NAME REACTIONS AND REAGENTS IN ORGANIC SYNTHESIS

Second Edition

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AND REAGENTS
IN ORGANIC SYNTHESIS

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Second Edition

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Preface

It has been a long haul. The start for this revision came almost the same way that the original edition started. For the first edition it was Mike Ellerd, then an undergraduate at Montana State, who organized my crude Name Reaction handouts so well that others encouraged the conversion into a book. At Colby College, Frank Favaloro did the same thing, making "study sheets" and adding to the list of Name Reactions. He graduated in 1996 and I started reformatting and expanding. With encouragement from Darla Henderson, this became a project. By then Frank had finished graduate school and was enthusiastic about participating. I had also retired from formal teaching and found much more time for creative work. The three of us started to work in earnest!

This edition differs substantially from the first by the inclusion of many modern Name Reactions instead of sticking exclusively with the old, tried and true. There are many reactions not covered; indeed, we ultimately eliminated those that had little contemporary use. We generally applied a "rule of thumb" that a newer name had to be cited by multiple authors. Therefore there are some relatively new protocols that have not stood the test of time; however the breadth of recent use warranted inclusion. As for reagents, we have focused on both Name Reagents and those whose acronyms are often used in place of the actual name. We have noted the common use of these forms in current literature.

First and foremost, this is a book to be used. Feel free to write in the text . . . use any available blank space to add your own notes. Transform this into ***your*** book of Name Reactions! It is intended to serve as a starting point. Within a two page format for reactions and one page for reagents, the reader will find a basic, generalized definition / formula, a mechanism that conveys a possible course from starting material to product, notes which describe a few of the major highlights of the reaction or which points the reader to related reactions (by name or similarity) and recent examples of use. We have tried to convey the current mechanistic thinking with special care to show intermediate steps, point out proton exchanges, and sometimes suggest transition states, but without going through kinetics, isotope effects, etc.

Wherever appropriate, we have included references to selected secondary sources. They contain more detailed discussions on the topics introduced in this book. In all cases, we recommend use of the primary literature. The examples in the following pages are but a small taste of the detail, variation, scope and experimental detail available. Our choices reflect our personal interests; there is no "better or worse" implied! We tried to use current examples from journals that seem to be most commonly accessible, both in paper form and electronically, to student and professional alike. When recent references were difficult to come by, we made use of the abstracts and reaction-search engine of *SciFinder* (American Chemical Society). In these cases, we supplied a number [AN year: XXXX] that will allow ready access to the abstract. To the authors of the works we have chosen to describe, we hold the most sincere gratitude and we hope we have faithfully represented your work.

Colby College
Waterville, ME
Feb 1, 2005

ACKNOWLEDGMENTS

As always, completion of a project requires more than just the work of the authors. Without the consideration, support and patience of spouses: Margaret (Brad), Mary (Mike) and Michelle (Frank), this probably could not have been completed.

Special thanks goes to the chemistry community for their endless development of new methods for creating C-C and C-heteroatom bonds. It has been an enlightening experience to chronicle the explosion of new "named" reactions and protocols. We have not lost view of the obvious new participation of the world chemical community.

Each of us can thank mentors and special people that have given us encouragement:

Brad:
I still owe much to my formal mentors:
Richard F. Smith who first provided the excitement of chemistry, A.Paul Krapcho, graduate mentor and friend, and the late Henry Rapoport, postdoctoral advisor.

I thank my colleagues from Colby College, Dasan Thamattoor and Jeff Katz, for their help in reading parts of this manuscript. And, of course my former graduate and undergraduate students . . . two of the latter are now coauthors, who were the reason for my continued interest in the academic life. Special thanks goes to Prof.Tom Poon (Claremont McKenna, Pitzer, & Scripps Colleges) for a great two years as a Dreyfus Fellow with me at Colby. He taught me much, and worked closely with Frank Favaloro.

I would like to thank several Colby staff that made my working easier: Susan W. Cole of the Science Library could always be depended on to solve any library problem that developed in the absolutely great electronic resources of Colby College, and patiently put up with my many requests, piled up books and journals and general use of the library. The Colby College ITS staff was extremely good-natured and helpful for computer questions. Their help was greatly appreciated.

Mike:
My appreciation goes out to all of my professors at Montana State, who,years ago sparked my interest in chemistry, and to those who still today keep that interest very much alive.

Frank:
I would like to thank all of those who not only taught me organic chemistry, but also to be excited for the art it contains: Gordon W. Gribble, Tadashi Honda, Thomas Spencer, Peter Jacobi, David Lemal, Thomas Poon, Philip Previte and, most importantly, Brad Mundy. Thank you to the many friends and co-workers who provided support, advice and the occasional reference: Erin Pelkey, Janeta Popovici-Müller, Tara Kishbaugh, Jeanese Badenock, Alison Rinderspacher and Chaoyang Dai.

Of course a project with a publisher requires interaction. Darla Henderson, Amy Byers, Camille Carter and Dean Gonzalez were the people who kept the ball rolling and the project in focus.

Colby College
Waterville, ME

Feb 1, 2005

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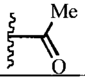
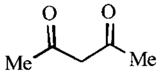
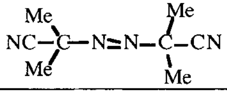
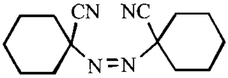
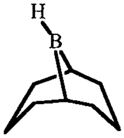
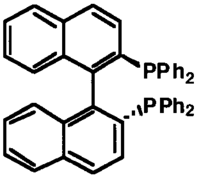
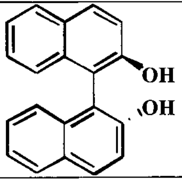
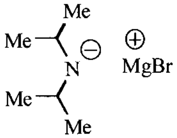
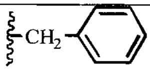
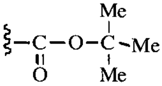
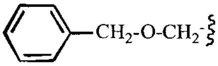
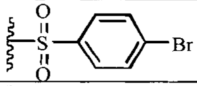
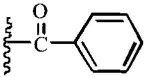
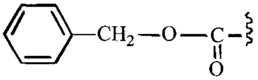
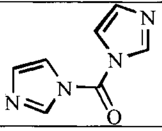
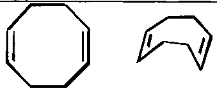
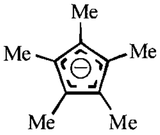
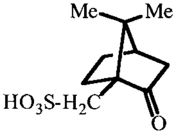
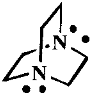
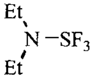
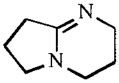
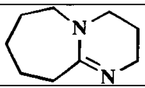
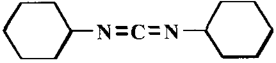
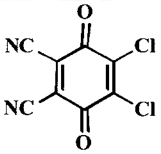
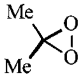
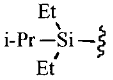
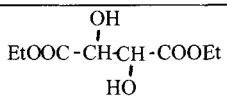
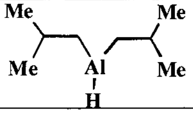
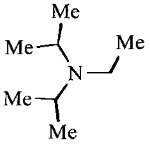
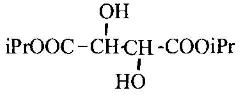
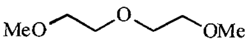
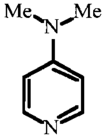
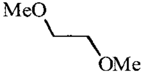
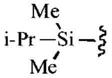
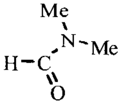
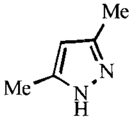
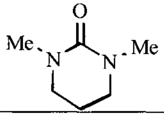
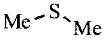
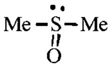
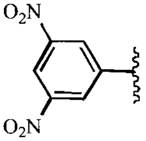
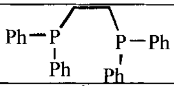
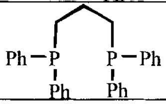
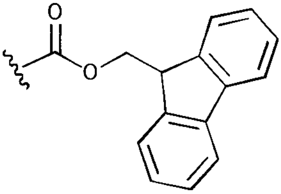
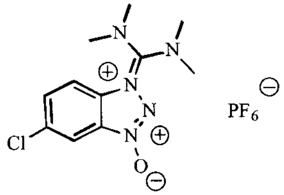
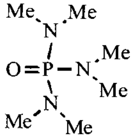
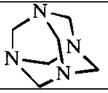
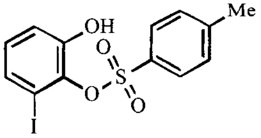
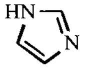
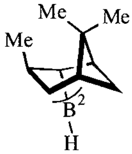
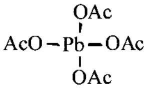
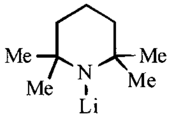
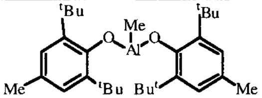
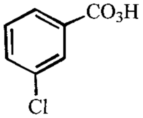
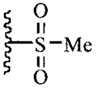
ACRONYMS AND ABBREVIATIONS

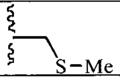
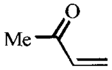
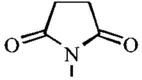
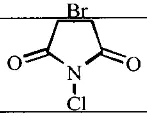
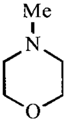
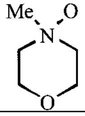
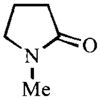
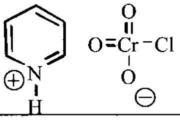
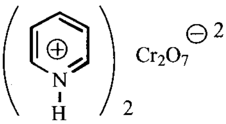
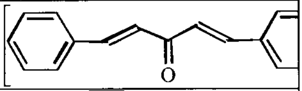
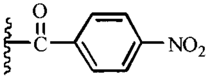
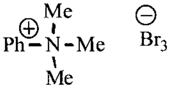
Acronym	Name	
Ac	Acetyl	
Acac	Acetylacetonate	
AcOH (HOAc)	Acetic acid	Me-COOH
AIBN	2,2'-Azobisisobutyronitrile	
ACN	1,1′-Azobis-1-cyclohexanenitrile	
9-BBN	9-Borobicyclo[3.3.1]nonane	
BINAP	2,2'-Bis(Diphenylphosphino)-1,1'-binaphththyl	
BINOL	1,1'-bi-2,2'-naphthol	
BITIP	Binol/Titanium isopropoxide	$Ti(iPrO)_4$ / BINOL
BMDA	Bromomagnesium Diisopropylamide	
BMS	Borane Dimethylsulfide	BH_3-Me_2S

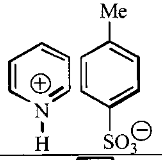
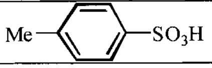
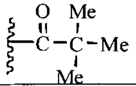
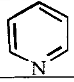
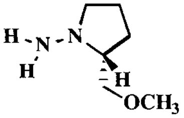
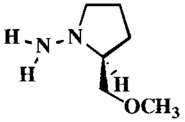
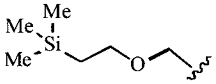
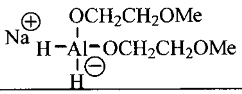
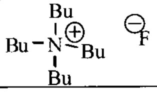
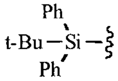
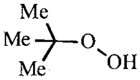
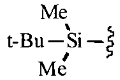
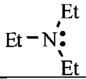
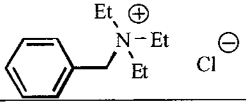
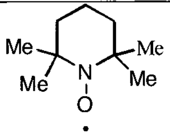
BMS	Borane Dimethylsulfide	BH_3-Me_2S
Bn-	Benzyl	
Boc- (t-Boc)	t-Butoxycarbonylchloride	
BOM-	Benzyloxymethyl-	
Bs	Brosylate	
Bu_3SnH	tri-^{n}butylstannane	$^nBu)_3SnH$
Bz	Benzoyl	
CAN	Ceric ammonium nitrate	$Ce(NH_4)_2(NO_3)_6$
CAS	Ceric ammonium sulfate	$Ce(NH_4)_4(SO_4)_4$
Cbz-	Carbobenzyloxy	
CDI	1,1'-Carbonyldiimidazole	
Cetyl	Hexadeca-	$C_{16}H_{33}$-
cod	Cyclooctadiene	
cp	Cyclopentadienyl	
cp*	Tetramethylcyclopentadienyl	
CSA	Camphorsulfonic Acid	
DABCO ***TED***	1,4-Diazabicylo[2.2.2]octane, TED, triethylenediamine	

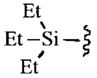
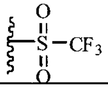
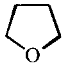
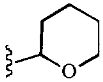
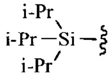
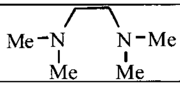
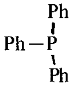
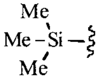
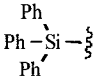
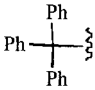
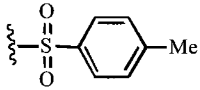
DAST	Diethylamino)sulfur trifluoride	 $\mathrm{Et_2N{-}SF_3}$
DBN	1,5-Diazabicyclo[4.3.0]non-5-ene	
DBU	1,5-Diazabicyclo[5.4.0]undec-7-ene	
DCC	Dicyclohexylcarbodiimide	
DDQ	2,3-Dichloro-5,6-dicyano-1,4-benzoquinone	
DDO	Dimethyldioxirane	
DEAD	Diethyl Azodicarboxylate	EtOOC−N=N−COOEt
DEIPS	Diethylisopropylsilyl	 $\mathrm{i\text{-}Pr{-}SiEt_2{-}}$
DET	Dietkyl tartrate	 $\mathrm{EtOOC{-}\overset{OH}{CH}{-}\underset{HO}{CH}{-}COOEt}$ in R-, S, and meso forms
DIBAL ***DIBAL-H***	Disobutylaluminum hydride	
DIEA ***DIPEA***	Diisopropylethylamine ***Hunig's base***	
DIPT	Diisopropyl tartrate	 $\mathrm{iPrOOC{-}\overset{OH}{CH}{-}\underset{HO}{CH}{-}COOiPr}$ in R-, S, and meso forms
Diglyme	Diethylene glycol dimethyl ether	

DMAP	4-(Dimethylamino)pyridine	
DME	1,2-Dimethoxyethane Glyme	
DMIPS	Dimethylisopropylsilyl	
DMF	Dimethylformamide	
DMP	Dimethylpyrazole	
DMPU	N,N'-Dimethylpropyleneurea	
DMS	Dimethylsulfide	
DMSO	Dimethylsulfoxide	
DNP	2,4-dinitrophenyl	
dppe	1,2-Bis(diphenylphosphino)ethane (DIPHOS)	
dppp	1,2-Bis(diphenylphosphino)propane	
ee	enantiomeric excess = % major enantiomer - % minor enantiomer	
Fmoc	9-Fluorenylmethoxycarbonyl	

HCTU	2-(6-Chloro-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate	
HMPT ***HMPA***	Hexamethylphosphoric triamide	
HMTA	Hexamethylenetetramine	
HTIB	Hydroxy(tosyloxy)-iodobenzene	
Im	Imidazoyl	
Icp$_2$BH	Diisopinocampheylborane	
LTA	Lead tetraacetate	 $\mathrm{AcO{-}\overset{OAc}{\underset{OAc}{Pb}}{-}OAc}$
LTMP ***LiTMP***	Lithium 2,2,6,6-tetramethylpiperidide	
MAD	Methylaluminum bis(2,6-di-t-butyl-4-methylphenoxide)	
MCPBA	m-Chlorperoxybenzoic acid	
MeCN	Acetonitrile	$Me-C\equiv N$
MEM-	2-Methoxyethoxymethyl	
Ms	Mesyl , Methanesulfonyl	

MTM	Methylthiomethyl	
MVK	Methyl Vinyl Ketone	
NBS	N-Bromosuccinimide	
NCS	N-Chlorosuccinimide	
NMM	4-Methylmorpholine	
NMO	N-Methylmorpoline-N-oxide	
NMP	N-Methylpyrrolidone	
PCC	Pyridinium chlorochromate Corey's Reagent	
PDC	Pyridinium dichromate	
Pd(dba)$_2$	Bis(dibenzylideneacetone)palladium (0)	
PMB	p-Methoxybenzyl	
PNB	para-Nitrobenzoyl	
PPA	Polyphosphoric Acid	Unspecified mixture with High concentration of P_2O_5
PTT ***(PTAB)***	Phenyltrimethylammonium tribromide Phenyltrimethylammonium perbromide	

PPTS	Pyridinium para-toluenesulfonate	
PTSA	p-Toluenesulfonic acid; Tosic acid	
Pv	Pivaloyl	
Py	Pyridine	
RAMP	(R)-1-Amino-2-Methoxymethylpyrrolidine	
SAMP	(S)-1-Amino-2-Methoxymethylpyrrolidine Ender's Reagent	
SEM	2-Trimethylsilylethoxy-methoxy	
SMEAH	Sodium Bis(2-methoxyethoxy)aluminum Hydride	
TBAF	Tetrabutylammonium fluoride	
TBDPS	*tert*-Butyldiphenylsilyl	
TBHP	*t*-Butyl hydroperoxide	
TBS TBDMS	*tert*-Butyldimethylsilyl	
TEA	Triethylamine	
TEBA ***TEBAC***	Benzyltriethylammonium chloride	
TEMPO	2,2,6,6-Tetramethylpiperidin-1-oxyl	

TES	Triethylsilyl	
Tf	Triflate	
THF	Tetrahydrofuran	
THP	Tetrahydropyranyl	
TIPS	Triisopropylsilyl	
TMEDA	N,N,N',N'-Tetramethylethylenediamine	
TPAP	Tetra-n-Propylammonium Perruthenate	$Pr_4N^+RuO_4^-$
TPP	Triphenyl phosphine	
TMS	Trimethylsilyl	
TMSOTf	Trimethylsilyltrifluoromethanesulfonate	$TMS{-}O{-}SO_2CF_3$
TPS	Triphenylsilyl	
Trt	Trityl	
Ts- Tos-	Tosyl p-toluenesulfonyl	

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NAME REACTIONS

In this section we provide a summary of Name Reactions. The format is slightly modified from our previous book, but maintains the essential features:

Reaction:

Summary reaction.

Proposed Mechanism:

Currently accepted mechanisms. We have tried to be complete in showing steps, intermediates and the necessary curly arrow notations.

Notes:

Additional comments and references from key sources.

Examples:

Current examples if possible.

When a term is underlined, (for example, ***Aldol Condensation***) it means that the concept can be found under an independent heading in the book.

General Bibliography:

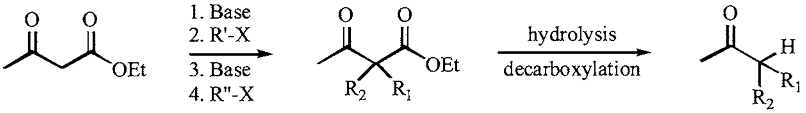
B. P. Mundy, M. G. Ellerd, *Name Reactions and Reagents in Organic Synthesis*, John Wiley and sons, Inc., New York, 1988;
M. B. Smith, J. March in *March's Advanced Organic Chemistry,* 5th ed., John Wiley and Sons, Inc., New York, 2001;
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998;
V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002;
J. J. Li, *Name Reactions*, Springer, Berlin, 2002;
Comprehensive Organic Synthesis, B. M. Trost, editor-in-chief, Pergamon Press, Oxford, 1991;
M. B. East, D. J. Ager, *Desk Reference for Organic Chemists*, Krieger Publishing Company, Malabar, FL, 1995;
M. Orchin, F. Kaplan, R. S. Macomber, R. M. Wilson, H. Zimmer, *The Vocabulary of Organic Chemistry*, John Wiley and Sons, Inc., New York, 1980;
A. Hassner, C. Stumer, *Organic Syntheses Based on Name Reactions and Unnamed Reactions*, Pergamon, Oxford, 1994;
The Merck Index, Merck & CO., Inc., Whitehouse Station, N. J. (now in the 13th Edition) Each edition has an updated list of Named Reactions.
See also: http://themerckindex.cambridgesoft.com/TheMerckIndex/NameReactions/TOC.asp

Other URL's to Name Reaction Websites:
www.monomerchem.com/display4.html
www.chempensoftware.com/organicreactions.htm
www.organic-chemistry.org/namedreactions/
http://orgchem.chem.uconn.edu/namereact/named.html

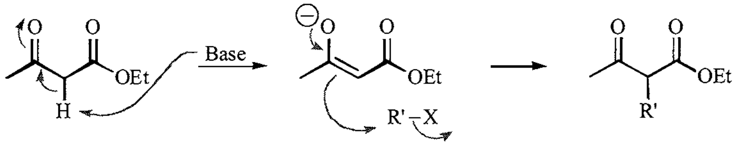
Some references are provided with a SciFinder (American Chemical Society) number so that one can access the abstract if needed.

Acetoacetic Ester Synthesis

The Reaction:

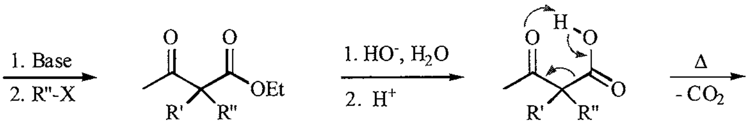


Proposed Mechanism:



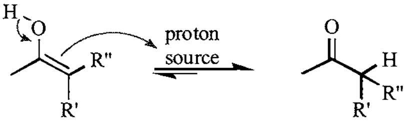
The methylene protons are the most acidic by influence from both carbonyls.

X can be Cl, Br, I, OTs, etc.



Alkylation can be done a second time (with a different R) if desired.

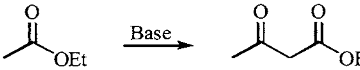
Ester hydrolysis/saponification, then with heat, the β-keto acid decarboxylates to give an enol.



keto-enol tautomerism

Notes:

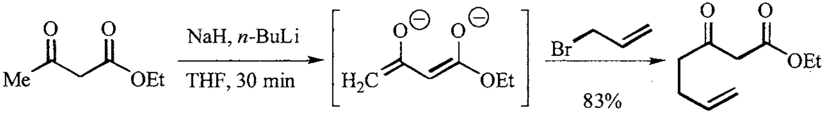
Acetoacetic Ester can be prepared by the condensation of ethyl acetate, called the ***Acetoacetic Ester Condensation Reaction***, a **Claisen Condensation**:



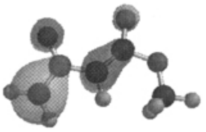
J. K. H. Inglis and K. C. Roberts *Organic Syntheses* CV1, 235

See M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p 549; and C. R. Hauser, B. E. Hudson, Jr., *Organic Reactions* **1**, 9

Weiler Modification: By using very strong bases, a dianion can be formed that will preferentially alkylate at the methyl group:

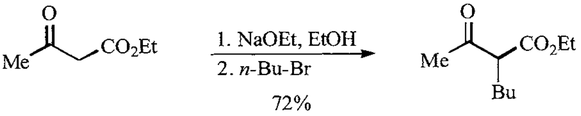


S. N. Huckin, L. Weiler *Journal of the American Chemical Society* **1974**, 96, 1082

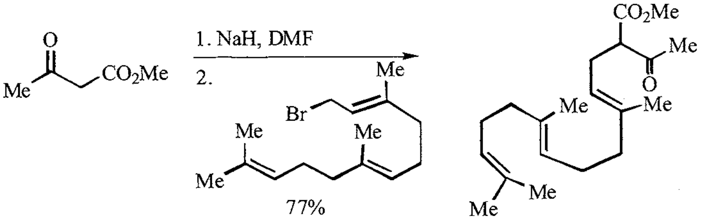


Simple AM1 calculation on Me ester shows the *HOMO* corresponding to the reactive intermediate

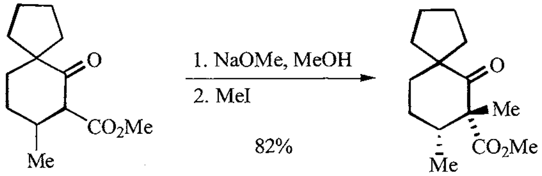
Examples:



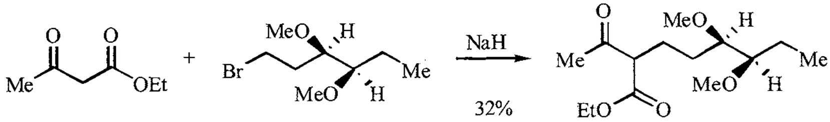
C. S. Marvel, F. D. Hager, *Organic Syntheses* **1941**, 1, 248



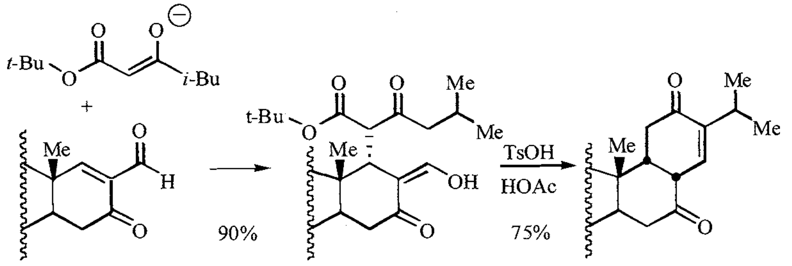
K. A. Parker, L. Resnick, *Journal of Organic Chemistry* **1995**, 60, 5726



Y.-Q. Lu, C.-J. Li, *Tetrahedron Letters* **1996**, 37, 471



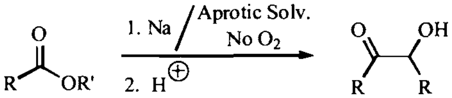
K. Mori, *Tetrahedron* **1974**, 30, 4223



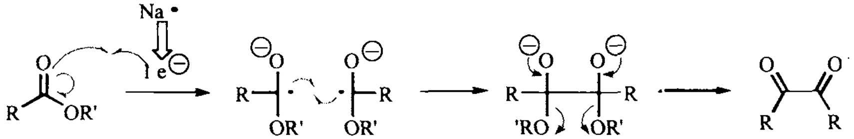
W. L. Meyer, M. J. Brannon, C. da G. Burgos, T. E. Goodwin, R. W. Howard, *Journal of Organic Chemistry* **1985**, 50, 438

Acyloin Condensation

The Reaction:



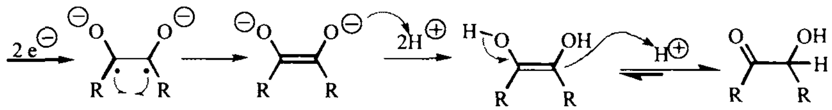
Proposed Mechanism:



An electron adds to the LUMO of the ester.

Two of these radical anions react.

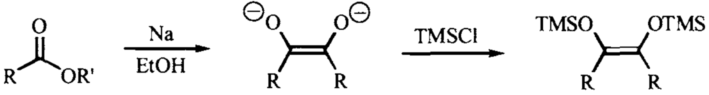
Alkoxide leaves to give a 1,2 dione that further reacts with electrons in solution.



Notes:

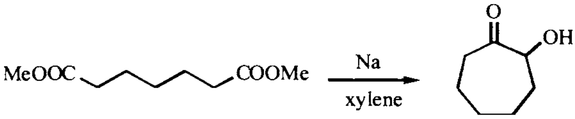
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p 1562; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 1-3; S. M. McElvain, *Organic Reactions*, **4**, 4; J. P. Schaefer, J. J. Bloomfield, *Organic Reactions*, **4**, 15; J. J. Bloomsfield, J. M. Owsley, J. M. Nelke, *Organic Reactions* **23**, 2

The ***Rühlmann modification (Bouveault-Blanc Condensation or Rühlmann Reaction)*** traps the dienolate as a TMS derivative. This protocol generally results in improved yields.

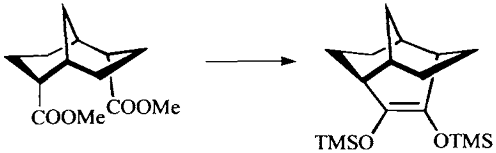


This reaction is better than either the ***Dieckmann*** or ***Thorpe-Zeigler*** reactions for preparing large rings.

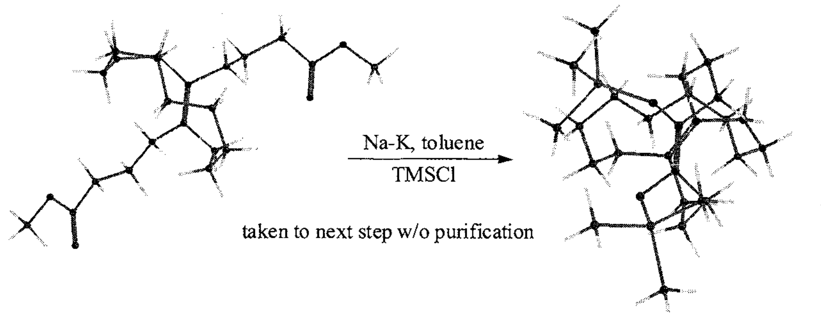
Examples:



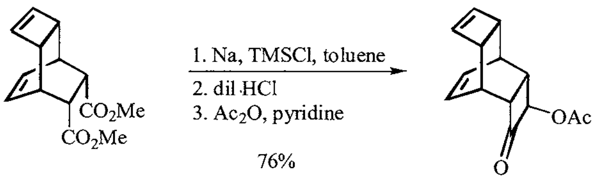
N. L. Allinger, *Organic Syntheses* **1963**, 4, 840



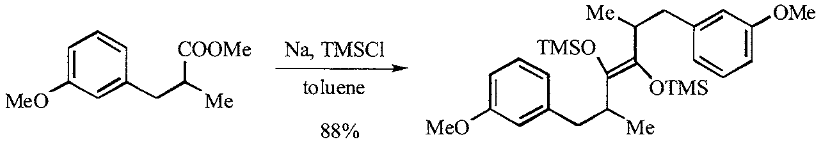
E. Butkus, A. Ilinskasa, S. Stoniusa, R. Rozenbergasa, M. urbanovàb, V. Setnikac, P. Bouc, K. Volkac, *Tetrahedron: Asymmetry* **2002**, 13, 633



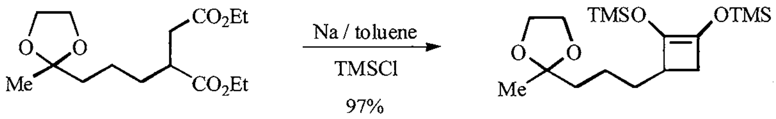
J. A. Marshall, J. C. Peterson, L. Lebioda, *Journal of the American Chemical Society* **1984**, 106, 6006



G. Mehta, R. Vidya, *Journal of Organic Chemistry* **2001**, 66, 6913



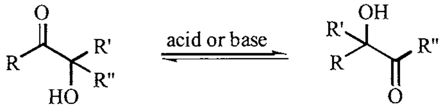
M. J. Meyers, J. Sun, K. E. Carlson, B. S. Katzenellenbogen, J. A. Katzenellenbogen, *Journal of Medicinal Chemistry* **1999**, 42, 2456



A. N. Blanchard, D. J. Burnell, *Tetrahedron Letters* **2001**, 42, 4779

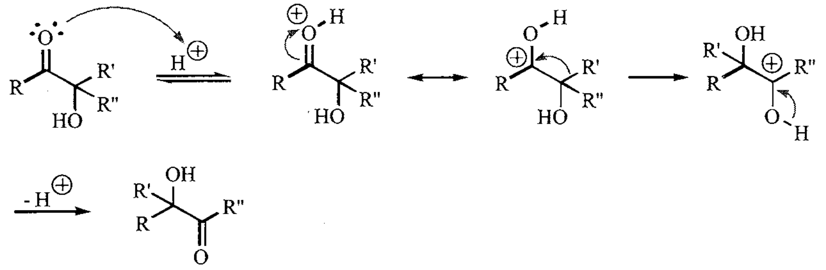
Acyloin Rearrangement

The Reaction:

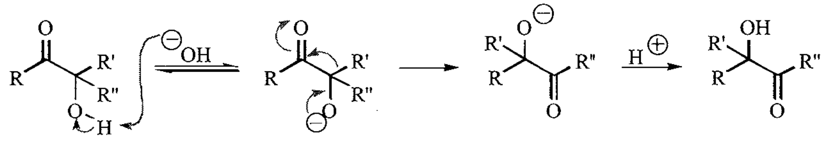


Proposed Mechanism:

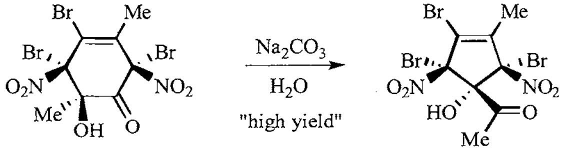
In acid:



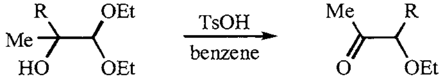
In base:



Examples:

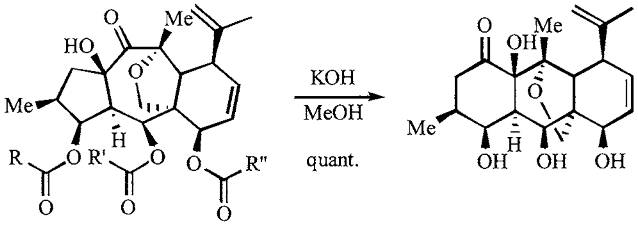


P. A. Bates, E. J. Ditzel, M. P. Hartshorn, H. T. Ing, K. E. Richards, W. T. Robinson, *Tetrahedron Letters* **1981**, 22, 2325



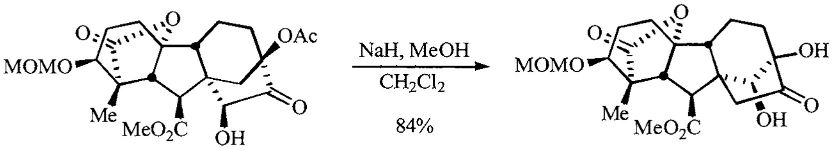
R = *i*-Pr 43%
R = Ph 80%

T. Sate, T. Nagata, K. Maeda, S. Ohtsuka, *Tetrahedron Letters* **1994**, 35, 5027



a mixture of acyl esters

M. Rentzea, E. Hecker, *Tetrahedron Letters* **1982**, 23, 1785



J. Liu, L. N. Mander, A. C. Willis, *Tetrahedron* **1998**, 54, 11637

Adamantane Rearrangement (Schleyer Adamantization)

The Reaction:

Proposed Mechanism:

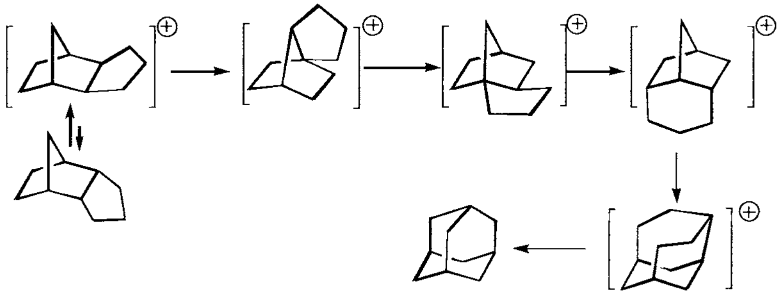
P. von R. Schleyer, P. Grubmcller, W. F. Maier, O. Vostrowsky, *Tetrahedron Letters* **1980**, 21, 921

M. Farcasiu, E. W. Hagaman, E. Wenkert, P. von R. Schleyer *Tetrahedron Letters* **1981**, 22, 1501

E. M. Engler, M. Farcasiu, A. Sevin, J. M. Cense, P. V. R. Schleyer, *Journal of the American Chemical Society* **1973**, 95, 5769

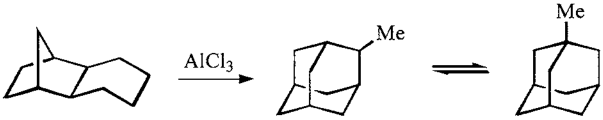
M. A. McKervey, *Tetrahedron* **1980**, 36, 971 provides a useful review:

This reaction consists of a series of deprotonations, protonations, hydride transfers and ***Wagner-Meerwein rearrangements***. There are postulated to be 2897 possible routes between starting material and product! A few of the steps have been tested experimentally; most of the data are computational. The following structural features seem to be supported:



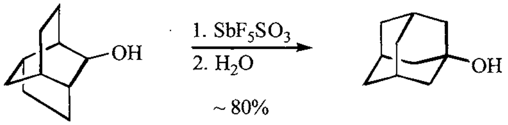
Notes:

Tricyclic molecules having 10 carbon atoms are converted to adamantane with Lewis acids. Additional carbon atoms become alkyl appendages:



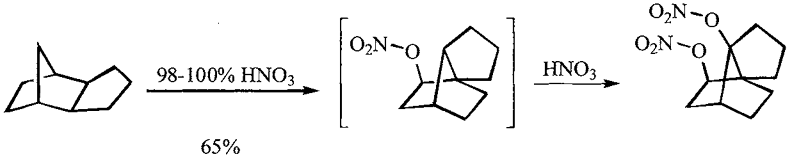
M. A. McKervey, *Tetrahedron* **1980**, 36, 971

Examples:



H. W. Whitlock, Jr., M. W. Siefken, *Journal of the American Chemical Society* **1968**, 90, 4929

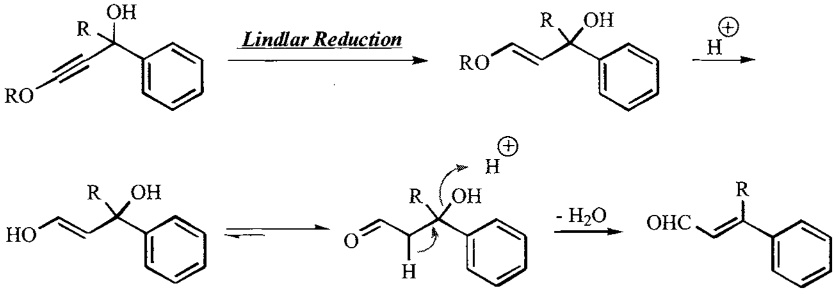
Verification of the first steps:



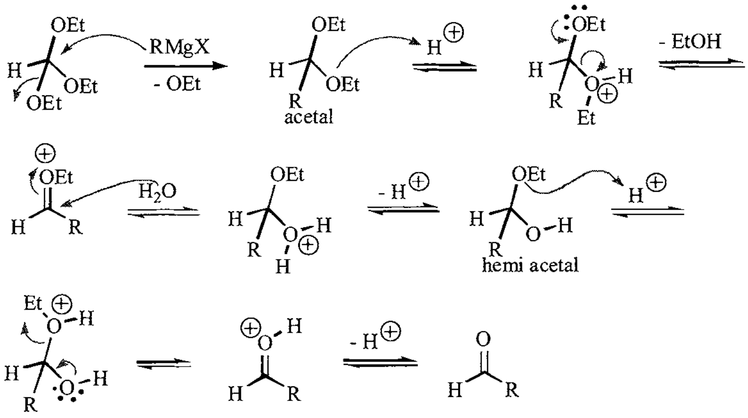
P. A. Krasutsky, I. R. Likhotvorik, A. L. Litvyn, A. G. Yurchenko, D. Van Engen *Tetrahedron Letters* **1990**, 31, 3973

Aldehyde Syntheses

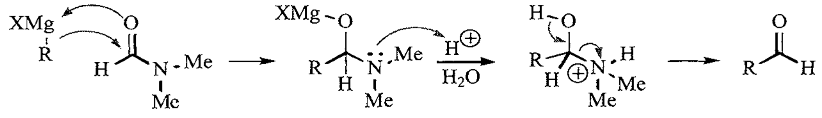
Arens-van Dorp Cinnamaldehyde Synthesis



Bodroux-Chichibabin Aldehyde Synthesis

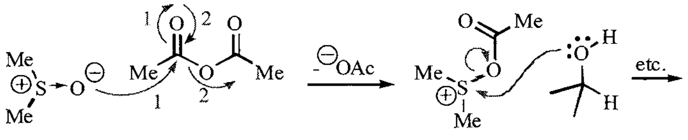


Bouveault Aldehyde Synthesis

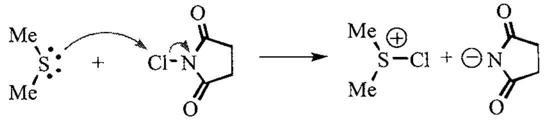


DMSO-based Oxidations

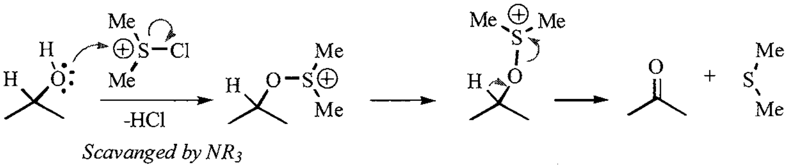
Albright-Goldman Oxidation / Albright-Goldman Reagent



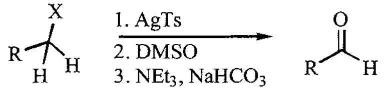
Corey-Kim Oxidation / Corey-Kim Reagent



NCS
N-ChloroSuccinimide

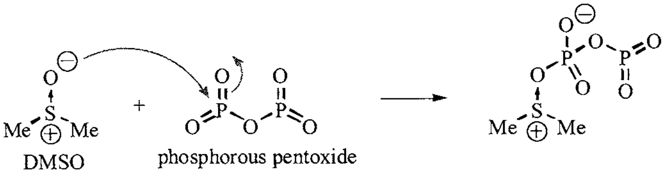


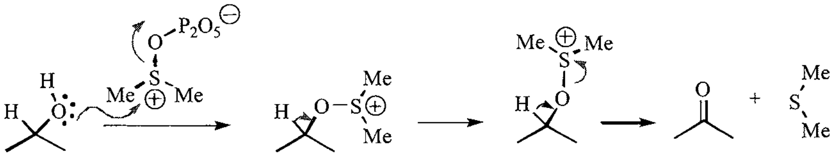
Kornblum Aldehyde Synthesis



X = I, Br, OTs

Onodera Oxidation

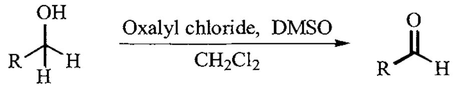




Pfitzner-Moffatt Oxidation

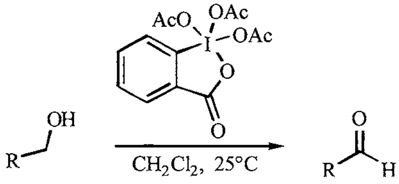
also for ketones

Swern Oxidation



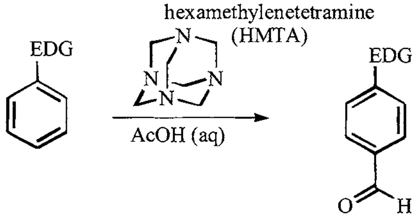
also for ketones

Dess-Martin Oxidation

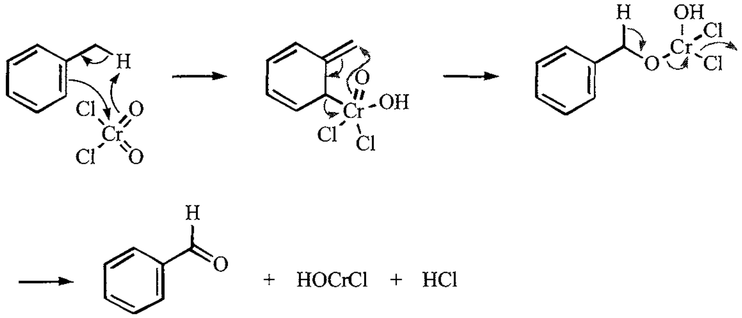


also for ketones

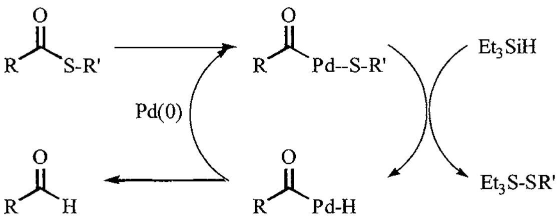
Duff Reaction



Étard Reaction

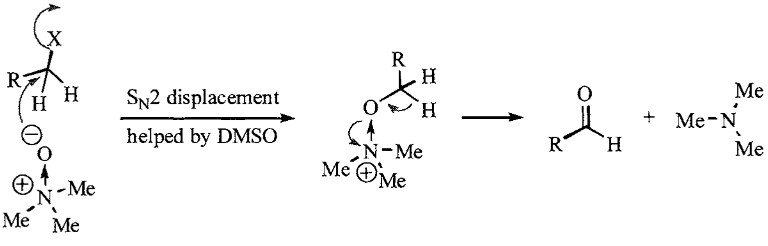


Fukuyama Reduction



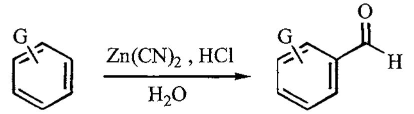
M. Kimura, M. Seki, *Tetrahedron Letters* **2004**, 45, 3219

Ganem Oxidation



TMNO

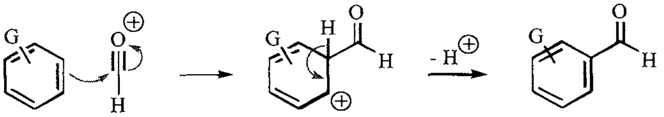
Gattermann Reaction (Gatterman Aldehyde Synthesis) / Gattermann Reagent



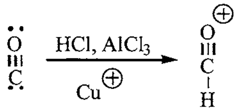
G = alkyl, OR

Gatterman-Koch Reaction (see under <u>Gatterman Reaction</u>)

There seems to be agreement that the product-forming part of the mechanism is:

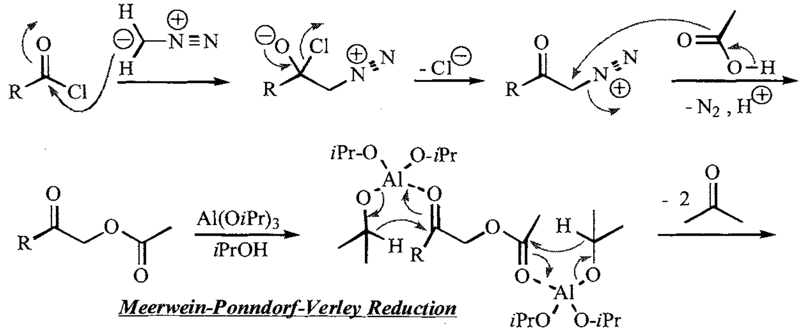


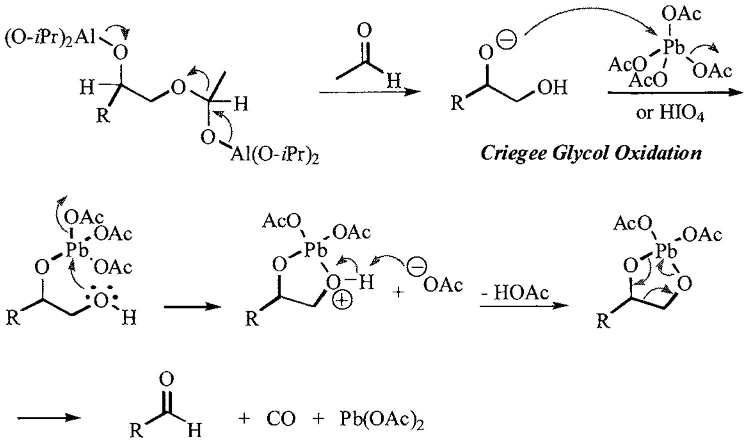
However, the details of the formation of the formyl cation seem to be less assured.



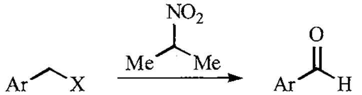
See S. Raugei, M. L. Klein, *Journal of Physical Chemistry B*, **2001**, 105, 8213 for pertinent references to experiment, and their computational study of the formyl cation.

Grundmann Aldehyde Synthesis

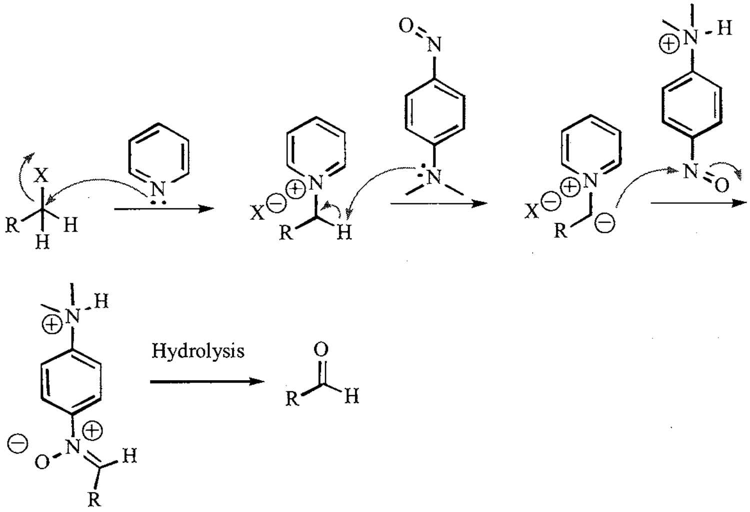




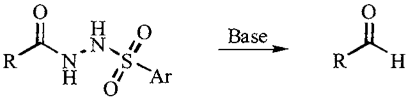
Hass-Bender Reaction



Kröhnke Aldehyde Synthesis

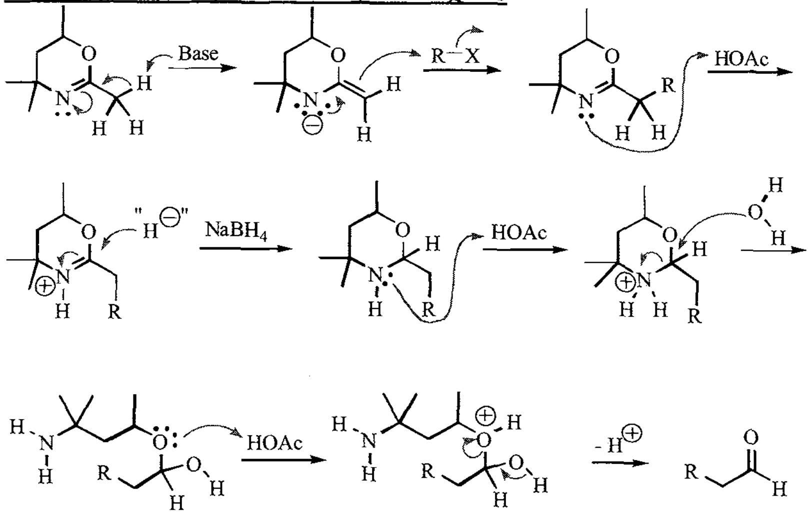


McFadyen-Stevens Aldehyde Synthesis

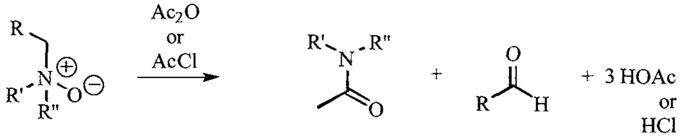


R = Ar or alkyl with no α-protons

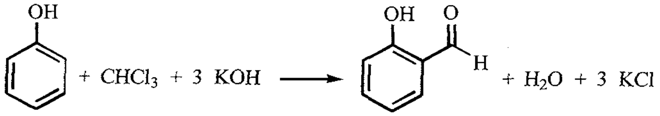
Meyers Aldehyde Synthesis / Meyers Reagents



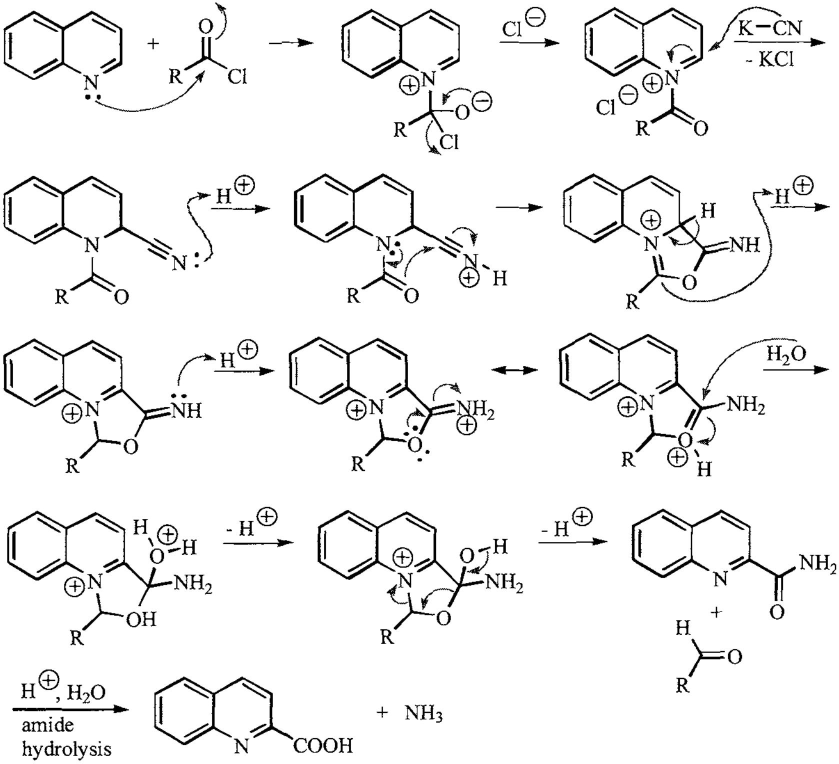
Polonovski Reaction



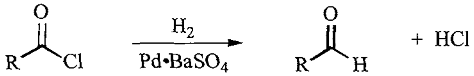
Reimer-Tiemann Reaction



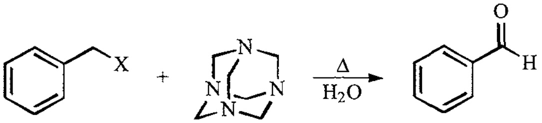
Reissert Reaction (Grosheintz-Fischer-Reissert Aldehyde Synthesis)



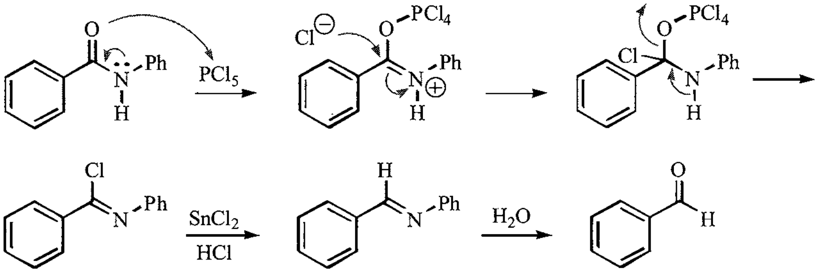
Rosenmund Reduction



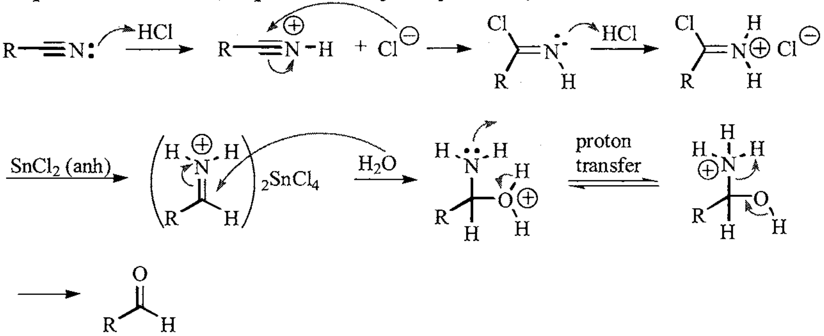
Sommelet Reaction



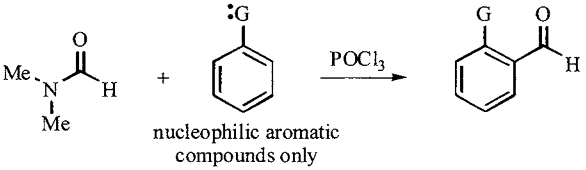
Sonn-Muller Method



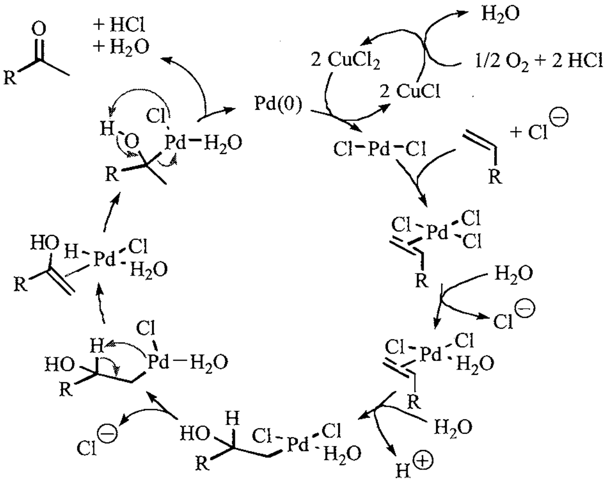
Stephen Reduction (Stephen Aldehyde Synthesis)



Vilsmeier-Haack Reaction

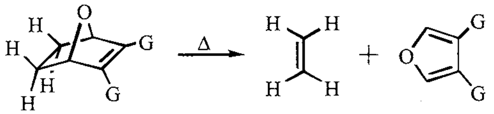


Wacker Oxidation Reaction

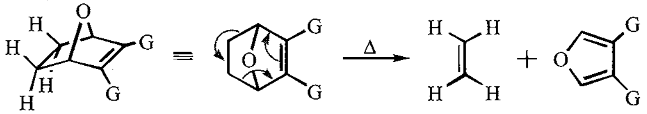


Alder-Rickert Reaction

The Reaction:



Proposed Mechanism:

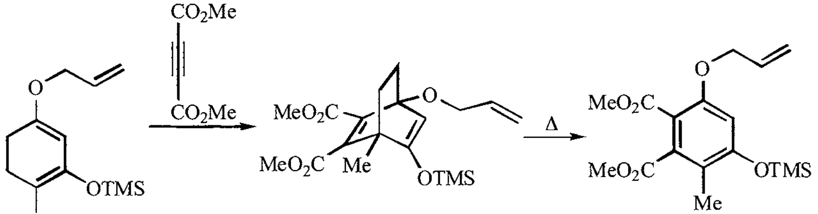


This reaction is a reverse ***Diels-Alder Reaction***. The orbital considerations controlling the “backward: reaction are the same as the “forward” reaction.

Notes:

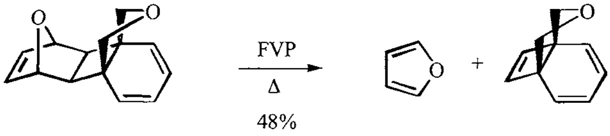
It seems accepted that almost any "***retro-Diels-Alder***" reaction can be included in the grouping, "***Alder-Rickert Reaction***".

Examples:

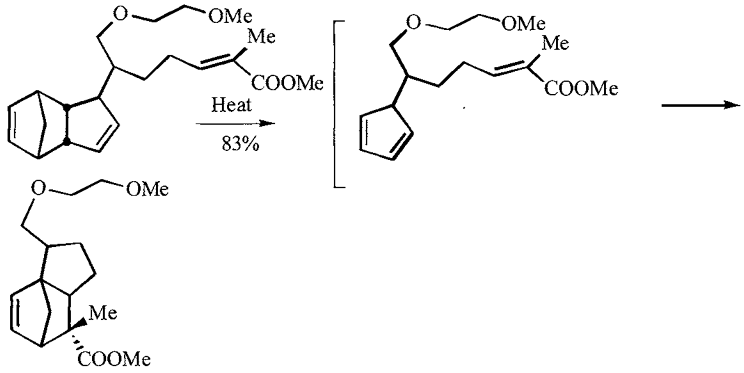


59% for the two steps.

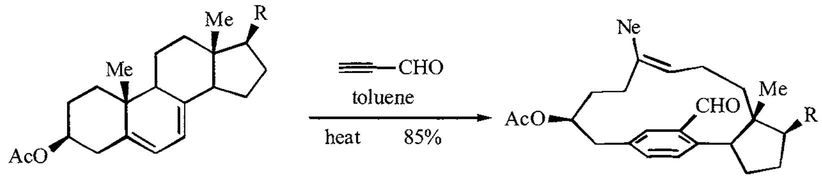
J. W. Patterson, *Tetrahedron* **1993**, 49, 4789



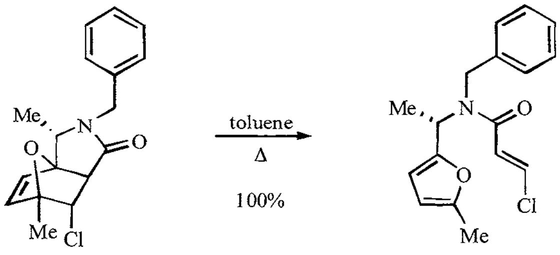
R. N Warrener, J.-M. Wang, K. D. V. Weerasuria, R. A. Russell, *Tetrahedron Letters* **1990**, 31, 7069



D. W. Landry, *Tetrahedron* **1983**, 39, 2761



D. Schomburg, M. Thielmann, E. Winterfeldt, *Tetrahedron Letters* **1985**, 26, 1705



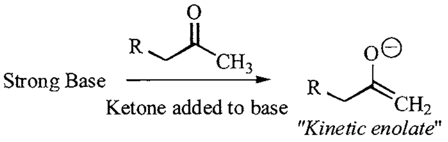
M. E. Jung, L. J. Street, *Journal of the American Chemical Society* **1984**, 106, 8327

Aldol Type Reactions

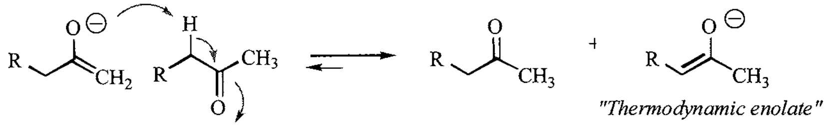
The Reaction:

This reaction has become an extremely important tool in the reaction toolbox of organic chemists. Because of the variety of approaches to the aldol products, this summary section is prepared.

Most synthetically useful approaches use a preformed enolate as one of the reactants.

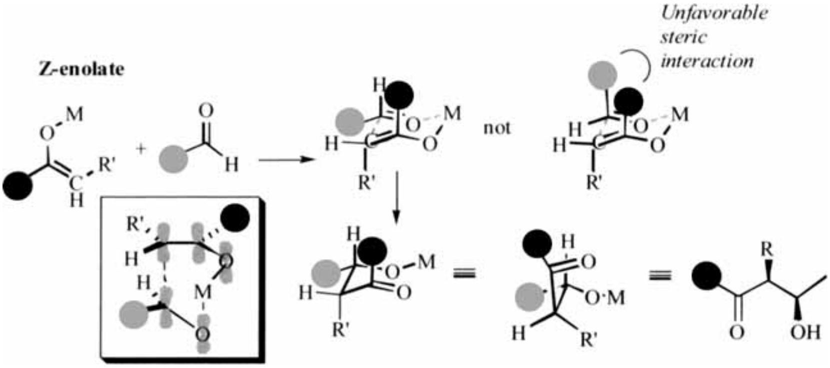


With a weaker base and / or slow addition of base to the ketone, an equilibrium will be established and a *"thermodynamic enolate"* will predominate.



The most useful approach is when the enolate can be trapped and used in a configurationally stable form.

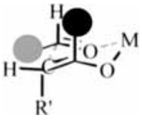
A generic analysis of enolate addition to an aldehyde:



A similar exercise can be provided for the E-enolate.

Zimmerman-Traxler model

An analysis of the steric effects in a chair-transition state for the reaction:

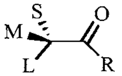


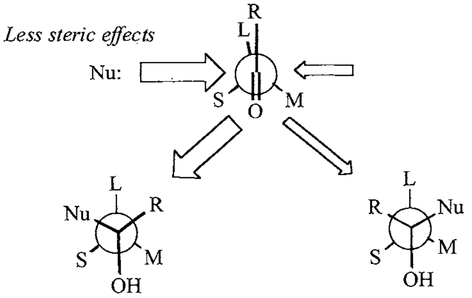
A ***directed aldol reaction*** requires that one partner provides a preformed enolate (or chemically equivalent reactive species) and is then added to the second carbonyl-containing molecule.

When one of the reactants is chiral, asymmetric induction can provide enantioselective products:

Cram's Rule and Related Views on Asymmetric Induction

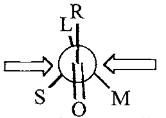
This rule was developed to rationalize the steric course of addition to carbonyl compounds.[1] The conformations of the molecules are shown in their ***Newman structures***, and a preferred conformation is selected in which the *largest group,* **L**, is situated *anti* to the carbonyl oxygen. This conformation assumes a model having a *large* oxygen, sometimes referred to as the "big O" model.[2] Examination of steric hindrance to nucleophile trajectory determined the major product.[3] We might point out, at the start, that Reetz has recently reported that "how" the reaction is carried out; for example "slow" vs. "fast" mixing, can dramatically alter product ratios.[4]





Major product **Minor product**

In cases where the alpha-carbon is chiral, attack at the carbonyl carbon introduces a new stereogenic center. The two carbonyl faces are *diastereotopic* and attack at the *re* and *se* faces are different



The two faces are diastereotopic

A modification of the ***Cram model***, in which the medium sized group, **M**, eclipsed the carbonyl oxygen, was developed by Karabatsos[5]; however, it generally predicted the same product as the ***Cram model***. In this model, which assumes two major conformations, the major product is that which is derived from attack at the less hindered side of the more stable conformer.

---

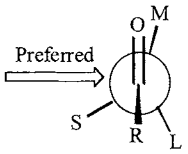
[1] a. See J. D. Morrison, H. S. Mosher, *Asymmetric Organic Reactions*, Prentice-Hall, Englewood Cliffs, 1971, Chapter 3, for a somewhat dated, but excellent account of this concept.
b Cram's first work, (D. J. Cram, F. A. Abd Elhafez, *Journal of the American Chemical Society* **1952**, 74, 5828) set the stage for intense studies that have spanned 50 years.

[2] The original thought included the notion that there was a large steric bulk associated with the oxygen by nature of metal complexing.

[3] Application of the ***Curtin-Hammett Principle*** would suggest that the different ground state conformers have minimal influence on the product composition. It is the difference in activation energies for the two different isomers that controls the reaction, and the diastereomeric transition states would be attained from either ground state conformation.

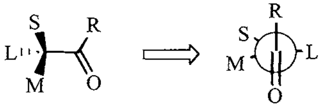
[4] M. T. Reetz, S. Stanchev, H. Haning, *Tetrahedron* **1992**, 48, 6813

[5] a G. J. Karabatsos *Journal of the American Chemical Society* **1967**, 89, 1367;
b. G. J. Karabatsos, D. J. Fenoglio, *Topics in Stereochemistry* **1970**, 5, 167



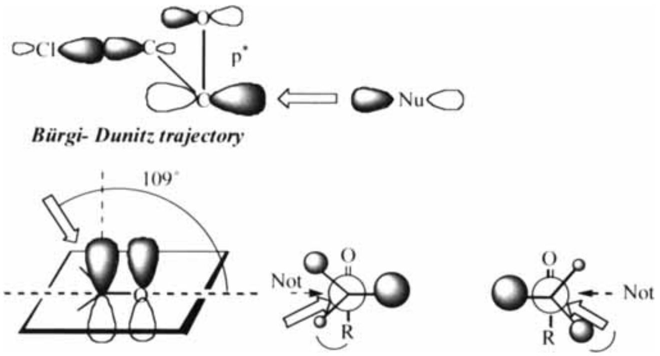
Felkin–Cherest-Anh Rule

Like ***Cram's Rule***, the ***Felkin-Cherest-Anh model***, developed by Felkin and coworkers[6], is an attempt to understand and predict the stereochemistry of addition to a carbonyl group. This model requires a "small O" interpretation in which the largest group is oriented *anti* to the attacking nucleophile's trajectory. One should note that the ***Felkin-Cherest-Anh model*** neglects the interaction of the carbonyl oxygen. In this approach, the *R/S* or *R/M* interactions dominate.



This is the important interaction that must be minimized. Note that in this approach the carbonyl substituent plays an important role.

Calculations in this model are based on an orbital interaction as described below. It should also be noted that the trajectory of delivery of nucleophile to the carbonyl carbon is defined by an angle of about 109°.

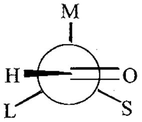


Preferred conformation. Less interaction between the small group and the R-group. We also note that this model "feels" the influence of increasing size of R.

We see in this coformer an increased interaction between the medium group and R. Also, there is more interaction with the nucleophile.

This model often leads to the same conclusions obtained from the other models. It does, however, recognize the nonpassive role of the **R**-group in ketones. In this model one would predict an *increase* of stereodifferentiation as the size of **R**- increases. This has been found experimentally.

For aldehydes the transition state model will be:



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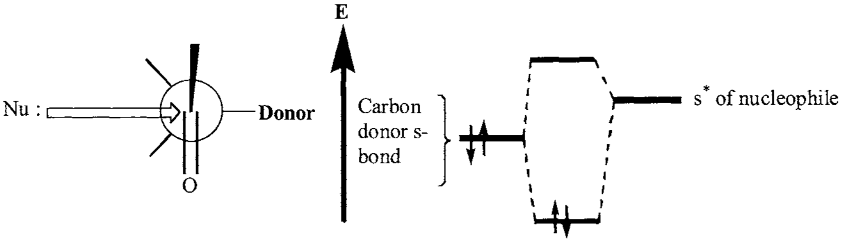
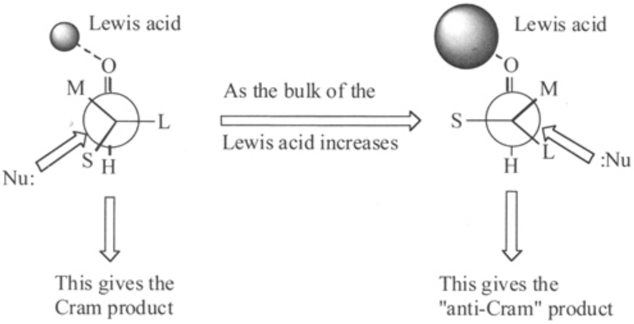
[6] M. Cherest, H. Felkin, N. Prudent, *Tetrahedron Letters*, **1968**, 9, 2199

A useful orbital approach by Cieplak[7] has suggested that the nucleophile will attack the carbonyl *anti* to the best donor ligand.



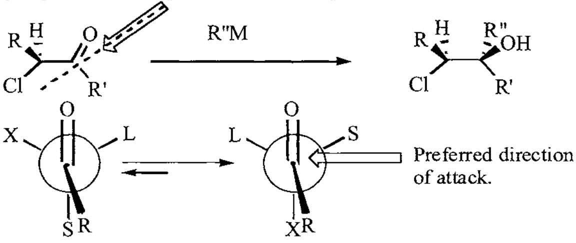
Cases for Modification of the Models

Sometimes the Lewis acid that coordinates with the carbonyl oxygen is sufficiently bulky that it seriously influences the stereochemistry of attack. Sometimes these reaction products, which seem opposite of the expected ***Cram Rule*** analysis, are termed ***"anti-Cram" products***. Compare the "normal" situation with the influence of a sterically bulky Lewis acid:



Dipolar Model

There is evidence to suggest that competing dipole effects will alter the preferred conformation. Thus, for example, halogens will prefer a conformation in which the dipoles are *anti* to one another. This is often described as the ***Cornforth model.***[8] In this model the highly polarized group will take the place of the L-group of the ***Cram model.***



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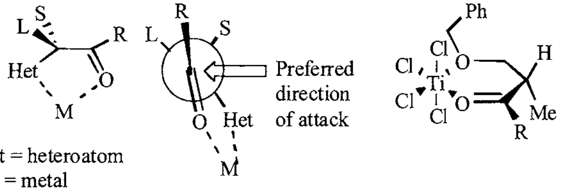
7. a. A. S. Cieplak, B. D. Yait, C. R. Johnson, *Journal of the American Chemical Society* **1989** 111, 8447

   b. A. S. Cieplak, *Journal of the American Chemical Society* **1981**, 103, 4548

8. J. W. Cornforth, R. H. Cornforth, K. K. Methew, *Journal of the Chemical Society* **1959**, 112

Chelation Control[9]

Neighboring heteroatoms can provide a site for complexing.



Het = heteroatom
M = metal

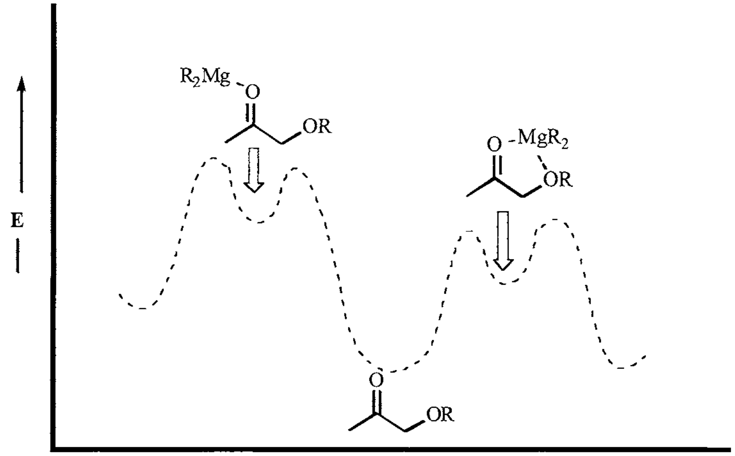
Product stereochemistries can be greatly influenced by these chelation control effects. This was first observed by Cram.[10] There are many controversies about this topic, and the issue remains a topic of investigative interest.[11] Without kinetic data, it has been suggested that it is impossible to distinguish the following two mechanistic types:[12]

$$\text{Chelate} \rightleftharpoons \text{Ketone} + MgMe_2 \longrightarrow \text{Product} \quad \text{(Non-chelation)}$$

$$\text{Ketone} + MgMe_2 \rightleftharpoons \text{Chelate} \longrightarrow \text{Product} \quad \text{(Chelation)}$$

Rate enhancement should be a requirement for chelation control because if chelation is the source of stereoselectivity it necessarily follows that the chelation transition state should be of a lower energy pathway.[13]

These concepts are seen on the energy diagram below. It should be noted that an interesting conclusion from this analysis is that *increased selectivity* is associated with *increased reactivity*. This might be considered to run counter to a number of other analyses of reactivity and selectivity.



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9. M. T. Reetz, *Accounts of Chemical Research* **1993**, 26, 462

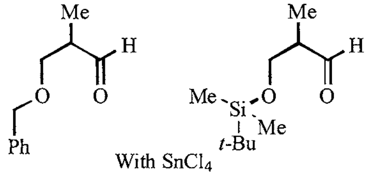
10. D. J. Cram, K. R. Kopecky, *Journal of the American Chemical Society* **1959**, 81, 2748

11. a. W. C. Still, J. H. McDonald, *Tetrahedron Letters*, **1984**, 1031
   b. M. T. Reetz, *Angewandte Chemie, International Edition in English*, **1984**, 23, 556
   c. G. E. Keck, D. E. Abbott, *Tetrahedron Letters* **1984**, 25, 1883
   d. S. V. Frye, E. L. Eliel, *Journal of the American Chemical Society* **1988**, 110, 484

12. J. Laemmle, E. C. Ashby, H. M. Neumann, *Journal of the American Chemical Society* **1971**, 93, 5120

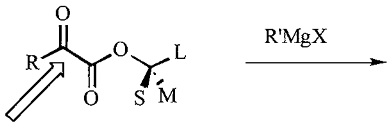
13. X. Chen, E. R. Hortelano, E. L. Eliel, S. V. Frye *Journal of the American Chemical Society* **1992**, 114, 1778

The *a priori* prediction of which functional groups will provide complexation are not always obvious. Keck[14] demonstrated some dramatic differences in oxygen chelation resulting from minor differences in substitution.



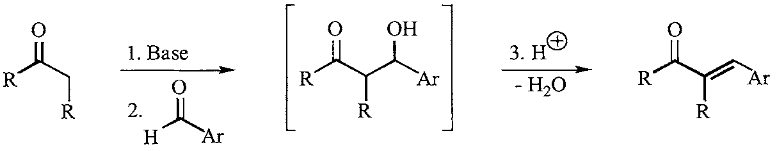
Stong chelate *No chelate*

A potentially useful extension of the ***Cram's rule*** is the asymmetric induction provided by a remote ester (***Prelog's rule***):

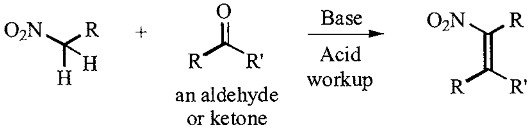


Reactions based on the Aldol Reaction:

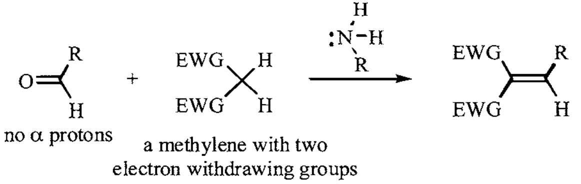
Claisen-Schmidt:



Henry Reaction



Knoevenagel Reaction



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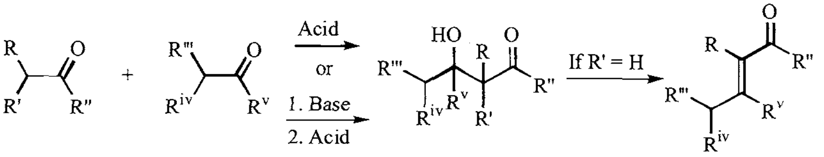
[14] G. E. Keck, S. Castellino, *Tetrahedron Letters* **1987**, 28, 281

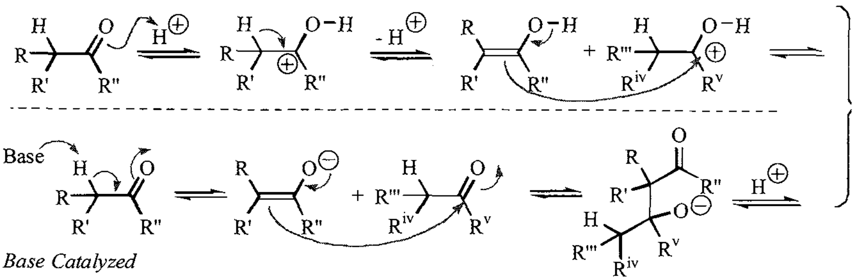
Aldol Condensation

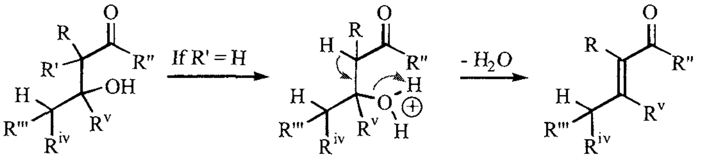
The Reaction:



Proposed Mechanism:

Acid Catalyzed



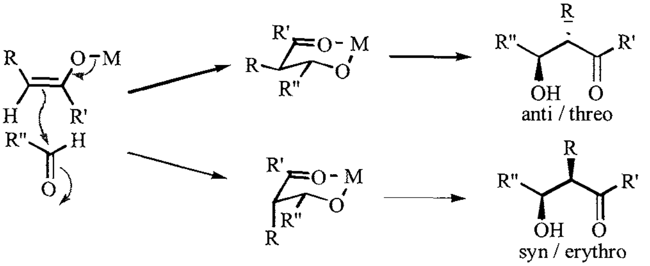


If R' = H, dehydration is possible to give the α, β unsaturated ketone.

Dehydration is often irreversible and a driving force.

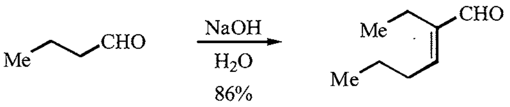
Notes:

If the starting materials are not the same, the reaction is known as a ***"mixed" aldol condensation.***

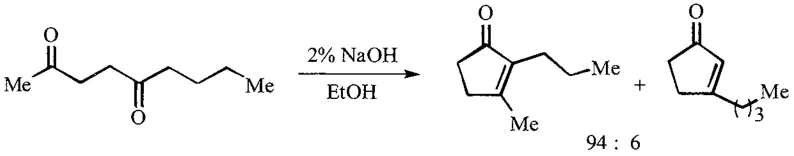


M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1218-1213; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 4-10; A. T. Nielsen, W. J. Houlihan, *Organic Reactions* **16** (full volume); T. Mukaiyama, *Organic Reactions*, **28**, 3; C. J. Cowden, I. Patterson, *Organic Reactions* **51**, 1.

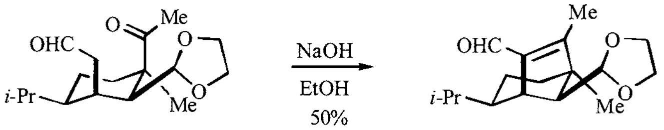
Examples:



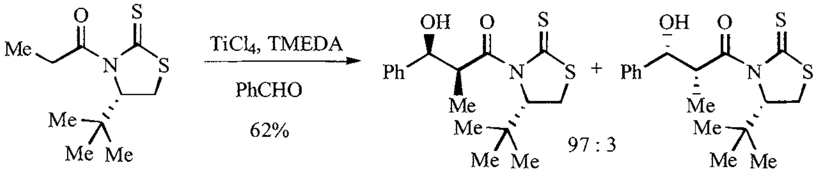
M. Haussermann, *Helvetica Chimica Acta* **1951**, 34, 1482 (Reported in A. T. Nielsen, W. J. Houlihan, *Organic Reactions* **16**, page 8).



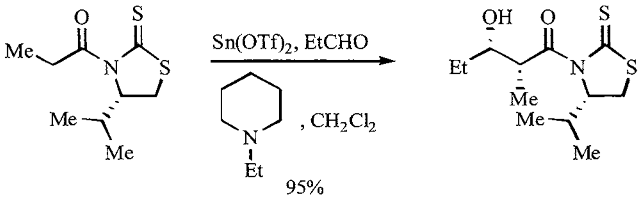
P. M. McCurry, Jr., R. K. Singh, *Journal of Organic Chemistry* **1974**, 39, 2316



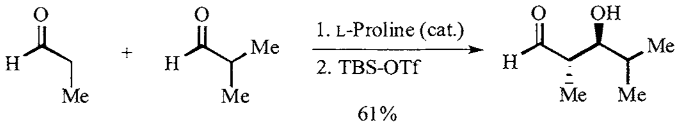
E. J. Corey, S. Nozoe, *Journal of the American Chemical Society* **1965**, 87, 5728



M. T. Crimmins, K. Chaudhary, *Organic Letters* **2000**, 2, 775



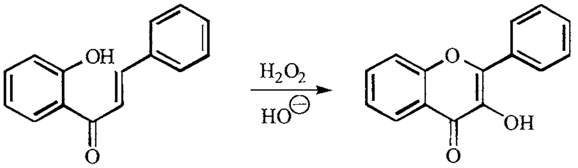
D. Zuev, L. A. Paquette, *Organic Letters* **2000**, 2, 679



P. M. Pihko, A. Erkkila, *Tetrahedron Letters* **2003**, 44, 7607

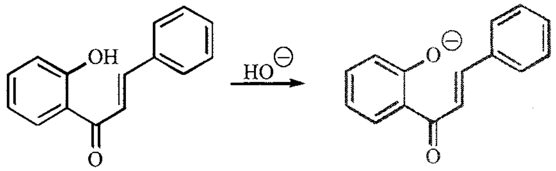
Algar-Flynn-Oyamada Reaction

The Reaction:

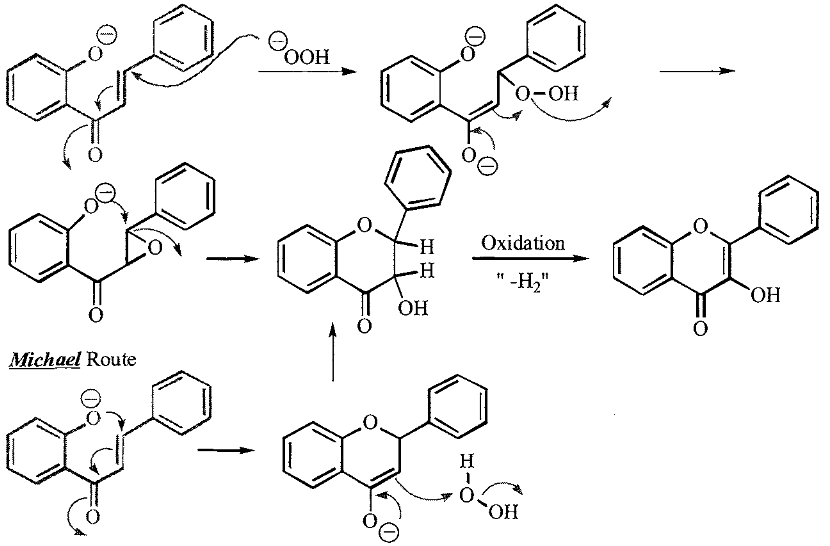


Proposed Mechanism:

$H_2O_2 + HO^{\ominus} \longrightarrow {}^{\ominus}OOH + H_2O$



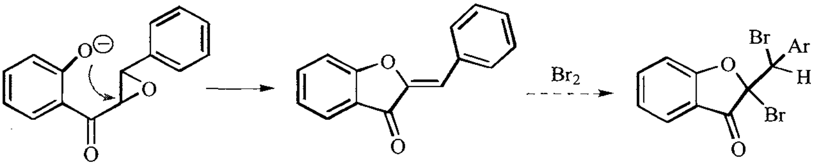
Enone Epoxidation Route:



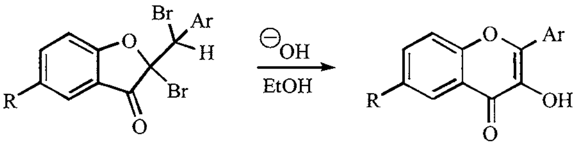
T. M. Gormley, W. I. O'Sullivan, *Tetrahedron* **1973**, 29, 369
See: M. Bennett, A. J. Burke, W. I. O'Sullivan, *Tetrahedron* **1996**, 52, 7178 for a detailed analysis of the role of the epoxide intermediate.

Notes:

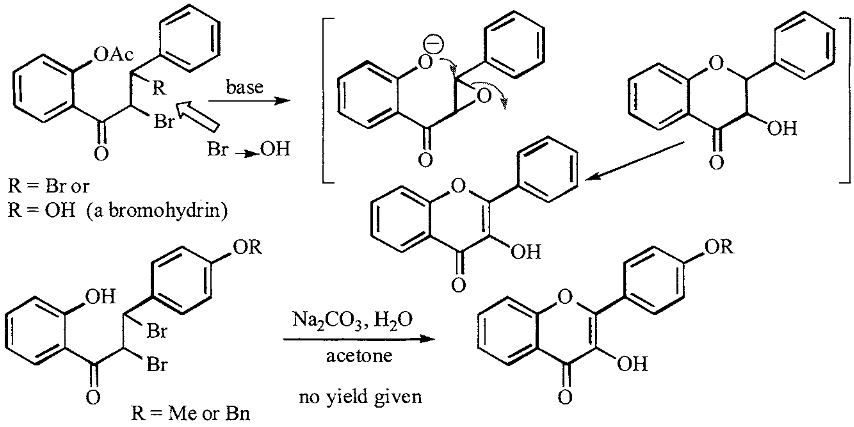
Sometimes an "arone" can be formed.



Auwers Synthesis



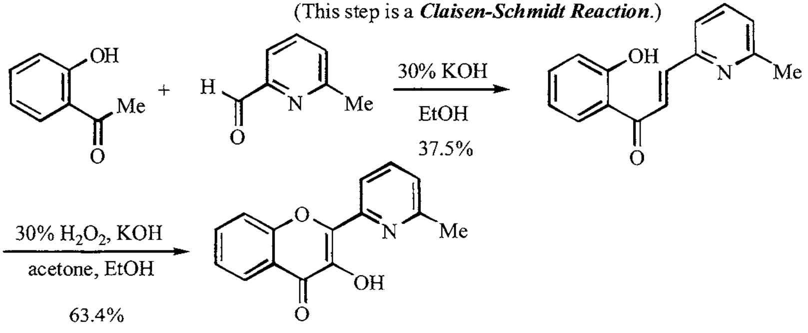
The Rasoda Reaction:



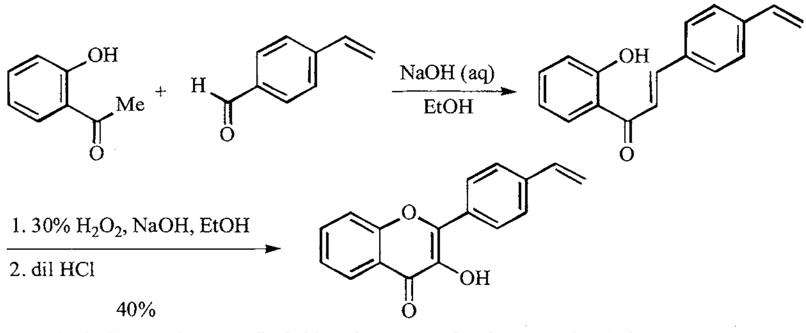
M. G. Marathey, *Journal of Organic Chemistry* **1955**, 20, 563

Examples:

(This step is a ***Claisen-Schmidt Reaction***.)



K. B. Raut, S. H. Wender, *Journal of Organic Chemistry* **1960**, 25, 50



J. R. Dharia, K. F. Johnson, J. B. Schlenof, *Macromolecules* **1994**, 27, 5167

Alkyne Coupling

The Reaction:

$$2\ R{-}{\equiv}{-}H \longrightarrow R{-}{\equiv}{-}{\equiv}{-}R$$

General Discussion:

See P. Siemsen, R. C. Livingston, F. Diederich, *Angewandte Chemie International Edition in English* **2000**, 39, 2632 and K. Sonogashira, *Comprehensive Organic Synthesis*, Vol 3, Chapter 2.5

The earliest of the alkyne coupling reactions is that of Glaser, who had noted:

$$Ph{-}{\equiv}{-}Cu \xrightarrow{O_2} Ph{-}{\equiv}{-}{\equiv}{-}Ph$$

In much of the early work, the copper acetylides were prepared from the reaction of a terminal alkyne with Cu(I) salts.

$$Ph{-}{\equiv}{-}H \xrightarrow[NH_4OH]{CuX} Ph{-}{\equiv}{-}Cu$$

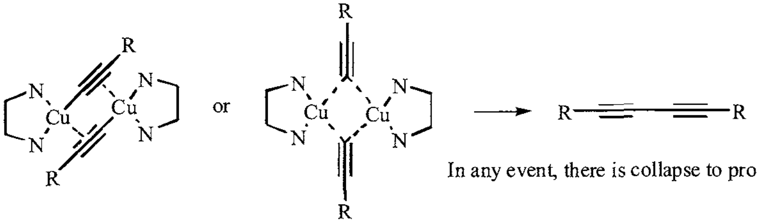
The reaction was of limited use due to the explosive nature of copper acetylides.

In the ***Hay modification*** of the ***Glaser reaction***, it was noted that the reaction could be modified to avoid isolation of the acetylide:

$$R{-}{\equiv}{-}H \xrightarrow[\text{Solvent and } O_2]{\text{CuX, TMEDA (catalytic)}} R{-}{\equiv}{-}{\equiv}{-}R$$

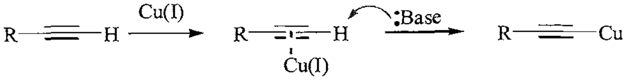
A. S. Hay, *Journal of Organic Chemistry* **1962**, 27, 3320

In this process the TMEDA-Cu complex readily binds to the alkyne. Various interpretations of the binding are possible:



In any event, there is collapse to product.

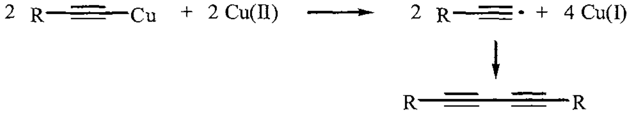
There is evidence that the role of oxidant is to convert Cu(I) to Cu(II). It may be:



$$R{-}{\equiv}{-}H \xrightarrow{Cu(I)} R{-}\underset{Cu(I)}{\equiv}{-}H \xrightarrow{:Base} R{-}{\equiv}{-}Cu$$

$$R{-}{\equiv}{-}Cu(I) \dashrightarrow R{-}{\equiv}{-}\underset{(II)}{Cu}{-}{\equiv}{-}R \dashrightarrow R{-}{\equiv}{-}{\equiv}{-}R$$

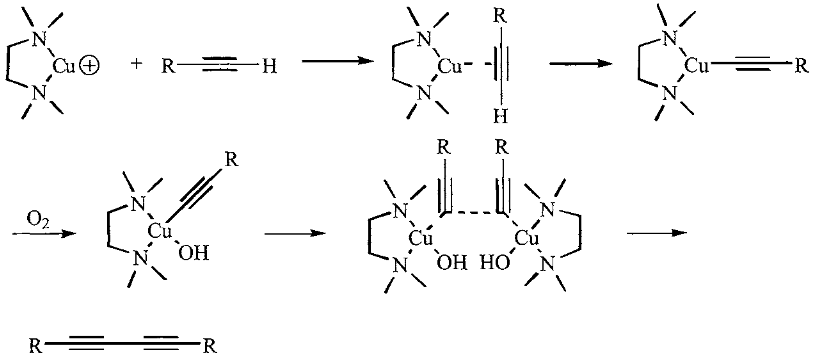
An older view of these reactions involved formation of a radical:



This would require that hetero-coupling of two different alkynes give a statistical product mix. This is not observed.

A computational study of the ***Glaser reaction*** provides additional mechanistic insight.
L. Fomina, B. Vazquez, E. Tkatchouk, S. Fomine, *Tetrahedron* **2002**, 58, 6741

Selected intermediates are shown:



There is much to learn about the details of these reactions. In different sections the following reactions will be described:

Cadiot-Chodkiewicz Coupling

$R-\equiv-H \;+\; X-\equiv-R' \longrightarrow R-\equiv-\equiv-R'$

Castro-Stephens Coupling

$R-\equiv-H \;+\; Ar-X \xrightarrow[\text{CuCl}, \Delta]{\text{base}} R-\equiv-Ar$

Eglinton Reaction

$2\,R-\equiv-H \xrightarrow[\text{pyridine}]{\text{CuX}_2} R-\equiv-\equiv-R$

Glaser Coupling

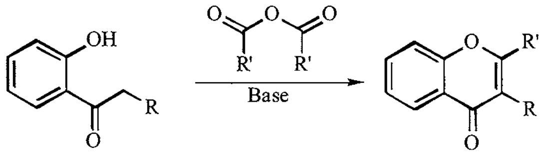
$R-\equiv-H \xrightarrow[\text{Solvent and O}_2]{\text{CuX, TMEDA (catalytic)}} R-\equiv-\equiv-R$

Sonogashira Coupling

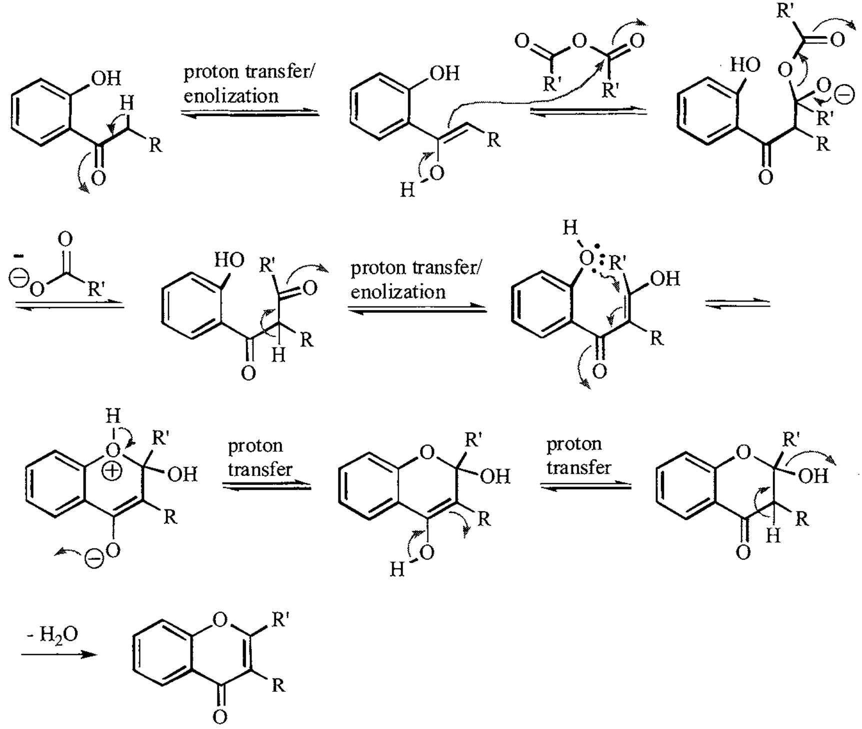
$R-X \;+\; H-\equiv-R' \xrightarrow[\text{CuI, NEt}_3]{\text{PdCl}_2(\text{PPh}_3)_2} R-\equiv-R'$

Allan-Robinson Reaction

The Reaction:



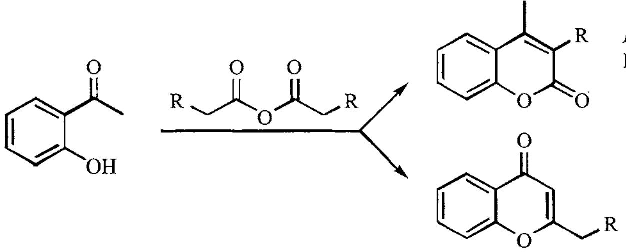
Proposed Mechanism:



Notes:

The rate determining step is dependent on both the concentration of enolacetate and acetate ion. T. Szell, D. M. Zorandy, K. Menyharth, *Tetrahedron* **1969**, 25, 715

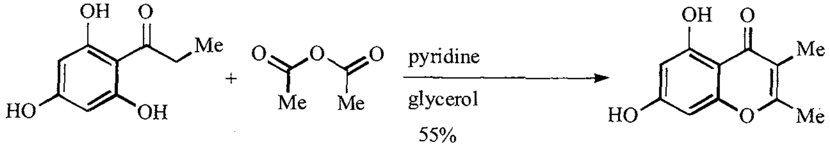
In the related ***Kostanecki Reaction***, the same reagents give a different product. In that case, the attacking species is the phenol oxygen, rather than the enol tautomer of the ketone.



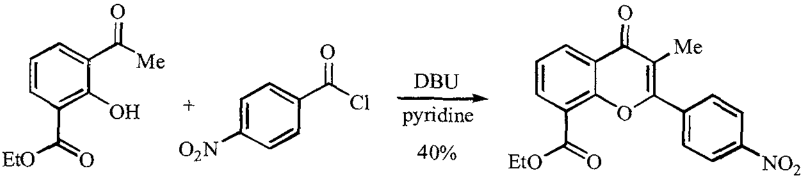
Kostanecki Acylation Product
= Coumarin

Allan-Robinson Reaction Product
= Chromone

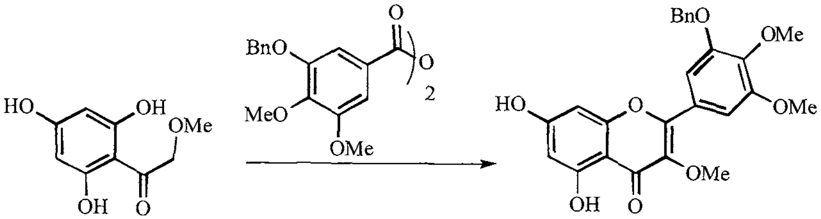
Examples:



T. Szell, *Journal of the Chemical Society*, C, **1967**, 2041 (AN 1968:2779)



C. Riva, C. De Toma, L. Donadel, C. Boi, R. Pennini, G. Motta, A. Leosardi, *Synthesis* **1997**, 195



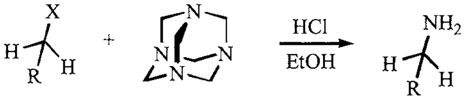
No yield given, product synthesis to confirm structure of an isolated compound.

G. Berti, O. Liv, D. Segnini, I. Cavero, *Tetrahedron* **1967**, 23, 2295

Amine Preparations

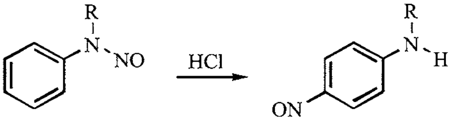
See R. E. Gawley, *Organic Reactions* **1988**, 35, 1

Delépine Reaction



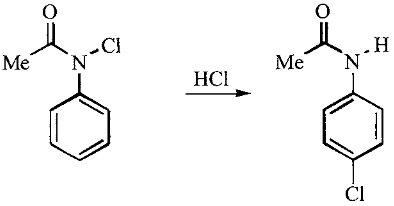
Fischer-Hepp and Related Rearrangements

Fischer-Hepp Rearrangement

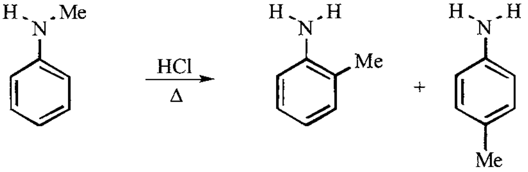


HCl is the preferred acid.

Orton Rearrangement

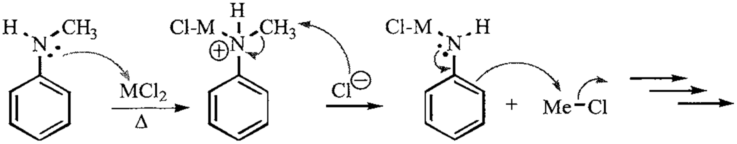


Hofmann-Martius Rearrangement



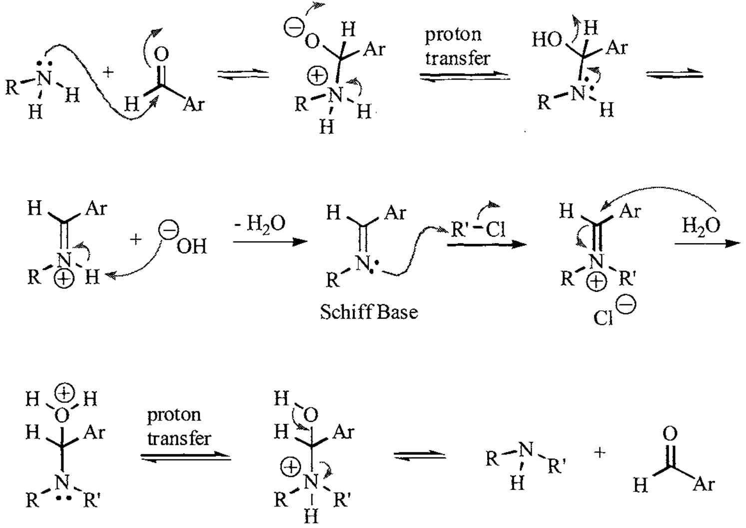
Reilly-Hickinbottom Rearrangement

Similar to ***Hoffmann-Martius Rearrangement*** except that it uses Lewis acids and the amine rather than protic acid and the amine salt.

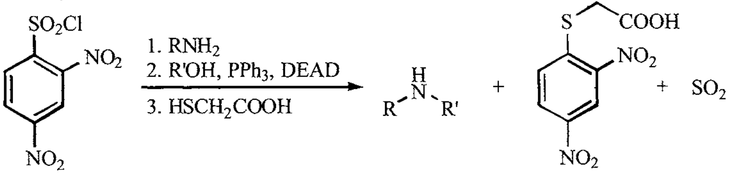


M = Co, Cd, Zn

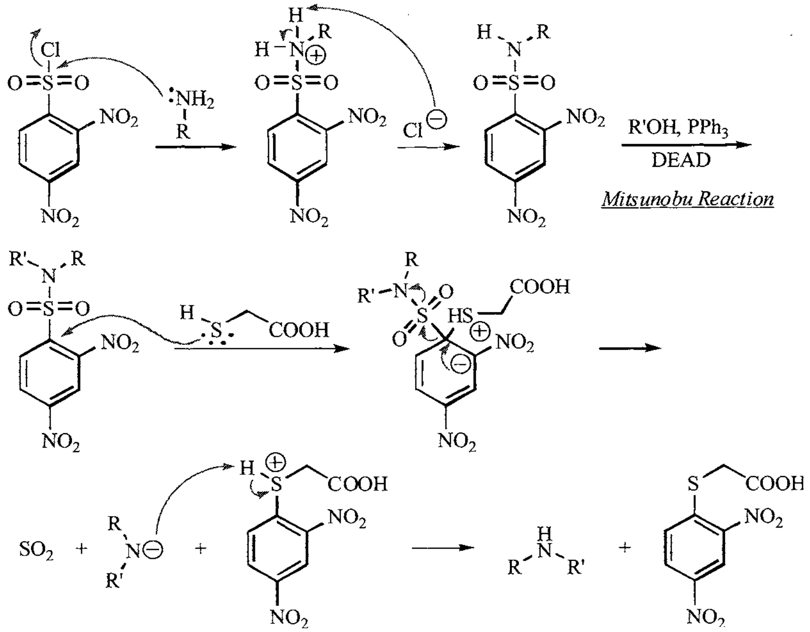
Forster Reaction (Forster-Decker Method)



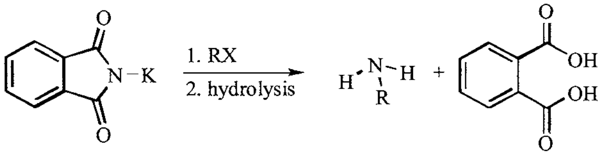
Fukuyama Amine Synthesis



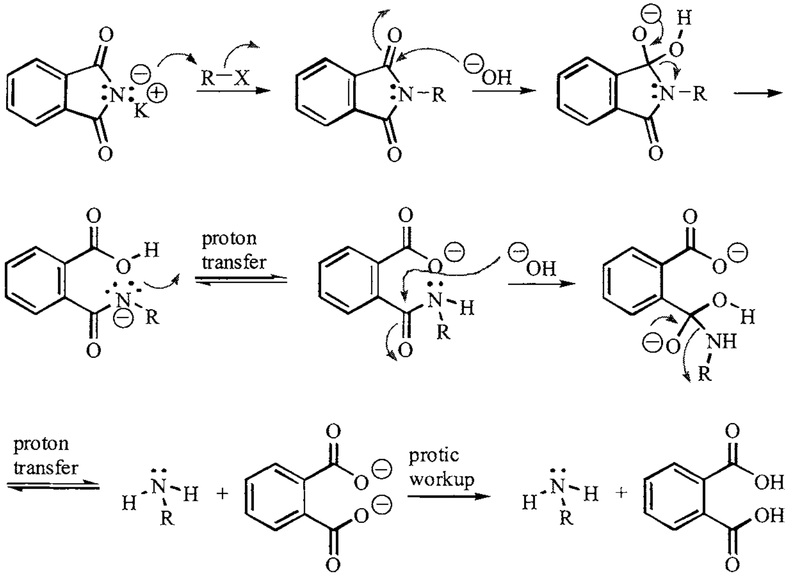
via:



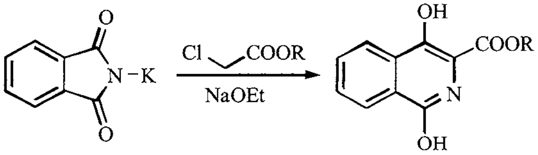
Gabriel Synthesis



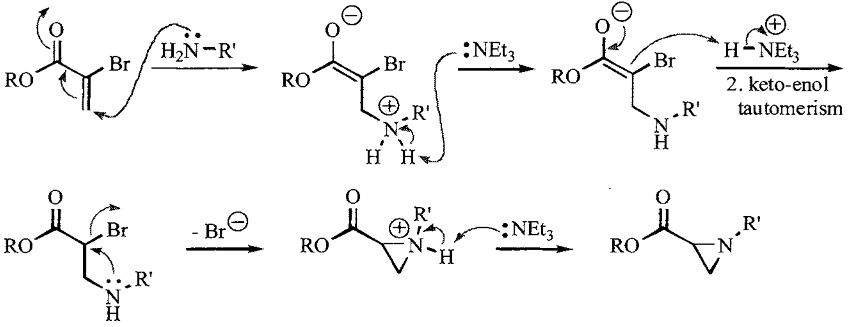
via:



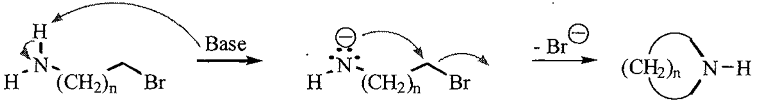
Gabriel-Colman Rearrangement



Gabriel-Cromwell Reaction

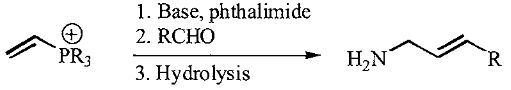


Gabriel (-Marckwald) Ethylenimine Method

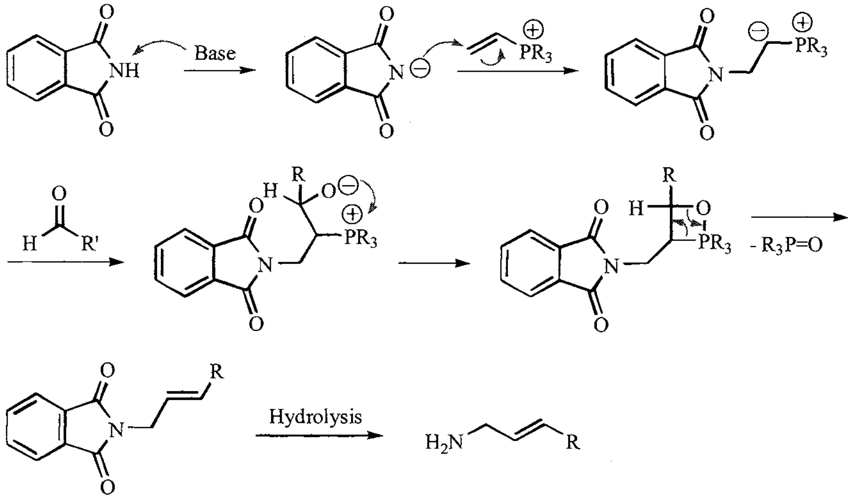


Schweizer Allyl Amine Synthesis

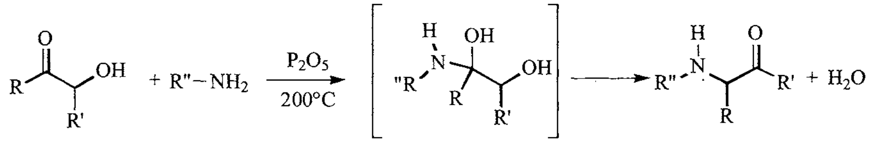
A combination of ***Gabriel*** and ***Wittig*** chemistry



via:

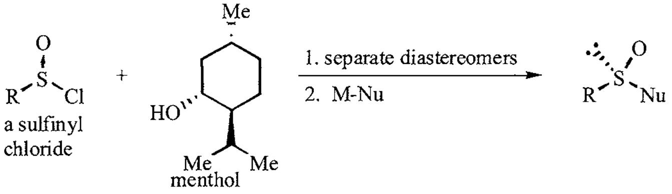


Voight Amination / Reaction

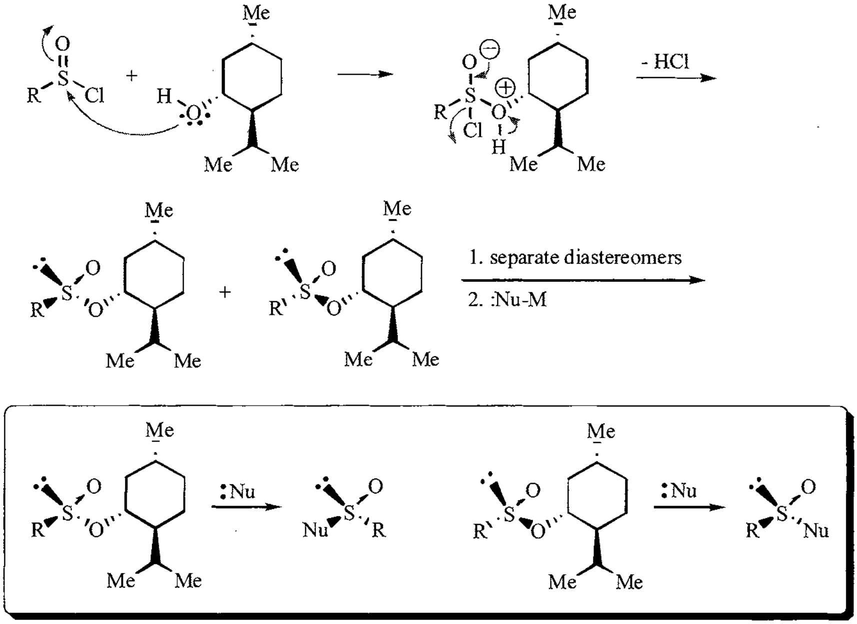


Andersen Sulfoxide Synthesis

The Reaction:



Proposed Mechanism:

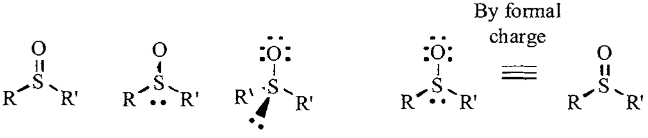


K. K. Andersen, *Tetrahedron Letters* **1962**, 3, 93

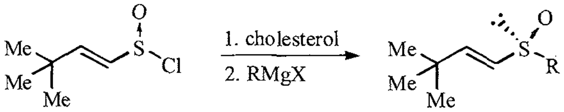
Notes:

Other chiral auxiliaries have been used besides menthol.

Sulfoxide Designations:

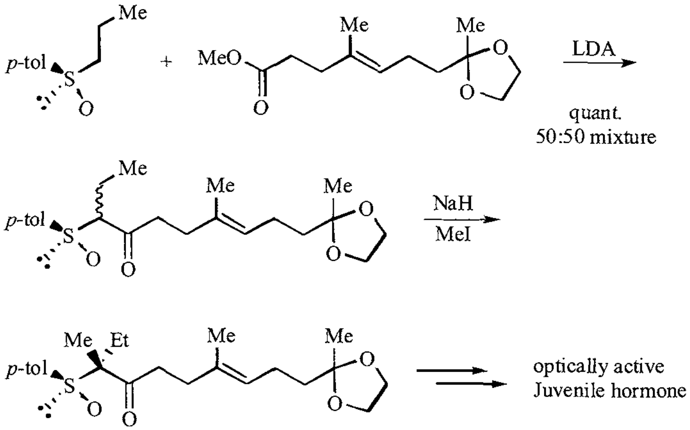


Examples:



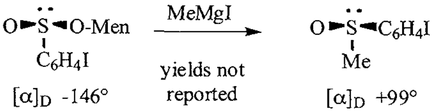
R = *n*-Bu: yield = 61%, 83% ee
R = Ph-CH_2: yield = 78%, 91% ee

R. R. Strickler, A. L. Schwan, *Tetrahedron: Asymmetry* **1999**, 10, 4065



9:1 diastereoselectivity

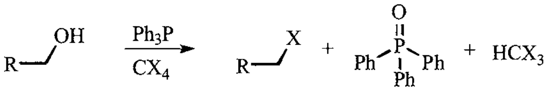
H. Kosugi, O. Kanno, H. Uda, *Tetrahedron: Asymmetry* **1994**, 5, 1139



P. Bickart, M. Axelrod, J. Jacobs, K. Mislow, *Journal of the American Chemical Society* **1967**, 89, 697

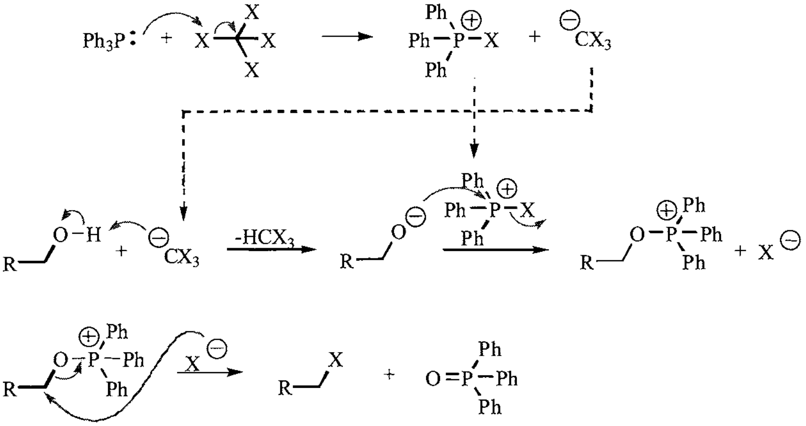
Appel Reaction

The Reaction:



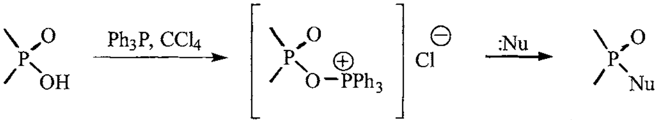
X = Cl or Br

Proposed Mechanism:



Notes:

There are two processes called the ***Appel Reaction***. Although similar, the second is concerned with reactions of phosphorous:

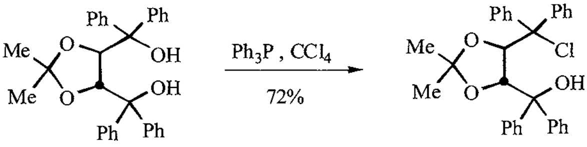


With inversion of configuration around P..

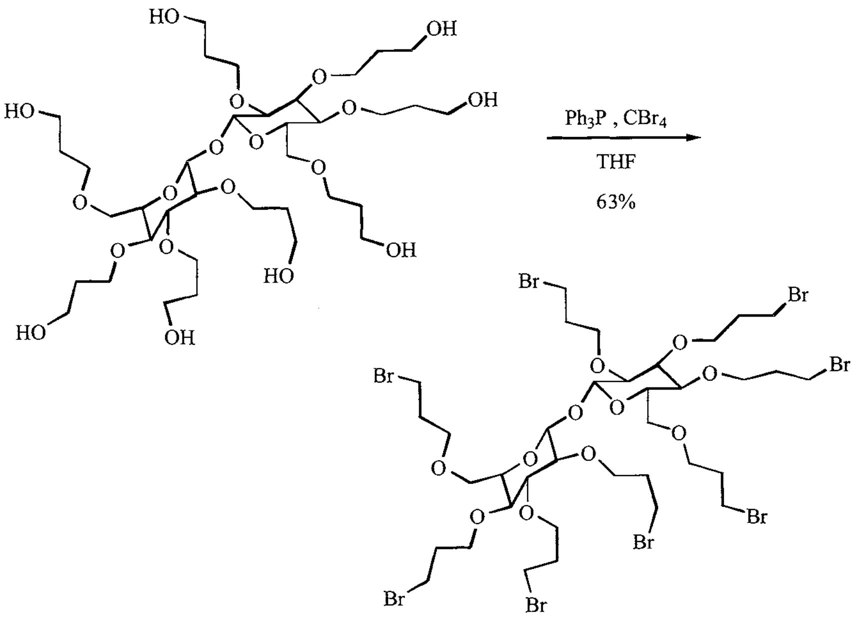
J. Baraniak, W. J. Stec, *Tetrahedron Letters* **1985**, 26, 4379

See also: J. Beres, W. G. Bentrude, L. Parkanji, A. Kalman, A. E. Sopchik, *Journal of Organic Chemistry* **1985**, 50, 1271

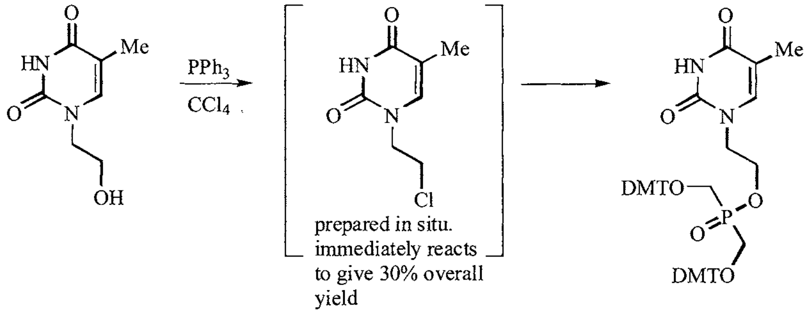
Examples:



D. Seebach, A. Pichota, A. K. Beck, A. B. Pinkerton, T. Litz, J. Karjalainen, V. Gramlich, *Organic Letters* **1999**, 1, 55

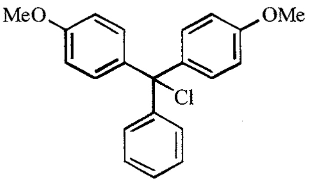


M. Dubber, T. K. Lindhorst, *Organic Letters* **2001**, 3, 4019



prepared in situ. immediately reacts to give 30% overall yield

ODMT (ODMTr) is the 4,4'-dimethoxytrityl group, a common –OH protecting group for the carbohydrate moieties in syntheses of polynucleotides.

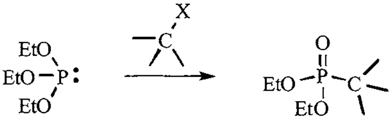


4,4'-dimethoxytrityl chloride [40615-36-9]

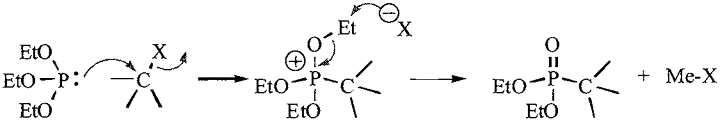
B. Nawrot, O. Michalak, M. Nowak, A. Okruszek, M. Dera, W. J. Stee, *Tetrahedron Letters* **2002**, 43, 5397

Arbuzov Reaction (Michaelis-Arbuzov Reaction)

The Reaction:



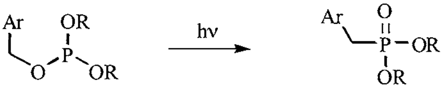
Proposed Mechanism:



Notes:

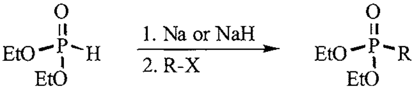
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, p. 12.; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1234.

The Photo-Arbuzov Reaction:

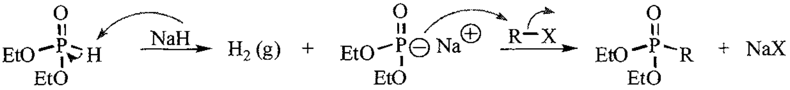


Michaelis-Becker Reaction (Michaelis Reaction)

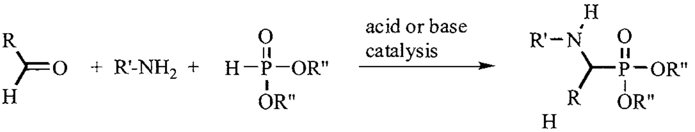
The Reaction:

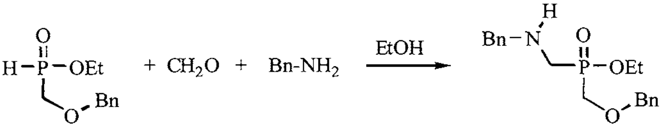


Proposed Mechanism:



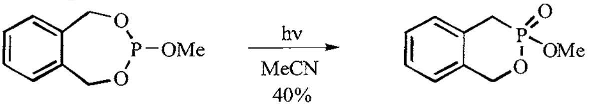
Kabachnik-Fields Reaction



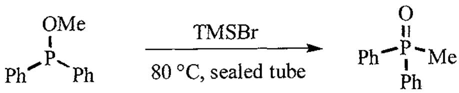


H.-J. Cristan, A. Herve, D. Virieux, *Tetrahedron* **2004**, 60, 877

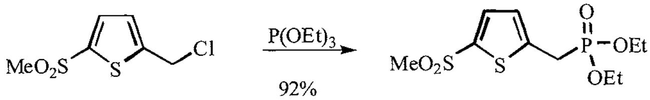
Examples:



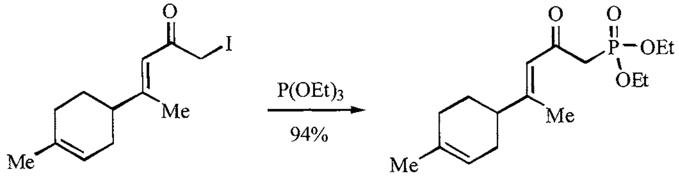
M. S. Landis, N. J. Turro, W. Bhanthumnavin, W. G. Bentrude, *Journal of Organometallic Chemistry* **2002**, 646, 239



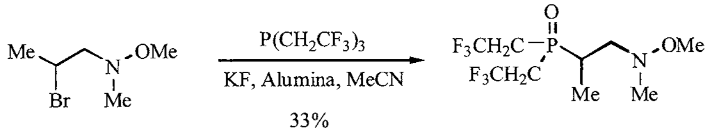
P.-Y. Renard, P. Vayron, C. Mioskowski, *Organic Letters* **2003**, 5, 1661



S.-S Chou, D.-J. Sun, J.-Y. Huang, P.-K. Yang, H.-C. Lin, *Tetrahedron Letters* **1996**, 37, 7279

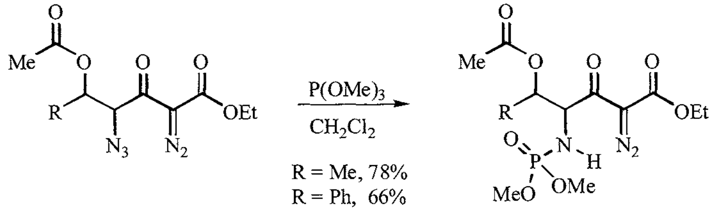


R. W. Driesen, M. Blouin, *Journal of Organic Chemistry* **1996**, 61, 7202

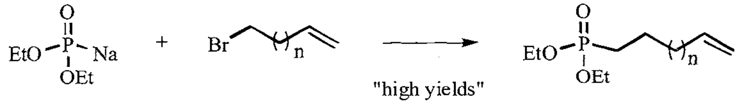


S. Fortin, F. Dupont, P. Deslongchamps, *Journal of Organic Chemistry* **2002**, 67, 5437

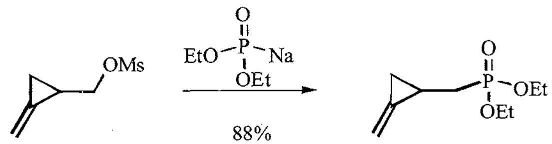
Described as a tandem ***Staudinger-Arbuzov Reaction***:



M. M. Sá, G. P. Silveira, A. J. Bortoluzzi, A. Padwa, *Tetrahedron* **2003**, 59, 5441



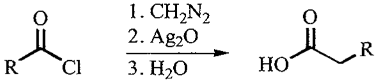
I. Pergament, M. Srebnik, *Organic Letters* **2001**, 3, 217



H.-P. Guan, Y.-L. Qui, M. B. Ksebati, E. A. Kern, J. Zemlicka, *Tetrahedron* **2002**, 58, 6047

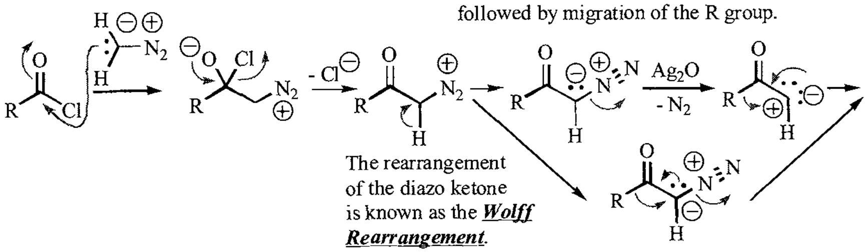
Arndt-Eistert Homologation Reaction

The Reaction:



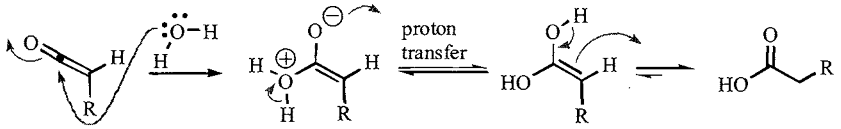
Proposed Mechanism:

Elimination of nitrogen gives a carbene, followed by migration of the R group.



The rearrangement of the diazo ketone is known as the ***Wolff Rearrangement***.

Alternatively, R migration and N_2 elimination may be concerted, avoiding the formation of a carbene.



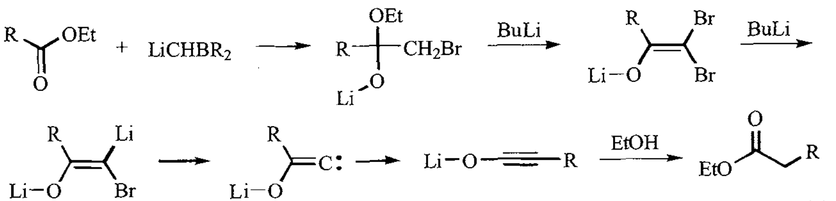
keto-enol tautomerism

Notes:

See: *Diazomethane*

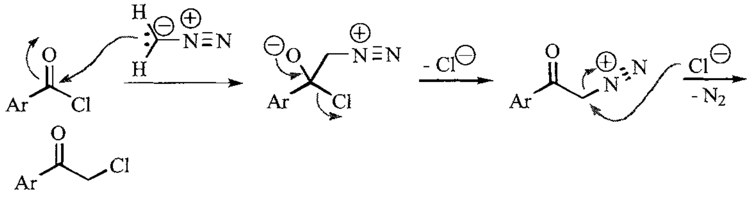
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1405-1407; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 13-15; W. E. Bachmann, W. S. Struve, *Organic Reactions* **1**, 2

The ***Kowalski Ester Homologation*** provides a similar conversion (C. Kowalski, M. S. Haque, *Journal of Organic Chemistry* **1985**, 50, 5140)

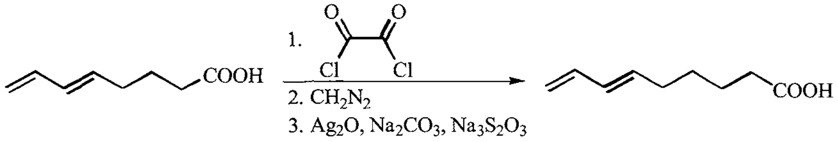


See also: P. Chen, P. T. W. Cheng, S. H. Spergel, R. Zahler, X. Wang, J. Thottathil, J. C. Barrish, R. P. Polniaszek, *Tetrahedron Letters* **1997**, 38, 3175

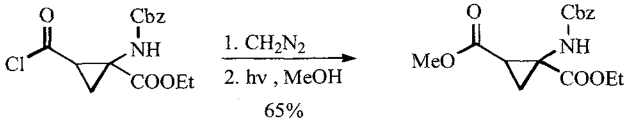
Nierenstein Reaction



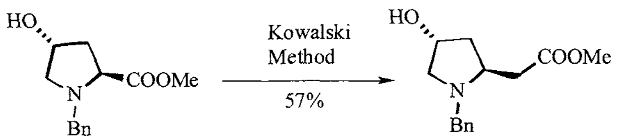
Examples:



T. Hudlicky, J. P. Sheth, *Tetrahedron Letters* **1979**, 29, 2667

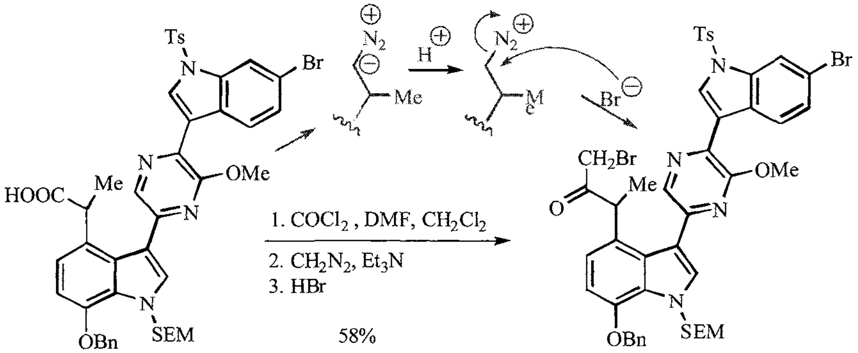


J. M. Jimenez, R. M. Ortuno, *Tetrahedron: Asymmetry* **1996**, 7, 3203

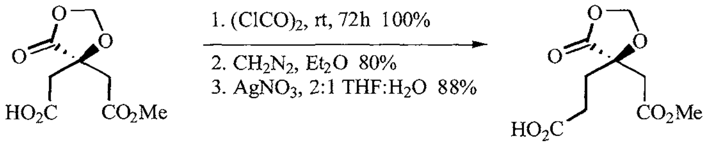


A number of examples to show that this method is more mild than the ***Arndt-Eistert*** reaction

D. Gray, C. Concello', T. Gallagher, *Journal of Organikc Chemistry* **2004**, 69, 4849



N. J. Garg, R. Sarpong, B. M. Stoltz, *Journal of the American Chemical Society* **2002**, 124, 13179

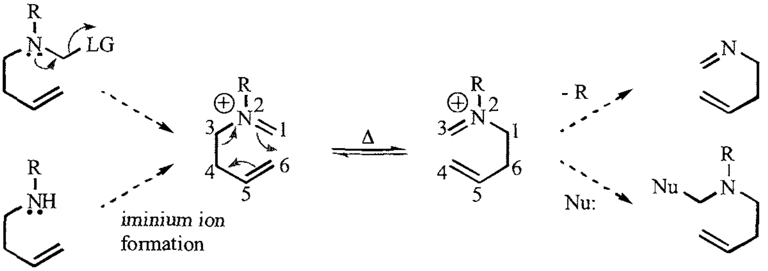


R. A. Ancliff, A. T. Russell, A. J. Sanderson *Tetrahedron: Asymmetry* **1997**, 8, 3379

Aza-Cope Rearrangement

The Reaction:

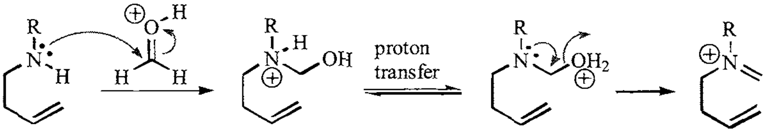
Proposed Mechanism:



Notes:

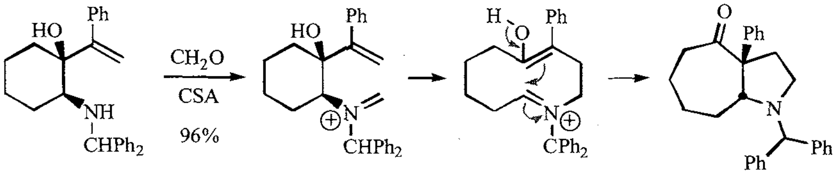
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1445.

iminium ion formation

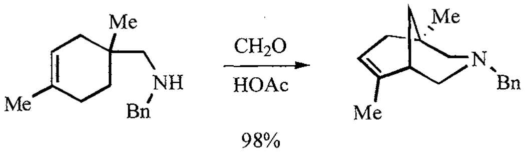


The ***Azo-Cope Rearrangement***:

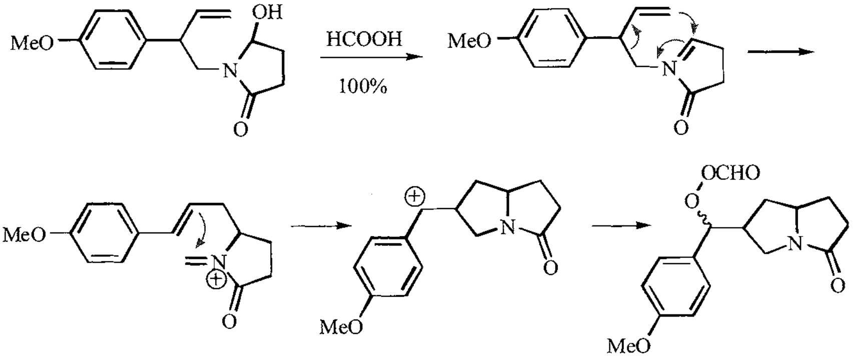
Examples:



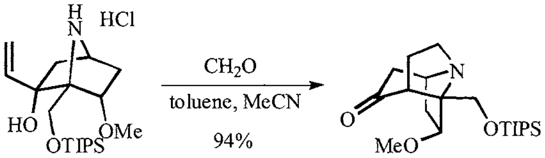
L. E. Overman, E. J. Jacobsen, R. J. Doedens, *Journal of Organic Chemistry* **1983**, 48, 3393



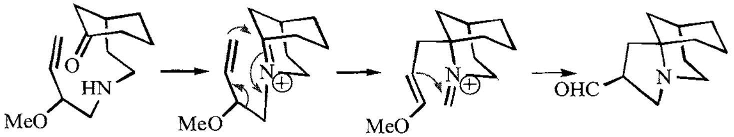
K. Shishido, K. Hiroya, K. Fukumoto, T. Kametani, *Tetrahedron Letters* **1986**, 27, 1167



H. Ent, H. De Koning, W. N. Speckamp *Journal of Organic Chemistry* **1986**, 51, 1687



M. Bruggemann, A. I. McDonald, L. E. Overman, M. D. Rosen, L. Schwink, J. P. Scott, *Journal of the American Chemical Society* **2003**, 125, 15284

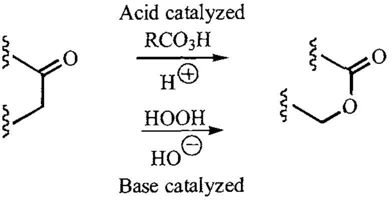


No yield given for this step, catalyzed by tosic acid in benzene.

K. M. Brummond, J. Lu, *Organic Letters* **2001**, 3, 1347

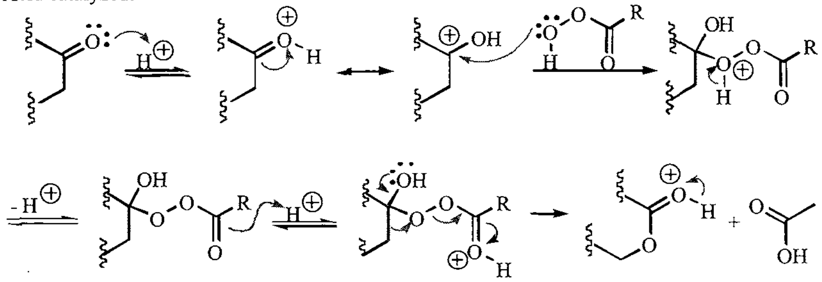
Baeyer-Villiger Reaction

The Reaction:

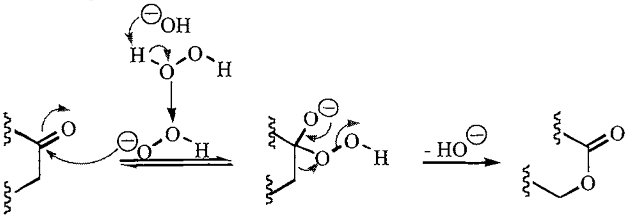


Proposed Mechanism:

Acid catalyzed:



Base catalyzed:

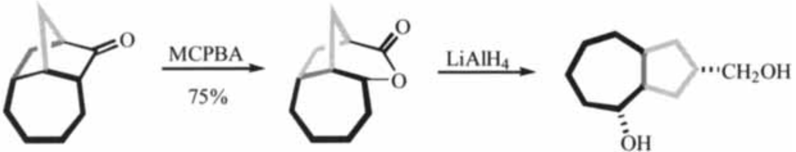


Notes:

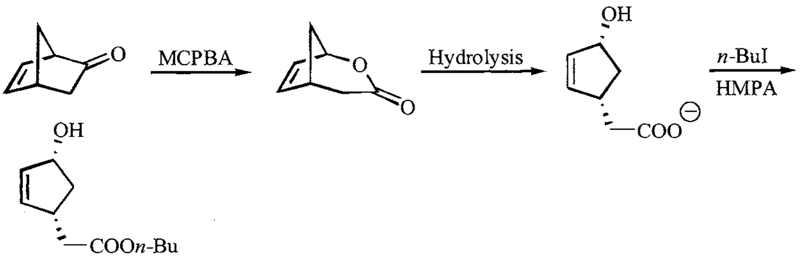
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1417-1418; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 16-19; C. H. Hassall, *Organic Reactions* **9**, 3; G. R. Krow, *Organic Reactions* **43**, 3.

Migratory Apptitude: 3° > 2°> Ph-CH_2-> Ph- > 1°> Me > H

Hydrolysis or reduction of the lactone ring provided by reaction with cyclic ketones provides a useful strategy for construction of ring systems:



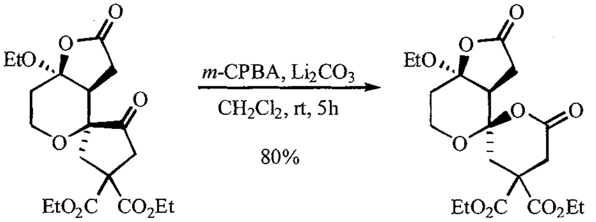
Y. Chen, J. K. Snyder, *Tetrahedron Letters* **1997**, 38, 1477



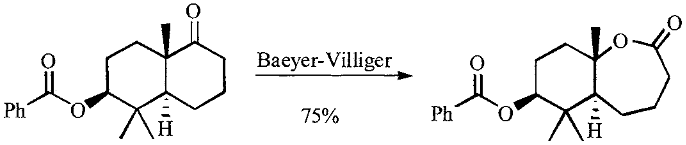
A. E. Greene, C. Le Drian, P. Crabbe, *Journal of the American Chemical Society* **1980**, 102, 7584

Examples:

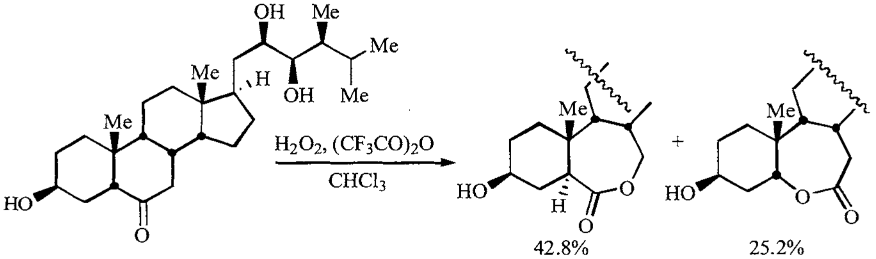
Note the retention of stereochemistry after the oxygen insertion. This is a general observation.



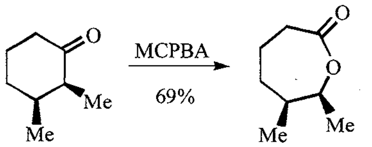
N. Haddad, Z. Abramovich, I. Ruhman *Tetrahedron Letters* **1996**, 37, 3521



F. W. J. Demnitz, R. A. Parhael, *Synthesis* **1996**, 11, 1305



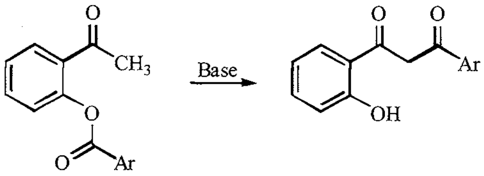
B. Voigt, J. Schmidt, G. Adam, *Tetrahedron* **1996**, 52, 1997



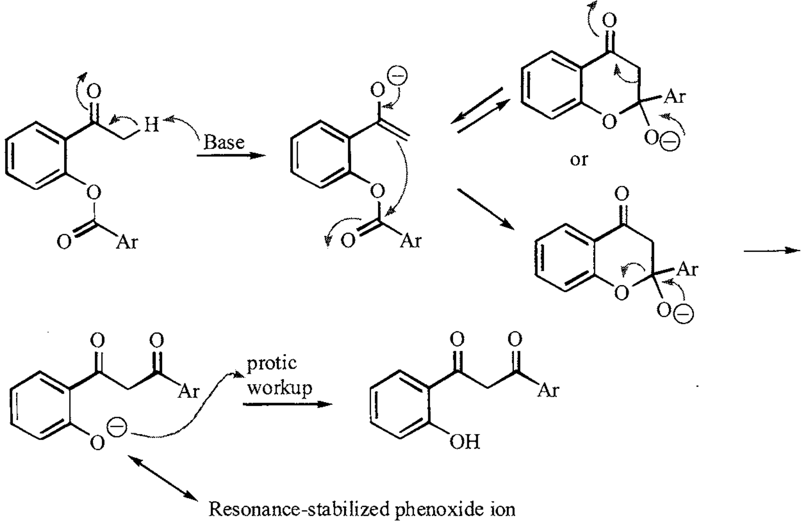
G. Magnusson, *Tetrahedron Letters* **1977**, 18, 2713

Baker-Venkataraman Rearrangement

The Reaction:



Proposed Mechanism:

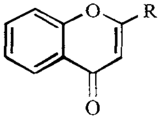


Resonance-stabilized phenoxide ion

See: T. Szell, G. Balaspiri, T. Balaspiri, *Tetrahedron* **1969**, 25, 707

Notes:

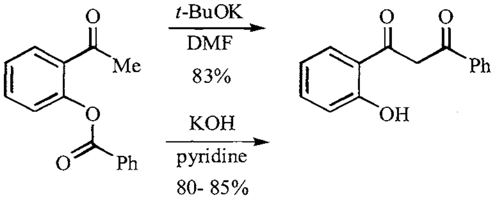
These β-diketones are useful intermediates for the synthesis of flavones and chromones:



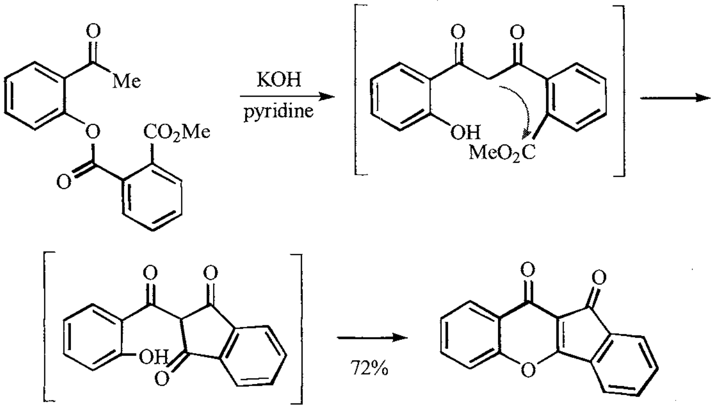
R = Ph: Flavone; R = Me: Chromone

V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002, pp. 277-278

Examples:

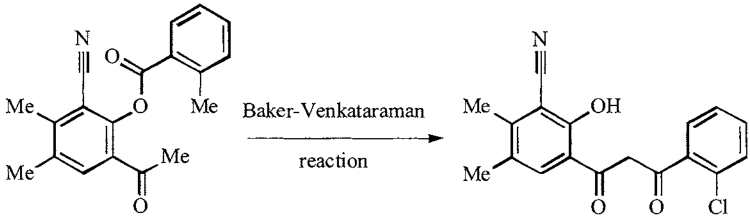


A. Nishinaga, H. Ando, K. Maruyama, T. Mashino, *Synthesis* **1992**, 839
T. S. Wheeler, *Organic Syntheses*, CV4, 478

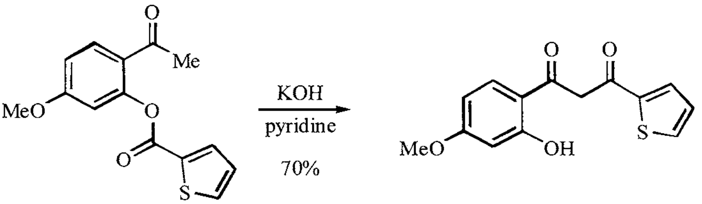


A ring closure that is often associated with the reaction is called the ***Baker-Venkataraman Reaction***.

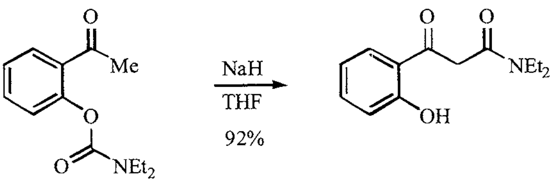
N. Thasana, S. Ruchirawat, *Tetrahedron Letters* **2002**, 43, 4515



S. J. Cutler, F. M. El-Kabbani, C. Keane, S. L. Fisher-Shore, C. D. Blanton, *Heterocycles* 1990, 31, 651 (AN 1990:552089)



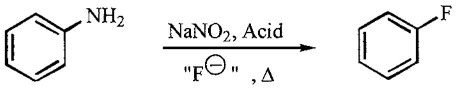
P. F. Devitt, A. Timoney, M. A. Vickars, *Journal of Organic Chemistry* **1961**, 26, 4941



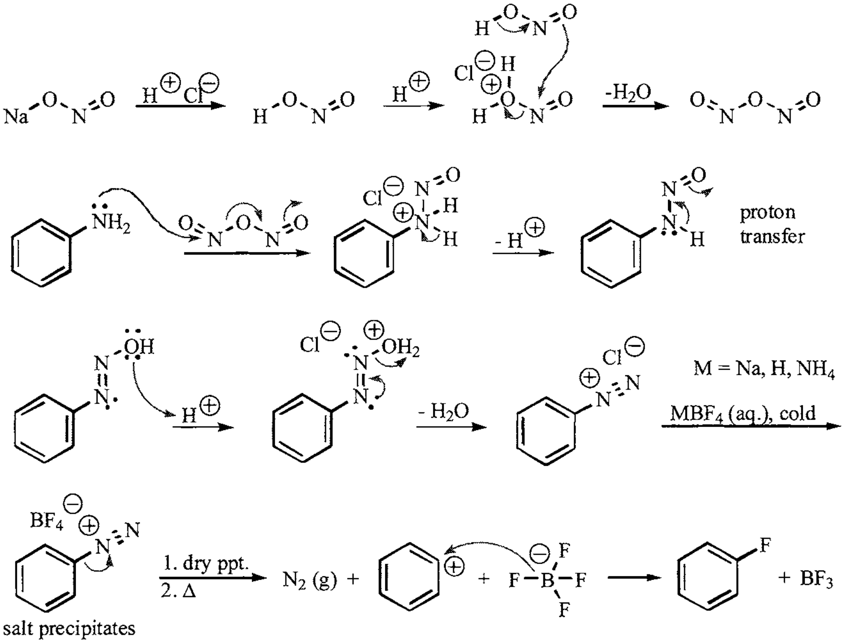
A. V. Kalinin, A. J. M. da Silva, C. C. Lopes, R. S. C. Lopes, V. Snieckus *Tetrahedron Letters* **1998**, 39, 4995

Balz-Schiemann Reaction (Schiemann Reaction)

The Reaction:

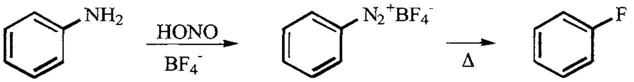


Proposed Mechanism:



Notes:

The original work:



G. Balz, G. Schiemann,*Berichte der Deutschen Chemischen Gesellschaft* **1927**, 60, 1186

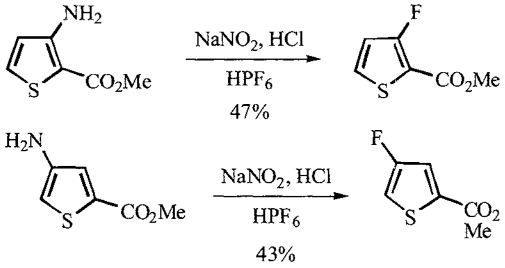
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 237-238; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 875; A. Roe, *Organic Reactions* 5, 4

Reaction is often incorporated into the ***Sandmeyer Reactions*** series,

Procedural improvement to avoid isolation of the (toxic) intermediate:
D. J. Milner, P. G. McMunn, J. S. Moilliet, *Journal of Fluorine Chemistry* **1992**, 58, 317 and D. J. Milner, *Journal of Fluorine Chemistry* **1991**, 54, 382

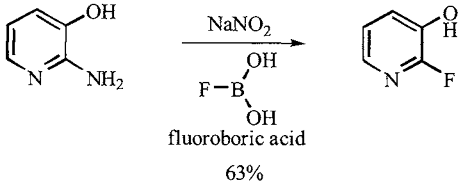
Reaction improvement by using ionic liquid salts:
K. K. Laali, V. J. Gettwert, *Journal of Fluorine Chemistry* **2001**, 107, 31

Examples:

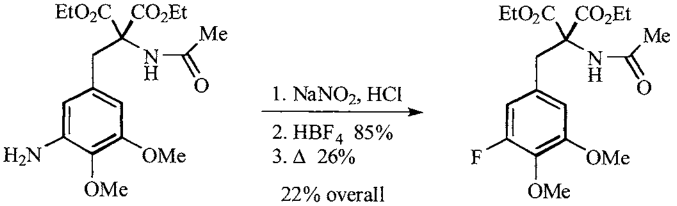


A. Kiryanov, A. Seed, P. Sampson, *Tetrahedron Letters* **2001**, 42, 8797

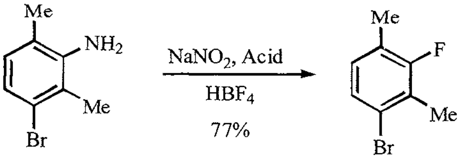
A modified ***Balz-Schiemann Reaction***:



F. Dolle, L. Dolci, H. Valette, F. Hinnen, F. Vaufrey, H. Guenther, C. Fuseau, C. Coulon, M. Buttalender, C. Crouzel *Journal of Medicinal Chemistry* **1999**, 42, 2251



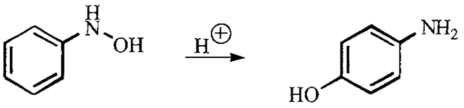
M. Argentini, C. Wiese, R. Weinreich, *Journal of Fluorine Chemistry* **1994**, 68, 141



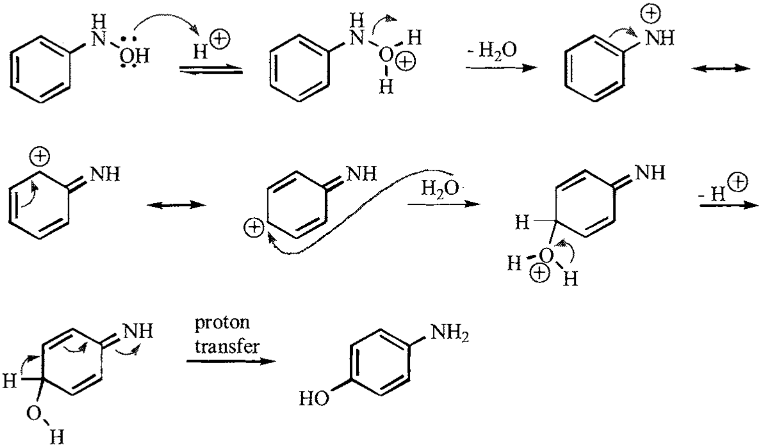
H. Hart, J. F. Janssen, *Journal of Organic Chemistry* **1970**, 35, 3637

Bamberger Rearrangement

The Reaction:



Proposed Mechanism:

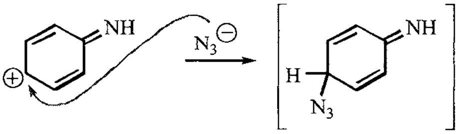


See discussion in: N. Haga, Y. Endo, K.-i. Kataoka, K. Yamaguchi, K. Shudo, *Journal of the American Chemical Society* **1992**, 114, 9795

Notes:

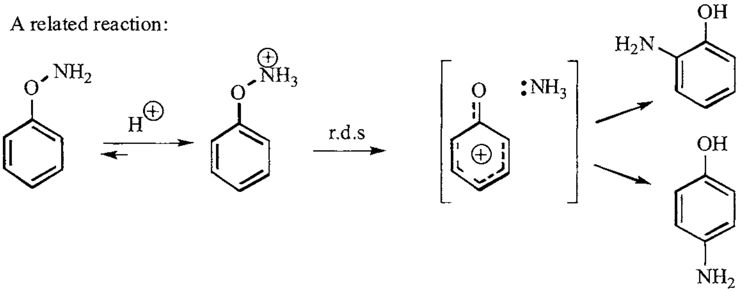
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 878; V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002, p. 449

By addition of azide ion to the reaction, the intermediate can be competitively trapped:



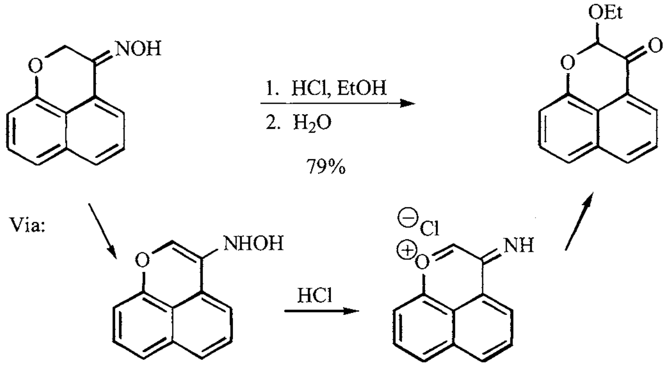
J. C. Fishbein, R. A. McClelland, *Journal of the American Chemical Society* **1987**, 109, 2824

A related reaction:

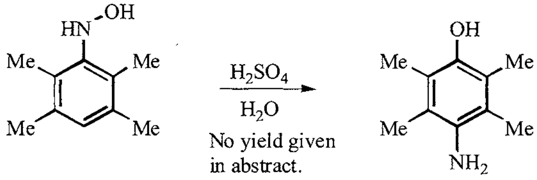


N. Haga, Y. Endo, K.-i. Kataoka, K. Yamaguchi, K. Shudo, *Journal of the American Chemical Society* **1992**, 114, 9795

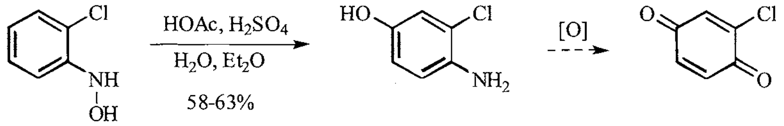
Examples:



J. C. Jardy, M. Venet, *Tetrahedron Letters* **1982**, 23, 1255



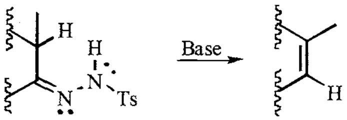
G. G. Barclay, J. P. Candlin, W. Lawrie, P. L. Paulson, *Journal of Chemical Research Synopses* **1992**, 245



R. E. Harman, *Organic Syntheses* CV4, 148

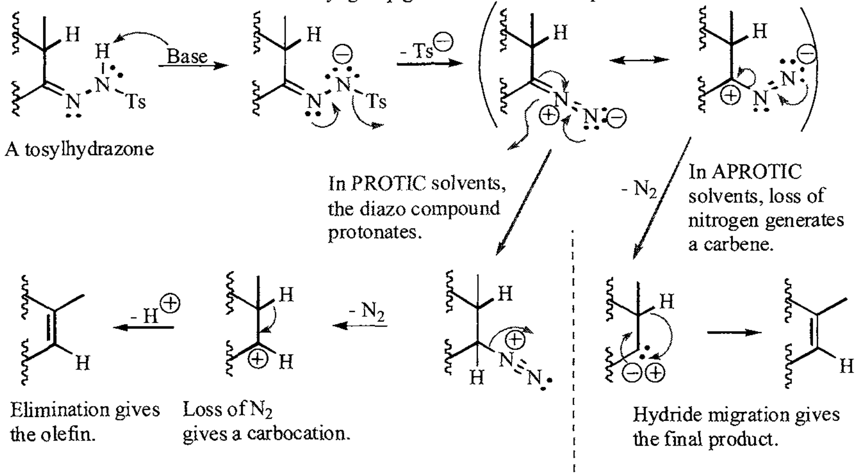
Bamford-Stevens Reaction

The Reaction:



Proposed Mechanism:

Loss of the tosyl group generates a diazo compound.



A tosylhydrazone

In PROTIC solvents, the diazo compound protonates.

In APROTIC solvents, loss of nitrogen generates a carbene.

Elimination gives the olefin.

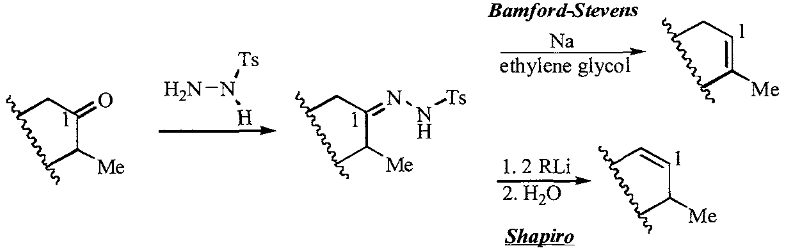
Loss of N_2 gives a carbocation.

Hydride migration gives the final product.

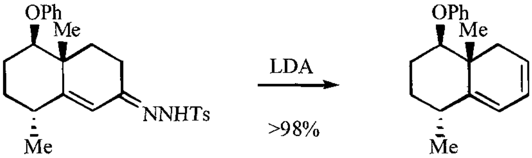
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1335; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 19-22; R. H. Shapiro, *Organic Reactions* **23**, 3

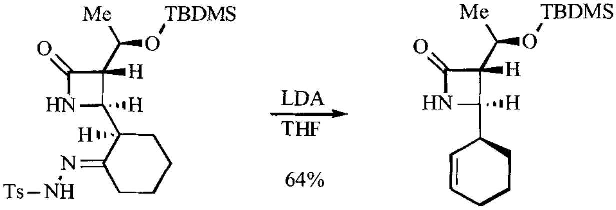
In the related ***Shapiro reaction***, two equivalents of an alkyl lithium are used and the less substituted alkene is formed.



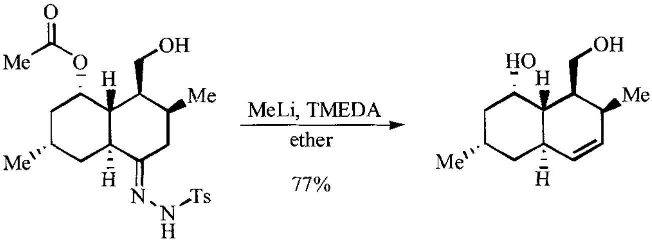
Examples:



P. A. Grieco, T. Oguri, C.-L. J. Wang, E. Williams, *Journal of Organic Chemistry* **1977**, 42, 4113

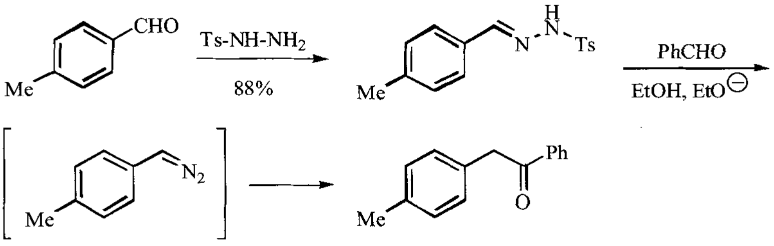


C. Marchioro, G. Pentassuglia, A. Perboni, D. Donati, *Journal of the Chemical Society Perkin Transactions 1* **1997**, 463



S. J Hecker, C. H. Heathcock, *Journal of the American Chemical Society* **1986**, 108, 4586

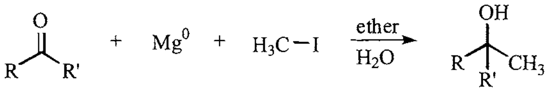
A general method for the homologation of aldehydes to benzylic ketones makes use of the ***Bamford-Stevens*** approach, via intermediate aryldiazomethanes:

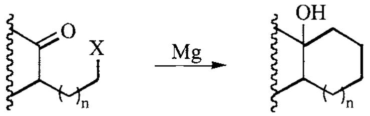


S. R. Angle, M. L. Neitzel, *Journal of Organic Chemistry* **2000**, 65, 6458

Barbier (Coupling) Reaction

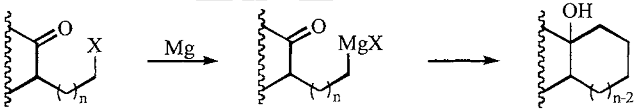
The Reaction:





Proposed Mechanism:

Resembles an internal ***Grignard reaction***:



Notes:

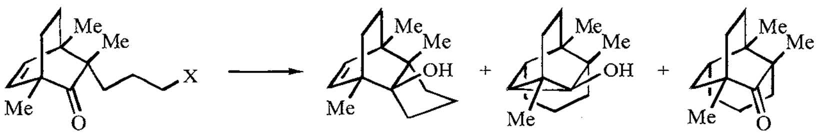
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1205

This reaction was used before it was noted that adding the halide to magnesium prior to the addition the carbonyl gave a better reaction. See the ***Grignard Reaction***.

Other metals may be used.

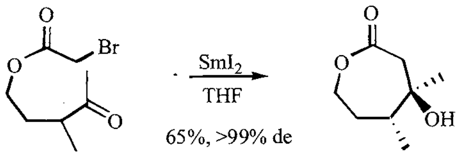
A variety of reactions of a carbonyl and an organohalogen compound are classified as ***Barbier and Barbier-type***.

Examples:



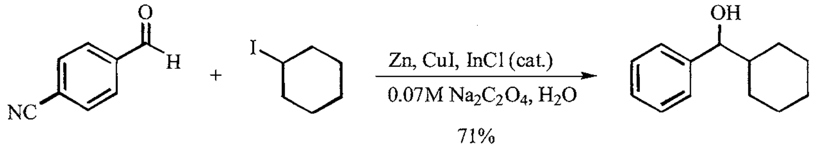
X	Conditions	Ratio		
Br	Li powder, ultrasound, Et_2O	34	50	-
Br	Mg turning, $HgCl_2$, ultrasound, THF	10	12	37
I	BuLi, THF	71	-	-

W. Zhang, P. Dowd, *Tetrahedron Letters* **1993**, 34, 2095

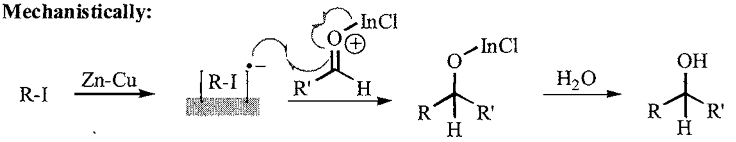


C. A. Molander, J. B. Etter, L. S. Harring, P.-J. Thorel, *Journal of the American Chemical Society* **1991**, 113, 3889

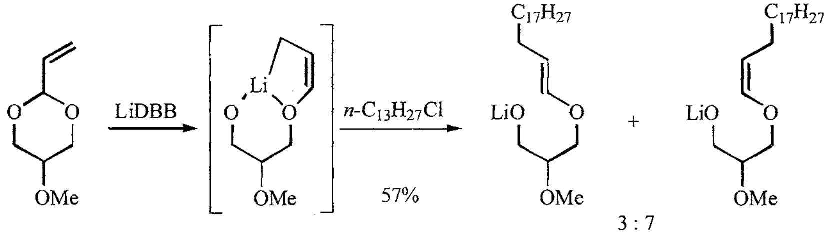
For a review of diiodosamarium chemistry (including ***Barbier Reactions***) see:
H. Kagan, *Tetrahedron* **2003**, 59, 10351



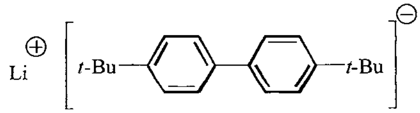
Mechanistically:



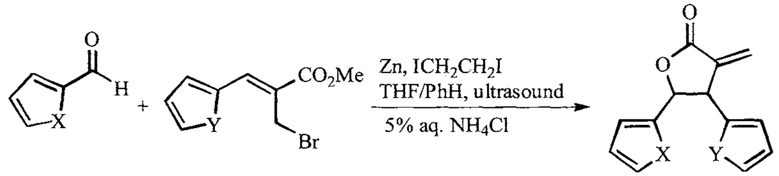
C. C. K. Keh, C. Wei, C.-J, Li, *Journal of the American Chemical Society* **2003**, 125, 4062



LiDBB =Lithium 4,4'-dit-butylbiphenyl =



J. Shin, O. Gerasimov, D. H. Thompson, *Journal of Organic Chemistry* **2002**, 67, 6503

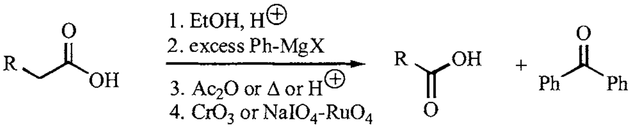


X = O, Y = S 68% (cis/trans = 95/5) X = S, Y = S 72% (cis/trans = 95/5)
X = O, Y = O 71% (cis/trans = 56/44) X = S, Y = O 43% (cis/trans = 52/48)

A. S.-Y. Lee, Y.-T. Chang, S.-H. Wang, S.-F. Chu, *Tetrahedron Letters* **2002**, 43, 8489

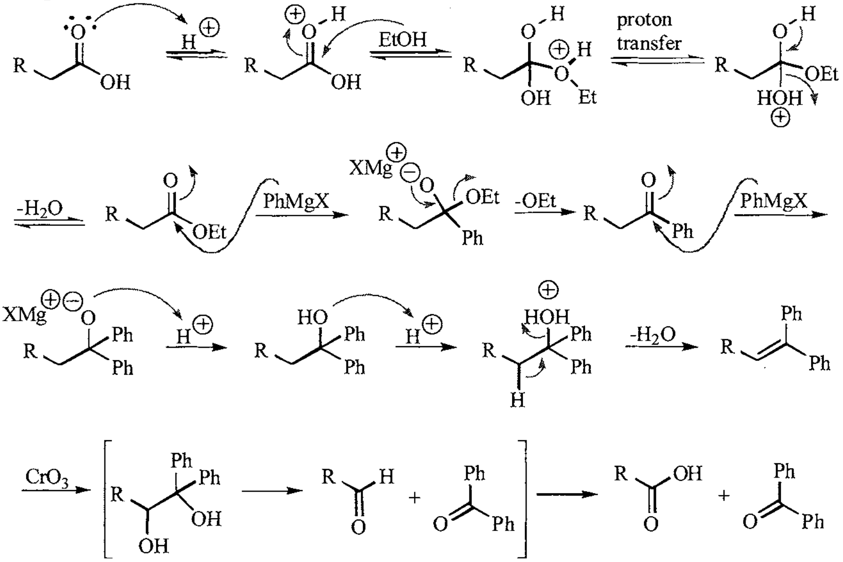
Barbier-Wieland Degradation (Barbier-Locquin Degradation)

The Reaction:



A procedure for decreasing a chain length by one carbon.

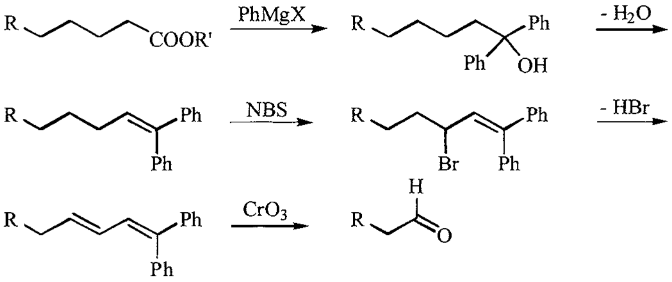
Proposed Mechanism:



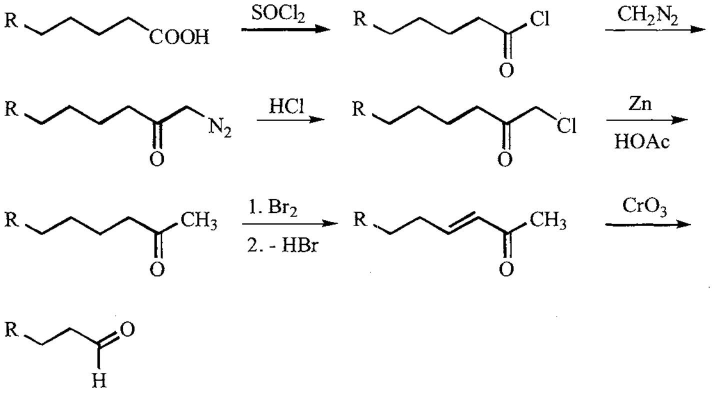
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1526.

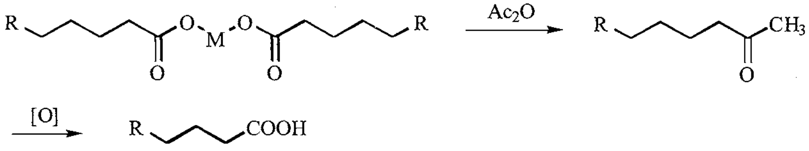
A variation of this procedure, the ***Meystre-Miescher-Wettstein Degradation (Miescher Degradation)*** removes three carbons from the chain:



Gallagher-Hollander Degradation

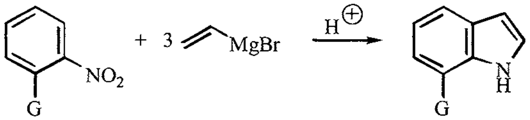


Krafft Degradation

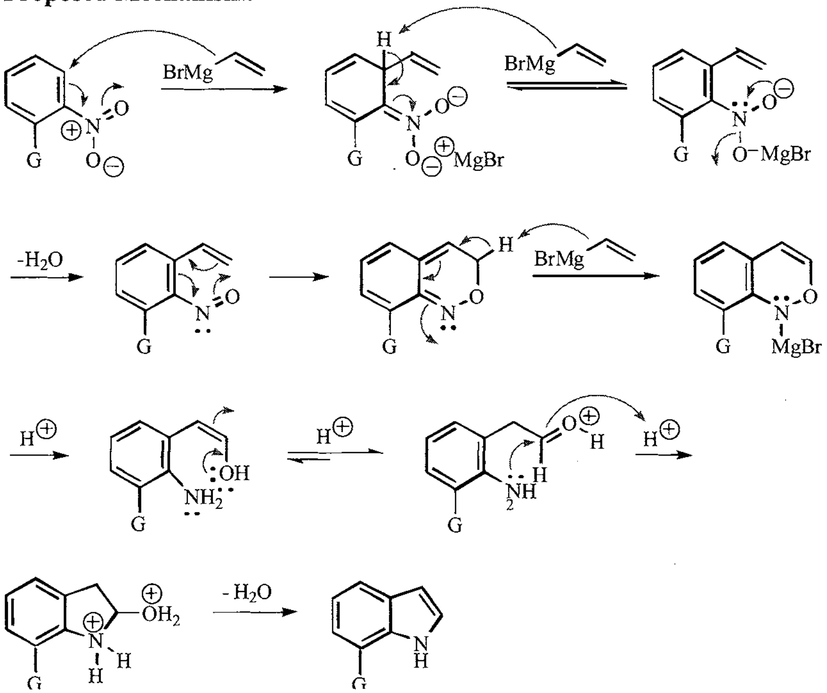


Bartoli Indole Synthesis

The Reaction:



Proposed Mechanism:

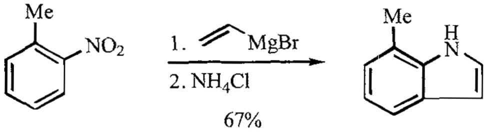


Notes:

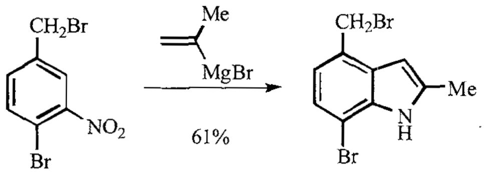
G. Bartoli, G. Palmieri, M. Bosco, R. Dalpozzo, *Tetrahedron Letters* **1989**, 30, 2129;
G. Bartoli, M. Bosco, R. Dalpozzo, *Tetrahedron Letters* **1985**, 26, 115

The reaction works only with the ortho position of the nitrobenzene occupied.

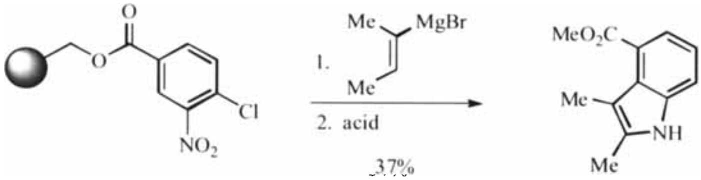
Examples:



G. Bartoli, G. Palmieri, M. Bosco, R. Dalpozzo, *Tetrahedron Letters* **1989**, 30, 2129



A. Dobbs, *Journal of Organic Chemistry* **2001**, 66, 638

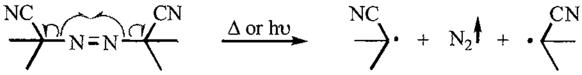


K. Knepper, S. Brase, *Organic Letters* **2003**, 5, 2829

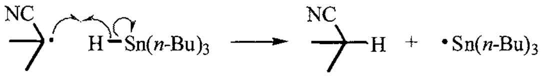
Barton Decarboxylation

The Reaction:

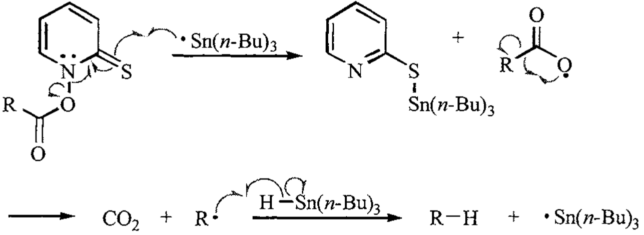
Proposed Mechanism:



AIBN = Azo-*bis*-isobutyronitrile

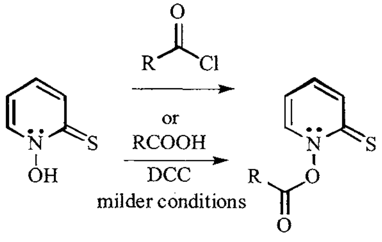


The decarboxylation step:

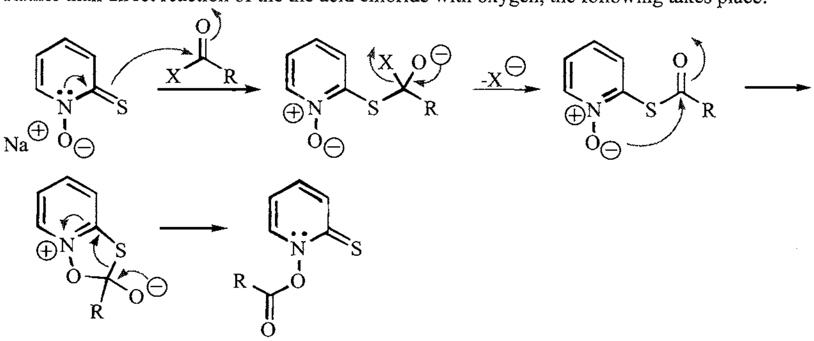


Notes:

Starting material preparation:

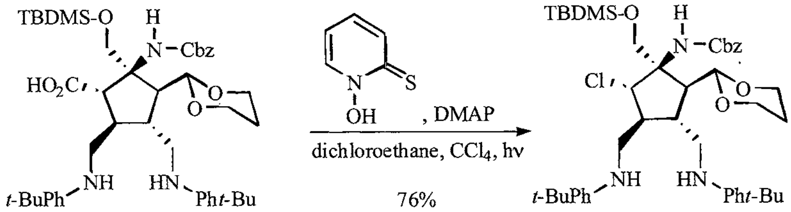


Rather than direct reaction of the the acid chloride with oxygen, the following takes place:

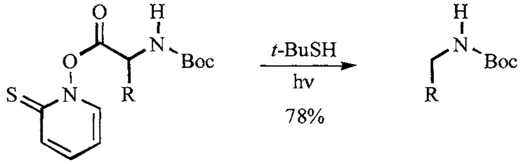


D. Crich *Aldrichimica Acta* **1987**, 20, 35

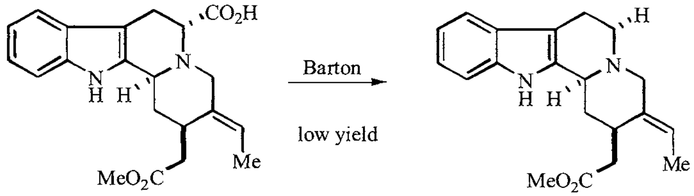
Examples:



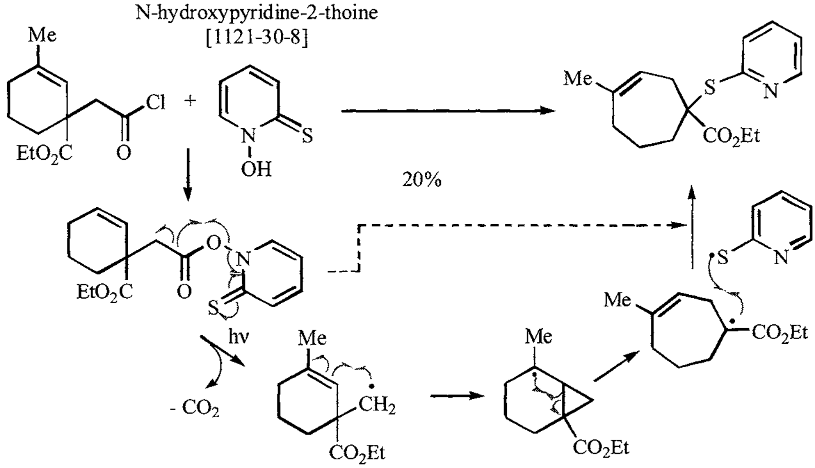
J. T. Starr, G. Koch, E. M. Carreira, *Journal of the American Chemical Society* **2000**, 122, 8793



D. H. R. Barton, Y. Herve, P. Potier, J. Thierry, *Tetrahedron*, **1988**, 44, 5479



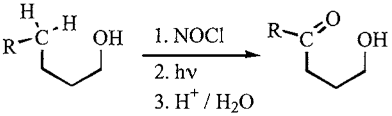
S. F. Martin, K. X. Chen, C. T. Eary, *Organic Letters* **1999**, 1, 79



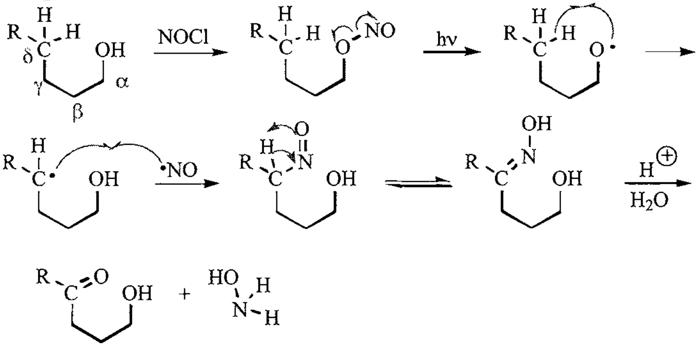
E. Bacque, F. Pautrat, S. Z. Zand, *Organic Letters* **2003**, 5, 325

Barton Reaction (Barton Nitrite Photolysis Reaction)

The Reaction:

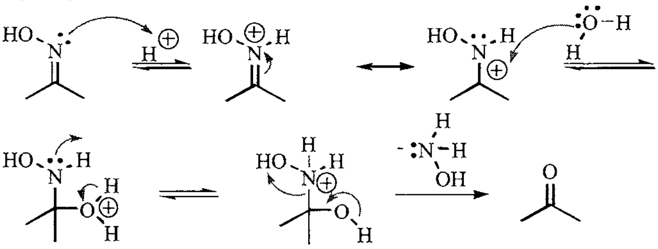


Proposed Mechanism:



Notes:

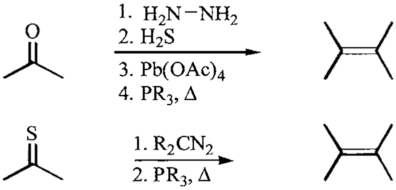
Hydrolysis mechanism



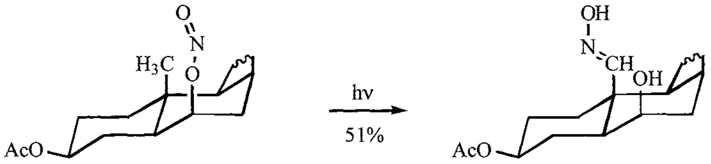
This reaction is a useful method for functionalizing a remote position (the δ–position).

Also by Barton is the

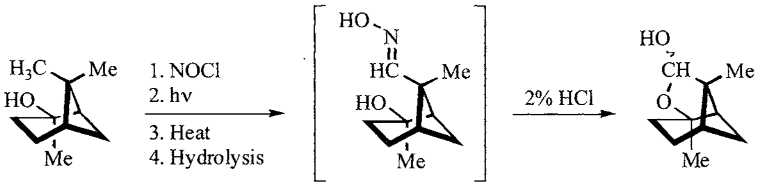
Barton-Kellogg Reaction (Barton Olefin Synthesis)



Examples:



D. H. R. Barton, I. M. Beaton, L. E. Geller, M. M. Pechet, *Journal of the American Chemical Society* **1960**, 82, 2640



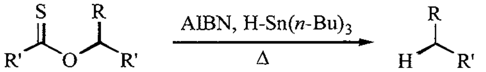
Not purified

51% yield of hemiacetal

P. D. Hobbs, P. D. Magnus *Journal of the American Chemical Society* **1976**, 98, 4594

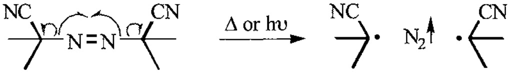
Barton-McCombie Reaction (Barton-Deoxygenation)

The Reaction:

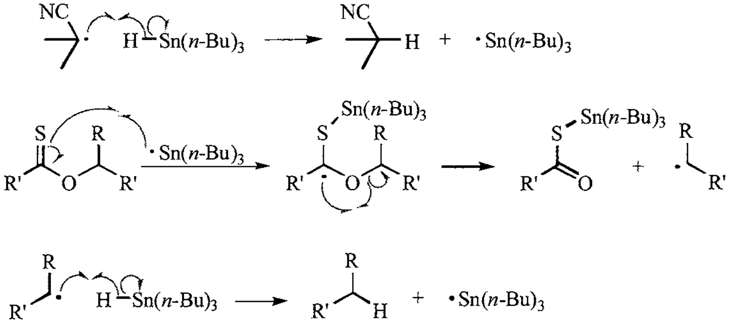


R' = H, CH_3, SCH_3 (= xanthate, see ***Chugaev Reaction***), Ph, OPh, imidazolyl

Proposed Mechanism:



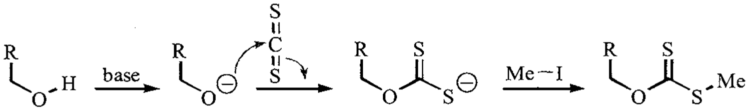
AIBN = Azo-*bis*-isobutyronitrile



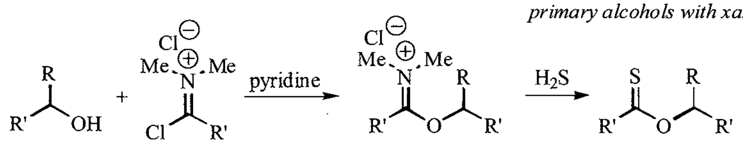
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 527.
For a discussion of mechanism: D. Crich, *Tetrahedron Letters* **1988**, 29, 5805

Depending on the substrate, different thiocarbonyl compounds have been used:

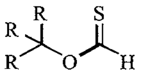


primary alcohols with xanthates



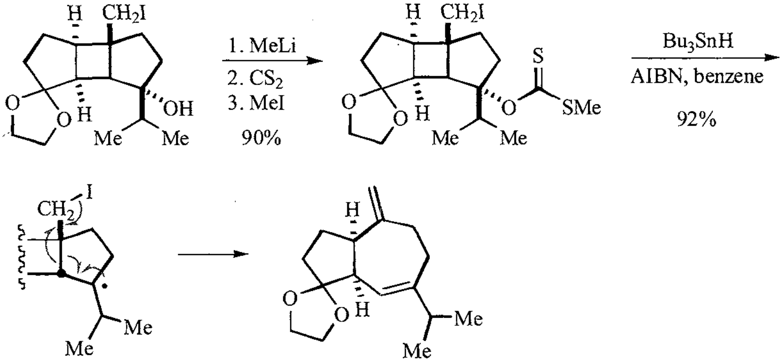
imidoyl chloride methochloride
(from phosgene and an amide)

secondary alcohols with thiocarbonyl esters

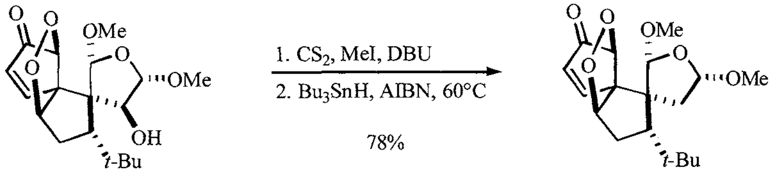


tertiary alcohols with thioformates

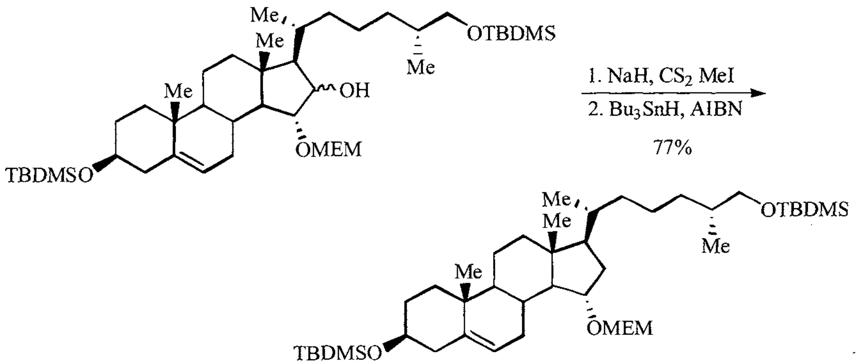
Examples:



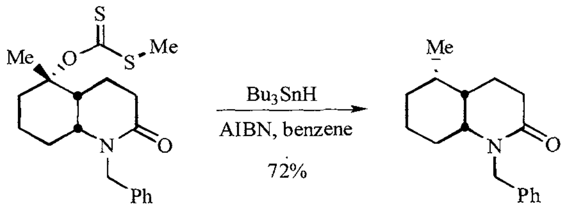
G. L. Lange, C. Gottardo, *Tetrahedron Letters* **1994**, 35, 8513



M. T. Crimmins, J. M. Pace, P. G. Nantermet, A. S. Kim-Meade, J. B. Thomas, S. H. Watterson, A. S. Wagman, *Journal of the American Chemical Society* **1999**, 121, 10249



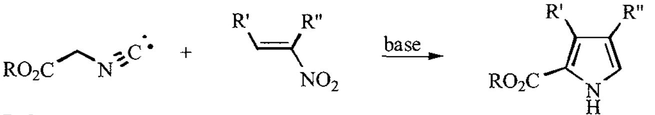
J. R. Williams, D. Chai, J. D. Bloxton, II, H. Gong, W. R. Solvibile, *Tetrahedron* **2003**, 59, 3183



K. Paulvannan, J. R. Stille, *Tetrahedron Letters* **1993**, 34, 6673

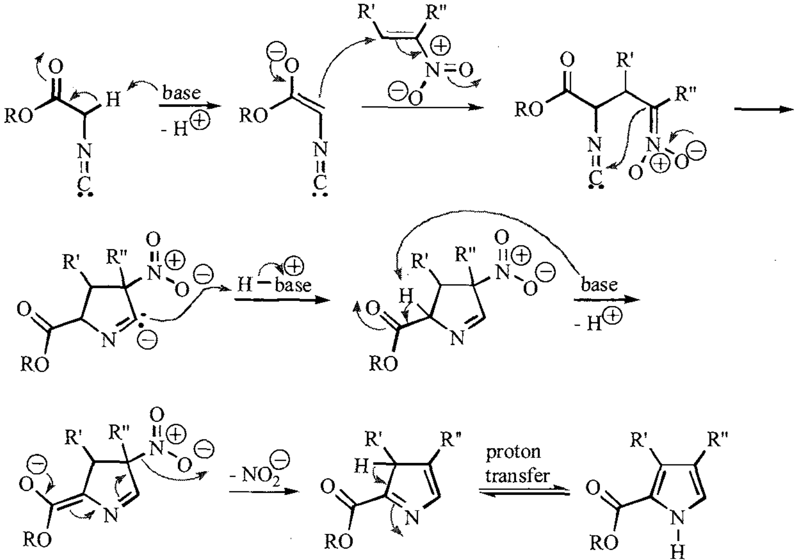
Barton-Zard Pyrrole Synthesis

The Reaction:



D. H. R. Barton, S. Z. Zard, *Journal of the Chemical Society, Chemical Communications* **1985**, 1098
D. H. R. Barton, J. Kervagoret, S. Zard, *Tetrahedron* **1990**, 46, 7587

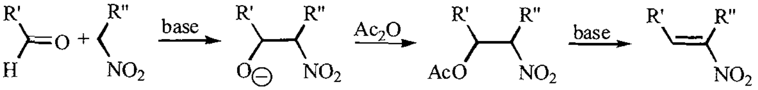
Proposed Mechanism:



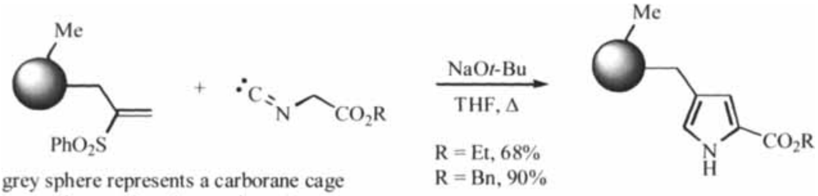
D. H. R. Barton, J. Kervagoret, S. Zard, *Tetrahedron* **1990**, 46, 7587

Notes:

One possible starting material preparation: A ***Henry Reaction*** followed by trapping with Ac_2O and elimination of the resultant acetate.

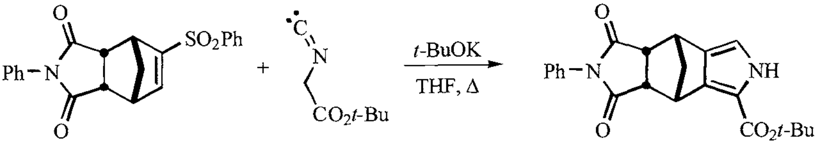


Examples:



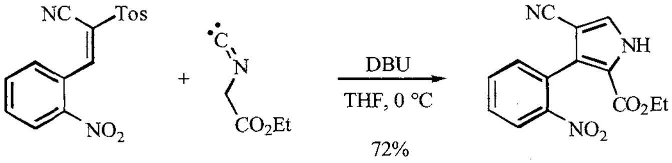
grey sphere represents a carborane cage
(see reference for a better picture)

S. Chayer, L. Jaquinod, K. M. Smith, M. G. H. Vicente *Tetrahedron Letters* **2001**, 42, 7759

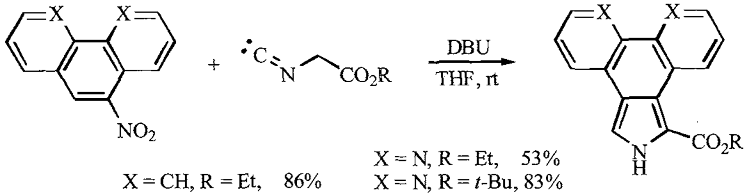


part of a 7 step procedure of overall 32% yield

D. Lee, T. M. Swager *Journal of the American Chemical Society* **2003**, 125, 6870



J. Bergman, S. Rehn *Tetrahedron* **2002**, 58, 9179

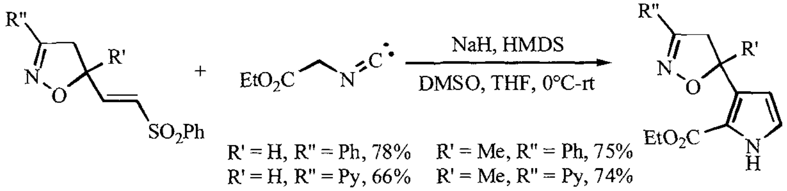


X = N, R = Et, 53%

X = CH, R = Et, 86% X = N, R = *t*-Bu, 83%

X = CH, R = *t*-Bu, 65% X = N, R = Bz, 73% (refluxing THF / *i*-PrOH)

T. D. Lash, B. H. Novak, Y. Lin *Tetrahedron Letters* **1994**, 35, 2493

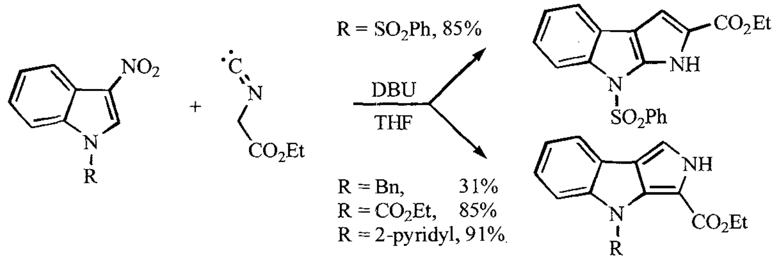


R' = H, R'' = Ph, 78% R' = Me, R'' = Ph, 75%

R' = H, R'' = Py, 66% R' = Me, R'' = Py, 74%

S. H. Hwang, M. J. Kurth *Tetrahedron Letters* **2002**, 43, 53

A rearranged / abnormal ***Barton-Zard Pyrrole*** product is observed when the protecting group on nitrogen is phenyl sulfonyl. However, when R = Bn, CO_2Et or 2-pyridyl, the expected pyrrolo[3,4,*b*]indole is obtained.



R = SO_2Ph, 85%

R = Bn, 31%

R = CO_2Et, 85%

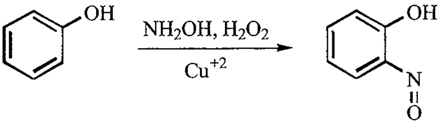
R = 2-pyridyl, 91%

E. T. Pelkey, L. Chang, G. W. Gribble *Chemical Communications* **1996**, 1909

E. T. Pelkey, G. W. Gribble *Chemical Communications* **1997**, 1873

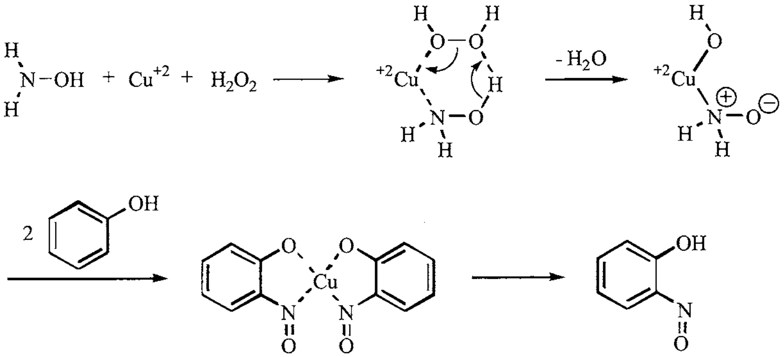
Baudisch Reaction

The Reaction:



Proposed Mechanism:

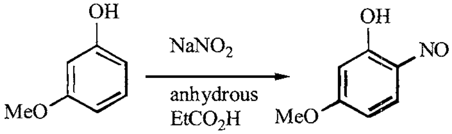
There is much not known about the details of this reaction.



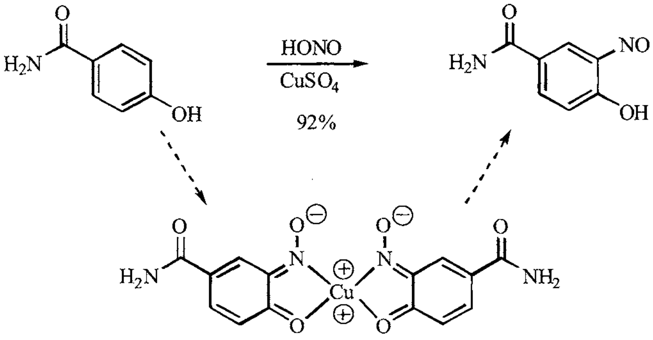
Notes:

For studies on the mechanism: See K. Maruyama, I. Tanimoto, R. Goto, *Tetrahedron Letters* **1966,** 47, 5889

Examples:



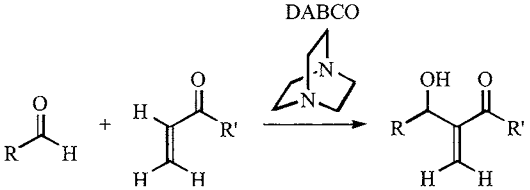
R. J. Maleski, M. Kluge, D. Sicker, *Synthetic Communications* **1995**, 25, 2327 (AN 1995-63432)



M. C. Cone, C. R. Melville, J. R. Carney, M. P. Gore, S. J. Gould, *Tetrahedron* **1995**, 51, 3095

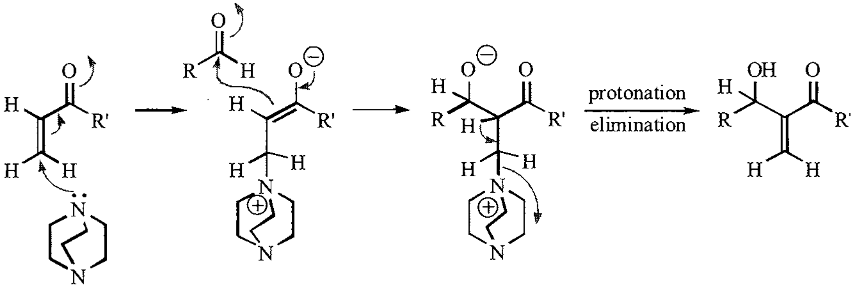
Baylis-Hillman Reaction (Morita-Baylis-Hillman)

The Reaction:



DABCO = 1,4-Diazabicyclo[2.2.2]octane

Proposed Mechanism:



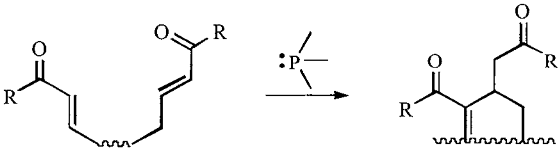
Attack of the tertiary amine generates the enolate which will attack the aldehyde.

Protonation of the alkoxide and elimination of the amine gives the final product.

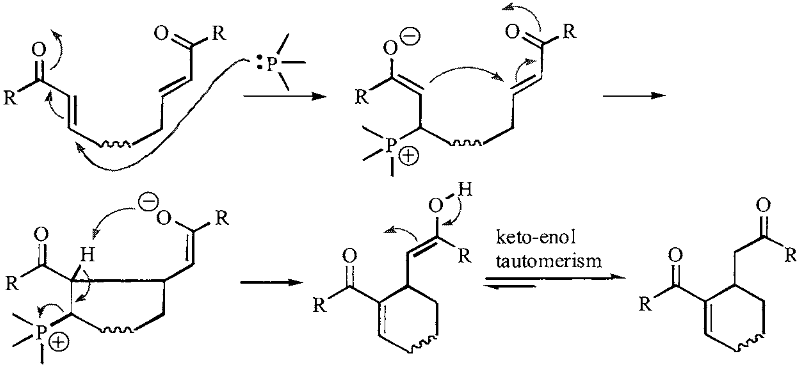
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5^{th} ed., John Wiley and Sons, Inc., New York, 2001, p. 1212; E. Ciganek, *Organic Reactions* **51**, 2; D. Basavaiah, A. J. Rao, T. Satyanarayana, *Chemical Reviews* **2003**, 103, 811

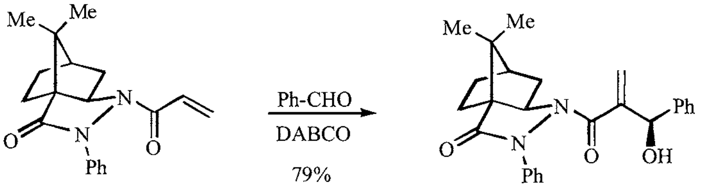
The ***Rauhut-Currier Reaction*** is a similar reaction involving two enone coupling partners:



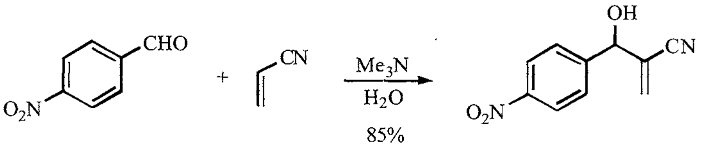
Proposed Mechanism:



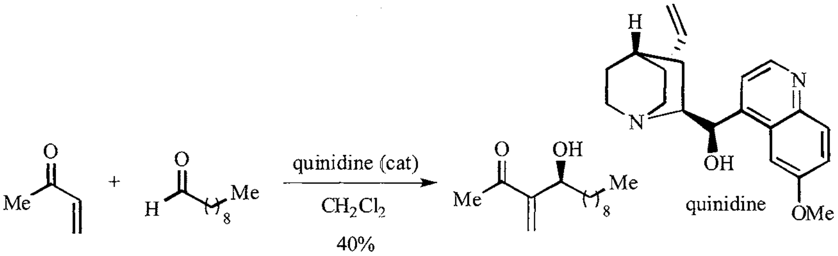
Examples:



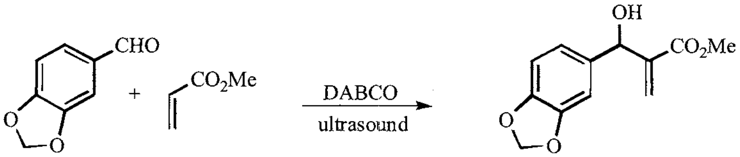
K.-S. Yang, K. Chen, *Organic Letters* **2000**, 2, 729



K,-S. Yang, K. Chen, *Organic Letters* **2000**, 2, 729

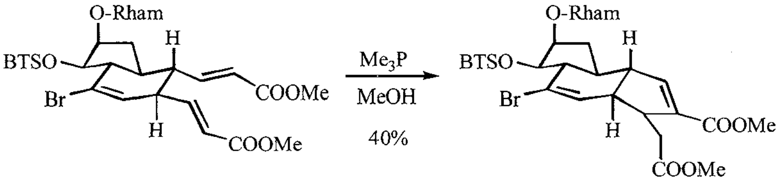


I. E. Mariko, P. R. Giles, N. J. Hindley, *Tetrahedron* **1997**, 53, 1015

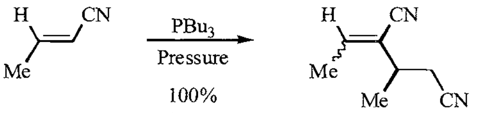


F. Coelho, W. P. Almeida, D. Veronese, C. R. Mateus, E. C. S. Lopes, R. C. Rossi, G. P. C. Silveira, C. H. Pavam, *Tetrahedron* **2002**, 58, 7437

Examples for the *Rauhut-Currier Reaction*:



D. J. Mergott, S. A. Frank, W. R. Roush, *Organic Letters* **2002**, 4, 3157

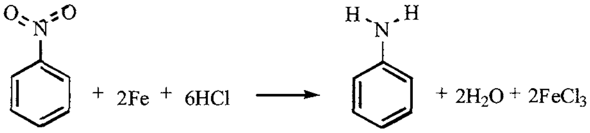


(77:23 *cis:trans*)

G. Jenner, *Tetrahedron Letters* **2000**, 41, 3091

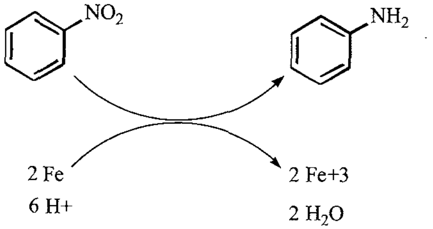
Béchamp Reduction

The Reaction:



Proposed Mechanism:

$\text{Ar-NO}_2 + 6e^{\ominus} + 6\,H^{\oplus} \longrightarrow \text{Ar-NH}_2 + 2\,H_2O$



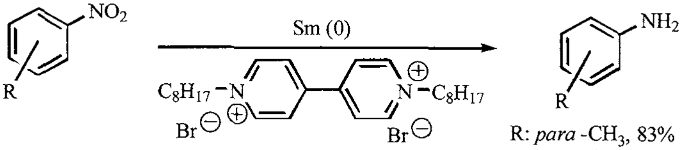
The reaction is a metal-catalyzed oxidation-reduction process.

Notes:

C. S. Hamilton, J. F. Morgan, *Organic Reactions* **2**, 10

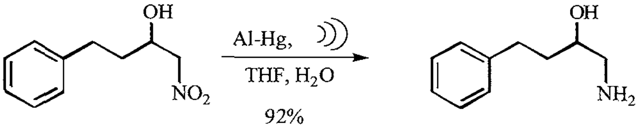
Other new approaches to the reduction:

1,1'-Dialkyl-4,4-bipyridinium halides (viologens) are useful electron-transfer catalysts.

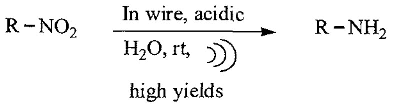


R: *para* -CH_3, 83%
R: *para* -$CH_2CH_2N_3$, 92%

C. Yu, B. Liu, L. Hu, *Journal of Organic Chemistry* **2001**, 66, 919

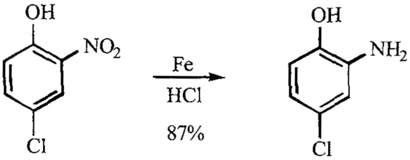


R. W. Fitch, F. A. Luzzio, *Tetrahedron Letters* **1994**, 35, 6013

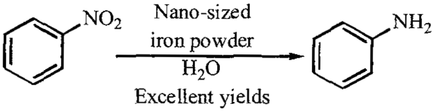


Y. Se.Cho, B. K. Jun, S. Kim, J. H. Cha, A. N. Pae, H. Y. K., M. C. Ho, S.-Y. Han *Bulletin of the Korean Chemical Society* **2003**, 24, 653 (AN 2003:513428)

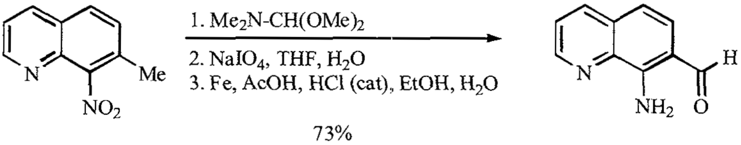
Examples:



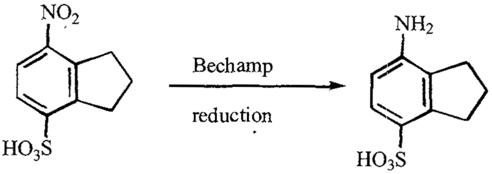
S. Mukhopadhyay, G. K. Gandi, S. B. Chandalia, *Organic Process Research & Development* **1999**, 3, 201



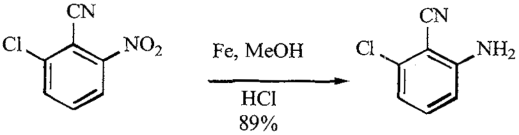
L. Wang, P. Li, Z. Wu, J. Yan, M. Wang, Y. Ding, *Synthesis* **2003**, 2001



E. C Riesgo, X. Jin, R. P. Thummel, *Journal of Organic Chemistry* **1996**, 61, 3017



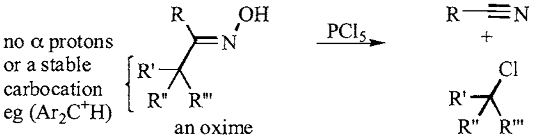
A. Courtin, *Helvetica Chemica Acta* **1980**, 63, 2280 (AN 1981: 406876)



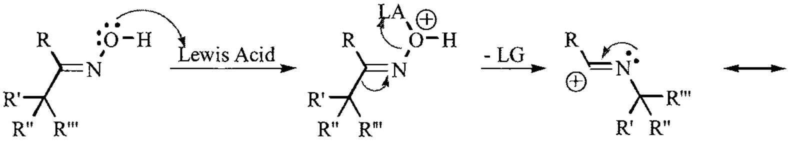
M. W. Zettler, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **4**, 2871

Beckmann Fragmentation

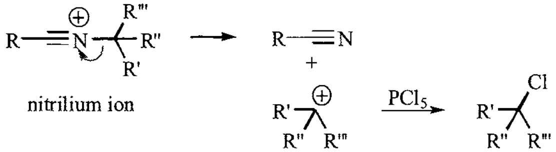
The Reaction:



Proposed Mechanism:



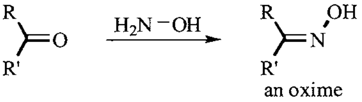
A better leaving group is made when oxygen bonds to the Lewis Acid



Because a stable carbocation can be formed, the nitrile is liberated before it can be trapped by water as in the usual ***Beckmann Rearrangement***.

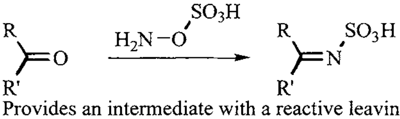
Notes:

Starting material preparation:



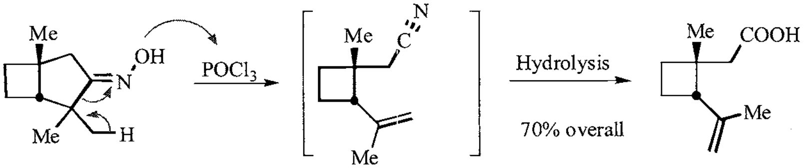
The -OH group is generally anti to the larger R

Hydroxylamine-O-sulfonic acid
(HOSA)

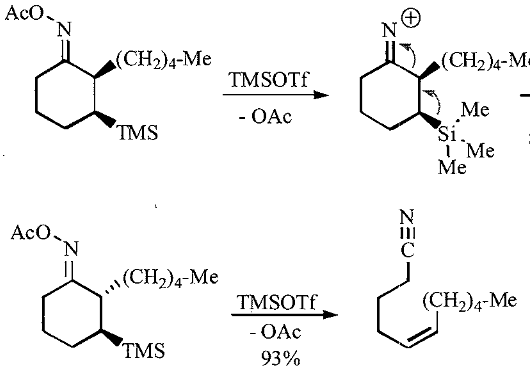


Provides an intermediate with a reactive leaving group already incorporated.

Examples:

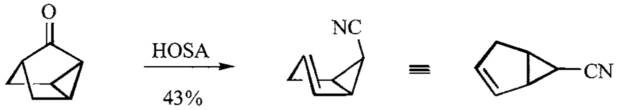


G. Rosini, M. Greir, E. Marcotta, M. Petrini, R. Ballini, *Tetrahedron* **1986**, 42, 6027

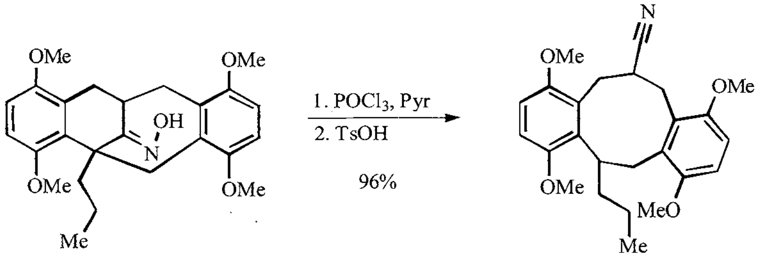


TMSOTf = TMS-O-SO$_2$-CF$_3$

H. Nishiyama, K. Sakuta, N. Osaka, H. Arai, M. Matsumoto, K. Itoh, *Tetrahedron* **1988**, 44, 2413



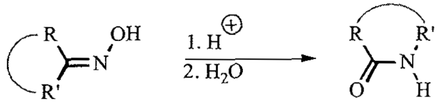
M. G. Rosenberg, U. Haslinger, U. H. Brinker, *Journal of Organic Chemistry* **2002**, 67, 450



J. D. White, J. Kim, N. E. Drapela, *Journal of the American Chemical Society* **2000**, 122, 8665

Beckmann Rearrangement

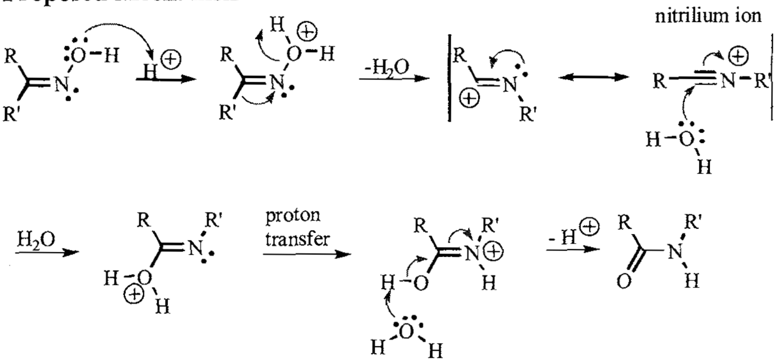
The Reaction:



Can be a ring enlargement.

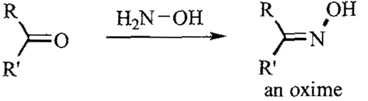
The reaction can also be carried out with PCl_5, PPA, P_2O_5 or TsCl.

Proposed Mechanism:



Notes:

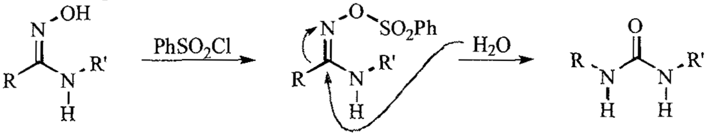
Starting Material Preparation:



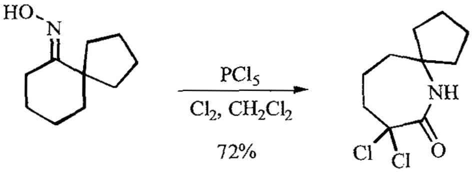
The -OH group is generally anti to the larger R.

T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 22-24; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1349, 1381, 1384, 1415-1416; L. G. Donaruma, W. Z. Heldt, *Organic Reactions* **11**, 1; R. E. Gawley, *Organic Reactions* **35**, 1

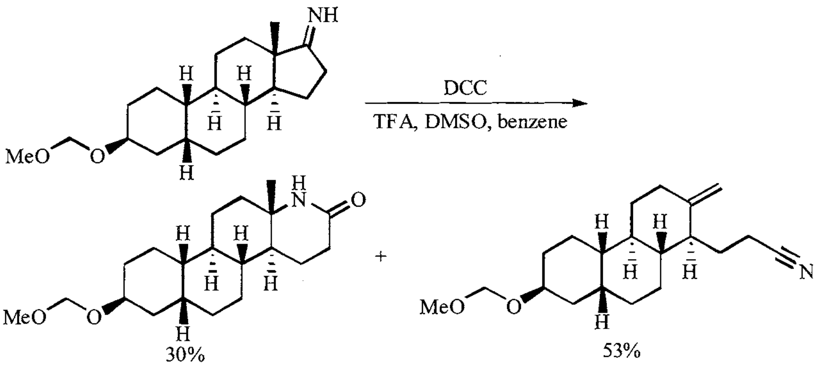
The rearrangement of amidoximes to derivatives of urea is called the ***Tiemann Rearrangement***.



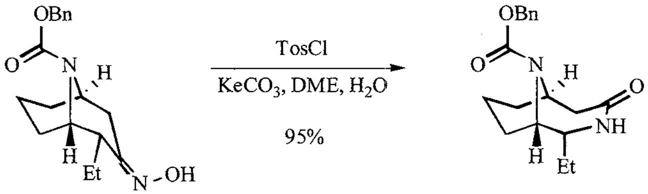
Examples:



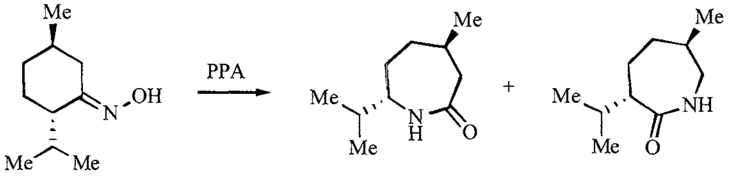
J. A. Robl, E. Dieber-McMaster, R. Sulsky, *Tetrahedron Letters* **1996**, 37, 8985



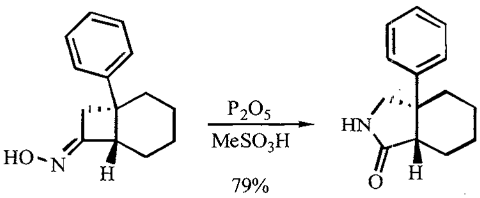
M. Han, D. F. Covey, *Journal of Organic Chemistry* **1996**, 61, 7614



O. Muraoka, B.-Z. Zheng, K. Okumura, G. Tanabe, T. Momose, C. H. Eugster, *Journal of the Chemical Society, Perkin Transactions 1* **1996**, 13, 1567

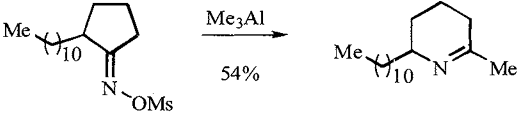


N. Komatsu, S. Simizu, T. Sugita, *Synthetic Communications* **1992**, 22, 277 (AN 1992:151543)



P. W. Jeffs, G. Molina, N. A. Cortese, P. R. Hauck, J. Wolfram, *Journal of Organic Chemistry* **1982**, 47, 3876

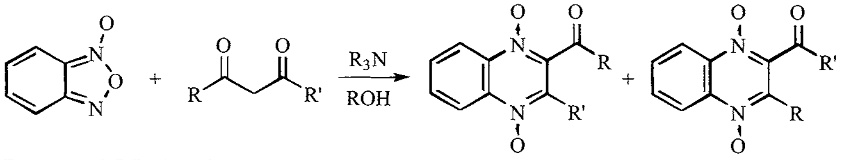
In this example, the intermediate carbocation is trapped by Me$_3$Al rather than water:



Y. Matsmura, K. Maruoka, H. Yamamoto, *Tetrahedron Letters* **1982**, 23, 1929

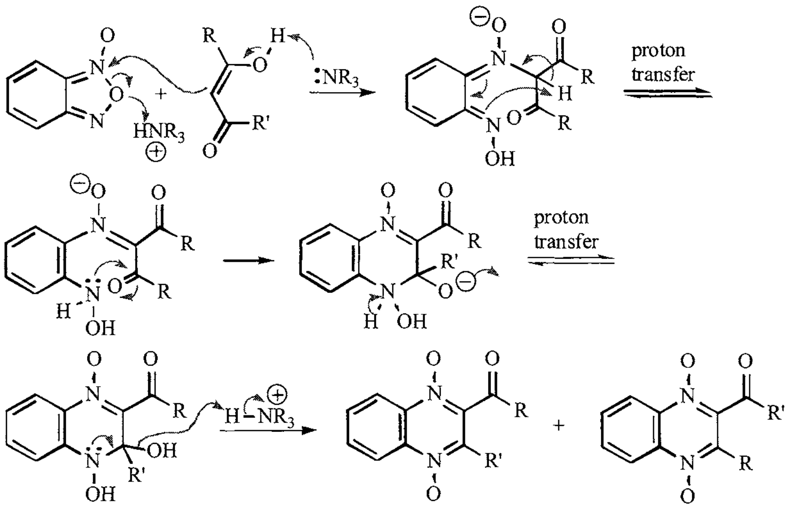
Beirut Reaction

The Reaction:



Proposed Mechanism:

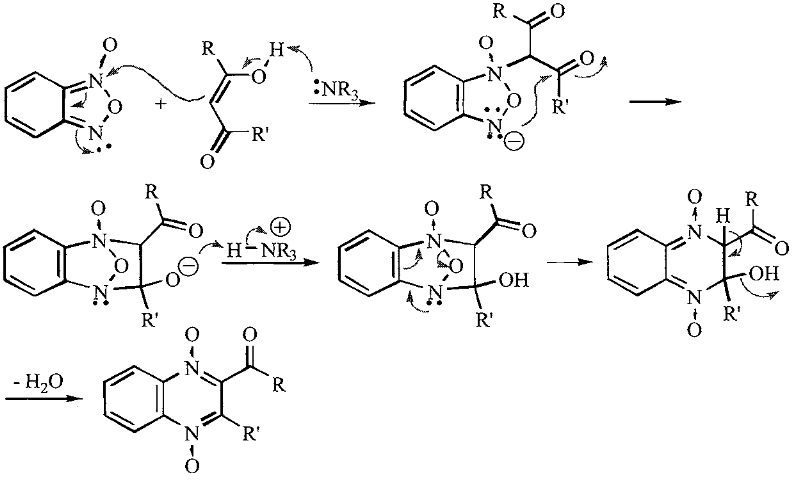
L. Turker, E. Dura, *Journal of Molecular Structure (Theochem)* **2002**, 593, 143



For 1,3-diketones both isomers can be observed.

A second mechanistic interpretation:

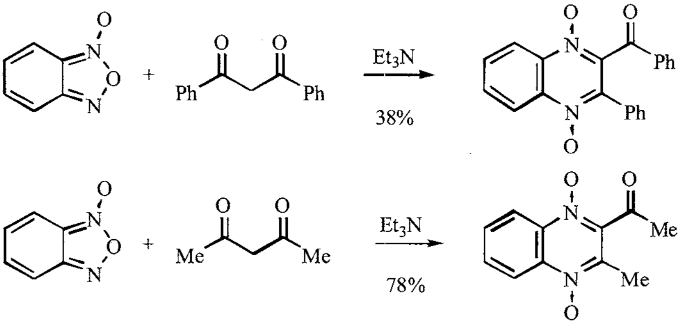
C. H. Issidorides, M. J. Haddadin, *Journal of Organic Chemistry* **1996**, 31, 4067



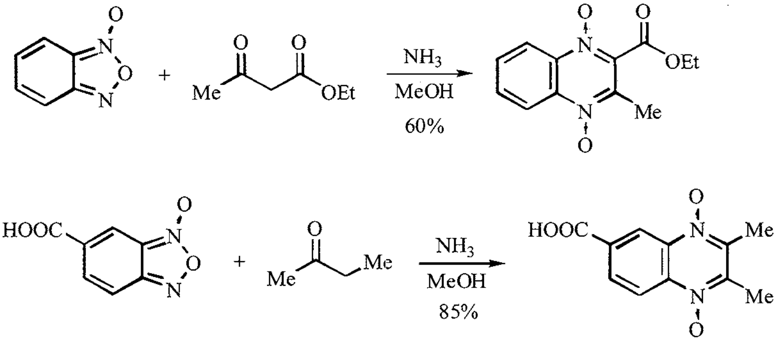
Notes:

The reaction provides access to a number of quinoxaline-1,4-dioxide derivatives, by reaction of the benzofurazan oxide with 1,3-diketones, β-ketoesters, enals, enamines, phenols and α,β-unsaturated ketones.

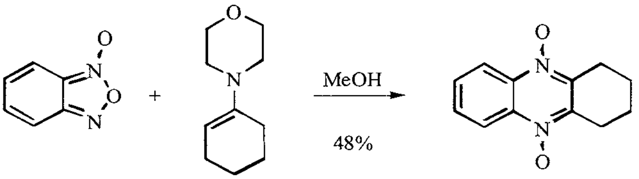
Examples:



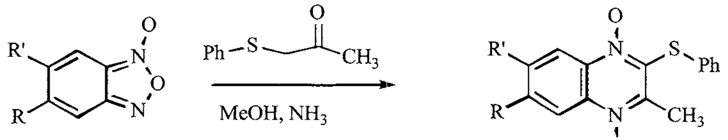
C. H. Issidorides, M. J. Haddadin, *Journal of Organic Chemistry* **1966**, 31, 4067



M. L. Edwards, R. E. Bambury, H. W. Ritter, *Journal of Medicinal Chemistry* **1976**, 19, 330



M. J. Haddadin, C. H. Issidorides, *Tetrahedron Letters* **1965**, 6, 3253

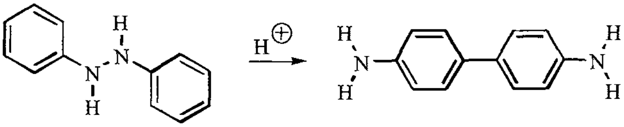


A large series prepared for screening

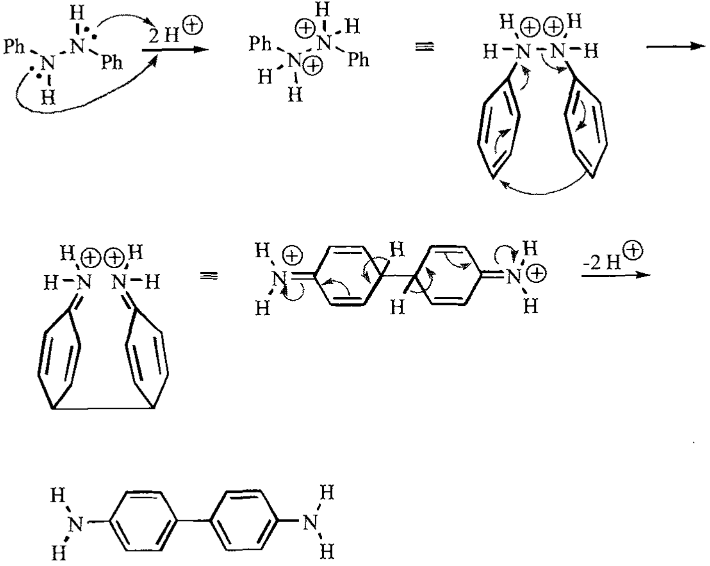
A. Carta, G. Paglietti, M. E. R. Nikookar,P. Sanna, L. Sechi, S. Zanetti, *European Journal of Medicinal Chemistry* **2002**, 37. 355

Benzidine Rearrangement (Zinin Benzidine Rearrangement)

The Reaction:



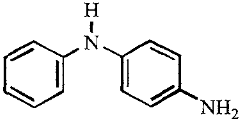
Proposed Mechanism:



Notes:

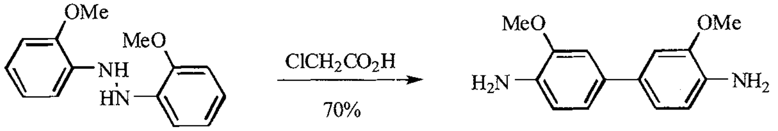
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp. 1455-1456; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 24-26.

Byproducts sometimes include *semidines*:

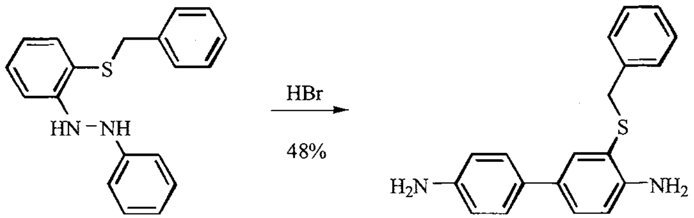


Examples:

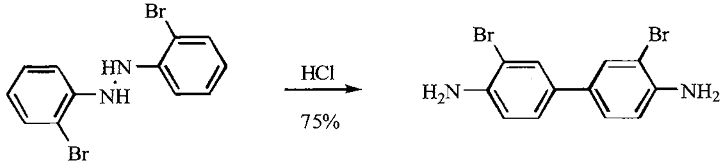
This work included kinetic details.



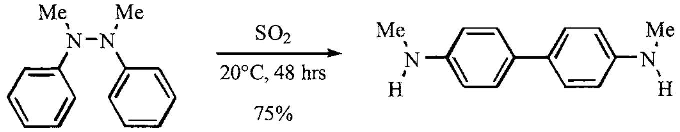
H. J. Shine, K. H. Park, M. L. Brownawell, J. S. Filippo, Jr., *Journal of the American Chemical Society* **1984**, 106, 7077



A. Burawoy, C. E. Vellins *Journal of the Chemical Society* **1954**, 90

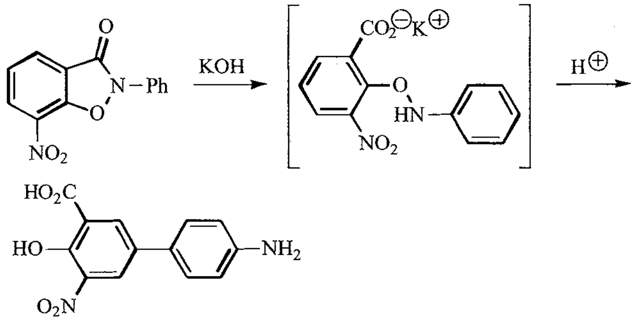


H. R. Snyder, C. Weaver, C. D. Marshall, *Journal of the American Chemical Society* **1949**, 71, 289



M. Nojima, T. Ando, N. Tokura, *Journal of the Chemical Society, Perkin Transaction 1* **1976**, 14, 1504

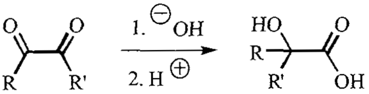
The following is an example of the ***Sheradsky Rearrangement***. It is an oxygenated analog of the ***Benzidine Rearrangement***.



T. Sheradsky, S. Auramovki-Grisaru, *Journal of Heterocyclic Chemistry* **1980**, 17, 189 (AN 1980:407167)

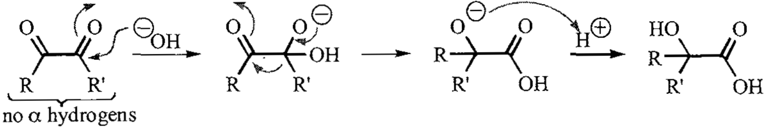
Benzilic Acid Rearrangement

The Reaction:



Typically the R groups are aromatic, but if not, must be devoid of α-hydrogens.

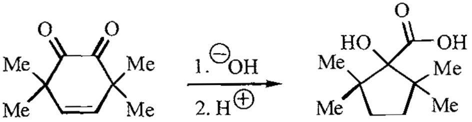
Proposed Mechanism:



Notes:

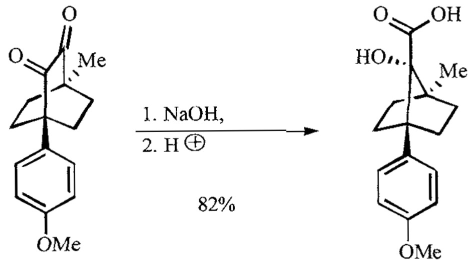
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1403; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 26-27.

This reaction can be a ring contraction:

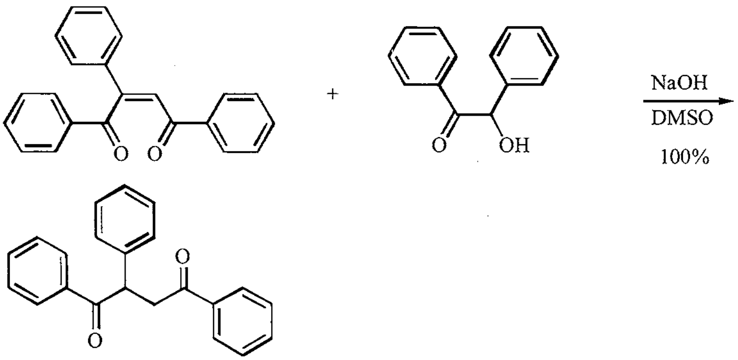


Reported in: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, p 27 (A. Schaltegger, P. Bigler, *Helvetica Chemica Acta*, **1986**, 69, 1666)

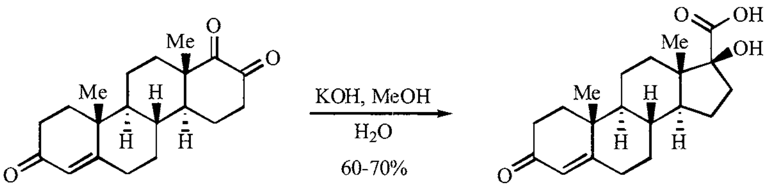
Examples:



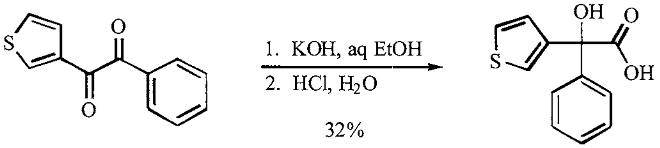
S. Deb, R. Chakraborti, U. R. Ghatak, *Synthetic Communications* **1993**, 23, 913 (AN 1993:494997)



J. M. Robinson, E. T. Flynn, T. L. McMahan, S. L. Simpson, J. C. Trisler, K. B. Conn, *Journal of Organic Chemistry* **1991**, 56, 6709



V. Georgian, N. Kundu, *Tetrahedron* **1963**, 19, 1037



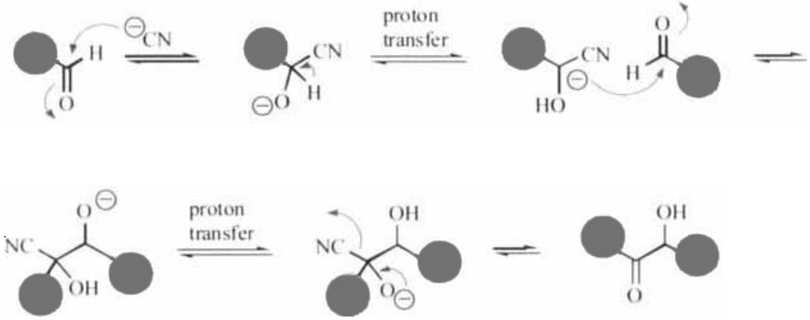
E. Campaigne, R. C. Bourgeois, *Journal of the American Chemical Society* **1953**, 75, 2702

Benzoin Condensation

The Reaction:

No protons on the α carbon. The group is typically aromatic.

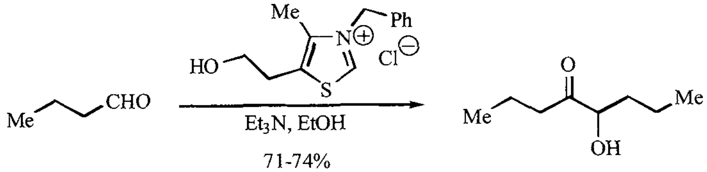
Proposed Mechanism:



Notes:

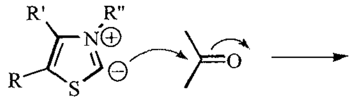
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p 1240, 1243; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 27-29; W. S. Ide, J. S. Buck, *Organic Reactions* **4**, 5.

Use of thiazolium ion catalysis allows the ***benzoin condensation*** of aldehydes with α-protons.

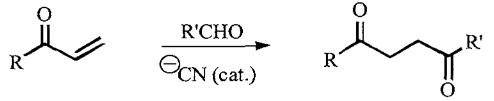


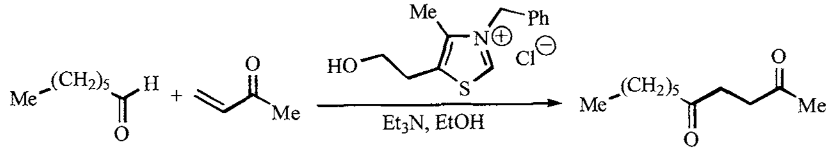
H. Stetter, H. Kuhlmann, *Organic Syntheses*, CV 7, 95

In these reactions a thiazolium salt forms an ion that participates much like cyanide:



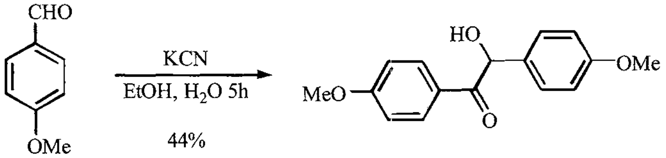
Stetter Reaction (Stetter 1,4-Dicarbonyl Synthesis)



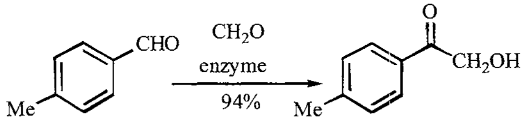


H. Stetter, H. Kuhlmann, W. Haese, *Organic Syntheses*, CV 8, 620

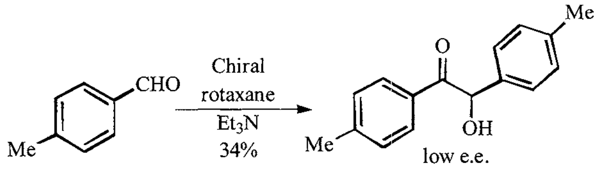
Examples:



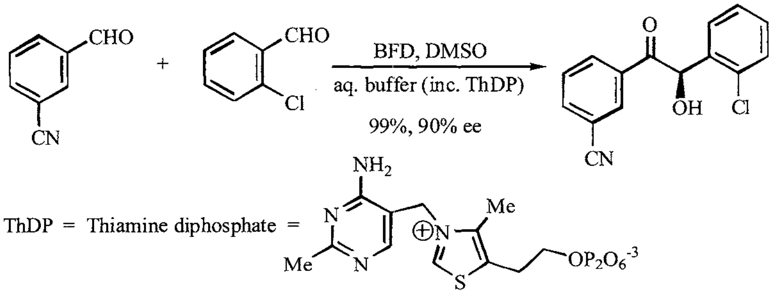
G. Sumrell, J. I. Stevens, G. Goheen, *Journal of Organic Chemistry* **1957**, 22, 39



A. S. Demir, P. Ayhan, A. C. Igdir, A. N. Duygu, *Tetrahedron* **2004** 60 6509



Y. Tachibana, N. Kihara, T. Takata, *Journal of the American Chemical Society* **2004**, 126, 3438

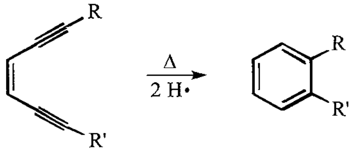


BFD = Benzoylformate decarboxylase

P. Dünkelmann, D. Kolter-Jung, A. Nitsche, A. S. Demir, P. Siegert, B. Lingen, M. Baumann, M. Pohl, M. Müller, *Journal of the American Chemical Society* **2002**, 124, 12084

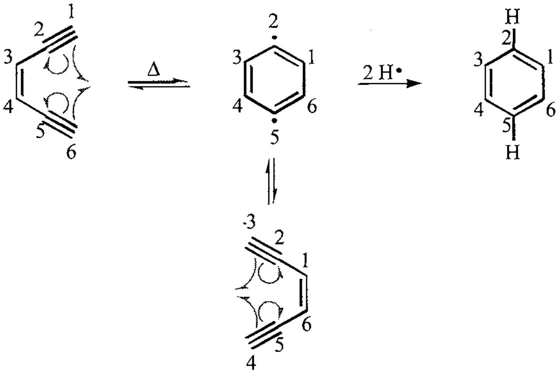
Bergman Cyclization

The Reaction:



The source is frequently 1,4-dihydrobenzene

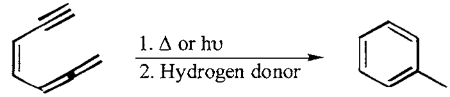
Proposed Mechanism:



Notes:

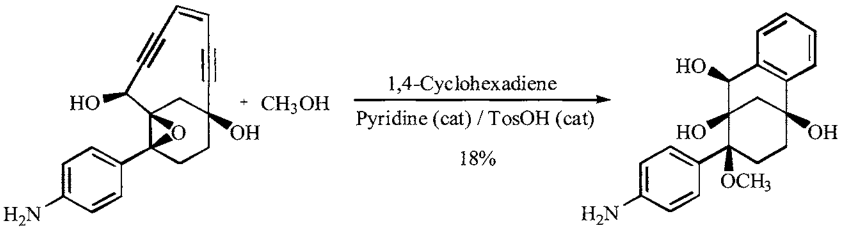
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1432; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 29-33.

The ***Myers-Saito Cyclization*** is a similar reaction with a different substrate:

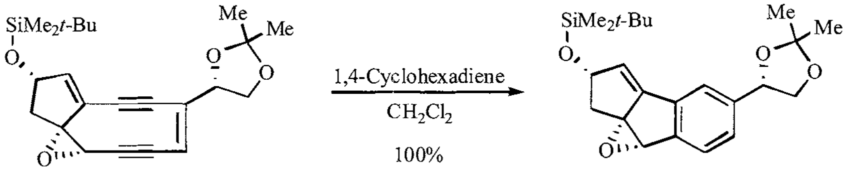


allenyl enyne

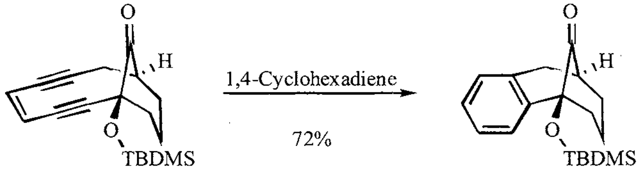
Examples:



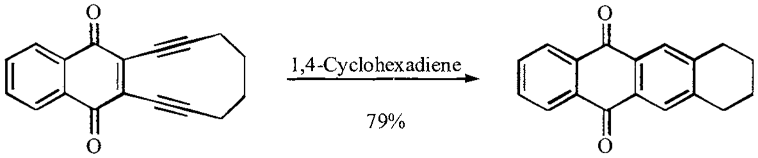
H. Mastalerz, T. W. Doyle, J. F. Kadow, D. M. Vyas, *Tetrahedron Letters* **1996**, 37, 8683



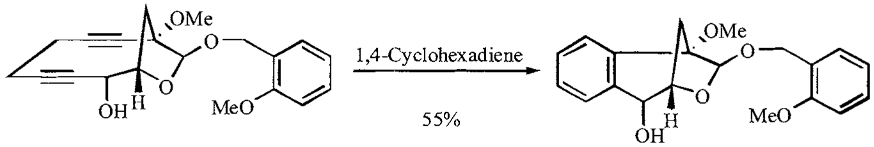
K. Iida, M. Kirama, *Journal of the American Chemical Society* **1995**, 117, 8875



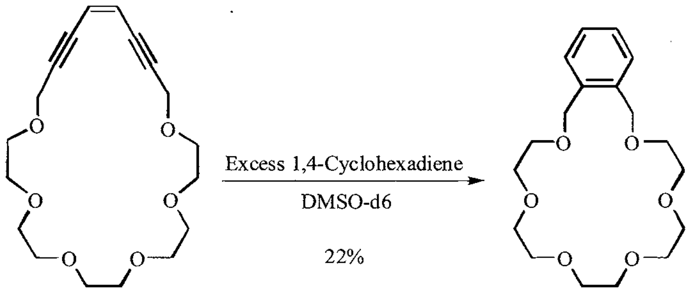
D. P. Magnus, R. T. Lewis, J. C. Huffman, *Journal of the American Chemical Society* **1988**, 110, 6921



M. F. Semmelhack, T. Neu, F. Foubelo, *Tetrahedron Letters* **1992**, 33, 3277



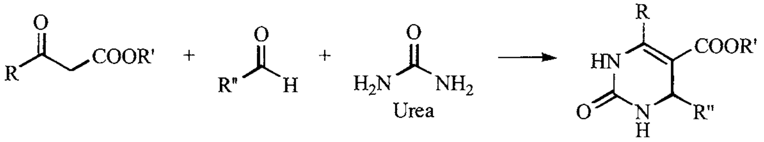
T. Brandstetter, M. E. Maier, *Tetrahedron* **1994**, 50, 1435



M. M. McPhee, S. M. Kerwin, *Journal of Organic Chemistry* **1996**, 61, 9385

Biginelli Reaction (Biginelli Pyrimidone Synthesis)

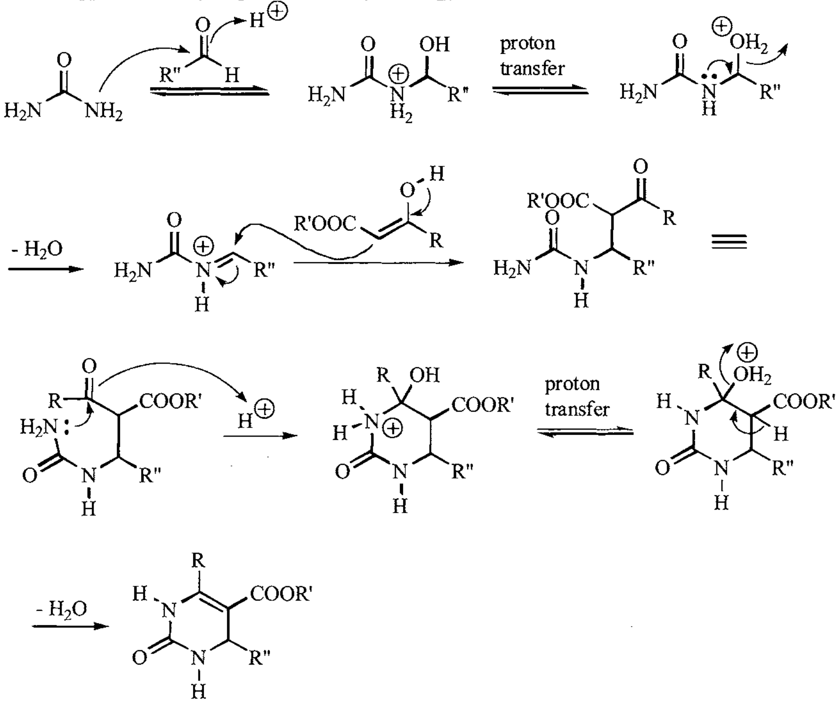
The Reaction:



Proposed Mechanism:

G. Jenner, *Tetrahedron Letters* **2004**, 45, 6195

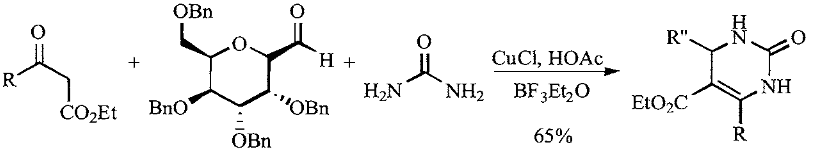
C. O. Kappe, *Journal of Organic Chemistry* **1997**, 62, 7201



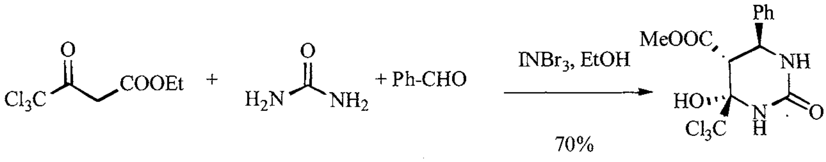
Notes:

C. O. Kappe, A. Stadler, *Organic Reactions* **63**, 1

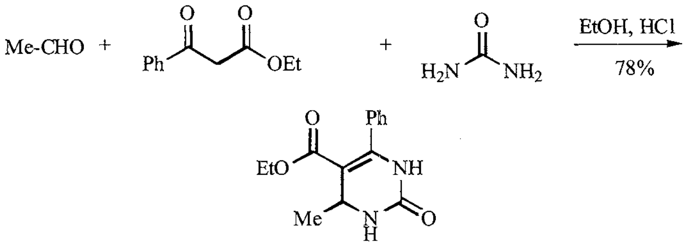
Examples:



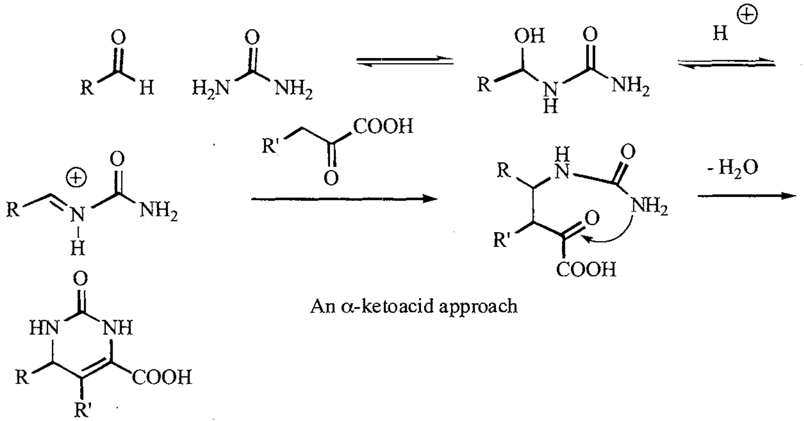
A. Dondoni, A. Mass, S. Sabbatini, V. Bertolasi, *Journal of Organic Chemistry* **2002**, 67, 6979



M. A. P. Martins, M. V. M. Teixeira, W. Cunico, E. Scapin,a, R. Mayer, C. M. P. Pereira, N. Zanatta, H.G. Bonacorso, C.Peppeb Y.-F. Yuan, *Tetrahedron Letters* **2004** , 45, 8991

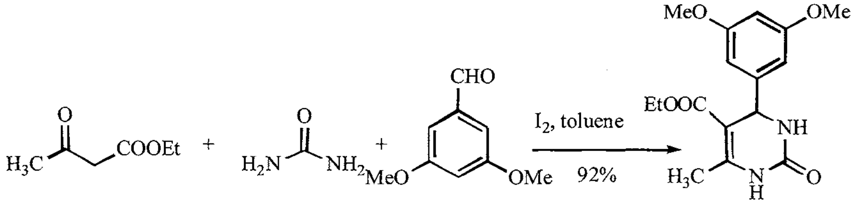


H. E. Zaugg, W. B. Martin, *Organic Reactions* **1965**, 14, 130

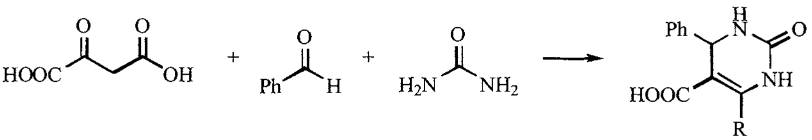


An α-ketoacid approach

M. M. Abelman, S. C. Smith, D. R. James, *Tetrahedron Letters* **2003**, 44, 4559



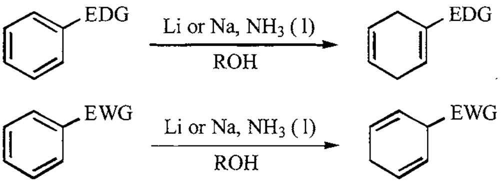
R. S. Bhosale, S. V. Bhosale, S. V. Bhosale, T. Wang, P. K. Zubaidha, *Tetrahedron Letters* **2004**, 45, 9111



J. C. Bussolari, P. A. McDonnel *Journal of Organic Chemistry* **2000**, 65, 6777

Birch Reduction

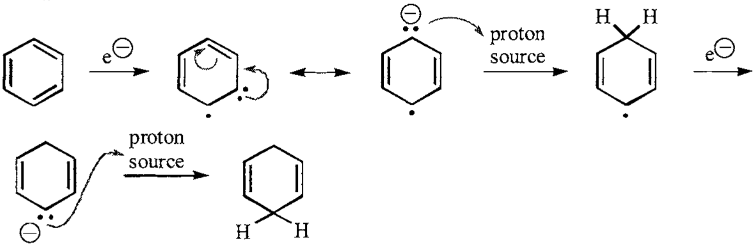
The Reaction:



EDG can be
-R, -OR

EWG can be
-COOH

Proposed Mechanism:

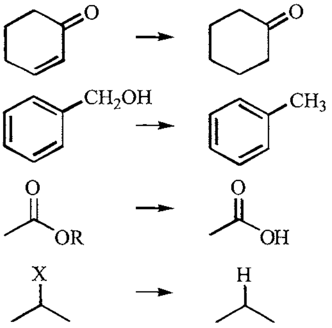


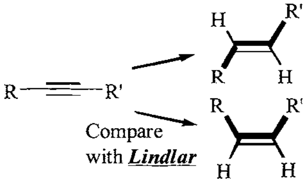
Notes:

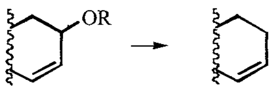
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1010; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 33-35; D. Caine, *Organic Reactions* **23**,1; P. W. Rabideau, Z. Marcinow, *Organic Reactions* **42**,1.

Na / NH_3 is more prone to Fe-catalyzed conversion to $NaNH_2$. The ***Wilds Modification*** (A. L. Wilds, N. A. Nelson, *Journal of the American Chemical Society* **1953**, 75, 5360) uses Li, and is less likely to be converted to amide ion. It is often helpful to distill the liquid ammonia before use.

Other susceptible functional groups:

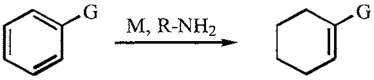






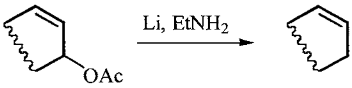
R = OAc, H, $POCl_2$

Benkeser Reduction

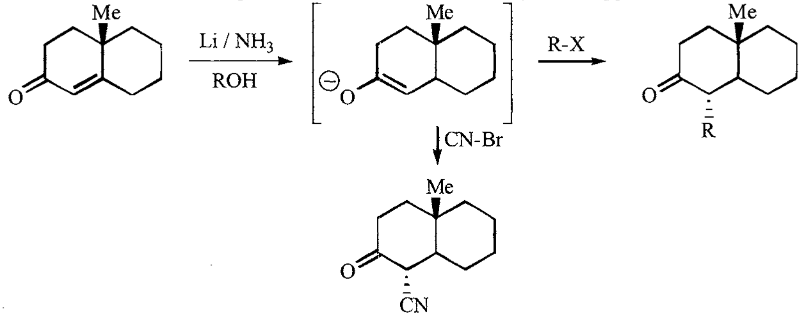


$R\text{-}NH_2$ = various amines eg. Et_2NH and Me_2NH
M = Na. Li, Ca

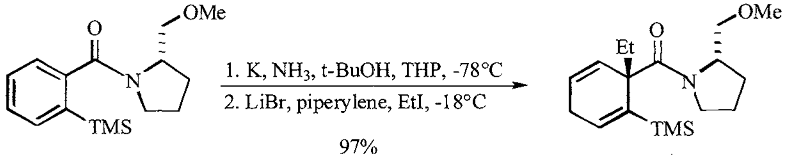
Henbest Reductino



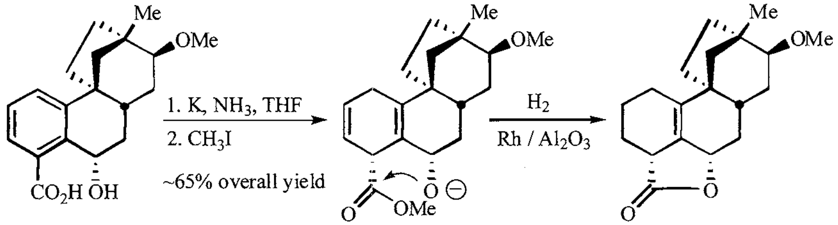
Birch reduction of enones provides for a number of useful synthetic applications:



Examples:

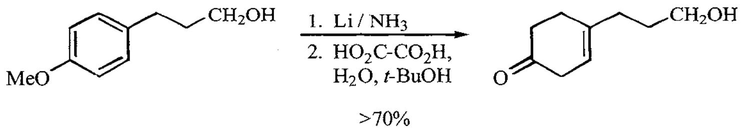


A. G. Schultz, L. Pettus, *Journal of Organic Chemistry* **1997**, 62, 6855



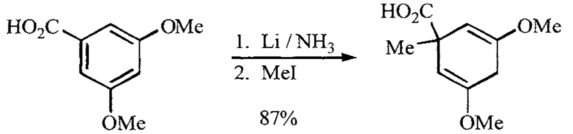
L. E. Overman, D. J. Riccan, V. D. Tran, *Journal of the American Chemical Society* **1997**, 119, 12031

With a weaker organic acid used in workup, the enol ether can be selectively converted to the ketone without conjugation of the resulting enone.



E. J. Corey, N. W. Boaz, *Tetrahedron Letters* **1985**, 26, 6015

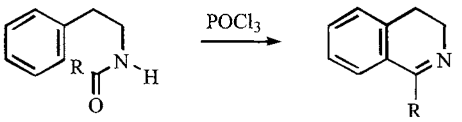
The intermediate anion can be captured by electrophiles other than protons.



A. Gopalan, P. Mangus, *Journal of the American Chemical Society* **1980**, 102, 1756

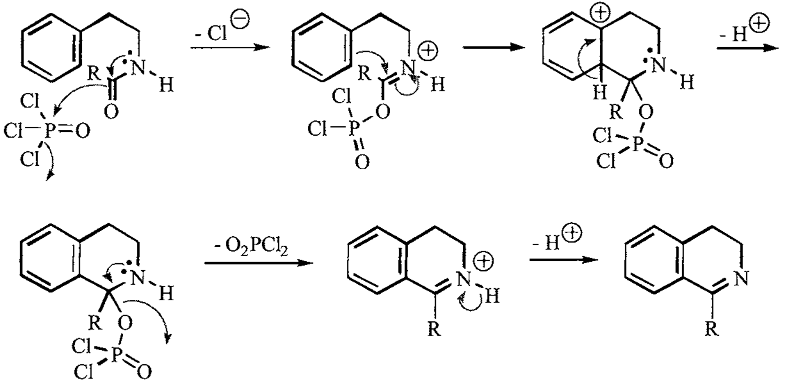
Bischler-Napieralski Reaction

The Reaction:



Other catalysts are possible. (e.g. $ZnCl_2$ and PO_5)

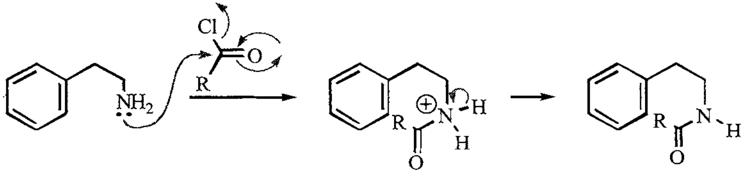
Proposed Mechanism:



Notes:

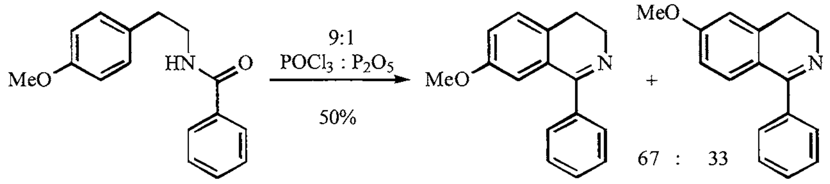
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 721; W. M. Whaley, T. R. Govindachari, *Organic Reactions* **6**, 12

Starting Material Preparation:

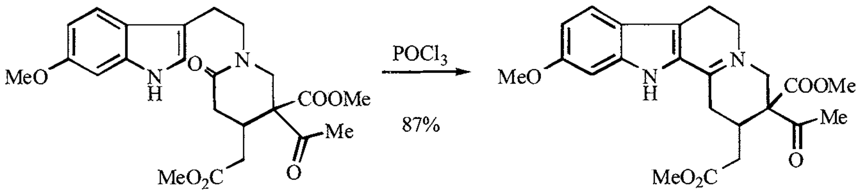


Anhydrides can also be used.

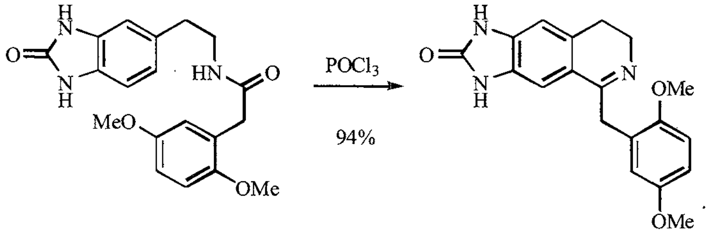
Examples:



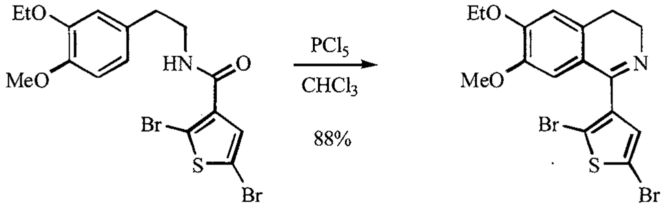
S. Doi, N. Shirai, Y. Sato, *Journal of the Chemical Society, Perkin Transactions 1* **1997**, 15, 2217



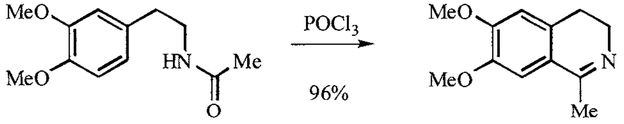
E. E. Van Tamelen, C. Placeway, G. P. Schiemenz, I. G. Wright, *Journal of the American Chemical Society* **1969**, 91, 7359



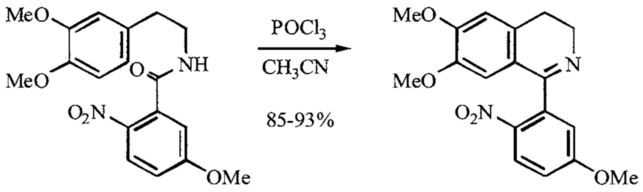
C. V. Denyer, J. Bunyan, D. M. Loakes, J. Tucker, J. Gillam, *Tetrahedron* **1995**, 51, 5057



S. Jeganathan, M. Srinivasan, *Synthesis* **1980**, 1021



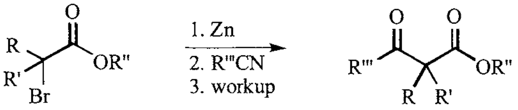
A. Brossi, L. A. Dolan, S. Teitel, *Organic Synthesis* **1977**, 56, 3



C. S. Hilger, B. Fugmann, W. Steglich, *Tetrahedron Letters* **1985**, 26, 5975

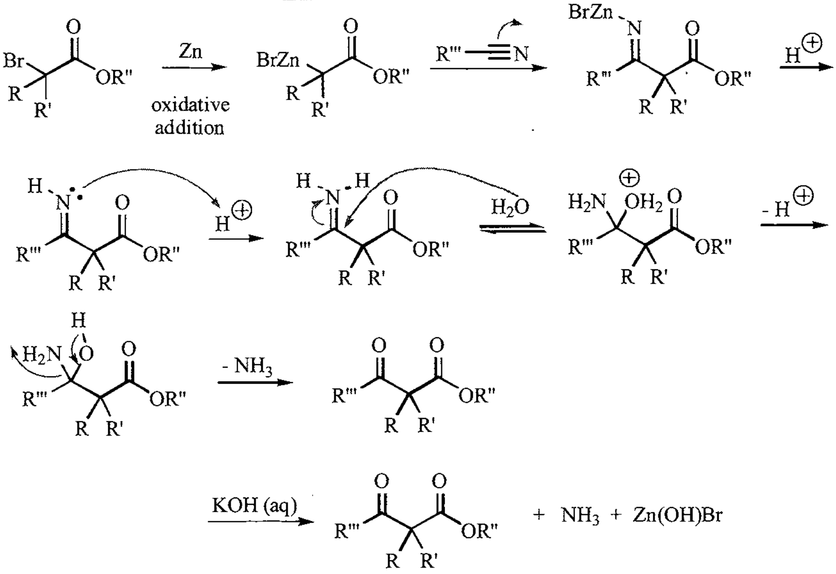
Blaise Reaction

The Reaction:



Proposed Mechanism:

The starting reagent is the ***Reformatsky***-type. In this case, instead of adding to a carbonyl group, addition is to the nitrile. See ***Reformatsky Reaction*** for a discussion of reagent.

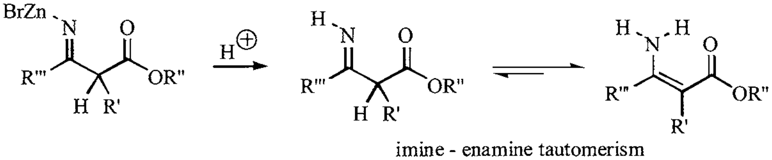


Notes:

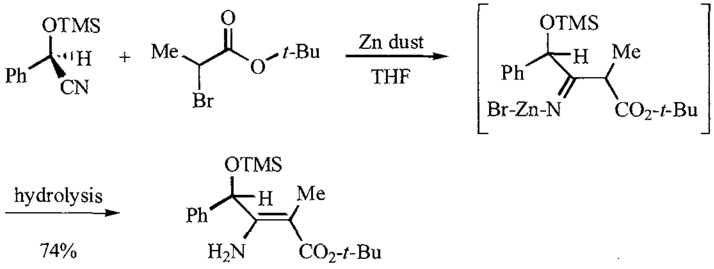
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1213.

See ***Reformatsky Reaction*** for further comments on the organo-zinc reagent.

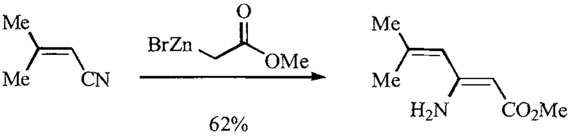
It is possible to arrest the workup to provide the enamine product:



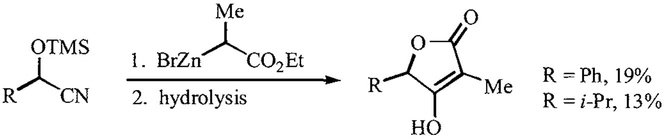
Examples:



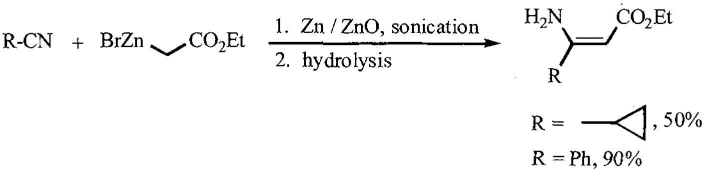
J. Syed, S. Forster, F. Effenberger, *Tetrahedron: Asymmetry* **1998**, 9, 805



M. Mauduit, C. Kouklovsky, Y. Langlois, C. Riche, *Organic Letters* **2000**, 2, 1053



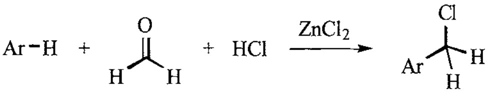
J. J. Duffield, A. C. Regan, *Tetrahedron: Asymmetry* **1996**, 7, 663



A. S.-Y. Lee, R.-Y. Cheng, O.-G. Pan, *Tetrahedron Letters* **1997**, 38, 443

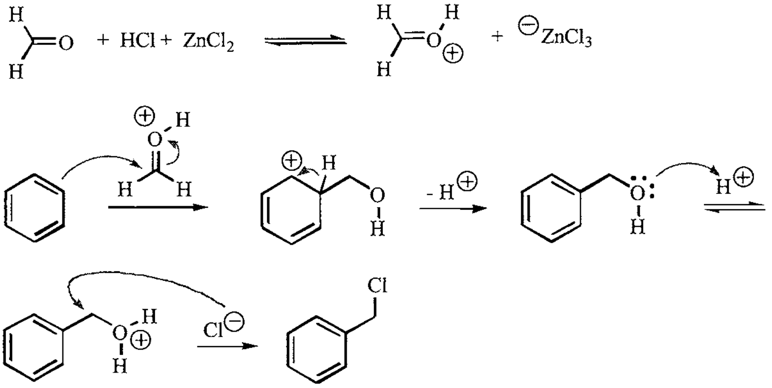
Blanc Chloromethylation Reaction

The Reaction:



Proposed Mechanism:

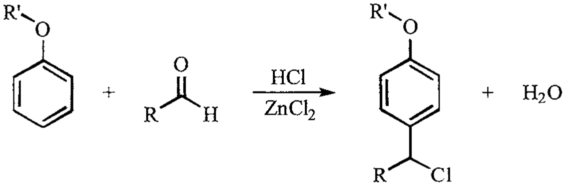
The HCl and ZnCl$_2$ form the reactive reagent with formaldehyde:



Notes:

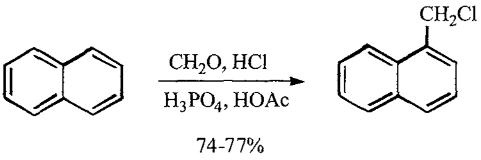
See: ***Formaldehyde***. The use of aqueous formaldehyde sometimes gives better yield than using paraformaldehyde.

See the similar ***Quelet Reaction***:

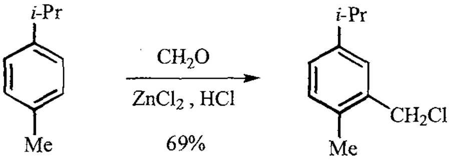


If the *p*-position is filled, the substitution will go to an open *ortho* position.

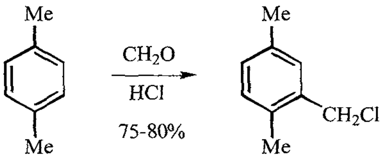
Examples:



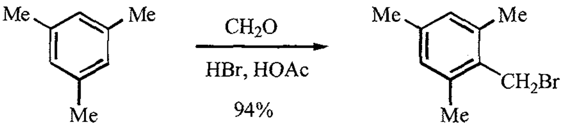
O. Grummitt, A. Buc, *Organic Syntheses* CV 3, 195



W. G. Whittleston, *Journal of the American Chemical Society* **1937**, 59, 825



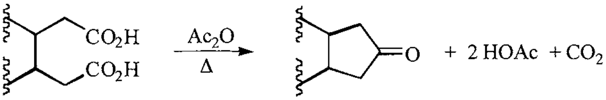
J. V. Braun, J. Nelles, *Journal of the American Chemical Society* **1951**, 73, 766



A. W. Van der Made R. H Van Der Made, *Journal of Organic Chemistry* **1993**, 58, 1262

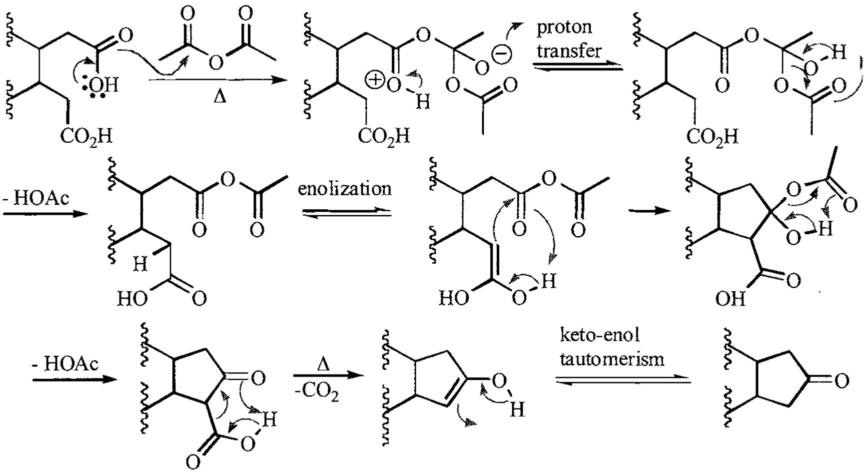
Blanc Cyclization / Reaction (Blanc Rule)

The Reaction:



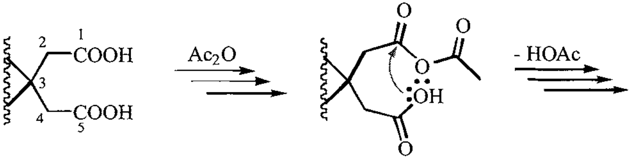
This reaction works for 1,6 dicarboxylic acids or larger.

Proposed Mechanism:

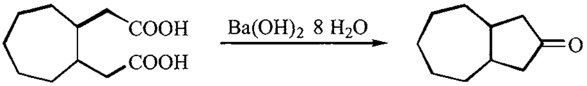


Notes:

For 1,4 or 1,5 diacids the following is observed:

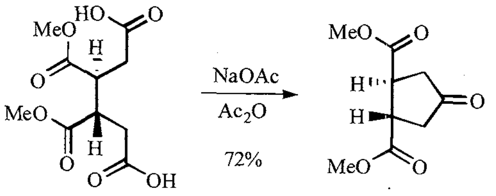


The ***Ruzicka Cyclization (or Ruzicka Large Ring Synthesis)*** is a similar reaction in which cyclic ketones are formed from salts (Ca or Ba for smaller rings and Th or Ce for larger rings) of diacids:

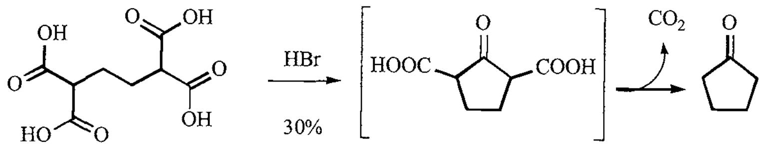


P. A. Plattner, A. Furst, K. Jirasek, *Helvetica Chimica Acta* **1944**, 29, 730 (AN 1946:23967)

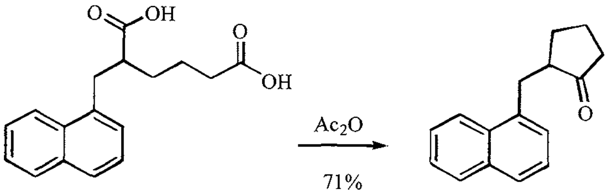
Examples:



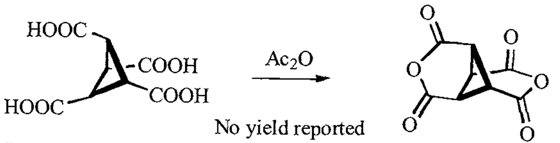
H.-J. Gais, G. Bülow, A. Zatorski, M. Jentsch, P. Maidonis, *Journal of Organic Chemistry* **1989**, 54, 5115



L. Crombie, J. E. H. Hancock, R. P. Linstead, *Journal of the Chemical Society* **1953**, 3496

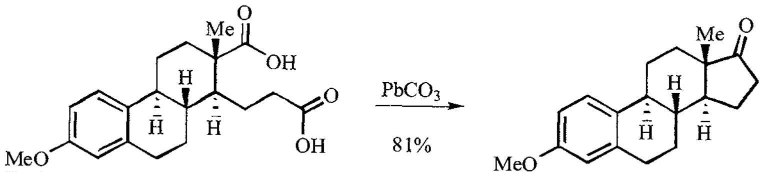


W. E. Backmann, N. C. Deno, *Journal of the American Chemical Society* **1949**, 71, 3540

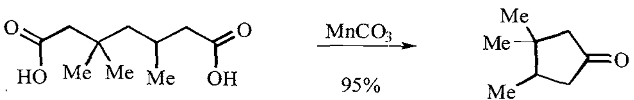


J. Dressel, K. L. Chasey, L. A. Paquette, *Journal of the American Chemical Society* **1988**, 110, 5479

Examples of the *Ruzicka Cyclization*:



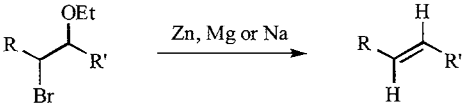
W. S. Johnson, D. K. Banerjee, W. P. Schneider, C. D. Gutsche, W. E. Shelberg, L. J. Chinn, *Journal of the American Chemical Society* **1952**, 74, 2832



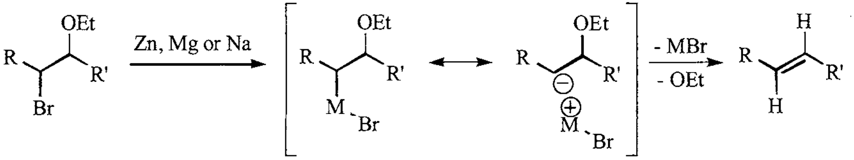
H. E. Baumgarten, D. C. Gleason, *Journal of Organic Chemistry* **1951**, 16, 1658

Boord Olefin Synthesis

The Reaction:



Proposed Mechanism:

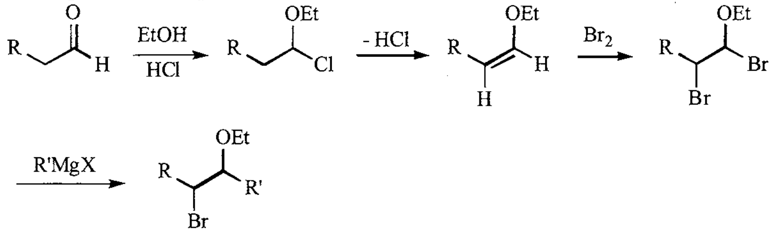


The E1-CB mechanism associated with this reaction results in similar product yields independent of stereochemistry.

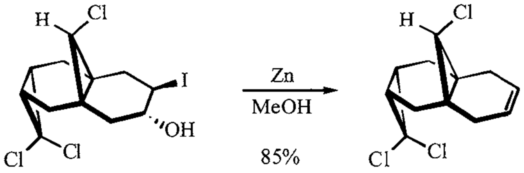
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1344.

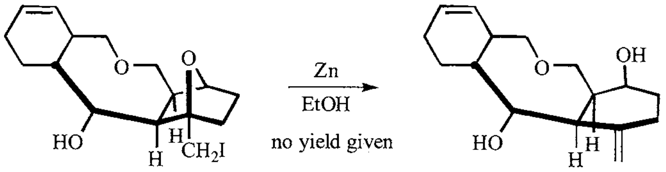
Starting Material Preparation:



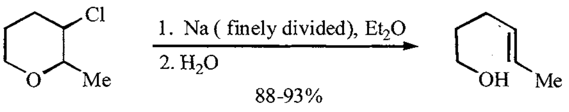
Examples:



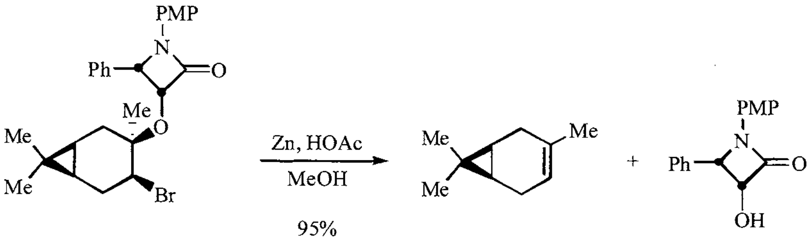
B. Halton, S. G. G. Russell, *Journal of Organic Chemistry* **1991**, 56, 5553



J. S. Yadav, R. Renduchintala, L. Samala, *Tetrahedron Letters* **1994**, 35, 3617



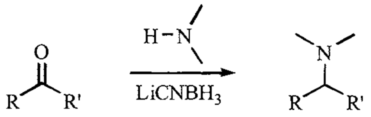
R. Paul, O. Riobé, M. Maumy, *Organic Syntheses* CV 6, 675



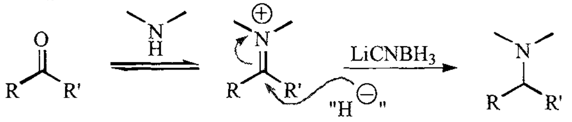
S. N. Joshi, A. R. A. S. Deshmukh, B. M. Bhawal, *Tetrahedron: Asymmetry* **2000**, 11, 1477

Borche Reduction

The Reaction:

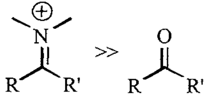


Proposed Mechanism:



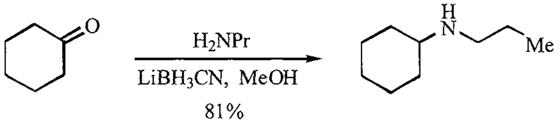
Notes:

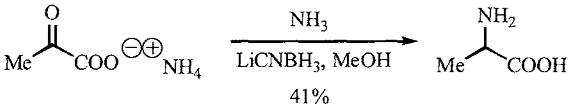
The success of this procedure rests on the much greater reactivity of



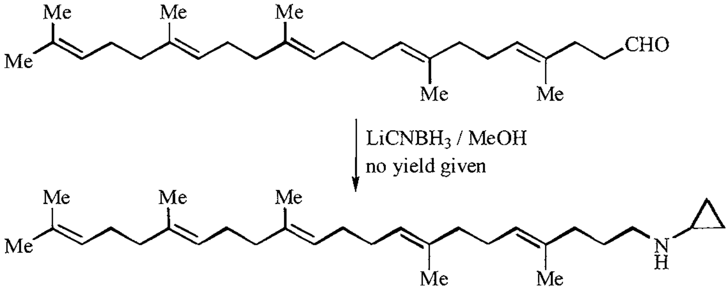
to the reducing agent

Examples:

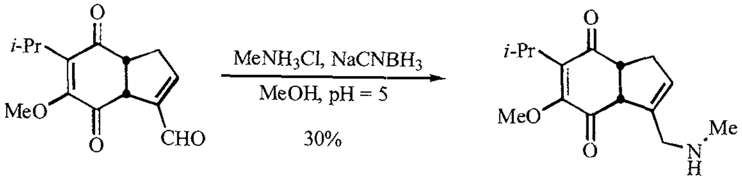




R. F. Borch, H. D. Durst, *Journal of the American Chemical Society* **1969**, 91, 3996

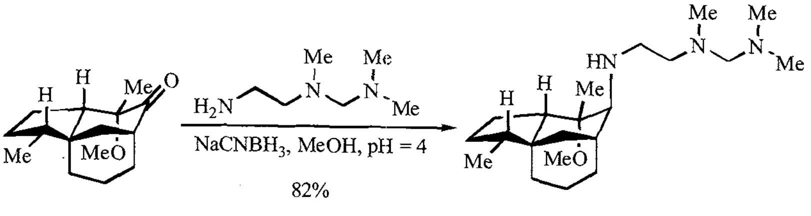


S. E. Sen, G. D. Prestwich, *Journal of the American Chemical Society* **1989**, 111, 8761

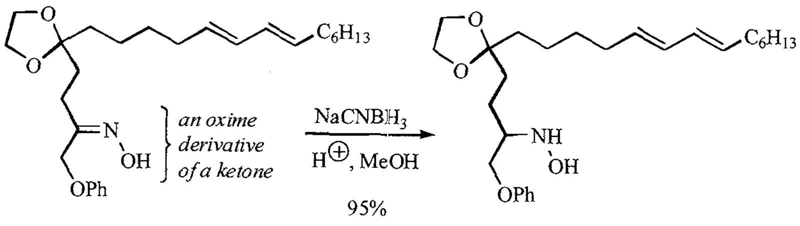


A. S. Kende, T. J. Bentley, R. A. Mader, D. Ridge, *Journal of the American Chemical Society* **1974**, 96, 4332

To see the use of the method for generating a library, with a modification of the reducing agent:
R. A. Tommasi, L. W. Whaley, H. R. Marepalli, *Journal of Combinatorial Chemistry* **2000**, 2, 447



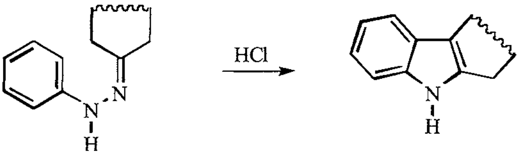
A. J. Frontier, S. Raghaven, S. J. Danishefsky, *Journal of the American Chemical Society* **1997**, 119, 6686



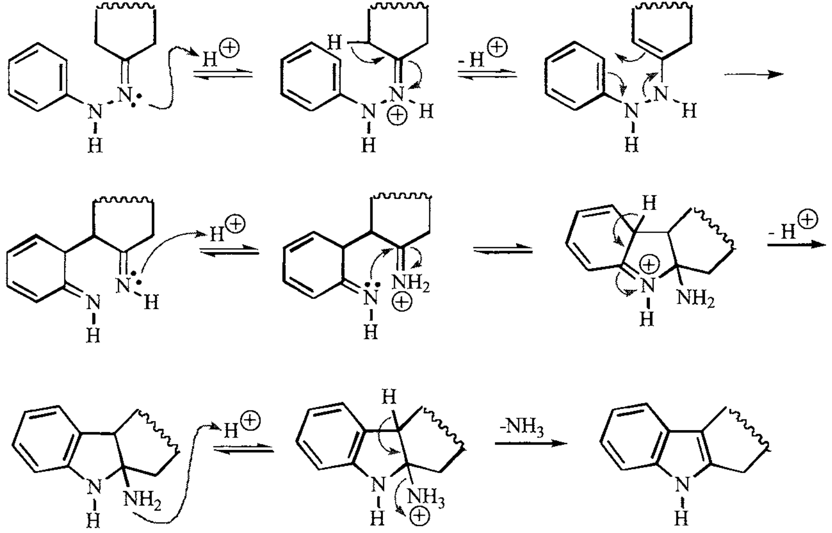
K. M. Werner, J. M. de los Santos, S. M. Weinreb, M. Shang, *Journal of Organic Chemistry* **1999**, 64, 686

Borsche-Drechsel Cyclization

The Reaction:



Proposed Mechanism:



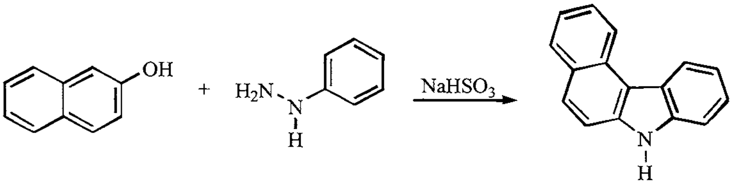
Notes:

See this general concept in the ***Fischer Indole Synthesis*** and the ***Bucherer Carbazole Synthesis***.

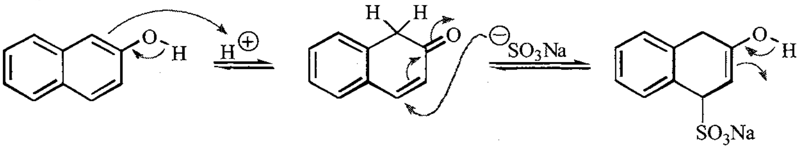
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 865-66; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, p. 37

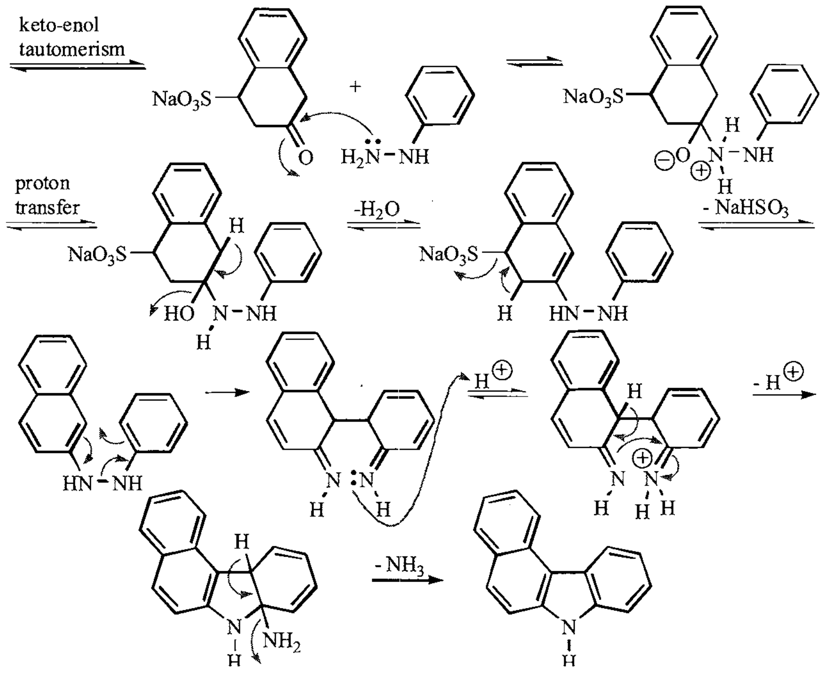
Bucherer Carbazole Synthesis

The Reaction:

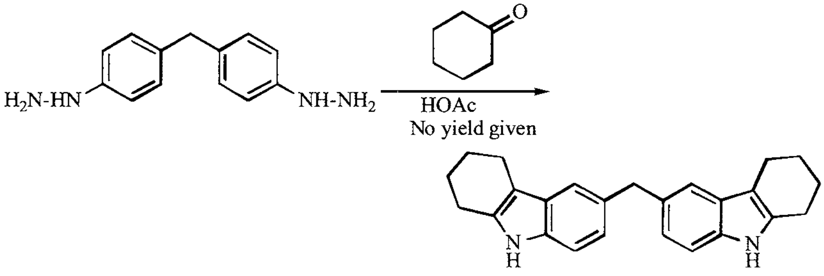


Proposed Mechanism:

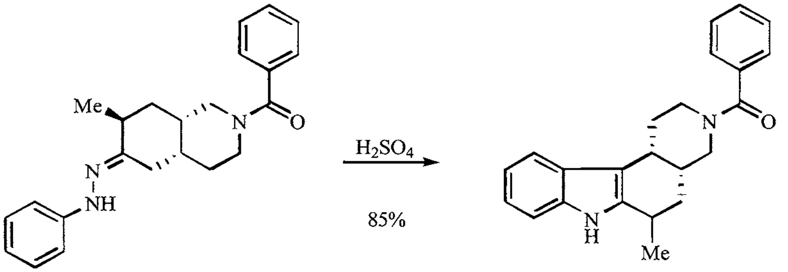




Examples of *Borsche-Drechsel Cyclization*



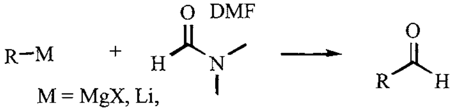
P. Bruck, *Journal of Organic Chemistry* **1970**, 35, 2222



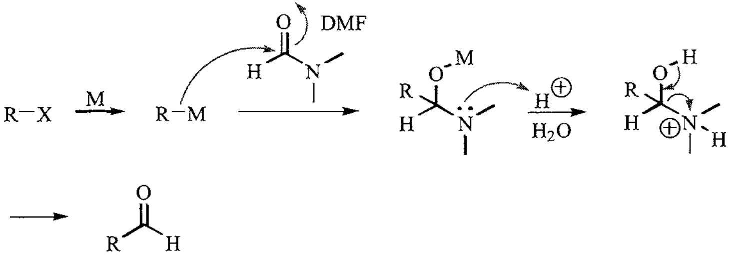
K. Freter, V. Juchs, T. P. Pitner, *Journal of Organic Chemistry* **1983**, 48, 4593

Bouveault Aldehyde Synthesis / Reaction

The Reaction:

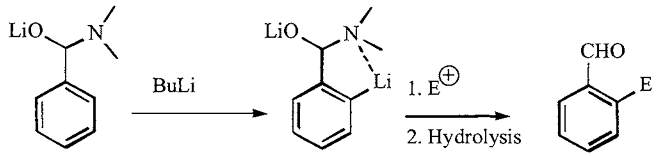


Proposed Mechanism:



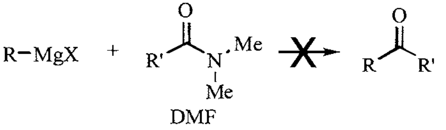
***Comin modification*:**

D. L. Comins, J. D. Brown, *Journal of Organic Chemistry* **1984**, 49, 1078



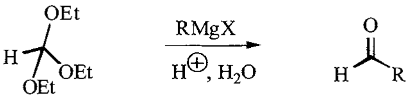
Notes:

Based on the mechanism, one might suggest an extension to ketone synthesis. This is not a useful reaction. (M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p 1215).

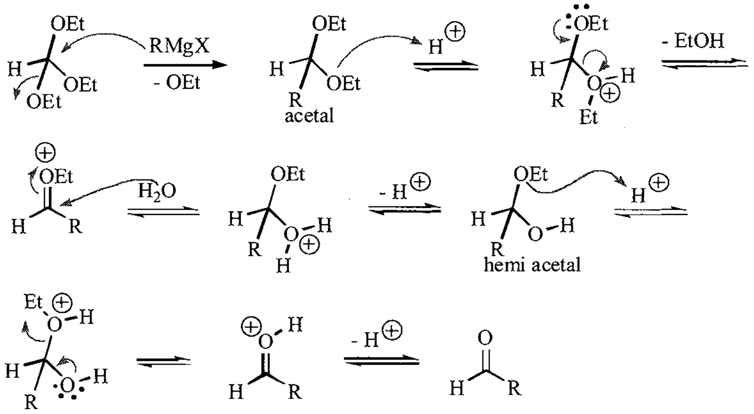


Bodroux-Chichibabin Aldehyde Synthesis

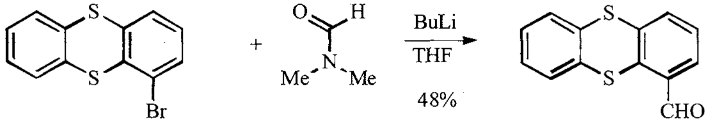
The Reaction:



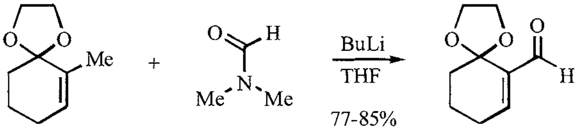
Proposed Mechanism:



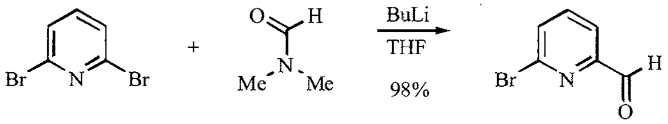
Examples:



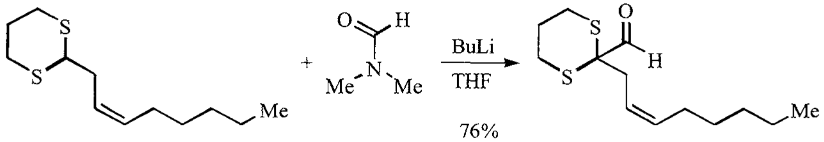
J. M. Lovell, J. A. Joule, *Journal of the Chemical Society, Perkin Transactions 1* **1996**, 2391



G. J. Bodwell, Z. Pi, *Tetrahedron Letters* **1997**, 38, 309



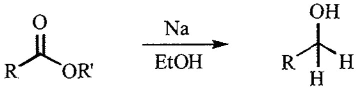
D. Cai, D. L. Hughes, T. R. Verhoeven, *Tetrahedron Letters* **1996**, 37, 2537



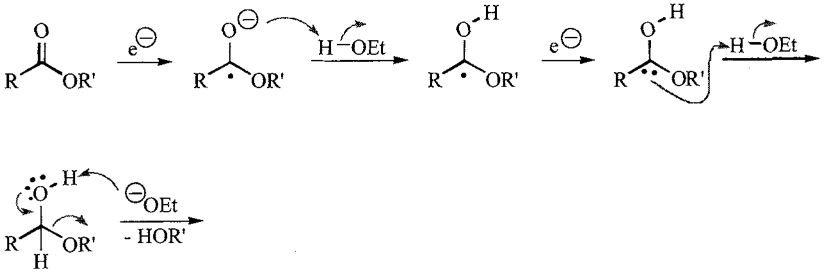
S. P. Khanapure, S. Manna, J. Rokach, R. C. Murphy, P. Wheelan, W. S. Powell, *Journal of Organic Chemistry* **1995**, 60, 1806

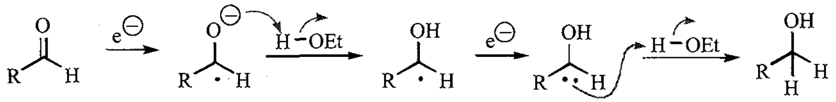
Bouveault-Blanc Reduction

The Reaction:



Proposed Mechanism:





Dissolving metal reduction of carbonyl group

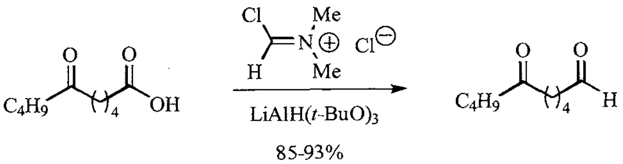
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1191, 1551.

The related reduction of simple carbonyl groups with Na / alcohol (see boxed portion of mechanism) has been largely replaced by hydride reduction. However, the method has some advantages:

1. "thermodynamic products" are favored;
2. Oximes are converted to amines.

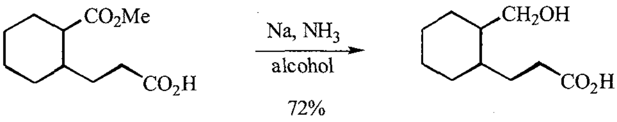
For direct conversion of an acid to an aldehyde in the presence of a ketone:



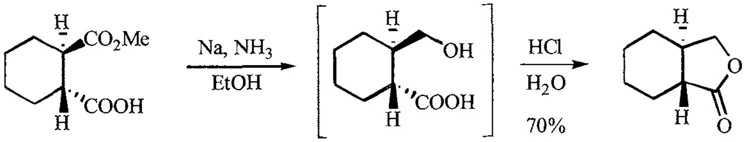
T. Fujisawa, T. Sato, *Organic Syntheses* CV 8, 498

Examples:

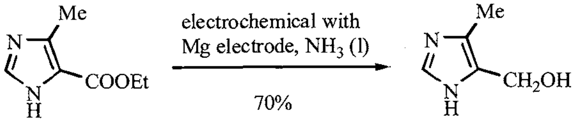
It is appropriate here to mention that in the following example $LiAlH_4$ would reduce both the acid and the ester; diborane would preferentially reduce the acid; and DIBAH would convert the ester to an aldehyde.



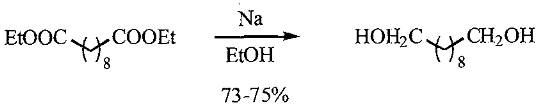
L. A. Paquette, N. A. Nelson, *Journal of Organic Chemistry* **1962**, 27, 2272



R. M. Borzilleri, S. M. Weinreb, M. Parvez, *Journal of the American Chemical Society* **1995**, 117, 10905



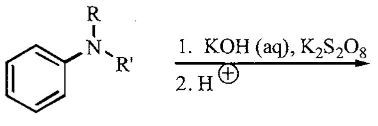
J. Chaussard, C. Combellas, A. Thiebault, *Tetrahedron Letters* **1987**, 28,1173



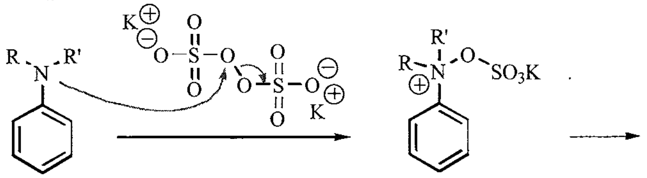
R. H. Manske, *Organic Syntheses* CV 2, 154

Boyland-Sims Oxidation

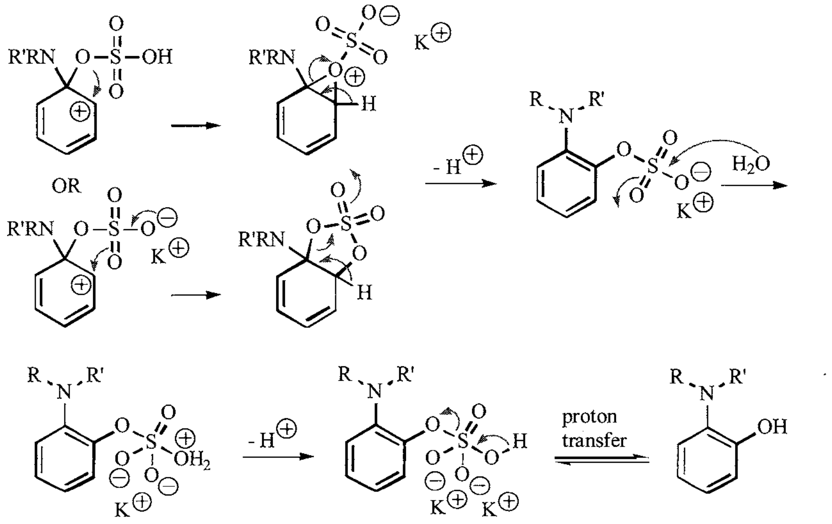
The Reaction:



Proposed Mechanism:



E. J. Behrman, *Journal of Organic Chemistry* **1992**, 57, 2266



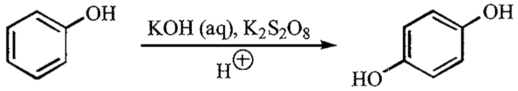
Notes:

For comments on this and the ***Elbs Reaction***, see: M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p 724; E. J. Behrman, *Organic Reactions* **35**, 2

See the similarity in the:

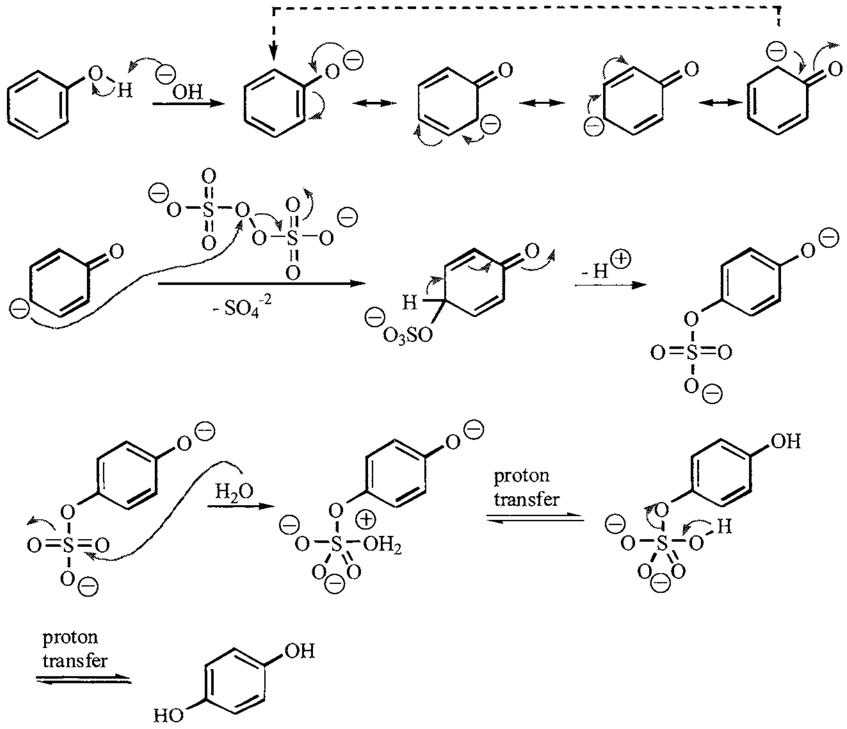
Elbs Persulfate Oxidation (Elbs Reaction)

The Reaction:



Proposed Mechanism:

T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 92-93; V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International, Ltd., Pangbourne, U.K., 2002, pp 320-321.

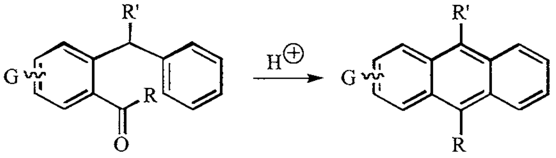


Notes:

Oxidation usually occurs at the *para* position. If the *para* position is occupied, the *ortho* position is the next likely site for reaction.

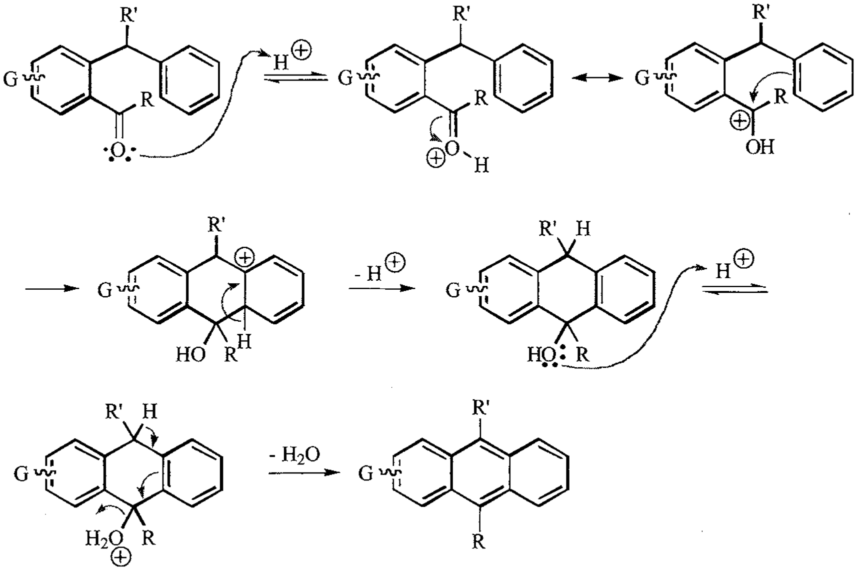
Bradsher Reaction

The Reaction:



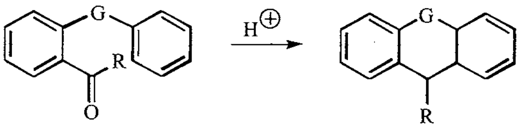
Proposed Mechanism:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p 720



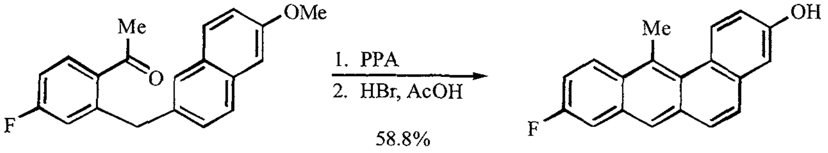
Notes:

This reaction also works with heterocyclic derivatives, where G = O, S, or Se.

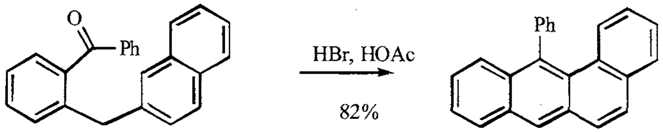


See: ***Polycarbocyclic Syntheses***

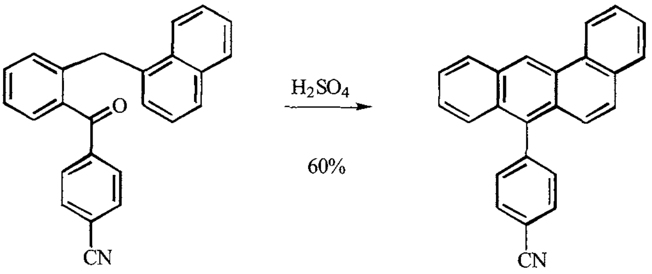
Examples:



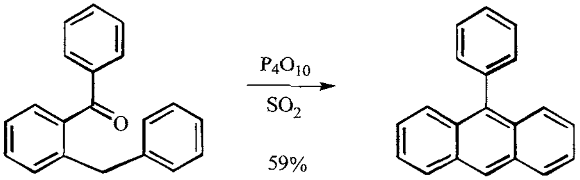
R. G. Harvey, C. Cortez, Tetrahedron **1997**, 53, 7101



C. K Bradsher, *Journal of the American Chemical Society* **1940**, 62, 486



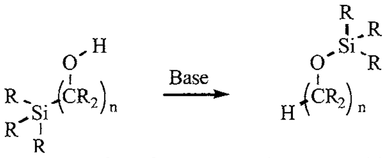
F. A. Vingiello, R. K. Stevens, *Journal of the American Chemical Society* **1958**, 80, 5256



C. K. Bradsher, E. F. Sinclair, *Journal of Organic Chemistry* **1957**, 22, 79

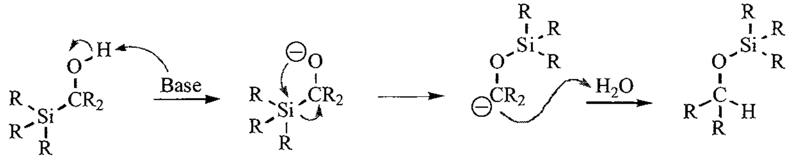
Brook Rearrangement

The Reaction:

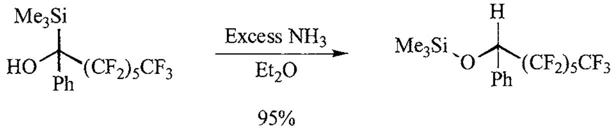


n = 1 – 3, where for 3 – 5 membered transition states can be formed.

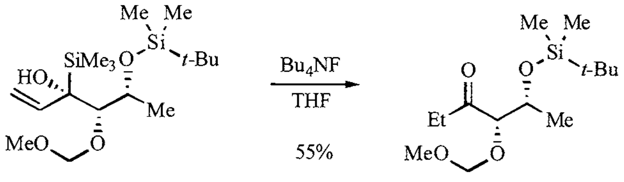
Proposed Mechanism:



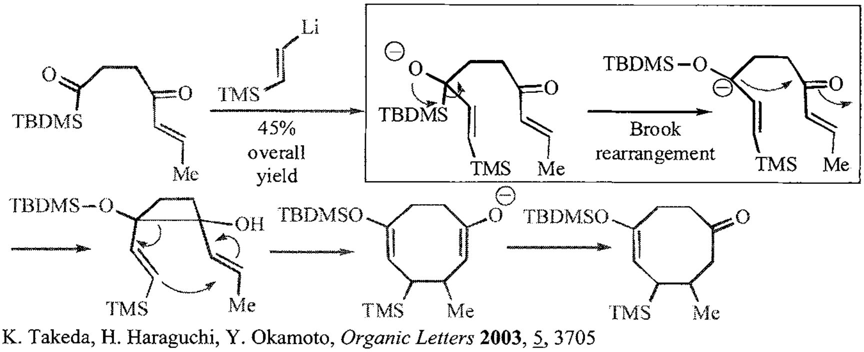
Examples:



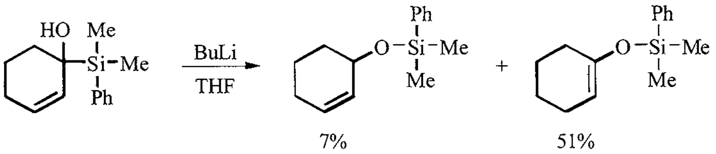
B. Dondy, P. Doussot, C. Portella, *Tetrahedron Lett*ers **1994**, 35, 409



P. F. Cirillo, J. S. Panek, *Journal of Organic Chemistry* **1990**, 55, 6071

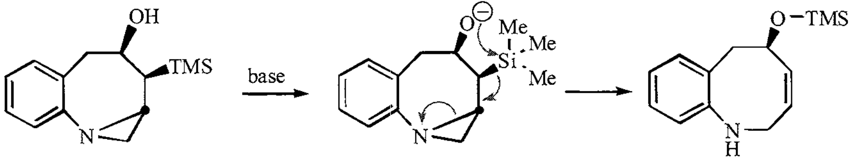


K. Takeda, H. Haraguchi, Y. Okamoto, *Organic Letters* **2003**, 5, 3705

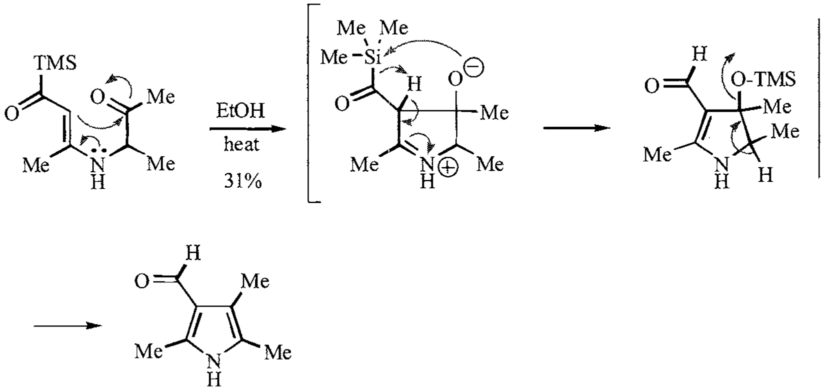


M. Koreeda, S. Koo, *Tetrahedron Letters* **1990**, 31, 831

An example of a ***Homo-Brook Rearrangement***



Yields were varied, depending on base used.
R. Ducray, N. Cramer, M. A. Ciufolini, *Tetrahedron Letters* **2001**, 42, 9175

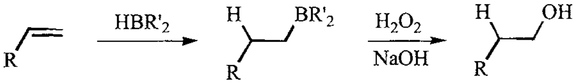


L. A. Calvo, A. M. Gonza´lez-Nogal, A. Gonza´lez-Ortega, M. C. San˜udo, *Tetrahedron Letters* 2001, 42, 8981

Brown's Hydroboration

See: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 157-160.

The Reaction:

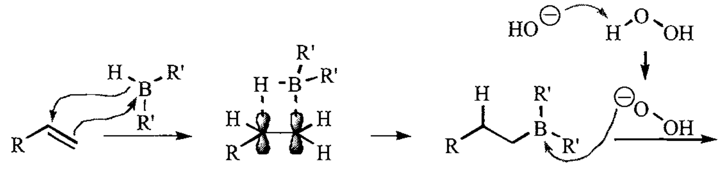


HBR'$_2$ may be BH_3 (B_2H_6 = diborane) or other borane derivatives (see below).

Proposed Mechanism:

In the presence of ethers (and especially dimethyl sulfide) diborane can dissociate into a complexed borane:

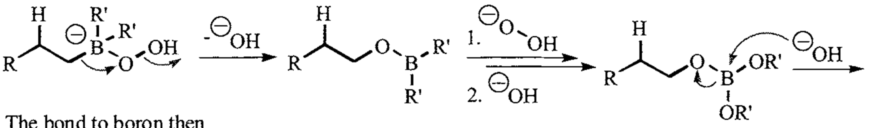
Z = O, S, generally from Et_2O, THF, and DMS



Borane attacks from the least hindered face. *Stereochemical control.*

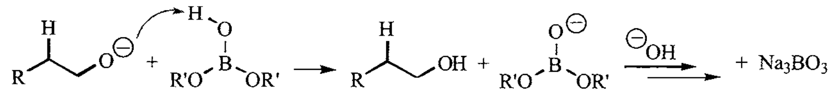
Boron adds as an electrophile and hydride as the nucleophile in a cis-fashion. *Regiochemical control.*

Boron hydrolysis begins with the attack of peroxide.



The bond to boron then migrates to oxygen.

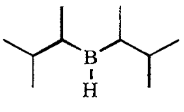
Two more addition / migrations take place



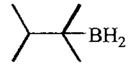
The result is a cis, anti-Markownikoff addition of water. The C-B bond is converted into a C-OH bond *with retention of stereochemistry.*

Notes:

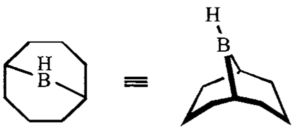
With hindered alkenes, it is more difficult to add three alkenes to borane. This becomes the basis for unique, borane derivatives. See ***Hydroboration Reagents***.



Disiamylborane
Sia_2BH

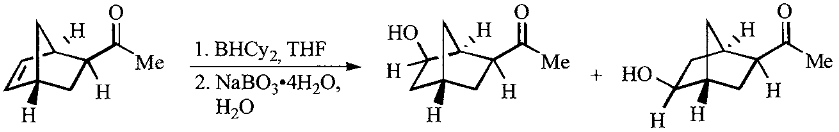


Thexylborane

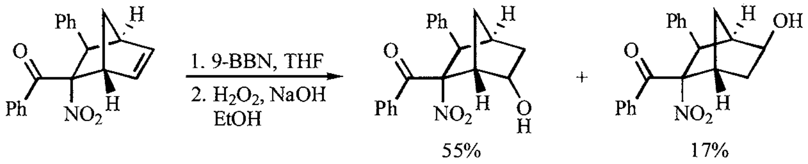


9-BBN
9-borabicyclo[3.3.1]nonane

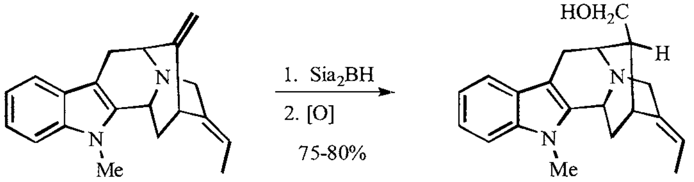
Examples:



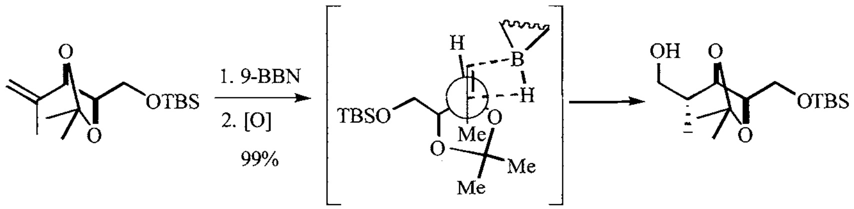
G. W. Kabalka, S. Yu, N.-S. Li, *Tetrahedron Letters* **1997**, 38, 5455



D. L. Gober, R. A. Lerner, B. F. Cravatt, *Journal of Organic Chemistry* **1994**, 59, 5078



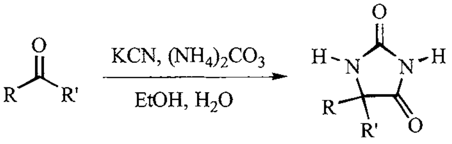
D. L. Gober, R. A. Lerner, B. F. Cravatt, *Journal of Organic Chemistry* **1994**, 59, 5078



K. Suenaga, K. Araki, T. Sengoku, D. Uemura, *Organic Letters* **2001**, 3, 527

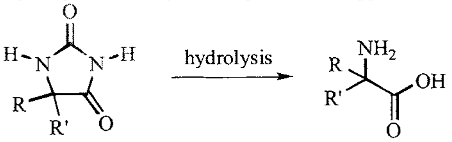
Bucherer-Bergs Reaction

The Reaction:

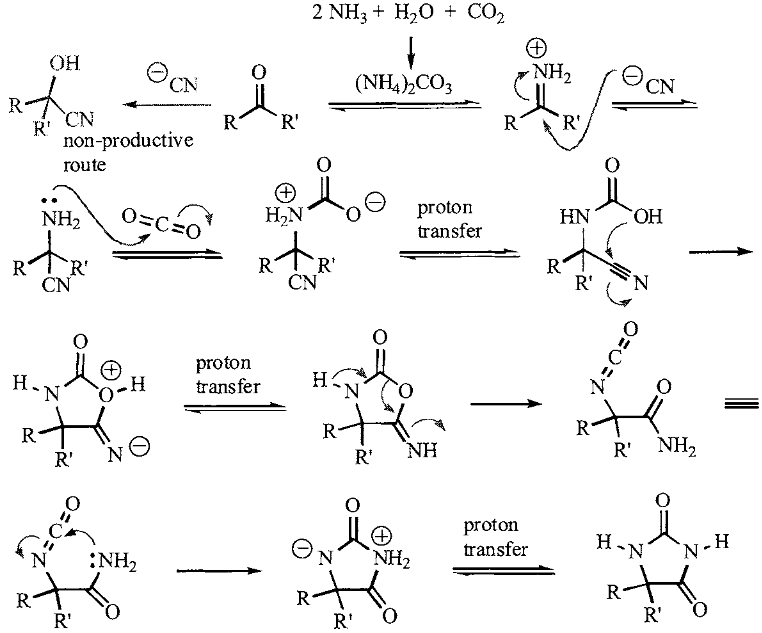


hydantoin

Hydrolysis of the hydantoin provides an approach to amino acids:

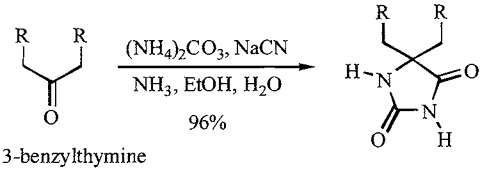


Proposed Mechanism:

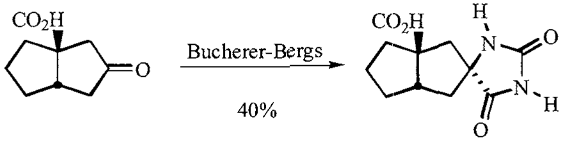


F. L. Chubb, J. T. Edward, S. C. Wong, *Journal of Organic Chemistry* **1980**, 45, 2315
An intermediate α-aminonitrile carbamate is found. A. Rousset, M. Lasperas, J. Taillades, A. Commeyras, *Tetrahedron* **1980**, 36, 2649

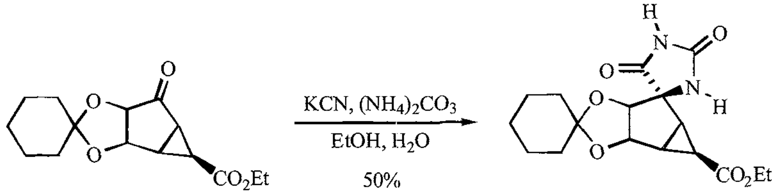
Examples:



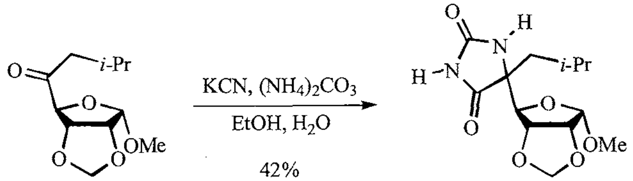
R: 3-benzylthymine
F. L. Chubb, J. T. Edward, S. C. Wong, *Journal of Organic Chemistry* **1980**, 45, 2315



J. Ezquerra, B. Yruretaguyena, C. Avendano, E. de la Cuesta, R. Gonzalez, L. Prieto, C. Peqregal, M. Espada, W. Prowse, *Tetrahedron* **1995**, 51, 3271



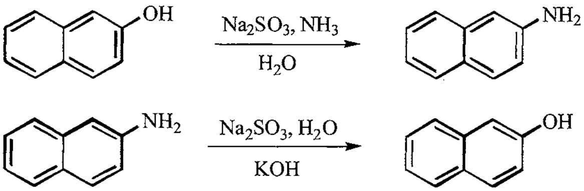
C. Dominguez, J. Ezquerra, S. R. Baker, S. Burrelly, L. Prieto, M. Espada, C. Pedregal, *Tetrahedron Lett*ers **1998**, 39, 9305



B. Steiner, J. Micova, M. Koos, V. Langer, D. Gyepesova, *Carbohydrate Research* **2003**, 338, 1349

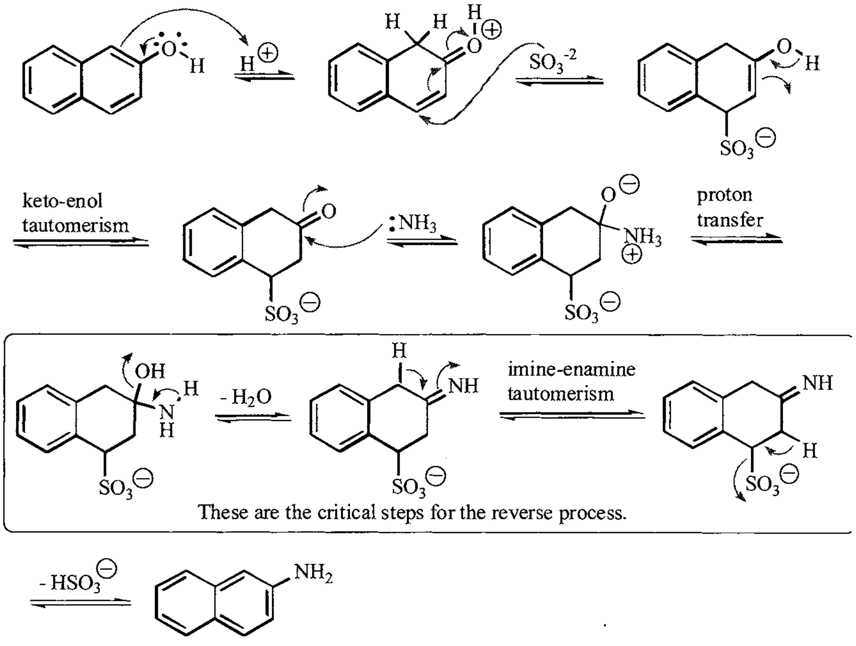
Bucherer Reaction

The Reaction:



This reaction can be carried out in either direction with modest modifications of reaction conditions.

Proposed Mechanism:

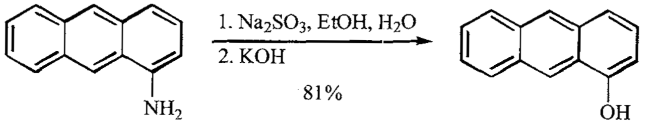


These are the critical steps for the reverse process.

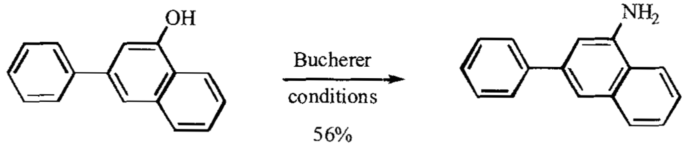
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 861, 865; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 37-39; N. L. Drake, *Organic Reactons* **1**, 5.

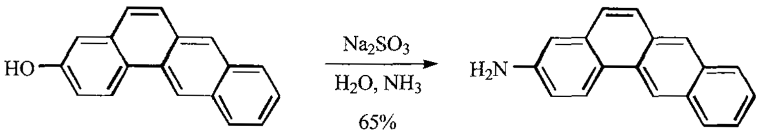
Examples:



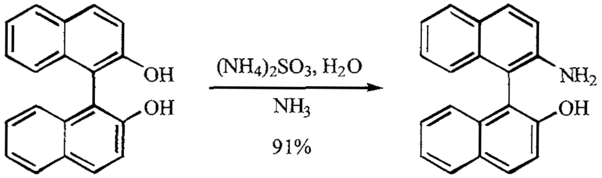
R. S. Coleman, M. A. Mortensen, *Tetrahedron Letters* **2003**, 44, 1215



S. Vyskocil, M. Smrcina, M. Lorenc, I. Tislerova, R. D. Brooks, J. J. Kulagowski, V. Langer, L. J. Farrugia, P. Kocovsky, *Journal of Organic Chemistry* **2001**, 66, 1359



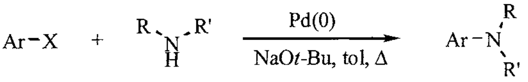
L. F. Fieser, E. B. Hershberg, L. Long, Jr., M. S. Newman, *Journal of the American Chemical Society* **1937**, 59, 475



K. Korber, W. Tang, X. Hu, X. Zhang, *Tetrahedron Letters* **2002**, 43, 7163

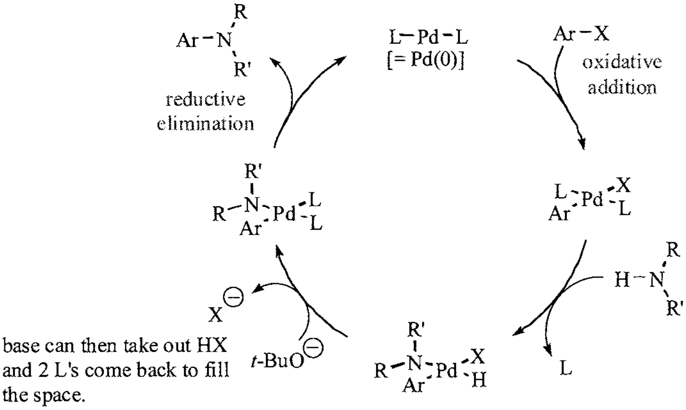
Buchwald-Hartwig Reactions

The Reaction:



Proposed Mechanism:

Buchwald calls the replacement of halide by nitrogen metathesis.

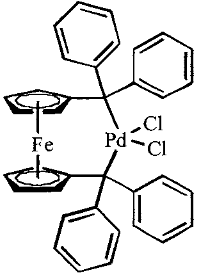


base can then take out HX and 2 L's come back to fill the space.

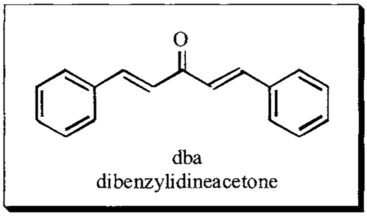
Sources for mechanism:
J. P. Wolfe, S. Wagaw, S. L. Buchwald, *Accounts of Chemical Research* **1998**, 31, 805
J. Louie, J. F. Hartwig, *Tetrahedron Letters* **1995**, 36, 3609
B. H. Yang, S. L. Buchwald, *Journal of Organometallic Chemistry* **1999**, 576, 125

Notes:

Representative catalysts:



$$\mathrm{Pd_2(dba)_3} \xrightarrow{\mathrm{PPh_3}} 2\ \mathrm{Pd(PPh_3)_4}$$



dba
dibenzylidineacetone

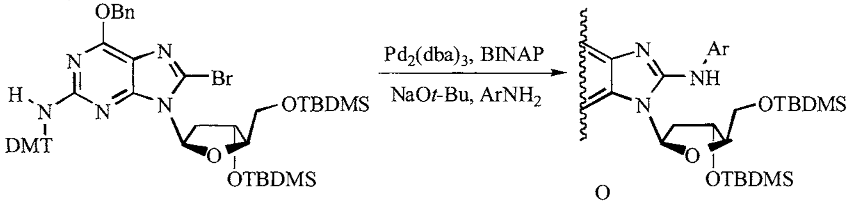
Pd(dppf)Cl$_2$ =
[1,1'-Bis(diphenylphosphino)ferrocene]dichloropalladium(II)

A useful Review describes the use of BINAP for the conversion:

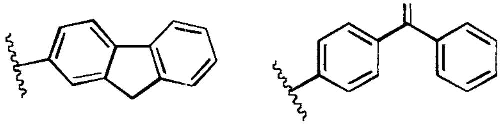
$$\text{Ar-Br} + \text{R'NH}_2 \xrightarrow[\text{BINAP, NaO}t\text{-Bu}]{0.25\ \text{mol\% Pd}_2(\text{dba})_3} \text{Ar-NHR'}$$

J. P. Wolfe, S. Wagaw, S. L. Buchwald, *Accounts of Chemical Research* **1998**, 31, 805

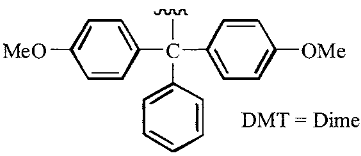
Examples:



When Ar =



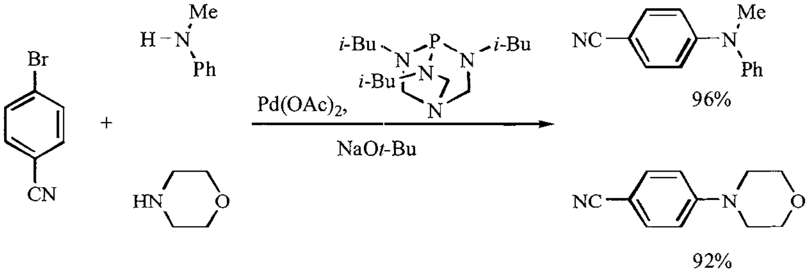
72% 83%



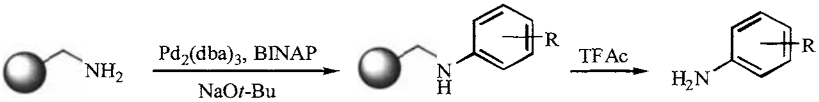
DMT = Dimethoxytrityl, a useful protecting group

L. C. J. Gillet, O. D. Scharer, *Organic Letters* **2002**, 4, 4205

See ***Verkade's Base***



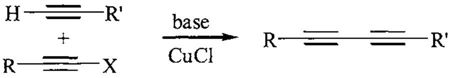
S. Urgaonkar, J.-H. Xu, J. G. Verkade, *Journal of Organic Chemistry* **2003**, 68, 8416



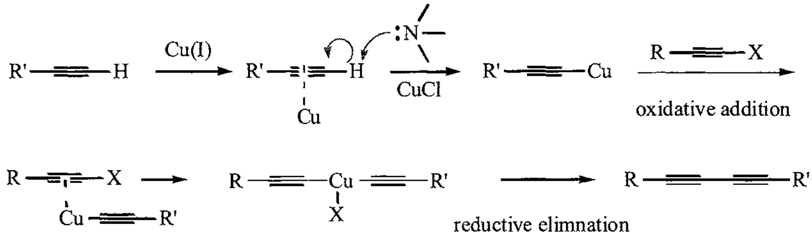
A number of ligands and resins were examined.
K. Weigand, S. Pelka, *Organic Letters* **2002**, 4, 4689

Cadiot-Chodkiewicz Coupling

The Reaction:



Proposed Mechanism:

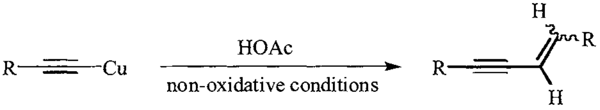


Notes:

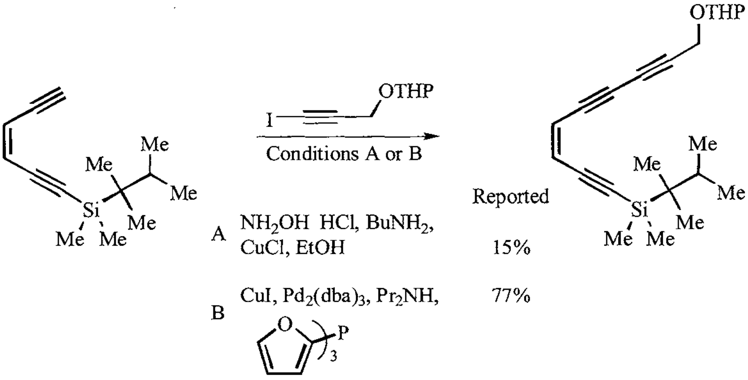
See ***Alkyne Coupling***,
CuCl = Cu_2Cl_2

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 937.

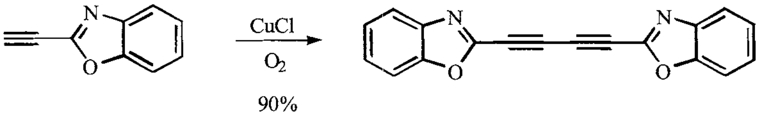
Strauss Coupling:
In the absence of oxygen or oxidizing atmosphere:



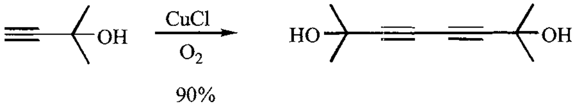
Examples:



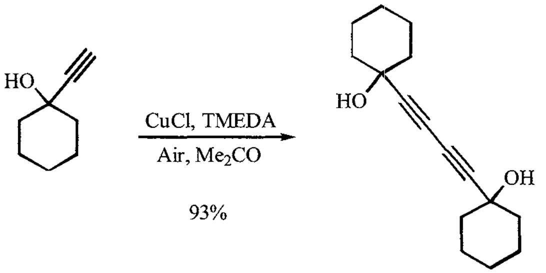
D. Elbaum, T. B. Nguyen, W. L. Jorgensen, S. L. Schreiber, *Tetrahedron* **1994**, 50, 1503



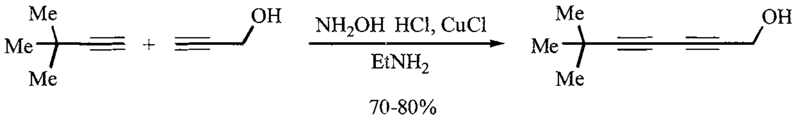
U. Fritzsche, S. Hunig, *Tetrahedron Letters* **1972**, 13, 4831



H. A. Stansbury, W. R. Proops, *Journal of Organic Chemistry* **1962**, 27, 320



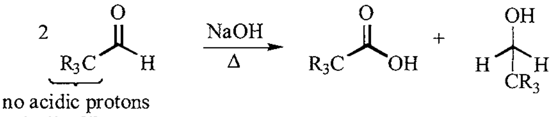
A. S. Hay, *Journal of Organic Chemistry* **1962**, 27, 3320



J.-P. Gotteland, I. Brunel, F. Gendre, J. Desire, A. Delhon, D. Junquero, P. Oms, S. Halazy, *Journal of Medicinal Chemistry* **1995** 38, 3207

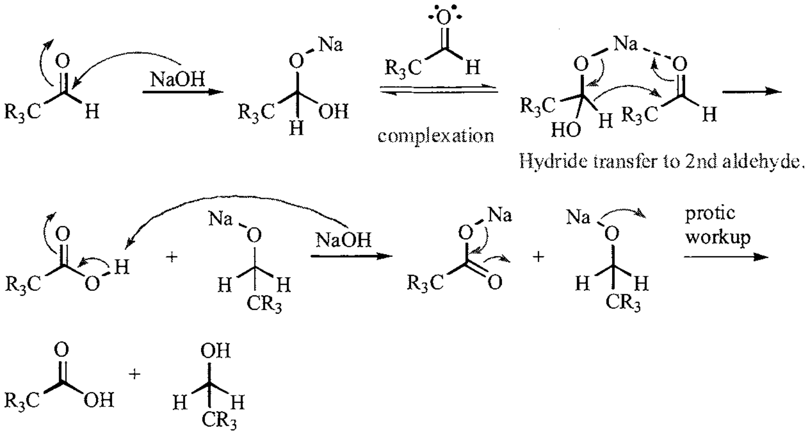
Cannizzarro Reaction / Aldehyde Disproportionation

The Reaction:



no acidic protons
typically CR_3 = Ar

Proposed Mechanism:



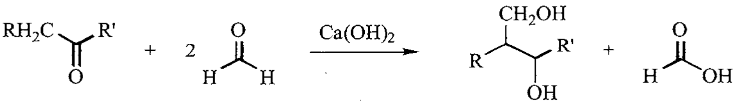
Notes:

T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp 40-42; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1564-1565; T. A. Geissman, *Organic Reactions* **2**, 3.

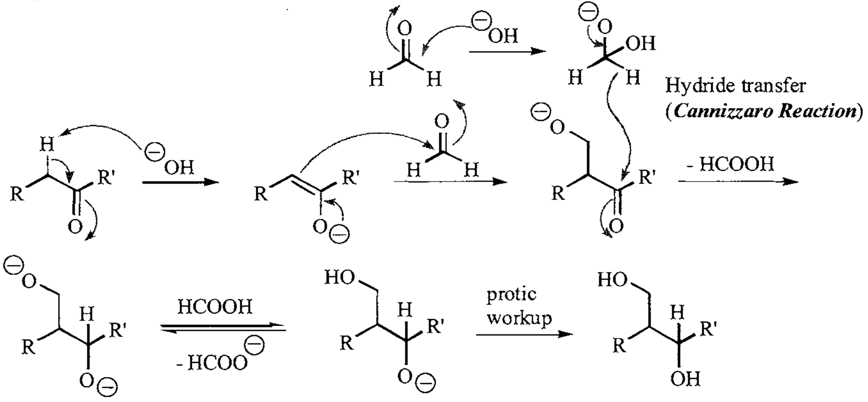
Tollens Reaction

The reaction is an ***aldol condensation*** followed by a ***Cannizzarro reaction***.

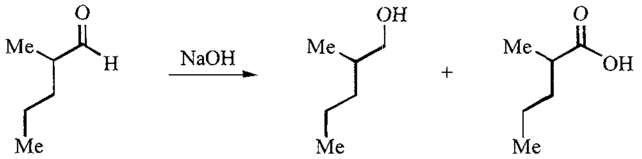
The Reaction:



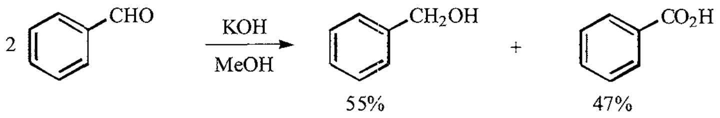
Proposed Mechanism:



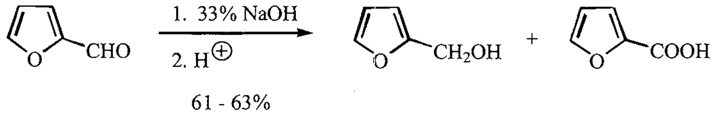
Examples:



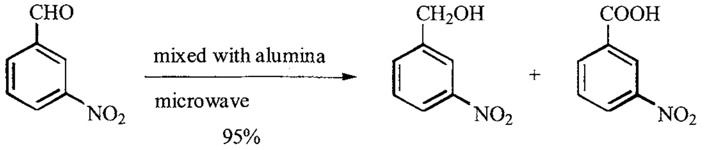
M. Hausermann, *Helvetica Chemica Acta* **1951**, 34, 1211 (AN 1952:2485)



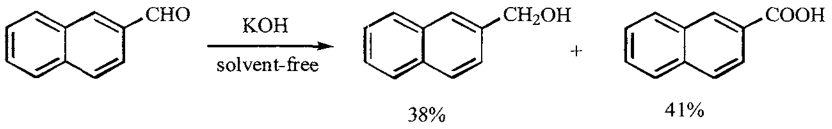
C. G. Swain, A. L. Powell, W. A. Sheppard, C. R. Morgan, *Journal of the American Chemical Society* **1979**, 101, 3576



W. C. Wilson, *Organic Syntheses*, CV1, 276



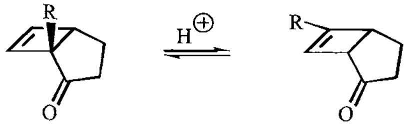
A. Pourjavadi, B. Soleimanzadeh, G. B. Marandi, *Reactive & Functional Polymers* **2002**, 51, 49



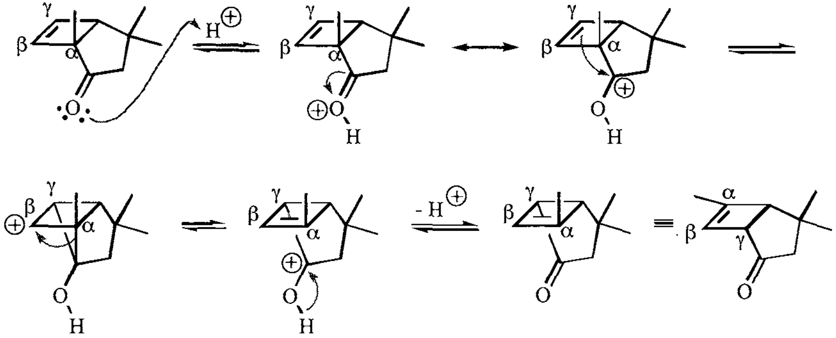
K. Yoshizawa, S. Toyota, F. Toda, *Tetrahedron Letters* **2001** 42, 7983

Cargill Rearrangement

The Reaction:



Proposed Mechanism:

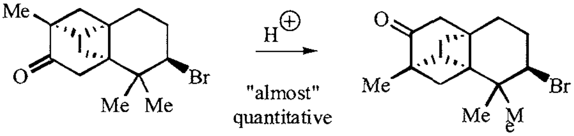


R. L. Cargill, T. E. Jackson, N. P. Peet, D. M. Pond, *Accounts of Chemical Research* **1974**, 7, 106

Notes:

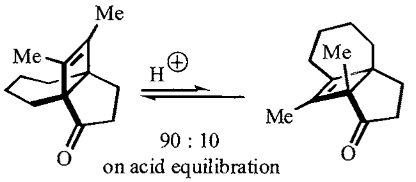
The name of this rearrangement is applied to acid conditions on β-γ unsaturated ketones where either (or both) the carbonyl and/or alkene bond is in a strained environment.

In later works, the name seems to include highly congested and strained multi-ring systems.

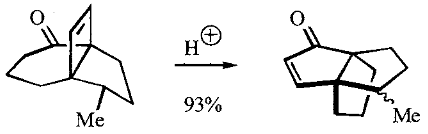


S. N. Fedorov, O. S. Radchenko, L. K. Shubina, A. I. Kalinovsky, A. V. Gerasimenko, D. Y. Popov, V. A. Stonik *Journal of the American Chemical Society* **2001**, 123, 504

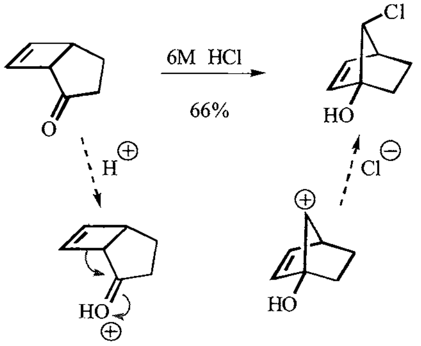
Examples:



R. L. Cargill, T. E. Jackson, N. P. Peet, D. M. Pond, *Accounts of Chemical Research* **1974**, 7, 106



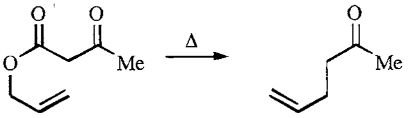
A. B. Smith, III, P. J. Jerris, *Journal of the American Chemical Society* **1981**, 103, 194



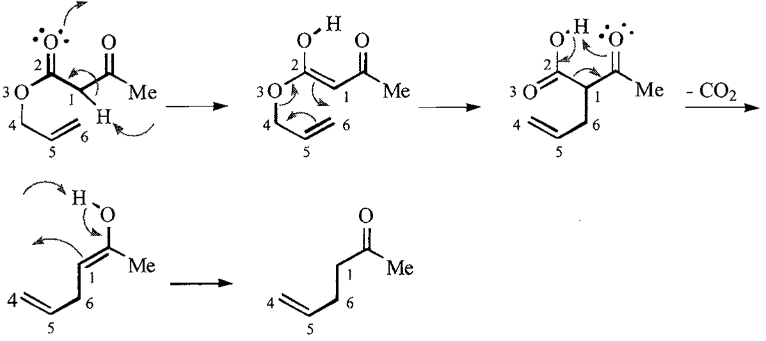
R. L. Cargill, D. M. Ponds, S. O. LeGrande *Journal of Organic Chemistry* **1970**, 35, 359

Carroll Rearrangement (Kimel-Cope Rearrangement)

The Reaction:



Proposed Mechanism:

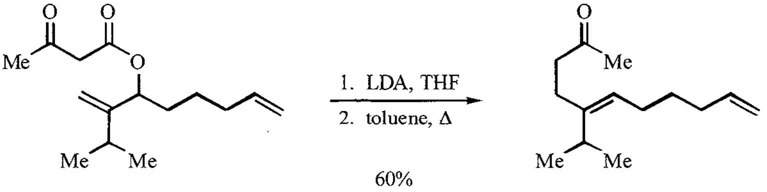


Notes:

See ***Claisen, Cope and Related Rearrangements***.

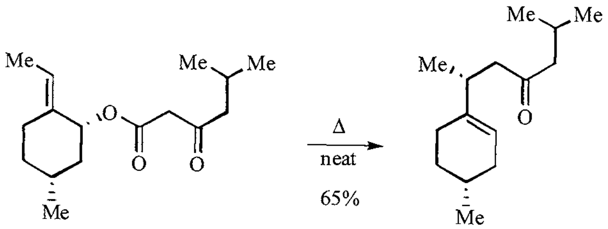
Enol formation provides the necessary "1,5-diene" for the "***Cope-like***" rearrangement. If one provides an enolate anion, the ionic nature of the reaction provides the expected acceleration of rate.

Anion-accelerated Carroll Rearrangement:

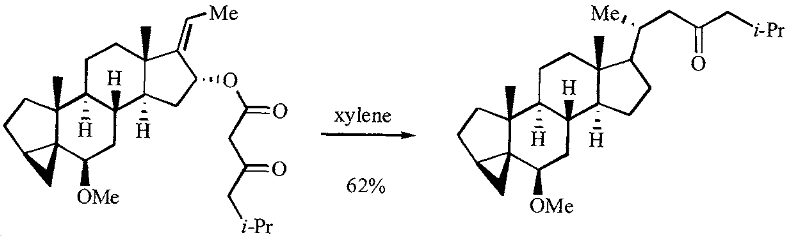


B. Shi, N. A. Hawrylik, B. B. Snider, *Journal of Organic Chem*istry **2003**, 68, 1030

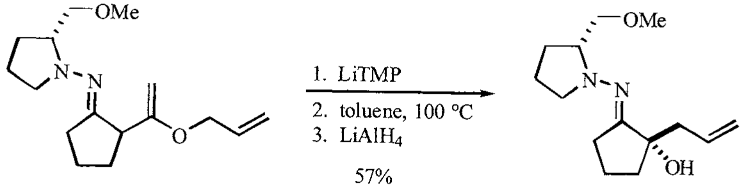
Examples:



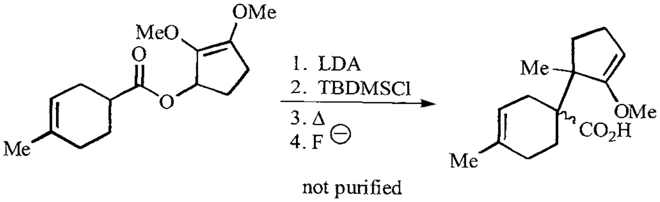
M. Koreeda, L. Brown, *Journal of Organic Chemistry* **1983**, 48, 2122



M. Tanabe, K. Hayashi, *Journal of the American Chemical Society* **1980**, 102, 862



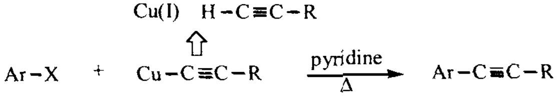
D. Enders, M. Knopp, *Tetrahedron* **1996**, 52, 5805



G. A. Kraus, P. J. Thomas, *Journal of Organic Chemistry* **1986**, 51, 503

Castro-Stephens Coupling

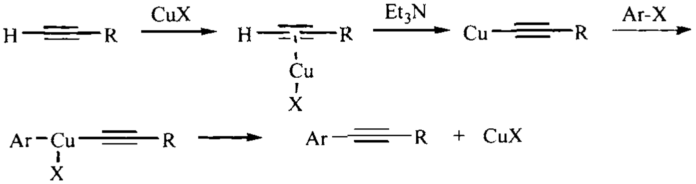
The Reaction:



$$\mathrm{Ar{-}X} + \overset{\mathrm{Cu(I)}\ \ \mathrm{H{-}C{\equiv}C{-}R}}{\mathrm{Cu{-}C{\equiv}C{-}R}} \xrightarrow[\Delta]{\text{pyridine}} \mathrm{Ar{-}C{\equiv}C{-}R}$$

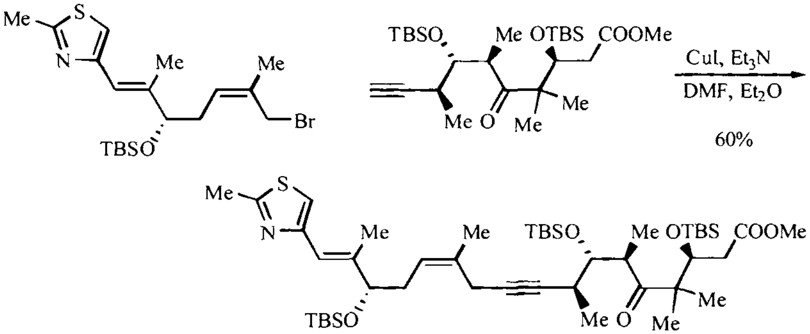
Proposed Mechanism:

See ***Alkyne Coupling***



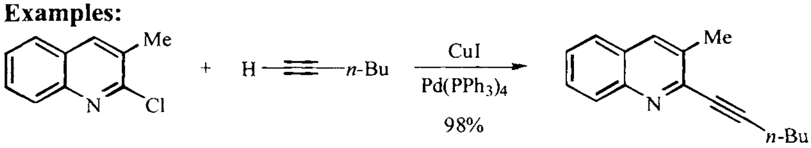
Notes:

It appears that common use of the Name now extends to halides other than Ar-X. Thus, for example:



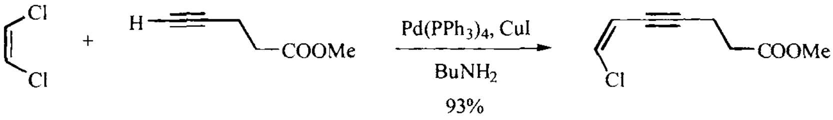
J. D. White, R. G. Carter, K. F. Sundermann, M. Wartmann, *Journal of the American Chemical Society*, **2001**, 123, 5407

Examples:

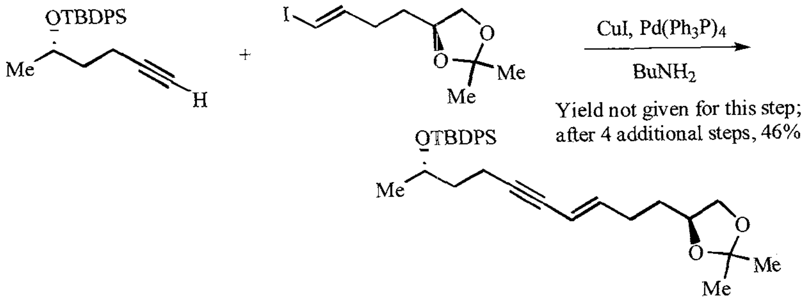


M. A. Ciufolini, J. W. Mitchell, F. Roschangar, *Tetrahedron Letters* **1996**, 37, 8281

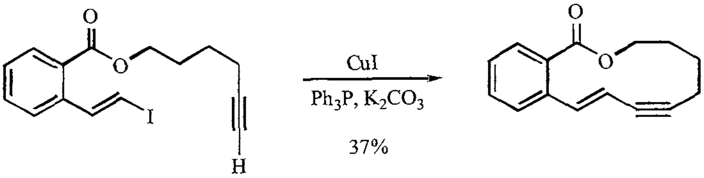
Although the authors call this reaction a ***Castro-Stephens reaction***, they point out that it is really a ***Linstrumelle modification of the Sonogashira protocol.***



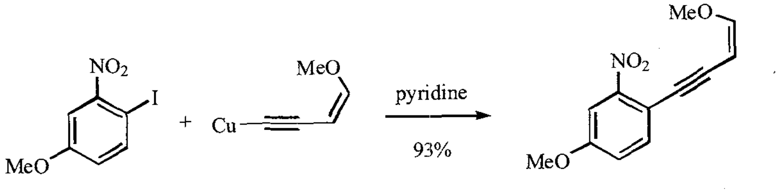
D. Guillerm, G. Linstrumelle, *Tetrahedron Letters* **1985**, 26, 3811



J. Mulzer, M. Berger, *Tetrahedron Letters*, **1998**, 39, 803



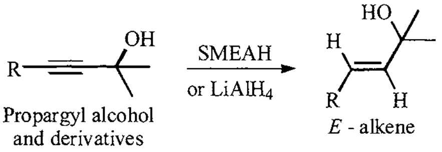
R. Garg, R. S. Coleman, *Organic Letters*, **2001**, 3, 3487



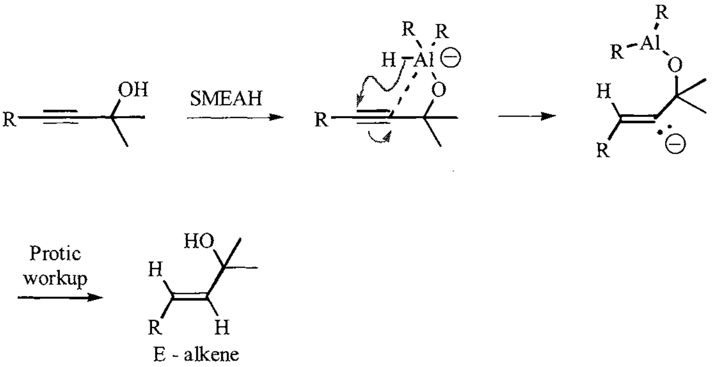
G. A. Krause, K. Frazier, *Tetrahedron Letters*, **1978**, 19, 3195

Chan Alkyne Reduction

The Reaction:

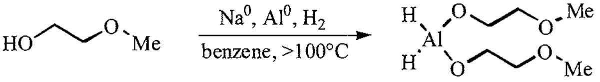


Proposed Mechanism:



Notes:

Reagent preparation:

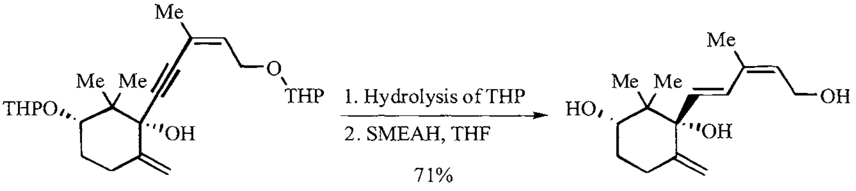


SMEAH

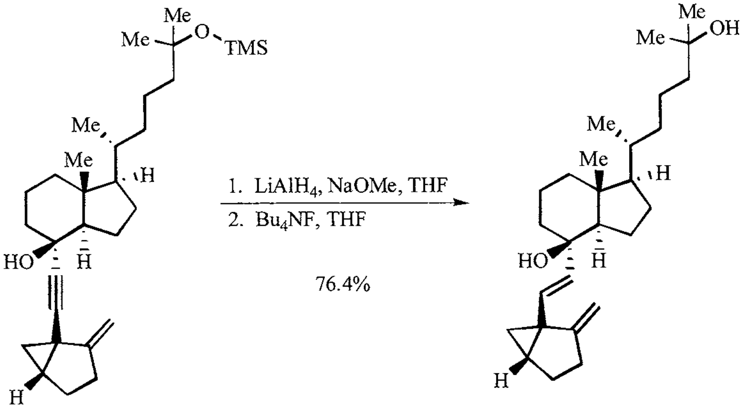
Sodium bis(2-methoxymthoxy)aluminum Hydride

The reaction bears similarity to the ***Whiting Reaction***:

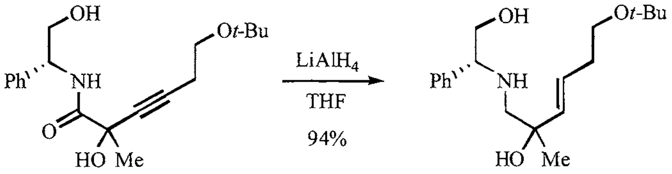
Examples:



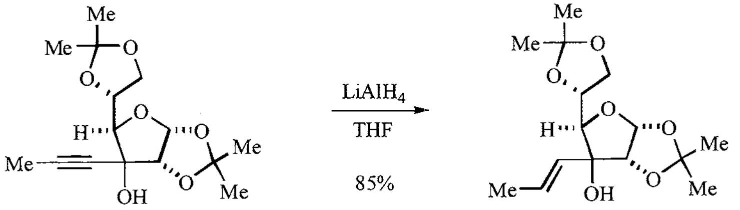
H. Yamamoto, T. Oritani, *Phytochemistry*, **1995**, 40, 1033



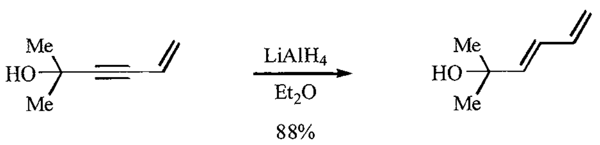
M. M. Kabat, J. Kiegiel, N. Cohen, K. Toth, P. M. Wovkulich, M. R. Uskokovic, *Journal of Organic Chemistry*, **1996**, 61, 118



C. Agami, M. Cases, F. Couty, *Journal of Organic Chemistry*, **1994**, 59, 7937



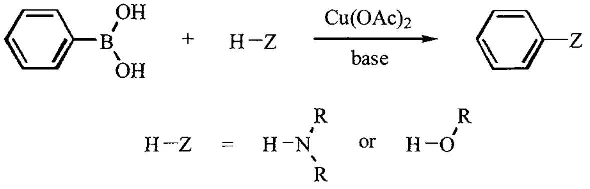
T. Eguchi, T. Koudate, K. Kakinuma, *Tetrahedron*, **1993**, 49, 4527



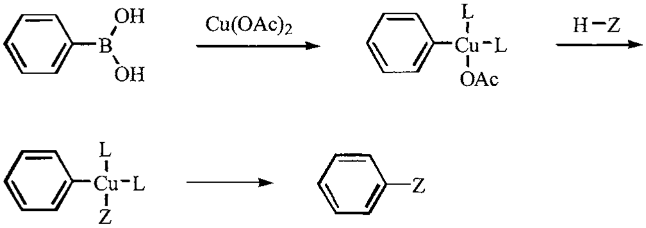
E. B. Bates, E. R. H. Jones, M. C. Whiting, *Journal of the Chemical Society*, **1954**, 1854

Chan-Lam Coupling

The Reaction:



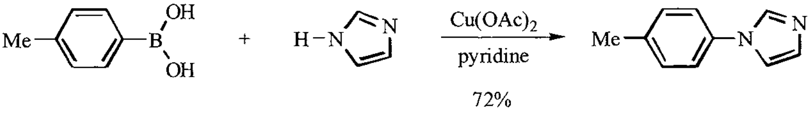
Proposed Mechanism:



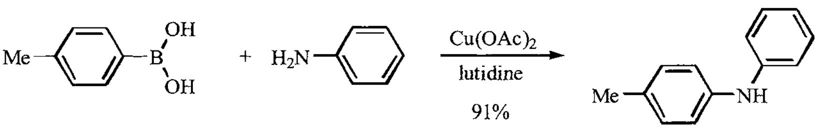
Notes:

Evans describes the possibility of a common intermediate for the ***Ullman*** and ***Chan-Lam reactions***. D. A. Evans, J. Katz, T. R. West, *Tetrahedron Letters* **1998**, 39, 2937

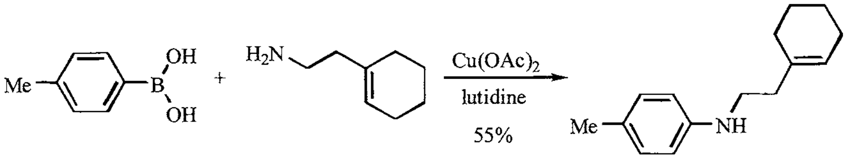
Examples:



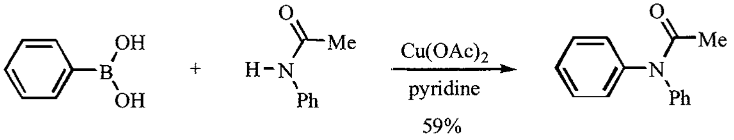
P. Y. S. Lam, C. G. Clark, S. Saubern, J. Adams, M. P. Winters, D. M. T. Chan, A. Combs, *Tetrahedron Letters* **1998**, 39, 2941

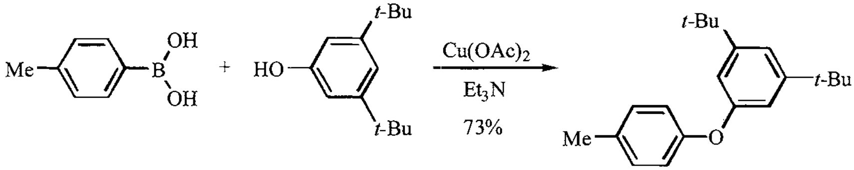


J. C. Antilla, S. L. Buchwald, *Organic Letters* **2001**, 3, 2077

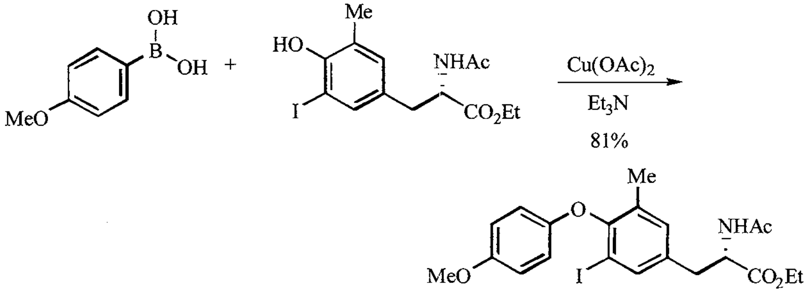


J. C. Antilla, S. L. Buchwald, *Organic Letters* **2001**, 3, 2077





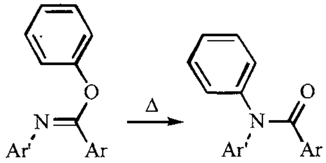
D. M. T. Chan, K. L. Monaca, R.-P. Wanag, M. P. Winters, *Tetrahedron Letters* **1998**, 39, 2933



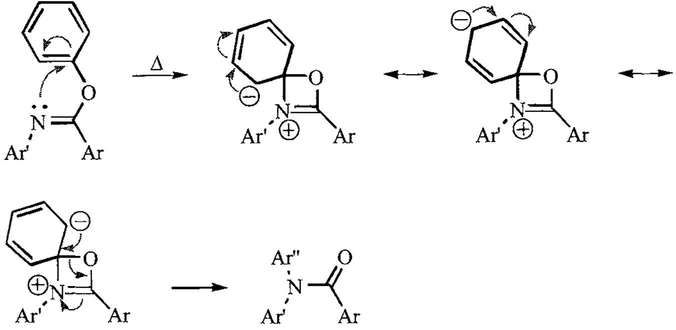
D. A. Evans, J. Katz, T. R. West, *Tetrahedron Letters* **1998**, 39, 2937

Chapman Rearrangement

The Reaction:

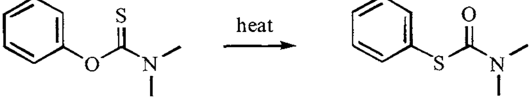


Proposed Mechanism:

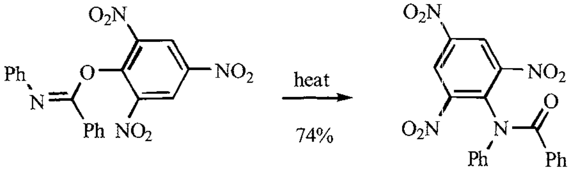


Notes:

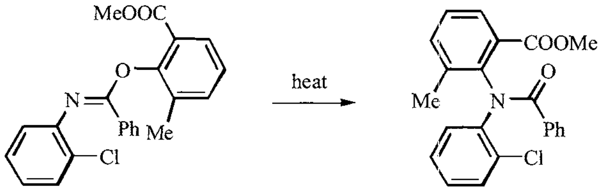
Similar to the ***Newman-Kwart Rearrangement***:



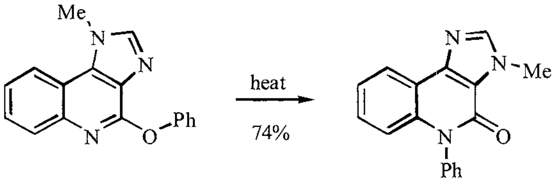
Examples:



J. D. McCullough, Jr., D. Y. Curtin, I. C. Paul, *Journal of the American Chemical Society* **1972**, 94, 874

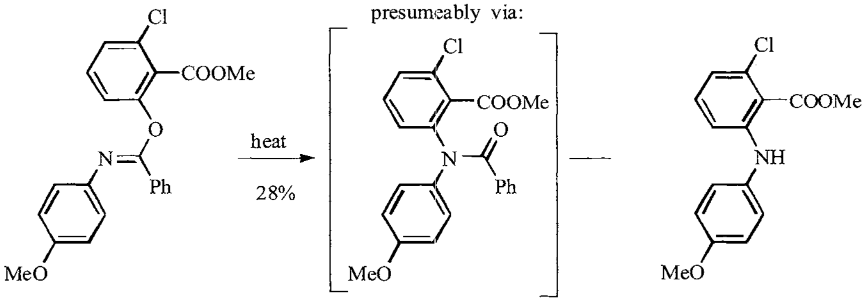


D. M. Hall, E. E. Turner, *Journal of the Chemical Society* **1945**, 694



The methyl migration is rationalized.

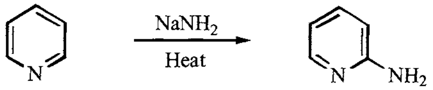
T. Kuroda, F. Zuzuki, *Tetrahedron Letters* **1992**, 33, 2027



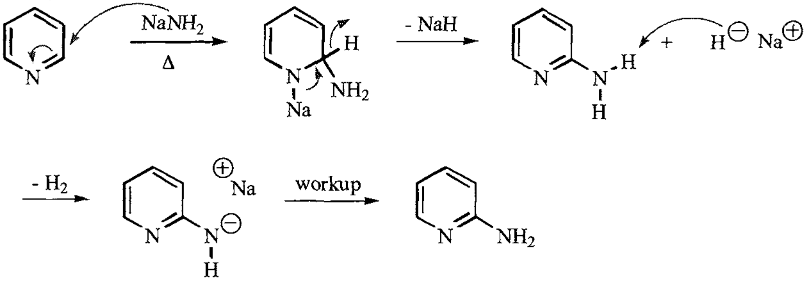
W. G. Dauben, R. L. Hodgson, *Journal of the American Chemical Society* **1950**, 72, 3479

Chichibabin Reaction

The Reaction:



Proposed Mechanism:



Notes:

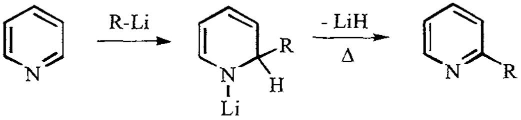
See: M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 873.

This reaction will work with other nitrogen containing heterocycles such as quinoline.

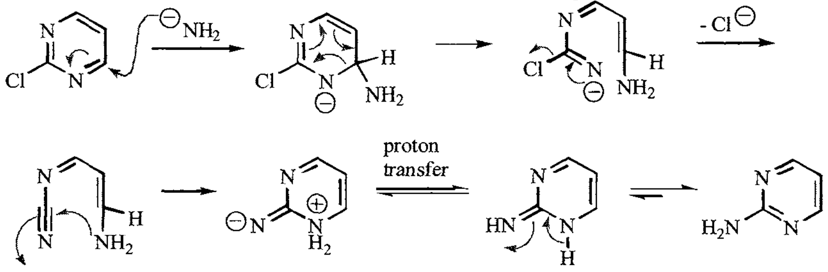
$RNH^{\ominus}$ and $R_2N^{\ominus}$ will also work

Attack at the 2- or 4- positions can leave negative charge on the ring nitrogen.

A related reaction: ***Ziegler alkylation***:

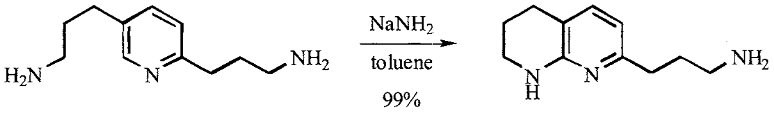


In the pyrimidine series an S_N(ANRORC) mechanism has been proposed:

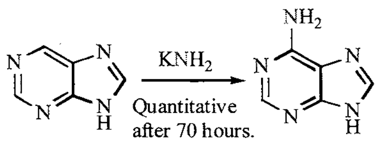


H. C. van der Plas, *Accounts of Chemical Research* **1978**, 11, 462

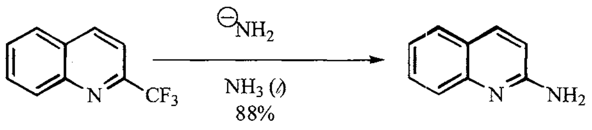
Examples:



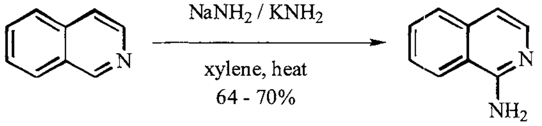
M. Palucki, D. L. Hughes, N. Yasuda, C. Yang, P. J. Reider, *Tetrahedron Letters* **2001**, 42, 6811



N. J. Kos, H. C. van der Plas, B. van Veldhuizen, *Journal of Organic Chemistry* **1979**, 44, 3140



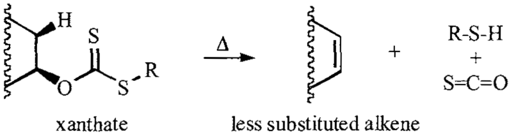
Y. Kobayashi, I. Kumadaki, S. Taguchi, Y. Hanzawa, *Tetrahedron Letters* **1970**, 11, 3901



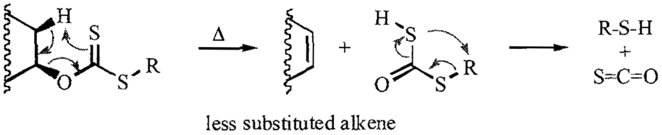
F. W. Bergstrom, H. G. Sturz, H. W. Tracy, *Journal of Organic Chemistry* **1945**, 11, 239

Chugaev Reaction

The Reaction:



Proposed Mechanism:

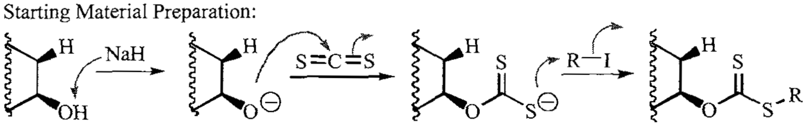


A *cis* elimination, often providing the least substituted alkene.

Notes:

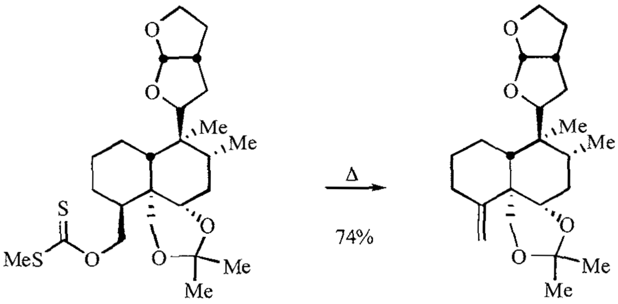
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 42-44; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1330; H. R. Nace, *Organic Reactions* **12**, 2.

Starting Material Preparation:

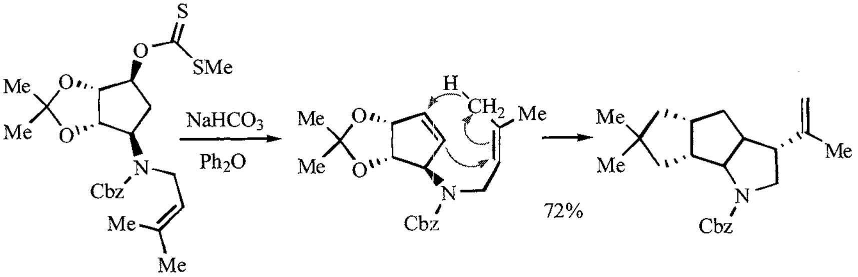


See the related ***Grieco-Sharpless Elimination***.

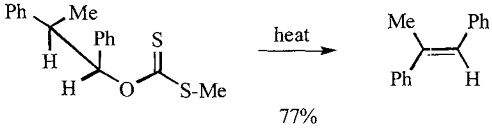
Examples:



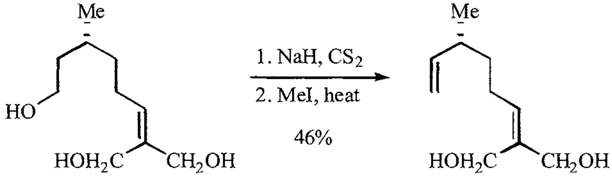
T. M. Meulemans, G. A. Stork, F. Z. Macaev, B. J. M. Jansen, A. deGroot, *Journal of Organic Chemistry* **1999**, 64, 9178



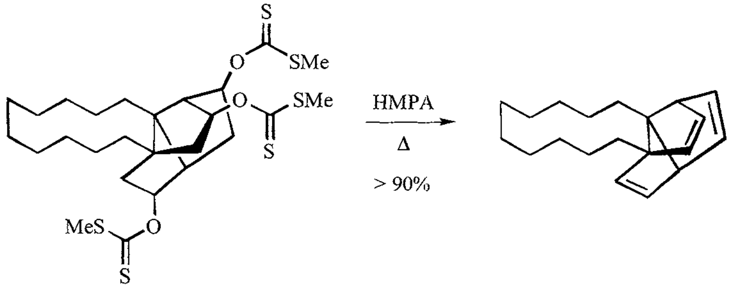
H. Nakagawa, T. Sugahara, K. Ogasawara, *Organic Letters* **2000**, 2, 3181



D. J. Cram and F. A. A. Elhafez, *Journal of the American Chemical Society* **1952**, 74, 5828



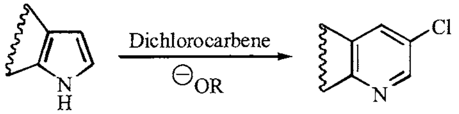
G. Cernigliano, P. Kocienski, *Journal of Organic Chemistry* **1977**, 42, 3622



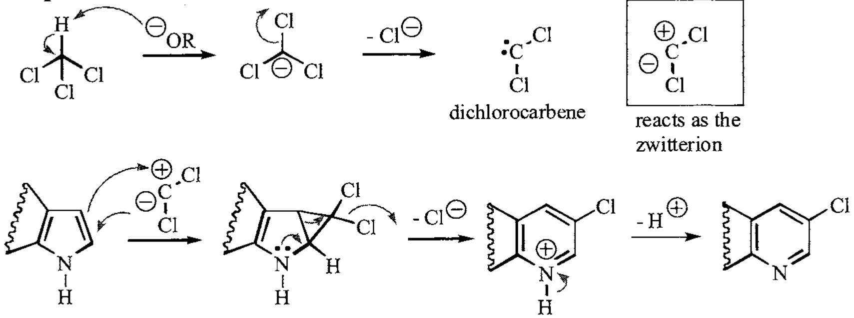
X. Fu, C. M. Cook, *Tetrahedron Letters* **1990**, 31, 3409

Ciamician-Dennstedt Rearrangement

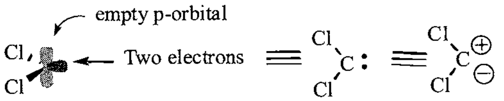
The Reaction:



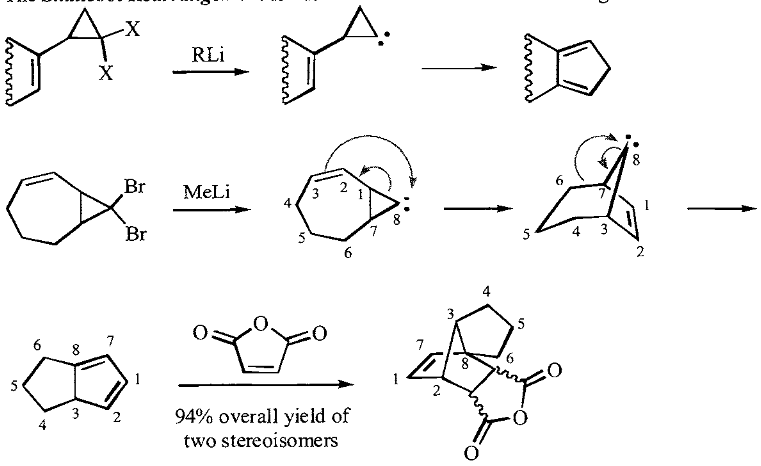
Proposed Mechanism:



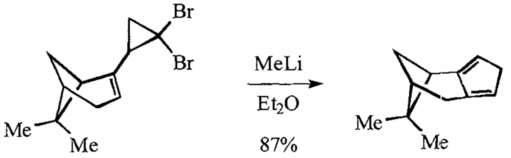
Notes:



The ***Skattebol Rearrangement*** is another dihalocarbene-based rearrangement:

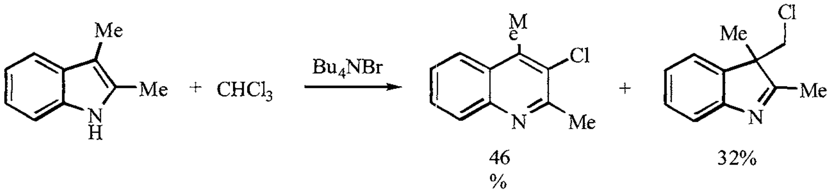


K. H. Holm, L. Skattebol, *Tetrahedron Letters* **1977**, 18, 2347

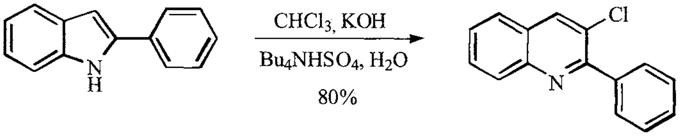


L. A. Paquette, M. Gugelchuk, M. L. McLaughlin, *Journal of Organic Chemistry* **1987**, 52, 4372

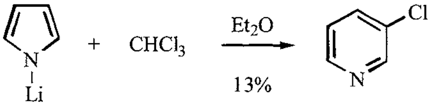
Examples:



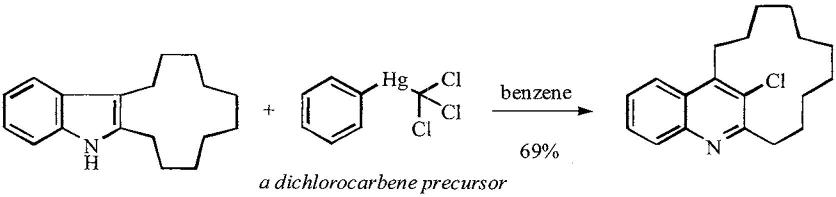
F. DeAngelis, A. Inesi, M. Feroci, R. Nicoletti, *Journal of Organic Chemistry* **1995**, 60, 445



K. C. Joshi, R. Jain, S. Arora, *Journal of the Indian Chemical Society* **1993**, 70, 567 (AN 1994:508439)



E. R. Alexander, A. B. Herrick, T. M. Roder, *Journal of the American Chemical Society* **1950**, 72, 2760

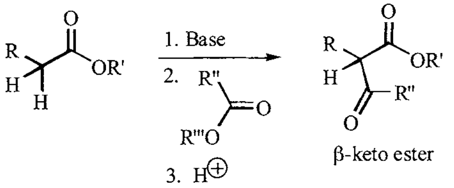


W. E. Parham, R. W. Davenport, J. B. Biasotti, *Tetrahedron Letters* **1969**, 10, 557

Ph-Hg-CX$_3$ are known as ***Seyferth Reagents***.

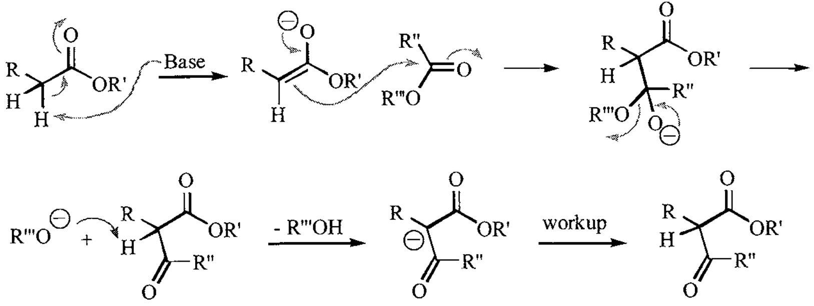
Claisen Condensation (ester attacking ester)

The Reaction:



β-keto ester

Proposed Mechanism:



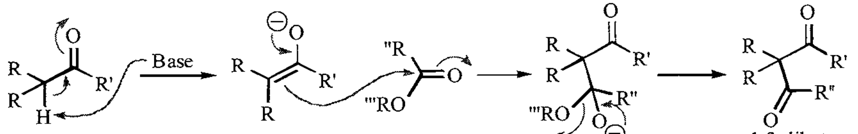
β-keto ester

Notes:

R" is usually a group that cannot form an enolate, such as a phenyl ring.

It is important to note that an equivalent of base must be used for this reaction; unlike the ***Aldol Condensation***, this cannot be used catalytically.
See: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 45-48.

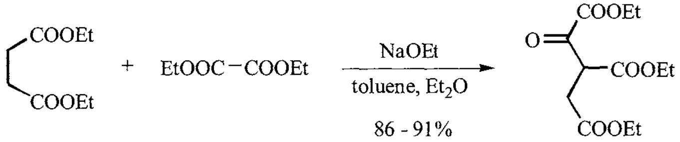
Aldehyde or ketone attacking ester



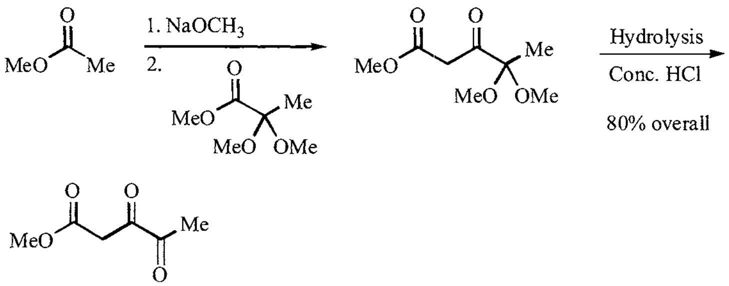
1,3-diketone

R" is usually a group that cannot form an enolate.

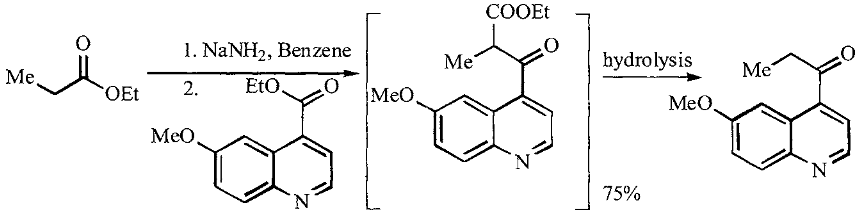
Examples:



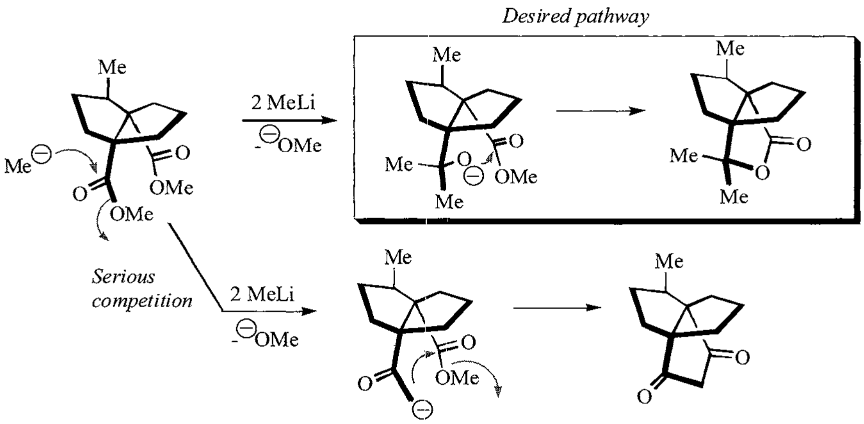
L. Friedman, E. Kosower, *Organic Syntheses*, CV3, 510



A. G. Cameron, A. T. Hewson, M. I. Osammur *Tetrahedron Letters* **1984**, 25, 2267



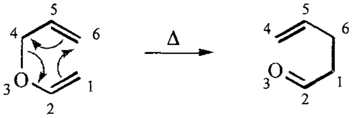
J. W. Cornforth, R. H. Cornforth, *Journal of the Chemical Society* **1948**, 93



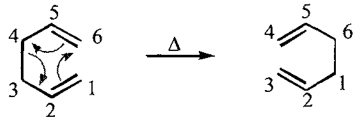
B. P. Mundy, D. Wilkening, K. B. Lipkowitz *Journal of Organic Chemistry* **1985**, 50, 5727

Claisen, Cope and Related Rearrangements

Claisen-Type Reactions:

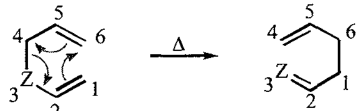


Cope-Type Reactions:



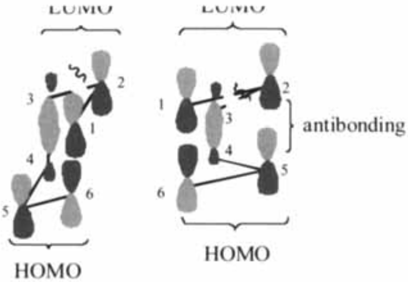
Notes:

All reactions are classified as [3,3]-sigmatropic reactions. They are orbital symmetry regulated processes.



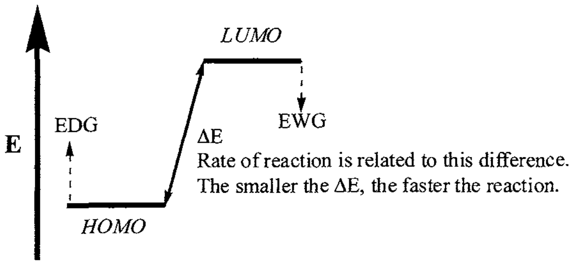
Z = C or heteroatom

By Frontier Molecular Orbital theory several important predictions can be made:
1. There will be a preferred chair transition-state for the reaction:



In the boat transition-state there is an *antibonding* interaction between C-2 and C-5.

2. Reactions will be accelerated by charged intermediates:



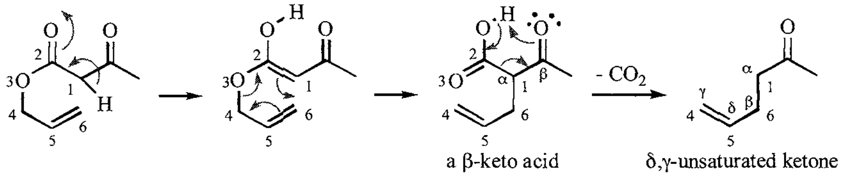
Rate of reaction is related to this difference.
The smaller the ΔE, the faster the reaction.

Claisen and Related Rearrangements

This reaction has developed a number of related protocols and variations. Some have earned sufficient recognition to act as "stand alone" reactions and will be found under their own headings in this monograph.

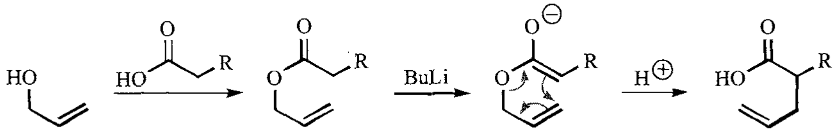
<u>Carroll Rearrangement (Kimel-Cope Rearrangement)</u>

β-keto esters can rearrange to give β-keto acids which will decarboxylate to give δ,γ-unsaturated ketones.



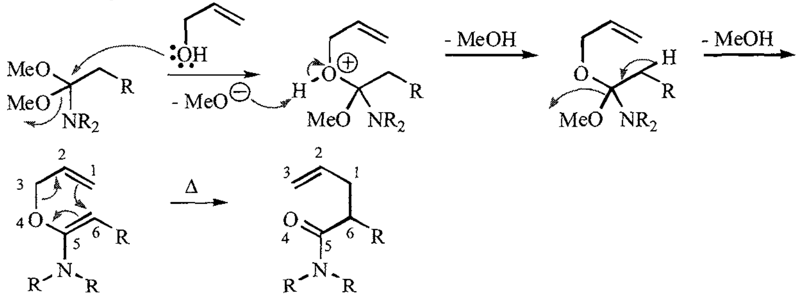
***Claisen-Arnold Reaction*:**

Enolate formation with an allyl ester can give 2-substituted carboxylic acids.



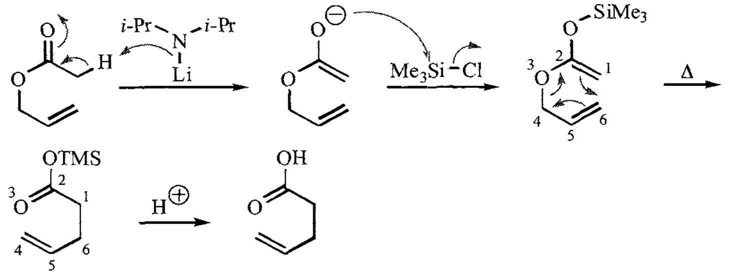
***Claisen-Eschenmoser Reaction (Eschenmoser-Claisen Rearrangement)*:**

Amides are produced after rearrangement with heating.

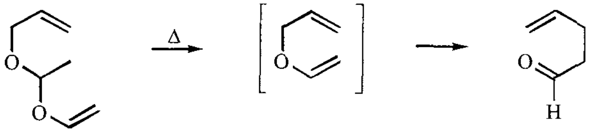


***Claisen-Ireland Reaction (Ireland-Claisen Rearrangement)*:**

Formation of a silyl enol ether will generate an allyl vinyl ether which after rearrangement can be desilylated to give a carboxylic acid.

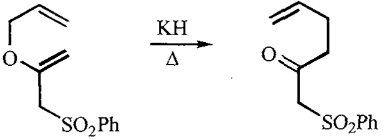


Dauben-Dietsche Rearrangement:



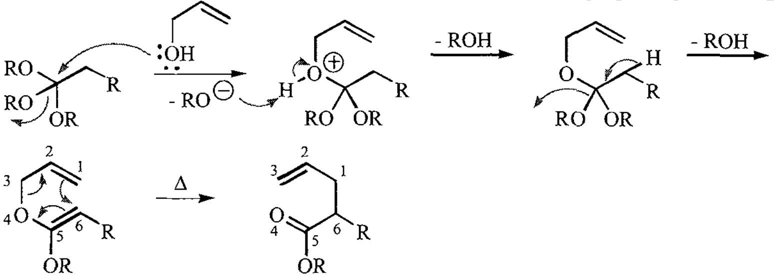
Denmark Rearrangement:

The **Claisen rearrangement** of phenyl sulfonyl substituted allyl vinyl ethers.



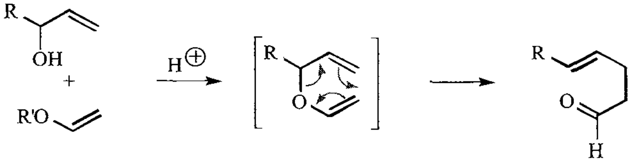
Johnson-Claisen Rearrangement (Johnson Orthoester Rearrangement)

Elimination of two equivalents of ROH after condensation between an allyl alcohol and an orthoester will provide the allyl vinyl ether which undergoes the [3,3]-sigmatropic rearrangement.



Marbet-Saucy Reaction / Variation

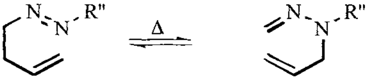
A vinyl ether and allyl alcohol will react under acidic conditions to give the allyl vinyl ether which then rearranges under the reaction conditions.



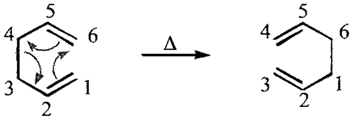
Cope and Related Reactions

Aza-Cope Rearrangement

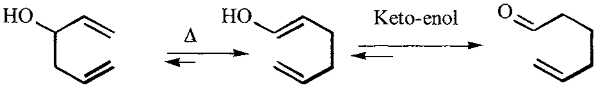
Azo-Cope Rearrangement



Cope Rearrangement

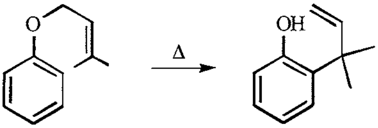


Oxy-Cope Rearrangement

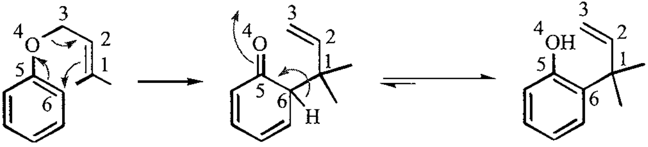


Claisen Rearrangement (allyl phenyl ethers)

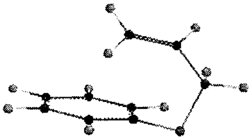
The Reaction:



Proposed Mechanism: a [3.3]-sigmatropic rearrangement



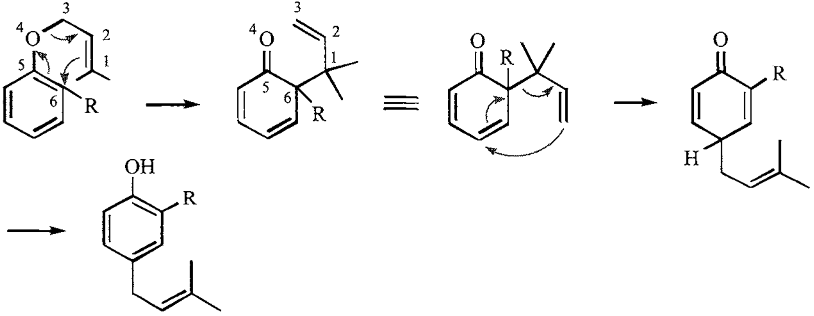
keto-enol tautomerism



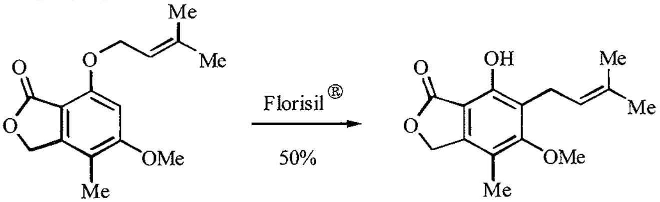
Note that the pi-system of the allyl group is readily aligned over the aromatic ring, providing a 1,5-diene motif for the sigmatropic rearrangement.

Notes:

If the ortho-positions are blocked (only one shown, below), rearrangement continues:

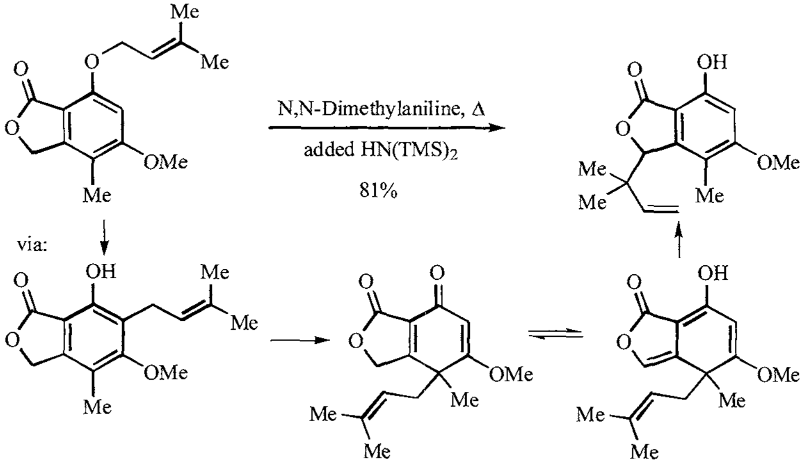


Simple [1,3]-rearrangements have been observed:

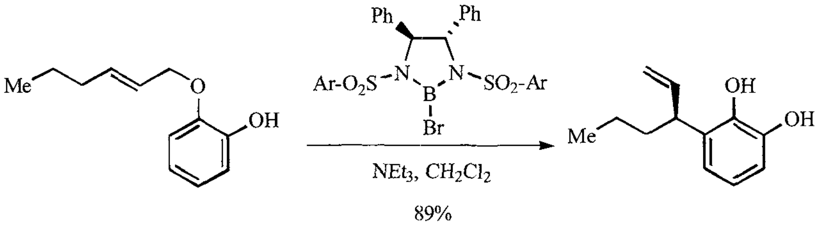


F. X. Talams, D. B. Smith, A. Cervantes, F. Franco, S. T. Cutler, D. G. Loughhead, D. J. Morgans, Jr., R. J. Weikert *Tetrahedron Letters* **1997**, 38, 4725

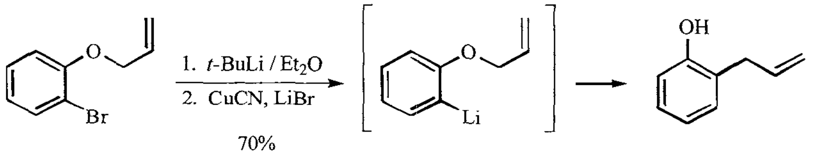
Examples:



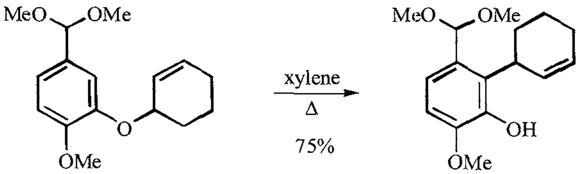
D. B. Smith, T. R. Elworthy, D. J. Morgns, Jr., J. T. Lenson, J. W. Patterson, A. Vasquez, A. M. Waltos, *Tetrahedron Letters* **1996**, 37, 21



***Reagent used for the enantioselective rearrangement**:*
(*S,S*)-2-Bromo-4,5-diphenyl-1,3-tosyl-1,3-diaza-2-borolidine
H. Ito, A. Sato, T. Taguchi, *Tetrahedron Letters* **1997**, 38, 4815



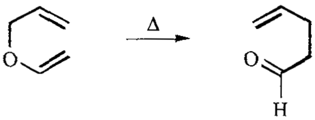
J. Barluenga, R. Sanz, F. J. Fananas, *Tetrahedron Letters* **1997**, 38, 6103



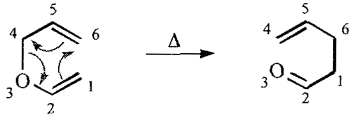
S. Lambrecht, H. J. Schaefer, R. Froehlich, M. Grehl, *Synlett*, **1996**, 283 (AN 1996:201759)

Claisen Rearrangement (allyl vinyl ethers)

The Reaction:



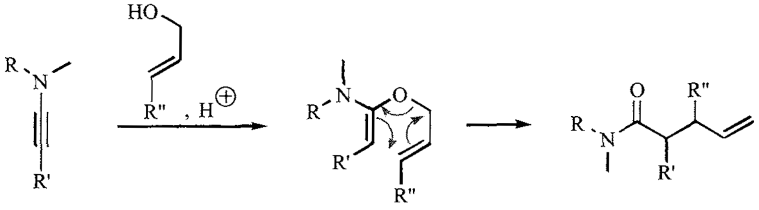
Proposed Mechanism:

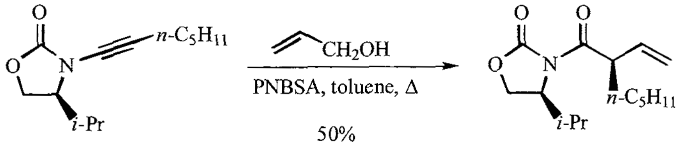


Notes:

See: ***Claisen, Cope and Related Rearrangements***

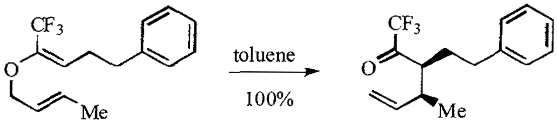
Ficini-Ynamine-Claisen Rearrangement



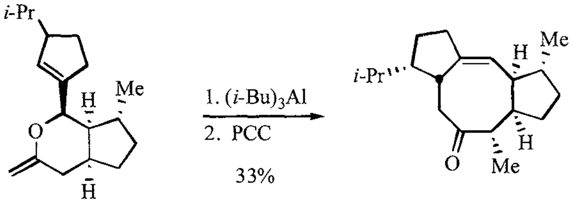


J. A. Mulder, R. P. Hsung, M. O. Frederick, M. R. Tracey, C. A. Zificsak, *Organic Letters* **2002**, 4, 1383

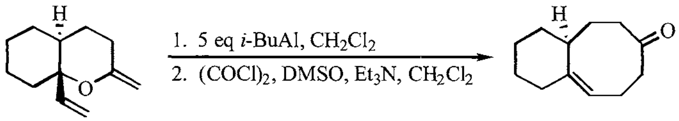
Examples:



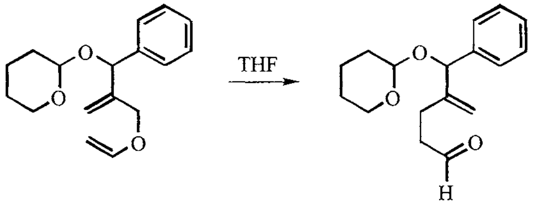
J.-P. Begue, D. Bonnet-Delpon, S.-W. Wu, A. M'Bida, T. Shintani, T. Nakai, *Tetrahedron Letters*, **1994**, 35, 2907



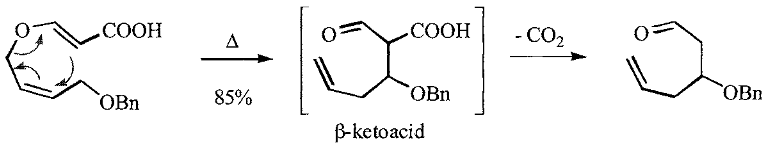
L. A. Paquette, S.-Q. Sun, D. Friedrich, P. G. Savage, *Journal of the American Chemical Society* **1997**, 119, 8438



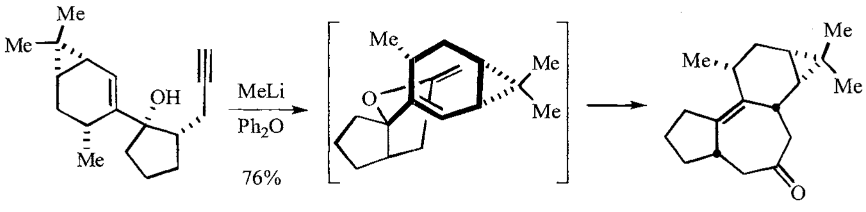
C. M. G. Philippo, V. Nha Huu, L. A. Paquette, *Journal of the American Chemical Society* **1991**, 113, 2762



Y. Masuyama, Y. Nimura, Y. Jurusu, *Tetrahedron Letters* **1992**, 33, 6477



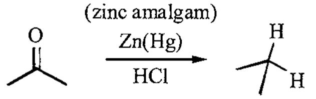
E. Marotta, P. Righi, G. Rosini, *Organic Letters* **2000**, 2, 4145



T. V. Ovaska, S. E. Reisman, M. A. Flynn, *Organic Letters* **2001**, 3, 115

Clemmensen Reduction

The Reaction:

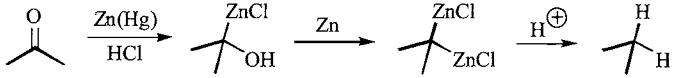


Aldehydes and Ketones

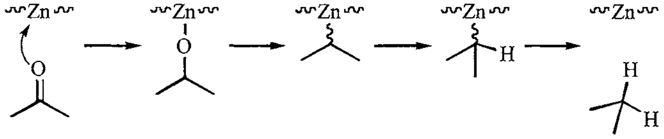
Proposed Mechanism:

This mechanism is not yet resolved. There are a number of possibilities:

1.



2.

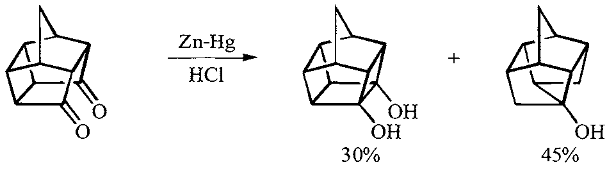


Notes:

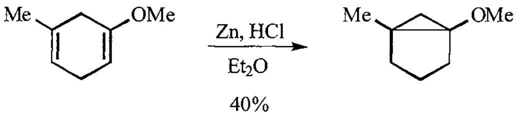
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 52-53; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1547; E. L. Martin, *Organic Reactions* **1**, 7; E. Vedejs, *Organic Reactions* **22**, 3.

Other mechanistic interpretations:
Zn-carbene: J. Burdon, R. C. Price, *Chemical Communications* **1986**, 893
One electron transfer: M. L. DiVona, V. Ruanati, *Journal of Organic Chemistry* **1991**, 56, 4269

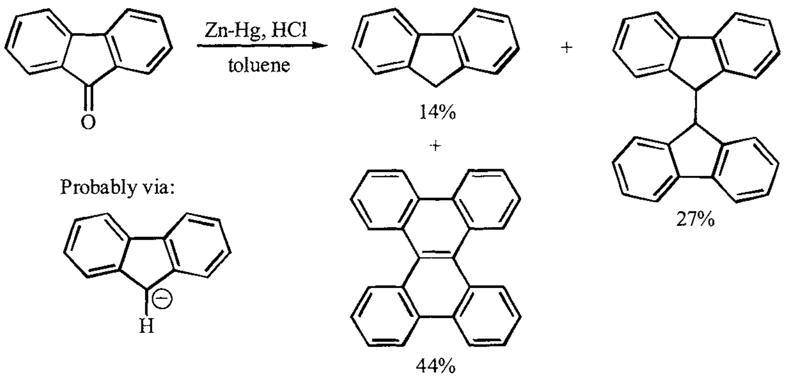
Examples:



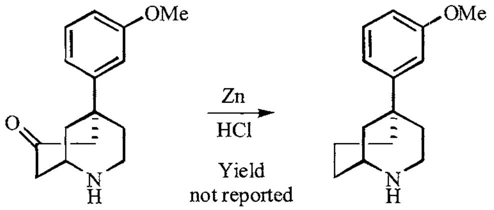
F. J. C. Martins, L. Fourie, H. J. Venter, P. L. Wessels *Tetrahedron* **1990**, 46, 623



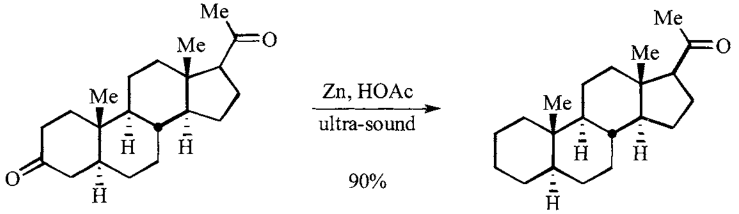
I. Elphimoff-Felkin, P. Sarda, *Tetrahedron Letters* **1983**, 24, 4425



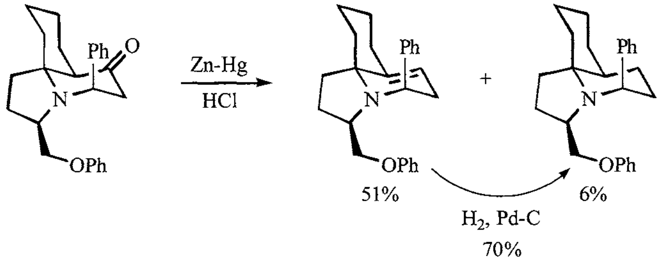
S. K. Talapatra, S. Chakrabarti, A. K. Mallik, B. Talapatra, *Tetrahedron* **1990**, 46, 6047



J. B. Thomas, K. M. Gigstad, S. E. Fix, J. P. Burgess, J. B. Cooper, S. W. Mascarella, B. E. Cantrell, D. M. Zimmerman, F. I. Carroll, *Tetrahedron Letters* **1999**, 40, 403



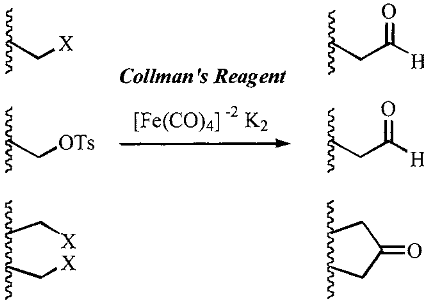
J. A. R. Salvador, M. L. SaeMelo, A. S. Campos Neves *Tetrahedron Letters* **1993**, 34, 361



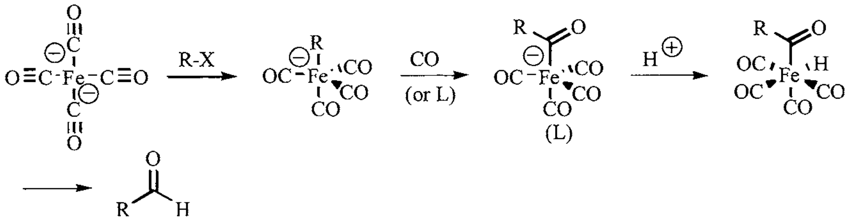
K. M. Werner, J. M. de los Santos, S. M. Weinreb, M. Shang, *Journal of Organic Chemistry* **1999**, 64, 686

Collman Carbonylation Reaction

The Reaction



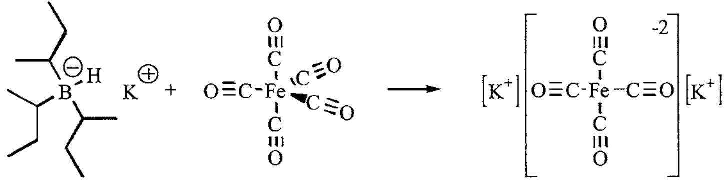
Proposed Mechanism:



J. P. Collman, *Accounts of Chemical Research* **1975**, 8, 342

Notes:

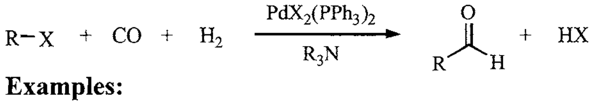
Reagent preparation:



K- Selectride

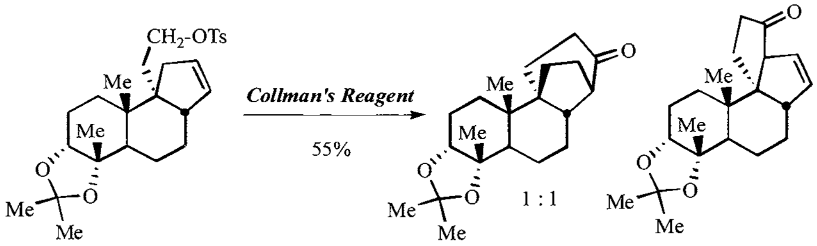
Collman's Reagent

For an alternative approach: A. Schoenberg, R. F. Heck, *Journal of the American Chemical Society* **1974**, 96, 7761

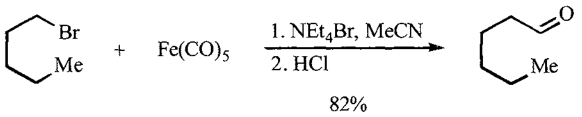


$$R{-}X + CO + H_2 \xrightarrow[R_3N]{PdX_2(PPh_3)_2} RCHO + HX$$

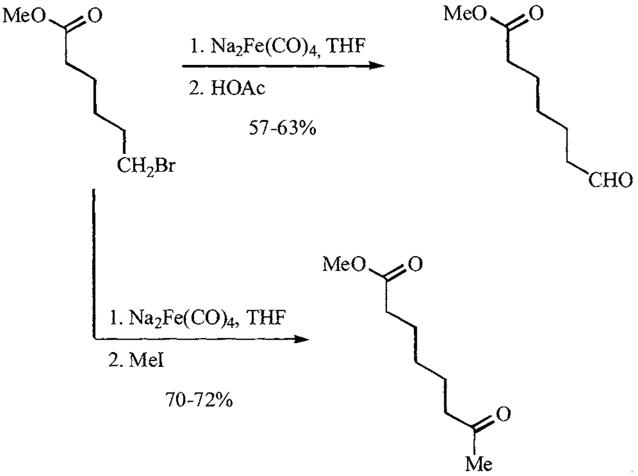
Examples:



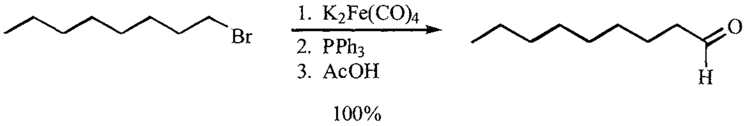
D. Bankston, F. Fang, E. Huie, S. Xie, *Journal of Organic Chemistry* **1999**, 64, 3461



K. Yoshida, H. Kuwata, *Journal of the Chemical Society, Perkin Transactions 1* **1996**, 1873



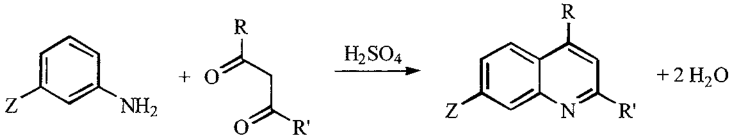
R. G. Finke, T. N. Sorrel, *Organic Synthesis* CV6, 807



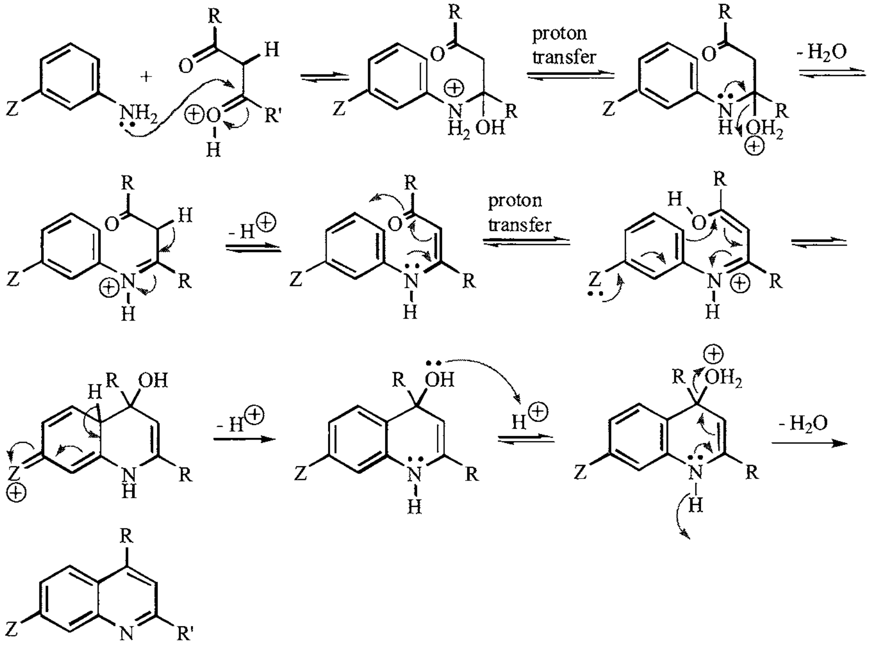
J. A. Gladysz, W. Tam, *Journal of Organic Chemistry* **1978**, 43, 2279

Combes Quinoline Synthesis

The Reaction:



Proposed Mechanism:

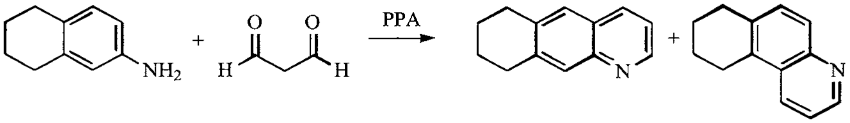


Notes:

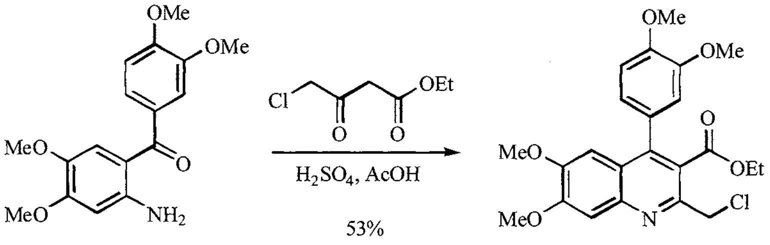
The rate of cyclization is enhanced when Z = EDG. G. R. Newkome, W. W. Paudler, *Contemporary Heterocyclic Chemistry*, John Wiley and Sons, New York, 1982, p. 203

J. L. Born, *Journal of Organic Chemistry* **1972**, 37, 3952 provides mechanistic insight based on deuterium incorporation.

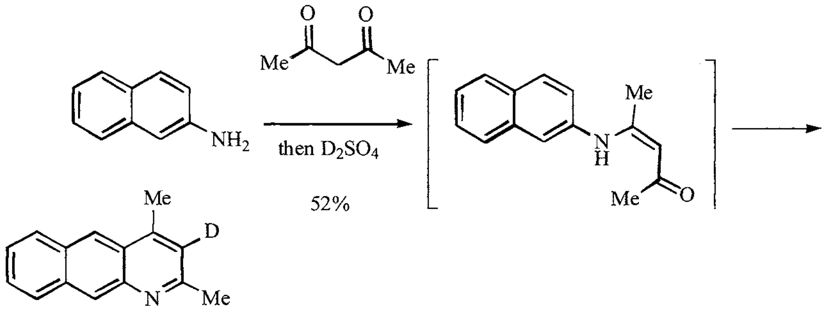
Examples:



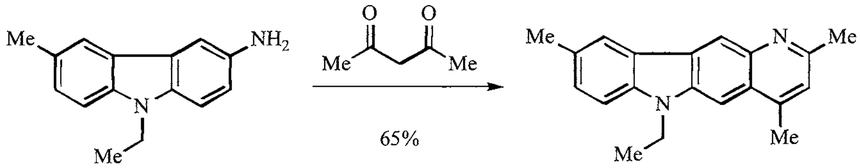
L. Takeuchi, M. Ushida, Y. Hamada, T. Yuzure, H. Suezawa, M. Hirota, *Heterocycles* **1995**, 41, 2221 (AN 1996:201759)



A. Baba, N. Kawamura, H. Makino, Y. Ohta, S. Taketome, T. Sohda, *Journal of Medicinal Chemistry* **1996**, 39, 5176



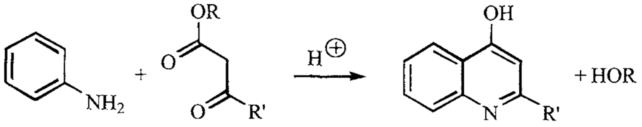
J. L. Born, *Journal of Organic Chemistry* **1972**, 37, 3952



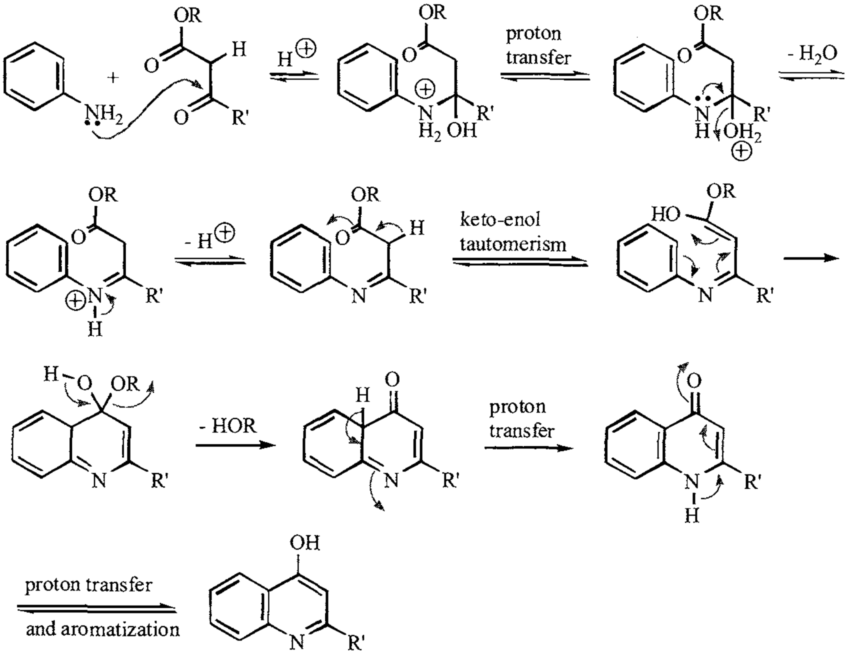
J.-C. Perche, G. Saint-Ruf, N. P. Buu-Hoi, *Journal of the Chemical Society Perkin Transactions 1* **1972**, 260

Conrad-Limpach Reaction

The Reaction:



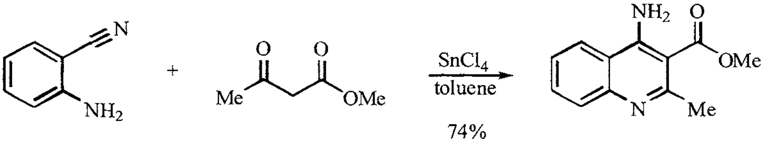
Proposed Mechanism:



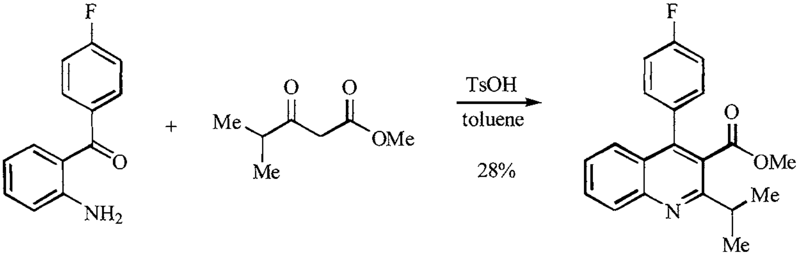
Notes:

See the very similar ***Knorr Quinoline Reaction***, conducted with the same reagents at elevated temperatures.

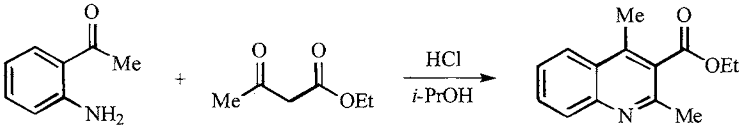
Examples:



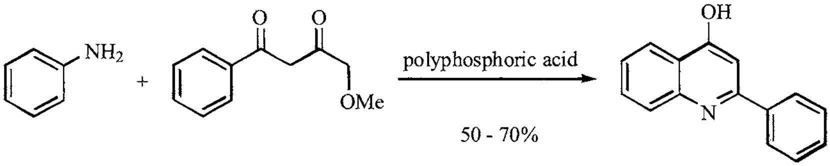
A. C. Veronese, R. Callegari, D. F. Morelli, *Tetrahedron* **1995**, 51, 12227



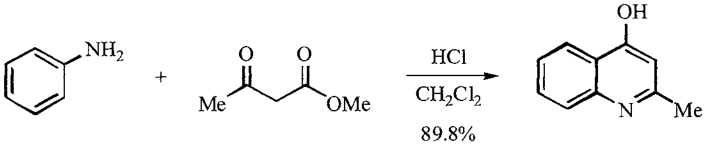
D. R. Sliskovic, J. A. Picard, W. H. Roark, B. D. Roth, E. Ferguson, B. R. Krause, R. S. Newton, C. Sekerke, M. K. Shaw, *Journal of Medicinal Chemistry* **1991**, 34, 267



L. A. Bastiaansen, J. A. M. V. Schijndel, H. M. Buck, *Organic Preparations and Procedures International* **1988**, 20, 102 (AN 1998:510222)



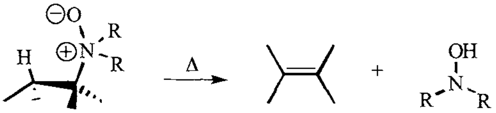
B. Staskun, S. S. Isrealstam, *Journal of Organic Chemistry* **1961**, 26, 3191



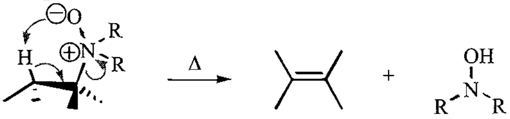
C. E. Kaslow, M. M. Marsh, *Journal of Organic Chemistry* **1947**, 12, 456

Cope Elimination (Reaction)

The Reaction:



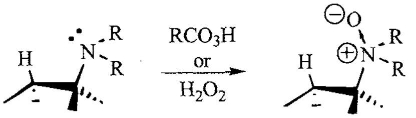
Proposed Mechanism:



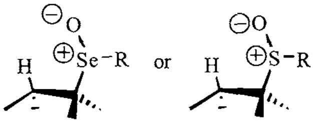
Notes:

See: M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1322-1326; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 54-56; A. C. Cope, E. R. Trumbull, *Organic Reactions* **11**, 5.

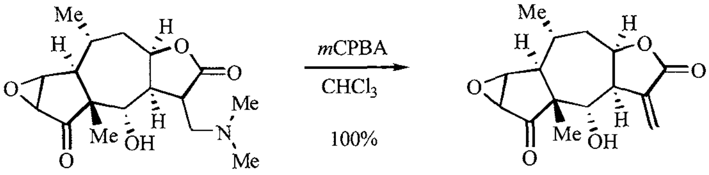
Starting Material Preparation:



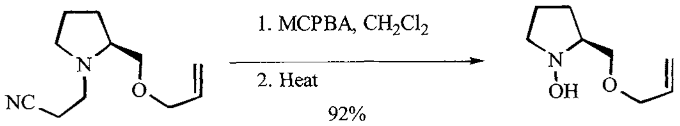
Alternate Starting Materials:



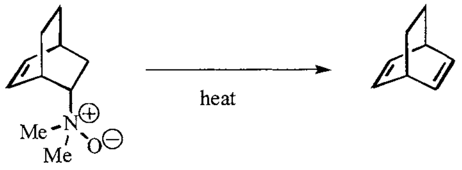
Examples:



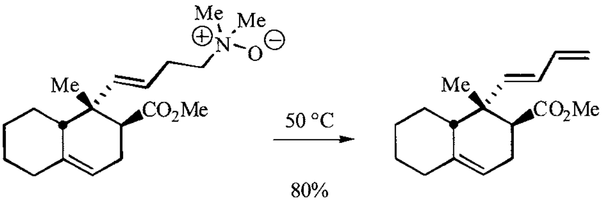
K.-H. Lee, S.-H. Kim, H. Furukawa, C. Piantadosi, E.-S. Huang, *Journal of Medicinal Chemistry* **1975**, 18, 59



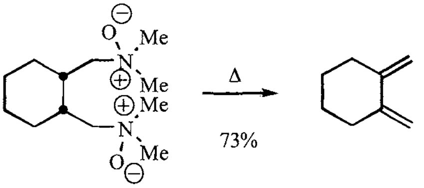
I. A. O'Neil, E. Cleator, V. E. Ramos, A. P. Chorlton, D.J. Topolczay, *Tetrahedron Letters* **2004**, 45, 3655



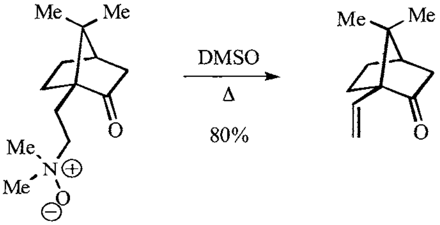
C. A. Grob, H. Kny, A. Gagneux, *Helvetica Chimica Acta* **1957**, 40, 130 (AN 1958:20977)



E. J. Corey, M. C. Desai, *Tetrahedron Letters* **1985**, 5747



L. D. Quin, J. Leimert, E. D. Middlemass, R. W. Miller, A. T. McPhail, *Journal of Organic Chemistry* **1979** 44, 3496



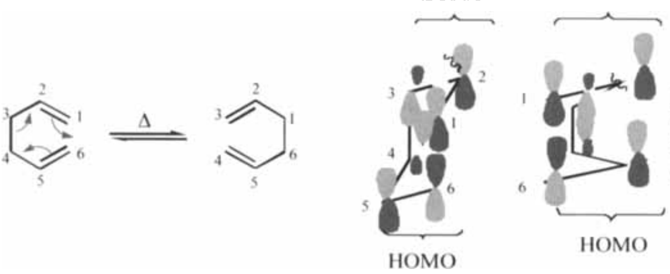
A. G. Martinez, E. T. Vilar, A. G. Fraile, S. de la Moya Cereo, B. L. Maroto, *Tetrahedron: Asymmetry* **2002**, 13, 17

Cope Rearrangement

The Reaction:

Proposed Mechanism:

The preferred chair transition state geometry by FMO theory:



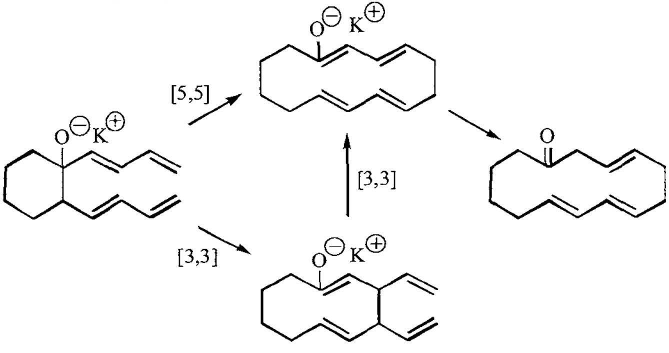
In the boat T.S. there is an *antibonding* interaction between C-2 and C-5.

T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 56-59.

Notes:

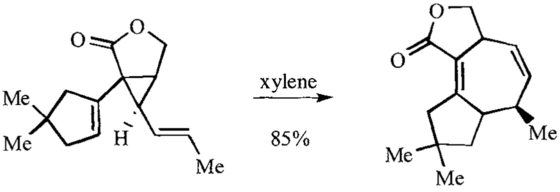
See ***Claisen, Cope and Related Rearrangements***.

An interesting study of competing pathways:

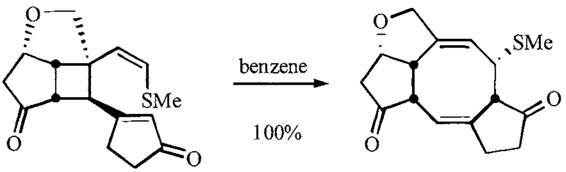


P. A. Wender, R. J. Ternansky, S. McN. Sieburth, *Tetrahedron Letters* **1985**, 26, 4319

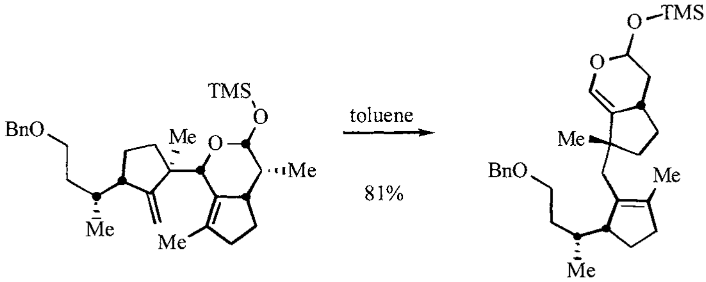
Examples:



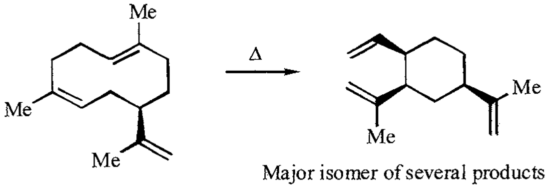
H. M. L. Davies, B. D. Doan, *Tetrahedron Letters* **1996**, 37, 3967



G. Jomme, F. Orsini, M. Resmini, M. Sisti, *Tetrahedron Letters* **1991**, 32, 6969



N. Kato, H. Takeshita, S. Tanaka, H. Kataoka, *Journal of the Chemical Society Perkin: Transactions 1* **1989**, 1833

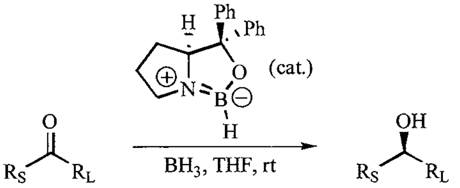


Major isomer of several products formed

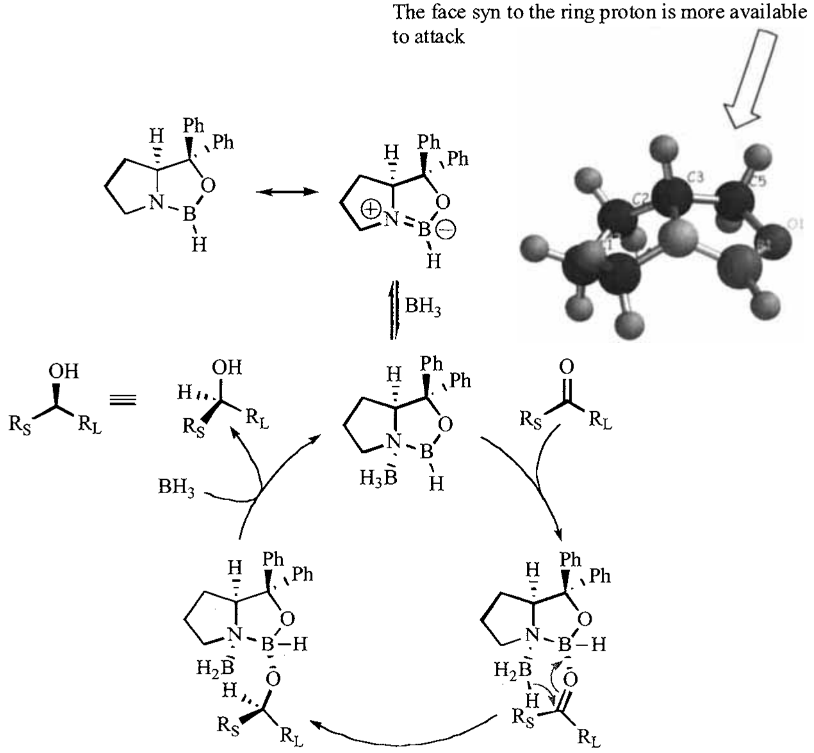
A. M. Adio, C. Paul, P. Kloth, W. A. König, *Phytochemistry* **2002**, 65, 199

Corey-Bakshi-Shibata (CBS Reduction)

The Reaction:



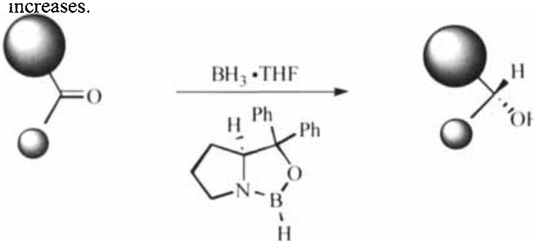
Proposed Mechanism:


The face syn to the ring proton is more available to attack

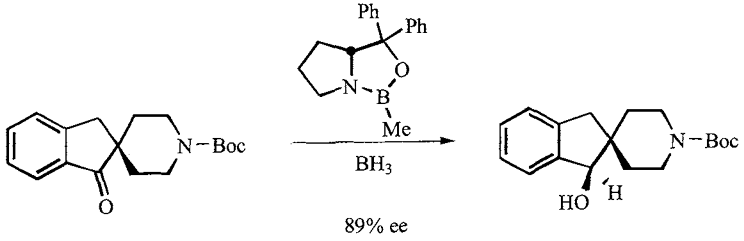
Notes:

For a discussion of the reaction, see D. J. Mathre, I. Shinkai, *Encyclopedia of Reagents for Organic Synthesis,* John Wiley and Sons, Inc., NewYork, 1995, 7, 4767

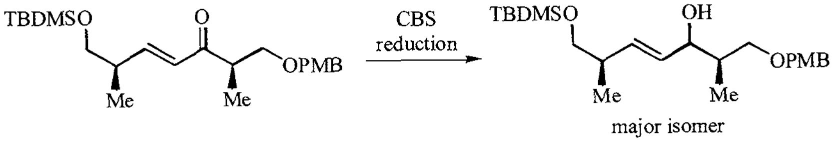
Enatioselectivity for the reduction improves as the size differential of the groups on the carbonyl increases.



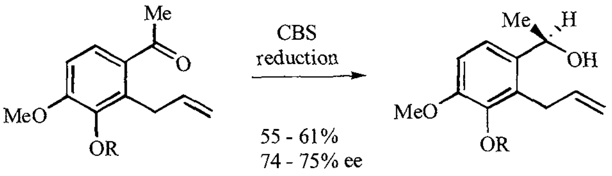
Examples:



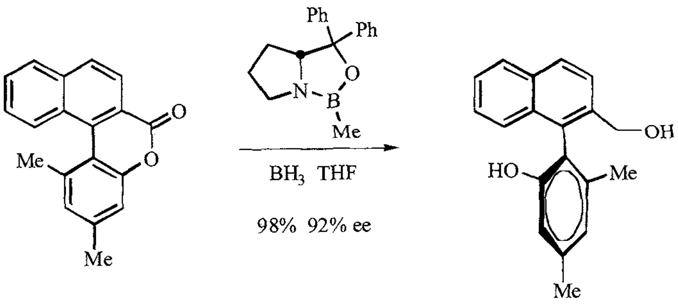
T. Takemoto, K. Nakajima, Y. Iio, M. Tamura, T. Nishi, *Tetrahedron Asymmetry* **1999**, 10, 1787



J. Mulzer, M. Berger, *Tetrahedron Letters* **1998**, 39, 803



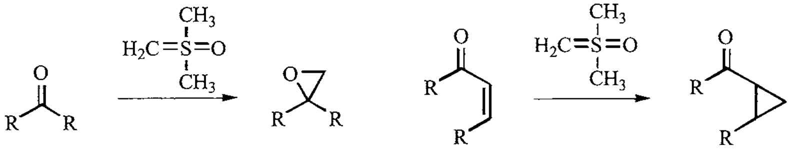
C. B. de Koning, R.-G. F. Giles, I. R. Green, N. M. Jahed, *Tetrahedron Letters* **2002**, 43, 4199



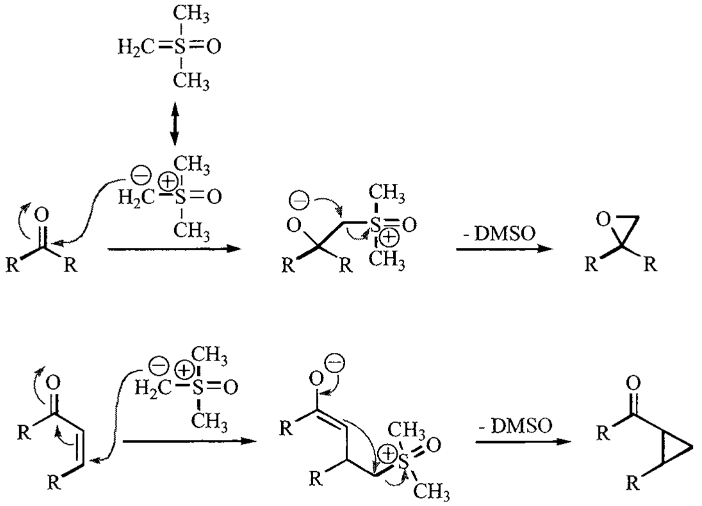
G. Bringmann, M. Breuning, P. Henschel, J. Hinrichs, *Organic Syntheses*, 79, 72

Corey-Chaykovsky Reaction

The Reaction:



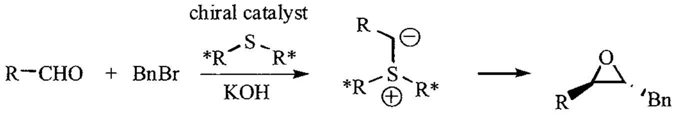
Proposed Mechanism:



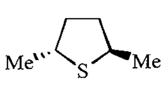
Notes:

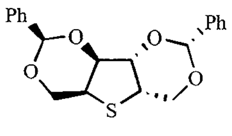
See: ***Corey-Chaykovsky Reagent***.

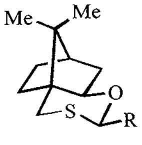
A chiral approach: See V. K. Aggarwal C. L. Winn, *Accounts of Chemical Research* **2004**, 37, 611



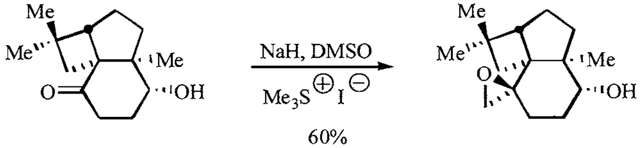
Examples of chiral sulfide catalysts:



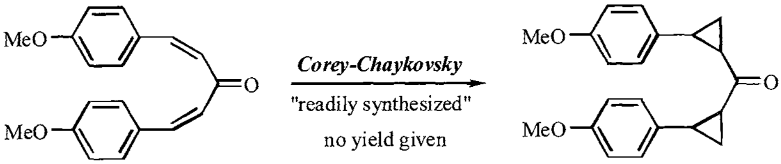




Examples:

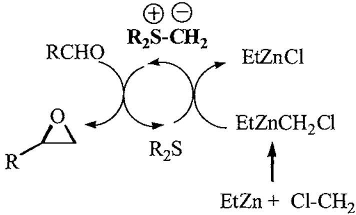


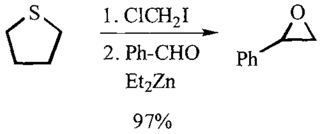
C. F. D. Amigo, I. G. Collado, J. R. Hanson, R. Hernandez-Galan, P. B. Hitchcock, A. J. Macıas-Sanchez, D. J. Mobbs, *Journal of Organic Chemistry* **2001**, 66, 4327



K. Hantawong, W. S. Murphy, N. Russell, D. R. Boyd, *Tetrahedron Letters* **1984**, 25, 999

A novel-in-situ preparation of an epoxidation reaction (***Simmons-Smith Epoxidation***):

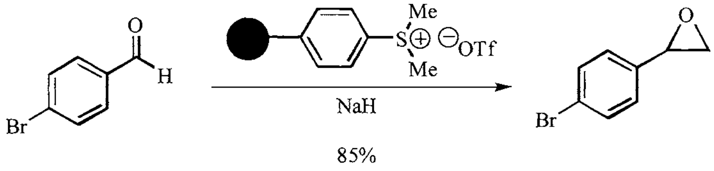




This reaction is useful for base-sensitive aldehydes; no epimerization.

V. K. Aggarwal, M. P. Coogan, R. A. Stenson, R. V. H. Jones, R. Fieldhouse, J. Blacker, *European Journal of Organic Chemistry* **2002**, 319

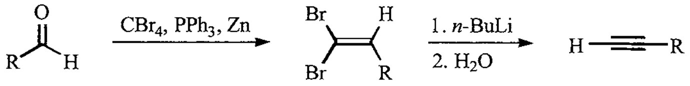
A polymer-bound reagent:



M. K. W. Choi, P. H. Toy, *Tetrahedron* **2004**, 60, 2875

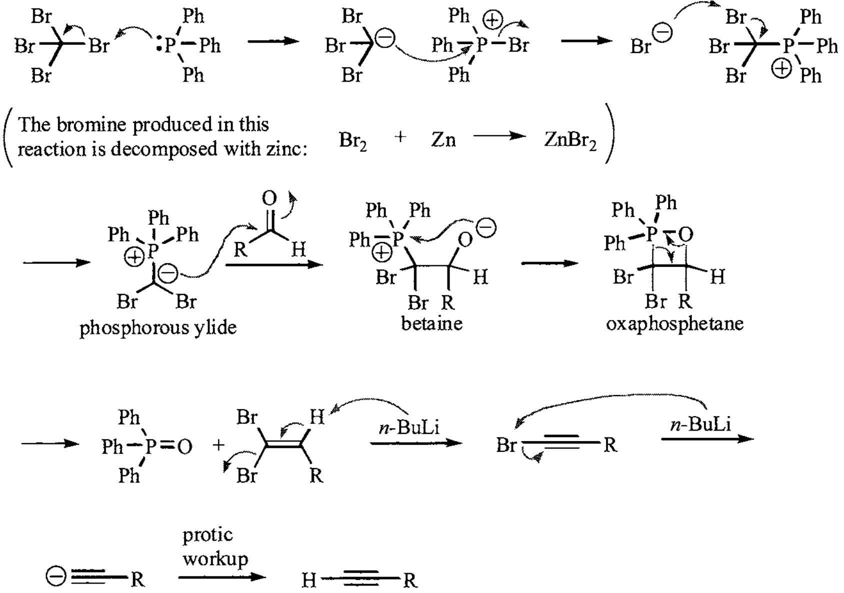
Corey-Fuchs Reaction

The Reaction:



E. J. Corey, P. L. Fuchs, *Tetrahedron Letters* **1972**, 36, 3769

Proposed Mechanism:



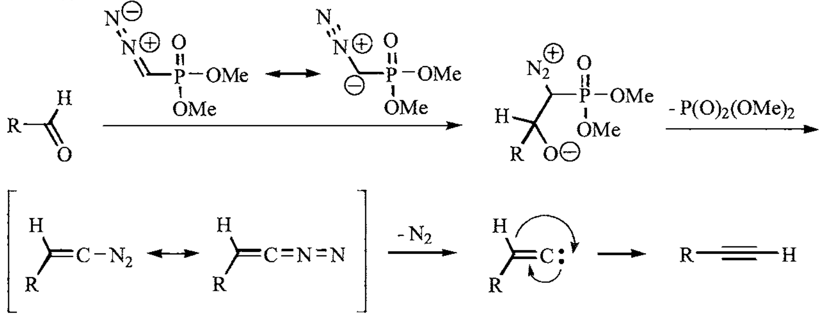
(The bromine produced in this reaction is decomposed with zinc: $Br_2 + Zn \rightarrow ZnBr_2$)

Notes:

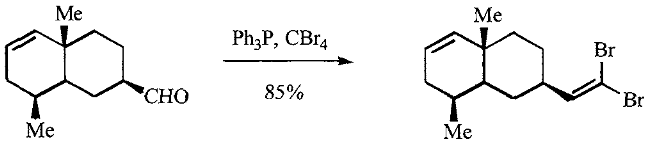
This is an alkyne-analog of the ***Wittig reaction***. Since organocopper chemistry finds utility in converting the C-Br bond to other alkyl groups, we show only the first part of the transformation in most examples.

See: ***Fritsch-Buttenberg-Wiechell Rearrangement.***

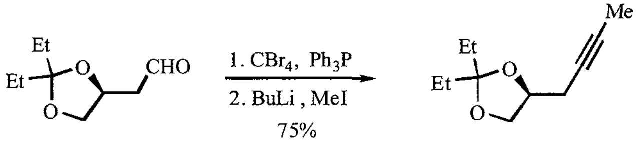
The ***Seyferth Protocol:*** is another method for the conversion:



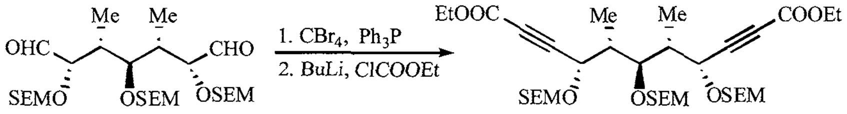
Examples:



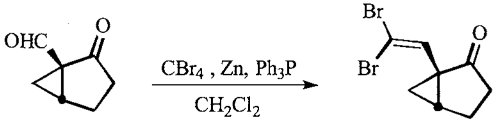
Y. Mizuno, R. Mori, H. Irie, *Journal of the Chemical Society, Perkin Transactions 1* **1982**, 2849



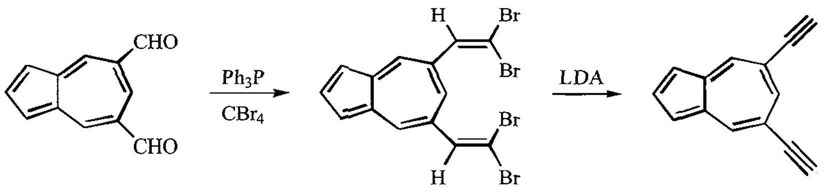
A. B. Smith, S. S.-Y. Chen, F. C. Nelson, J. M. Reichert, B. A. Salvatore, *Journal of the American Chemical Society* **1995**, 117, 12013



It was reported that these were just two of nice steps with average yield of 90%
W. C. Still, J. C. Barrish, *Journal of the American Chemical Society* **1983**, 105, 2487



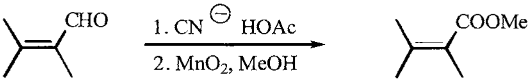
W. H. Okamura, G.-D. Zhu, D. K. Hill, R. J. Thomas, K. Ringe, D. B. Borchardt, A. W. Norman, L. J. Mueller, *Journal of Organic Chemistry* **2002**, 67, 1637



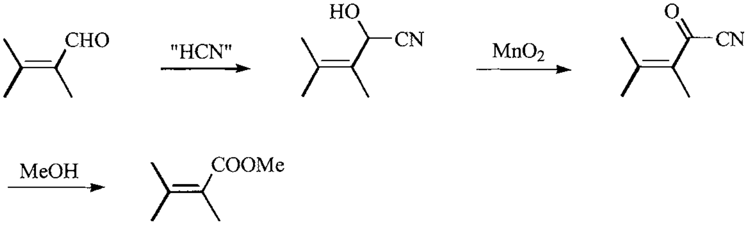
K. H. H. Fabian, A. H. M. Elwahy, K. Hafner, *Tetrahedron Letters* **2000**, 41, 2855

Corey-Gilman-Ganem Oxidation

The Reaction:

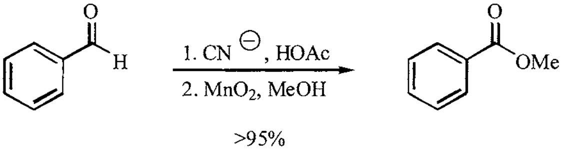


Proposed Mechanism:

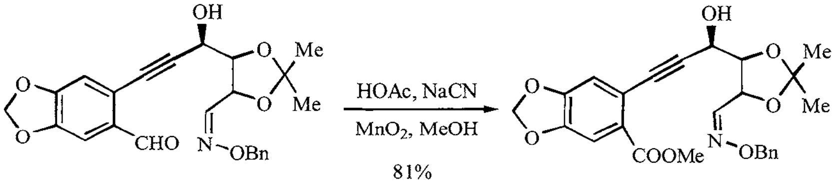


E. J. Corey, N. W. Gilman, B. E. Ganem, *Journal of the American Chemical Society* **1968**, 90, 5616

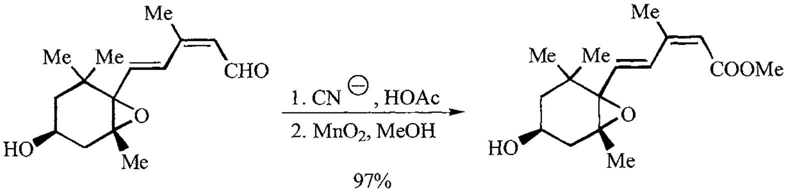
Examples:



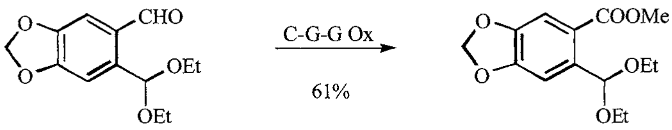
E. J. Corey, N. W. Gilman, B. E. Ganem, *Journal of the American Chemical Society* **1968**, 90, 5616



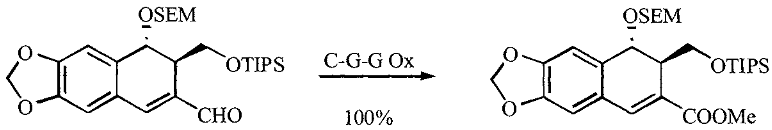
G. E. Keck, T. T. Wagner, J. F. D. Rodriguez, *Journal of the American Chemical Society* **1999**, 121, 5176



H. Yamamoto, T. Oritani, *Tetrahedron Letters* **1995**, 36, 5797



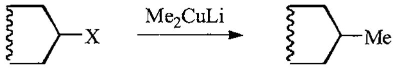
D. L. Boger, S. E. Wolkenberg, *Journal of Organic Chemistry* **2000**, 65, 9120



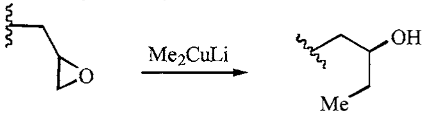
D. B. Berkowitz, S. Choi, J.-H. Maeng, *Journal of Organic Chemistry* **2000**, 65, 847

Corey-House-Posner-Whitesides Reaction

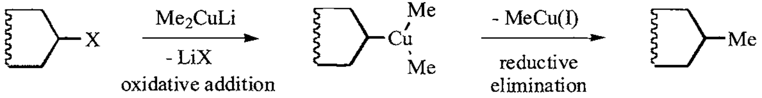
The Reaction:



X = halogen or tosylate



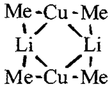
Proposed Mechanism:



See: N. Yoshikai, N. Eiichi, *Journal of the American Chemical Society* **2004**, 126, 12264 for a mechanistic discussion of the reaction at sp_2 centers.

Notes:

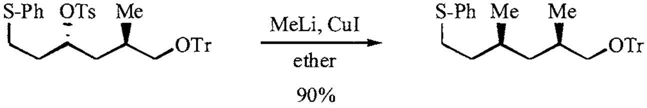
The reagent is most likely a more complex species.



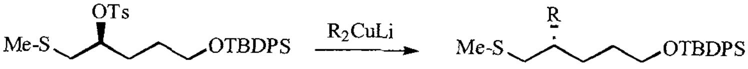
When X = tosylate there is evidence of a direct S_N2 displacement with inversion of stereochemistry.

The general reaction of R_2CuLi is often included in this class.

Examples:

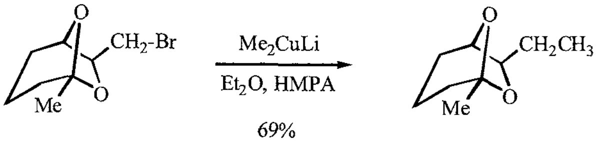


S. Hanessian, N. G. Cooke, B. DeHoff, Y. Sakito *Journal of the American Chemical Society* **1990**, 112, 5276

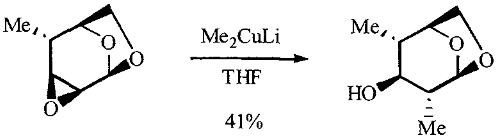


R =	Me	83%
R =	Bu	72%
R=	Allyl	98%

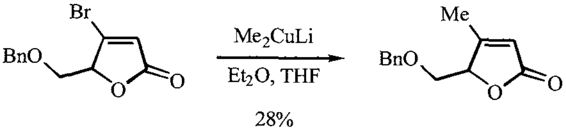
S. Hanessian, B. Thavonekham, B. DeHoff, *Journal of Organic Chemistry* **1989**, 54, 5831



B. D. Johnstone, A. C. Oelschlager, *Journal of Organic Chemistry* **1982**, 47, 5384



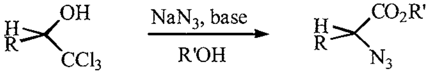
T. Wakamatsu, H. Nakamura, M. Taniguchi, Y. Ban, *Tetrahedron Letters* **1986**, 27, 6071



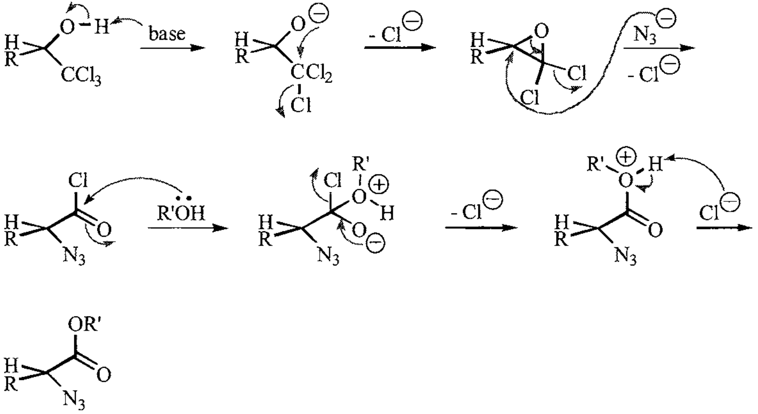
D. Caine, A. S. Frobese, V. C. Ukachukwu, *Journal of Organic Chemistry* **1983**, 48, 740

Corey-Link Reaction

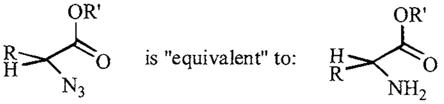
The Reaction:



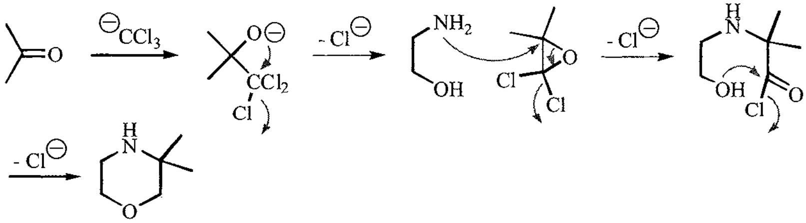
Proposed Mechanism:



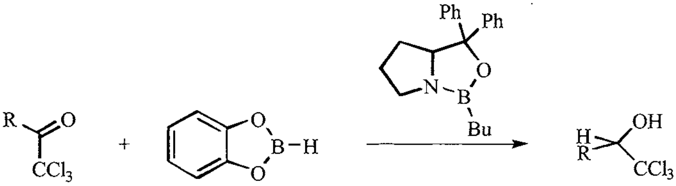
Notes:



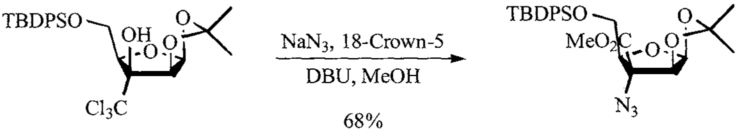
See a similar mechanistic reaction in the ***Bargellini Reaction***:



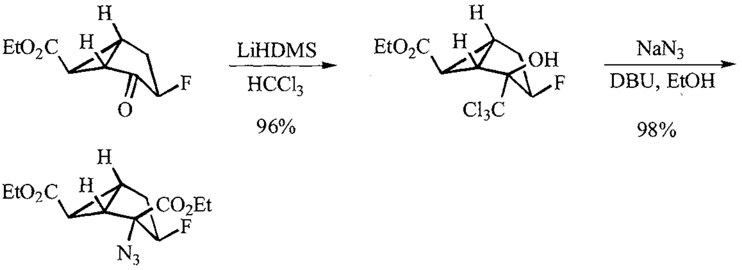
Starting material preparation:



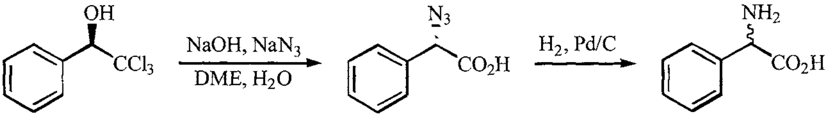
Examples:



M. H. Sorensen, C. Nielsen, P. Nielsen, *Journal of Organic Chemistry* **2001**, 66, 4878

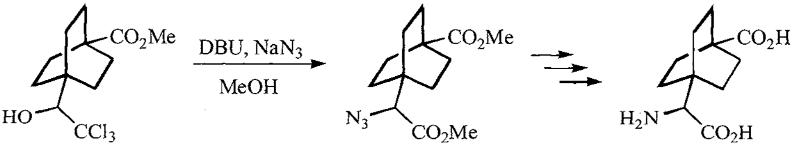


C. Pedregal, W. Prowse, *Bioorganic and Medicinal Chemistry Letters* **2002**, 10, 433



70%, 0% ee
when DBU is the base used, 62%, 99% ee

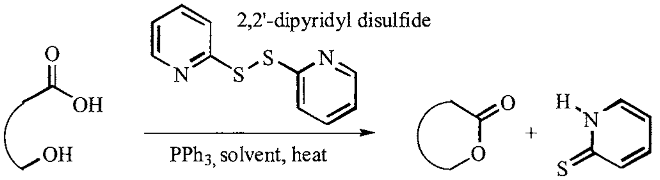
C. Mellin-Morliere, D. J. Aitken, S. D. Bull, S. G. Davies, H.-P. Husson, *Tetrahedron: Asymmetry* **2001**, 12, 149



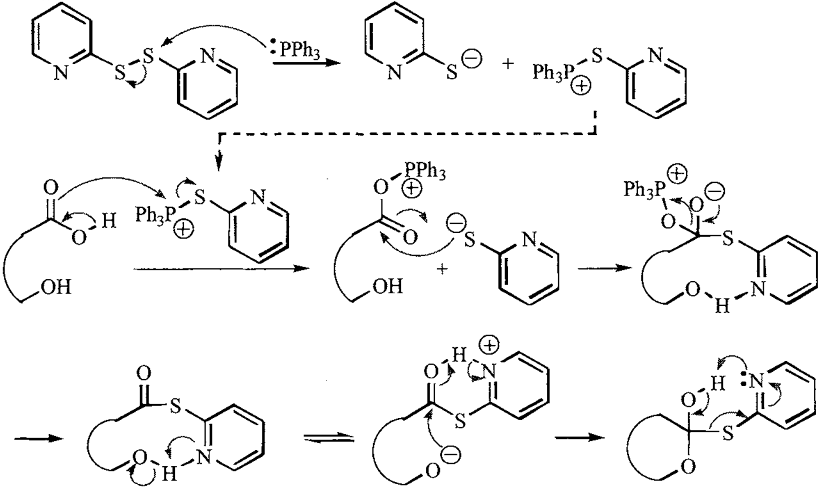
S. R. Baker, T. C. Hancox, *Tetrahedron Letters* **1999**, 40, 781

Corey-Nicoloau Macrocyclization

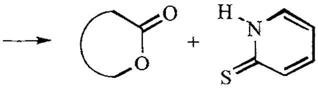
The Reaction:



Proposed Mechanism:

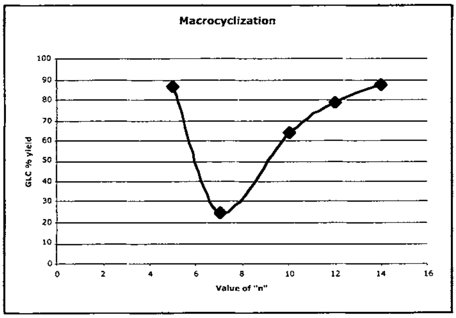


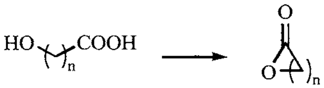
This thiopyridyl ester uniquely activates the carbonyl as well as the hydroxyl group by proton exchange.



Notes:

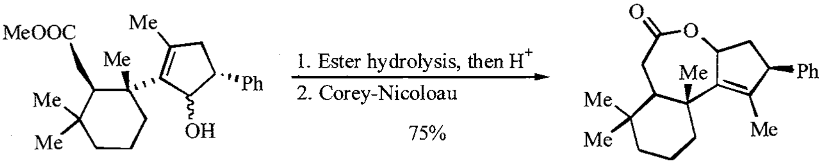
See: ***Macrolactonization Methods***



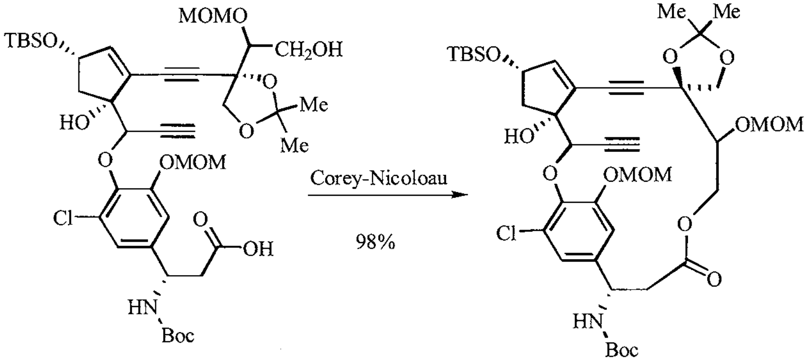


E. J. Corey, K. C. Nicolaou, *Journal of the American Chemical Society* **1974**, 96, 5614

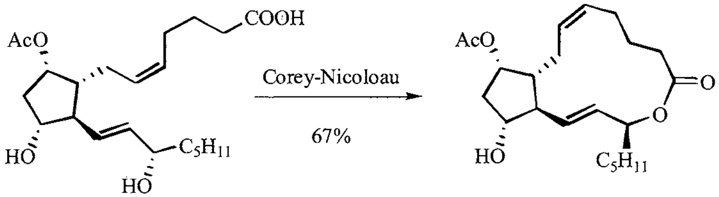
Examples:



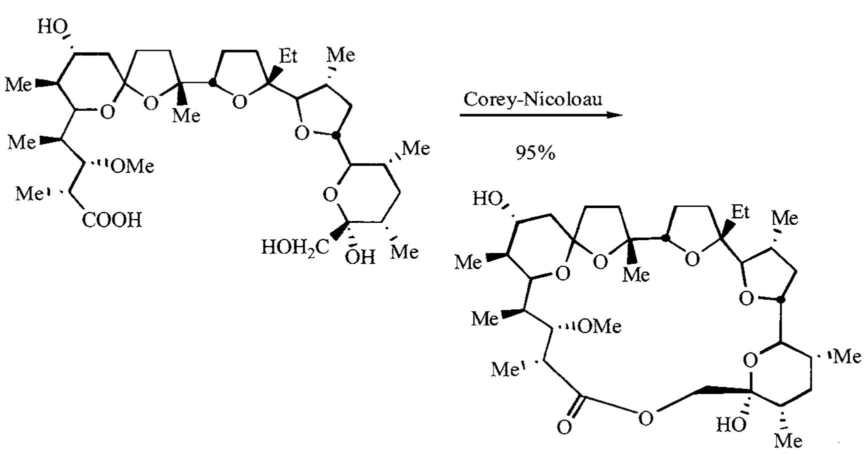
A. Fernandez, E. M. M. de la Nava, R. R. Gonzalez, *Journal of Organic Chemistry*, **2001**, 66, 7632



T. Sasaki, M. Inoue, M. Hirama, *Tetrahedron Letters*, **2001**, 42, 5299



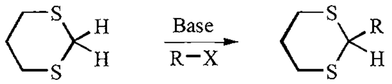
E. J. Corey, K. C. Nicoloau, L. S. Melvin, Jr., *Journal of the American Chemical Society* **1975**, 97, 653



E. J. Corey, K. C. Nicoloau, L. S. Melvin, Jr., *Journal of the American Chemical Society*, **1975**, 97, 653

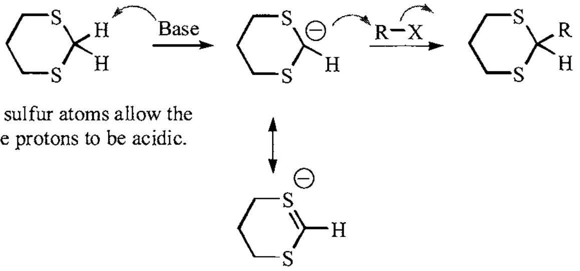
Corey-Seebach Reaction

The Reaction:



Alkylation can take place twice.

Proposed Mechanism:



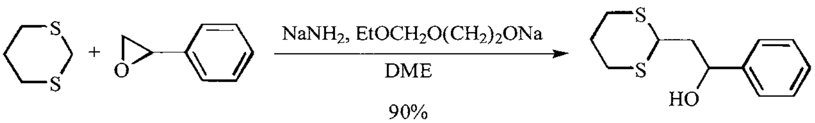
Adjacent sulfur atoms allow the methylene protons to be acidic.

Notes:

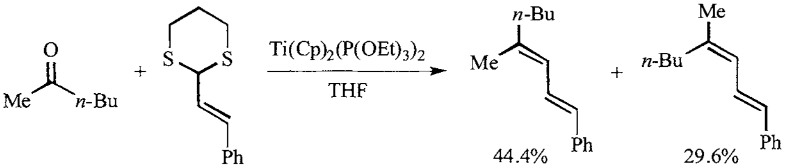
Although the five-ring analog is easily prepared, it is not useful for the transformation due to the tendency for base-induced decomposition:

See: A. B. Smith, III, C. M. Adams, *Accounts of Chemical Research* **2004**, 37, 365 for an excellent tour through the authors' use of the dithiane-based chemistry for the construction of complex molecules.

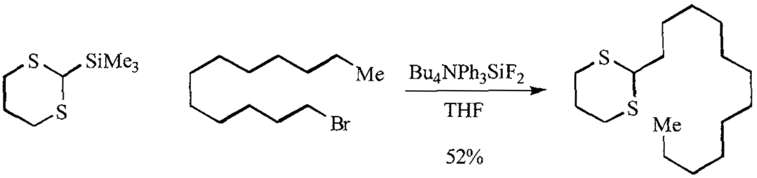
Examples:



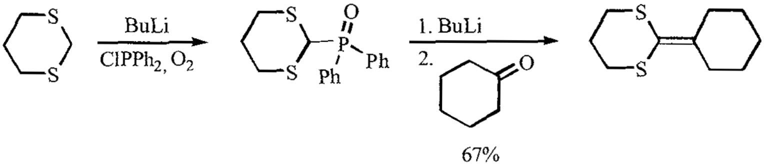
P. Gros, P. Hansen, P. Caubere, *Tetrahedron* **1996**, 52, 15147



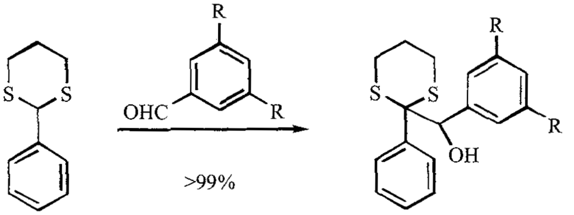
Y. Horikawa, M. Watanabe, T. Fujiwara, T. Takeda, *Journal of the American Chemical Society* **1997**, 119, 1127



A. S. Pilcher, P. Deshong, *Journal of Organic Chemistry* **1996**, 61, 6901



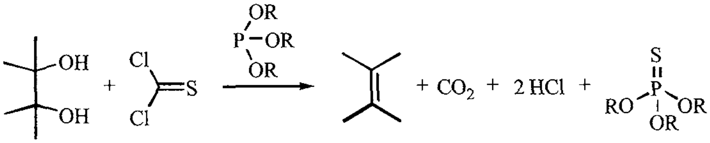
E. Juaristi, B. Gordillo, L. Valle, *Tetrahedron* **1986**, 42, 1963



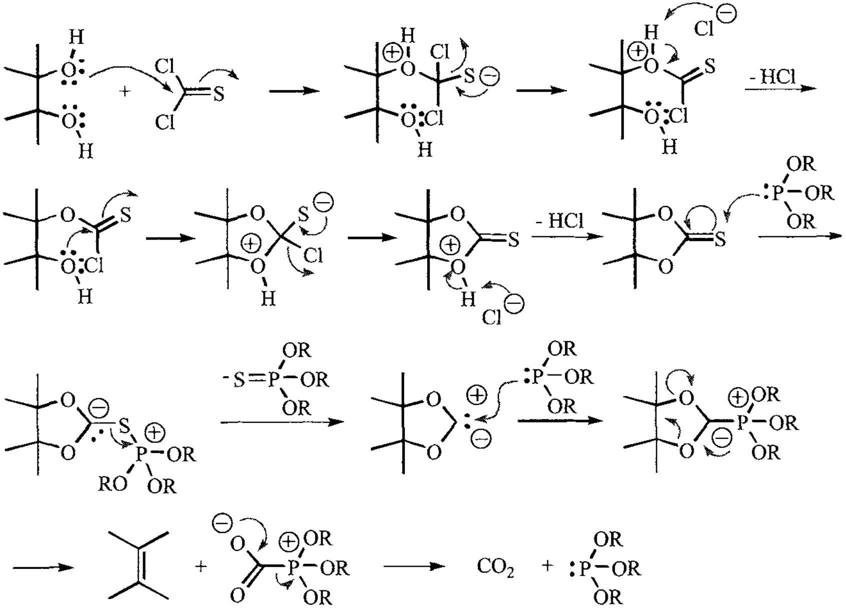
M. H. B. Stowell, R. S. Rock, D. C. Rees, S. I. Chan, *Tetrahedron Letters* **1996**, 37, 307

Corey-Winter Olefination

The Reaction:



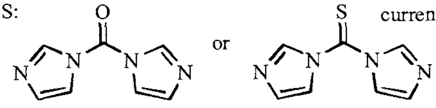
Proposed Mechanism:



See: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 59-61; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1340; E. Block, *Organic Reactions* **30**, 2

Notes:

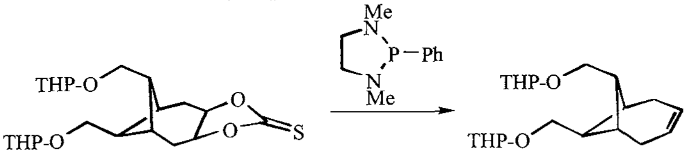
Instead of using $Cl_2C{=}S$:



current reagent of choice

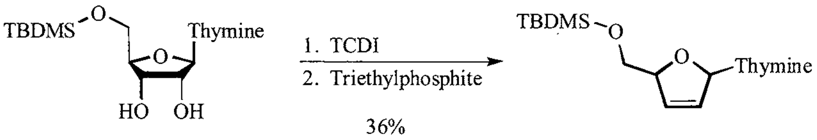
carbonyldiimidazole 1,1'-thiocarbonyldiimidazole TCDI

A modification is the ***Corey-Hopkins olefination***. See *Tetrahedron Letters*, **1982**, 23, 1979:

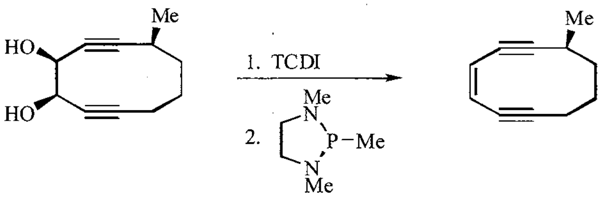


J. Dressel, K. L. Chasey, L. A. Paquette, *Journal of the American Chemical Society* **1988**, 110, 5479

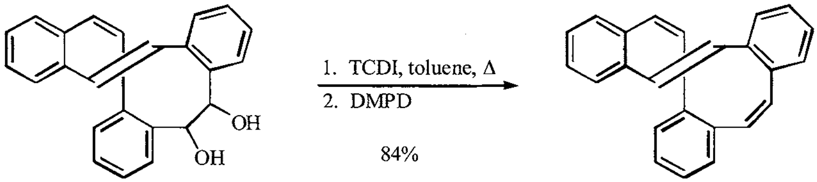
Examples:



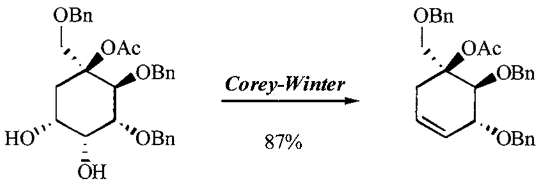
Y. Saito, T. A. Zevaco, L. A. Agrofoglio, *Tetrahedron* **2002**, 58, 9593



M. F. Semmelhack, J. Gallagher, *Tetrahedron Letters* **1993**, 34, 4121



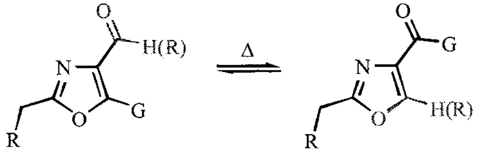
Y. Kuwatani, T. Yoshida, A. Kusaka, M. Iyoda, *Tetrahedron Letter* **2000**, 41, 359



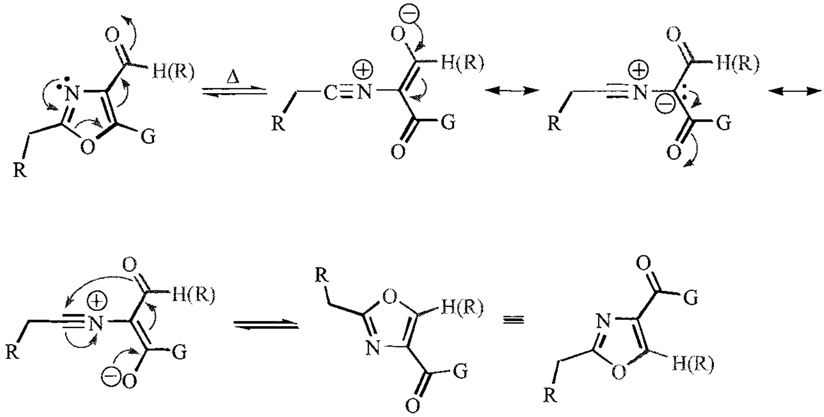
S. H.-L. Koc, C. C. Lee, T. K. M. Shing, *Journal of Organic Chemistry* **2001**, 66, 7184

Cornforth Rearrangement

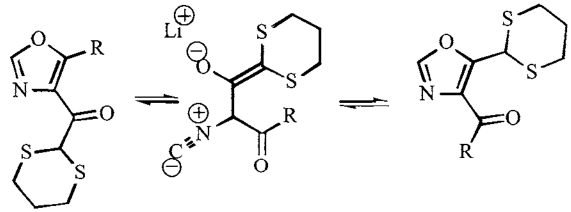
The Reaction:



Proposed Mechanism:



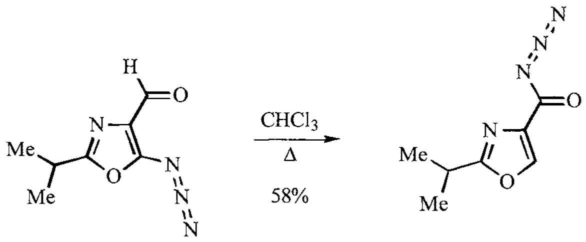
Notes:



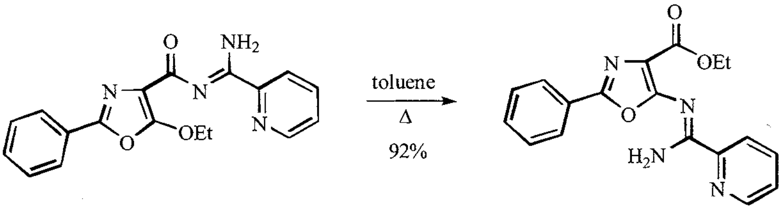
First reported base-catalyzed Cornforth equilibrium.

D. R. Williams, E. L. McClymont, *Tetrahedron Letters* **1993**, 34, 7705

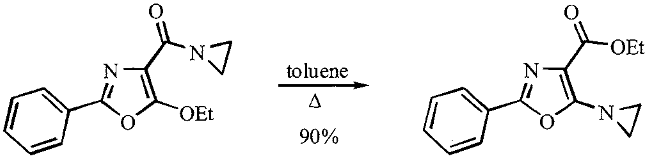
Examples:

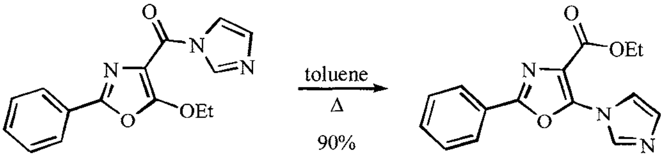


G. L'Abbe, A.-M. Llisiu, W. Dehaen, S. Toppett, *Journal of the Chemical Society Perkin Transactions 1* **1993**, 2259



I. J. Turchi, C. A. Maryanoff, *Synthesis* **1983**, 837

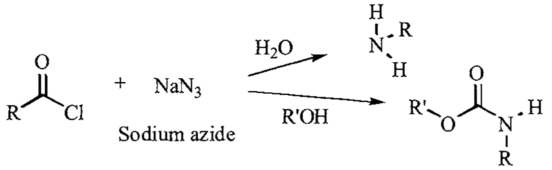




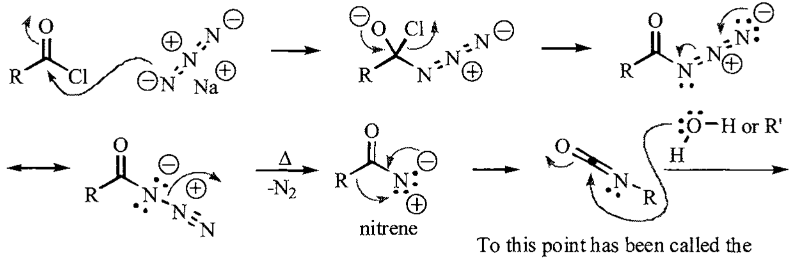
M. J. S. Dewar, I. K. Turchi, *Journal of Organic Chemistry* **1975**, 40, 1521

Curtius Rearrangement / Reaction / Degradation

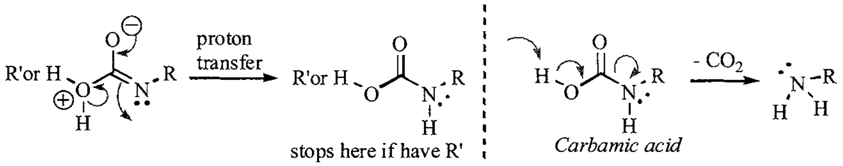
The Reaction:



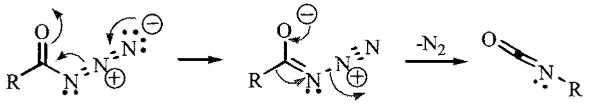
Proposed Mechanism:



To this point has been called the
Curtius Rearrangement / Reaction



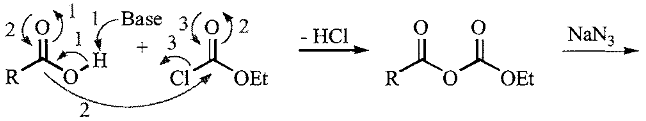
OR with no nitrene...



Notes:

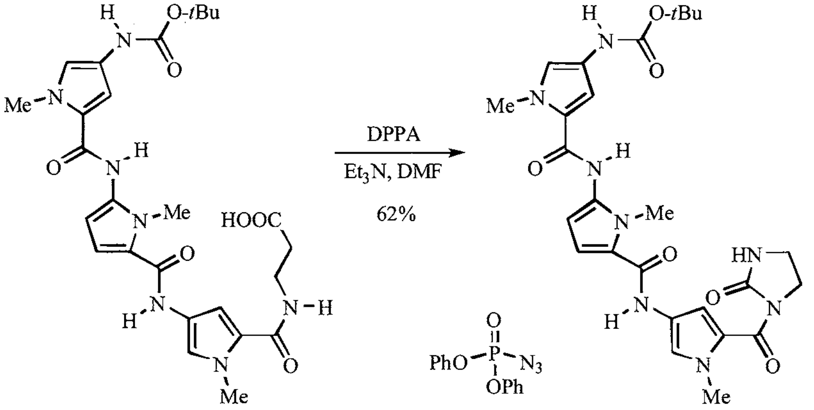
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 61-63; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1412-1413; P. A. S. Smith, *Organic Reactions* **3**, 9.

Alternate Starting Material:



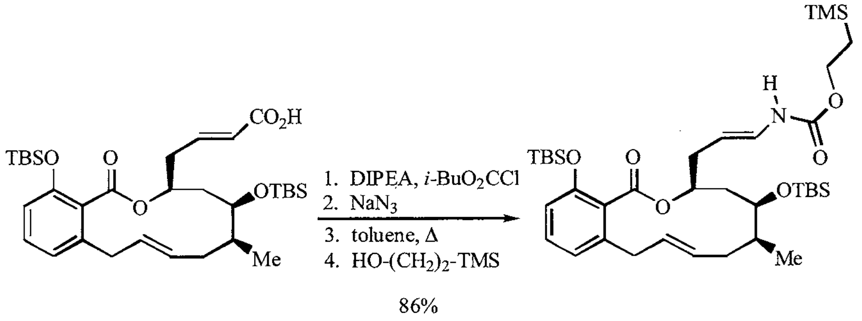
As with the***Hofmann***, ***Schmidt*** and ***Lossen Rearrrangements***, there is a common isocyanate intermediate.

Examples:

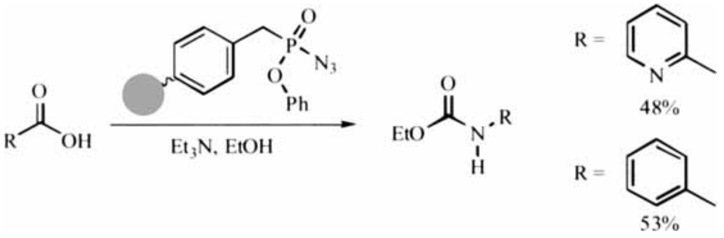


DPPA: Diphenyl phosphorazidate [26386-88-9]

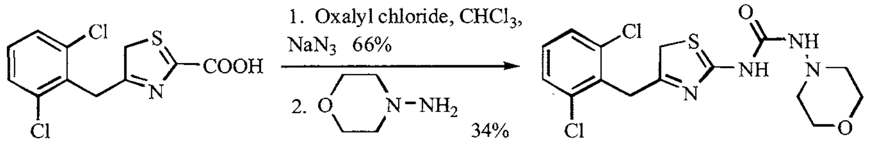
I. Beria, M. Nesi, *Tetrahedron Letters* **2002**, 43, 7323



A. B. Smith, III, J. Zheng, *Tetrahedron* **2002**, 43, 7323



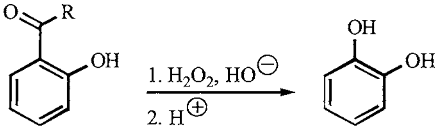
Y. Lu, R. T. Taylor, *Tetrahedron Letters* **2003**, 44 9267



S. D. Larsen, C. F. Stachew, P. M. Clare, J. W. Cubbage, K. L. Leach *Bioorganic & Medicinal Chemistry Letters* **2003**, 13, 3491

Dakin Reaction

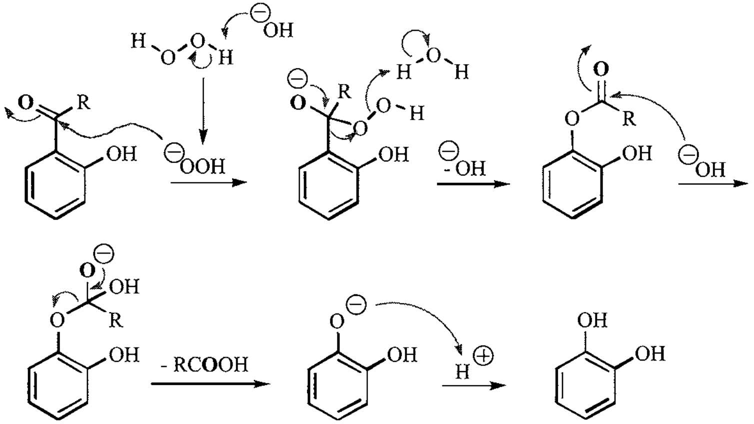
The Reaction:



The reaction requires an -OH or -NH_2 in the *ortho* or *para* position.
R = H or Me

Proposed Mechanism:

(The ketone oxygen is bolded to demonstrate labeling studies.)

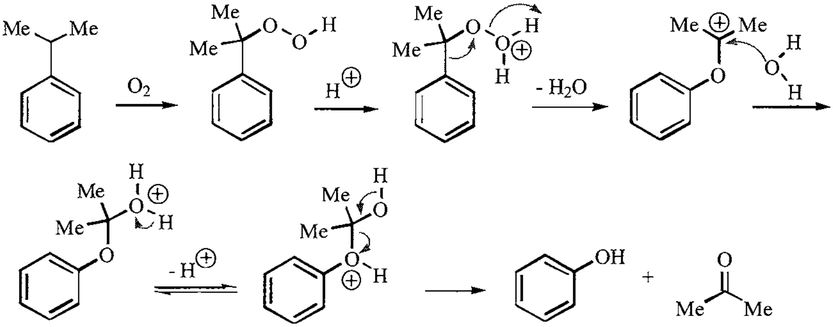


Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1528; V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002, pp. 432-433

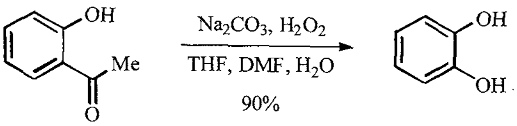
Peroxy acids (***Baeyer-Villiger Reaction***) can provide the same products.

Hydroperoxide Rearrangement

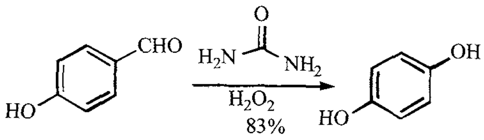


Phenol and acetone

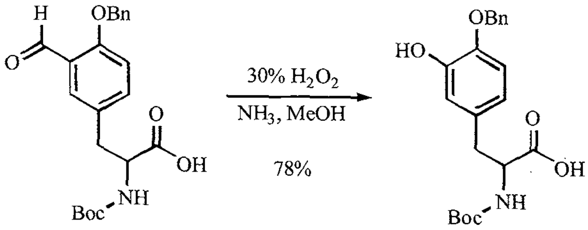
Examples:



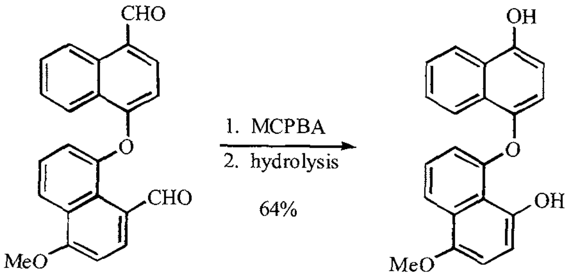
G. W. Kabalka, N. K. Reddy, C. Narayana, *Tetrahedron Letters* **1992**, 33, 865



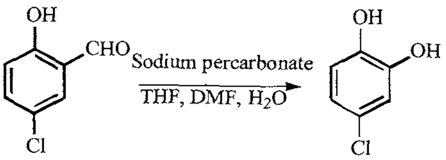
R. S. Varma, K. P. Naiker, *Organic Letters* **1999**, 1, 189



M. E. Jung, T. I. Lazarova, *Journal of Organic Chemistry* **1997**, 62, 1553



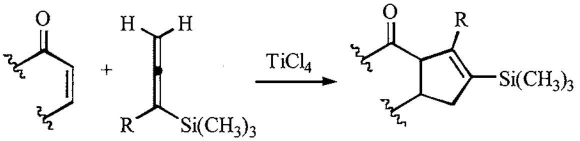
P. Wipf, S. M. Lynch, *Organic Letters*, **2003**, 5, 1155

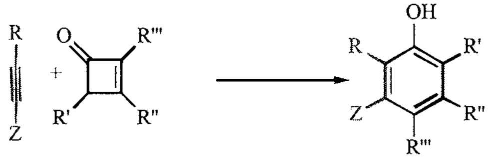


G. W. Kabalka, N. K. Reddy, C. Narayana, *Tetrahedron Letters* **1992**, 33, 865

Danheiser Annulation

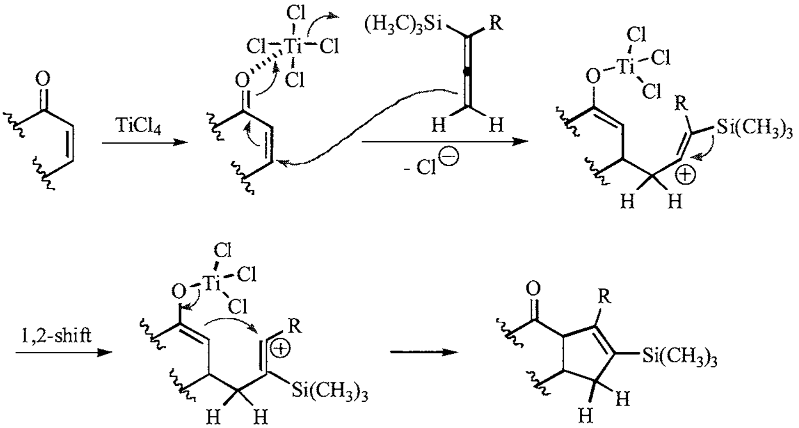
The Reactions:

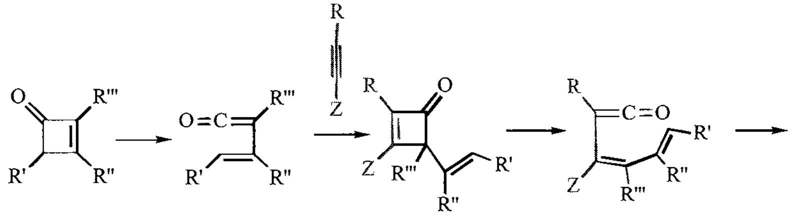




A number of examples are presented

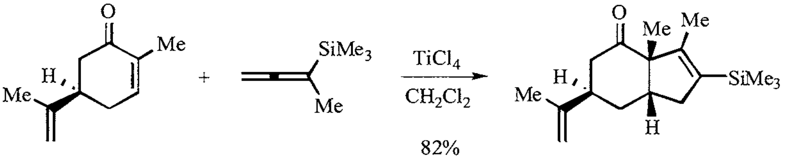
Proposed Mechanisms:



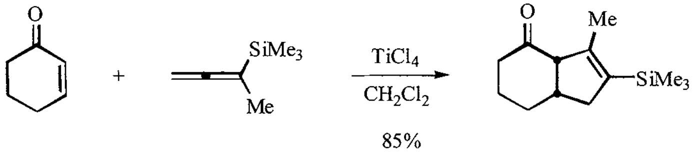


R. L. Danheiser, S. K. Gee, *Journal of Organic Chemistry* **1984**, 49, 1672

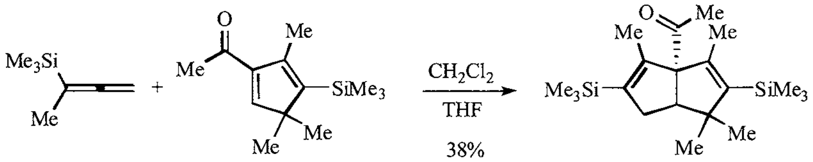
Examples:



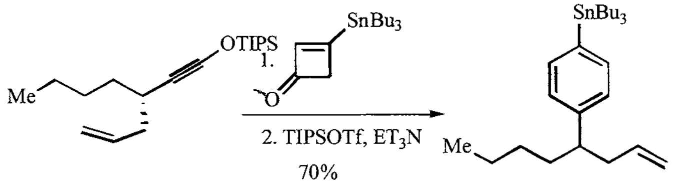
R. L. Danheiser, D. M. Fink, Y.-M. Tsai, *Organic Synthesis* **1988**, 66, 8



R. L. Danheiser, D. J. Carini, A. Basak, *Journal of the American Chemical Society* **1981**, 103, 1604



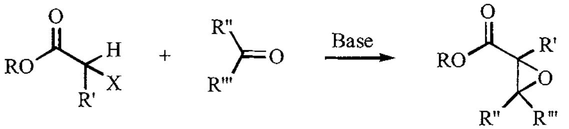
R. L. Danheiser, D. J. Carini, D. M. Fink, A. Basak *Tetrahedron*, **1983**, 39, 935



A. B. Smith, III, C. M. Adams, S. A. Kozmin, D. V. Paone, *Journal of the American Chemical Society* **2001**, 123, 5925

Darzens Condensation (Darzens-Claisen Reaction, Darzens Glycidic Ester Condensation)

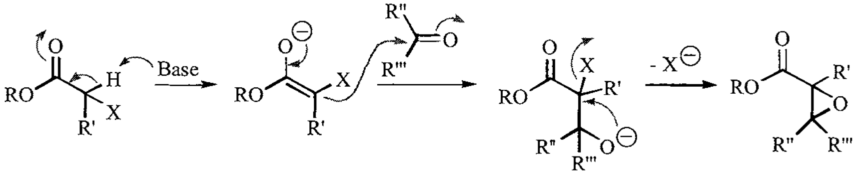
The Reaction:



X = halogen

glycidic ester = an α, β-epoxy ester

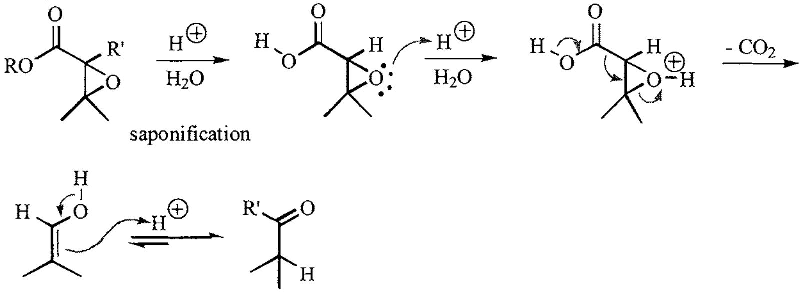
Proposed Mechanism:



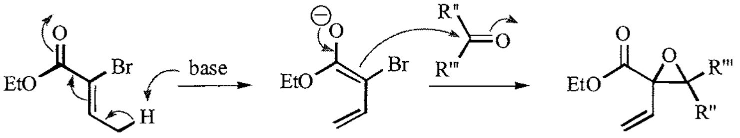
Notes:

T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 71-72; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1230; M. S. Newman, B. J. Magerlein, *Organic Reactions* **5**, 10.

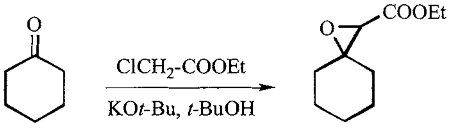
One possible extension:



In a reaction with enones:

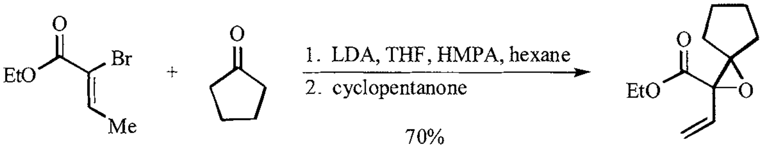


Examples:

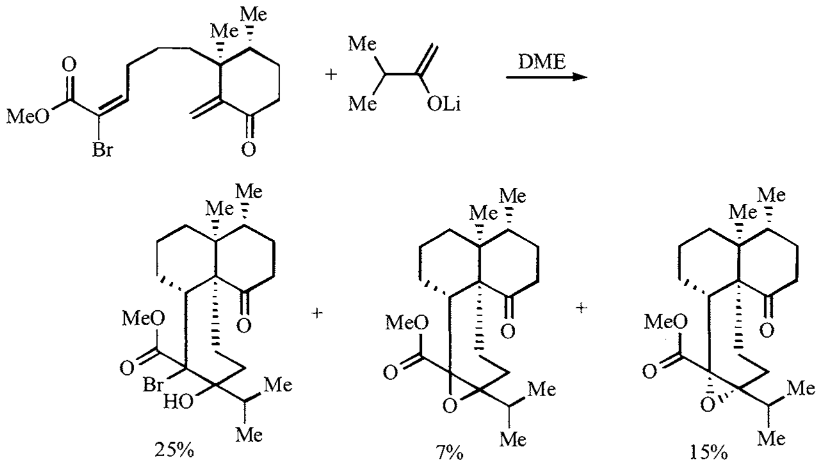


83-95%

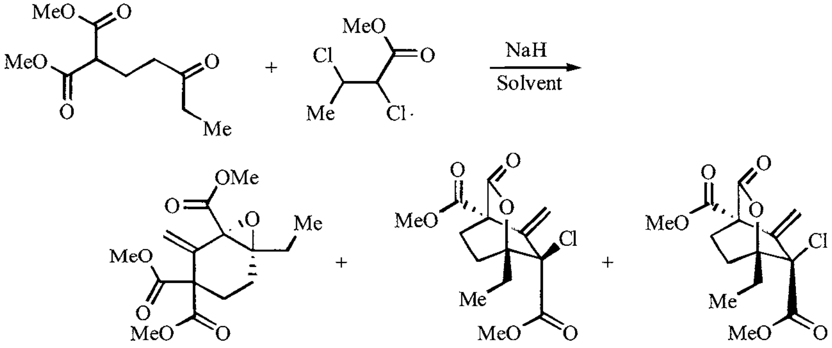
R. Hunt, L. Chinn, W. Johnson, *Organic Syntheses* CV4, 459



F. E. Anderson, H. Luna, T. Hudlicky, L. Radesca, *Journal of Organic Chemistry* **1986**, 51, 4746



S. Danishefsky, S. Chackalamannil, P. Harrison, M. Silvestri, P. Cole, *Journal of the American Chemical Society* **1985**, 107, 2474

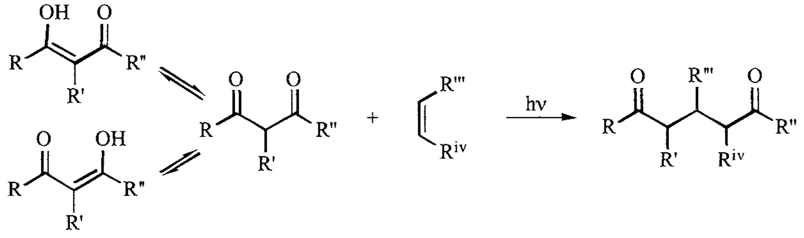


DMF	65%		
THF	15%	40%	20%

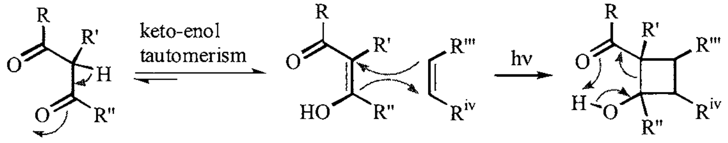
J. G. Bauman, R. C. Hawley, H. Rapoport, *Journal of Organic Chemistry* **1984**, 49, 3791

de Mayo Reaction

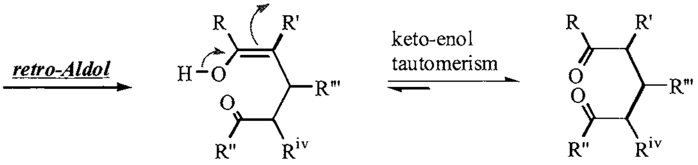
The Reaction:



Proposed Mechanism:

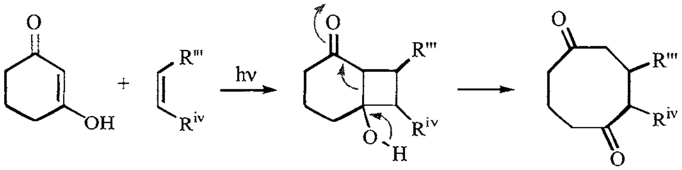


The orientation of the alkene is dictated by the identity of the R groups.

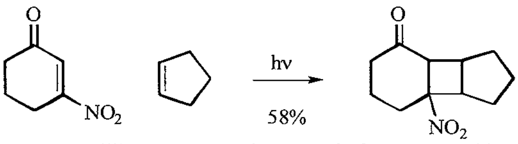


Notes:

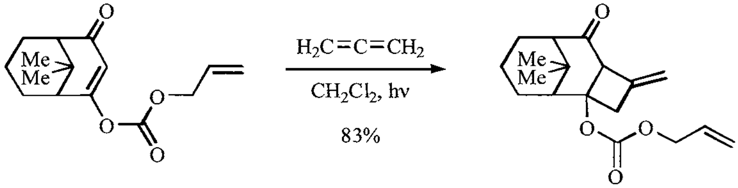
The reaction can be a ring expansion:



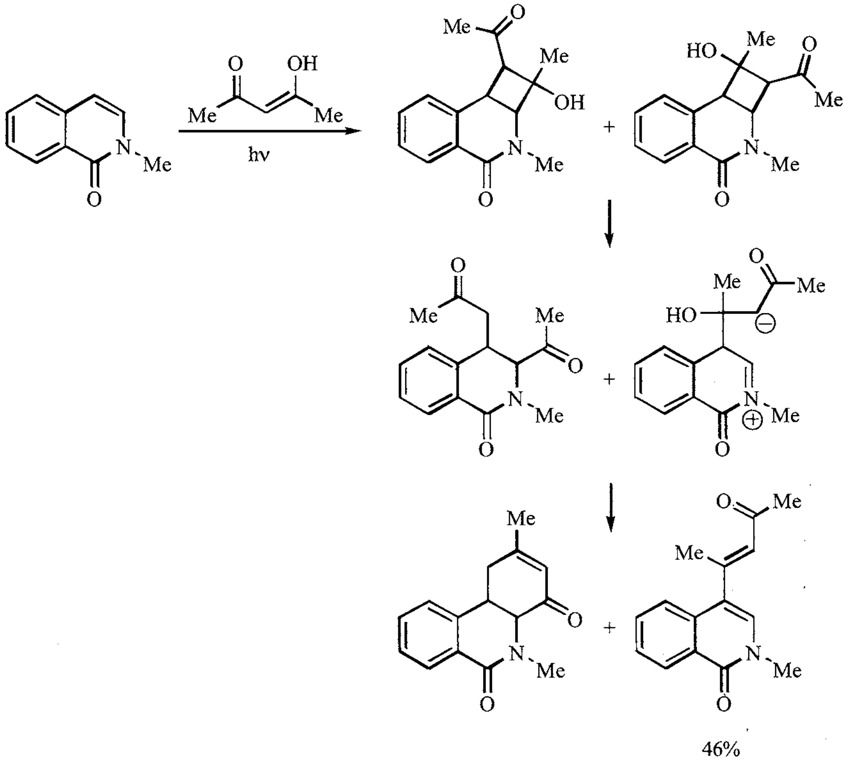
Examples:



T. M. Qaevilllon, A. C. Weedon, *Tetrahedron Letters* **1996**, 37, 3939



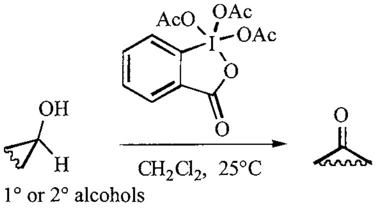
R. Kaczmarek, S. Blechert, *Tetrahedron Letters* **1986**, 27, 2845



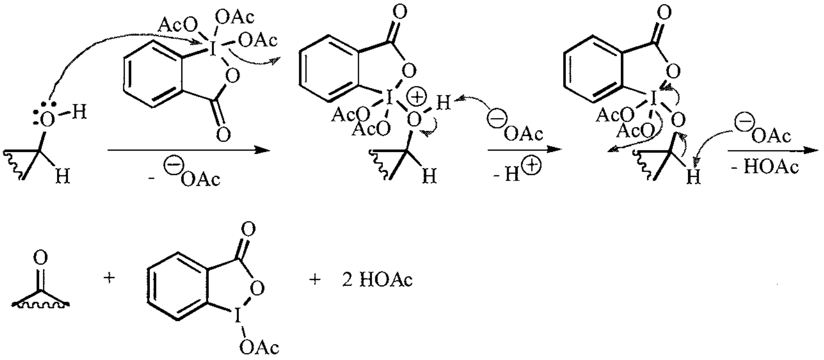
D. E. Minter, C. D. Winslow, *Journal of Organic Chemistry* **2004**, 69, 603

Dess-Martin Oxidation

The Reaction:



Proposed Mechanism:

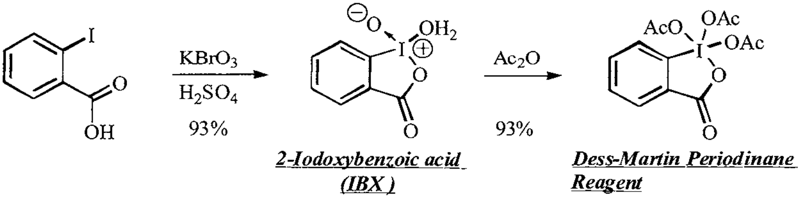


Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1516; F. A. Luzzio, *Organic Reactions* **53**, 1.

This reaction is noted for its mildness.

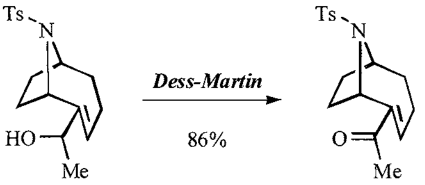
Reagent Preparation: D. B. Dess, J. C. Martin, *Journal of Organic Chemistry* **1983** 48, 4155



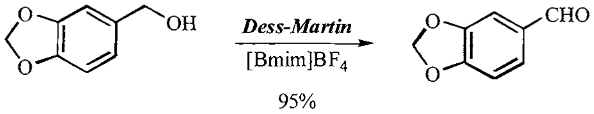
2-Iodoxybenzoic acid (IBX) is also a useful oxidizing reagent. Insoluble in most solvents (except DMSO) it can be used with other cosolvent mixtures.

See ***Dess-Martin Reagent*** and ***IBX Reagent***.

Examples:

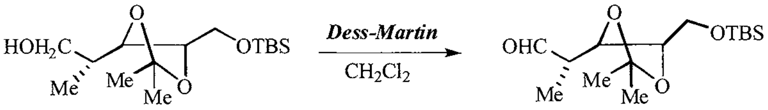


M. Mori, T. Tomita, Y. Kita, T. Kitamura, *Tetrahedron Letters* **2004**, 45, 4397

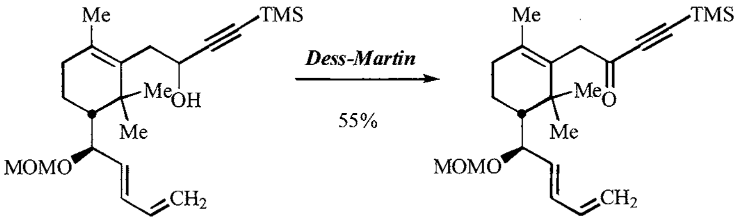


See: ***Bmim***

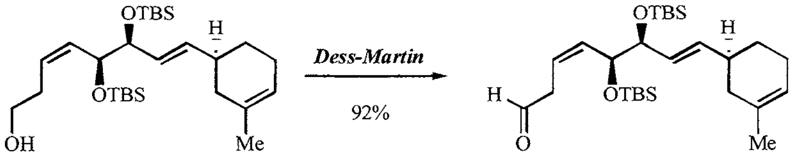
J. S. Yadav, B. V. S. Reddy, A. K. Basak, A. Venkat Narsaiah, *Tetrahedron* **2004**, 60, 2131



K. Suenaga, K. Araki, T. Sengoku, D. Uemura, *Organic Letters* **2001**, 3, 527



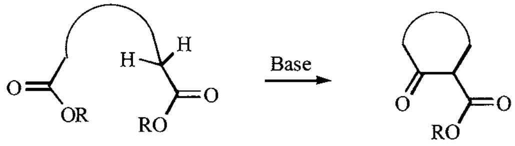
Y.-F. Lu, A. G. Fallis, *Tetrahedron Letters* **1993**, 34, 3367



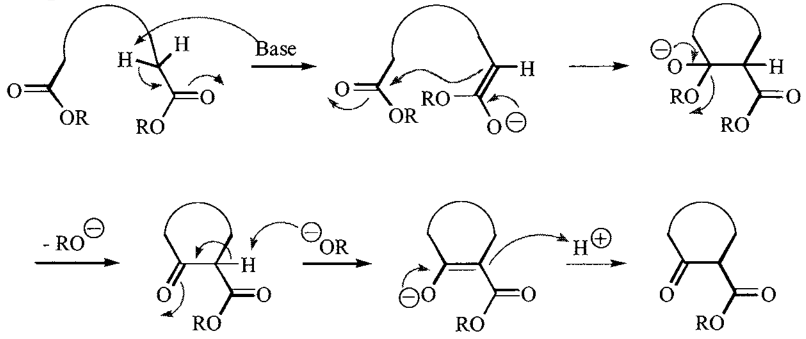
P. A. Wender, S. G. Hegde, R. D. Hubbard, L. Zhang, *Journal of the American Chemical Society* **2002**, 124, 4956

Dieckmann Condensation / Cyclization / Reaction

The Reaction:



Proposed Mechanism:

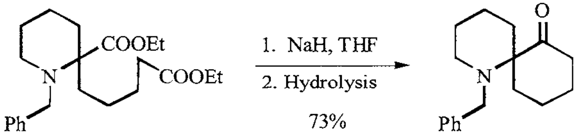


The product remains an enolate until protic workup.

Notes:

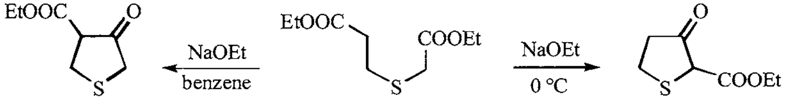
V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002, pp. 308-309; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 569-570; C. R. Hauser, B. E. Hudson, Jr., *Organic Reactions* **1**, 9; J. P. Schaefer, J. J. Bloomfield, *Organic Reactions*, **15**, 1.

Regiochemistry Issues:



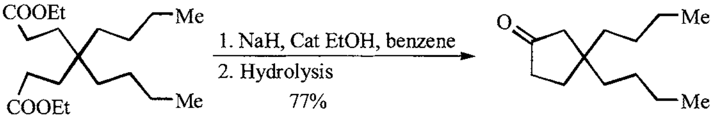
P. Compain, J. Gore, J.-M. Vatele, *Synthetic Communications* **1995**, 25, 3075 (AN 1995:752767)

Kinetic vs. Thermodynamic Control:

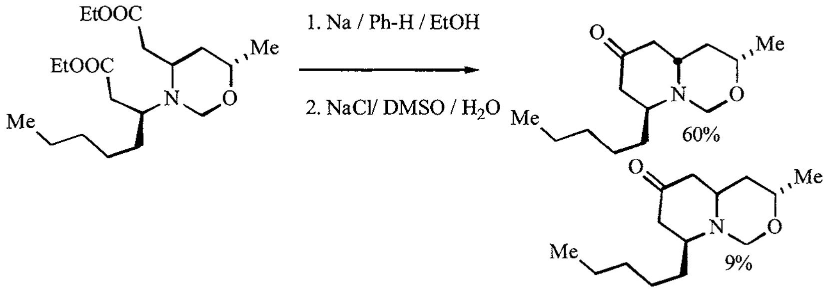


F. Duus, *Tetrahedron* **1981**, 57, 2633

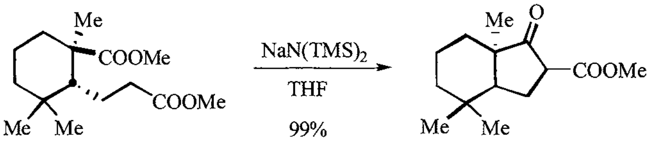
Examples:



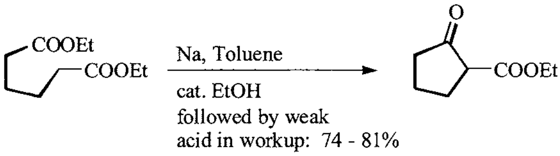
D. P. Provencal, J. W. Leahy, *Journal of Organic Chemistry* **1994**, 59, 5496



W. Zhu, D. Ma, *Organic Letters* **2003**, 5, 5063



L. A. Paquette, H.-L. Wang, *Journal of Organic Chemistry* **1996**, 61, 5352



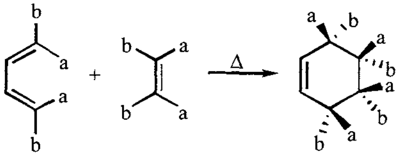
In the absence of solvent

*t*BuONa	74%
EtONa	61%

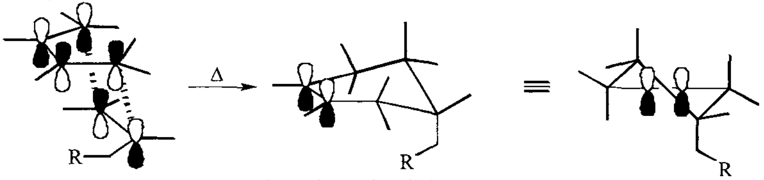
P. S. Pinkney, *Organic Syntheses*, CV2, 116
F. Toda, T. Suzuki, S. Higa, *Journal of the Chemical Society: Perkin Transactions 1* **1988**, 3207

Diels-Alder Reaction

The Reaction:

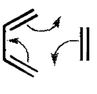


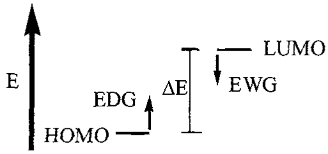
Proposed Mechanism:



The endo product is favored.

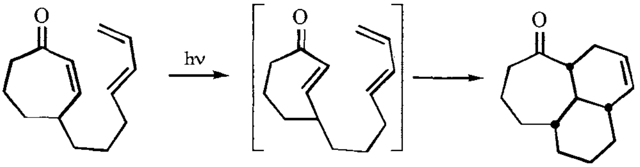
This is a [4+2] concerted reaction. Bonds are broken and formed simultaneously, however, the arrows shown below are usually used to illustrate the mechanism.





The smaller the ΔE, the faster the reaction. Therefore, electron donating groups on the diene and/or electron withdrawing groups on the dieneophile will accelerate the reaction.

Although FMO theory shows the reaction to be a ground-state process, photochemical reactions with a trans-ring juncture product have been observed. This has been attributed to an excited state isomerization of the ene-portion followed by a ground state ***Diels-Alder reaction***:



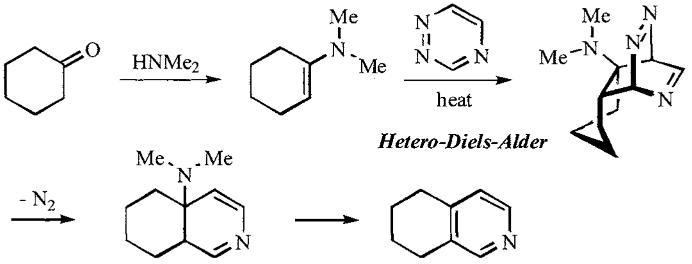
H. Dorr, V. H. Rawal, *Journal of the American Chemical Society* **1999**, 121, 10229

T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 78-85; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1062-1075; M. C. Klotzel, *Organic Reactions* **4**, 1; E. Ciganek, *Organic Reactions* **32**, 1.

Notes:

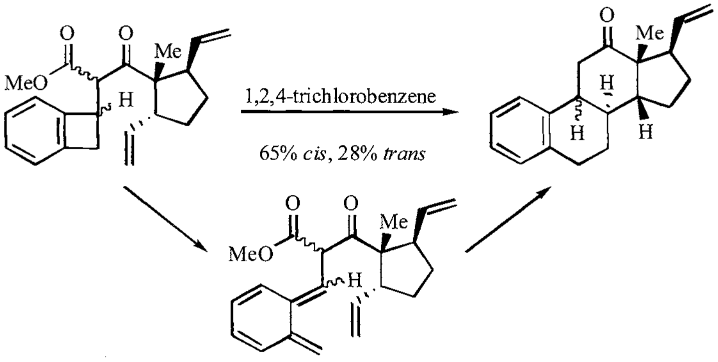
The reverse reaction can also be performed, particularly if one or both fragments are stable.

Boger Heterocycle Synthesis

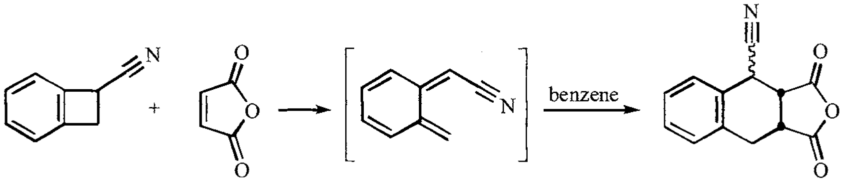


D. L. Boger, J. S. Panek, *Journal of Organic Chemistry* **1981**, 46, 2179

The ***Diels-Alder Reaction*** can be used in a number of creative ways. For example, extremely reactive dienes can be generated by thermal cycloreversion reactions:

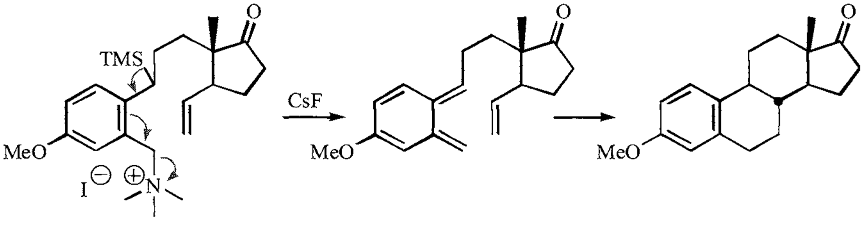


H. Pellissier, M. Santelli, *Tetrahedron* **1996**, 52, 9093



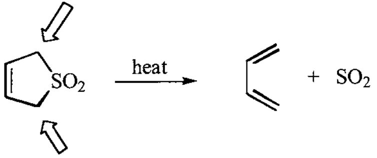
C. W. Jefford, G. Bernardinelli, Y. Wang, D. C. Spellmeyer, A. Buda, K. N. Houk, *Journal of the American Chemical Society* **1992**, 114, 1157

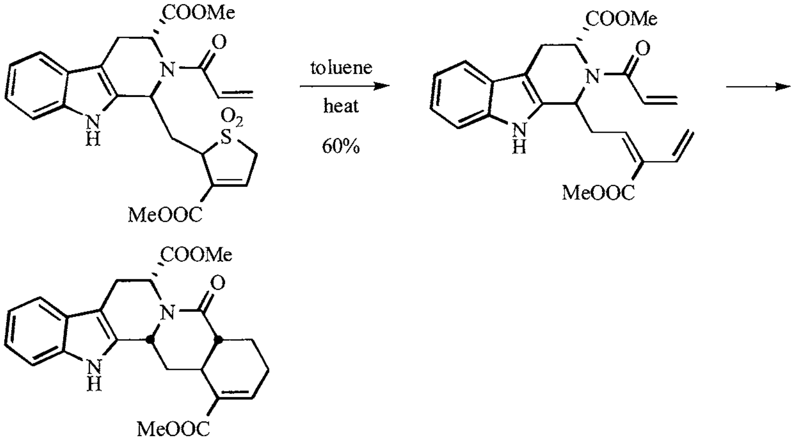
The driving force for the ***Diels-Alder reaction*** is, in part, due to the rearomatization process. Fluoride-induced elimination creates the same opportunity:



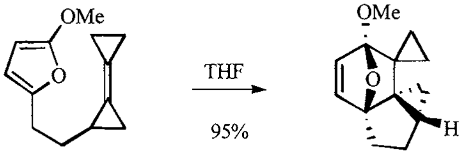
Y. Ito, M. Nakatsuka, T. Saeguso *Journal of the American Chemical Society* **1982**, 104, 7609

Extrusion of SO_2 provides a unique opportunity for diene preparation:
Because of the sulfoxide influence, substitution at these positions quite easy.

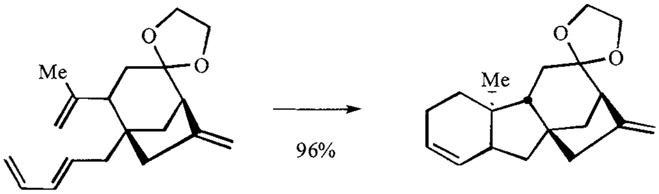




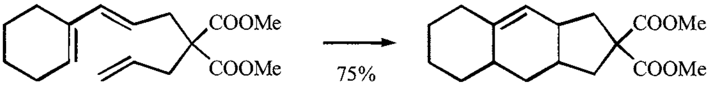
J. Leonard, A. B. Hague, G. Harms, M. F. Jones, *Tetrahedron Letters* **1999**, 40, 8141



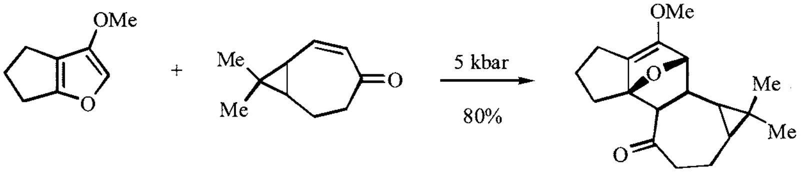
T. Heiner, S. I. Kozhushkov, M. Noltemeyer, T. Hauman, R. Boese, A. DeMeijere, *Tetrahedron* **1996**, 52, 12185



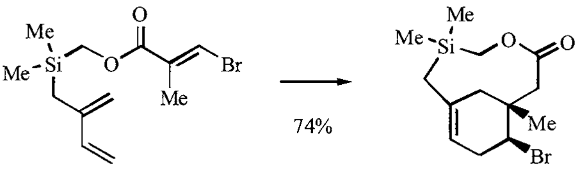
M. Toyota, T. Wada, Y. Nishikawa, K. Yanai, K. Fukumoto, C. Kabuto, *Tetrahedron* **1995**, 51, 6927



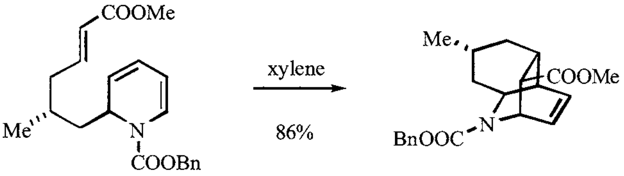
B. M. Trost, M. Lautens, *Journal of the American Chemical Society* **1983**, 105, 3345



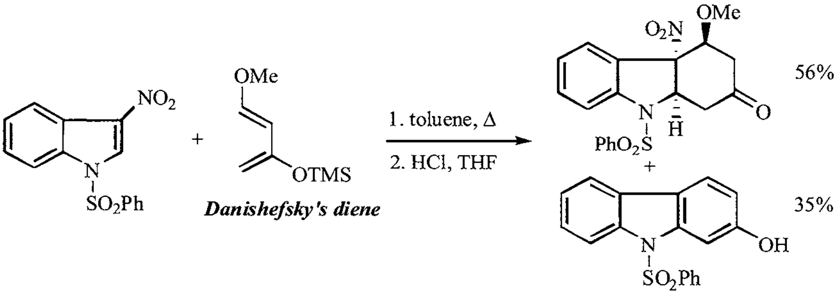
A. B. Smith, III, N. J. Liverton, N. J. Hrib, H. Sivaramakrishnan, K. Winzenberg, *Journal of Organic Chemistry* **1985**, 50, 3239

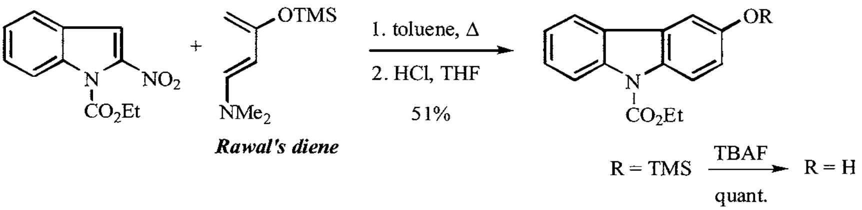


J. M. Whitney, J. S. Parner, K. J. Shea, *Journal of Organic Chemistry* **1997**, 62, 8962



D. L. Comins, C. A. Brooks, R. S. Al-awar, R. R. Goehring, *Organic Letters* **1999**, 1, 229

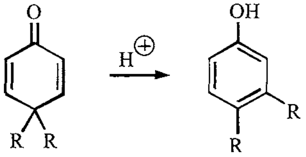




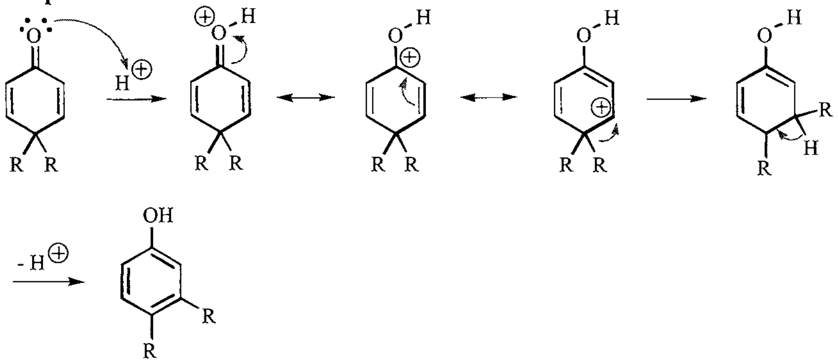
T. L. S. Kishbaugh, G. W. Gribble *Tetrahedron Letters* **2001**, 42, 4783

Dienone-Phenol Rearrangement

The Reaction:



Proposed Mechanism:

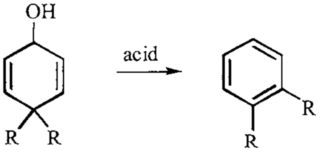


See: V. P. Vitullo, N. Grossman, *Journal of the American Chemical Society* **1972**, 94 3844

Notes:

If the R-groups are different, product mixtures to be expected.

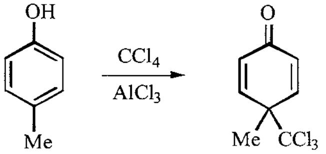
Dienol-Benzene Rearrangement



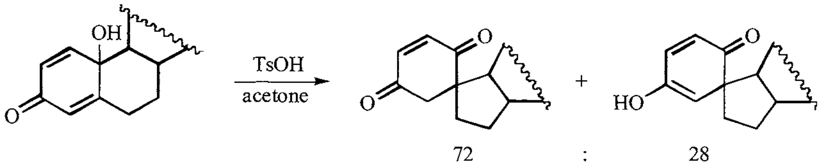
A dienone preparation:

Zincke-Suhl Reaction

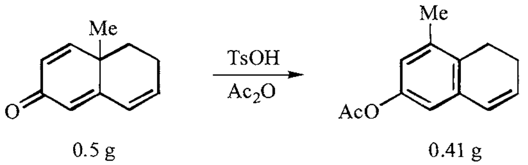
The Reaction:



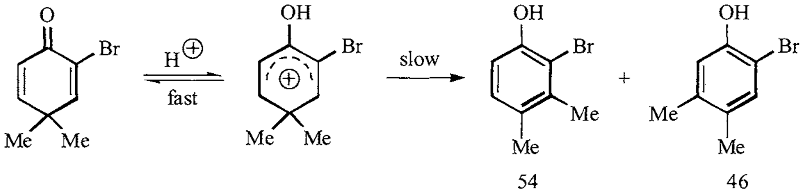
Examples:



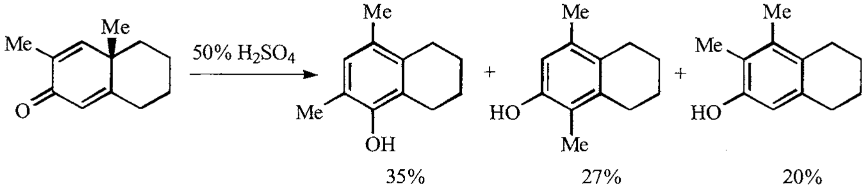
A. Planas, J. Tomas, J.-J. Bonet, *Tetrahedron Letters* **1978**, 28, 471



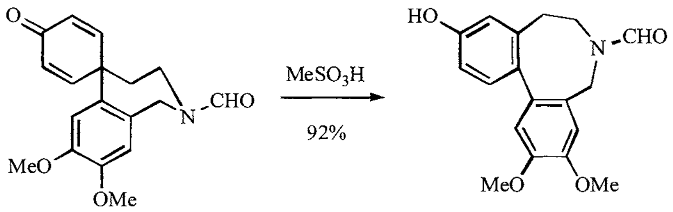
A. Sandoval, L. Miramontes, G. Rosenkranz, C. Djerassi, *Journal of the American Chemical Society* **1951**, 73, 990



A. J. Waring, *Tetrahedron Letters* **1975**, 12, 172



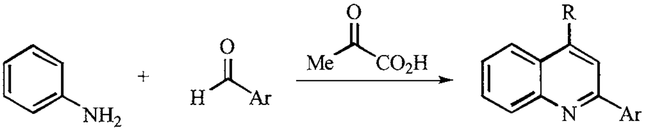
P. J. Kropp, *Tetrahedron Letters* **1963**, 4, 1671



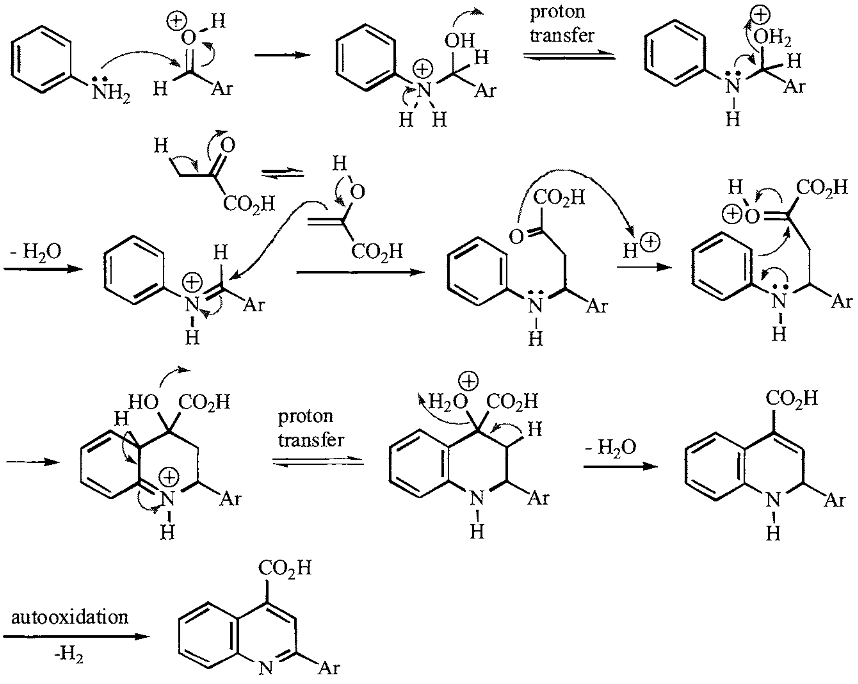
S. Kodama, H. Takita, T. Kajimoto, K. Nishide, M. Node, *Tetrahedron* **2004**, 60, 4901

Doebner Reaction (Beyer Synthesis, Beyer Method for Quinolines)

The Reaction:



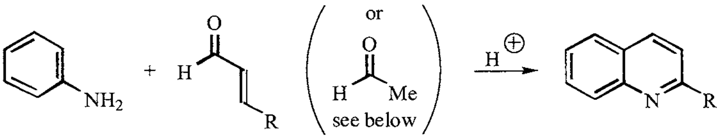
Proposed Mechanism:



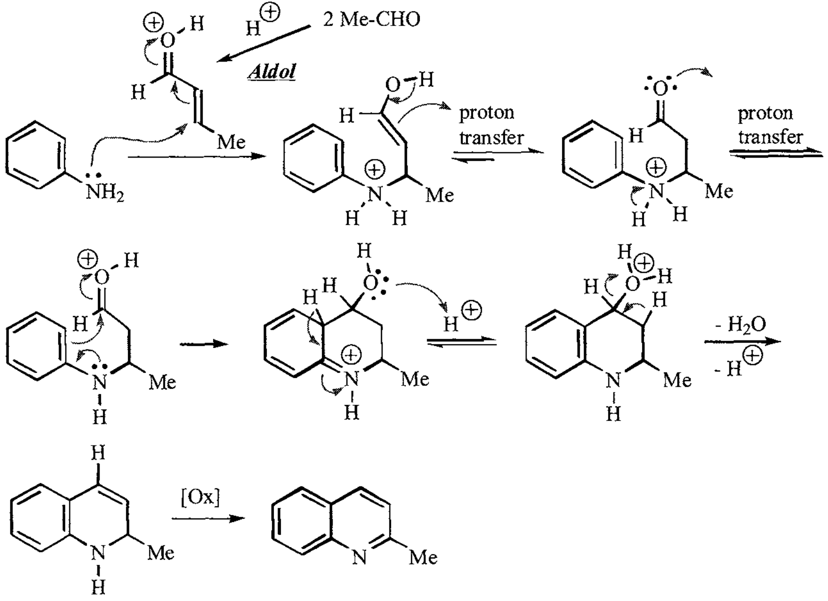
Notes:

Doebner-von Miller Reaction

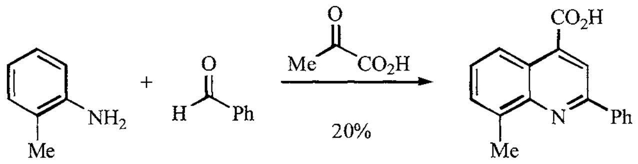
The Reaction: V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002, p. 314



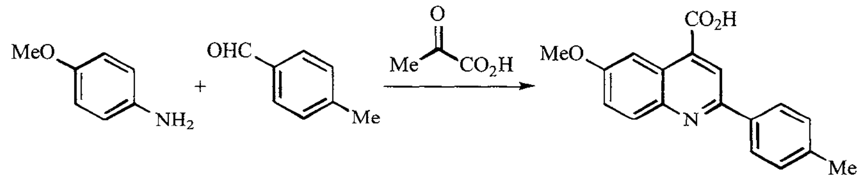
Proposed Mechanism:



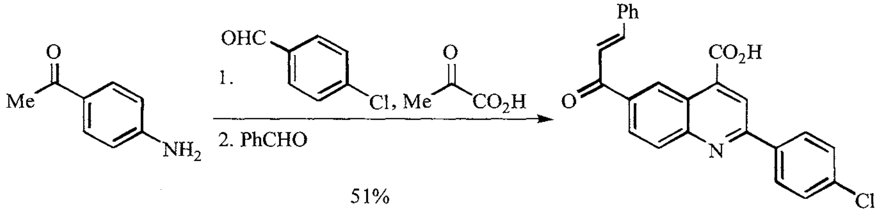
Examples:



G. J. Atwell, B. C. Baguley, W. A Denny, *Journal of Medicinal Chemistry* **1989**, 32, 396



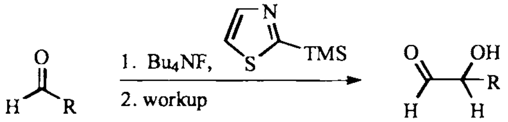
G. A. Epling, K. Y. Lin *Journal of Heterocyclic Chemistry* **1987**, 24, 853 (AN 1998: 55860)
See also: G. SA. Epling, A. A. Provatas, *Chemical Communications* **2002**, 1036



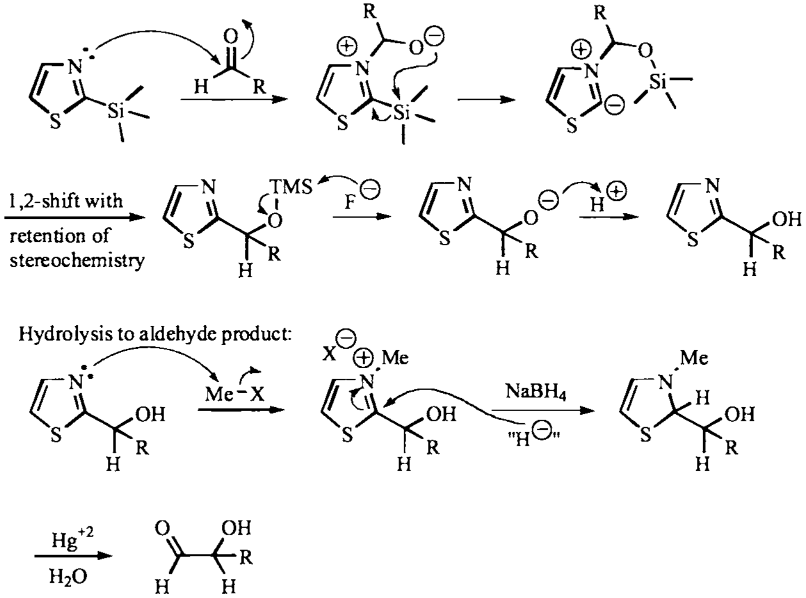
D. J. Bhatt, G. C. Kamdar, A. R. Parikh *Journal of the Indian Chemical Society* **1984**, 61, 816 (AN 1985:453938)

Dondoni Homologation

The Reaction:



Proposed Mechanism:

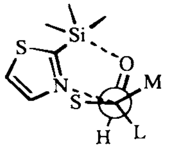


A. Dondoni,.G. Fantin, M. Fogagnolo, A. Medici, P. Pedrini, *Journal of Organic Chemistry* **1989**, 54, 693

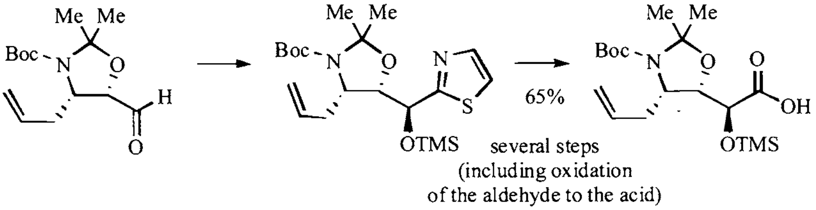
A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici, P. Pedrini, *Tetrahedron Letters* **1985**, 26, 5477

Notes:

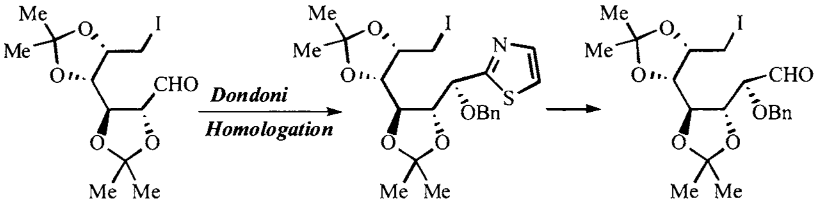
Rationalization of stereochemistry for addition given by:



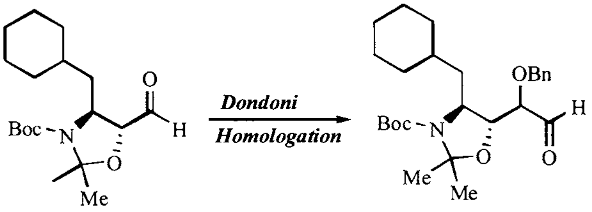
Examples:



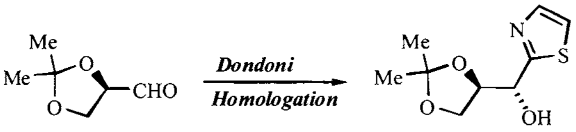
A. K. Ghosh, A. Bischoff, J. Cappiello, *Organic Letters* **2001**, 3, 2677



J. Marco-Contelles, E. de Opazo, *Journal of Organic Chemistry* **2002**, 67, 3705



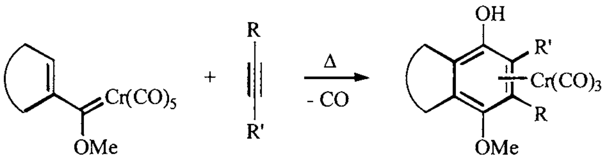
A. Wagner, M. Mollath, *Tetrahedron Letters* **1993**, 34, 619



A. Dondoni, G. Fantin, M. Fogagnolo, A. Medici, P. Pedrini, *Journal of Organic Chemistry* **1989**, 54, 693

Dötz Reaction

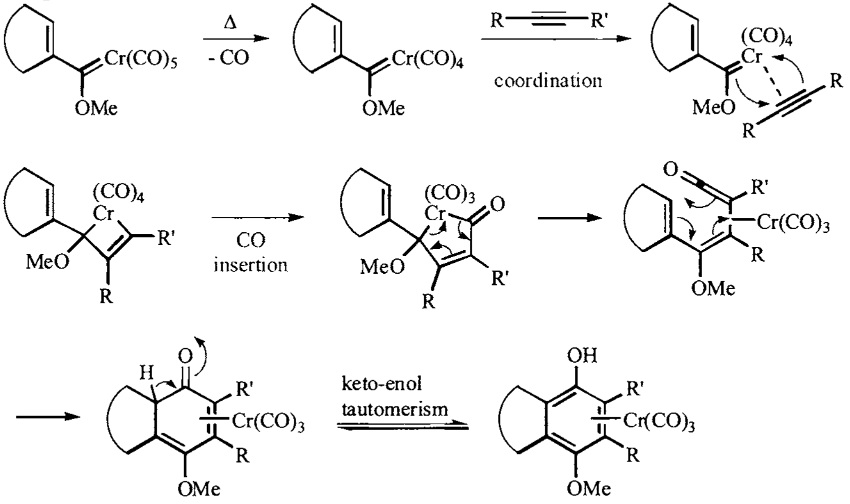
The Reaction:



vinyl or aromatic alkoxy pentacarbonyl chromium carbene complex

and sometimes the regioisomer for unsymmetrical alkynes

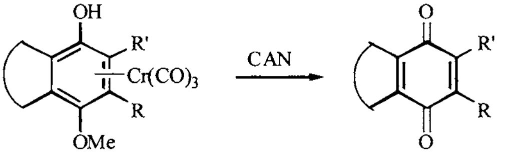
Proposed Mechanism:



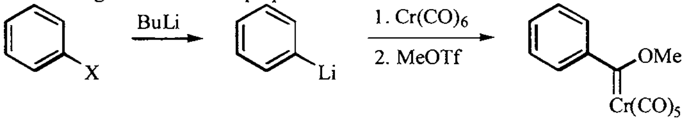
Notes:

See: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 88-91. These authors note that there is poor regioselectivity for non-symmetrical alkynes.

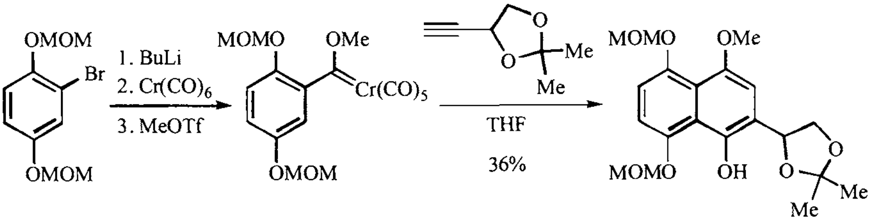
Often the product is directly oxidized:



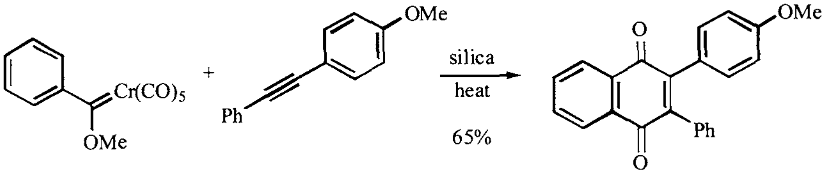
The starting material can be prepared:



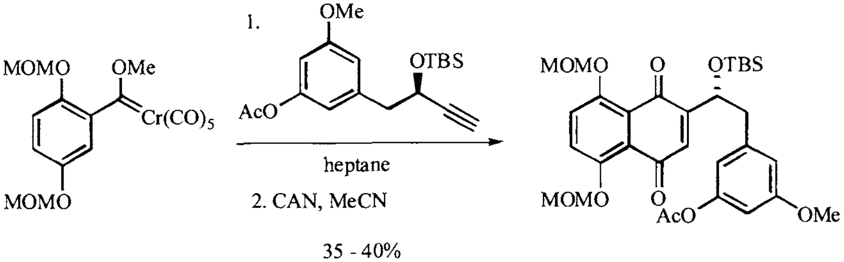
Examples:



S. R. Pulley, B. Czako, *Tetrahedron Letters* **2004**, 45, 5511



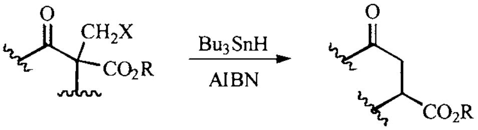
J. C. Anderson, J. W. Cran, N. P. King *Tetrahedron Letters* **2002**, 43, 3849



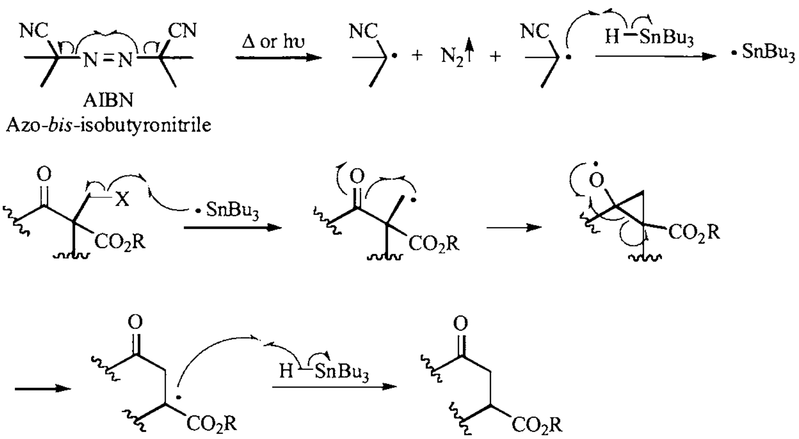
W. R. Roush, R. J. Neitz, *Journal of Organic Chemistry* **2004**, 69, 4906

Dowd-Beckwith Ring Expansion

The Reaction:

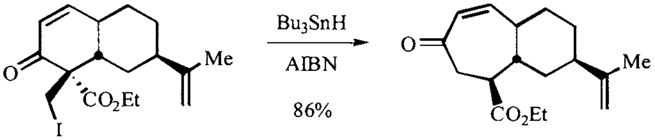


Proposed Mechanism:

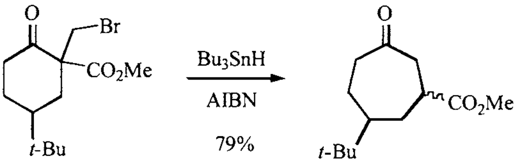


P. Dowd, S.-C. Choi, *Tetrahedron* **1989**, 45, 77

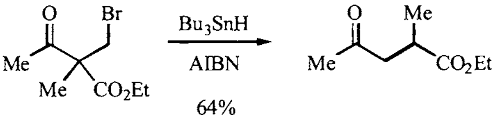
Examples:

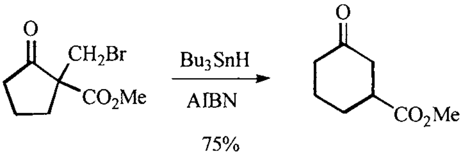


M. G. Banwell, J. M. Cameron, *Tetrahedron Letters* **1996**, 37, 525

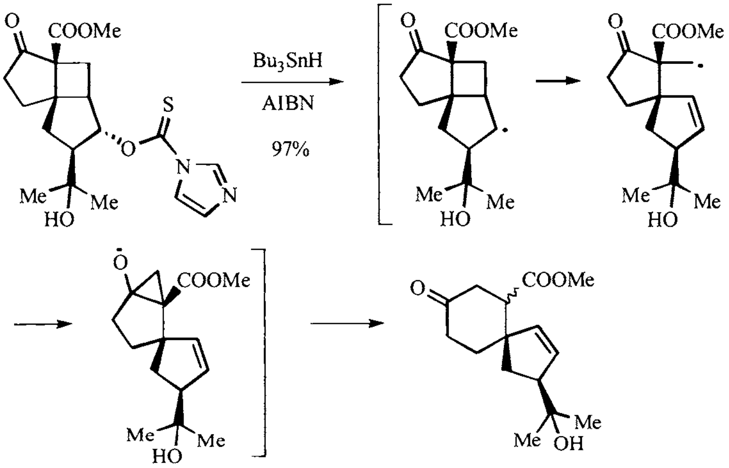


C. Wang, X. Gu, M. S. Yu, D. P. Curran, *Tetrahedron Letters* **1998**, 54, 8355





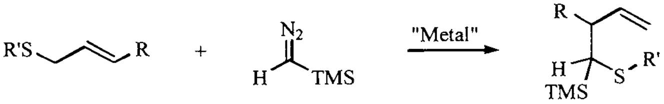
P. Dowd, S.-C. Choi, *Tetrahedron* **1989**, 45, 77



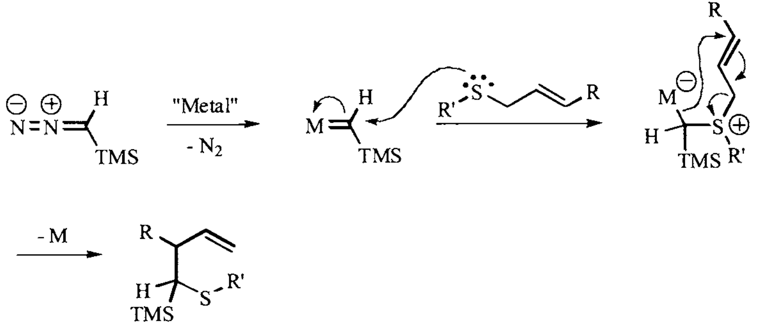
M. T. Crimmins, Z. Wang, L. A. McKerlie, *Journal of the American Chemical Society* **1998**, 120, 1747

Doyle-Kirmse Reaction

The Reaction:



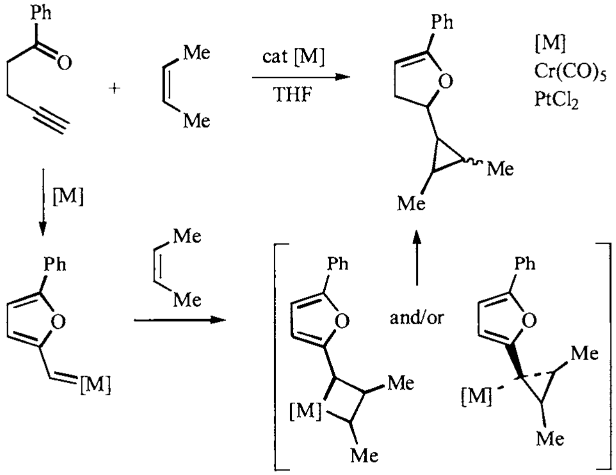
Proposed Mechanism:



M. P. Doyle, W. H. Tamblyn, V. Bagher, *Journal of Organic Chemistry* **1981**, 40, 5094

Notes:

Influence of metal catalyst:

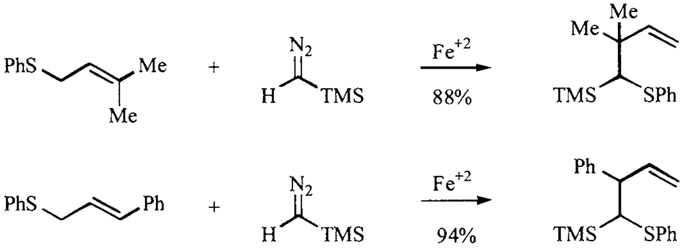


[M]	cis	trans
$Cr(CO)_5$	91	9
$PtCl_2$	75	25

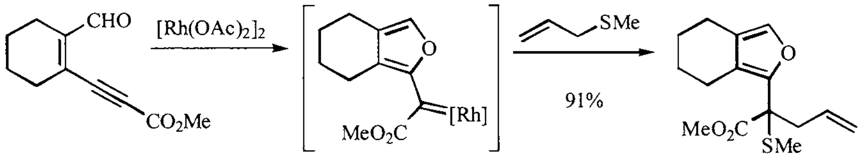
[M]	Yield
$Cr(CO)_5$	14
$PtCl_2$	26

K. Miki, T. Yokoi, F. Nishino, Y. Kato, Y. Washitake, K. Ohe, S. Uemura, *Journal of Organic Chemistry* **2004**, 69, 1557

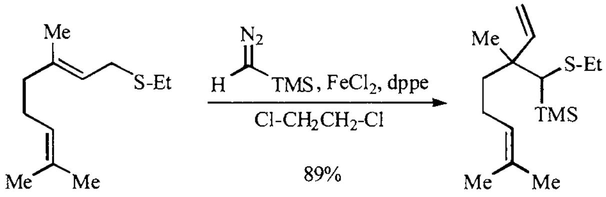
Examples:



D. S. Carter, D. L. Van Vranken, *Organic Letters* **2000**, 2, 1303



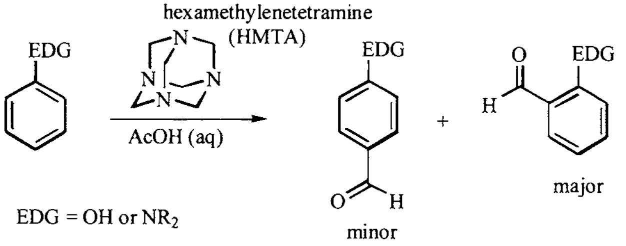
Y. Kato, K. Miki, F. Nishino, K. Ohe, S. Uemura, *Organic Letters* **2003**, 5, 2619



J. B. Perales, N. F. Makino, D. L. Van Vranken, *Journal of Organic Chemistry* **2002**, 67, 6711

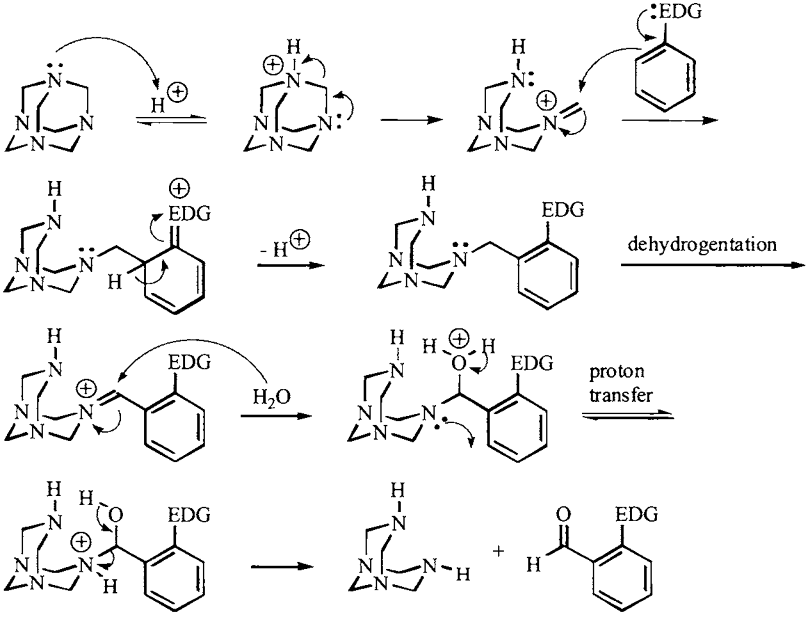
Duff Reaction

Reaction:



EDG = OH or NR_2

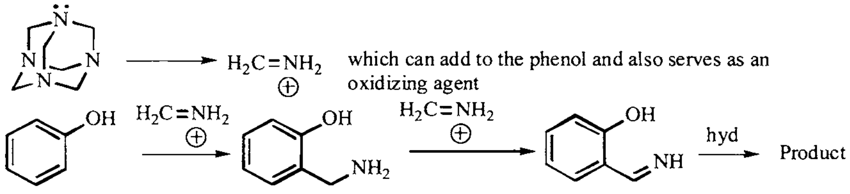
Proposed Mechanism:



Notes:

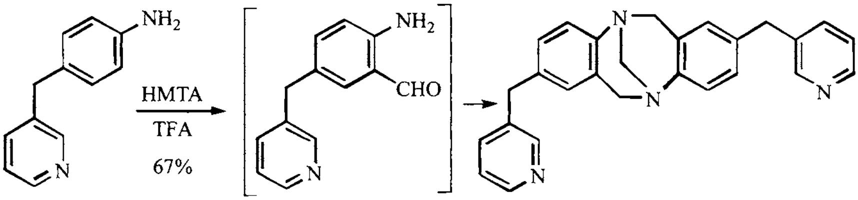
V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002, pp. 315-316; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 717.

A detailed kinetic and product (intermediate) study (Y. Ogata, A. Kawaqsaki, F. Sugiura, *Tetrahedron* **1968**, 24, 5001) describes the rapid decomposition of HMTA:

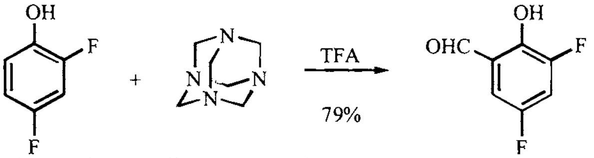


which can add to the phenol and also serves as an oxidizing agent

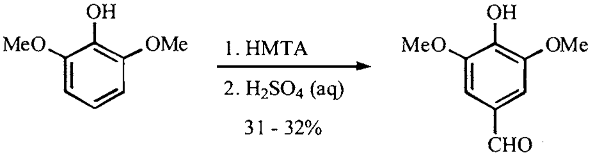
Examples:



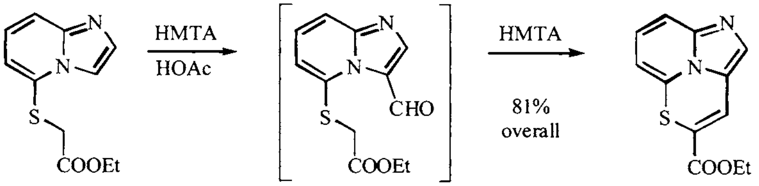
R. A. Johnson, R. R. Gorman, R. J. Wnuk, N. J. Drittenden, J. W. Aikem, *Journal of Medicinal Chemistry* **1993**, 36, 3202



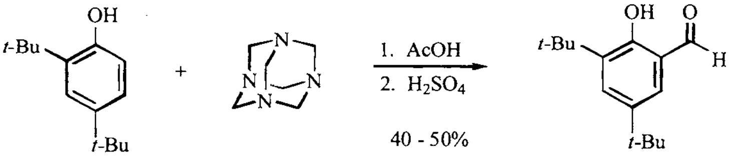
M. A. Weidner-Wells, S. A. Fraga-Spano, *Synthetic Communications* **1996**, 26, 2775



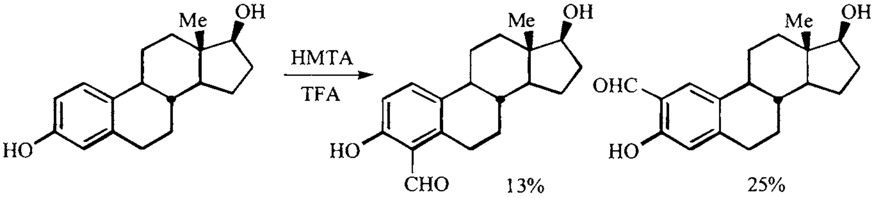
C. F. Allen, G. W. Leubner, *Organic Syntheses* CV4, 866



T. Ikemoto, T. Kawamoto, H. Wada, T. Ishida, T. Ito, Y. Isogami, Y. Miyano, Y. Mizuno, K. Tomimatsu, K. Hamamura, M. Takatani, M. Wakimasu, *Tetrahedron* **2002**, 58, 489



J. F. Larrow, E. N. Jacobson, Y. Gao, Y. Hong, X. Nie, C. M. Zepp, *Journal of Organic Chemistry* **1994**, 59, 1939



H.-M. He, M. Cushman, *Bioorganic & Medicinal Chemistry Letters* **1994**, 4, 1725

Eglinton Reaction

The Reaction:

$$2\ R-\equiv-H \xrightarrow[\text{pyridine}]{CuX_2} R-\equiv-\equiv-R$$

terminal alkyne

$X = OAc, Cl$

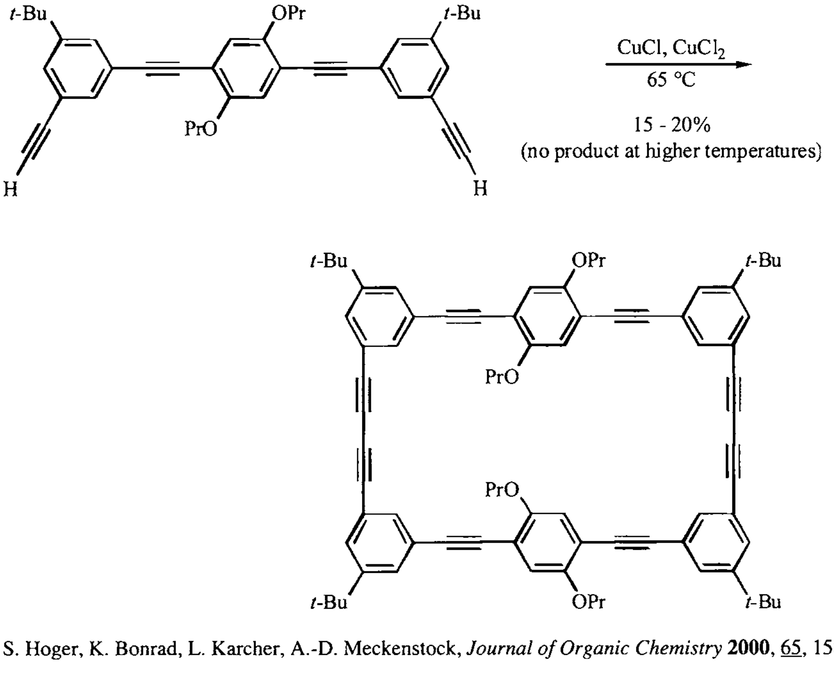
Proposed Mechanism:

See ***Alkyne Coupling*** for a general discussion.

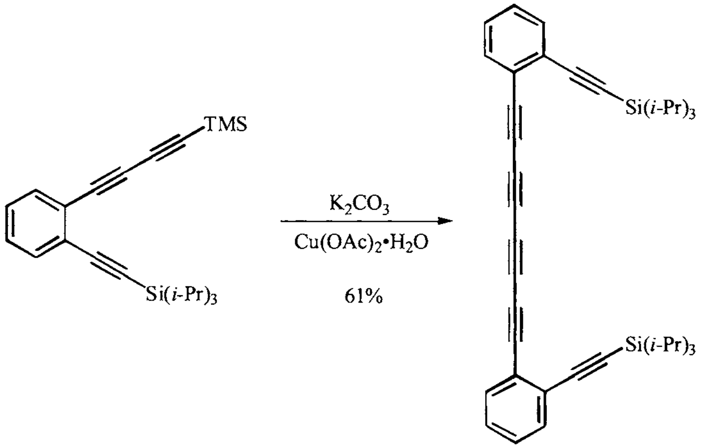
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p 927.

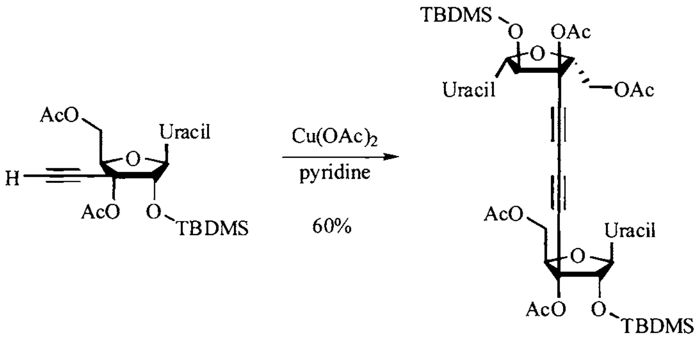
Examples:



S. Hoger, K. Bonrad, L. Karcher, A.-D. Meckenstock, *Journal of Organic Chemistry* **2000**, 65, 1588

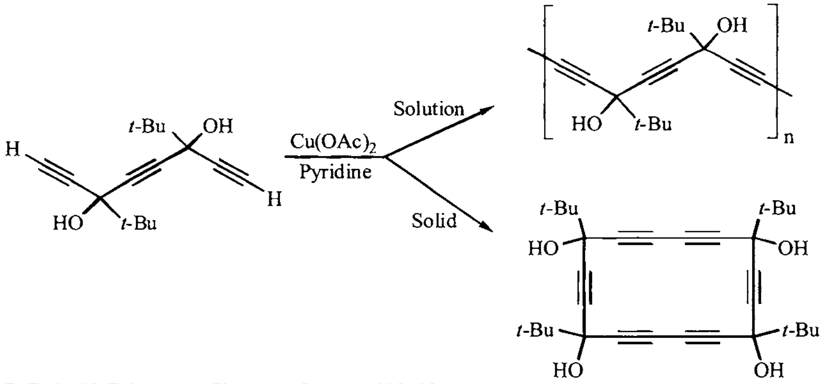


M. H. Haley, M. L. Bell, S. C. Brand, D. B. Kimball, J. J. Pak, W. B. Wan, *Tetrahedron Letters* **1997**, 38, 7483



F. Jung, A. Berger, J.-F. Biellmann, *Organic Letters* **2003**, 5, 383

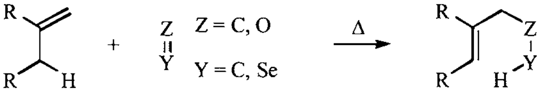
The product composition can differ depending on whether the reaction is carried out in solid or solution:



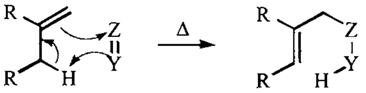
F. Toda, Y. Tokumaru, *Chemistry Letters* **1990**, 987
(Reported in P. Siemsen, R. C. Livingston, F. Diederich, *Angewandte Chemie International Edition in English* **2000**, 39, 2632)

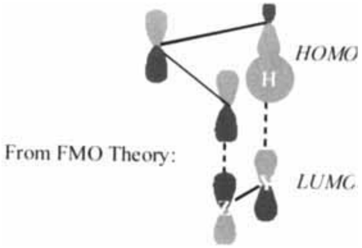
Ene Reaction (Alder-Ene Reaction)

The Reaction:



Proposed Mechanism:





Notes:

See: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 93-97.

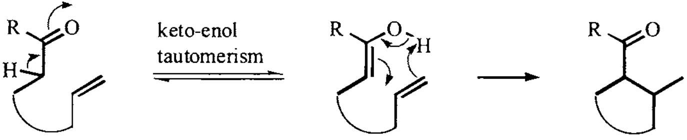
Other reactions following the "ene" mechanistic interpretation:

Reactions of singlet oxygen (***Schenck ene reaction***),

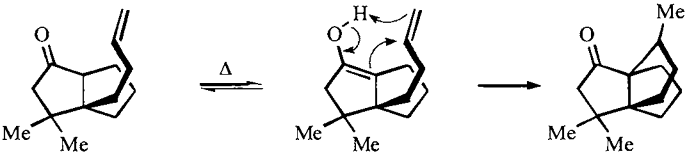
SeO_2 oxidations,

Etard Reaction,

Conia Cyclization:

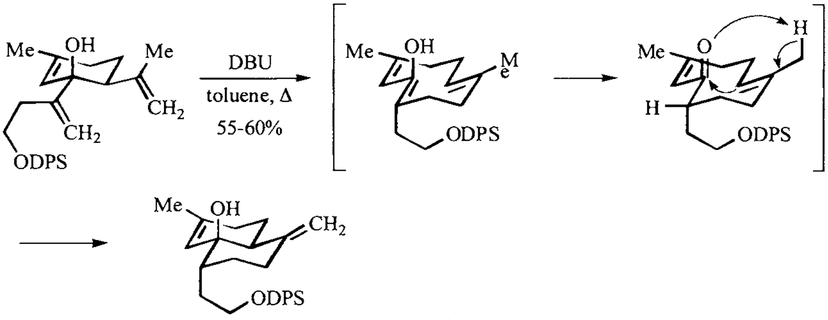


The enol serves as the ene component in the reaction.



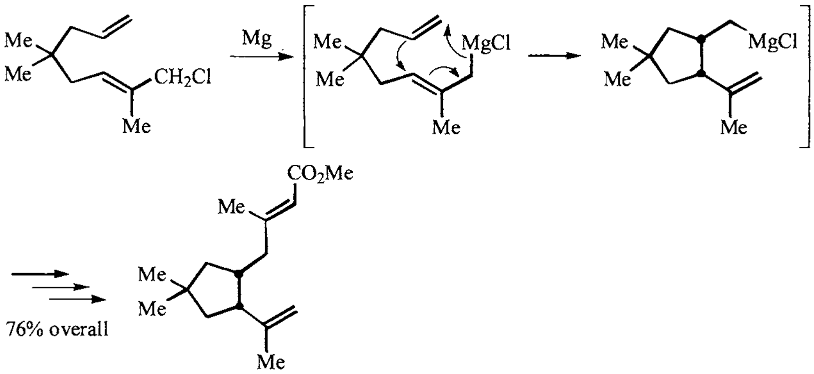
H. Schostarez, L. A. Paquette, *Tetrahedron* **1981**, 37, 4431

Examples:



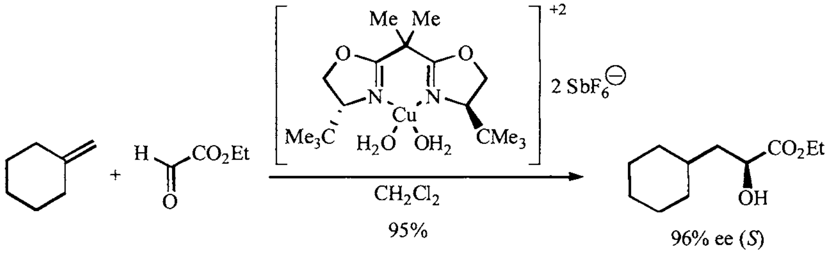
L. Barriault, D. H. Deon, *Organic Letters* **2001**, 3, 1925

The ***magnesium-ene reaction*** provides a unique approach to remote functional groups:

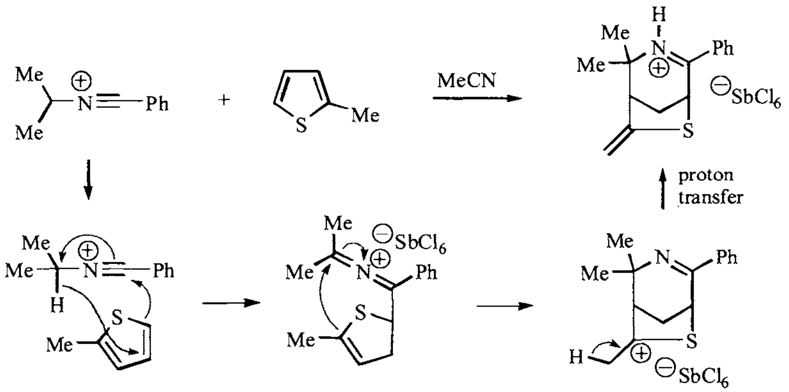


W. Oppolzer, A. Nakao, *Tetrahedron Letters* **1986**, 27, 5471

Carbonyl-ene Reaction:



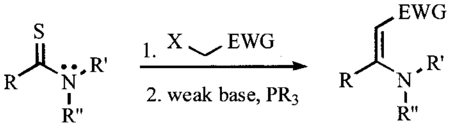
D. A. Evans, S. W. Tregay, C. S. Burgey, N. A. Paras, T. Vojkovsky, *Journal of the American Chemical Society* **2000**, 122, 7936



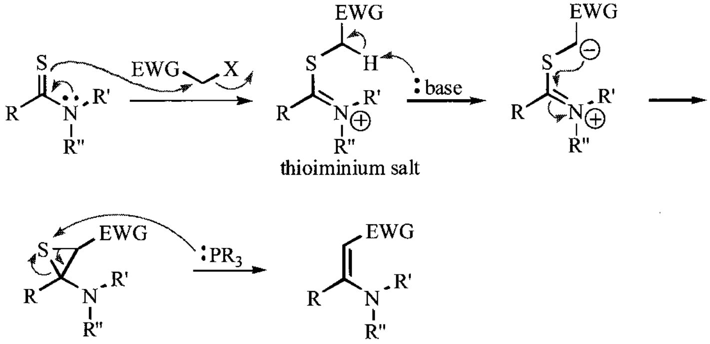
J. Henninger, K. Polborn, H. Mayr, *Journal of Organic Chemistry* **2000**, 65, 3569

Eschenmoser Coupling Reaction

The Reaction:

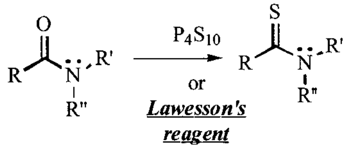


Proposed Mechanism:

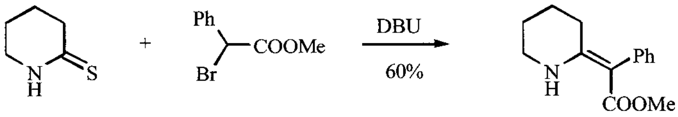


Notes:

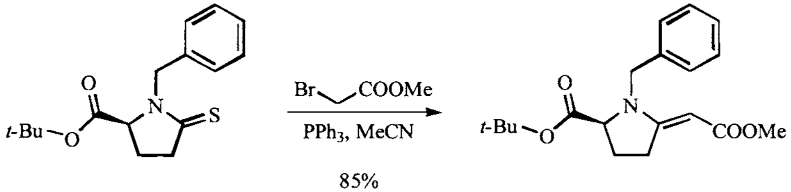
Possible starting material preparation:



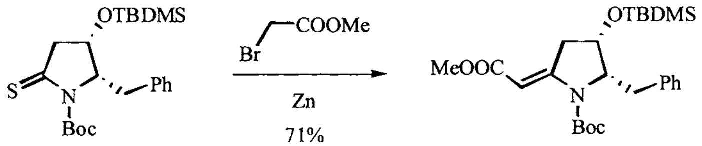
Examples:



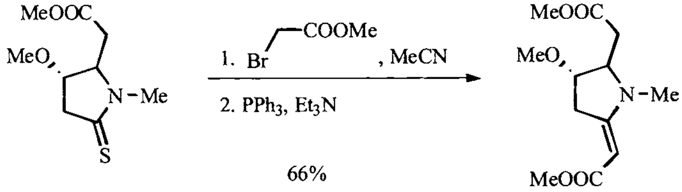
D. Russowsky, B. A. da Silveira Neto, *Tetrahedron Letters* **2004**, 45, 1437



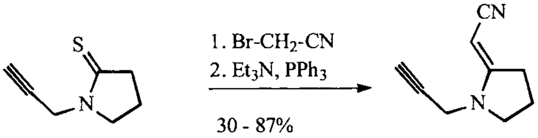
J. S. Petersen, G. Fels, H. Rapoport, *Journal of the American Chemical Society* **1984**, 106, 4359



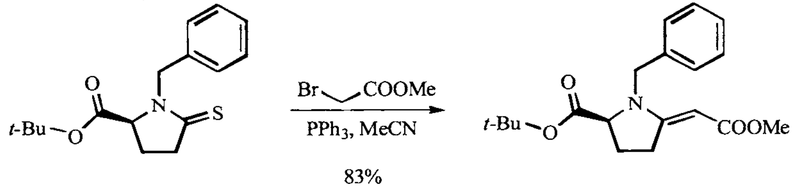
H. K. Lee, J. Kim, C. S. Pak, *Tetrahedron Letters* **1999**, 40, 2173



D. J. Hart, L.-Q. Sun, A. P. Kozikowski, *Tetrahedron Letters* **1995**, 36, 7787



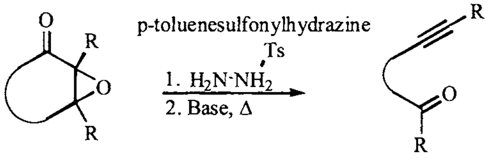
D. Gravenstock, I. G. Pierson, *Tetrahedron Letters* **2000**, 41, 3497



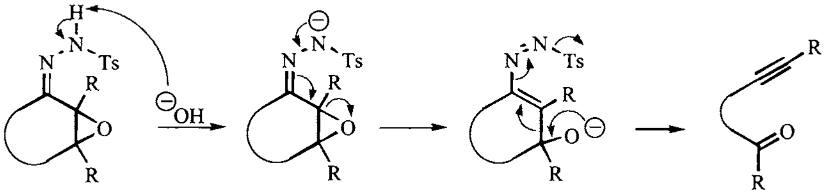
J. A. Campbell, H. Rapoport, *Journal of Organic Chemistry* **1996**, 61, 6313

Eschenmoser Fragmentation (Eschenmoser-Tanabe Fragmentation / Ring Cleavage)

The Reaction:



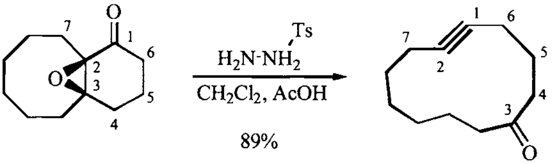
Proposed Mechanism:



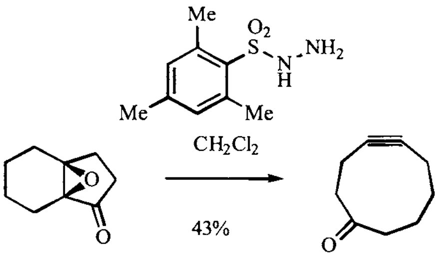
Notes:

See: M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1347. The authors note that aldehydes can be formed if 2,4-dinitrophenylhydrazine is used.

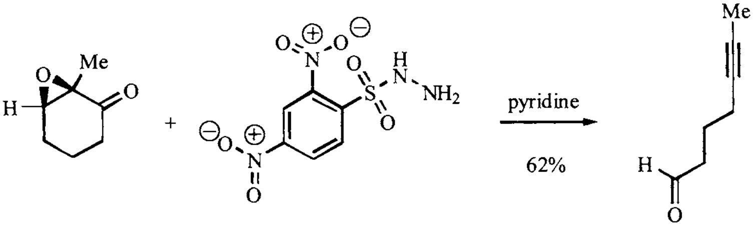
Examples:



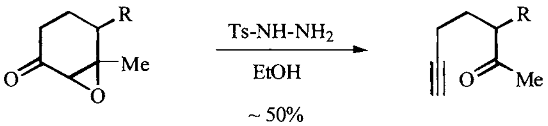
P. Kraft, W. Tochtermann, *Justus Liebig's Annalen der Chemie* **1994**, 1161 (AN 1994:700495)



C. B. Reese, H. P. Sander, *Synthesis* **1981**, 276

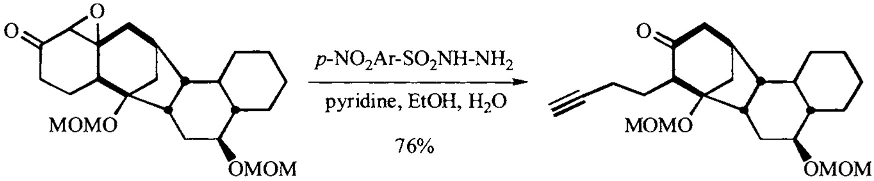


E. J. Corey, H. S. Sachdev, *Journal of Organic Chemistry* **1975**, 40, 579



R = Pr, *i*-Bu, *i*-Pr,

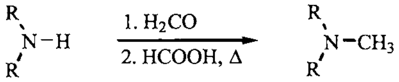
W. Dai, J. A. Katzenellenbogen, *Journal of Organic Chemistry* **1993**, 58, 1900



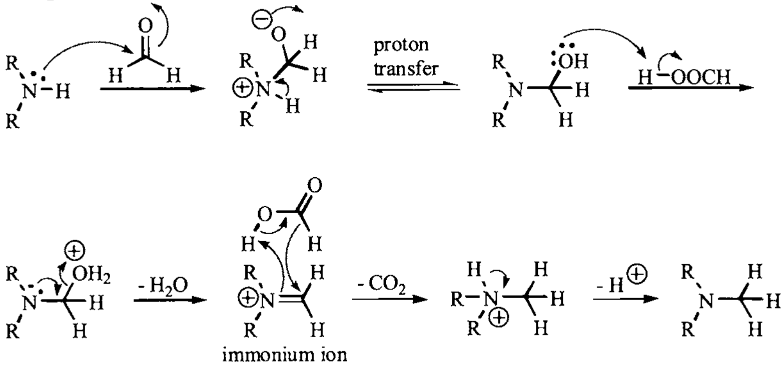
L. N. Mander, M. M. McLachlan, *Journal of the American Chemical Society* **2003**, 125, 2400

Eschweiler-Clarke (Clark) Methylation

The Reaction:



Proposed Mechanism:

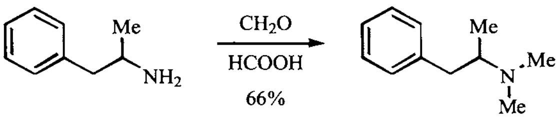


Notes:

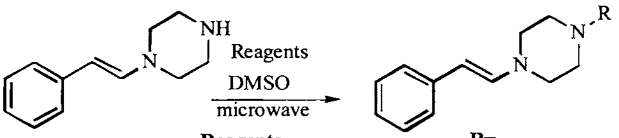
This reaction specifically refers to the case when a primary or secondary amine is reductively methylated with formaldehyde and formic acid.

See also the ***Wallach Reaction*** and the ***Leuckart(-Wallach) Reaction***.

Examples:

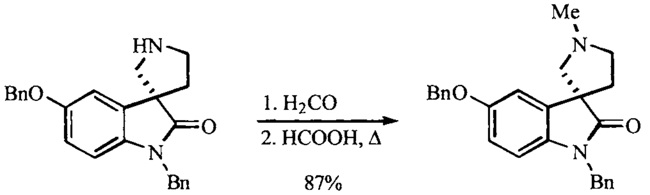


W. E. Parham, W. T. Hunter, R. Hanson, T. Lahr, *Journal of the American Chemical Society* **1952**, 74, 5646

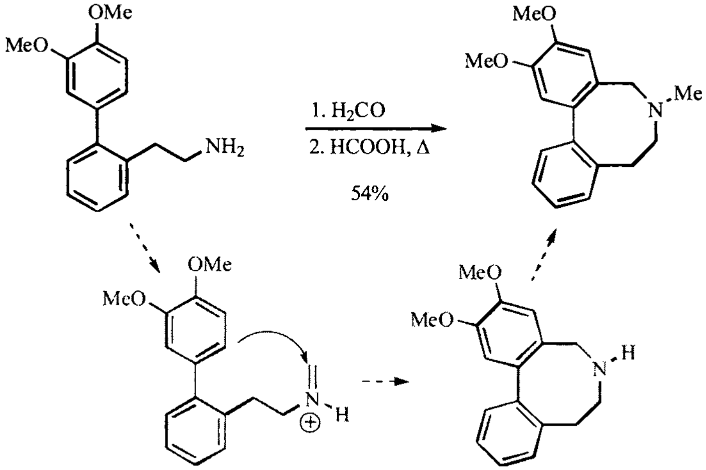


Reagents	R=
HCHO, DCOOD	$-CH_2D$
DCHO, HCOOH	$-CHD_2$
DCDO, DCOOD	$-CD_3$

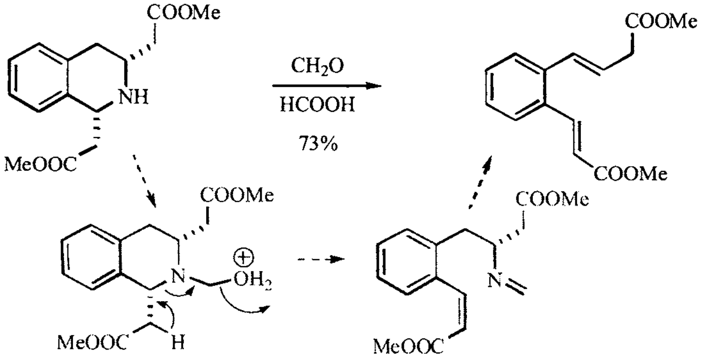
J. R. Harding, J. R. Jones, S.-Y. Lu, R. Wood, *Tetrahedron Letters* **2002**, 43, 9487



G. Lakshmaiah, T. Kawabata, M. Shang, K. Fuji, *Journal of Organic Chemistry* **1999**, 64, 1699



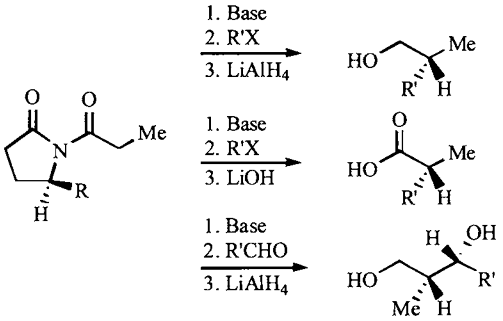
P. Sahakitpichan, S. Ruchirawat, *Tetrahedron Letters* **2003**, 44, 5239



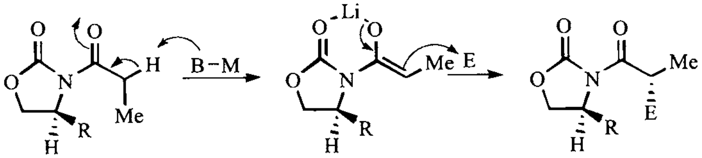
K. Watanabe, T. Wakabayashi, *Journal of Organic Chemistry* **1980**, 45, 357

Evans Chiral *N*-Acyloxazolidinone Methodology

The Reaction:



Proposed Mechanism:



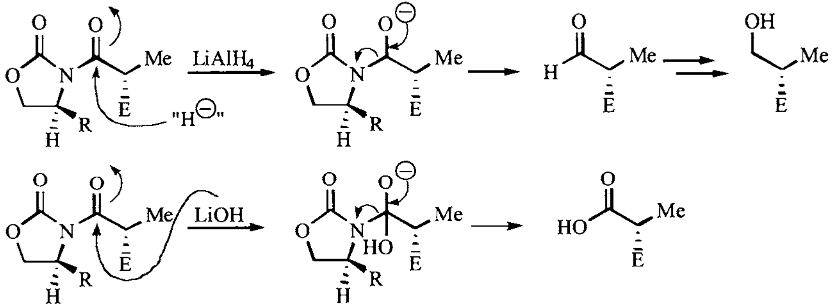
Notes:

R is often *i*-Pr or Bn.

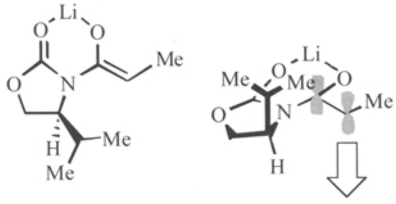
Bases (B-M) include LDA, Li or NaHMDS, amines with Lewis acids, etc.

E = electrophile (halide, aldehyde).

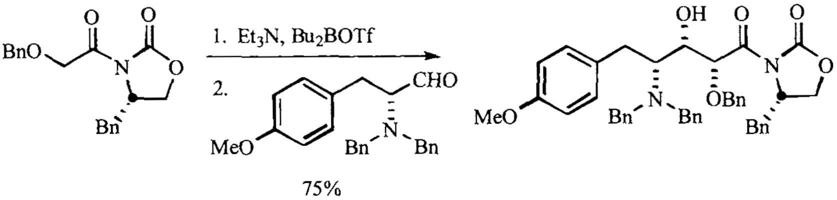
Removal of chiral auxiliary:



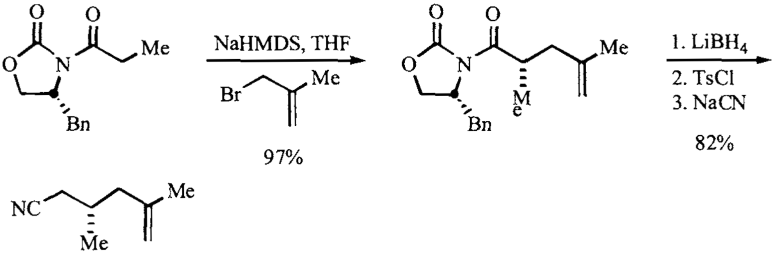
Z-enolates produced. Steric effects on direction of enolate alkylation are quite obvious:



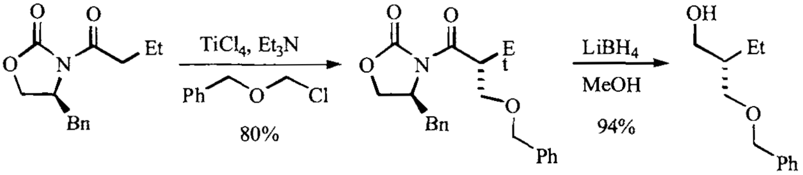
Examples:



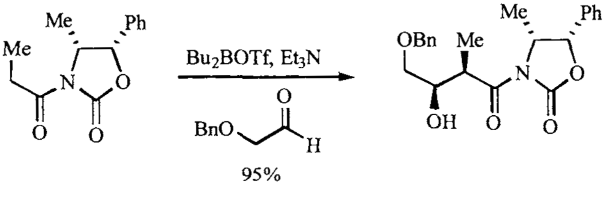
A. N. Hulme, E. M. Rosser, *Organic Letters* **2002**, 4, 265



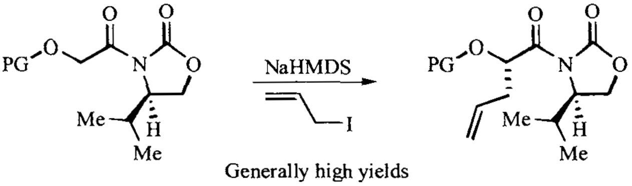
M. R. Pitts, J. Mulzer, *Tetrahedron Letters* **2002**, 43, 8471



A. K. Ghosch, J.-H. Kim, *Tetrahedron Letters* **2003**, 44, 7659



A. K. Mandal, *Organic Letters* **2002**, 4, 2043

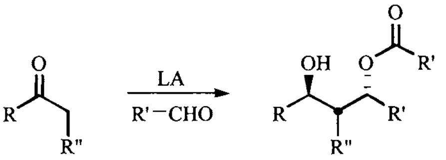


Protecting Groups = Bn-, Et$_3$Si-, Me-, MOM-.

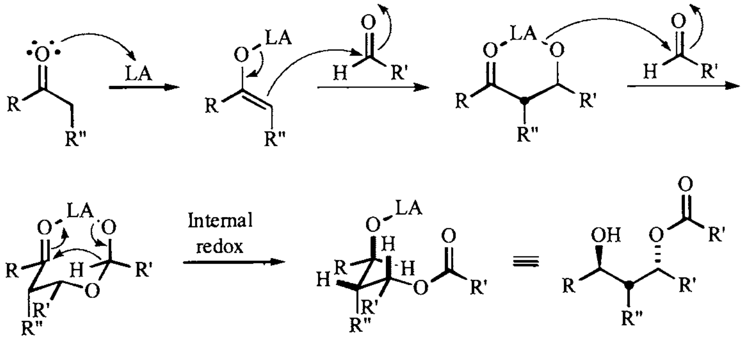
M. T. Crimmins, K. A. Emmitte, J. D. Katz, *Organic Letters* **2000**, 2, 2165

Evans-Tischenko Reaction

The Reaction:



Proposed Mechanism:

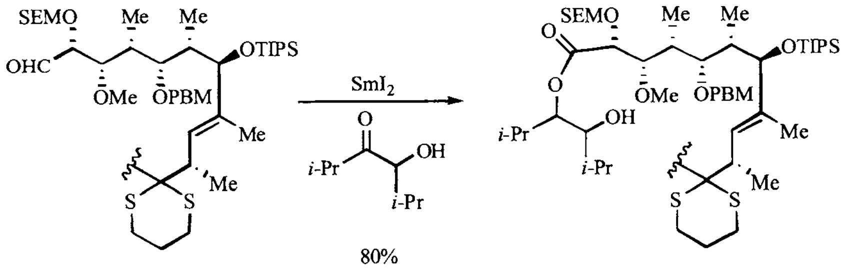


Note syn-relationships (highlighted bonds)

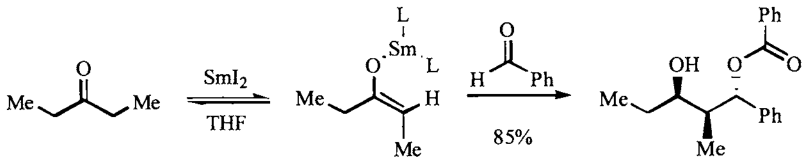
Notes:

The ***Evans-Tischenko Reaction*** generally requires a β-hydroxyketone (developed from an ***Aldol reaction***) to react with an aldehyde. The resulting glycol monoester will be characterized as having high anti-selectivity.

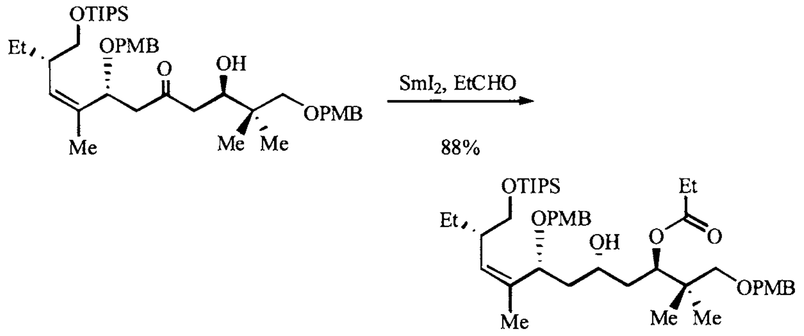
Examples:



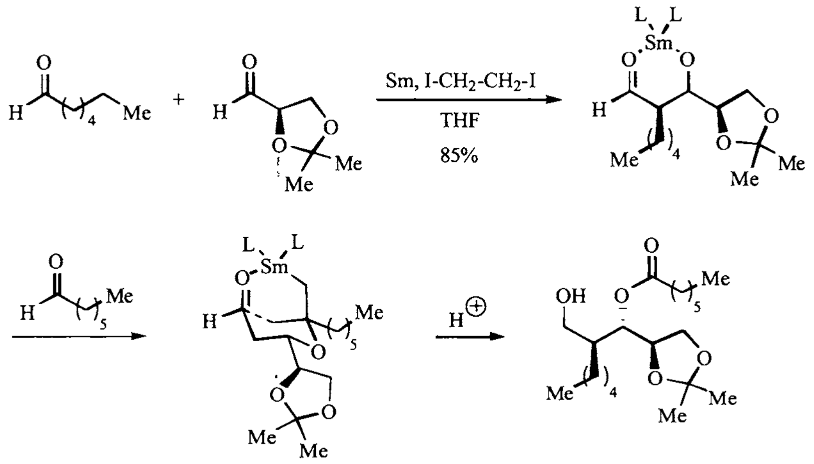
A. B. Smith, III, C. M. Adams, S. A. L. Barbosa, A. P. O. Degnan, *Journal of the American Chemical Society* **2003**, 125, 350



L. Lu, H.-Y. Chang, J.-M. Fang, *Journal of Organic Chemistry* **1999**, 64, 843



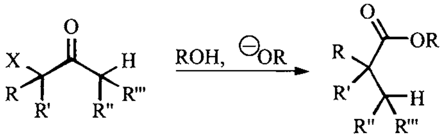
I. Paterson, M. E. DiFrancesco, T. Kuhn, *Organic Letters* **2003**, 5, 599



L. Lu, H.-Y. Chang, J.-M. Fang, *Journal of Organic Chemistry* **1999**, 64, 843

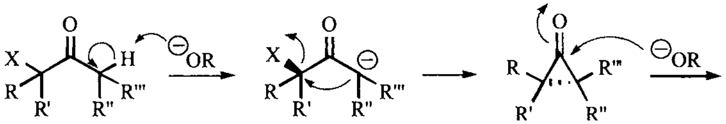
Favorskii Rearrangement (Favorsky)

The Reaction:

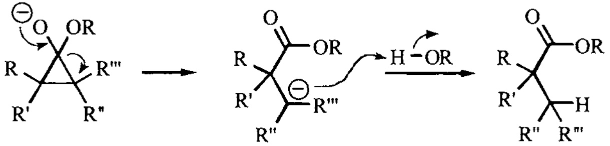


Can be a ring contraction.

Proposed Mechanism:



The new C-C is of opposite stereochemistry from the departing X-group.
G. Stork, J. J. Borowitz, *Journal of the American Chemical Society* **1960**, 82, 4370.



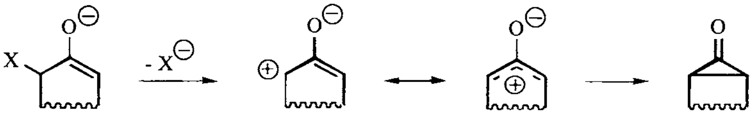
Either side of the cyclopropane can break.
The more stabilized carbanion will be favored.

Notes:

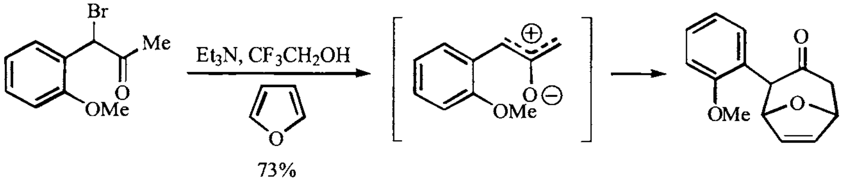
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 100-103; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1403-1405; A. S. Kende, *Organic Reactions* **11**, 4.

Alkoxide or hydroxide bases can be used, giving esters (as shown above) or acids, respectively.

An alternative rationale:

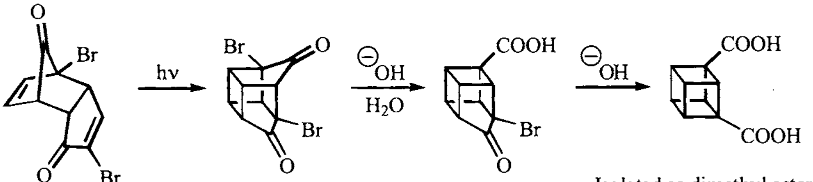


The oxyallyl intermediate has been trapped:



M. W. Finch, J. Mann, P. D. Wilde, *Tetrahedron* **1987**, 43, 5431

The rearrangement was essential for the design and execution of the first preparation of the cubane skeleton:

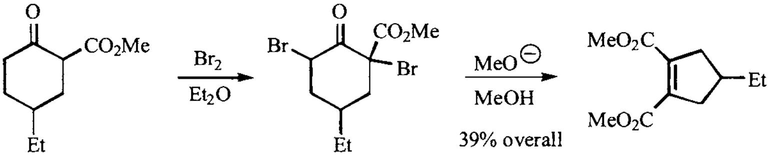


Isolated as dimethyl ester
in overall yield of 30%

P. E. Eaton, T. W. Cole, Jr., *Journal of the American Chemical Society* **1964**, 86, 962

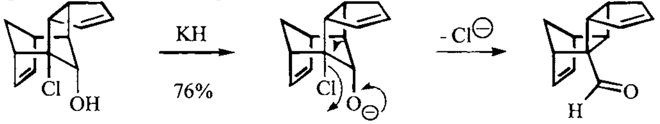
Examples:

R. Xu, G. Chu, D. Bai, *Tetrahedron Letters* **1996**, 37, 1463

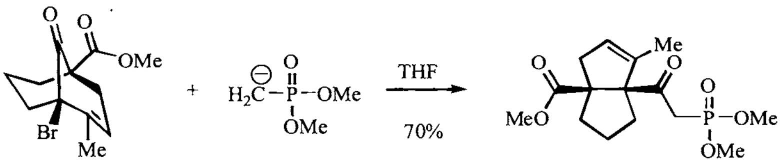


J. D. White, J. Kim, N. E. Drapela, *Journal of the American Chemical Society* **2000**, 122, 8665

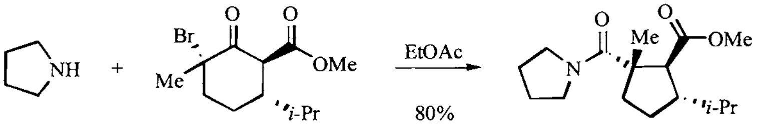
Quasi Favorski Rearrangement:



M. Harmata, P. Rashatasakhon, *Organic Letters* **2001**, 3, 2533



G. A. Kraus, J. Shi, *Journal of Organic Chemistry* **1991**, 56, 4147



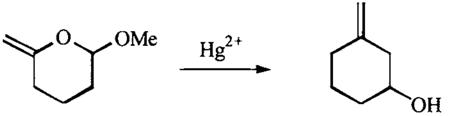
J. M. Llera, B. Fraser-Reid, *Journal of Organic Chemistry* **1989**, 54, 5544

Ferrier Rearrangement

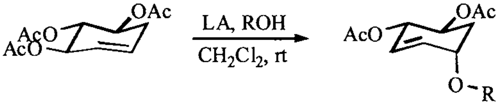
The Reaction:

Several reaction types appear to be covered under this heading:

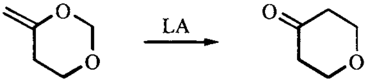
1.



2.



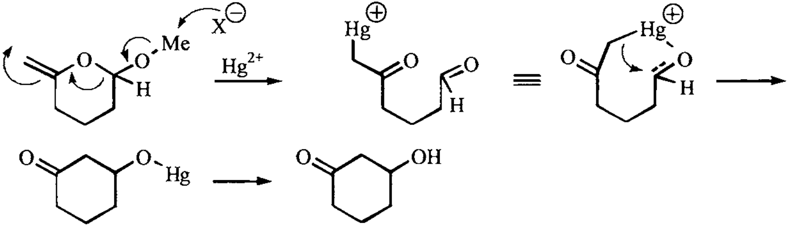
3. ***A Petasis-Ferrier rearrangement***



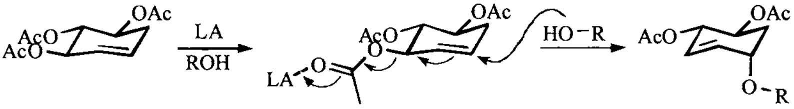
N. A. Petasis, S.-P. Lu, *Tetrahedron Letters* **1996**, 37, 141

Proposed Mechanism:

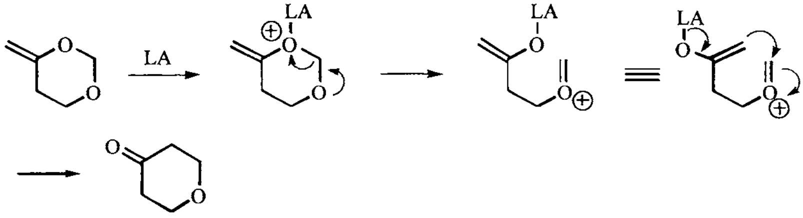
1.



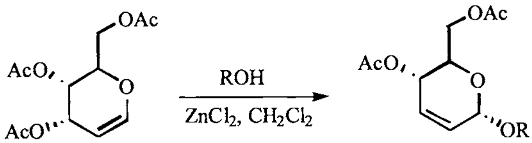
2.

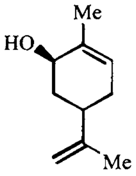


3.

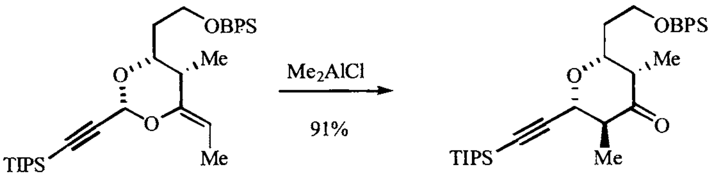


Examples:

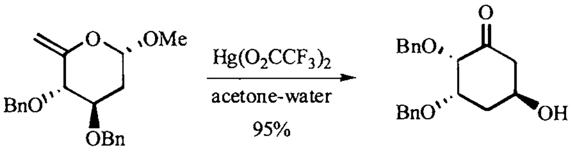


ROH	% Yield
	70%
Ph-CH_2OH	95%

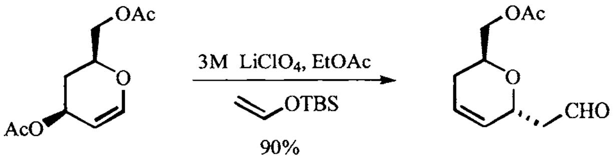
B. K. Bettadaiah, P. Srinivas, *Tetrahedron Letters* **2003**, 44, 7275



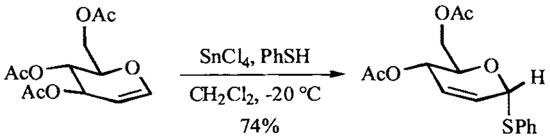
A. B. Smith, III, K. P. Minbiule, P. R. Verhoest, T. J. Beauchamp, *Organic Letters* **1999**, 1, 913



H. Fuwa, Y. Okamura, H. Natsugari, *Tetrahedron* **2004**, 60, 5341



P. A. Grieco, J. D. Speake, *Tetrahedron Letters* **1998**, 39, 1275



C. Kan, C. M. Long, M. Paul, C. M. Ring, S. E. Tully, C. M. Rojas, *Organic Letters* **2001**, 3, 381

Finkelstein Reaction

The Reaction:

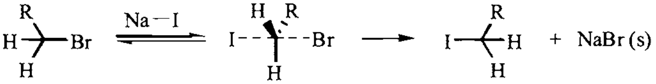
$$R{-}X + Na{-}X' \overset{\text{acetone}}{\rightleftharpoons} R{-}X' + Na{-}X\ (s)$$

X = Br or Cl
X' = I or F

Proposed Mechanism:

See: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 102-103; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5^{th} ed., John Wiley and Sons, Inc., New York, 2001, p. 517

This is a classical S_N2 reaction, therefore 1° > 2° > 3°.

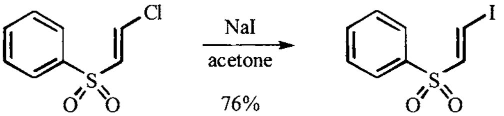


3° chlorides -> 3° iodides with NaI in CS_2 and $ZnCl_2$ catalyst.

NaBr and NaCl are not soluble in acetone, driving the equilibrium.

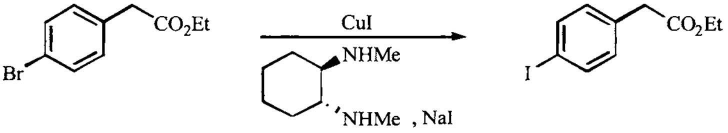
Notes:

Although the reaction was considered to involve simple displacement on alkyl halides, an interpretation now appears to include other systems:



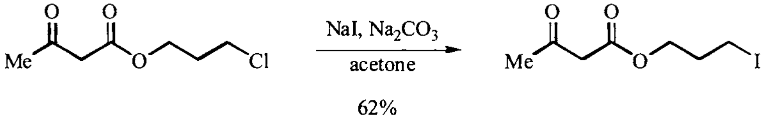
T. Zoller, D. Uguen, A. DeCian, J. Fischer, *Tetrahedron Letters* **1998**, 39, 8089

An "***Aromatic Finkelstein***" reaction:

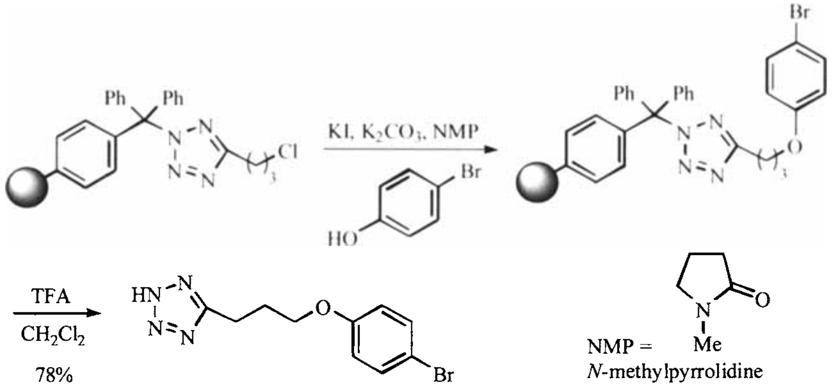


A. Klapars, S. L. Buchwald, *Journal of the American Chemical Society* **2002**, 124, 14844

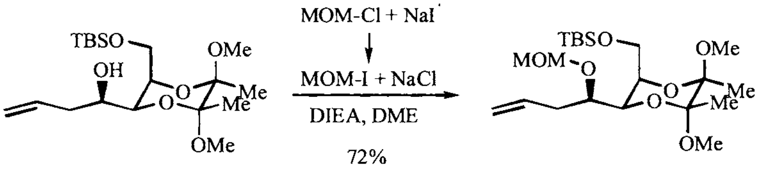
Examples:



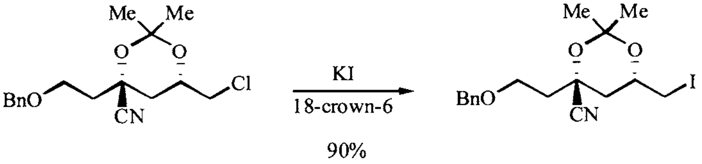
J. Christoffers, H. Oertling, P. Fischer, W. Frey, *Tetrahedron* **2003**, 59, 3769



D. P. Matthews, J. E. Green, A. J. Shuker, *Journal of Combinatorial Chemistry* **2000**, 2, 19



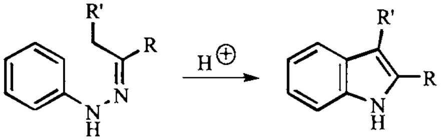
DIEA = ***Hunig's Base*** = diisopropylethylamine
D. J. Dixon, A. C. Foster, S. V. Ley, *Organic Letters* **2000**, 2, 123



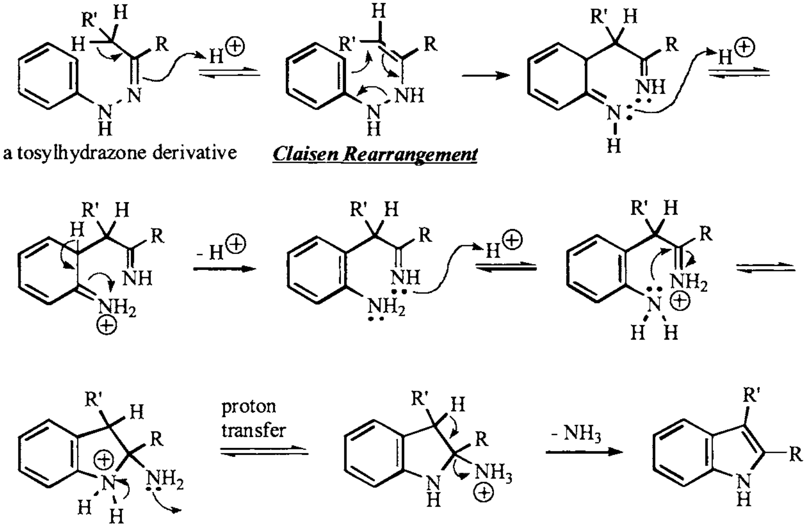
T. I. Richardson, S. D. Rychnovsky, *Journal of the American Chemical Society* **1997**, 119, 12360

Fischer Indole Synthesis

The Reaction:



Proposed Mechanism:

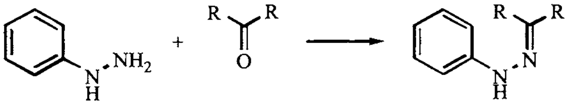


See: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 103-106; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1452-1453

Notes:

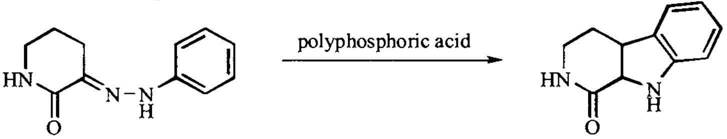
A variety of Lewis acids can be used.

The ***Barry Reaction***:

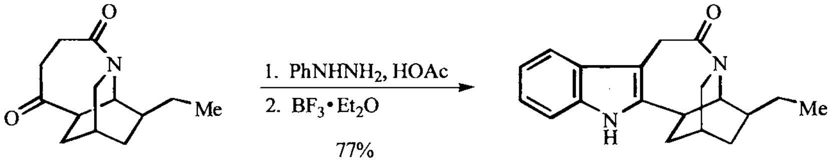


V. C. Barry, *Nature* **1948**, 152, 537

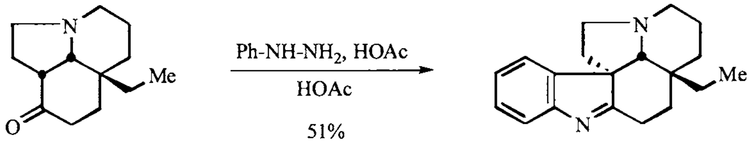
Abramovitch-Shapiro Protocol



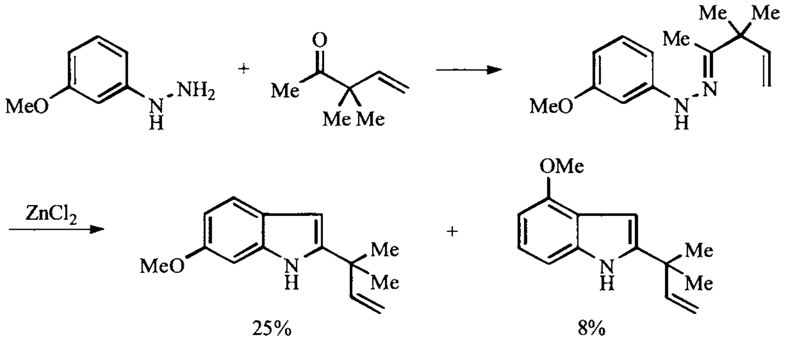
Examples:



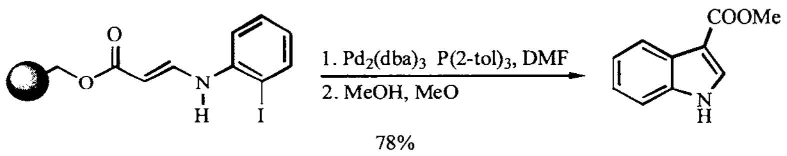
J. D. White, Y. Choi, *Organic Letters*, **2000**, 2, 2373



R. Iyengar, K. Schildknegt, J. Aube, *Organic Letters* **2000**, 2, 1625



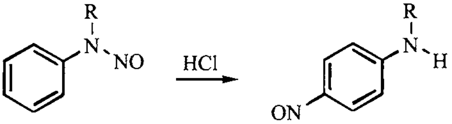
R. J. Cox, R. M. Williams, *Tetrahedron Letters* **2002**, 43, 2149



K. Yamazaki, Y. Kondo, *Journal of Combinatorial Chemistry* **2002**, 4, 191

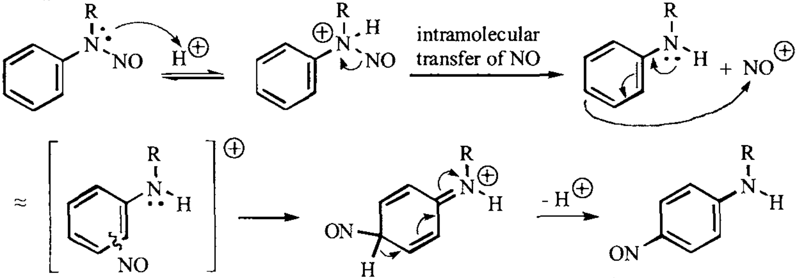
Fischer-Hepp and Related Rearrangements

The Reaction:



HCl is the preferred acid.

Proposed Mechanism:



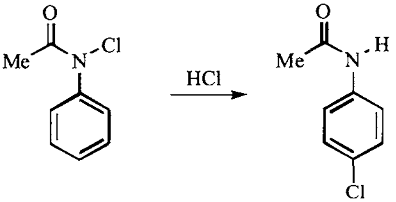
See: M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp. 728-730 for the ***Fischer-Hepp Rearrangement*** as well as the ***Orton and Hofmann-Martius Rearrangements***.

D. L. H. Williams, *Tetrahedron* **1975**, 31, 1343

See similarity to:

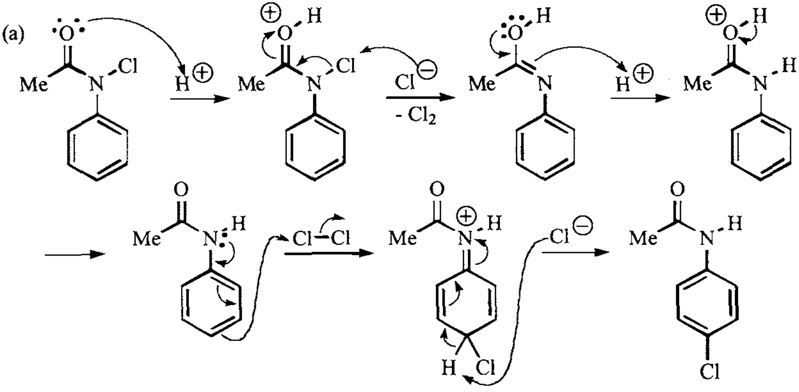
Orton Rearrangement

The Reaction:

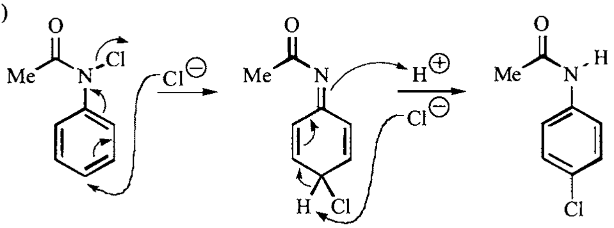


D. L. H. Williams, *Tetrahedron* **1975**, 31, 1343 comments on the similarities.

Proposed Mechanism:

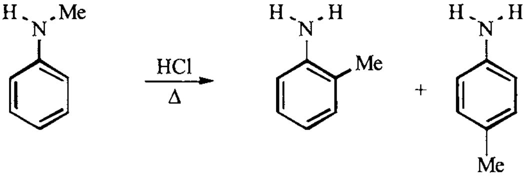


(b)

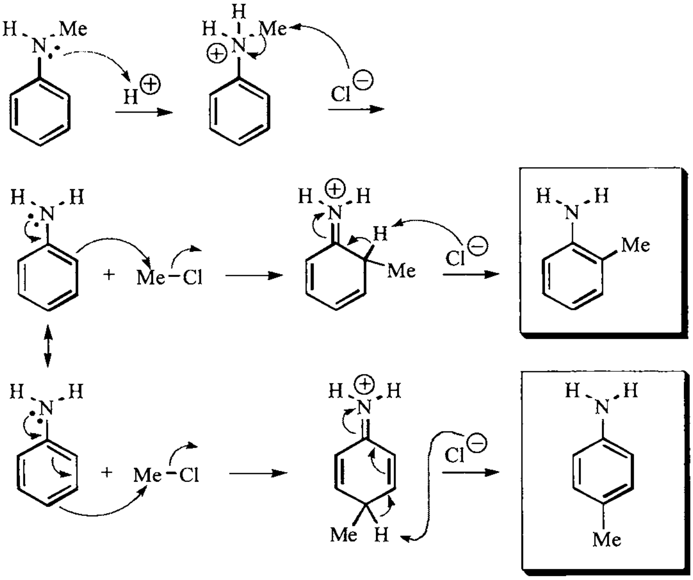


Hofmann-Martius Rearrangement

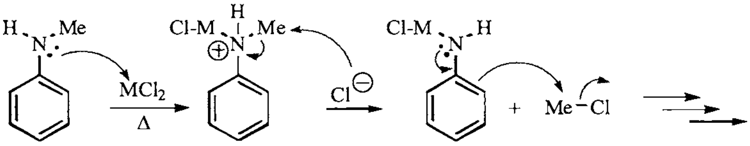
The Reaction:



Proposed Mechanism:



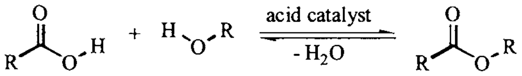
Reilly-Hickinbottom Rearrangement - uses Lewis acids and the amine rather than protic acid and the amine salt.



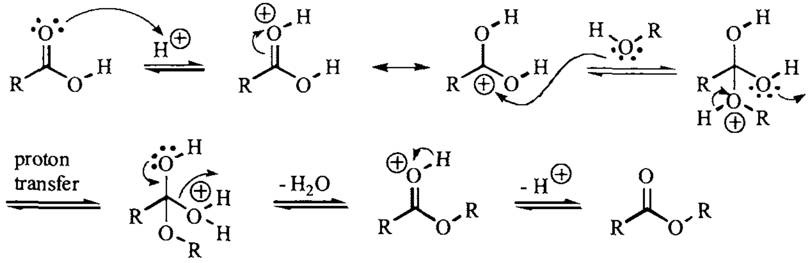
M = Co, Cd, Zn

Fischer Esterification / Fischer-Speier Esterification

The Reaction:



Proposed Mechanism:

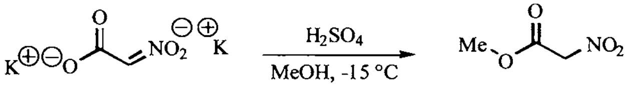


Notes: R. Bruchner, *Advanced Organic Chemistry, Reaction Mechanisms*, Academic Press, San Diego, CA, 2002, p. 247

This is an equilibrium process, and the extent of reaction is controlled by forcing the equilibrium to the right. Trapping of water, or forcing by having one reactant (clearly the most available!) in excess are methods often employed.

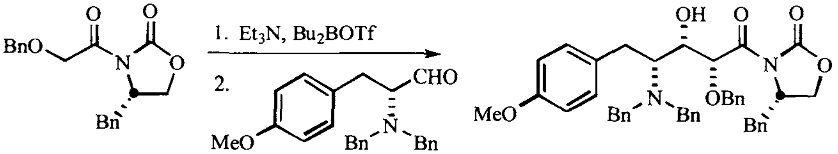
See: K. G. Kabza, B. R. Chapados, J. E. Gestwicki, J. L. McGrath, *Journal of Organic Chemistry* **2000**, 65, 121 for an interesting overview in the context of microwave use.
This process is common for undergraduate laboratory experiments.

Examples:



66-70%

S. Zen, M. Koyama, S. Koto, *Organic Syntheses* CV 6, 797



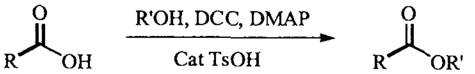
75%

A. N. Hulme, E. M. Rosser, *Organic Letters* **2002**, 4, 265

Steglich Esterification

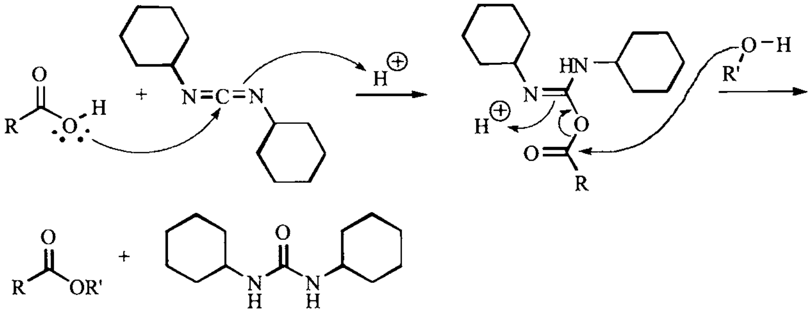
Useful method for sterically-hindered esterification reactions.

Reaction:

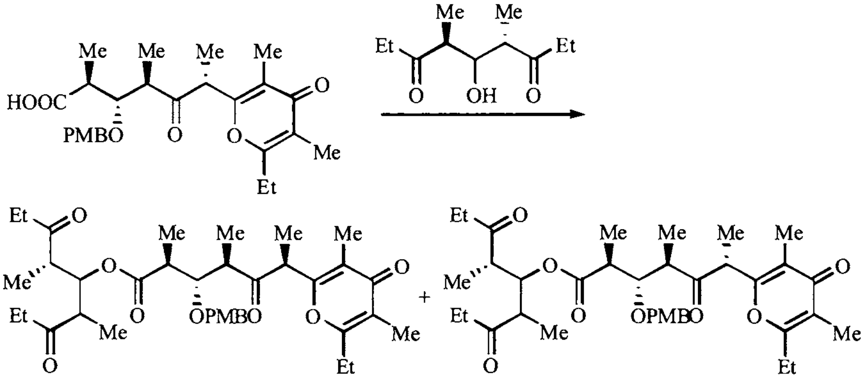


See: B. Neises, W. Steglich, *Organic Syntheses* CV 7, 93

Mechanism:

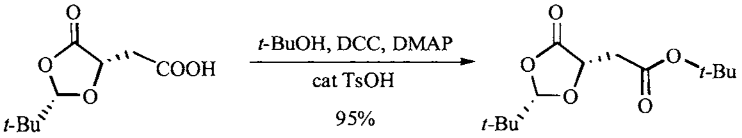


Examples:



Conditions	Ratio		
DCC, DMAP, DMAP-HCl	2.5	:	1
DMAP, Et_3N, 2,4,6-$Cl_3(C_6H_2)COC$	1	:	10

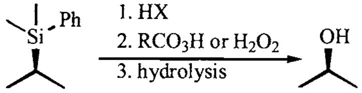
I. Paterson, D. Y.-K. Chen, J. L. Acena, A. S. Franklin, *Organic Letters* **2000**, 2, 1513



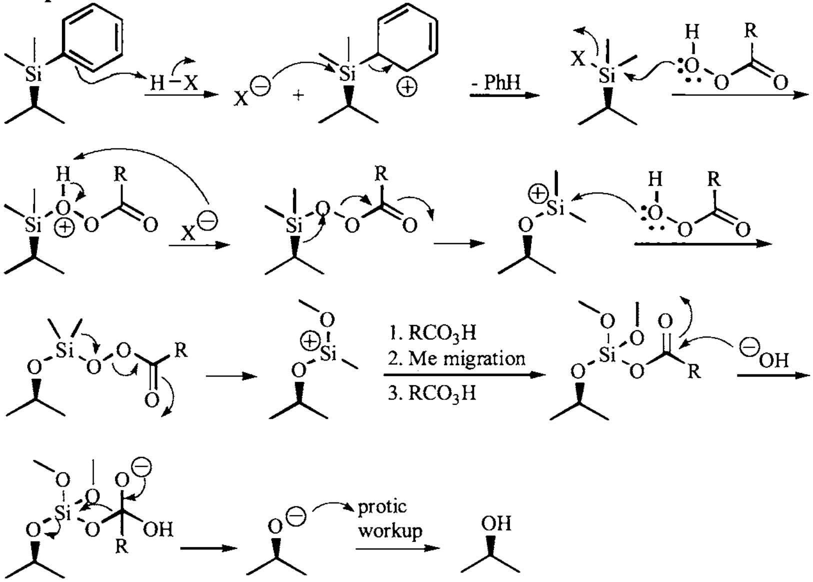
M. Sefkow, *Journal of Organic Chemistry* **2001**, 66, 2343

Fleming Oxidation

The Reaction:



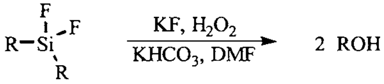
Proposed Mechanism:



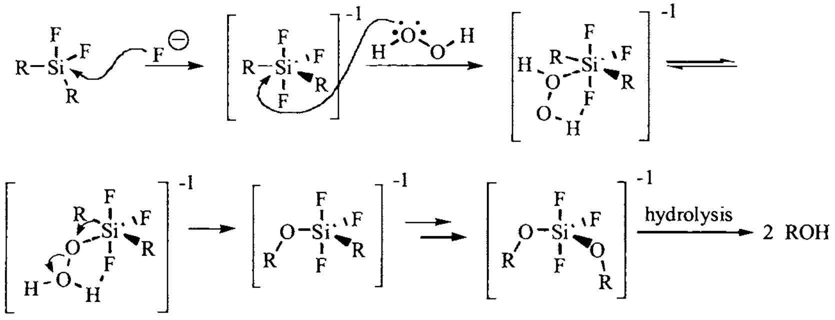
Notes:

This reaction, depending on the details of the reaction, is known as the ***Fleming Oxidation***, the ***Fleming-Tamao Oxidation***, the ***Tamao-Fleming Oxidation***, or the ***Tamao-Kumada Oxidation***.

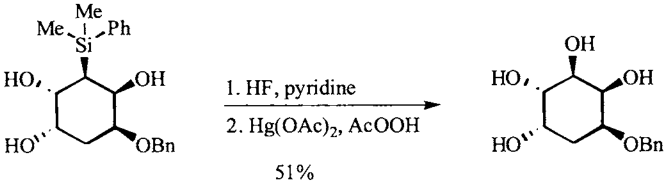
Fleming-Tamao-Kumada Oxidation



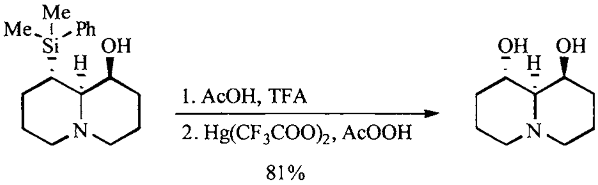
Proposed Mechanism:



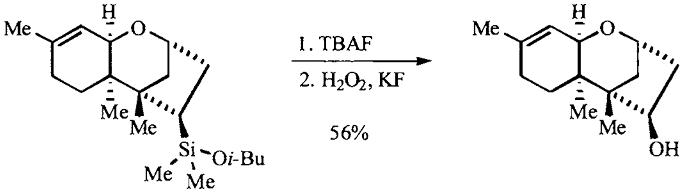
Examples:



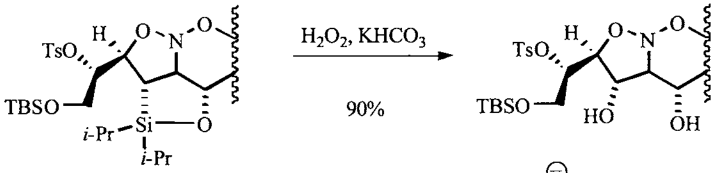
J. N. Heo, E. B. Holson, W. R. Roush, *Organic Letters* **2003**, 5, 1697



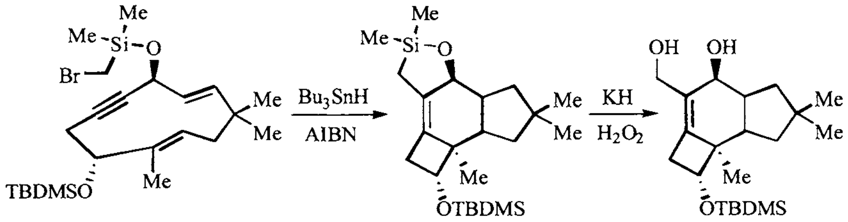
J. A. Vanecko, F. G. West, *Organic Letters* **2002**, 4, 2813



M. K. O'Brien, A. J. Pearson, A. A. Pinkerton, W. Schmidt, K. Willamn, *Journal of the American Chemical Society* **1989**, 111, 1499



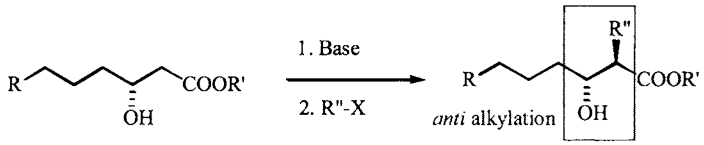
Note: When the silicon unit is part of an oxasilacycloalkane, $F^{\ominus}$ is not needed.
S. E. Denmark, J. J. Cottell, *Journal of Organic Chemistry* **2001**, 66, 4276



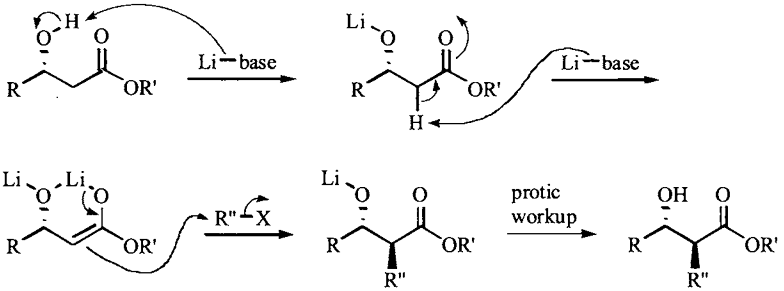
M. R. Elliot, A.-L. Dhimane, M. Malacria, *Journal of the American Chemical Society* **1997**, 119, 3427

Frater-Seebach Alkylation

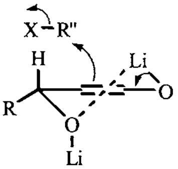
The Reaction:



Proposed Mechanism:

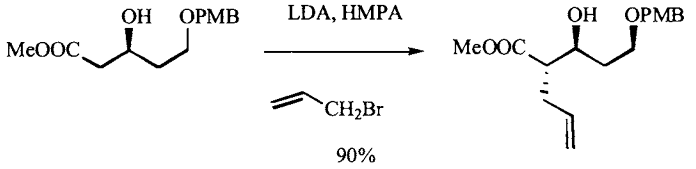


Notes:

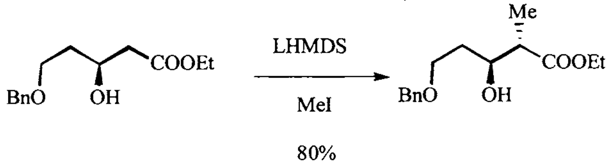


Preferential alkylation is *anti* to the hydroxyl group.

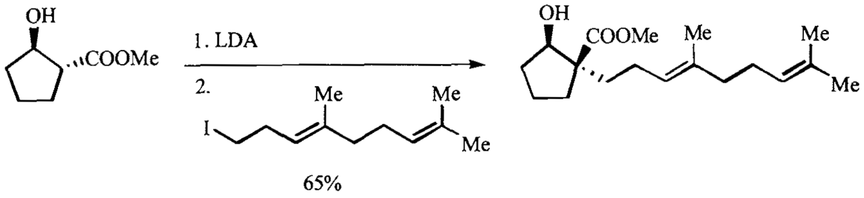
Examples:



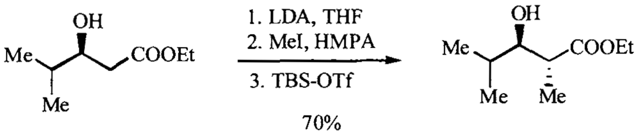
M. Nakatsuka, J. A. Ragan, T. Sammakia, D. B. Smith, D. E. Vehling, S. L. Schreiber, *Journal of the American Chemical Society* **1990**, 112, 5583



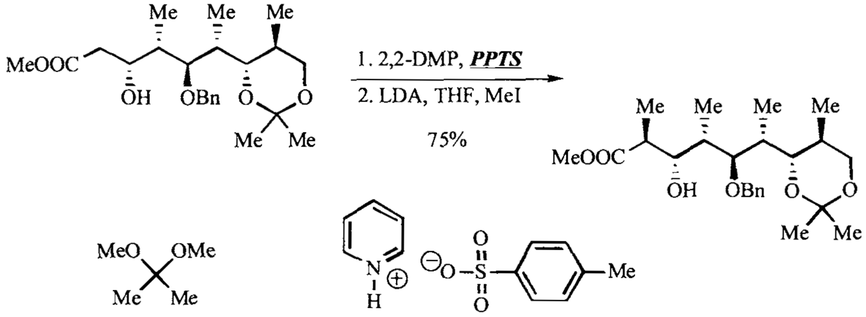
S. D. Rychnovsky, C. Rodriguez, *Journal of Organic Chemistry* **1992**, 57, 4793



C. H. Heathcock, C. J. Kath, R. B. Ruggeri, *Journal of Organic Chemistry* **1995**, 60, 112

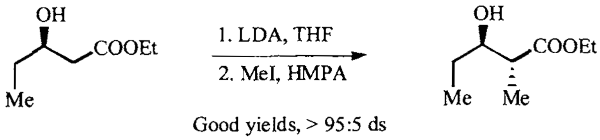


W. R. Roush, T. D. Bannister, M. D. Wendt, J. A. Jablonowski, K. A. Scheidt, *Journal of Organic Chemistry* **2002**, 67, 4275



2,2-DMP = 2,2-dimethoxypropane **PPTS = pyridinium p-toluenesulfonate**
[77-76-9]

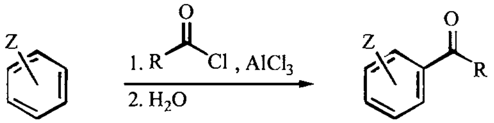
K. W. Hunt, P. A. Grieco, *Organic Letters* **2001**, 3, 481



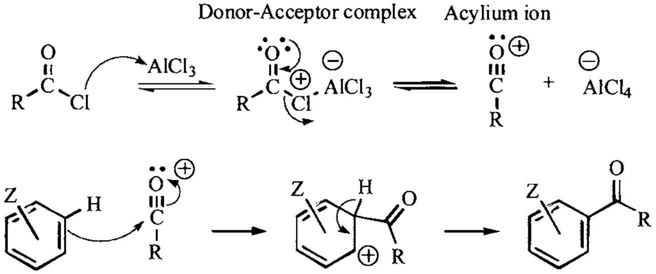
W. R. Roush, J. S. Newcom, *Organic Letters* **2002**, 4, 4739

Friedel-Crafts Acylation

The Reaction:



Proposed Mechanism:



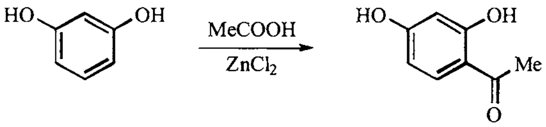
Notes:

Unlike the carbocation intermediate on the ***Friedel-Crafts alkylation***, this ***acylium ion*** intermediate will not undergo rearrangement.

See: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 106-109.

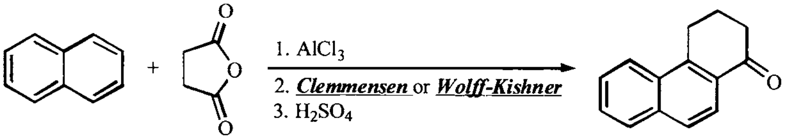
Nencki Reaction: Acylation of polyphenolic compounds.

Example:

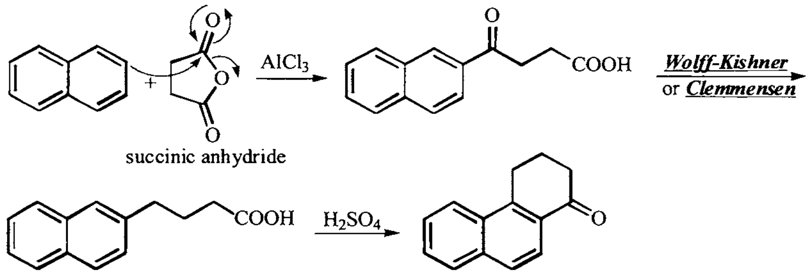


Haworth (Phenanthrene) Synthesis

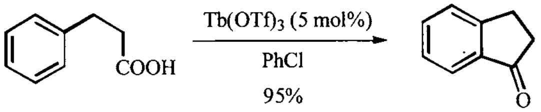
The Reaction:



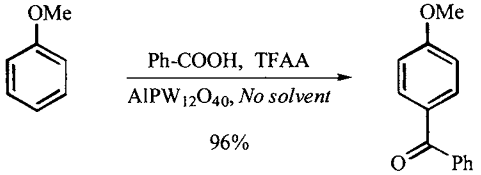
Proposed Mechanism:



Examples:

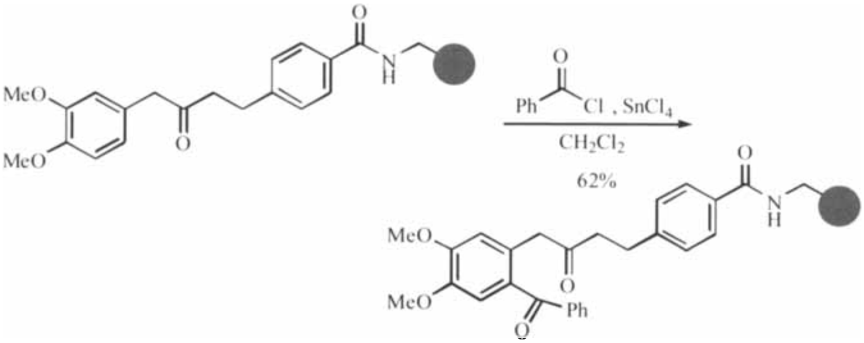


D.-M. Cui, C. Zhang, M. Kawamura, S. Shimada, *Tetrahedron Letters* **2004**, 45, 1741

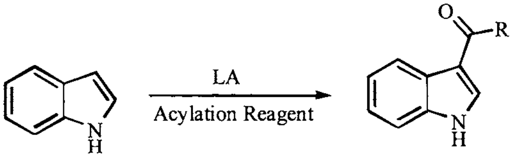


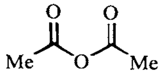
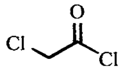
aluminum dodecatungstophosphate
($AlPW_{12}O_{40}$),
stable and non-hygroscopic

H. Firouzabadi, N. Iranpoor, F. Nowrouzi, *Tetrahedron Letters* **2003**, 44, 5343



F. Bevacqua, A. Basso, R. Gitto, M. Bradley, A. Chimirri, *Tetrahedron Letters* **2001**, 42 7683

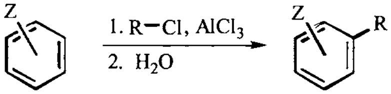


LA	Reagent	R=	Yield
$AlCl_3$		CH_3	78%
$SnCl_4$	Me-CN	CH_3	96%
$SnCl_4$		$ClCH_2$	80%

O. Ottoni, A. de V. F. Neder, A. K. B. Dias, R. P. A. Cruz, L. B. Aquino, *Organic Letters* **2001**, 3, 1005

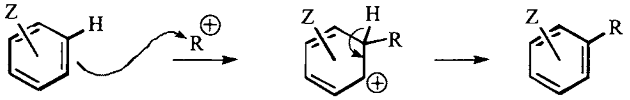
Friedel-Crafts Alkyation

The Reaction:



Proposed Mechanism:

$$R{-}Cl + AlCl_3 \rightleftharpoons \overset{\oplus}{R} + \overset{\ominus}{AlCl_4}$$

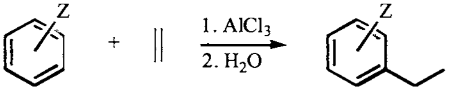


See: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 110-113; C. A. Price, *Organic Reactions* **3**, 1; E. Berliner, *Organic Reactions* **5**, 5.

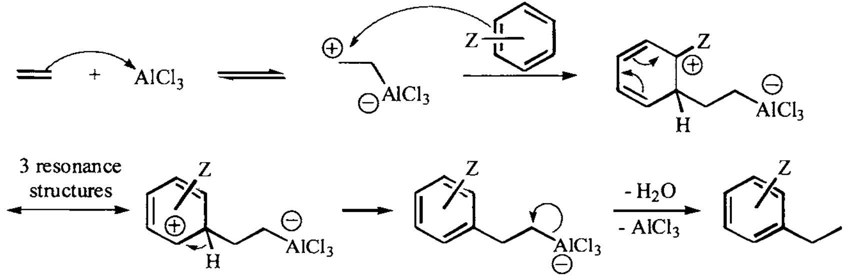
Alcohols and alkenes are also useful alkylating agents. Some classify the latter reactions as:

Darzens-Nenitzescu Alkylation

The Reaction:



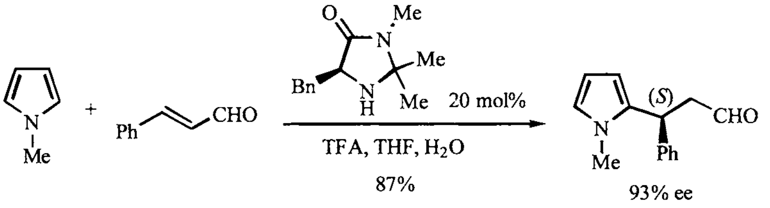
Proposed Mechanism:



Notes:

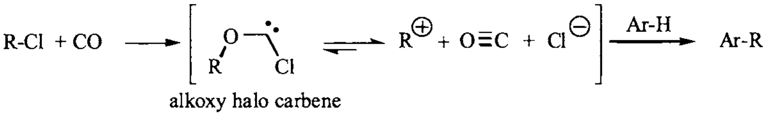
A variety of protic and Lewis acids have been used.

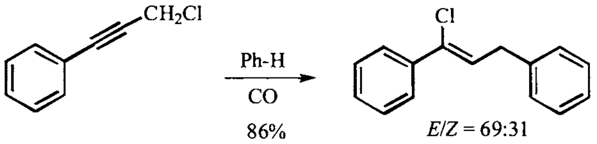
Examples:



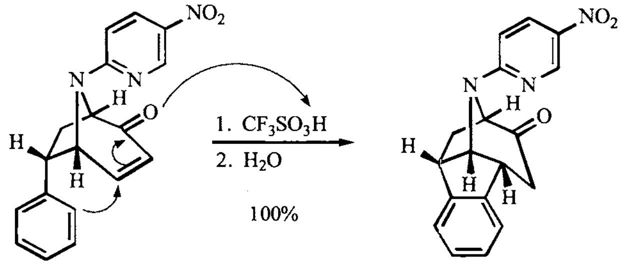
N. A. Paras, D. W. C. MacMillan, *Journal of the American Chemical Society* **2001**, 123, 4370

Use of CO as a catalyst:

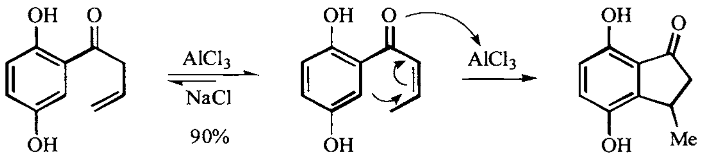




S. Ogoshi, H. Nakashima, K. Shimonaka, H. Kurosawa, *Journal of the American Chemical Society* **2001**, 123, 8626



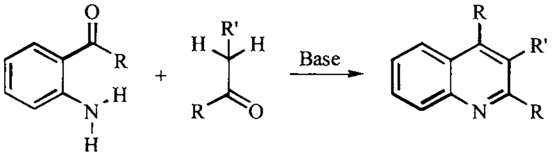
N. Dennis, B. E. D. Ibrahim, A. R. Katritzky, *Synthesis* **1976**, 105



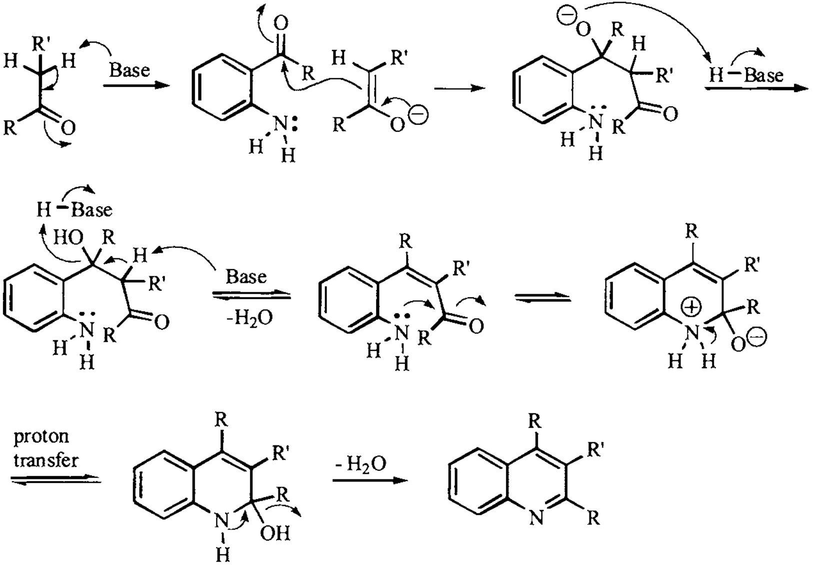
D. B. Bruce, A. J. S. Sorrie, R. H. Thomson, *Journal of the Chemical Society* **1953**, 2403

Friedlander Quinoline Synthesis

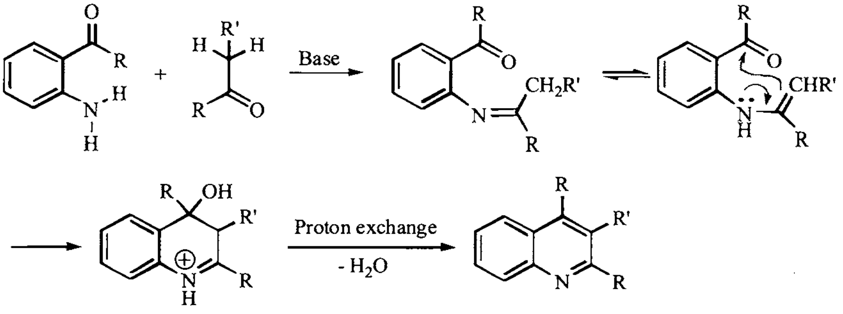
The Reaction:



Proposed Mechanism:



The Imine-enamine Approach

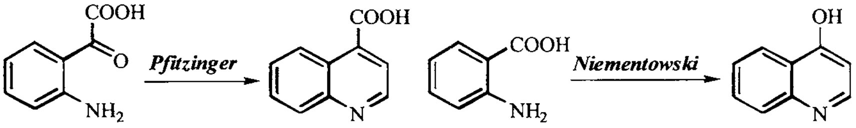


Notes:

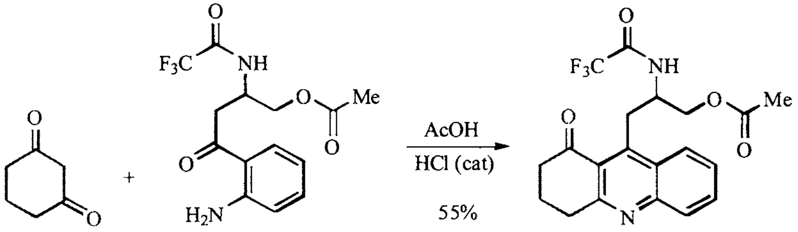
See: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 114-116

Intermediates from both interpretations have been isolated.

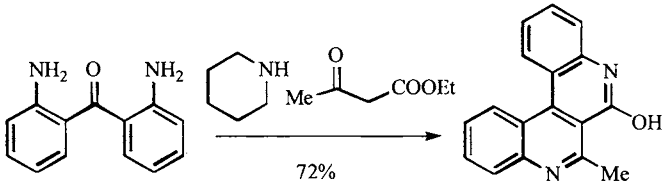
The ***PfitzingerReaction*** and the ***Niementowski Quinoline Synthesis*** are based on this concept:



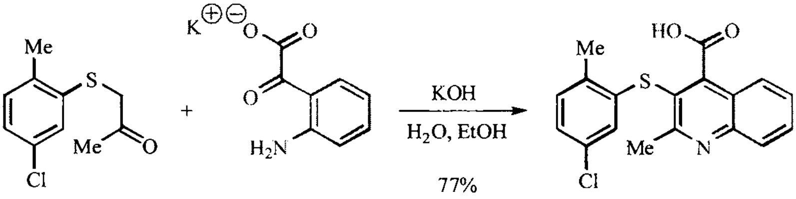
Examples:



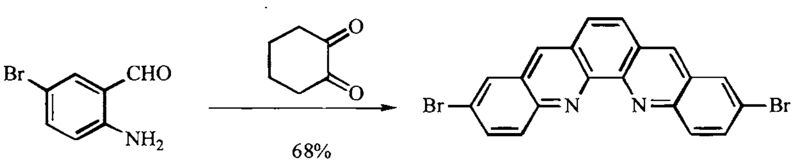
G. Gellerman, A. Rudi, Y. Kashman, *Tetrahedron* **1994**, 50, 12959



R. T. Parfitt, *Journal of Medicinal Chemistry* **1966**, 9, 161



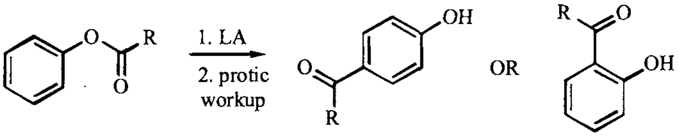
M. Croisy-Delcey, C. Huel, A. Croisy, E. Bisagni, *Heterocycles* **1991**, 32, 1933 (AN 1992:128706)



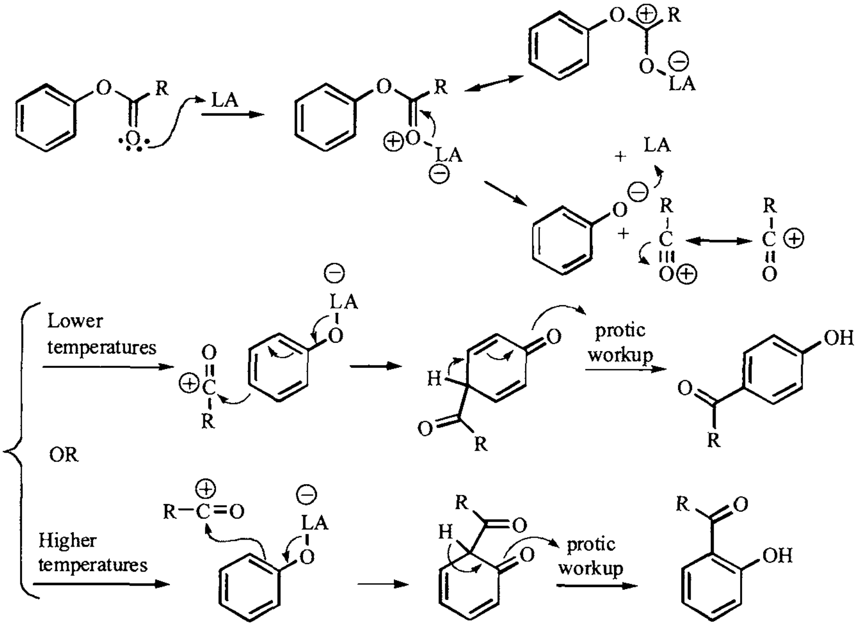
Y.-Z Hu, G. Zhang, R P. Thummel *Organic Letters* **2003**, 5, 2251

Fries Rearrangement / Photo Fries Rearrangement

The Reaction:



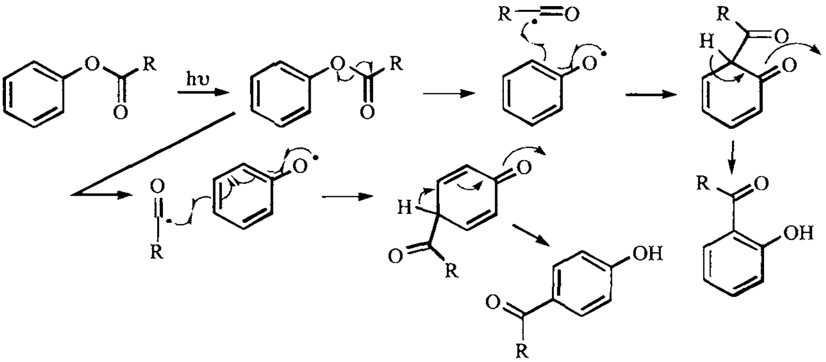
Proposed Mechanism:



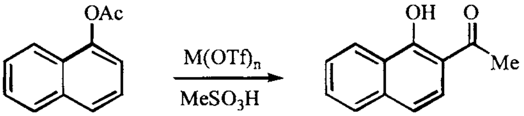
Notes:

See:T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 116-119; A. H. Blatt, *Organic Reactions* **1**, 11.

The Photo-Fries Reaction:

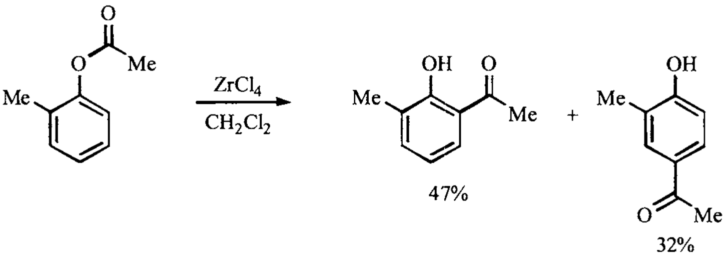


Examples:



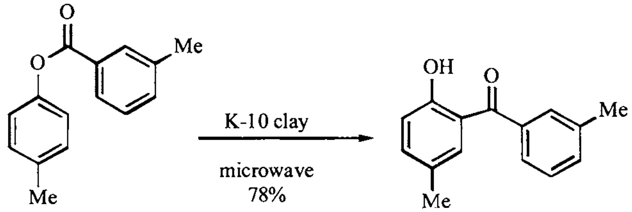
Both $Cu(OTf)_2$ and $Y(OTf)_3$ gave the product in 90% yield.

O. Mouhtady, H. Gaspard-Iloughmane, N. Roques, C. LeRoux, *Tetrahedron Letters* **2003**, 44, 6379

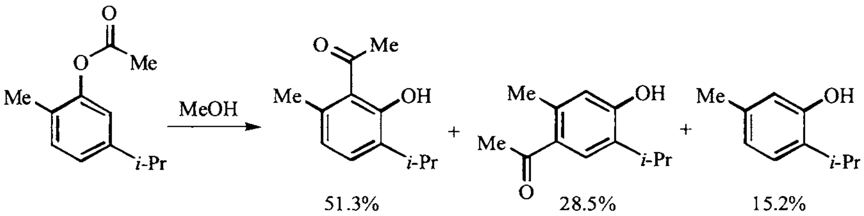


D. C. Harrowven, R. F. Dainty, *Tetrahedron Letters* **1996**, 37, 7659

Montmorillonite clays are layered silicates; montmorillonite K-10 is a specially manufactured acidic catalyst (Montmorillonite K10, [1318-93-0] A. Cornélis, P. Laszlo, M. W. Zettler in *eEROS Encyclopedia of Reagents for Organic Synthesis*, L. A. Paquette, Ed., John Wiley and Sons, Inc., online reference available at http://www.intersciene.wiley.com)



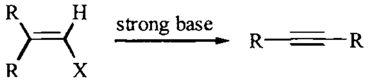
S. A. Khanum, V. T. D, S. Shashikantha, A. Firdouseb, *Bioorganic & Medicinal Chemistry Letters* **2004**, 4, 5351



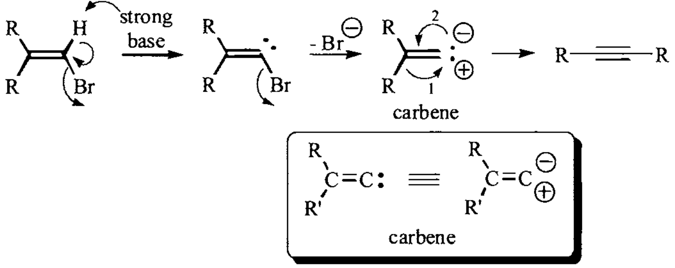
R. Saua, G. Torres, M. Valpuesta, *Tetrahedron Letters* **1995**, 36, 1311

Fritsch-Buttenberg-Wiechell Rearrangement

The Reaction:



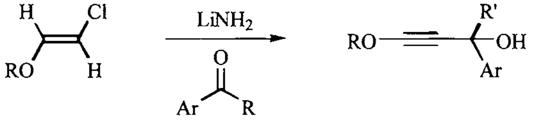
Proposed Mechanism:



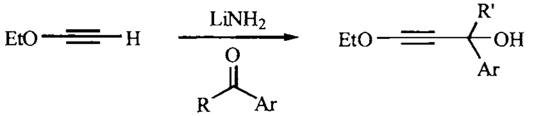
Notes:

See the similarities in:

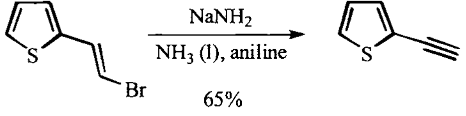
Arens-van Dorp Synthesis - Isler Modification



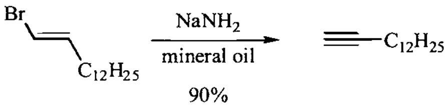
The original ***Arens-van Dorp Synthesis*** (see below) used ethoxyacetylene, which is difficult to make, as the starting material. The advantage of the ***Isler Modification*** is the use of β-chlorovinyl ether which will generate lithium ethoxyacetylene in situ.



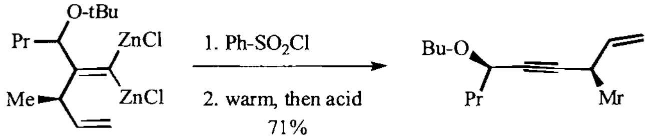
Examples:



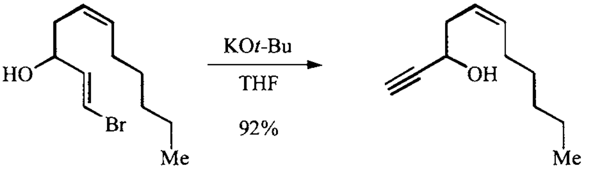
A. Vaitiekunas, F. F. Nord, *Journal of Organic Chemistry* **1954**, 19, 902



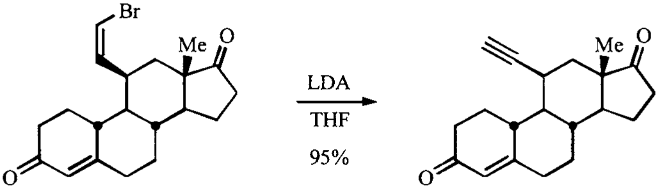
W. G. Knipprath, R. A. Stein, *Lipids* **1966**, 1, 81



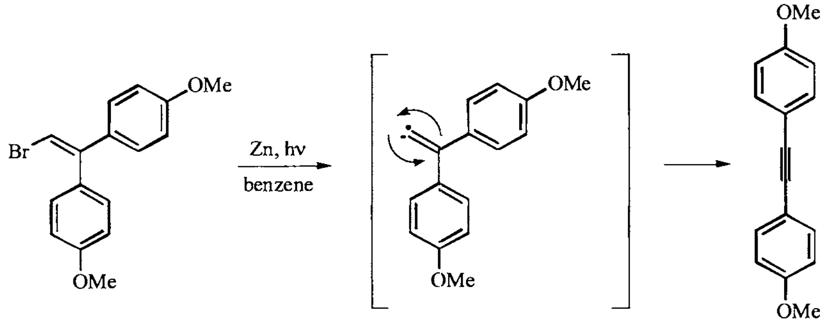
I. Creton, H. Rezaei, I. Marek, J. F. Normant, *Tetrahedron Letters* **1999**, 40, 1899



P. Pianetti, P. Rollin, J. R. Poughny, *Tetrahedron Letters* **1987**, 27, 5853



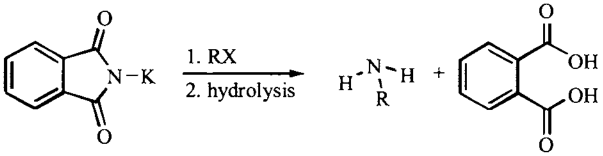
E. Ottow, R. Rohde, W. Schwede, R. Wiechert, *Tetrahedron Letters* **1993**, 34, 5253



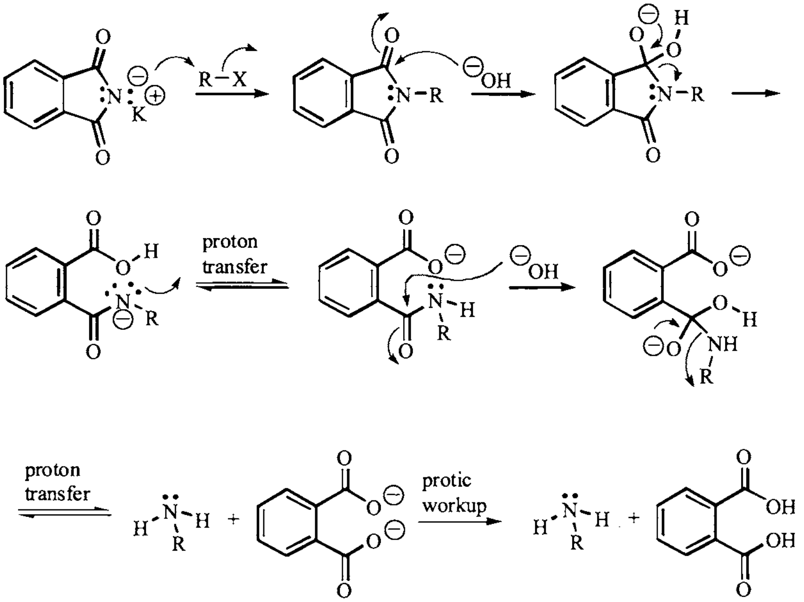
T. Suzuki, T. Sonoda, S. Kobayashi, H. Taniguchi, *Journal of the Chemical Society, Chemical Communications* **1976**, 180

Gabriel Synthesis

The Reaction:

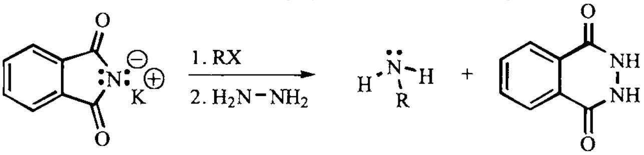


Proposed Mechanism:



Notes:

The ***Manske Modification***: Using hydrazine to release the primary amine.

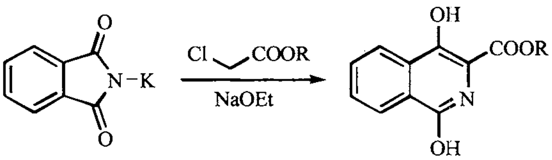


The use of hydrazine is useful in that it is gentle to other functional groups.

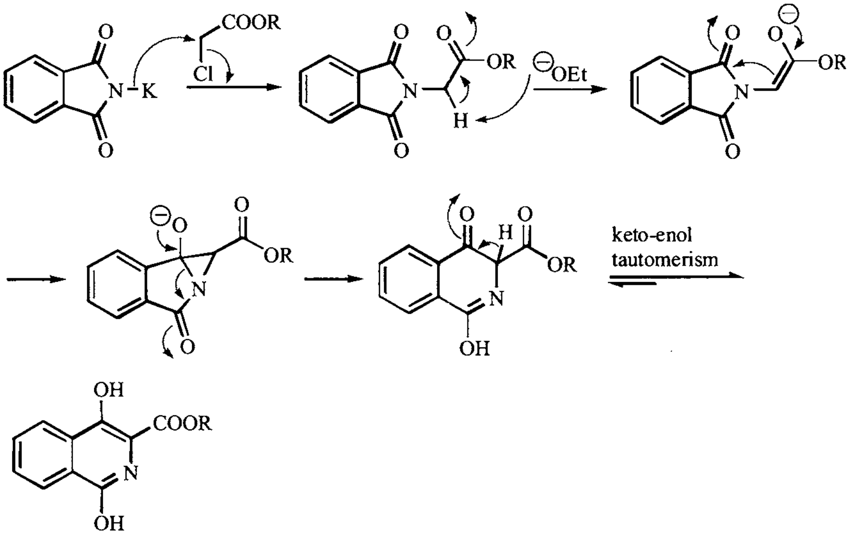
See T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 120-122; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 500, 513, 864.

Gabriel-Colman Rearrangement

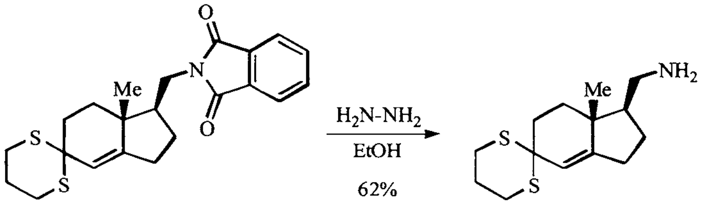
The Reaction:



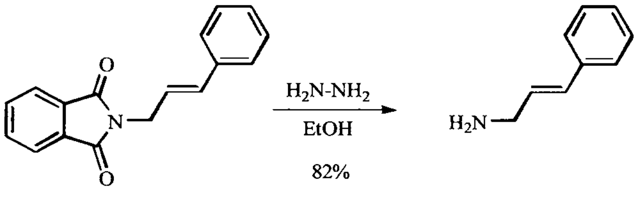
Proposed Mechanism:



Examples:



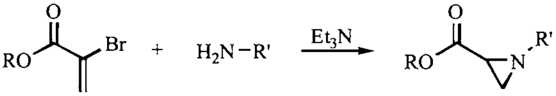
L. G. Sevillano, C. P. Melero, E. Caballero, F. Tome, L. G. Lelievre, K. Geering, G. Crambert, R. Carron, M. Medarde, A. San Feliciano, *Journal of Medicinal Chemistry* **2002**, 45, 127



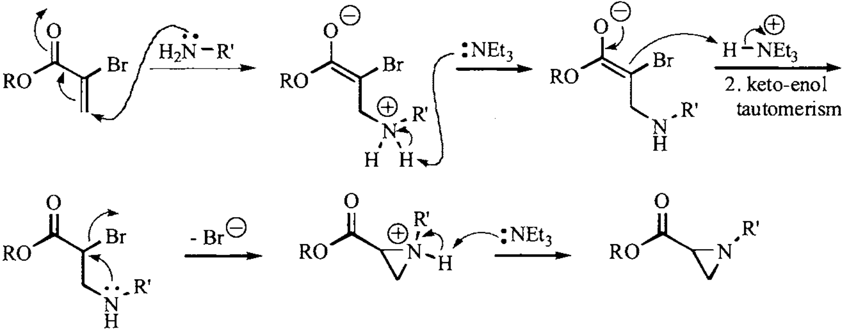
C. Serino, N. Stehle, Y. S. Park, S. Florio, P. Beak, *Journal of Organic Chemistry* **1999**, 64, 1160

Gabriel-Cromwell Reaction

The Reaction:

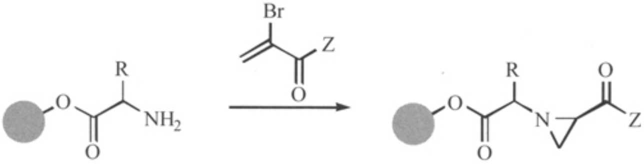


Proposed Mechanism:



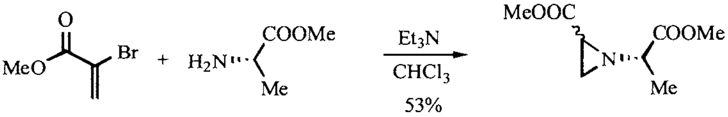
Notes:

General reactions on solid phase are described in a review:

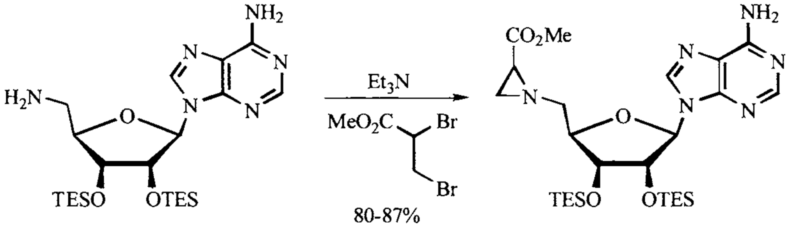


R. G. Franzen, *Journal of Combinatorial Chemistry* **2000**, 2, 195

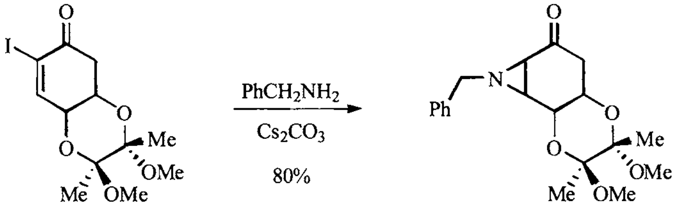
Examples:



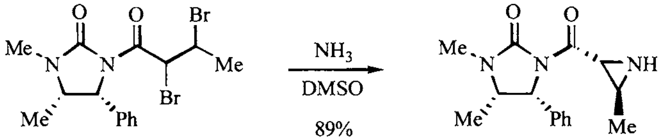
S. N. Filigheddu, M. Taddei, *Tetrahedron Letters* **1998**, 39, 3857



L. R. Comstock, S. R. Rajski, *Tetrahedron* **2002**, 58, 6019



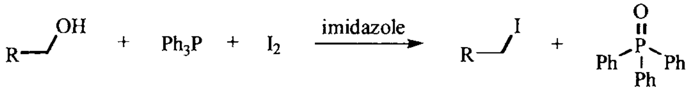
M. T. Barros, C. D. Maycock, M. R. Ventura, *Tetrahedron Letters* **2002**, 43, 4329



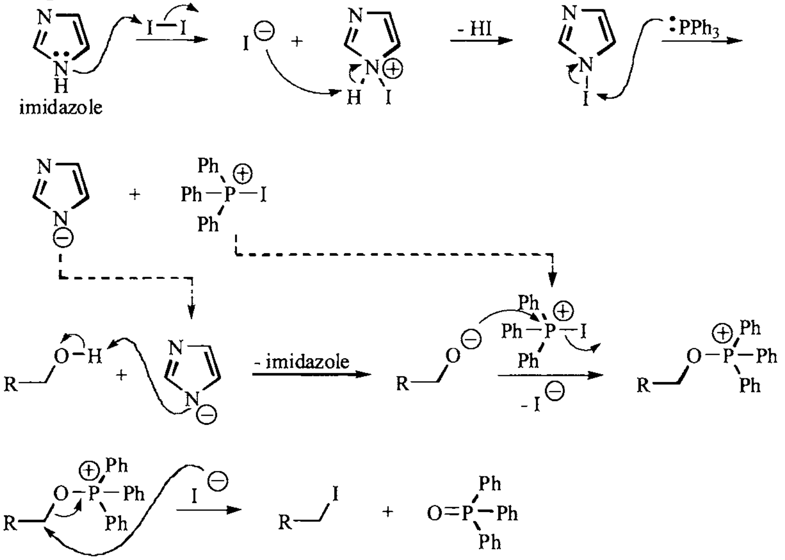
G. Cardillo, L. Gentilucci, C. Tomasini, M. P. V. Castjon-Bordas, *Tetrahedron Asymmetry* **1998**, 39, 3857

Garegg-Samuelsson Reaction

The Reaction:

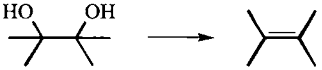


Proposed Mechanism:

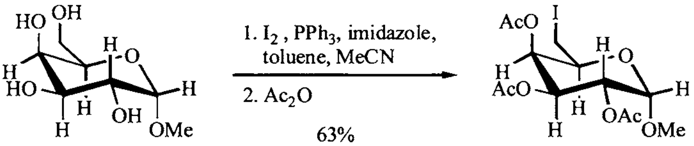


Notes:

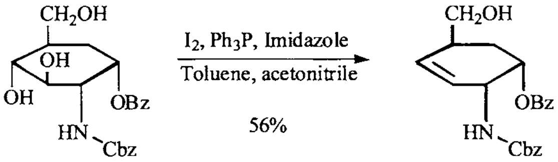
1. The reaction will also work with bromine.
2. General reactivity: 1° > 2° alcohols.
3. Secondary alcohols often experience inversion of configuration.
4. 1,2-diols in this reaction result in alkene formation [***Garegg-Samuelsson Olefination***]



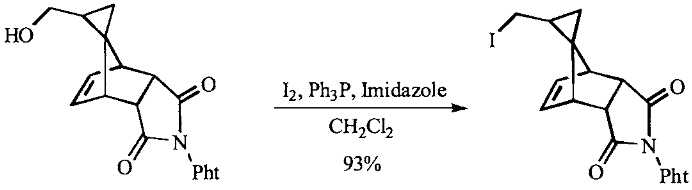
Examples:



P. J. Garegg, R. Johansson, C. Ortega, B. Samuelsson, *Journal of the Chemical Society, Perkin Transaction I*, **1982**, 681

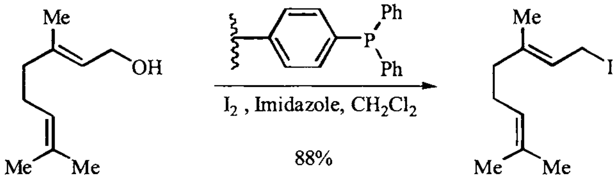


Z. Pakulski, A. Zamojski, *Carbohydrate Research* **1990**, 205, 410

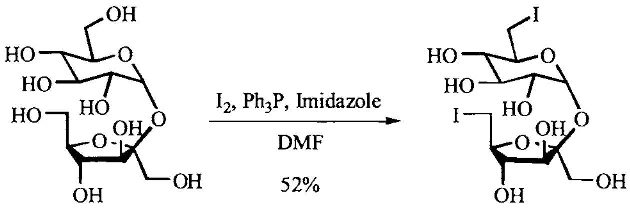


Pht = phthalyl

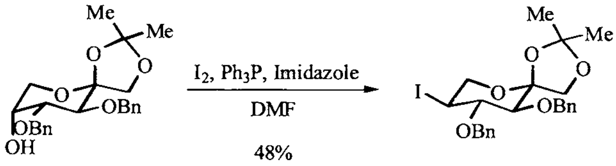
J. T. Starr, G. Koch, E. M. Carreira, *Journal of the American Chemical Society* **2000**, 122, 8793



G. Anikumar, H. Nambu, Y. Kita, *Organic Process and Research Development* **2002**, 6, 190



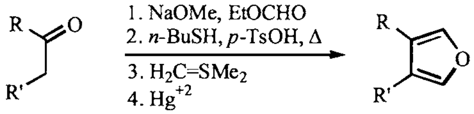
J. M. G. Fernandez, A. Gadelle, J. Defaye, *Carbohydrate Research* **1994**, 265, 249



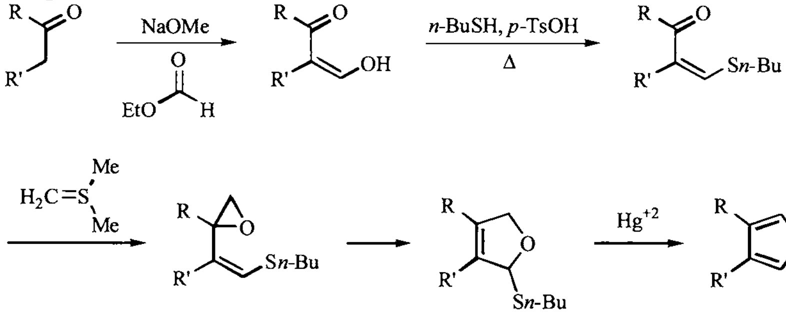
I. Izquierdo, M. T. Plaza, F. Franco, *Tetrahedron Asymmetry* **2002**, 13, 1503

Garst-Spencer Furan Annulation

The Reaction:

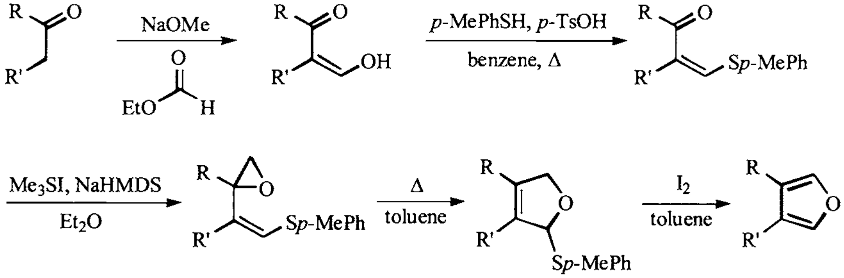


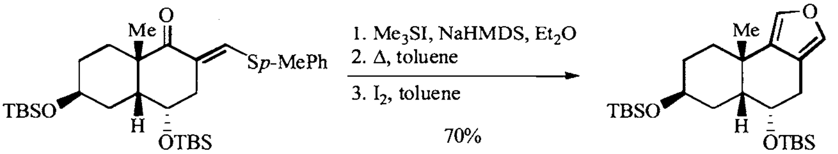
Proposed Mechanism:



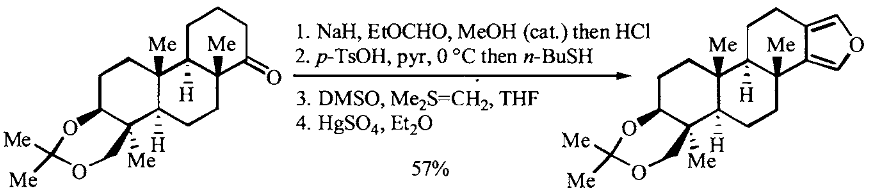
Examples:

An improvement by Kurosu, Marcin and Kishi:



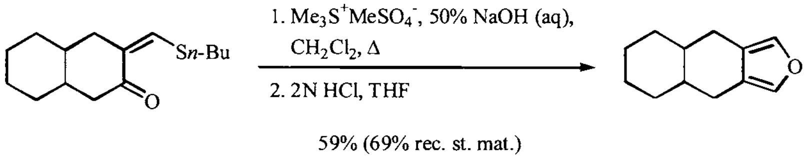


M. Kurosu, L. R. Marcin, Y. Kishi, *Tetrahedron Letters* **1989**, 39, 8929
see also M. Kurosu, L. R. Marcin, T. J. Grinsteiner, Y. Kishi *Journal of the American Chemical Society* **1998**, 120, 6627

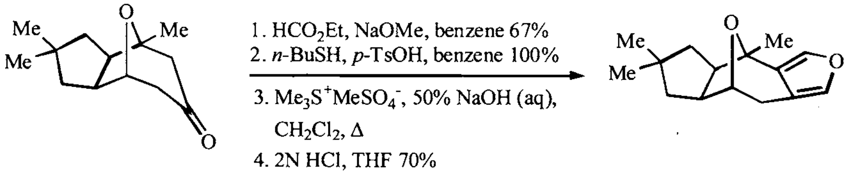


P. A. Zoretic, M. Wang, Y. Zhang, Z. Shen, *Journal of Organic Chemistry* **1996**, 61, 1806

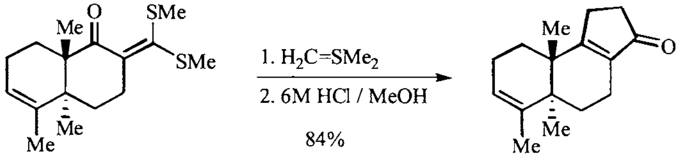
Phase-transfer conditions are used in this example:



M. E. Price, N. E. Schore *Journal of Organic Chemistry* **1989**, 54, 2777



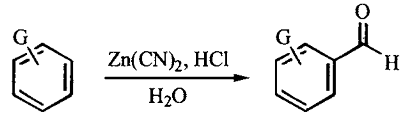
M. E. Price, N. E. Schore *Journal of Organic Chemistry* **1989**, 54, 5662



L. C. Garver, E. E. van Tamelen, *Journal of the American Chemical Society* **1982**, 104, 867

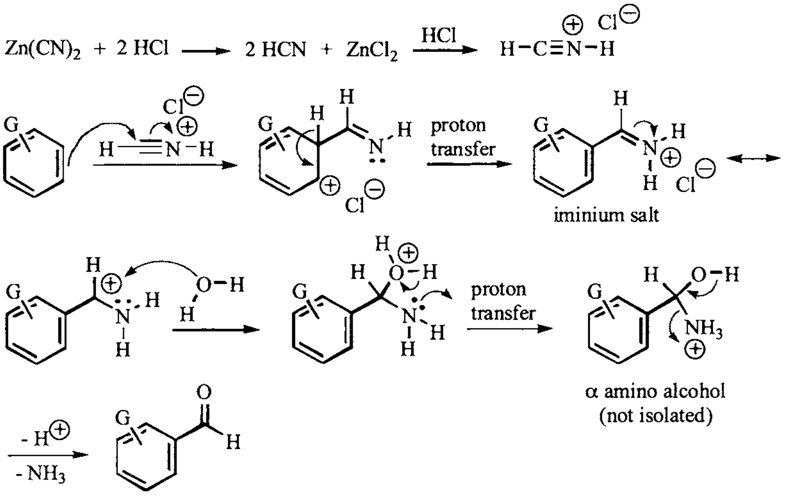
Gattermann Aldehyde Synthesis (Gattermann-Adams Formylation)

The Reaction:



G = alkyl, OR

Proposed Mechanism:

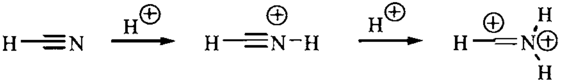


Notes:

T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 123-124; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 715; W. E. Truce, *Organic Reactions* **9**, 2.

The reaction works with alkylbenzenes, phenols, their ethers, and many heterocycles, it doesn't work with aromatic amines.

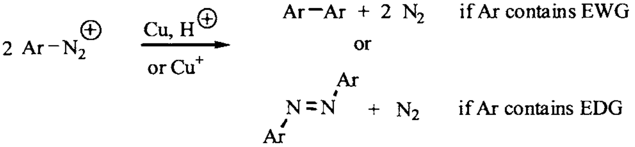
In strong acid solutions, there is evidence of a dication intermediate:



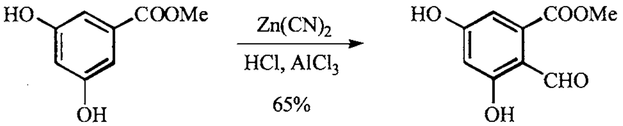
Y. Sato, M. Yato, T. Ohwada, S. Saito, K. Shudo, *Journal of the American Chemical Society* **1995**, 117, 3037

The original conditions, called the ***Gattermann Reaction / Formylation***, were to add HCN, HCl and $ZnCl_2$ (known as ***Adam's Catalyst***) directly. Use of ***Adam's catalyst*** avoids using gaseous HCN.

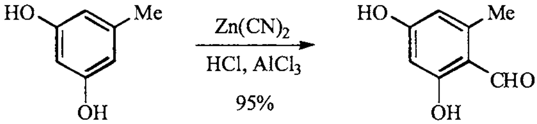
Gattermann Method



Examples:



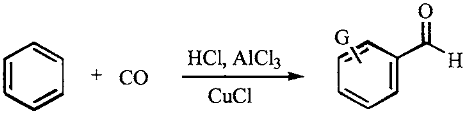
A. V. Rama Rao, N. Sreenivasan, D. Reddeppa Reddy, V. H. Deshpande, *Tetrahedron Letters* **1987**, 28, 455



G. Solladie, A. Rubio, M. C. Carreno, J. L. G. Ruano, *Tetrahedron Asymmetry* **1990**, 1, 187

Gattermann-Koch Reaction

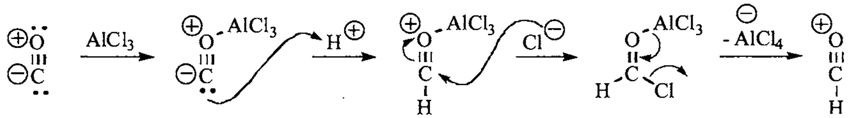
The Reaction:



Proposed Mechanism:

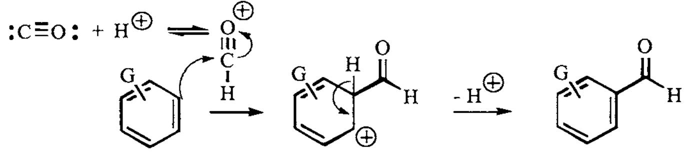
The details of the formation of the formyl cation seem to be less assured.

See S. Raugei, M. L. Klein, *Journal of Physical Chemistry B* **2001** 105, 8212 for pertinent references to experiment, and their computational study of the formyl cation. The work shows the uncertainty associated with acid concentration, counter ion and relative O- vs-C protonation possibilities. We provide a very simplistic possibility:



The probable role of copper is to facilitate the transport of carbon monoxide, with which it binds. See: N. N. Crouse, *Organic Reactions* **5**, 6.

There seems to be agreement that the product-forming part of the mechanism is:



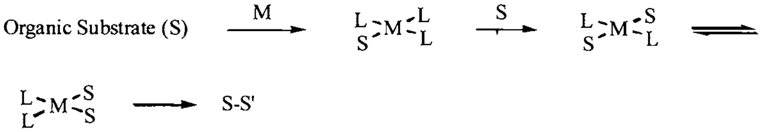
This reaction is limited to benzene and alkylbenzenes.

General Coupling Reactions

A number of coupling reactions have already been summarized under the title ***Alkyne Coupling***. This section summarizes a number of other common coupling protocols.

The Reaction:

These important synthesis reactions have a common mechanistic theme:

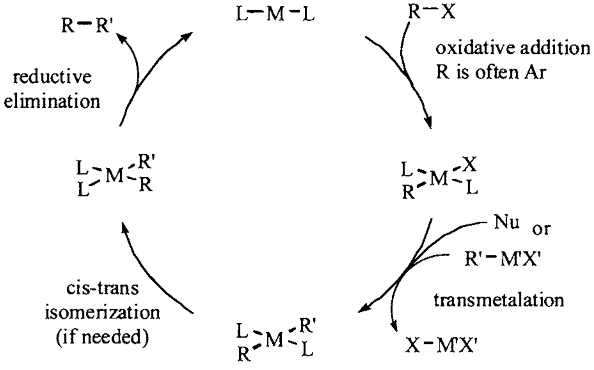


The difference in the reactions is in: M (Ni, Cu, Pd).

In these reactions there are many variables: Ligand (type and number), Metal (oxidation state and identity), X (halogen, triflate, etc), M'.

Proposed Mechanism:

In a catalytic cycle the common trend is:

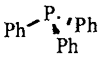


This step generally has some nucleophile replace a ligand. In the cases where the nucleophile is derived from an organometallic reagent it is called a ***transmetallation***.

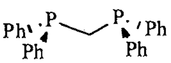
Named Reaction	Metal	Nucleophile
Buchwald-Hartwig	Pd	R_2NH or ROH
Fukuyama	Pd	R-Zn-I *
Heck	Pd	alkene
Kumada	Pd or Ni	R-MgX
Negishi	Pd or Ni	R-ZnX
Sonogashira	Pd	R-≡-Cu
Stille	Pd	$R\text{-}SnBu_3$
Suzuki	Pd	$R\text{-}B(OH)_2$

Under the specific heading one can find details and examples specific for the reaction.

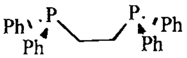
Common Ligands:



Triphenylphosphine



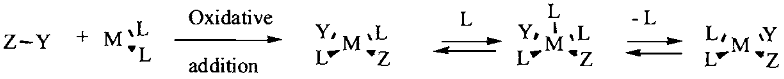
dppm



dppe

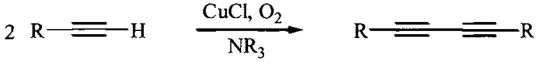
The ligands can be particularly useful in preparing the organometallic-substrate for reductive elimination.

In this generic example, the oxidation state of the metal is reduced by two, while the product is released in the reductive elimination step. In many reactions the oxidative addition does not provide the proper stereochemistry for elimination; an isomerization must occur.



Glaser (Oxidative) Coupling (Reaction)

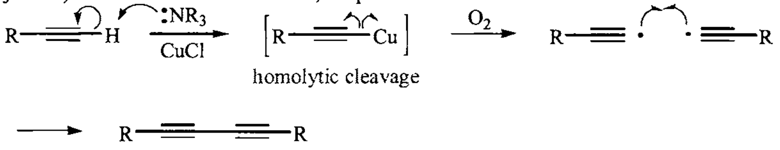
The Reaction:



Proposed Mechanism:

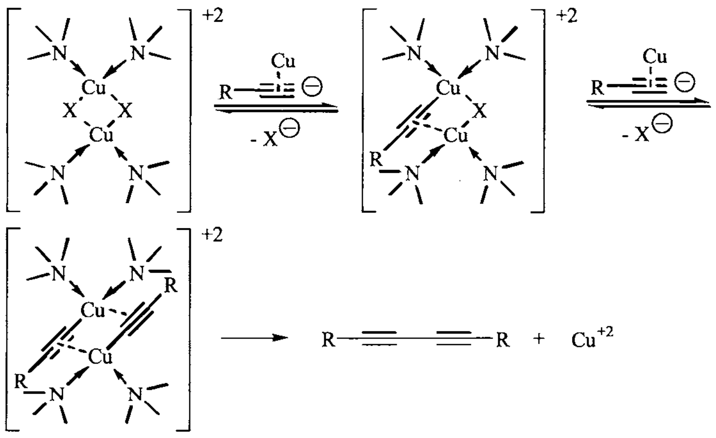
Mechanistic details are not well understood. It is known that the reaction has been successfully accomplished with a variety of solvents, amines and copper salts.

There seems to be consensus that a copper-alkyne bond is homolytically broken by oxygen (often just air) and the radicals thus formed, couple:



A more detailed interpretation is available:

P. Siemsen, R. C. Livingston, F. Diederich, *Angewandte Chemie International Edition* **2002**, 39, 2632



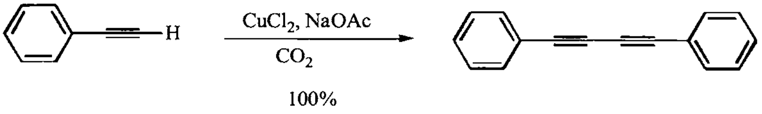
Notes:

See: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 125-127; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 927

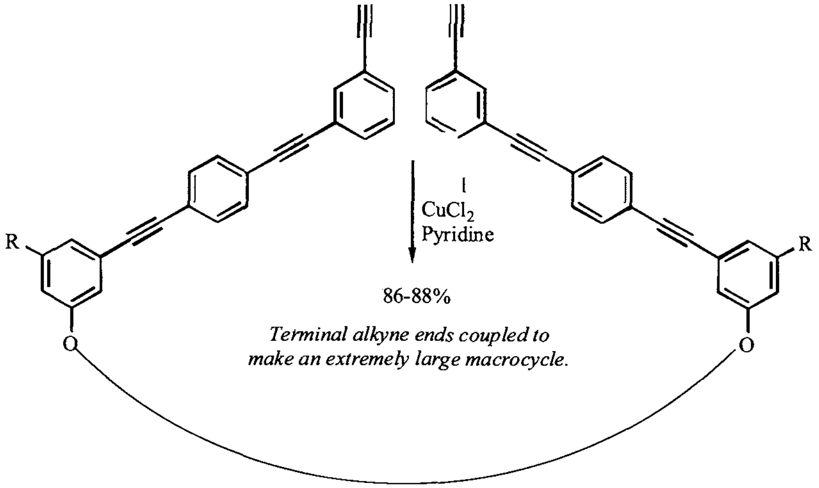
O_2 was an early choice for oxidant; however, other oxidants have been used.

Examples:

The reaction can be carried out without amines, using sodium acetate in super-critical CO_2.



J. Li, H. Jiang, *Chemical Communications* **1999**, 2369



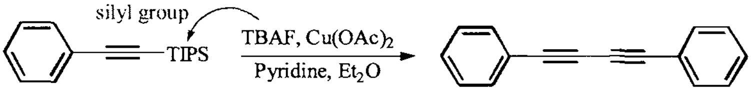
86-88%

Terminal alkyne ends coupled to make an extremely large macrocycle.

Large Carbon Span

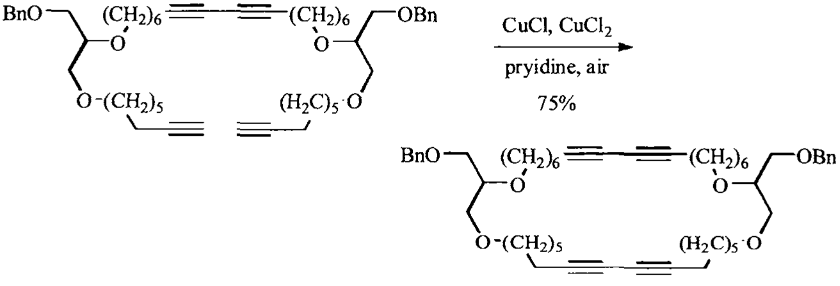
S. Hoger, A.-D. Meckenstock, H. Pellen, *Journal of Organic Chemistry* **1997**, 62, 4556

Removes the silyl group



68%

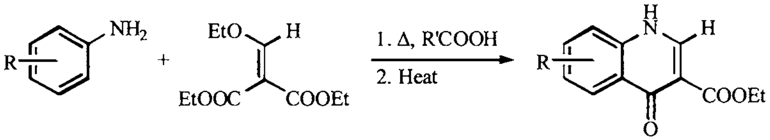
M. A. Heuft, S. K. Collins, G. P. A. Yap, A. G. Fallis, *Organic Letters* **2001**, 3, 2883



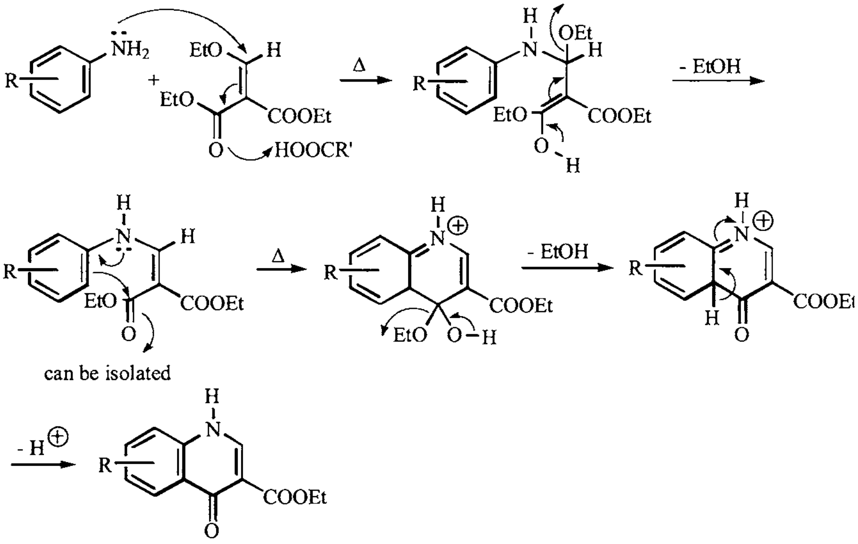
A. P. Patwardhan, D. H. Thompson, *Organic Letters* **1999**, 1, 241

Gould-Jacobs Reaction

The Reaction:

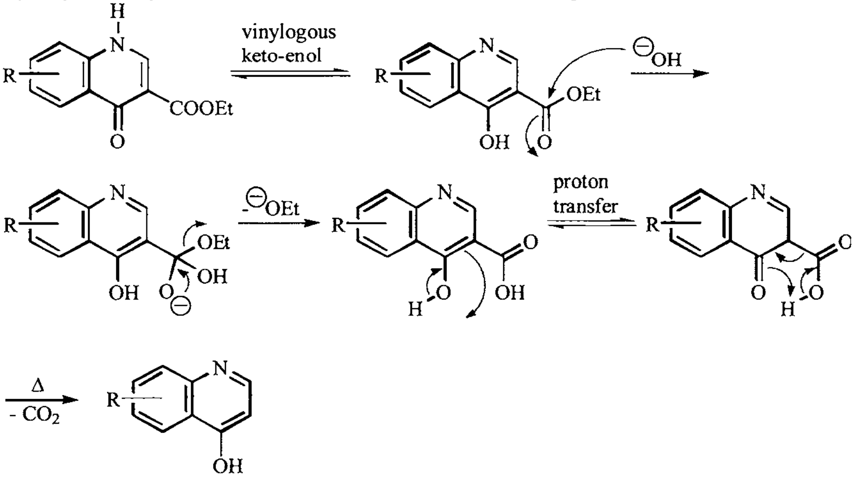


Proposed Mechanism:

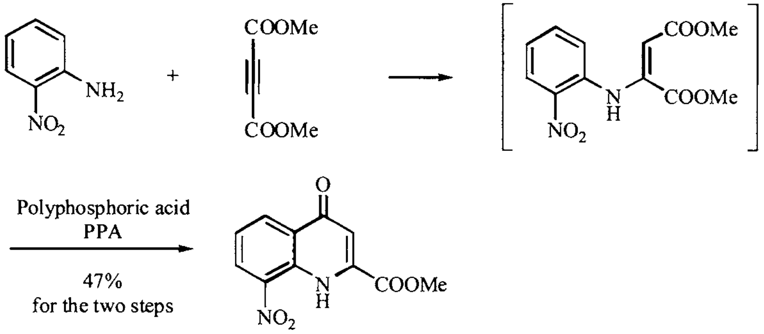


Notes:

Hydrolysis readily removes the ester and aromatizes the second ring:

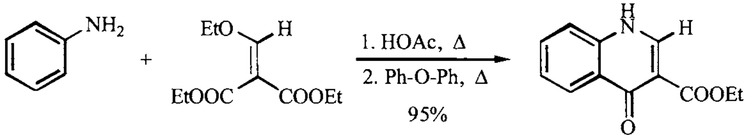


A different approach to similar molecules:

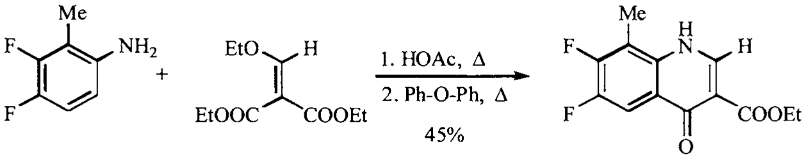


N. D. Heindel, I. S. Bechara, T. F. Lemke, V. B. Fish, *Journal of Organic Chemistry* **1967**, 32, 4155

Examples:



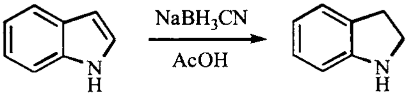
J. N. Kim, K. Y. Lee, H. S. Kim, T. Y. Kim, *Organic Letters* **2000**, 2, 343



J. C. Carretero, J. L. Garcfa Ruano, M. Vicioso, *Tetrahedron* **1992**, 48, 7373

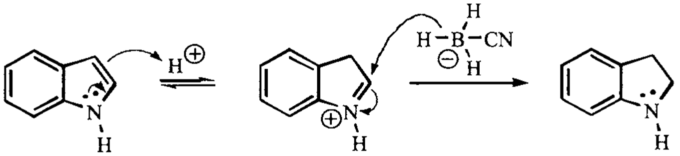
Gribble Indole Reduction

The Reaction:



G. W. Gribble, P. D. Lord, J. Skotnicki, S. E. Dietz, J. T. Eaton, J. L. Johnson, *Journal of the American Chemical Society* **1974**, 96, 7812

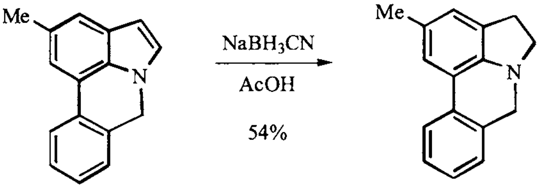
Proposed Mechanism:



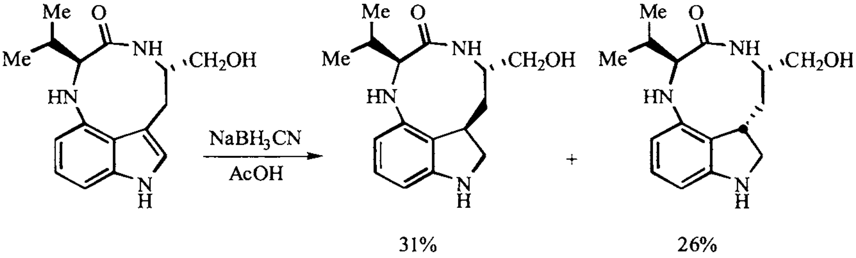
Notes:

G. W. Gribble, *Chemical Society Reviews* **1998**, 27, 395

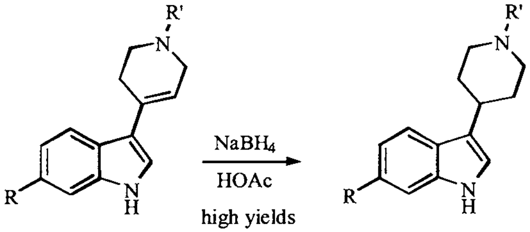
Examples:



J. C. Torres, A. C. Pinto, S. J. Garden *Tetrahedron* **2004**, 60, 9889



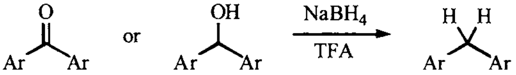
Y. Nakagawa, K. Irie, Y. Komiya, H. Ohigashia, K. Tsuda, *Tetrahedron* **2004**, 60 7077



A. Borghese, L. Antoine, G. Stephenson, *Tetrahedron Letters* **2002**, 43, 8087

Gribble Reduction of Diaryl Ketones and Methanols

The Reaction:

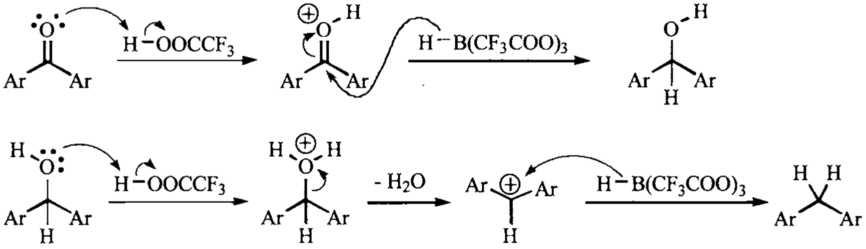


G. W. Gribble, M. Leese, B. E. Evans, *Synthesis* **1977**, 172
G. W. Gribble, W. J. Kelley, S. E. Emery, *Synthesis* **1978**, 763

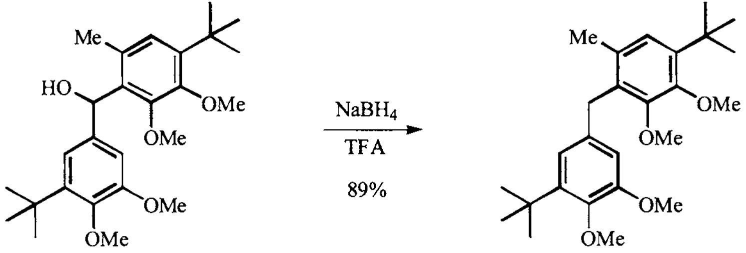
Proposed Mechanism:

$NaBH_4 + CF_3CO_2H \longrightarrow (CF_3CO_2)_3BH$

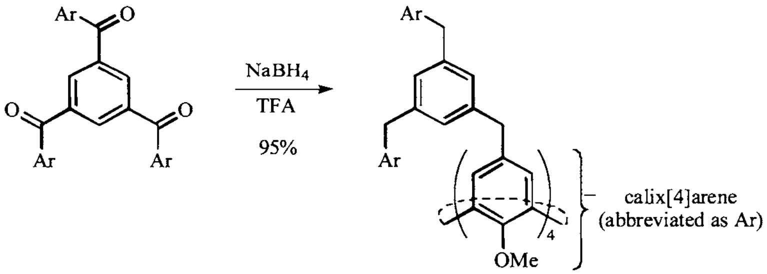
(TFA = trifluoroacetic acid = CF_3CO_2H)



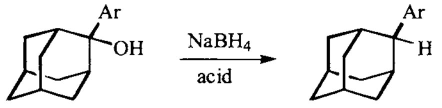
Examples:



G. Bringmann, T. Pabst, P. Henschel, M. Michel, *Tetrahedron* **2001**, 57, 1269



J. Wang, C. D. Gutsche, *Journal of Organic Chemistry* **2002**, 67, 4423

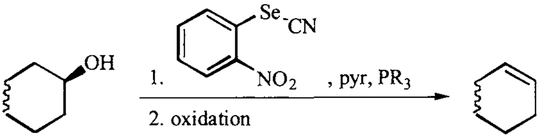


Acid	yield
CF_3CO_2H	70 - 81%
CF_3SO_3H	94 - 99%

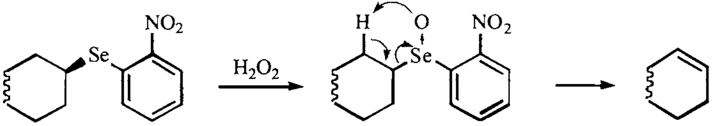
G. A. Olah, A.-h. Wu, O. Farooq, *Journal of Organic Chemistry* **1988**, 53, 5143

Grieco-Sharpless Elimination

The Reaction:



Proposed Mechanism:

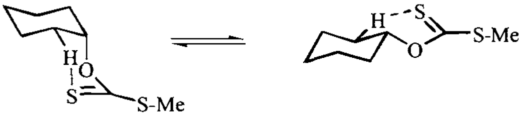


Notes:

Selenium-based reactions are generally very mild, often with the advantage of preparing the selenium derivative and carrying out the oxidative elimination as a one-pot sequence.

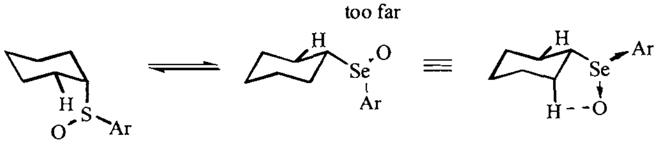
The five-membered transition state for selenoxide elimination is more restrictive than the six-membered transition state of the ***Chugaev Elimination***.

Chugaev:



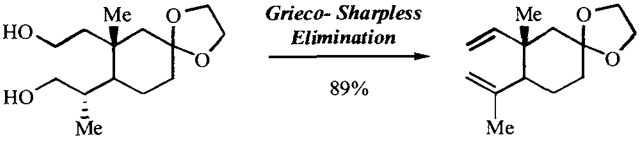
syn elimination *anti* elimination

Selenoxide:

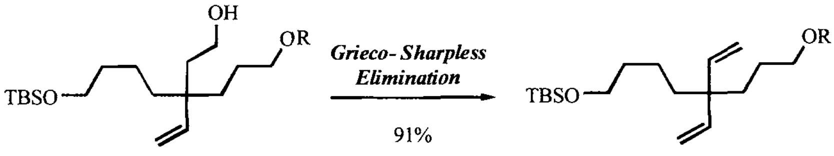


syn elimination *syn* elimination

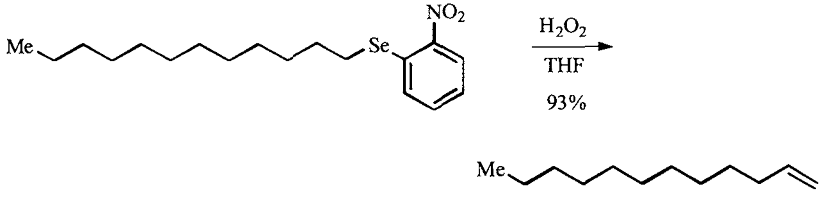
Examples:



G. Majetich, P. A. Grieco, M. Nishizawa, *Journal of Organic Chemistry* **1977**, 42, 2327



Y. Fukuda, M. Shindo, K. Shishido, *Organic Letters* **2003**, 5, 749



K. B. Sharpless, M. Y. Young, *Journal of Organic Chemistry* **1975**, 40, 947

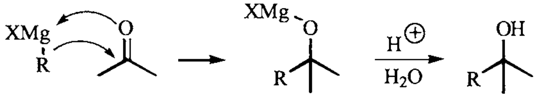
Grignard Reactions

The Reaction:

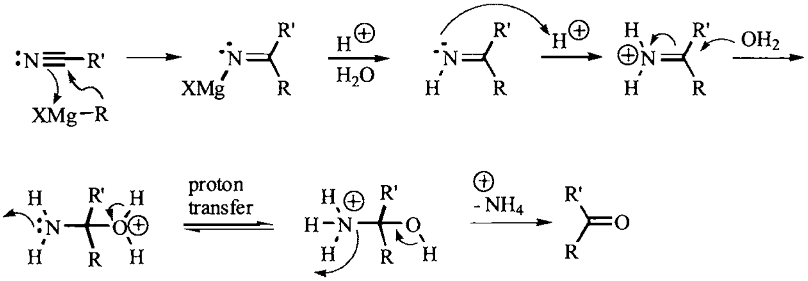
$R{-}X + Mg \longrightarrow R{-}MgX$ The ***Grignard reagent***

formaldehyde $\xrightarrow{R-MgX}$ 1° alcohols
aldehydes $\longrightarrow$ 2° alcohols
ketones $\longrightarrow$ 3° alcohols
esters $\longrightarrow$ 3° alcohols
CO_2 $\longrightarrow$ carboxylic acid
nitrile $\longrightarrow$ ketone
Chloramine $\longrightarrow$ Amine
NC-CN $\longrightarrow$ Nitrile
$HC(OR)_3$ $\longrightarrow$ Aldehyde

Proposed Mechanism:



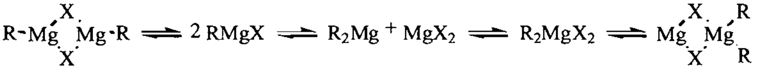
nitrile ⟶ ketone



Notes:

T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 132-138; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1205-1209.

Schlenk equilibrium - The "***Grignard reagent***" is really an equilibrium. Shown below are some of the structures:

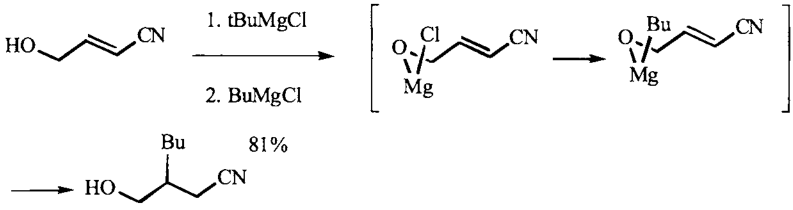


$R{-}Mg(\mu{-}X)_2Mg{-}R \rightleftharpoons 2\,RMgX \rightleftharpoons R_2Mg + MgX_2 \rightleftharpoons R_2MgX_2 \rightleftharpoons Mg(\mu{-}X)_2Mg(R)_2$

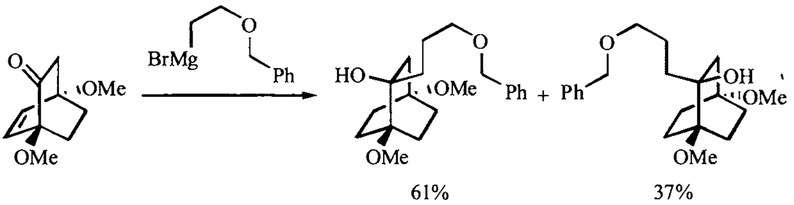
Iron-Catalyzed Cross-Coupling Reactions

B. Scheiper, M. Bonnekessel, H. Krause, A. Fürstner *Journal of Organic Chemistry* **2004**, 69, 3943

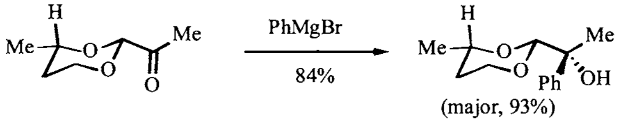
Examples:



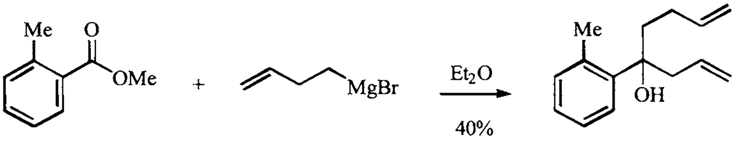
F. F. Fleming, Q. Wang, Z. Zhang, O. W. Steward, *Journal of Organic Chemistry* **2002**, 67, 5953



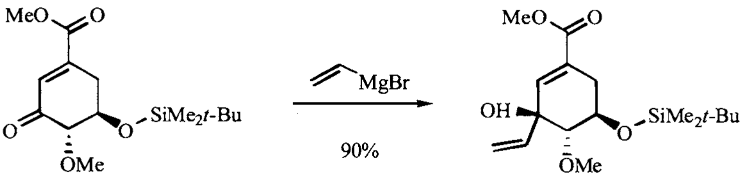
T. Uyehara, T. Marayama, K. Sakai, M. Ueno, T. Sato, *Tetrahedron Letters* **1996**, 37, 7295



W. F. Bailey, D. P. Reed, D. R. Clark, G. N. Kapur, *Organic Letters* **2001**, 3, 1865



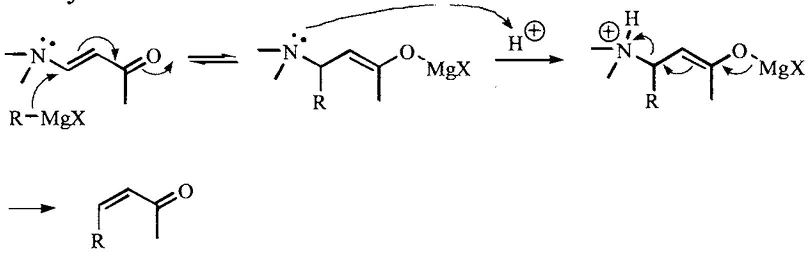
P. A. Wender, T. M. Dore, M. A. Delong, *Tetrahedron Letters* **1996**, 37, 7687



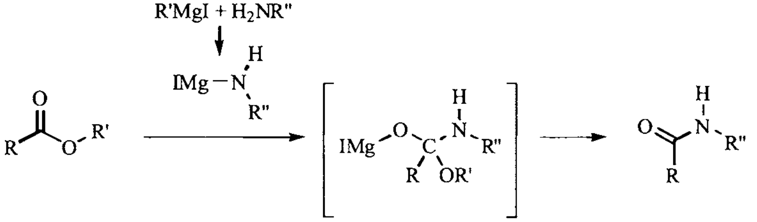
S. Hanessian, J. Pan, A. Carnell, H. Bouchard, L. Lesage, *Journal of Organic Chemistry* **1997**, 62, 465

There are a number of reactions employing ***Grignard reagents*** that have their own names:

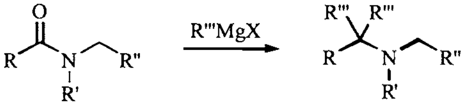
Bénary Reaction



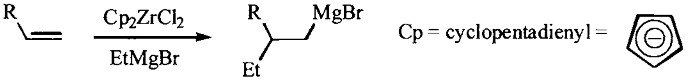
Bodroux Reaction



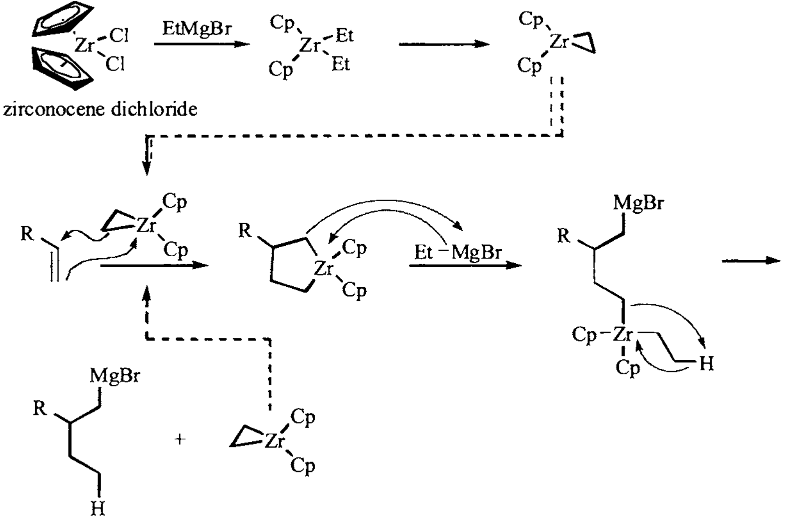
Bouveault Reaction



Dzhemilev Reaction

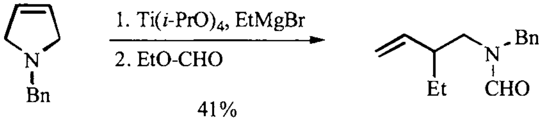


Proposed Mechanism:



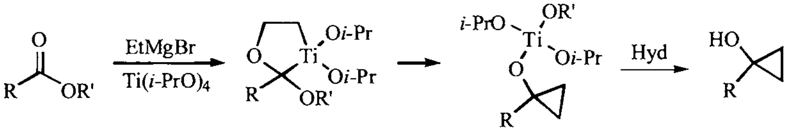
U. M. Dzhemilev, O. S. Vostrikova, *Journal of Organometallic Chemistry* **1985**, 285, 43

Example:
Titanium Analog

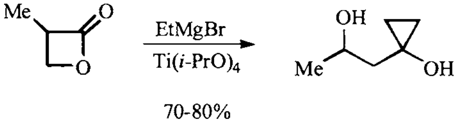


G.-D. Tebben, K. Rauch, C. Stratmann, C. M. Williams, A. deMeijere, *Organic Letters* **2003**, 5, 483

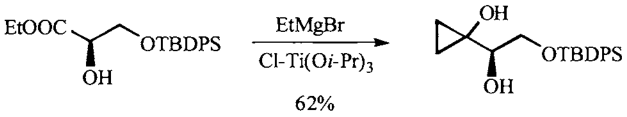
Kulinkovich Reaction



Examples:

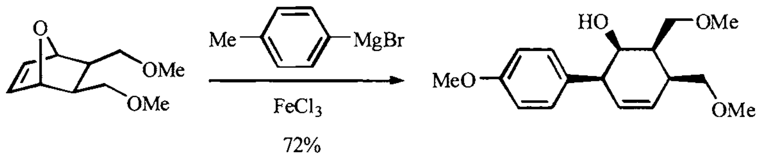


A. Esposito, M. Taddei, *Journal of Organic Chemistry* **2000**, 65, 9245

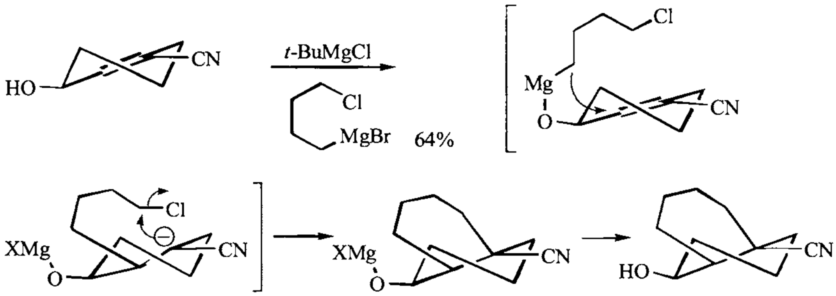


S. Y. Cha, J. K. Cha, *Organic Letters* **2000**, 2, 1337

Other Examples of novel *Grignard* use:



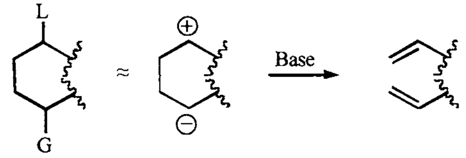
M. Nakkamura, K. Matsuo, T. Inoue, E. Nakamura, *Organic Letters* **2003**, 5, 1373



F. F. Fleming, Z. Zhang, Q. Wang, O. W. Steward, *Organic Letters* **2002**, 4, 2493

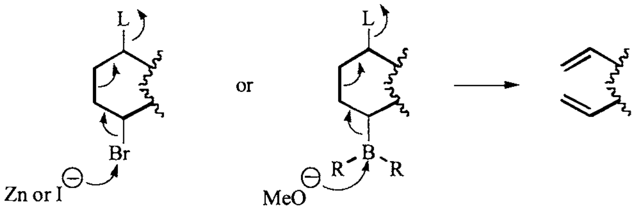
Grob Fragmentation

The Reaction:



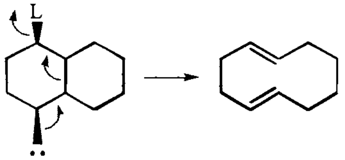
G = OH, Br, BH_2, BR_2
L = Cl, Br, OTs

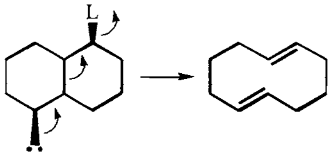
Proposed Mechanism:

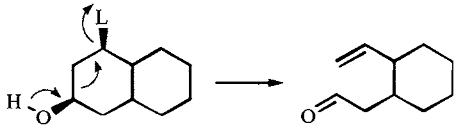


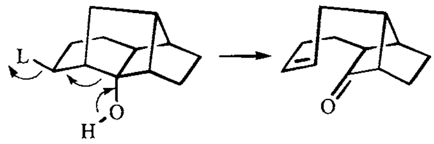
Notes:

Proper stereoelectronic effects are required, but can lead to a variety of interesting structural products. For a somewhat dated, but readable account, see: P. Deslongchamps, *Stereoelectronic Effects in Organic Chemistry*, Pergamon Press, Oxford, England, 1983

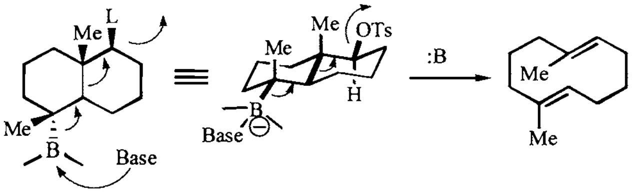






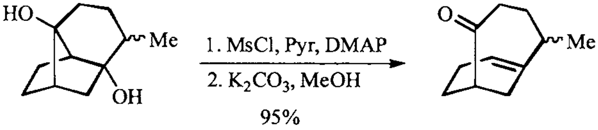


The stereoelectronic bond orientations are critical to the success of these reactions. This is easily seen in a generic ***Marshall Boronate Fragmentation***.

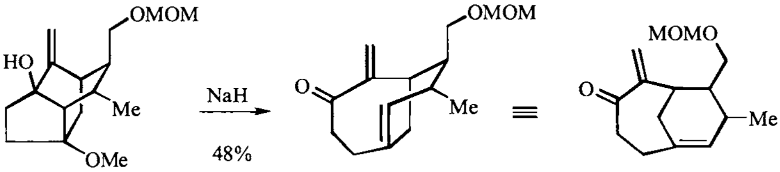


J. A. Marshall, G. L. Bundy, *Journal of the American Chemical Society* **1966**, 88, 4291

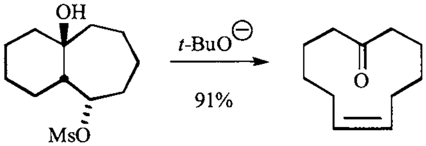
Examples:

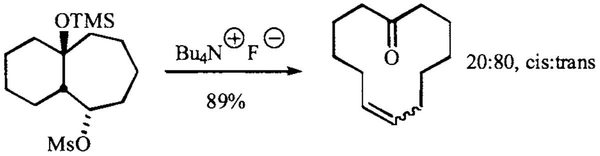


J. T. Njardarson, J. L. Wood, *Organic Letters* **2001**, 3, 2431

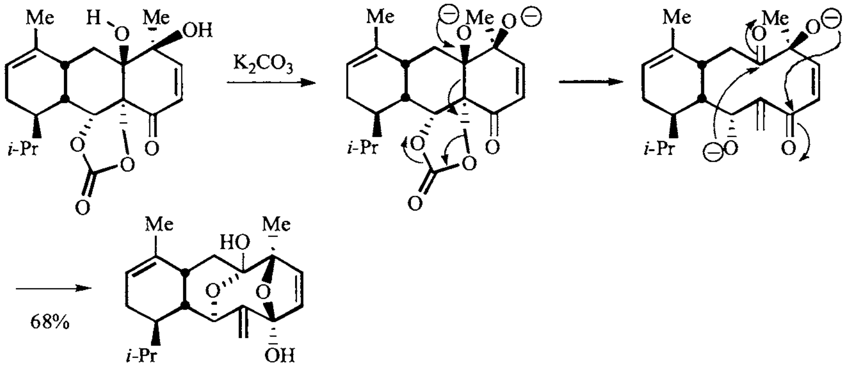


T. Yoshimitsu, M. Yanagiya, J. Nagaoka, *Tetrahedron Letters* **1999**, 40, 5215





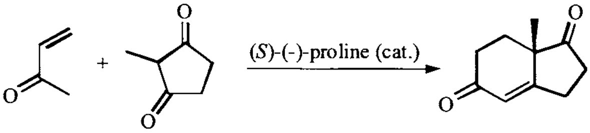
W. Zhang, P. Dowd, *Tetrahedron Letters* **1996**, 37, 957



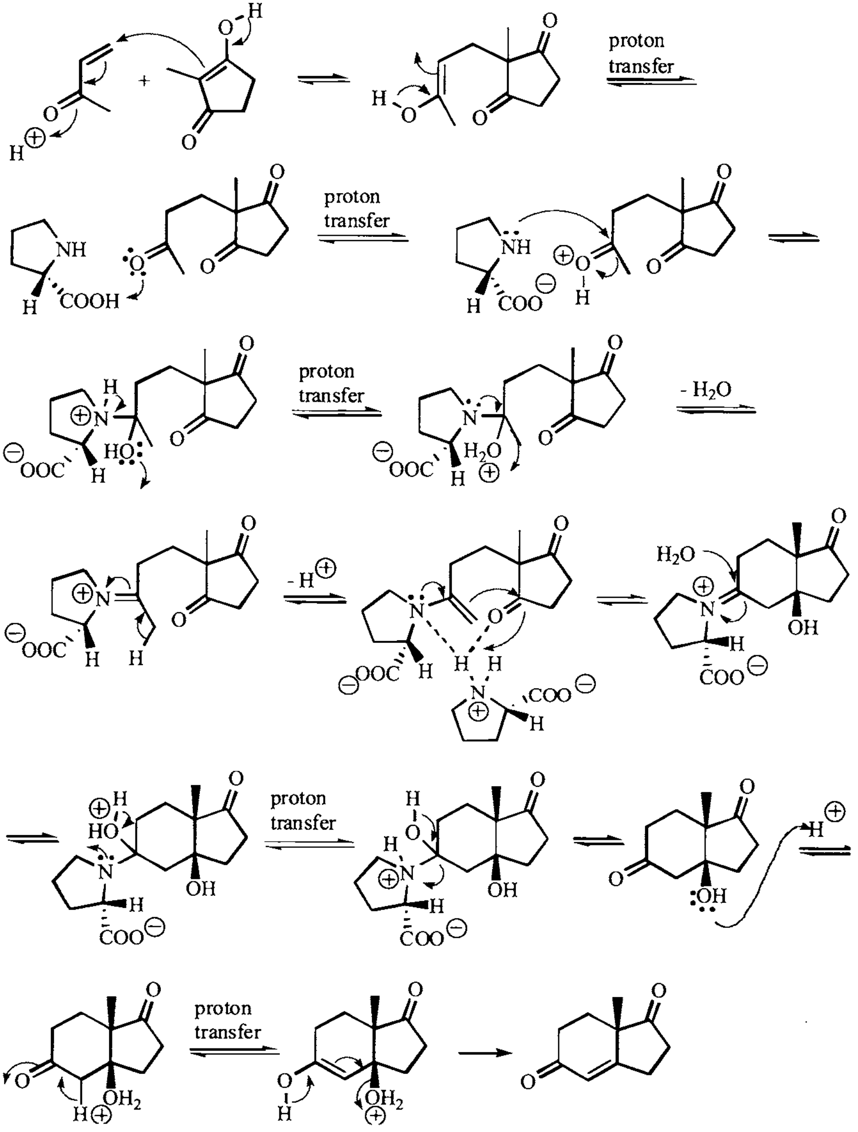
J. D. Winkler, K. J. Quinn, C. H. MacKinnon, S. D. Hiscock, E. C. McLaughlin, *Organic Letters* **2003**, 5, 1805

Hajos-Weichert Reaction

The Reaction:



Proposed Mechanism:

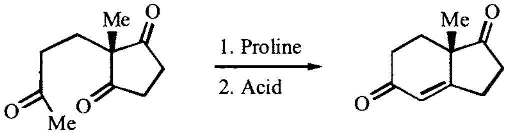


Notes:

See: S. Wallbaum, J. Martens, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 6, 4301 for a discussion on proline-initiated ***aldol*** cyclizations, including chemical and optical yields.

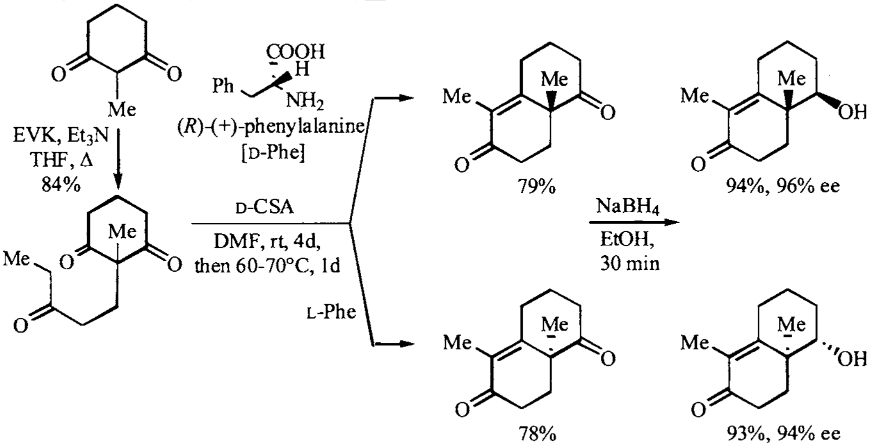
Examples:

The preparation of the ***Hajos-Parrish ketone:***



Z. G. Hajos, D. R. Parrish, *Journal of Organic Chemistry* **1974**, 39, 1615

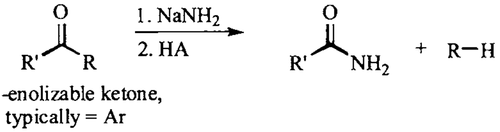
Phenylalanine can also be used as the source of chirality, sometimes with improved yields. See: H. Hagiwara, H. Uda, *Journal of Organic Chem*istry **1988**, 53, 2308 and S. Takahashi, T. Oritani, K. Yamashita, *Tetrahedron* **1988**, 44, 7081



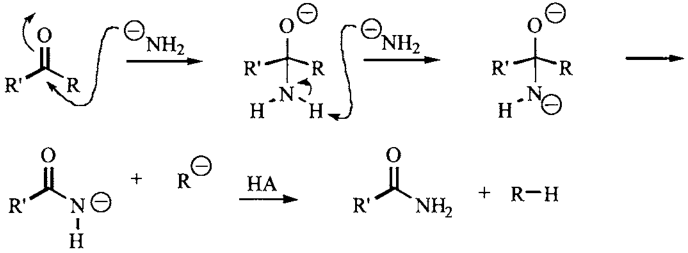
F. G. Favaloro, Jr., T. Honda, Y. Honda, G. W. Gribble, N. Suh, R. Risingsong, M. B. Sporn, *Journal of Medicinal Chemistry* **2002**, 45, 4801

Haller-Bauer Reaction

The Reaction:



Proposed Mechanism:



Notes:

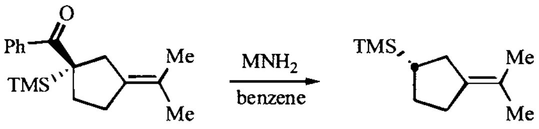
This is a reaction of non-enolizable ketones. Optical activity in the R- group is maintained.

See: G. Mehta, R. V. Venkateswaran, *Tetrahedron* **2000**, 56, 1399. In this updated Review, the authors indicate the inclusion of alkoxide cleavages as ***Haller-Bauer***. March describes these as "Hydro-de-Acylation" reactions. See also: M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 814; K. E. Hamlin, A. W. Weston, *Organic Reactions* **9**, 1.

L. A. Paquette, J. P. Gilday, *Organic Preparations and Procedures International* **1990**, 22, 167

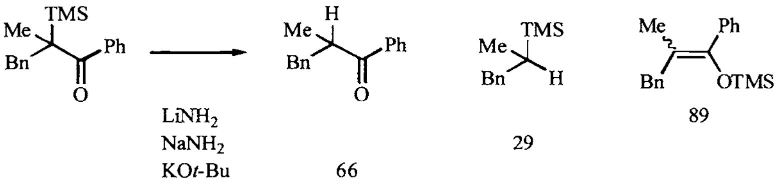
For an improved procedure see: W. Kaiser, *Synthesis* **1975**, 395

Examples:

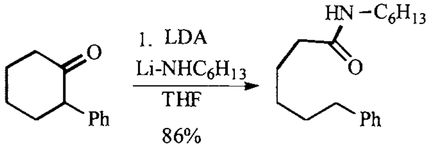


M = Na > M = K for reaction ee

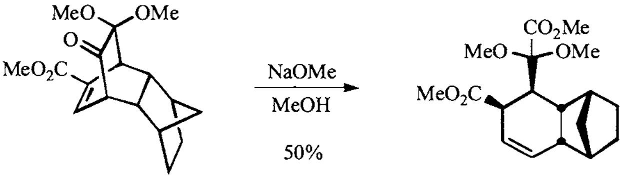
L. A. Paquette, G. D. Maynard, C. S. Ra, M. Hoppe, *Journal of Organic Chemistry* **1989**, 54, 1408



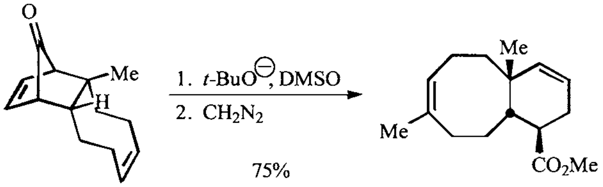
J. P. Gilday, J. C. Gallucci, L. A. Paquette, *Journal of Organic Chemistry* **1989**, 54, 1399



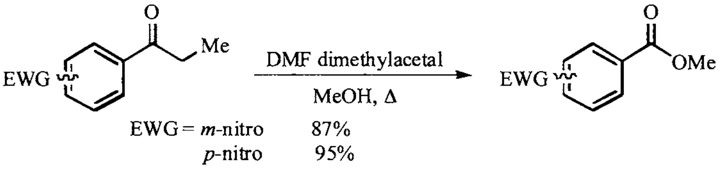
K. Ishihara, T. Yano, *Organic Letters* **2004**, 6, 1983



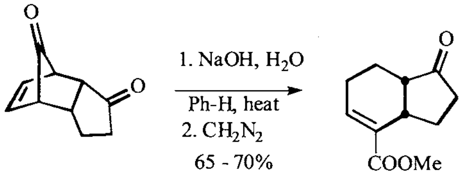
O. Arjona, R. Medel, J. Plumet, *Tetrahedron Letters* **2001**, 42, 1287



G. Mehta, K. S. Reddy, A. C. Kunwar, *Tetrahedron Letters* **1996**, 37, 2289



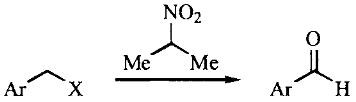
N. Zhang, J. Vozzolo, *Journal of Organic Chemistry* **2002**, 67, 1703



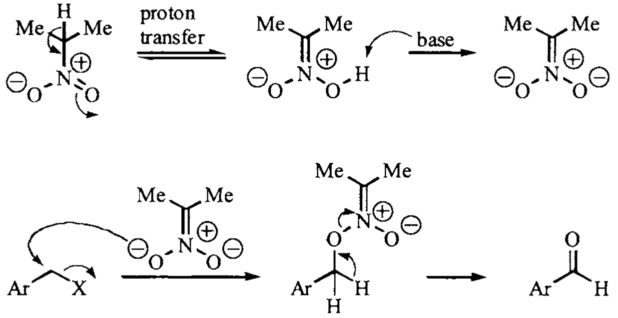
C. Mehta, D. S. Reddy, *Journal of the Chemical Society, Perkin Transactions 1*, **2001**, 1153

Hass-Bender Reaction

The Reaction:



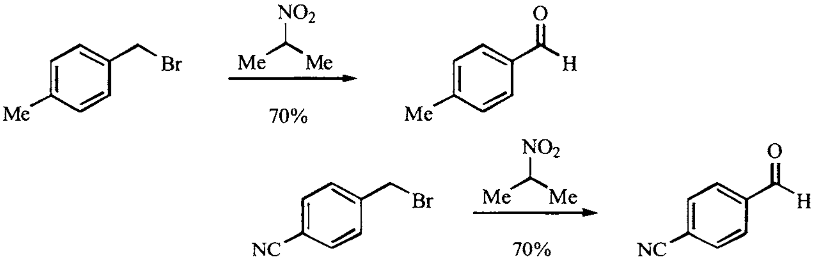
Proposed Mechanism:



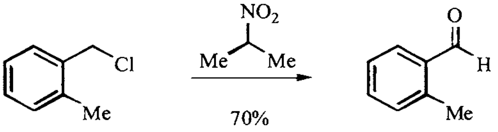
Notes:

See related reactions; ***Aldehyde Syntheses***

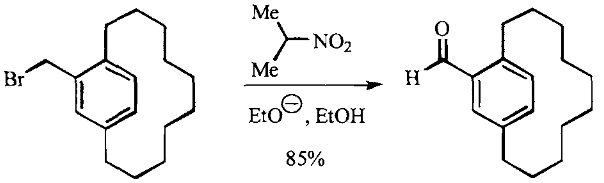
Examples:



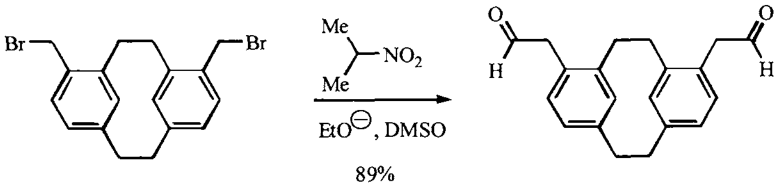
The authors state that non-aromatic ketones have been made.
H. B. Hass, M. L. Bender *Journal of the American Chemical Society* **1949**, 71, 1767



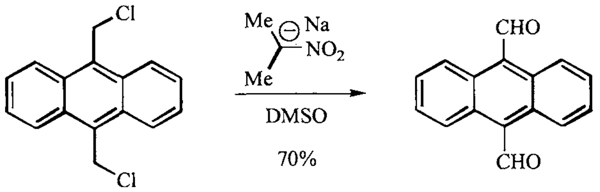
H. B. Hass M. L. Bender, *Organic Syntheses, Coll. Vol 4,* **1963**, 932



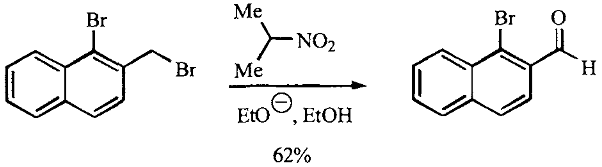
Note: Only 20% by the ***Sommelet Oxidation***.
A. T. Blomquist, R. E. Stahl, J. Meinwald, B. H. Smith, *Journal of Organic Chemistry* **1961**, 26, 1687



Note: Only 57% by the ***Sommelet Oxidation***.
S. Akabori, T. Sato, K. Hata, *Journal of Organic Chemistry* **1968**, 33, 3277



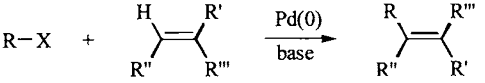
Note: Without DMSO, no product is observed.
B. H. Klandermann, *Journal of Organic Chemistry* **1966**, 31, 2618



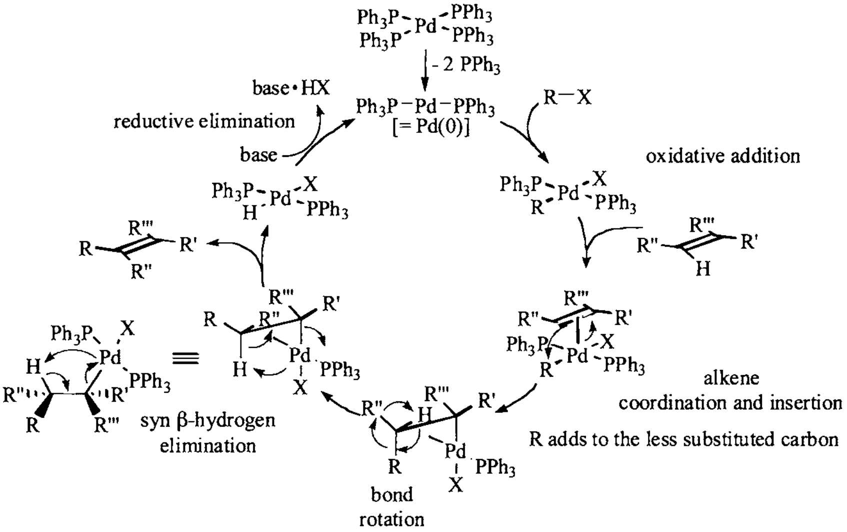
J. Clayden, C. McCarthy, N. Westlund, C. S. Frampto *Journal of the Chemical Society, Perkin Transactions I* **2000**, 1363

Heck Reaction

The Reaction:



Proposed Mechanism:

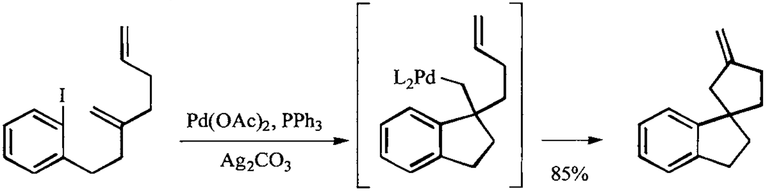


Notes:

T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 144-147; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 930; J. T. Link, *Organic Reactions* **60**, 2.

For a review on applications to Natural Product synthesis, see:
A. B. Dounay, L. E. Overman, *Chemical Reviews* **2003**, 103, 2945

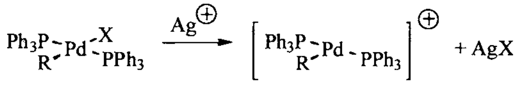
The ***Overman Spirocyclization***:



M. M. Abelman, L. E. Overman *Journal of the American Chemical Society* **1988**, 110, 2328

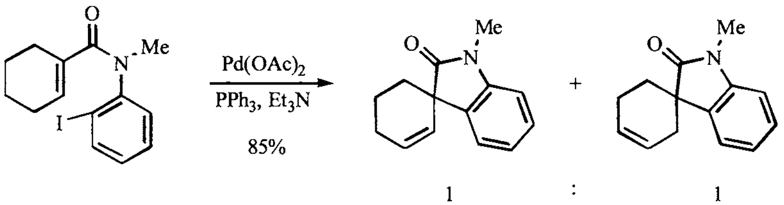
Examples:

Silver ion is sometimes added:



$$Ph_3P\text{-}Pd(R)(X)\text{-}PPh_3 \xrightarrow{Ag^{\oplus}} \left[Ph_3P\text{-}Pd(R)\text{-}PPh_3\right]^{\oplus} + AgX$$

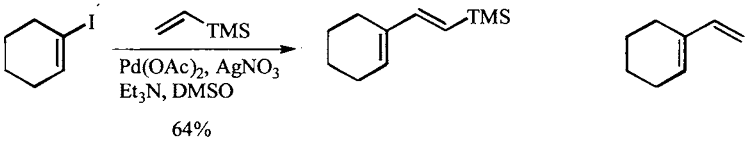
The charged species is carried through the reaction until the last step when $H^{\oplus}$ is eliminated.



1 : 1

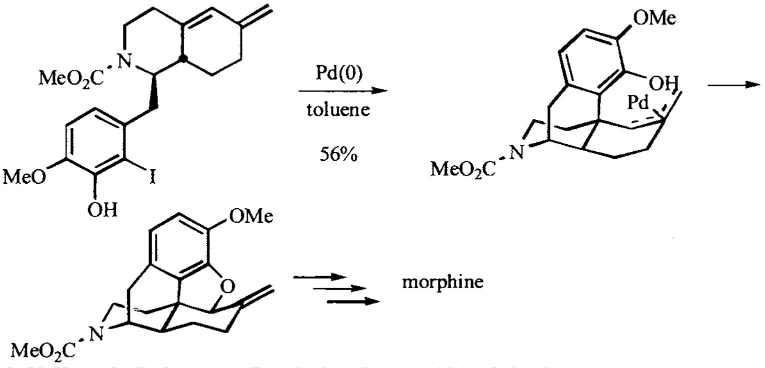
with $AgNO_3$ added: 26 : 1

M. M. Abelman, T. Oh, L. E. Overman *Journal of Organic Chemistry* **1987**, 52, 4130

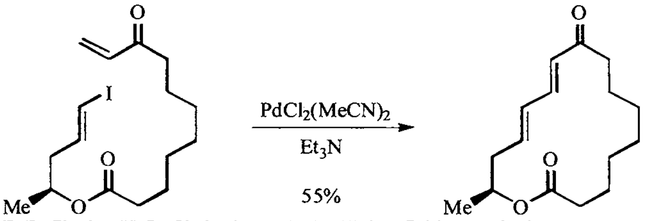


In this case, the silver suppresses desilylation. Without silver included, the product was obtained in 12% yield and the major product was the above right.

K. Karabelas, A. Hallber *Journal of Organic Chemistry* **1988**, 53, 4909



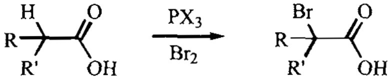
C. Y. Hong, L. E. Overman, *Tetrahedron Letters* **1994**, 35, 3453



F. E. Ziegler, U. R. Chakroborty, R. B. Weisenfield, *Tetrahedron* **1981**, 37, 4035

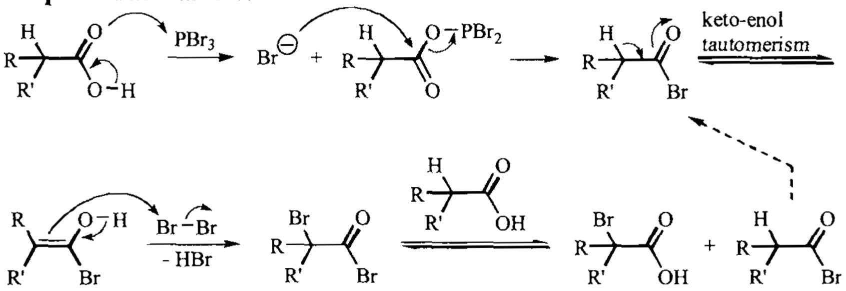
Hell-Volhard-Zelinski Reaction

The Reaction:



The halogen from PX_3 is not transferred to the alpha position.

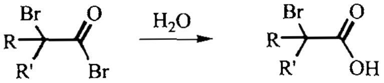
Proposed Mechanism:

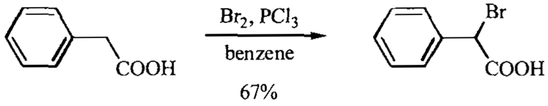


Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry,* 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 777; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 147-149. These authors note that α-F or α-I cannot be obtained by this method,

Some describe:

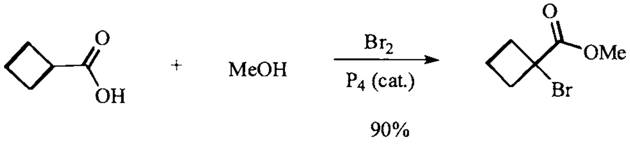




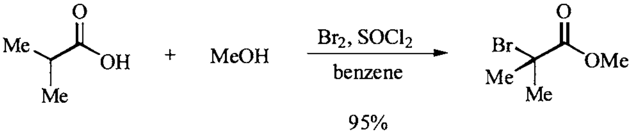
There is no water in the experimental.

L. A. Carpino, L. V. McAdams, III, *Organic Syntheses*, CV6, 403

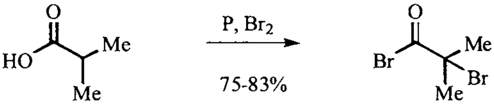
Examples:



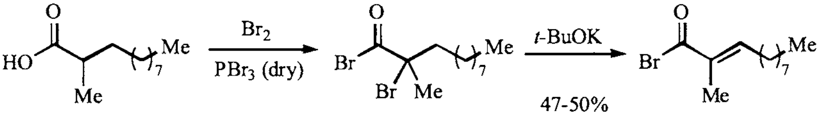
K. Estieu, J. Ollivier, J. Salauen, *Tetrahedron Letters* **1996**, 37, 623



Y. Ogata. T. Sugimaot, *Journal of Organic Chemistry* **1978**, 43, 3684



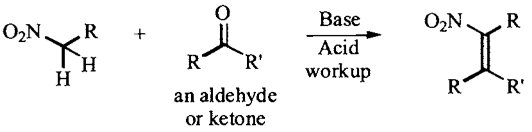
C. W. Smith, D. G. Norton, *Organic Syntheses* CV4, 348



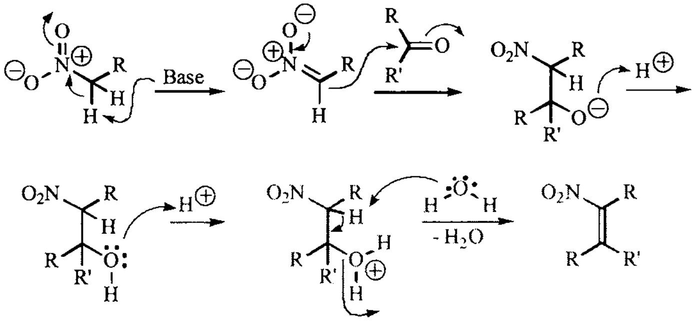
C. F. Allen, M. J. Kalm, *Organic Syntheses* CV4, 398

Henry Reaction / Kamlet Reaction

The Reaction:



Proposed Mechanism:

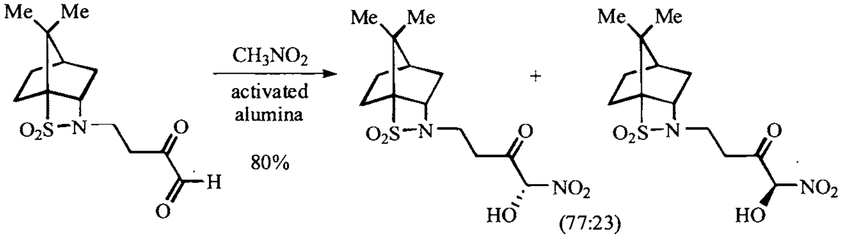


Notes:

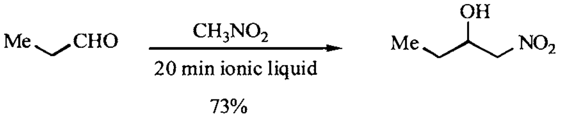
The reaction is mechanistically similar to the ***Aldol reaction***.

See: V. K. Ahluwalia, R.K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002, p. 329

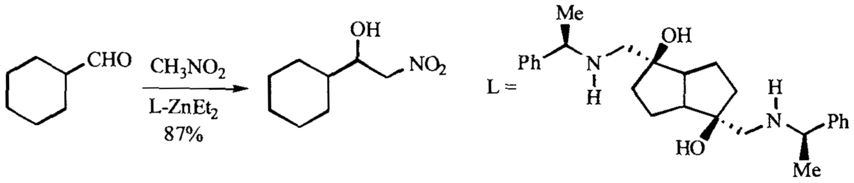
Examples:



I.Kudyba, J. Raczko, Z. Urbanczyk-Lipkowska J. Jurczak, *Tetrahedron* **2004**, 60 4807

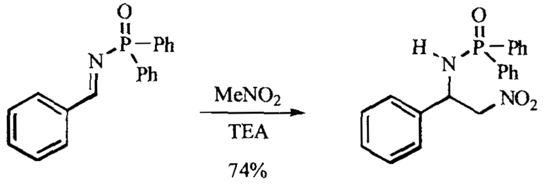


T. Jiang, H. Gao, B. Han, G. Zhao, Y. Chang, W. Wu, L. Gao, G. Yang, *Tetrahedron Letters* **2004**, 45, 2699

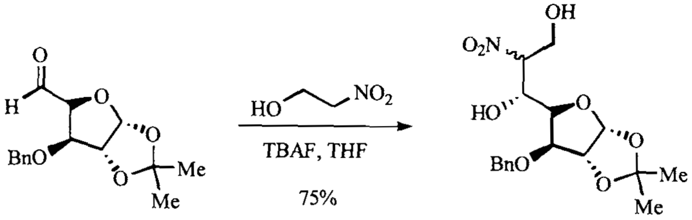


Y.-W. Zhong, P. Tian, G.-Q. Lin, *Tetrahedron: Asymmetry* **2004**, 15, 771

***Aza-Henry Reaction*:**



T. Okino, S. Nakamura, T. Furukawa, Y. Takemoto, *Organic Letters* **2004**, 6, 625

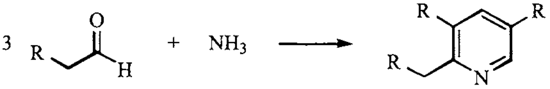


R. G. Soengas, J. C. Estevez, R. J. Estevez, *Organic Letters* **2003**, 5, 4457

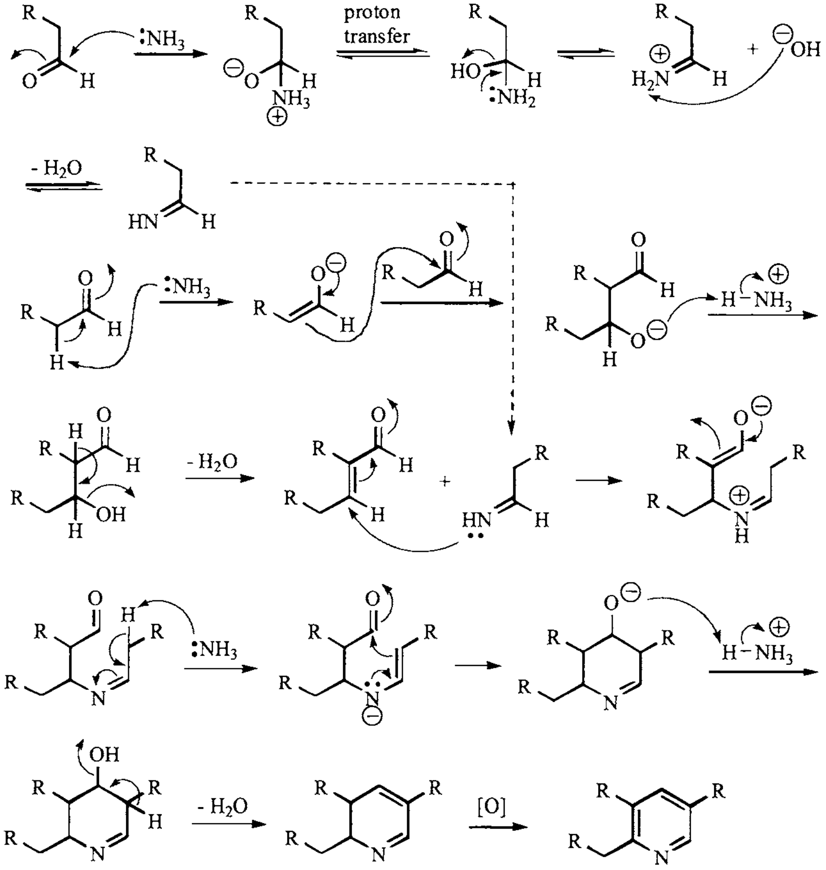
Heterocyclic Syntheses

Pyridine Syntheses

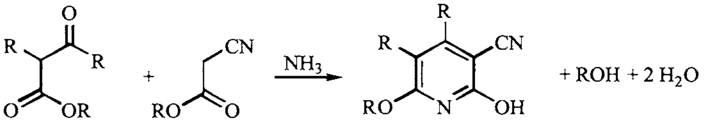
Chichibabin Pyridine Synthesis



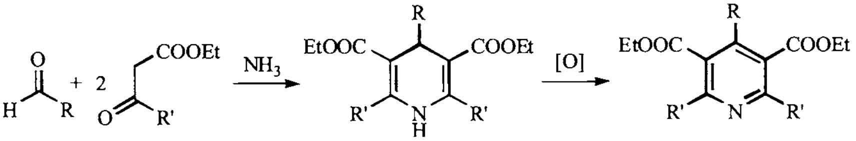
Proposed Mechanism:



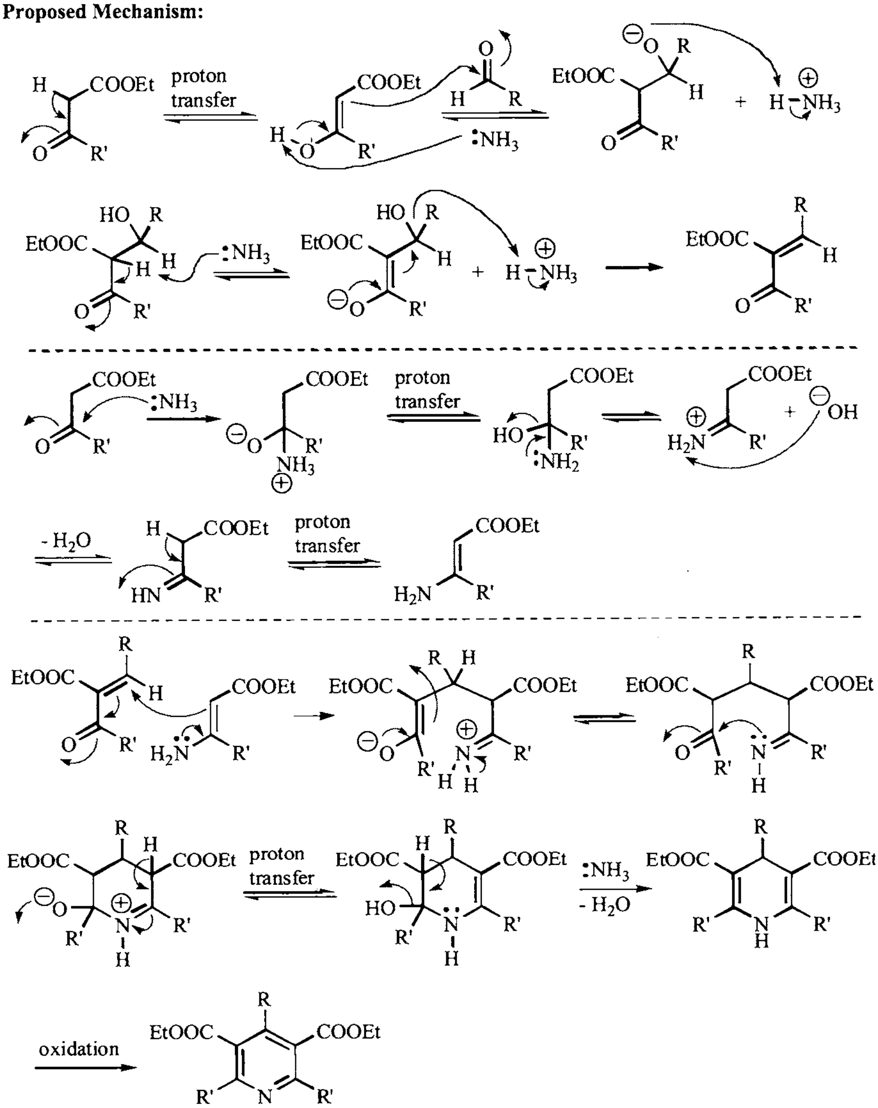
Guareschi-Thorpe Condensation



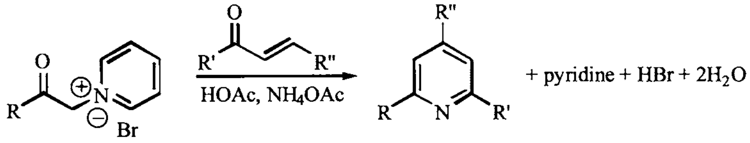
Hantzsch (Dihydro) Pyridine Synthesis



Proposed Mechanism:



Krohnke Pyridine Synthesis



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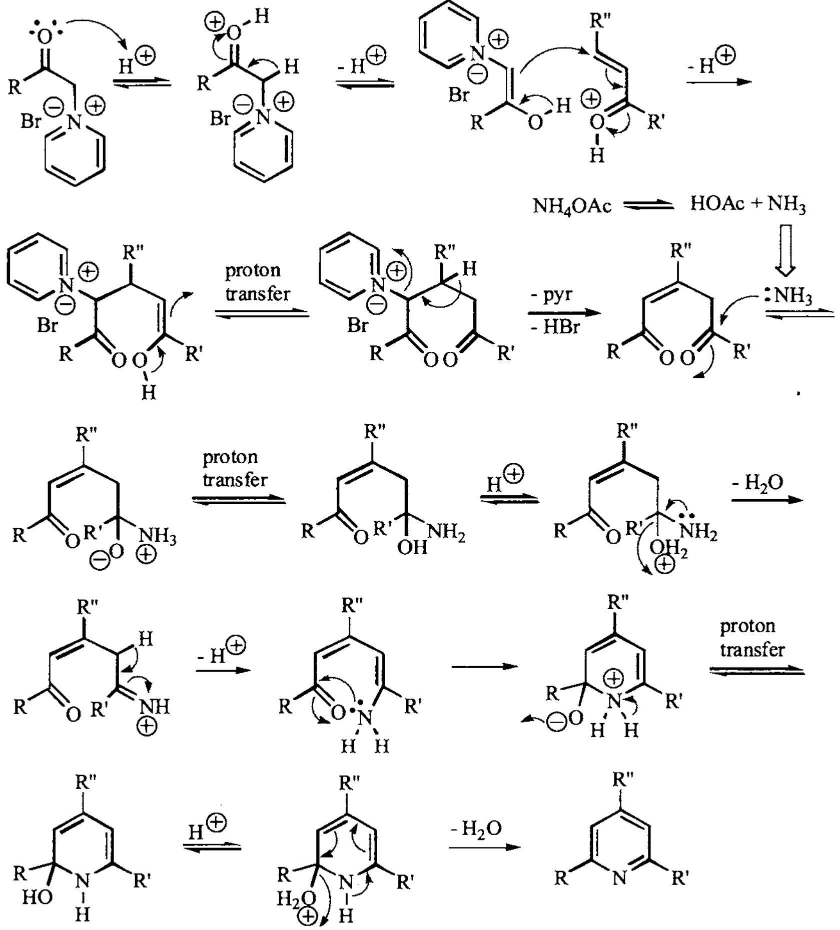
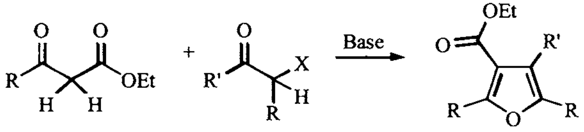


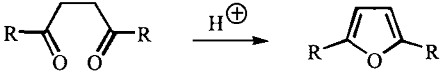
Furan, Pyrrole, Thiophene Syntheses

Furan Syntheses

Feist-Benary Furan Synthesis

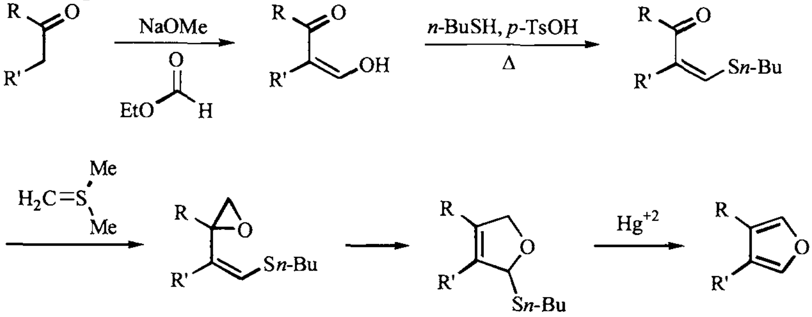


Paal-Knorr Furan Synthesis



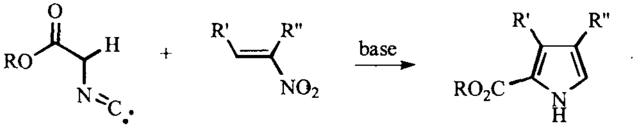
or other Lewis Acids eg P_2O_5

Garst-Spencer Furan Annulation

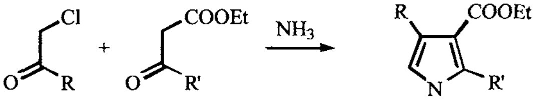


Pyrrole Syntheses

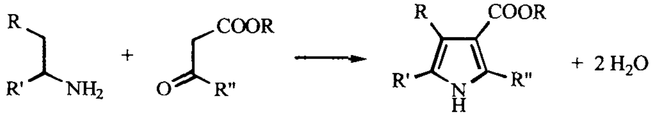
Barton-Zard Pyrrole Synthesis



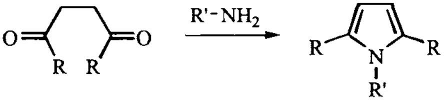
Hantzsch Pyrrole Synthesis



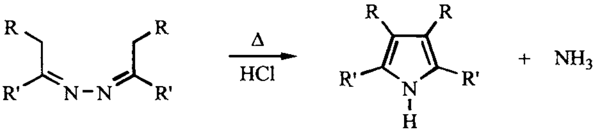
Knorr Pyrrole Synthesis



Paal-Knorr Pyrrole Synthesis

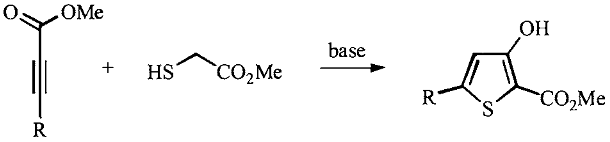


Piloty-Robinson Synthesis

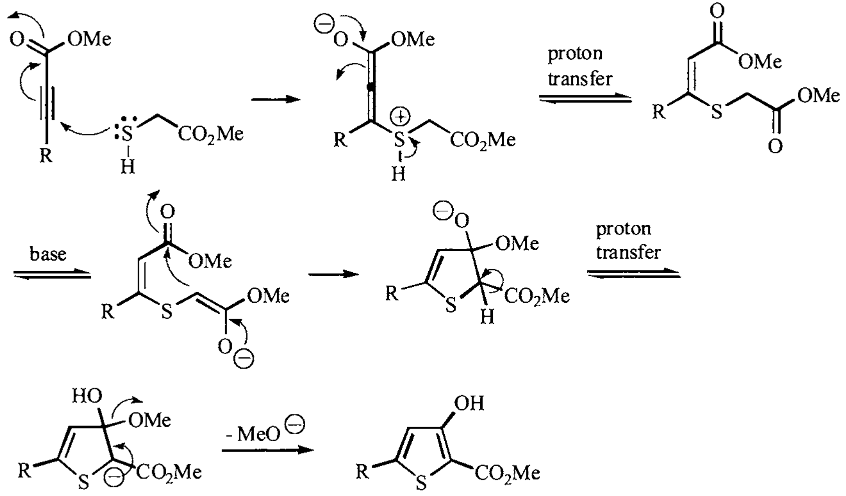


Thiophene Syntheses

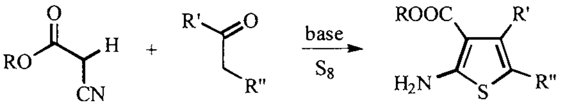
Fiesselmann Thiophene Synthesis



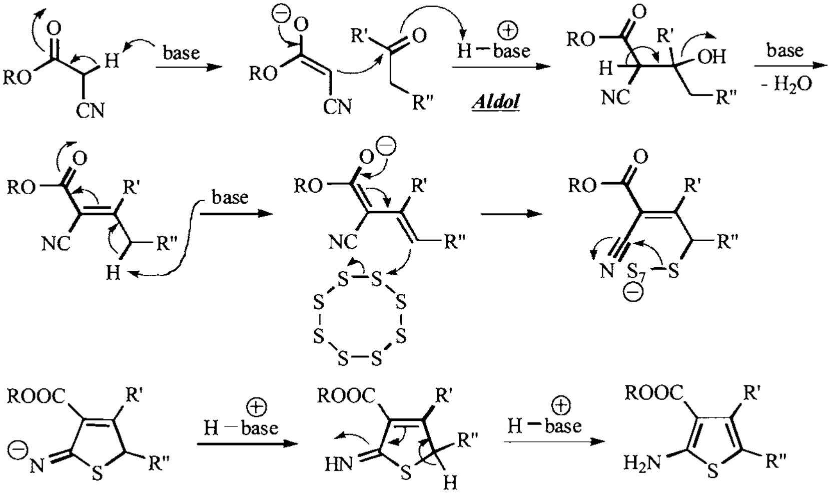
Proposed Mechanism:



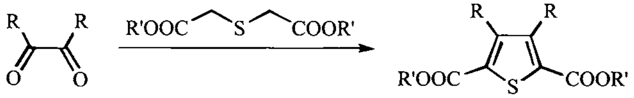
Gewald Aminothiophene Synthesis



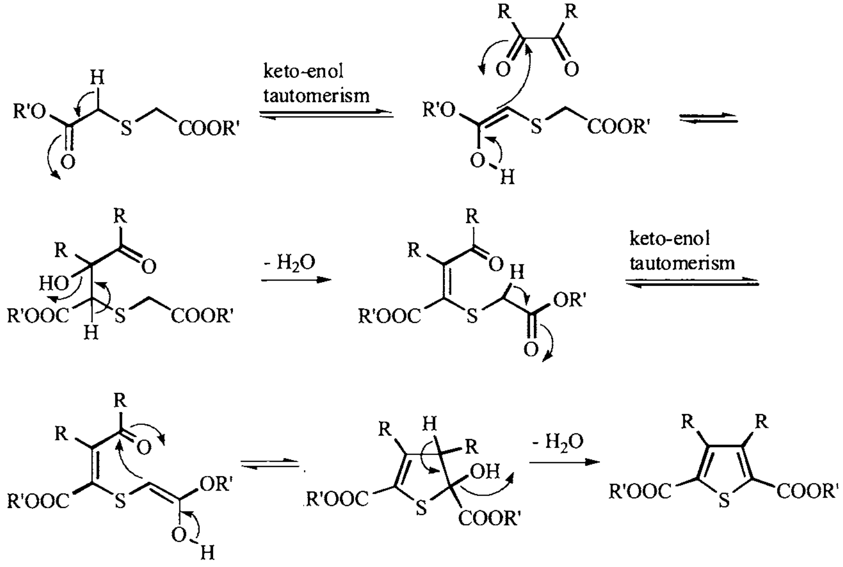
Proposed Mechanism:



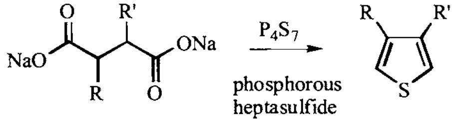
Hinsberg Synthesis of Thiophene Derivatives



Proposed Mechanism:

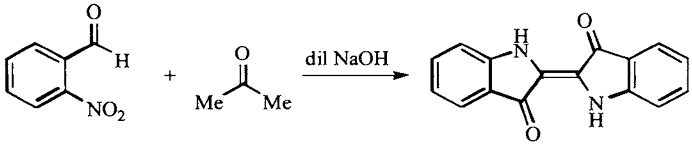


Vollhard-Erdmann Cyclization

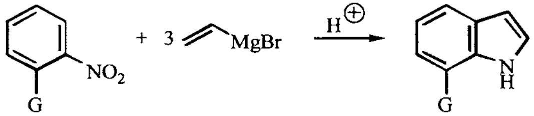


Indole Syntheses

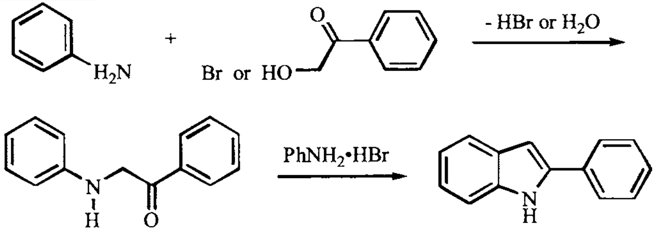
Baeyer-Drewson Indigo Synthesis



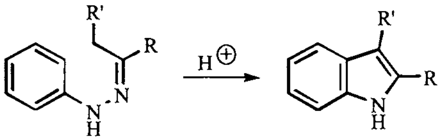
Bartoli Indole Synthesis



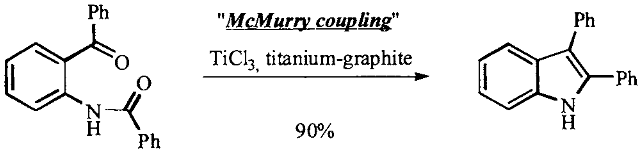
Bischler-Möhlau Indole Synthesis



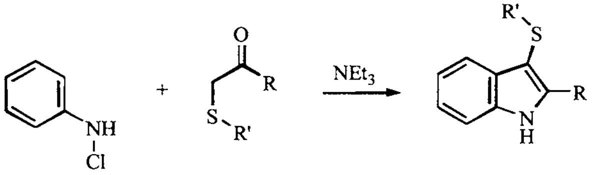
Fischer Indole Synthesis



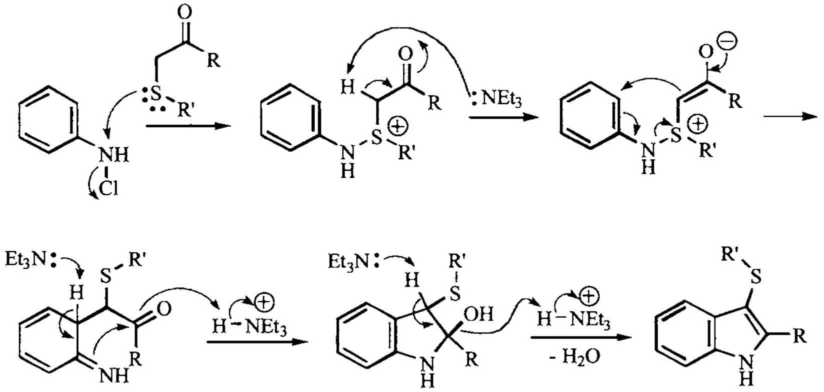
Furstner Indole Synthesis



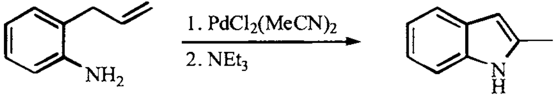
Gassman Indole Synthesis



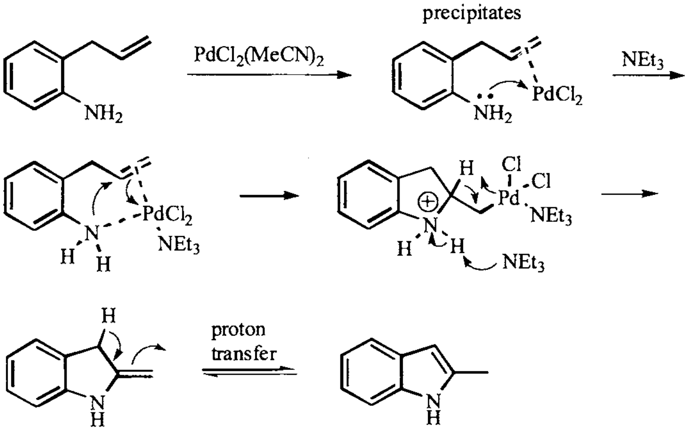
Proposed Mechanism:



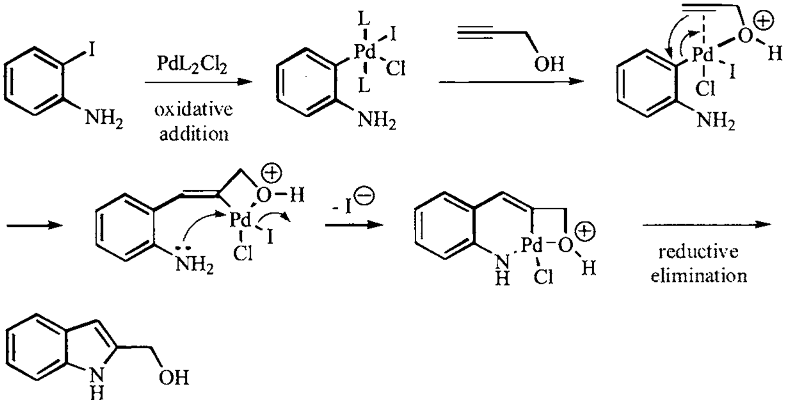
Hegedus Indole Synthesis



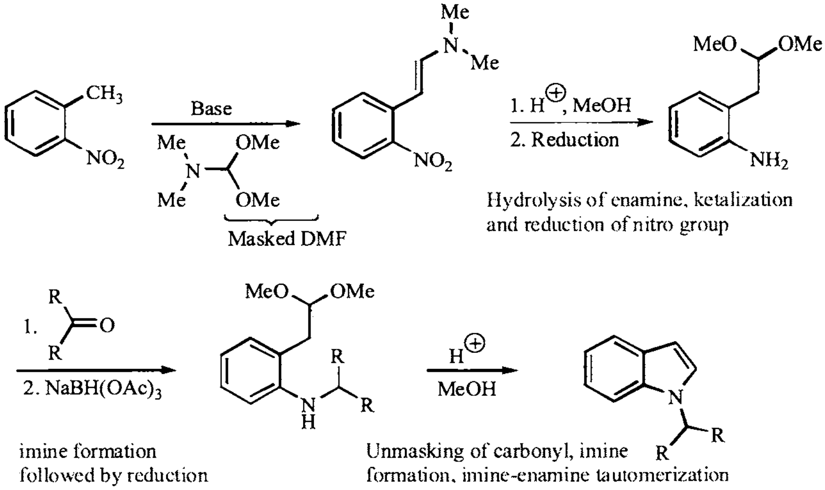
Proposed Mechanism:



Larock Indole Synthesis



Leimgruber-Batcho Indole Synthesis

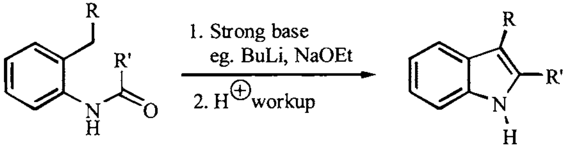


Hydrolysis of enamine, ketalization and reduction of nitro group

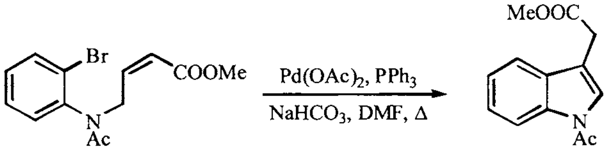
imine formation followed by reduction

Unmasking of carbonyl, imine formation, imine-enamine tautomerization

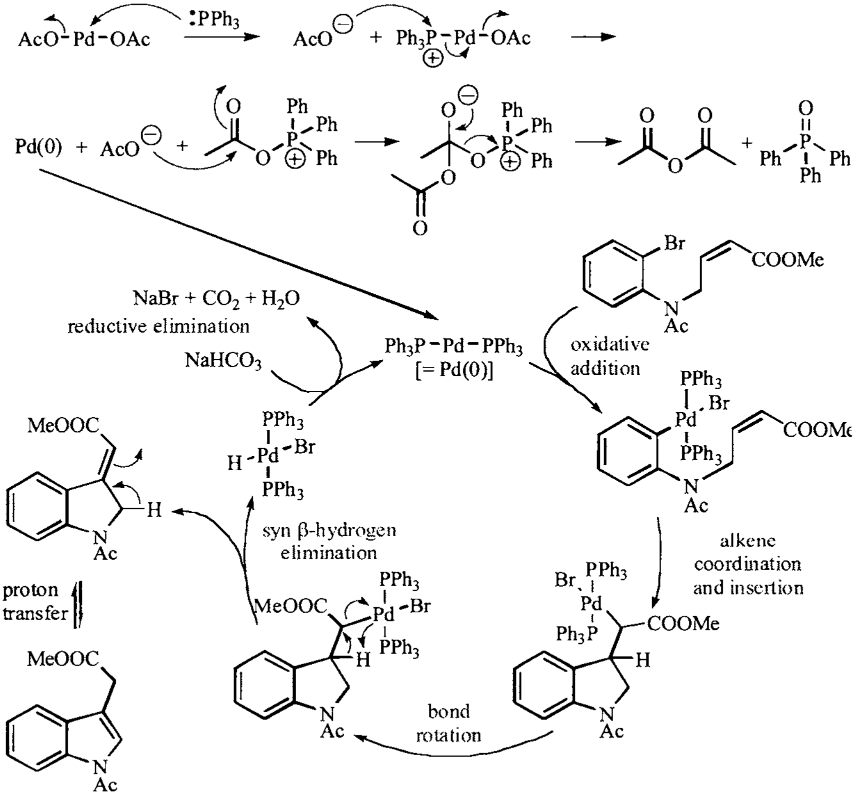
Madelung Indole Synthesis



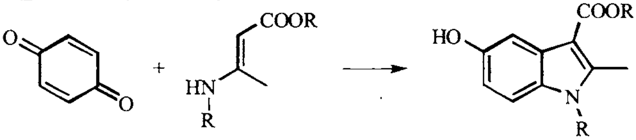
Mori-Ban Indole Synthesis

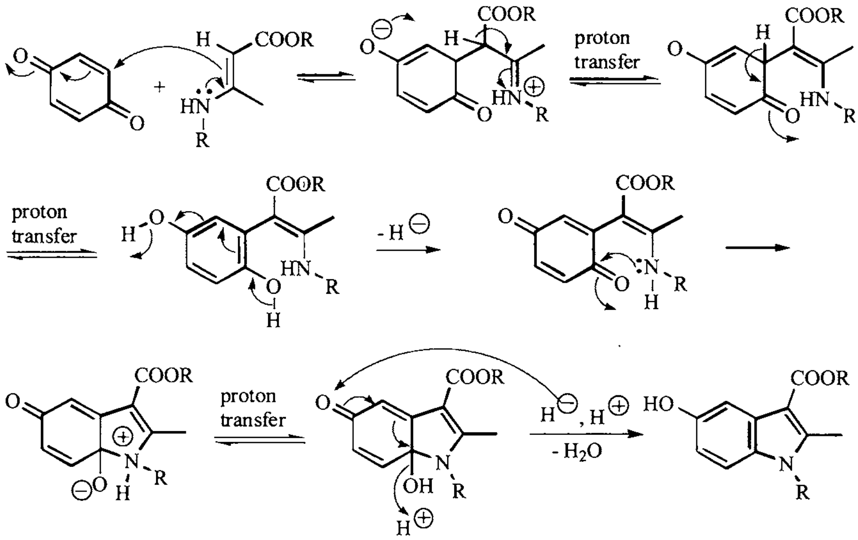


Proposed Mechanism:

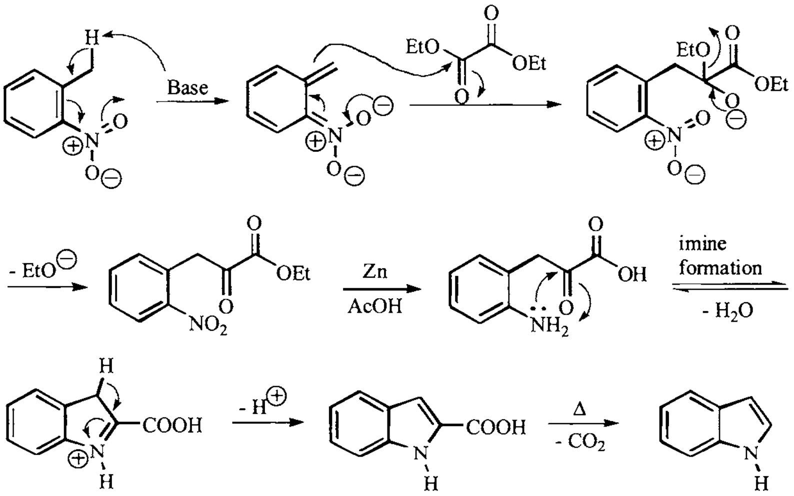


Nenitzescu Indole Synthesis

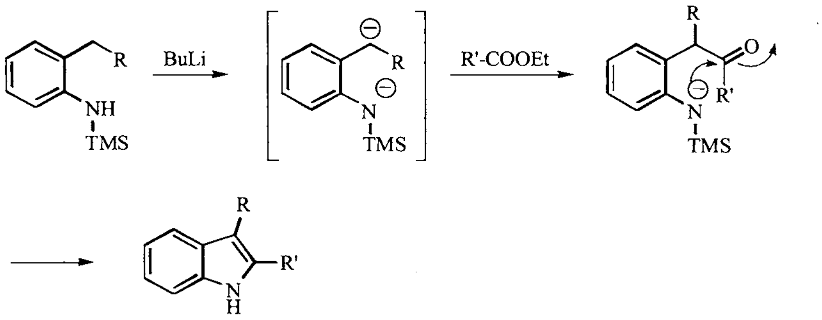




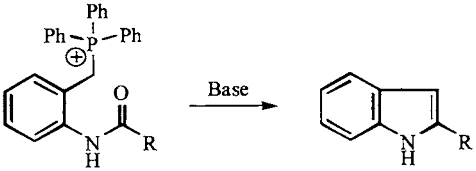
Reissert Indole Synthesis



Smith Indole Synthesis

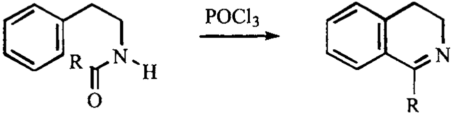


Wittig Indole Synthesis

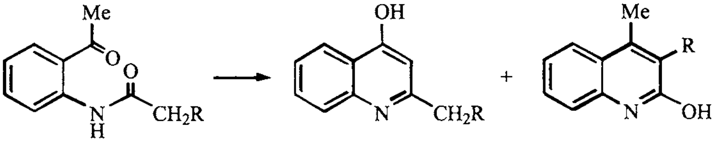


Quinoline-Isoquinoline Syntheses

Bischler-Napieralski Reaction

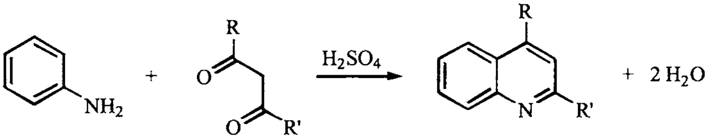


Camps Quinoline Synthesis

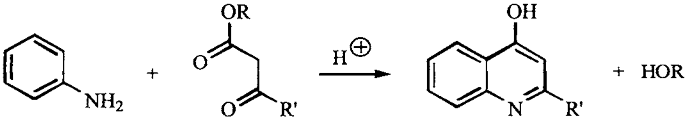


The identity of R influences the product distribution.

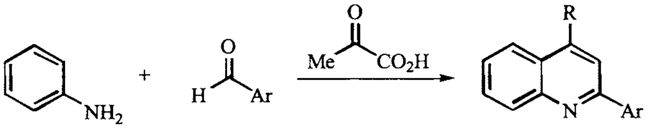
Combes Quinoline Synthesis



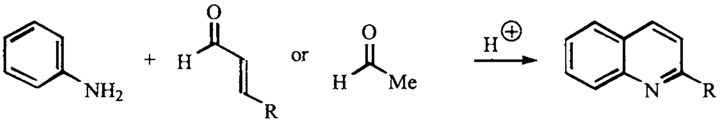
Conrad-Limpach Reaction



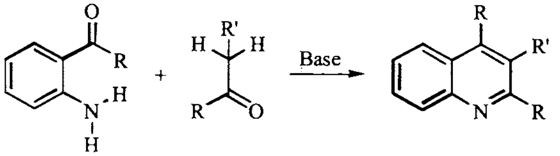
Doebner Reaction



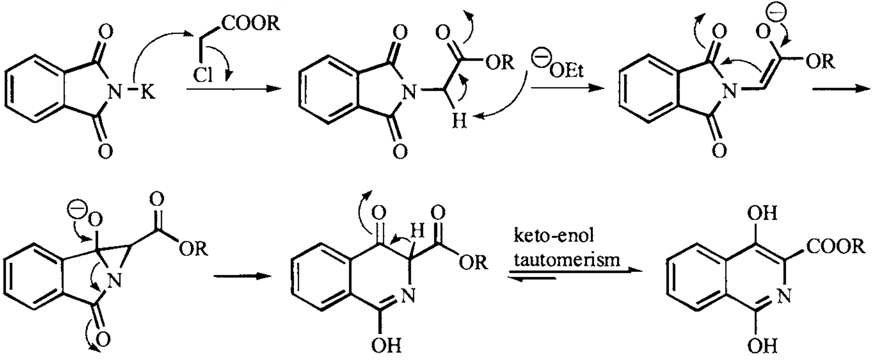
Doebner-von Miller Reaction



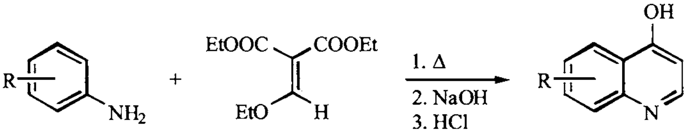
Friedlander Quinoline Synthesis



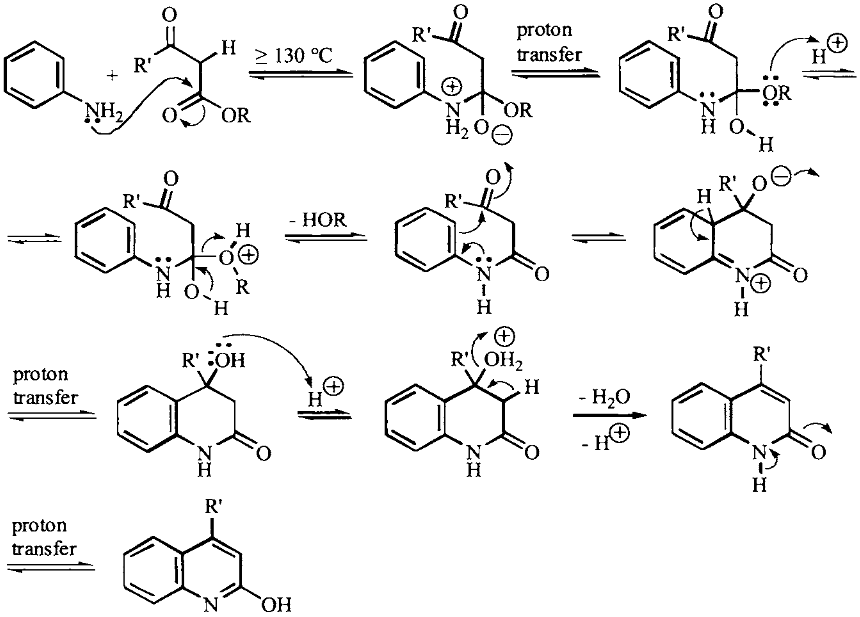
Gabriel-Colman Rearrangement



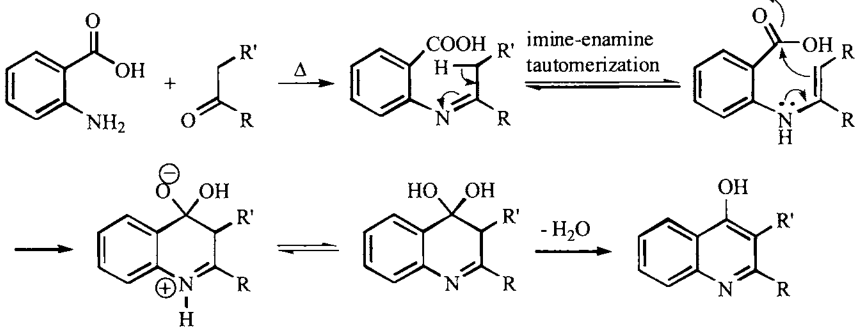
Gould-Jacobs Reaction



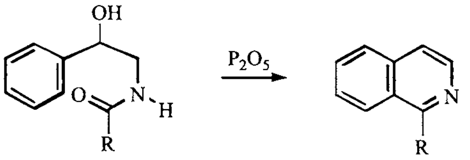
Knorr Quinoline Synthesis



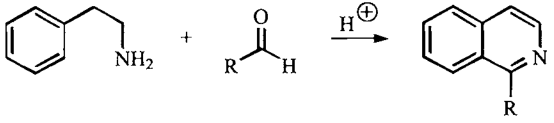
Niementowski Quinoline Synthesis



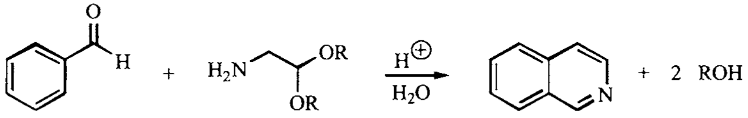
Pictet-Gams Isoquinoline Synthesis



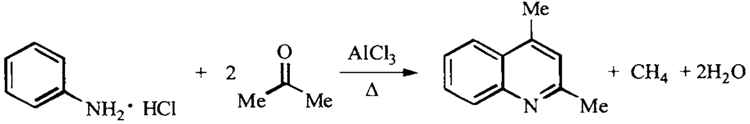
Pictet-Spengler Isoquinoline Synthesis



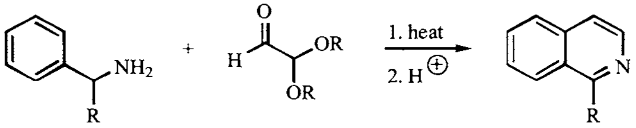
Pomeranz-Fritsch Reaction



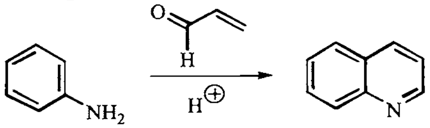
Riehm Quinoline Synthesis



Schlittler-Müller Reaction (Modification of the Pomeranz-Fritsch Reaction)

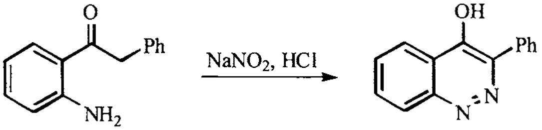


Skraup Reaction

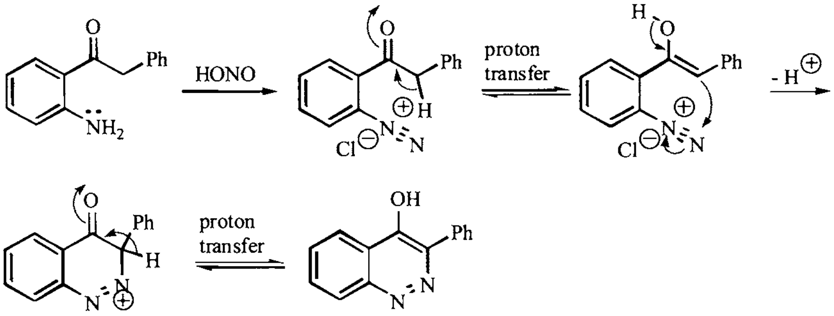


Cinnoline Syntheses

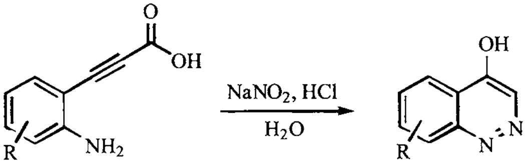
Borsche Cinnoline Synthesis



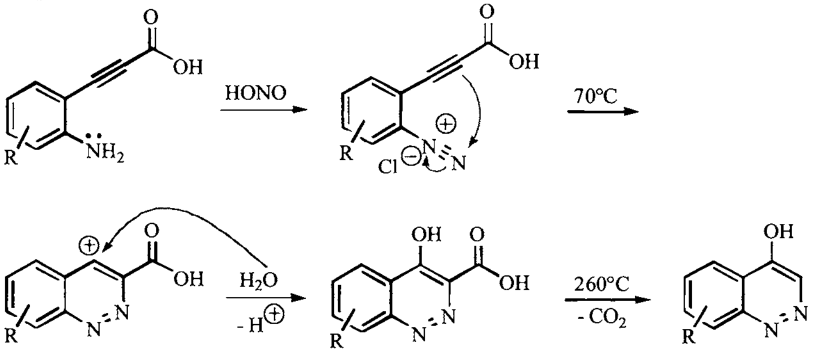
Proposed Mechanism:



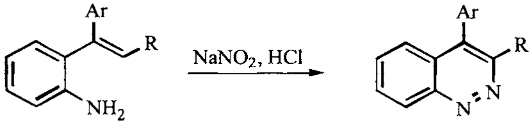
von Richter (Cinnoline) Synthesis



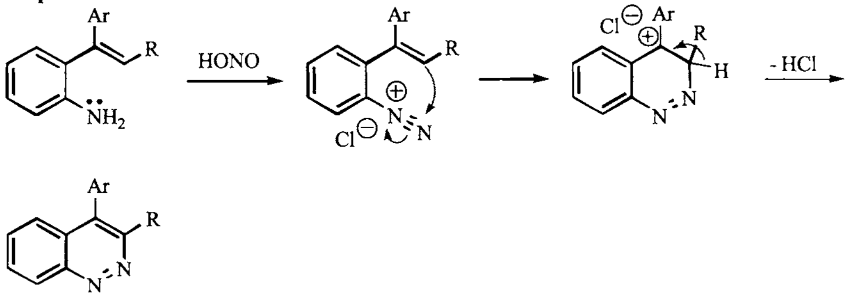
Proposed Mechanism:



Widman-Stoermer (Cinnoline) Synthesis

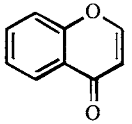


Proposed Mechanism:

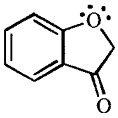


Flavone-Chromone Syntheses

General Structures

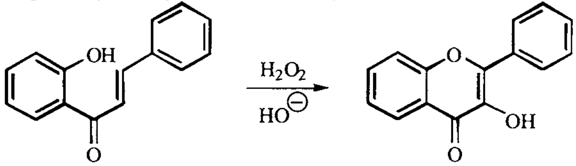


Flavone



Chromone

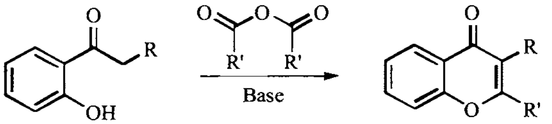
Algar-Flynn-Oyamada Reaction

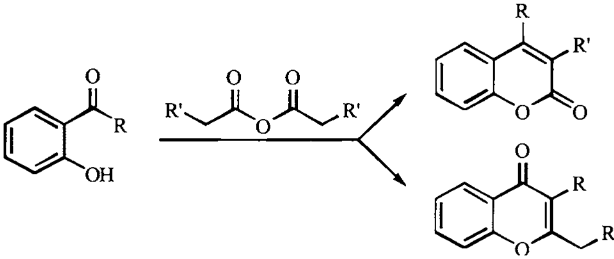


ortho-hydroxyphenyl styryl ketones

flavonols

Allan-Robinson Reaction

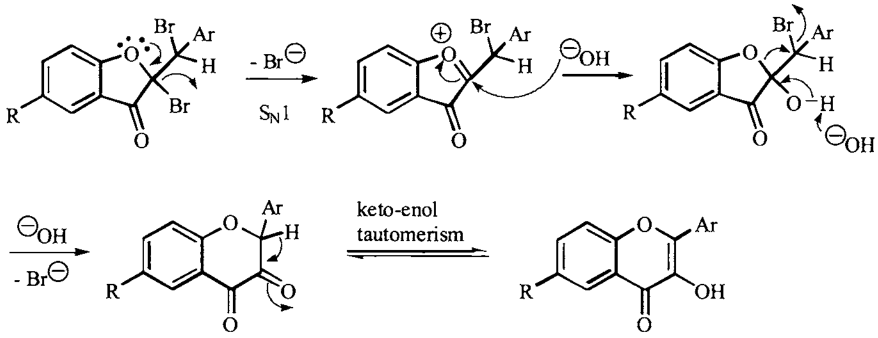




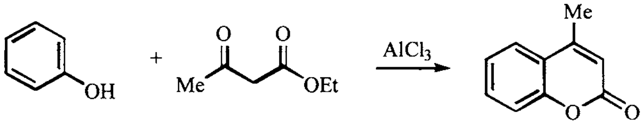
Kostanecki Acylation
product, a coumarin

Allan-Robinson Reaction
product, a chromone

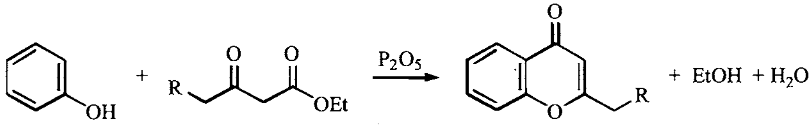
Auwers Synthesis



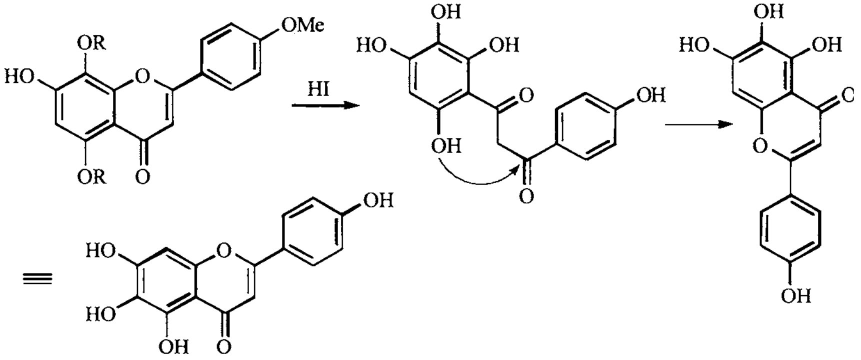
Pechmann Condensation



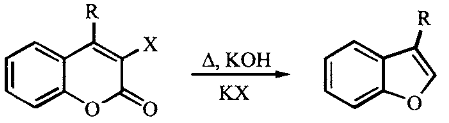
Simonis Chromone Cyclization



Wessely-Moser Rearrangement

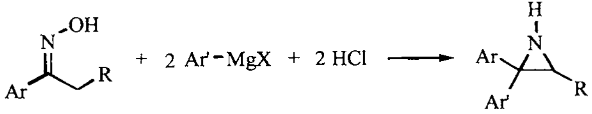


Perkin Rearrangement (Coumarin-Benzofuran Ring Contraction)

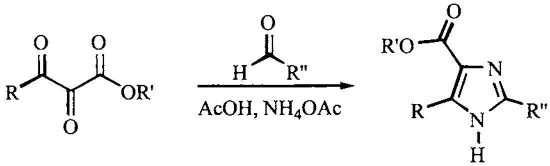


Miscellaneous

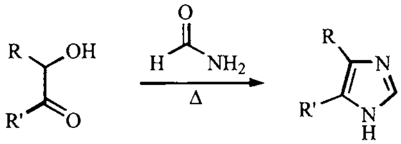
Hoch-Campbell Aziridine Synthesis



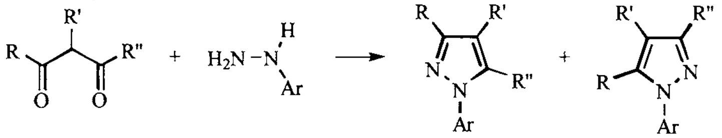
Brackeen Imidazole Synthesis



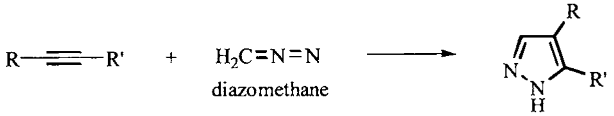
Bredereck Imidazole Synthesis



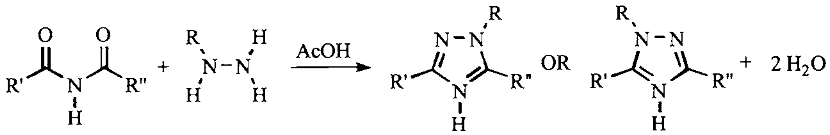
Knorr Pyrazole Synthesis



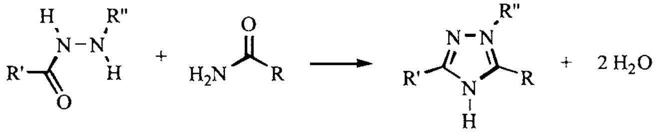
Pechmann Pyrazole Synthesis



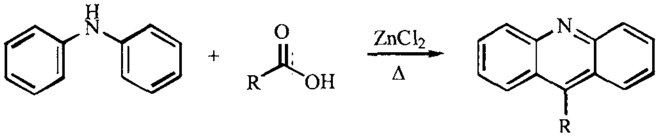
Einhorn-Brunner Reaction



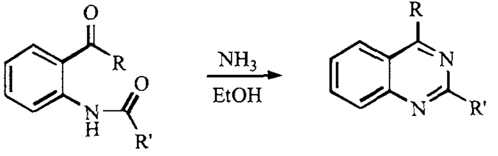
Pellizzari Reaction



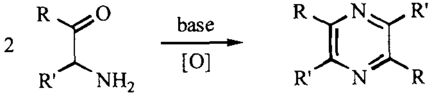
Bernthsen Acridine Synthesis



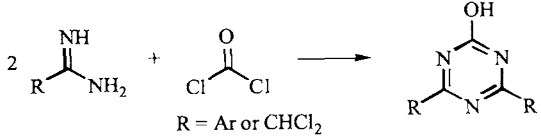
Bischler Quinoxaline Synthesis



Gutknecht Pyrazine Synthesis

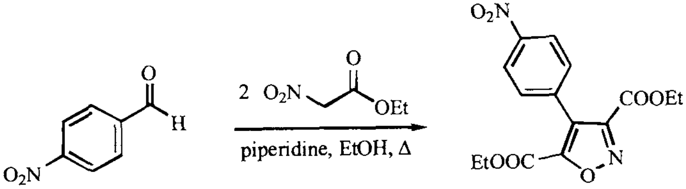


Pinner Triazine Synthesis

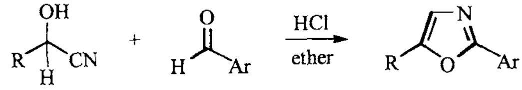


R = Ar or CHCl$_2$

Dornow-Wiehler Oxazole Synthesis



Fischer Oxazole Synthesis



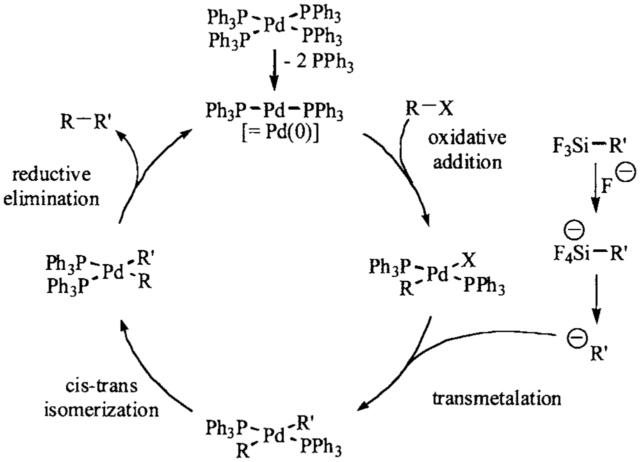
a cyanohydrin

Hiyama Cross-Coupling Reaction

The Reaction:

$$R{-}X \quad + \quad F_3Si{-}R' \xrightarrow[\text{base or } F^{\ominus}]{Pd(0)} R{-}R'$$

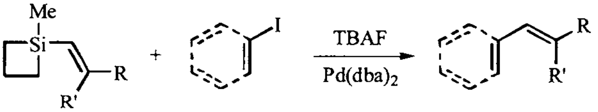
Proposed Mechanism:



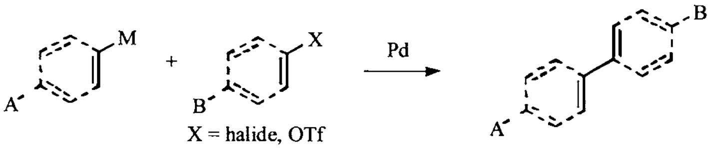
Notes:

Denmark-Mori Modification

See: S. E. Denmark, R. F. Sweis, *Accounts of Chemical Research* **2002**, 35, 835

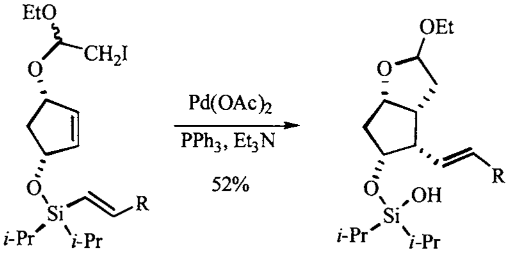


In this account they summarize related coupling reactions:

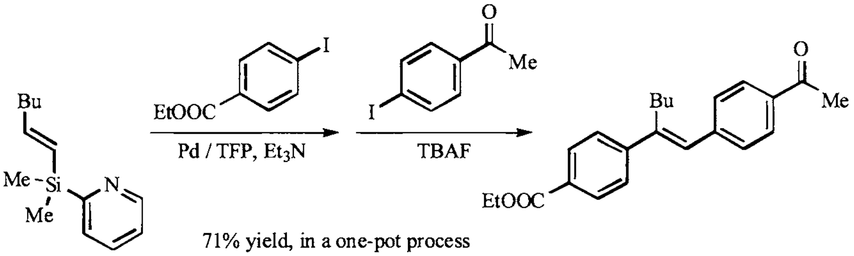


Stille-Migata-Kosugi	$M = SnR_3$
Suzuki-Miyaura	$M = BR_2$ or $B(OR)_2$
Hiyama	$M = SiR_{(3-n)}F_{(n)}$
Tamao-Ito	$M = Si(OR)_3$

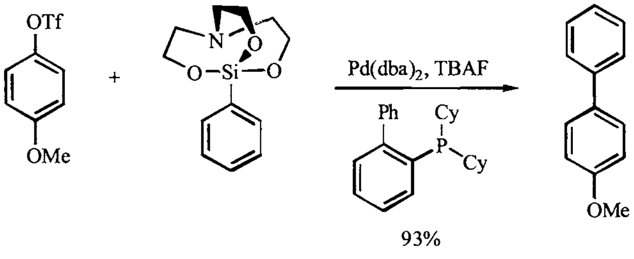
Examples:



L. G. Quan, J. K. Cha, *Journal of the American Chemical Society* **2002**, 124, 12424



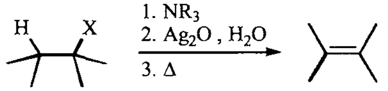
K. Itami, T. Nakami, J. Yoshida, *Journal of the American Chemical Society* **2001**, 123, 5600



S. Riggleman, P. DeShong, *Journal of Organic Chemistry* **2003**, 68, 8106

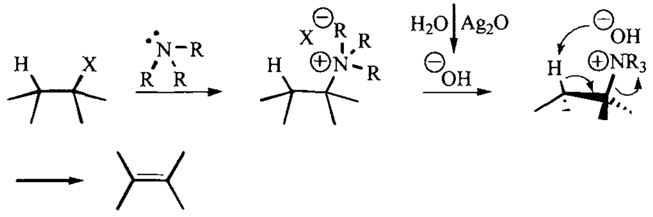
Hofmann Elimination (Exhaustive Methylation, Degradation)

The Reaction:



generally gives the less substituted alkene

Proposed Mechanism:

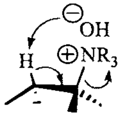


Notes:

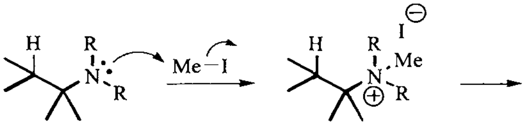
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 149-153: M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1331-1333; A. C. Cope, E. R. Turnbull, *Organic Reactions* **11**, 5; S. H. Pine, *Organic Reactions* **18**, 4.

With amines, the first step is generally exhaustive methylation.

This reaction is conducted in a solvent that won't separate the ion pairs. This necessitates an eclipsed / syn orientation for elimination to take place. If there is a choice of eclipsed states, elimination will take place during the most stable, which generally gives the less substituted alkene.



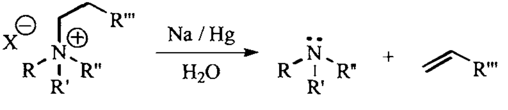
The starting material can also be achieved with an amine that is exhaustively alkylated with alkyliodide. The alkyl group must not have β hydrogens, methyl and phenyl are common.



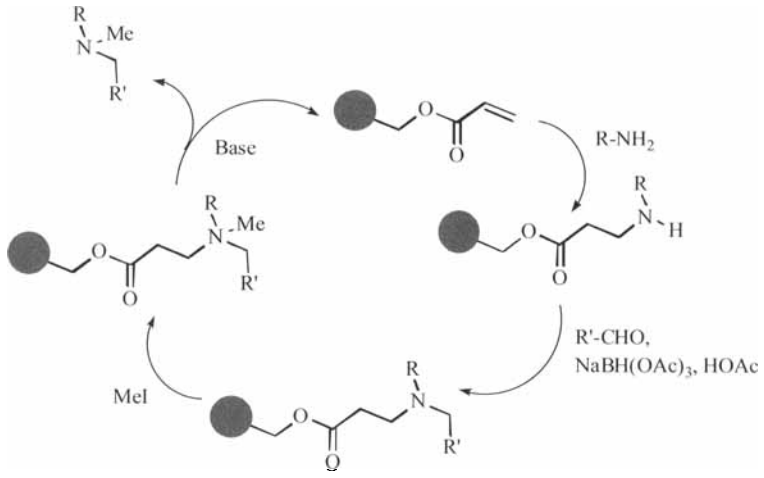
The reaction can be carried out with leaving groups other than amines.

Hofmann Rule: *Elimination from quaternary ammonium and tertiary sulfonium salts generally provides the lesser-substituted alkene as major product.*

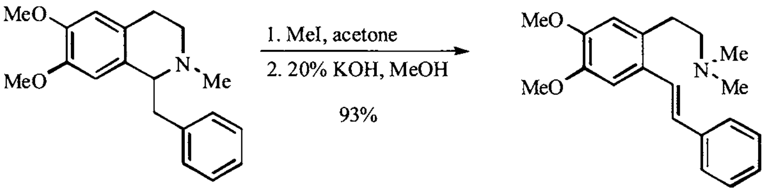
Emdė Degradation / Reduction



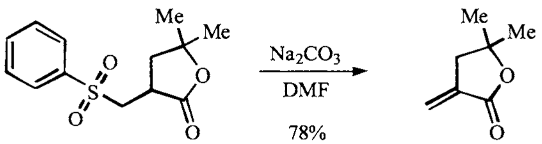
Examples:



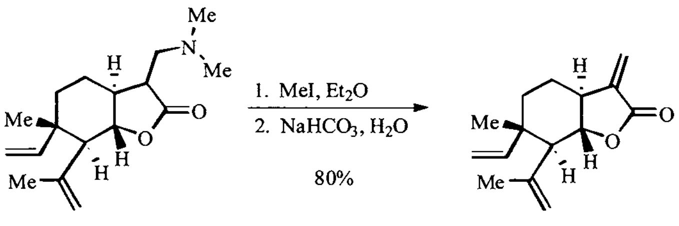
C. Alhambra, J. Castro, J. L. Chiara, E. Fernandez, A. Fernandez-Mayoralas, J. M. Fiandor, S. Garcıa-Ochoab, M. D. Martın-Ortegaa,*Tetrahedron Letters 2001,* 42, 6675



S. V. Kini, M. M. V. Ramana, *Tetrahedron Letters* **2004**, 45, 4171



T. Shono, Y. Matsumara, S. Kashimura, K. Hatanaka, *Journal of the American Chemical Society* **1979**, 101, 4752



T. C. Jain, C. M Banks, J. E. McCloskey, *Tetrahedron* **1976**, 32, 765

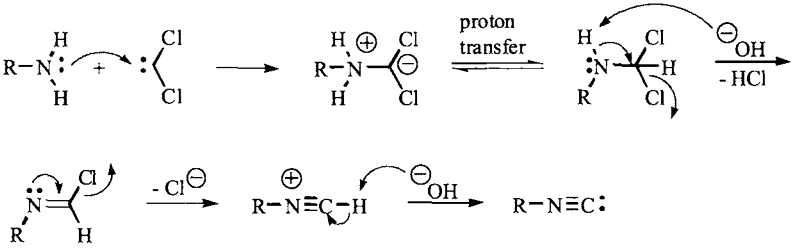
Hofmann Isonitrile Synthesis (Carbylamine Reaction)

The Reaction:

$R{-}NH_2 + CHCl_3 + 3\,NaOH \longrightarrow R{-}N{\equiv}C\colon + 3\,NaCl + 3\,H_2O$

Proposed Mechanism:

$CHCl_3 + NaOH \longrightarrow \colon CCl_2 + NaCl + H_2O$

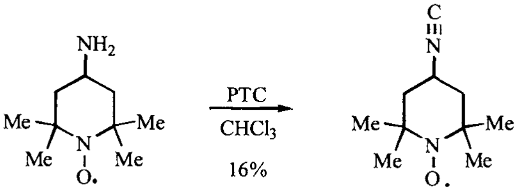


Notes:

This is a carbene reaction.

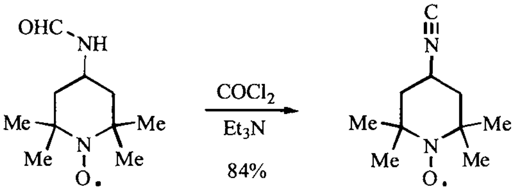
See: V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002, p. 333

Examples:



PTC = phase transfer conditions

Under different reaction conditions:



J. Zakrzewski, J. Jezierska, J. Hupko, *Organic Letters* **2004**, 6, 695

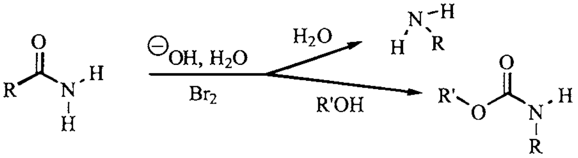
$$\text{R-NH}_2 \xrightarrow[\text{Et}_3\overset{\oplus}{\text{N}}\text{BnCl}^{\ominus}\text{, 50\% NaOH}]{\text{CHCl}_3\text{ (alcohol free), CH}_2\text{Cl}_2} \text{R-N}\equiv\text{C}$$

R = *n*-Bu	60%
R = Bn	55%

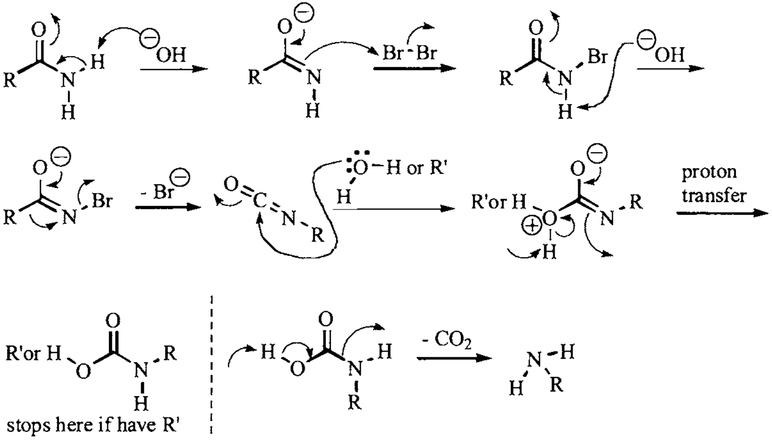
W. P. Weber, G. W. Gokel, *Tetrahedron Letters* **1972**, 17, 1637

Hofmann Rearrangement

The Reaction:



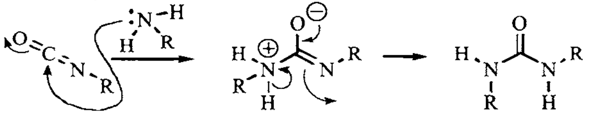
Proposed Mechanism:



Notes:

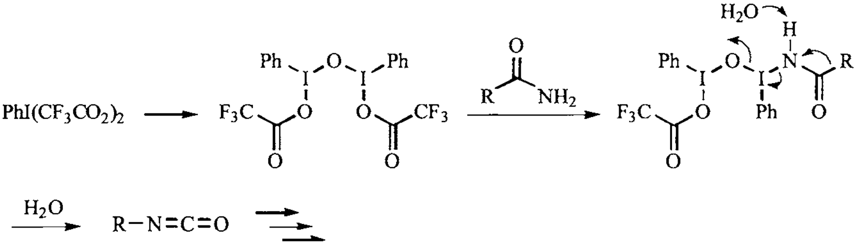
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1380, 1384; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp, 153-154; E. L. Wallis, J. F. Lane, *Organic Reactions* **3**, 7.

The workup can also be with RNH_2 to give urea derivatives.

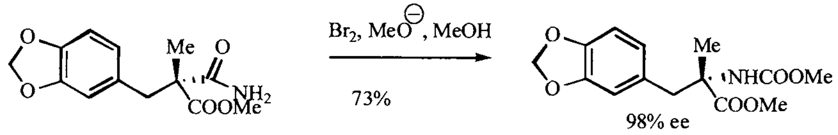


It has been found that $PhI(OAc)_2$ [iodosobenzene diacetate] and $PhI(CF_3CO_2)_2$ [bis(trifluoroacetoxy)iodosobenzene] are much better reagents for the reaction. See: L.-h. Zhang, G. S. Kauffman, J. A. Pesti, J. Yin, *Journal of Organic Chemistry* **1997**, 62, 6918

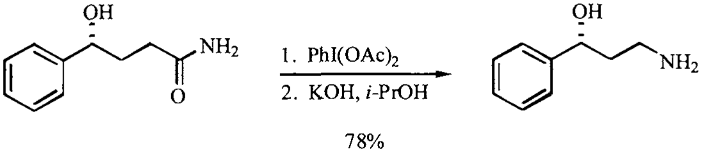
The mechanism (abbreviated below) for the $PhI(CF_3CO_2)_2$ reaction has been discussed: R. H. Boutin G. M. Loudon, *Journal of Organic Chemistry* **1984**, 49, 4211



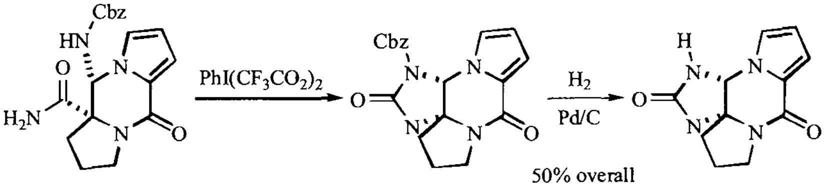
Examples:



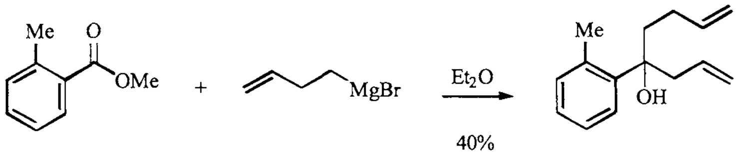
M.Yokoyaa, M. Kashiwagi, M. Iwasaki, K. Fuhshuku,H.Ohtab, T. Sugaia,
Tetrahedron: Asymmetry **2004**, 15, 2817



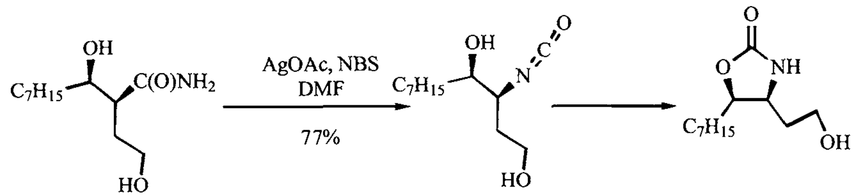
J. W. Hilborn, Z.-H. Lu, A. R. Jurgens, Q. K. Fang, P. Byers, S. A. Wald, C. H. Senanayaka,
Tetrahedron Letters **2001**, 42, 8919



K. G. Poullennec, D. Romo, *Journal of the American Chemical Society* **2003**, 125, 6344



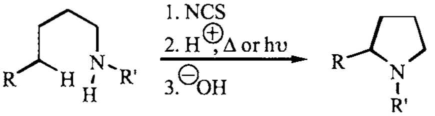
D. E. DeMong, R. M. Williams, *Journal of the American Chemical Society* **2003**, 125, 8561



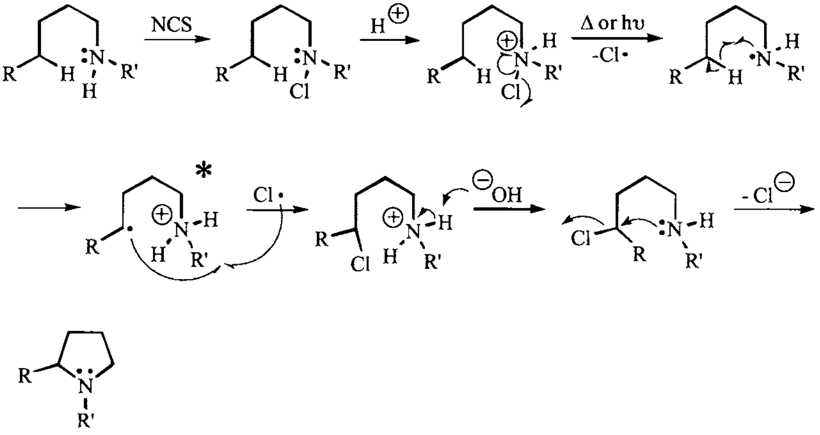
T. Hakogi, M. Taichi, S. Katsumura, *Organic Letters* **2003**, 5, 2801

Hofmann-Loffler-Freytag Reaction

The Reaction:



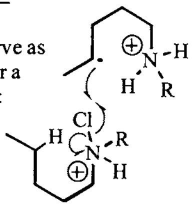
Proposed Mechanism:



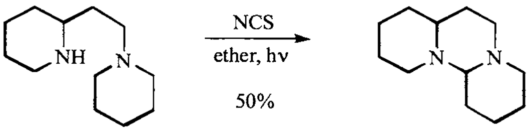
Notes:

See Reagents: *NCS*

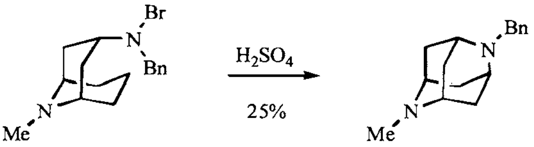
* This step can serve as the propagation for a series of reactions:



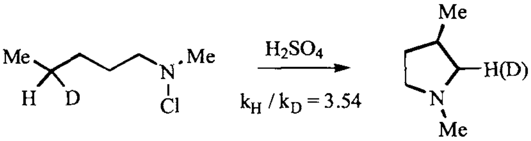
Examples:



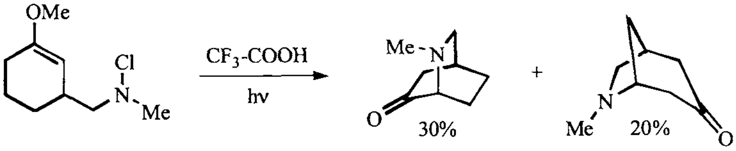
K. Kimura, Y. Ban, *Synthesis* **1978**, 201



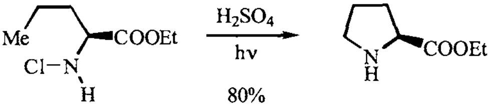
R.-M. Dupeyre, A. Rassat, *Tetrahedron Letters* **1973**, 14, 2699



E. J. Corey, W.R. Hertler, *Journal of the American Chemical Society* **1960**, 82, 1657



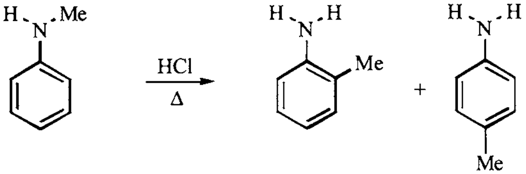
R. Furstoss, P. Teissier, B. Waegell, *Tetrahedron Letters* **1970**, 11, 1263



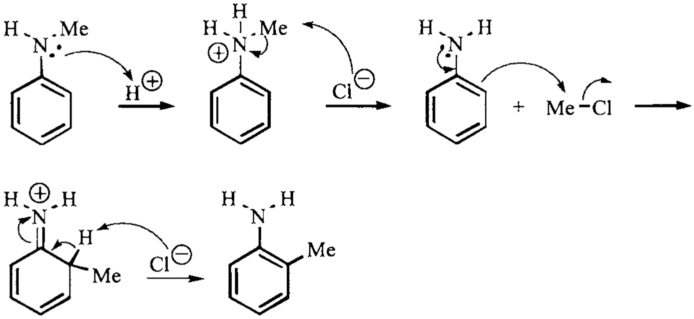
S. L. Titouani, J.-P. Lavergne, P. Viallefont, *Tetrahedron* **1980**, 36, 2961

Hofmann-Martius Rearrangement

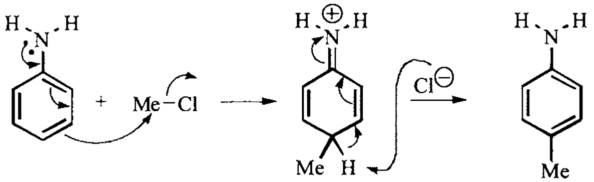
The Reaction:



Proposed Mechanism:



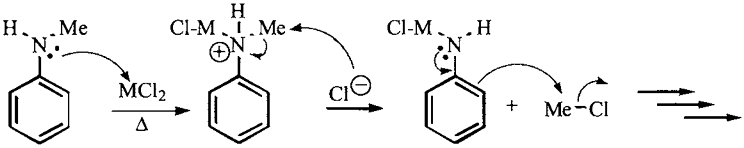
OR



Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 729.

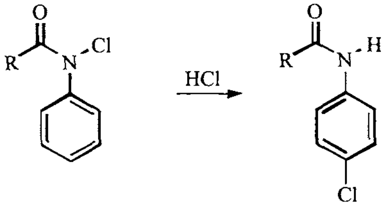
The ***Reilly-Hickinbottom Rearrangement*** uses $CoCl_2$, $CdCl_2$ or $ZnCl_2$ and the amine rather than protic acid and the amine salt.



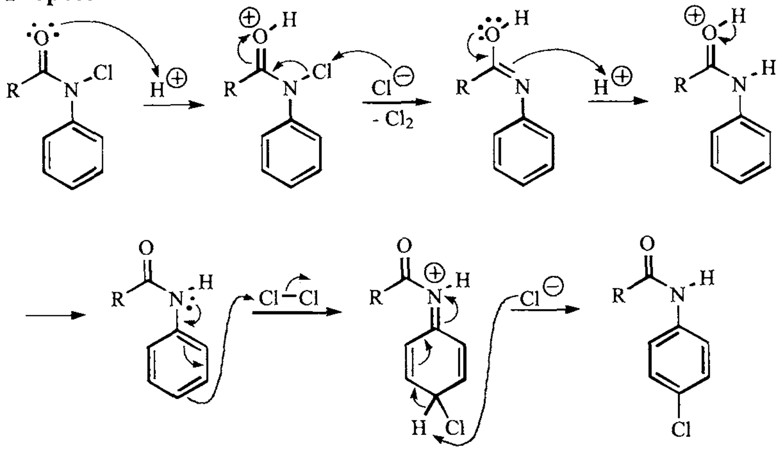
M = Co, Cd, Zn; Δ = 200-350 °C

Orton Rearrangement

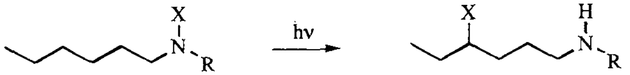
The Reaction:



Proposed Mechanism:



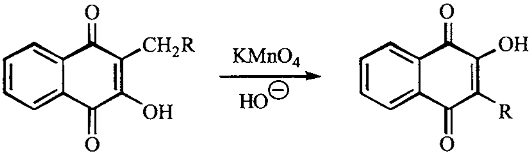
R. S. Neale, N. L. Marcus, R.G. Schepers, *Journal of the American Chemical Society* **1966**, 88, 305
The authors describe a radical reaction for



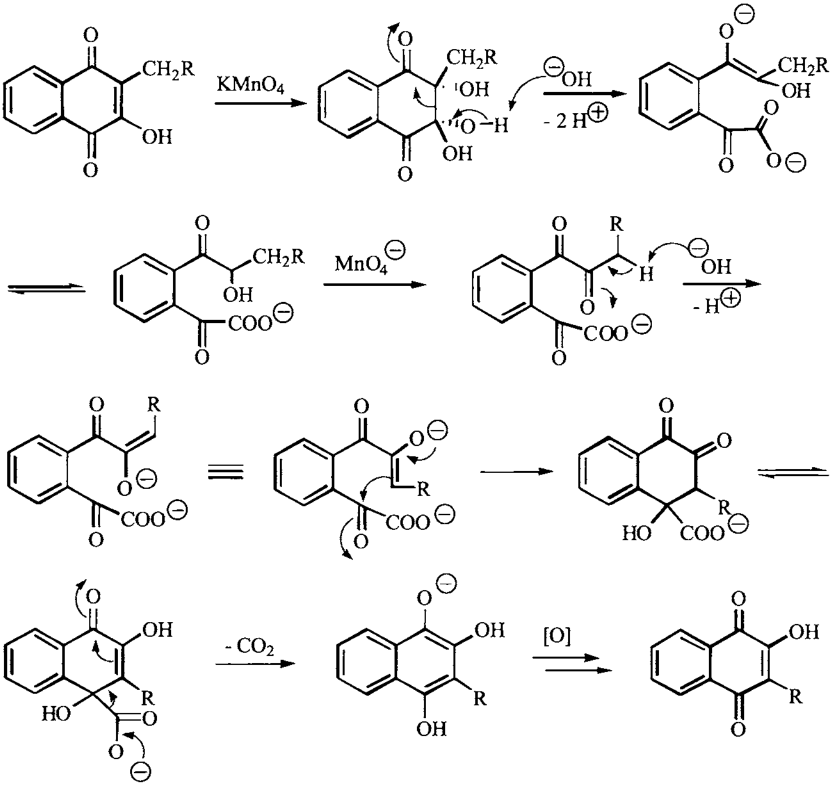
See: R. S. Neale, N. L. Marcus, *Journal of Organic Chemistry* **1969**, 34, 1808 for related reactions of *N*-halo-cyano compounds. A radical process is discussed.

Hooker Reaction

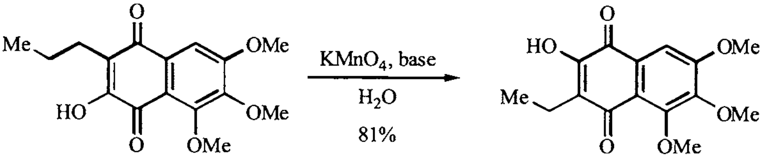
The Reaction:



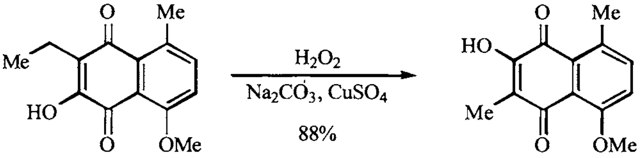
Proposed Mechanism:



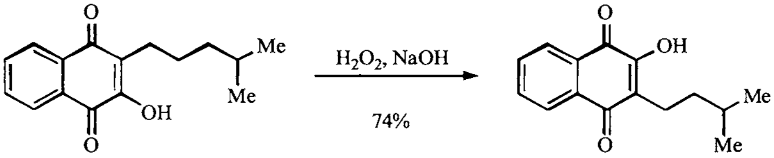
Examples:



K. H. Lee, H. W. Moore, *Tetrahedron Letters* **1993**, 34, 235



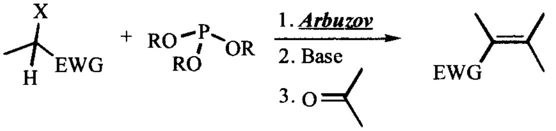
K. H. Lee, H. W. Moore, *Tetrahedron Letters* **1993**, 34, 235



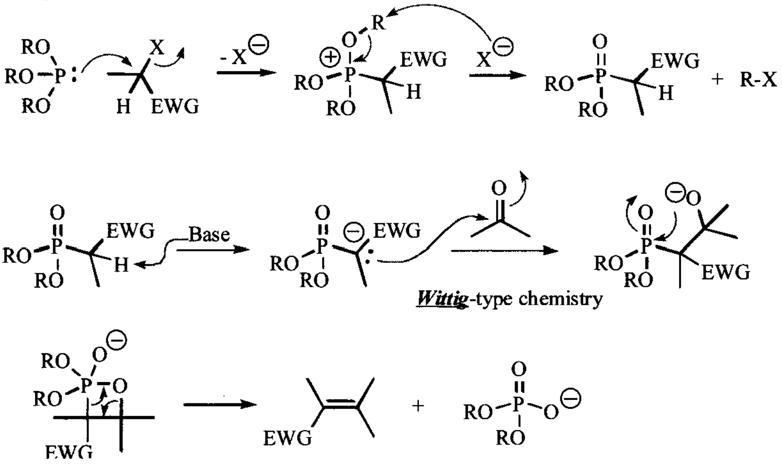
L. F. Fieser, M. Fieser, *Journal of the American Chemical Society* **1948**, 70, 3215

Horner-Wadsworth-Emmons-Wittig Reaction

The Reaction:



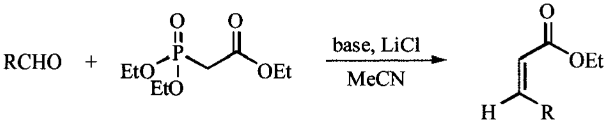
Proposed Mechanism:



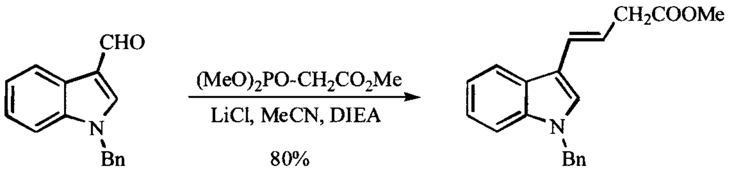
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1233.

See also the ***Masamune-Roush*** conditions for this reaction. Generally useful for base-sensitive aldehydes.

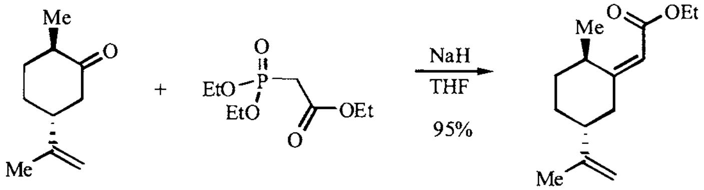


M. A. Blanchette, W. Choy, J. T. Davis, A. P. Essenfeld, S. Masamune, W. R. Roush, T. Sakai, *Tetrahedron Letters* **1984**, 25, 2183

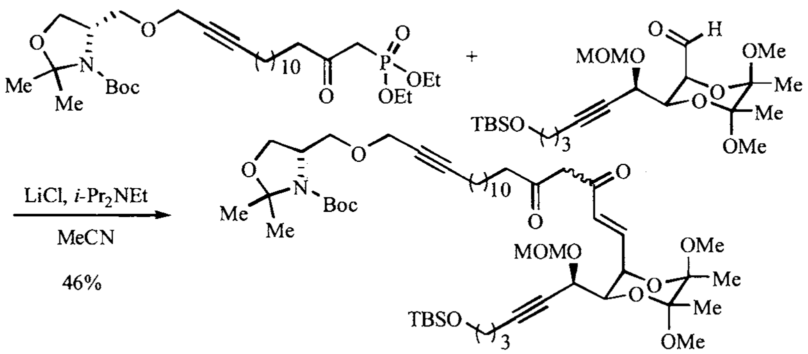


N. P. Pavri, M. L. Trudell, *Journal of Organic Chemistry* **1997**, 62, 2649

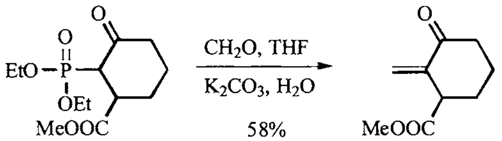
Examples:



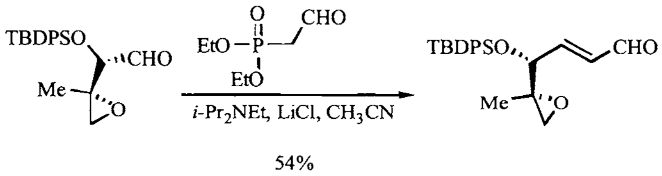
A. Srikrishna, D. Vijaykumar, T. J. Reddy, *Tetrahedron* **1997**, 53, 1439



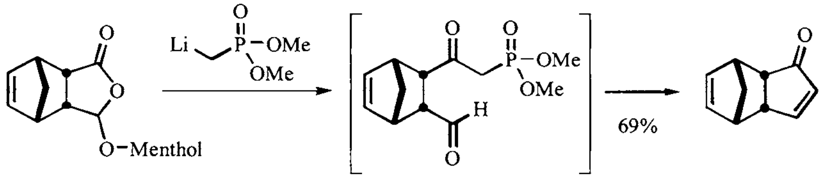
H. Kiyota, D. J. Dixon, C. K. Luscombe, S. Hettstedt, S. V. Ley, *Organic Letters* **2002**, 4, 322



A. Samarat, V. Fargeas, J. Villieras, J. Lebreton, H. Amri, *Tetrahedron Letters* **2001**, 42, 1273



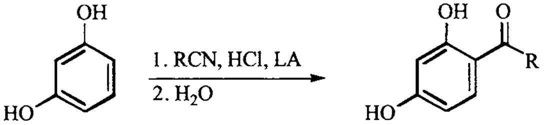
I. Vemura, H. Miyagawa, T. Veno, *Tetrahedron* **2002**, 58, 2351



J. Knol, B. L. Feringa, *Tetrahedron Letters* **1997**, 38, 2527

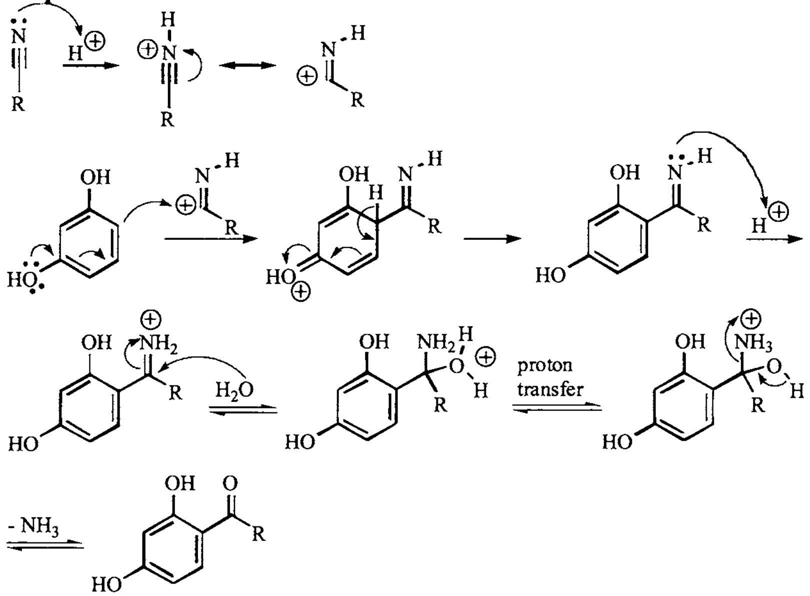
Houben-Hoesch Reaction / Hoesch Reaction

The Reaction:



Lewis Acids include $ZnCl_2$, $AlCl_3$, BCl_3, etc.

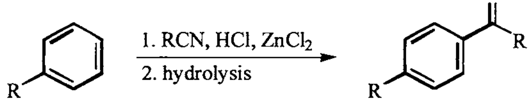
Proposed Mechanism:



Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p.722; P. E. Sperri, A. S. DuBois, *Organic Reactions* **5**, 9.

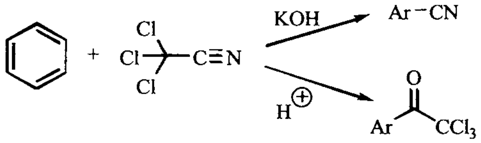
The ***Hoesch Reaction (Acylation)***:



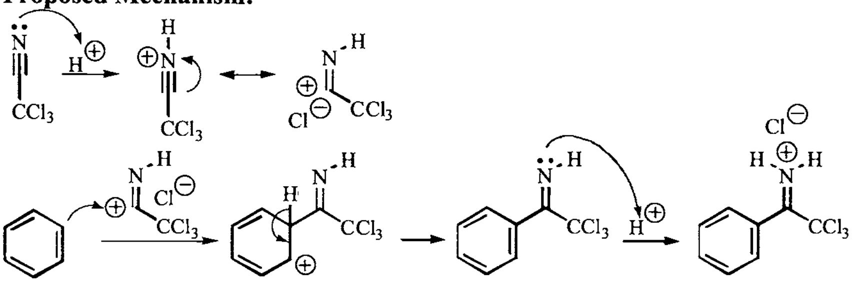
R = OH, OR, NR_2

The ***Houben-Hoesch Reaction*** refers specifically to phenols as substrates, where the reaction is generally most useful.

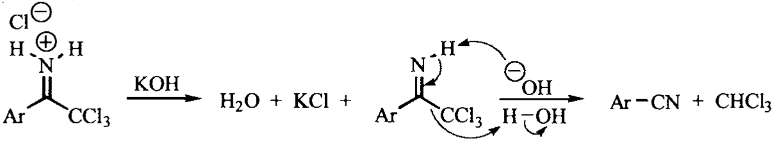
Houben-Fischer Synthesis



Proposed Mechanism:

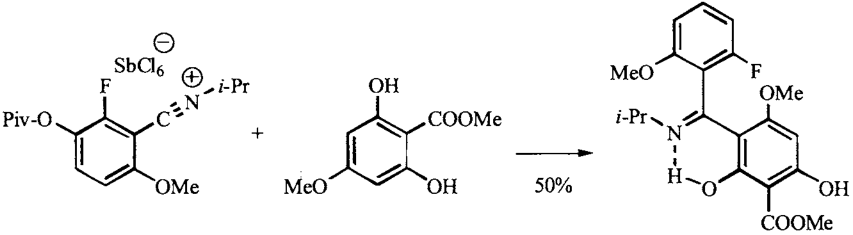


Basic Hydrolysis:

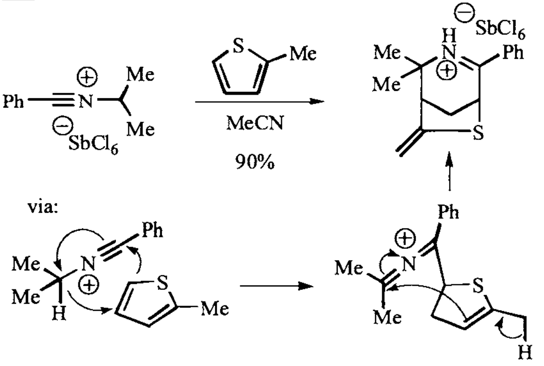


Acidic Hydrolysis:

Examples:



D. W. Udwary, L. K. Casillas, C. A. Townsend *Journal of the American Chemical Society* **2002**, 124, 5294

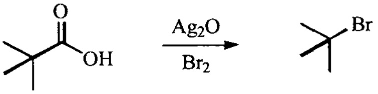


J. Henninger, K. Polborn, H. Mayr, *Journal of Organic Chemistry* **2000**, 65, 3569

Hunsdiecker Reaction (Borodine Reaction, Borodine-Hunsdiecker Reaction)

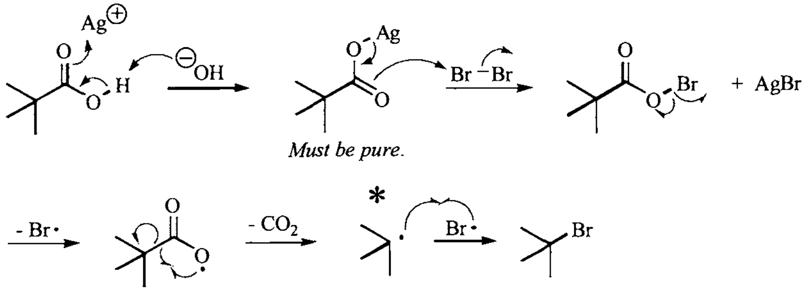
A. Borodin, composer, is best noted for the work "*Prince Igor*".

The Reaction:



Proposed Mechanism:

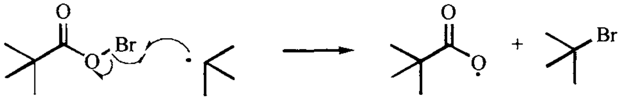
$$Ag_2O + H_2O \rightleftharpoons AgOH + HO^{\ominus} + Ag^{\oplus}$$



Must be pure.

Any optical activity is lost

* This step can also be the propagation step:

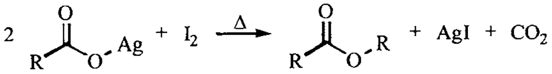


Notes:

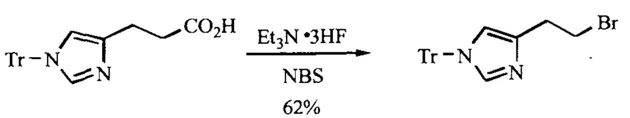
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 942-943; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 155-157; C. V. Wilson, *Organic Reactions* **9**, 5.

The ***Christol-Firth Modification*** or ***Christol-Firth-Hunsdiecker Reaction*** uses HgO in place of Ag_2O. In this modification it is not necessary to isolate an intermediate.

The ***Simonini Reaction*** differs by the ratio of I_2. The products are significantly different, this reaction produces esters:

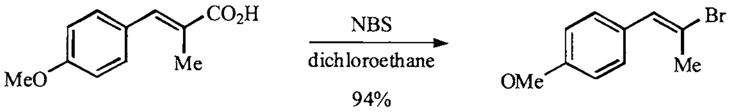


Examples:

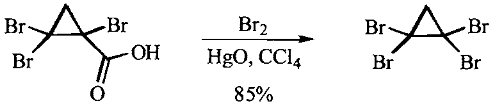


Tr = trityl
—CPh_3

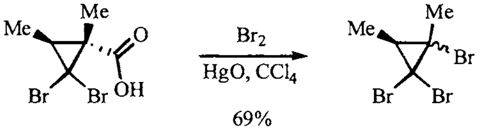
B. Dolensky, K. L. Kirk, *Journal of Organic Chemistry* **2002**, 67, 3468



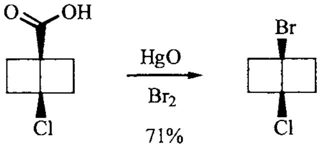
D. Naskar, S. Chowdhury, S. Roy, *Tetrahedron Letters* **1998**, 39, 699



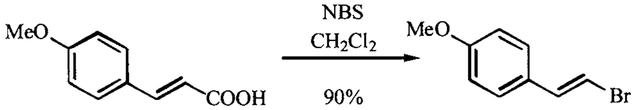
A. R. Al Dulayymi, J. R. Al Dulayymi, M. S. Baird, M. E. Gerrard, G. Koza, S. D. Harkins, E. Roberts, *Tetrahedron* **1996**, 52, 3409



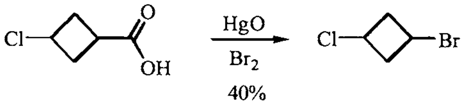
M. S. Baird, H. L. Fitton, W. Clegg, A. McCamley, *Journal of the Chemical Society: Perkin Transactions I* **1993**, 321



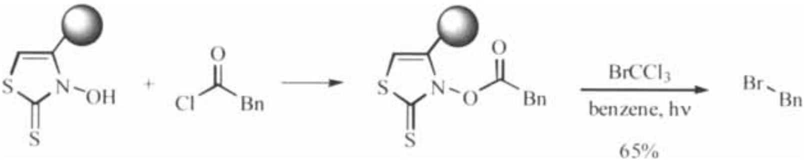
K. B. Wilberg, M. G. Matturo, P. J. Okarma, M. E. Jason, *Journal of the American Chemical Society* **1984**, 106, 2194



J. P. Das, S. Roy, *Journal of Organic Chemistry* **2002**, 67, 7861



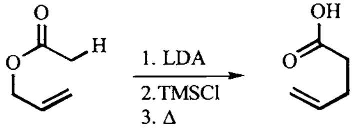
G. M. Lampman, J. C. Aumiller, *Organic Syntheses* **1971**, 206



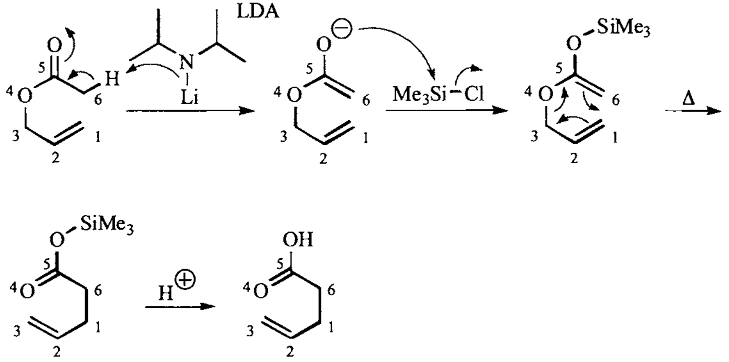
L. DeLuca, G. Giacomelli, G. Porcu, M. Taddei, *Organic Letters* **2001**, 3, 855

Ireland-Claisen Rearrangement

The Reaction:



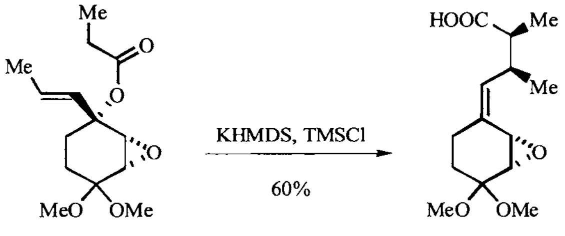
Proposed Mechanism:



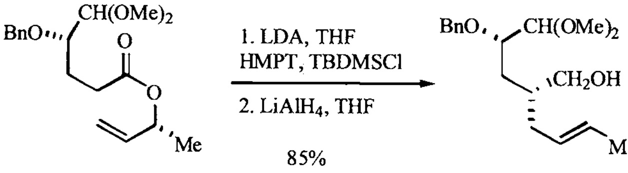
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1452.

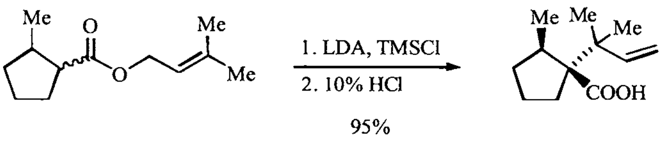
Examples:



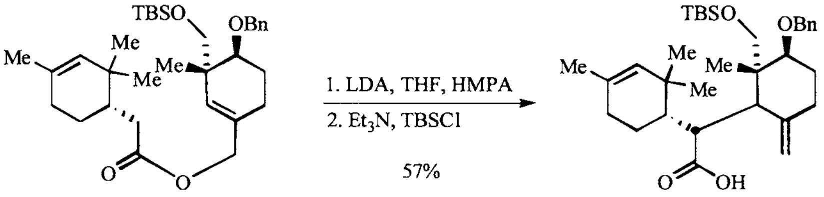
S.-p. Hong, M. C. McIntosh, *Organic Letters* **2002**, 4, 19



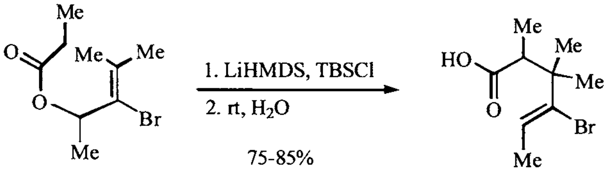
S. Höck, F. Koch, H.-J. Borschberg *Tetrahedron: Asymmetry* **2004**, 15, 1801



J. C. Gilbert, J. Yin , F. H. Fakhreddine, M. L. Karpinski *Tetrahedron* **2004**, 60, 51



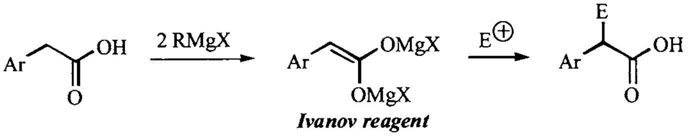
P. Magnus, N. Westwood, *Tetrahedron Letters* **1999**, 40, 4659



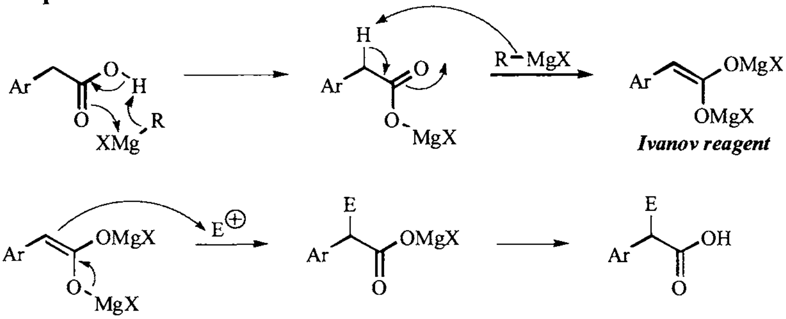
P. A. Jacobi, Y. Li, *Organic Letters* **2003**, 5, 701

Ivanov Reaction

The Reaction:



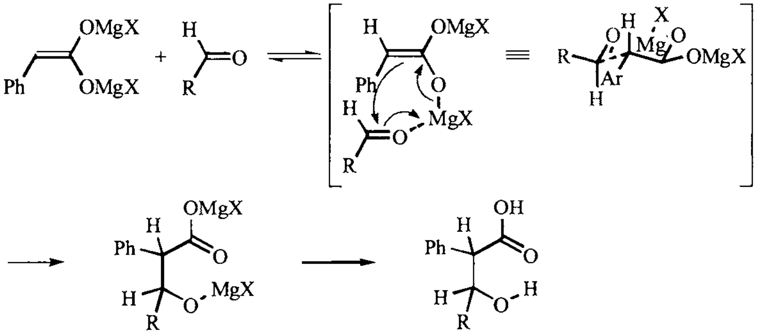
Proposed Mechanism:



Notes:

The stereochemistry of the ***Ivanov Reactions***:
H. E. Zimmerman, M. D. Traxler; *Journal of the American Chemical Society* **1957**, 79, 1920

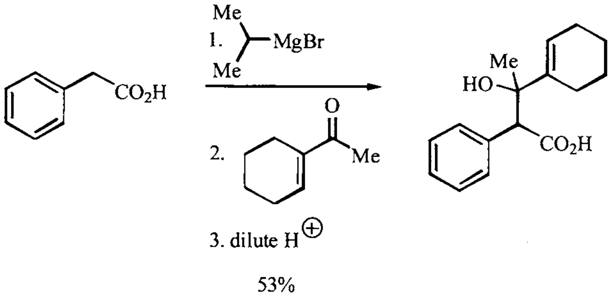
The reaction is particularly useful with the electrophile being an aldehyde or ketone:



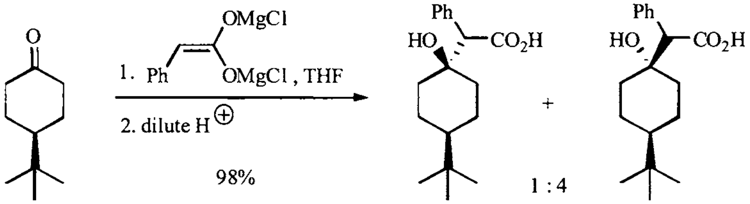
R	Rel Rate
i-Pr	6.3
t-Bu	1

J. Toullec, M. Mladenova, C. F. Gaudemar-Bardone, C. B. Blagoev, *Tetrahedron Letters* **1983**, 24, 589

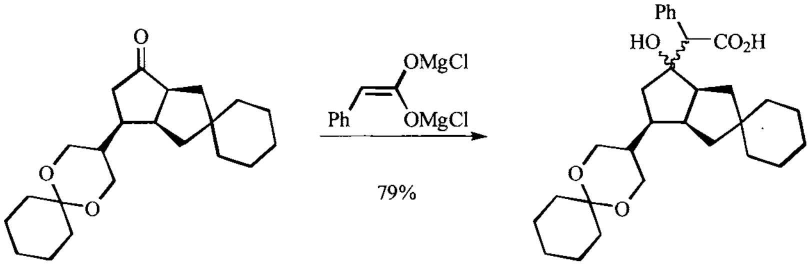
Examples:



F. F. Blicke, H. Zinnes, *Journal of the American Chemical Society* **1955**, 77, 6247



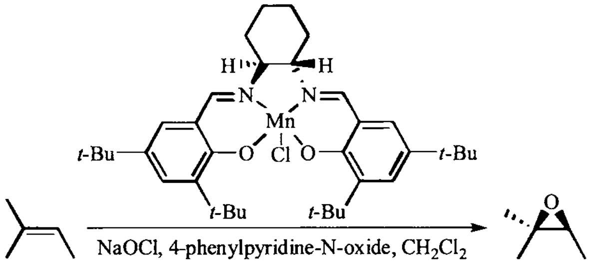
M. Mladenova, B. Blagoev, M. Gaudemar, F. Gaudemar-Bardone, J. Y. Lallemand *Tetrahedron* **1981**, 37, 2157



Y. A. Zhdanov, G. V. Bogdanova, O. Y. Riabuchina *Carbohydrate Research* **1973**, 29, 274

Jacobsen-Katsuki Epoxidation

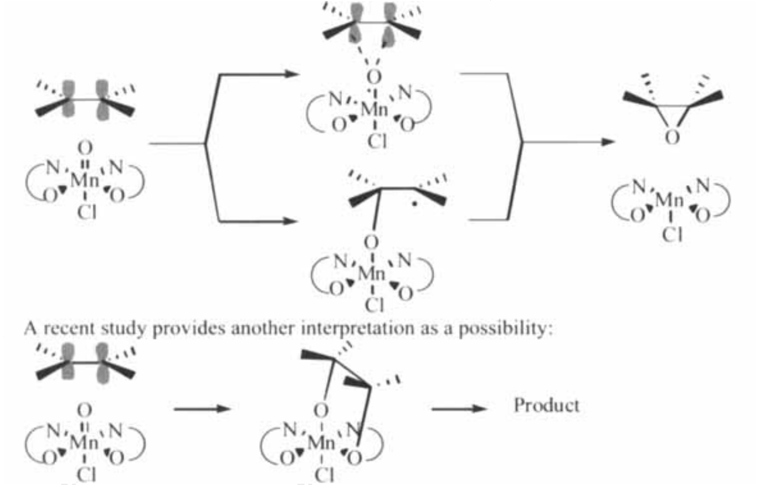
The Reaction:



E. N. Jacobsen, L. Deng, Y. Furukawa, L. E. Martinez *Tetrahedron* **1994**, 50, 4323

Proposed Mechanism:

The mechanistic details are still being studied. Two interpretations most thought about include:



A recent study provides another interpretation as a possibility:

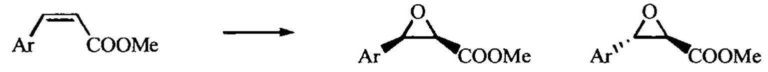
Y. G. Abashkin, S. K. Burt, *Organic Letters* **2004**, 6, 59

See: D. L. Hughes, G. B. Smith, J. Liu, G. C. Dezeny, C. H. Senanayake, R. D. Larsen, T. R. Verhoeven, P. J. Reider, *Journal of Organic Chemistry* **1997**, 62, 2222, for details of the mechanistic interpretation.

Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1053.

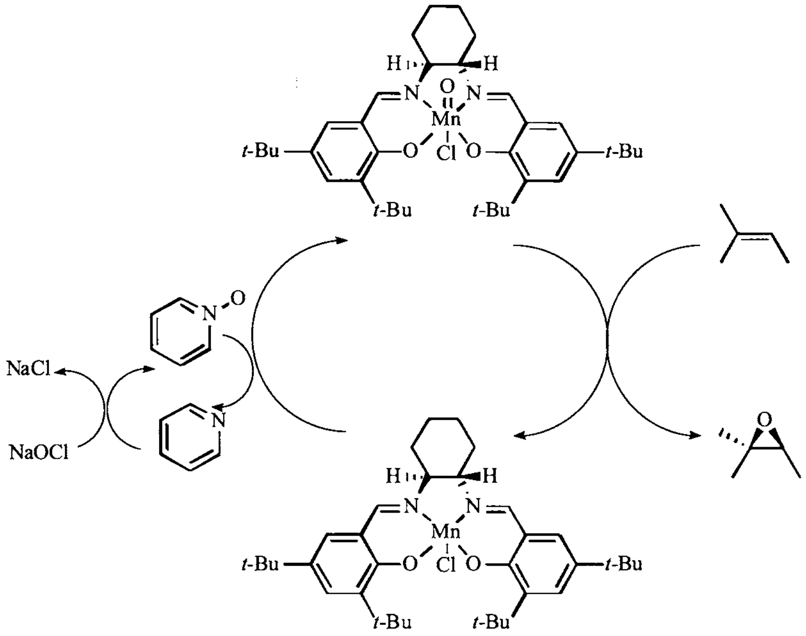
Selectivity depends on substrate structure:



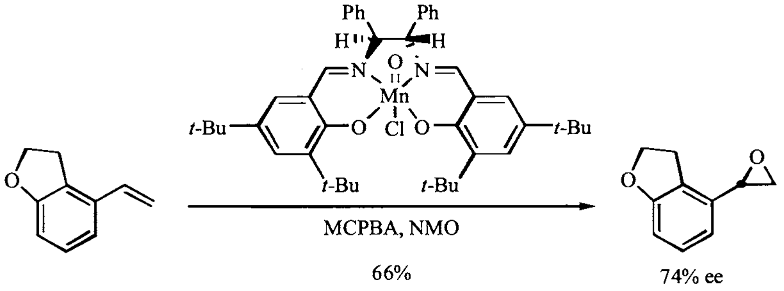
Ar = *p*-MeO-phenyl	~ 11	:	1
Ar = *p*-NO_2-phenyl	~ 1	:	4

E. N. Jacobsen, L. Deng, Y. Furukawa, L. E. Martinez, *Tetrahedron* **1994**, 50, 4323

The oxygen has its origins in the NaOCl:



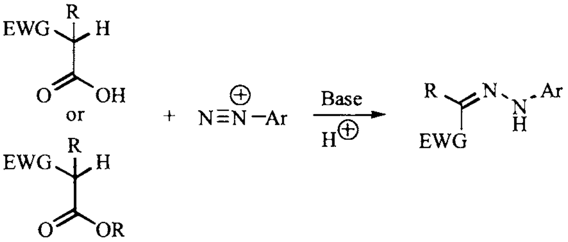
Examples:



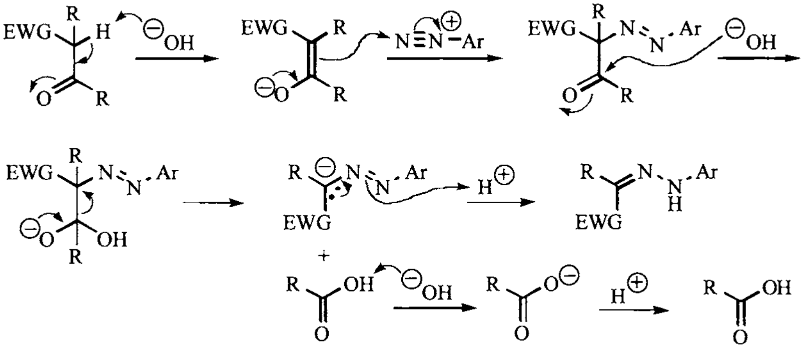
J. S. Prasad, T. Vu, M. J. Totleben, G. A. Crispino, D. J. Kacsur, S. Swaminathan, J. E. Thornton, A. Fritz, A. K. Singh, *Organic Process Research & Development* **2003**, 7, 821

Japp-Klingemann Reaction

The Reaction:



Proposed Mechanism:



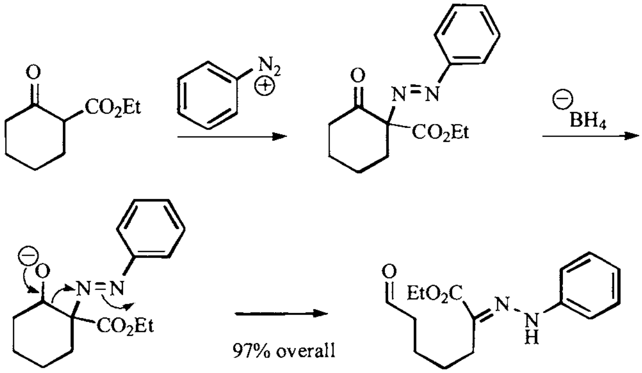
The carboxylic acid byproduct would exist as a carboxylate until acid is added.

Notes:

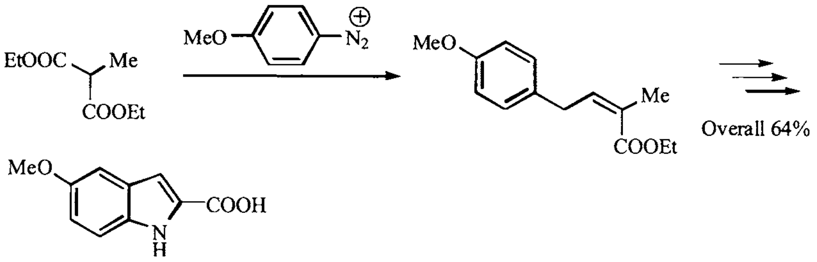
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 779; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 161-163; R. R. Philips, *Organic Reactions* **10**, 2.

Examples:

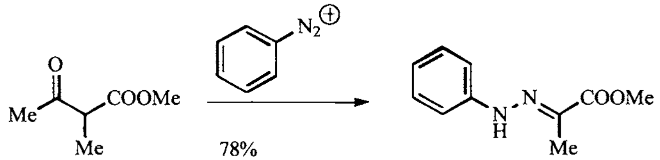
A variation where the intermediate is reduced:



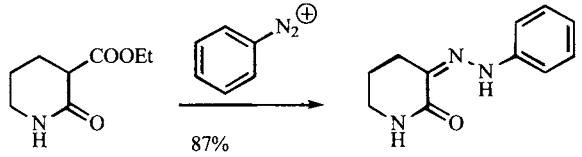
A. P. Kosikowski, W. C. Floyd, *Tetrahedron Letters* **1978**, 19, 19



Y. Bessard, *Organic Process Research & Development* **1993**, 2, 214



H. C. Yao, P. Resnick, *Journal of the American Chemical Society* **1962**, 84, 3514

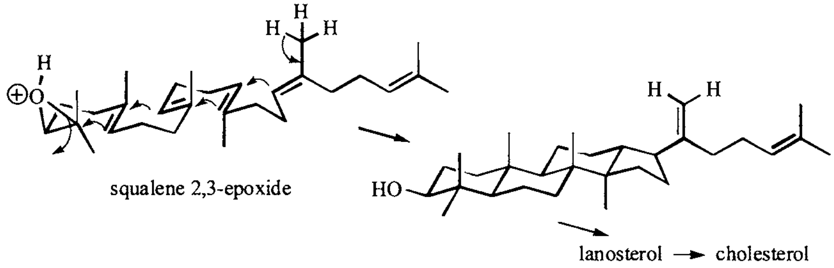


D. Shapiro, R. A. Abramovitch, *Journal of the American Chemical Society* **1955**, 77, 6690

Johnson Polyene Cyclization

The Reaction:

The reactions encompass the attempts to mimic the suggested biosynthetic cyclization for multi-ring terpenes and steroids, such as:



W. S. Johnson, *Accounts of Chemical Research* **1968**, 1, 1

Proposed Mechanism:

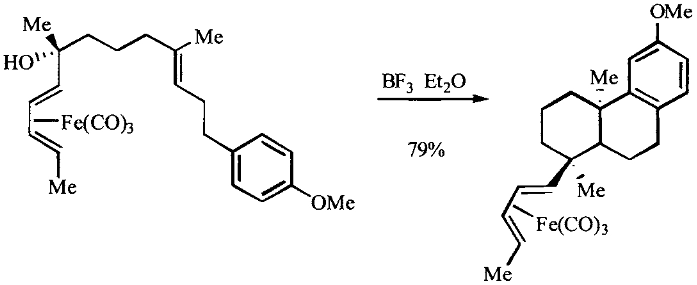
These are generally cationic processes where correct alignment of alkenes bonds will allow for ring formation:

Notes:

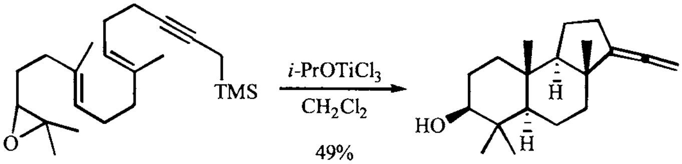
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1019.

Success in this reaction requires control of the *E*/*Z* configuration of the alkene bonds and often a good terminator step.

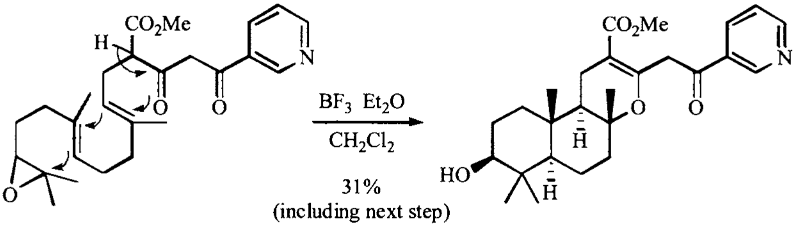
Examples:



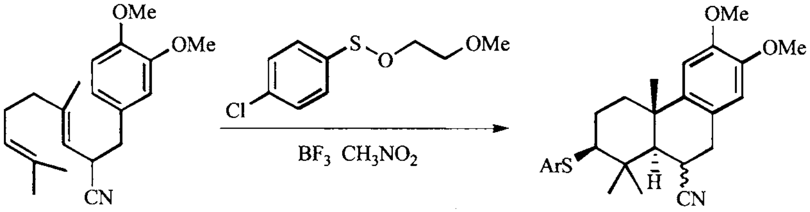
M. Franck-Neumann, P. Geoffroy, D. Hanss *Tetrahedon Letters* **2002**, 43, 2277



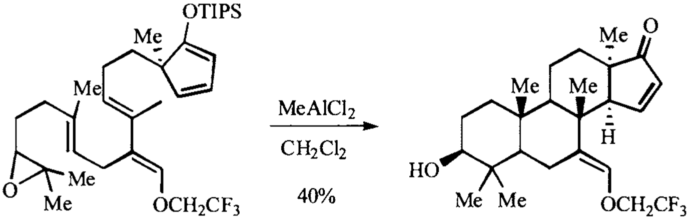
P. V. Fish, A. R. Sudhakar, W. S. Johnson, *Tetrahedron Letters* **1993**, 34, 7849



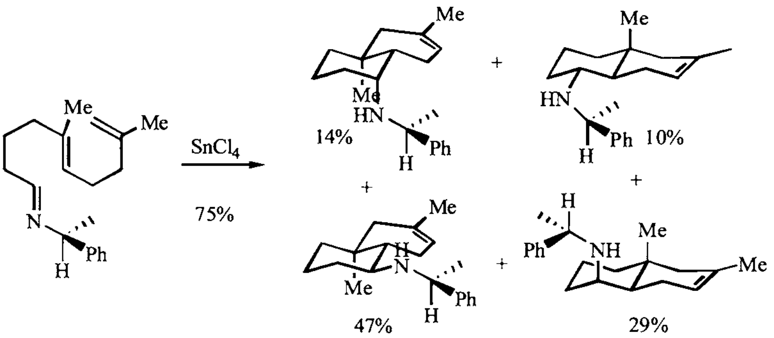
A. B. Smith, III, T. Kinsho *Tetrahedron Letters* **1996**, 37, 6461



S. R. Harring and T. Livinghouse, *Journal of Organic Chemistry* **1997**, 62, 6388



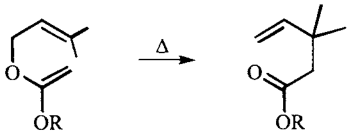
E. J. Corey, H. B. Wood, Jr., *Journal of the American Chemical Society* **1996**, 118, 11982



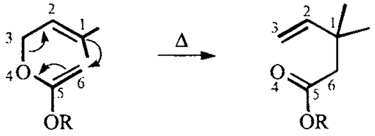
G. Demailly, G. Solladie, *Tetrahedron Letters* **1980**, 21, 3355

Johnson-Claisen Rearrangement (Johnson Orthoester Rearrangement)

The Reaction:

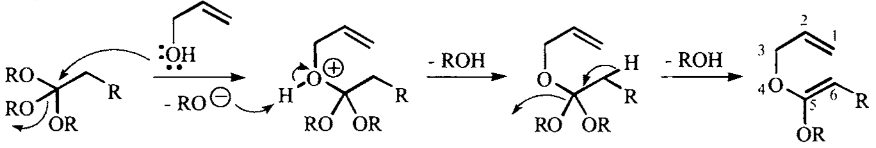


Proposed Mechanism:

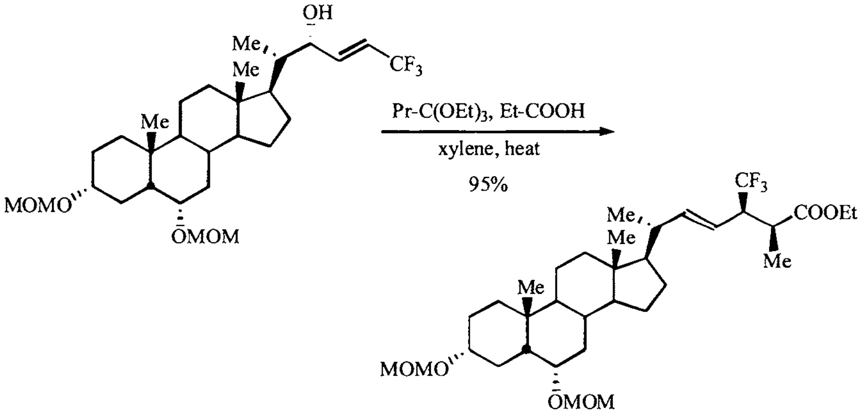


Notes:

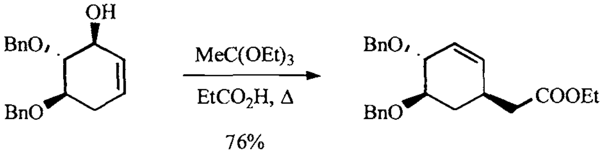
Preparation of starting material:



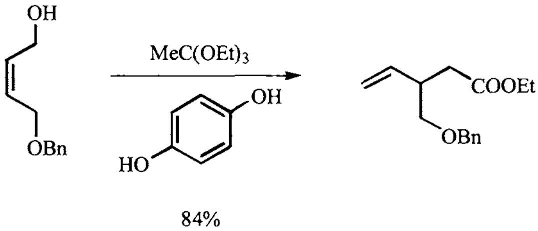
Examples:



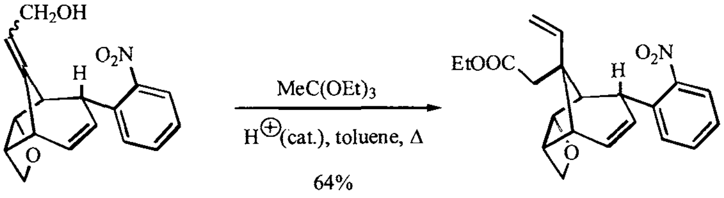
B. Jiang, Y. Liu, W.-s. Zhou, *Journal of Organic Chemistry* **2000**, 65, 6231



H. Fuwa, Y. Okamura, H. Natsugari, *Tetrahedron* **2004**, 60, 5341



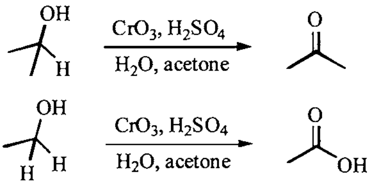
E. Marotta, P. Righi, G. Rosini, *Organic Letters* **2000**, 2, 4145



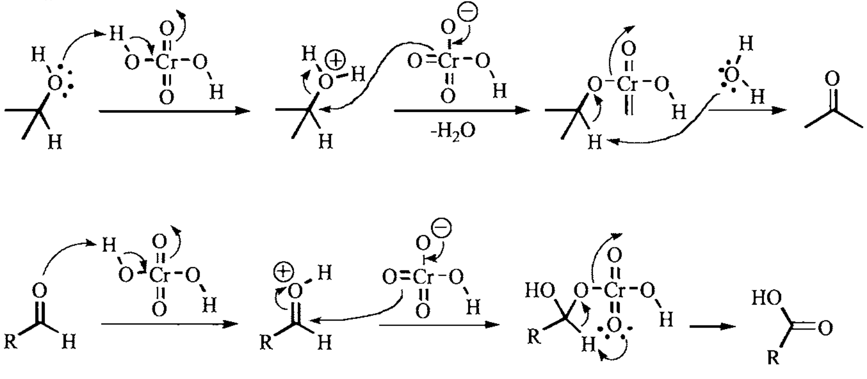
F. W. Ng, H. Lin, S. J. Danishefsky, *Journal of the American Chemical Society* **2002**, 124, 9812

Jones Oxidation

The Reaction:

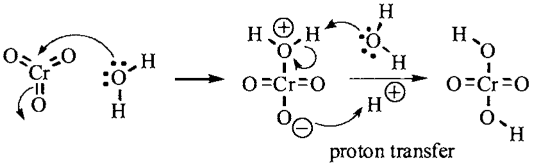


Proposed Mechanism:



Notes:

Chromium Reagent Formation:

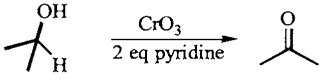


See ***Jones Reagent***.

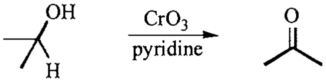
This is a useful and simple reaction to carry out. The oxidizing solution can be slowly titrated into the reaction flask until the color of the oxidant persists.

Primary alcohols are readily converted to acids, secondary alcohols to ketones. 1,2-Diols can suffer fragmentation. Allylic alcohols are readily oxidized.

Collins Oxidation

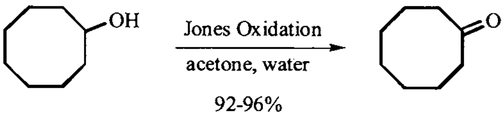


Sarrett Oxidation

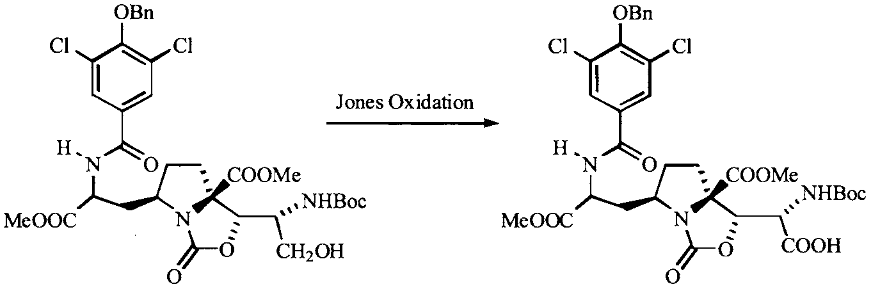


Note: Must add CrO_3 to pyridine solution.

Examples:

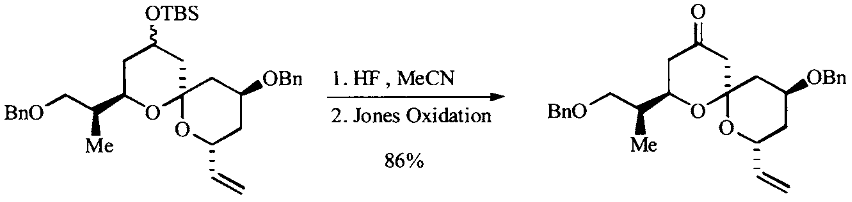


E. J. Eisenbraun, *Organic Syntheses,* CV5, 597

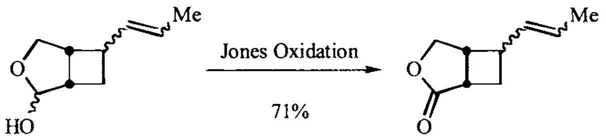


This was the last step in a four-step sequence. No individual yields presented. Overall yield 54%

D. Ma and J. Yang, *Journal of the American Chemical Society* **2001**, 123, 9706



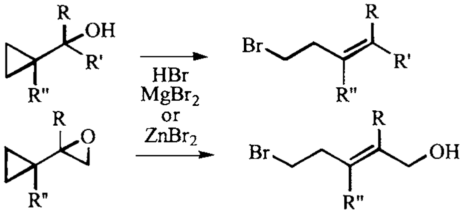
M. T. Crimmins, C. A. Carroll, B. W. King, *Organic Letters* **2000**, 2, 597



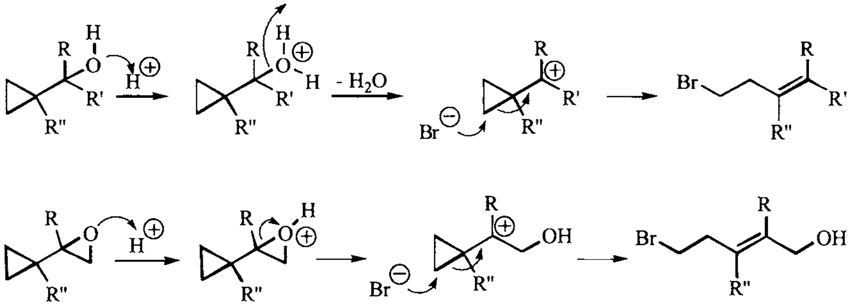
J. Panda, S. Ghosh, S. Ghosh *Journal of the Chemical Society, Perkin Transactions 1* **2001**, 3013

Julia-Bruylants Cyclopropyl Carbinol Rearrangement

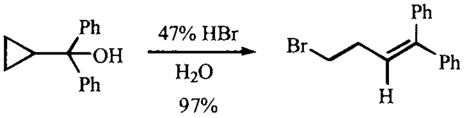
The Reaction:



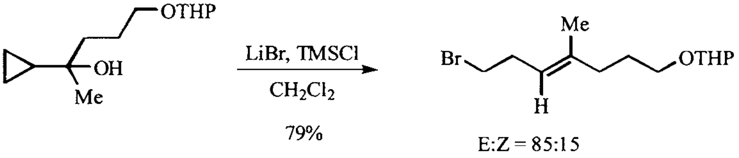
Proposed Mechanism:



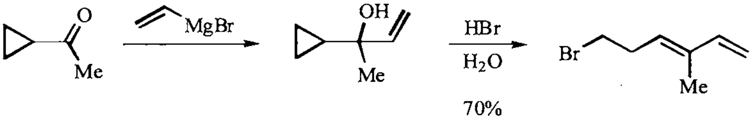
Examples:



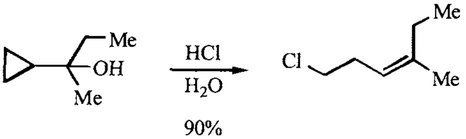
A. Van der Bent, A. G. S. Blommaert, C. T. M. Melman, A. P. IJzerman, I. Van Wijngaarden, W. Soudijn, *Journal of Medicinal Chemistry* **1992**, 35, 1042



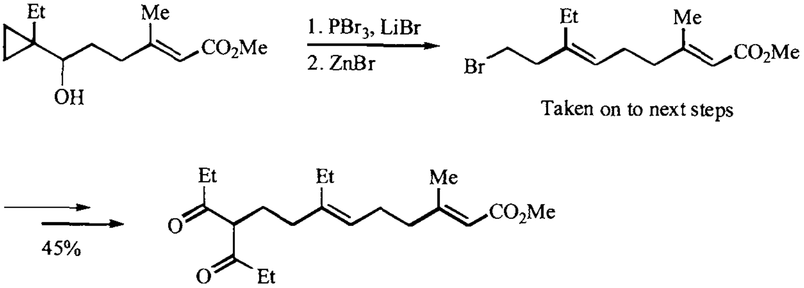
Z. Liu, W. Z. Li, Y. Li, *Tetrahedron: Asymmetry* **2001**, 12, 95



P. A. Wender, J. M. Nuss, D. B. Smith, A. Suarez-Sobrina, J. Vagberg, D. Decosta, J. Bordner, *Journal of Organic Chemistry* **1997**, 62, 4908



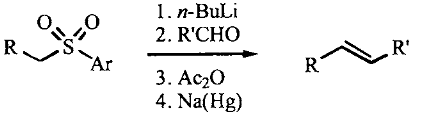
C. A. Henrick, F. Schaub, J. B. Siddall, *Journal of the American Chemical Society* **1972**, 94, 5374



W. S. Johnson, T.-T. Li, D. J. Faulkner, S. F. Campbell, *Journal of the American Chemical Society* **1968**, 90, 6225

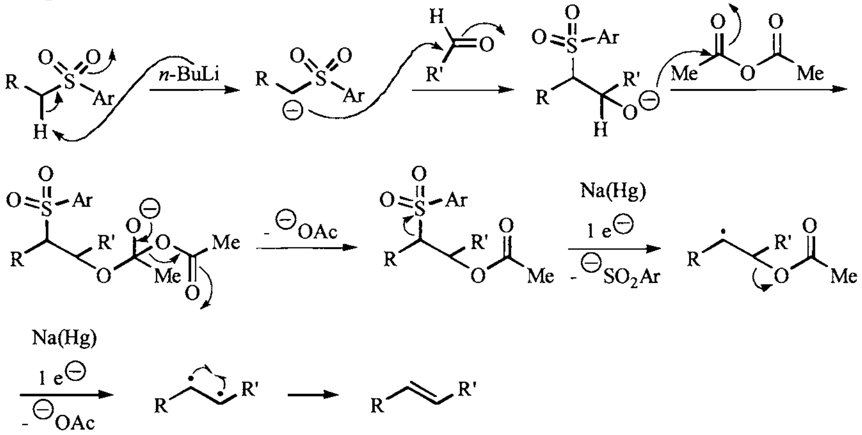
Julia Olefination (Julia-Lythgoe Olefination)

The Reaction:



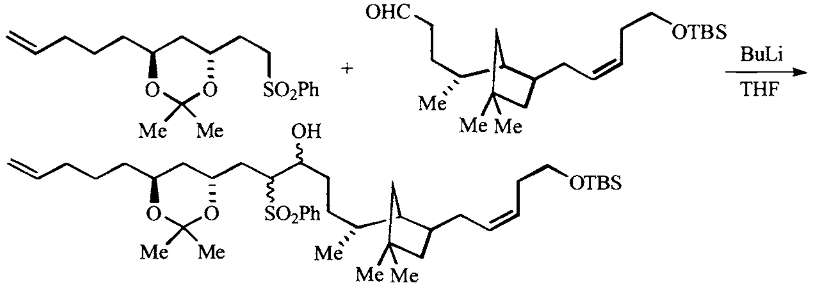
M. Julia, J. M. Paris, *Tetrahedron Letters* **1973**, 14, 4833

Proposed Mechanism:



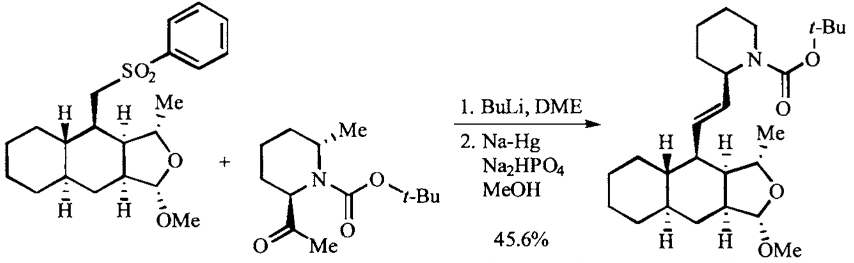
Julia Coupling

Utilizes the first part of the reaction sequence:

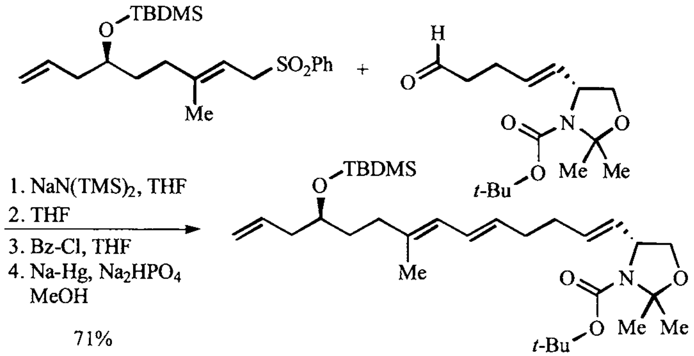


K. Suenaga, K. Araki, T. Sengoku, D. Uemura, *Organic Letters* **2001**, 3, 527

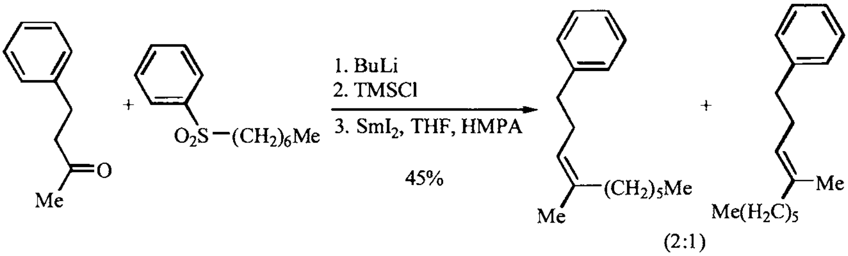
Examples:



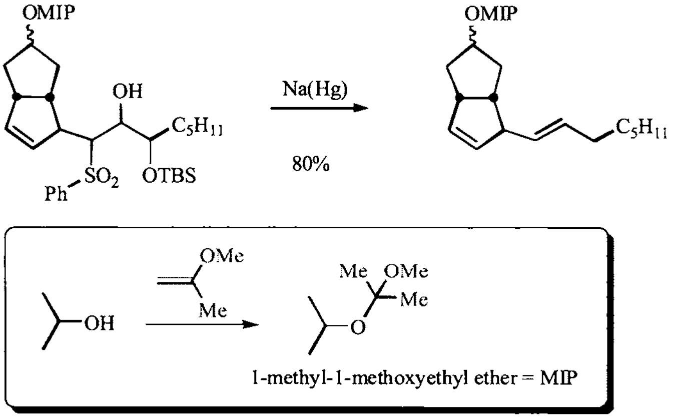
D. J. Hart, J. Li, W.-L. Wu, A. P. Kozikowski, *Journal of Organic Chemistry* **1997**, 62, 5023



M. Z. Hoemann, K. A. Agriosw, J. Aube, *Tetrahedron Letters* **1996**, 37, 953



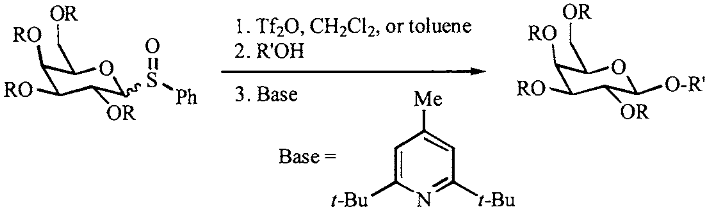
I. E. Marko, F. Murphy, S. Donlan, *Tetrahedron Letters* **1996**, 37, 2089



G. Zanoni, A. Porta, F. Castronovo, G. Vidari, *Journal of Organic Chemistry* **2003**, 68, 6005

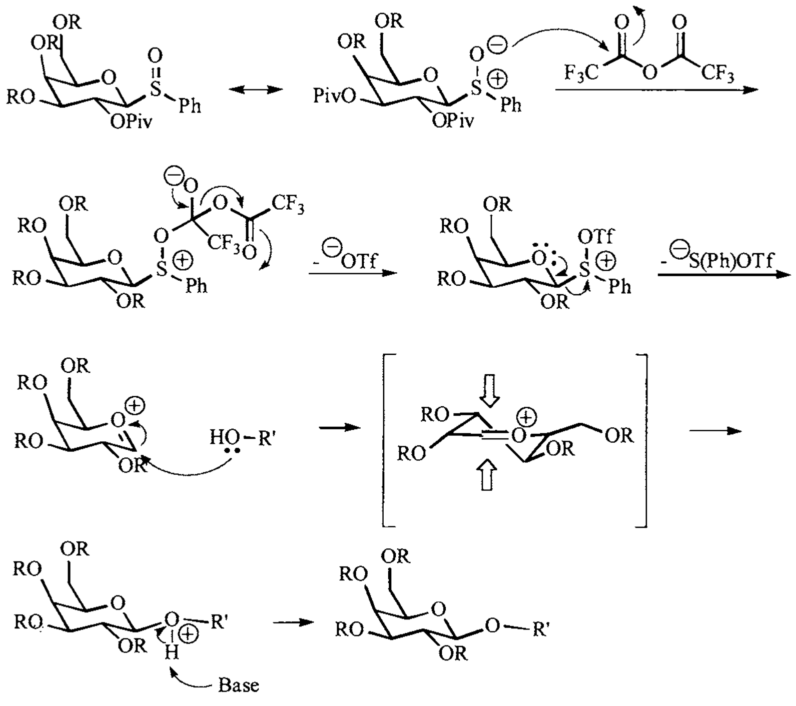
Kahne Glycosylation

The Reaction:

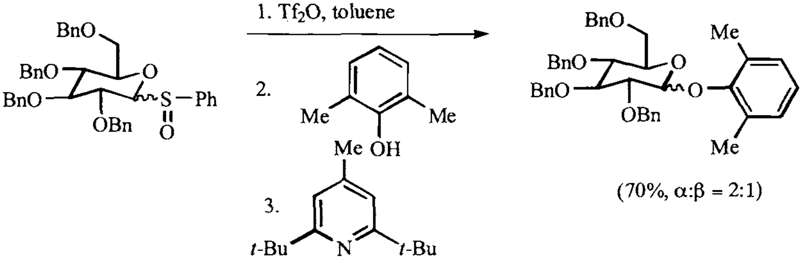


D. Kahne, S. Walker, Y. Cheng, D. Van Engen *Journal of the American Chemical Society* **1989**, 111, 6881

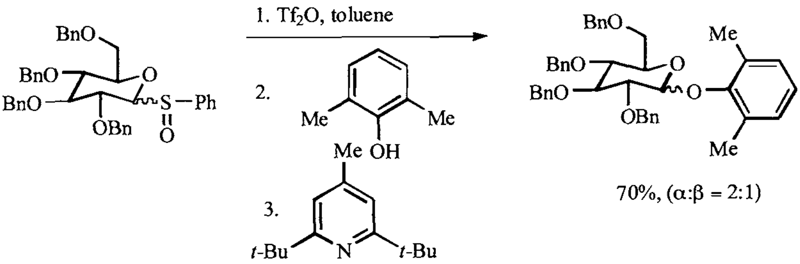
Proposed Mechanism:



Examples:

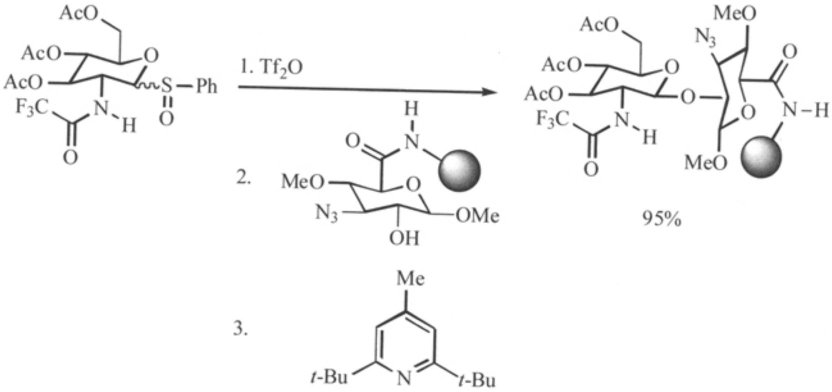


D. Kahne, S. Walker, Y. Cheng, D. Van Engen *Journal of the American Chemical Society* **1989**, 111, 6881



(part of a large sequence, no yield for this step)

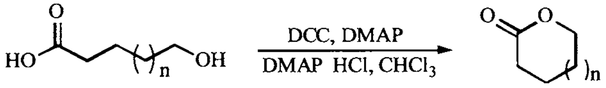
L. Yan, C. M. Taylor, R. Goodnow, Jr., D. Kahne, *Journal of the American Chemical Society* **1994**, 116, 6953



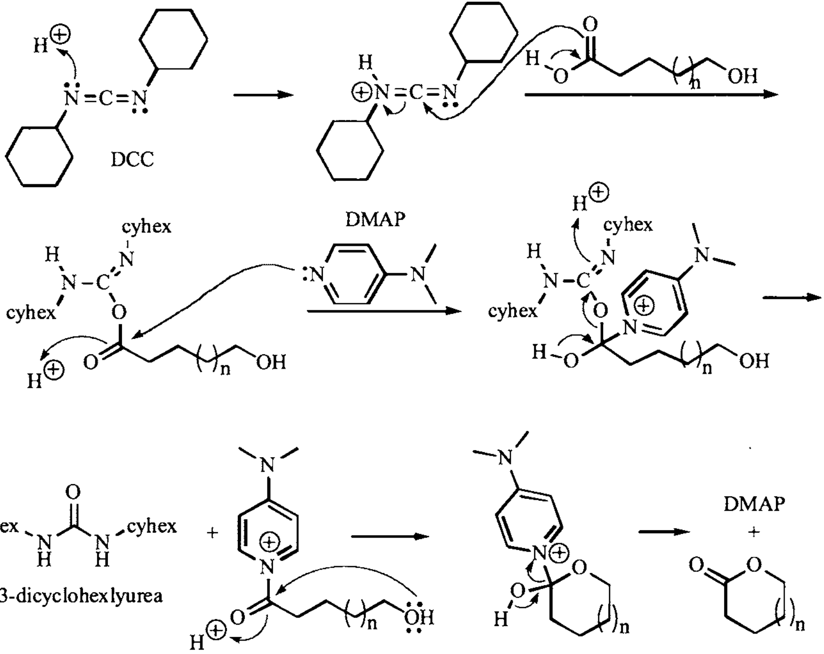
D. J. Silva, H. Wang, N. M. Allanson, R. K. Jain, M. J. Sofia, *Journal of Organic Chemistry* **1999**, 64, 5926

Keck Macrolactonization

The Reaction:



Proposed Mechanism:



Notes:

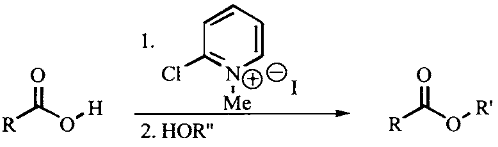
See *Macrolactonization* for related methods.

This reaction is an extension of the ***Steglich esterification reaction***. See: E. P. Boden, G. E. Keck, *Journal of Organic Chemistry* **1985**, 50, 2394.

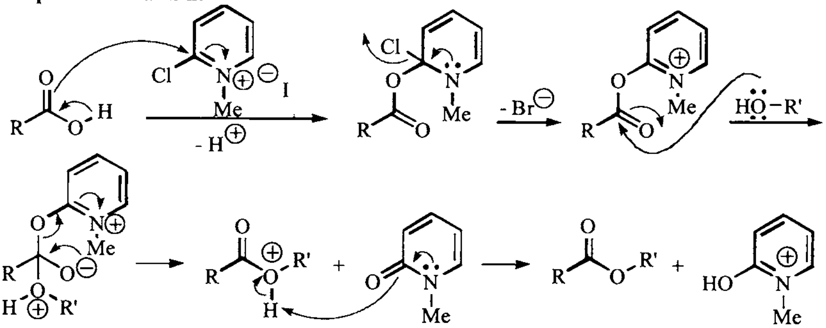
For another approach to macrolactonization, see:

Mukaiyama Esterification

The Reaction:

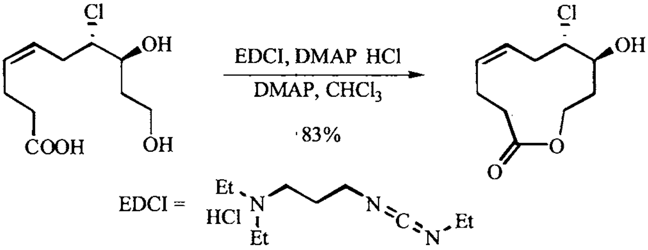


Proposed Mechanism:

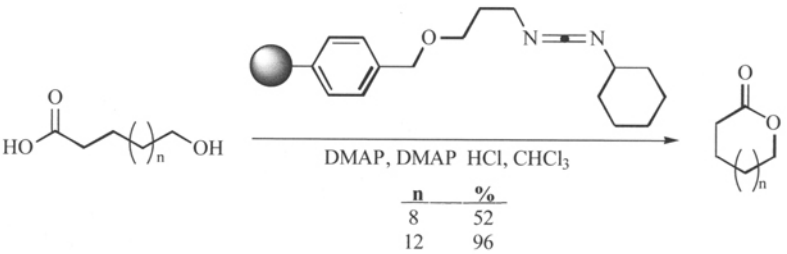


Notes:
See: ***Mukaiyama's Reagent*** for examples.

Examples (of the Keck Macrolactonization):



F. Fujiwara, D. Awakura, M. Tsunashima, A. Nakamura, T. Honma, A. Murai, *Journal of Organic Chemistry* **1999**, 64, 2616

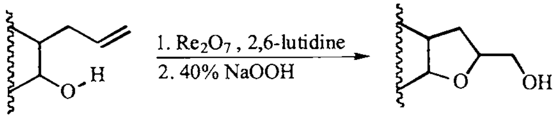


n	%
8	52
12	96

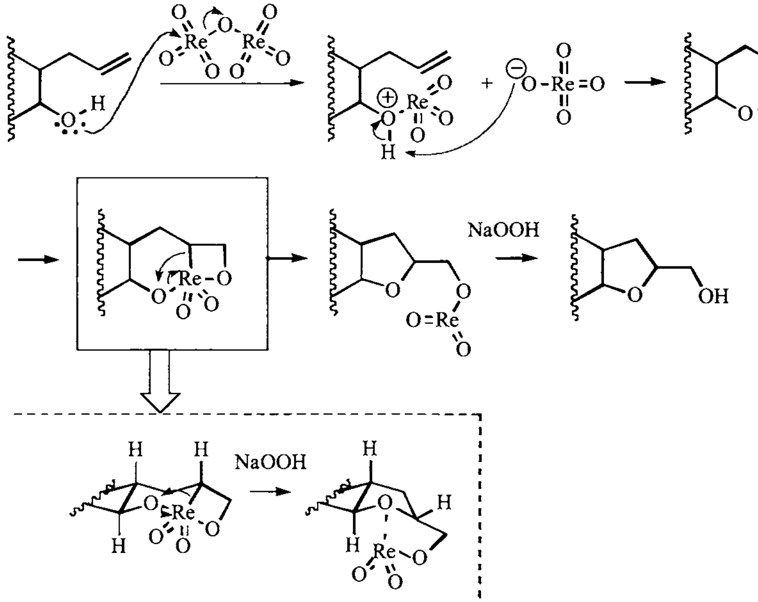
G. E. Keck, C. Sanchez, C. A. Wagner, *Tetrahedron Letters* **2000**, 41, 8673

Kennedy Oxidative Cyclization

The Reaction:



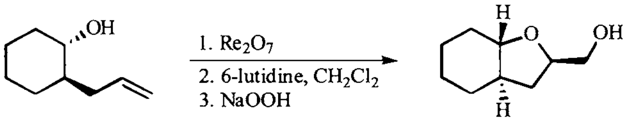
Proposed Mechanism:



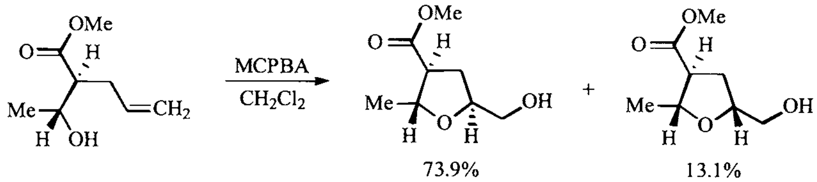
Notes:

For comments on mechanism, see: S. Tang, R. M. Kennedy, *Tetrahedron Letters* **1992**, 33, 5299, 5303 ; S. C. Sinha, E. Keinan, S. C. Sinha, *Journal of the American Chemical Society* **1998**, 120, 9076

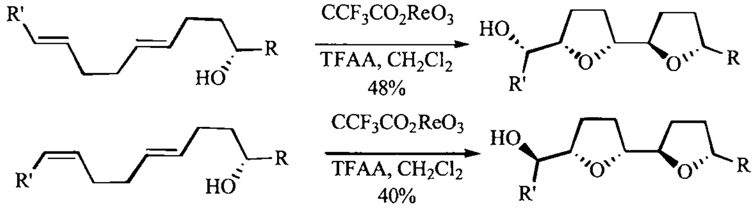
Examples:



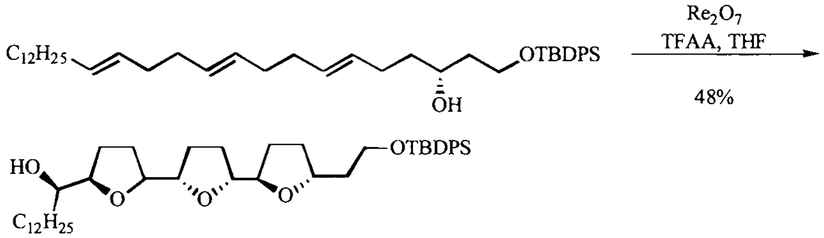
S. Tang, R. M. Kennedy, *Tetrahedron Letters* **1992**, 33, 5299



S. Tang, R. M. Kennedy, *Tetrahedron Letters* **1992**, 33, 5299.



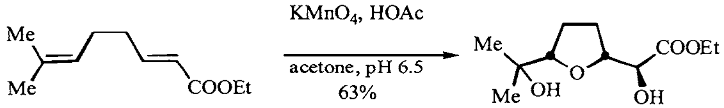
S. C. Sinha, E. Keinan, S. C. Sinha, *Journal of the American Chemical Society* **1998**, 120, 9076



S. C. Sinha, A. Sinha, S. C. Sinha, E. Keinan, *Journal of the American Chemical Society* **1997**, 119, 12014

There are other oxidative cyclizations related to the Kennedy protocol:

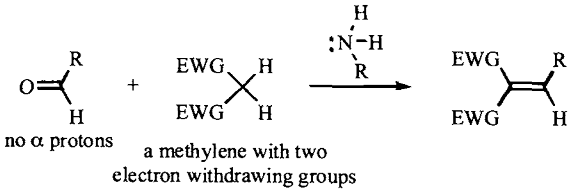
For example:



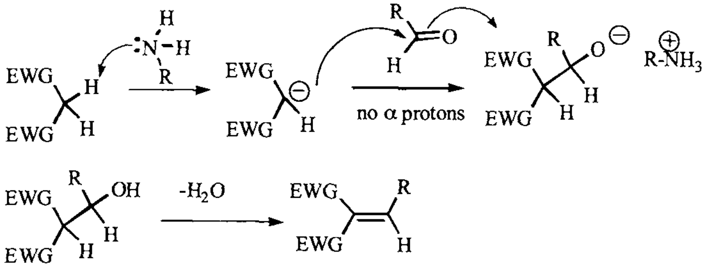
A. R. L. Cecil, Y. Hu, M. J. Vinent, R. Duncan, R. C. D. Brown, *Journal of Organic Chemistry* **2004**, 69, 3368

Knoevenagel Condensation (Reaction)

The Reaction:



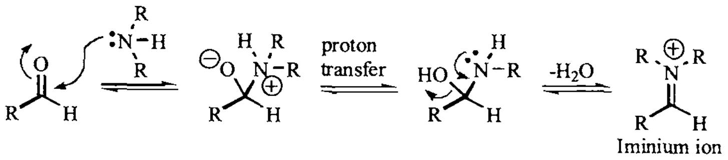
Proposed Mechanism:



Notes:

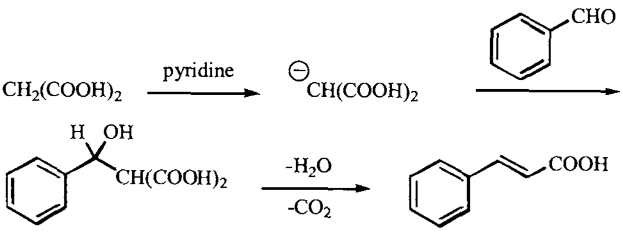
See: R. Bruckner, *Advanced Organic Chemistry*, Harcourt/Academic Press, San Diego, 2002, pp 419-422, for an interesting discussion of the active nucleophile in this reaction.

Another interpretation involves the formation of an intermediate iminium species as the electrophile: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, 164-167.

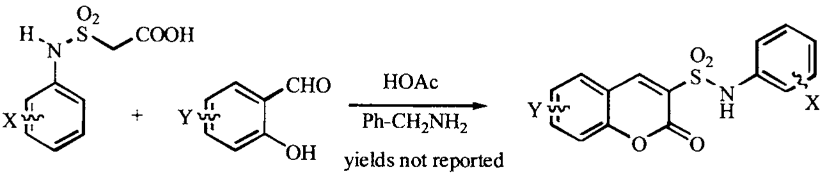


M. B. Smith, J. March in March's *Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1225-1228; G, Jones, *Organic Reactions* **15**, 2.

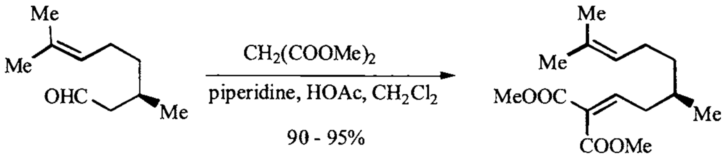
When the amine catalyst is specifically pyridine, the reaction is known as the ***Doebner Modification of the Knoevenagel Reaction***:



Examples:



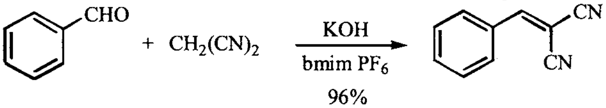
N. S. Reddy, M. R. Mallireddigari, S. Cosenza, K. Gumireddy, S. C. Bell, E. P. Reddy, M.V.R. Reddy, *Bioorganic & Medicinal Chemistry Letters* **2004**, 14, 4093



L. F. Tietze, U. Beifuss, *Organic Syntheses* CV 9, 310

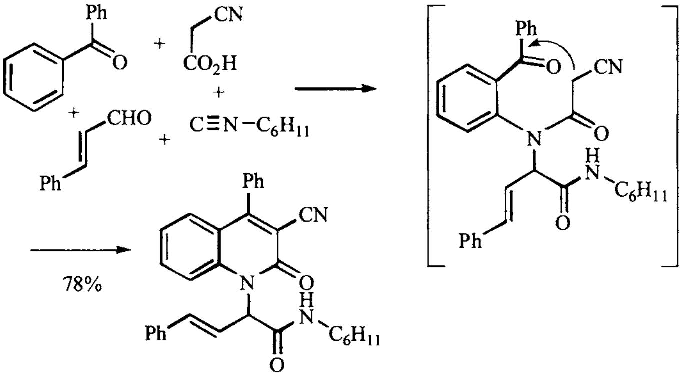
Use of ionic liquids:

Solvent used several times, without additional base, to carry out the reaction.

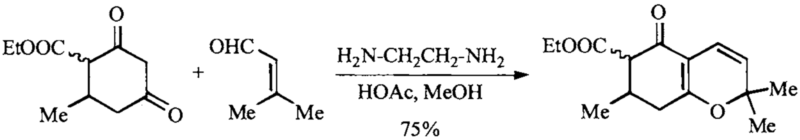


P. Formentin, H. Garcia, A. Leyva, *Journal of Molecular Catalysis A: Chemical* **2004**, 214, 137

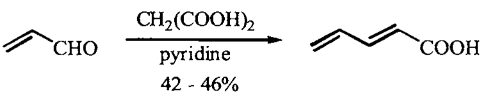
Tandem ***Ugi-Knoevenagel Reaction***:



S. Marcaccini, R. P. M. Cruz Pozo, S. Basurto, M. Garcı`a-Valverdeb, T. Torrobab, *Tetrahedron Letters* **2004**, 45, 3999



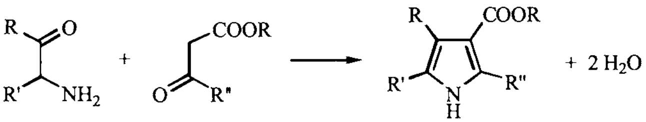
H. Hu, T. J. Harrison, P. D. Wilson, *Journal of Organic Chemistry* **2004**, 69, 3782



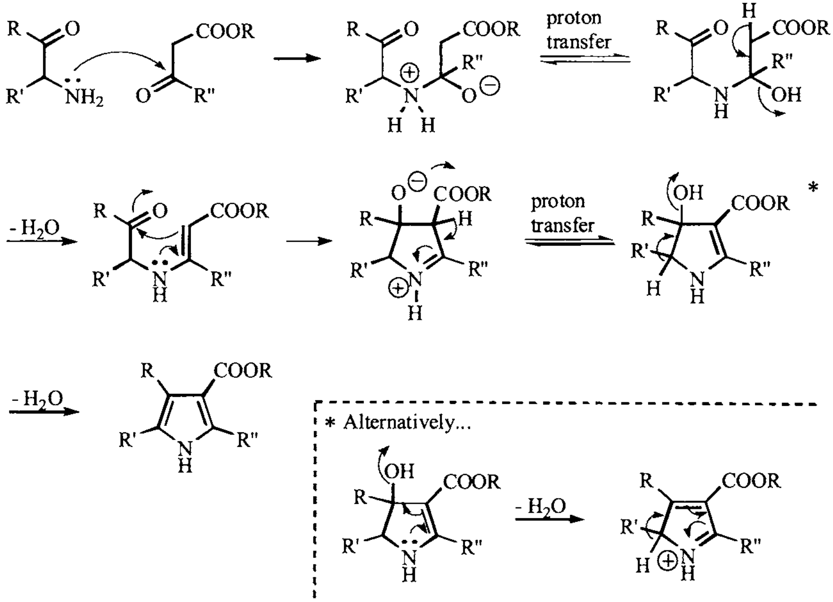
P. J. Jessup, C. B. Petty, J. Roos, L. E. Overman, *Organic Syntheses*, CV6, 95

Knorr Pyrrole Synthesis

The Reaction:



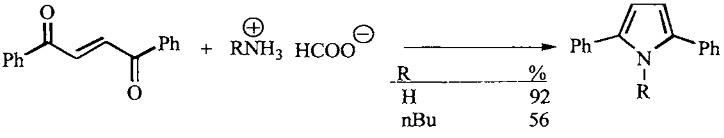
Proposed Mechanism:



Notes:

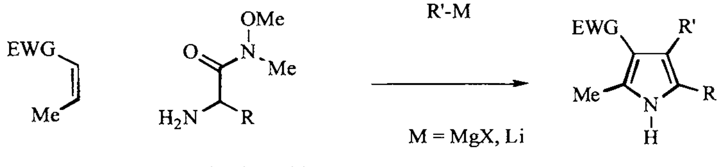
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 168-170.

Examples:



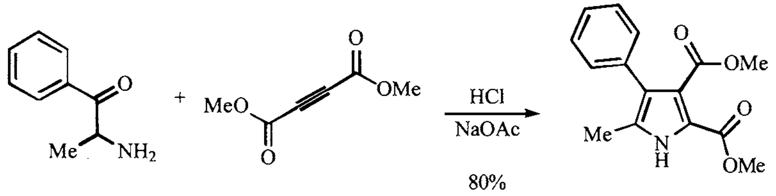
R	%
H	92
nBu	56

H. Surya P. Rao, S. Jothilingam, *Tetrahedron Letters* **2001**, 42, 6595

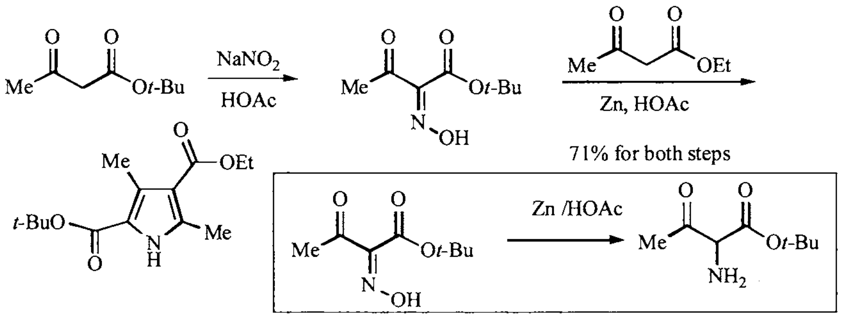


Weinreb Amide

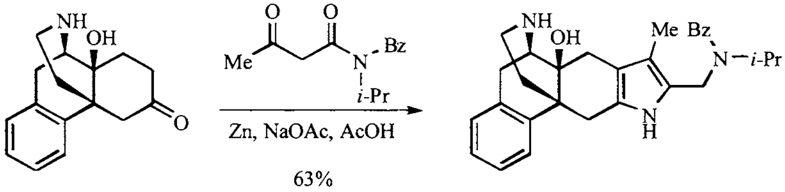
A. Alberola, A. G. Ortega, M. L. Sidaba, C. Safiudo, *Tetrahedron* **1999**, 55, 6555



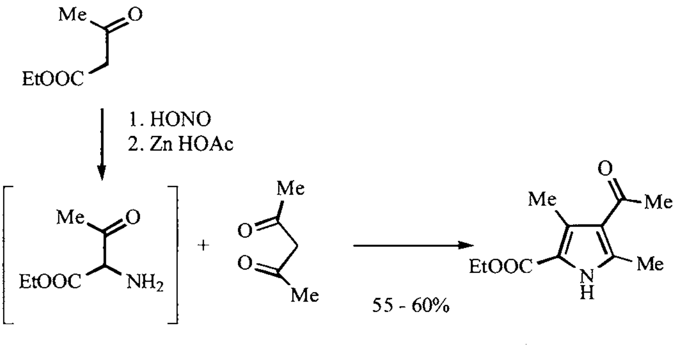
J. B. Hendrickson, R. Rees, *Journal of the American Chemistry Society* **1961**, 83, 1250



J. M. Manley, M. J. Kalman, B. G. Conway, C. C. Ball, J. L. Havens, R. Vaidyanathan, *Journal of Organic Chemistry* **2003**, 68, 6447



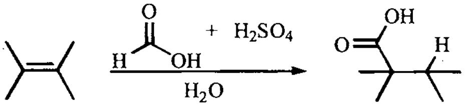
R. K. Bellingham, J. S. Carey, N. Hussain, D. O. Morgan, P. Oxley, L. C. Powling *Organic Process Research & Development* **2004**, 8, 279



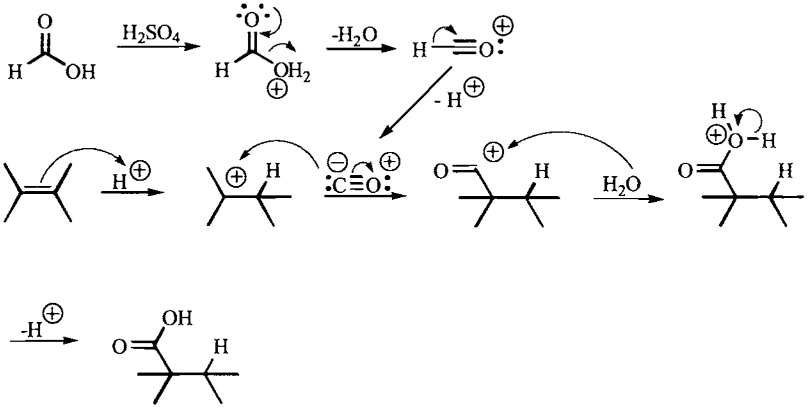
H. Fischer, *Organic Syntheses* CV3, 513

Koch-Haaf Carbonylation (Reaction)

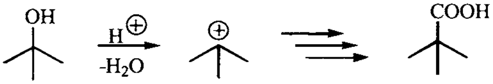
The Reaction:



Proposed Mechanism:



The carbocation can also come from an alcohol.

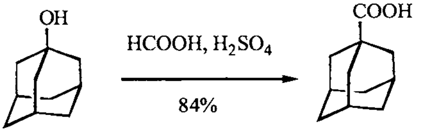


Notes:

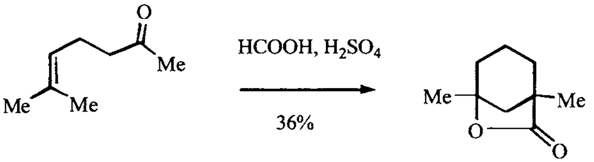
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp. 564, 1035.

The acid-catalyzed hydrocarboxylation of an alkene is known as the ***Koch Reaction***. When the source of both the CO and the H_2O is formic acid, the process is called the ***Koch-Haaf Carbonylation***.

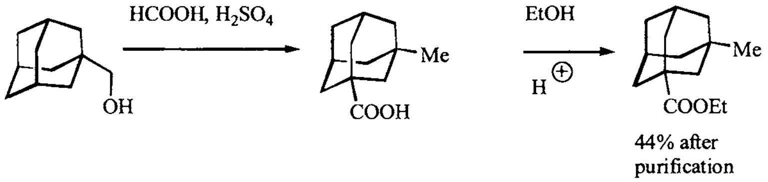
Examples:



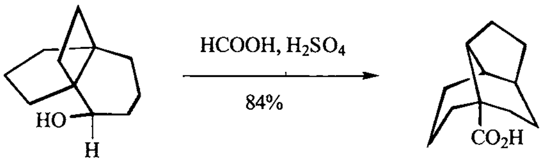
H. Langhals, I. Vergelsberg, C. Riichardt, *Tetrahedron Letters* **1981**, 22, 2365



M. E. N. Nambudiry, G. S. K. Rao, *Tetrahedron Letters* **1972**, 13, 4707



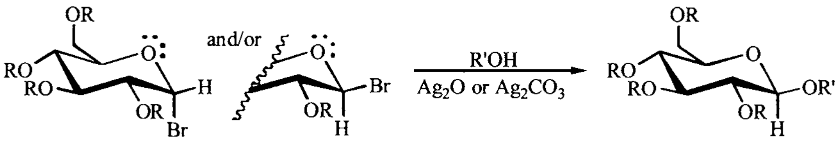
D. J. Raber, R. C. Fort, E. Wiskoit, C. W. Woodworth, P. v. R. Schleyer, J. Weber, H. Steer, *Tetrahedron* **1971**, 27, 3



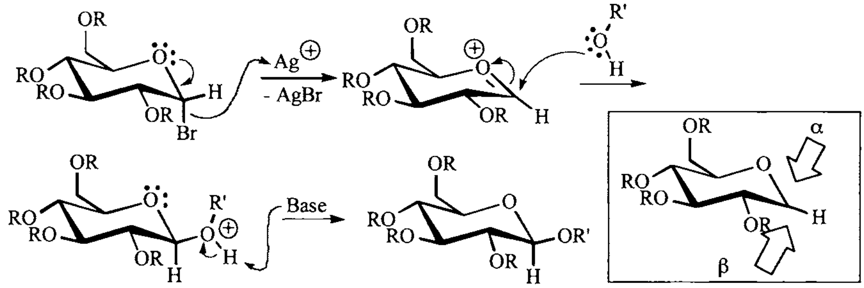
K. Kakiuchi, M. Ue, I. Wakaki, Y. Tobe, Y. Odaira, M. Yasuda, K. Shimal, *Journal of Organic Chemistry* **1986**, 51, 282

Köenigs-Knorr Synthesis / Reaction / Method / Glycosidation

The Reaction:



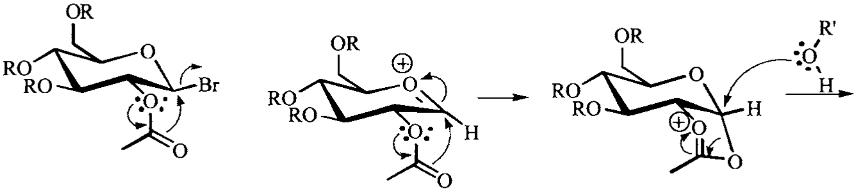
Proposed Mechanism:



α– attack preferred.

Notes:

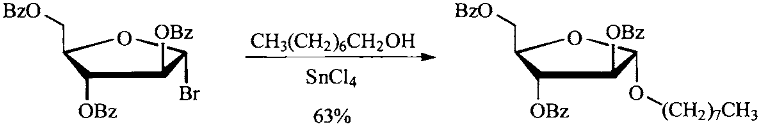
An adjacent acetoxy group can participate in the reaction:



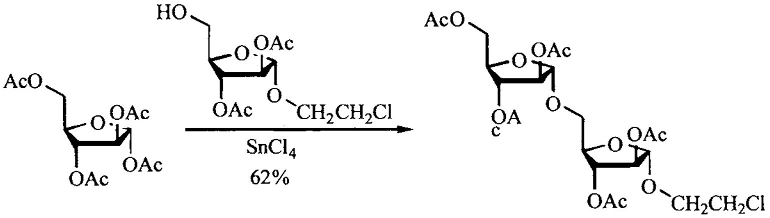
In the early works, Hg salts were often used in place of the Ag salts to initiate the reaction. This has been called the ***Zemplen-Helferich modification***.

Examples:

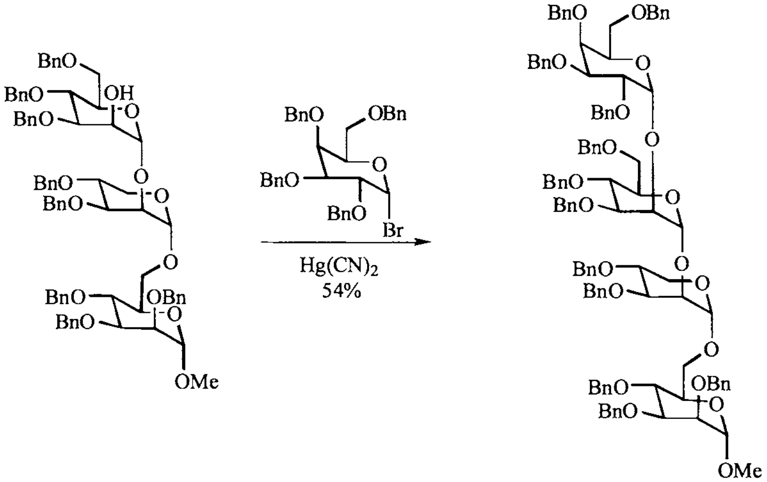
An improvement over the traditional method to avoid use of Hg salts.



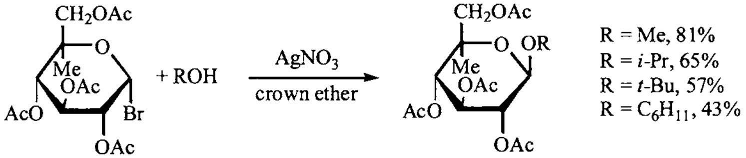
The procedure also replaces anomeric acetate groups.



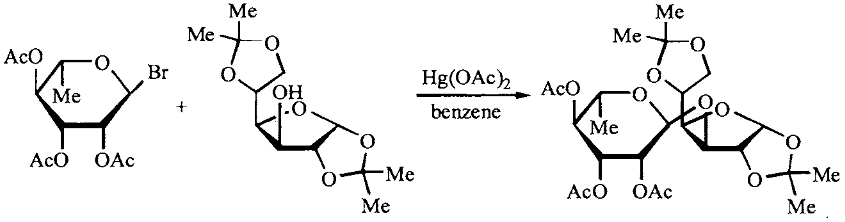
A. K. Pathak, Y. A. El-Kattan, N. Bansal, J. A. Maddry, R. C. Reynolds, *Tetrahedron Letters* **1998**, 39, 1497



H. Li, Q. Li, M.-S. Cai, Z.-J. Li, *Carbohydrate Research* **2000**, 328, 611



A. Knochel, G. Rudopph, J. Thiem, *Tetrahedron Letters* **1974**, 15, 55

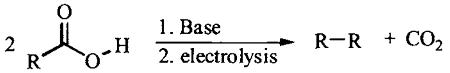


yield described as "low"
(10% after deprotection)

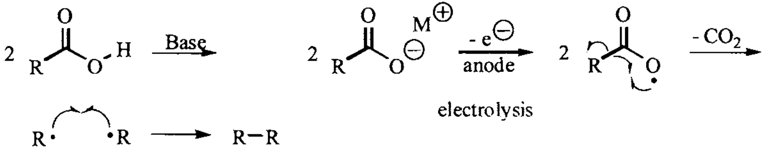
F. Imperato, *Journal of Organic Chemistry* **1976**, 41, 3478

Kolbé Electrolysis

The Reaction:



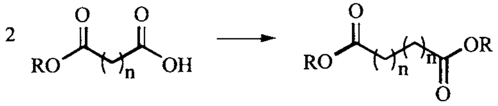
Proposed Mechanism:



Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 942; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 170-171.

1. The ***Brown-Walker Electrolysis*** is useful for dimerizing half-acid-esters:



2. Mixed coupling can be accomplished by relying on statistics and using the less-costly acid in excess. Prediction of yield of R-R' for the reaction:

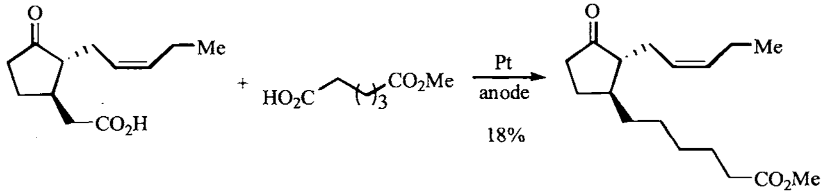
$$\text{R-COOH} + \text{R'-COOH} \longrightarrow \text{R-R} + \text{R'-R'} + \text{R-R'}$$

YIELD = 100N / (1+N), assuming a 1:N ratio of the two acids.

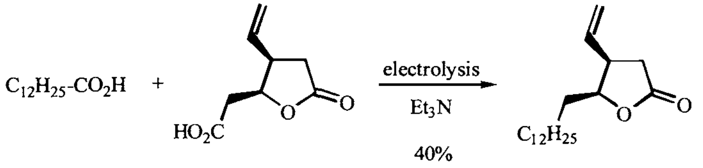
H.J. Schafer, in *Comprehensive Organic Synthesis*, B. M. Trost, editor-in-chief, Pergamon Press, Oxford, 1991, **3**, Chapter 2.8

See: M.A. Iglesias-Arteaga, E. Juaristi, F. J. Gonzalez, *Tetrahedron* **2004**, 60, 3605 for a detailed discussion of the electrochemistry.

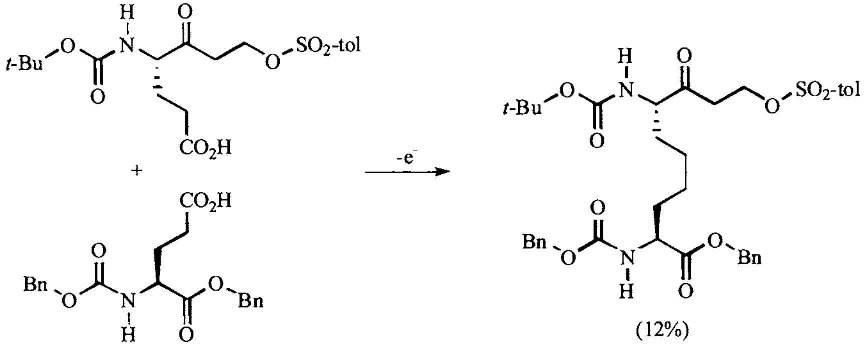
Examples:



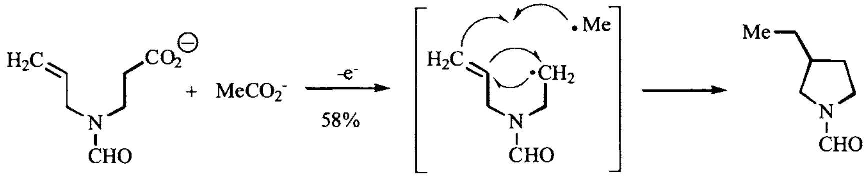
K. Schierle, J. Hopke, M.-L. Niedt, W. Boland, E. Steckhan, *Tetrahedron Letters* **1996**, 37, 8715



A. Forster, J. Fitremann, P. Renaud, *Tetrahedron Letters* **1998**, 39, 7097



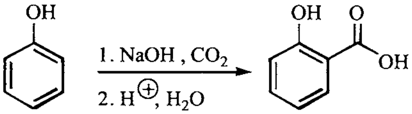
J. Hiebl, H. Kollmann, F. Rovenszky, K. Winkler *Bioorganic & Medicinal Chemistry Letters* **1997,** 7, 2963



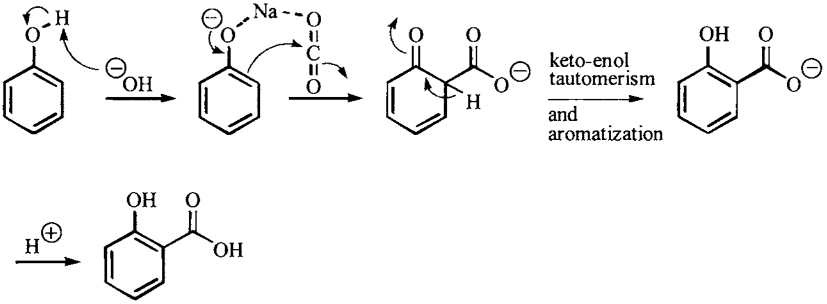
L. Becking, H. J. Schafer, *Tetrahedron Letters* **1988**, 29, 2797

Kolbé-Schmitt Reaction (Kolbé Synthesis, Schmitt Synthesis)

The Reaction:



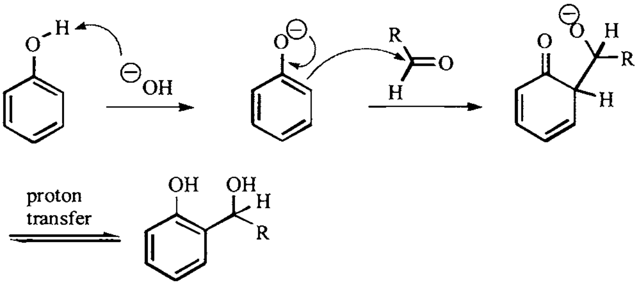
Proposed Mechanism:



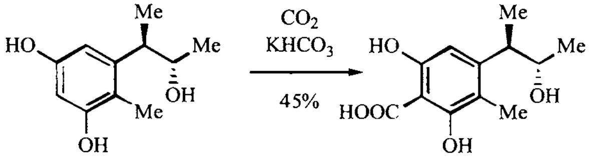
Notes:

Recent work shows that a phenoxide-CO_2 complex is formed competitively with direct carboxylation. This does not go on to form products, but rather decomposes to phenoxide and carbon dioxide. (Y. Kosugi, Y. Imaoka, F. Gotoh, M. A. Rahim, Y. Matsui, K. Sakanishi, *Organic and Biomolecular Chemistry* **2003**, 1, 817)

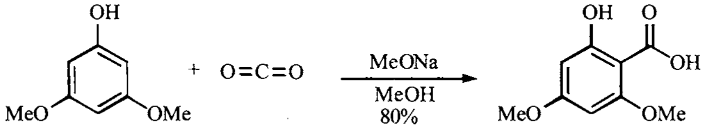
Lederer-Manasse Reaction



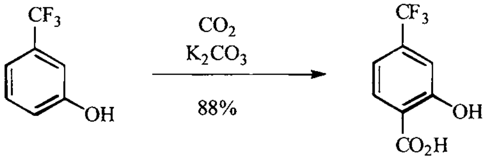
Examples:



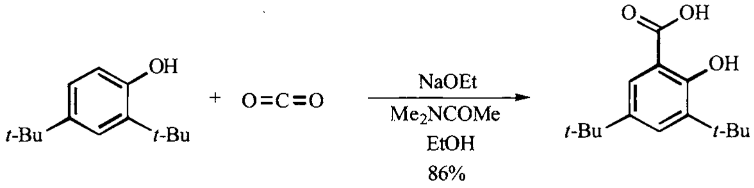
A. C. Regan, J. Staunton, *Journal of the Chemical Society, Chemical Communications* **1987**, 520

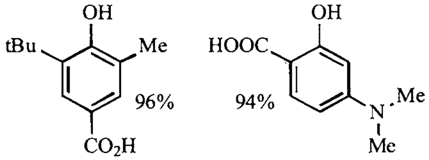


A. Fuerstner, N. Kindler, *Tetrahedron Letters* **1996**, 37, 7005



M. Hauptschein, E. A. Nodiff, A. J. Saggiomo, *Journal of the American Chemical Society* **1954**, 76,1051

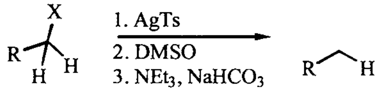




W. H Meek, C. H. Fuchsman, *Journal of Chemical and Engineering Data* **1969**, 14, 388

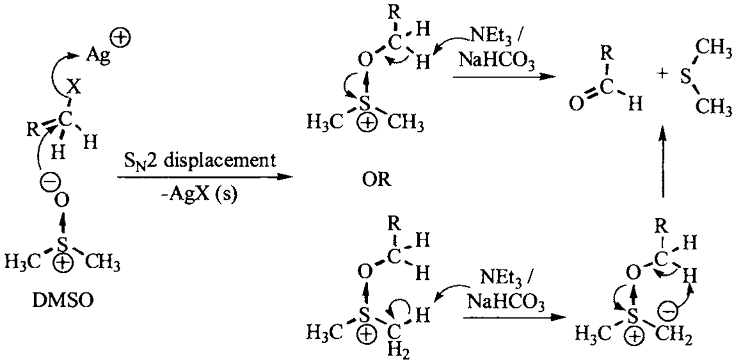
Kornblum Aldehyde Synthesis

The Reaction:



X = I, Br, OTs

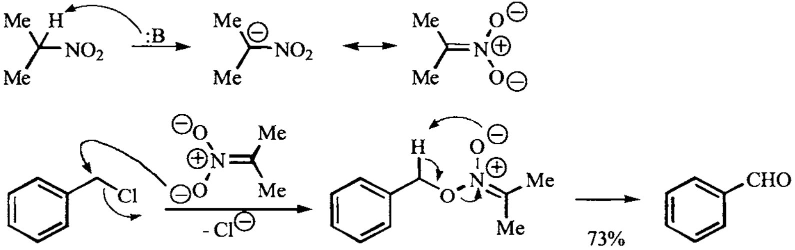
Proposed Mechanism:



Notes:

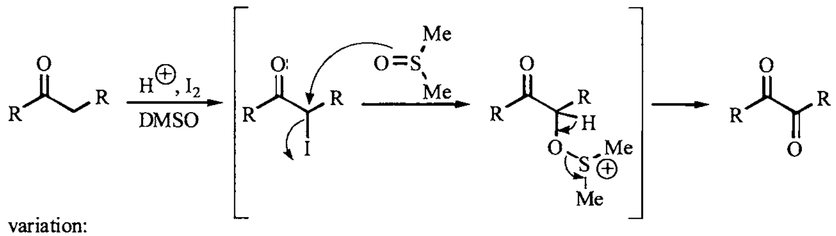
T. T. Tidwell, *Organic Reactions* **39**, 3

The ***Hass or Hass-Bender Reaction*** will specifically convert a benzylic halide to an aldehyde:

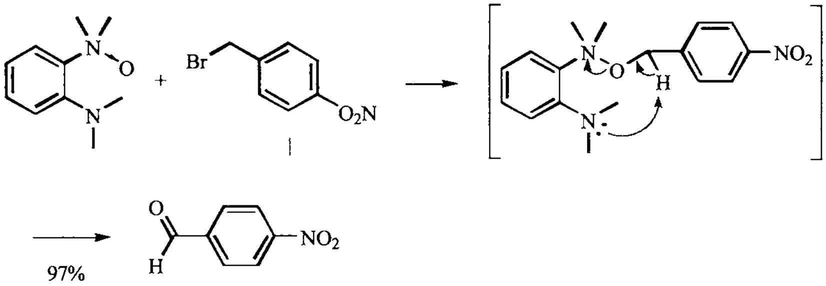


H. B. Hass, M. L. Bender, *Journal of the American Chemical Society* **1949**, 71, 1767

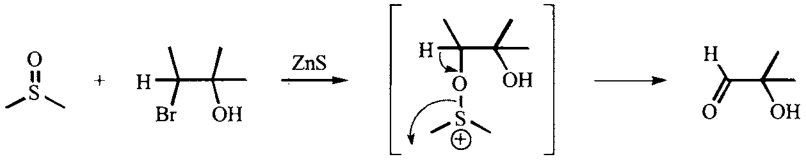
Examples:

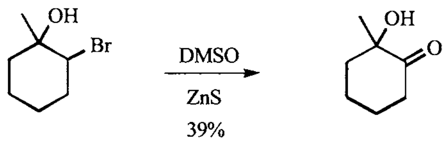


variation:

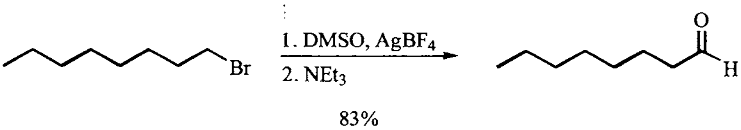


S. Chandrasekhar, M. Sridhar, *Tetrahedron Letters* **2000**, 41, 5423





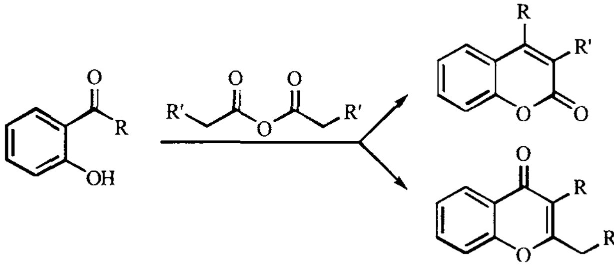
B. K. Bettadaiah, K. N. Burudutt, P. Srinivas, *Journal of Organic Chemistry* **2003**, 68, 2460



B. Ganem, R. K. Boeckman, *Tetrahedron Letters* **1974**, 917

Kostanecki Acylation

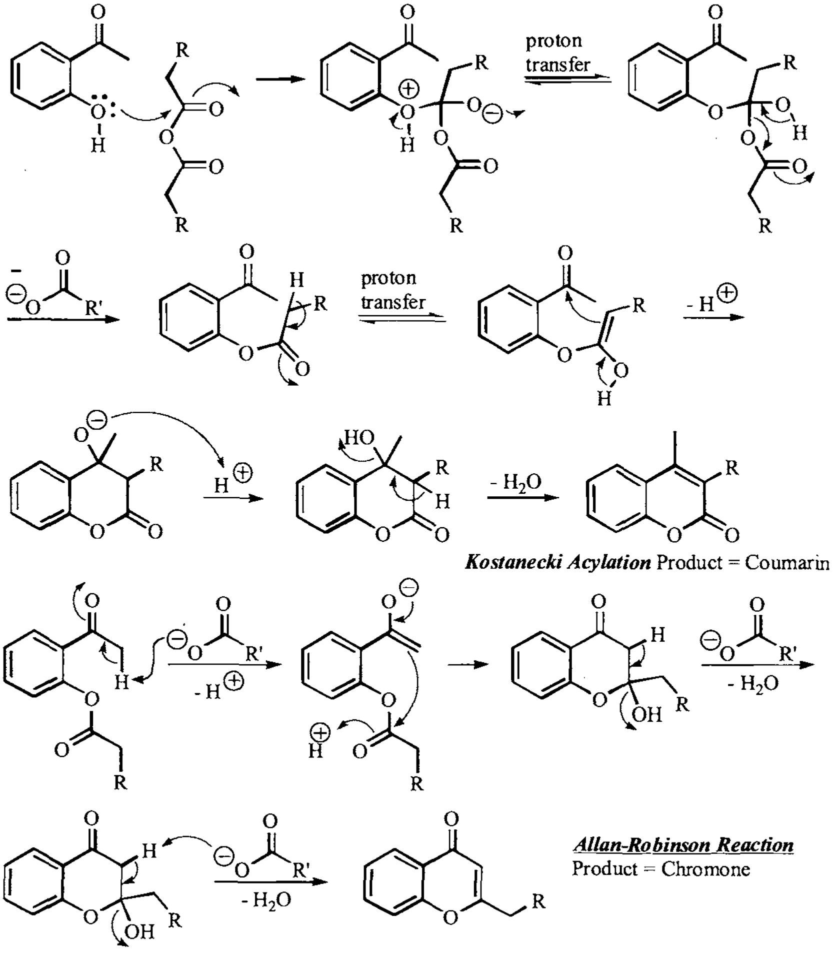
The Reaction:



Kostanecki Acylation product, a coumarin

Allan-Robinson Reaction product, a chromone

Proposed Mechanism:



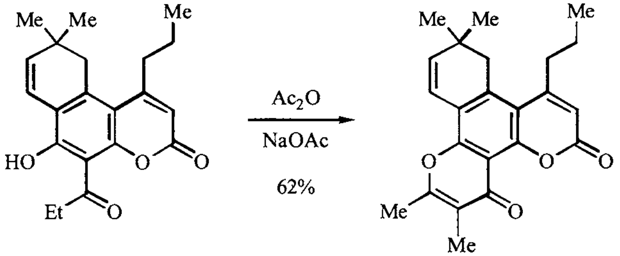
Kostanecki Acylation Product = Coumarin

Allan-Robinson Reaction
Product = Chromone

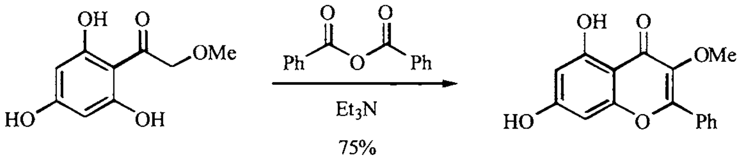
Notes:

There is competition between products from ***Allan - Robinson*** and ***Kostanecki Acylation***. A search of literature shows that both product types are often classified as the latter. This is exemplified with examples, all of which are searchable under ***Kostanecki Acylation***.

Examples:

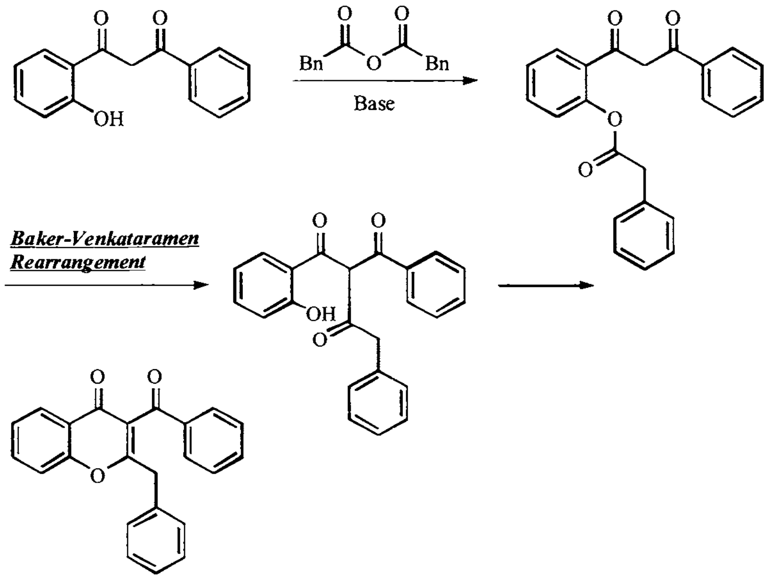


M. I. T. Flavin, J. D. Rizzo, A. Khilevich, A. Kucherenko, A. K. Sheinkman, V. Vilaychack, L. Lin, W. Chen, E. M. Greenwood, T. Pengsuparp, J. M. Pezzuto, S. H. Hughes, T. M. Flavin, M. Cibulski, W. A. Boulanger, R. L. Shone, Z.- Q. Xu, *Journal of Medicinal Chemistry* **1996**, 39, 1303



J. H. Looker, J. H. McMechan, J. W. Mader, *Journal of Organic Chemistry*, **1978**, 43, 2344

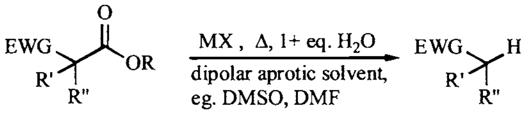
Using the Scheme shown below, a series of substituted chromones was prepared. Yields ranged from 13 - 67%



V. Rossollin, V. Lokshin, A. Samat, R. Guglielmetti, *Tetrahedron* **2003**, 59, 7725

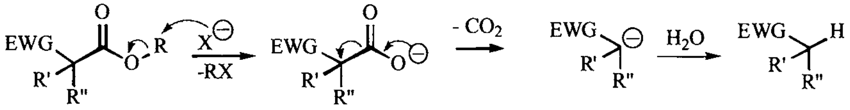
Krapcho Dealkoxycarbonylation

The Reaction:



MX =(Li or Na)MCl, LiI, (Na or K) MCN

Proposed Mechanism:

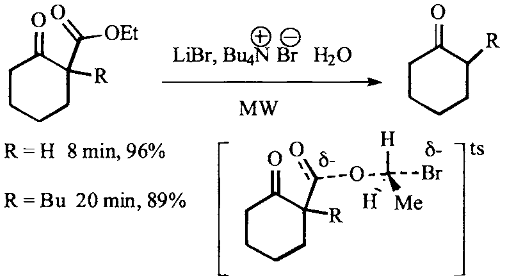


As evidence for an intermediate anion, there have been applications where an electrophile is captured.

Notes:

In solvents such as DMSO and DMF, the Cl⁻ is not solvated; thus, it's nucleophilicity is enhanced for the required S_N2 displacement.

This reaction is greatly accelerated under microwave conditions.

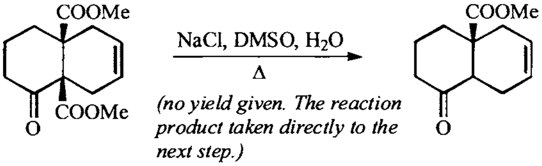


R = H 8 min, 96%

R = Bu 20 min, 89%

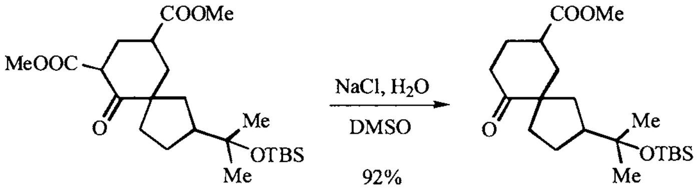
L. Perreux, A. Loupy, *Tetrahedron* **2001**, 57, 9199.

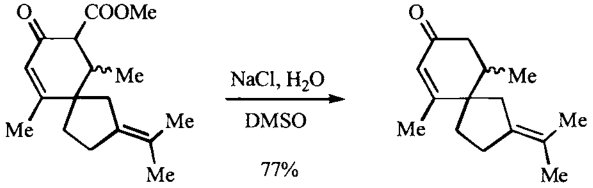
Examples:



(no yield given. The reaction product taken directly to the next step.)

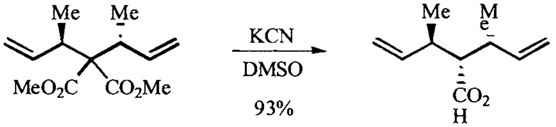
P. J. Garratt, J. R. Porter, *Journal of Organic Chemistry* **1986**, 51, 5450



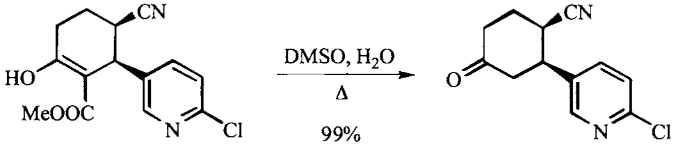


(1.7 : 1
mixture)

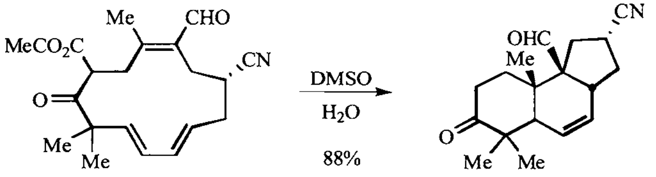
G. H. Posner, E. M. Shulman-Roskes, *Tetrahedron* **1992**, 48, 4677



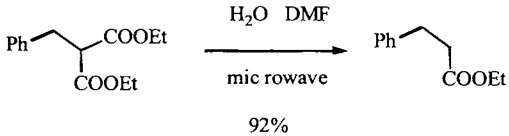
P. A. Evans, L. J. Kennedy, *Journal of the American Chemical Society* **2001**, 123, 1234



D. A. Evans, K. A. Scheidt, C. W. Downey, *Organic Letters* **2001**, 3, 3009



A. Toro, P. Nowak, P. Deslongchamps, *Journal of the American Chemical Society* **2000**, 122, 4526

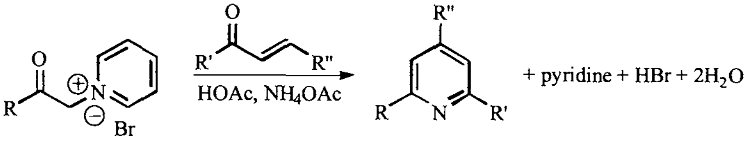


Via direct attack of the carbonyl by water, followed by decarboxylation of the resulting half acid.

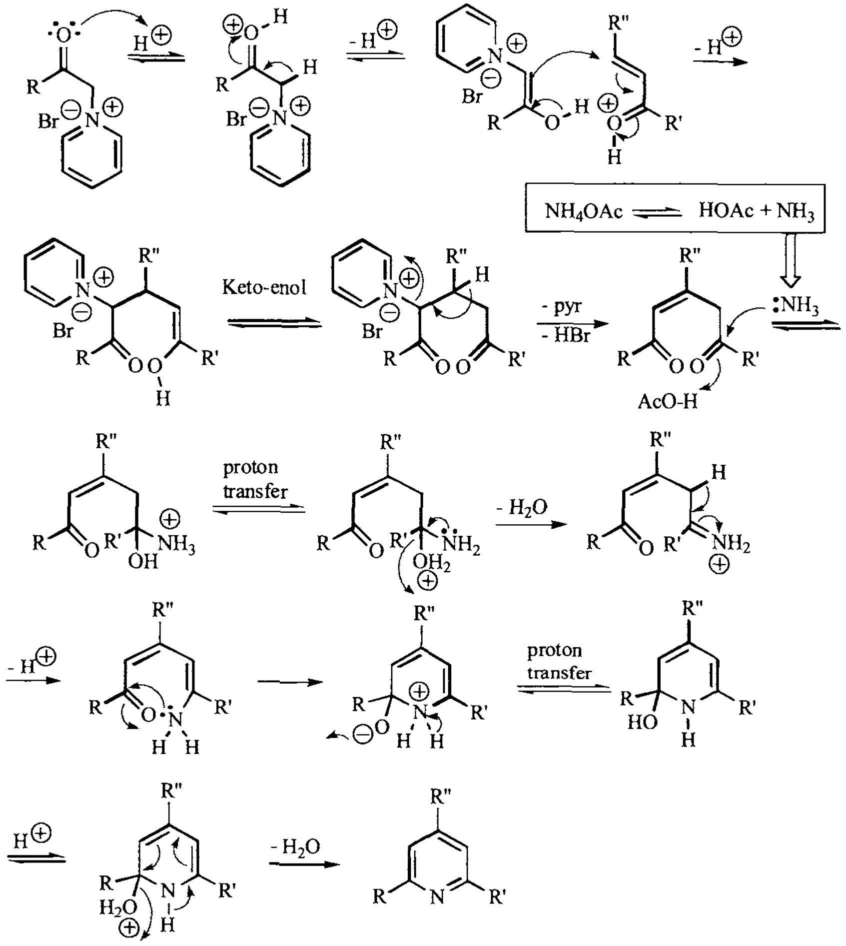
D. P. Curran, Q. Zhang, *Advanced Synthesis and Catalysis* **2003**, 345, 329

Kröhnke Pyridine Synthesis

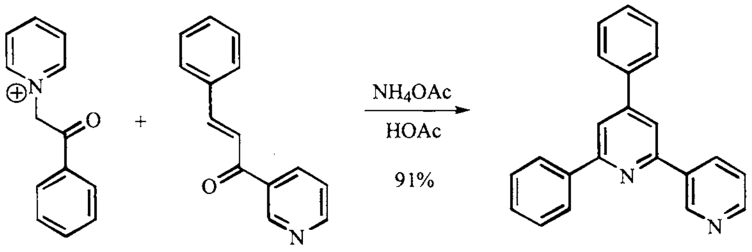
The Reaction:



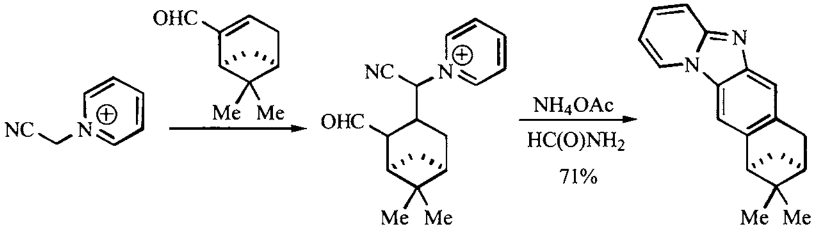
Proposed Mechanism:



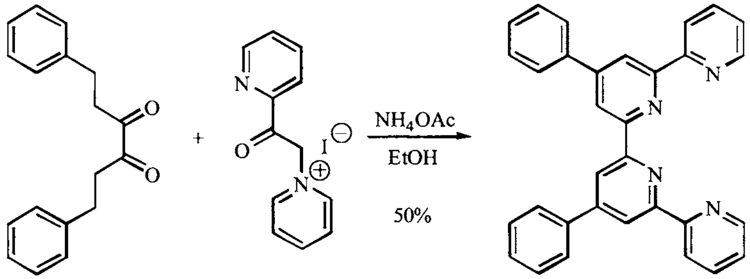
Examples:



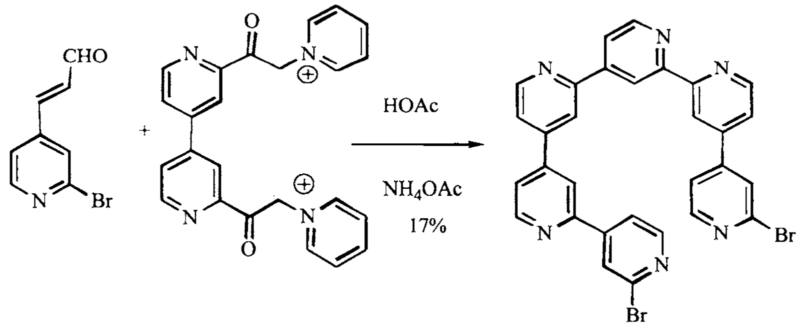
F. Krohnke, *Synthesis* **1976**, 1 (Review)



N. C. Fletcher, D. Abeln, A. von Zelewsky *Journal of Organic Chemistry* **1997**, 62, 8577



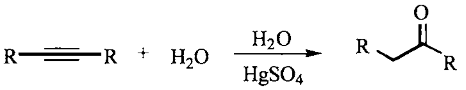
E. C. Constable, M. J. Hannon, D. R. Smith, *Tetrahedron Letters* **1994**, 35, 6657



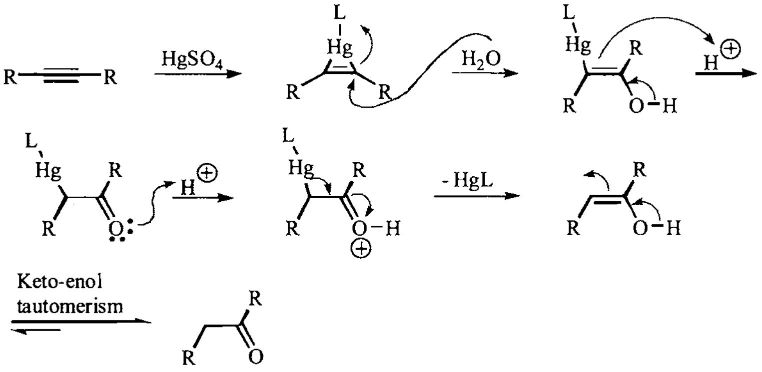
T. R. Kelly, Y.-J. Lee,R. J. Mears, *Journal of Organic Chemistry.* **1997**, 62, 2774

Kucherov Reaction

The Reaction:



Proposed Mechanism:

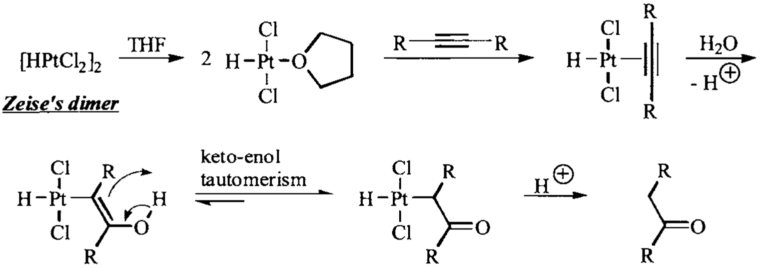


Notes:

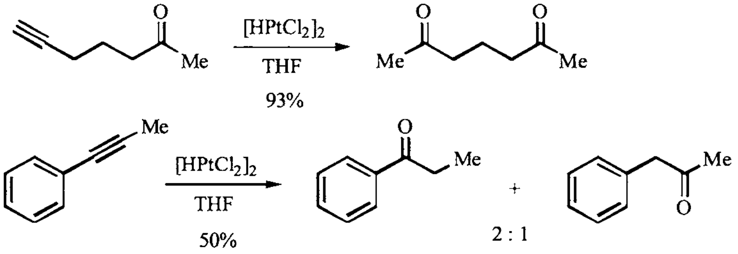
See also: ***Oxy-and Solvomercuration***

A discussion about the protonation of acetylene: V. Lucchini and G. Modena, *Journal of the American Chemical Society* **1990**, 112, 6291

Other alkyne hydration reactions:



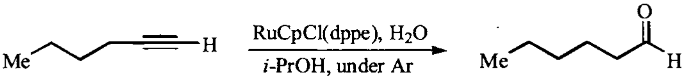
By this method:



W. Hiscox, P. W. Jennings, *Organometallics* **1990** 9, 1997

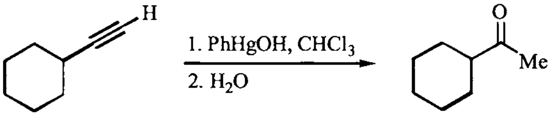
Examples:

Anti-Markovnikov hydration of a terminal alkyne:



>99%

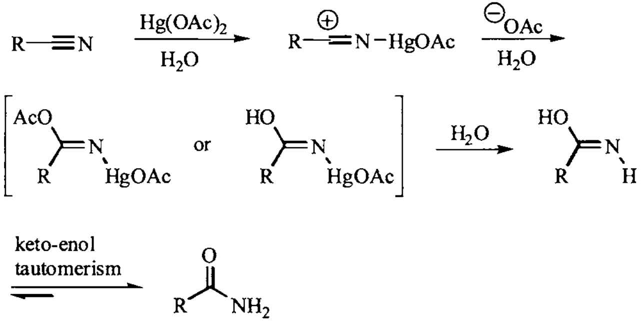
T. Suzuki, M. Tokunaga, Y. Wakatsuki, *Organic Letters* **2001**, 3, 735



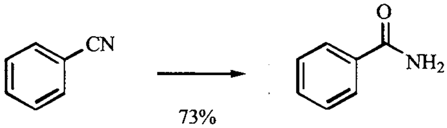
49%

V. Janout, S. L. Regen, *Journal of Organic Chemistry* **1982**, 47, 3331

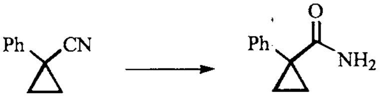
Hydration of a nitrile:



By this method:



73%



92%

K. Maeyama, N. Iwasawa, *Journal of the American Chemical Society* **1998**, 120, 1928

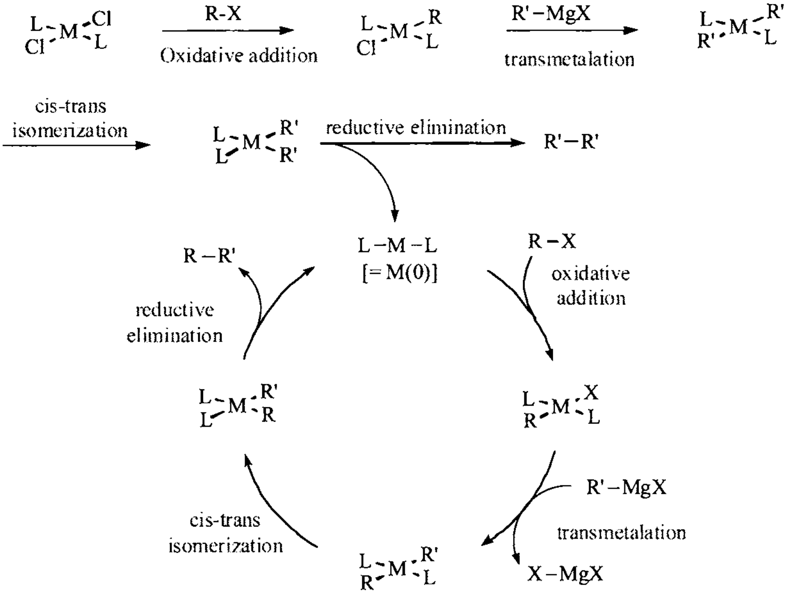
Kumada Coupling Reaction

The Reaction:

$$R{-}X + R'{-}MgX \xrightarrow[\text{THF or DMF}]{M(0)} R{-}R'$$

M = Ni or Pd

Proposed Mechanism:

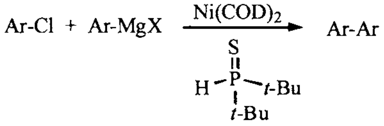


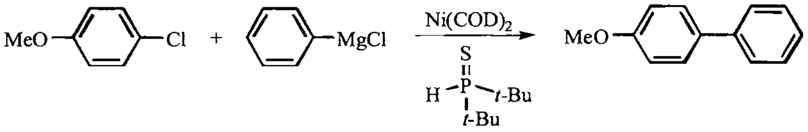
Notes:

For R-X: When M = Ni, Cl > Br > I; when M = Pd, I > Br > Cl

Reaction is limited by any functional group that will normally react with a ***Grignard reagent***.

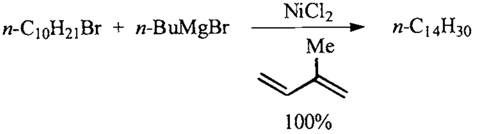
Examples:



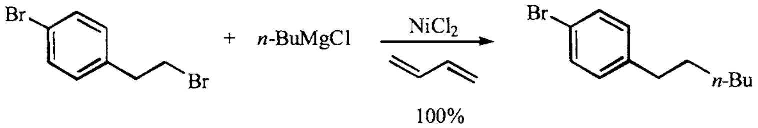


G. Y. Li, W. J. Marshall, *Organometallics* **2002**, 21, 590

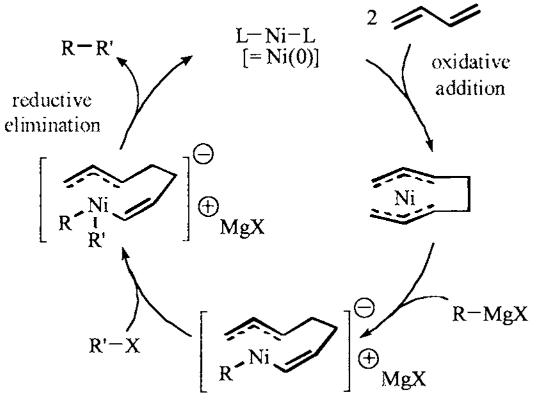
An important influence of butadiene on the reaction has been noted:



PdCl$_2$ catalysis provides only 38% yield.

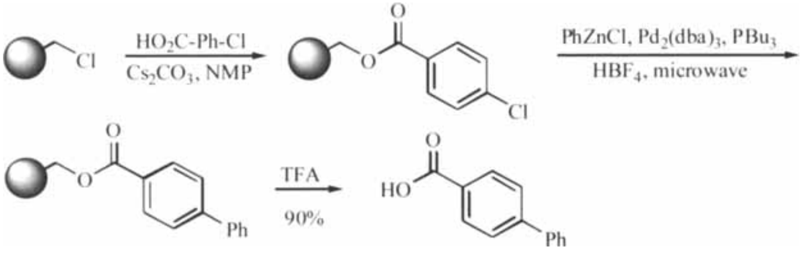


Mechanistically:

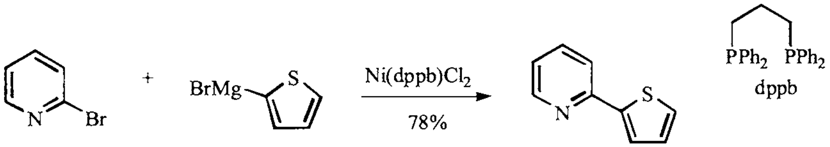


J. Terao, H. Watanabe, A. Ikumi, H. Kuniyasu, N. Kambe, *Journal of the American Chemical Society* **2002**, 124, 4222

Examples:



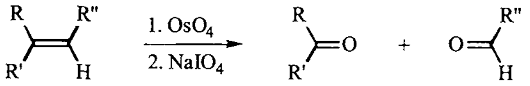
P. Walla, C. O. Kappe, *Chemical Commmunications* **2004**, 564



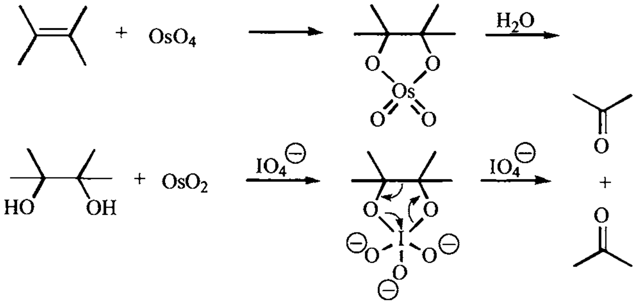
K. Tamoa, S. Kodama, I. Nakajima, M. Kumada, A. Minato, K. Suzuki, *Tetrahedron* **1982**, 38, 3347

Lemieux-Johnson Oxidation

The Reaction:



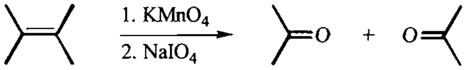
Proposed Mechanism:



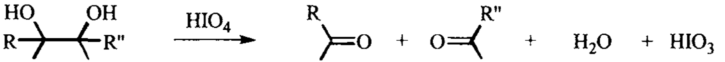
The $NaIO_4$ serves two purposes: (1) cleavage of the diol generated from the OsO_4 and, (2) reoxidation of the reduced osmium.

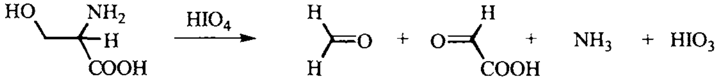
Notes:

See also the ***Lemieux-von Rudloff Reagent***, where catalytic $KMnO_4$ is used in place of OsO_4:



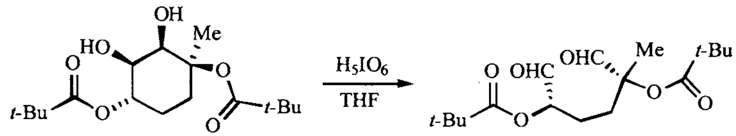
The ***Malaprade Periodic Acid Oxidation Reaction*** oxidizes 1,2 diols or 2-amino alcohols with periodic acid:





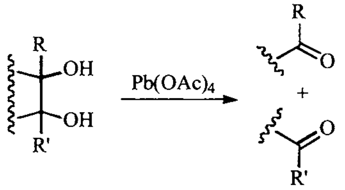
B. H. Nicolrt, L. A. Shinn, *Journal of the American Chemical Society* **1939**, 61, 1615

Recent example of ***Malaprade Reaction***:



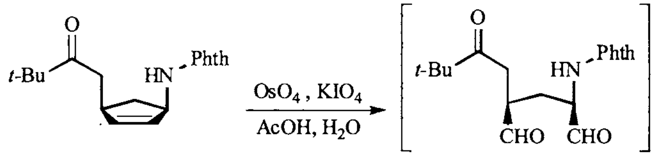
L. Vares, T. Rein, *Journal of Organic Chemistry* **2002**, 67, 7226

Criegee Glycol Oxidation



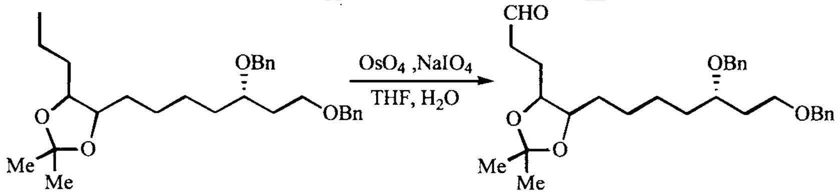
See: ***Criegee Reagent***

Examples:



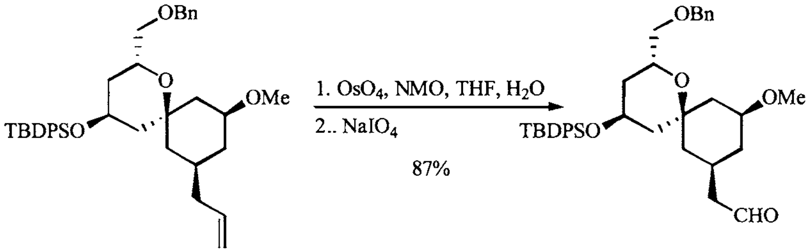
Not isolated; carried on to the next step.

F. A. Luzzio, A. V. Mayrov, W. D. Figg, *Tetrahedron Letters* **2000**, 41, 2275

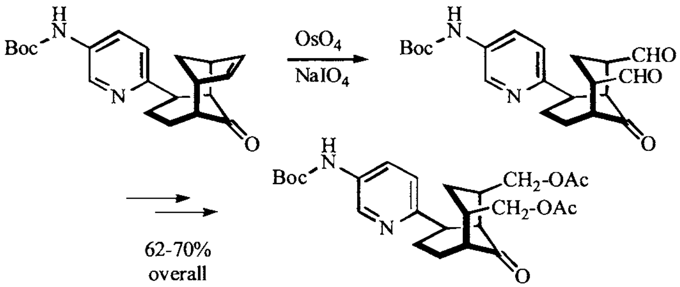


Taken directly to the next step.

S. Takahashi, A. Kubota, T. Nakata, *Organic Letters* **2003**, 5, 1353



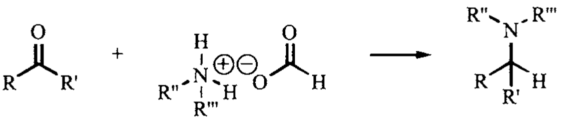
D. Zuev, L. A. Paquette, *Organic Letters* **2000**, 2, 679



M. J. Sung, H. I. Lee, Y. Chong, J. K. Cha, *Organic Letters* **1999**, 1, 2017

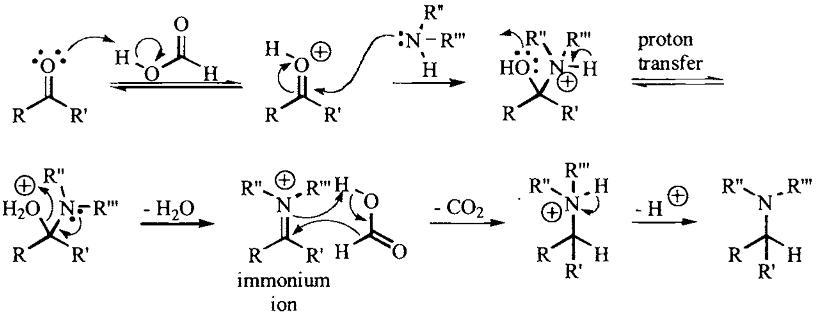
Leuckart Reaction / Reductive Amination

The Reaction:

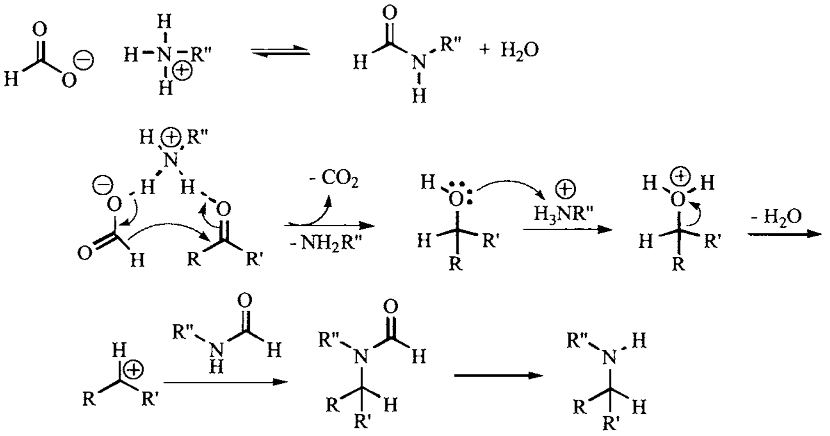


Proposed Mechanism:

A common mechanistic interpretation involves hydride transfer in the reduction of the immonium ion intermediate:



Another interpretation:
See: P. I. Awachie, V. C. Agwada, *Tetrahedron* **1990**, 46, 1899



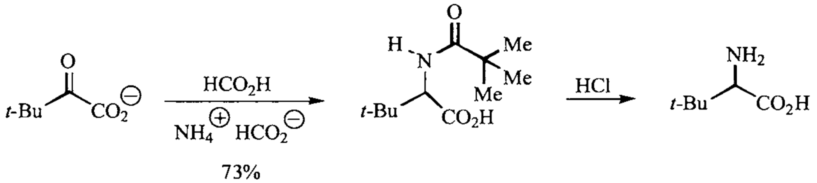
Notes:

This reaction refers to the case when a ketone or aldehyde is reductively aminated, using ammonium formate or another amine salt of formic acid.

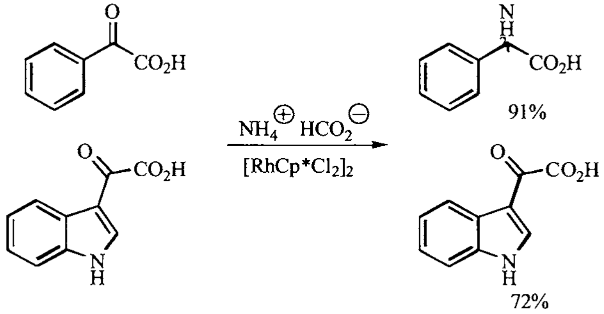
When conducted in excess formic acid, so that the formic acid is the hydride source, the reaction is called the ***Wallach Reaction***.

See also the ***Eschweiler-Clarke Methylation*** and the ***Borche Reduction***.

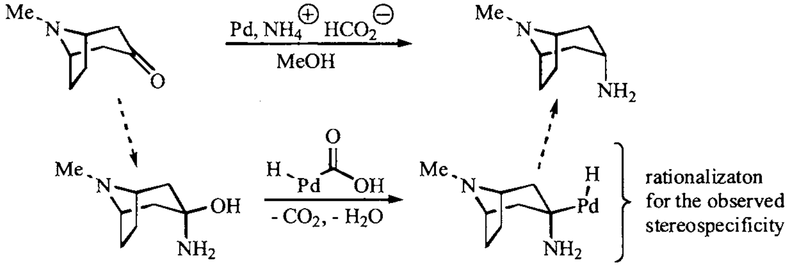
Examples:



B. M. Adger, U. C. Dyer, I. C. Lennon, P. D. Tiffin, S. E. Ward, *Tetrahedron Letters* **1997**, 38, 2153



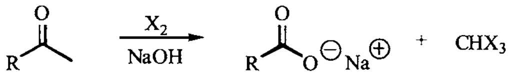
M. Kitamura, D. Lee, S. Hayashi, S. Tanaka, M. Yoshimura, *Journal of Organic Chemistry* **2002**, 67, 8685



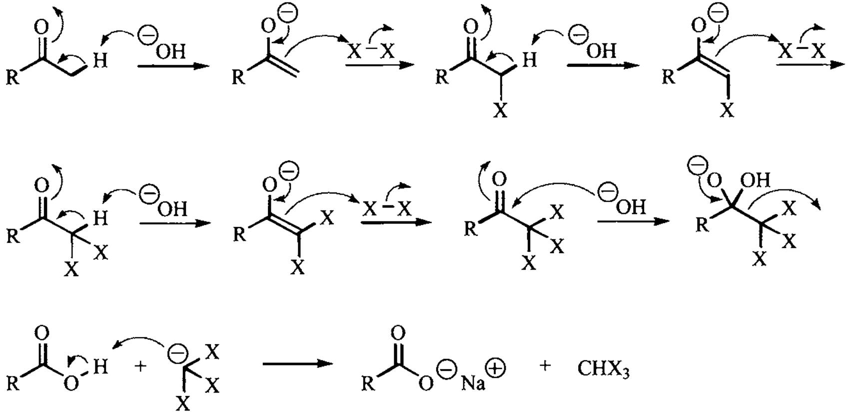
M. Allegretti, R. Anacardio, M. C. Cesta, R. Curti, M. Mantovanini, G. Nano, A. Topai, G. Zampella, *Organic Process Research & Development* **2003**, 7, 209

Lieben Haloform (Iodoform) Reaction

The Reaction:



Proposed Mechanism:

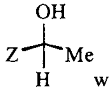


Notes:

Cl_2 and Br_2 can also be used besides I_2.

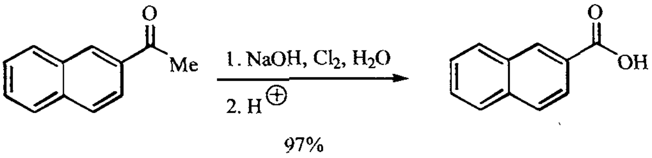
This reaction has long been considered a chemical test.

Since the reaction conditions are oxidative, alcohols such as

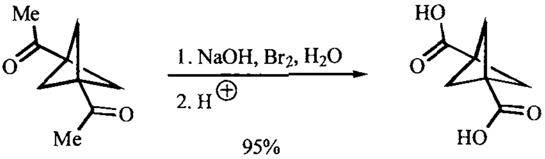


will oxidize to the corresponding carbonyl compound and give a positive iodoform test.

Examples:



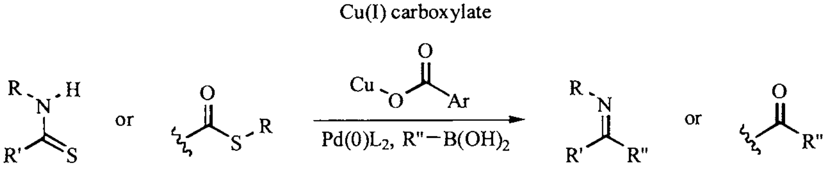
M. S. Newman, H. L. Holme, *Organic Syntheses*, CV2, 428



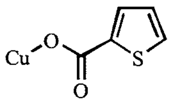
M. D. Levin, P. Kosznski, J. Michl, *Organic Syntheses*, 77, 249

Liebeskind–Srogl Coupling

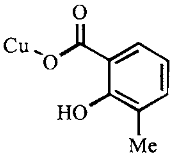
The Reaction:



Cu(I) carboxylates include:

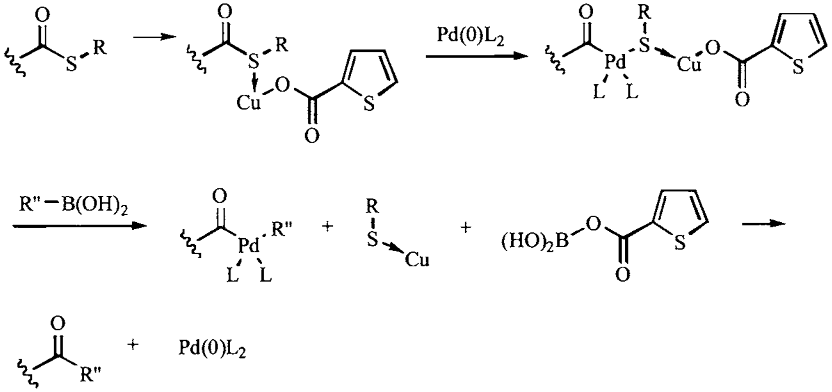


CuTC = Cu(I)thiophene-2-carboxylate



CuMeSal = copper(I) 3-methylsalicylate

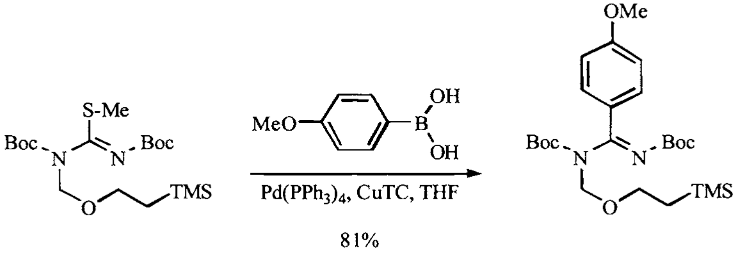
Proposed Mechanism:



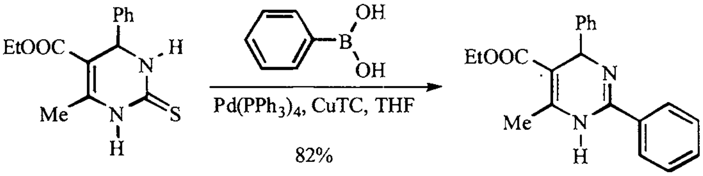
Notes:

The reaction proceeds under nonbasic conditions.

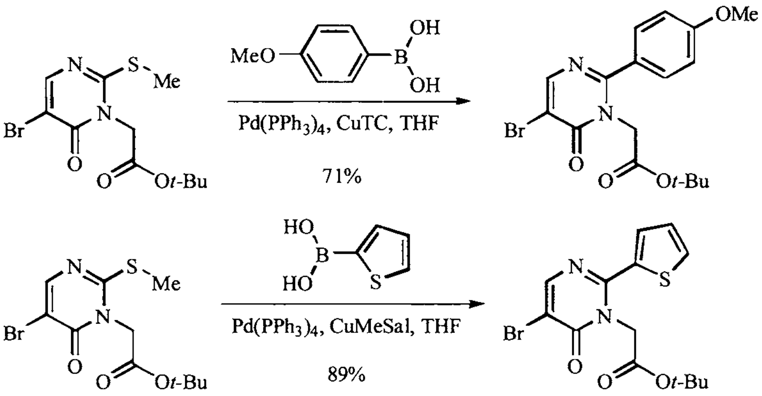
Examples:



C. L. Kusturin, L. S. Liebeskind, W. L. Neumann, *Organic Letters* **2002**, 4, 983

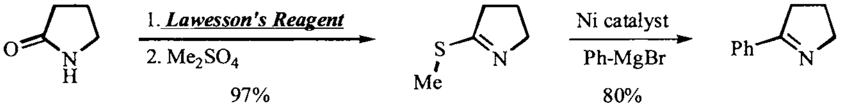


A. Lengar, C. O. Kappe, *Organic Letters* **2004**, 6, 771



C. Kusturin, L. S. Liebeskind, H. Rahman, K. Sample, B. Schweitzer, J. Srogl, W. L. Neumann, *Organic Letters* **2003**, 5, 4349

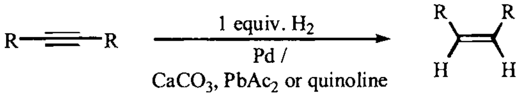
Thioimidate-Kumuda Cross-Coupling variation:

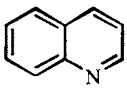


D. M. Mans, W. H. Pearson, *Journal of Organic Chemistry* **2004**, 69, 6419

Lindlar Reduction

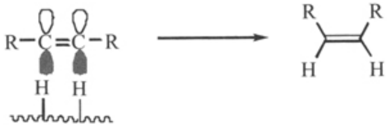
The Reaction:





= quinoline

Proposed Mechanism:

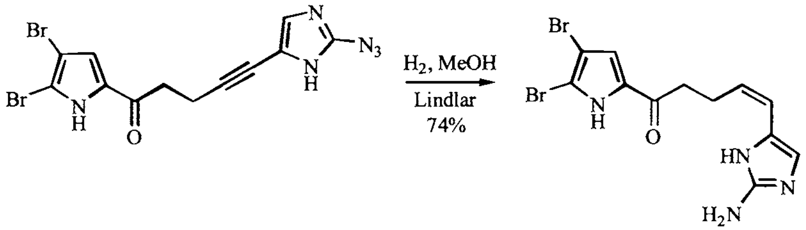


Notes:

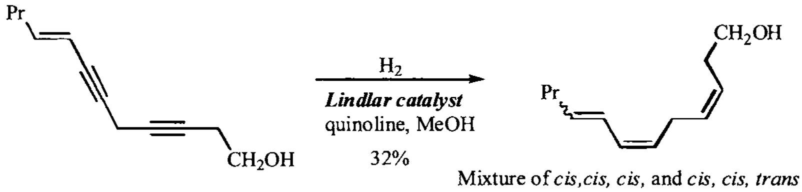
Generally an alkene will reduce to an alkane, however, the "poisoned" catalyst suppresses the ability for this to readily occur.

See ***Lindlar catalyst***

Examples:

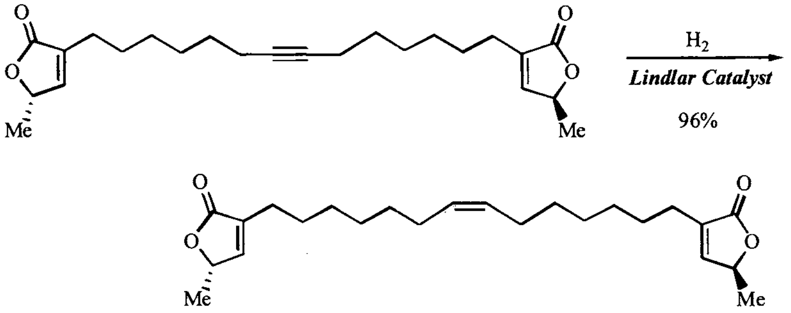


T. Lindel, M. Hochgurtel, *Journal of Organic Chemistry* **2000**, 65, 2806

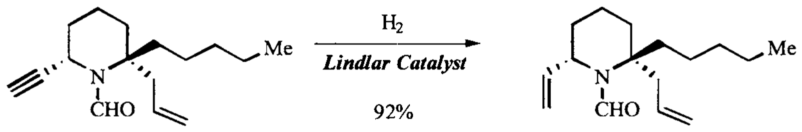


Mixture of *cis,cis, cis,* and *cis, cis, trans*

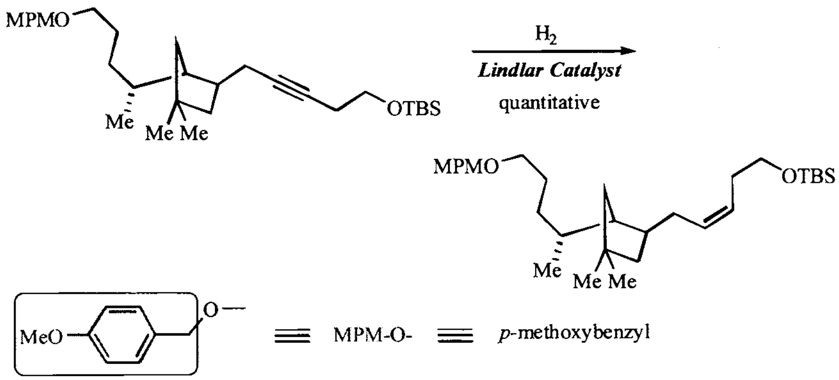
A. Tai, F. Matsumura, H. C. Coppel, *Journal of Organic Chemistry* **1969**, 34, 2180



Quinoline was added to the reduction mixture.
A. Furstner, T. Dierkes, *Organic Letters* **2000**, 2, 2463



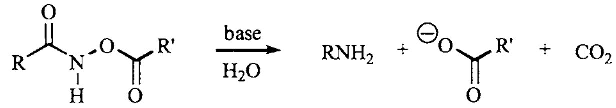
T. Itoh, N. Yamazaki, C. Kibayashi, *Organic Letters* **2002**, 4, 2469

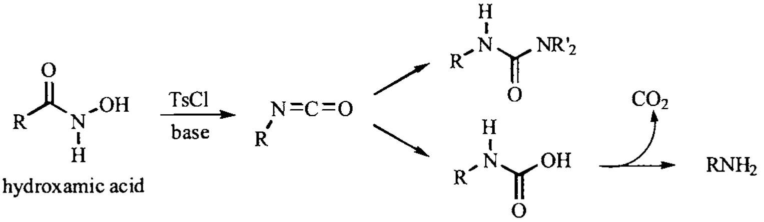


K. Suenaga, K. Araki, T. Sengoku, D. Uemura, *Organic Letters* **2001**, 3, 527

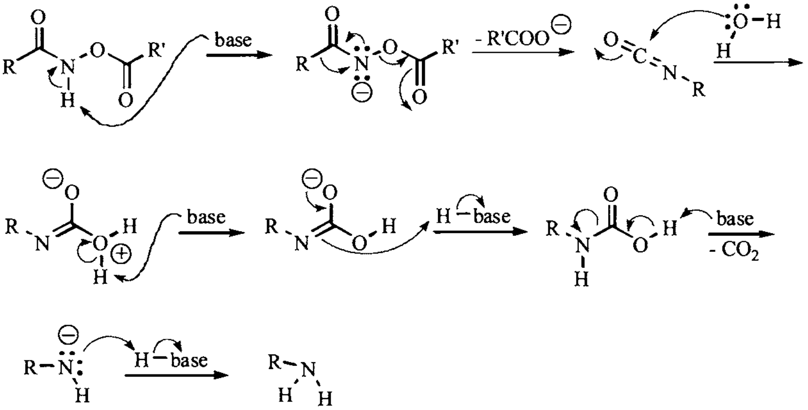
Lössen Rearrangement

The Reaction:

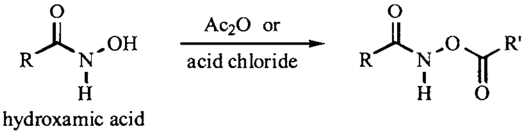




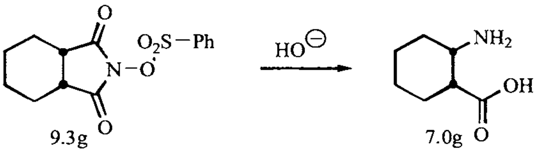
Proposed Mechanism:



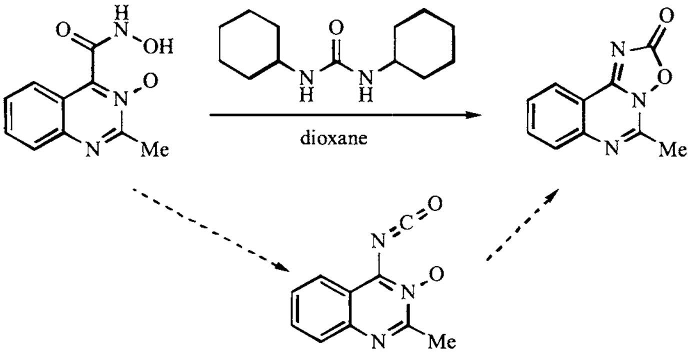
Notes:



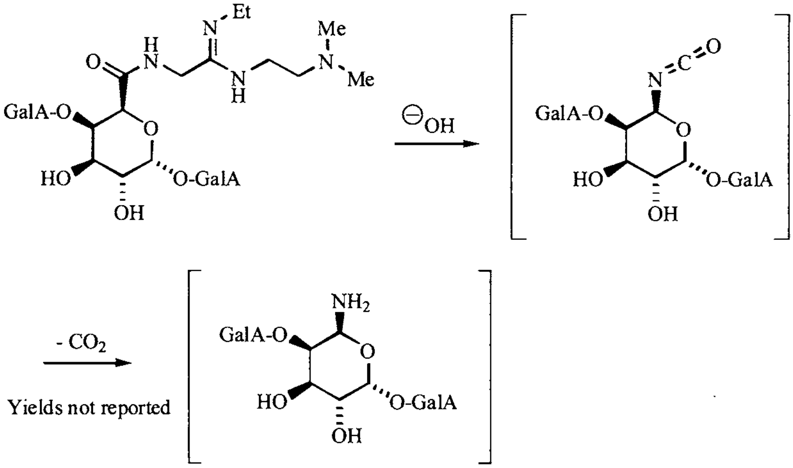
Examples:



L. Baue, S. V. Miarha, *Journal of Organic Chemistry* **1959**; 24, 1293



J.Bergman, J.-O. Lindstriim, *Tetrahedron Letters* **1976**, 17, 3615

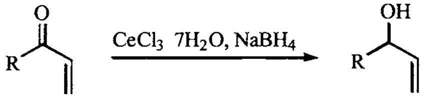


Yields not reported

P. W. Needs, N. M. Rigby, S. G. Ring, A. J. MacDougall, *Carbohydrate Research*, **2001**, 333, 47

Luche Reduction

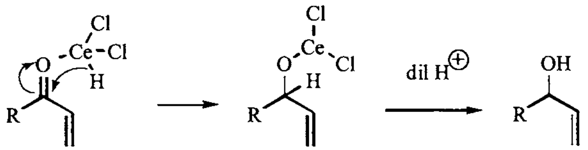
The Reaction:



Proposed Mechanism:

A. L. Gemal, J. -L. Luche, *Journal of the American Chemical Society* **1981**, 103, 5454

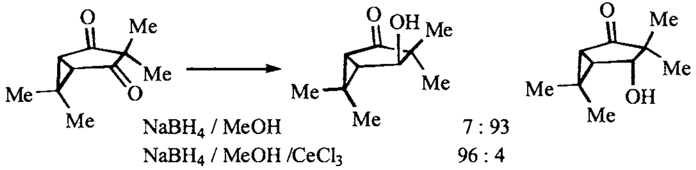
$CeCl_3 + NaBH_4 \longrightarrow HCeCl_2$



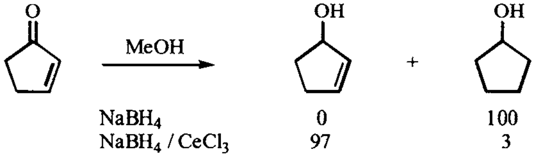
The cerium reagent coordinates to the carbonyl, making only a 1,2 addition possible.

Notes:

The major use of the ***Luche conditions*** is found in applications where conjugate addition needs to be suppressed. However, there are a number of reports where stereoselectivity has been modified with this reducing protocol.

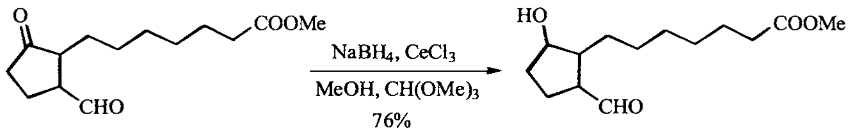


Reported in: L. A. Paquette, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1031

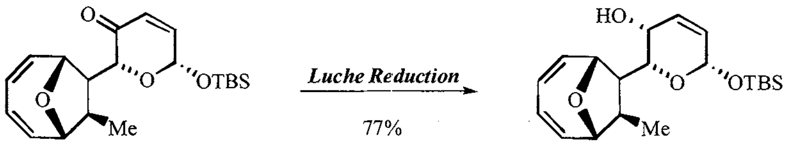


J. L. Luche, *Journal of the American Chemical Society* **1978**, 100, 2226

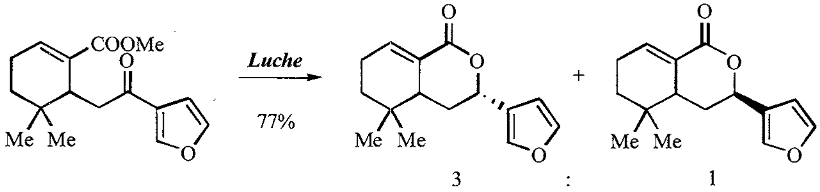
Examples:



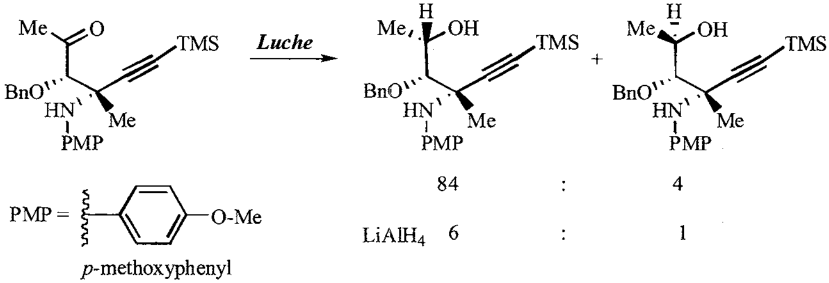
A. L. Gemal, J. L. Luche, *Journal of Organic Chemistry* **1979**, 44, 4187



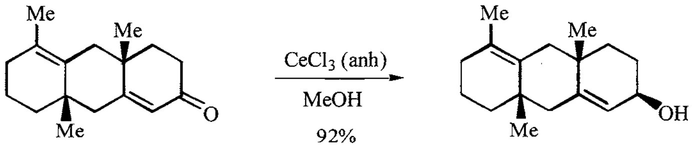
K. Takao, G. Watanabe, H. Yasui, K. Tadano, *Organic Letters* **2002**, 4, 2941



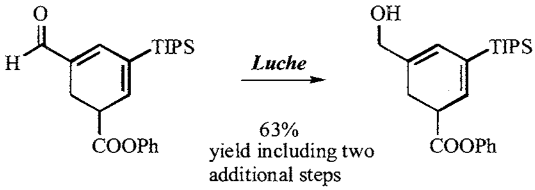
K. Agapiou, M. J. Krische, *Organic Letters* **2003**, 5, 1737



W. W. Cutchins, F. E. McDonald, *Organic Letters* **2002**, 4, 749



L. A. Paquette, D. T. Belmont, Y. -L. Hsu, *Journal of Organic Chemistry* **1985**, 50, 4667



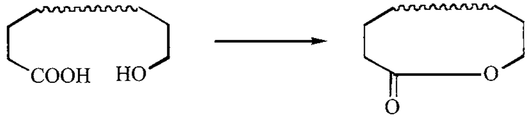
D. L. Comins, A. L. Williams, *Organic Letters* **2001**, 3, 3217

Macrolactonization Methods

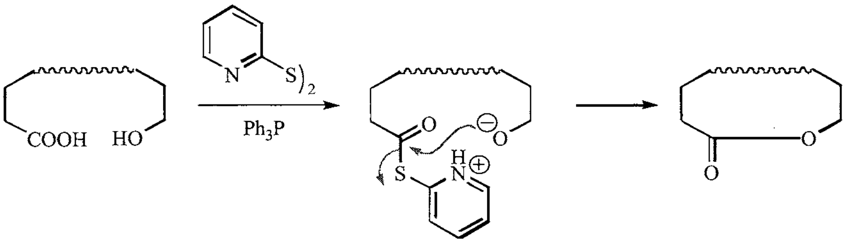
See: R. H. Boeckman, Jr., S. W. Goldstein, *in The Total Synthesis of Natural Products,* edited by J. ApSimon, John Wiley and Sons, Inc., New York, 1988, Chapter 1, for a useful review of macrocyclic lactone syntheses.

A key feature of most macrolactonization protocols is enhancement of the acyl group.

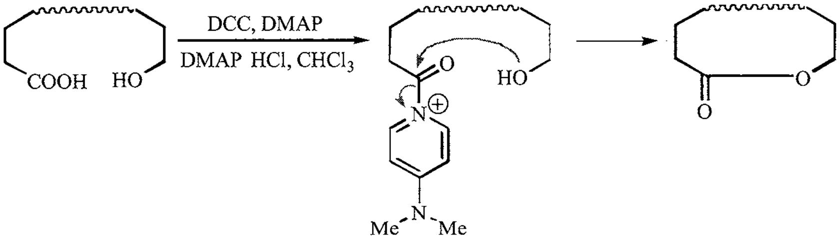
The Reaction:



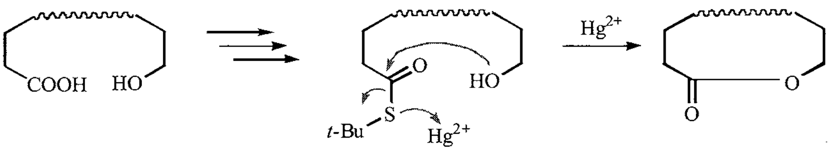
Corey-Nicoloau Macrocyclization



Keck Macrolactonization

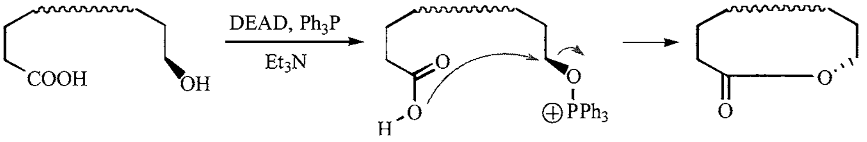


Masamune Macrolactonization



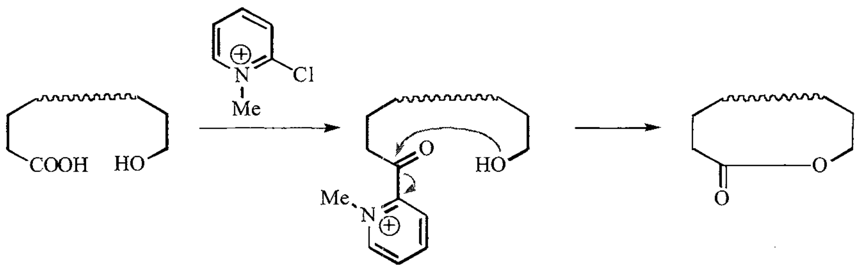
Mitsunobu Macrolactonization

See: ***Mitsunobu Lactonization***



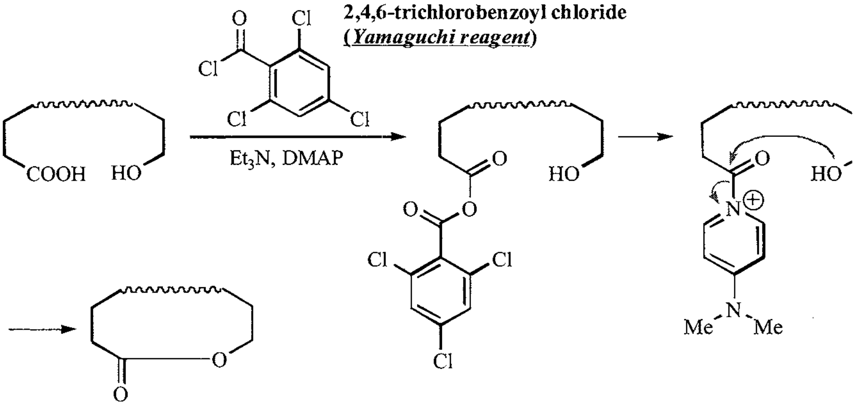
Mukaiyama's Macrolactonization

See ***Mukaiyama's Reagent***



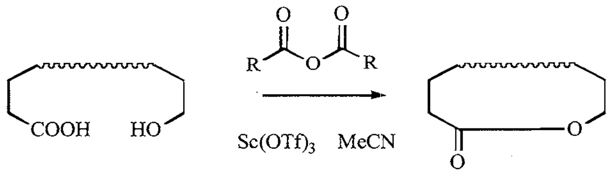
Yamaguchi's Macrolactonization

*See: **Yamaguchi's Esterification***



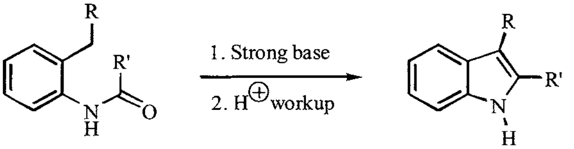
Yamamoto's Macrolactonization

See: ***Yamamoto's Reagent***, ***Yamamoto's Esterification***

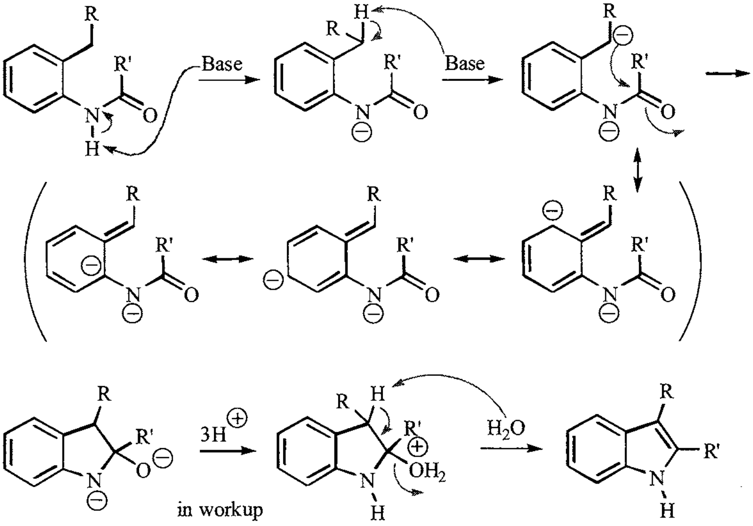


Madelung Indole Synthesis

The Reaction:



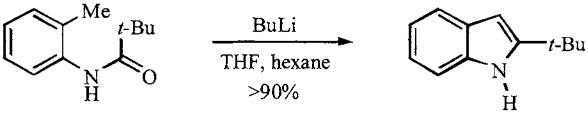
Proposed Mechanism:



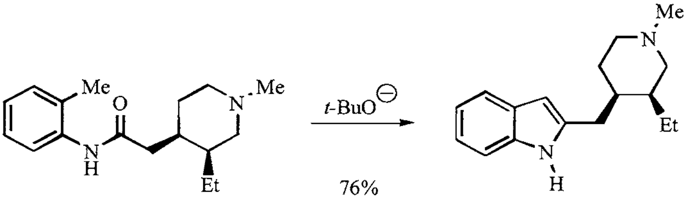
Notes:

See other Indole Syntheses, in ***Heterocyclic Syntheses***

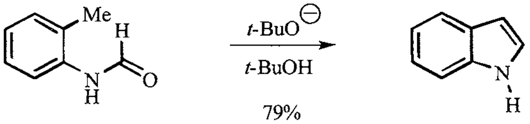
Examples:



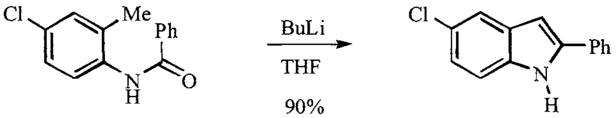
W. Fuhrer, H. W. Gschwend, *Journal of Organic Chemistry* **1979**, 44, 1133



A. Wu, V. Snieckus, *Tetrahedron Letters* **1975**, 16, 2057



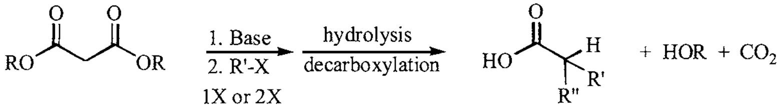
F. T. Tyson, *Organic Syntheses* **1943**, 23, 42



W. J. Houlihan, V. A. Parrino, Y. Uike, *Journal of Organic Chemistry* **1981**, 46, 4511

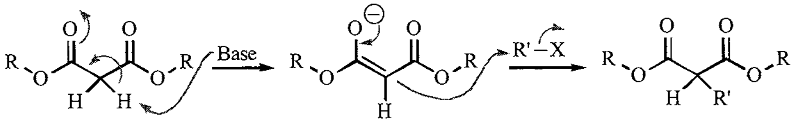
Malonic Ester Synthesis

The Reaction:



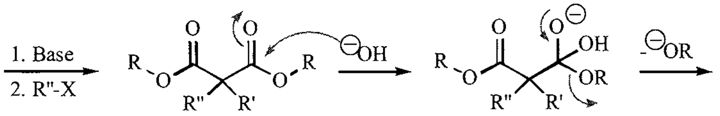
R often = ethyl = malonic ester

Proposed Mechanism:



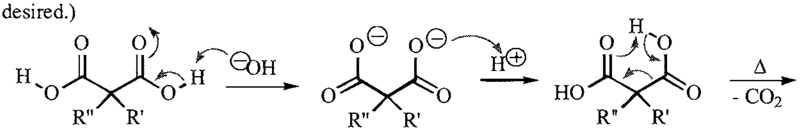
The methylene protons, being influenced by two carbonly groups, are the most acidic.

This part of the sequence is an enolate alkylation.



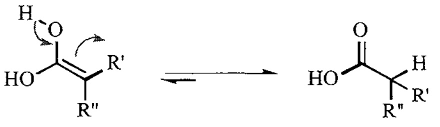
A second alkylation may occur (with a different electrophile if desired.)

Under basic conditions, the both esters are saponified to acids. (Arrows are shown for one.)



Carboxylic acids exist as carboxylate ions in base.

The carboxylates are protonated in acid and with heat, α-keto acids can decarboxylate, liberateing CO_2

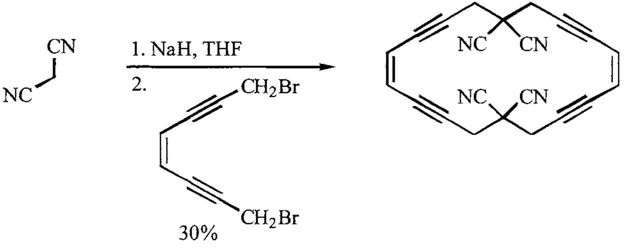


The resulting enol undergoes keto-enol tautomerism to give the final acid product.

Notes:

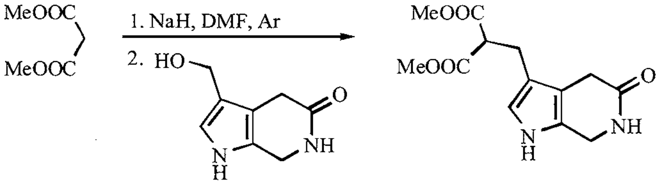
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 549; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 178-181

Malonitrile provides similar chemistry

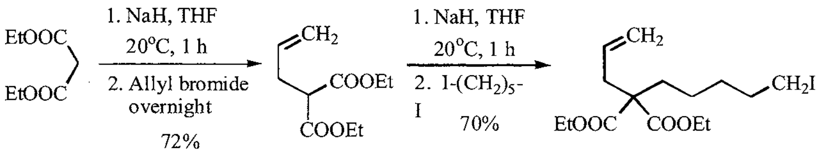


B. Koenig, W. Pitsch, I. Dix, P. G. Jones, *Synthesis* **1996**, 446

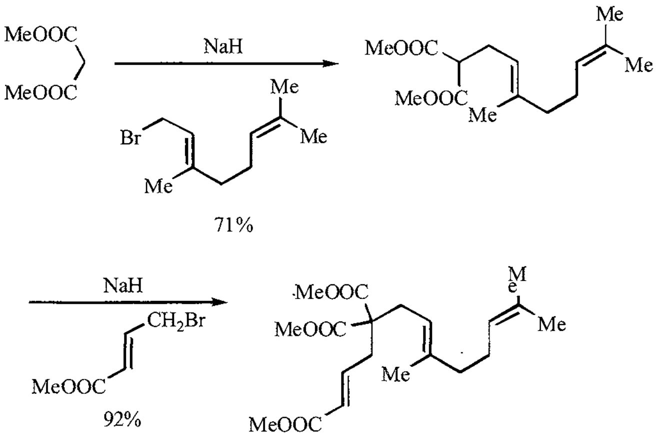
Examples:



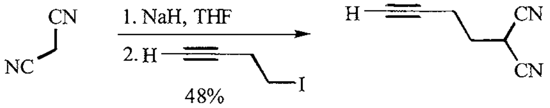
C. Y. DeLeon, B. Ganem, *Journal of Organic Chemistry* **1996**, 61, 8730



T. Yamazaki, A. Kasatkin, Y. Kawanaka, F. Sata, *Journal of Organic Chemistry* **1996**, 61, 2266



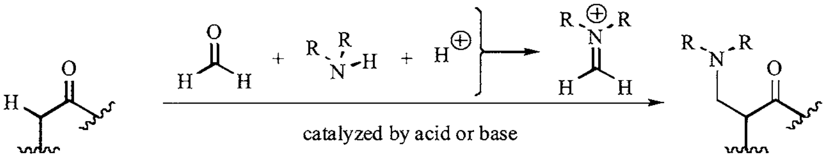
T. Takasu, S. Maiti, A. Katsumata, M. Mihara, *Tetrahedron Letters* **2001**, 42, 2157



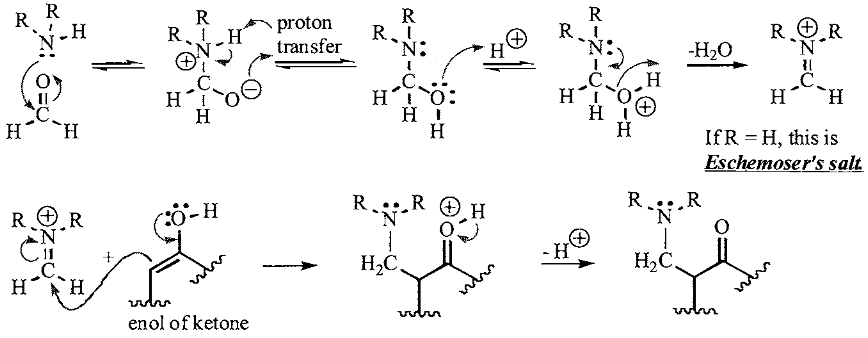
E. C. Taylor, J. E. Macor, L. G. French, *Journal of Organic Chemistry* **1991**, 56, 1807

Mannich Reaction

The Reaction:



Proposed Mechanism:

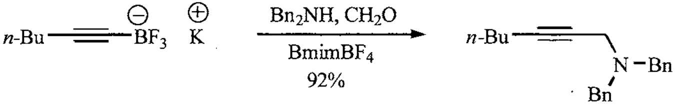


If R = H, this is ***Eschemoser's salt***

Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1189; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 182-184; F. F. Blicke, *Organic Reactions* **1**, 10; J. H. Brewster, E. L. Eliel, *Organic Reactions* **7**, 3.

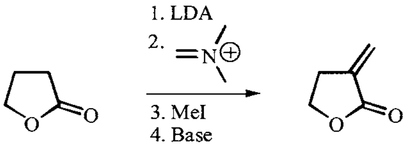
The imminium ion can be trapped by other nucleophiles:



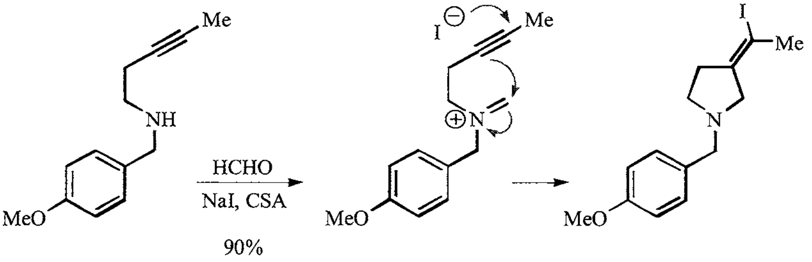
$BmimBF_4$ = butylmethylimidazolium tetrafluoroborate

G. W. Kabalka, B. Venkataiah, G. Dong *Tetrahedron Letters* **2004**, 45, 729

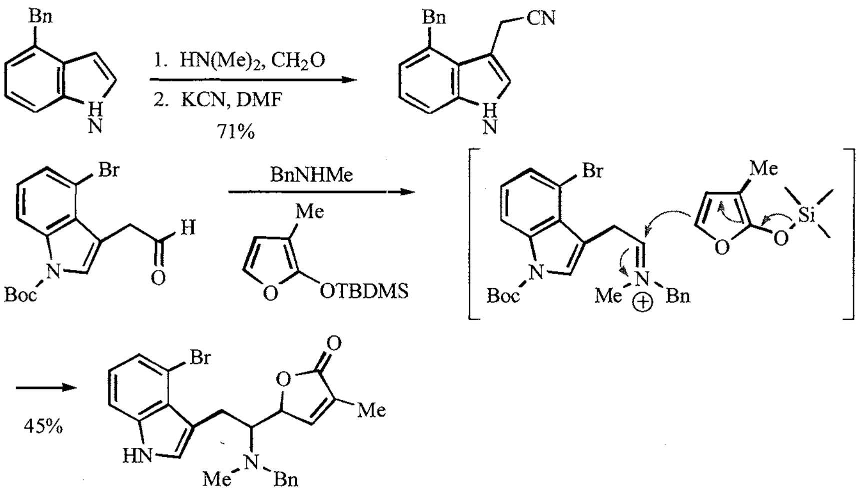
Mannich-Eschenmoser Methylenation



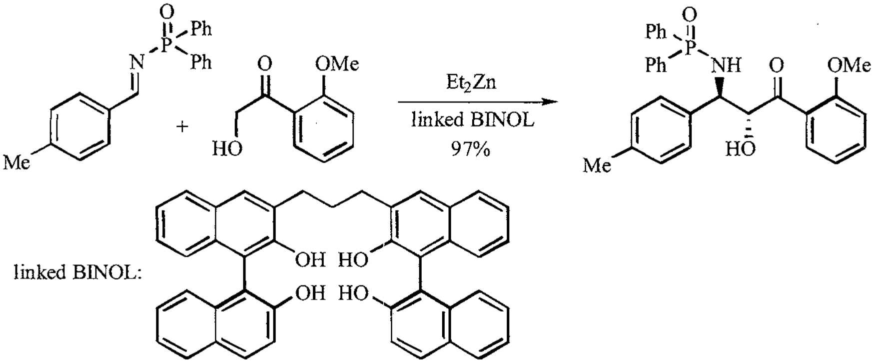
Examples:



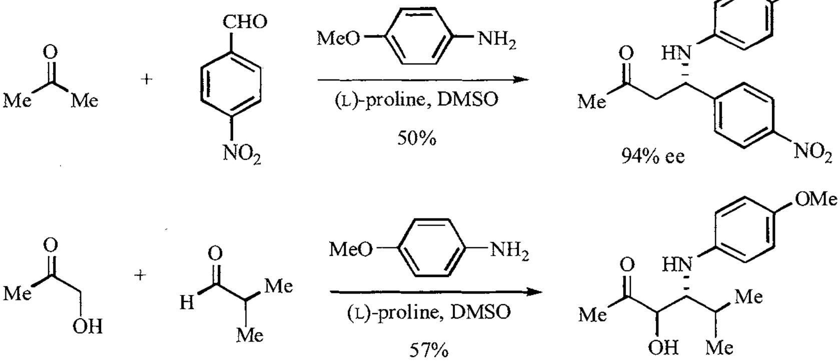
H. Arnold, L. E. Overman, M. J. Sharp, M. C. Witschel *Organic Syntheses* **1992**, 70, 111



S. Liras, C. L. Lynch, A. M. Fryer, B. T. Vu, S. F. Martin, *Journal of the American Chemical Society* **2001**, 123, 5918



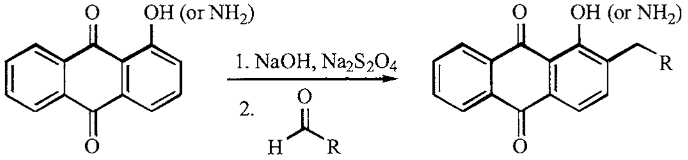
S. Matsunaga, N. Kumagai, S. Harada, M. Shibasaki, *Journal of the American Chemical Society* **2003**, 125, 4712



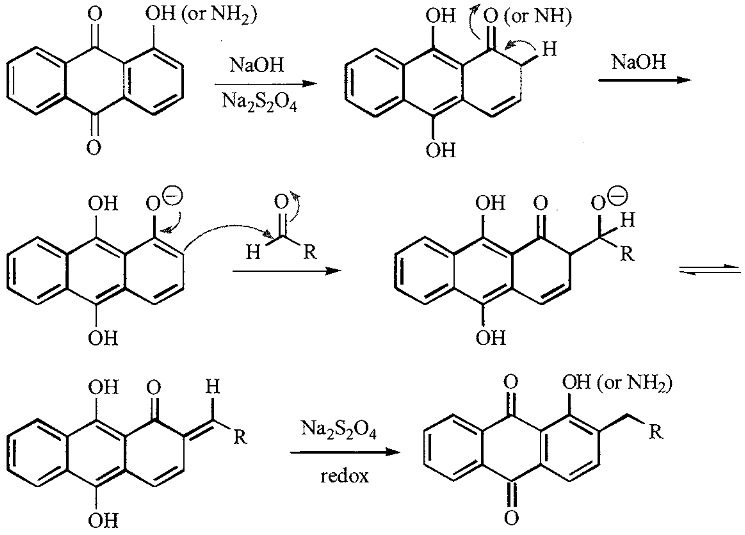
B. List, *Journal of the American Chemical Society* **2000**, 122, 9336

Marschalk Reaction

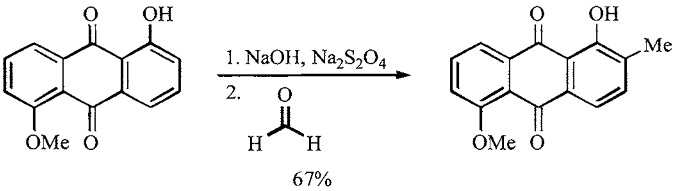
The Reaction:



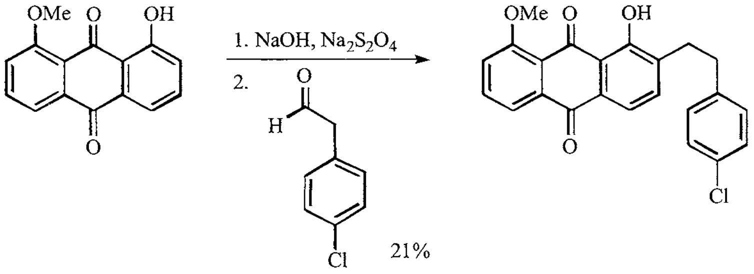
Proposed Mechanism:



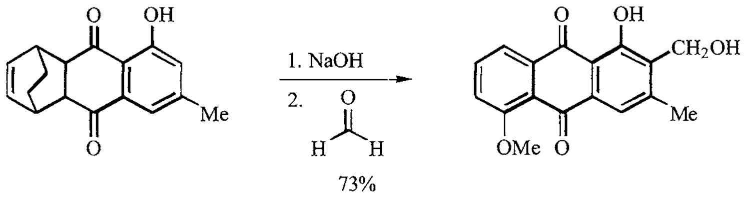
Examples:



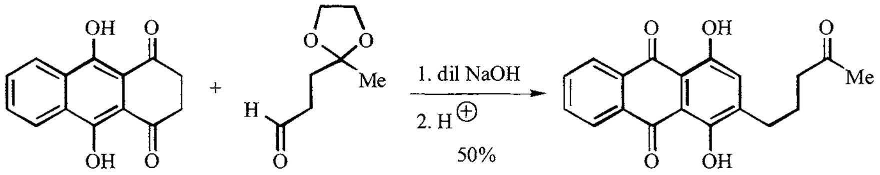
K. Krohn, W. Baltus, *Tetrahedron* **1988**, 44, 49



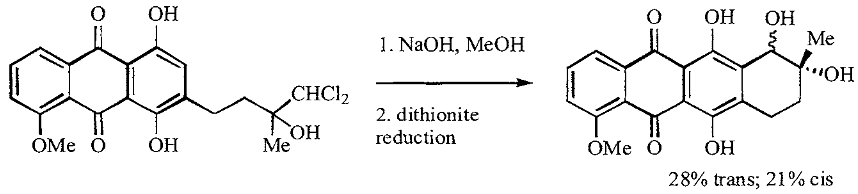
K. Muller, R. Altmann, H. Prinz, *European Journal of Medicinal Chemistry* **2002**, 37, 83



K. Krohn, E. Broser, *Journal of Organic Chemistry* **1984**, 49, 3766



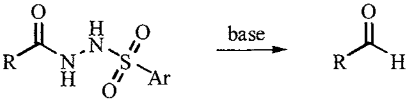
A. B. Argade, A. R. Mehendale, N. R. Ayyangar, *Tetrahedron Letters* **1986**, 27, 3529



K. Krohn, W. Priyono, *Tetrahedron* **1984**, 40, 4609

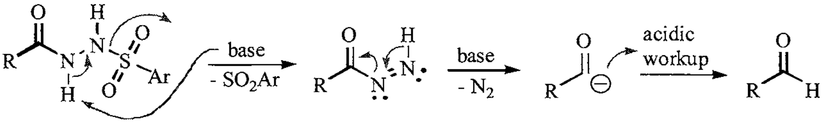
McFadyen-Stevens Aldehyde Synthesis (McFadyen-Stevens Reduction)

The Reaction:

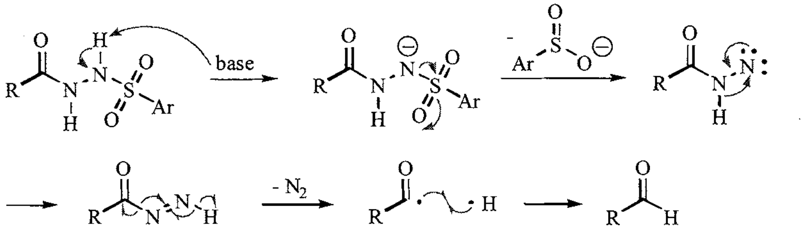


R = Ar or alkyl with no α-protons

Proposed Mechanism:



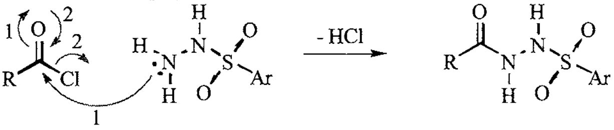
Alternate carbene mechanism:



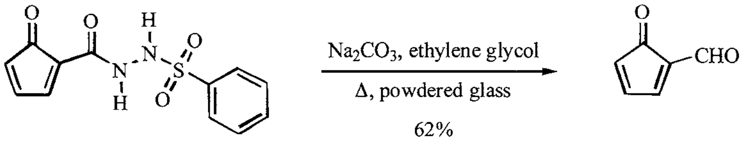
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 534.

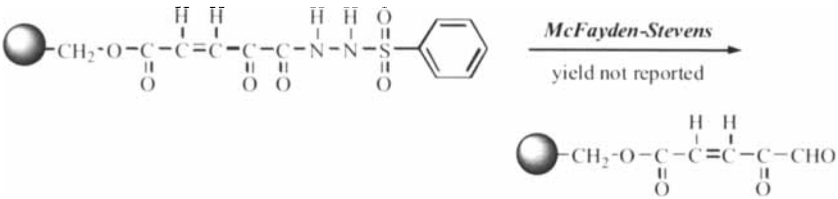
Starting material preparation:



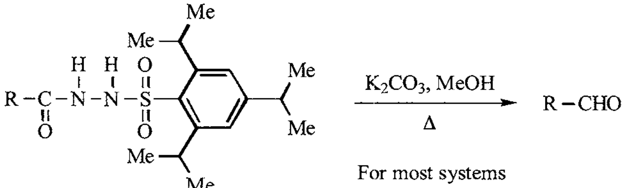
Examples:



M. S. Newman, E. G. Caflisch, Jr., *Journal of the American Chemical Society* **1958**, 80, 862

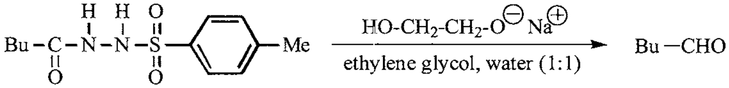


F. Gavina, A. M. Costero, A. M. Gonzalez, *Journal of Organic Chemistry* **1990**, 55, 2060



For most systems
yields about 50%

C. C. Dudman, P. Grice, C. B. Reese, *Tetrahedron Letters* **1980**, 21, 4645

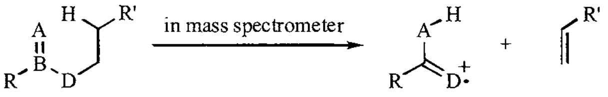


10%

H. Babad, W. Herbert, A. W. Stiles, *Tetrahedron Letters* **1966**, 7, 2927

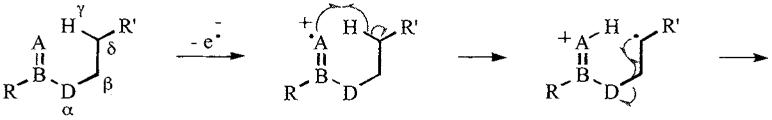
McLafferty Rearrangement

The Reaction:

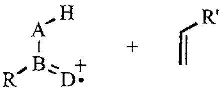


A, B, X = carbon or heteroatom

Proposed Mechanism:



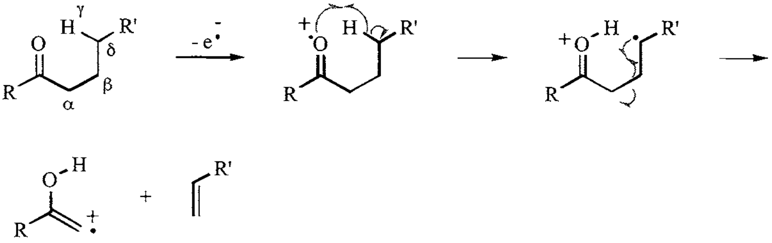
After an electron is lost, the γ hydrogen is abstracted, followed by fragmentation.



D. G. I. Kingston, J. T. Bursey, M. M. Bursey, *Chemical Reviews* **1974**, 74, 215

Notes:

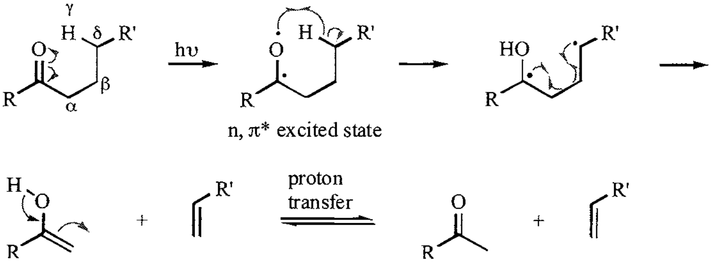
The reaction is most commonly associated with the mass spectral fragmentations of carbonyl derivatives.



A secondary hydrogen atom will migrate about ten times better than a primary hydrogen atom.

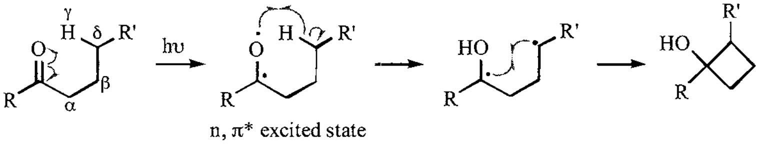
The reaction is often compared to a similar photochemical reaction:

Norrish Type II Cleavage



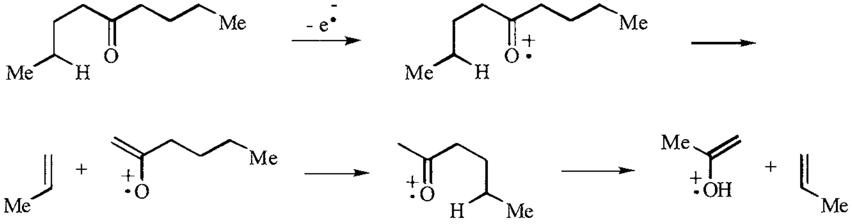
There is also the **Norrish Type I Cleavage**:

Rather than fragmentation of ***Norrish Type II*** biradicals, cyclization can occur. This is called the ***Yang Cyclization***:



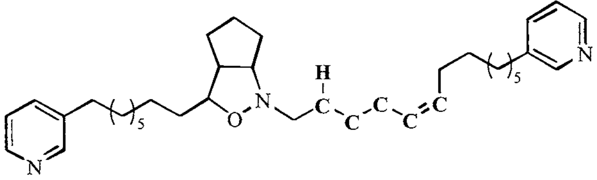
Examples:

A double ***McLafferty Rearrangement***:

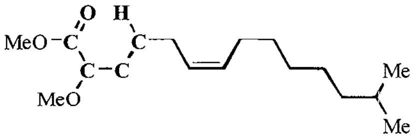


G. Eadon, *Journal of the American Chemical Society* **1972**, 94, 8938

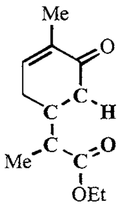
The utility of the ***McLafferty rearrangement*** in assigning structures is easily documented: For each example, the important atoms are shown **in bold**.



J. E. Baldwin, S. P. Romeril, V. Lee, T. D. W. Claridge, *Organic Letters* **2001**, 3, 1145



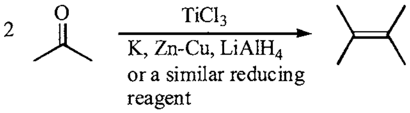
N. Carballeira, V. Pagan, *Journal of Natural Products* **2001**, 64, 620



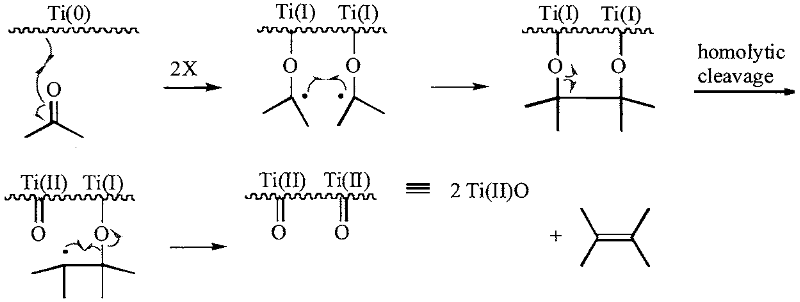
W. Engel, *Journal of Agricultural and Food Chemistry* **2002**, 50, 1686

McMurry (Olefination) Reaction

The Reaction:



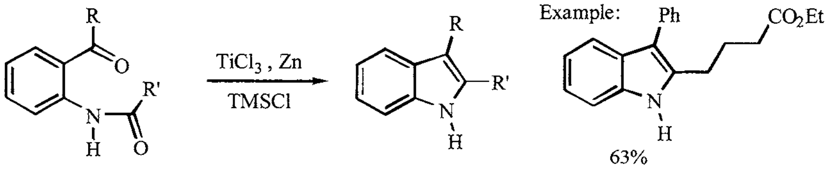
Proposed Mechanism:



Notes:

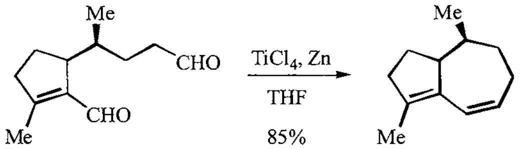
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1561; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 184-187
See: ***McMurry Reagent***

The reaction of a ketone with an amide provides a unique entry into the indole skeleton (***Furstner Indole Synthesis***).

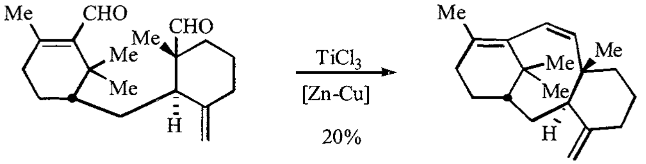


A. Furstner, B. Bogdanovic, *Angewandte Chemie International Edition in English* **1996**, 35, 2442; A. Furstner, D. N. Jumbam, *Tetrahedron* **1992**, 48, 5991

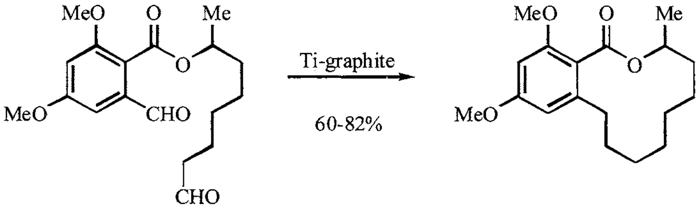
Examples:



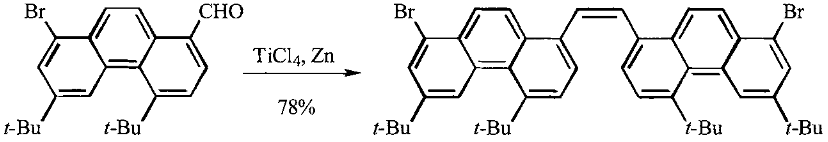
E. Lee, C. H. Yoon, *Tetrahedron Letters* **1996**, 37, 5929



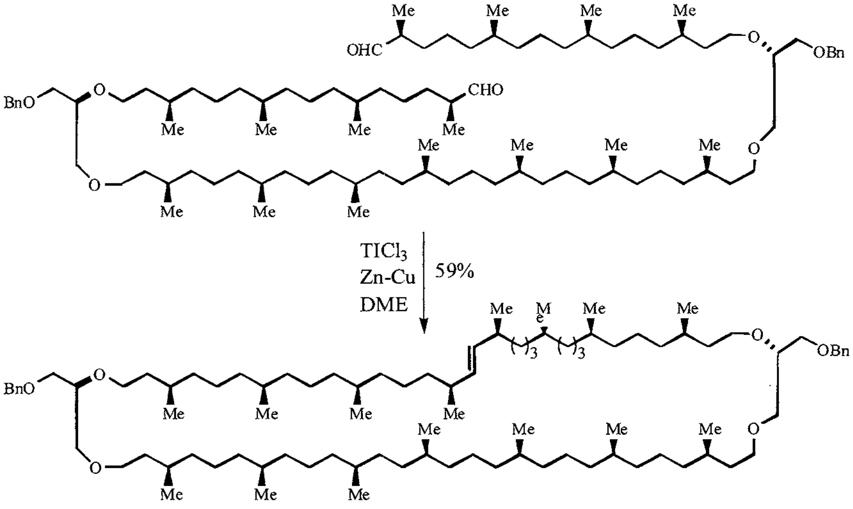
A. S. Kende, S. Johnson, P. San Filippo, J. C. Hodges, L. N. Jungheim, *Journal of the American Chemical Society* **1986**, 108, 3513



A. Furstner, O. R. Thiel, N. Kindlar, B. Bartkowska, *Journal of Organic Chemistry* **2000**, 65, 7990



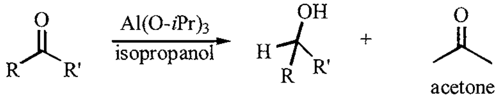
F. B. Mallory, K. E. Butler, A. Bérubé, E. D. Luzik, Jr., C. W. Mallory, E. J. Brondyke, R. Hiremath, P. Ngo, P. Carroll, *Tetrahedron* **2001**, 57, 3715



T. Eguchi, K. Ibaragi, K. Kakinuma, *Journal of Organic Chemistry* **1998**, 63, 2689

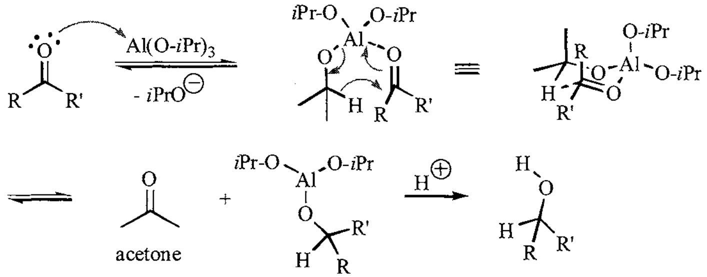
Meerwein-Ponndorf-Verley Reduction

The Reaction:



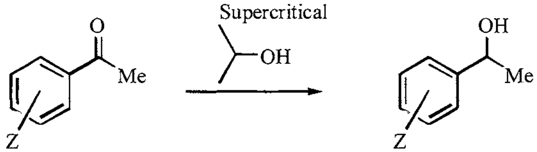
This is the reverse of the ***Oppenauer Oxidation***.

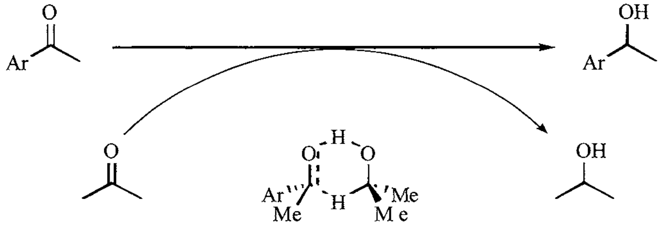
Proposed Mechanism:



Notes:

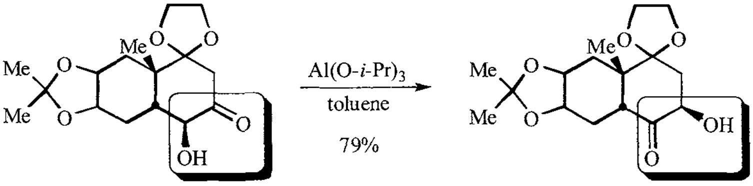
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1199; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 187-188; A. Wilds, *Organic Reactions* **2**, 5.





A Hamett analysis provides $\rho = 0.33$; suggestive of a not-strongly ionized transition state.
T. Kamitanaka, T. Matsuda, T. Haradon, *Tetrahedron Letters* **2003**, 44, 4551

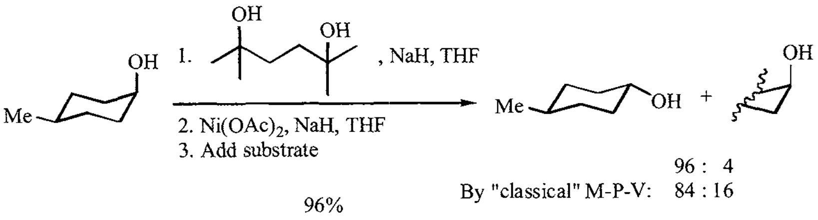
Examples:



Note also the oxidation

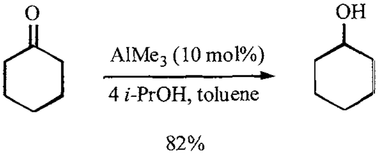
T. K. M. Shing, C. M. Lee, H. Y. Lo, *Tetrahedron Letters* **2001**, 42, 8361

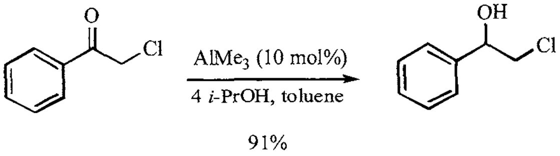
Simple alcohol epimerization via a redox system:



R. Vanderesse, G. Feghouli, Y. Fort, P. Caubere, *Journal of Organic Chemistry* **1990**, 55, 5916

A catalytic reaction:



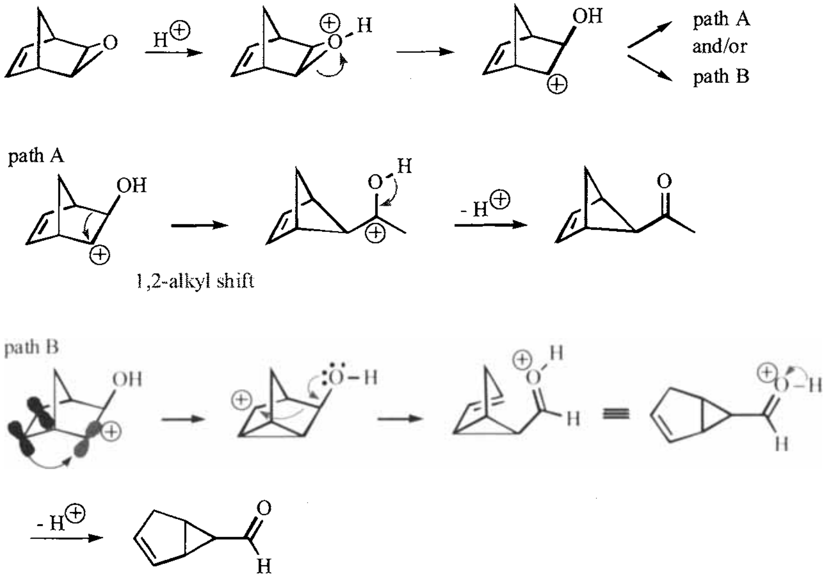


E. J. Campbell, H. Zhou, S. T. Nguyen, *Organic Letters* **2001**, 3, 2391

Meinwald Rearrangement

The Reaction:

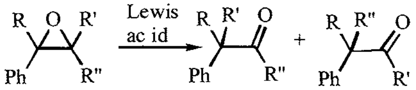
Proposed Mechanism:



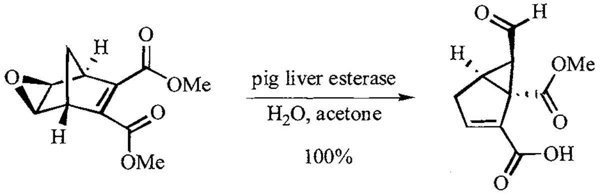
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1398.

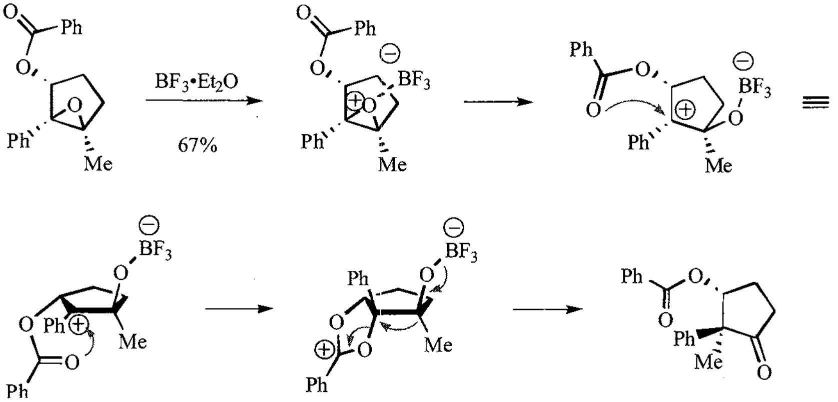
A more generic reaction generally associated with this Name Reaction is:



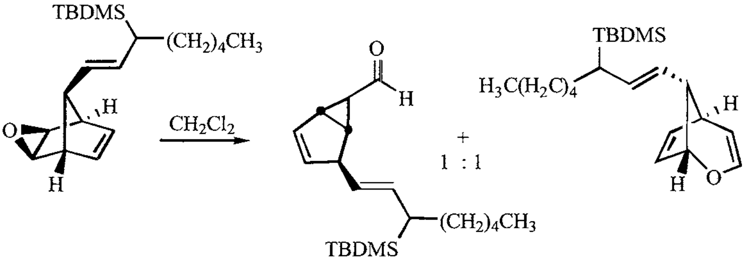
Examples:



S. Niwayama, S. Kobayashi, M. Ohno, *Journal of the American Chemical Society* **1994**, 116, 3290

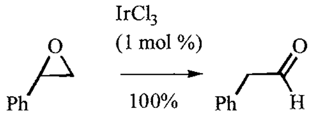


Y. Kita, A. Furukawa, J. Futamura, K. Higuchi, K. Ueda, H. Fujioka, *Tetrahedron* **2001**, 57, 815



A.D. Baxter, S. M. Roberts, M. Roberts, F. Scheinmann, B. J. Wakefield, R. F. Newton, *Journal of the Chemical Society, Chemical Communications* **1983**, 932

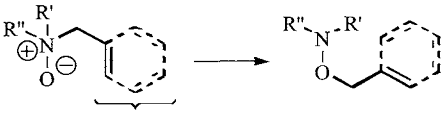
Use of IrCl$_3$ catalyst:



I. Karame, M. L. Tommasino, M. Lemaire, *Tetrahedron Letters* **2003**, 44, 7687

Meisenheimer Rearrangement

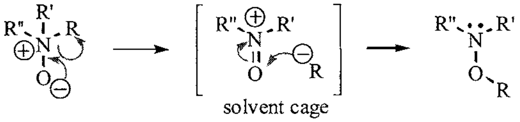
The Reaction:



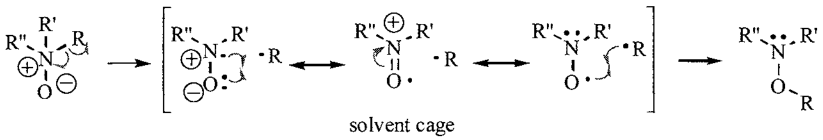
Usually allyl or benzyl.

Proposed Mechanism:

Ionic and radical mechanisms have been proposed:



or

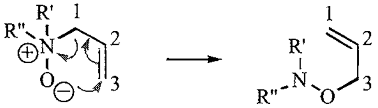


U. Schöllkopf, M. Patsch, H. Schäfer, *Tetrahedron Letters* **1964**, 5, 2515;
N. Castagnoli, Jr., J. C. Craig, A. P. Melikian, S. K. Roy, *Tetrahedron* **1970**, 26, 4319

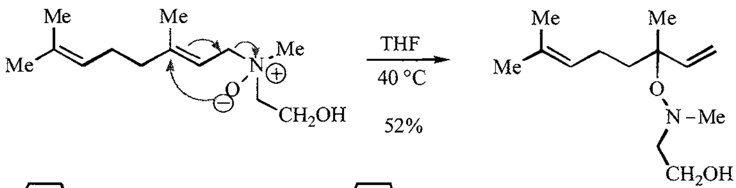
Notes:

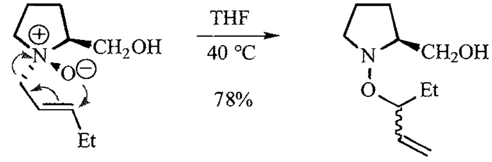
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1420

A 2,3-sigmatropic rearrangement is possible:

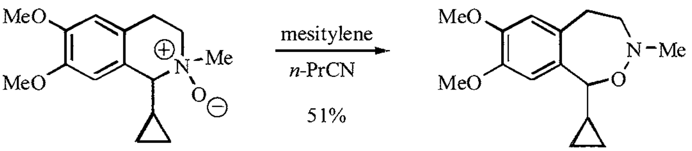


Examples:

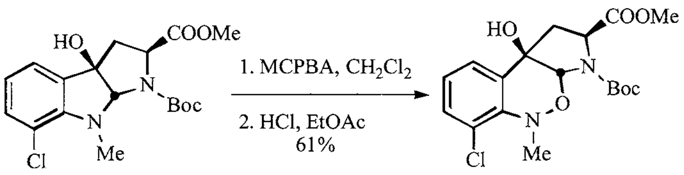




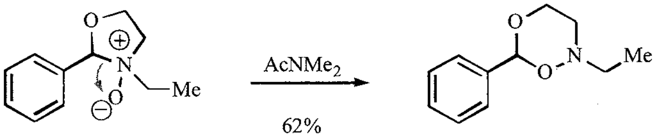
J. E. H. Buston, I. Coldham, K. R. Mulholland, *Tetrahedron: Asymmetry* **1998**, 9, 1995



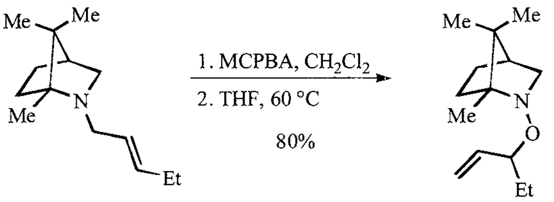
T. S. Bailey, J. B. Bremner, D. C. Hockless, B. W. Skelton, A. H. White, *Tetrahedron Letters* **1994**, 35, 2409



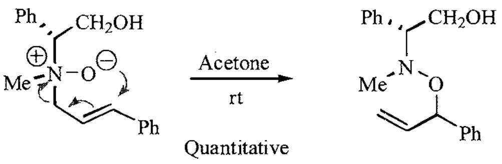
C. Didier, D. J. Critcher, N. D. Walshe, Y. Kojima,Y. Yamauchi, A. G. M. Barrett, *Journal of Organic Chemistry* **2004**, 69, 7875



S. Saba, P. W. Domkowski, F. Firooznia, *Synthesis* **1990**, 921



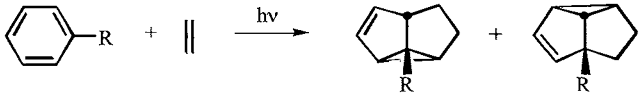
J. E. H. Buston, I. Coldham, K. R. Mulholland, *Journal of the Chemical Society, Perkin Transactions* **1999**, 2327



J. Blanchet, M. Bonin, L. Micouin, H.-P. Husson, *Tetrahedron Letters* **2000**, 41, 8279

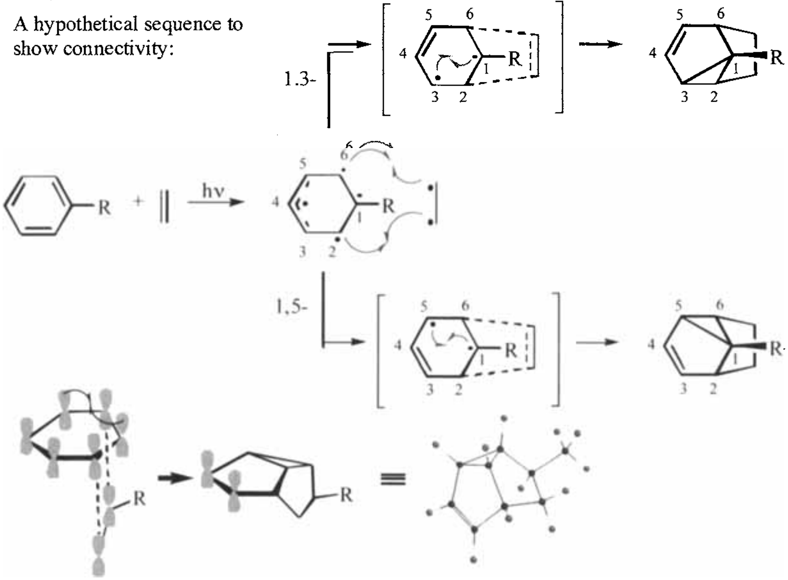
Meta Photocycloaddition Reaction of Arenes

The Reaction:



Proposed Mechanism:

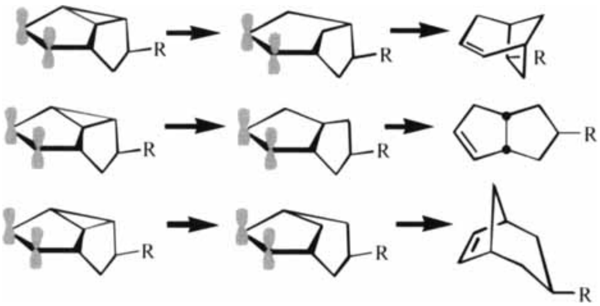
A hypothetical sequence to show connectivity:

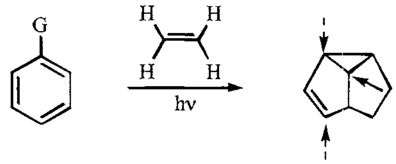


Notes:

See: http://www.stanford.edu/group/pawender/html/photo.html for a useful overview of the important work of the Wender group and its use of this reaction.

In this drawing it is apparant that the ring has excellent potential for synthesis.
By proper design of cyclopropane cleavage one can arrive at a number of important ring systems:

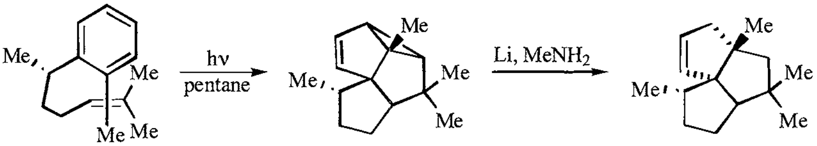




G = Electron donating
or withdrawing group.

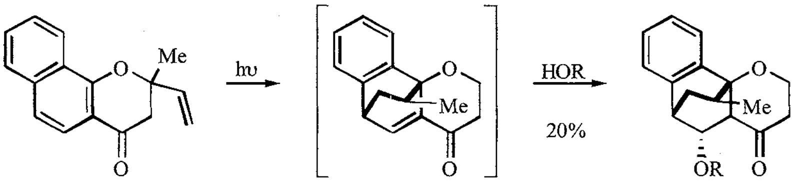
—— Position for EDG
- - - Position for EWG

Examples:

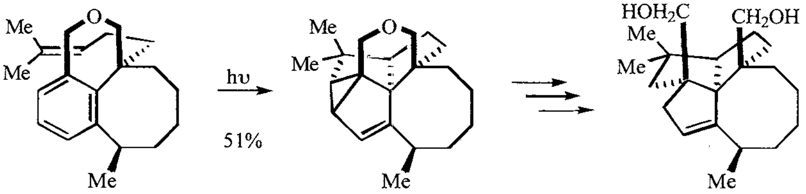


Silphinene

P. A. Wender, R. J. Ternansky, *Tetrahedron Letters* **1985**, 26, 2625



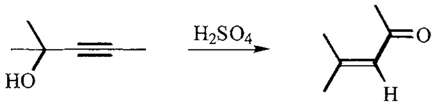
G. P. Kalena, P. Pradhan, V. S. Puranik, A. Banerji, *Tetrahedron Letters* **2003**, 44, 2011



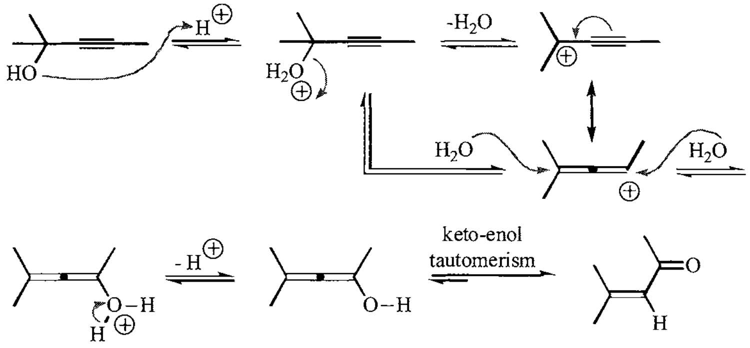
P. A. Wender, T. W. von Geldern, B. H. Levine, *Journal of the American Chemical Society* **1988**, 110, 4858

Meyer-Schuster propargyl alcohol rearrangement

The Reaction:



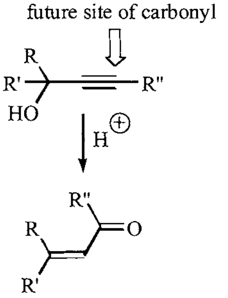
Proposed Mechanism:



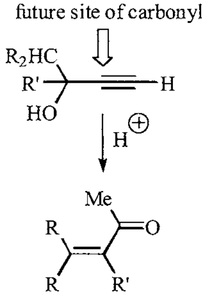
M. Edens, D. Boerner, C. R. Chase, D. Nass, M. D. Schiavelli, *Journal of Organic Chemistry* **1977**, 42, 3403

Notes:

The ***Meyer-Schuster Rearrangement*** is similar to the ***Rupe Rearrangement***.

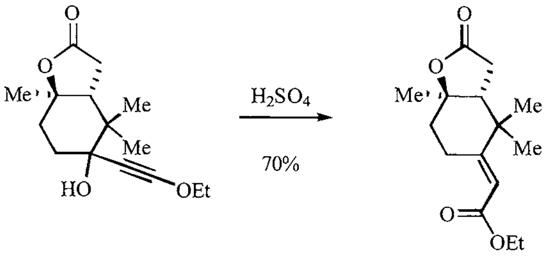


When R'' = H, an aldehyde is the product.
R' may be H

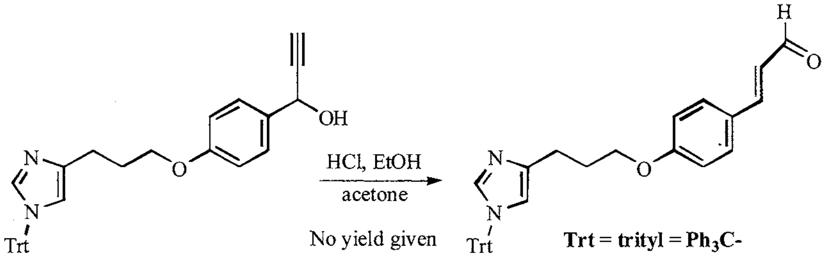


No aldehyde product

Examples:

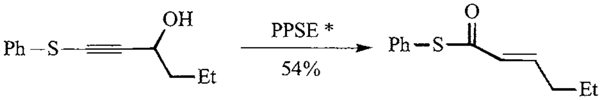


D. Crich, S. Natarajan, J. Z. Crich, *Tetrahedron* **1997**, 53, 7139



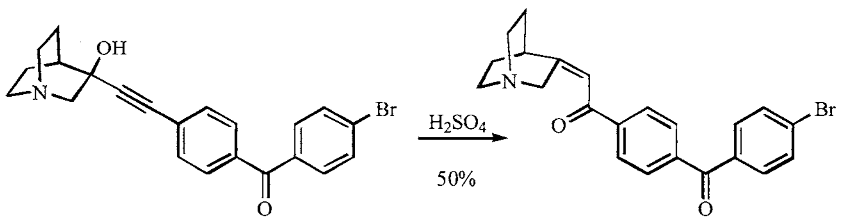
Trt = trityl = Ph_3C-

H. Stark, B. Sadek, M. Krause, A. Huls, X. Ligneau, C. R. Ganellin, J.-M. Arrang, J.-C. Schwartz, W. Schunak, *Journal of Medicinal Chemistry* **2000**, 43, 3987



* polyphosphoric acid trimethylsilylester

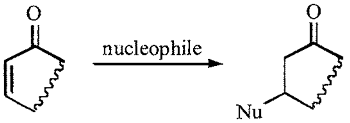
M.Yoshimatsu, M. Naito, M. Kawahigashi, H. Shimizu, T. Kataoka, *Journal of Organic Chemistry* **1995**, 60, 4798



G. R. Brown, D. M. Hollinshead, E. S. E. Stokes, D. S. Clarke, M. Eakin, A. J. Foubister, S. C. Glossop, D. Griffiths, M. C. Johnson, F. McTaggart, D. J. Mirrlees, G. J. Smith, R. Wood, *Journal of Medicinal Chemistry* **1999**, 42, 1306

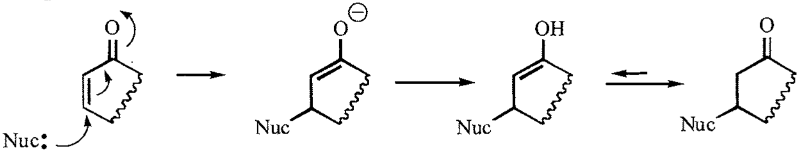
Michael Reaction

The Reaction:



1,4 additions to enones

Proposed Mechanism:



See: T. Poon, B. P. Mundy, T. W. Shattuck, *Journal of Chemical Education,* **2002**, 79, 264

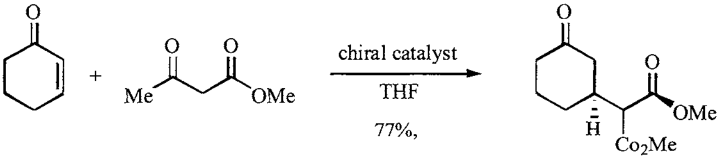
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp. 1022-1024; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 189-191; E. D. Bergmann, D. Ginsburg, R. Pappo, *Organic Reactions* **10**, 3; T. Mukaiyama, S. Kobayashi, *Organic Reactions* **46**, 1; R. D. Little, M. R. Masjedizadeh, O. Wallwuist, J. I. McLoughlin, *Organic Reactions* **47**, 2.

In a strict sense the name of this reaction should only be applied to C-based 1,4-nucleophilic addition reactions. There have been interpretations to include other hetero-based nucleophiles.

For these reactions one can always consider the potential competition of 1,2- vs. 1,4 addition:

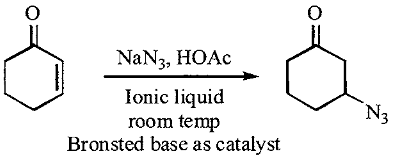
Examples:

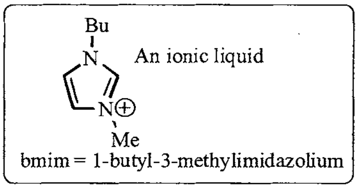


(92% ee)

K. Majima, R. Takita, A. Okada, T. Ohshima, M. Shibasaki, *Journal of the American Chemical Society* **2003**, 125, 15837

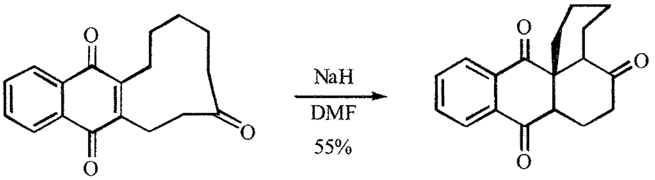
An *Aza-Michael Addition*:



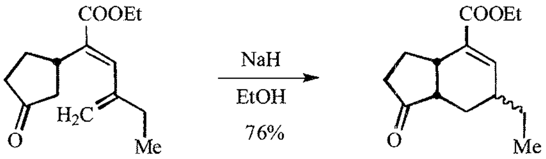


Ionic liquids: ***BmimPF$_6$***, BmimBr, BmimBF$_4$
Catalysts: Et$_3$N, pyridine

L.-W. Xu, L. Li, C.-G. Xia, S.-L. Zhou, J.-W. Li, *Tetrahedron Letters* **2004**, 45, 1219

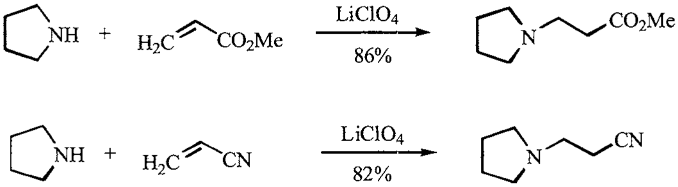


D. M. Gordon, S. J. Danishefsky, G. K. Schulte, *Journal of Organic Chemistry* **1992**, 57, 7052

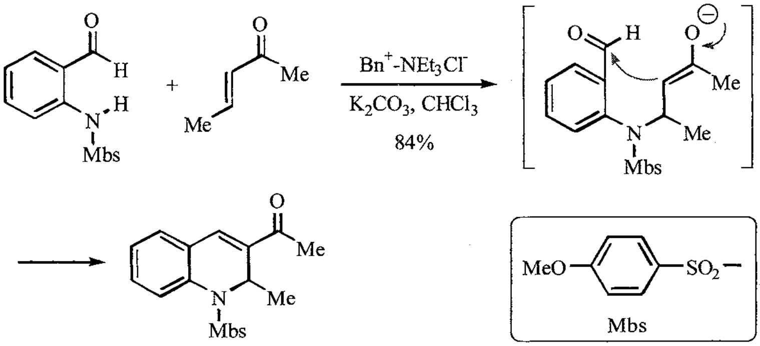


S. Nara, T. Toshima, A. Ichihara, *Tetrahedron* **1997**, 53, 9509

$LiClO_4$ accelerated reactions under solvent-free conditions:



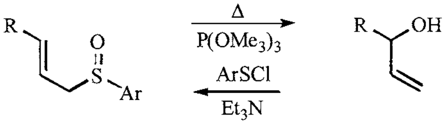
N. Azizi, M. R. Saidi, *Tetrahedron* **2004**, 60, 383



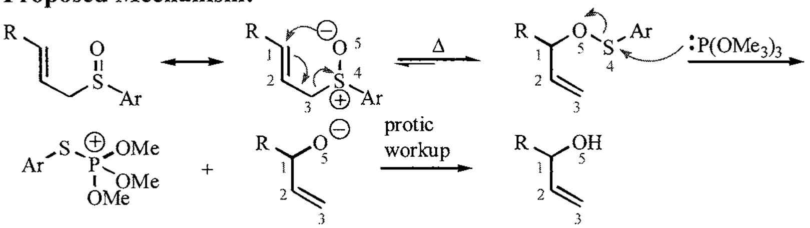
K. Makino, O. Hara, Y. Takiguchi, T. Katano, Y. Asakawa, K. Hatano, Y. Hamada, *Tetrahedron Letters* **2003**, 44, 8925

Mislow-Evans Rearrangement (Evans (-Mislow) Rearrangement)

The Reaction:



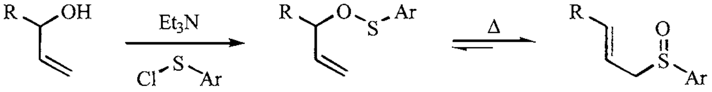
Proposed Mechanism:

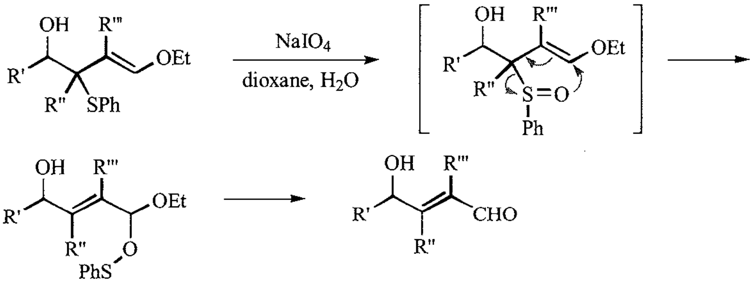


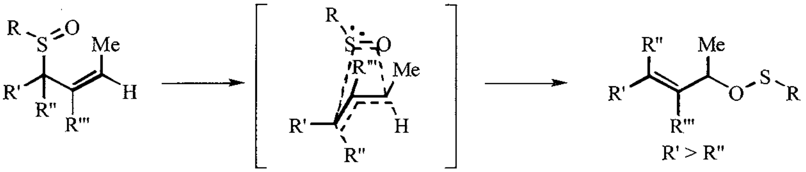
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1455.

The reverse reaction is accomplished by a reaction with ArSCl and thermal rearrangement.



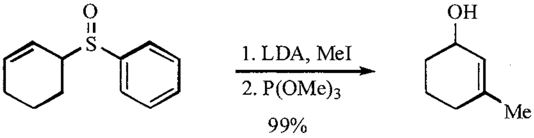




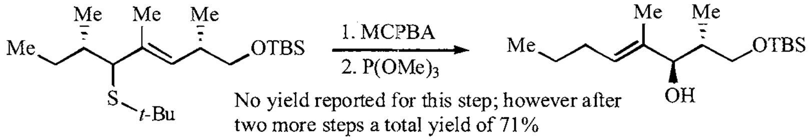
The selectivity for *E*-isomers should increase as $R^1 > R^2$ increases.

T. Sato, J. Otera, H. Nozaki, *Journal of Organic Chemistry* **1989**, 54, 2779

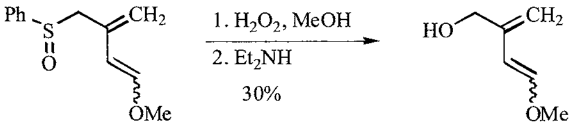
Examples:



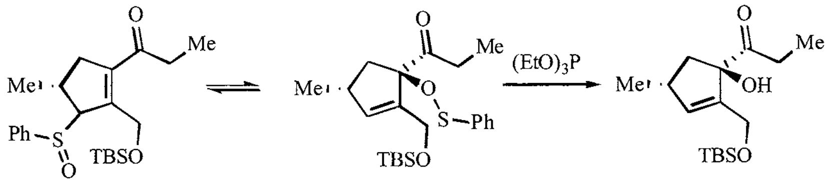
D. A. Evans, G. C. Andrews, T. T. Fujimi, D. Wells, *Tetrahedron Letters* **1973**, 14, 1385



A. K. Mapp, C. H Heathcock, *Journal of Organic Chemistry* **1999**, 64, 23



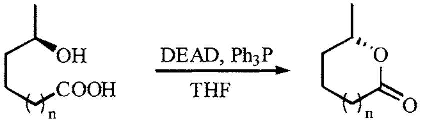
T. Mandai, K. Osaka, M. Kawagishi, M. Kawada, J. Otera, *Journal of Organic Chemistry* **1984**, 49, 3595



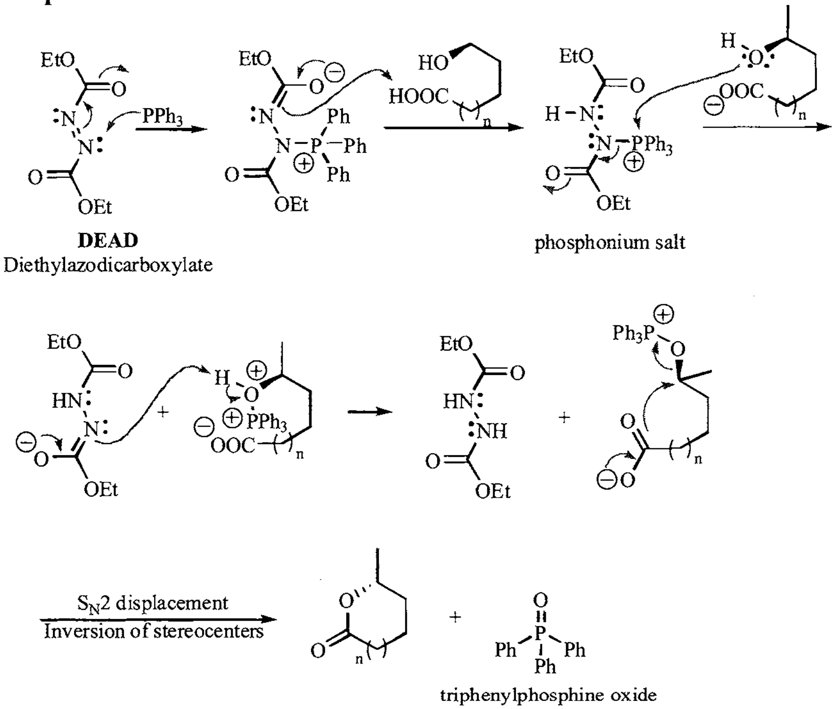
Reported in a Review: A. B. Smith, III, C. M. Adams, *Accounts of Chemical Research* **2004**, 37, 365

Mitsunobu Lactonization

The Reaction:



Proposed Mechanism:

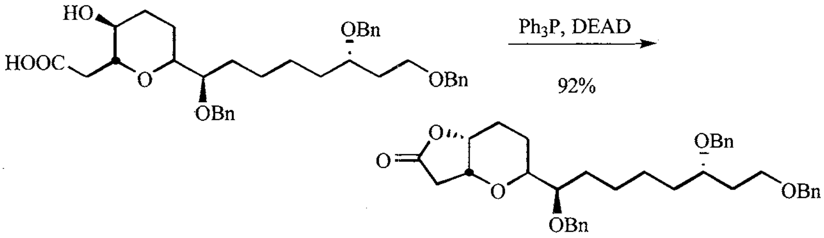


Notes:

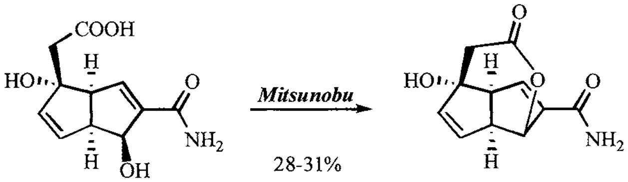
See: ***Mitsunobu Reaction*** and ***Macrolactonization Methods***.

This lactonization process inverts the stereochemistry of the alcohol portion of the lactone.

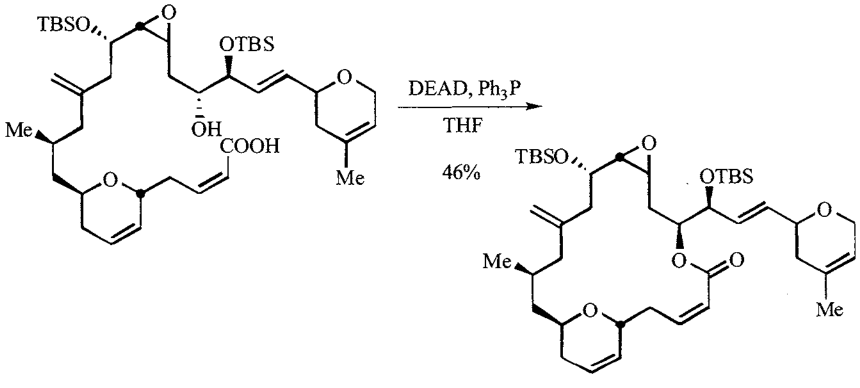
Examples:



S. Takahashi, A. Kubota, T. Nakata, *Organic Letters* **2003**, 5, 1353



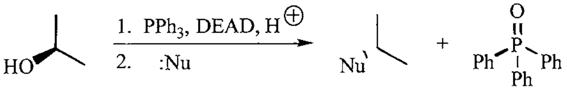
A. B. Smith, III, G. A. Sulikowski, K. Fujimoto, *Journal of the American Chemical Society* **1989**, 111, 8039



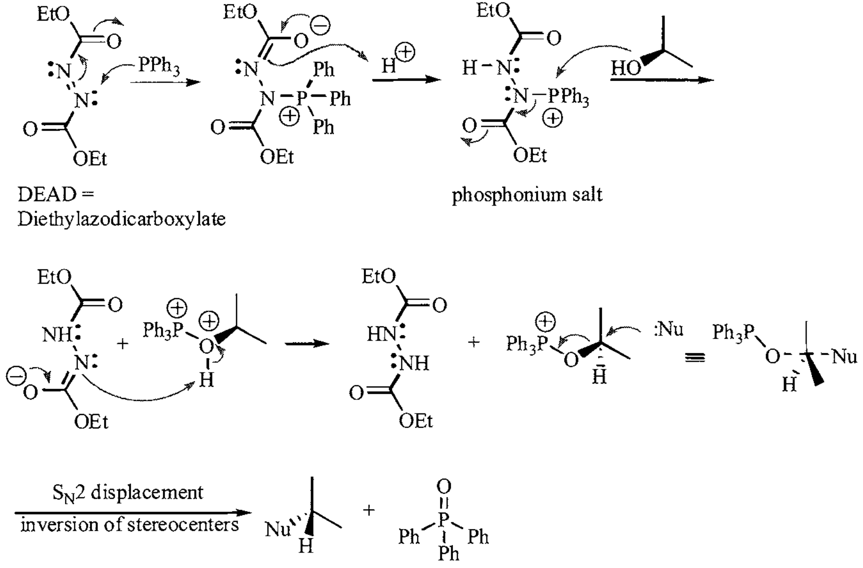
M. T. Crimmins, M. G. Stanton, S. P. Allwein, *Journal of the American Chemical Society* **2002**, 124, 5959

Mitsunobu Reaction

The Reaction:



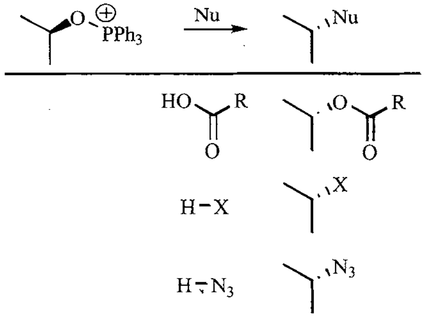
Proposed Mechanism:



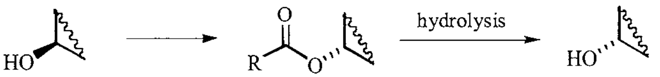
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 486; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 192-194; D. L. Hughes, *Organic Reactions* **42**, 2

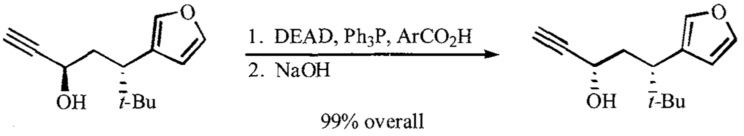
A number of nucleophilic displacements from the ***Mitsunobu*** intermediate are possible:



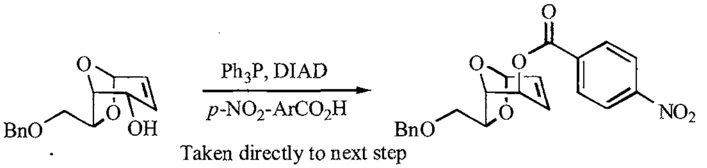
When a carboxylic acid is used as the nucleophile, simple ester hydrolysis releases the alcohol, providing an inversion of alcohol stereochemistry.



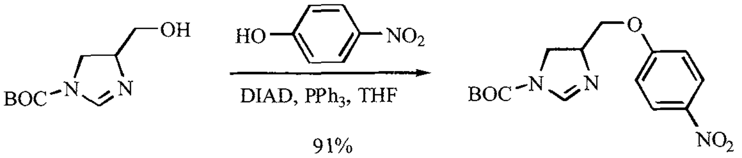
Examples:



M. T. Crimmins, J. M. Pace, P. G. Nantermet, A. S. Kim-Meade, J. B. Thomas, S. H. Watterson, A. S. Wagman, *Journal of the American Chemical Society* **1999**, 121, 10249

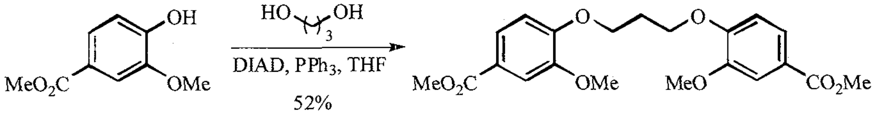


K. Kadota, M. Takeuchi, T. Taniguchi, K. Ogasawdra, *Organic Letters* **2001**, 3, 1769



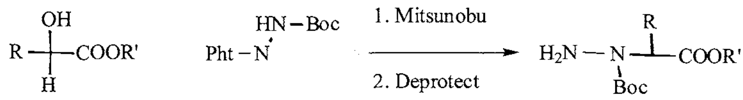
N. Defacqz, V. Tran-Trieu, A. Cordi, J. Marchand-Brynaert, *Tetrahedron Letters* **2003**, 44, 9111

***Mitsunobu Etherification*:**



S. J. Gregson, P. W. Howard, D. R. Gullick, A. Hamaguchi, K. E. Corcoran, N. A. Brooks, J. A. Hartley, T. C. Jenkins, S. Patel, M. J. Guille, D. E. Thurston, *Journal of Medicinal Chemistry* **2004**, 47, 1161

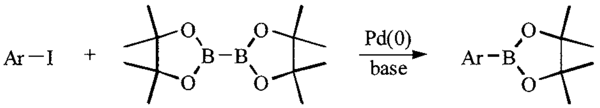
A general protocol:



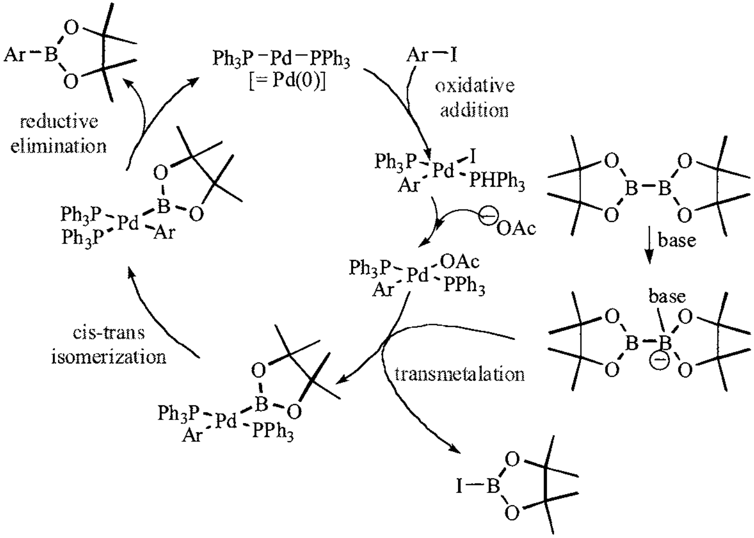
N. Brosse, A. Grandeury, B. Jamart-Gregoire, *Tetrahedron Letters* **2002**, 43, 2009

Miyaura Boration Reaction

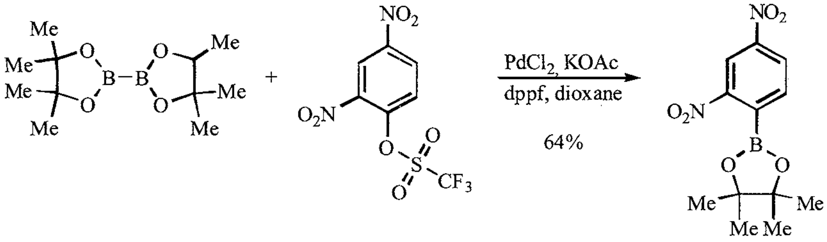
The Reaction:



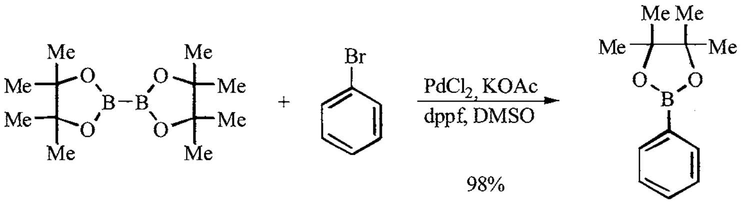
Proposed Mechanism:

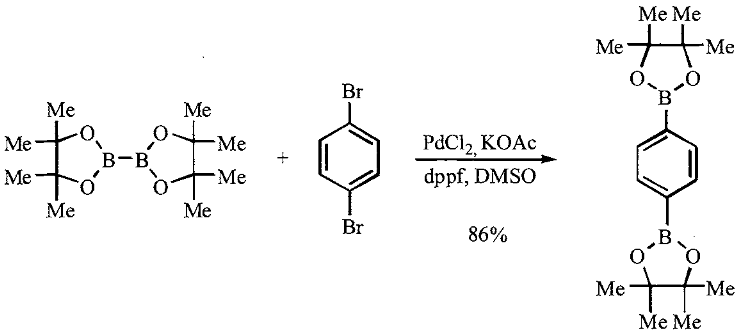


Examples:



T. Ishiyama, Y. Itoh, T. Kitano, N. Miyaura, *Tetrahedron Letters* **1997**, 38, 3447

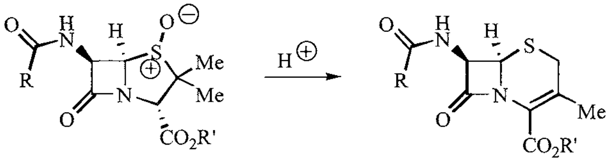




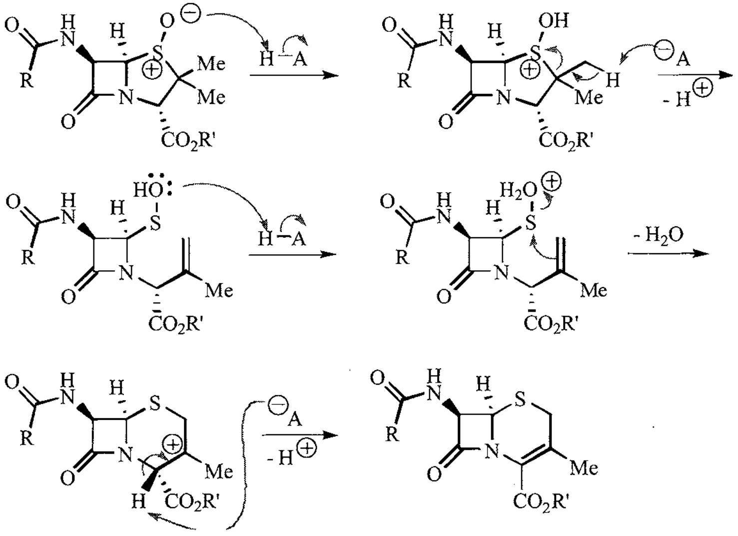
T. Ishiyama, M. Murata, N. Miyaura, *Journal of Organic Chemistry* **1995**, 60, 7508

Morin Rearrangement

The Reaction:



Proposed Mechanism:

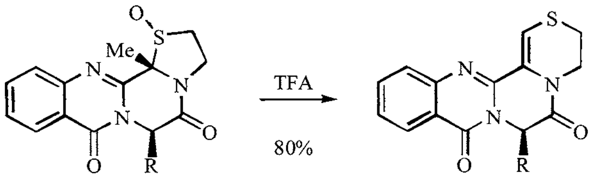


Notes:

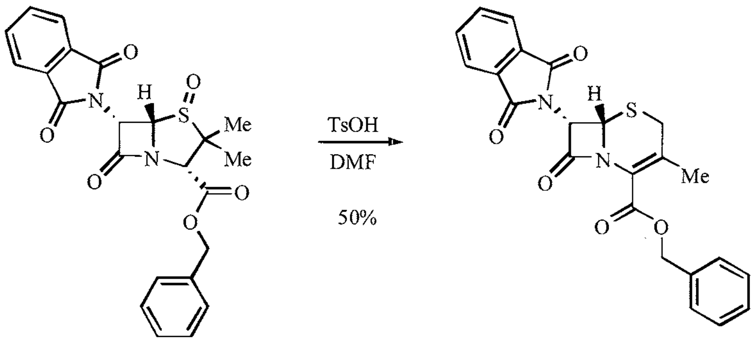
R. B. Morin, B. G. Jackson, R. A. Mueller, E. R. Lavagnino, W. B. Scanlon, S. L. Andrews, *Journal of the American Chemical Society* **1963**, 85, 1896

An intermediate of this rearrangement has been trapped:
J. D. Freed, D. J. Hart, N. A. Magomedov, *Journal of Organic Chemistry* **2001**, 66, 839

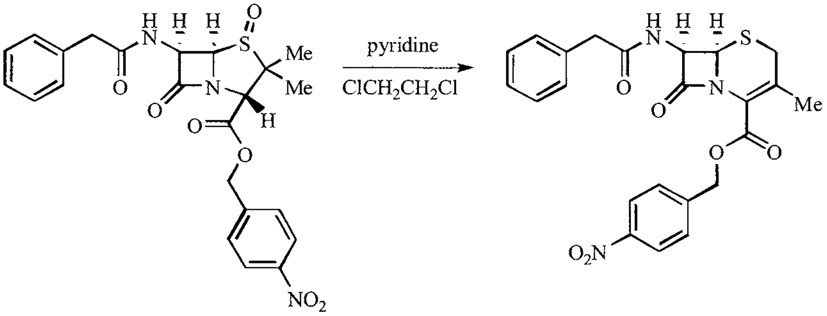
Examples:



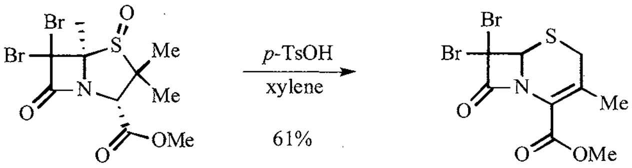
D. J. Hart, N. Magomedov, *Journal of Organic Chemistry* **1999**, 64, 2990



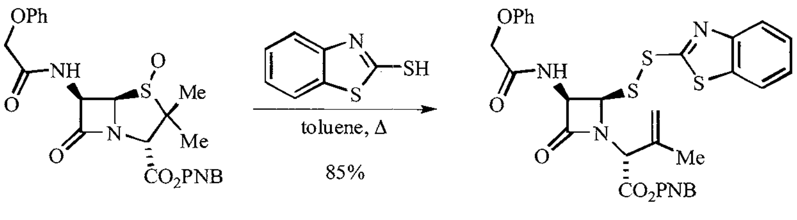
T. Fekner, J. E. Baldwin, R. M. Adlington, D. J. Schofield, *Journal of the Chemical Society, Chemical Communications* **1996**, 1989



A. Nudelman, R. J. McCaully, *Journal of Organic Chemistry* **1977**, 42, 2887



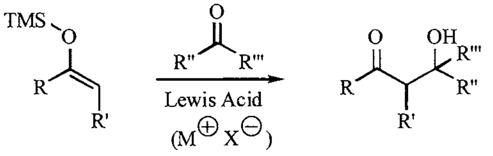
J. P. Clayton, J. H. C. Nayler, M. J. Pearson, R. Southgate, *Journal of the Chemical Society, Perkin Transactions 1* **1974**, 22



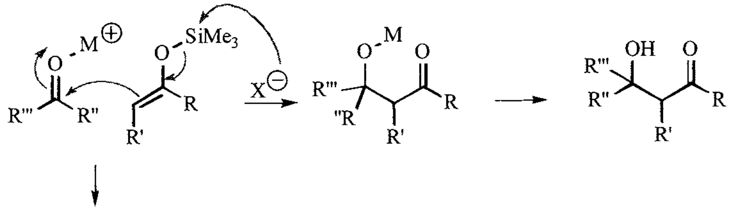
V. Farina, J. Kant, *Tetrahedron Letters* **1992**, 33, 3559

Mukaiyama Reaction

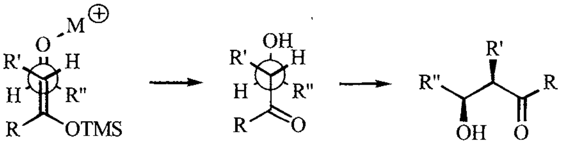
The Reaction:



Proposed Mechanism:



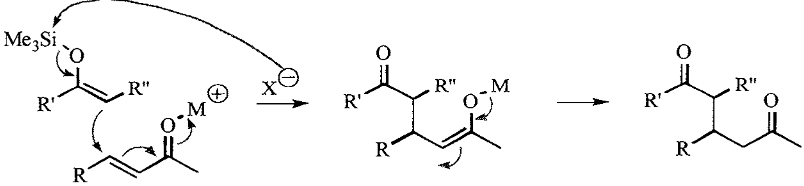
alternate view to address stereochemistry, R''' = H



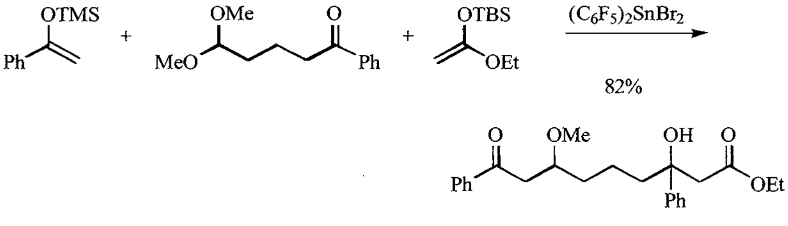
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001,p.1223.

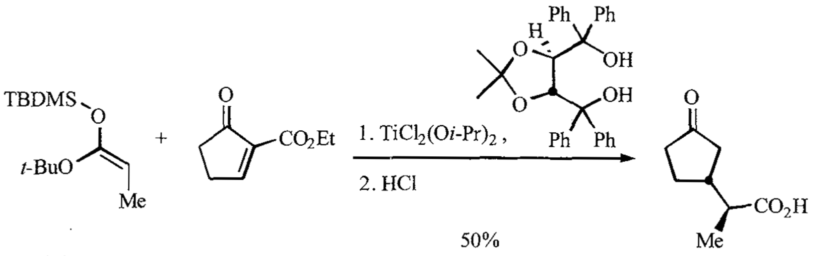
A variant with enones: the ***Mukaiyama Michael Reaction***:



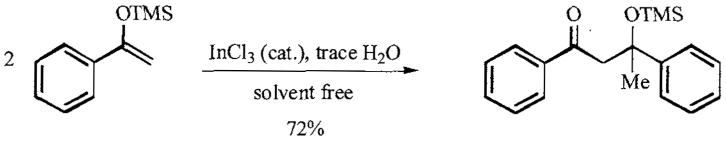
Examples:



J.-x. Chen, J. Otera, *Angewandte Chemie International Edition in English* **1998**, 37, 91

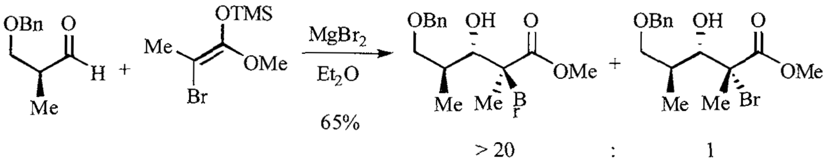


A. Ishii, J. Kojima, K. Mikami, *Organic Letters* **1999**, 1, 2013

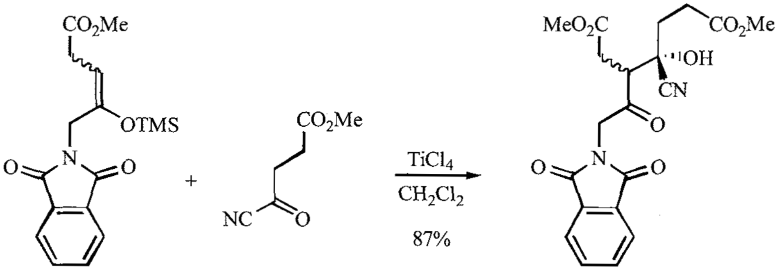


Control of water with the $InCl_3$ is critical to the reaction.

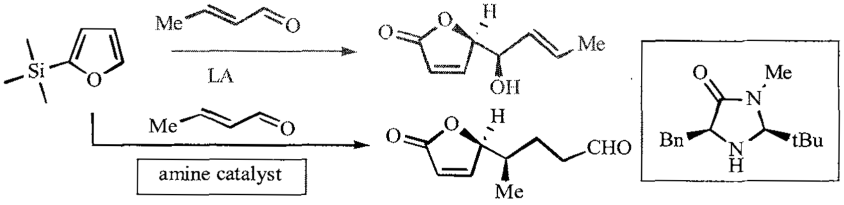
S. Chancharunee, P. Perlmutter, M. Statton, *Tetrahedron Letters* **2002**, 44, 5683



Y. Guindon, K. Houde, M. Prevost, B. Cardinal-David, B. Daoust, M. Benchegroun, B. Guerin, *Journal of the American Chemical Society* **2001**, 123, 8496



A. R. Chaperon, T. M. Engeloch, R. Neier, *Angewandte Chemie International Edition in English* **1998**, 37, 358

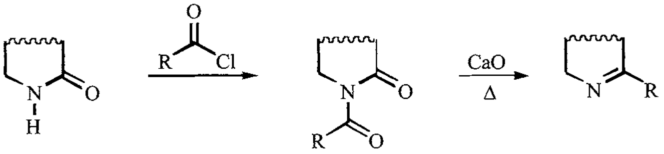


Developed and tested a new approach to a common natural products subunit

S. P. Brown, N. C. Goodwin, D. W. C. MacMillan, *Journal of the American Chemical Society* **2003**, 125, 1192

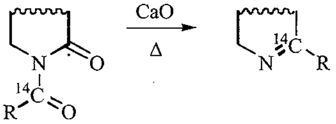
Mundy *N*-Acyllactam Rearrangement

The Reaction:



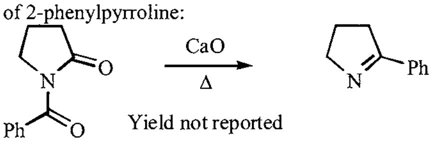
Proposed Mechanism:

Not established, however the path of ^{14}C label as follows:



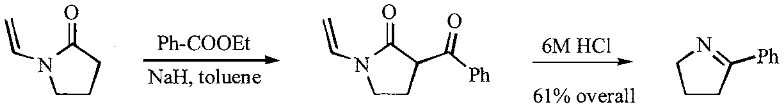
Notes:

This sequence can provide easy access to substituted pyrrolines. For example, the simple synthesis of 2-phenylpyrroline:



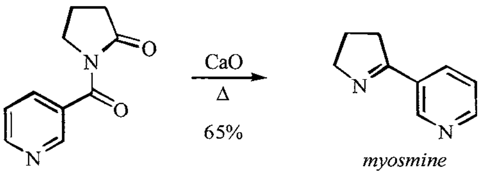
B. P. Mundy, B. R. Larsen, L. F. McKenzie, G. Braden, *Journal of Organic Chemistry* **1972**, 37, 1635

is also accomplished by:

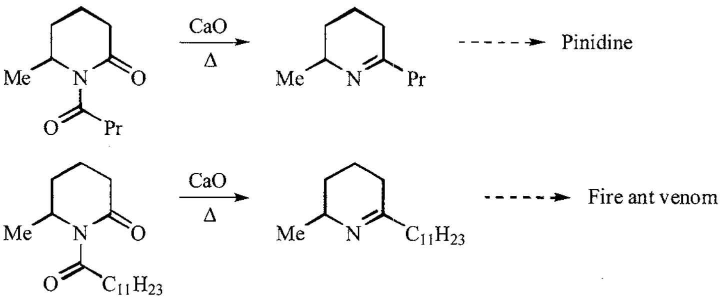


K. L. Sorgi, C. A. Maryanoff, D. F. McComsey, B. E. Maryanoff, *Organic Syntheses*, Vol. 75, 215

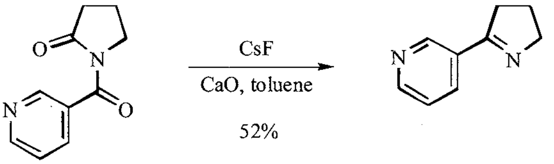
Examples:



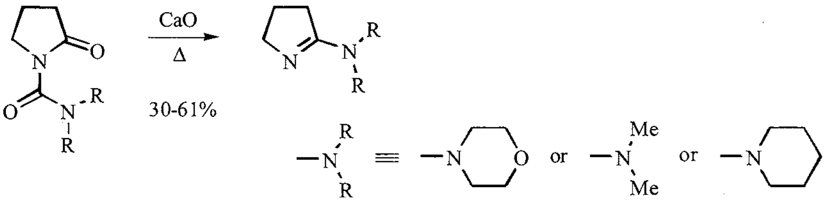
B. P. Mundy, B. R. Larsen, L. F. McKenzie, G. Braden, *Journal of Organic Chemistry* **1972**, 37, 1635



R. K. Hill, T. Yuri, *Tetrahedron* **1977**, 33, 1569



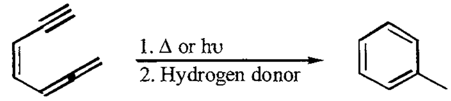
D. Villemin, M. Hachemi, *Reaction Kinetics and Catalysis Letters* **2001**, 72, 3



S. Ravi, M. Easwatamourthy, *Oriental Journal of Chemistry* **2001**, 17, 349 (AN 2001:775237)

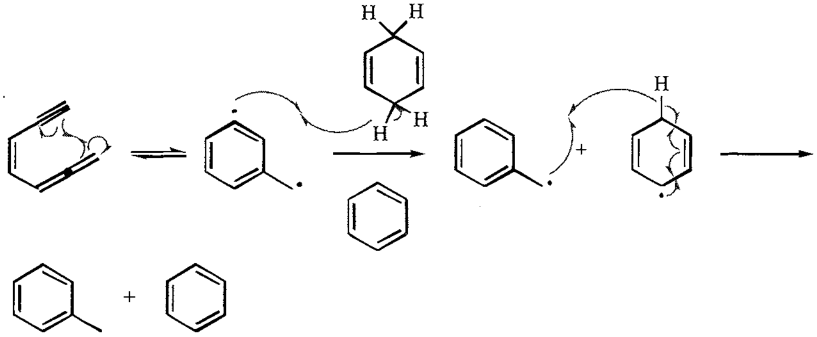
Myers-Saito Cyclization / Schmittel Cyclization

The Reaction:



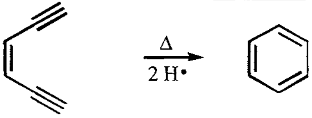
allenyl enyne

Proposed Mechanism:

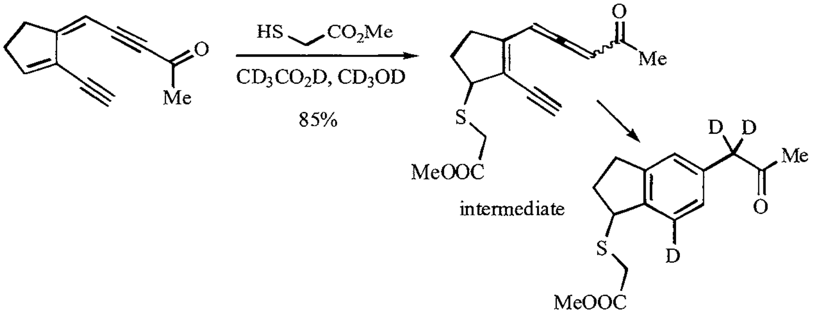


Notes:

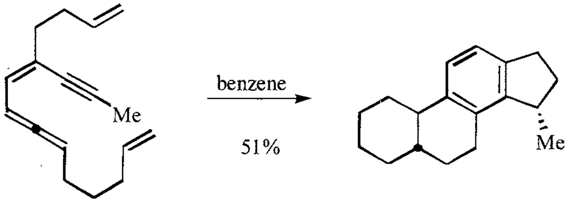
See related chemistry of ***Bergman Cyclization***:



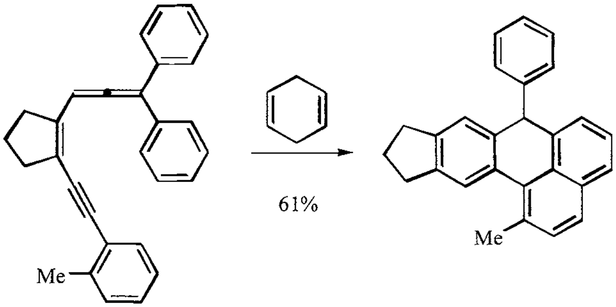
Examples:



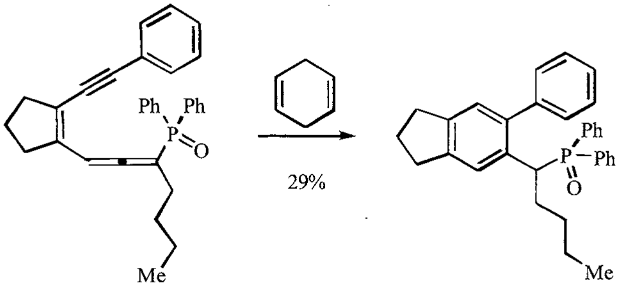
P. A. Wender, M. J. Tebbe, *Tetrahedron* **1994**, 50, 1419



K. K. Wang, Z. Wang, A. Tarli, P. Gannett, *Journal of the American Chemical Society* **1996**, 118, 10783



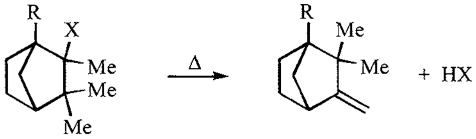
B. Liu, K. K. Wang, J. L. Petersen, *Journal of Organic Chemistry* **1996**, 61, 8503



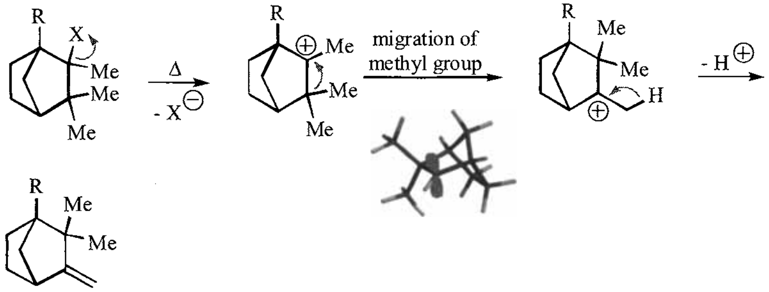
M. Schmittel, J.-P. Steffen, D. Auer, M. Maywald, *Tetrahedron Letters* **1997**, 38, 611

Nametkin Rearrangement

The Reaction:



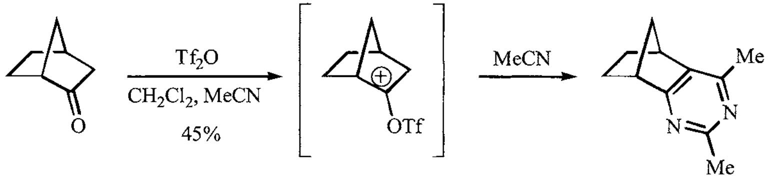
Proposed Mechanism:

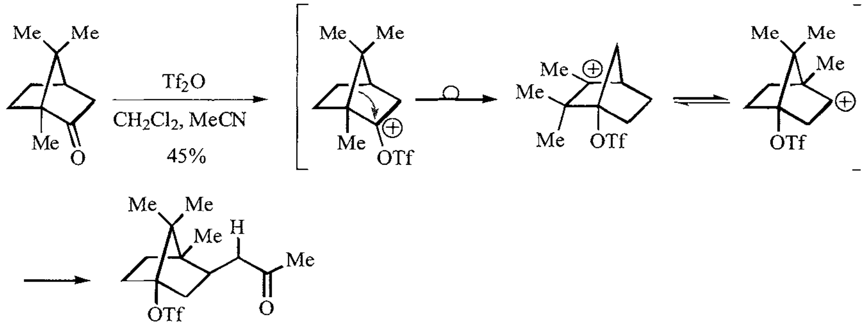


Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1394.

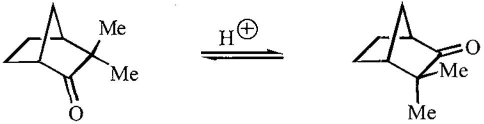
A specific example of a ***Wagner - Meerwein rearrangement***
An interesting experiment to analyze for trapping carbocation:





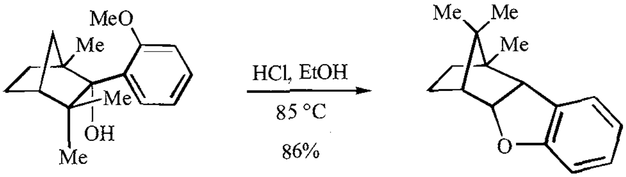
A. G. Martinez, E. T. Vilar, A. G. Fraile, A. H. Fernandez, S. De La Moya Cerero, F. M. Jimenez, *Tetrahedron* **1998**, 54, 4607

An examination of torsional factors in the rearrangement:

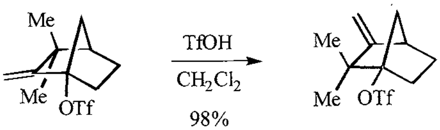


P. C. Moews, J. R. Knox, W. R. Vaughan, *Journal of the American Chemical Society* **1978**, 100, 260

Examples:



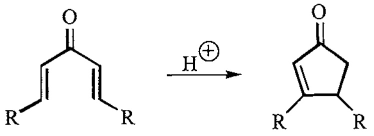
S. M. Starling, S. C. Vonwiller, J. N. H. Reek, *Journal of Organic Chemistry* **1998**, 63, 2262



A. G. Martinez, E. Teso Vilar, A. G. Fraile, S. de la Cerero, M. E. R. Herrero, P. M. Ruiz, L. R. Subramanian, A. G. Gancedo, *Journal of Medicinal Chemistry* **1995**, 38, 4474

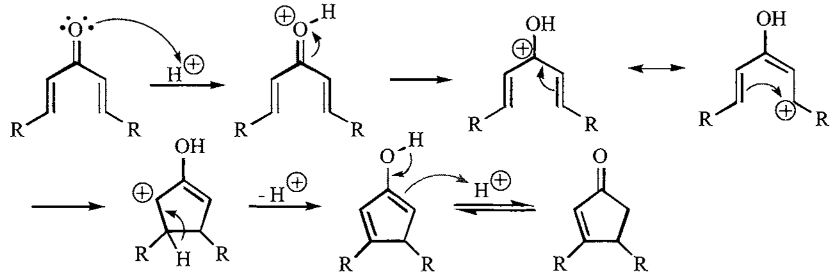
Nazarov Cyclization

The Reaction:

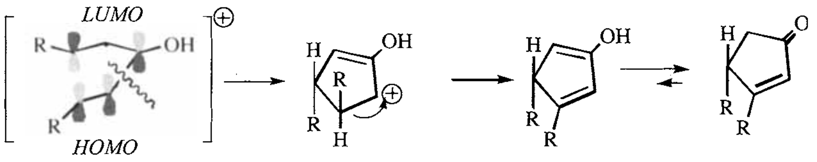


Proposed Mechanism:

"Curly Arrow Formalism"



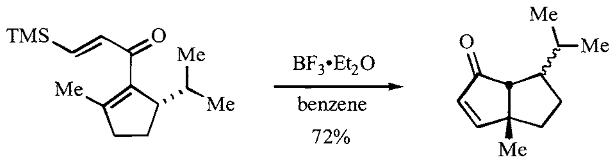
"Electrocyclization Formalism"



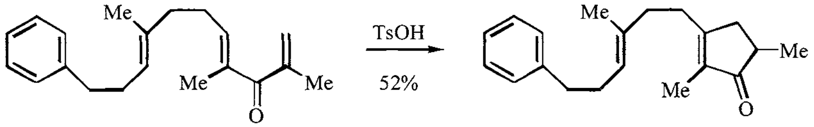
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry,* 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1021; T. Laue, A. Plagens, *Named Organic Reactions,* John Wiley and Sons, Inc., New York, 1998, pp. 195-196; K. L. Habermas, S. C. Denmark, T. K. Jones, *Organic Reactions* **45**, 1.

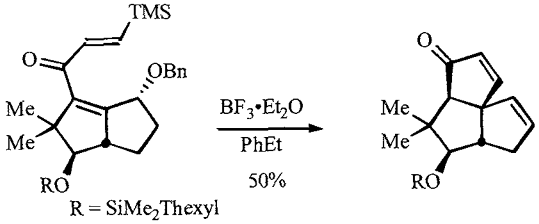
Examples:



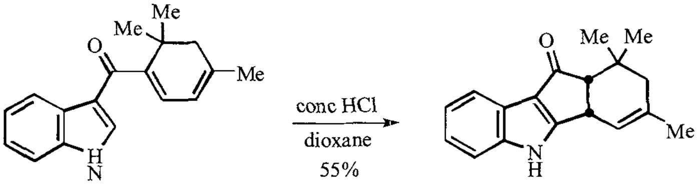
L. A. Paquette, H.-J. Kang, *Journal of the American Chemical Society* **1991**, 113, 2610



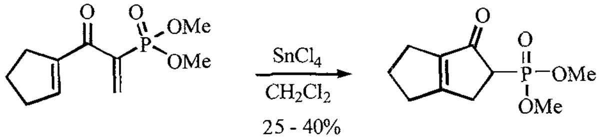
J. A. Bender, A. M. Arif, F. G. West, *Journal of the American Chemical Society* **1999**, 32, 7443



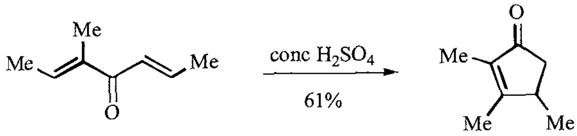
M. Meisch, L. Miesch-Gross, M. Franck-Neumann, *Tetrahedron* **1997**, 53, 2103



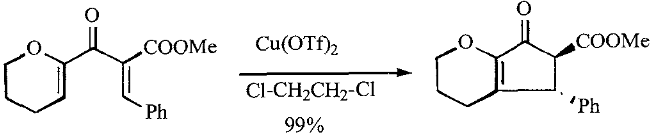
K.-F. Cheng, M.-K. Cheung, *Journal of the Chemical Society, Perkin Transaction 1* **1996**, 11, 1213



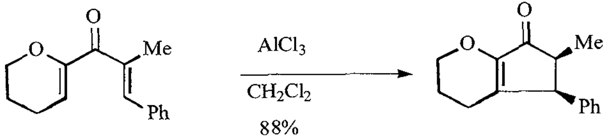
T. Minami, M. Makayama, K. Fujimoto, S. Matsuo, *Journal of the Chemical Society, Chemical Communications* **1992**, 2, 190



J. Motoyoshiya, T. Yazaki. S. Hayashi, *Journal of Organic Chemistry* **1991**, 56, 735. This work studied rearrangements during the cyclization process.



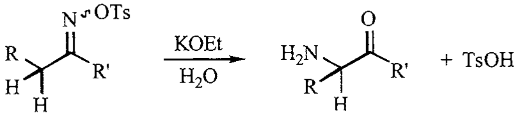
W. He, X. Sun, A. J. Frontier, *Journal of the American Chemical Society* **2003**, 125, 14278



G. Liang, S. N. Gradl, D. Trauner, *Organic Letters* **2003**, 5, 4931

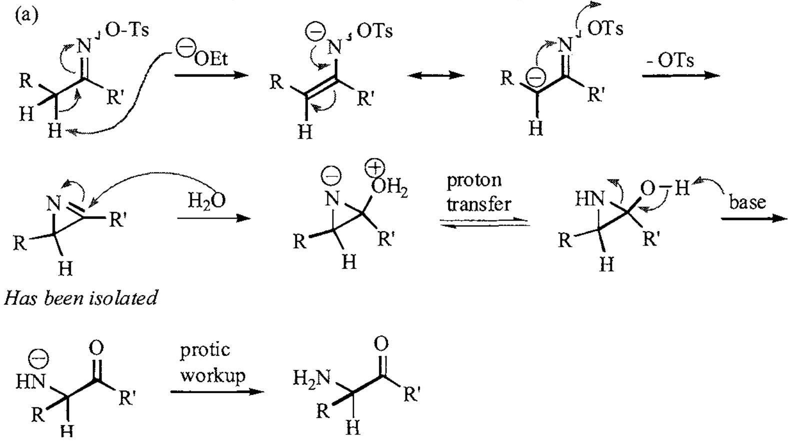
Neber Rearrangement

The Reaction:



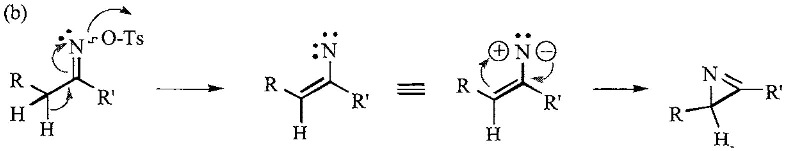
Proposed Mechanism:

Syn or *anti* orientation gives same product



Has been isolated

M. M. H. Verstappen, G. J. A. Ariaans, B. Zwanenburg, *Journal of the American Chemical Society* **1996**, 118, 8491

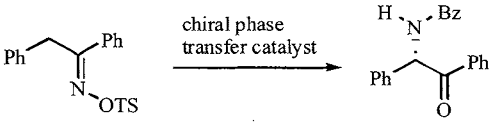


"Nitrene"

Notes:

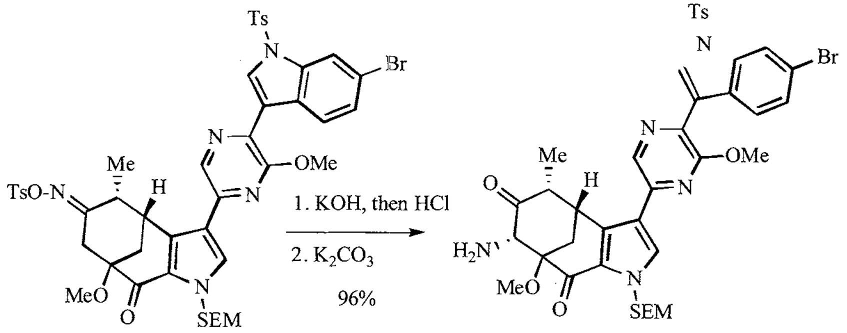
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp. 288, 1410; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, p. 197

The nitrene mechanism is not consistent with the outcome of a chiral-based study:
T. Ooi, M. Takahashi, K. Doda, K. Maruoka, *Journal of the American Chemical Society* **2002**, 124, 7640.

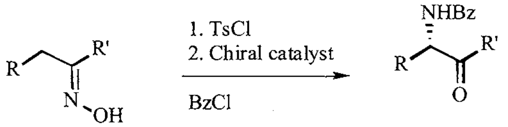


Unlike the similar ***Beckmann rearrangement***, the stereochemistry of the oxime is not critical to the outcome of the reaction.

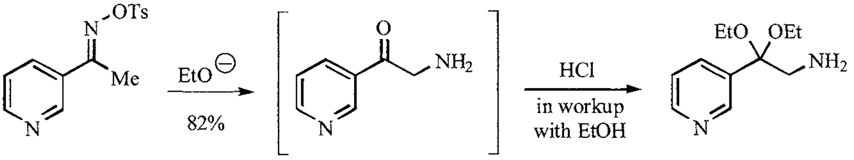
Examples:



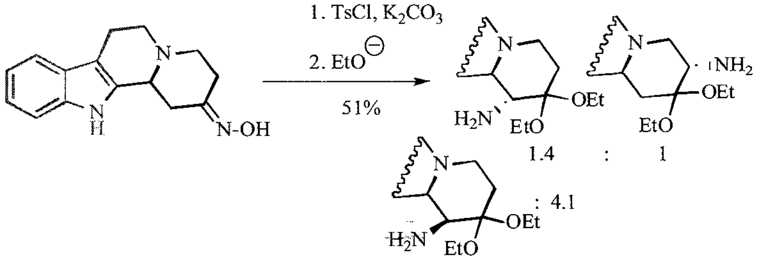
N. K. Garg, D. D. Caspi, B. M. Stoltz, *Journal of the American Chemical* **2004**, 126, 9552



T. Ooi, M. Takahashi, K. Doda, K. Maruoka *Journal of the American Chemical* **2002**, 124, 7640



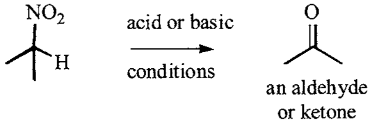
J. Y. L. Chung, G.-J. Ho, M. Chartrain, D. Zhao, J. Leazer, R. Farr, M. Robbins, K. Emerson, D. J. Mathre, J. M. McNamaro, D. L. Hughes, E. J. J. Grabowski, P. J. Reider, *Tetrahedron Lett*ers **1999**, 40, 6739



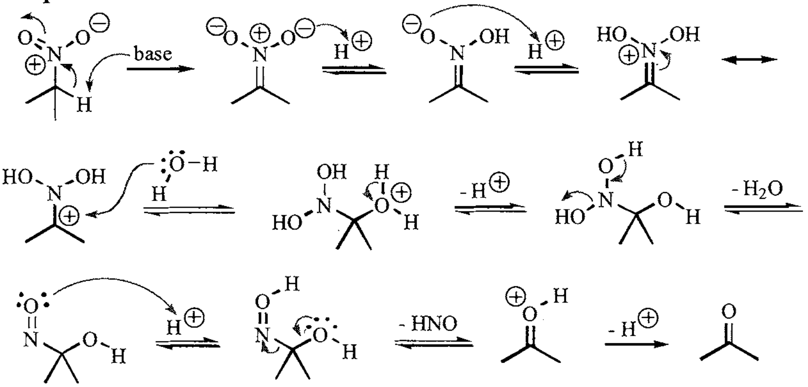
I. Lopez, A. Diez, M. Rubiralta, *Tetrahedron* **1996**, 52,. 8581-

Nef Reaction

The Reaction:



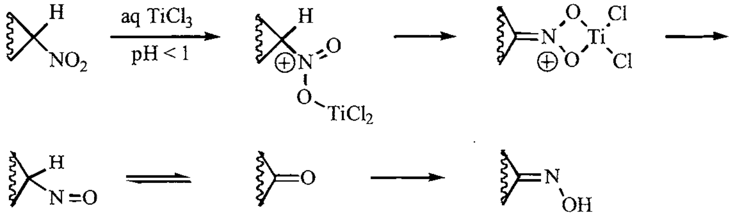
Proposed Mechanism:

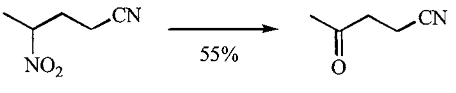


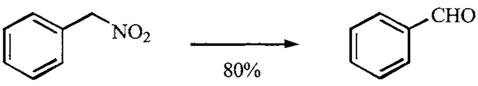
$$2\,HNO \rightleftharpoons H_2O + N_2O$$

Notes:

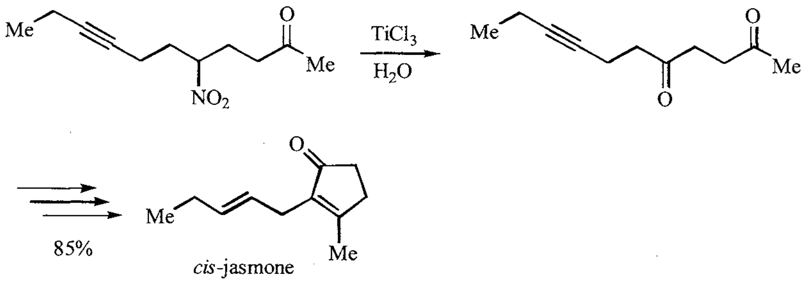
$TiCl_3$ can be very effective for this reaction. This is called the ***McMurry Modification of the Nef Reaction***.



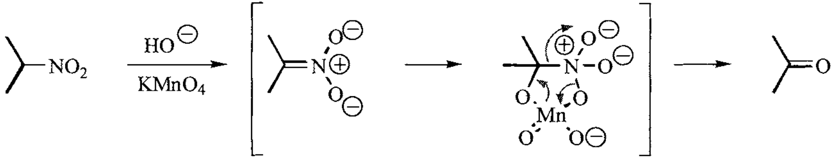




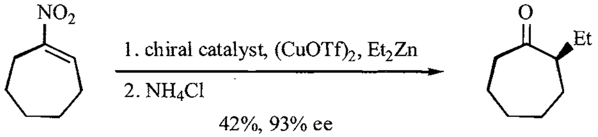
J. E. McMurry, J. Melton, *Journal of Organic Chemistry* **1973**, 38, 4367



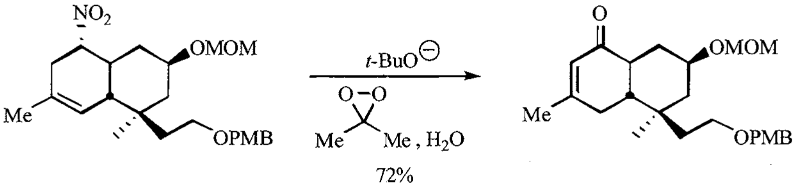
Basic permanganate can accomplish this conversion:



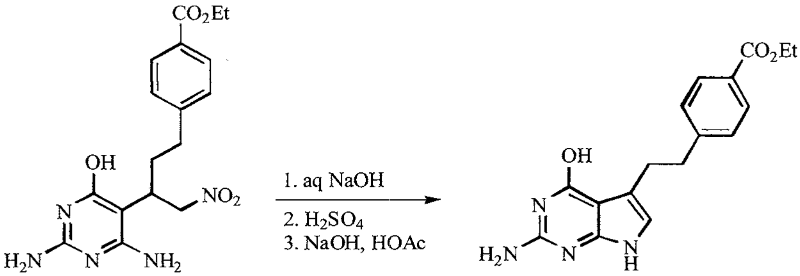
Examples:



C. A. Luchaco-Cullis, A. H. Hoveyda, *Journal of the American Chemical Society* **2002**, 124, 8192



R. Williams, T. A. Brugel, *Organic Letters* **2000**, 2, 1023



E. C. Taylor, B. Liu, *Journal of Organic Chemistry* **2003**, 68, 9938

Negishi Coupling

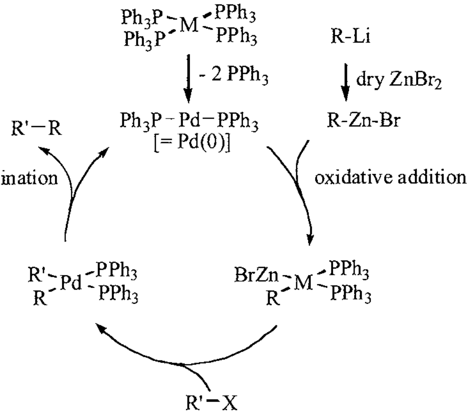
The Reaction:

$$R{-}ZnX \xrightarrow[\text{R'-X}]{\text{Ni or Pd}} R{-}R'$$

R = alkyl, alkenyl, aryl, allylic, benzylic
R' = Alkenyl, alkynyl, aryl, allylic, benzylic

E. Negishi, M. Kotora, C. Xu, *Journal of Organic Chemistry* **1997**, 62, 8957

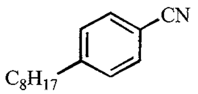
Proposed Mechanism:



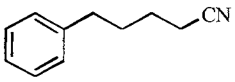
Notes:

For unactivated halides:

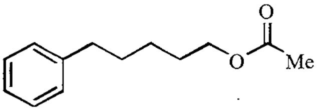
$$R{-}Br \xrightarrow{\text{Zn, cat. } I_2} [R{-}ZnBr] \xrightarrow[\text{cat. Ni}]{\text{Ar}-\text{X}} R{-}Ar$$



91%

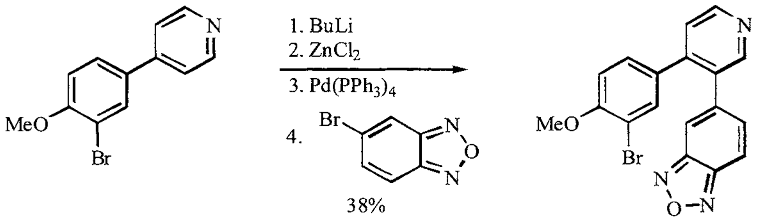


98%



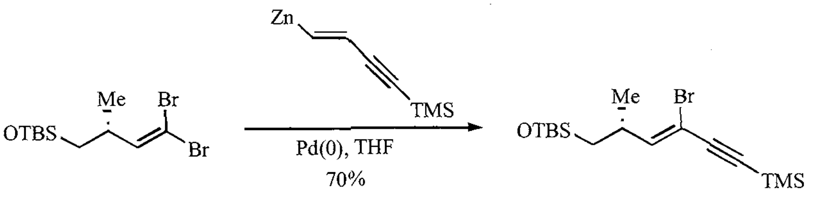
91%

S. Huo, *Organic Letters* **2003**, 5, 423

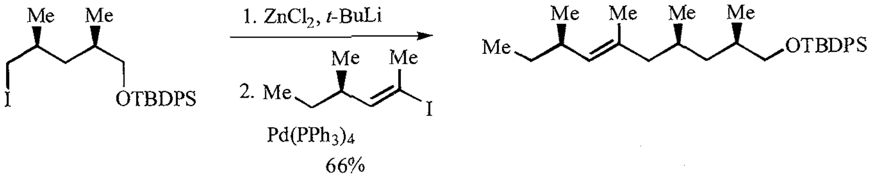


P. W. Manley, M. Acemoglu, W. Marterer, W. Pachinger, *Organic Processes and Research Development* **2003**, 7, 436

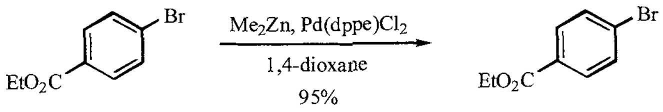
Examples:



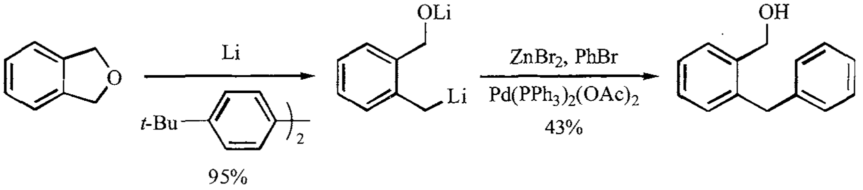
X. Zeng, Q. Hu, M. Qian, E.-i.Negishi, *Journal of the American Chemical Society* **2003**, 125, 13636



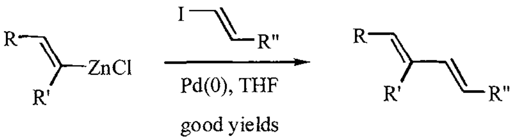
G. D. McAllister, R. J. K. Taylor, *Tetrahedron Letters* **2004**, 45, 2551



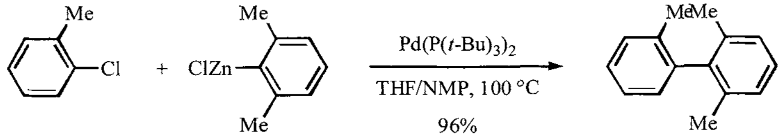
J. M. Herbert, *Tetrahedron Letters* **2004**, 45, 817



M. Yus, J. Gomis, *Tetrahedron Letters*, **2001**, 42, 5721



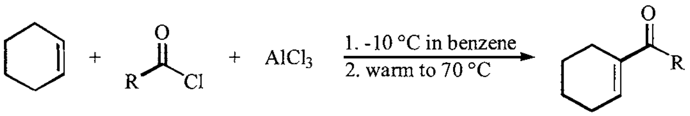
J. A. Panek, T. Hu, *Journal of Organic Chemistry* **1997**, 62, 4912



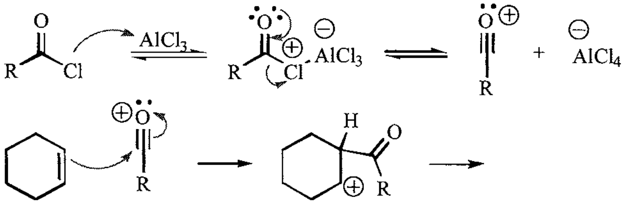
C. Dai, G. C. Fu, *Journal of the American Chemical Society* **2001**, 123, 2719

Nenitzescu Acylation

The Reaction:



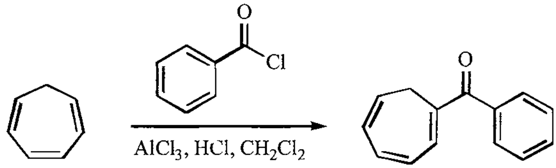
Proposed Mechanism:



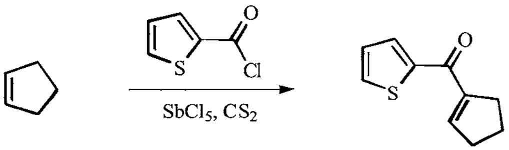
Notes:

Note similarities to the ***Friedel-Crafts Acylation***.

Examples:

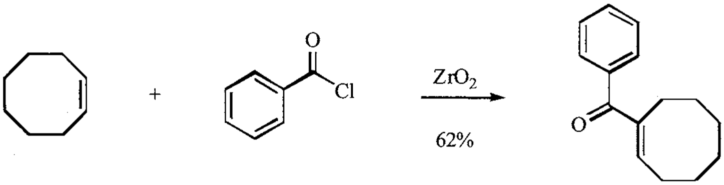


J. A. Blair, C. J. Tate, *Chemical Communications* **1969**, 1506

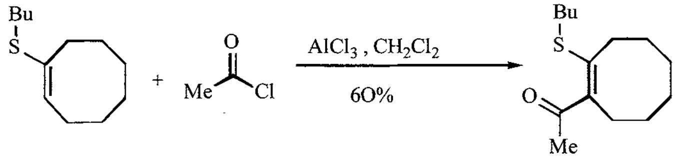


Yield not reported. Crude product was converted to the 2,4-D derivative.

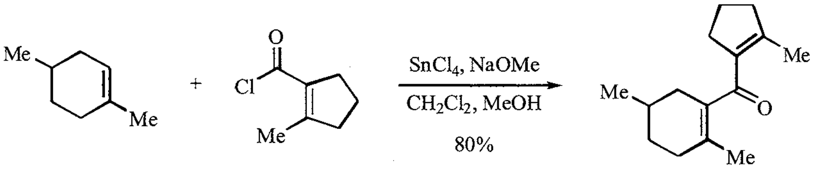
L. H. Klemm, T. Largman, *Journal of the American Chemical Society* **1952**, 74, 4458



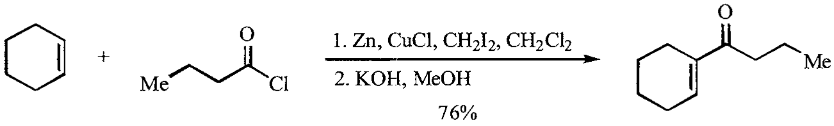
M. L. Patil, G. K. Jnaneshwara, D. P. Sabde, M. K. Dongare, A. Sudalai, F. H. Deshpande, *Tetrahedron Letters*, **1997**, 38, 2137



D. Villemin, B. Labiad, *Synthetic Communications* **1992**, 22, 3181 (AN 1993:168726)



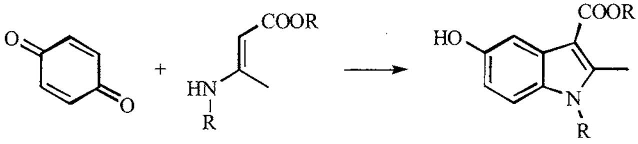
K. E. Harding, K. S. Clement, *Journal of Organic Chemistry* **1984**, 49, 3870



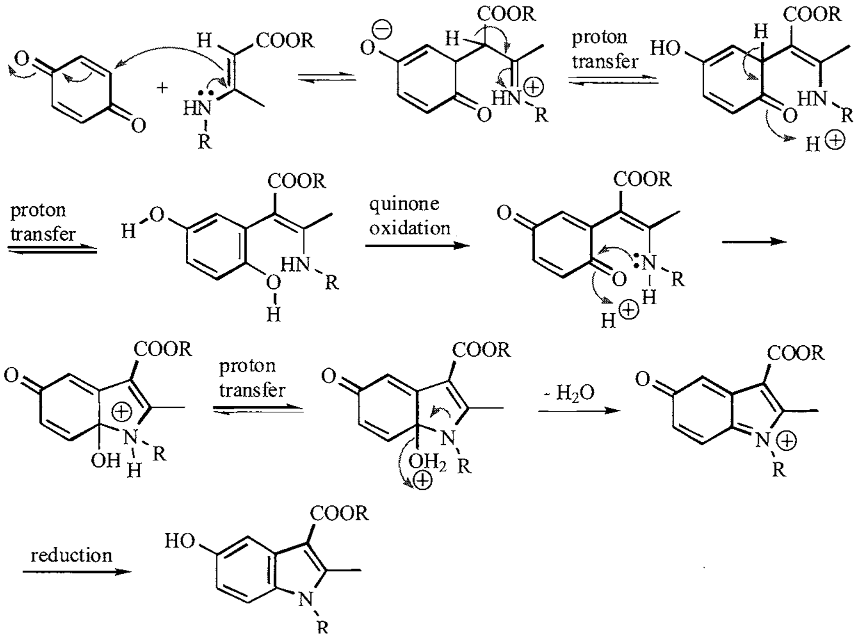
T. Shono, I. Sishiguchi, M. Sasaki, H. Ikeda, M. Kurita, *Journal of Organic Chemistry* **1983**, 48, 2503

Nenitzescu Indole Synthesis

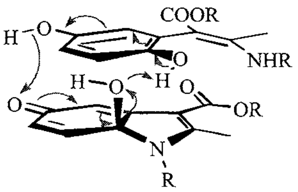
The Reaction:



Proposed Mechanism:

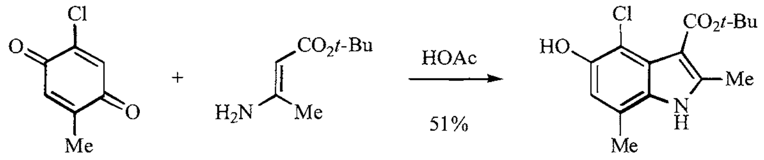


Notes:



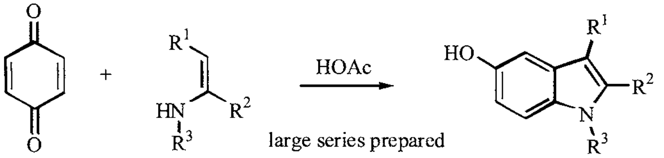
The hydride transfer may be a bimolecular oxidation / reduction process.

Examples:



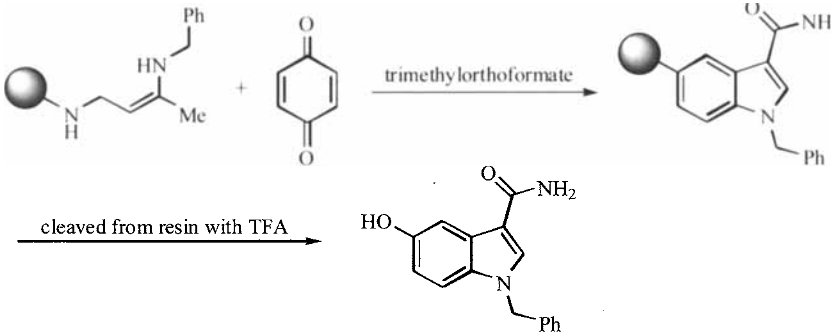
J. F. Poletto, M. J. Weiss, *Journal of Organic Chemistry* **1970**, 35, 1190

A large assortment of substitution patterns prepared:

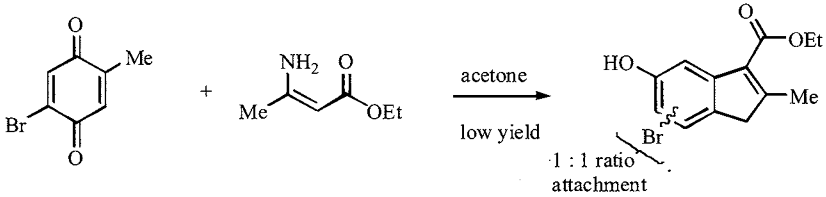


T. M. Boehme, C. E. Augelli-Szafran, H. Hallak, T. Pugsley, K. Serpa, R. D. Schwarz, *Journal of Medicinal Chemistry* **2002**, 45, 3094

A solid-phase synthesis:

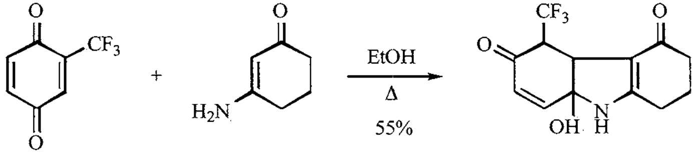


D. M. Ketcha, L. J. Wilson, D. E. Portlock, *Tetrahedron Letters* **2000**, 41, 6253



R. Littell, G. R. Allen, Jr., *Journal of Organic Chemistry* **1968**, 33, 2064

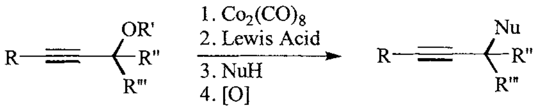
A modification used to prepare carbazoles:



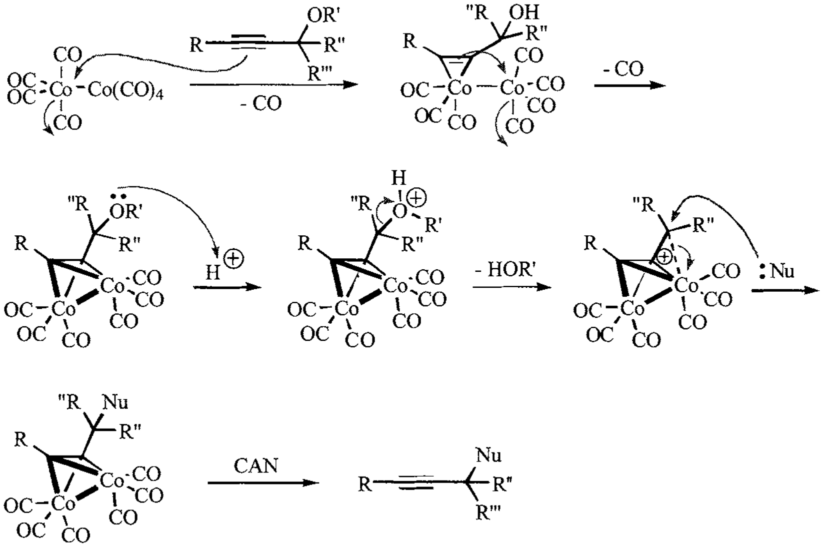
R. Littell, G. O.Morton, G. R. Allen, Jr., *Journal of the American Chemical Society* **1970**, 92, 3740

Nicholas Reaction

The Reaction:

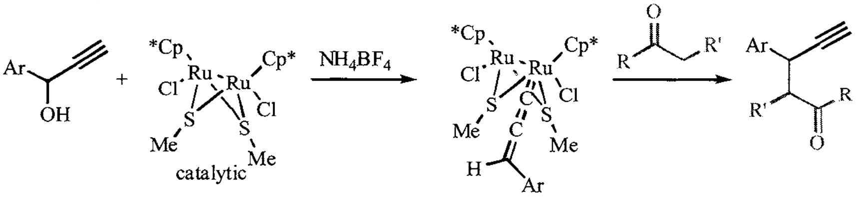


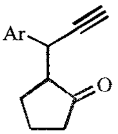
Proposed Mechanism:



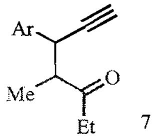
Notes:

A Ru-catalyzed variation:

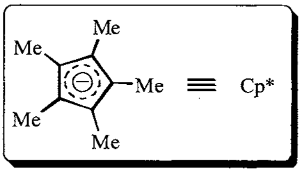




52%

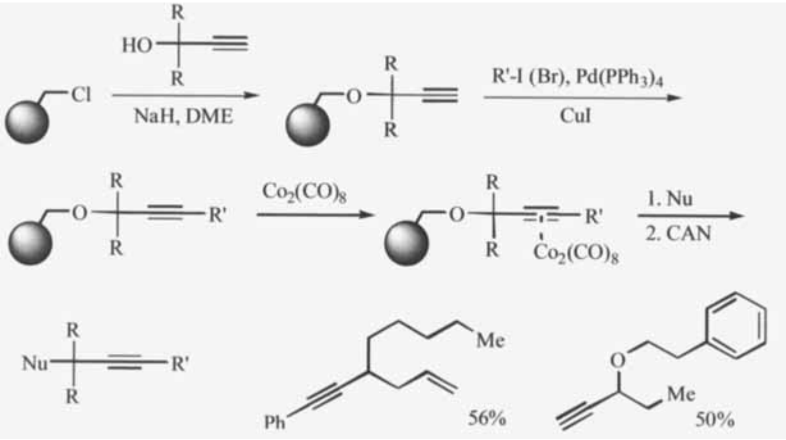


71%

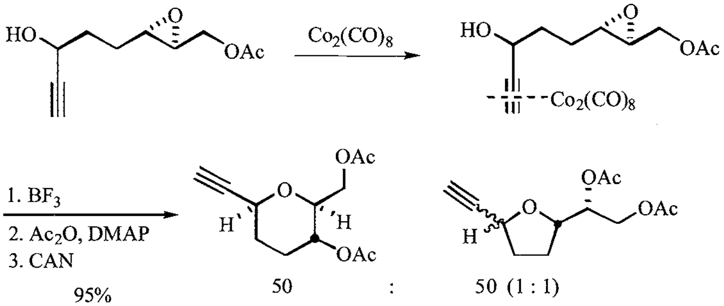


Y. Nishibayashi, I. Wakiji, Y. Ishii, S. Uemura, M. Hidai, *Journal of the American Chemical Society* **2001**, 123, 3393

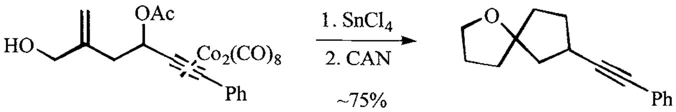
Examples:



J. A. Cassel, S. Leue, N. I. Gachkova, N. C. Kann, *Journal of Organic Chemistry* **2002**, 67, 9460



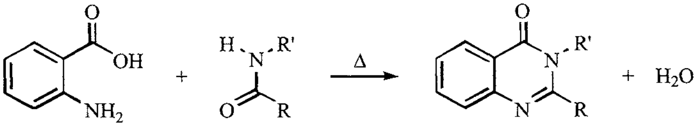
F. R. P. Crisostomo, T. Martın, V. S. Martın, *Organic Letters* **2004**, 6, 565



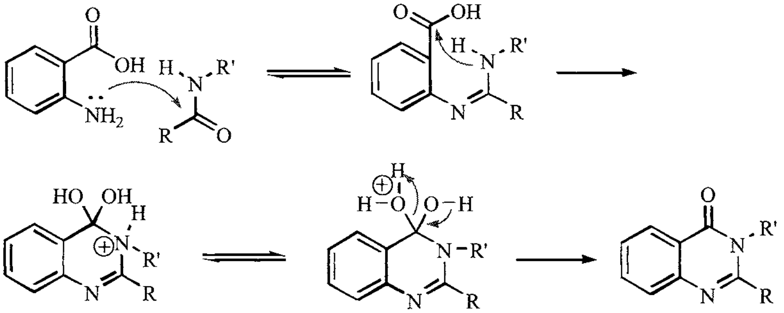
C. Mukai, H. Yamashita, M. Sassa, M. Hanaoka, *Tetrahedron* **2002**, 58, 2755

Niementowski Quinazoline Synthesis

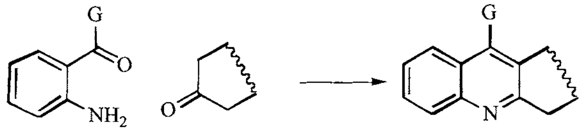
The Reaction:



Proposed Mechanism:



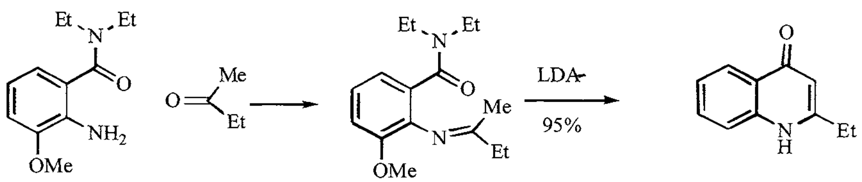
Notes:



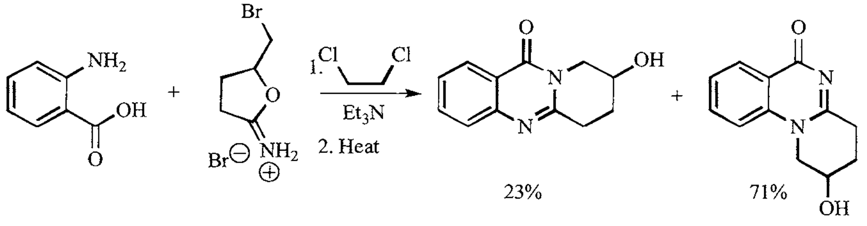
G	Name Reaction
H, R	Friedlander
C(O)O	Pfitzinger
OH, OR	Niementowski

R .J. Chong, M. A. Siddiqui, V. Snieckus, *Tetrahedron Letters* **1986**, 27, 5323

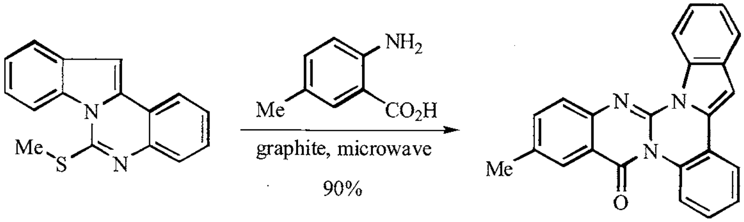
Examples:



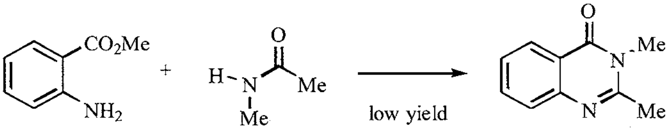
R .J. Chong, M. A. Siddiqui, V. Snieckus, *Tetrahedron Letters* **1986**, 27, 5323



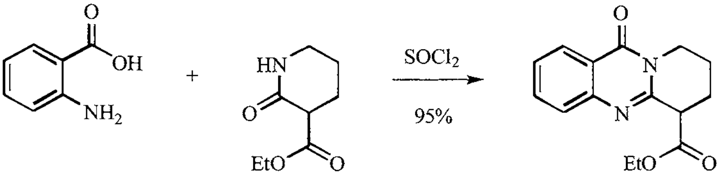
G. Fantin, M. Fogagnolo, A. Medici, P. Pedrini, *Journal of Organic Chemistry* **1993**, 58, 741



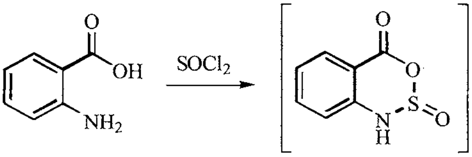
L. Domon, C. Le Coeur, A. Grelard, V. Thiery, T. Besson, *Tetrahedron Letters* **2001**, 42, 6671



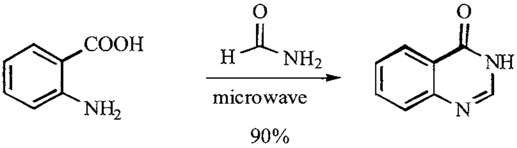
J. F. Meyer, E. C. Wagner, *Journal of Organic Chemistry* **1943**, 8, 239



The major reactant, formed in situ, was



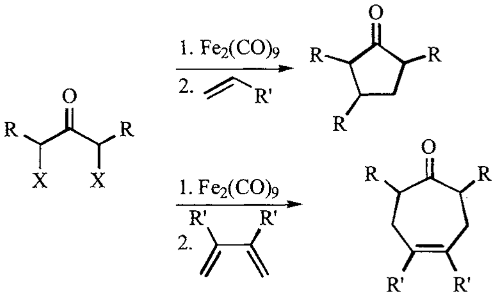
T. Kametani, C. V. Loc, T. Higa, M. Koizumi, M. Ihara, K. Fukumoto, *Journal of the American Chemical Society* **1977**, 99, 2306



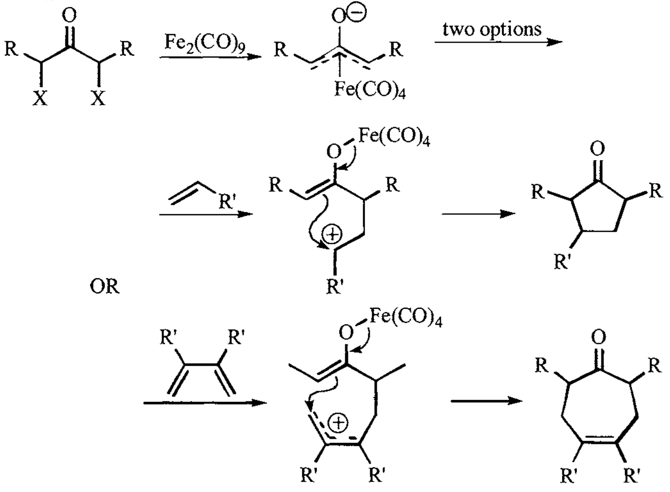
F. Alexandre, A. Berecibar, R. Wrigglesworth, T. Bessonb, *Tetrahedron* **2003**, 59, 1413

Noyori Annulation

The Reaction:

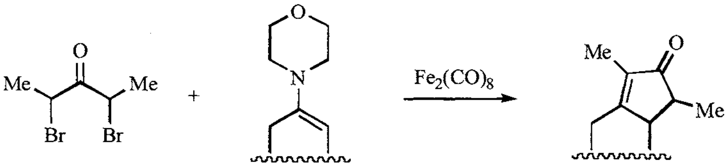


Proposed Mechanism:

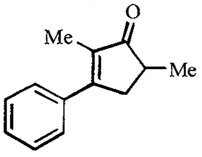


Notes:

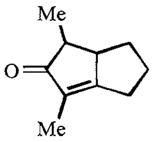
In the original work, reaction with enamines:



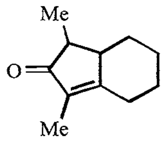
By this approach:



91%



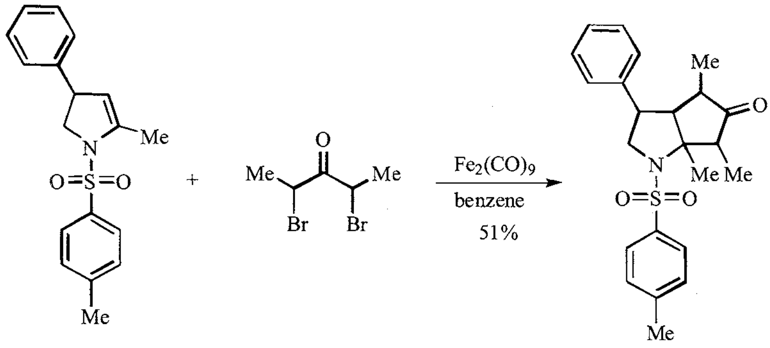
74%



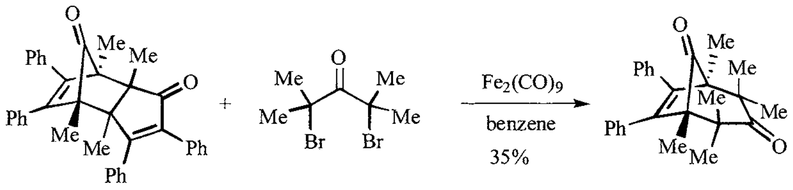
100%

Y. Hayakawa, K. Yokoyama, R. Noyori, *Journal of the American Chemical Society* **1978**, 100, 1799

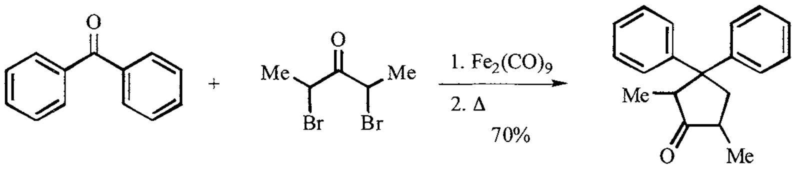
Examples:



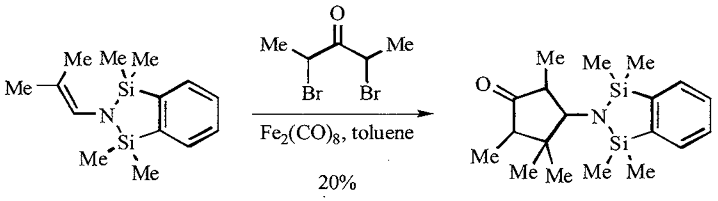
L. S. Hegedus, M. S. Holden, *Journal of Organic Chemistry* **1985**, 50, 3920



T. Ishizu, M. Mori, K. Kanematsu, *Journal of Organic Chemistry* **1981**, 46, 526



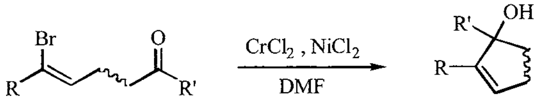
Y. Hayakawa, K. Yokiyama, R. Noyori, *Journal of the American Chemical Society* **1978**, 100, 1791



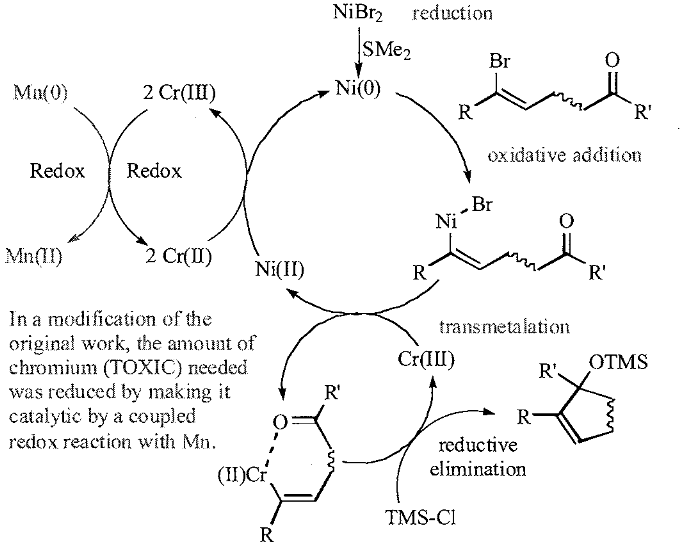
R. J. P. Corriu, J. J. E. Moreau, M. Pataud-Sat, *Journal of Organic Chemistry* **1990**, 55, 2878

Nozaki-Hiyama-Kishi Reaction

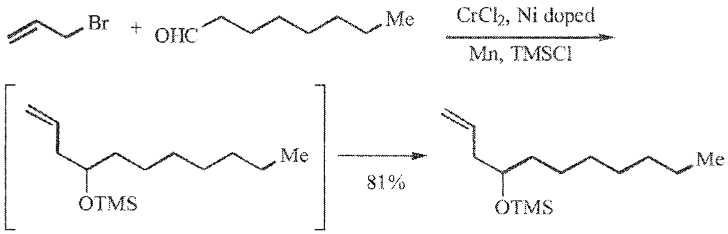
The Reaction:



Proposed Mechanism:



In a modification of the original work, the amount of chromium (TOXIC) needed was reduced by making it catalytic by a coupled redox reaction with Mn.

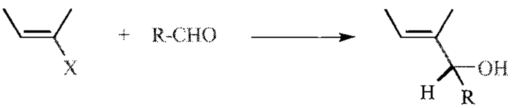


A. Furstner, N. Shi, *Journal of the American Chemical Society* **1996**, 118, 12349

Notes:

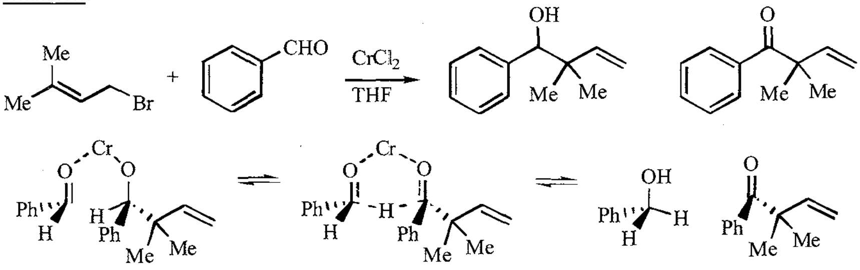
P. Cintas, *Synthesis* **1992**, 248

Disubstituted alkenyl halides maintain streochemistry in the product:



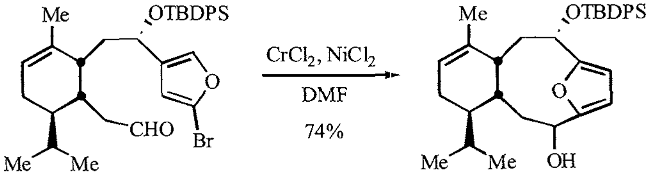
K. Takai, K. Kimura, T. Kuroda, T. Hiyama, H. Nozaki, *Tetrahedron Letters* **1983**, 24, 5281

The occasional observation of ketone products can be rationalized by a Cr-mediated ***Oppenauer oxidation***:

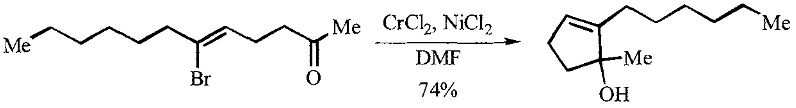


H. S. Schrekker, M. W. G. de Bolster, R. V. A. Orru, L. A. Wessjohann, *Journal of Organic Chemistry* **2002**, 67, 1977

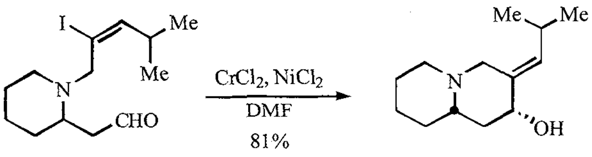
Examples:



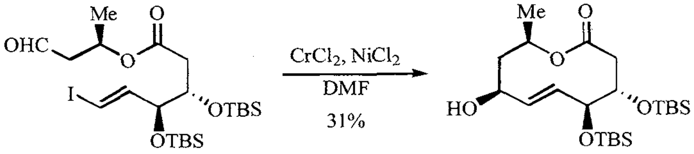
X.-T. Chen, S. K. Bhattacharya, B. Zhou, C. E. Gutteridge, T. R. R. Pettus, S. J. Danishefsky, *Journal of the American Chemical Society* **1999**, 121, 6563



B. M. Trost, A. B. Pinkerton, *Journal of Organic Chemistry* **2001**, 66, 7714



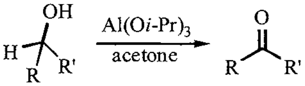
X.-Q. Tang, J. Montgomery, *Journal of the American Chemical Society* **2000**, 122, 6950



R. A. Pilli, M. M. Victor, *Tetrahedron Letters* **2002**, 43, 2815

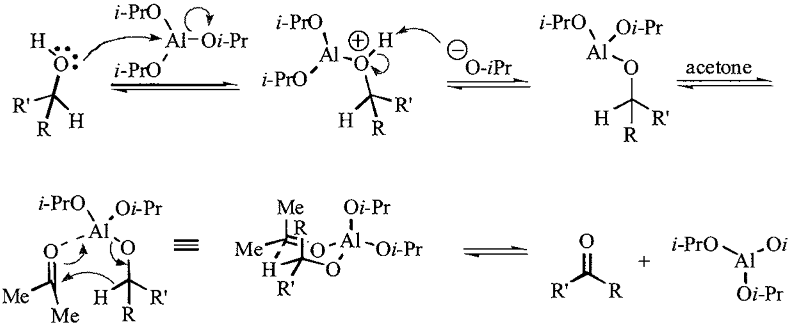
Oppenauer Oxidation

The Reaction:



This is the reverse of the ***Meerwein-Ponndorf-Verley Reduction***.

Proposed Mechanism:



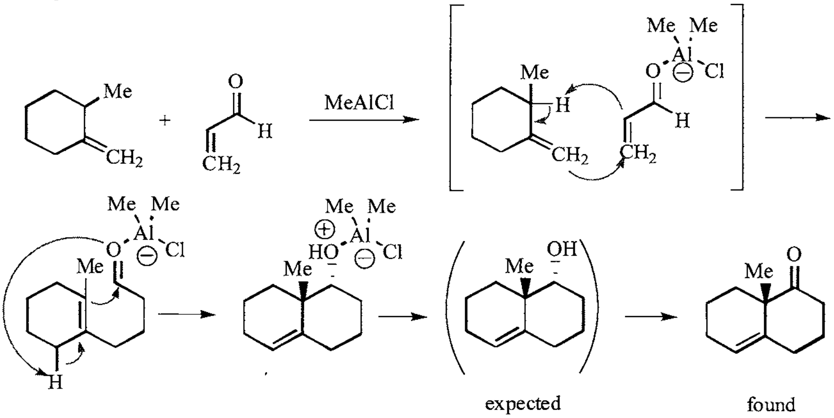
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1516; C. Djerassi, *Organic Reactions* **6**, 5

An important feature of this reaction is the lack of over oxidation.

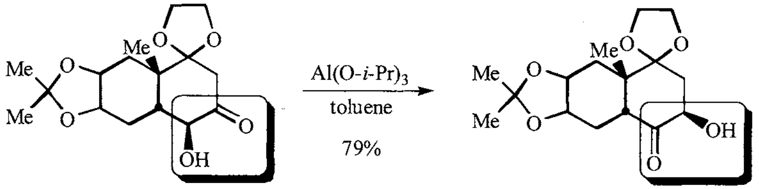
Examples:

A unique in-situ oxidation:



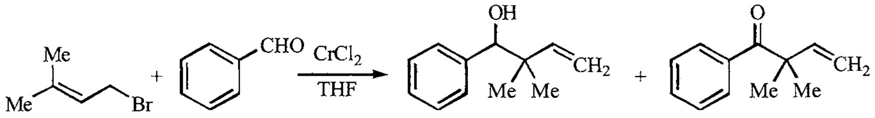
formed from  as the oxidizing agent

B. B. Snider, B. E. Goldman, *Tetrahedron* **1986**, 42, 2951



Note also the oxidation

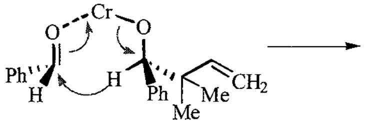
T. K. M. Shing, C. M. Lee, H. Y. Lo, *Tetrahedron Letters* **2001**, 42, 8361



78%, 1:1

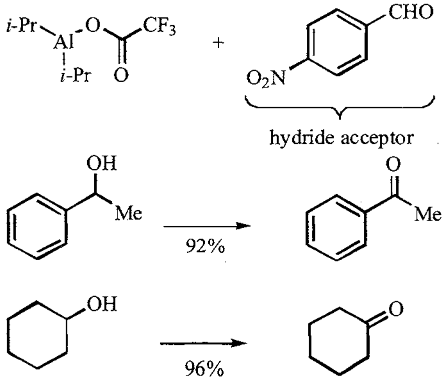
Hiyama-Nozaki product ***Oppenauer*** product

The ***Oppenauer*** product formed from an interaction of the expected product reacting with benzaldehyde in a Cr-catalyzed oxidation



H. S. Schrekker, M. W. G. de Bolster, R. V. A. Orru, L. A. Wessjohann, *Journal of Organic Chemistry* **2002**, 67, 1975

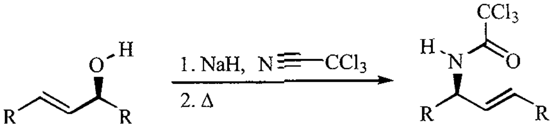
New oxidation system:



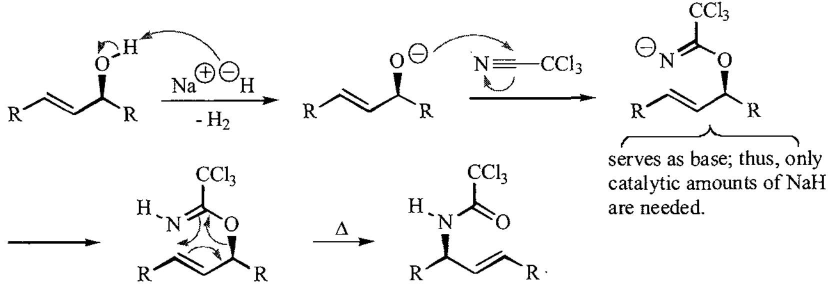
K. G. Akamanchi, B. A. Chaudhari, *Tetrahedron Letters* **1997**, 38, 6925

Overman Rearrangement

The Reaction:



Proposed Mechanism:



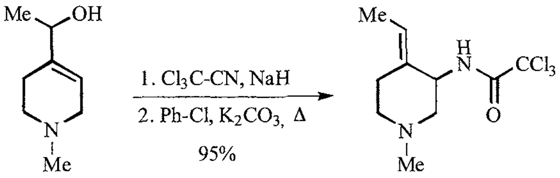
serves as base; thus, only catalytic amounts of NaH are needed.

Catalytic amounts of Hg(II) or Pd(II) work in some cases.

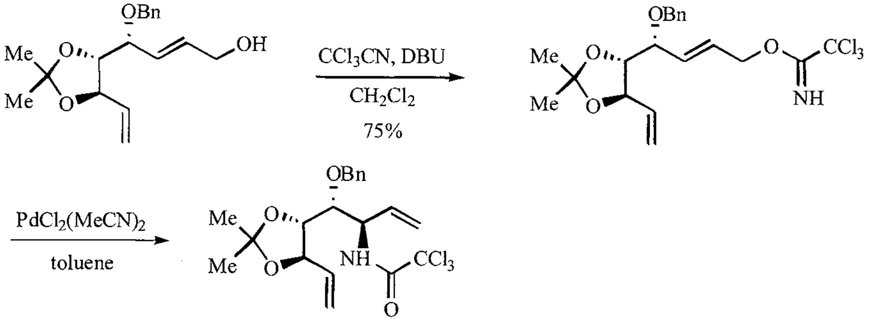
Notes:

Only catalytic amounts of NaH are needed (see above).

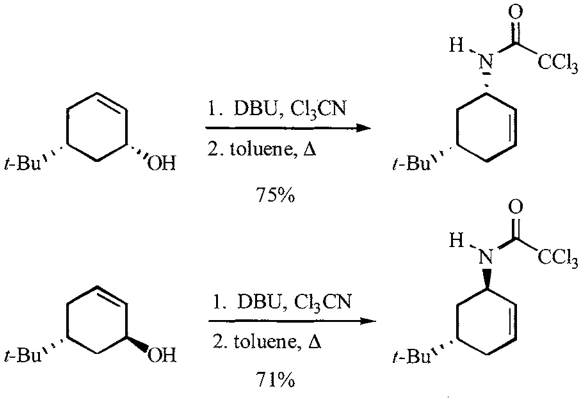
Examples:



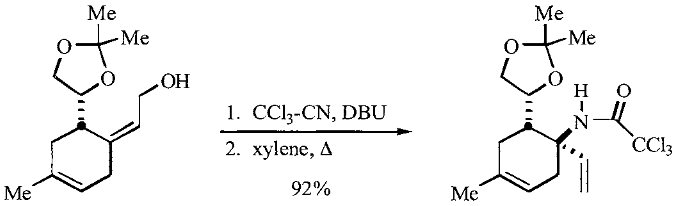
M. Reilly, D. R. Anthony, C. Gallagher, *Tetrahedron Letters* **2003**, 44, 2927



H. Ovaa, J. D. C. Codée, B. Lastdrager, H. S. Overkleeft, G. A. van der Marel, J. H. van Boom, *Tetrahedron Letters* **1999**, 40, 5063



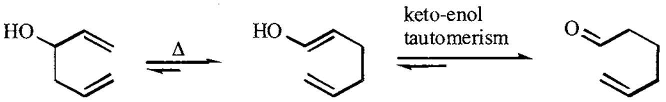
T. J. Donohoe, K. Blades, M. Helliwell, P. R. Moore, J. J. G. Winter, *Journal of Organic Chemistry* **1999**, 64, 2980



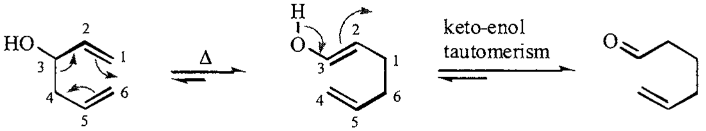
T. Nishikawa, M. Asai, N. Ohyabu, N. Yamamoto, Y. Fukuda, M. Isobe, *Tetrahedron* **2001**, 57, 3875

Oxy-Cope Rearrangement

The Reaction:



Proposed Mechanism:

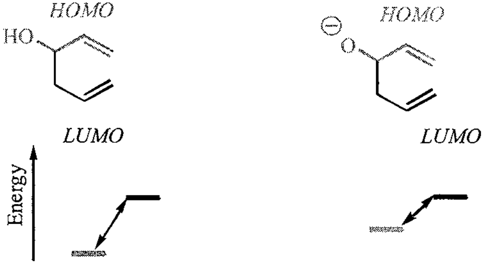


Notes:

Useful Review: L. A. Paquette, *Tetrahedron* **1997**, 53, 13971

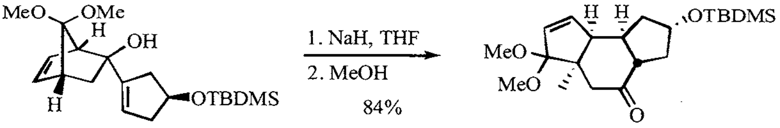
FMO theory predicts, and it is observed, that the reaction is greatly accelerated if the alcohol proton is removed (anion-accelerated). Many reactions of this type can be carried out at low temperature.

Anion-accelerated Oxy-Cope

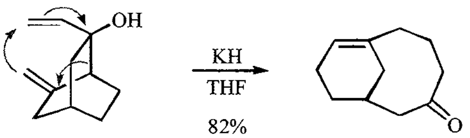


From FMO theory we imagine the *LUMO* portion of the reacting pair will be of the same energy in both reactions; however, the *HOMO* is raised for the anion.

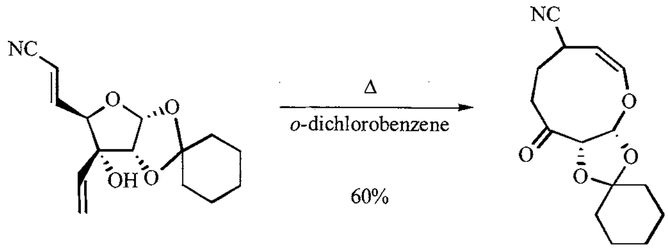
Examples:



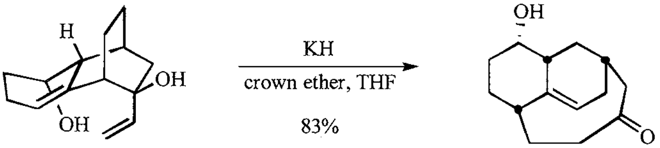
L. A. Paquette, Z. Gao, Z. Ni., G. F. Smith, *Tetrahedron Letters* **1997**, 38, 1271



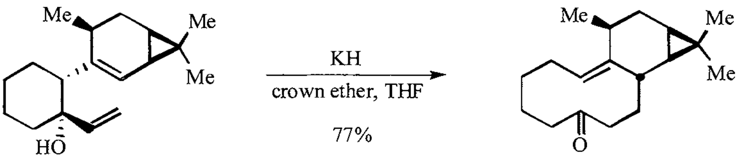
S. F. Martin, J.-M. Assercq, R. E. Austin, A. P. Dantanarayana, J. R. Fishpaugh, C. Gluchowski, D. E. Guinn, M. Hartmann, T. Tanaka, R. Wagner, J. B. White, *Tetrahedron* **1995**, 51, 3455



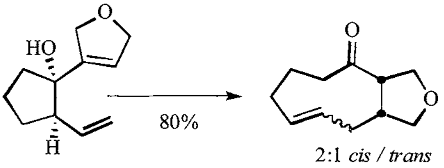
A.V. R. L. Sudha, M. Nagarajan, *Journal of the Chemical Society, Chemical Communications*, **1996**, 1359



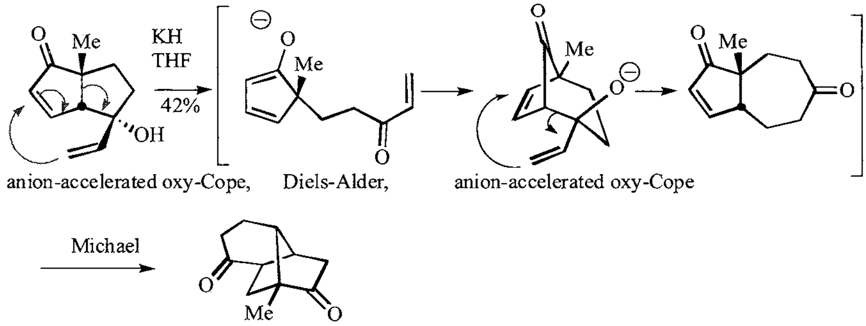
J.-F. Devaux, I. Hanna, J.-Y. Lallemand, *Journal of Organic Chemistry* **1997**, 62, 5062



L. A. Paquette, D. R. Sauer, S. D. Edmondson, D. Friedrich, *Tetrahedron* **1994**, 50, 4071



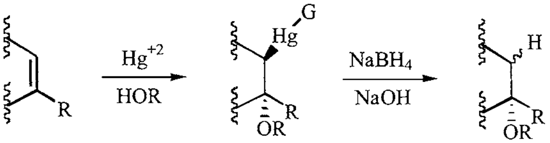
B. H. White, M. L. Snapper, *Journal of the American Chemical Society* **2003**, 125, 14901



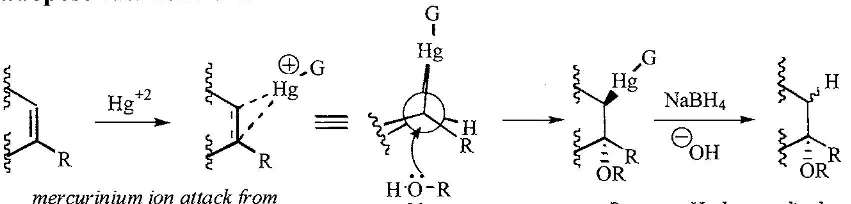
C. M. Tice, C. H. Heathcock, *Journal of Organic Chemistry* **1981**, 46, 9

Oxy- and Solvomercuration

The Reaction:



Proposed Mechanism:



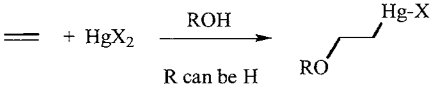
mercurinium ion attack from the less-hindered face.

Water or alcohol adds to the more substituted carbon.

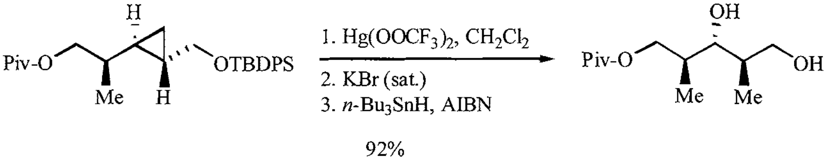
Removes Hg by a radical mechanism and is replaced by H radical.

Notes:

This is a useeful extension of the much older ***Hofmann-Sand reaction***, where an alkene reacts with a mercuric salt:

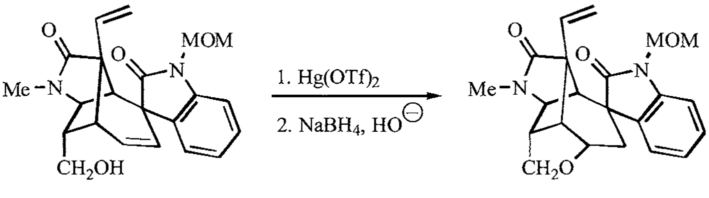


Cyclopropane rings can undergo the oxymercuration/ demercuration reaction:



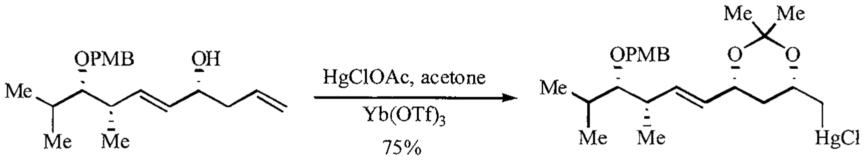
J. Cossy, N. Blanchard, C. Meyer, *Organic Letters* **2001**, 3, 2567

An intramolecular reaction sometimes known as the ***Speckamp procedure***

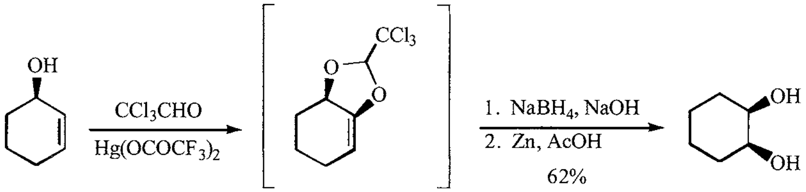


T. Fukuyama, G. Liu, *Journal of the American Chemical Society* **1996**, 118, 7426

Examples:

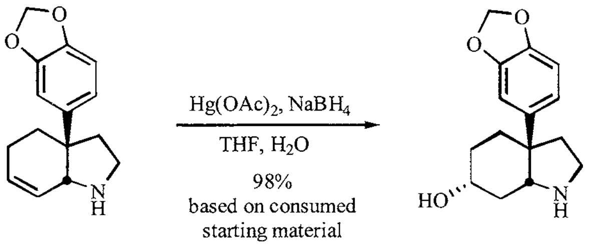


S. D. Dreher, J. L. Leighton, *Journal of the American Chemical Society* **2001**, 123, 341

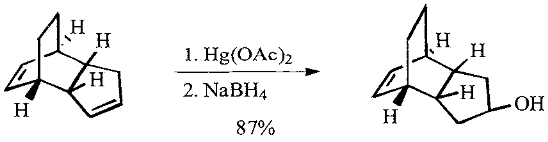


Chloral has a high propensity for forming hemiacetals

L. E. Overman, C. B. Campbell, *Journal of Organic Chemistry* **1974**, 39, 1474

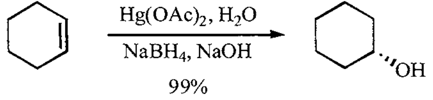


L. E. Overman, R. M. Burk, *Tetrahedron Letters* **1984**, 25, 5739



N. Takaishi, Y. Fujikura, Y. Inamoto, *Journal of Organic Chemistry* **1975**, 40, 3767

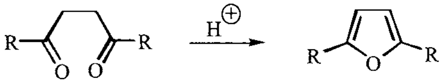
This early start of the investigations into this reaction provides useful insights into looking at reactivity.



H. C. Brown, P. Geoghegan, Jr., *Journal of the American Chemical Society* **1967**, 89, 1522

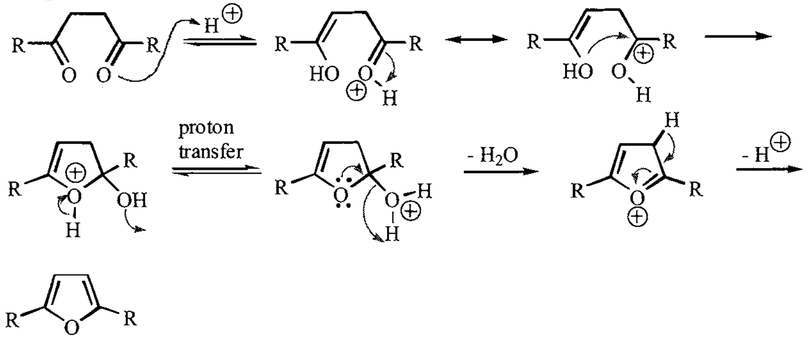
Paal-Knorr Furan Synthesis

The Reaction:



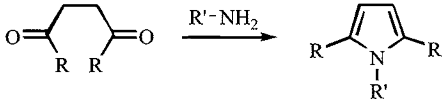
or other Lewis Acids

Proposed Mechanism:

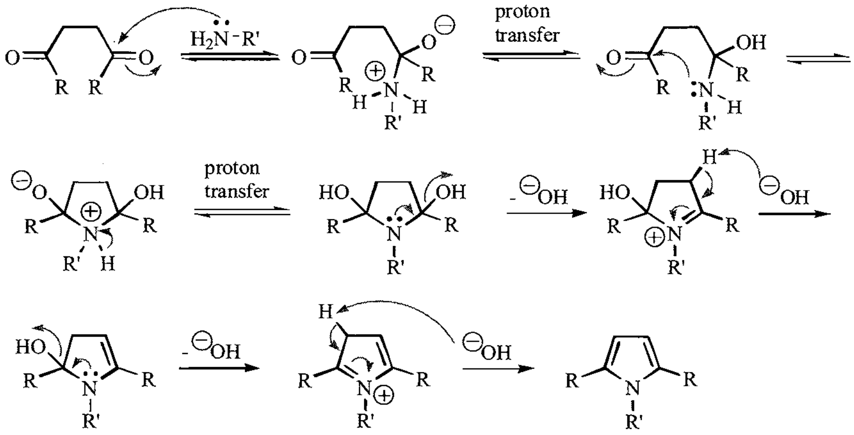


Paal-Knorr Pyrrole Synthesis

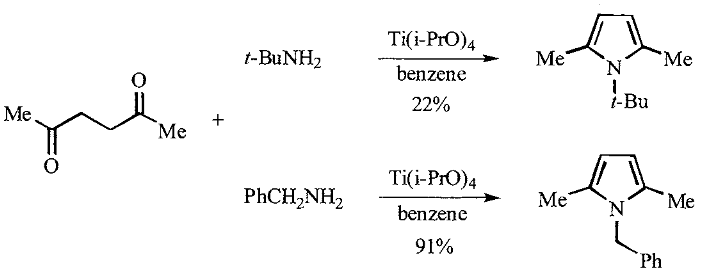
The Reaction:



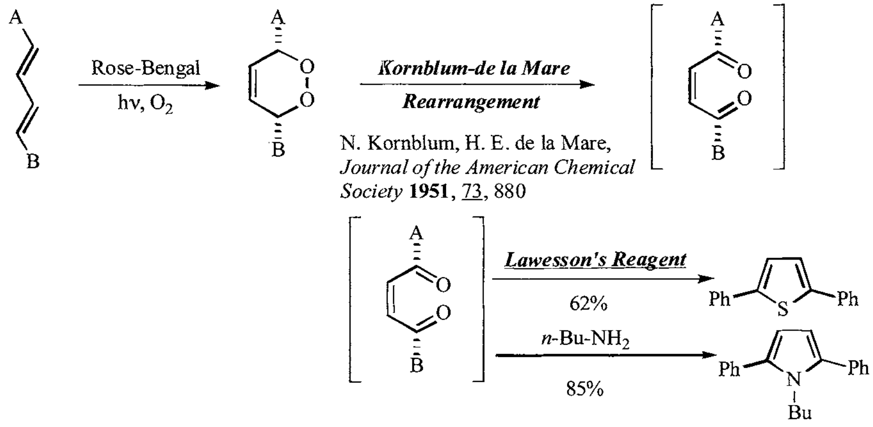
Proposed Mechanism:



Examples:

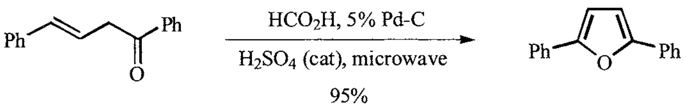


Y. Dong, N. N. Pai, S. L. Ablaza, S.-X. Yu, S. Bolvig, D. A. Forsyth, P. W. LeQuesne, *Journal of Organic Chemistry* **1999**, 64, 2657



N. Kornblum, H. E. de la Mare, *Journal of the American Chemical Society* **1951**, 73, 880

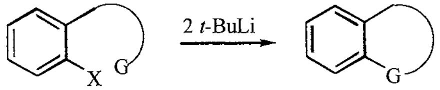
C. E. Hewton, M. C. Kimber, D. K. Taylor, *Tetrahedron Letters* **2002**, 43, 3199



H. S. P. Rao, S. Jothilingam, *Journal of Organic Chemistry* **2003**, 68, 5392

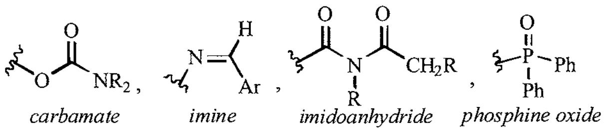
Parham Cyclization

The Reaction:

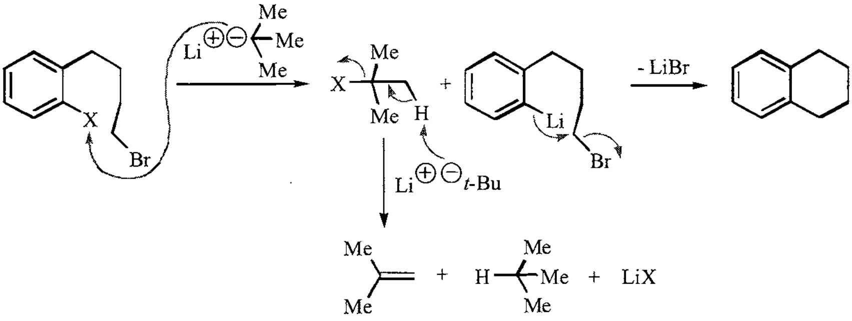


$X = Br, I_2$

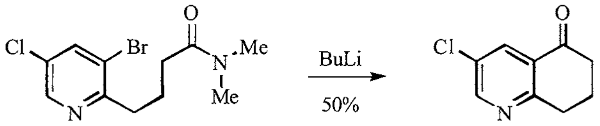
G = electrophilic groups:
-COOH, $-CONR_2$,
$-CH_2Br$, $-CH_2Cl$,
epoxide,



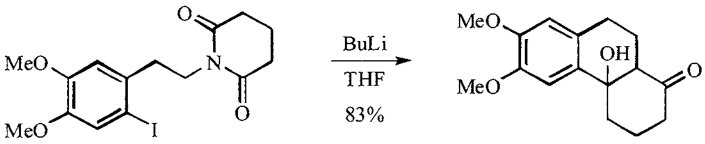
Proposed Mechanism:



Examples:

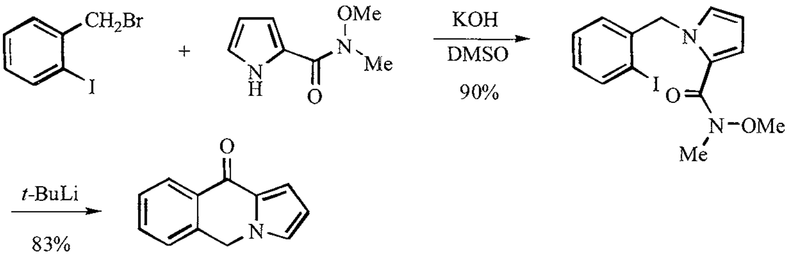


G. J. Quallich, D. E. Fox, R. C. Friedmann, C. W. Murtiashaw, *Journal of Organic Chemistry* **1992**, 57, 761

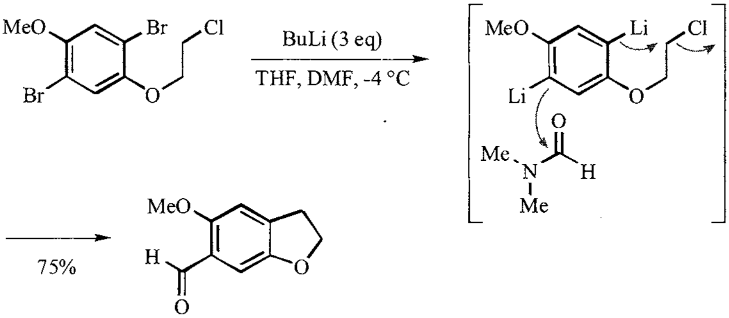


M. I. Collado, N. Sotomayor, M.-J. Villa, E. Lete, *Tetrahedron Letters* **1996**, 37, 6193

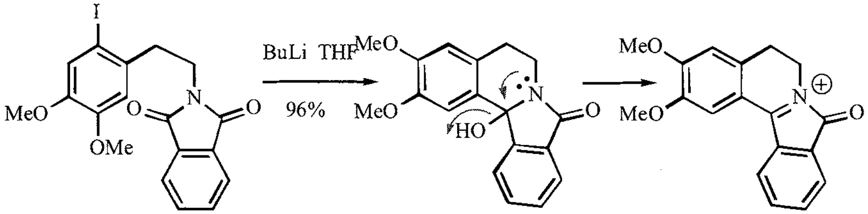
Using ***Weinreb amides***:



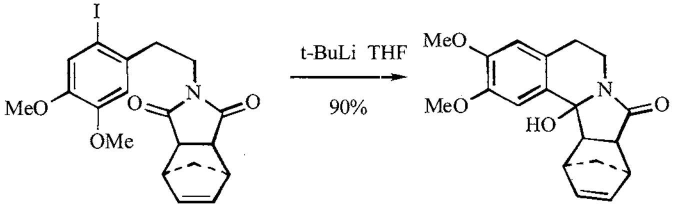
J. Ruiz, N. Sotomayer, E. Lete, *Organic Letters* **2003**, 5, 1115



M. Plotkin, S. Chen, P. G. Spoors, *Tetrahedron Letters* **2000**, 41, 2269



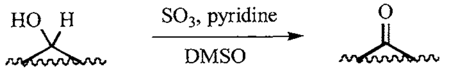
I. Osante, E. Lete, N. Sotomayor, *Tetrahedron Letters* **2004**, 45, 1253



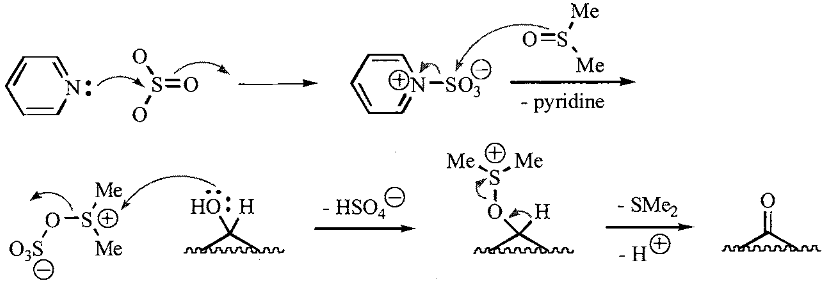
I. Gonza´lez-Temprano, I. Osante, E. Lete, N. Sotomayor, *Journal of Organic Chemistry* **2004**, 69, 3875

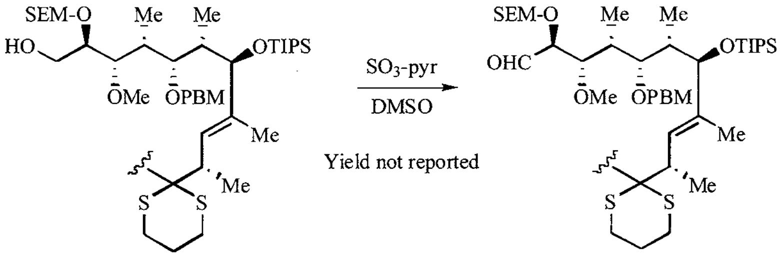
Parikh-Doering Oxidation

The Reaction:

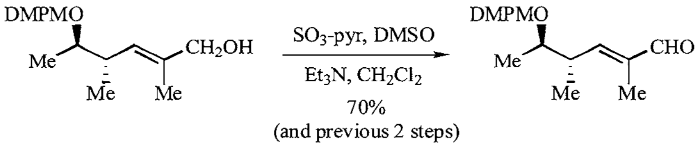


Proposed Mechanism:

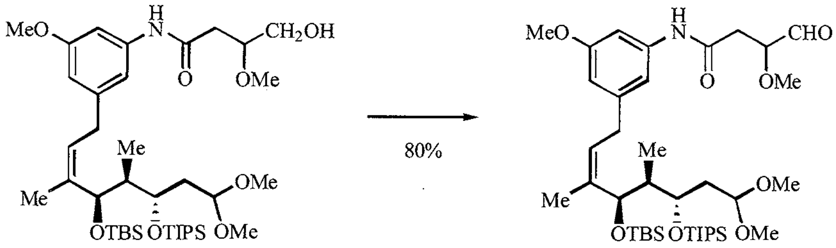




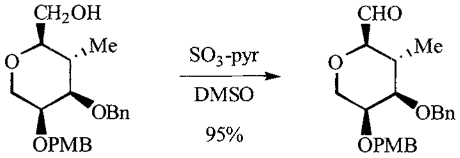
A. B. Smith, III, C. M. Adams, S. A. L. Barbosa, A. P. O. Degnan, *Journal of the American Chemical Society* **2003**, 125, 350



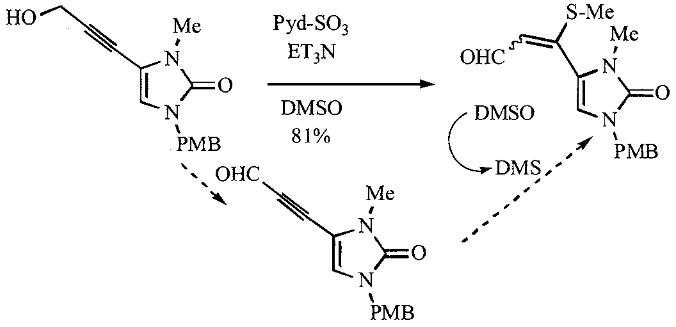
W. R. Roush, J. S. Newcom, *Organic Letters* **2002**, 4, 4739



J. A. Panek, C. E. Masse, *Journal of Organic Chemistry* **1997**, 62, 8290



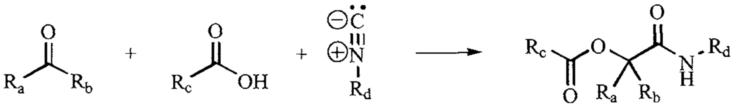
A. B. Smith, III, W. Zhu, S. Shirakami, C. Sfouggatakis, V. A. Doughty, C. S. Bennett, Y. Sakamoto, *Organic Letters* **2003**, 5, 761



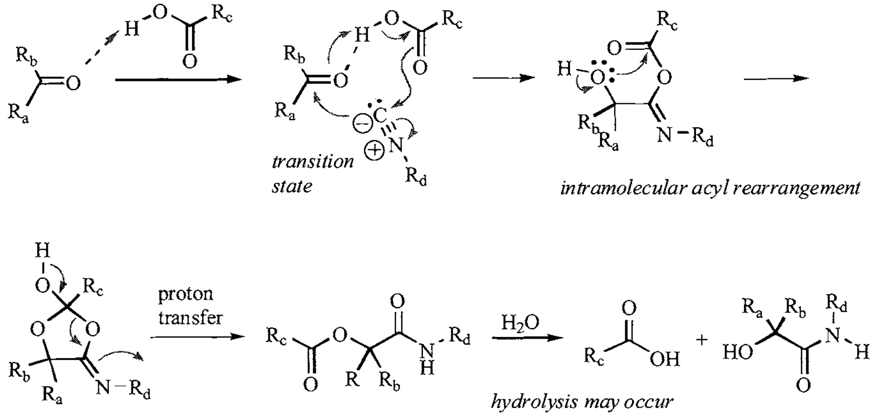
M. J. Porter, N. J. White,.G. E. Howells, D. D. P. Laffan, *Tetrahedron Letters* **2004**, 45, 6541

Passerini Reaction

The Reaction:



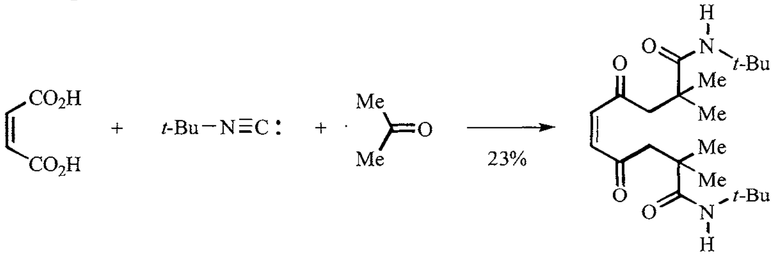
Proposed Mechanism:



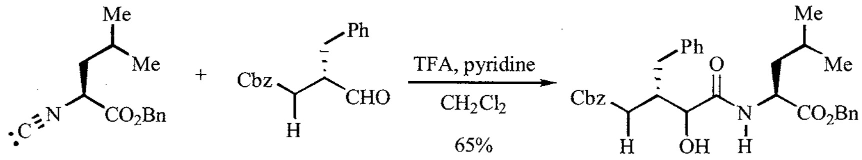
Notes:

See: M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1252

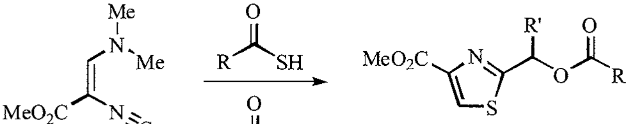
Examples:

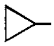


I. Lengyel, V. Cesare, T. Taldone, *Tetrahedron* **2004**, 60, 1107

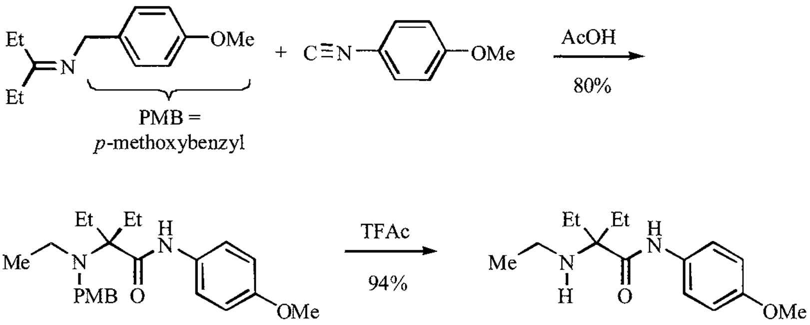


J. E. Sample, T. D. Owens, K. Nguyen, O. E. Levy, *Organic Letters* **2000**, 2, 2769



R	R'	Yield
Me-	Ph(CH$_2$)$_2$-	32%
Me-		35%

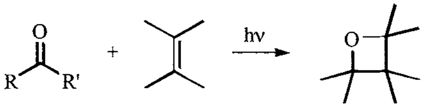
B. Henkel, B. Beck, B. Westner, B. Mejat, A. Domling, *Tetrahedron Letters* **2003**, 44, 89



S. P. G. Costa, H. L. S. Maia, S. M. M. A. Pereira-Lima, *Organic & Biomolecular Chemistry* **2003**, 1, 1475

Paterno-Buchi Reaction

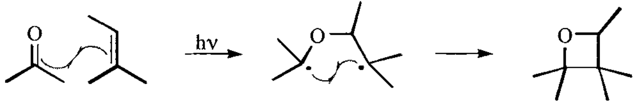
The Reaction:

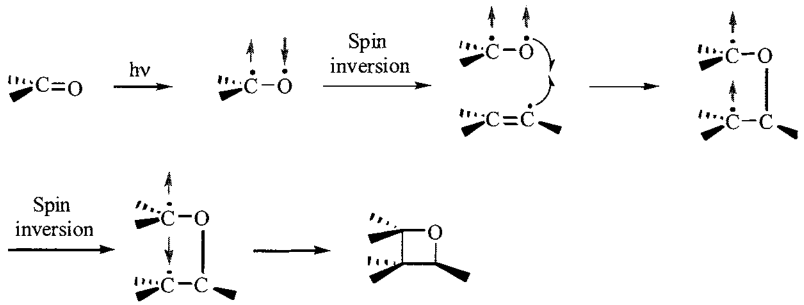


expect a mixture
of regioisomers

Proposed Mechanism:

This is a stepwise reaction with a diradical intermediate.



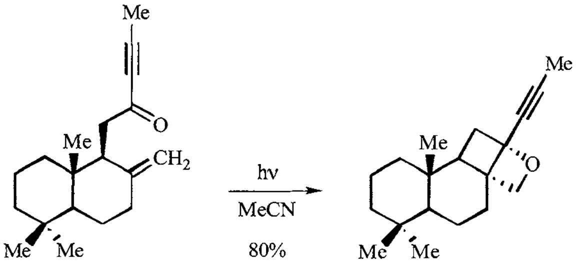


Notes:

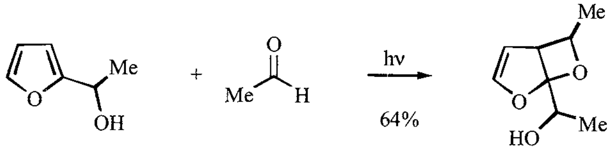
T. Laue, A. Plagens, *Named Organic Reactions,* John Wiley and Sons, Inc., New York, 1998, pp. 209-210; M. B. Smith, J. March in *March's Advanced Organic Chemistry,* 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1249-1250

The reaction is not concerted, as evidenced by reactions of *cis* and *trans* alkenes giving the same product mixture.

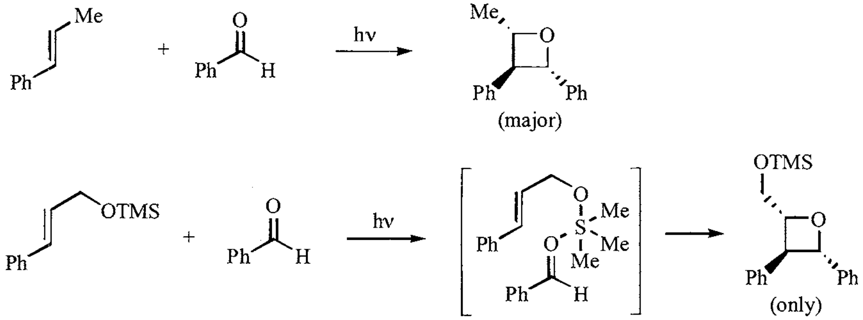
Examples:



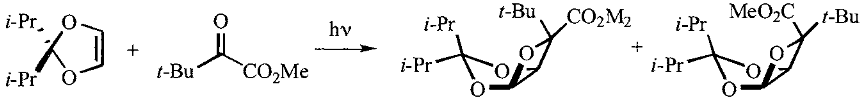
M. C. de la Torre, I. Garcia, M. A. Sierra, *Journal of Organic Chemistry* **2003**, 68, 6611



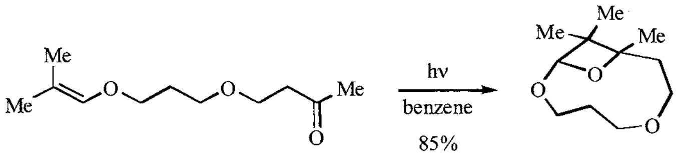
M. D'Auria, L. Emanuele, G. Poggi, R. Racioppi, G. Romaniello, *Tetrahedron* **2000**, 58, 5045



S. A. Fleming, J. J. Gao, *Tetrahedron Letters* **1997**, 38, 5407



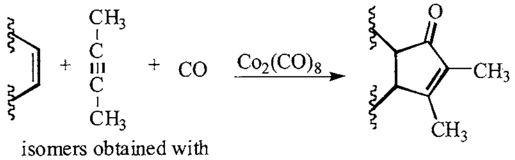
S. Buhr, G. Axel, J. Lex, J. Mattay, J. Schroeer, *Tetrahedron Letters* **1996**, 37, 1195



H. A. J. Car-less, J. Beanland, S. Mwesigye-Kibende, *Tetrahedron Letters* **1987**, 28, 5933

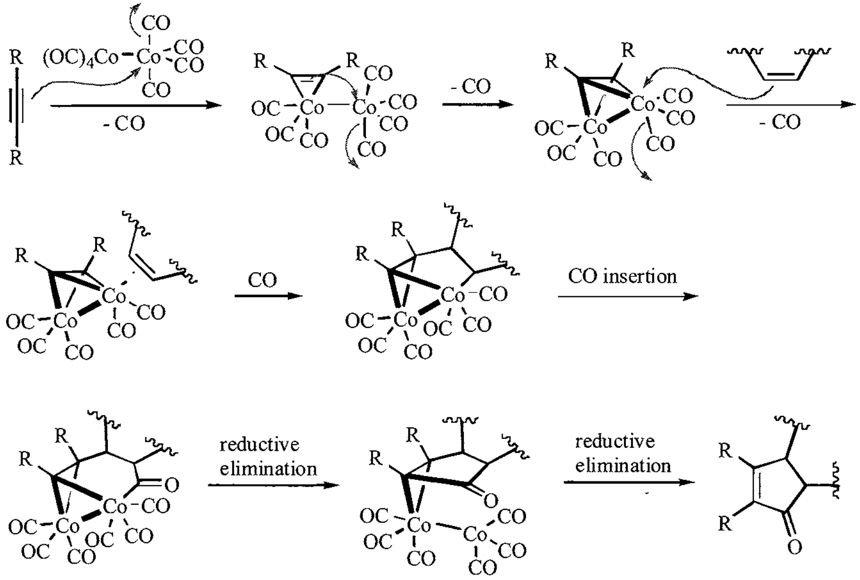
Pauson-Khand Cyclopentenone Annulation

The Reaction:



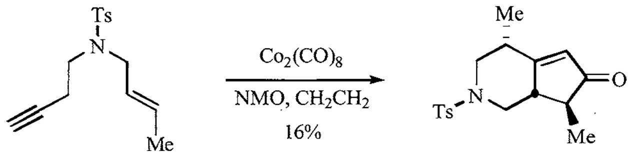
isomers obtained with unsymmetrical alkyne

Proposed Mechanism:

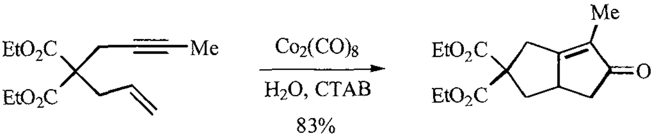


Notes:

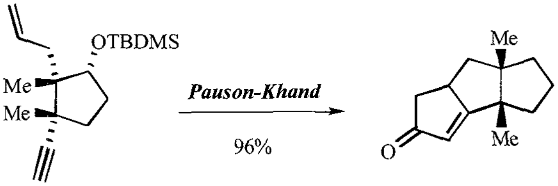
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1091; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 210-213; N. E. Schore, *Organic Reactions* **40**, 1.



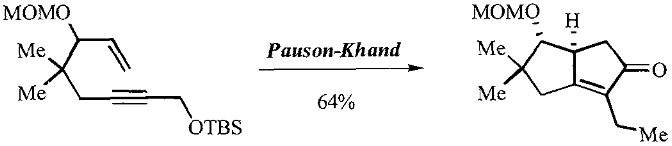
D. A. Ockey, M. A. Lewis, N. E. Schore, *Tetrahedron* **2003**, 59, 5377



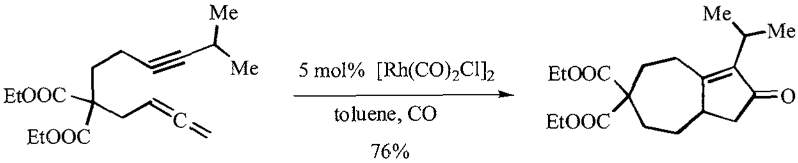
M. E. Krafft, J. A. Wright, L. V. R. Bonaga, *Tetrahedron Letters* **2003**, 44, 3417



C. Mukai, M. Kobayashi, I. J. Kim, M. Hanacka, *Tetrahedron* **2002**, 58, 5225



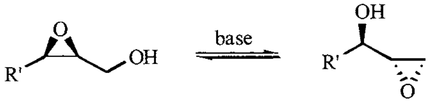
P. Magnus, M. J. Slater, L. M. Principe, *Journal of Organic Chemistry* **1989**, 54, 5148



K. M. Brummond, D. Gao, *Organic Letters* **2003**, 5, 3491;
K. M. Brummond, H. Chen, K. D. Fisher, A. D. Kerekes, B. Rickards, P. C. Sill, S. J. Geib, *Organic Letters*, **2002**, 4, 1931

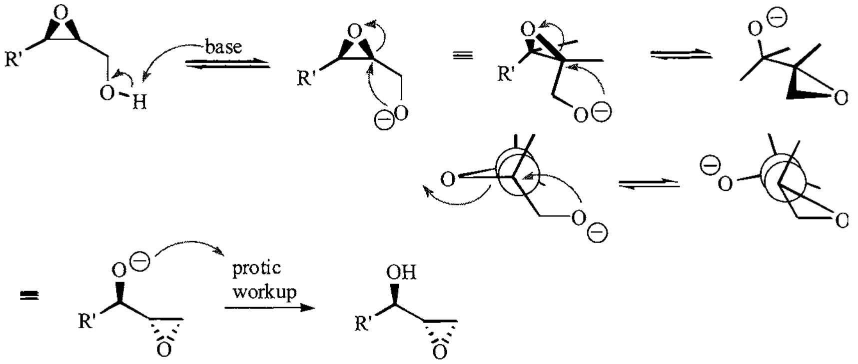
Payne Rearrangement

The Reaction:



base = NaOH, KOH, NaOR, NaSR

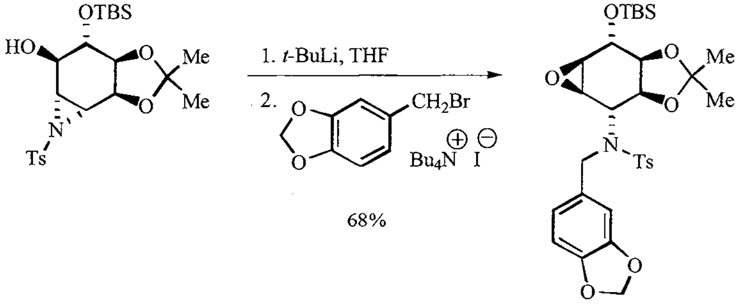
Proposed Mechanism:



Notes:

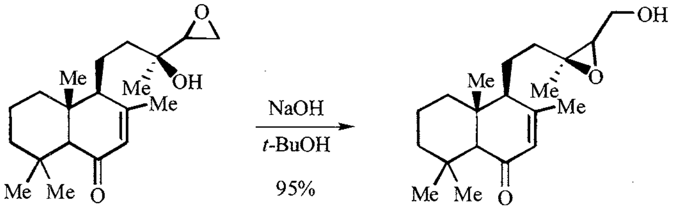
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 481; R. M. Hanson, *Organic Reactions* **60**, 1

An ***Aza-Payne reaction*** is also possible:

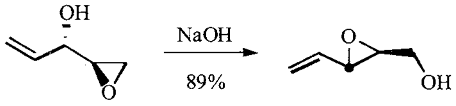


U. Rinner, P. Siengalewicz, T. Hudlicky, *Organic Letters* **2002**, 4, 115

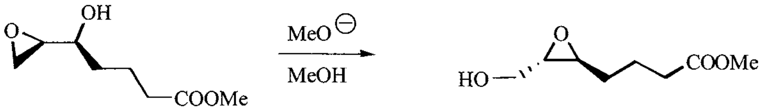
Examples:



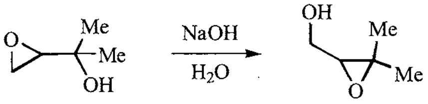
D. Herlem, F. Khuong-Huu, *Tetrahedron* **1997**, 53, 673



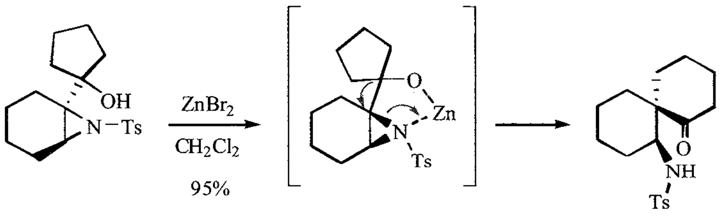
V. Jaeger, D. Schroeter, B. Koppenhoefer, *Tetrahedron* **1991**, 47, 2195



N. Cohen, B. L. Banner, R. J. Lopresti, F. Wong, M. Rosenberger, Y. Y. Liu, E. Thom, A. A. Liebman, *Journal of the American Chemical Society* **1983**, 105, 3661



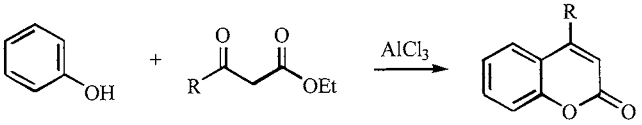
G. B. Payne, *Journal of Organic Chemistry* **1962**, 27, 3819



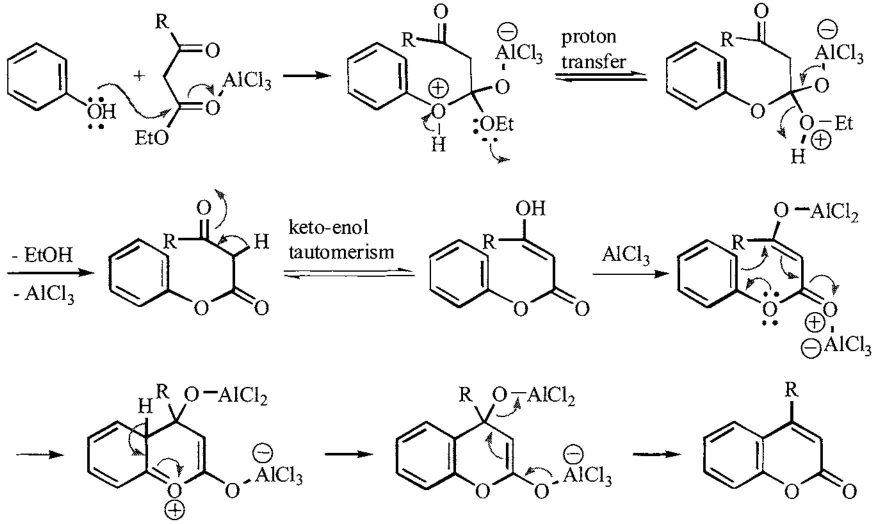
B. M. Wang, Z. L. Song, C. A. Fan, Y. Q. Tu, Y. Shi, *Organic Letters* **2002**, 4, 363

Pechmann Condensation

The Reaction:



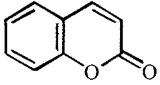
Proposed Mechanism:



Notes:

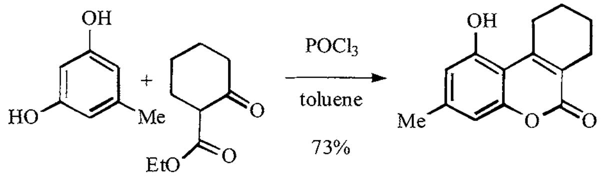
S. Sethna, R. Phadke, *Organic Reactions*, 7, 1

This reaction provides a simple entry into the ***coumarins***:

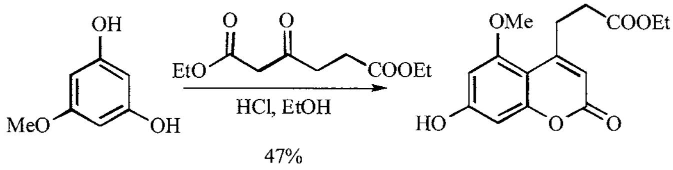


Many catalysts can be used, including sulfuric acid, aluminum chloride, phosphorous pentoxide, etc.

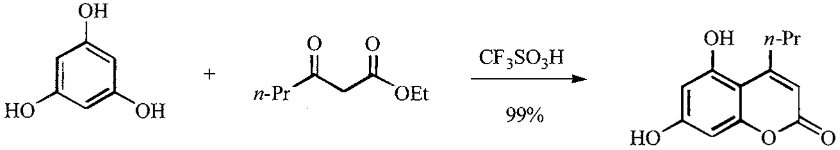
Examples:



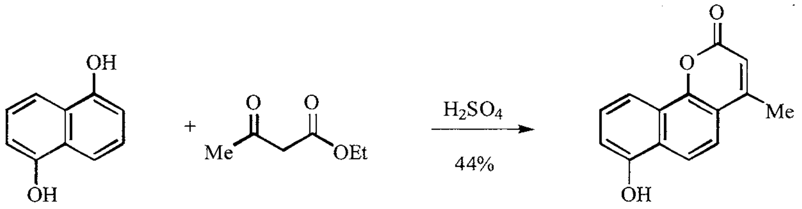
P. Selle's, U. Mueller, *Organic Letters* **2004**, 6, 277



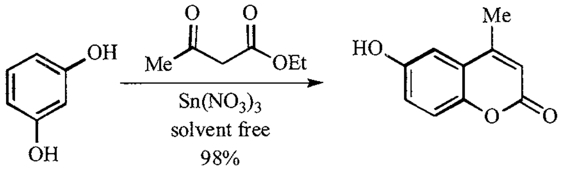
B. M. Trost, F. D. Toste, *Journal of the American Chemical Society* **2003**, 125, 3090



B. Chenera, M. L. West, J. A. Finkelstein, G. B. Dreyer, *Journal of Organic Chemistry*, **1993**, 58, 5605



W. Adam. X. Qian, C. R. Shah-Moeller, *Journal of Organic Chemistry* **1993**, 58, 3769

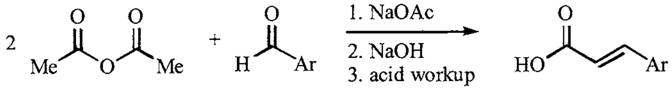


S. S. Bahekara, D, B. Shindeb,*Tetrahedron Letters* **2004,** 45, 7999

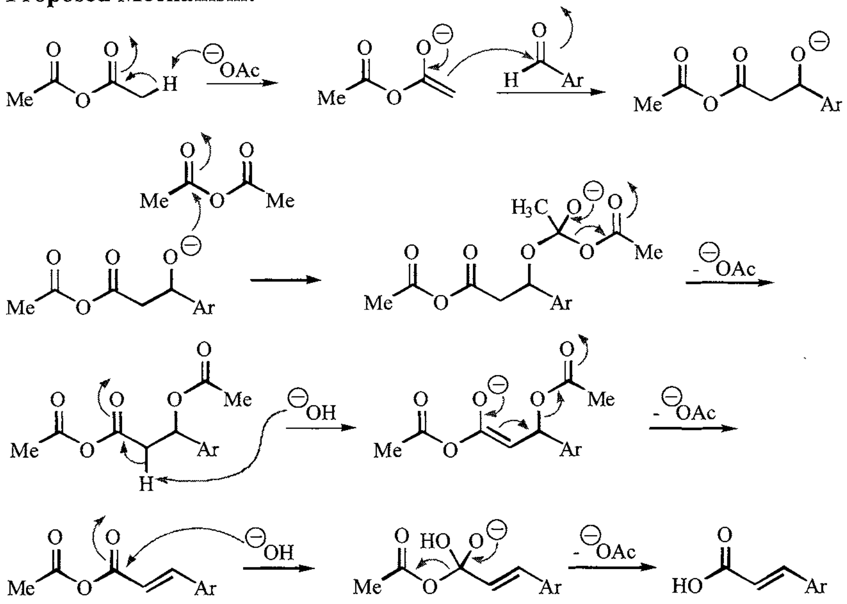
The use of indium(III) can do the same reaction: D. S. Bose, A. P. Rudradas, M. H. Babu, *Tetrahedron Letters* **2002**, 43 , 9195.

Perkin Reaction (Perkin cinnamic acid synthesis)

The Reaction:

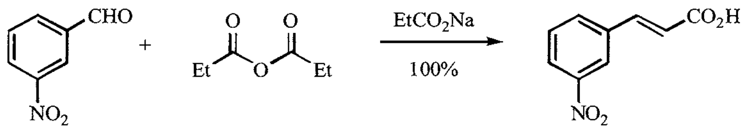


Proposed Mechanism:

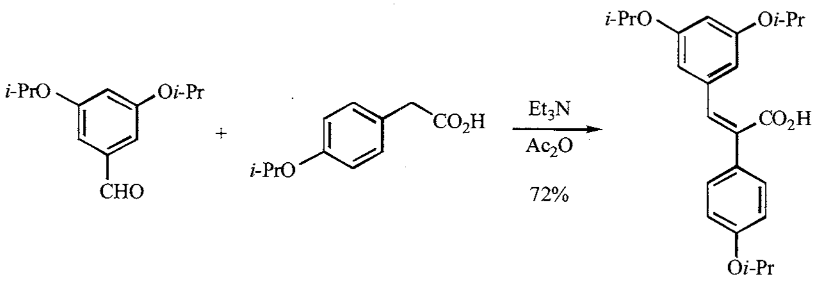


Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p.p. 1217, 1229; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 213-215; J. R. Johnson, *Organic Reactions* **1**, 8.

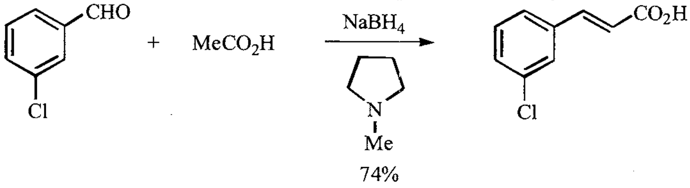


R. W. Maxwell, R. Adams, *Journal of the American Chemical Society* **1930**, 52, 2967

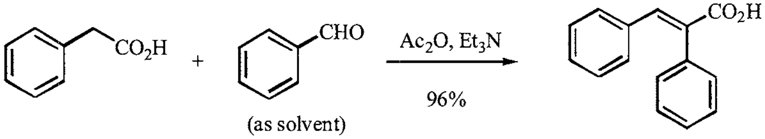


G. Solladie, Y. Pasturel-Jacope, J. Maignan, *Tetrahedron* **2003**, 59, 3315.

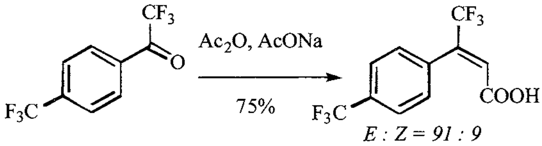
This method allows for the use of acids as a replacement for anhydrides.



C. I. Chiriac, F. Tanasa, M. Onciu, *Tetrahedron Letters* **2003**, 44, 3579



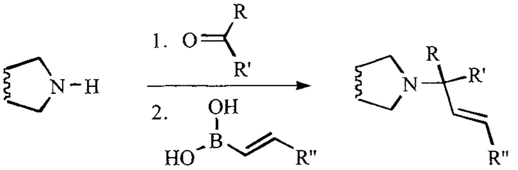
R. F. Buckles, J. A. Cooper, *Journal of Organic Chemistry* **1965**, 30, 1588

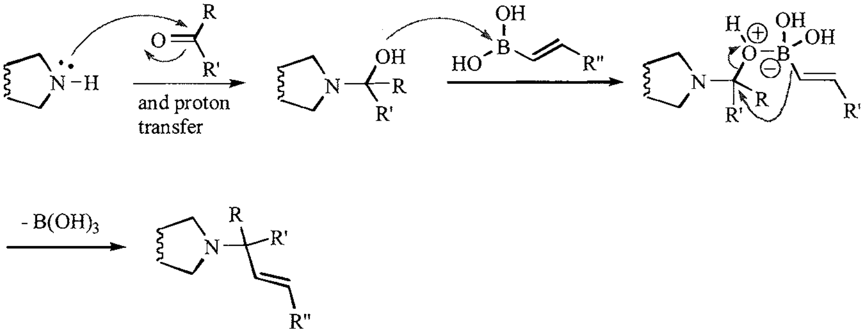


D. V. Sevenard, *Tetrahedron Letters* **2003**, 44, 7119

Petasis Reaction

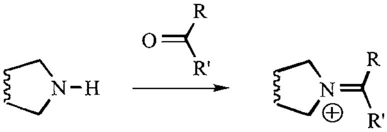
The Reaction:



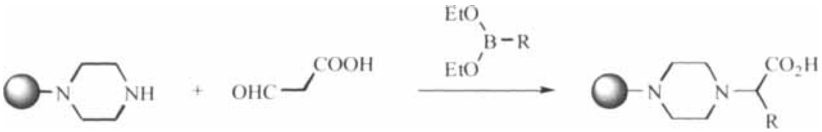


See: J. P. Tremblay-Morin, S. Raeppel, F. Gaudette, *Tetrahedron Letters* **2004**, 45, 3471

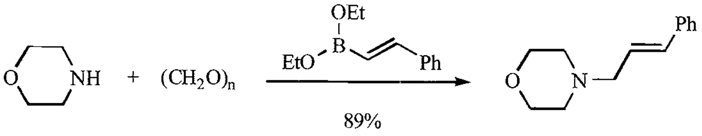
This is an example of a ***boronic-Mannich reaction***. The mechanism is not fully established; however it has been shown that an intermediate of the type:



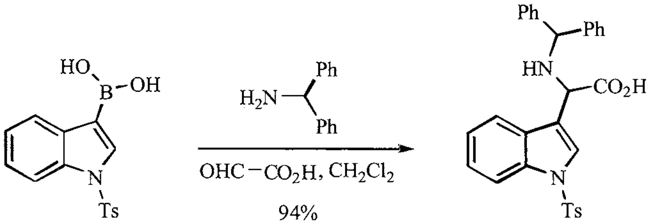
is not involved since an ***Eschenmoser salt*** will not react.



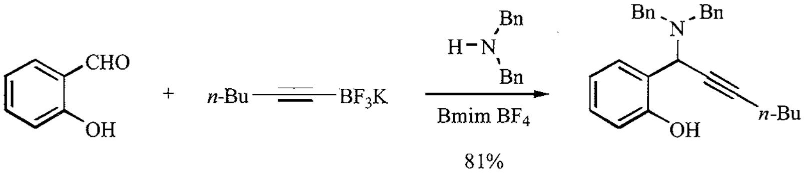
A series was prepared using a reusable resin. Yields were good.
K. A. Thompson, D. G. Hall, *Chemical Communications* **2000**, 2379



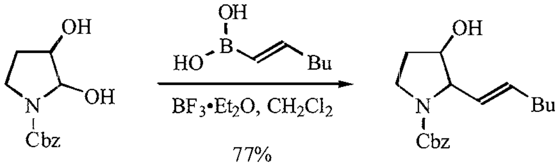
N. A. Petasis, I. Akritopoulou, *Tetrahedron Letters* **1993**, 34, 583



B. Jiang, C.-G. Yang, X.-H. Gu, *Tetrahedron Letters* **2001**, 42, 2546



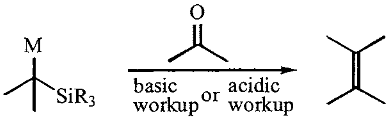
G. W. Kalbaka, B. Venkataiah, G. Dong, *Tetrahedron Letters* **2004**, 45, 727



R. A. Batey, D. B. MacKay, V. Santhakumar, *Journal of the American Chemical Society* **1999**, 121, 5075

Peterson Olefination Reaction (Peterson Elimination, Silyl-Wittig Reaction)

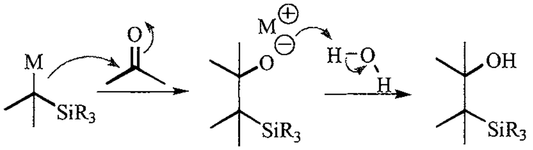
The Reaction:



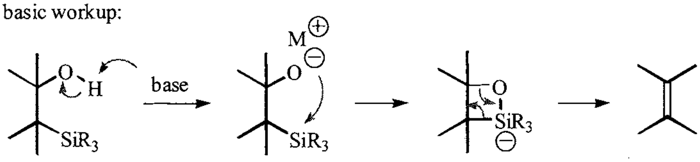
M = Lithium or Magnesium

Proposed Mechanism:

Different alkenes can be obtained, depending on how the reaction is carried out. In both approaches the same intermediate is obtained:

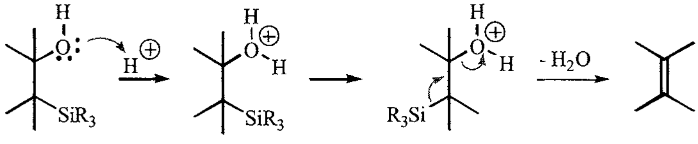


basic workup:



cis elimination

acidic workup:



anti elimination

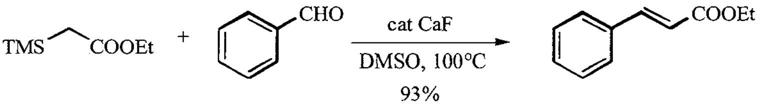
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1228; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 215-217; D. J. Ager, *Organic Reactions* **38**, 1.

For an altenative approach, see ***Tebbe Reagent***, ***Lombardo Reagent*** or the ***Wittig Reaction***.

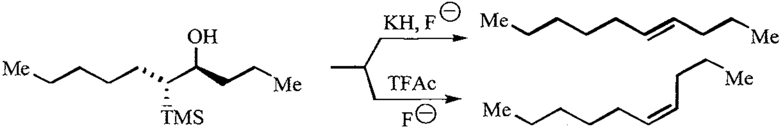
The steric requirements for the ***Peterson*** approach are less than for the ***Wittig*** approach.

A variation using fluoride-based elimination has been reported:



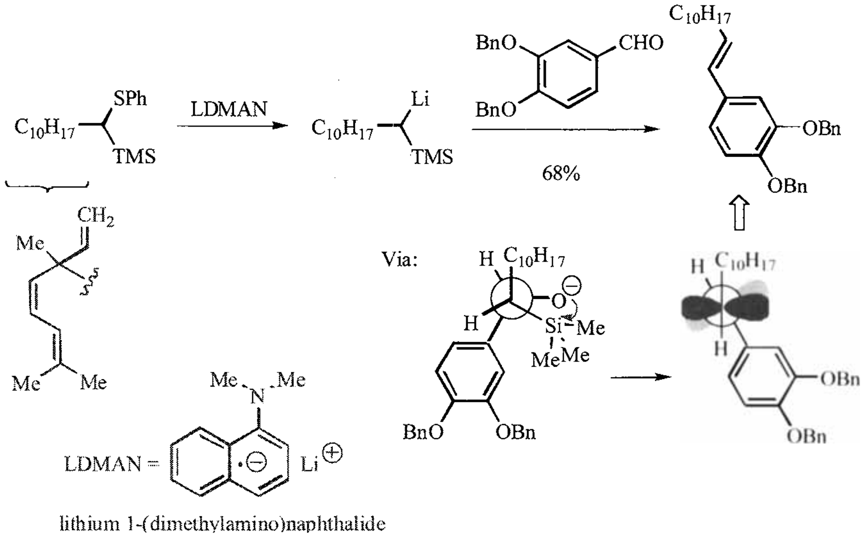
M. Bellassoued, N. Ozanne, *Journal of Organic Chemistry* **1995**, 60, 6582

Unique control of stereochemistry:

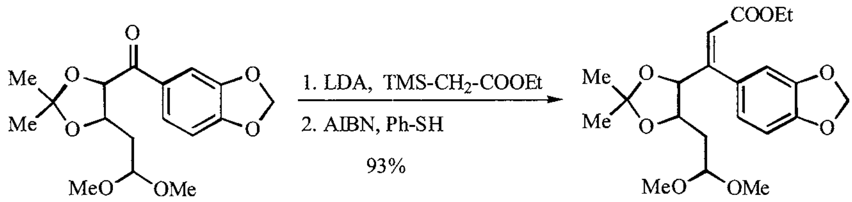


A. G. M. Barrett, J. A. Flygare, *Journal of Organic Chemistry* **1991**, 56, 638

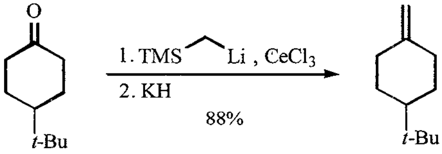
Examples:



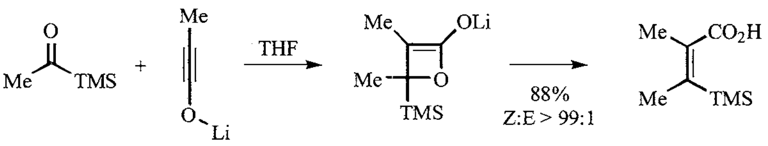
I. Lengyel, V. Cesare, T. Taldone, *Tetrahedron* **2004**, 60, 1107



J. E. Sample, T. D. Owens, K. Nguyen, O. E. Levy, *Organic Letters* **2000**, 2, 2769



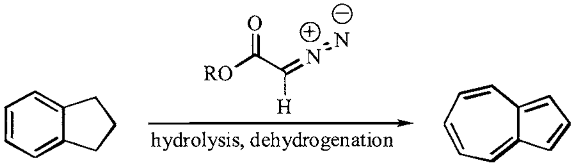
B. Henkel, B. Beck, B. Westner, B. Mejat, A. Domling, *Tetrahedron Letters* **2003**, 44, 89



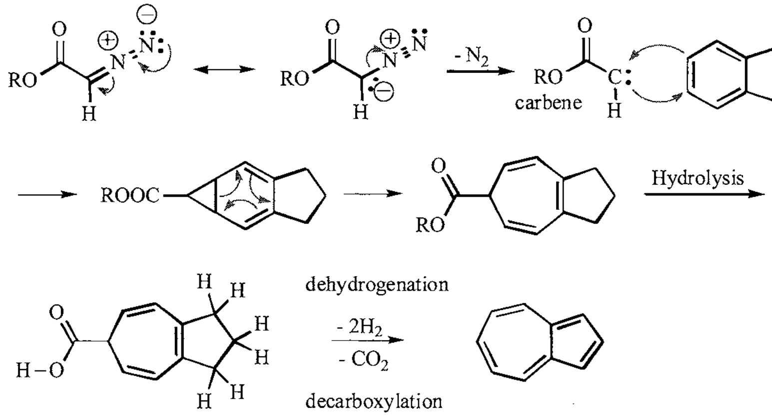
S. P. G. Costa, H. L. S. Maia, S. M. M. A. Pereira-Lima, *Organic & Biomolecular Chemistry* **2003**, 1, 1475

Pfau-Plattner Azulene Synthesis

The Reaction:

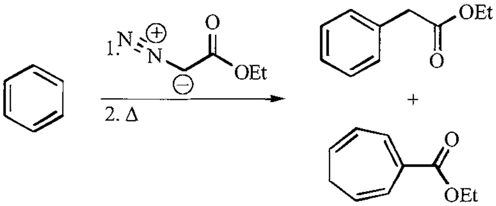


Proposed Mechanism:



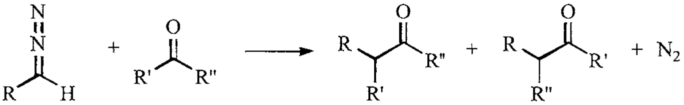
Notes:

This chemistry is an application of the ***Buchner Method of Ring Enlargement***:

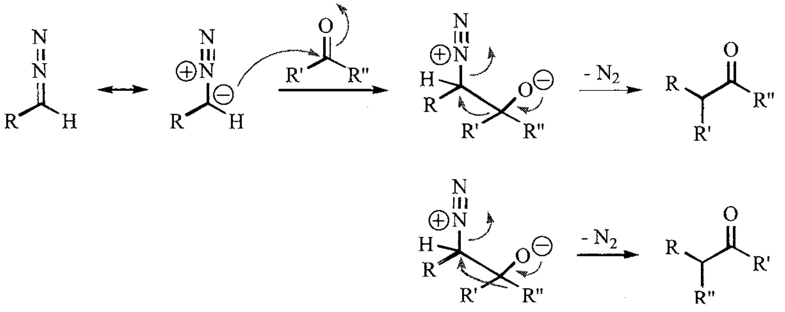


The reaction, as originally carried out, is of little contemporary use. Metal-mediated catalysis is more-often applied, where the reactive species are metal carbenoids.

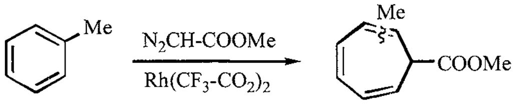
Buchner-Curtius-Schlotterbeck Reaction



Proposed Mechanism:

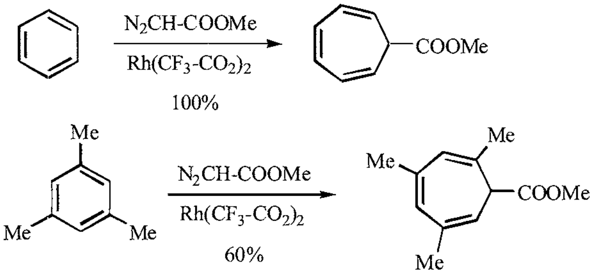


Examples:

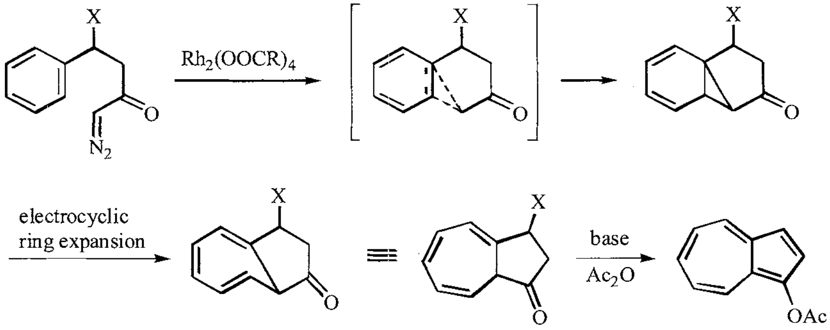


2-Me : 3-Me: 4-Me = 17 : 23 : 56

A. J. Anciaux, A. Demonceau, A. J. Hubert, A. F. Noels, N. Petiniot, P. Teyssie, *Journal of the Chemical Society, Chemical Communications* **1980**, 765



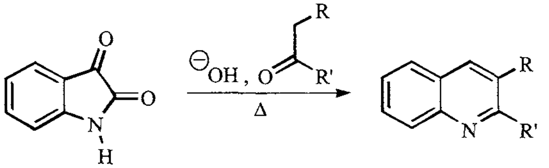
A. J. Anciaux, A. Demonceau, A. F. Noels, A. J. Hubert, R. Warin, P. Teyssi, *Journal of Organic Chemistry* **1981**, 46, 873



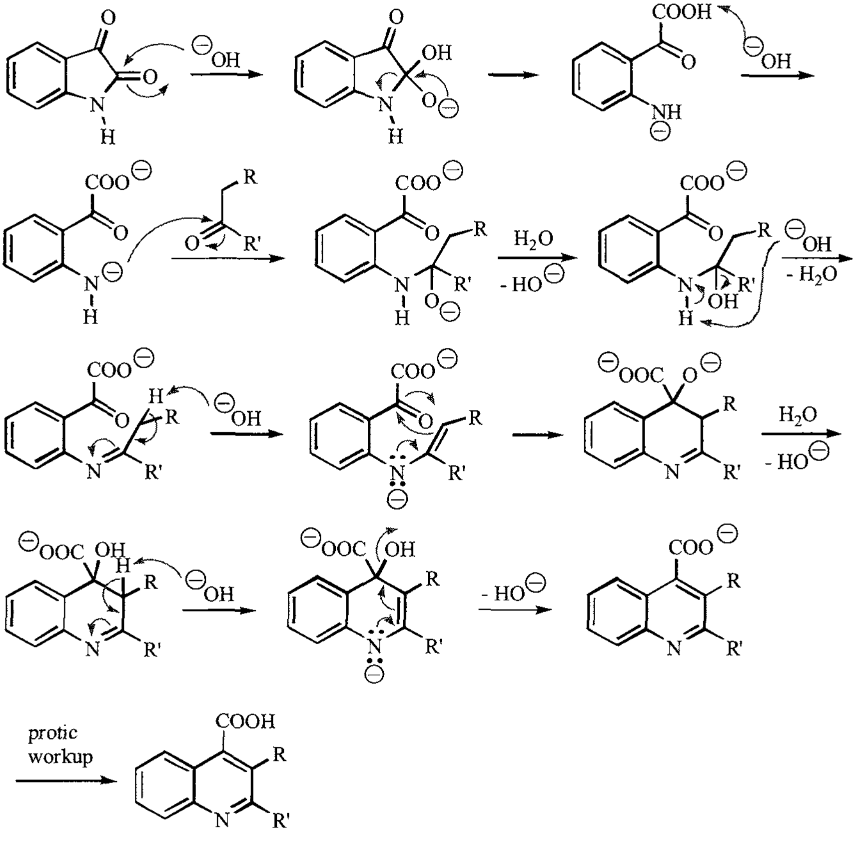
J. L. Kane, Jr., K. M. Shea, A. L. Crombie, R. L. Danheiser, *Organic Letters*, **2001**, 3, 1081

Pfitzinger Reaction

The Reaction:

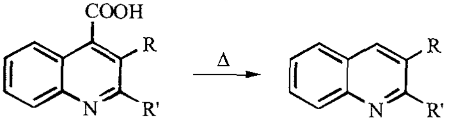


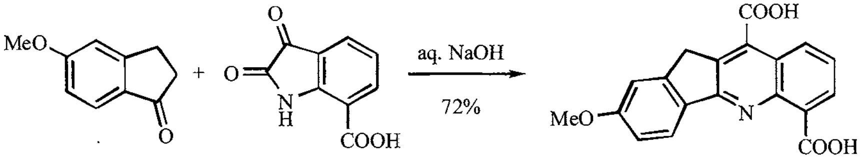
Proposed Mechanism:



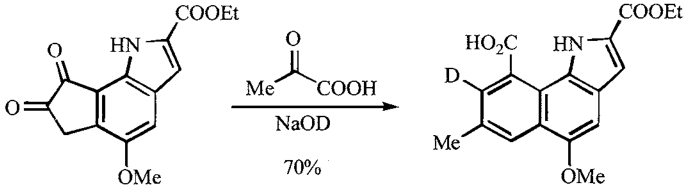
Notes:

Decarboxylation can take place

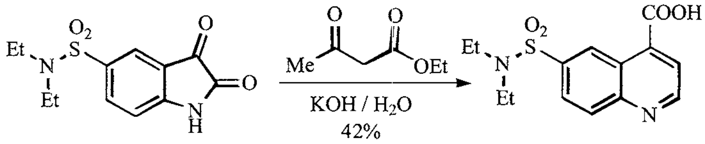




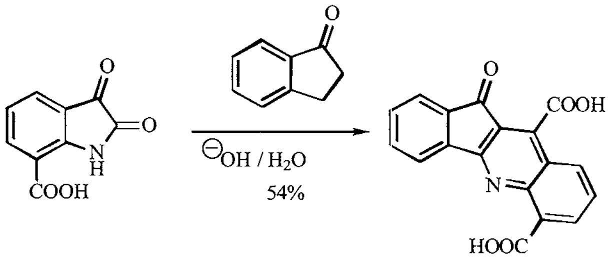
L. W. Deady, J. Â Desneves, A. J. Kaye, M. Thompson, G. J. Finlay, B. C. Baguley, W. A. Denny, *Bioorganic and Medicinal Chemistry* **1999**, 7, 2801



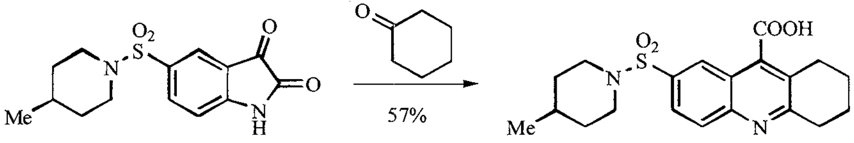
J. A. Jongejan, R. P. Bexemer, J. A. Duine, *Tetrahedron Letters* **1988**, 29, 3709



A. V. Ivachtchenko, A. V. Khvat, V. V. Kobak, V. M. Kysil, C. T. Williams, *Tetrahedron Letters* **2004**, 4, 5473



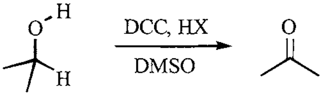
L. W. Deady, J. Desneves, A. J. Kaye, M,Thompson, G. J. Finlay, B. C. Baguley, W. A. Denny, *Bioorganic & Medicinal Chemistry* **1999**, 7, 2801



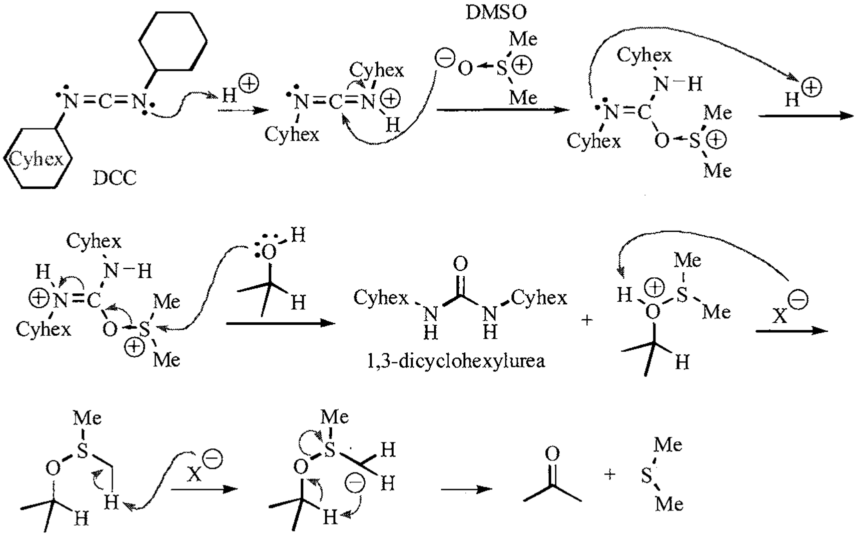
This paper describes the preparation of a number of libraries constructed with this reaction. A. V. Ivachtchenko, V. V. Kobak, A. P. Il'yin, A. S. Trifilenkov, A. A. Busel, *Journal of Combinatorial Chemistry* **2003**, 5, 645

Pfitzner-Moffatt Oxidation

The Reaction:



Proposed Mechanism:



A sulfur ylide is formed with base which then abstracts the α proton, generating dimethylsulfide and the aldehyde or ketone.

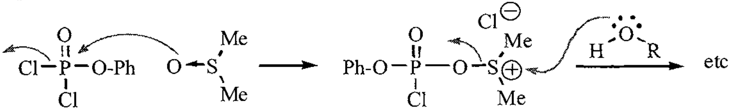
Notes:

T. T. Tidwell, *Organic Reactions* **39**, 3.

A number of oxidations belong to this general class.

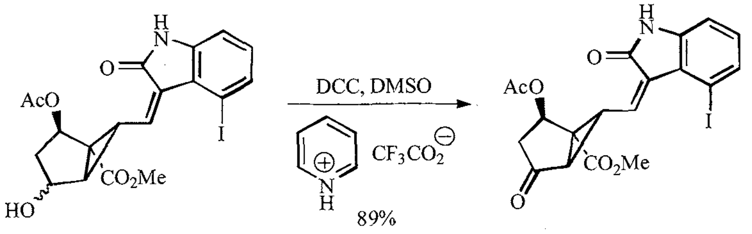
Dimethyl sulfoxide oxidations: W. W. Epstein, F. W. Sweat, *Chemical Reviews* **1967**, 67, 247

An "improved" reagent, based on the general idea associated with DMSO-based oxidations has been reported:

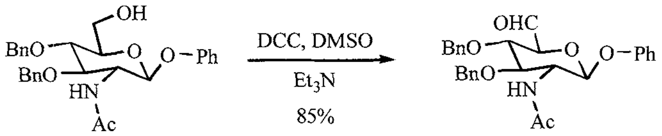


H.-J. Liu, J. M. Nyangulu, *Tetrahedron Letters* **1988**, 29, 3167

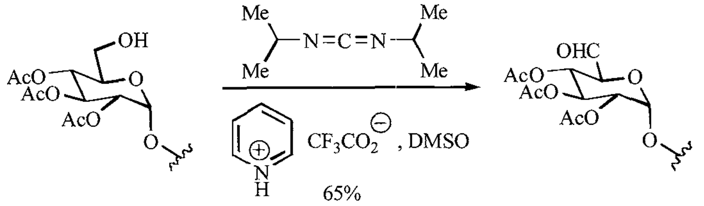
Examples:



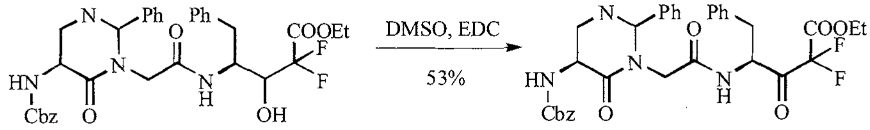
R. Schworer, R. R. Schmidt, *Journal of the American Chemical Society* **2002**, 124, 1632

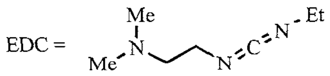


R. Schworer, R. R. Schmidt, *Journal of the American Chemical Society* **2002**, 124, 1632



B. Sauerbrei, J. Niggemann, S. Grisger, S. Lee, H. G. Floss, *Carbohydrate Research* **1996**, 280, 223

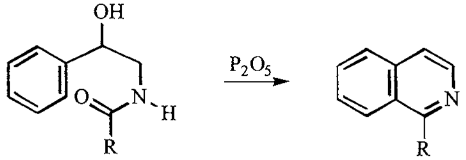




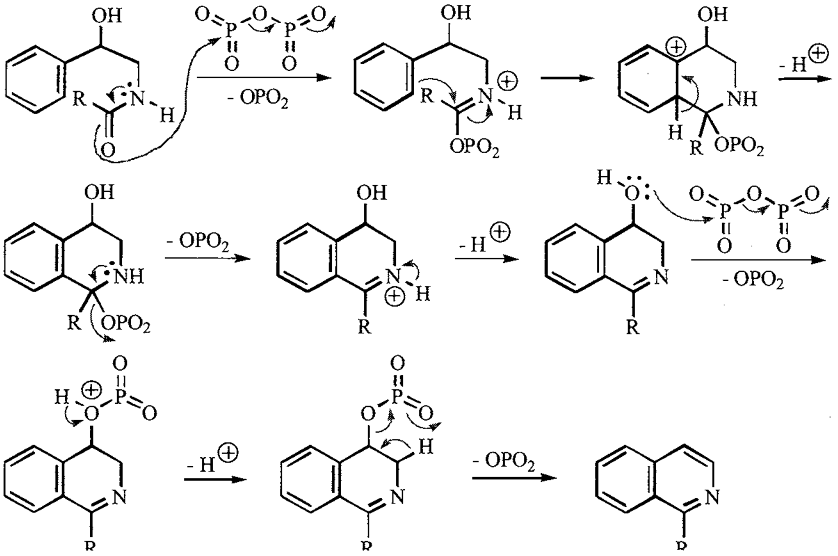
F. Akahoshi, A. Ashimori, Y. Sakashita, M. Eda, T. Imada, M. Nakajima, N. Mitsutomi, S. Kuwahara, T. Ohtsuka, C. Fukaya, M. Miyazaki, N. Nakamur, *Journal of Medicinal Chemistry*, **2001**, 44, 1297

Pictet-Gams Isoquinoline Synthesis

The Reaction:



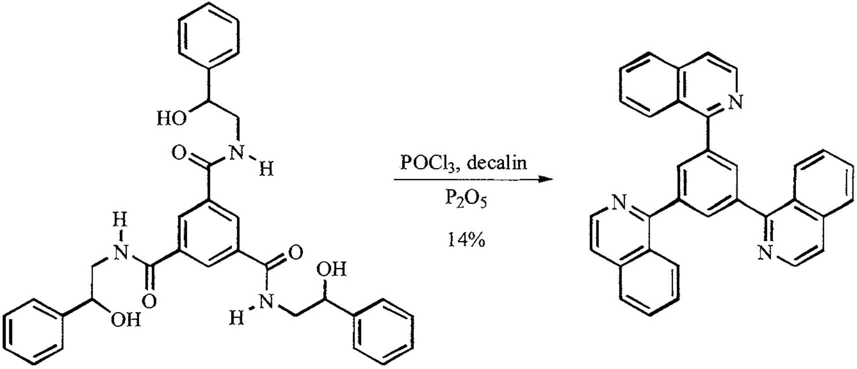
Proposed Mechanism:



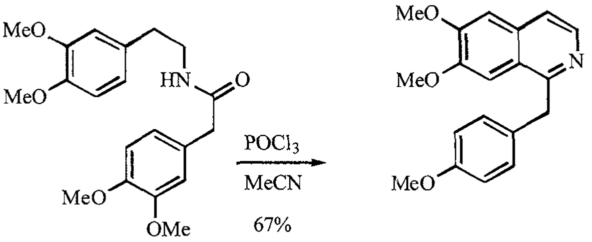
Notes:

Other condensing agents can be used: Examples: $POCl_3$, Polyphosphoric acid

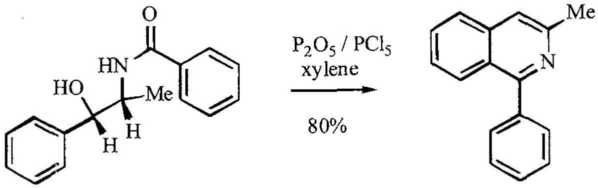
Examples:



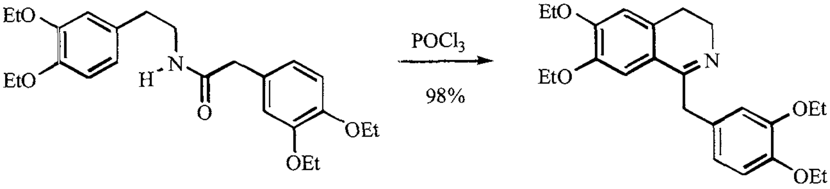
G. Dyker, M. Gabler, M. Nouroozian. P. Schulz, *Tetrahedron Letters* **1994**, 35, 9697



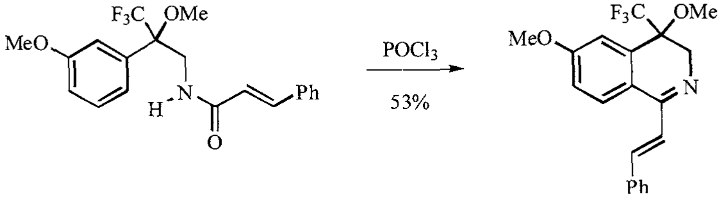
J. R. Falck, S. Manna, C. Mioskowski, *Journal of Organic Chemistry* **1981**, 46, 3742



A. O. Fitton. J. R. Frost, M. M. Zakaria, G. Andrew, *Journal of the Chemical Society, Chemical Communications* **1973**, 889



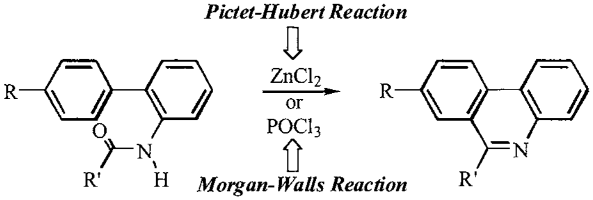
J. Wiejlard, E. F. Swanezy, E. Tashihan, *Journal of the American Chemical Society* **1949**, 71, 1889



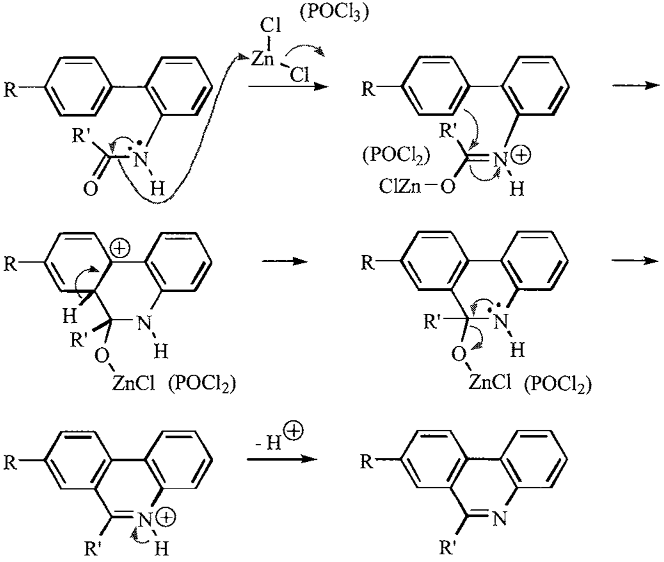
The CF$_3$ group appears to delay loss of the -OMe group under the reaction conditions.
L. Poszavacz, G. Simig, *Tetrahedron,* **2001**, 57, 8573

Pictet-Hubert Reaction / Morgan-Walls Reaction

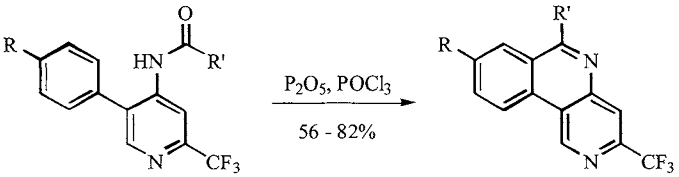
The Reaction:



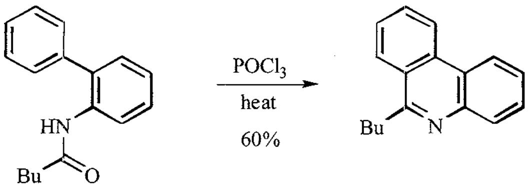
Proposed Mechanism:



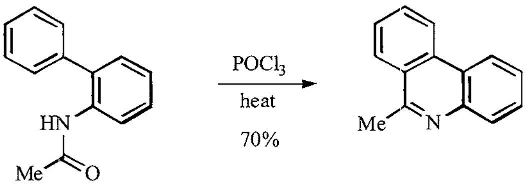
Examples:



A series of these products was prepared.
V. I. Tyvorskii, D. N. Bobrov, O. G. Kulinkovich, W. Aelterman, N. De Kimpe, *Tetrahedron* **2000**, 56, 7313



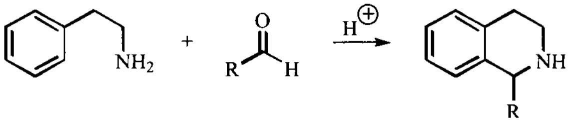
H. Gilman, J. Eisch, *Journal of the American Chemical Society* **1957**, 79, 4423



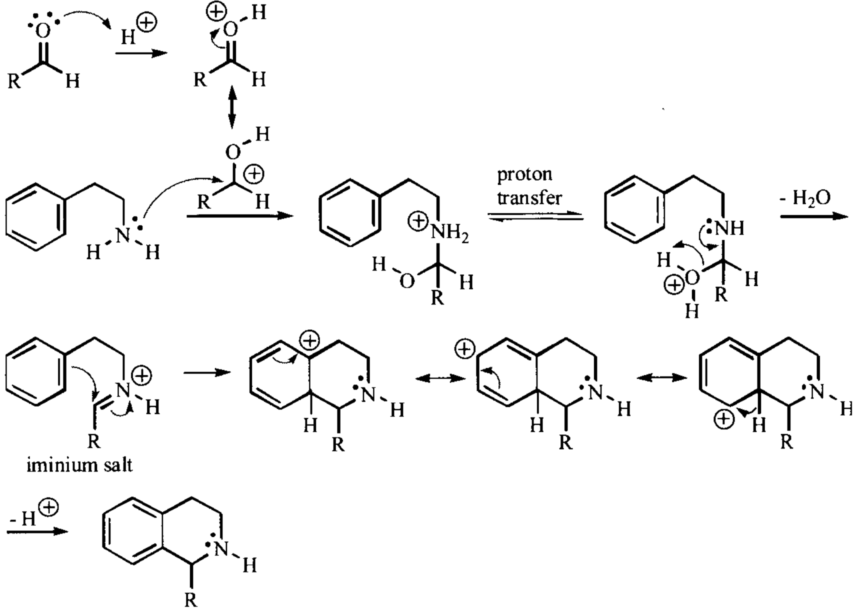
S. T. Mullins, N. K. Annan, P. R. Cook, G. Lowe, *Biochemistry* **1992**, 31, 842

Pictet-Spengler Isoquinoline Synthesis

The Reaction:

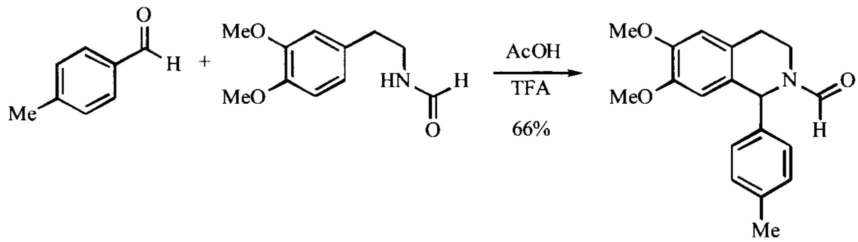


Proposed Mechanism:

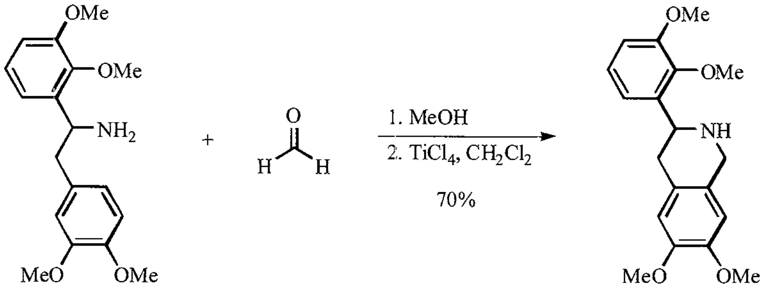


Notes:

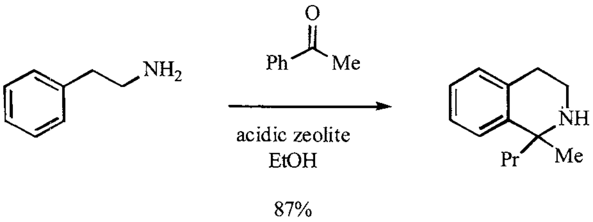
W. M. Whaley, T. Govindacharl, *Organic Reactions* **6**, 3.



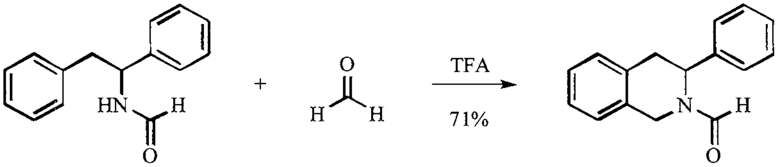
L. K. Lukanov, A. P. Venkov, N. M. Millov, *Synthesis* **1987**, 1031



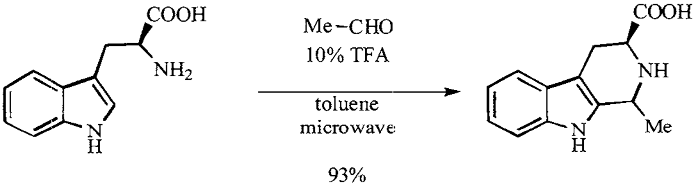
N. Totomayor, E. Dominguez, E. Lete, *Tetrahedron* **1995**, 51, 12159



A. Hegedus, Z. Hell, *Tetrahedron Letters* **2004**, 45, 8553



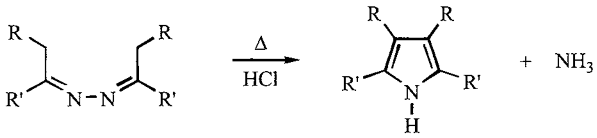
B. E. Maryanoff, M. C. Rebarchak, *Synthesis* **1992**, 1245



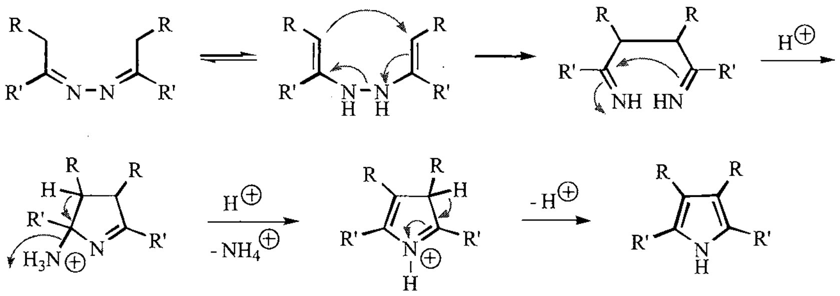
F.-M. Kuo, M.-C. Tseng, Y.-H. Yen, Y.-H. Chu, *Tetrahedron* **2004**, 60, 12075

Piloty-Robinson (Pyrrole) Synthesis

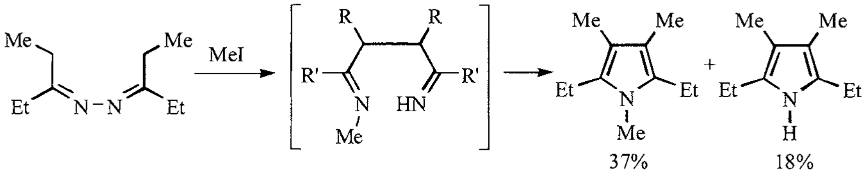
The Reaction:



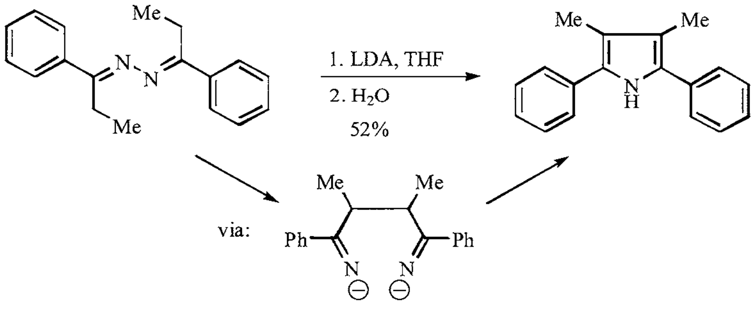
Proposed Mechanism:



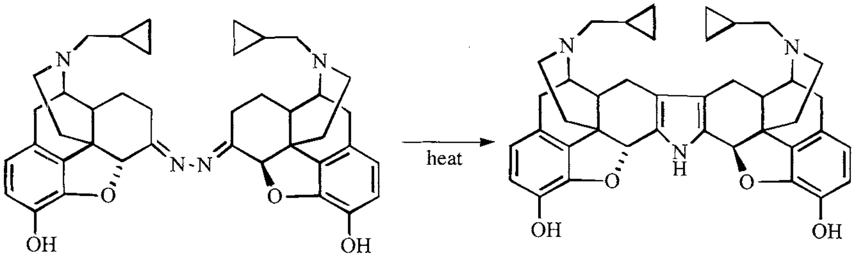
Notes:



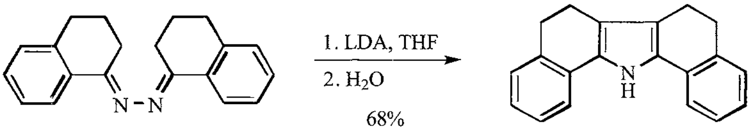
Examples:



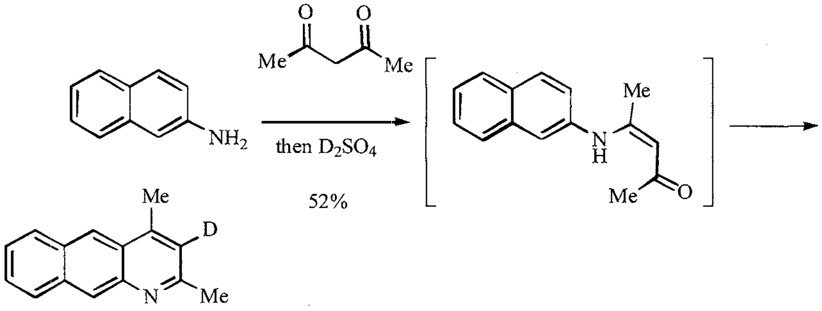
Z. Yoshida, T. Harada, Y. Tamura, *Tetrahedron Letters* **1976**, 17, 3823



P. S. Portoghese, A. W. Lipkowski, A. E. Takemor, *Journal of Medicinal Chemistry* **1987**, 30, 239



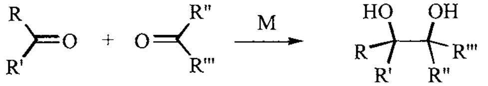
Y. Tamura, T. Harada, Z.-I. Yoshida, *Journal of Organic Chemistry* **1978**, 43, 3370



J. L. Born, *Journal of Organic Chemistry* **1972**, 37, 3952

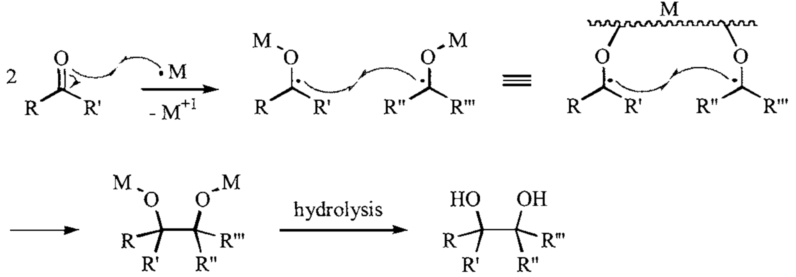
Pinacol Coupling Reaction

The Reaction:



Proposed Mechanism:

Most mechanistic interpretations have the metal providing an electron, followed by coupling of the ketyl moieties:

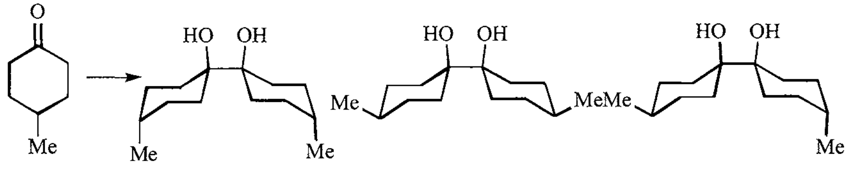


Notes:

There are many questions still to be answered. What is the role of different metals in the reaction? What are the factors governing mixed coupling?

Typical reductive coupling reaction mixtures: Al / Hg, Mg / Hg, Mg / $TiCl_4$, SmI_2, Mg / MgI_2, CeI_2, Yb.

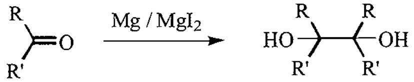
Influence of conditions on product composition:



[Hg-Al]	43	13	44
[Ti]	4	63	33

B. P. Mundy, D. R. Bruss, Y. Kim, R. D. Larsen, R. J. Warnet, *Tetrahedron Letters* **1985**, 26, 3927

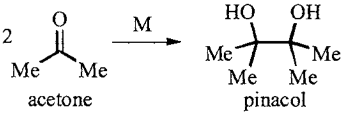
Gomberg-Bachmann Pinacol Synthesis

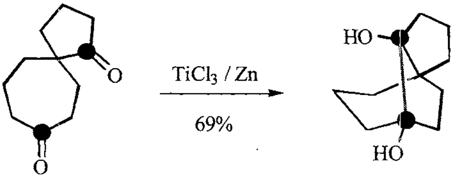


Enantioselective Pinacol Coupling of Aldehydes: A. Bensari, J. -L. Renaud, O. Riant, *Organic Letters* **2001**, 3, 3863

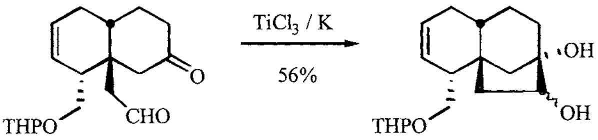
See: E. J. Corey, R. L. Danheiser, S. Chandrasekaran, *Journal of Organic Chemistry* **1976**, 41, 260; S. Talukdar, J.-M. Fang, *Journal of Organic Chemistry* **2001**, 66, 330; J. E. McMurry, W. Choy, *Journal of Organic Chemistry* **1978**, 43, 1800

The ***Pinacol Coupling*** of acetone gives 2,3-dimethyl-2,3-butanediol which is also known as pinacol and the source of the name of this reaction:

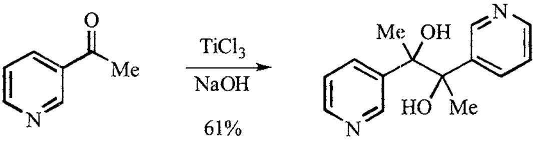




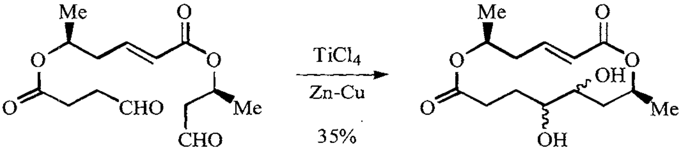
P. E. Eaton, P. G. Jobe, K. Nyi, *Journal of the American Chemical Society* **1980**, 102, 6636



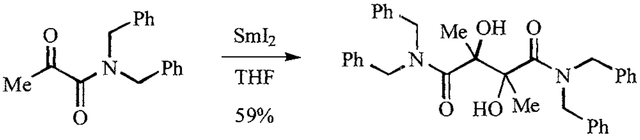
E. J. Corey, R. L. Danheiser, S. Chandrasekaran, P. Siret, G. E. Keck, J. -L. Gras, *Journal of the American Chemical Society* **1978**, 100, 8031, 8034



A. Clerici, O. Porta, *Tetrahedron Letters* **1982**, 23, 3517



D. Ghiringhelli, *Tetrahedron Letters* **1983**, 24, 287

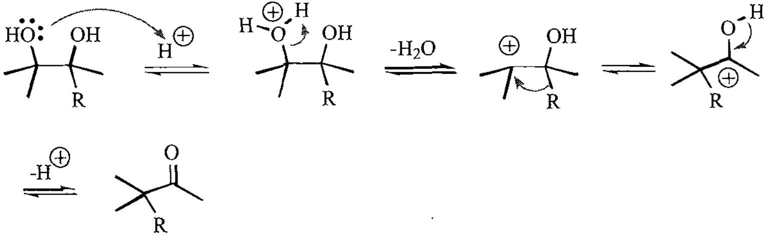


M. Yamashita, K. Okuyama, I. Kawasaki, S. Ohta, *Tetrahedron Letters* **1996**, 37, 7755

Pinacol Rearrangement

The Reaction:

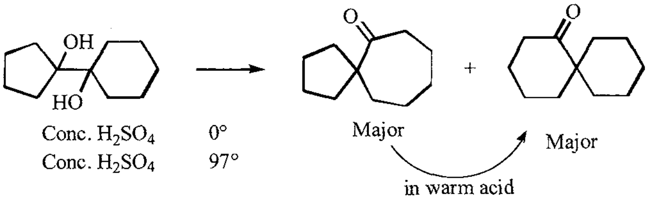
Proposed Mechanism:



Notes:

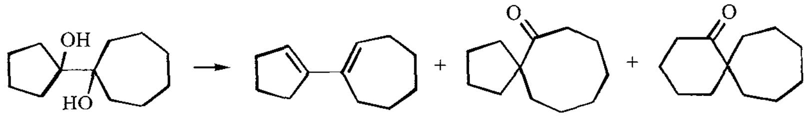
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 217-218; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1396-1398

Influence of temperature:



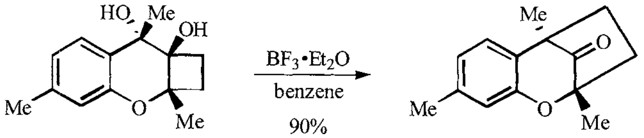
B. P. Mundy, R. Srinivasa, *Tetrahedron Letters* **1979**, 20, 2671

Concentration Effects

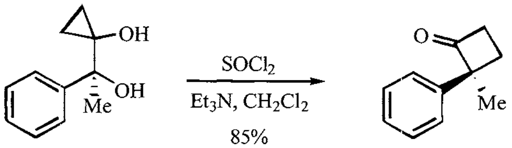


Conc. H$_2$SO$_4$	0°	0	5	95
25%. H$_2$SO$_4$	0°	30	1	69

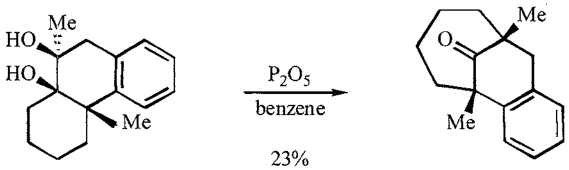
B. P. Mundy, R. Srinivasa, R. D. Otzenberger, A. R. DeBernardis, *Tetrahedron Letters* **1979**, 20, 2673



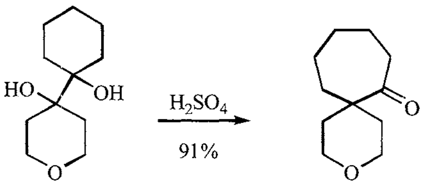
A. Nath, J. Mal, R. V. Venkateswaran, *Journal of Organic Chemistry* **1996**, 61, 4391



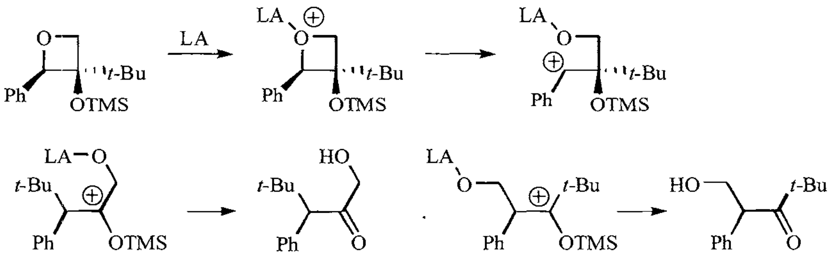
H. Nemoto, J. Miyuata, H. Hakamata, M. Nagamochi, K. Fukumoto, *Tetrahedron* **1995**, 51, 5511



C. M. Marson, S. Harper, A.J. Walker, J. Pickering, J. Campbell, R. Wrigglesworth, S.J. Edge, *Tetrahedron* **1993**, 49, 10339



B. P. Mundy, Y. Kim, R. J. Warnet, *Heterocycles* **1983**, 20, 1727

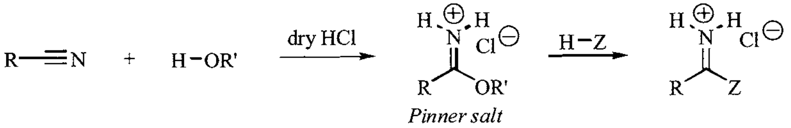


LA	RATIO	
$ZnCl_2$, CH_2Cl_2	43	57
$TiCl_4$, ether	100	0
$AlCl_3$, toluene	21	79

T. Bach, F. Eilers, *Journal of Organic Chemistry* **1999**, 64, 8041

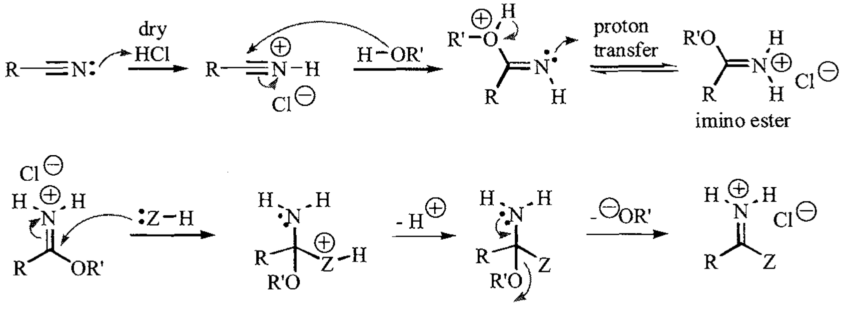
Pinner Reaction

The Reaction:



Z = -OH, -OR, -SH, NR_2

Proposed Mechanism:

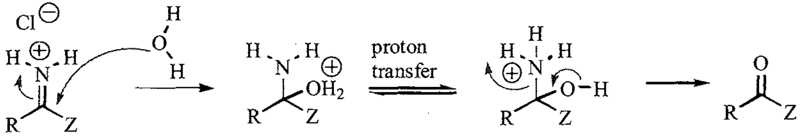


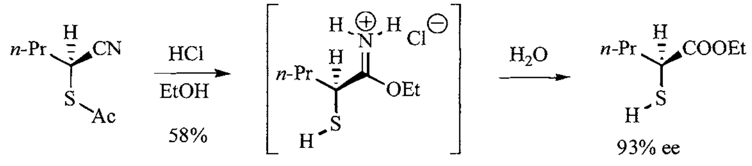
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1183

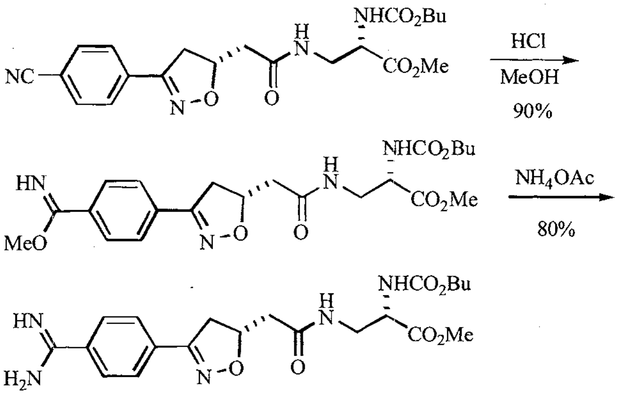
Imino esters are also known as imidates or imino ethers

Normally the product is subjected to hydrolysis:

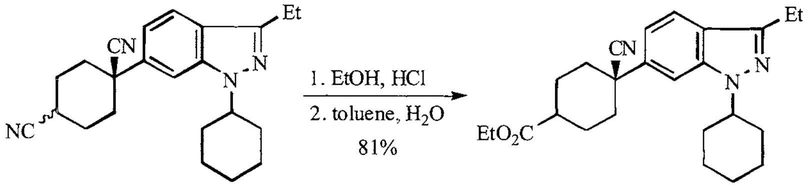




S. Gaupp, F. Effenberger, *Tetrahedron: Asymmetry* **1999**, 10, 1777

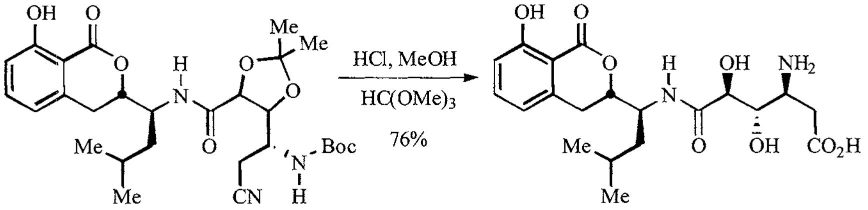


L.-H. Zhang, J. C. Chung, T. D. Costello, I. Valvis, P. Ma, S. Kauffman, R. Ward, *Journal of Organic Chemistry* **1997**, 62, 2466

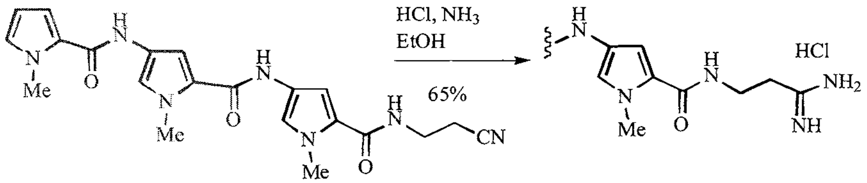


S. Caron, E. Vazquez, *Organic Process Research & Development* **2001**, 5, 587

Intermolecular Pinner Reaction:



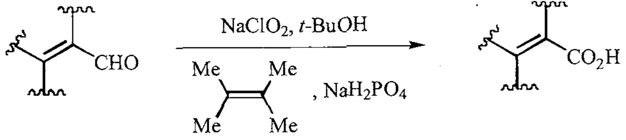
Y. Hamada, O. Hara, A. Kawai, Y. Kohno, T. Shioiri, *Tetrahedron* **1991**, 47, 8635



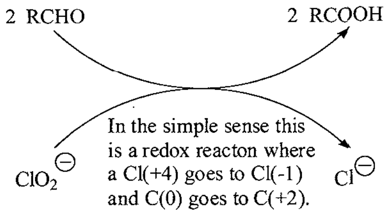
S. K. Sharma, M. Tandon, J. W. Lown, *Journal of Organic Chemistry* **2001**, 66, 1030

Pinnick Oxidation

The Reaction:

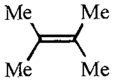


Proposed Mechanism:



In the simple sense this is a redox reacton where a Cl(+4) goes to Cl(-1) and C(0) goes to C(+2).

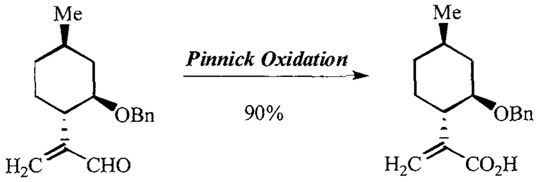
Notes:

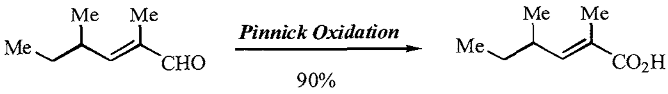


serves as a scavanger for other oxidants.

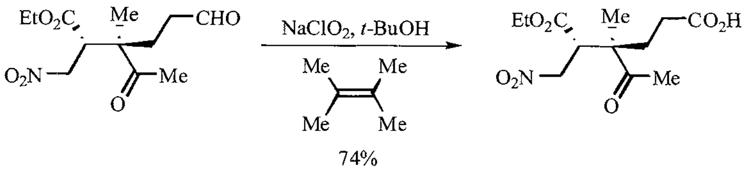
Idea for reaction based on
G. A. Krause, B. Roth, *Journal of Organic Chemistry* **1980**, 45, 4825

Examples:

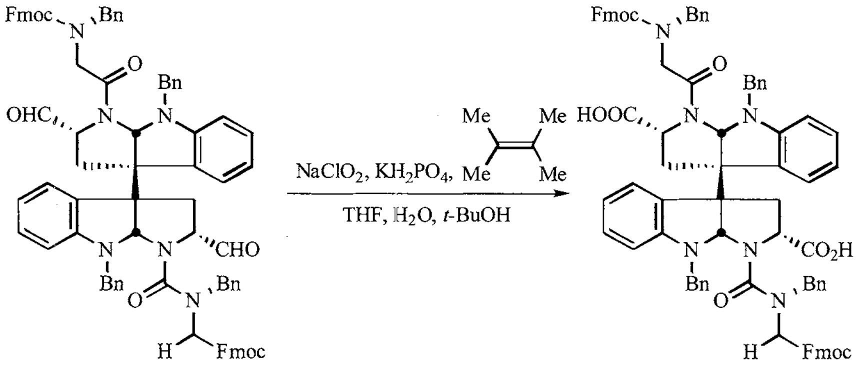




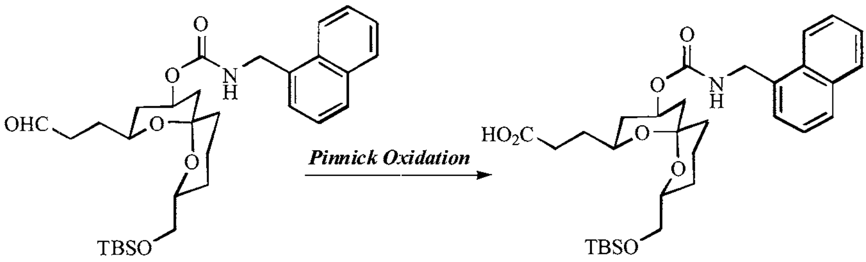
B. S. Bal, W. E. Childers, Jr., H. W. Pinnick, *Tetrahedron* **1981**, 37, 2091



J. Mulzer, D. Reither, *Organic Letters* **2000**, 2, 3139



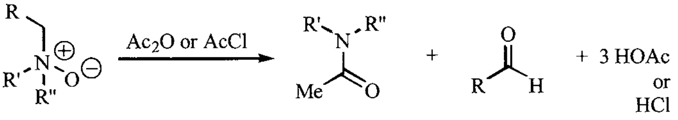
Yield not reported for this step. After two additional steps a total yield of 62%.
L. E. Overman, D. V. Paone, *Journal of the American Chemical Society* **2001**, 123, 9465



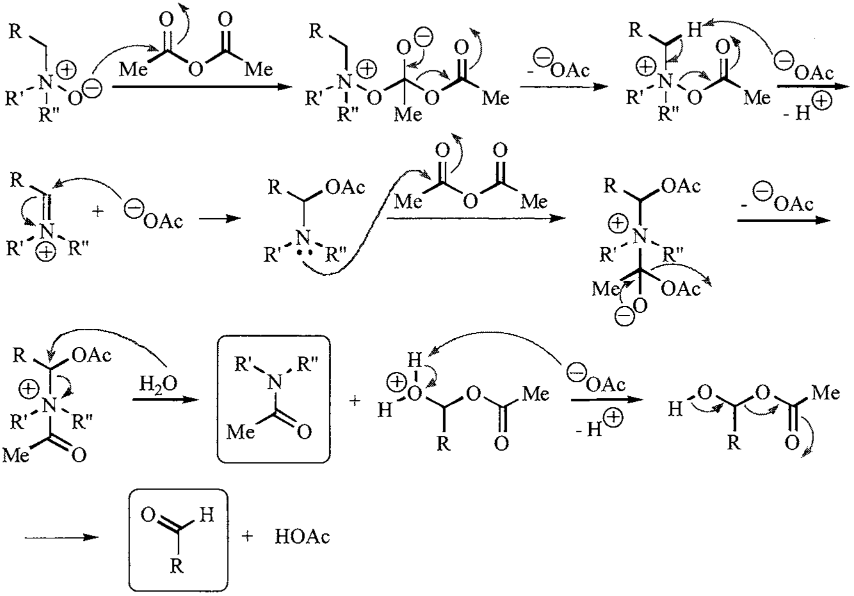
B. A. Kulkarni, G. P. Roth, E. Lobkovsky, J. A. Porco, Jr., *Journal of Combinatorial Chemistry* **2002**, 4, 56

Polonovski Reaction

The Reaction:



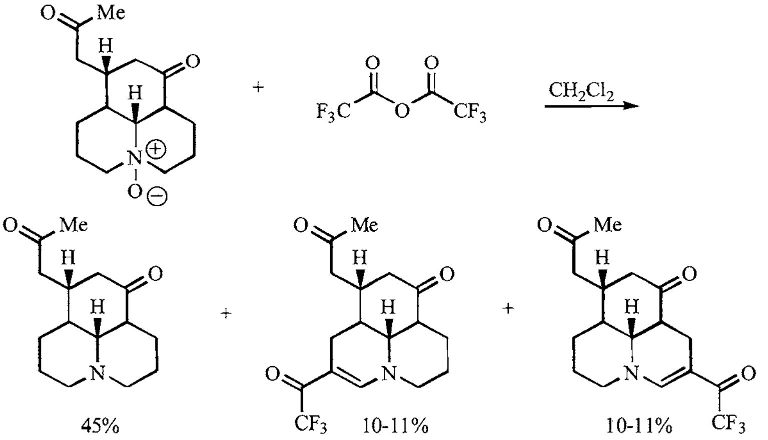
Proposed Mechanism:



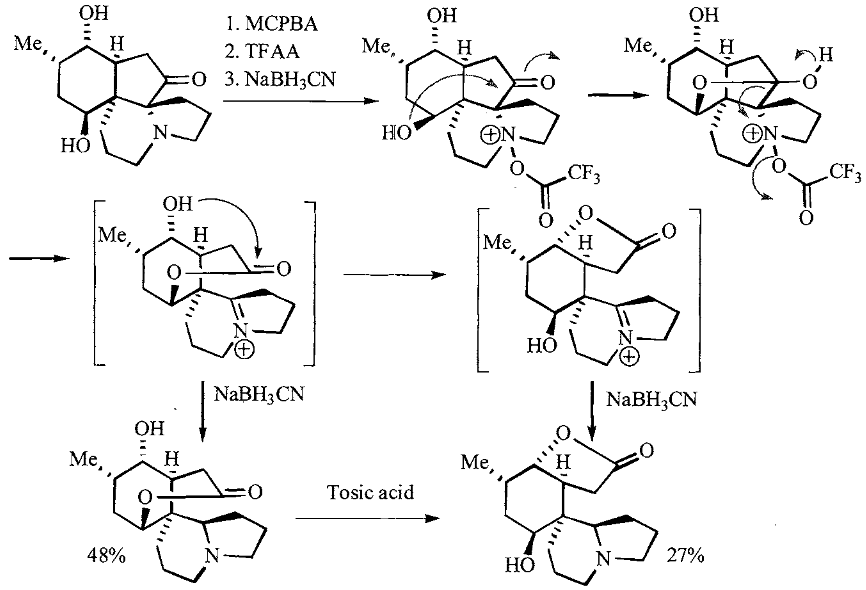
Notes:

D. Grierson, *Organic Reactions* **39**, 2

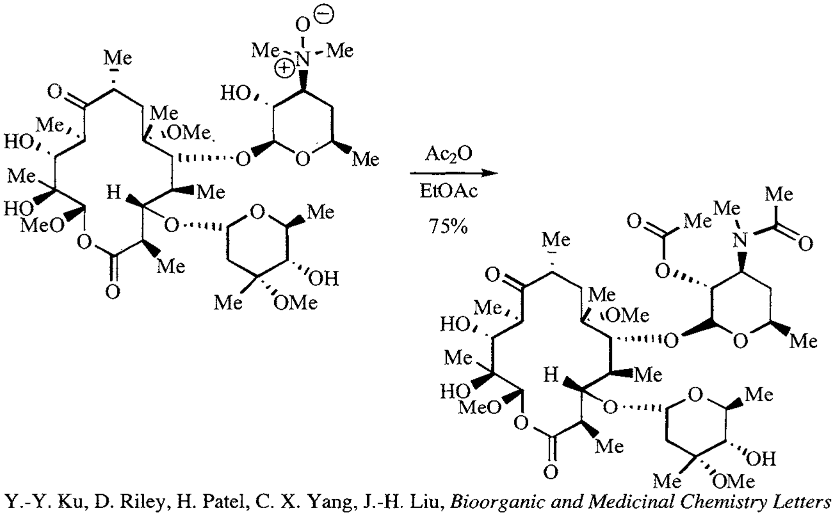
Examples:



E. Wenkert, B. Chauncy, K. G. Dave, A. R. Jeffcoat, F. M Schell, H. P. Schenk, *Journal of the American Chemical Society* **1973**, 95, 8427

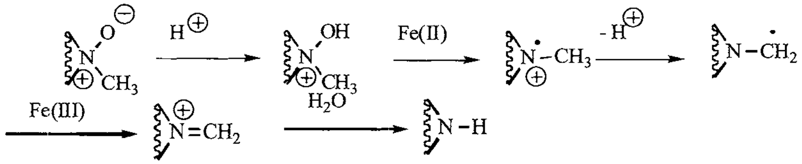


H. Morita, J. Kobayashi, *Journal of Organic Chemistry* **2002**, 67, 5378



Y.-Y. Ku, D. Riley, H. Patel, C. X. Yang, J.-H. Liu, *Bioorganic and Medicinal Chemistry Letters* **1997**, 7, 1203

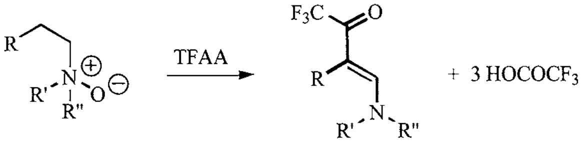
"Non-classical Polonvski" used as a new procedure for demethylation.



K. McCamley, J. A. Ripper, R. D. Singer, P. J. Srammells, *Journal of Organic Chemistry* **2002**, 68, 9847

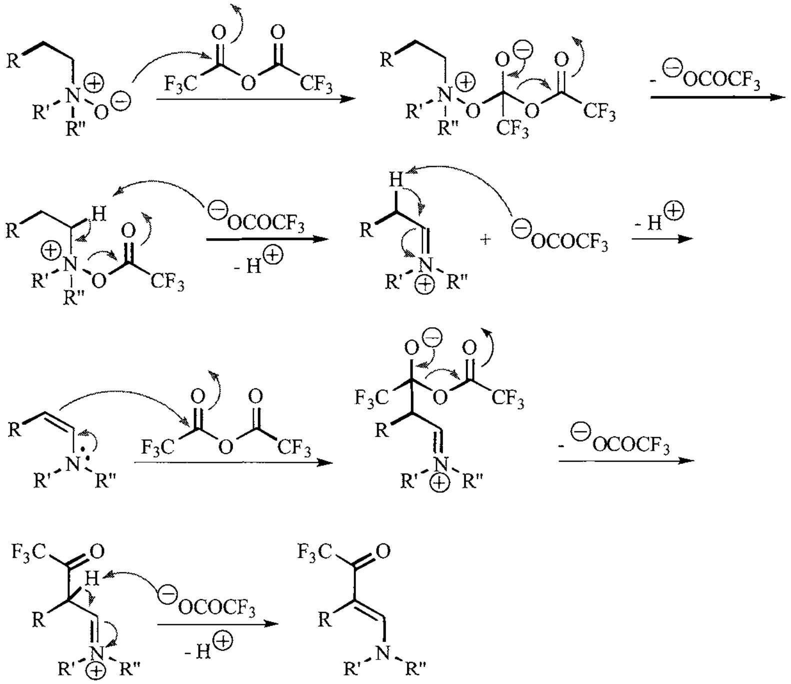
Polonovski-Potier Reaction

The Reaction:

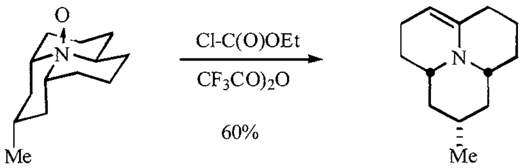


Proposed Mechanism:

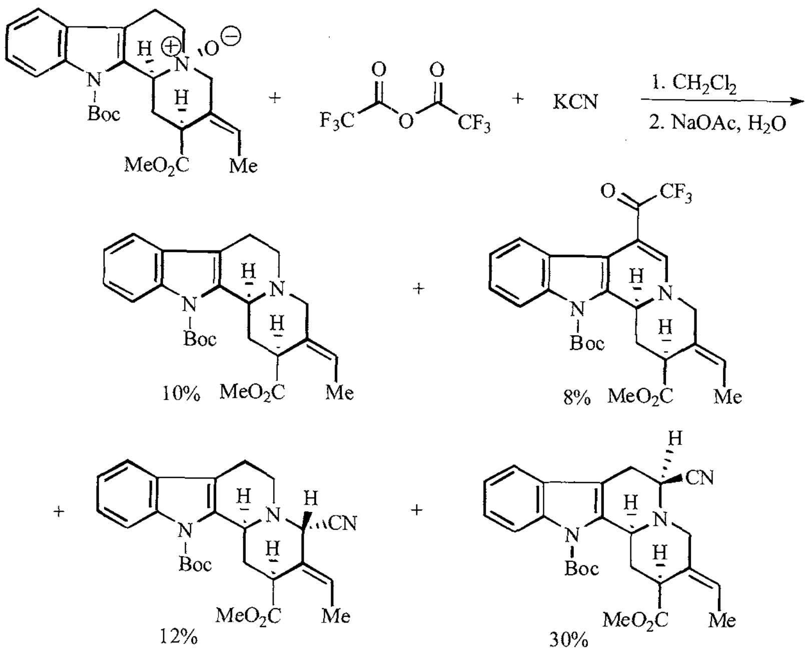
TFAA = Trifluoroacetic anhydride



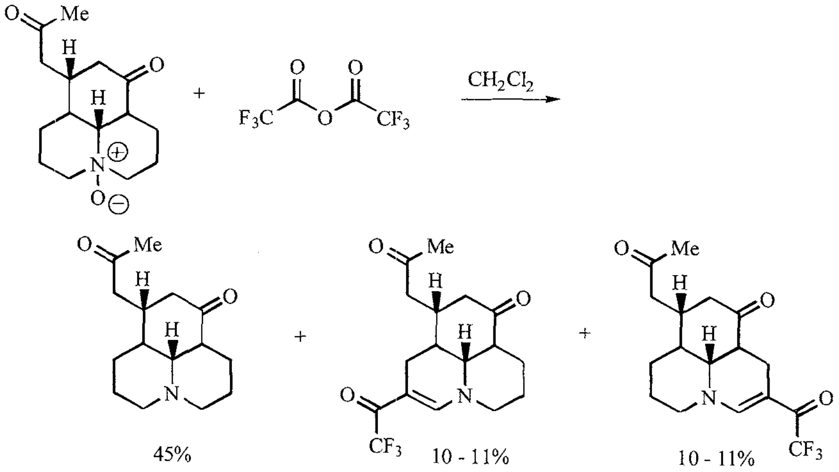
Examples:



B. Tursch, D. Daloze, J. C. Brakeman, C. Hootele, J. M. Pasteels, *Tetrahedron* **1975**, 31, 1541.



R. Jokela, M. Halonen, M. Lounasmaa, *Heterocycles* **1994**, 38, 189

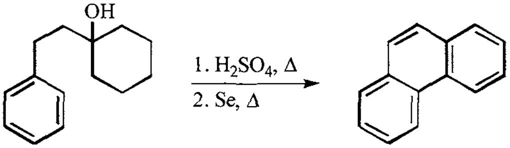


E. Wenkert, B. Chauncy, K. G. Dave, A. R. Jeffcoat, F. M Schell, H. P. Schenk, *Journal of the American Chemical Society* **1973**, 95, 8427

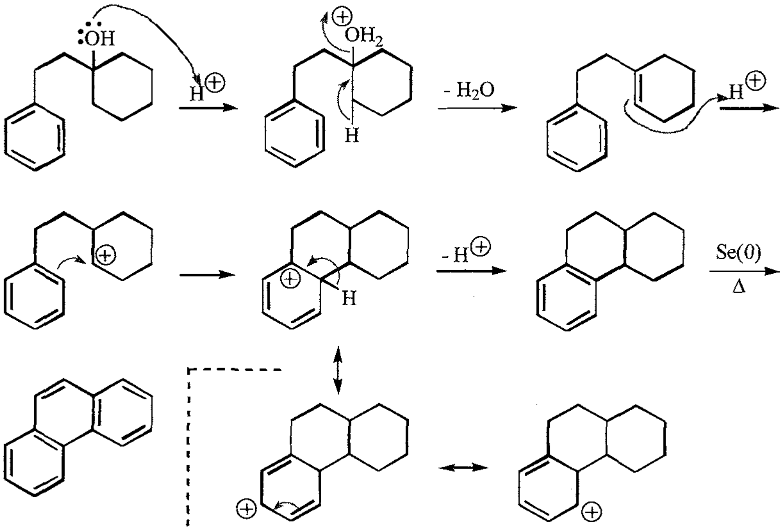
Polycarbocycle Syntheses

Bogert-Cook Synthesis

The Reaction:



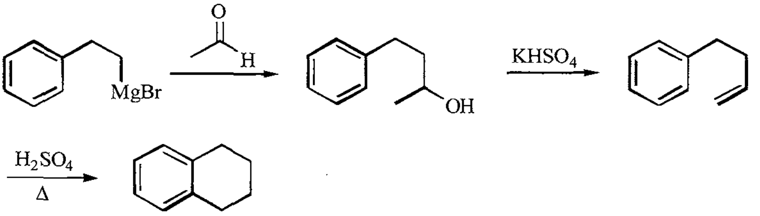
Proposed Mechanism:



Notes:

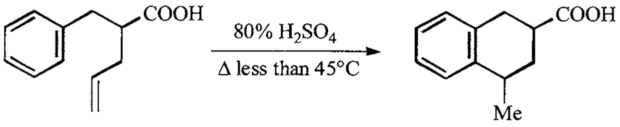
The Bardhan-Sengupta *Phenanthrene Synthesis uses* P_2O_5 *in place of* H_2SO_4.

When the alcohol containing portion is acyclic, the reaction is known as the ***Bogert Reaction***:

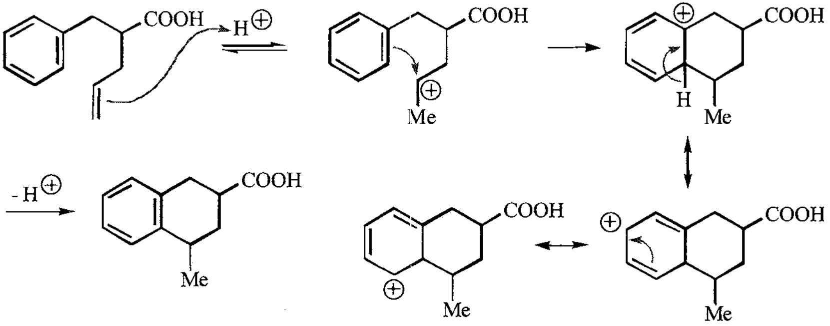


Darzens Synthesis of Tetralin Derivatives

The Reaction:

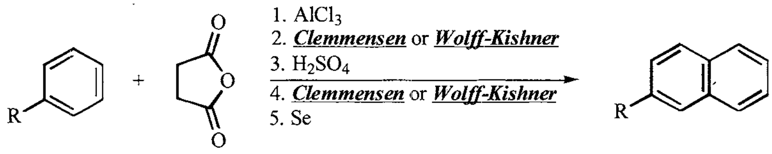


Proposed Mechanism:

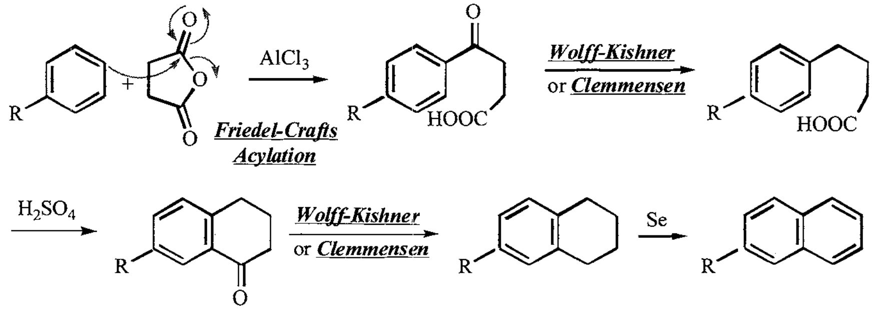


Haworth Reaction

The Reaction:

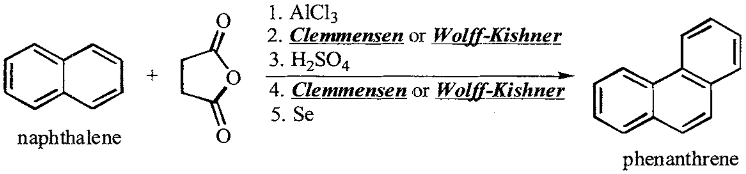


Proposed Mechanism:



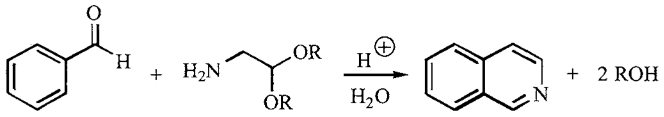
Notes:

On naphthalene based starting materials, a phenanthrene is produced and the reaction is called the ***Hayworth Phenanthrene Synthesis***:

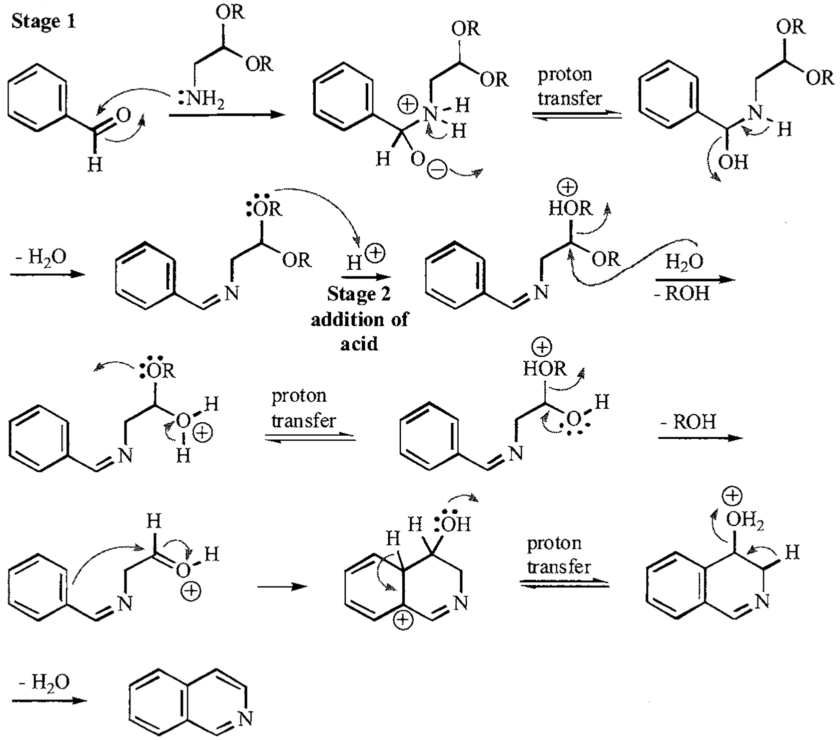


Pomeranz-Fritsch Reaction

The Reaction:



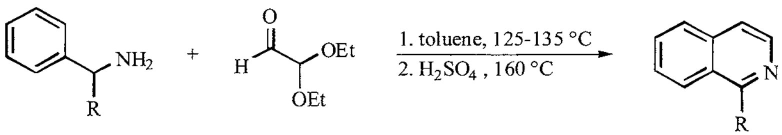
Proposed Mechanism:



Notes:

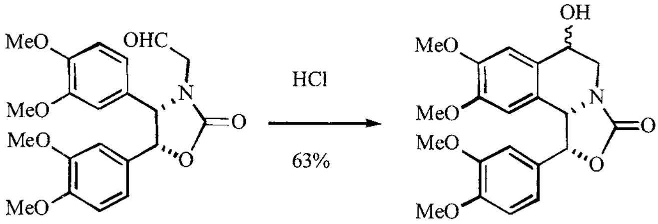
W. J. Gensler, *Organic Reactions* **6**, 4

Schlittler-Muller Modification:

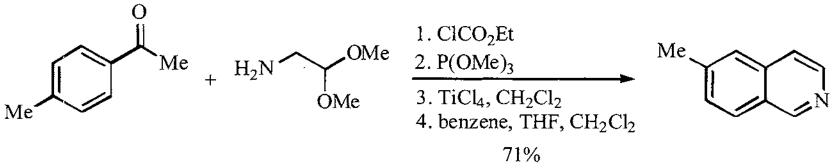


E. Schlittler, J. Muller, *Helvetica Chimica Acta* **1948**, 31, 914

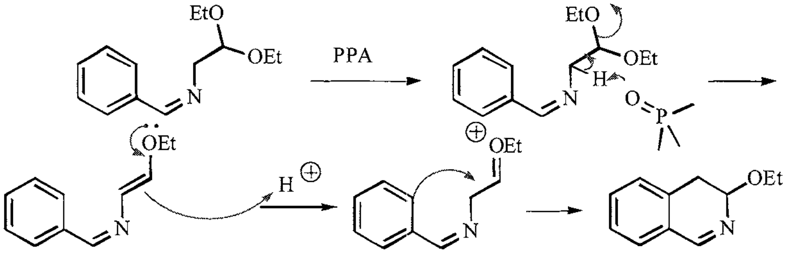
Examples:



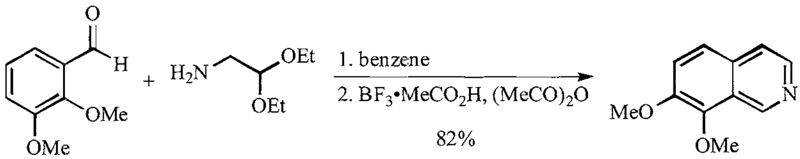
R. Hirkenkorn, *Tetrahedron Letters* **1991**, 32, 1775



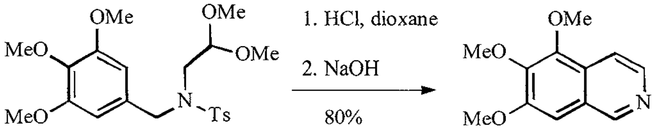
J. B. Hendrickson, C. Rodriquez, *Journal of Organic Chemistry* **1983**, 48, 3344



M. J. Bevis, E. J. Fobes, B. C. Uff, *Tetrahedron* **1969**, 25, 1585



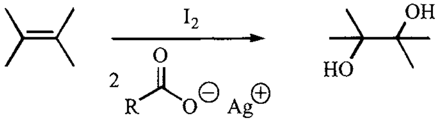
M. J. Bevis, E. J. Forbes, N. N. Naik, B. C. Uff, *Tetrahedron* **1971**, 27, 1253



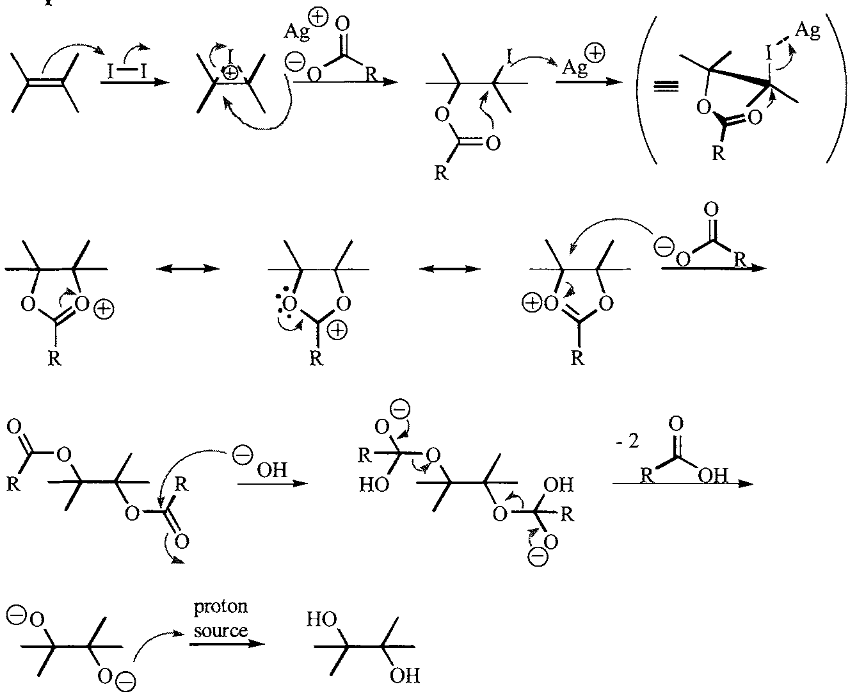
D. L. Boger, C. E. Brotherton, M. D. Kelley, *Tetrahedron* **1981**, 37, 3977

Prévost Reaction (Glycolization)

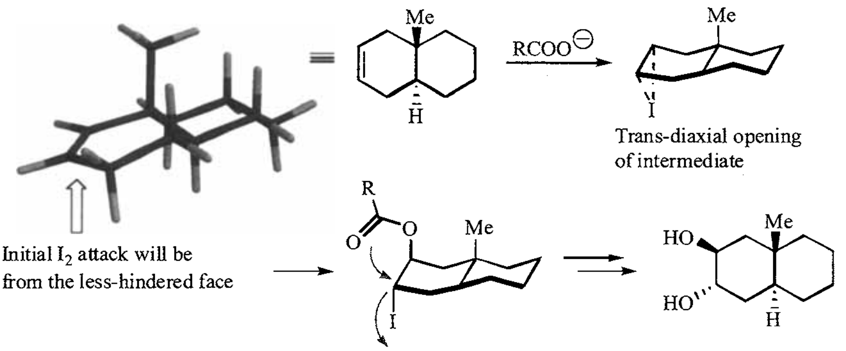
The Reaction:



Proposed Mechanism:



Notes:

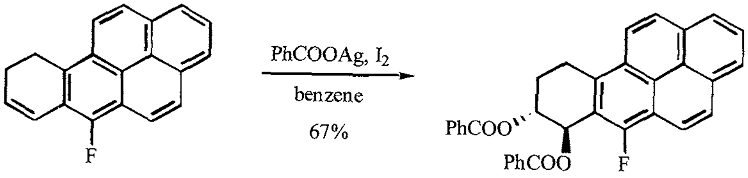


Trans-diaxial opening of intermediate

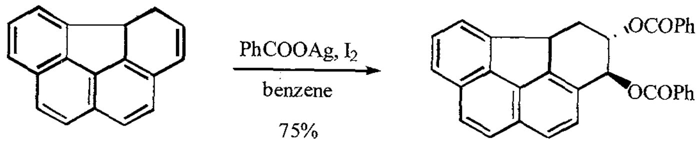
Initial I_2 attack will be from the less-hindered face

V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms,* Alpha Science International Ltd., Pangbourne, U.K., 2002, pp. 189-191; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1049-1050

Examples:



B. Zajc, *Journal of Organic Chemistry* **1999**, 64, 1902

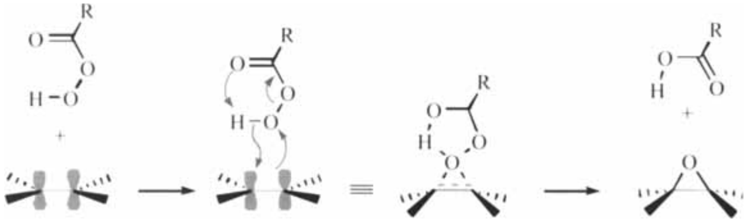


H.-F.Chang, B. P. Cho, *Journal of Organic Chemistry* **1999**, 64, 9051

Prilezhaev (Prileschajew) Reaction / Epoxidation

The Reaction:

Proposed Mechanism:



Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1052; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 218 - 220

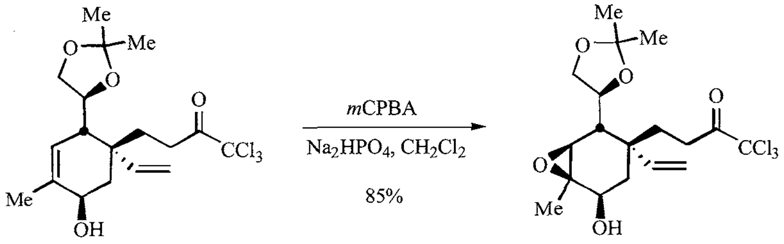
The name for this "Named Reaction" is not used much.

The reaction had its origins with the use of peroxyorganic acids. The simplest, formic, peracetic, and perbenzoic acid, are not so much in contemporary use. The workhorse of peroxy acids is *m*-chloroperoxybenzoic acid (*m*CPBA).

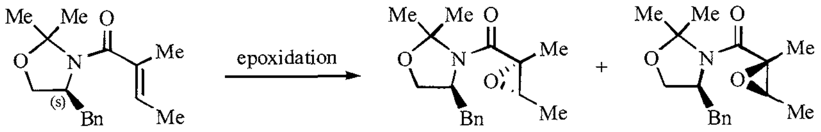
See other named reactions and reagents:

Oxone, ***DMD***, ***Sharpless Epoxidation***, ***Jacobsen-Katsuki Epoxidation***, ***Corey-Chaykovsky reagent and Reaction***, ***Shi (Asymmetric) Epoxidation***.

Examples:

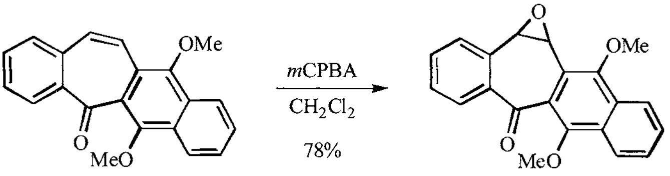


T. Nishikawa, D. Urabe, K. Yoshida, T. Iwabuchi, M. Asai, M. Isobe, *Organic Letters* **2002**, 4, 2679

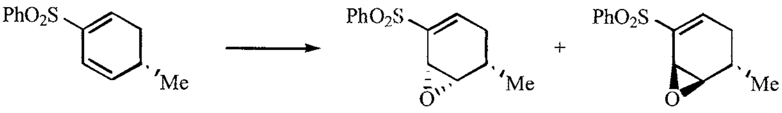


*m*CPBA	15	85
DMD	91	9

W. Adam, A. Pastor, K. Peters, E. Peters, *Organic Letters* **2000**, 2, 1019

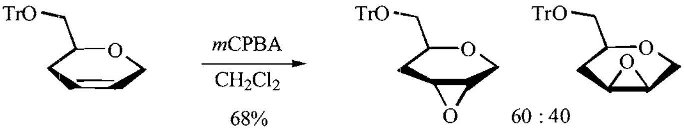


F. M. Hauser, H. Yin, *Organic Letters* **2000**, 2, 1045

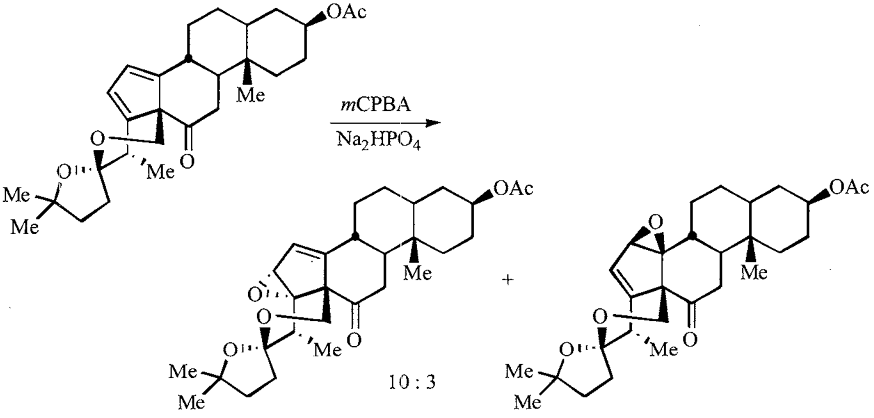


*m*CPBA	3	:	2
Jacobsen	6	:	1

Y. Chen, J. B. Evarts, Jr., E. Torres, P. L. Fuchs, *Organic Letters* **2002**, 4, 3571



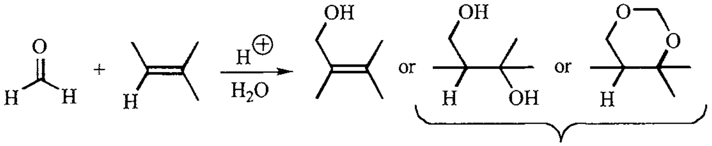
S. Aragones, F. Bravo, Y. Diaz, M. I. Matheu, S. Castillon, *Tetrahedron: Asymmetry* **2003**, 14, 1847



W. Li, P. L. Fuchs, *Organic Letters* **2003**, 5, 2849

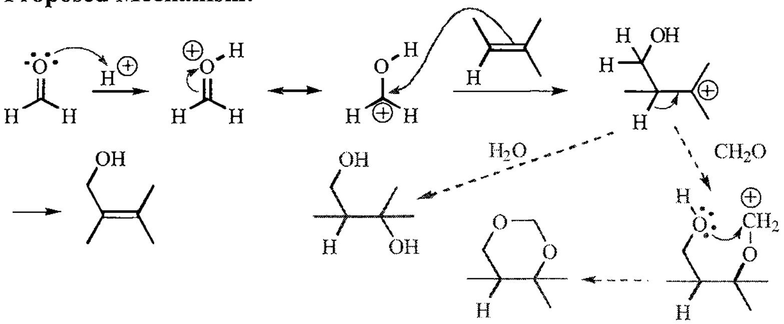
Prins Reaction

The Reaction:



Products sometimes seen with the reaction

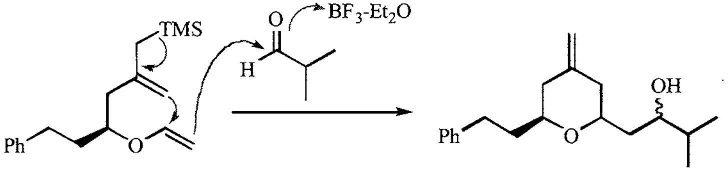
Proposed Mechanism:



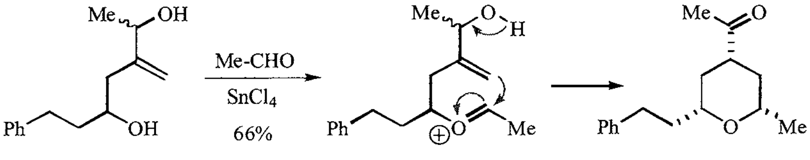
Notes:

T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 220-222; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1241-1242.; A. L. Henne, *Organic Reactions* **2**, 6; D. F. DeTar, *Organic Reactions* **9**, 7.

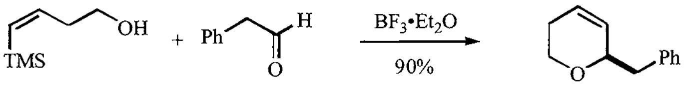
Examples:



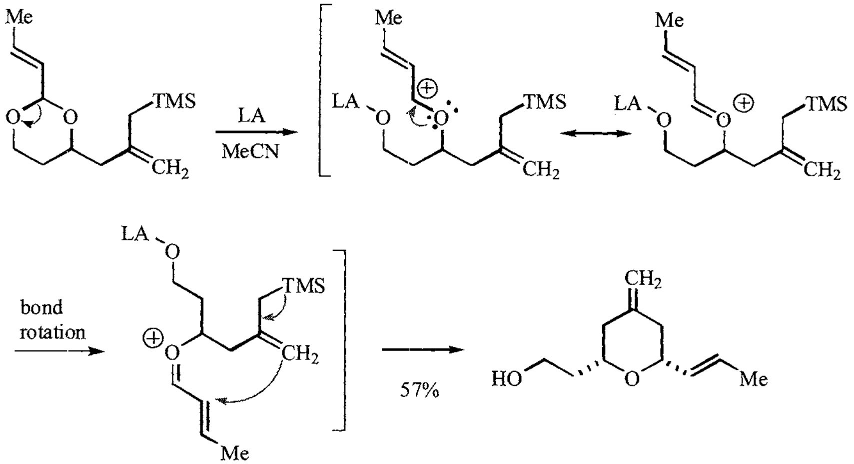
D. J. Kopecky, S. D. Rychnovsky, *Journal of the American Chemical Society* **2001** 123, 8420



M. J. Cloninger, L. E. Overman, *Journal of the American Chemical Society* **1999**, 121, 1092

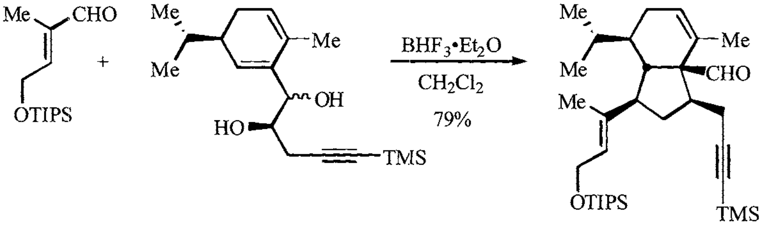


A. P. Dobbs, S. Martinovic, *Tetrahedron Letters* **2002**, 43, 7055

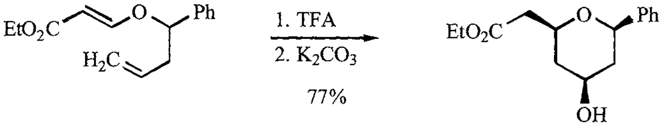


D. L. Aubele, C. A. Lee, P. E. Floreancig, *Organic Letters* **2003**, 5, 4521

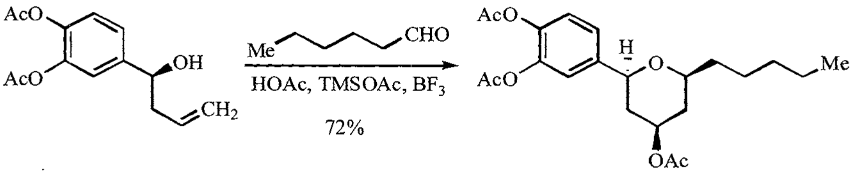
Tandem Prins-Pinacol Strategy:



L. E. Overman, L. D. Pennington, *Journal of Organic Chemistry* **2003**, 68, 7143



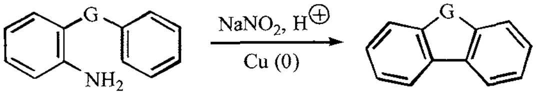
D. J. Hart, C. E. Bennett, *Organic Letters* **2003**, 5, 1499

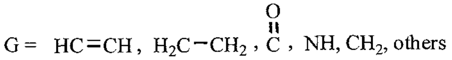


S. R. Crosby, J. R. Harding, C. D. King, G. D. Parker, C. L. Willis, *Organic Letters* **2002**, 4, 3407

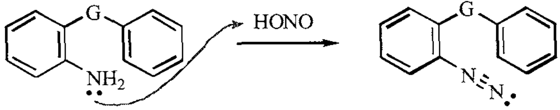
Pschorr Arylation (Reaction)

The Reaction:



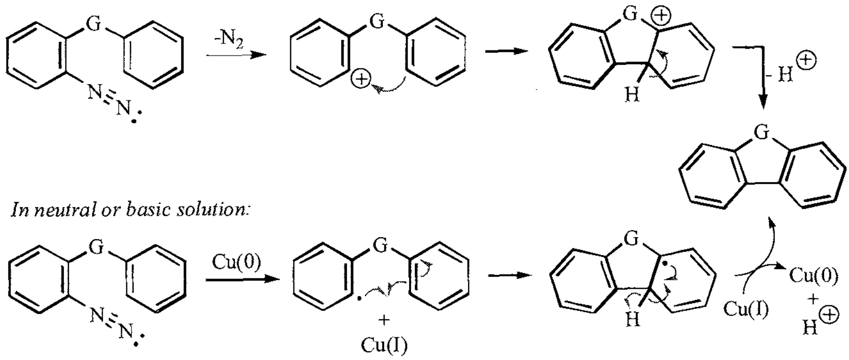

$G = HC{=}CH,\ H_2C{-}CH_2,\ \overset{\overset{O}{\|}}{C},\ NH,\ CH_2,\ \text{others}$

Proposed Mechanism:



For a discussion of the reactions under acidic or basic conditions, see: D. F. Detar, S. V. Sagmanli, *Journal of the American Chemical Society* **1951**, 73, 3240

In acid solution:

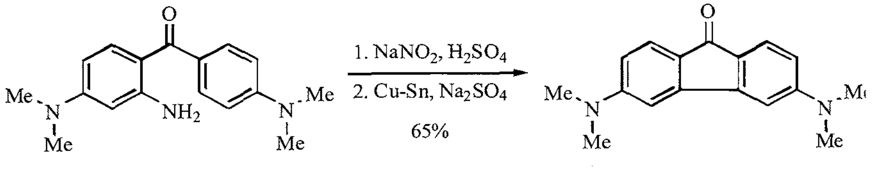


In neutral or basic solution:

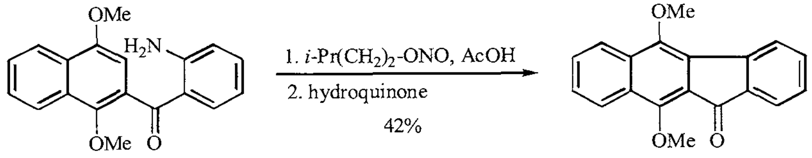
Notes:

Reactions are often difficult to control, with many side reactions observed.

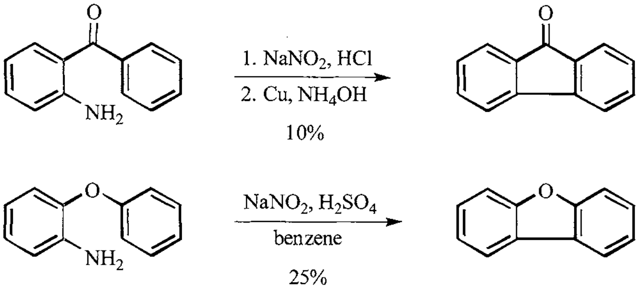
Examples:



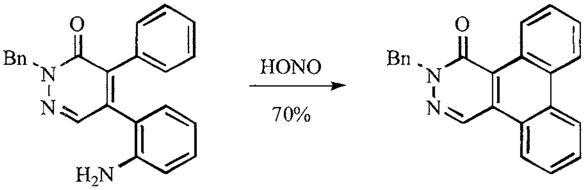
S. G. R. Guinot, J. D. Hepworth, M. Wainwright, *Journal of Chemical Research, Synopses* **1997**, 183 (AN 1977: 481656)



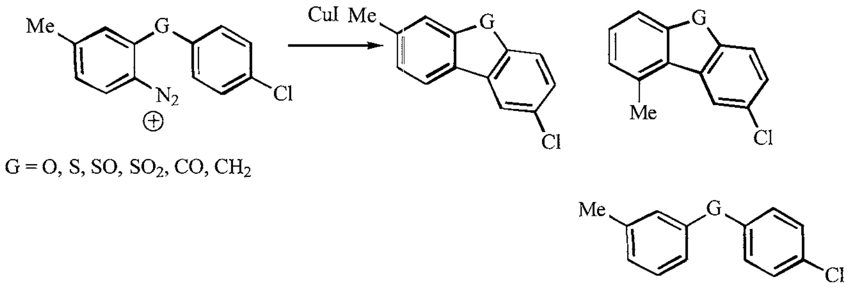
W. Williams, X. Sun, D. Jabaratnam, *Journal of Organic Chemistry* **1997**, 62, 4364



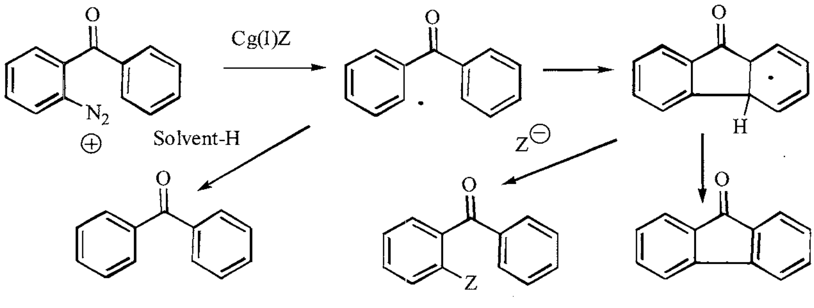
D. F. Detarand, S. V. Sagmanli, *Journal of the American Chemical Society* **1950**, 72, 965



P. Tapolcsanyi, B. U. W. Maes, K. Monsieurs, G. L. F. Lemiere, Z. Riedl, G. Hajos, B. Van den Driessche, R. A. Dommisse, P. Matyus, *Tetrahedron* **2003**, 59, 5919



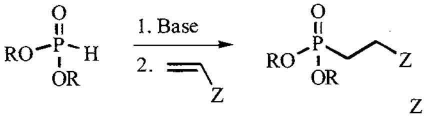
Mixtures were often obtained. Report provides calculational data.
S. Karady, J. M. Cummins, J. J. Dannenberg, E. del Rio, P. G. Dormer, B. F. Marcune, R. A. Reamer, T. L. Sordo, *Organic Letters* **2003**, 5, 1175



A. H. Lewin, T. Cohen, *Journal of Organic Chemistry* **1967**, 32, 3844

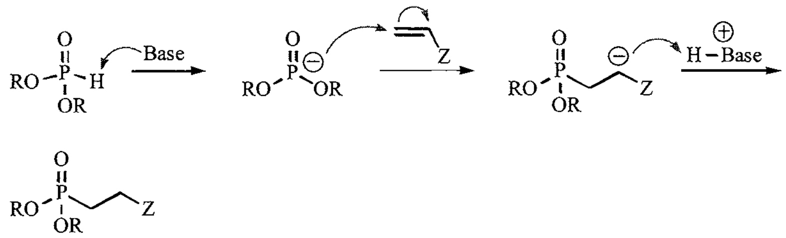
Pudovik Reaction

The Reaction:



Z = electron acceptor

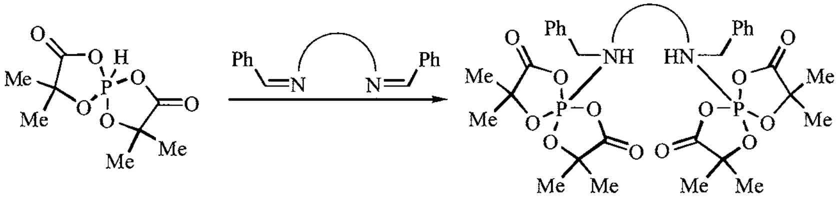
Proposed Mechanism:



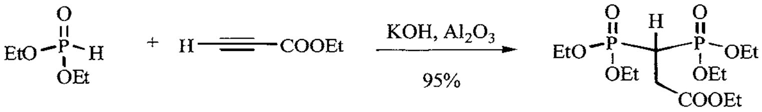
Notes:

A versatile and general method for generating C-P bonds; however, other connections are possible.

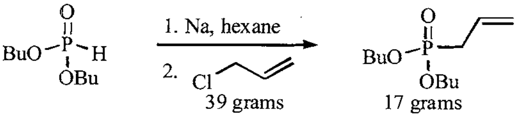
Examples:



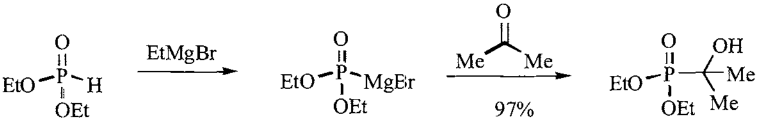
V. Pham, W. Zhang, V.Chen, V. Whitney, J. Yao, D. Froese, A. D. Friesen, J. M. Diakur, W. Haque, *Journal of Medicinal Chemistry* **2003**, 46, 3680



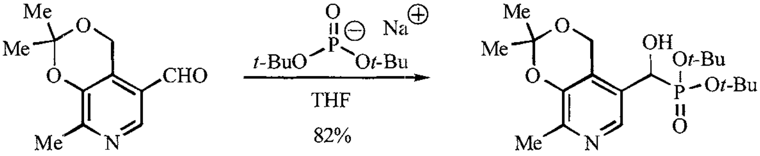
K. Vercruysse-Moreira, C. Déjugnat, G. Etemad-Moghada, *Tetrahedron* **2002**, 58, 5651



D. Albouy, M. Lasptras, G. Etemad-Moghadam, M. Koenig, *Tetrahedron Letters* **1999**, 40, 2311



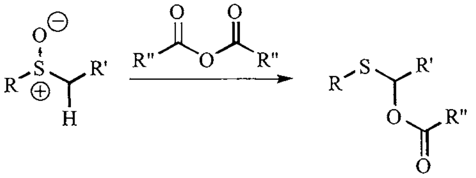
G. M. Kosolapoff, *Journal of the American Chemical Society* **1951**, 73, 4040



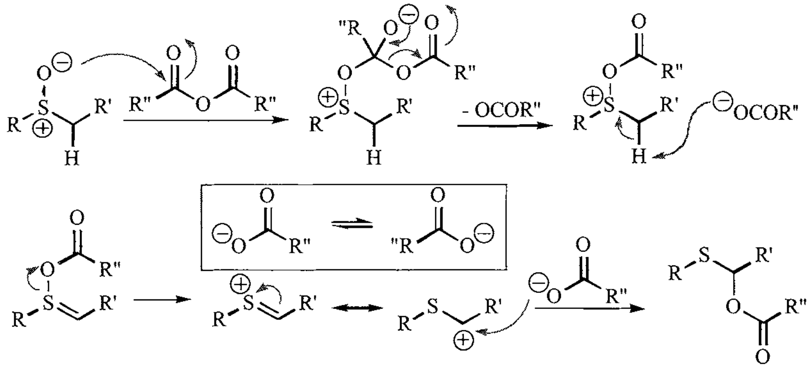
O. Gawron, C. Grelecki, W. Reilly, J. Sands, *Journal of the American Chemical Society* **1953**, 75, 3591

Pummerer Rearrangement

The Reaction:



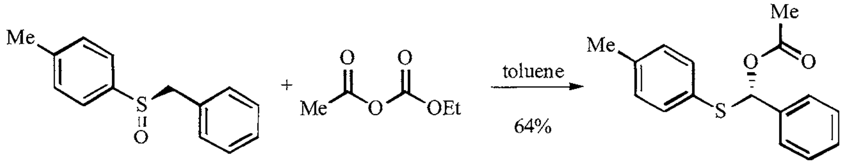
Proposed Mechanism:



Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p 1566; O. DeLucchi, U. Miotti, G. Modena, *Organic Reactions* **40**, 3.

Examples:

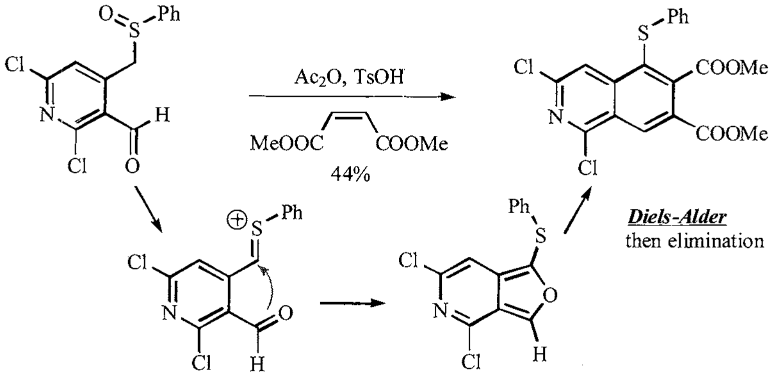


N. Shibata, M. Matsugi, N, Kawano, S. Fukui, C. Jujimori, K. Gotanda. K. Murata, Y. Kita, *Tetrahedron: Asymmetry* **1997**, 8, 303

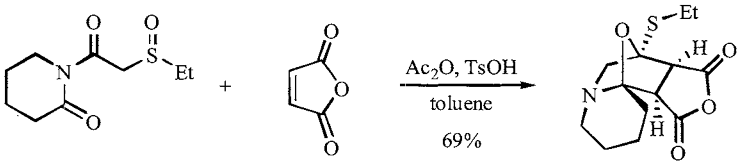
Solid phase Pummerer cyclization:

TFAA = Trifluoroaceticanhydride, *DMPU =N,N'-Dimethylpropyleneurea*

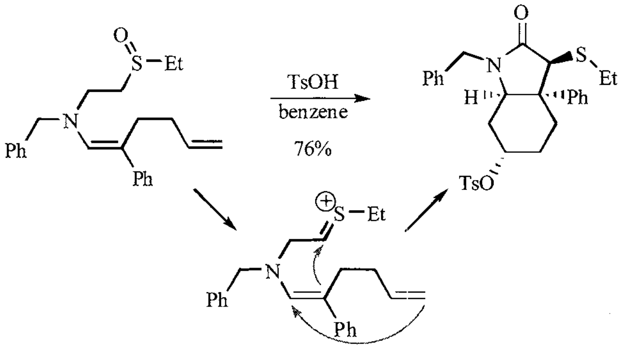
L. A. McAllister, S. Brand, R. de Gentile, D. J. Procter, *Chemical Communications* **2003**, 2380



T. K. Sarkar, N. Panda, S. Basak, *Journal of Organic Chemistry* **2003**, 68, 6919

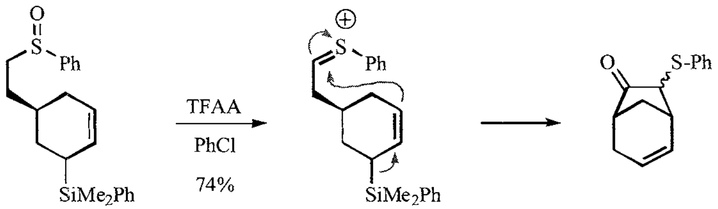


J. T. Kuethe, A. Padwa, *Journal of Organic Chemistry* **1997**, 62, 774



Trapping the intermediate in a ***Mannich reaction***.

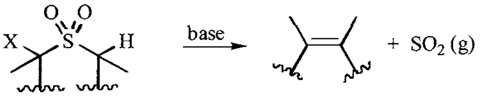
A. Padwa, M. D. Danca, K. I. Hardcastle, M. S. McClure, *Journal of Organic Chemistry* **2003**, 68, 929



P. Magnus, T. Rainey, V. Lynch, *Tetrahedron Letters* **2003**, 44, 2459

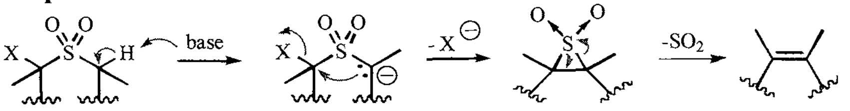
Ramberg-Backlund Olefin Synthesis

The Reaction:



X = Cl, Br, I

Proposed Mechanism:

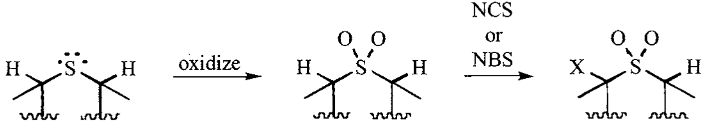


these intermediates have been isolated

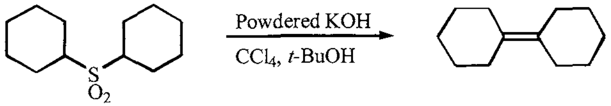
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1342; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 223-224; L. A. Paquette, *Organic Reactions* **25**, 1; R. J. K. Taylor, G. Casey, *Organic Reactions* **62**, 2

Starting material preparation:

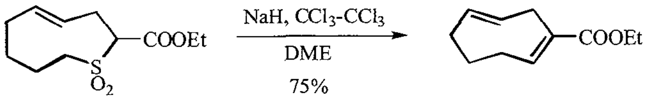


Meyers Procedure: Halogenates and eliminates in-situ



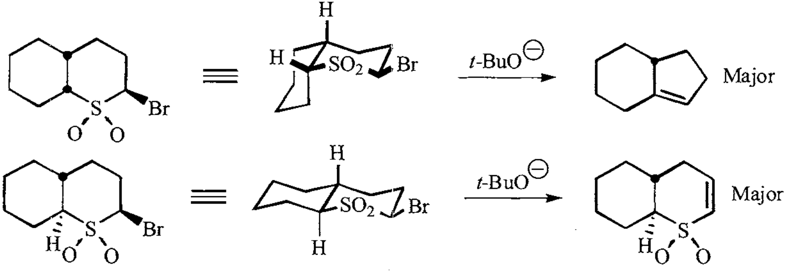
C. Y. Meyers, A. M. Malte, W. S. Matthews, *Journal of the American Chemical Society* **1969**, 91, 7510

Vedejs Procedure:



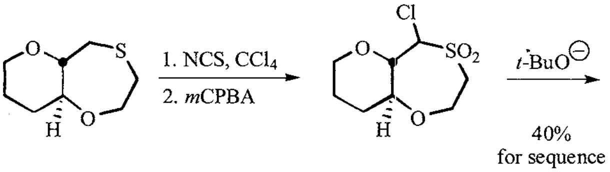
E. Vedejs, S. Singer, *Journal of Organic Chemistry* **1978**, 43, 4884

There is a stereochemical preference for the "W" arrangement of proton and leaving group.

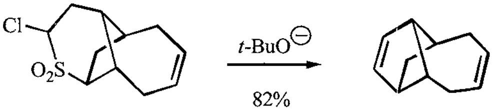


R. J. K. Taylor, G. Casy, *Organic Reactions* **2003**, 62, Chapter 2, pp361-362

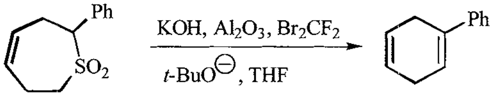
Examples:



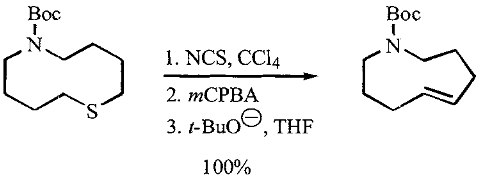
E. Alvarex, M. Delgado, M. T. Diaz, L. Harxing, R. Perez, J. D. Martin, *Tetrahedron Letters* **1996**, 37, 2865



J. Dressel, K. L. Chasey, L. A. Paquette, *Journal of the American Chemical Society* **1988**, 110, 5479



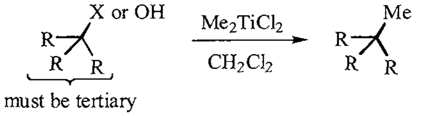
Q. Yao, *Organic Letters* **2002**, 4, 427

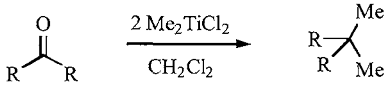


D. I. MaGee, E. J. Beck, *Journal of Organic Chemistry* **2000**, 65, 8367

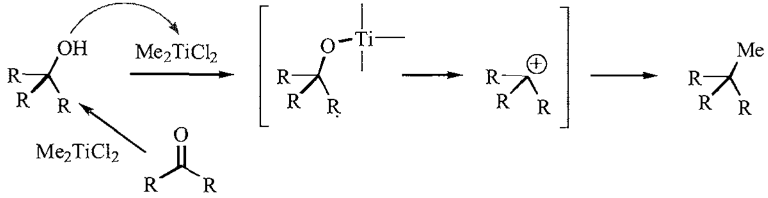
Reetz Alkylation

The Reaction:





Proposed Mechanism:

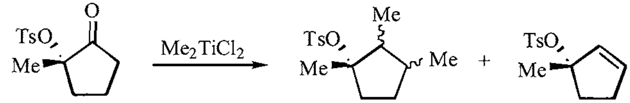


Notes:

Original Publication: M. T. Reetz, J. Westermann, R. Steinbach, *Journal of the Chemical Society: Chemical Communications* **1981**, 237

Reagent Preparation:
$(Me)_2Zn + TiCl_4 \longrightarrow Me_2TiCl_2$

Evidence for a carbocation rearrangement during the ***Reetz reaction***:

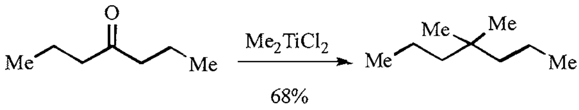


Optically active

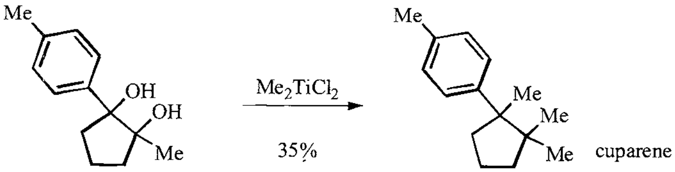
each product was racemic

G. H. Posner, T. P. Kogan, *Journal of the Chemical Society: Chemical Communications* **1983**, 1481

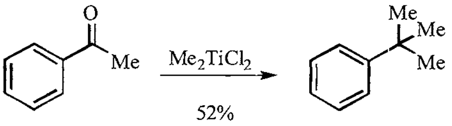
Examples:



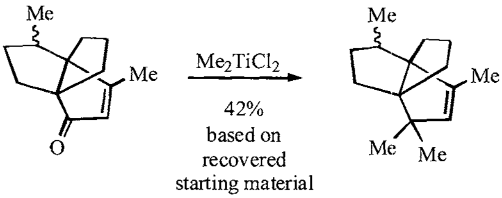
M. T. Reetz, R. Steinbach, B. Wenderoth, *Synthetic Communications* **1981**, 11, 261 (AN 1981:406655)



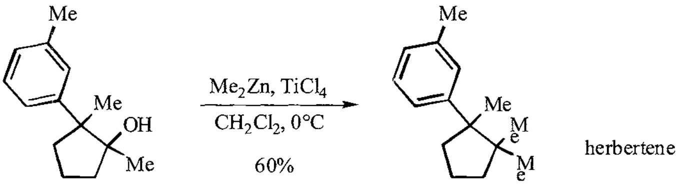
F. G. Favaloro, C. A. Goudreau, B. P. Mundy, T. Poon, S. V. Slobodzian, B. L. Jensen, *Synthetic Communications* **2001**, 31, 1847



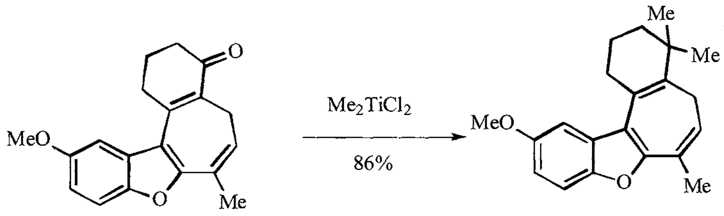
G. Haefelinger, M. Marb, *New Journal of Chemistry* **1987**, 11, 401 (AN 1988:149977)



B. P. Mundy, D. Wilkening, K. B. Lipkowitz, *Journal of Organic Chemistry* **1985**, 50, 5727



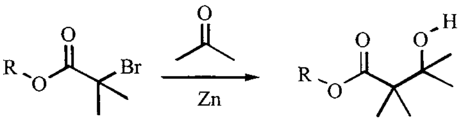
T. Poon, B. P. Mundy, F. G. Favaloro, C. A. Goudreau, A. Greenberg, R. Sullivan, *Synthesis* **1998**, 832



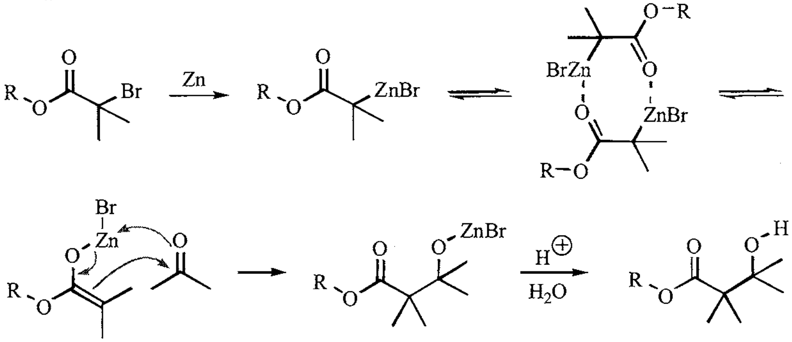
D. J. Kerr, A. C. Willis, B. L. Flynn ,*Organic Letters* **2004**, 6, 457

Reformatsky Reaction

The Reaction:



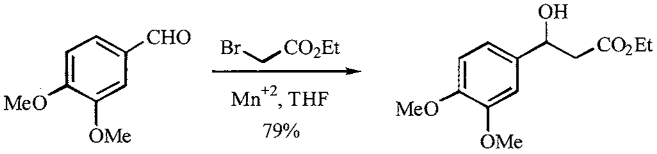
Proposed Mechanism:



Notes:

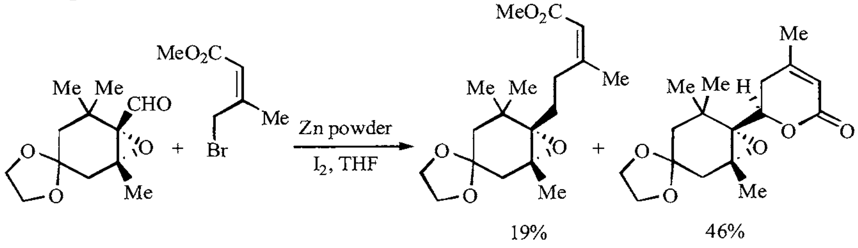
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 224-226; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1212; R. L. Shiner, *Organic Reactions* **1**, 1; M. W. Rathke, *Organic Reactions* **22**, 4.

Other metals can be used for the "***Reformatsky Reaction***":

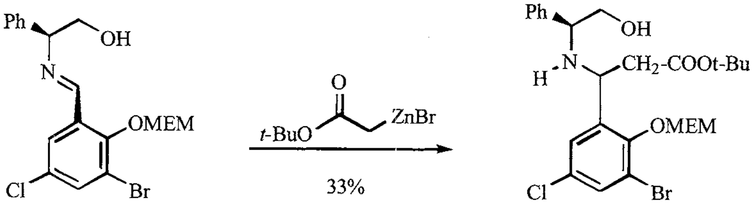


Y. S. Suh, R. D. Rieke, D. Reuben, *Tetrahedron Letters* **2004**, 45, 180

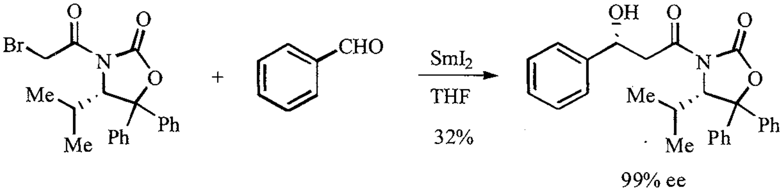
Examples:



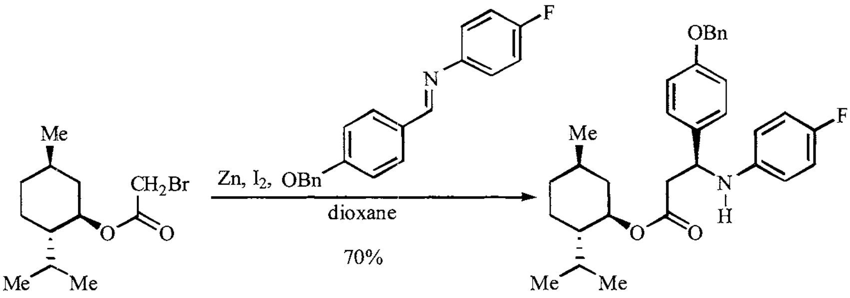
K. Sakai, K. Takahashi, T. Nukano, *Tetrahedron* **1992**, 48, 8229



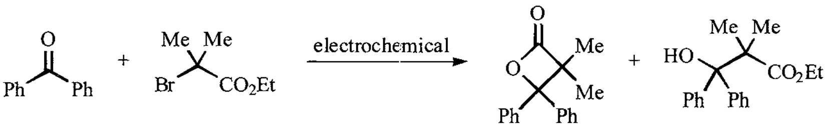
J. D. Clark, G. A. Weisenburger, D. K. Anderson, P.-J. Colson, A. D. Edney, D. J. Gallagher, H. P. Kleine, C. M. Knable, M. K. Lantz, C. M. V. Moore, J. B. Murphy, T. E. Rogers, P. G. Ruminski, A. S. Shah, N. Storer, B. E. Wise, *Organic Process Research & Development* **2004**, 8, 51



S.-i. Fukuzawa, H. Matsuzawa,S.-i. Yoshimitsu, *Journal of Organic Chemistry* **2000**, 65, 1702



B. B. Shankar, M. P. Kirkup, S. W. McCombie, J. W. Clader, A. K. Ganguly, *Tetrahedron Letters* **1996**, 37, 4095

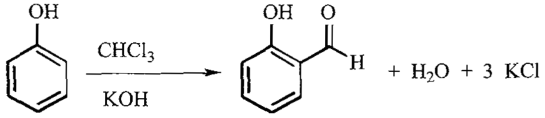


Zn anode:	100%	0%
Zn powder:	48%	9%

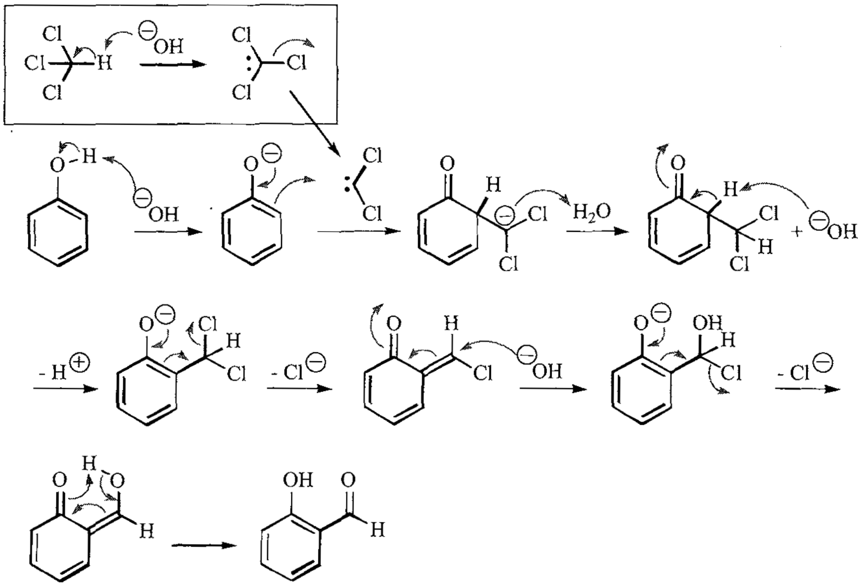
H. Schick, R. Ludwig, K.-H. Schwarz, K. Kleiner, A. Kunath, *Journal of Organic Chemistry* **1994**, 59, 3161

Reimer-Tiemann Reaction

The Reaction:



Proposed Mechanism:

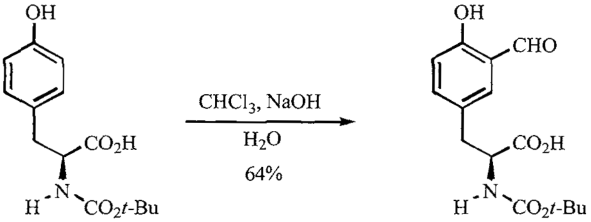


Notes:

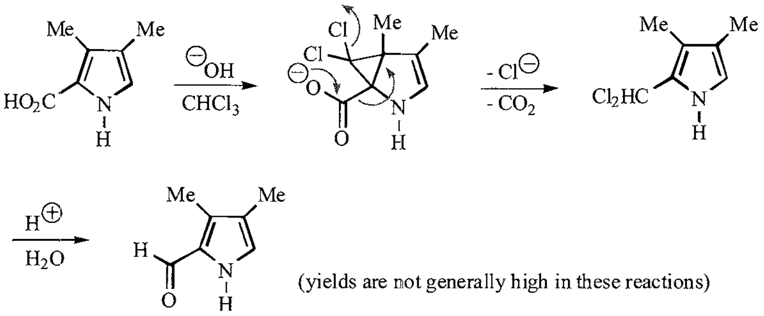
H. Wynberg, *Chemical Reviews* **1960**, 60, 169

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 716; T. Laue, A. Plagens, *Named Organic Reactions,* John Wiley and Sons, Inc., New York, 1998, pp. 226-227; H. Wynberg, E. W. Meijer, *Organic Reactions* **28**, 1

Examples:



M. E. Jung, T. I. Lazarova, *Journal of Organic Chemistry* **1997**, 62, 1553

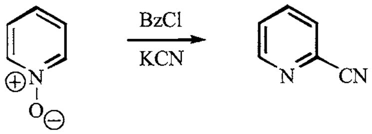


(yields are not generally high in these reactions)

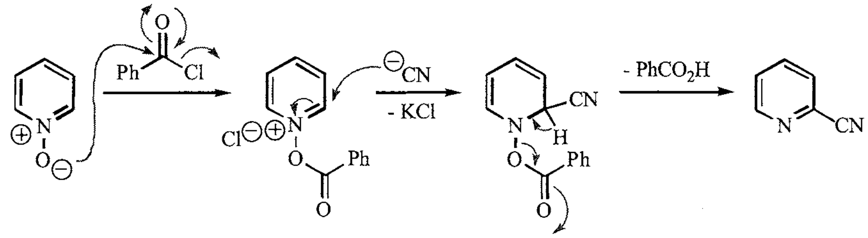
K. M. Smith, F. W. Bobe, O. M. Minnetian, H. Hope, M. D. Yanuck, *Journal of Organic Chemistry* **1985**, 50, 790

Reissert-Henze Reaction

The Reaction:



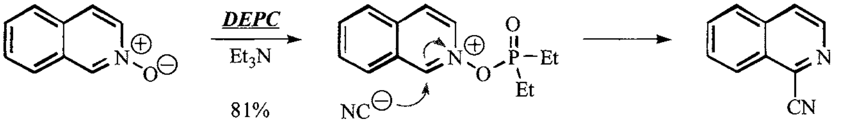
Proposed Mechanism:



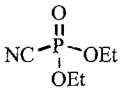
Notes:

As will be seen in the examples, there are a number of variations on the theme to deliver the cyanide and displace the *N*-oxide oxygen. However, all follow the same general mechanistic reasoning.

Examples:

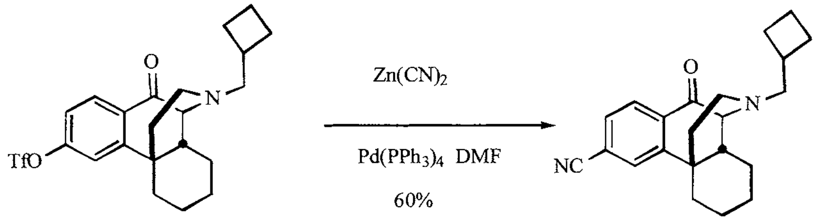


DEPC =

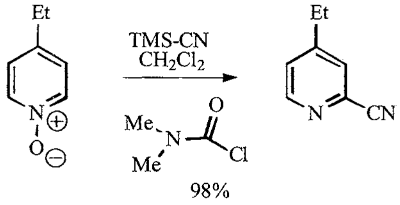


$NC-P(=O)(OEt)_2$

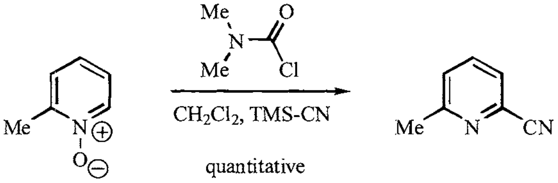
Reported in: H. H. Patel, *Encyclopedia of Reagents for Organic Synthesis,* John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1851



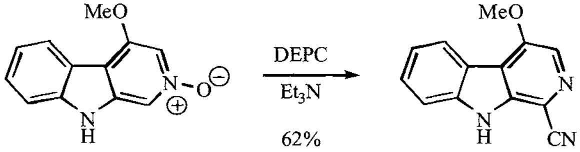
A. Zhang, J. L. Neumeyer, *Organic Letters* **2003**, 5, 201



R. T. Shuman, P. L. Ornstein, J. W. Paschal, P. D. Gesellchen, *Journal of Organic Chemistry* **1990**, 55, 738



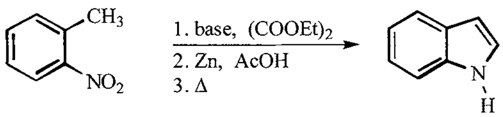
W. K. Fife, *Journal of Organic Chemistry* **1983**, 48, 1375



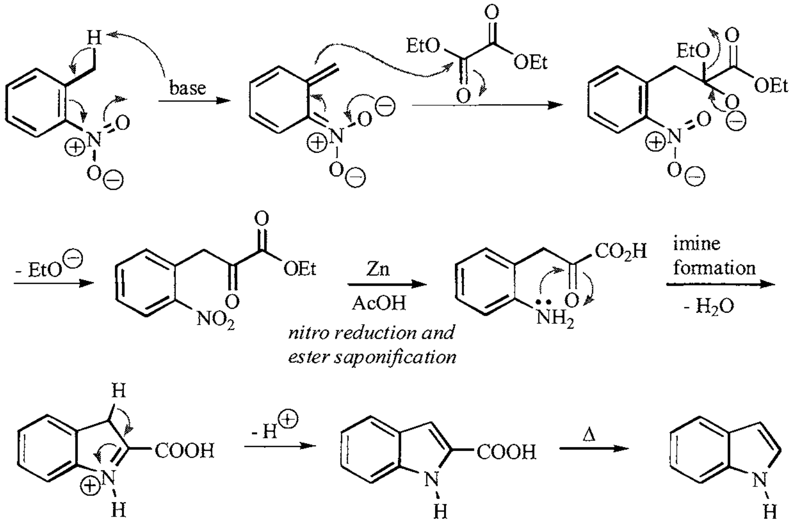
H. Suzuki, C. Iwata, K. Sakurai, K. Tokumoto, H. Takahashi, M. Hanada, Y. Yokoyama, Y. Murakami, *Tetrahedron* **1997**, 53, 1593

Reissert Indole Synthesis

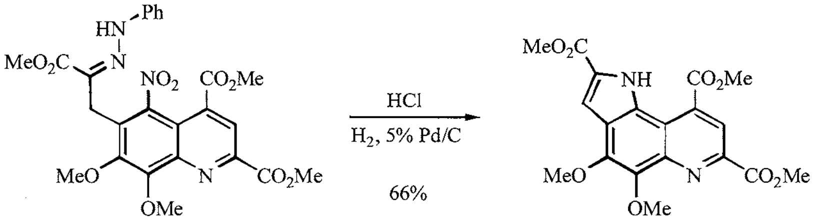
The Reaction:



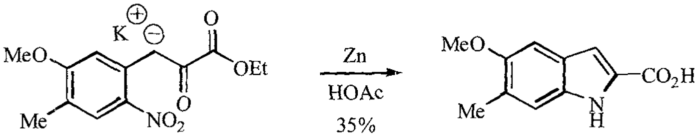
Proposed Mechanism:



Examples:



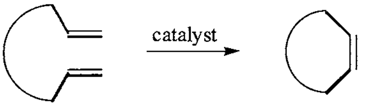
J. A. Gainor, S. M. Weinreb, *Journal of Organic Chemistry* **1982**, 47, 2833



G. Leadbetter, D. L. Fost, N. N. Ekwuribe, W. A. Remers, *Journal of Organic Chemistry* **1974**, 39, 3580; T. Hirata, Y. Yamada, M. Matsui, *Tetrahedron Letters* **1969**, 10, 19

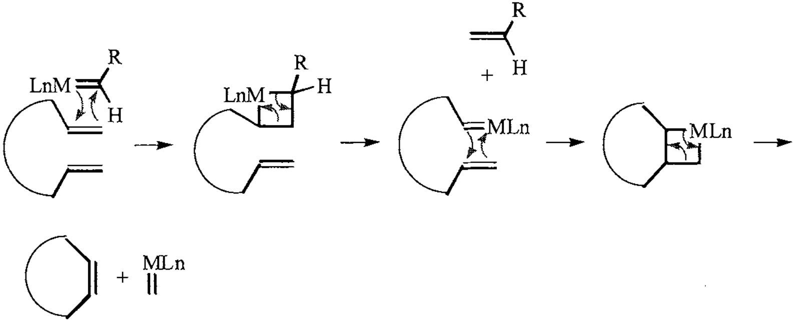
Ring Closing Metathesis (RCM)

The Reaction:

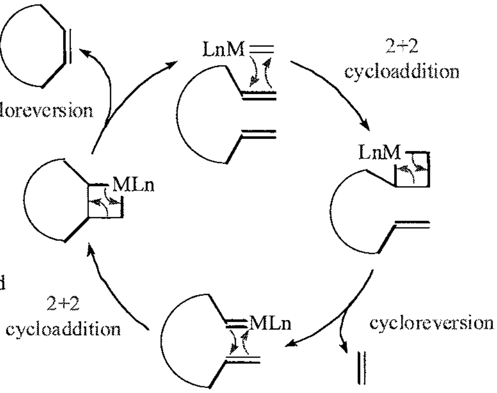


Proposed Mechanism:

1. Generation of catalyst (one cycle).



2. Catalytic cycle.



This is a simplified view of the ***Chauvin Mechanism***.

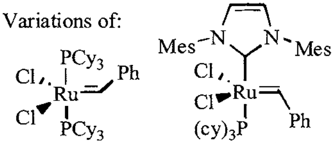
See: *Alkene Metathesis in Organic Synthesis*, edited by A. Fürstner, Springer, Berlin, 1998

Notes:

LnM$=$ = *Metal carbene complex*

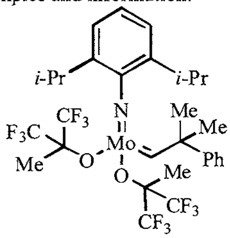
See ***Schrock*** and ***Grubbs*** Catalysts for additional examples and information.

Variations of:



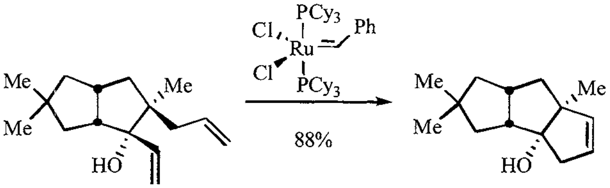
Cy = cyclohexyl
Mes = mesitylene

Grubbs' catalysts

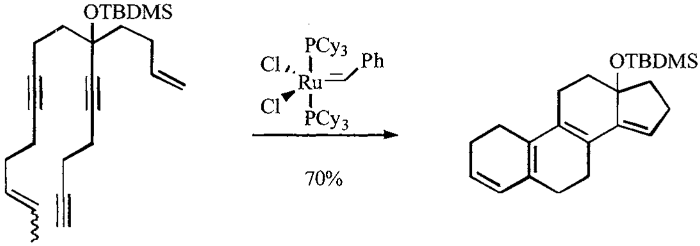


Schrock's catalyst

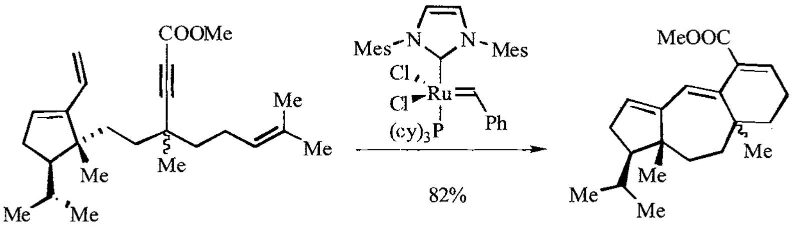
Examples:



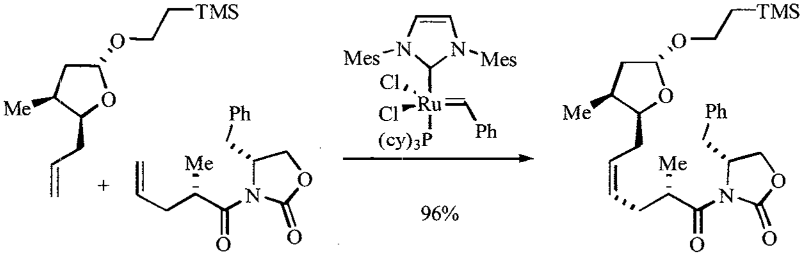
D. C. Harrowven, M. C. Lucas, P. D. Howes, *Tetrahedron Letters* **2000**, 41, 8985



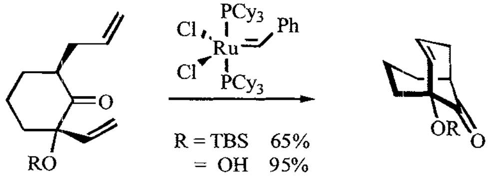
W. R. Zuercher, M. Scholl, R. M. Grubbs, *Journal of Organic Chemistry* **1998**, 63, 4291



F.-D. Boyer, I. Hanna, L. Ricard, *Organic Letters* **2004**, 6, 1817



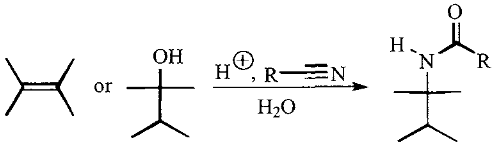
A. K. Ghosh, C. Liu, *Journal of the American Chemical Society* **2003**, 125, 2374



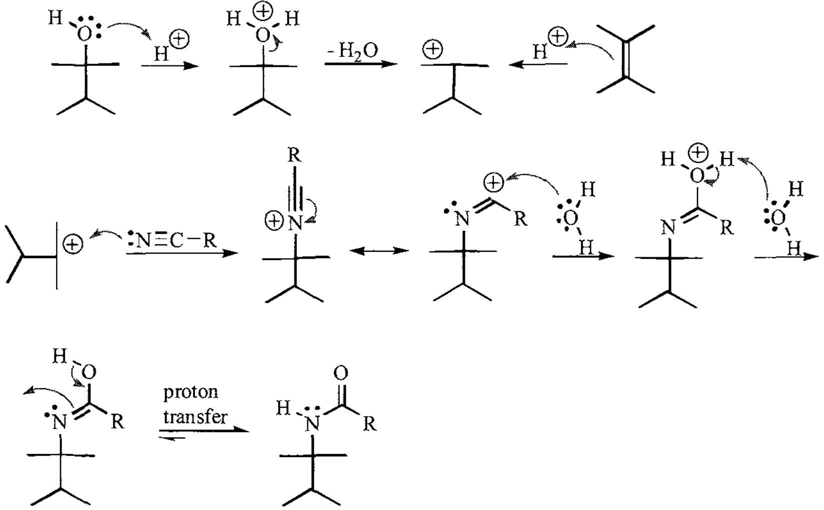
J. R. Rodrigues, L. Castedo, J. L. Mascarenas, *Organic Letters* **2000**, 2, 3209

Ritter Reaction

The Reaction:



Proposed Mechanism:

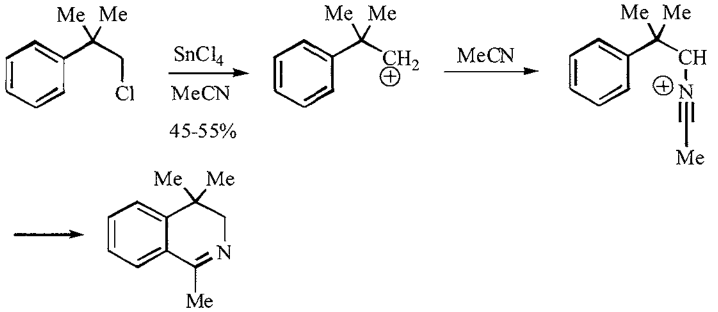


Notes:

V. K. Ahluwalia, R. K. Parashar, *Organic Reaction Mechanisms*, Alpha Science International Ltd., Pangbourne, U.K., 2002, pp. 371-372; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp 1244-1245; L. I. Krimen, D. J. Cota, *Organic Reactions* **17**, 3

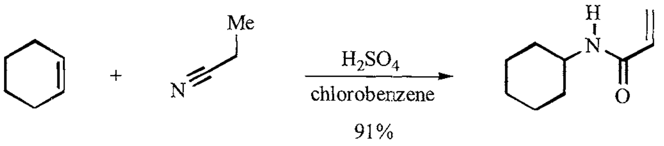
Hydrolysis of the amides provides a unique method for preparation of tertiary amines.

Examples:

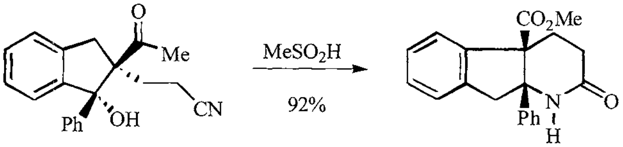


T.-L. Ho, R.-J. Chein, *Journal of Organic Chemistry* **2004**, 69, 591

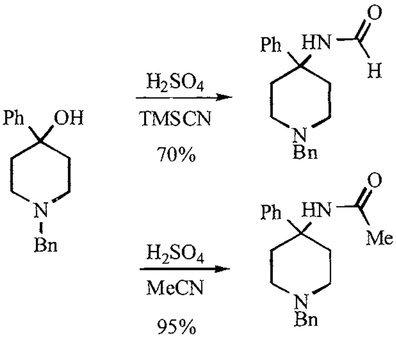
This work comments on the slow induction period of the H_2SO_4 reaction with acrylonitrile and alcohol, and on possible safety issues.



S. J. Chang, *Organic Process Research and Development* **1999**, 3, 232

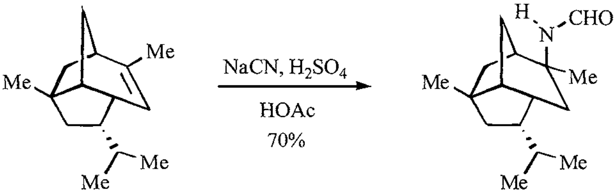


K. Van Emelen, T. DeWit, G. J. Hoornaert, F. Compernolle, *Organic Letters* **2000**, 2, 3083

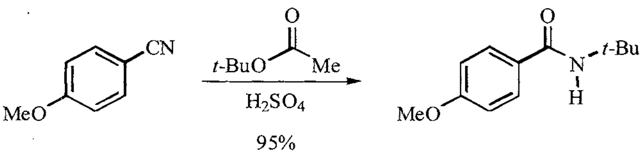


H. G. Chen, O. P. Goel, S. Kesten, J. Knobelsdorg, *Tetrahedron Letters* **1996**, 37, 8129

A ***modified Ritter Reaction***:



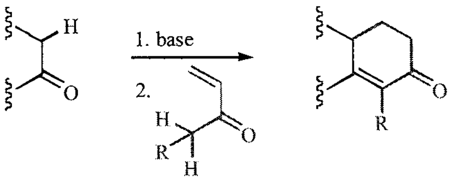
T.-L. Ho, L. R. Kung, *Organic Letters* **1999**, 1, 1051



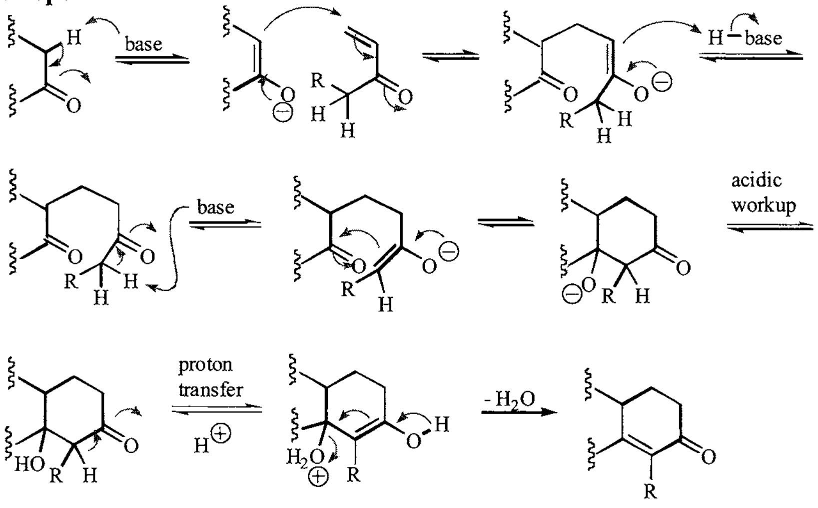
K. L Reddy, *Tetrahedron Letters* **2003**, 44, 1453

Robinson Annulation

The Reaction:



Proposed Mechanism:



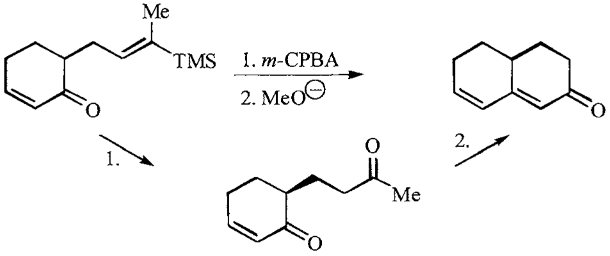
Notes:

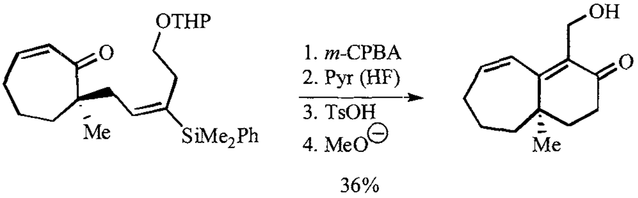
This is a ***Michael reaction*** followed by an ***Aldol reaction.***

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp. 1222-1224; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 228-232

See: D. Rajagopal, R. Narayanan, S. Swaminathan, *Tetrahedron Letters* **2001**, 42, 4887 for a one-pot asymmetric annulation procedure.

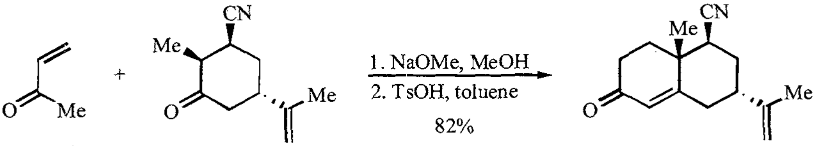
The related ***Stork-Jung Vinysilane annulation:***



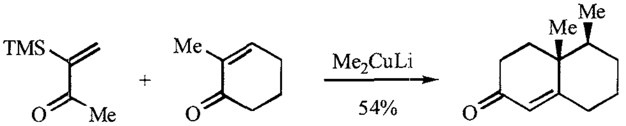


B. B. Snider, B. Shi, *Tetrahedron Letters* **2001**, 42, 9123

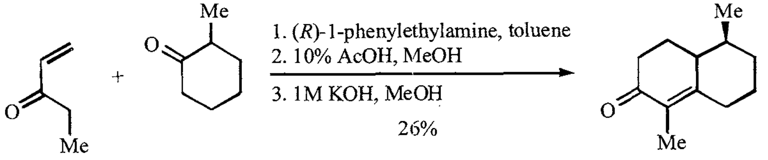
Examples:



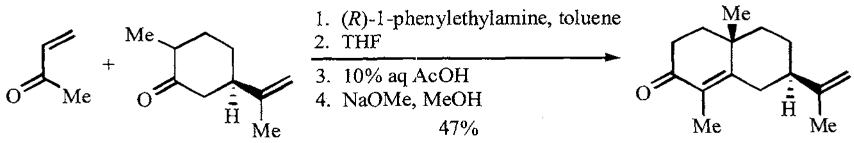
A. A. Verstegen-Haaksma, H. J. Swarts, J. M. B. Jansen, A. deGroot, *Tetrahedron* **1994**, 50, 10073



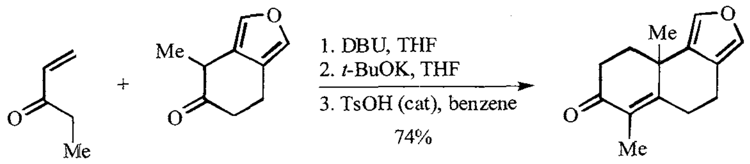
R. K. Boeckman, Jr., *Tetrahedron* **1983**, 39, 925



I. Jabin, G. Revial, K. Melloul, M. Pfau, *Tetrahedron: Asymmetry* **1997**, 8, 1101



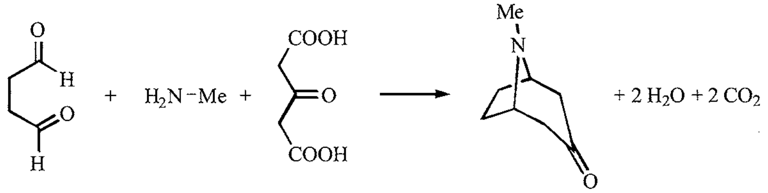
V. Zhabinskii, A. J. Minnaard, J. B. P. A. Wijnberg, A. deGroot, *Journal of Organic Chemistry* **1996**, 61, 4022



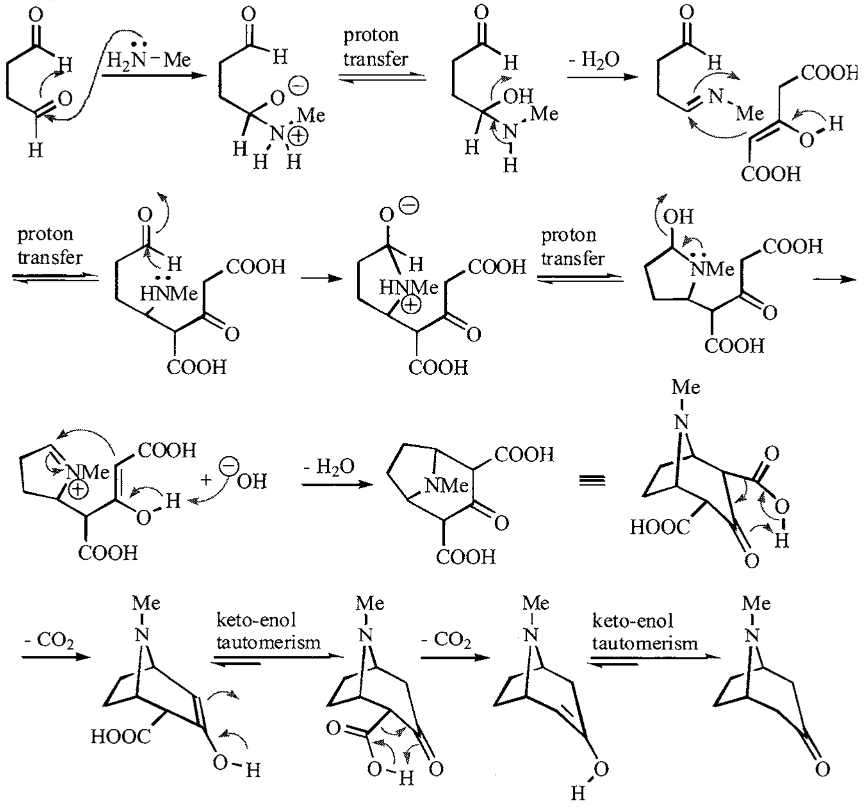
Y. Baba, T. Sakamoto, S. Soejima, K. Kanematsu, *Tetrahedron* **1994**, 50, 5645

Robinson-Schopf Reaction

The Reaction:



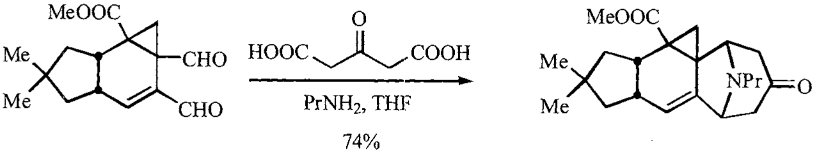
Proposed Mechanism:



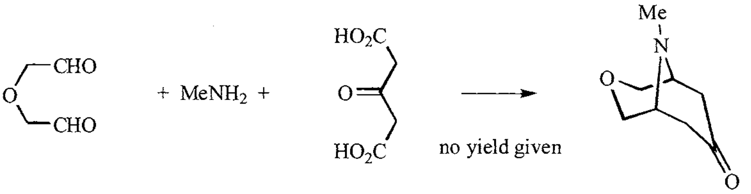
Notes:

This reaction is a “biomimetic” approach to forming alkaloids.

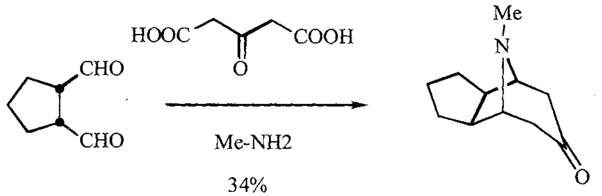
Examples:



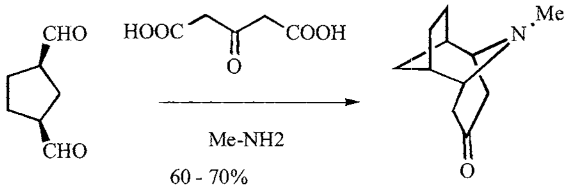
T. Jarevang, H. Anke, T. Anke, G. Erkel, O. Sterner, *Acta Chemica Scandinavica* **1998**, 52, 1350 (AN 1998:770310



J. Bermudez, J. A. Gregory, F. D. King, S. Starr, R. J. Summersell, *Bioorganic and Medicinal Chemistry Letters* **1992**, 2, 519



O. L. Chapman, T. H. Koch, *Journal of Organic Chemistry* **1966**, 31, 1043

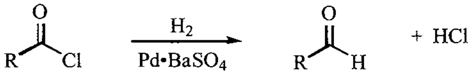


Detailed conformational study on the product

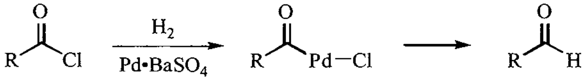
L. A. Paquette, J. W. Heimaster, *Journal of the American Chemical Society* **1966**, 88, 763

Rosenmund Reduction

The Reaction:



Proposed Mechanism:



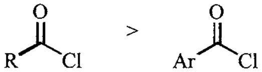
J. Tsuji, K. Ohno, *Journal of the American Chemical Society*, **1968**, 90, 94

Notes:

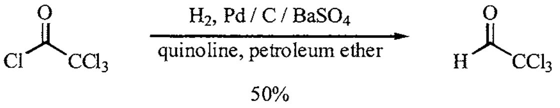
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 532; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 232-233; E. Mosettig, R. Mozingo, *Organic Reactions* **4**, 7

See: S. Siegel, *Encyclopedia of Reagents for Organic Synthesis,* John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3861

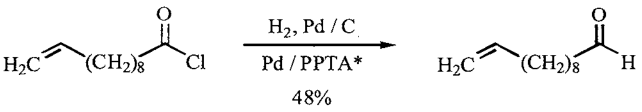
Pd-$BaSO_4$ binds less strongly to Pd-C, the product can leave the catalyst surface more readily and prevent over-reduction.



Examples:

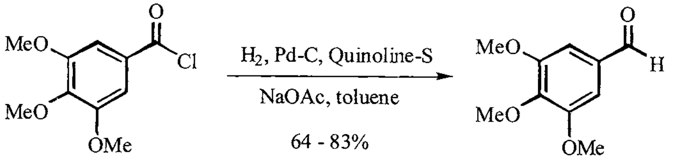


J. W. Sellers, W. E. Bissinger, *Journal of the American Chemical Society*, **1954**, 76, 4486



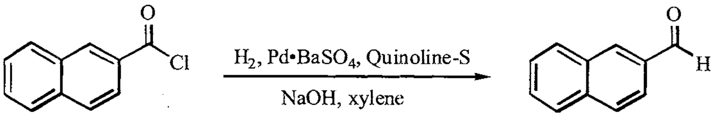
* $PdCl_2$ deposited on poly(*p*-phenylene terephthalamide) (PPTA)

V. G. Yadav, S. B. Chandalia, *Organic Process Research & Development* **1997**, 1, 226



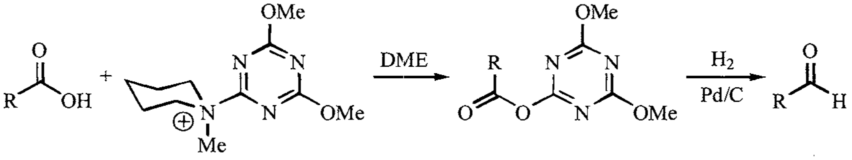
Quinoline-S prepared according to the recipe of E. B. Hershberg, J. Cason, Method 2, *Organic Syntheses* CV 3, 626

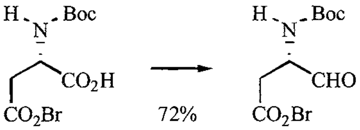
A. I. Rachlin, H. Gurien, D. P. Wagner, *Organic Syntheses* **1971**, 51 8

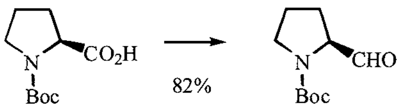


E. B. Hershberg and J. Cason, Method 2, *Organic Syntheses* CV 3, 626

Modification:



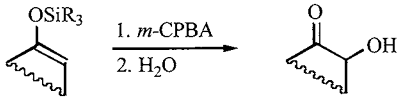




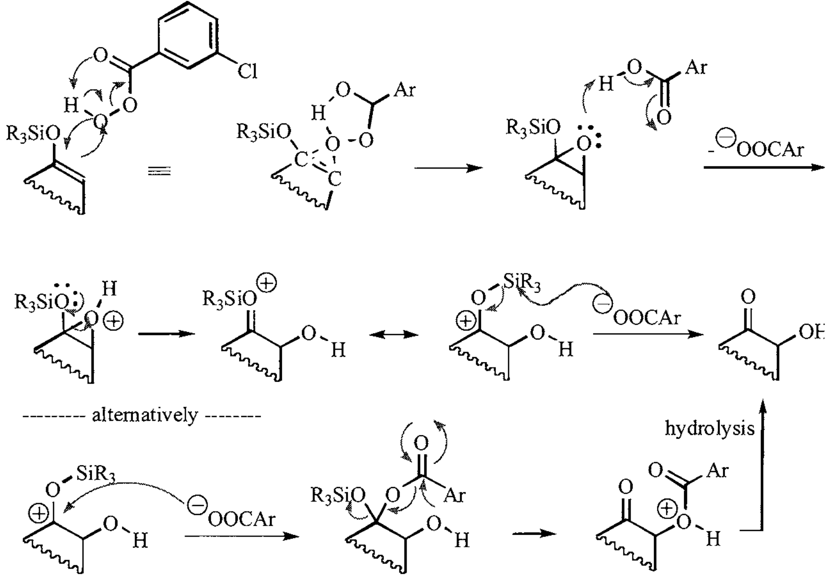
M. Falorni, G. Giacomelli, A. Porcheddu, M. Taddei, *Journal of Organic Chemistry* **1999**, 64, 8962

Rubottom Oxidation

The Reaction:

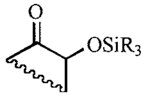


Proposed Mechanism:



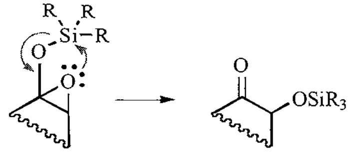
Notes:

Rubottom noted that, in the absence of a hydrolytic workup,

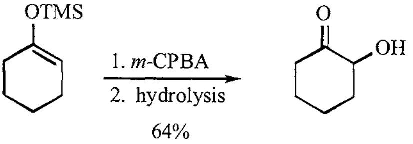


is obtained.

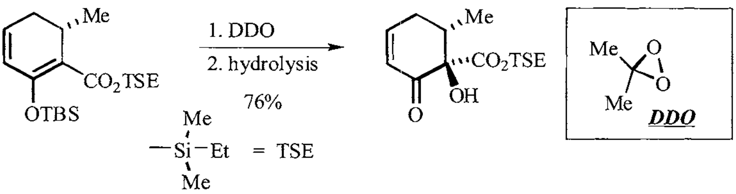
This is suggestive of:



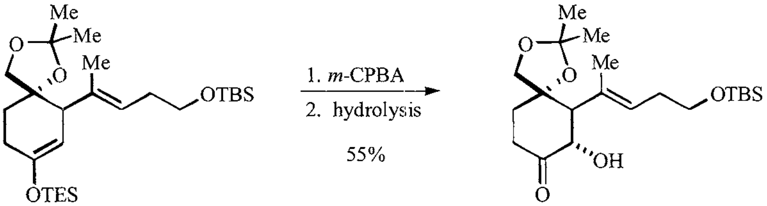
Examples:



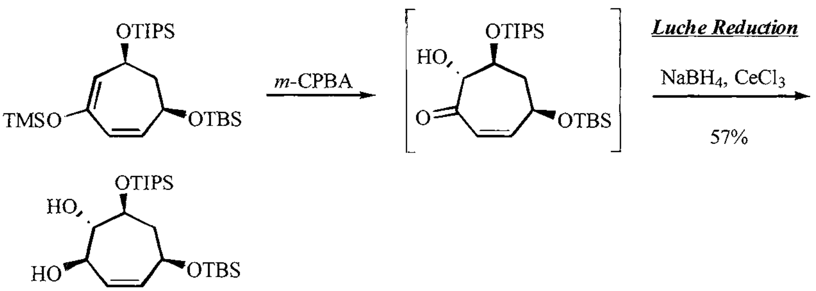
G. M. Rubottom, M. A. Vazquez, D. R. Pelegrins, *Tetrahedron Letters* **1974**, 15, 4319



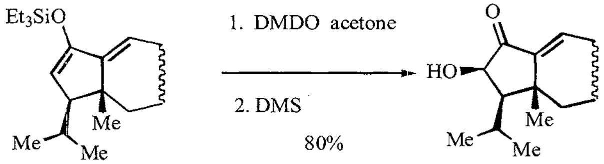
J. G. Allen, S. J. Danishefsky, *Journal of the American Chemical Society* **2001**, 123, 351



D. F. Taber, T. E. Christos, A. L. Rheingold, I. A. Guzei, *Journal of the American Chemical Society* **1999**, 121, 5589



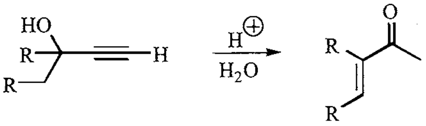
Y. Xu, C. R. Johnson, *Tetrahedron Letters* **1997**, 38, 1117



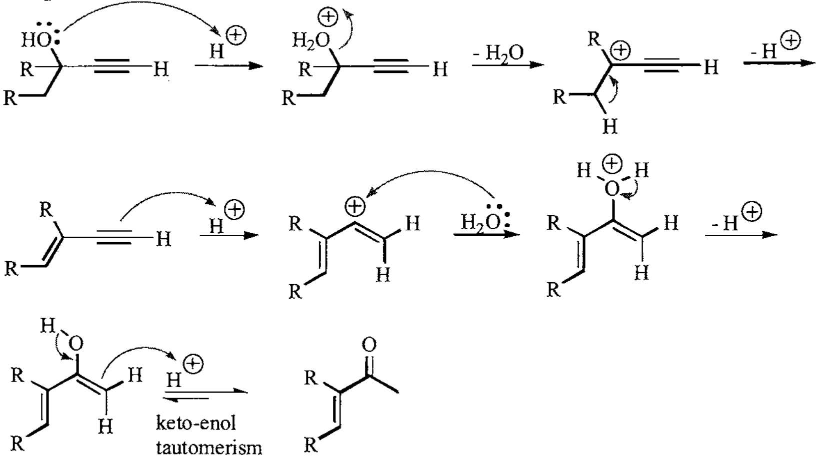
M. Mandel, S. Danishefsky, *Tetrahedron Letters* **2004**, 45, 3831

Rupe Rearrangement

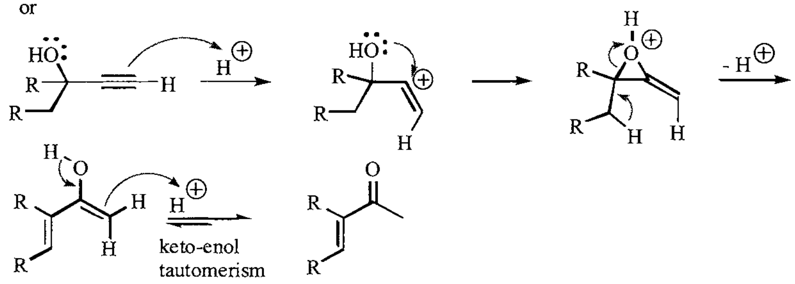
The Reaction:



Proposed Mechanism:



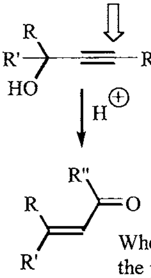
or



Notes:

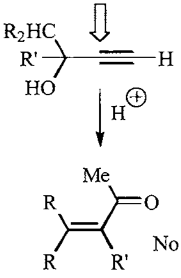
The ***Meyer-Schuster Rearrangement*** is similar to the ***Rupe Rearrangement***.

future site of carbonyl



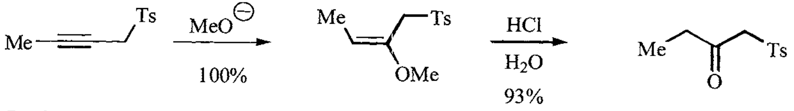
When R'' = H, an aldehyde is the product. R' may be H

future site of carbonyl

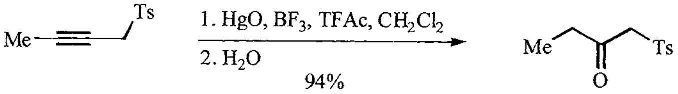


No aldehyde product

***Pseudo-Rupe Rearrangement*:**

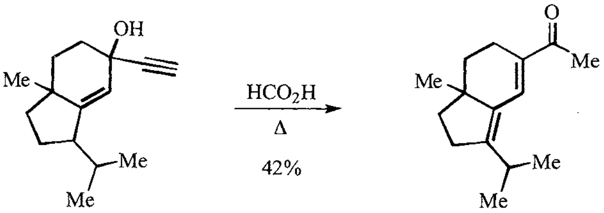


***Raphael Rearrangement*:**

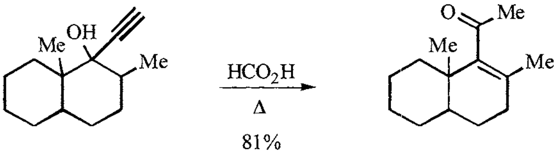


V. Barre, F. Massias, D. Uguen, *Tetrahedron Letters* **1989**, 30, 7389

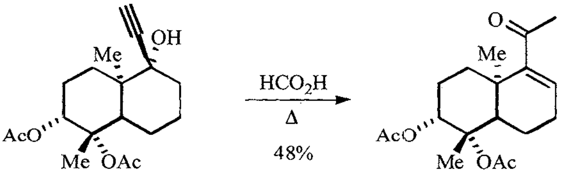
Examples:



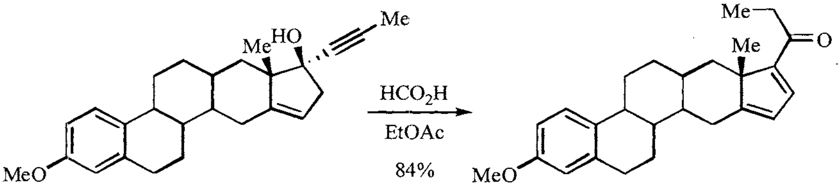
K. Takeda, D. Nakane, M. Takeda, *Organic Letters* **2000**, 2, 1903



W. S. Johnson, S. L.Gray, J. K. Crandall, D. M. Bailey, *Journal of the American Chemical Society* **1964**, 86, 1966



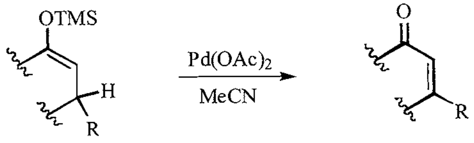
S. W. Pelletier, S. Prabhakar, *Journal of the American Chemical Society* **1968**, 90, 5318 and earlier references.



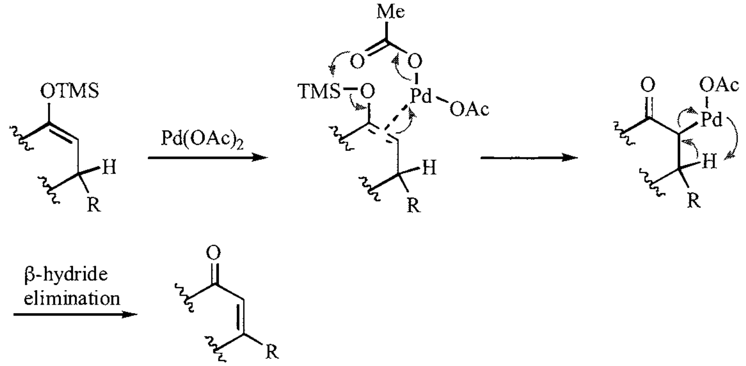
H. Weinman, M. Harre, H. Neh, K. Nickish, C. Skotsch, U. Tilstam, *Organic Process Research and Development* **2002**, 6, 216

Saegusa Oxidation

The Reaction:



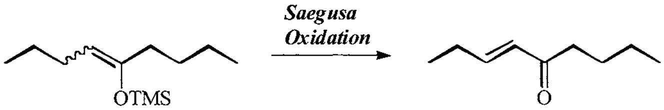
Proposed Mechanism:



Notes:

The original work shows that benzoquinone can be added to reoxidize the Pd reagent; however, the reaction proceeds well without it.

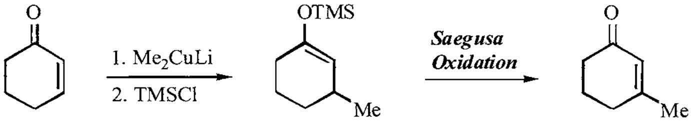
When applicable, there is selectivity for (*E*)-products:



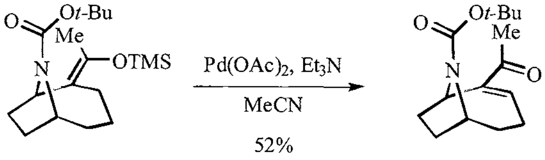
only isomer formed

A Pd-containing intermediate has been isolated and fully characterized:
S. Porth, J. W. Bats, D. Trauner, G. Giester, J. Mulzer, *Angewandte Chemie, International Edition in English* **1999**, 38, 2015

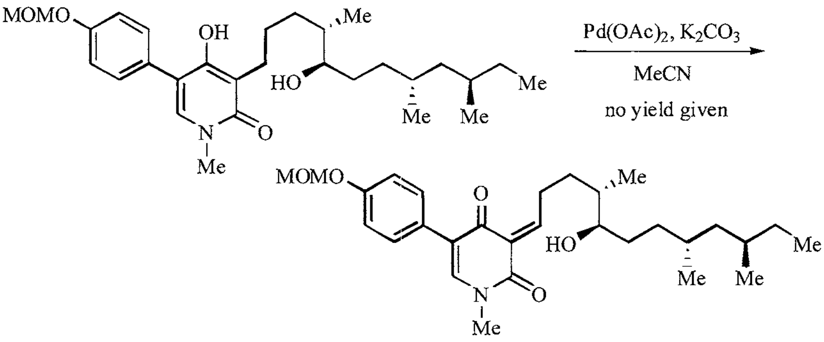
Examples:



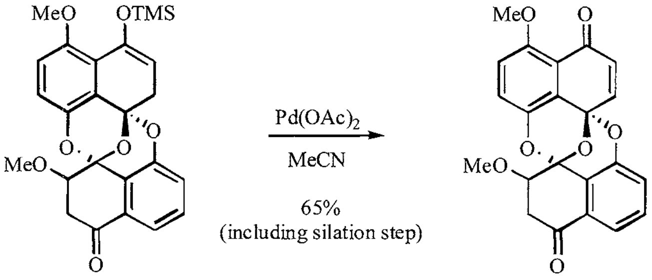
Y. Ito, T. Hirao, T. Saegusa, *Journal of Organic Chemistry* **1978**, 4, 1011



A. M. P. Koskinen, H. Rapoport, *Journal of Medicinal Chemistry* **1985**, 28, 1301



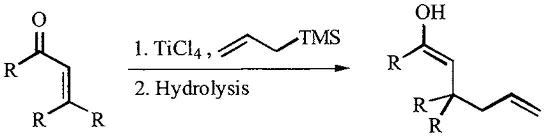
D. R. Williams, R. A. Turske, *Organic Letters* **2000**, 2, 3217



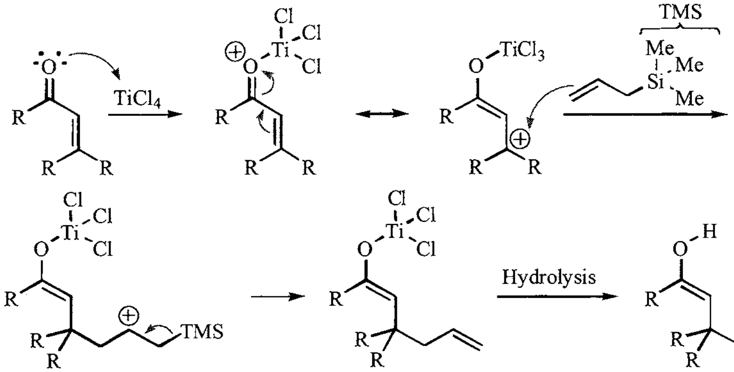
S. Chi, C. H. Heathcock, *Organic Letters* **1999**, 1, 3

Sakurai Reaction

The Reaction:



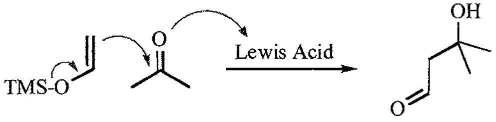
Proposed Mechanism:

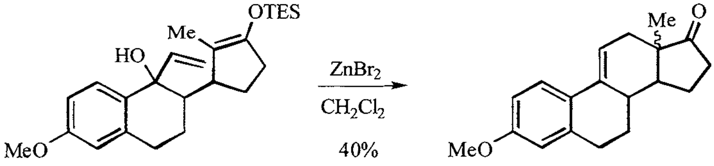


TMS/Silicon can
stabilize β carbocations.

Notes:

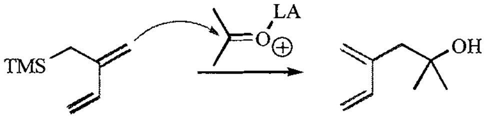
This reactionis similar to the ***Mukaiyama Reaction***, which employs silyl enol ethers:





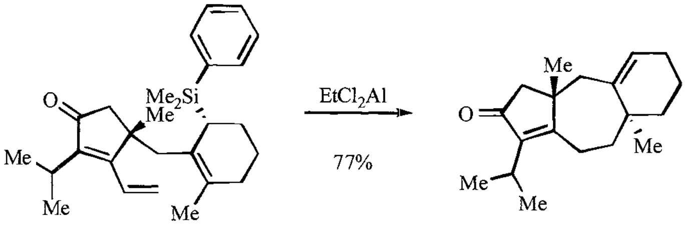
S. Dratch, T. Charnikhova, F. C. E. Saraber, B. J. M. Jansen, A. DeGroot *Tetrahedron* **2003**, 59, 4287

A useful isoprenylation reagent:

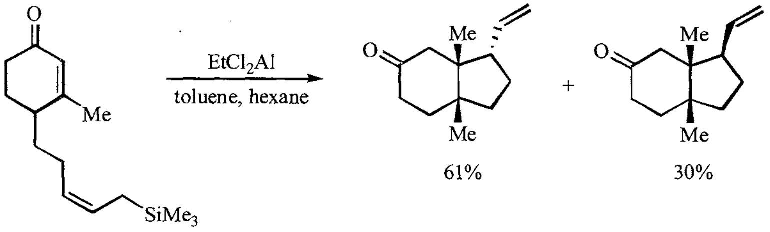


[70901-64-3]
See H. Sakurai, *Encyclopedia of Reagents for Organic Synthesis*, Ed. L. A. Paquette, John Wiley and Sons, Inc., New York, 1995, **7**, 5277

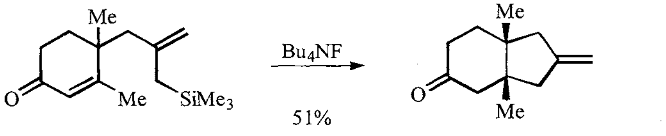
Examples:



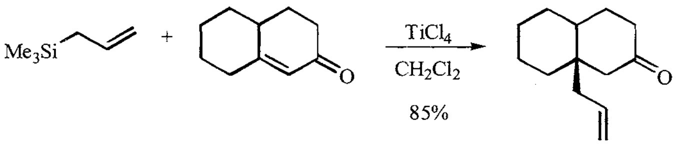
G. Majetich, J. S. Song, C. Ringold, G. A. Memeth, *Tetrahedron Letters* **1990**, 31, 2239



D. Schinzer, S. Solyon, M. Becker, *Tetrahedron Letters* **1985**, 26, 1831



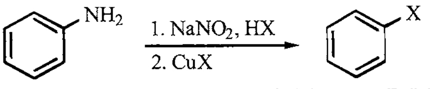
G. Majetich, K. Hull, J. Defauw, R. Desmond, *Tetrahedron Letters* **1985**, 26, 2747



A. Hosome, H. Sakurai, *Journal of the American Chemical Society* **1977**, 99, 1673

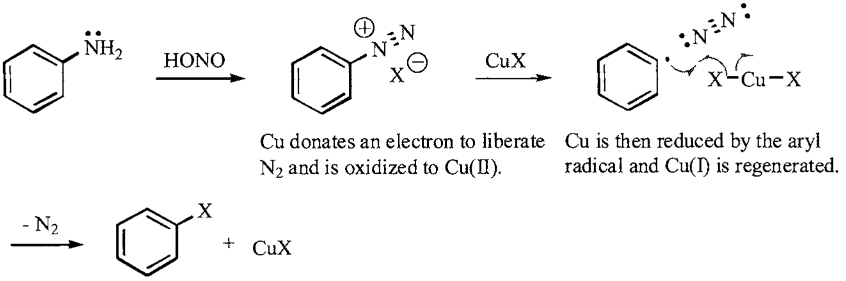
Sandmeyer Reaction

The Reaction:



Works best for X = Cl, Br, and CN, however F, I, R-S, OH are also possible.

Proposed Mechanism:

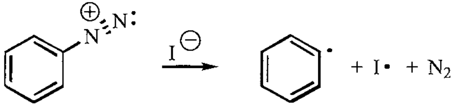


Cu donates an electron to liberate N_2 and is oxidized to Cu(II).

Cu is then reduced by the aryl radical and Cu(I) is regenerated.

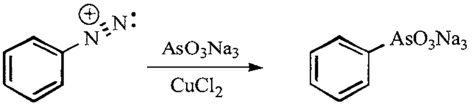
Notes:

For the iodination reaction, copper is not required. The iodide ion readily undergoes the necessary oxidation-reduction chemistry to push the reaction to completion:

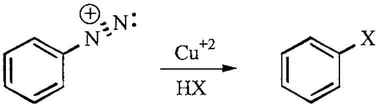


The iodine radical combines to form I_2, which undergoes further chemistry with I•. The result of complex reactions with other iodine intermediates provides the net capture of an iodine radical with the aryl radical to give product.

Bart-Scheller Arsonylation Reaction

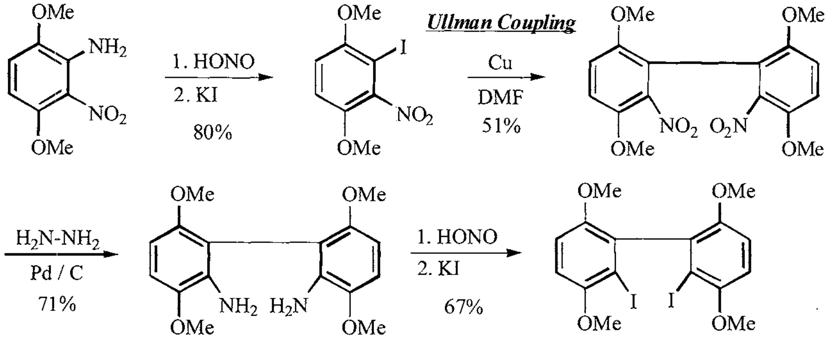


Körner-Contardi Reaction

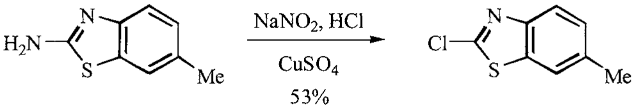


X = Cl, Br, CN

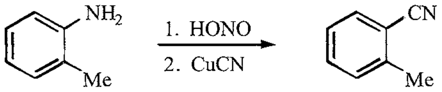
Examples:



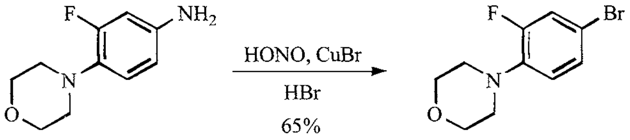
C. W. Lai, C. K. Lam, H. K. Lee, T. C. W. Mak, H. N. C. Wong, *Organic Letters* **2003**, 5, 823



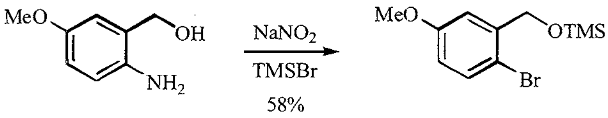
N. Zou, J.-F.Liu, B. Jiang, *Journal of Combinatorial Chemistry* **2003**, 5, 754



H. T. Clarke, R. R. Reed, *Organic Synthesis* **1941**, 1, 514



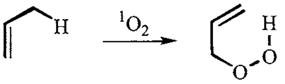
B. Mallesham, B. M. Rajesh, P. R. Reddy, D. Srinivas, S. Trehan, *Organic Letters* **2003**, 5, 7963



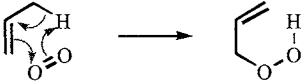
P. G. Tsoungas, M. Searcey, *Tetrahedron Letters* **2001**, 42, 6589

Schenck Ene Reaction

The Reaction:



Proposed Mechanism:



Notes:

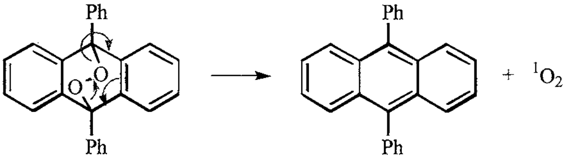
See H. H. Wasserman, R. W. DeSimone, *Encyclopedia of Reagents for Organic Synthesis*, Edited by L.A. Paquette, John Wiley and Sons, Inc., New York, 1995, **6**, 4478

Ways to Generate Singlet Oxygen:

1. Dye-sensitized photoexcitation (eg with TTP, below):

$$\text{Photosensitizer} + h\nu \longrightarrow {}^1\text{Photosensitizer}^*$$
$$^1\text{Photosensitizer}^* \longrightarrow {}^3\text{Photosensitizer}^*$$
$$^3\text{Photosensitizer}^* + {}^3O_2 \longrightarrow \text{Photosensitizer} + {}^1O_2$$

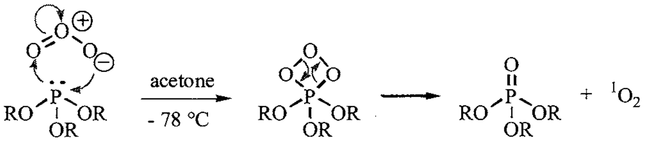
2.



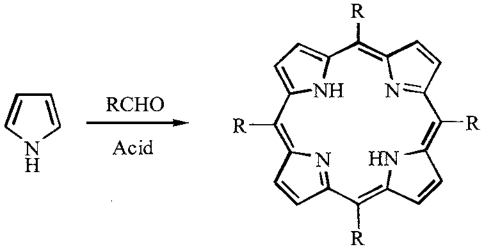
9.10-Diphenylanthracene Endoperoxide

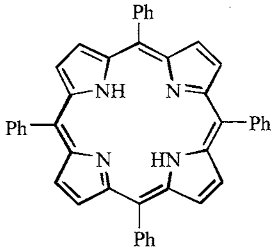
3. $H_2O_2 + {}^{\ominus}OCl \quad {}^1O_2 + H_2O + Cl^{\ominus}$

4.



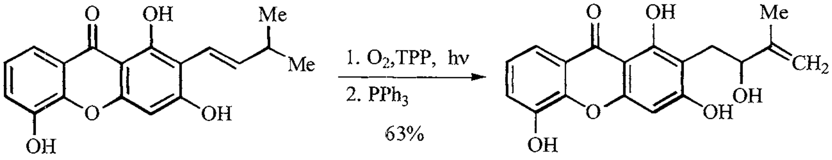
The ***Rothemund Reaction*** is useful for making substituted porphines (seen in examples on next page):



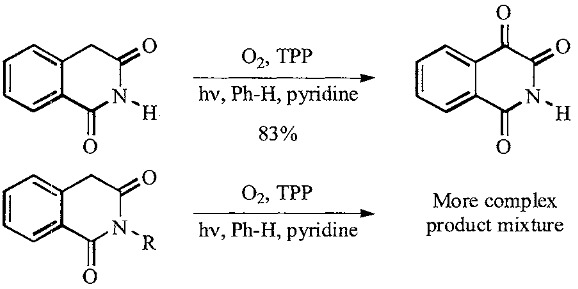


TTP - Tetraphenylporphine

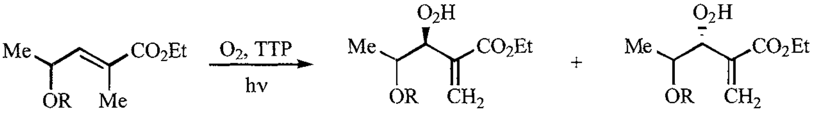
Examples:



J.-J. Helesbeux, O. Duval, C. Dartiguelongue, D. Seraphin, J.-M. Oger, P. Richomme, *Tetrahedron* **2004**, 60, 2293



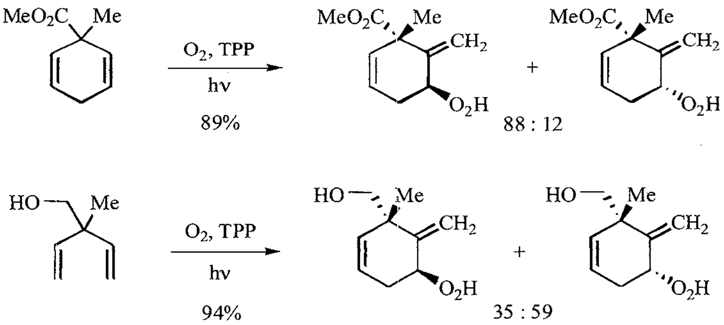
K.-Q. Ling, J.-H. Ye, X.-Y. Chen, D.-J. Ma, J.-H. Xu, *Tetrahedron* **1999**, 55, 9185



R = H, >95%, 84 : 16 threo : erythro

R = Si(i-Pr)$_3$, >95%, >95 : <5 threo : erythro

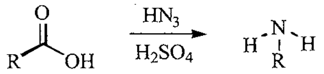
W. Adam, J. Renze, T. Wirth, *Journal of Organic Chemistry* **1998**, 63, 226



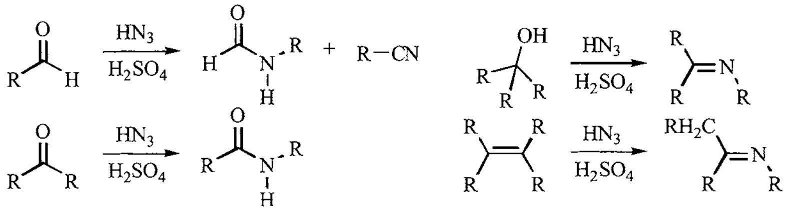
T. Linker, L. Froehlich, *Journal of the American Chemical Society* **1995**, 117, 2694

Schmidt Rearrangement, Schmidt Reaction

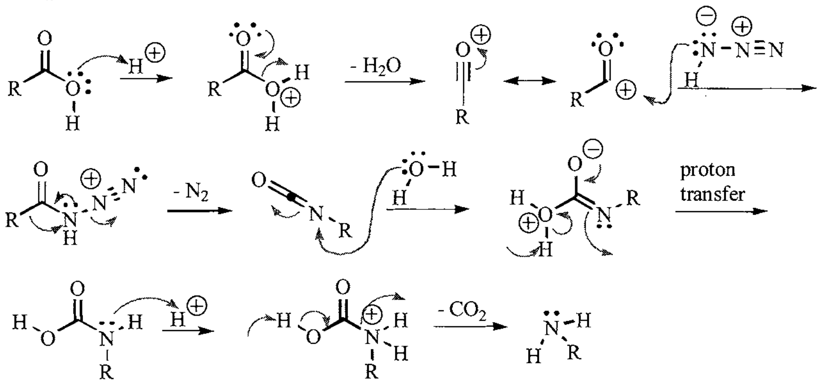
The Reaction:

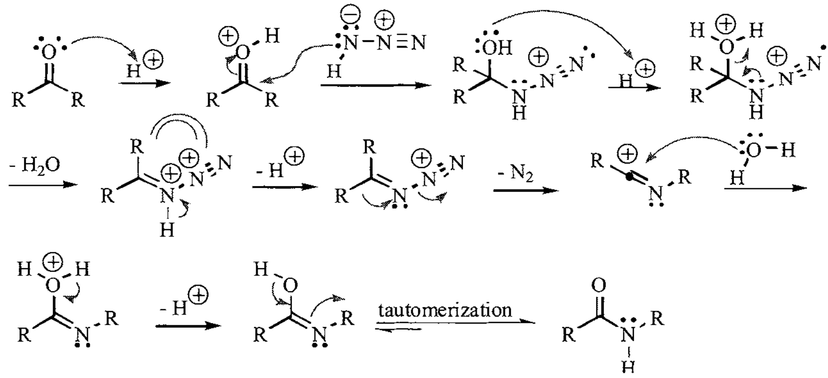


Also classified as Schmidt Reactions:



Proposed Mechanism:





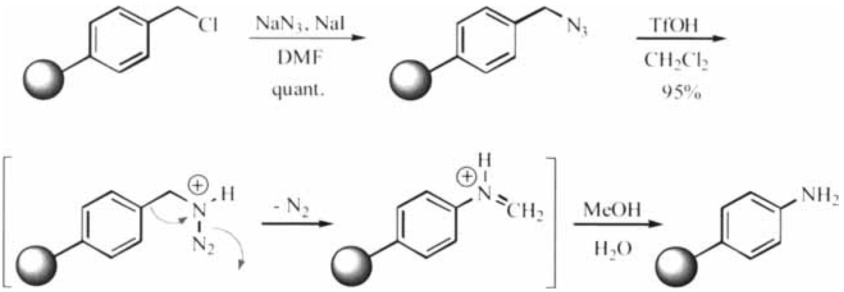
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp. 413-415; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 239-241; H. Wolff, *Organic Reactions* **3**, 8

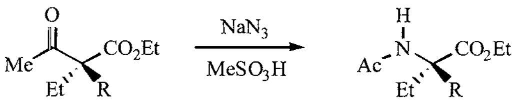
Loss of water will generally favor the less-hindered intermediate.

As with the ***Curtius***, ***Hofmann*** and ***Lossen Rearrangements***, there is a common isocyanate intermediate.

Examples:

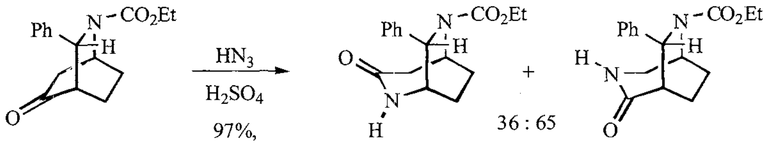


S. Arseniyadis, A. Wagner, C. Mioskowski, *Tetrahedron Letters* **2004**, 45, 2251

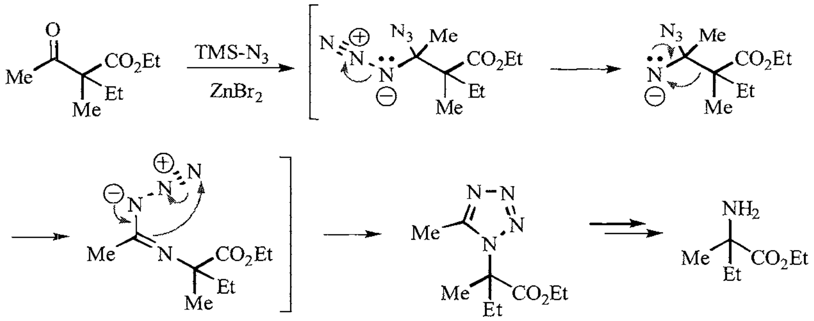


R = *n*-Bu, 55%
R = *t*-Bu, 35%

M. Tanaka, M. Oba, K. Tamai, H. Suemune, *Journal of Organic Chemistry* **2001**, 66, 2667



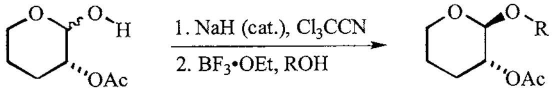
G. R. Krow, S. W. Szczepanski, J. Y. Kim, N. Liu, A. Sheikh, Y. Xiao, J. Yuan, *Journal of Organic Chemistry* **1999**, 64, 1254



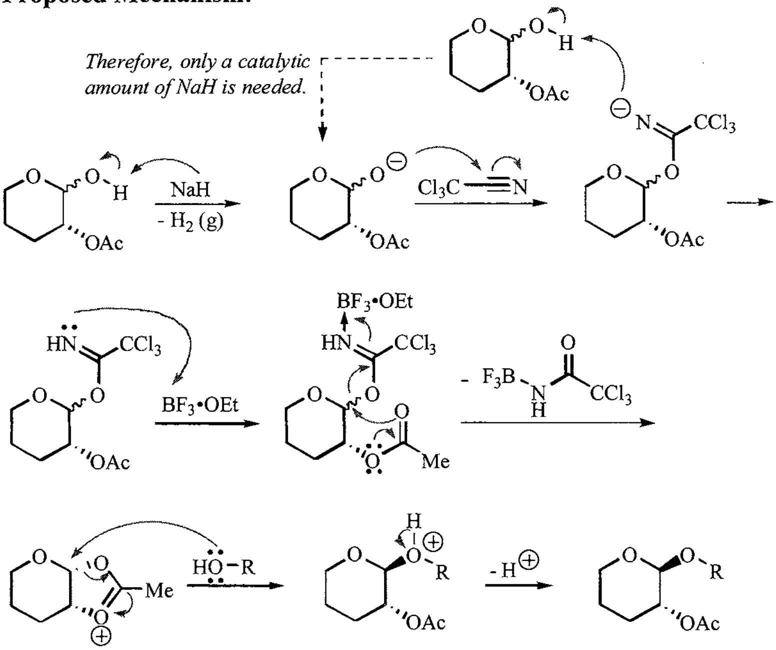
H.-J. Cristau, X. Marat, J.-P. Vors, J.-L. Pirat, *Tetrahedron Letters* **2003**, 44, 3179

Schmidt's Trichloroacetimidate Glycosidation Reaction

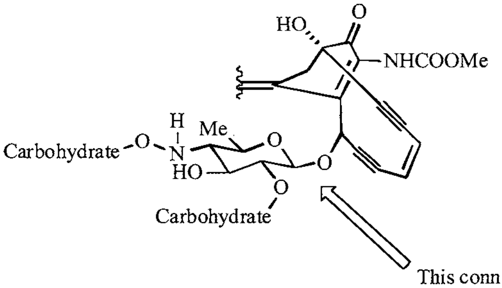
The Reaction:



Proposed Mechanism:


Therefore, only a catalytic amount of NaH is needed.

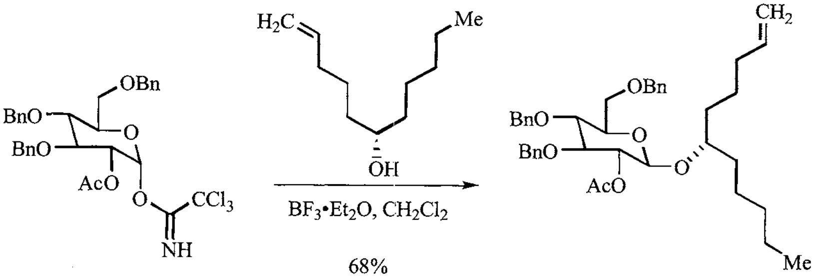
Notes:



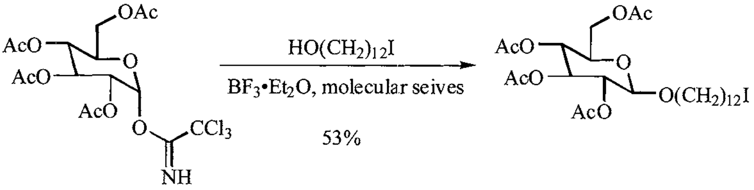
This connection established by ***Schmidt's Trichloroacetimidate Glycosidation Reaction***

K. C. Nicolaou, C. W. Hummel, M. Nakada, K. Shibayama, E. N. Pitsinos, H. Saimoto, Y. Mizuno, K. U. Baldenius, A. L. Smith, *Journal of the American Chemical Society* **1993**, 115, 7625

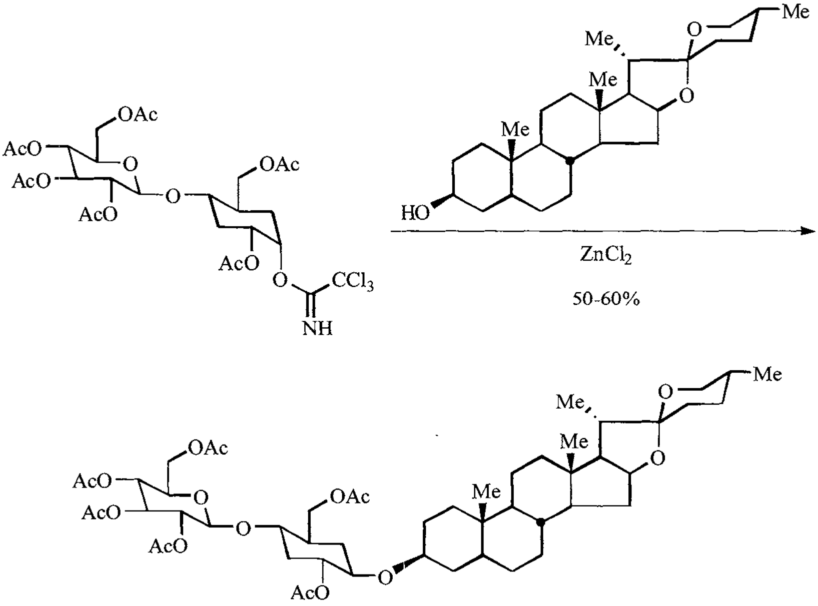
Examples:



A. Furstner, A. F. Jeanjean, P. Razon, *Angewandte Chemie, International Edition in English* **2002**, 41, 2097



T. Ren, D. Liu, *Tetrahedron Letters* **1999**, 40, 7621



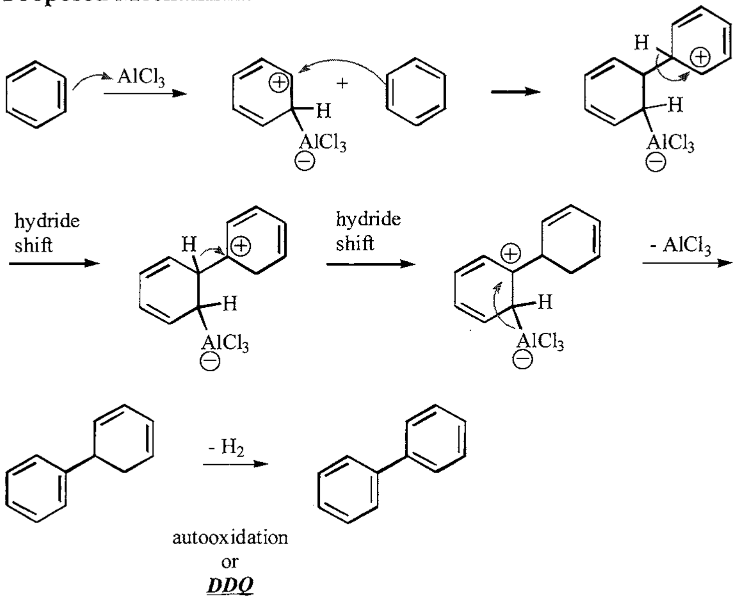
F. J. Urban, B. S. Moore, R. Breitenbach, *Tetrahedron Letters* **1990**, 31, 4421

Scholl Reaction

The Reaction:

$$2\ \mathrm{ArH} \xrightarrow{\mathrm{AlCl_3}} \mathrm{Ar{-}Ar} + \mathrm{H_2}$$

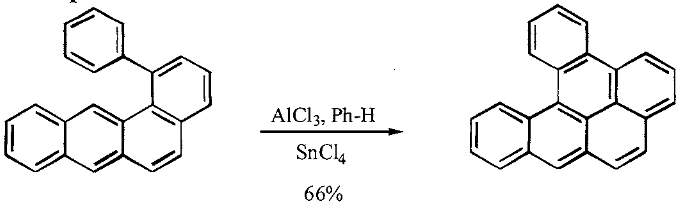
Proposed Mechanism:



Notes:

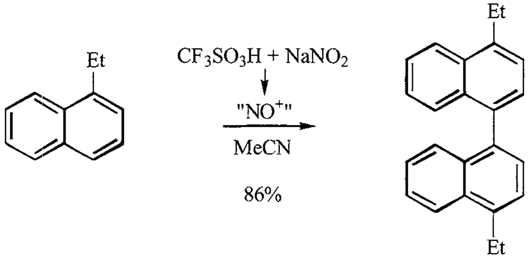
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 711

Examples:

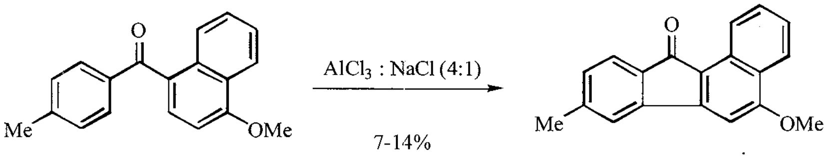


F. A. Vingiello, J. Yanez, J. A. Campbell, *Journal of Organic Chemistry* **1971**, 36, 2053

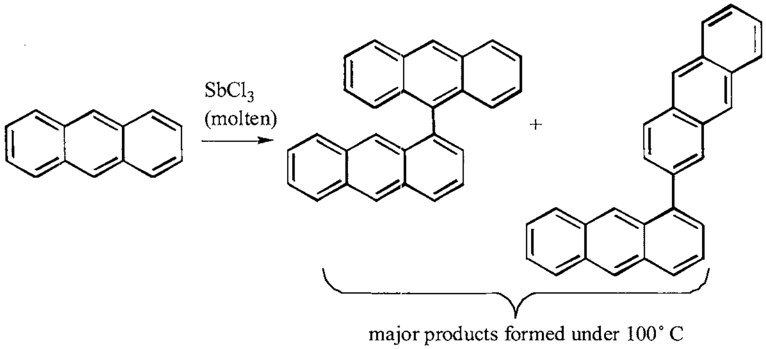
Radical-cation route:



M. Tanaka, H. Nakashima, M. Fujiwara, H. Ando, Y. Souma, *Journal of Organic Chemistry* **1996**, 61, 788



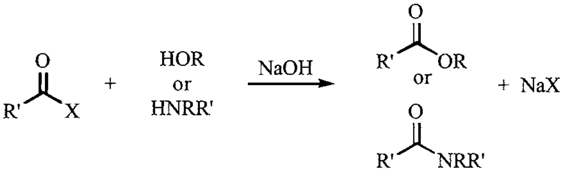
M. E. Gross, H. P. Lankelma, *Journal of the American Chemical Society* **1951**, 73, 3439



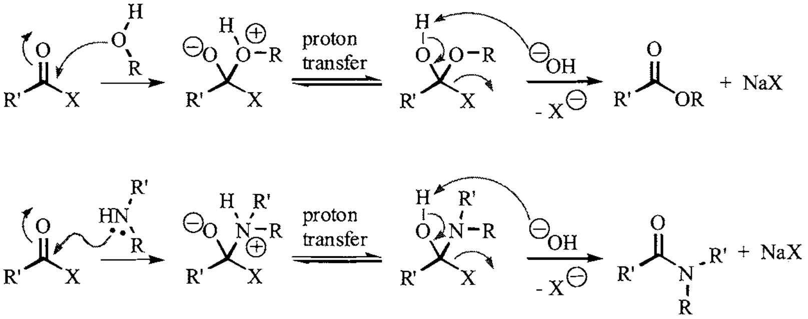
W. L. Poutsma, A. S. Dworkin, J. Brynestad, L. L. Brown, B. M. Bejamin, G. P. Smith, *Tetrahedron Letters* **1978**, 19, 873

Schotten-Baumann Reaction

The Reaction:



Proposed Mechanism:

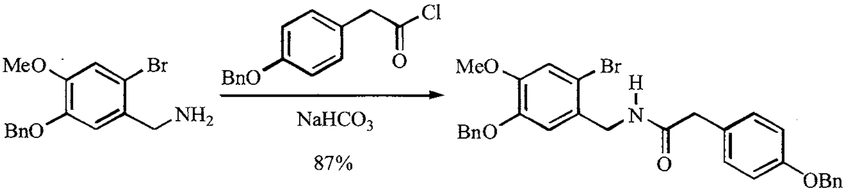


Notes:

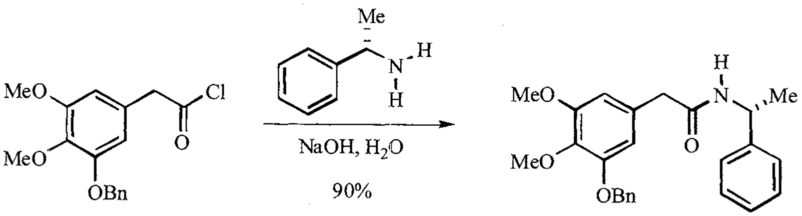
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp. 482, 506

Other methods for similar catalysis are known:
Einhorn Variation: Pyridine and DMAP (dimethylaminopyridine)
Steglich esterification: DMAP, trace of tosic acid, DCC (dicyclohexylcarbodiimide)
Yamaguchi Esterification: 2,4,6-trichlorobenzoyl chloride, (**Yamaguchii Reagent**), NEt_3, DMAP

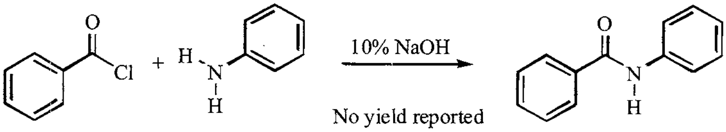
Examples:



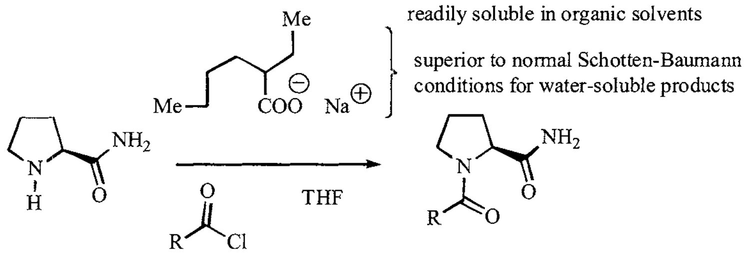
T. Honda, H. Namiki, F. Satch, *Organic Letters* **2001**, 3, 631



Y.-C. Wang, P. E. Georghiou, *Organic Letters* **2002**, 4, 2675



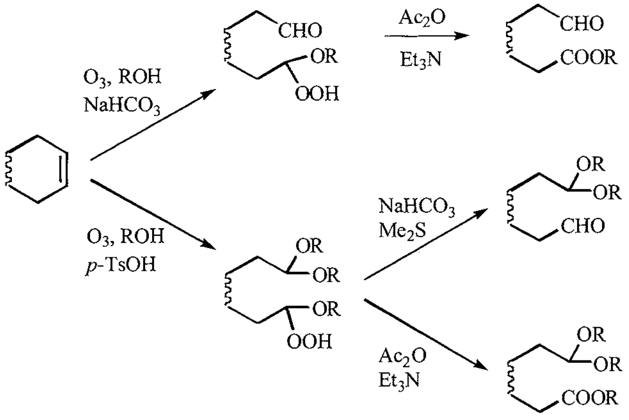
A. C. Hontz, E. C. Wagner, *Organic Syntheses* CV 4, 383



J. Fitt, K. Prasad, O. Repic, T. J. Blacklock, *Tetrahedron Letters* **1998**, 39, 6991

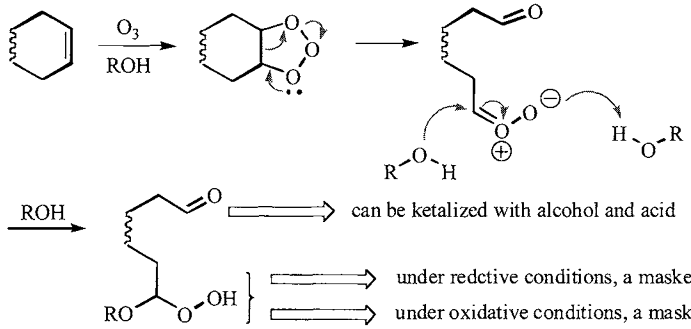
Schreiber Ozonolysis

The Reaction:



A protocol that allows for the differentiation of the two ends of the alkene bond during ozonolysis.

Proposed Mechanism:

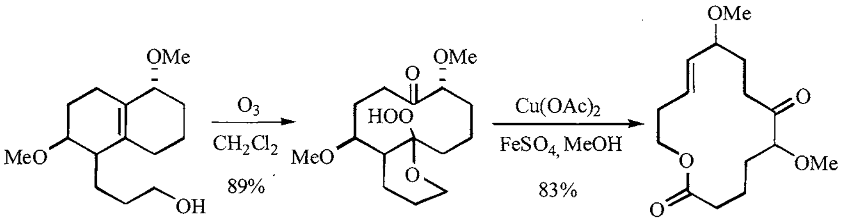


can be ketalized with alcohol and acid

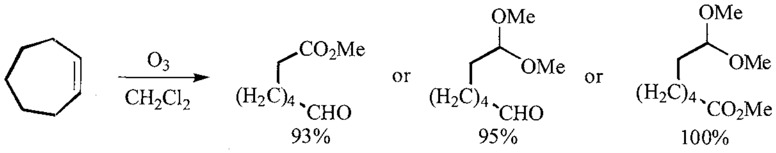
under redctive conditions, a masked aldehyde

under oxidative conditions, a masked acid

Examples:

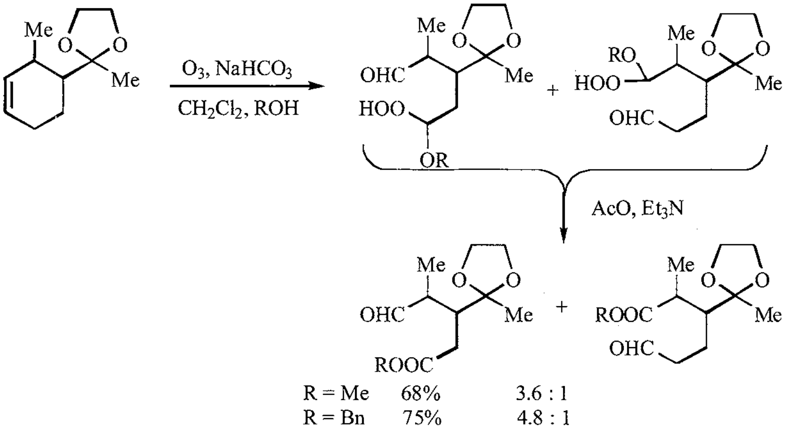


S. L. Schreiber, W. Liew, *Journal of the American Chemical Society* **1985**, 107, 2980



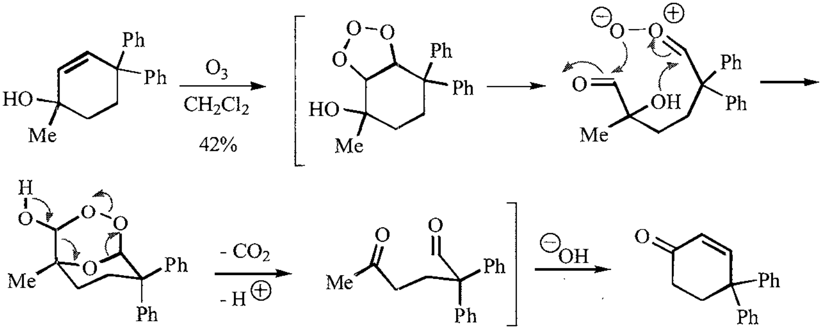
Different possible products possible by slight variation of workup

S. L. Schreiber, R. E. Claus, J. Regan, *Tetrahedron Letters* **1982**, 23, 3867



D. F. Taber, K. Nakajima, *Journal of Organic Chemistry* **2001**, 66, 2515

An anomolous ozonolysis

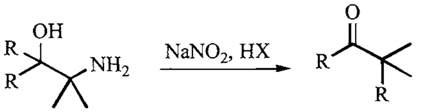


M. P. DeNinno, *Journal of the American Chemical Society* **1995**, 117, 9927

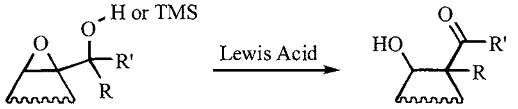
Semi-Pinacol Rearrangement

The Reaction:

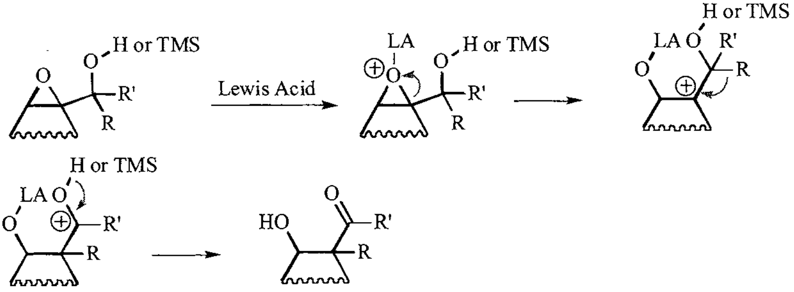
Originally:



But now commonly associated with ***Tiffeneau-Demjanov rearrangement***.
The classification now covers many reactions of the "***pinacol type***", including:



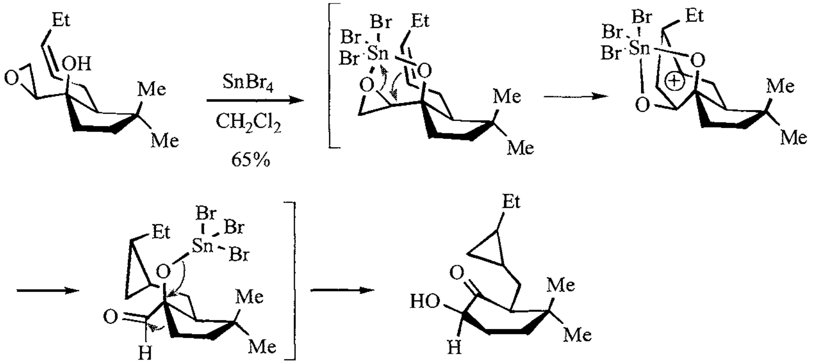
Proposed Mechanism:



Notes:

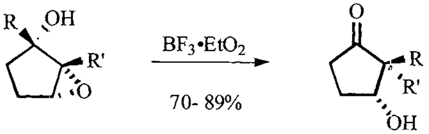
See ***Tiffineau- Demjanov*** for the hydroxy-amino rearrangement: T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 255-257; M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1397

A complex rearrangement:

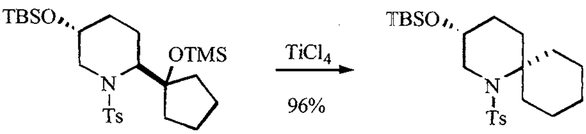


C. M. Marson, C. A. Oare, T. Walsgrove, T. J. Grinter, H. Adams. *Tetrahedron Letters* **2002**, 44, 141

Examples:

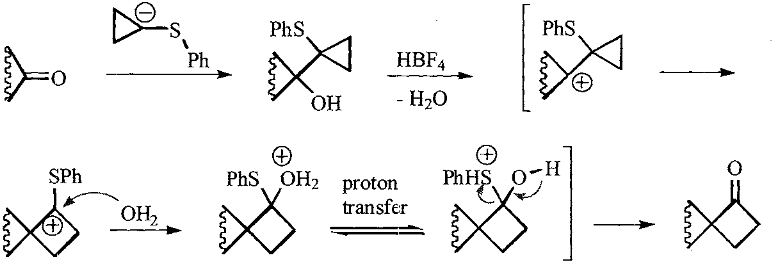


S.-J. Jeon, P. J. Walsh, *Journal of the American Chemical Society* **2003**, 125, 9544

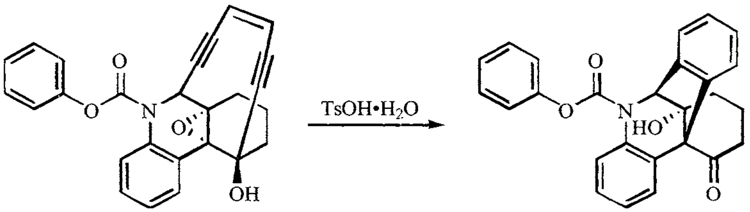


M. D. B. Fenster, G. R. Duke, *Organic Letters* **2003**, 5, 4313

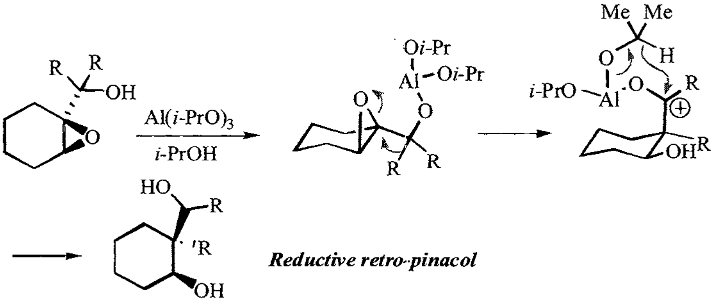
A useful methodology:



B. M. Trost, D. Keeley, M. J. Bogdanowicz, *Journal of the American Chemical Society* **1973**, 95, 3068



K. C. Nicolaou, A. L. Smith, S. V. Wendeborn, C.-K. Whang, *Journal of the American Chemical Society* **1991**, 113, 3106

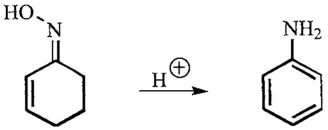


Reductive retro-pinacol

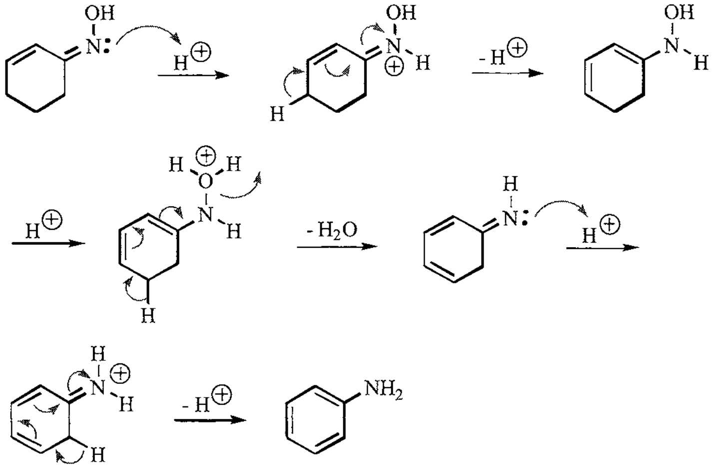
T. Q. Tu, L. D. Sun, P. Z. Wang, *Journal of Organic Chemistry* **1999**, 64, 629

Semmler-Wolff Reaction

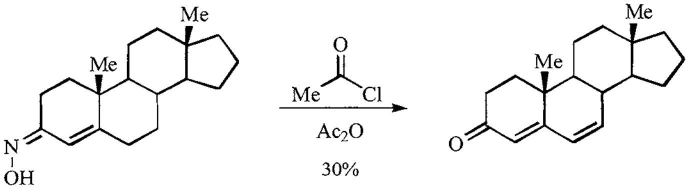
The Reaction:



Proposed Mechanism:

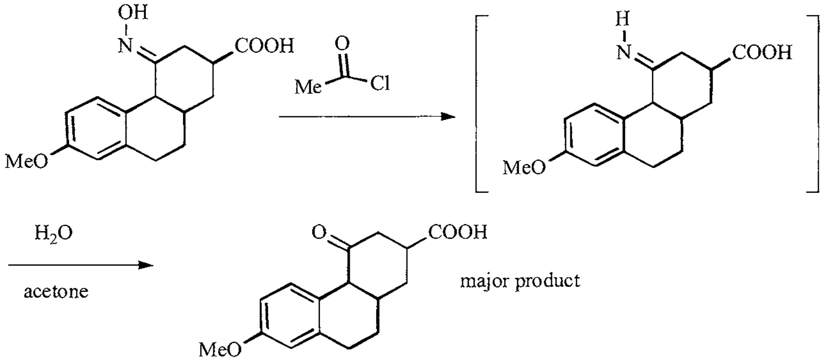


Examples:

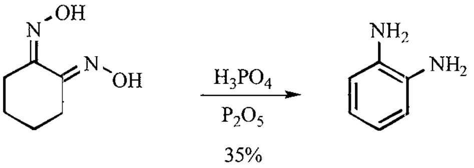


M. V. Bhatt, S. R. Raju, *Tetrahedron Letters* **1964**, 5, 2623

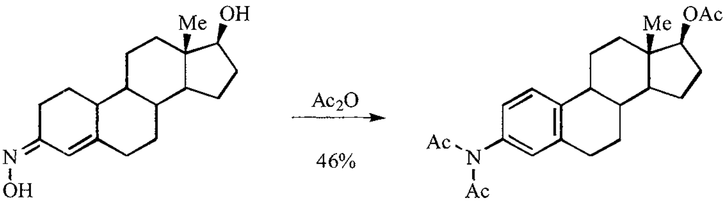
A similar "special case" moted:



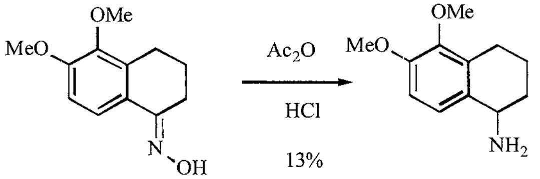
Z. G. Hajos, D. R. Parrish, M. W. Goldberg, *Journal of Organic Chemistry* **1968**, 33, 882



Y. Kobayashi, S. Wakamatsu, *Tetrahedron* **1967**, 23, 115



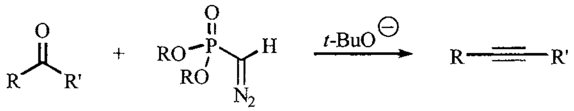
J. J. Weidner, P. M. Weintraub, R. A. Schnettler, N. P. Peet, *Tetrahedron* **1997**, 53, 6303



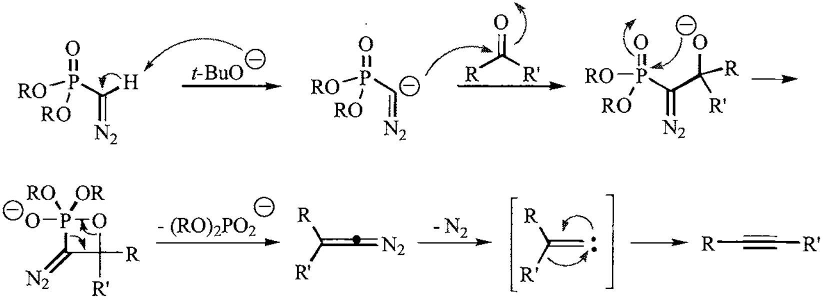
W. K. Sprenger, J. G. Cannon, H. F. Koelling, *Journal of Organic Chemistry* **1966, 31**, 2402

Seyferth-Gilbert Homolgation

The Reaction:

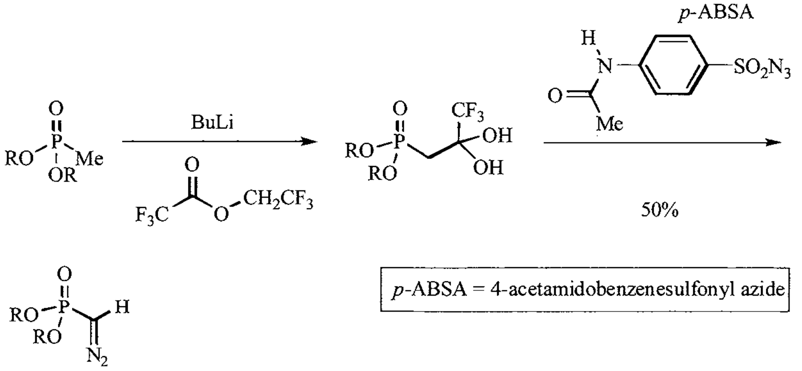


Proposed Mechanism:



Notes:

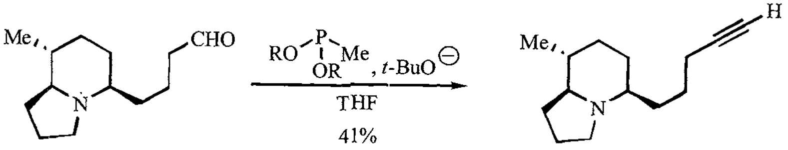
Starting material preparation:



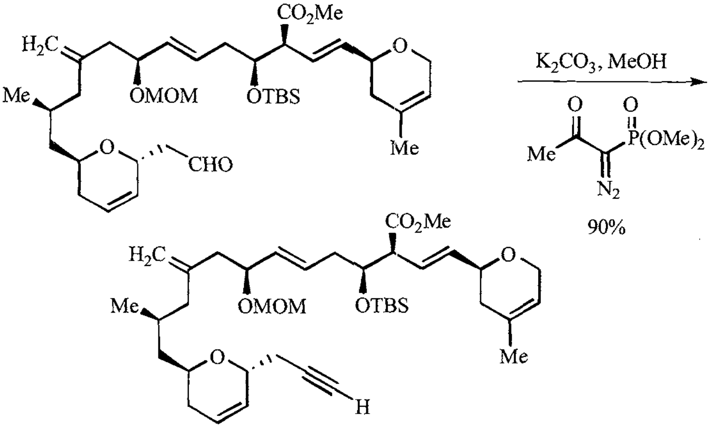
p-ABSA = 4-acetamidobenzenesulfonyl azide

D. G. Brown, E. J. Velthuisen, J. R. Commerford, R. G. Brisbois, T. R. Hoye, *Journal of Organic Chemistry* **1996**, 61, 2540

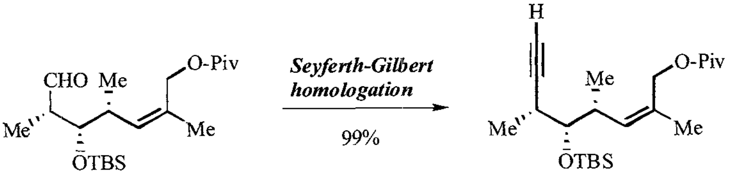
Examples:



D. L. Comins, D. H. LaMunyon, X. Chen, *Journal of Organic Chemistry* **1997**, 62, 8182



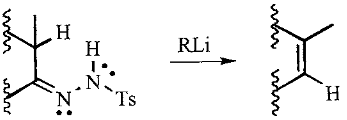
P. A. Wender, S. G. Hegde, R. D. Hubbard, L. Zhang, *Journal of the American Chemical Society* **2002**, 124, 4956



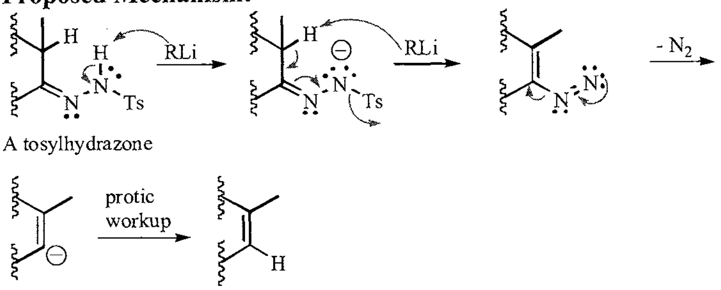
J. B. Nerenberg, D. T. Hung, P. K. Somers, S. L. Schreiber, *Journal of the American Chemical Society* **1993**, 115, 12621

Shapiro Reaction

The Reaction:



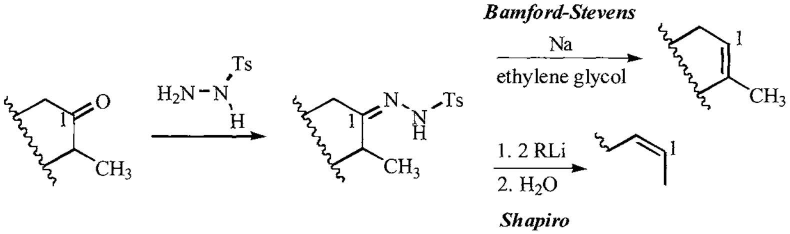
Proposed Mechanism:



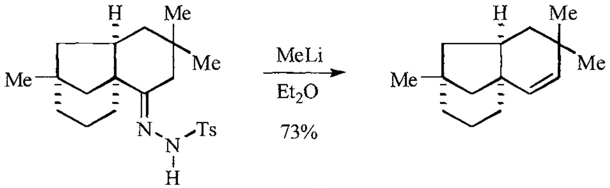
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1334; R. H. Shapiro, *Organic Reactions* **23**, 3; A. R. Chamberlin, S. H. Bloom, *Organic Reactions* **23**, 1

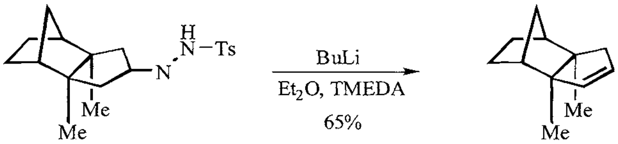
In the related ***Bamford-Stevens Reaction***, thermodynamic bases are used and the more substituted alkene is formed.



Examples:

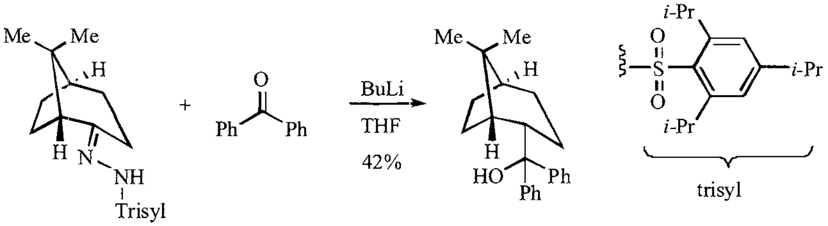


M. Ghosal, L. C. Pati, A. Roy, D. Mukherjee, *Tetrahedron* **2002**, 58, 6179

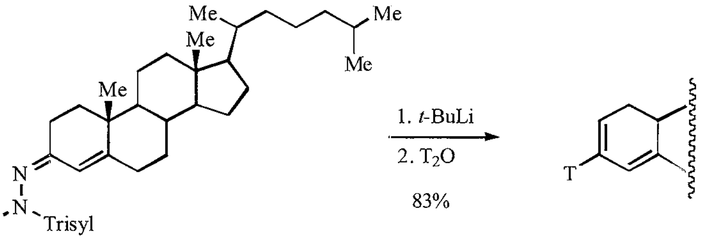


A. Srikrishna, S. Nagaraju, *Phytochemistry* **1995**, 40, 1699

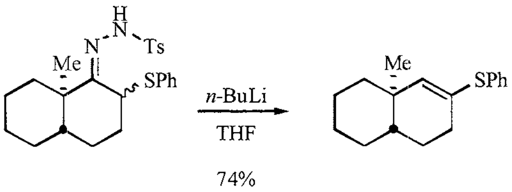
Trapping the anion formed in the reaction:



C. Liu, J.R. Sowa, *Tetrahedron Letters* **1996**, 37, 7241

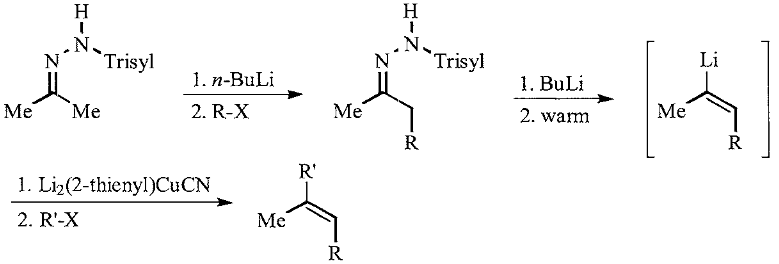


M. Saljoughian, H. Morimoto, C. Than, P. G. Williams, *Tetrahedron Letters* **1996**, 37, 2923

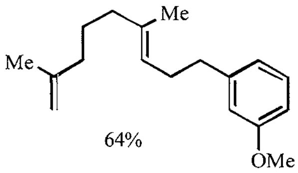


D. M. Coltart, S. J. Danishefsky, *Organic Letters* **2003**, 5, 1289

Interception of the anion intermediate in the ***Shapiro Reaction*** to form trisubstituted alkenes:



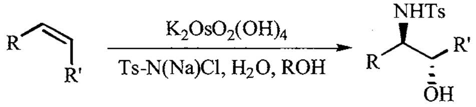
By this method:



E. J. Corey, J. Lee, B. E. Roberts, *Tetrahedron Letters* **1997**, 38, 8915

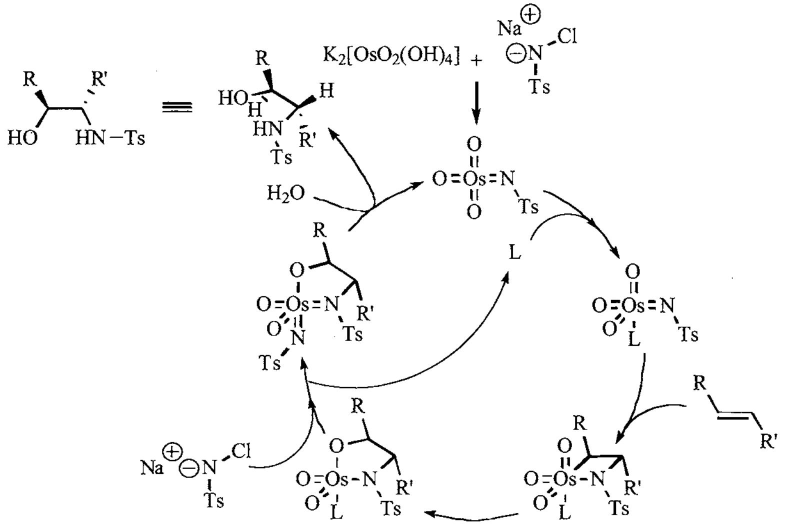
Sharpless (Catalytic Asymmetric) Aminohydroxylation

The Reaction:



Proposed Mechanism:

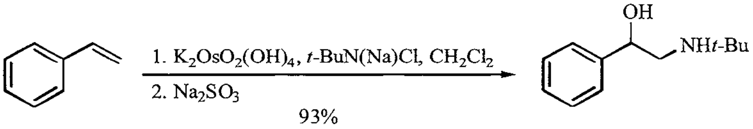
A simplified view. If L is chiral, the reaction can be rendered asymmetric:

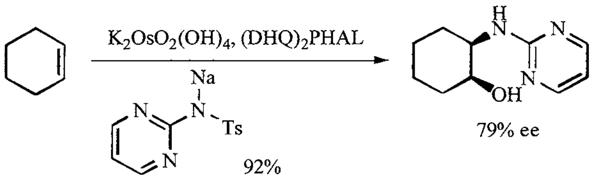


Notes:

For recent Reviews, see: K. Muñiz, *Chemical Society Reviews* **2004**, 33, 166; J. A. Bodkin, M. D. McLeod, *Journal of the Chemical Society, Perkin Transactions I*, **2002**, 2733

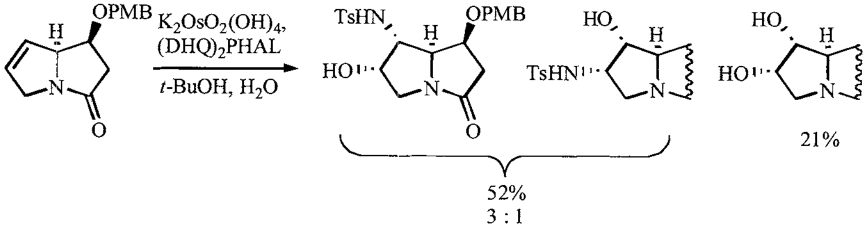
Examples:



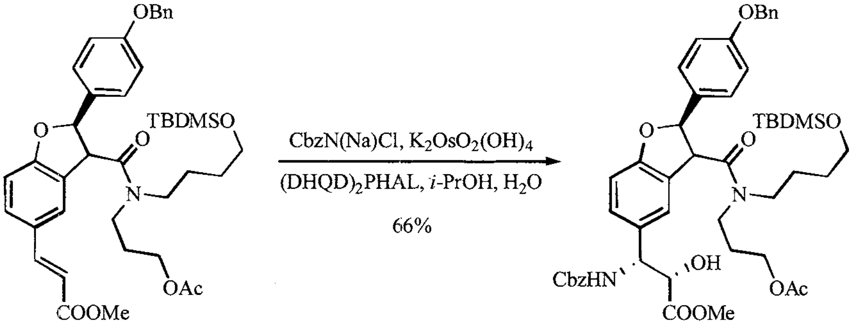


(DHQ)$_2$PHAL: See ***Sharpless Dihydroxylation***

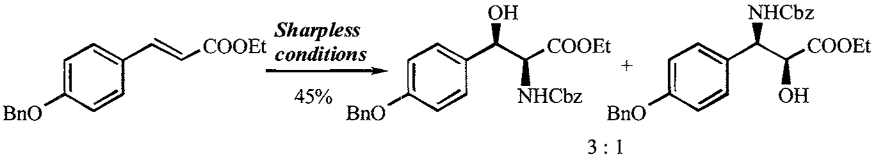
Reported in K. Muñiz, *Chemical Society Reviews* **2004**, 33, 166



P. R. Blakemore, S.-K. Kim, V. K. Schulze, J. D. White, A. F. T. Yokochi, *Journal of the Chemical Society, Perkin Transactions I*, **2001**, 1831



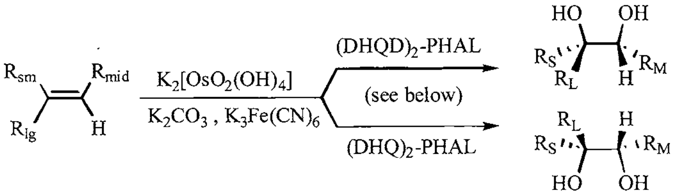
W. Kurosawa, T. Kan, T. Fukuyama, *Journal of the American Chemical Society* **2003**, 125, 8112



L. Dong, M. J. Miller, *Journal of Organic Chemistry* **2002**, 67, 4759

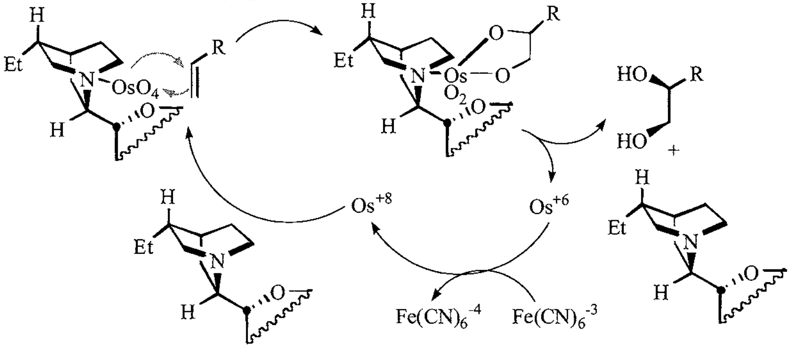
Sharpless (Asymmetric) Dihydroxylation

The Reaction:



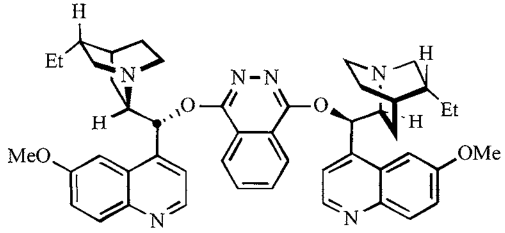
Proposed Mechanism:

The osmium is incorporated into the optically-active AD mix, where it undergoes hydroxylation in much the same way as proposed for simple hydroxylation. See Reagent: ***Osmium tetroxide***.

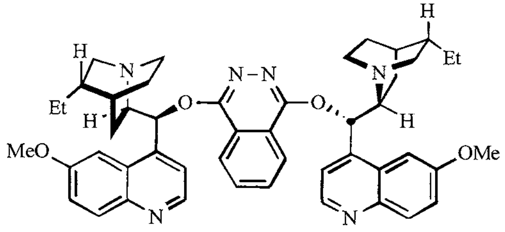


Notes:

Commercially available is AD [Asymmetric Dihydroxylation] mix (α) or (β):
α–mix contains
$(DHQ)_2$-PHAL = 1,4-bis(9-O-dihydroquinine)phtalazine

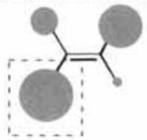


β–mix contains
$(DHQD)_2$-PHAL = 1,4-bis(9-O-dihydroquinidine)phtalazine

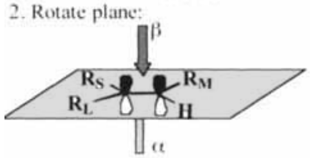


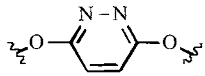
How to predict products:

1. Assign approximate "size" to groups, and place them on a plane according to:



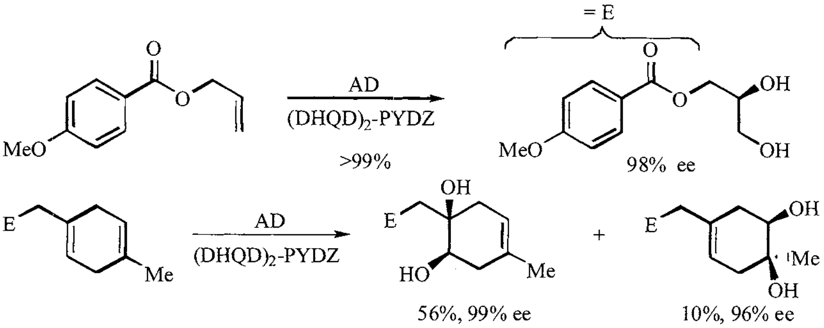
2. Rotate plane:





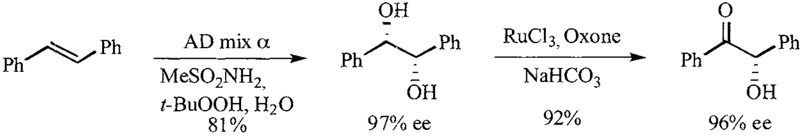
A pyridazine (PYDZ) core can also be incorporated into the catalyst.

Examples:

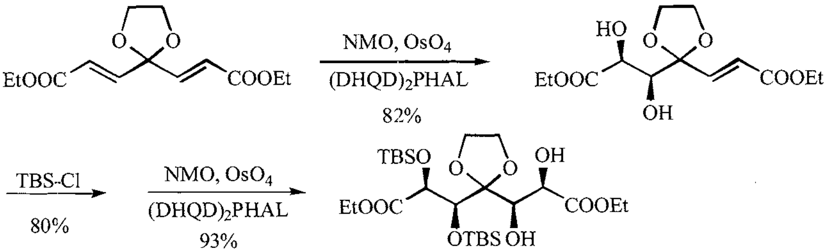


E. J. Corey, A. Guzman-Perez, M. C. Noe, *Journal of the American Chemical Society* **1995**, 117, 10805

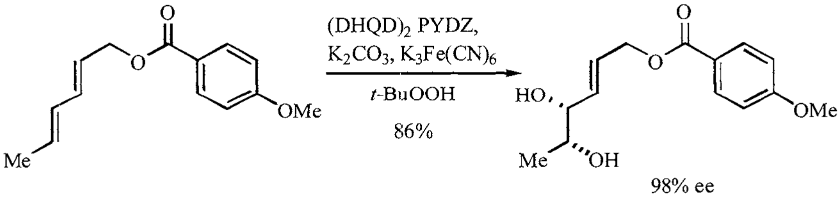
A keto-hydroxylation protocol:



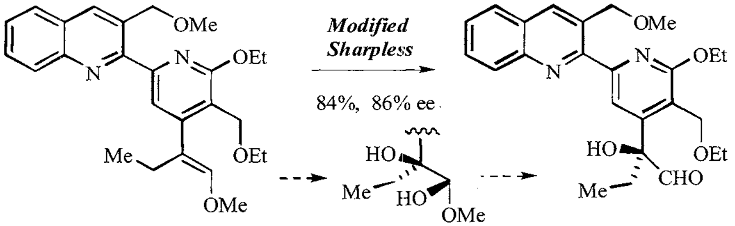
B. Plietker, *Organic Letters* **2004**, 6, 289



S. Lemaire-Audoire, P. Vogel, *Tetrahedron: Asymmetry* **1999**, 10, 1283



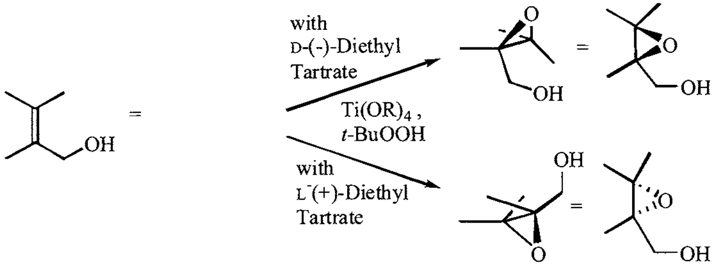
A. Guzman-Perez, E. J. Corey, *Tetrahedron Letters* **1997**, 38, 5941



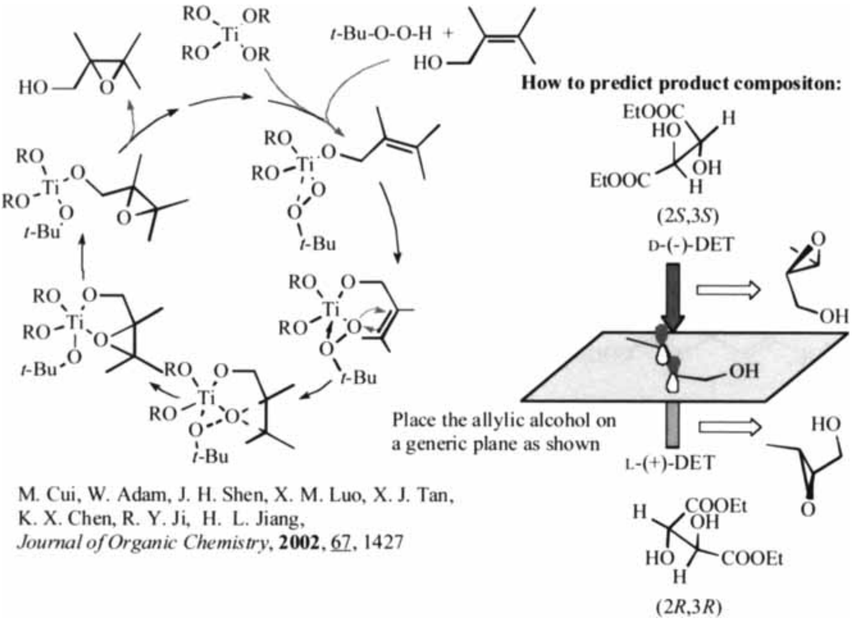
B. S. J. Blagg, D. L. Boger, *Tetrahedron* **2002**, 58, 6343

Sharpless Epoxidation

The Reaction:



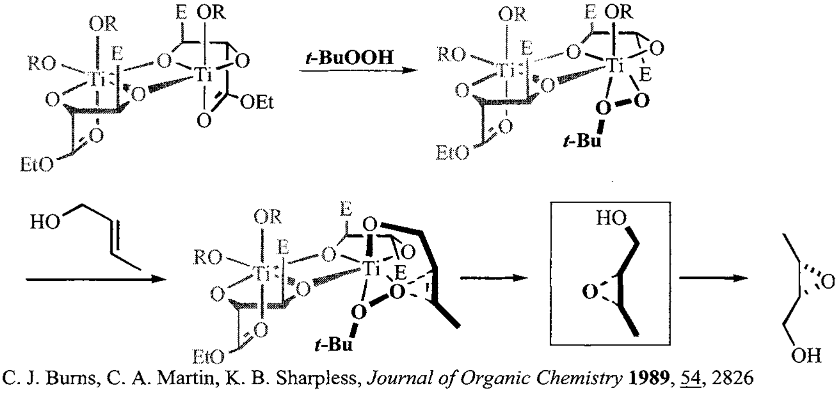
Proposed Mechanism:



M. Cui, W. Adam, J. H. Shen, X. M. Luo, X. J. Tan, K. X. Chen, R. Y. Ji, H. L. Jiang, *Journal of Organic Chemistry*, **2002**, 67, 1427

Notes:

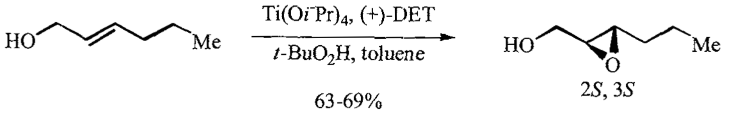
E= COOEt, R = *i*-Pr



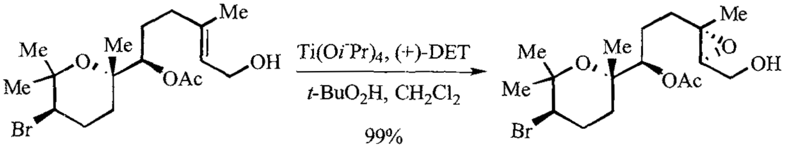
C. J. Burns, C. A. Martin, K. B. Sharpless, *Journal of Organic Chemistry* **1989**, 54, 2826

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1053; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 242-244

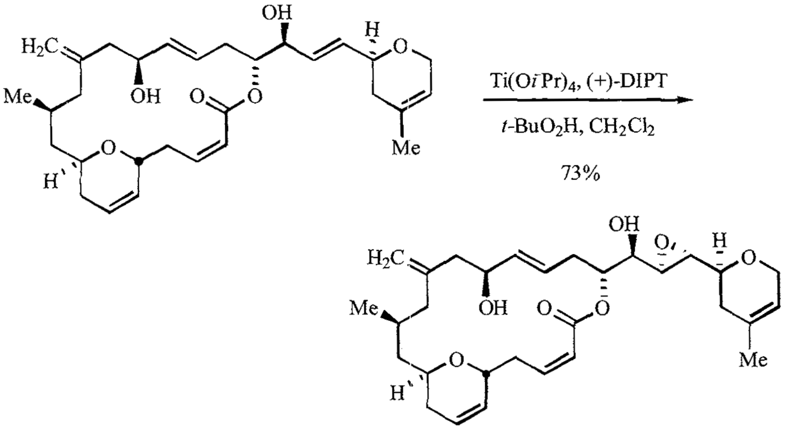
Examples:



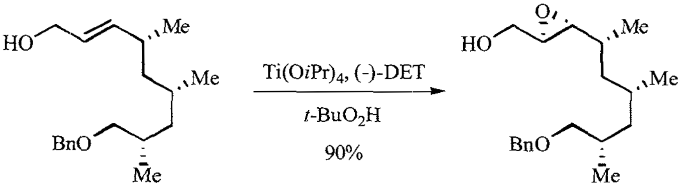
J. G. Hill, K. B. Sharpless, C. M. Exon, R. Regenye, *Organic Synthesis* CV7, 461



F. E. McDonald, X. Wei, *Organic Letters* **2002**, 4, 593



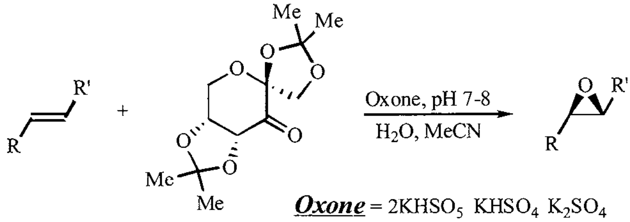
I. Patterson, C. D. Savi, M. Tudge, *Organic Letters* **2001**, 3, 3149



A. K. Ghosh, C. Liu, *Organic Letters* **2001**, 3, 635

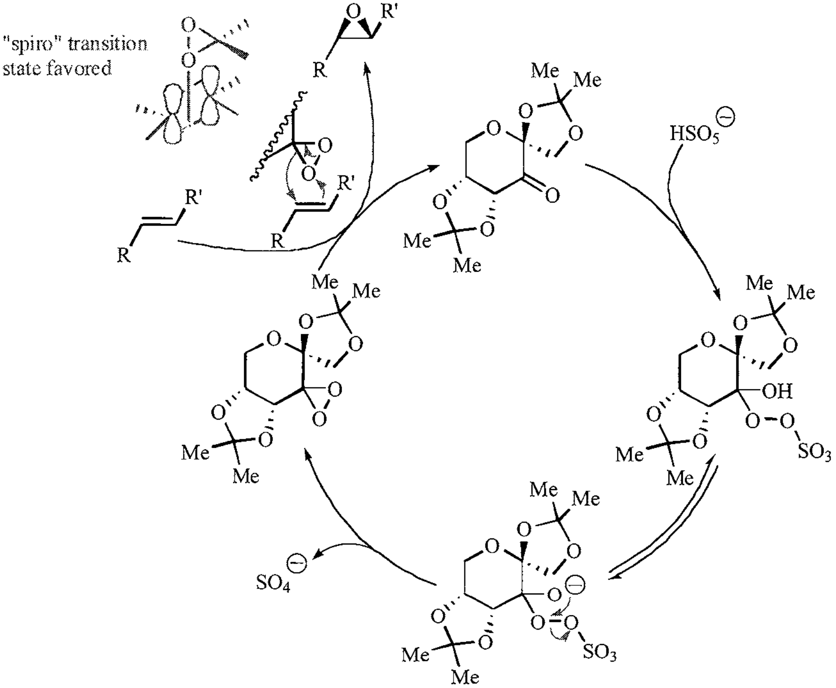
Shi (Asymmetric) Epoxidation

The Reaction:



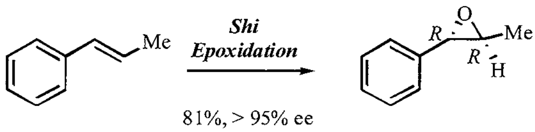
Oxone = $2KHSO_5\ KHSO_4\ K_2SO_4$

Proposed Mechanism:

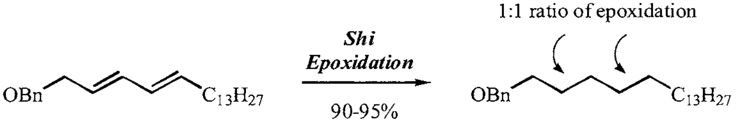


Y. Tu, Z.-X. Wang, Y. Shi, *Journal of the American Chemical Society* **1996**, 118, 9806; Y. Shi, *Accounts of Chemical Research* **2004**, 37, 488

Notes:

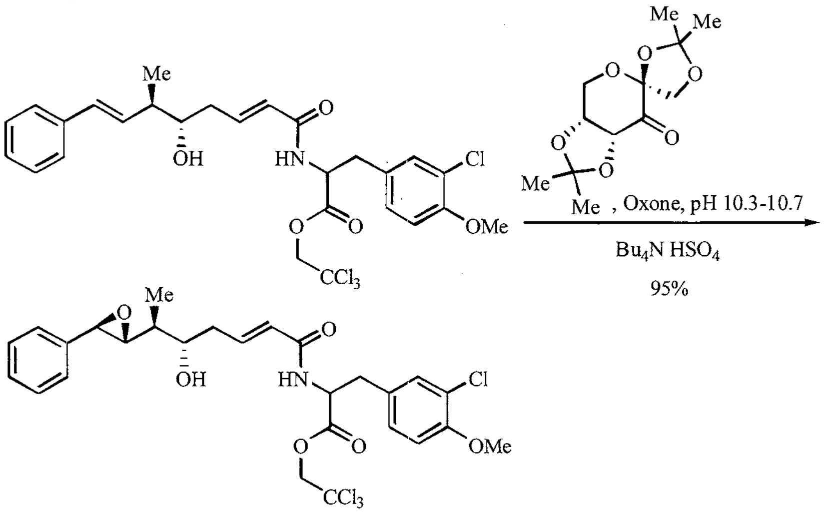


81%, > 95% ee

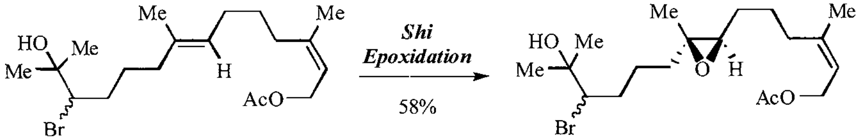


B. Olofsson, P. Somfai, *Journal of Organic Chemistry* **2003**, 68, 2514

Examples:

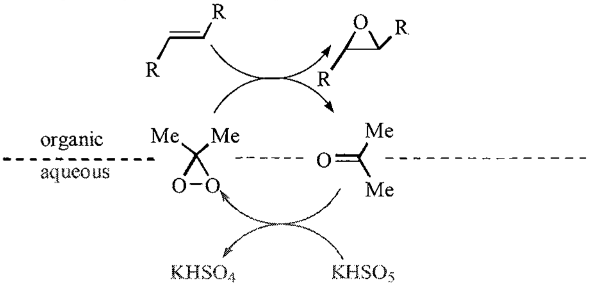


D. W. Hoard, E .D. Moher, M. J. Martinelli, B. H. Norman, *Organic Letters* **2002**, 4, 1813

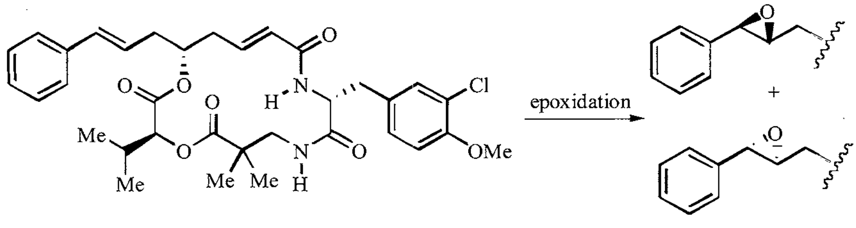


F. E. McDonald, X. Wei, *Organic Letters* **2002**, 4, 593

A two-phase system has been reported:



N. Hashimoto, A. Kanda, *Organic Process Research & Development* **2002**, 6, 405

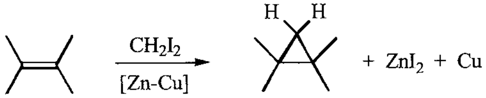


*m*CPBA ~2 : 1
Shi ~3.5 : 1

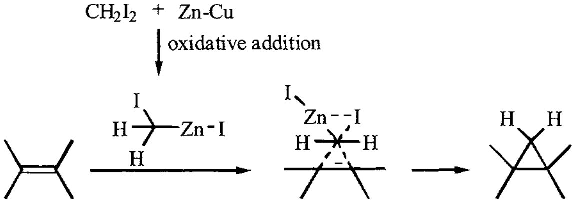
D. W. Hoard, E. D. Moher, M. J. Martinelli, B. H. Norman, *Organic Letters* **2002**, 4, 1813

Simmons-Smith Cyclopropanation

The Reaction:



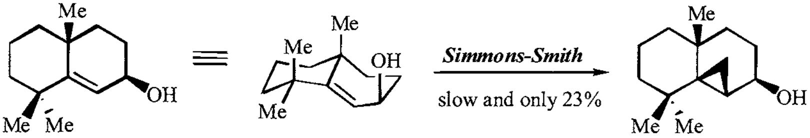
Proposed Mechanism:



Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1088; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 244-246; A. B. Charette, A. Beauchemin, *Organic Reactions* **58**, 1; H. E. Simmons, T. L. Cairns, S. A. Vladuchick, C. M. Hoiness, *Organic Reactions* **20**, 1

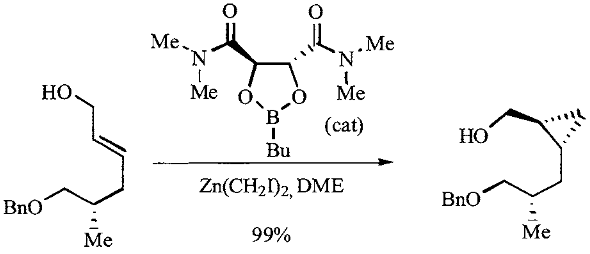
The cyclopropanation is sensitive to steric effects, adding from the less-hindered face. Having a neighboring hydroxyl group will generally accelerate the reaction, and will direct the cyclopropanation *syn* to the hydroxyl group; even into sterically congested alkenes.



W.G. Dauben, A.C. Ashcraft, *Journal of the American Chemical Society* **1963**, 85, 3673

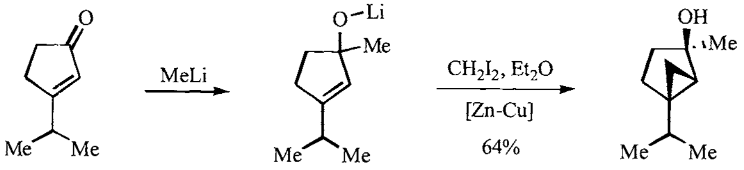
There are a number of modifications of this reaction; all providing the same product:

Furukawa's Reagent	$Et_2Zn + ICH_2I$ (1:1)
Sawada Reagent	$EtZnI + CH_2I_2$
Kobayashi Variation	$I_2 + Et_2Zn$

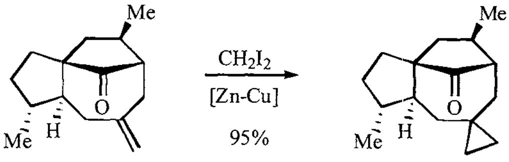


A. K. Ghosh, C. Liu, *Organic Letters* **2001**, 3, 635

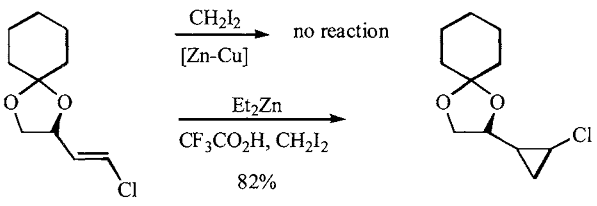
Examples:



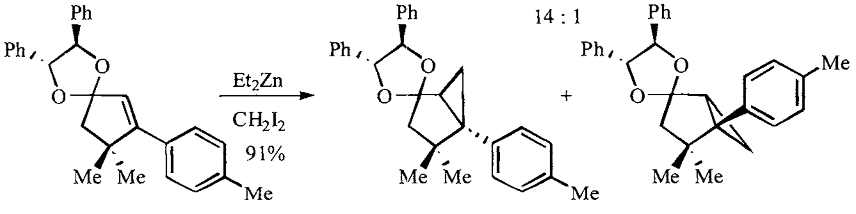
O. Cheng, T. Kreethadumrongdat, T. Cohen, *Organic Letters* **2001**, 3, 2121



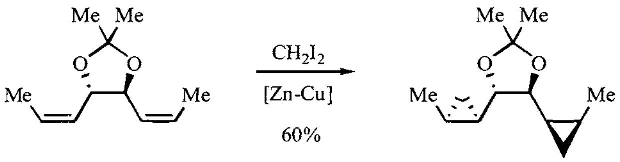
M. Harmata, P. Rashatasakhon, *Organic Letters* **2000**, 2, 2913



D. A. Evans, J. D. Burch, *Organic Letters* **2001**, 3, 503



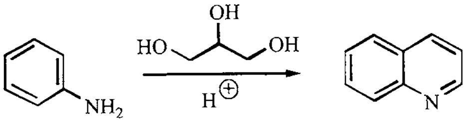
B. R. Aavula, Q. Cui, E. A. Mash, *Tetrahedron: Asymmetry* **2000**, 11, 4681



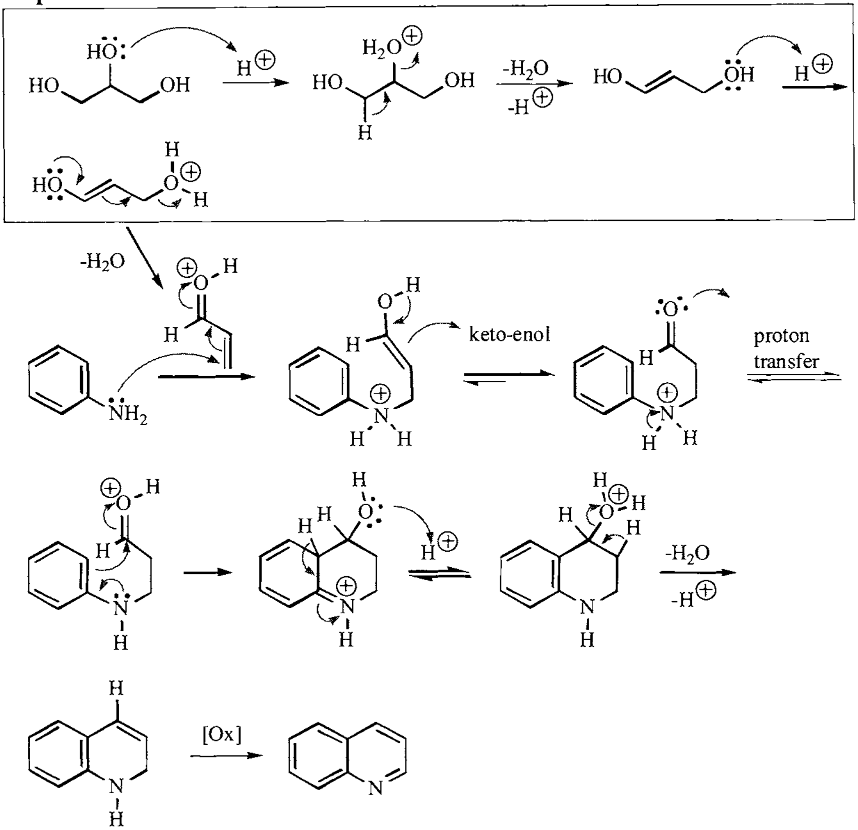
T. Onoda, R. Shirai, Y. Koiso, S. Iwasaki, *Tetrahedron Letters* **1996**, 37, 4397

Skraup Reaction

The Reaction:



Proposed Mechanism:



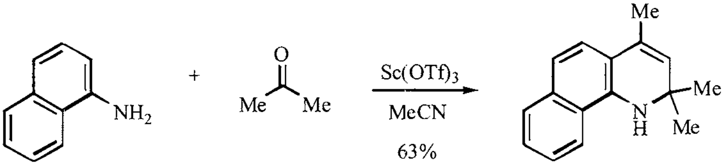
Notes:

T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 246-248; R. H. F. Manske, M. Kulka, *Organic Reactions* 7, 2

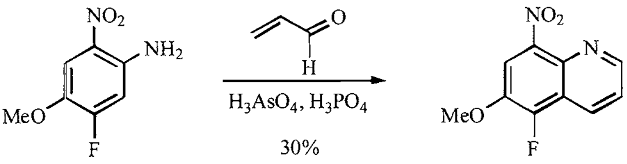
See also the very similar ***Deobner-von Miller reaction***.

Examples:

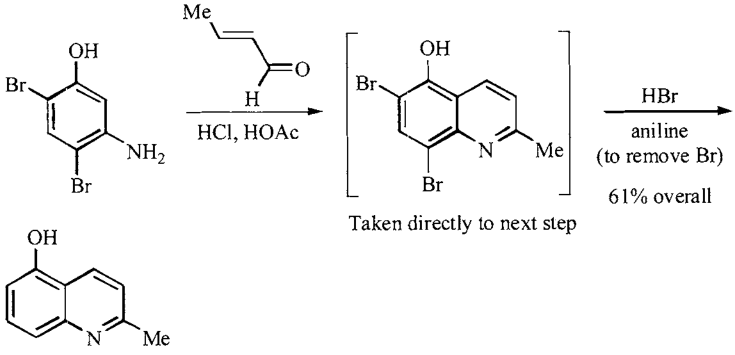
A "modified" ***Skraup***:



M.-E. Theoditou, L. A. Robinson, *Tetrahedron Letters* **2002**, 43, 3907



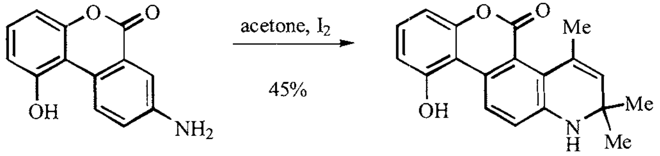
P. M. O'Neill, R. C. Storr, B. K. Park, *Tetrahedron* **1998**, 54, 4615



Taken directly to next step

H.-Y. Choi, D. Y. Choi, *Journal of the American Chemical Society* **2001**, 123, 9202

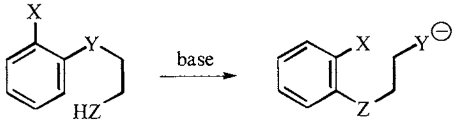
A "modified" ***Skraup***:



Y.-Y Ku, T. Grieme, P. Raje, P. Sharma, H. E. Morton, M. Rozema, S. A. King, *Journal of Organic Chemistry* **2003**, 68, 3238

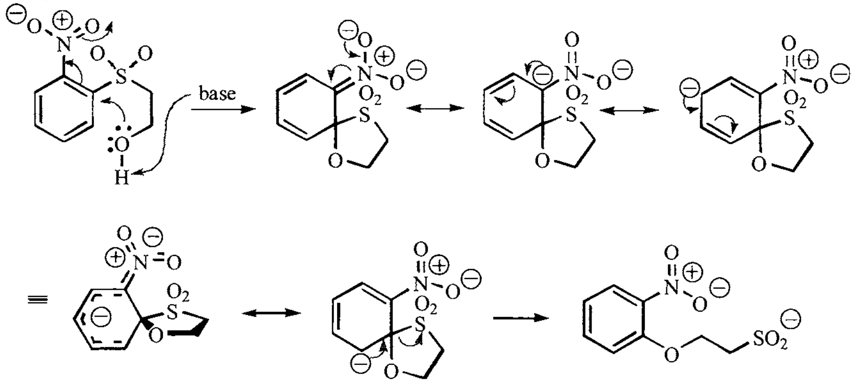
Smiles Rearrangement

The Reaction:



X = NO_2, SO_2R
Y = S, SO, SO_2, O, $COO^{\ominus}$
ZH = OH, NHR, SH, CH_2R, CONHR

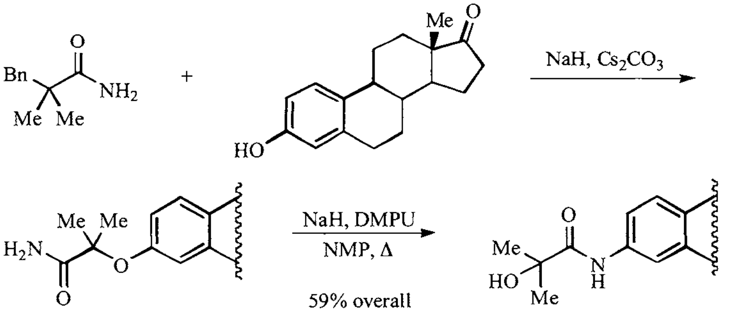
Proposed Mechanism:



Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 879; W. E. Truce, E. M. Kreider, W. W. Brand, *Organic Reactions* **18**, 2

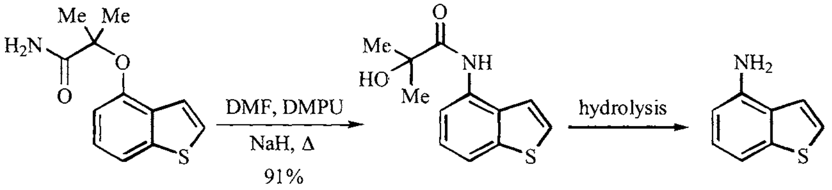
Examples:



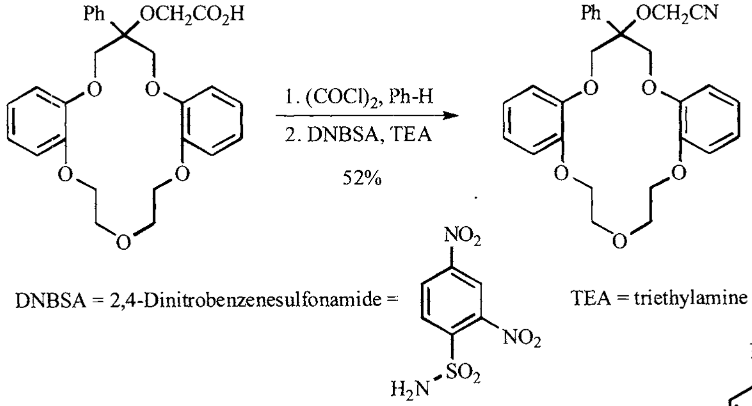
59% overall

DMPU =N,N'-Dimethylpropyleneura; NMP = *N*-methylpyrrolidine

J. J. Weidner, P. M. Weintraub, R. A. Schnettler, N. P. Peet, *Tetrahedron* **1997**, 53, 6303



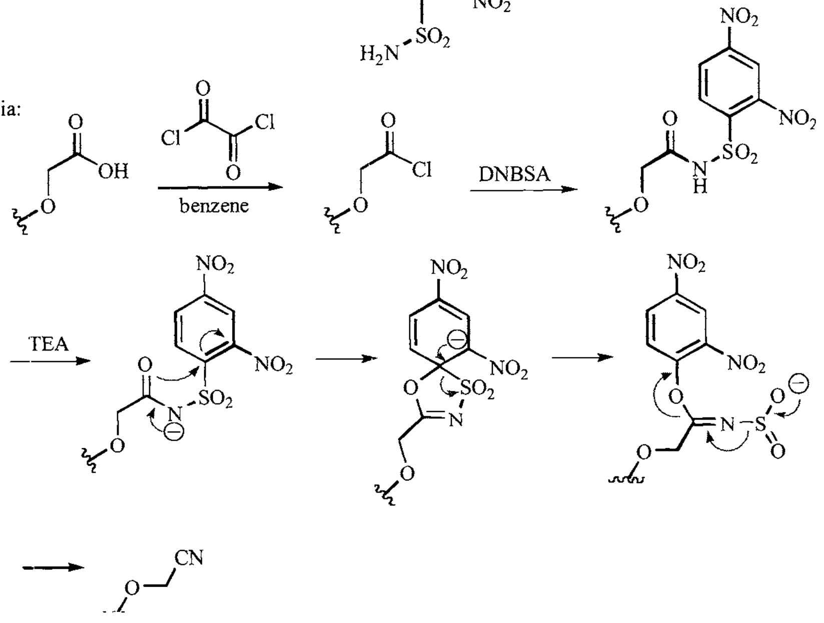
C. Bonini, M. Funicello, R. Scialpib, P. Spagnolob, *Tetrahedron* **2003**, 5, 7515



DNBSA = 2,4-Dinitrobenzenesulfonamide =

TEA = triethylamine = Et_3N

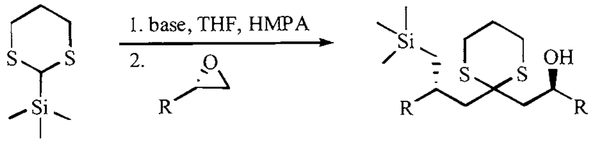
via:



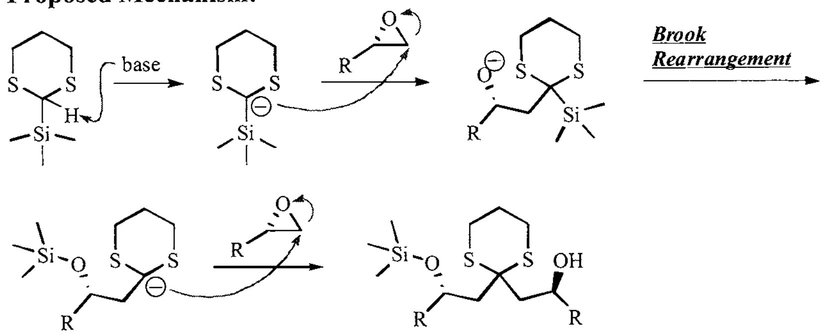
V. J. Huber, R. A. Bartsch, *Tetrahedron* **1998**, 54, 9281

Smith-Tietze Coupling

The Reaction:



Proposed Mechanism:

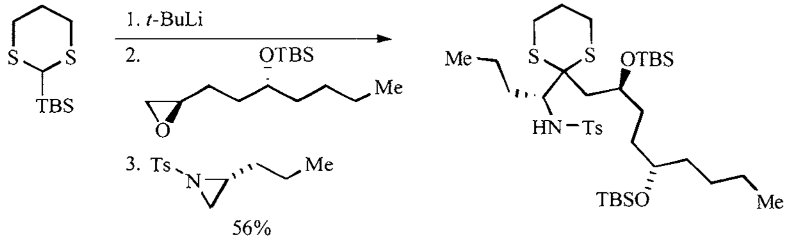


Notes:

a) A. B. Smith, III, A. M. Boldi, *Journal of the American Chemical Society* **1997**, 119, 6925; (b) A. B. Smith, III, L. Zhuang, C. S. Brook, Q. Lin, W. H. Moser, R. E. L. Trout, A. M. Boldi *Tetrahedron Letters* **1997**, 38, 8671; (c) L. F. Tietze, H. Geissler, J. A. Gewert, U. Jakobi, *Synlett* **1994**, 51

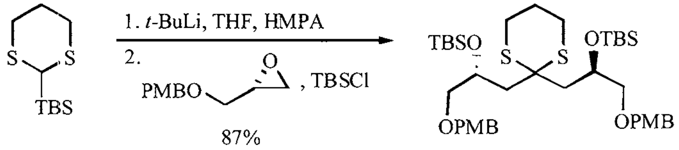
For the very first report of a *C*- to *O*-silyl rearrangement occurring after epoxide opening with 2-TMS-1,3-dithiane, see: P. F. Jones, M. F. Lappert, A. C. Szary, *Journal of the Chemical Society, Perkin Transactions 1* **1973**, 2272

For a recent variation of this theme:

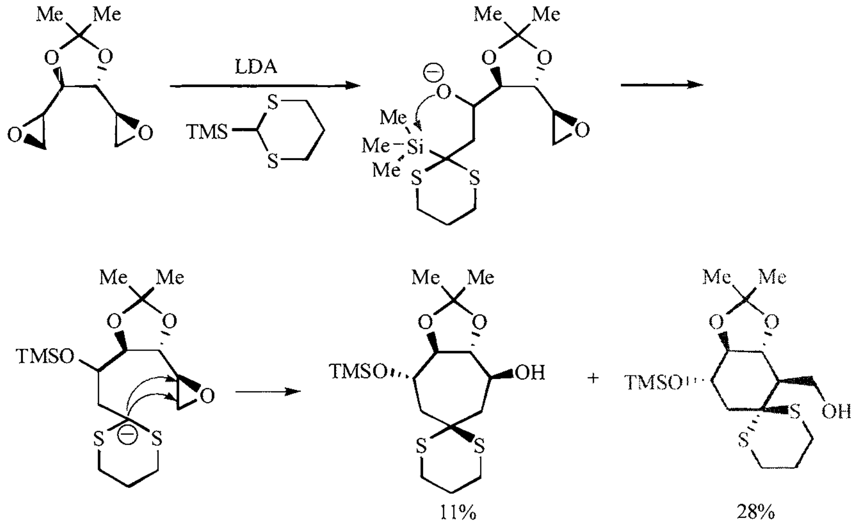


A. B. Smith, III, D.-S. Kim, *Organic Letters* **2004**, 6, 1493

Examples:



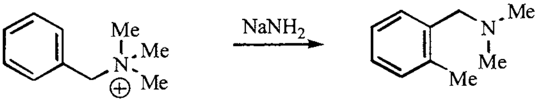
K.J. Hale, M. G. Hummersone, and G. S. Bhatia, *Organic Letters* **2000**, 2, 2189; K. J. Hale, M. G. Hummersone, J. Cai, S. Manaviazar, G. S. Bhatia, J. A. Lennon, M. Frigerio, V. M. Delisser, A. Chumnongsaksarp, N. Jogiya, A. Lemaitre, *Pure and Applied Chemistry* **2000**, 72, 1659



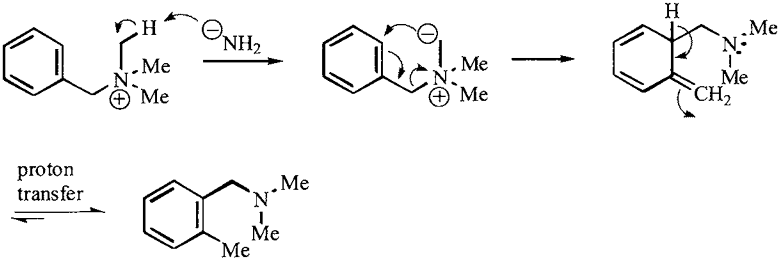
C. Gravier-Pelletier, W. Maton, T. Dintinger, C. Tellier, Y. Le Merrera, *Tetrahedron* **2003**, 59, 8705

Sommelet-Hauser Rearrangement

The Reaction:

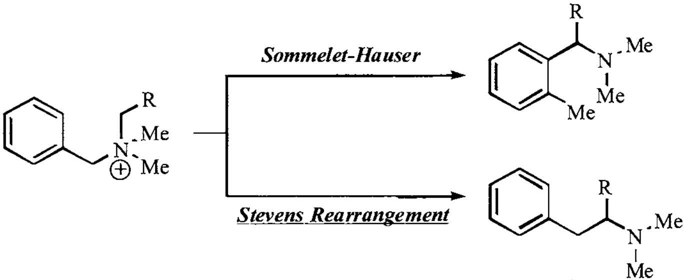


Proposed Mechanism:



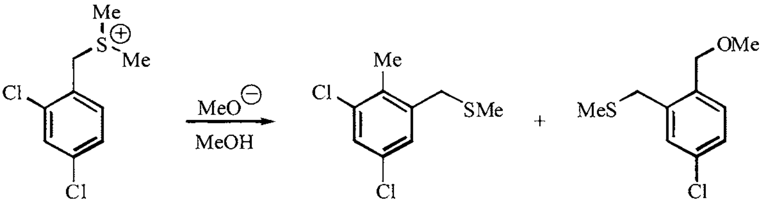
Notes:

There can be competition between ***Sommelet-Hauser*** and <u>***Stevens Rearrangement***</u> mechanisms:



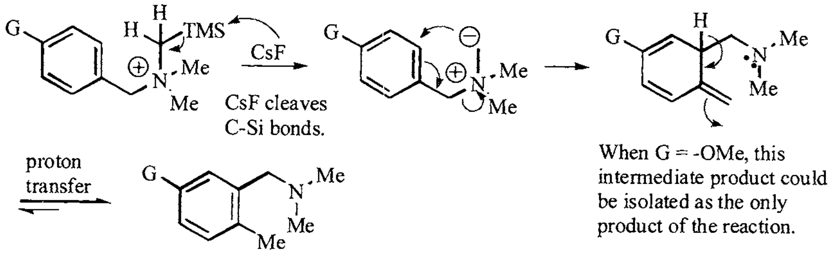
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp. 877, 1420, 1455; S. H. Pine, *Organic Reactions* **18**, 4

Examples:



58% 7%

T.-J. Lee, W. J. Holtz, *Tetrahedron Letters* **1983**, 24, 2071

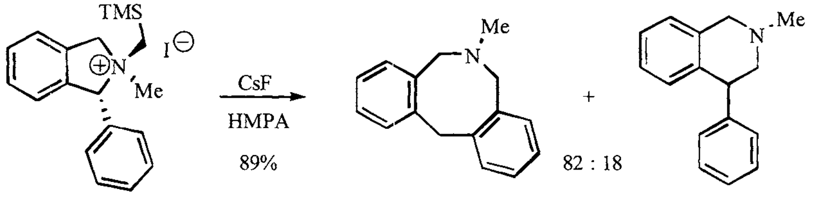


CsF cleaves C-Si bonds.

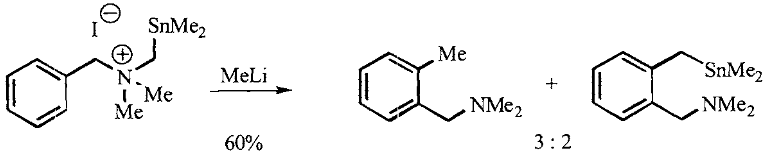
proton transfer

When G = -OMe, this intermediate product could be isolated as the only product of the reaction.

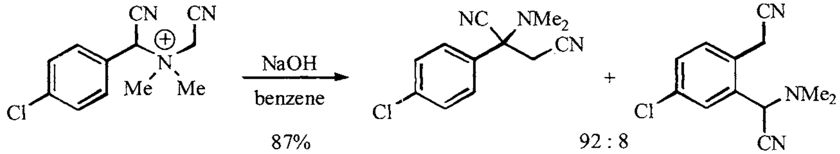
N. Shirai, Y. Watanabe, Y. Sato, *Journal of Organic Chemistry* **1990**, 55, 2767



A. Sakuragi, N. Shirai, Y. Sato, Y. Kurono, K. Hatano, *Journal of Organic Chemistry* **1994**, 59, 148



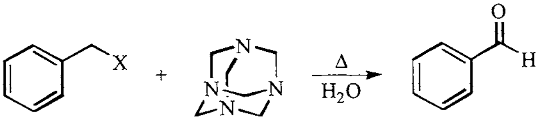
Y. Maeda, Y. Sato, *Journal of Organic Chemistry* **1966**, 61, 5188



A. Jonczyk, D. Lipiak, *Journal of Organic Chemistry* **1991**, 56, 6933

Sommelet Oxidation

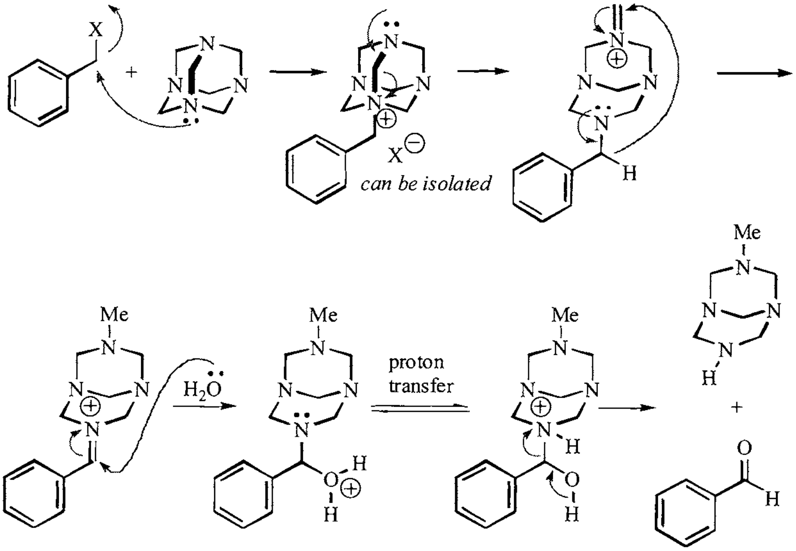
The Reaction:



HMTA
Hexamethylenetetramine

Proposed Mechanism:

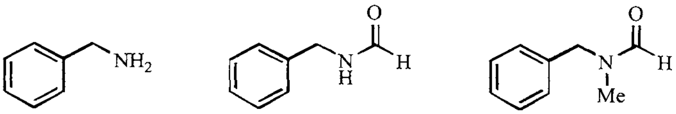
The mechanism is not clear, except for the first steps. Workup appears to play an important role in the product evolution: J. D. Hayler, S. L. B. Howie, R. G. Giles, A. Negus, P. W. Oxley, T. C. Walsgrove, M. Whiter, *Organic Process Research & Development* **1998**, 2, 3



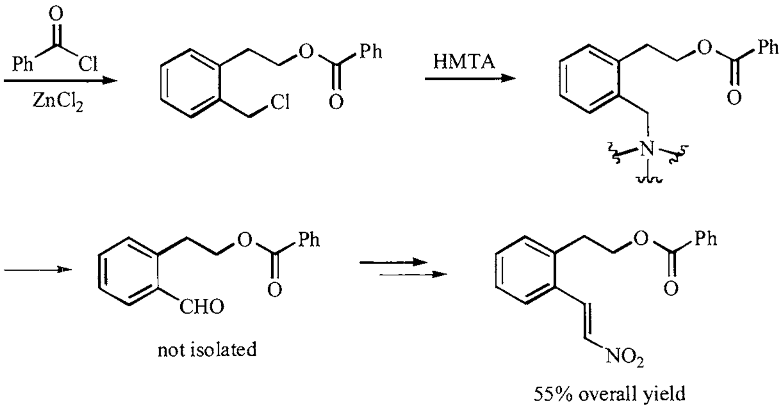
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p.1536; S. J. Angyal, *Organic Reactions* **8**, 4

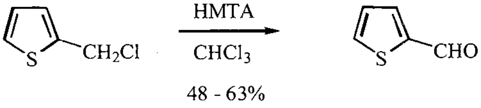
Other products from the reaction can be explained by different hydride transfers and cleavages:



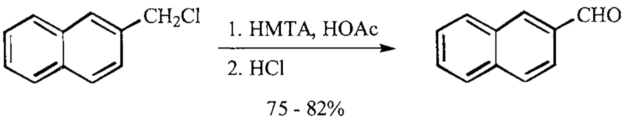
Examples:



J. D. Hayler, S. L. B. Howie, R. G. Giles, A. Negus, P. W. Oxley, T. C. Walsgrove, M. Whiter, *Organic Process Research & Development* **1998**, 2, 3



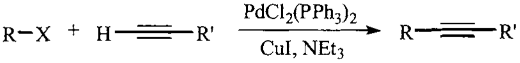
K. B. Wiberg, *Organic Syntheses*, CV 3, 811



S. J. Angyal, J. R. Tetaz, J. G. Wilson, *Organic Syntheses* CV 4, 690

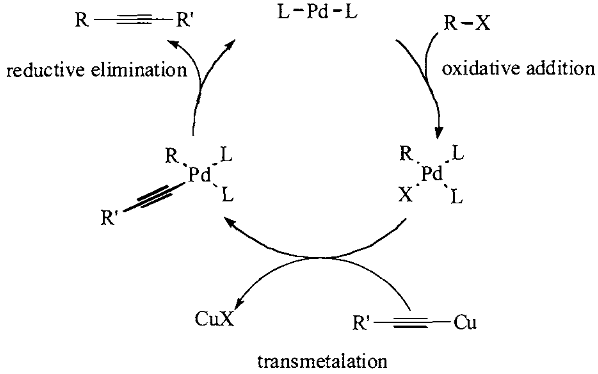
Sonogashira Coupling

The Reaction:



Proposed Mechanism:

R = aryl, vinyl, or pyridinyl
X = halogen

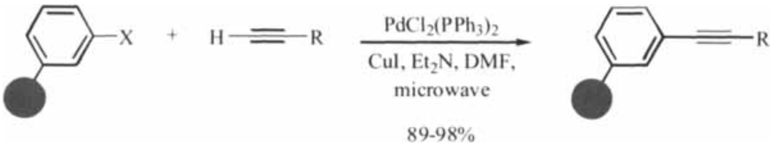


Notes:

For a recent summary of the reaction see:
R. R. Tykwinski, *Angewandte Chemie International Edition in English* **2003**, 42, 1566

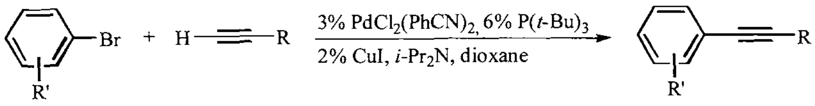
Examples:

A useful selection containing a number of functional groups is presented.

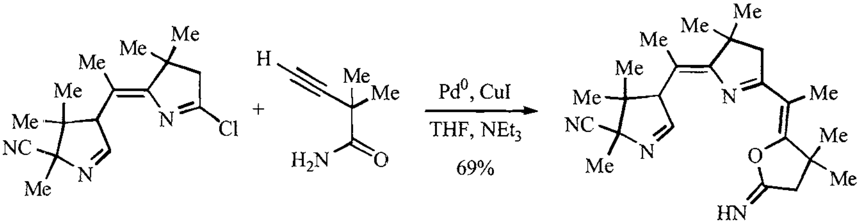


M. Erdelyi, A. Gogol, *Journal of Organic Chemistry* **2003**, 68, 6431

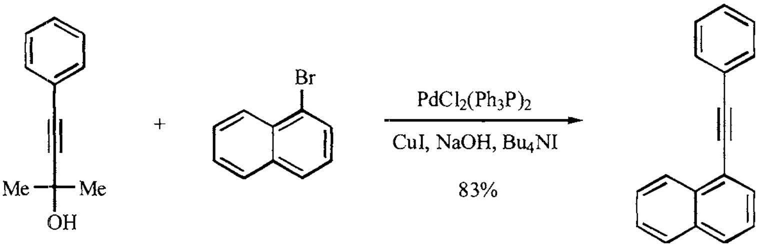
In a number of examples with high yields. P(t-Bu)$_3$ is useful for helping the reaction take place at room temperature.



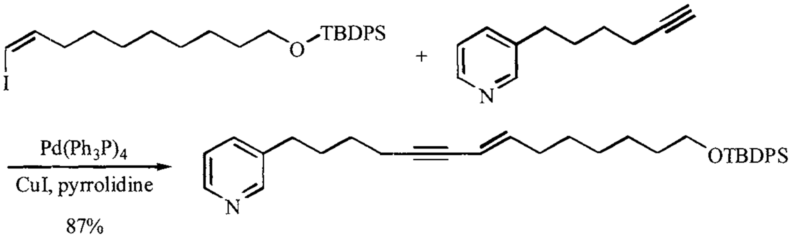
T. Hundertmark, A. F. Littke, S. L. Buchwald, G. C. Fu, *Organic Letters* **2000**, 2, 1729



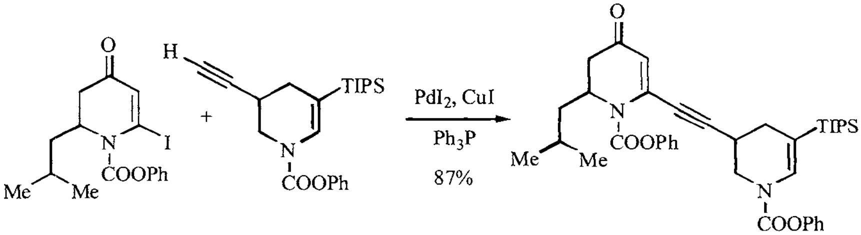
P. A. Jacobi, H. Lui, *Journal of Organic Chemistry* **1999**, 64, 1778



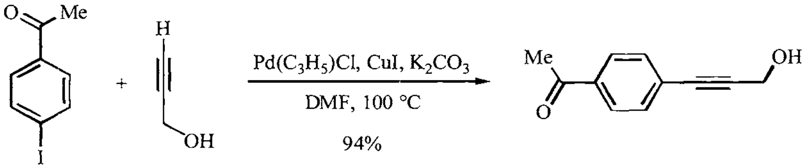
H.-F. Chow, C.-W. Wan, K.-H. Low, Y.-Y. Yeung, *Journal of Organic Chemistry* **2001**, 66, 1910



W. R. Goundry, J. E. Baldwin, V. Lee, *Tetrahedron* **2003**, 59, 1719



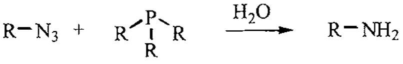
D. L. Comins, A. L. Williams, *Organic Letters* **2001**, 3, 3217



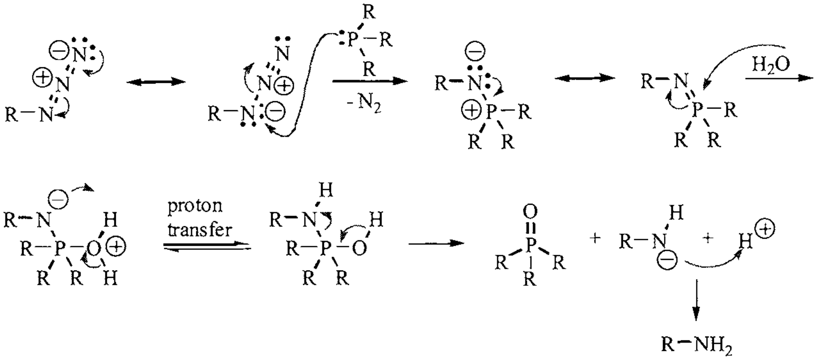
M. Feuerstein, H. Doucet, M. Santelli *Tetrahedron Letters* **2004**, 45, 1603

Staudinger Reaction

The Reaction:



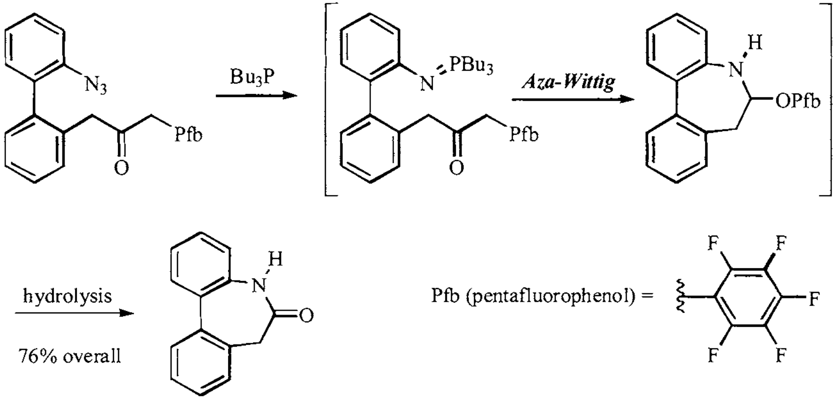
Proposed Mechanism:



Notes:

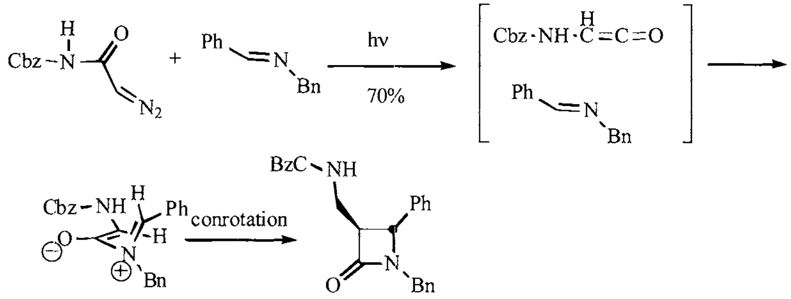
Other reducing agents can be used including $LiAlH_4$, Fe, and $Na_2S_2O_4$.

A unique tandem ***Staudinger-Wittig reaction*** finds application in lactam synthesis:

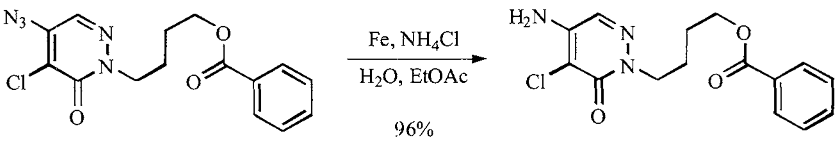


H. Fuwa, Y. Okamura, Y. Morohashi, T. Tomita, T. Iwatsubo, T. Kan, T. Fukuyam, H. Natsugari, *Tetrahedron Letters* **2004**, 45, 2320

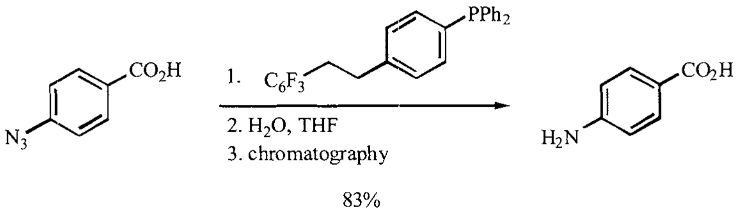
Examples:



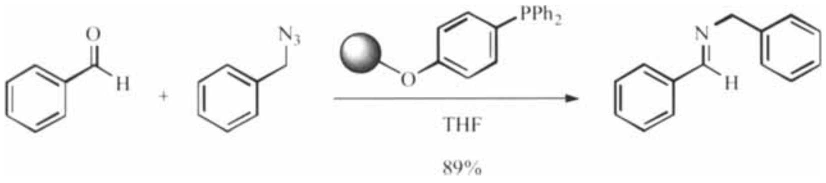
Y. Liang, L. Jiao, S. Zhang, J. Xu, *Journal of Organic Chemistry* **2005**, 70, 334



S.-D. Cho, W.-Y. Choi, S.-G. Lee, Y.-J. Yoon, S.-C. Shin, *Tetrahedron Letters* **1996**, 37, 7059



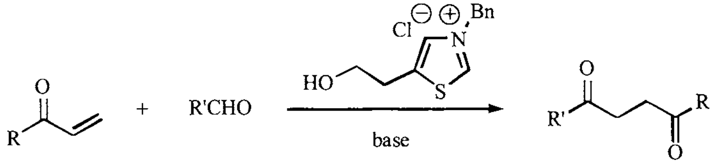
C. W. Lindsley, Z. Zhao, R. C. Newton, W. H. Leister, K. A. Strauss, *Tetrahedron Letters* **2002**, 43, 4467



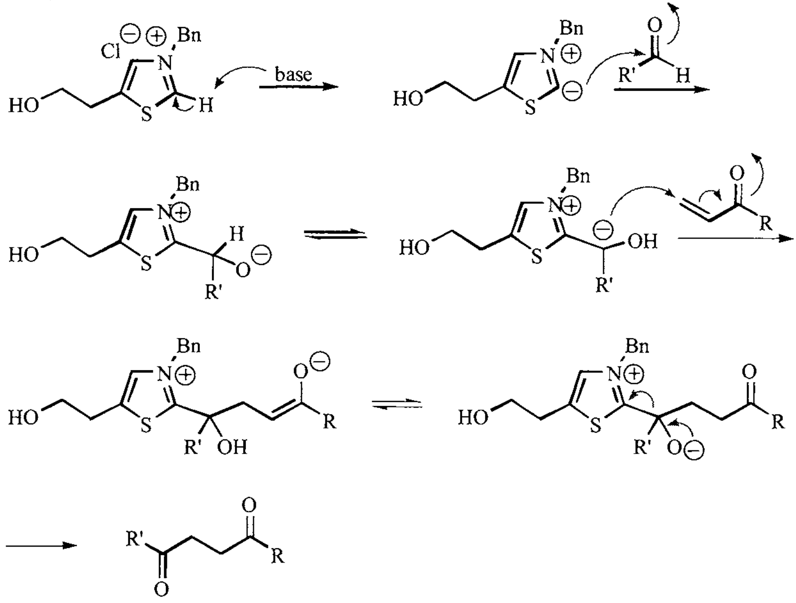
A. B. Charette, A. A. Boezio, M. K. Janes, *Organic Letters* **2000**, 2, 3777

Stetter Reaction (Stetter 1,4-Dicarbonyl Synthesis)

The Reaction:



Proposed Mechanism:

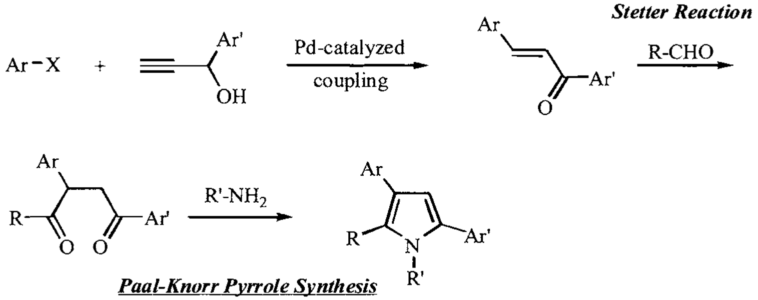


Notes:

H. Stetter, H. Kuhlmann, *Organic Reactions* **40**, 4

This reaction bears much mechanistic similarity to a vinylogous ***Benzoin Condensation***.

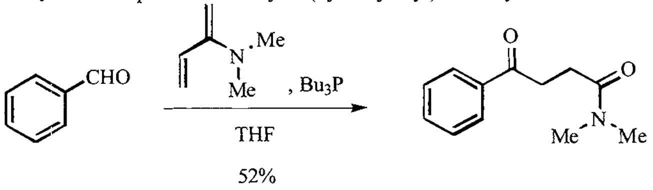
The 1,4-dicarbonyl compounds provide access to ***Paal-Knorr*** sequences. A one-pot, three-step reaction sequence has been reported:



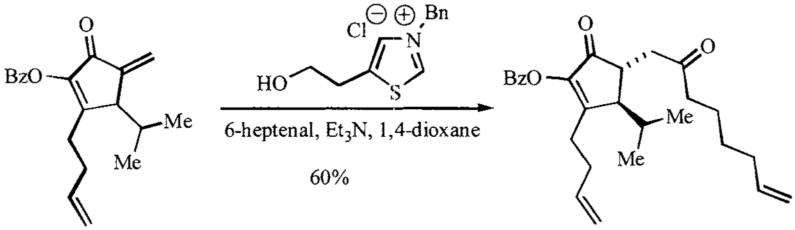
R. U. Braun, K. Zeitler, T. J. J. Muller *Organic Letters* **2001**, 3, 3297

Examples:

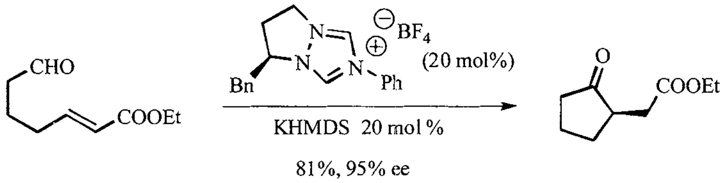
PBu_3 is used in place of 3-benzyl-5-(hydroxyethyl)-4-methylthiazolium chloride in this example.



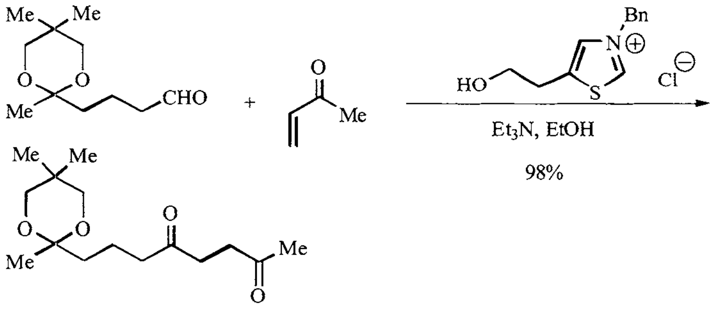
J. H. Gong, Y. J. Im, K. Y. Lee, J. N. Kim, *Tetrahedron Letters* **2002**, 43,1247



P. E. Harrington, M. A. Tius, *Organic Letters* **1999**, 1, 649



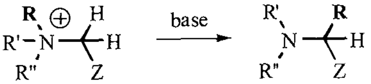
M. S. Kerr, J. R. de Alaniz, T. Rovis, *Journal of the American Chemical Society* **2002**, 124, 10298



M. P. Sant, W.B. Smith, *Journal of Organic Chemistry* **1993**, 58, 5479

Stevens Rearrangement

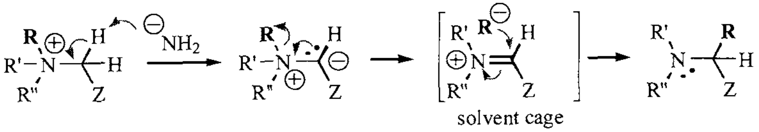
The Reaction:



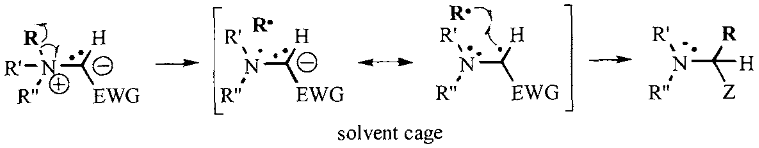
Z = ketone, ester, aryl
R (with approximate migratory aptitude) = propargyl > allyl > benzyl > alkyl (S. H. Pine, *Organic Reactions* **18**, 4)

Proposed Mechanism:

A much-used mechanism:



Evidence also favors:



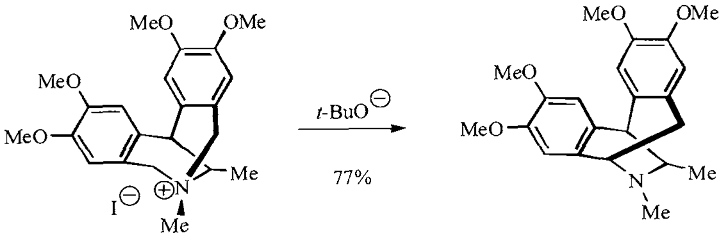
W. D. Ollis, M. Rey, I. O. Sutherland, *Journal of the Chemical Society, Perkin Transaction I* **1983**, 1009

Notes:

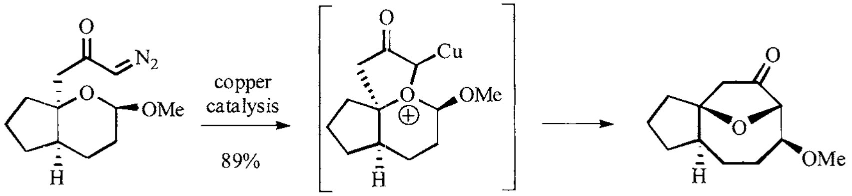
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1419; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 248-250; S. H. Pine, *Organic Reactions* **18**, 4

The reaction is often associated with migrations on sulfur:

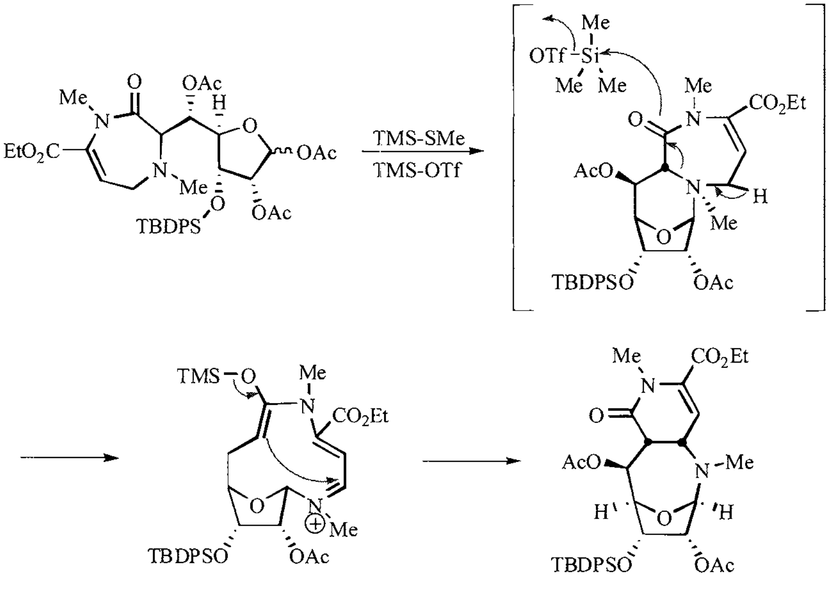
Examples:



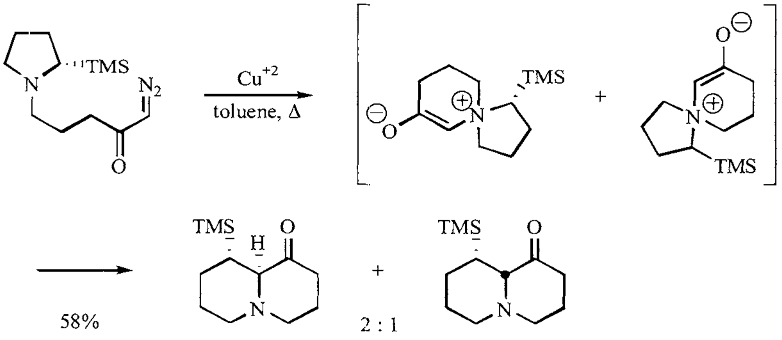
S. Hanessian, M. Mauduit, *Angewandte Chemie, International Edition in English* **2001**, 40, 3810



F. P. Marmsaeter, G. K. Murphy, F. G. West, *Journal of the American Chemical Society* **2003**, 125, 14724



S. Knapp, G. J. Morriello, G. A. Doss, *Tetrahedron Letters* **2002**, 43, 5797



J. A. Vanecko, J. F. G. West, *Organic Letters* **2002**, 4, 2813

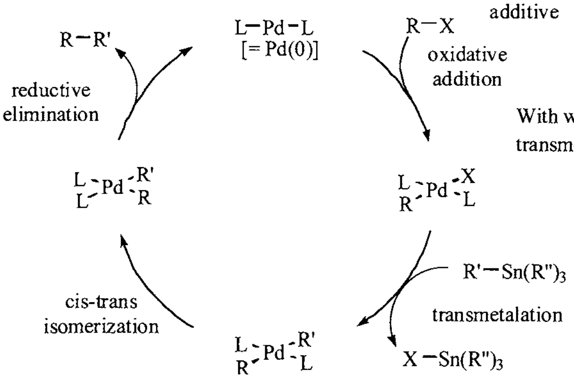
Stille Coupling

The Reaction:

$$R-X + R'-Sn(R'')_3 \xrightarrow[\text{THF or DMF}]{\text{Pd(0)}} R-R'$$

Proposed Mechanism:

Catalytic Cycle:



When X = Tf, LiCl is often needed as an additive

With weaker ligands, such as $AsPh_3$, transmetalation is enhanced.

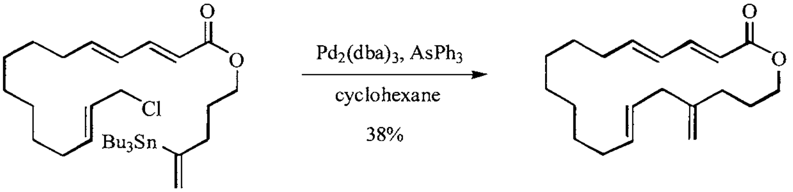
Notes:

In many respects this is a very general and useful reaction. It is compatible with a variety of functional groups and is run under relatively neutral conditions. The organotin intermediates are easy to prepare; however, toxicity of the tin reagents makes this method more of a problem than some of the other coupling protocols.

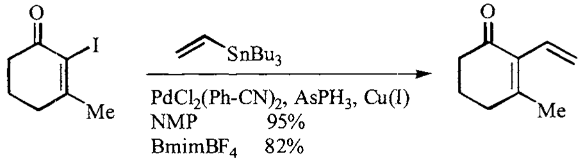
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 931; V. Farina, V. Krishnamurthy, W. J. Scott, *Organic Reactions* **50**.

See also the book based on the *Organic Reactions* article: V. Farina, V. Krishnamurthy, W. J. Scott, *The Stille Reaction*, John Wiley and Sons, Inc., New York, 1998,

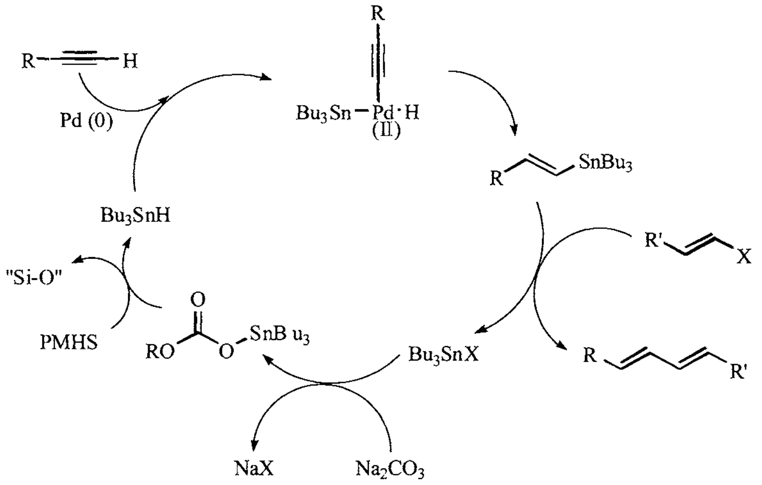
Examples:

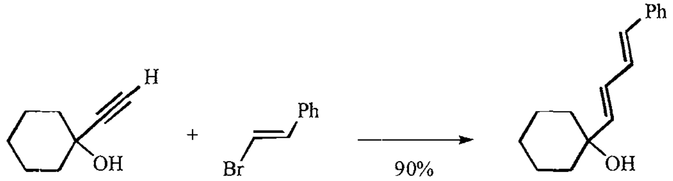


C. Boden, G. Pattenden, *Synlett* **1994**, 181 (AN 1995:6867)

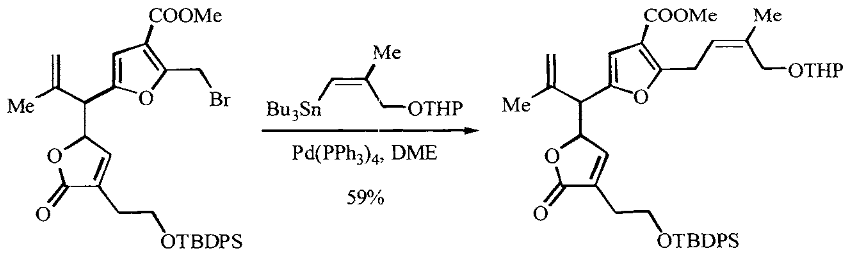


S. T. Handy, X. Zhang, *Organic Letters* **2001**, 3, 233





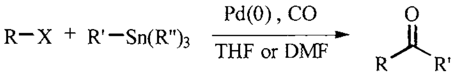
R. E. Maleczka, Jr., W. P. Gallagher, I. Terstiegee, *Journal of the American Chemical Society* **2000**, 122, 384



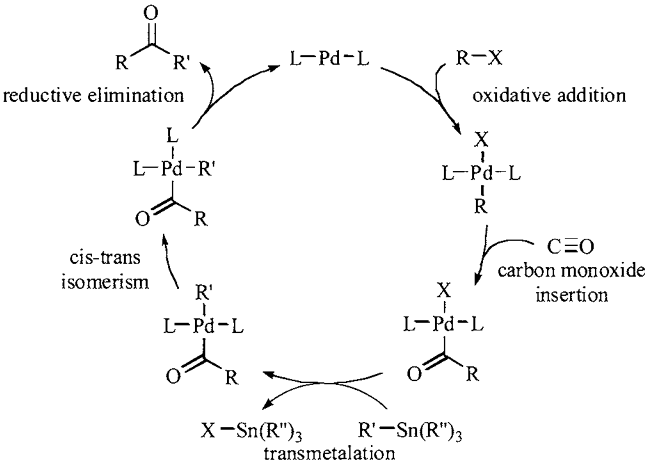
C. M. Rayner, P. C. Astles, L. A. Paquette, *Journal of Organic Chemistry* **1991**, 56, 1489

Stille Carbonylative Coupling

The Reaction:



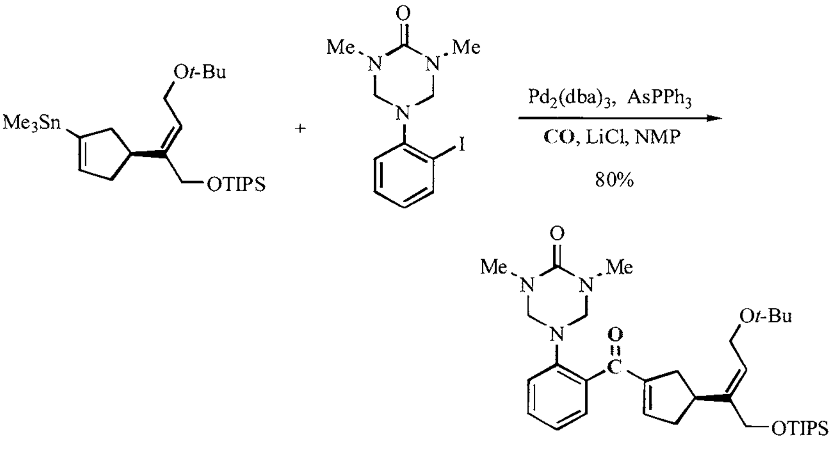
Proposed Mechanism:



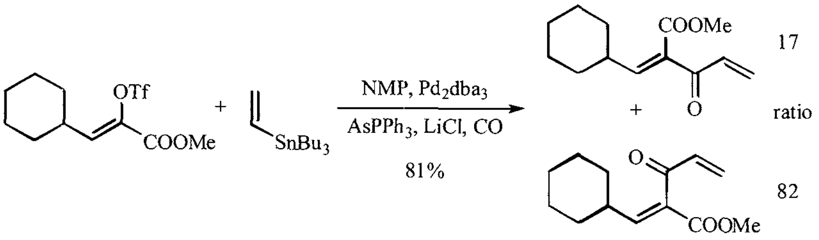
Notes:

See also the book based on the *Organic Reactions* article: V. Farina, V. Krishnamurthy, W. J. Scott, The *Stille Reaction*, John Wiley and Sons, Inc., New York, 1998,

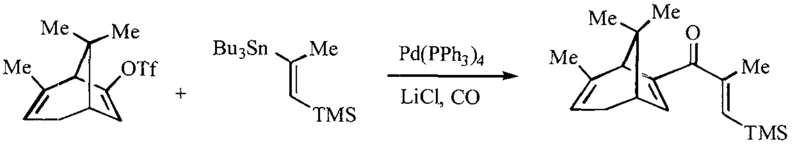
Examples:



S. D. Kight, L. E. Overman, G. Pairaudeau, *Journal of the American Chemical Society* **1993**, 115, 9293



S. Ceccarelli, U. Piarulli, C. Gennart, *Journal of Organic Chemistry* **2000**, 65, 6254

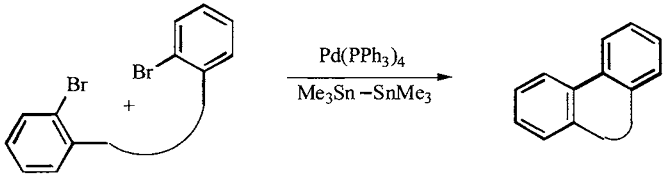


No added CuI	38%
added CuI	63%

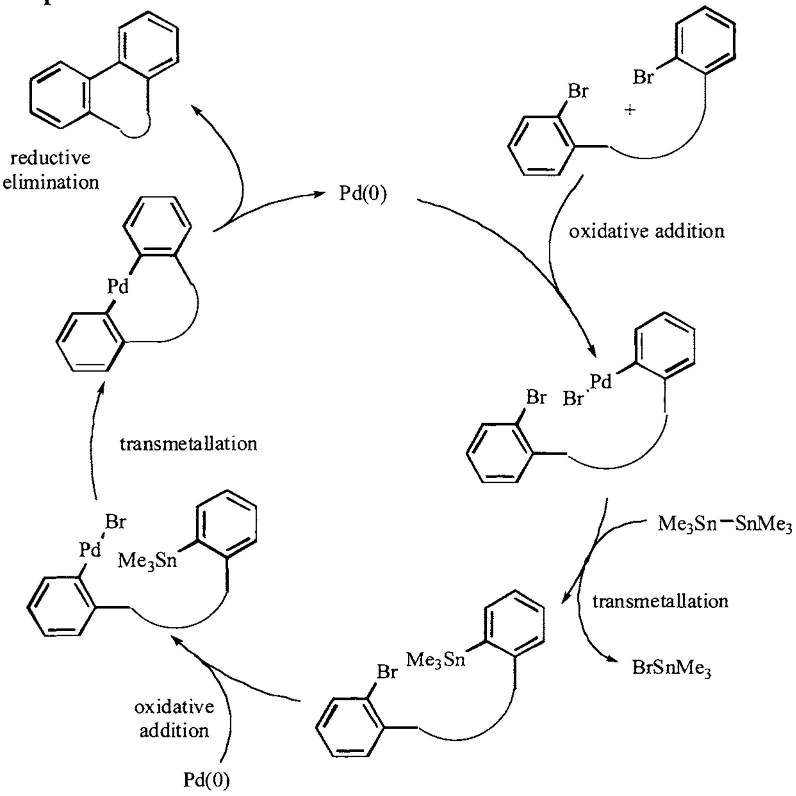
R. D. Mazzola, Jr., S. Giese, C. L. Benson, F. G. West, *Journal of Organic Chemistry* **2004**, 69, 220

Stille-Kelly Reaction

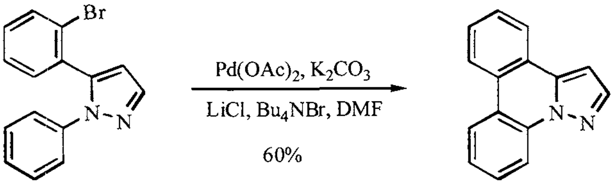
The Reaction:



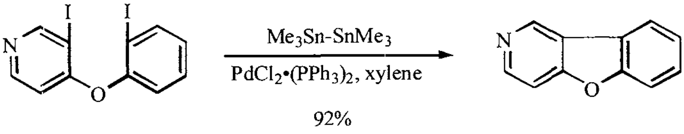
Proposed Mechanism:



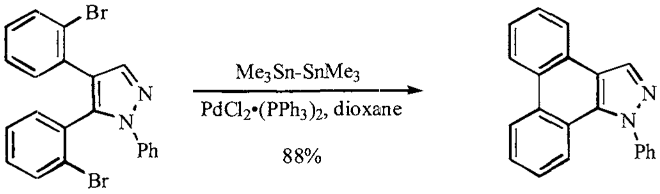
Examples:



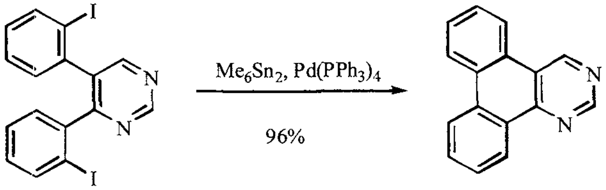
S. Hernandez, R. SanMartin, I. Tellitu, E. Dominguez, *Organic Letters* **2003**, 5, 1095



W. S. Yue, J. J. Li, *Organic Letters* **2002**, 4, 2201



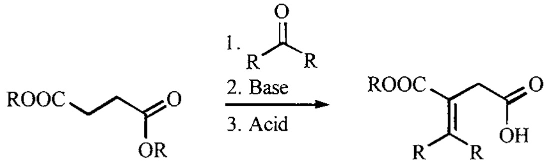
R.Olivera, R. SanMartin, E, Dominguez, *Journal of Organic Chemistry* **2000**, 65, 7010



R. Olivera, R. SanMartin, I. Tellitu, E. Domínguez, *Tetrahedron* **2002**, 58, 3021

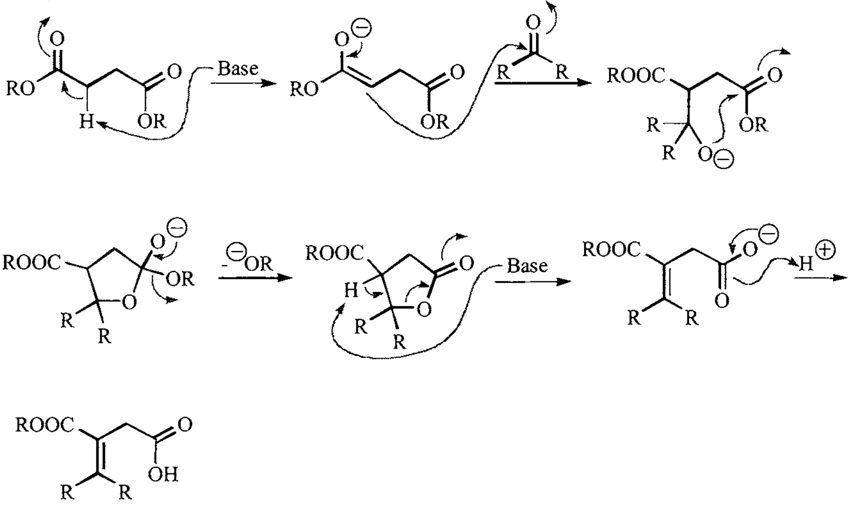
Stobbe Condensation

The Reaction:



a succinate derivative

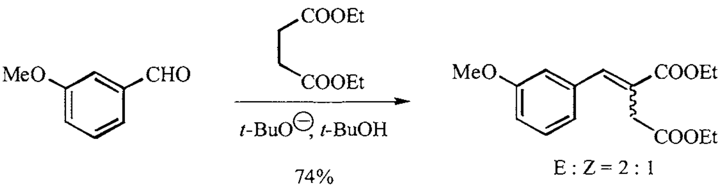
Proposed Mechanism:



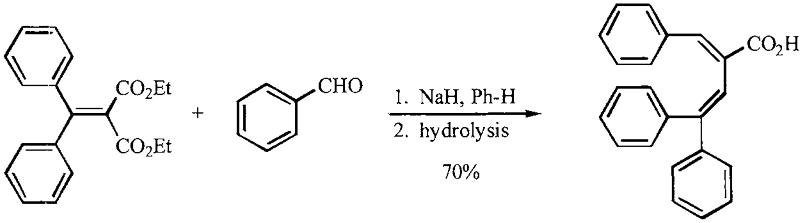
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1224; W. S. Johnson, G. H. Daub, *Organic Reactions* **6**, 1

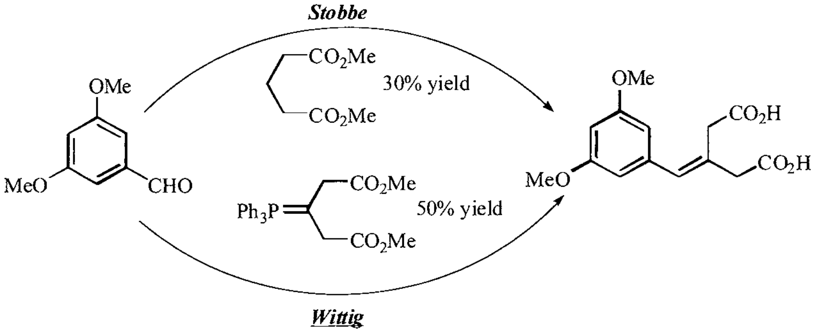
Examples:



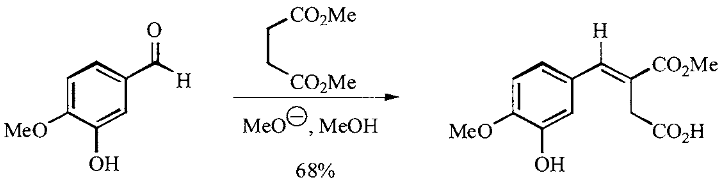
D. L. Boger, J. A. McKie, H. Cai, B. Cacciari, P. G. Baraldi, *Journal of Organic Chemistry* **1996**, 61, 1710



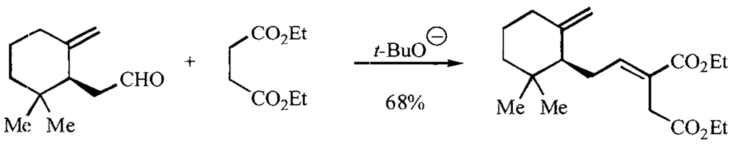
J. Liu, N. R. Brooks, *Organic Letters* **2002**, 4, 3521



A. Piettre, E. Chevenier, C. Massardier, Y. Gimbert, A. E. Green, *Organic Letters* **2002**, 4, 3139



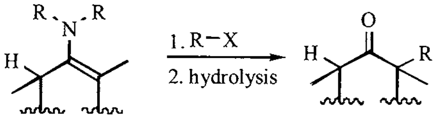
J. D. White, P. Hrnclar, F. Stappenbeck, *Journal of Organic Chemistry* **1999**, 64, 7871



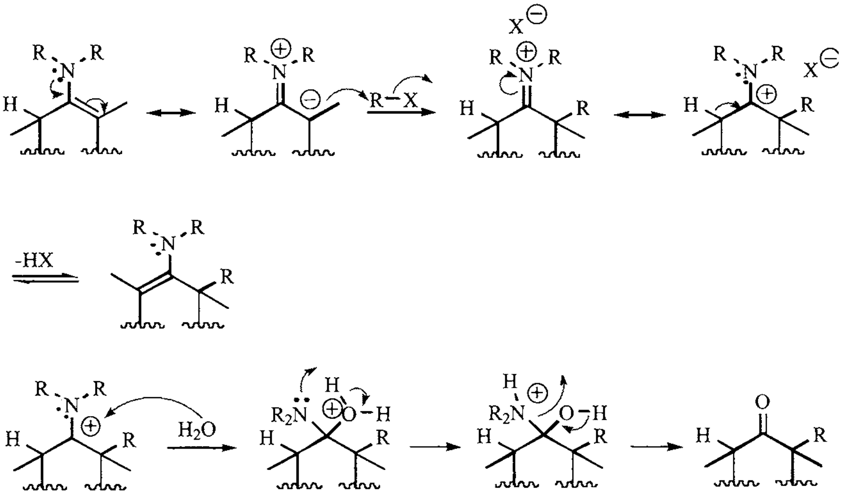
R. Baker, P. H. Briner, D. A. Evans, *Chemical Communications* **1978**, 410

Stork Enamine Synthesis

The Reaction:



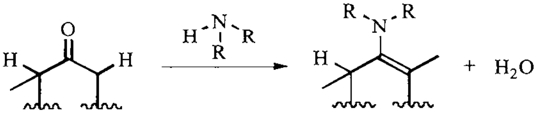
Proposed Mechanism:



Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp. 555, 787; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 250-253

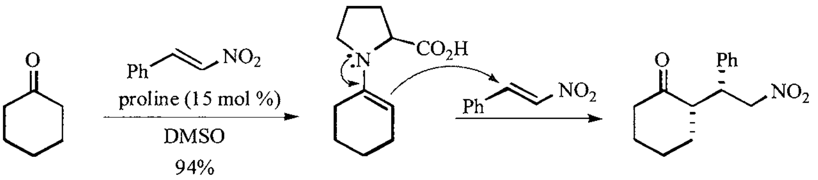
Starting material preparation:



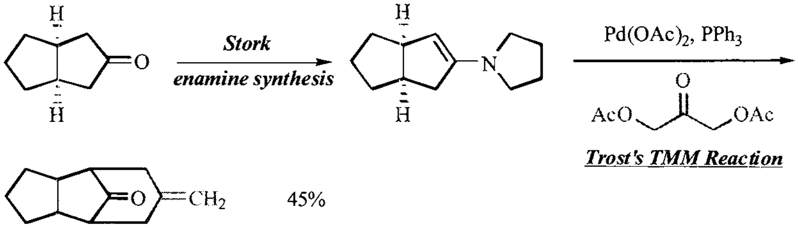
The amine used to make enamine is usually pyrrolidine, morpholine, piperidine or diethylamine.

Besides alkyl halides, the electrophile can be activated aryl halides, epoxides, anhydrides and ***Michael additions*** to activated alkenes.

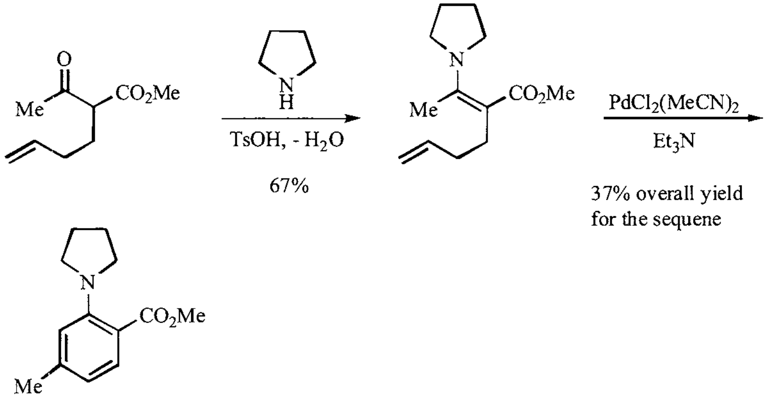
Examples:



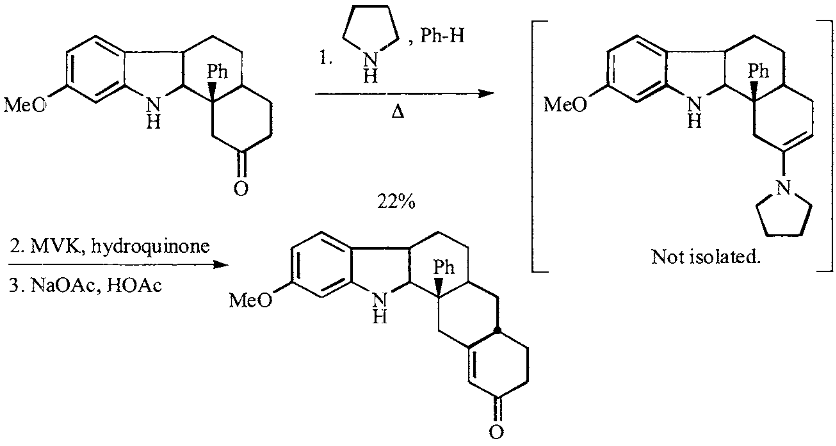
B. Kist, P. Pojarliev, H. J. Martin, *Organic Letters* **2001**, 3, 2423



F. Bouno, A. Tenaglia, *Journal of Organic Chemistry* **2000**, 65, 3869



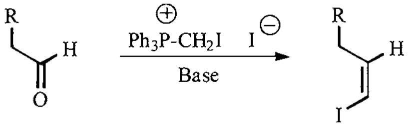
Method of: S. Hunig, E. Lücke, W. Brenninger, *Organic Syntheses*, CV 5, 808
in: T. Ishikawa, E. Vedo, R. Tani, S. Saito, *Journal of Organic Chemistry* **2001**, 66, 186



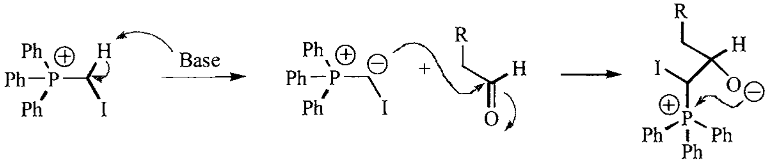
J. J. Li, B. K. Trivedi, J. R. Rubin, B. D. Roth, *Tetrahedron Letters* **1998**, 39, 6111

Stork-Wittig Olefination

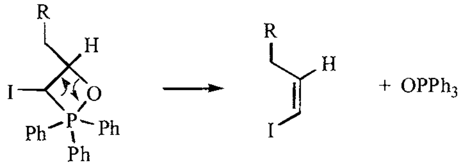
The Reaction:



Proposed Mechanism:



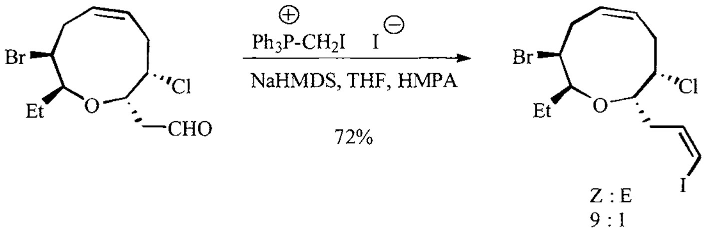
See: ***Wittig Reaction***



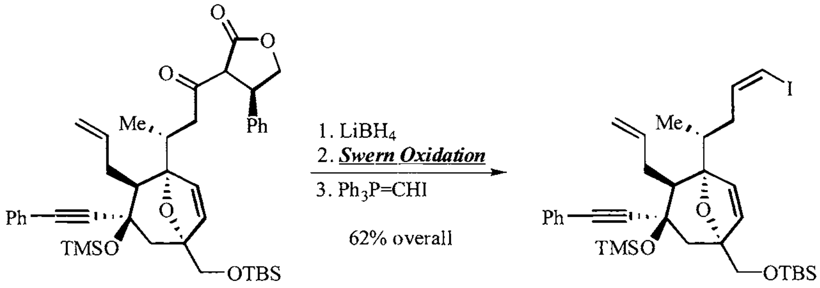
Notes:

The ***Takai Reaction*** provides the same transformation, but arrives at the *E*- configuration rather than the *Z*-.

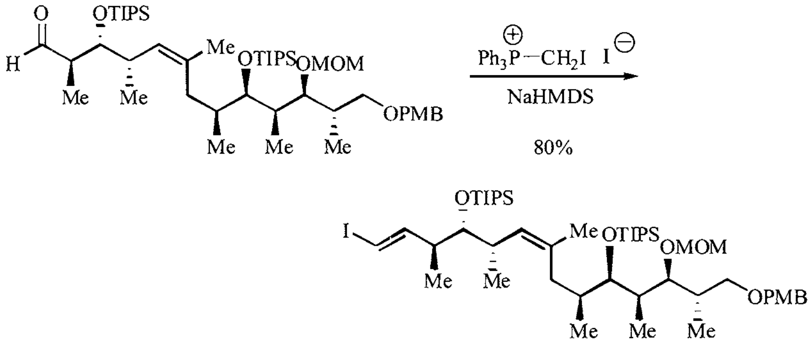
Examples:



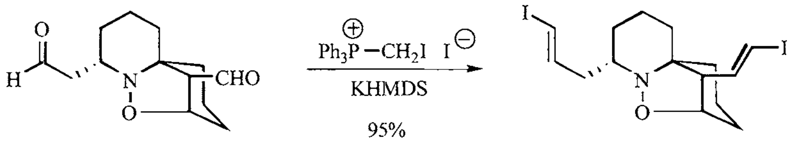
M. T. Crimmins, M. T. Powell, *Journal of the American Chemical Society* **2003**, 125, 7592



K. Lee, J. K. Cha, *Journal of the American Chemical Society* **2001**, 123, 559



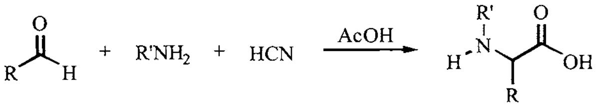
S. S. Harried, C. P. Lee, G. Yang, T. I. H. Lee, D. C. Myles, *Journal of Organic Chemistry* **2003**, 68, 6646



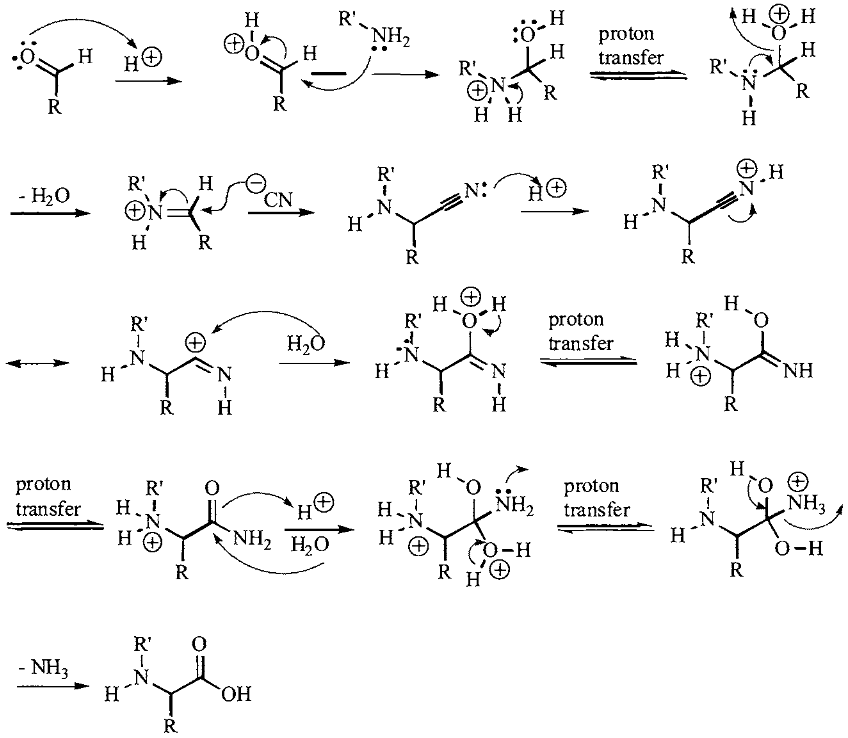
J. E. Davies, A. B. Holmes, J. P. Adams, *Journal of the American Chemical Society* **1999**, 121, 4900

Strecker Amino Acid Synthesis

The Reaction:



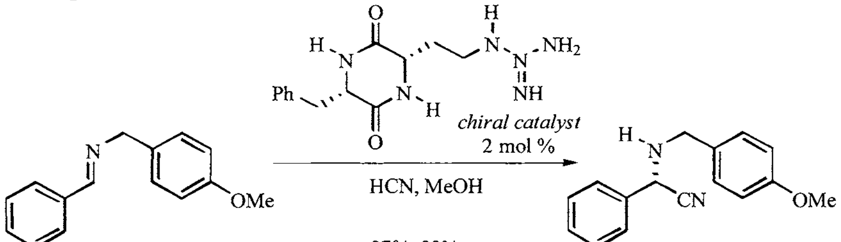
Proposed Mechanism:



Notes:

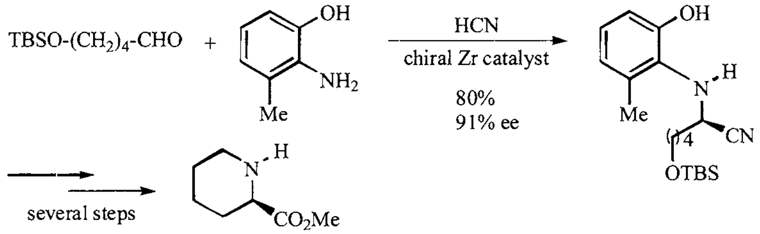
T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 253-254

Examples:



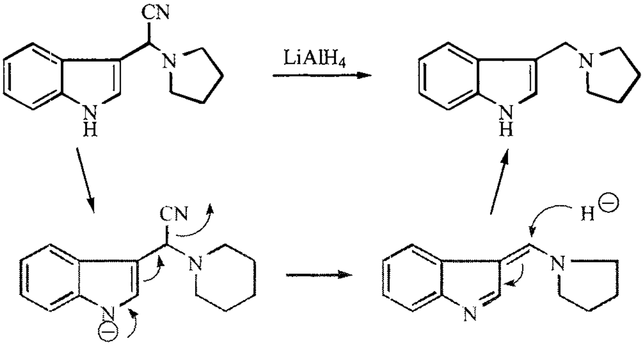
97%, 99% ee

M. S. Iyer, K. M. Gigstad, N. D. Namdev, M. Lipton, *Journal of the American Chemical Society* **1996**, 118, 4910



H. Ishitani, S. Komiyama, Y. Hasegawa, S. Kobayashi, *Journal of the American Chemical Society* **2000**, 122, 762

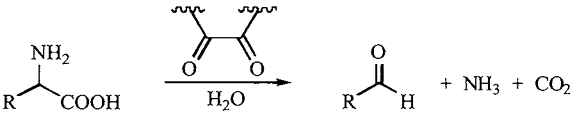
An anomolous reduction of a ***Strecker nitrile***:



P. Rajagopalan, B. G. Advani, *Tetrahedron Letters* **1965**, 6, 2197

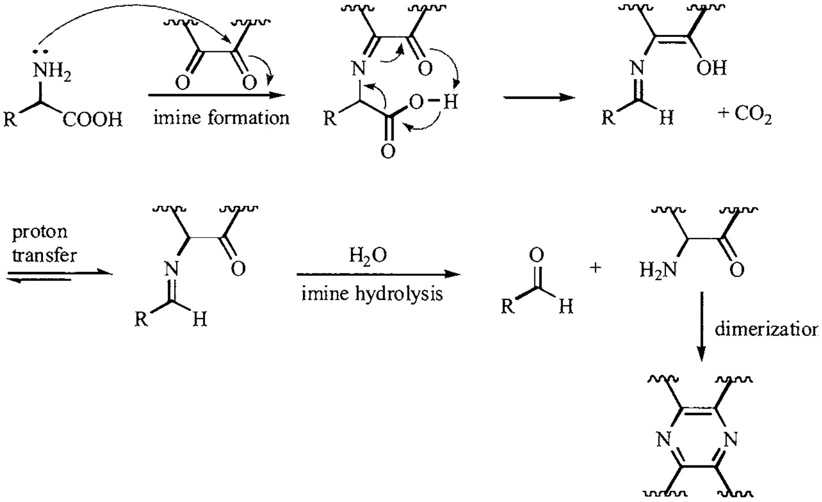
Strecker Degradation

The Reaction:



Proposed Mechanism:

G. P. Rizzi, *Journal of Organic Chemistry* **1969**, 34, 2002



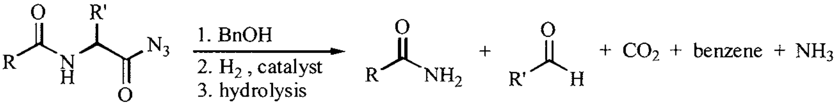
Notes:

The formation of aldehydes (flavorings) in roasting of cocoa beans, for example, is caused by ***Strecker degradation*** of amino acids.

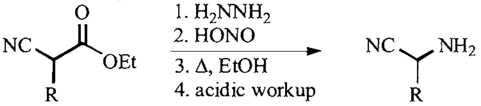
A. Arnoldi, C. Arnoldi, O. Baldi, A. Griffini, *Journal of Agricultural and Food Chemistry* **1987**, 35, 1035

Other degradation reactions:

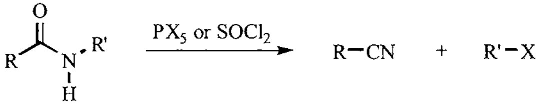
Bergmann Degradation



Darapsky Degradation (Procedure)

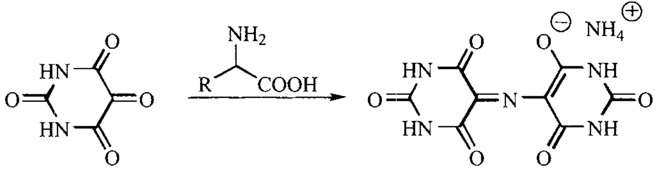


von Braun (Amide) Degradation / Reaction

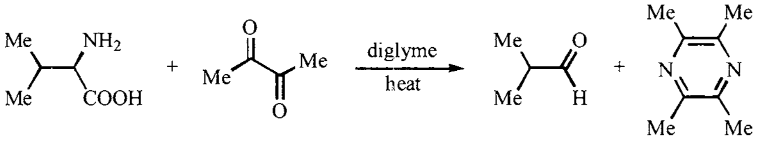


Examples:

This was used as a visual test for amino acids, where alloxane reacted with the amino acid to produce murexide, a colored compound:

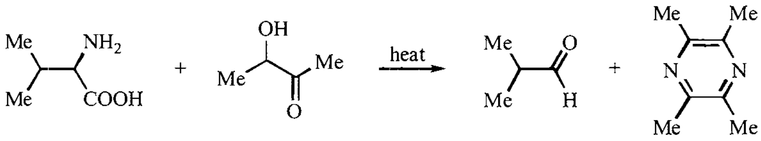


M. F. Aly, G. M. El-Nagger, T. I. El-Emary, R. Grigg, S. A. M. Metwally, S. Sivagnanam, *Tetrahedron* **1994**, 50, 895



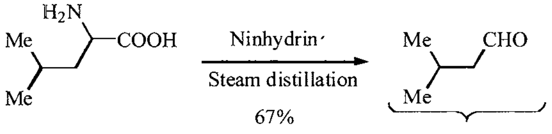
low yields of isolated products, but rapid loss of the butane dione.

G. P. Rizzi, *Journal of Organic Chemistry* **1969**, 34, 2002



GC-MS analysis of head space

C.-K. Shu, *Journal of Agricultural and Food Chemistry* **1998**, 46, 1515



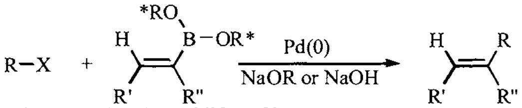
isolated as 2,4-D derivative

W. S. Fones, *Journal of the American Chemical Society* **1954**, 76, 1377

Suzuki Coupling

The Reaction:

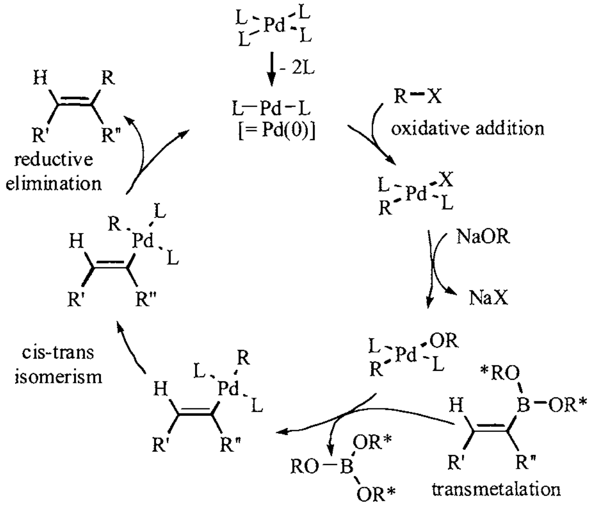
N. Miyauri, A. Suzuki, *Chemical Reviews* **1995**, 95, 2457



Where X = I >> Br > OTf >> Cl.

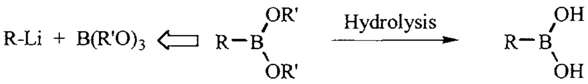
See: A useful review: S. R. Chemler, D. Trauner, S. J. Danishefsky, *Angewandte Chemie International Edition in English* **2001**, 40, 4544

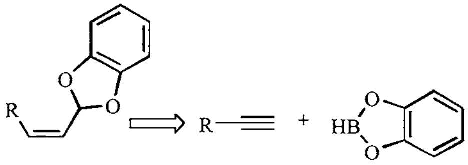
Proposed Mechanism:

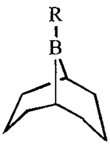


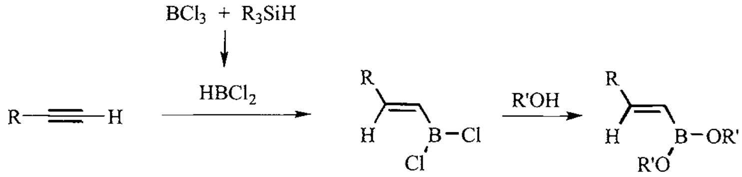
Notes:

General sources of common boron reagents:

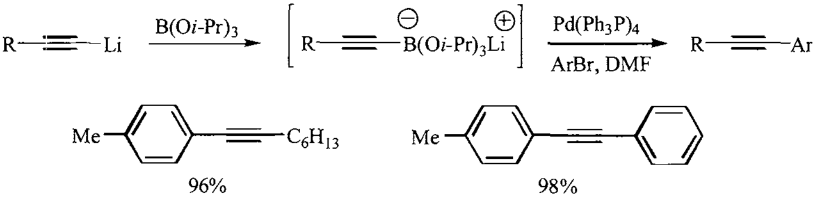




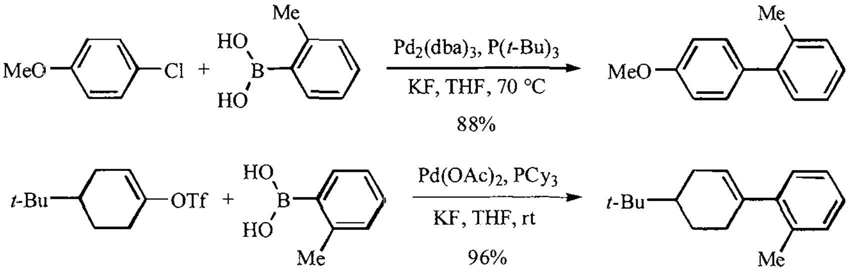




Examples:

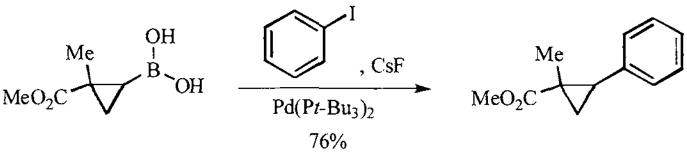


A.-S. Castanet, F. Colobert, T. Schlama, *Organic Letters*, **2000**, 2, 3559.

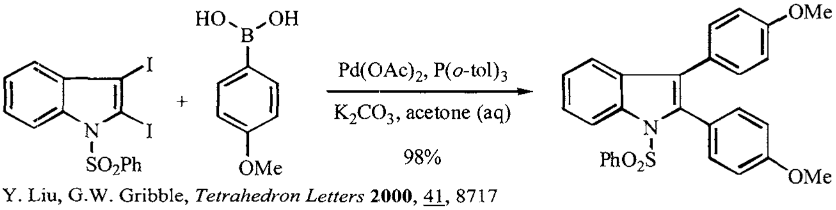


dba: dibenzylidene acetone

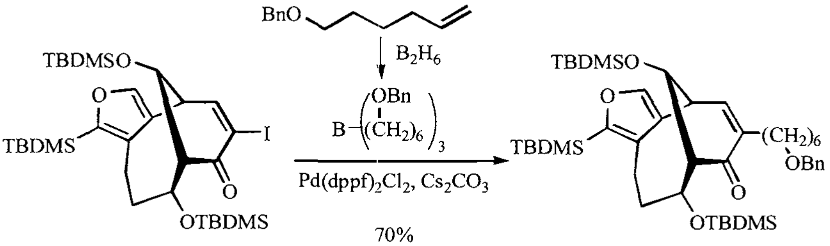
A.F. Littke, C. Dai, G.C. Fu, *Journal of the American Chemical Society* **2000**, 127, 4020



M. Rubina, M. Rubin, V. Geforgyan, *Journal of the American Chemical Society* **2003**, 125, 7198



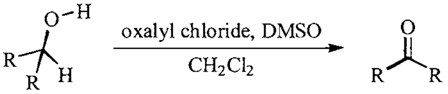
Y. Liu, G.W. Gribble, *Tetrahedron Letters* **2000**, 41, 8717



D. Meng, S. J. Danishfesky, *Angewandte Chemie, International Edition in English* **1999**, 38, 1485

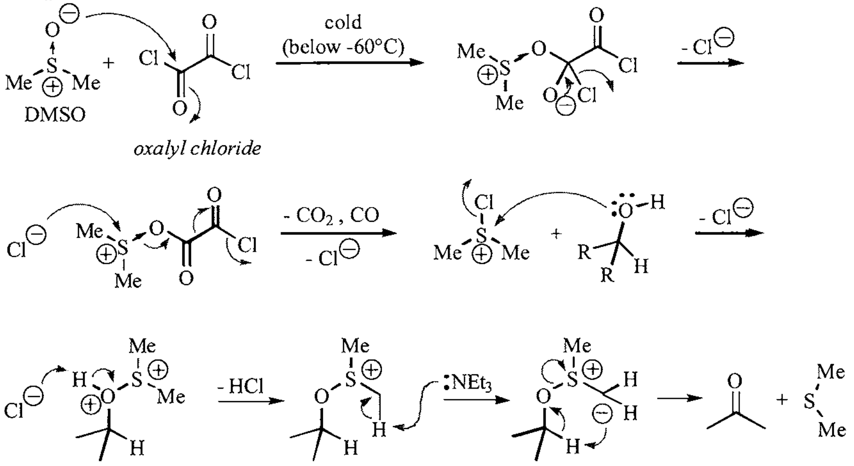
Swern Oxidation

The Reaction:



DMSO - Dimethylsulfoxide

Proposed Mechanism:

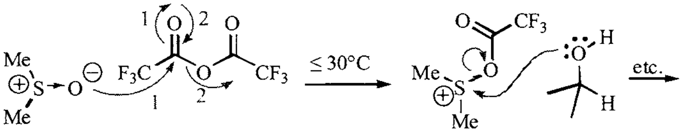


A sulfur ylide is formed with base which then abstracts the α proton, generating the carbonyl and dimethylsulfide.

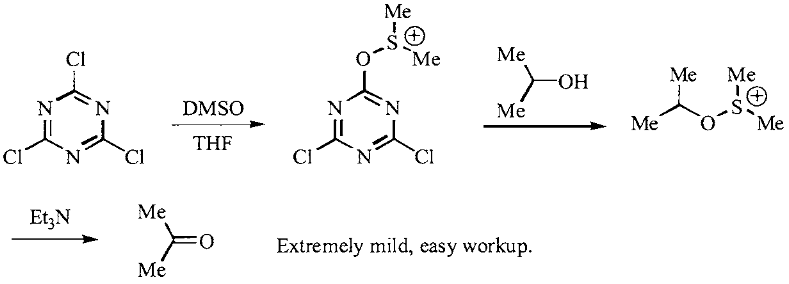
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1516; T. T. Tidwell, *Organic Reactions* **39**, 3

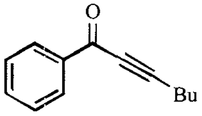
Triflouroacetic anhydride was used before oxalyl chloride and is also known as the ***Swern Oxidation***. Acetic anhydride can also be used. (***Albright-Goldman Oxidation)***



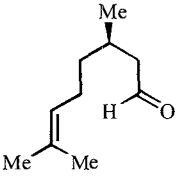
An alternative to the ***Swern Oxidation***:



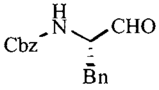
Extremely mild, easy workup.



90%



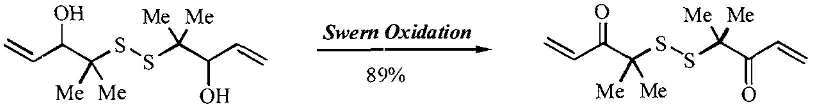
74%



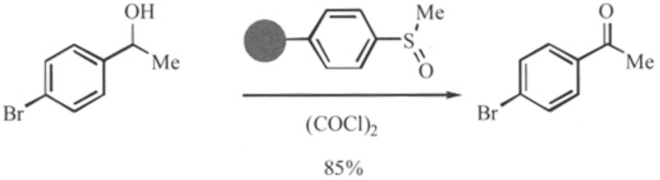
90%

L. DeLuca, G. Giacomelli, A. Porcheddu, *Journal of Organic Chemistry* **2001**, 66, 7807

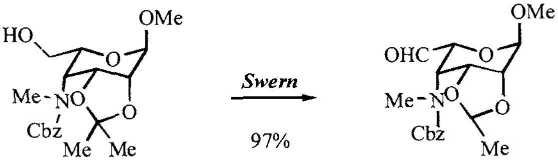
Examples:



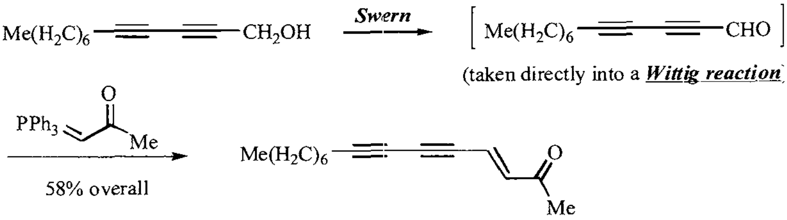
X. Fang, U. K. Gandarange, T. Wang, J. D. Sol, D. S. Garvey, *Journal of Organic Chemistry* **2001**, 66, 4019



M. K. W. Choi, P. H. Toy, *Tetrahedron* **2004**, 60, 2875



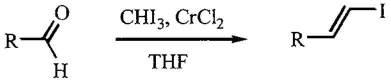
M. F. Semmelhack, Y. Jujang, D. Ho, *Organic Letters* **2001**, 3, 2403



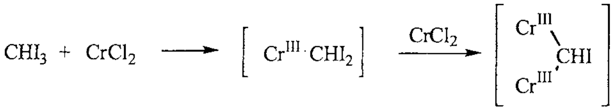
T. J. Speed, D. M. Thamattoor, *Tetrahedron Letters* **2002**, 43, 367

Takai Reaction

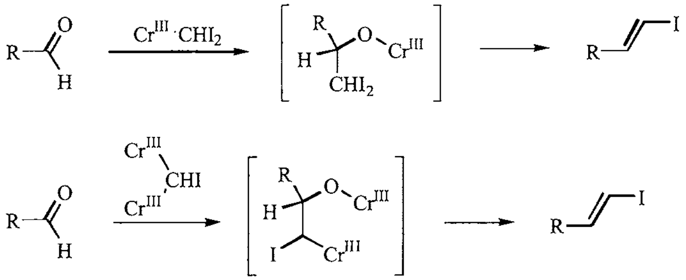
The Reaction:



Proposed Mechanism:

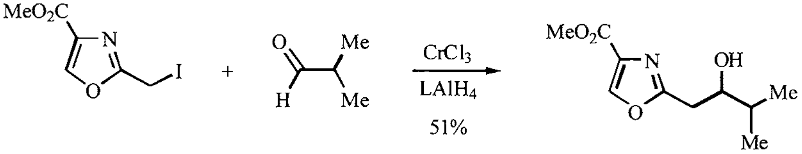


The two Cr-containing intermediates can distribute as shown below:



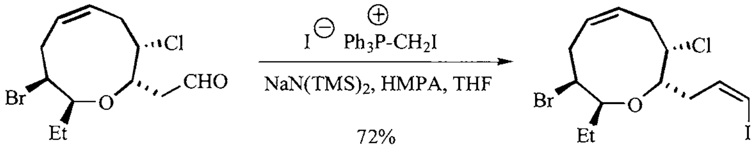
Notes:

There is also a ***Takai Coupling protocol***:



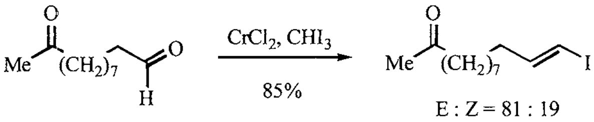
P. Breuilles, D. Uquen, *Tetrahedron Letters* **1998**, 39, 3149

See: ***Stork-Wittig Olefination*** for a related procedure:

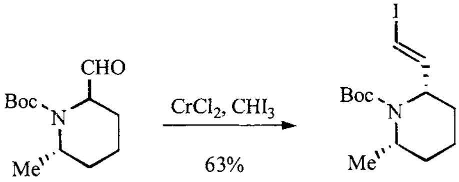


M. T. Crimmins, M. T. Powell, *Journal of the American Chemical Society* **2003**, 125, 7592

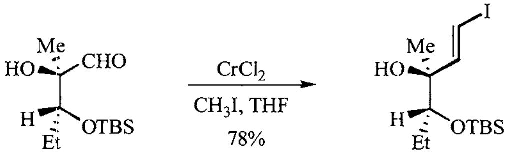
Examples:



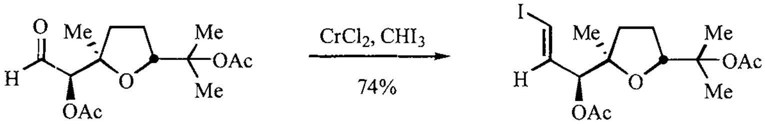
K. Takai, K. Nitta, K. Utimoto, *Journal of the American Chemical Society* **1986**, 108, 7408



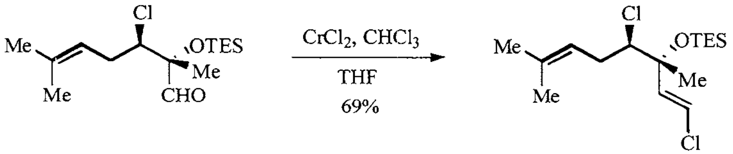
S. Chackalamannil, R. Davies, A. T. McPhail, *Organic Letters* **2001**, 3, 1427



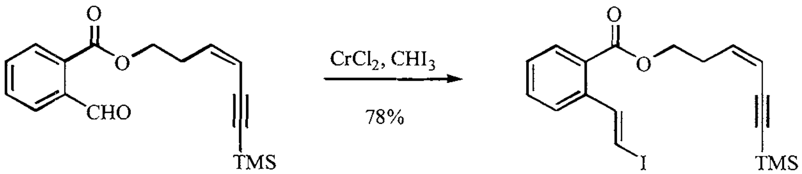
J. Cossy, D. Bauer, V. Bellosta, *Tetrahedron* **2002**, 58, 5909



I. C. Gonzalez, C. J. Forsyth, *Journal of the American Chemical Society* **2000**, 122, 9099



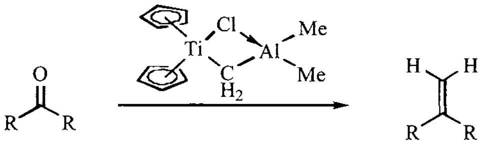
M. E. Jung, B. T. Fahr, D. C. D'Amico, *Journal of Organic Chemistry* **1998**, 63, 2982



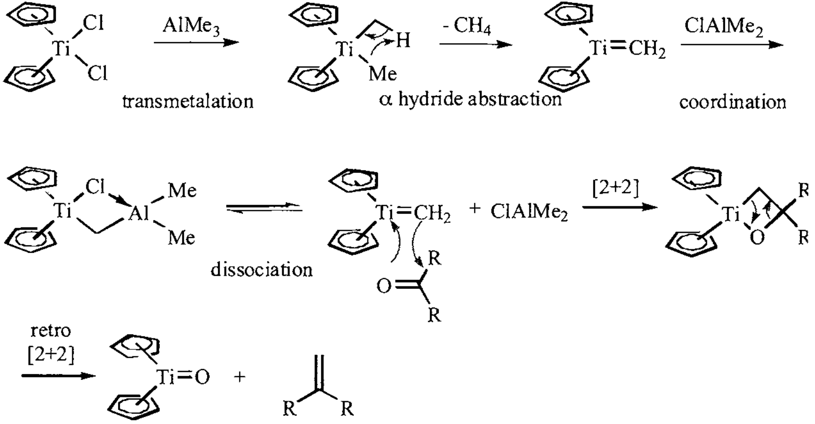
R. Garg, R. S. Coleman, *Organic Letters* **2001**, 3, 3487

Tebbe Reagent / Olefination

The Reaction:



Proposed Mechanism:



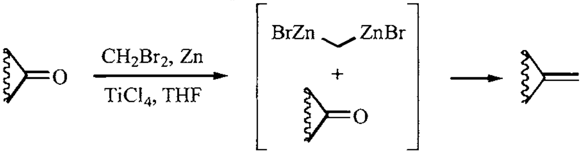
Notes:

See ***Tebbe Reagent***

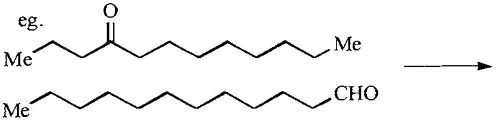
Tebbe reactions on beads:

A. G. M. Barrett, P. A. Procopiou, U. Voigtmann, *Organic Letters* **2001**, 3, 3165

The ***Oshima modification*** provides another entry into methylenation:



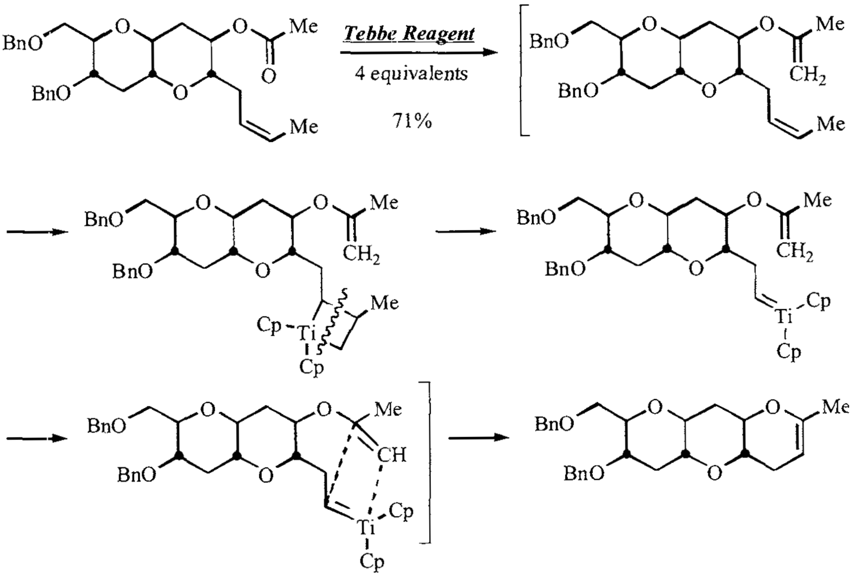
For details of competitive regiochemical analysis with a number of reagents, see:



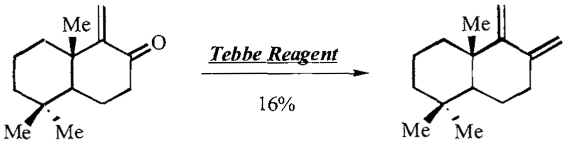
T. Okazoe, J.-I. Hibino, K. Takai, H. Nozakil, *Tetrahedron Letters* **1985**, 26, 5581

Examples:

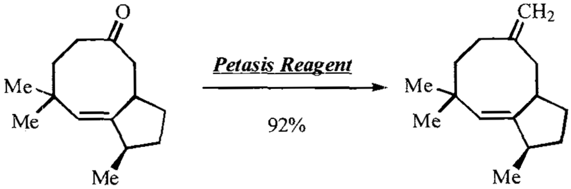
M. E. Jung, J. Pontillo, *Tetrahedron* **2003**, 59, 2729



K. C. Nicolaou, M. H. D. Postema, C. F. Claiborne, *Journal of the American Chemical Society* **1996**, 118, 1565



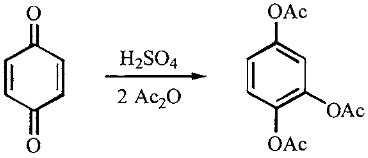
M. Cortés, J. A. Valderrama, M. Cuellar, V. Armstrong, M. Preite, *Journal of Natural Products* **2001**, 64, 348



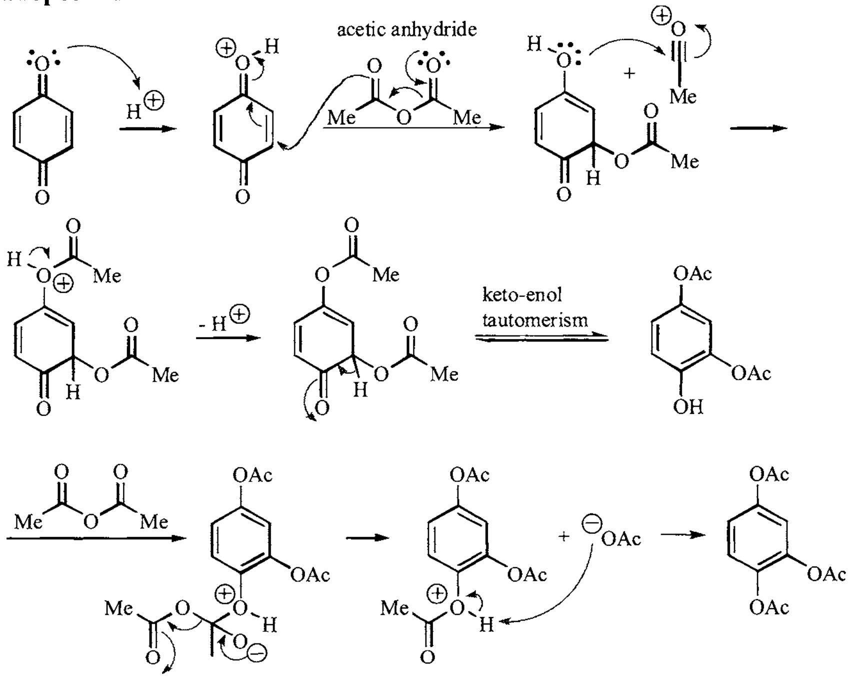
N. A. Petasis, M. A. Patane, *Tetrahedron Letters* **1990**, 31, 6799

Thiele-Winter Reaction (Acetoxylation) (Thiele Reaction)

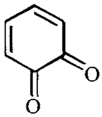
The Reaction:



Proposed Mechanism:

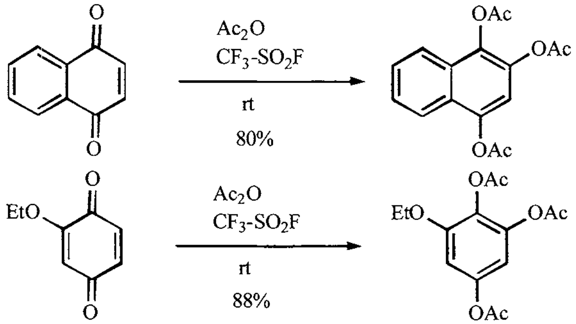


Notes:

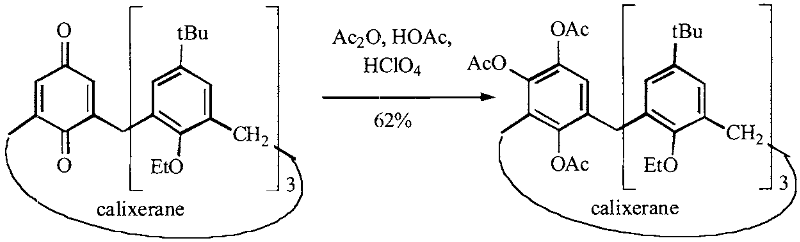


Ortho-quinones will give the same product.

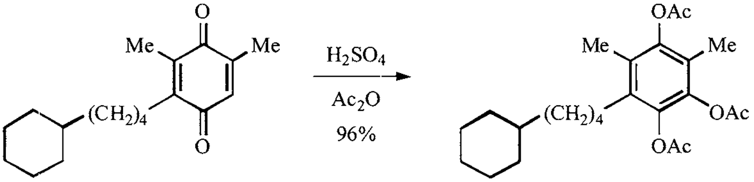
Examples:



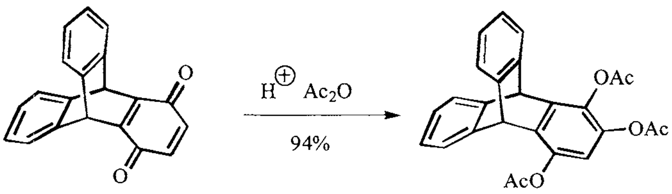
D. Villemin, N. Bar, M. Hammadi, *Tetrahedron Letters* **1997**, 38, 4777



P. A. Reddy, C. D. Gutsche, *Journal of Organic Chemistry* **1993**, 58, 3245



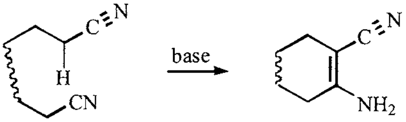
W. M. Mclamore, *Journal of the American Chemical Society* **1951**, 73, 2225



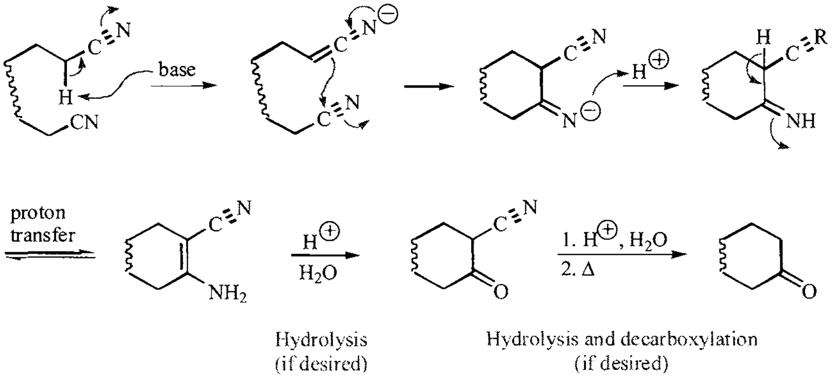
S. Spyroudis, N. Xanthopoulou, *Journal of Organic Chemistry* **2002**, 67, 4612

Thorpe Reaction (If intermolcular, known as the Thorpe-Ziegler Reaction.)

The Reaction:



Proposed Mechanism:

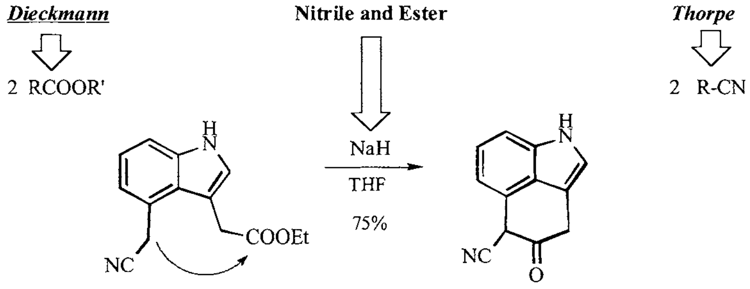


Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, pp. 1219, 1238; for ***Thorpe-Ziegler***, p. 1239.

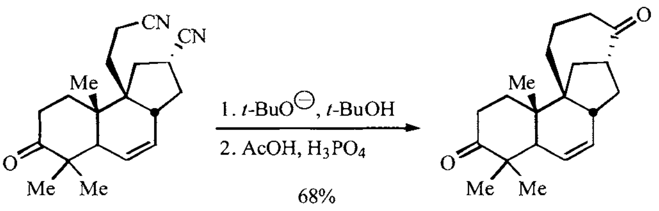
The ***Thorpe reaction*** is often better than the ***Diekmann Cyclization*** for ring sizes > 7.

What of the reaction of an ester and a nitrile?

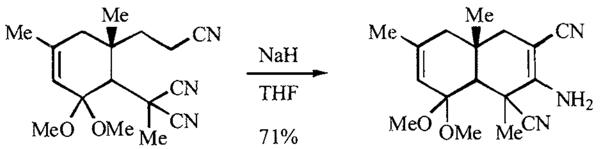


H. Plienenger, W. Muller, *Chemische Berichte* **1960**, 93, 2029 (AN 1961:13347)

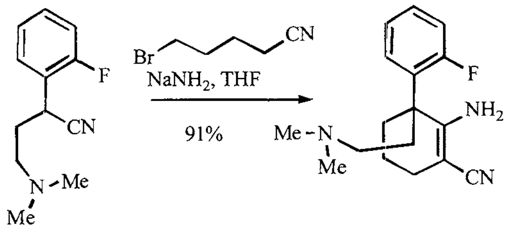
Examples:



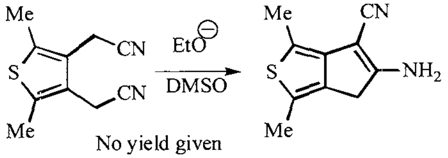
A. Toro, P. Nowak, P. Deslongchamps, *Journal of the American Chemical Society* **2000**, 122, 4526



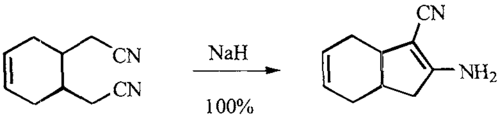
L. Lu, R. K. Shoemaker, D. M. S. Wheeler, *Tetrahedron Letters* **1989**, 30, 6993



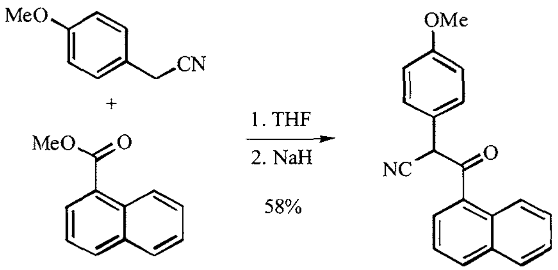
A. Hashimoto, A. K. Przybyl, J. T. M. Linders, S. Kodato, X. Tian, J. R. Deschamps, C. George, J. L. Flippen-Anderson, A. E. Jacobson, K. C. Rice, *Journal of Organic Chemistry* **2004**, 69, 5322



G. Seitz, H. Monnighoff, *Tetrahedron Letters* **1971**, 12, 4889



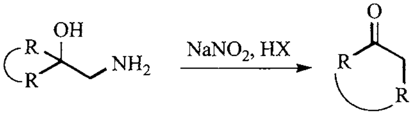
J. J. Bloomfield, P. V. Fennessey, *Tetrahedron Letters* **1964**, 5, 2273



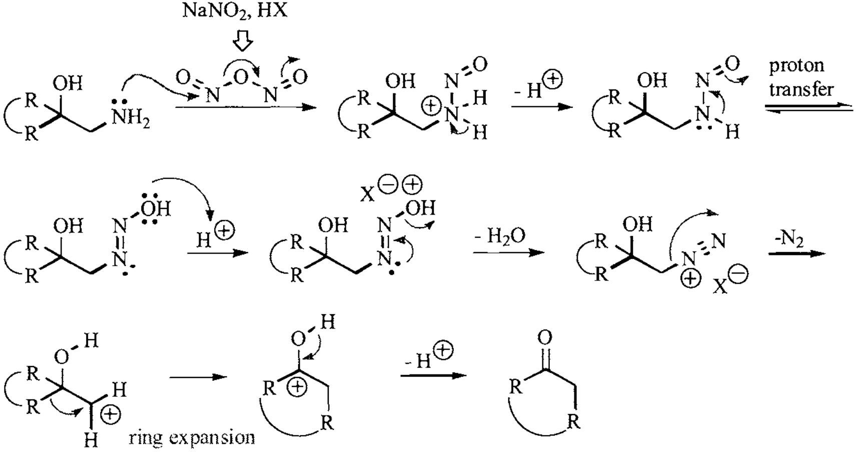
N. E. Kayaleh, R. C. Gupta, F. Johnson, *Journal of Organic Chemistry* **2000**, 65, 4515

Tiffeneau-Demjanov Rearrangement

The Reaction:



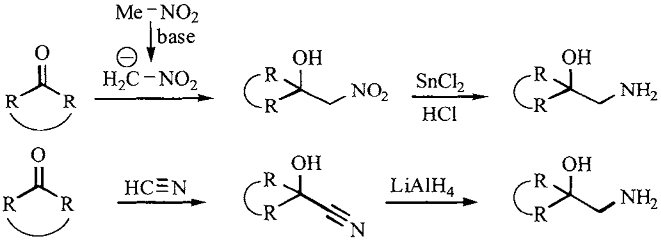
Proposed Mechanism:



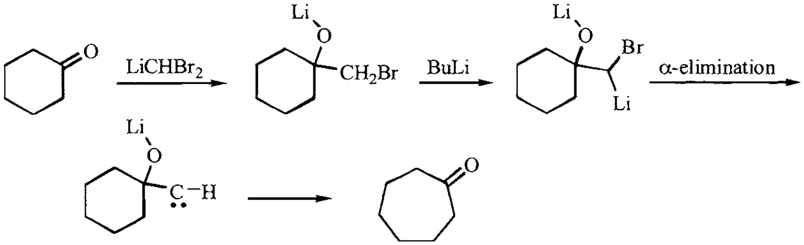
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry,* 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1399

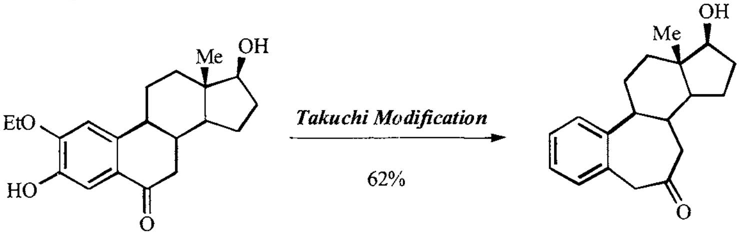
Possible sources of starting material:



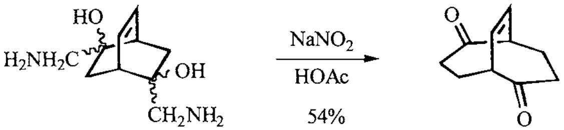
Takuchi Modification



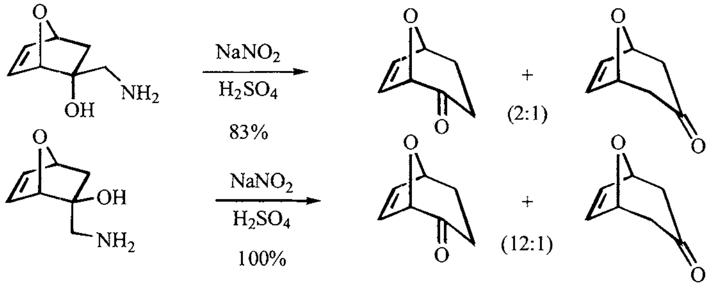
Examples:



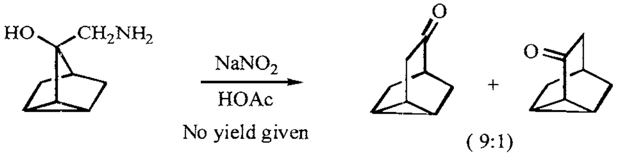
Z. Wang, D. Yang, A. K. Mohanakrishnan, E. Hamel, M. Cushman, *Journal of Medicinal Chemistry* **2000**, 43, 2419



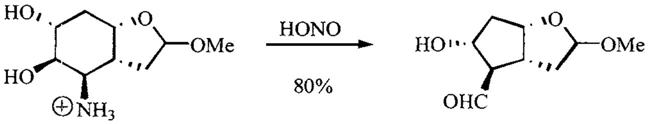
S. Kim, R. Bishop, D. C. Craig, I. G. Dance, M. L. Scudder, *Journal of Organic Chemistry* **2002**, 67, 3221



D. Fattori, S. Henry, P. Vogel, *Tetrahedron* **1993**, 49, 1649



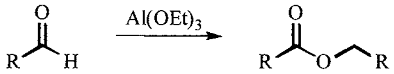
J. T. Lumb, G. H. Whitham, *Tetrahedron* **1965**, 21, 499



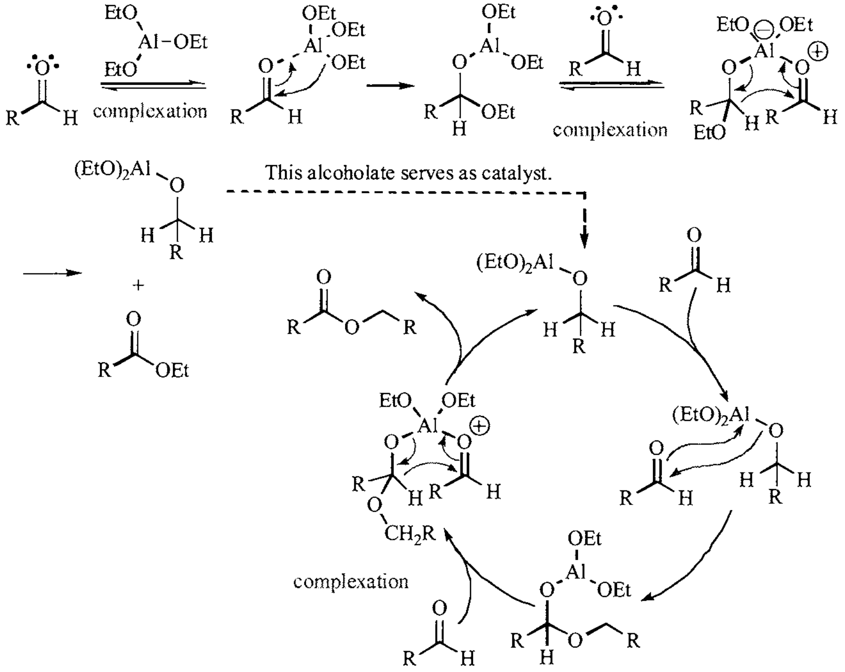
R. B. Woodward, J. Gostel, I. Ernest, R. J. Friary, G. Nestler, H. Raman, R. Sitrin, C. Suter, J. K. Whitesell, *Journal of the American Chemical Society* **1973**, 95, 6853

Tischenko Reaction

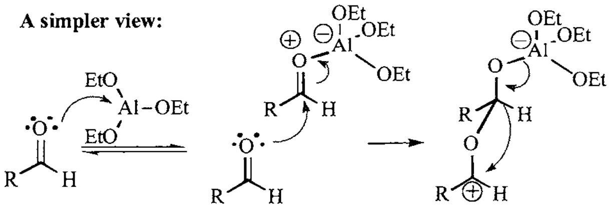
The Reaction:



Proposed Mechanism:

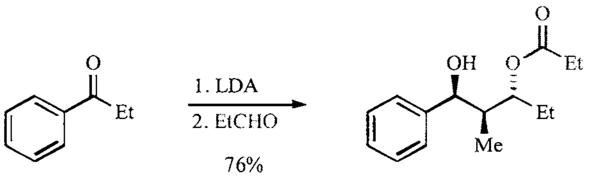


A simpler view:

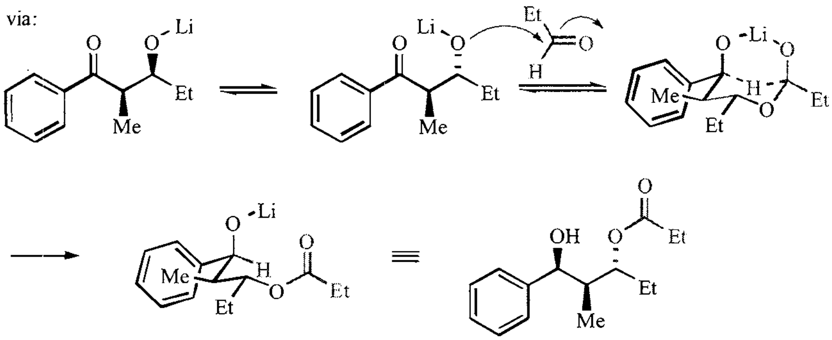


Notes:

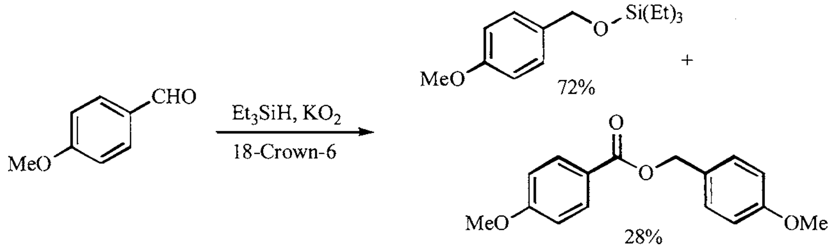
An "***Aldol-Tischenko reaction***" is sometimes observed as a byproduct of ***Aldol condensation***:



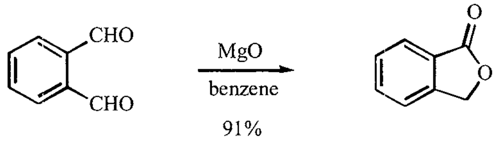
P. M. Bodnar, J. T. Shaw, K. A. Woerpel, *Journal of Organic Chemistry* **1997**, 62, 5674



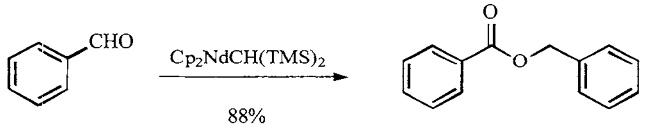
Examples:



F. LeBideau, T. Coradin, D. Gourier, J. Henique, E. Samuel, *Tetrahedron Letters* **2000**, 41, 5215

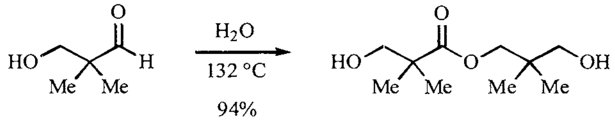


T. Sek, H. Tachikawa, T. Tamada, H. Hattori, *Journal of Catalysis* **2003**, 217, 117



S.-Y. Onozawa, T. Sakakura, M. Tanaka, M. Shiro, *Tetrahedron* **1996**, 52, 4291

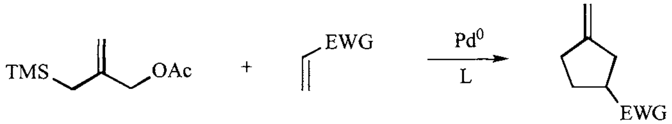
This reaction will take place slowly by storing an aqueous solution of the aldehyde at 60 °C.



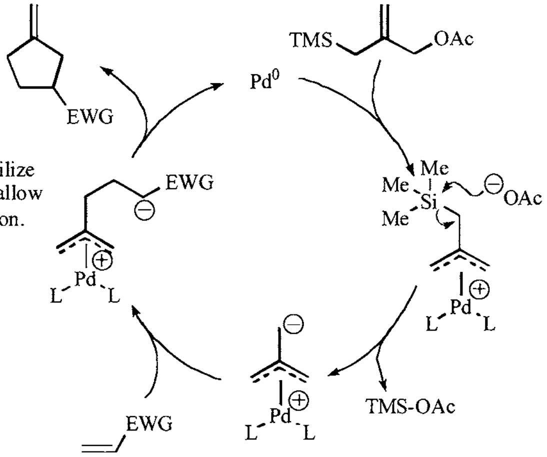
G. K. Finch, *Journal of Organic Chemistry* **1960**, 25, 2219

Trost's TMM (trimethylenemethane) Cycloaddition

The Reaction:



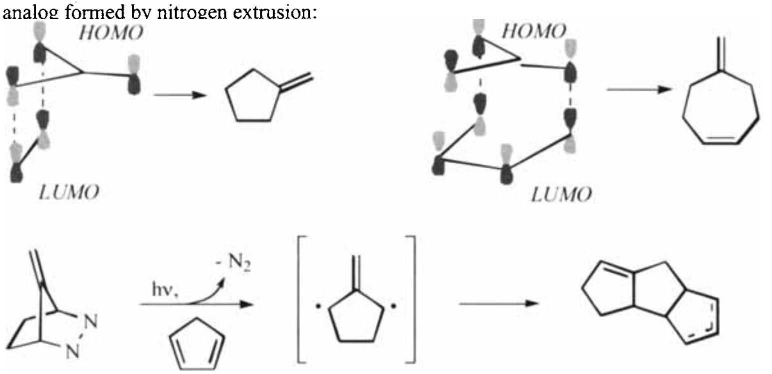
Proposed Mechanism:



EWG can stabilize the anion and allow for bond rotation.

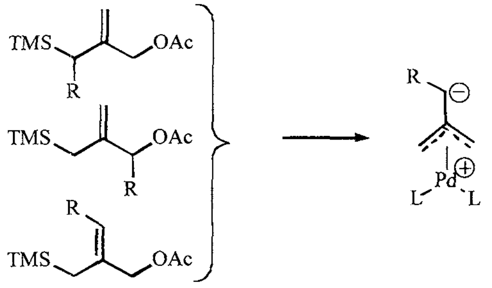
Notes:

An analysis of the use of orbital theory to rationalize product formation from the diradical TMM analog formed by nitrogen extrusion:

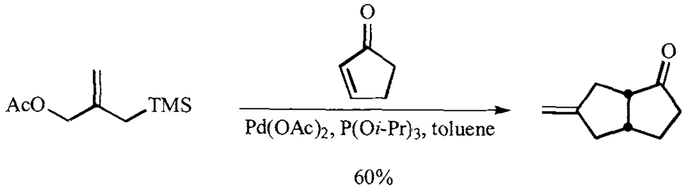


A series of products of which these are the major components.

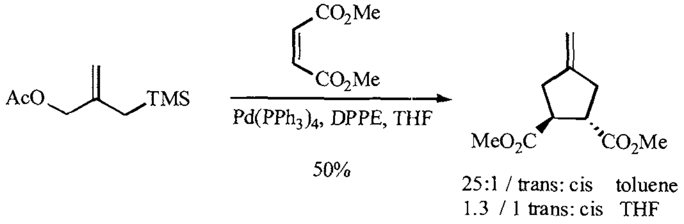
R. K. Siemionke, J. A. Berson, *Journal of the American Chemical Society* **1980**, 102, 3870



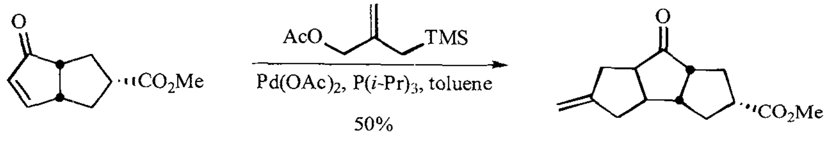
Examples:



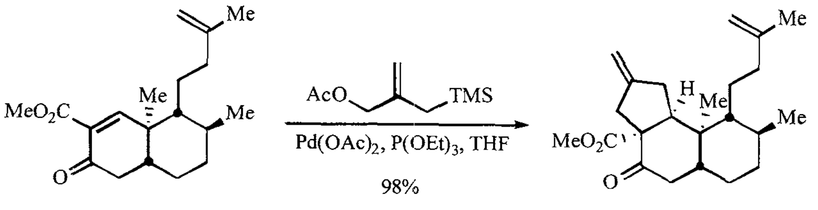
J. Cossy, D. Belotti, J. P. Pete, *Tetrahedron* **1990**, 46, 1859



B. M. Trost, D. M. T. Chan, *Journal of the American Chemical Society* **1983**, 105, 2315



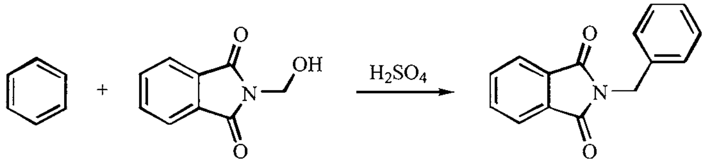
A. Heumann, S. Kadly, A. Tenagli, *Tetrahedron* **1994**, 50, 539



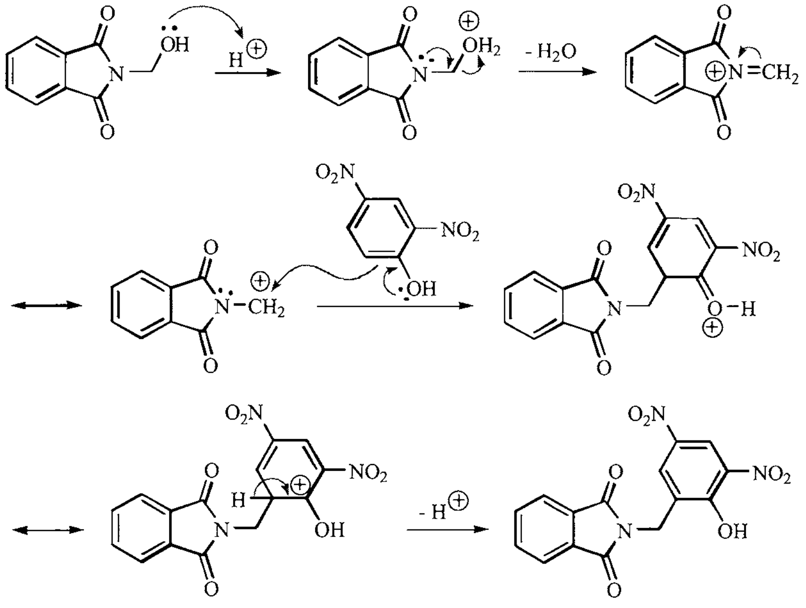
L. A. Paquette, D. R. Sauer, D. G. Cleary, M. A. Kinsella, C. M. Blackwell, L. G. Anderson, *Journal of the American Chemical Society* **1992**, 114, 7375

Tscherniac-Einhorn Reaction

The Reaction:



Proposed Mechanism:

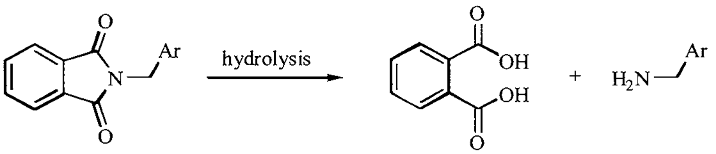


4 total resonance structures

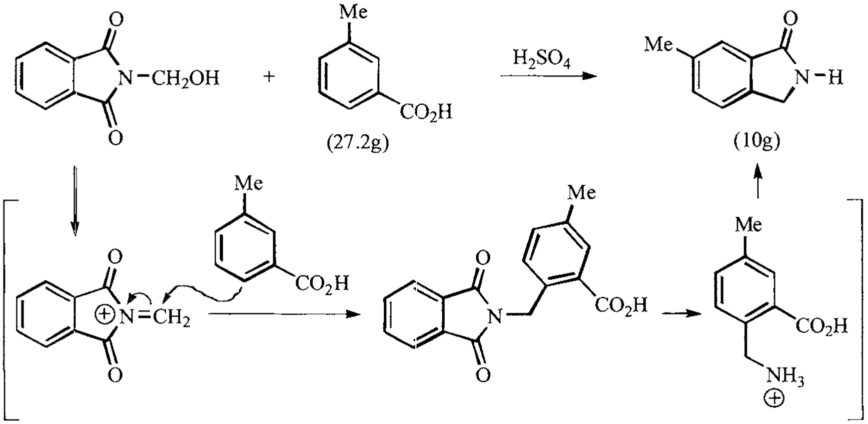
H. E. Zaugg, R. W. DeNet, J. E. Fraser, A. M. Kotre, *Journal of Organic Chemistry* **1969**, 34, 14

Notes:

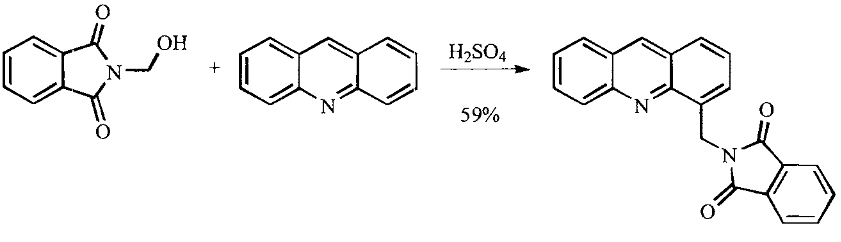
Sometimes the reaction can continue with hydrolysis of the phthalimide group:



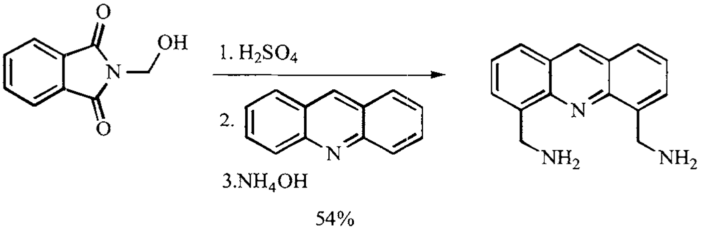
Examples:



P. S. Anderson, M. E. Christy, C. D. Colton, W. Halczenko, G. S. Ponticello, K. L. Shepard, *Journal of Organic Chemistry* **1979**, 44, 1519



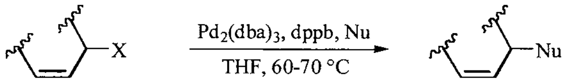
F. Hess, E. Cullen, K. Grozinger, *Tetrahedron Letters* **1971**, 12, 2591



F. K. Hess, P. B. Stewart, *Journal of Medicinal Chemistry* **1975**, 18, 320

Tsuji-Trost Reaction

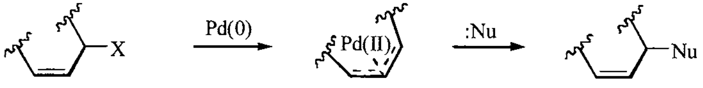
The Reaction:



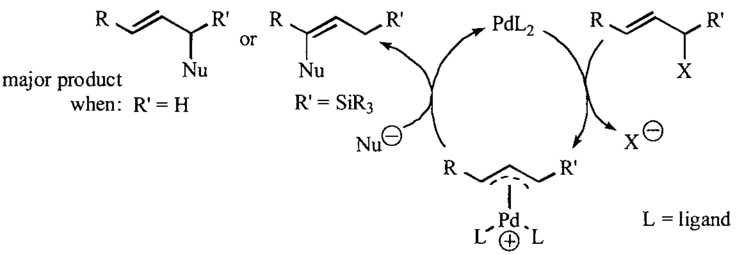
X = leaving group

J. Tsuji, H. Takahashi, M. Morikawa, *Tetrahedron Letters* **1965**, 6, 4387
B. M. Trost, T. J. Fullerton, *Journal of the American Chemical Society* **1973**, 95, 292

Proposed Mechanism:

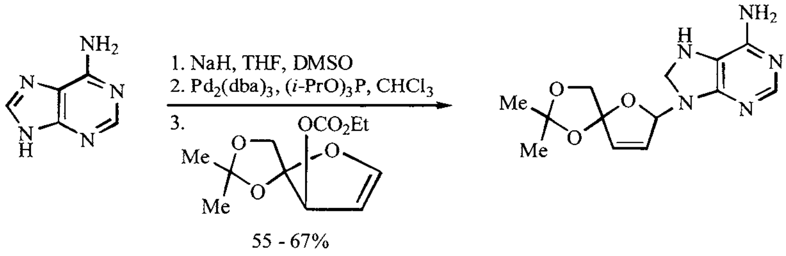


Notes:



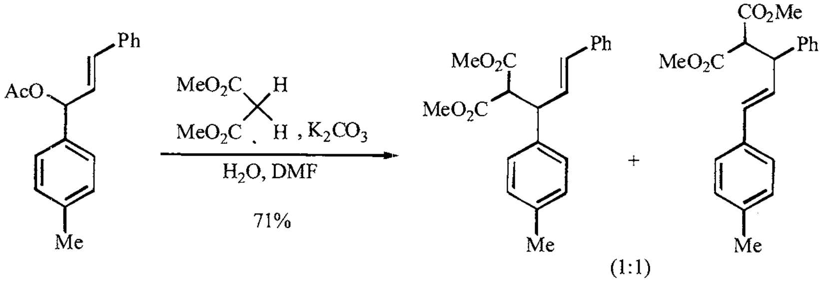
V. Branchadell, M. Moreno-Manas, R. Pleixats, S. Thorimbert, C. Commandeur, C. Boglio, M. Malacria, *Journal of Organometallic Chemistry* **2003**, 687, 337

Examples:

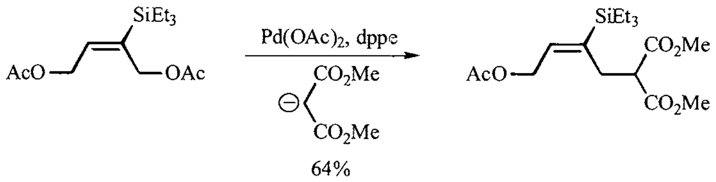


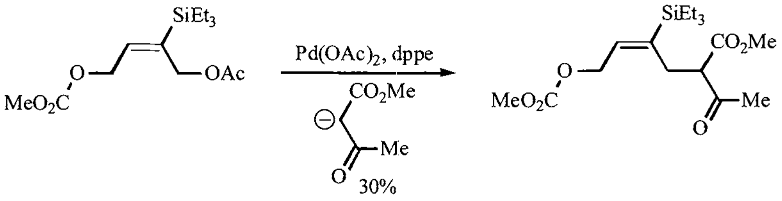
J. H. Hong, M. J. Shim, B. O. Ro, O. H. Ko, *Journal of Organic Chemistry* **2002**, 67, 6837

A water-mediated, transition metal free reaction:



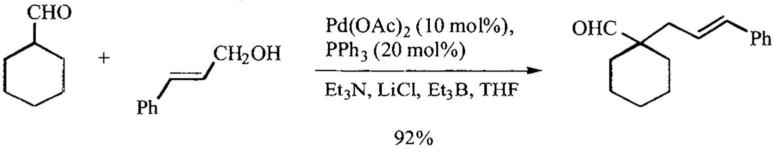
C. Chevrin, J. Le Bras, F. Henin, J. Muzart, *Tetrahedron Letters* **2003**, 44, 8099





V. Branchadell, M. Moreno-Manas, R. Pleixats, S. Thorimbert, C. Commandeur, C. Boglio, M. Malacria, *Journal of Organometallic Chemistry* **2003**, 687, 337

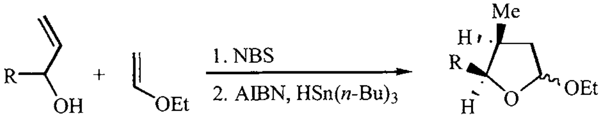
Catalytic allylation of aldehydes:



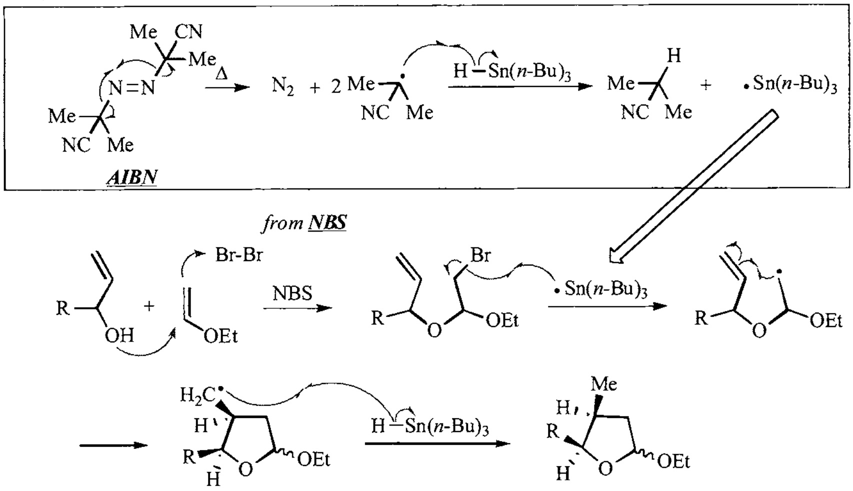
M. Kimura, Y. Horino, R. Mukai, S. Tanaka, Y. Tamaru, *Journal of the American Chemical Society* **2001**, 123, 10401

Ueno-Stork Cyclization

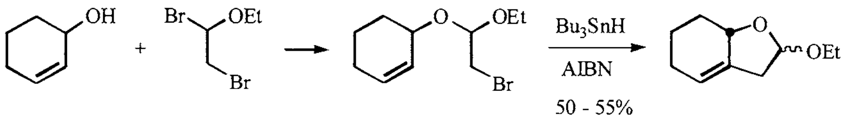
The Reaction:



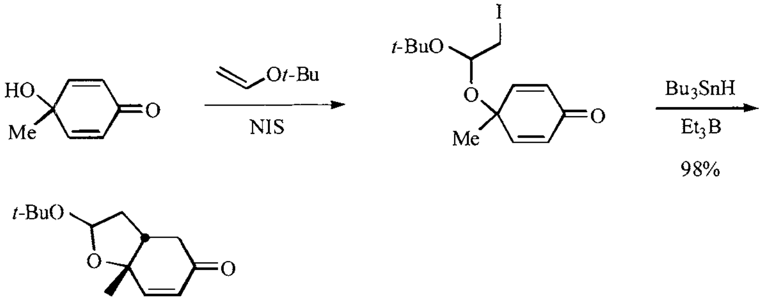
Proposed Mechanism:



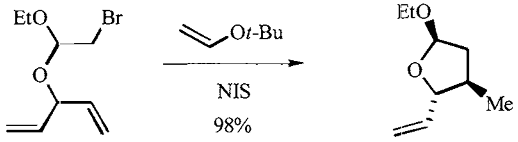
Examples:



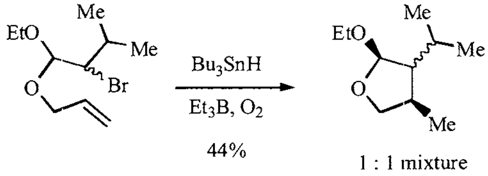
G. Stork, R. Mook, Jr., S. A. Biller, S. D. Rychnovsky, *Journal of the American Chemical Society* **1983**, 105, 3741



F. Villar, O. Equey, P. Renaud, *Organic Letters* **2000**, 2, 1061



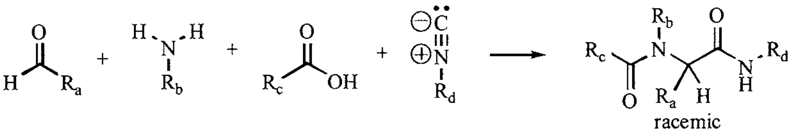
F. Villar, O. Equey, P. Renaud, *Organic Letters* **2000**, 2, 1061



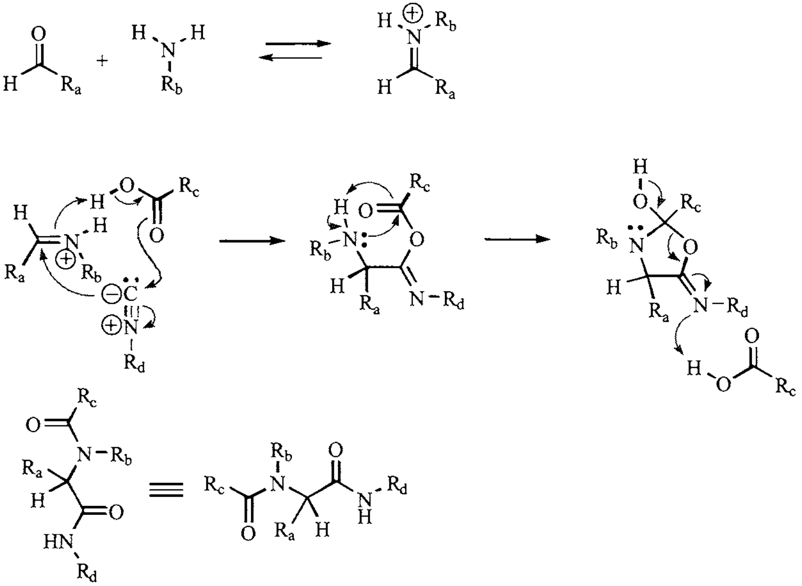
F. Villar, P. Renaud, *Tetrahedron Letters* **1998**, 39, 8655

Ugi Reaction

The Reaction:

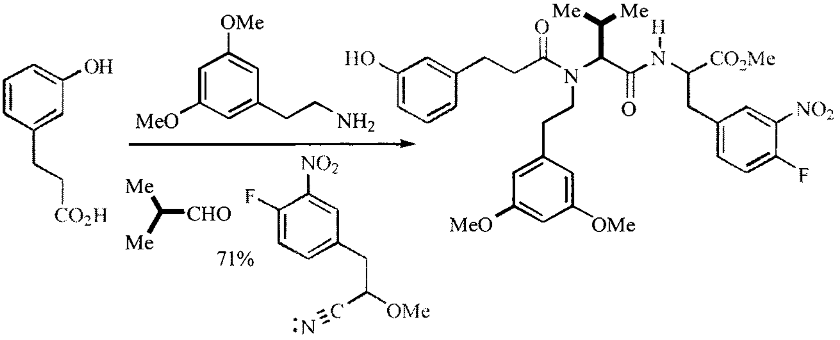


Proposed Mechanism:



Notes:

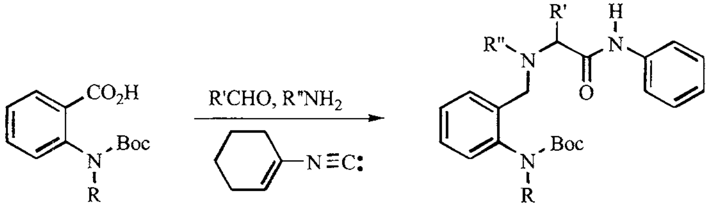
This reaction is similar to the ***Passerini reaction***. It is characterized by the four components going into the reaction mix:



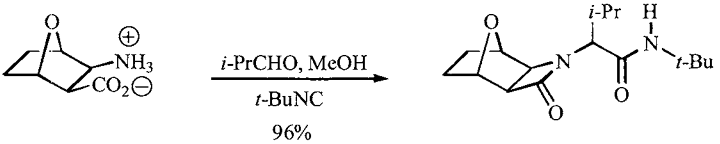
P. Cristau, J.-P. Vors, J. Zhu, *Organic Letters* **2001**, 3, 4079

Examples:

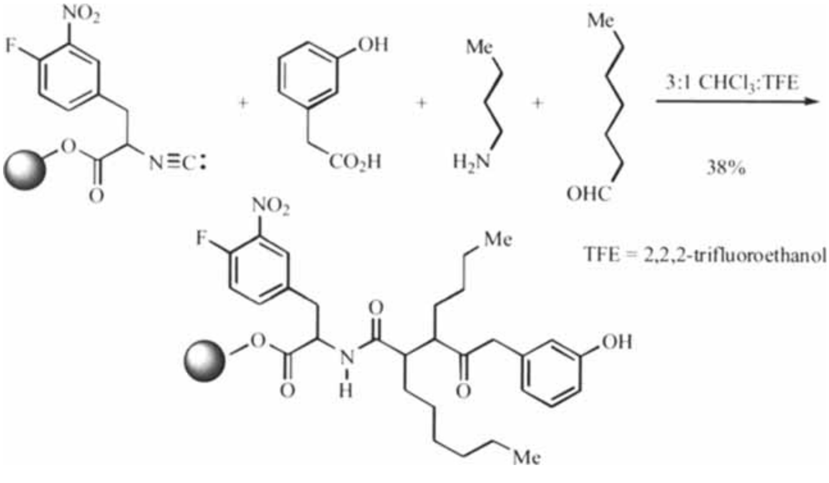
A chemical library developed



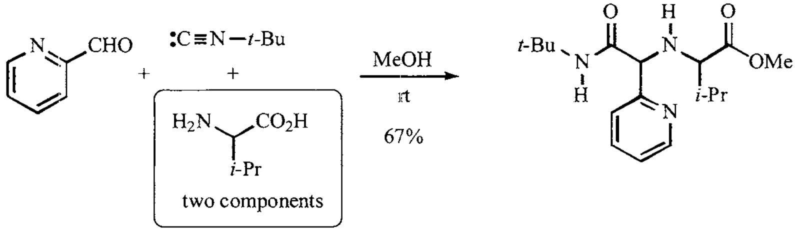
C. Hulme, J. Peng, S.-Y. Tang, C.J. Burns, I. Morize, R. Labaudiniere, *Journal of Organic Chemistry* **1998**, 63, 8021



A. Basso, L. Banfi, R. Riva, G. Guanti, *Tetrahedron Letters* **2004**, 45, 587



P. Cristau, J.-P. Vors, J. Zhu, *Tetrahedron* **2003**, 59, 7859



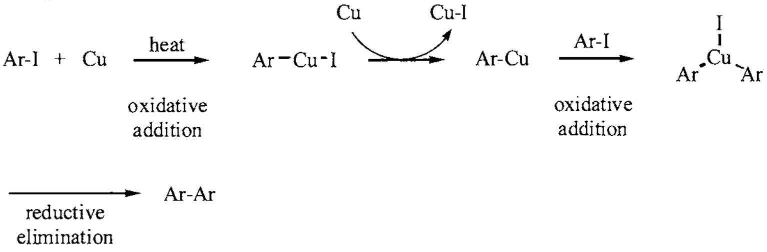
G. Dyker, K. Breitenstein, G. Henkel, *Tetrahedron: Asymmetry* **2002**, 13, 1929

Ullmann Coupling Reaction

The Reaction:

$$2\ Ar{-}I \xrightarrow[\Delta]{Cu} Ar{-}Ar + CuI_2$$

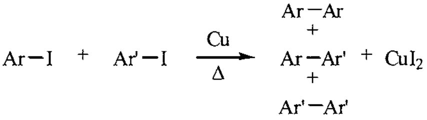
Proposed Mechanism:



Notes:

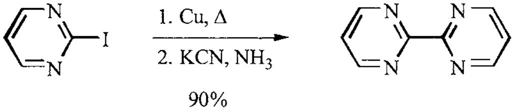
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 870.

Problem with mixed coupling:

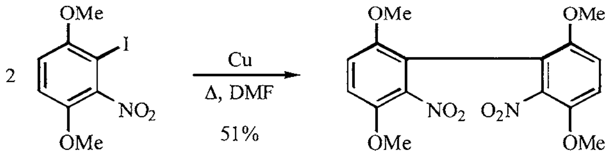


$$Ar{-}I + Ar'{-}I \xrightarrow[\Delta]{Cu} \begin{matrix} Ar{-}Ar \\ + \\ Ar{-}Ar' \\ + \\ Ar'{-}Ar' \end{matrix} + CuI_2$$

Examples:



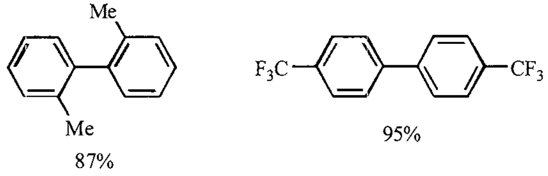
G. Vlád, I. Horváth, *Journal of Organic Chemistry* **2002**, 67, 6550



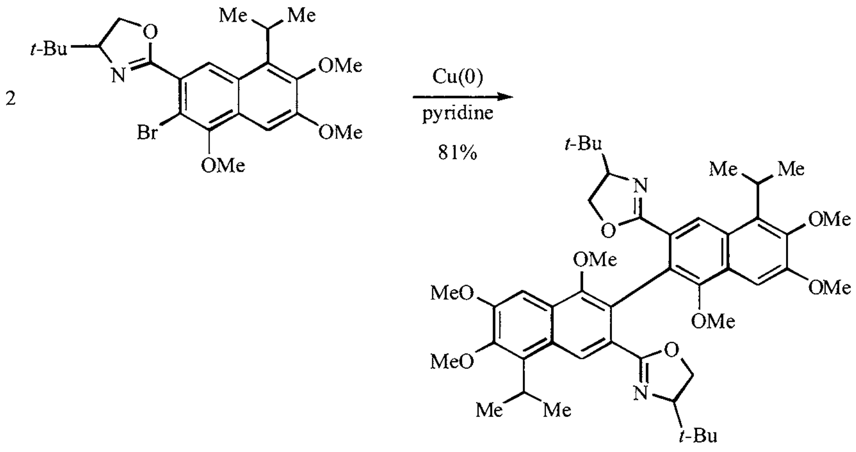
C. W. Lai, C. K. Lam, H. K. Lee, T. C. W. Mak, H. N. C. Wong, *Organic Letters* **2003**, 5, 823

$$\text{Ar-X} \xrightarrow[\text{H}_2\text{O, CO}_2\text{ (l)}]{\text{Pd/C, Zn}} \text{Ar-Ar}$$

X = I, Br, Cl



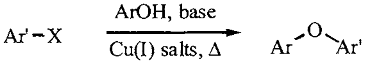
J.-H. Li, Y.-X. Xie, D.-L. Yin, *Journal of Organic Chemistry* **2003**, 68, 9867



A. I. Meyers, J. J. Willemsen, *Tetrahedron Letters* **1996**, 37, 791

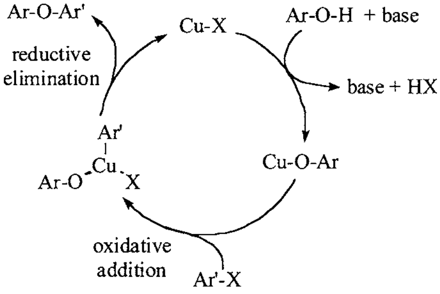
Ullmann Ether Synthesis

The Reaction:



X includes halides, $-NO_2$, $-NR_3^+$, -OR, or -OH

Proposed Mechanism:

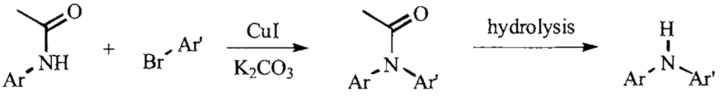


Notes:

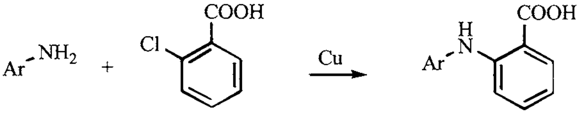
Ullmann-type reactions can replace Ar-O with Nu-H.

The copper-catalyzed addition of amines and amides (***Goldberg Reaction***) are placed in this section:

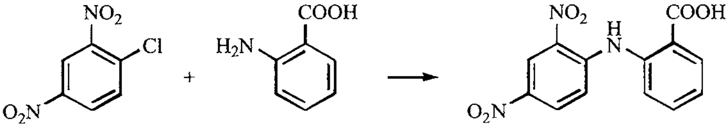
Goldberg Reaction



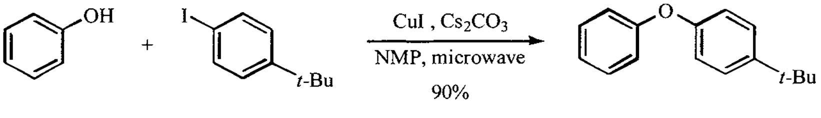
Ullmann Reaction (Jourdan-Ullmann Synthesis)



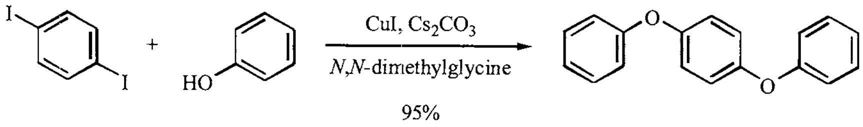
There is also the related **Jourdan Synthesis**:



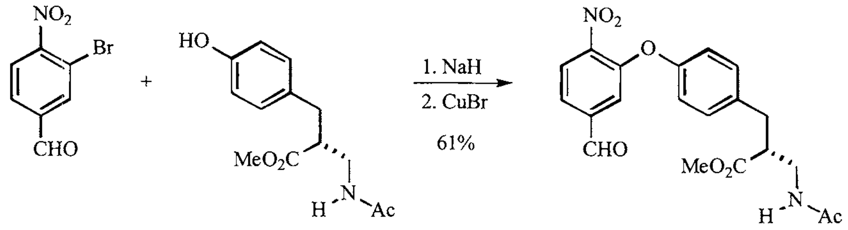
Examples:



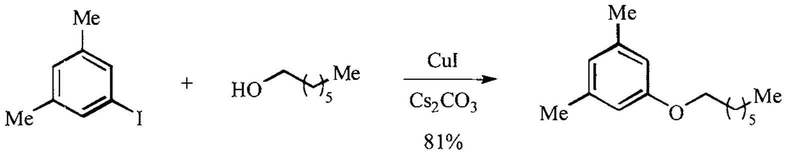
Y.-J. Wu, H. He, *Tetrahedron Letters* **2003**, 44, 3445



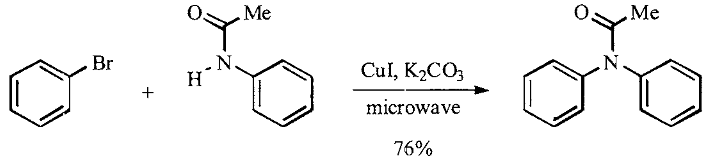
D. Ma, Q. Cai, *Organic Letters* **2003**, 5, 3799

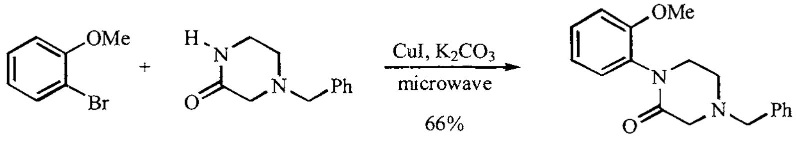


A. V. R. Rao, J. K. Chakraborty, K. L. Reddy, A. S. Rao, *Tetrahedron Letters* **1992**, 33, 4799

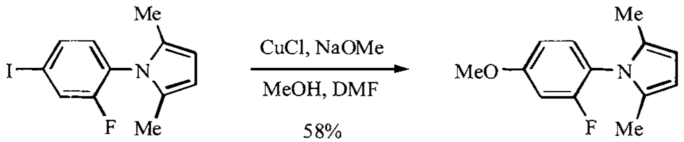


M. Wolter, G. Nordmann, G. E. Job, S. L. Buchwald, *Organic Letters* **2002**, 4, 973





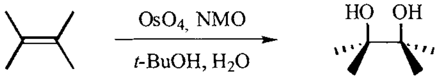
J. H. M. Lange, L. J. F. Hofmeyer, F. A. S. Hout, S. J. M. Osnabrug, P. C. Verveer, C. G. Kruse, R. W. Feenstra, *Tetrahedron Letters* **2002**, 43, 1101



J. A. Ragen, B. P. Jones, M. J. Castaldi, P. D. Hill, T. W. Makowski, *Organic Syntheses*, CV10, 418

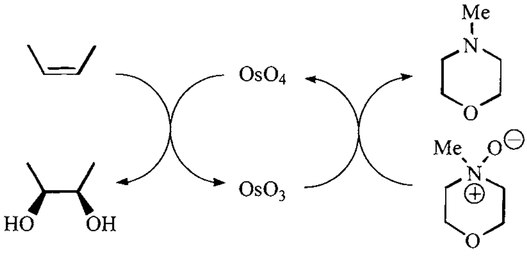
Upjohn Dihydroxylation Protocol

The Reaction:



V. VanRheenen, R. C. Kelly, D. Y. Cha, *Tetrahedron Letters* **1976**, 17, 1973

Proposed Mechanism:

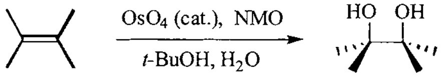


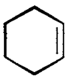
NMM
N-Methyl morpholine

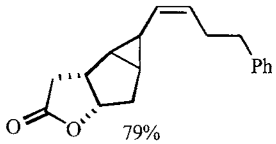
NMO
N-Methyl morpholine *N*-oxide

Notes:

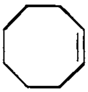
A procedure for the catalytic use of OsO_4:




91%



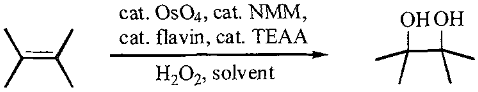
79%

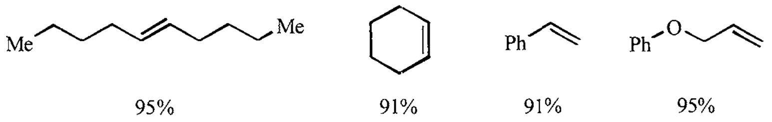

79%

V. VanRheenen, R. C. Kelly, D. Y. Cha, *Tetrahedron Letters* **1976**, 17, 1973

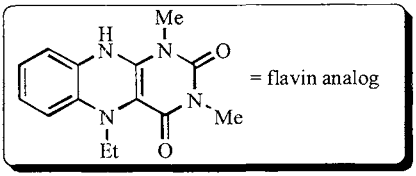
Examples:

Modification making H_2O_2 the terminal oxidant. general scheme: example substrates below.

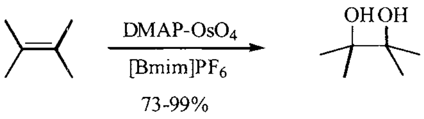




TEAA = $Et_4N^+AcO^-$ =
tetraethylammonium acetate

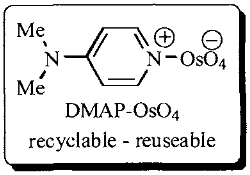


S. Y. Jonsson, K. Farnegårdh, J.-E. Backvall *Journal of the American Chemical Society* **2001**, 123, 1365

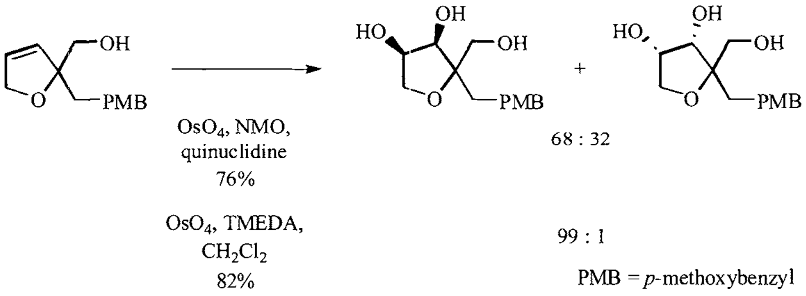


$[Bmim]PF_6$ =
1-butyl-3-methylimidazolium hexafluorophosphate

Modification using



Q. Yao *Organic Letters* **2002**, 4, 2197

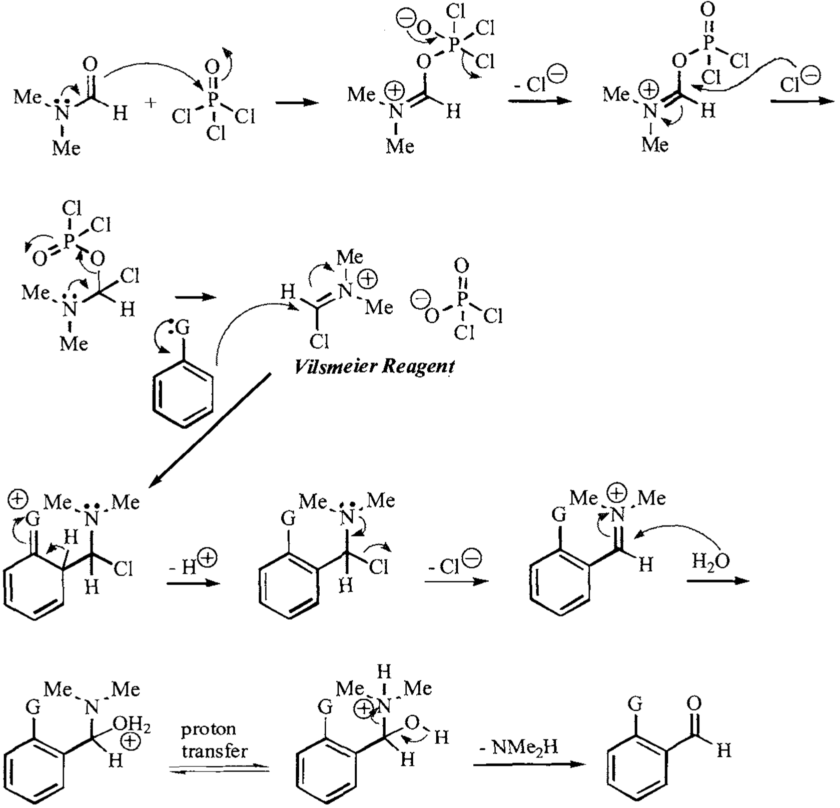


T. J. Donohoe, J. W. Fisher, P. J. Edwards *Organic Letters* **2004**, 6, 465

Vilsmeier-Haack Reaction

The Reaction:

Proposed Mechanism:



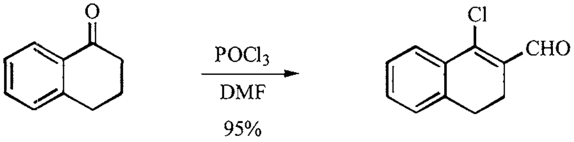
Notes:

A substituted phenyl group is shown for illustration. Heterocycles are also common substrates.

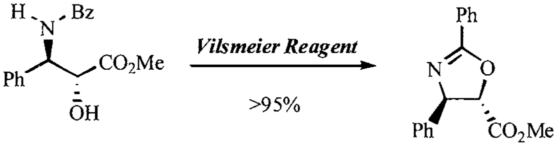
The reaction is more efficient when the aromatic ring has electron-donating groups as the G-substituent in the scheme above.

Vilsmeier chemistry can also be carried out on alkenes.

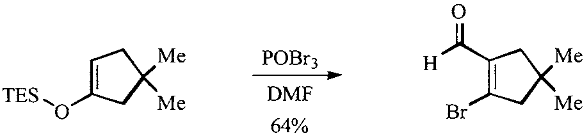
Examples:



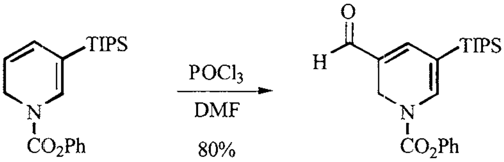
S. Hesse, G. Kirsch, *Tetrahedron Letters* **2002**, 43, 1213



P. G. M. Wutz, J. M. Northuis, T. A. Kwan, *Journal of Organic Chemistry* **2000**, 65, 9223



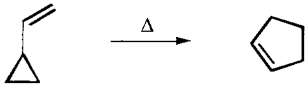
R. A. Aungst, Jr., C. Chan, R. L. Funk, *Organic Letters* **2001**, 3, 2611



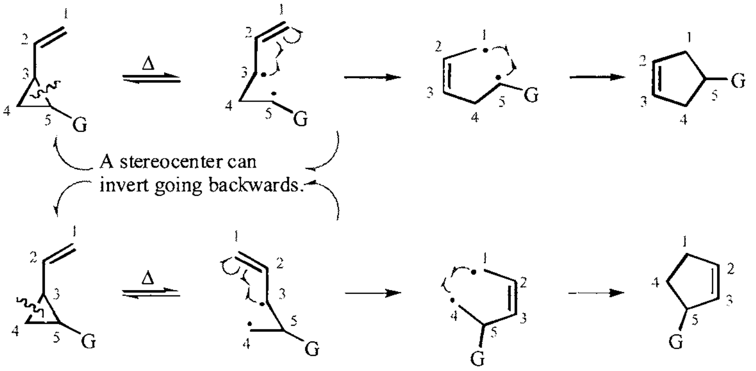
D. L. Comins, A. L. Williams, *Organic Letters* **2001**, 3, 3217

Vinylcyclopropane-Cyclopentene Rearrangement

The Reaction:

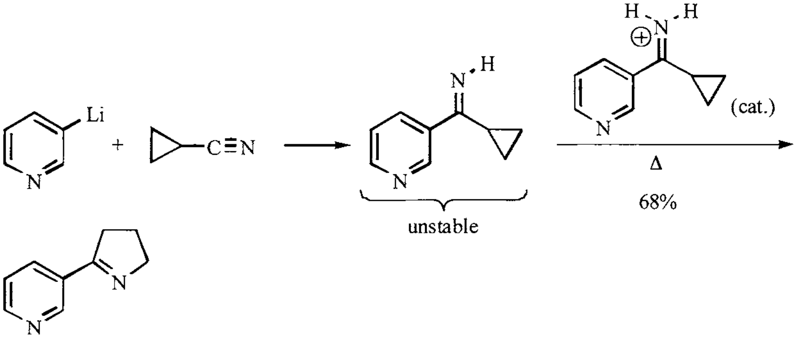


Proposed Mechanism:

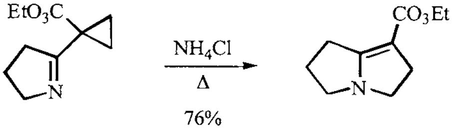


A stereocenter can invert going backwards.

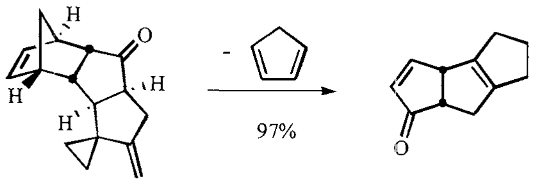
Examples:



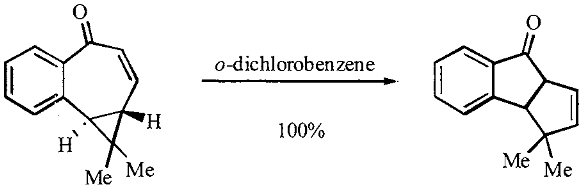
R. V. Stevens, M. C. Ellis, M. P. Wentland, *Journal of the American Chemical Society* **1968**, 90, 5576



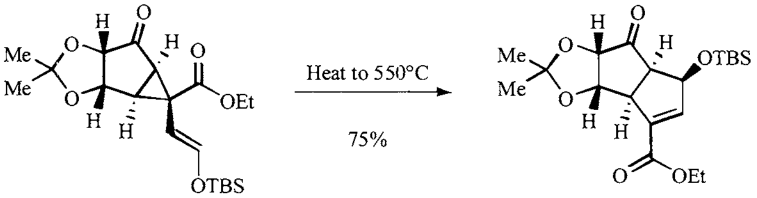
H. W. Pinnick, Y.-H. Chang, *Tetrahedron Letters* **1979**, 20, 837



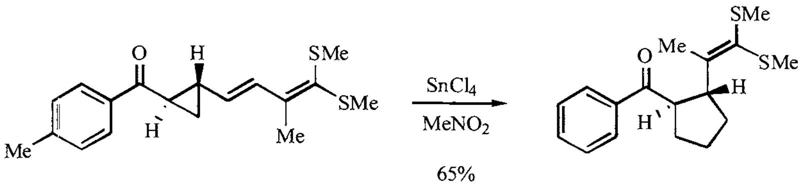
B. M. Trost, J. R. Paraquette, *Journal of Organic Chemistry* **1994**, 59, 7568



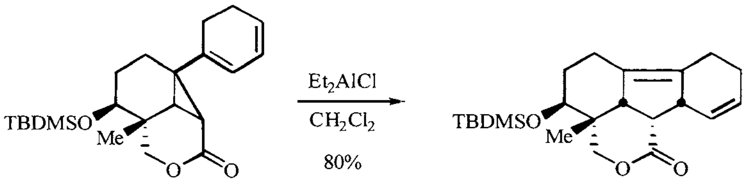
J. L. Wood, A. B. Smith, III, *Journal of the American Chemical Society* **1992**, 114, 10075



T. Hudlicky, A. Fleming, L. Radesca, *Journal of the American Chemical Society* **1989**, 111, 6691



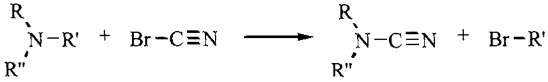
J. Satyanarayana, M. V. B. Rao, H. Ila, H. Junjappa, *Tetrahedron Letters* **1996**, 37, 3565



E. J. Corey, A. G. Myers, *Journal of the American Chemical Society* **1985**, 107, 5574

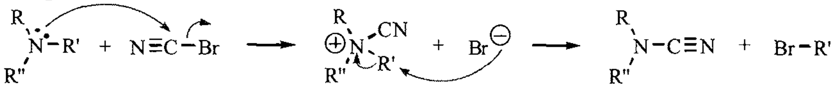
von Braun Reaction

The Reaction:



$$RR''N{-}R' + Br{-}C{\equiv}N \longrightarrow RR''N{-}C{\equiv}N + Br{-}R'$$

Proposed Mechanism:

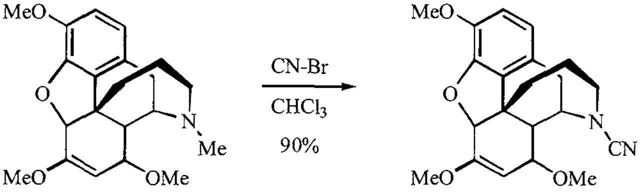


Notes:

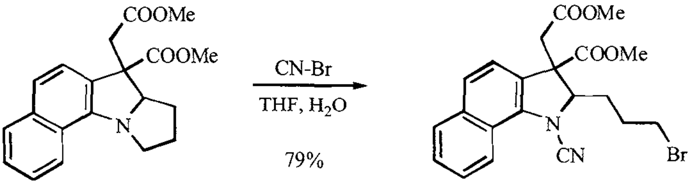
Cyanogen bromide has been classified as a "counter-attack" reagent.
See: J. R. Hwu, B. A. Gilbert, *Tetrahedron* **1989**, 45, 1233

After attack at the cyano group, the released bromide counter-attacks at the least hindered position.

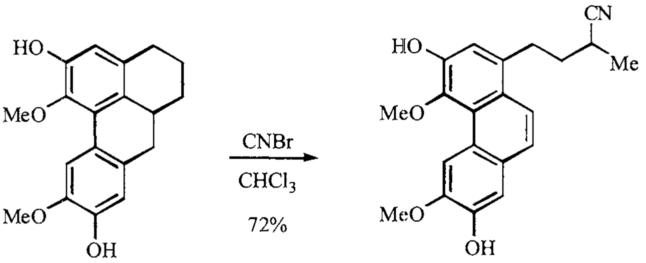
Examples:



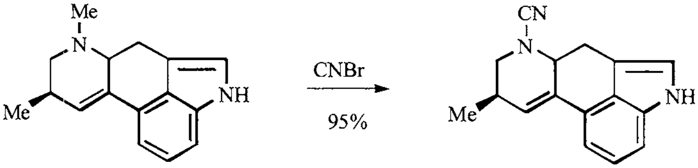
H. Rapoport, C. H. Lovell, H. R. Reist, M. E. Warren, Jr., *Journal of the American Chemical Society* **1967**, 89, 1942



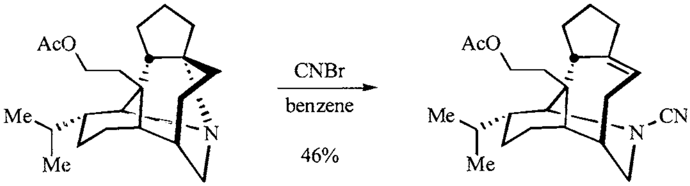
W. Verboom, G. W. Visser, D. N. Reinhoudt, *Tetrahedron* **1982**, 38, 1831



S. S.Lee, Y. J. Lin, M. Z. Chen, Y. C. Wu, C. H. Chen, *Tetrahedron Letters* **1992**, 33, 6309

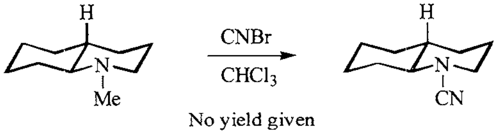


Y. Nakahara, T. Niwaguchi, H. Ishii, *Tetrahedron* **1977**, 33, 1591



H. Niwa, M. Toda, S. Ishimaru, Y. Hirata, S. Yamamura, *Tetrahedron* **1974**, 30, 3031

This work was a kinetic study showing the reaction is extremely fast.

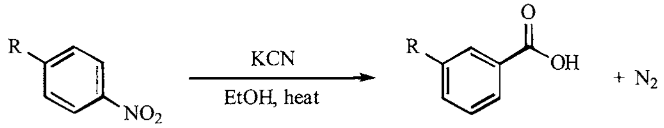


G. Fodor, S. Abidi, *Tetrahedron Letters* **1971**, 12, 1369

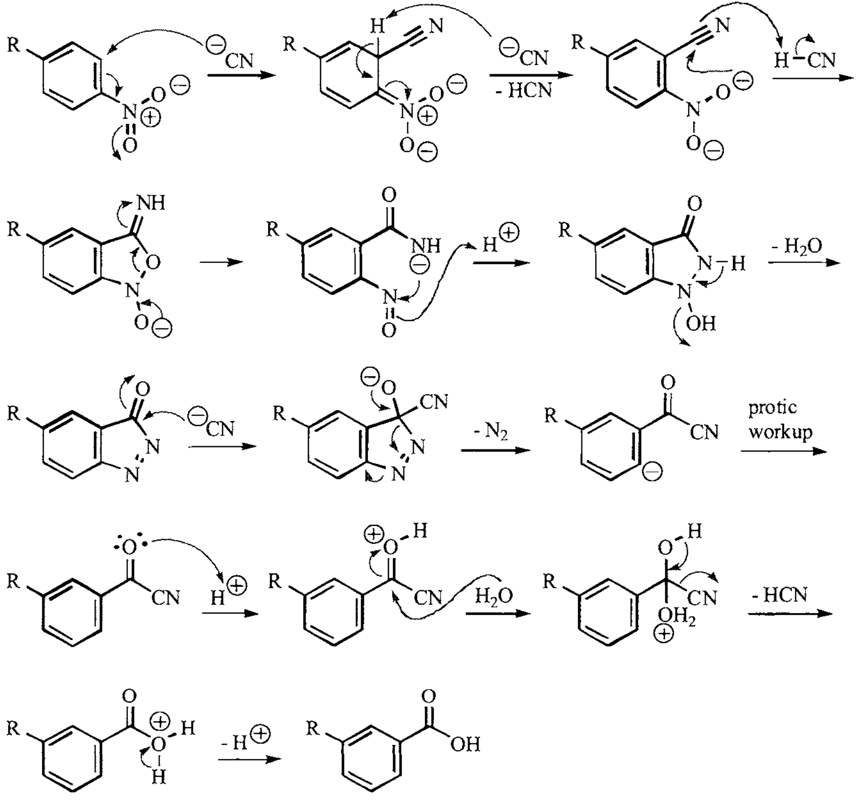
28

von Richter Reaction

The Reaction:



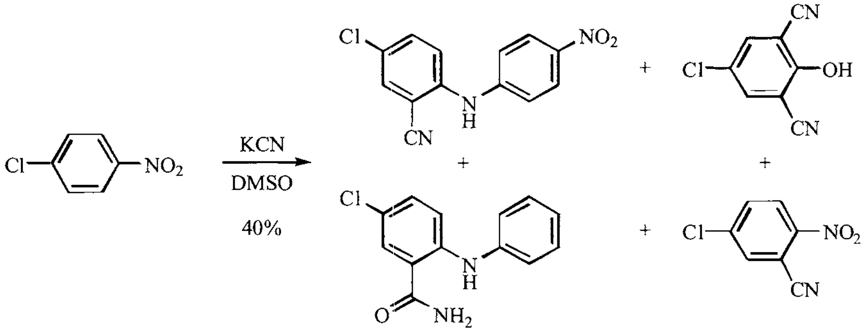
Proposed Mechanism:



M. Rosenblum, *Journal of the American Chemical Society* **1960**, 82, 3796

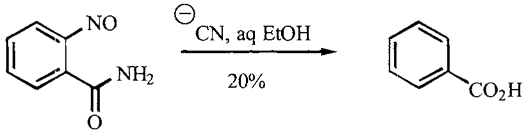
Examples:

Note solvent change:

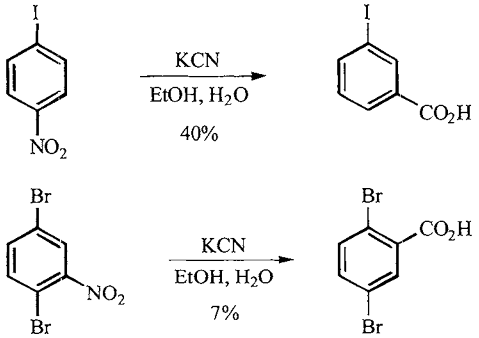


G. T. Rogers, T. L. V. Ulbricht, *Tetrahedron Letters* **1968**, 9, 1029

This substrate was subjected to the reaction conditions to test the validity of it being a proposed intermediate.



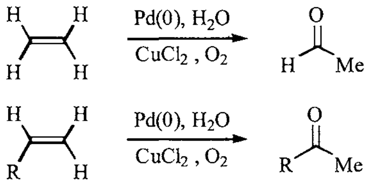
K. M. Ibne-Rasa, E. Koubak, *Journal of Organic Chemistry* **1963**, 28, 3240



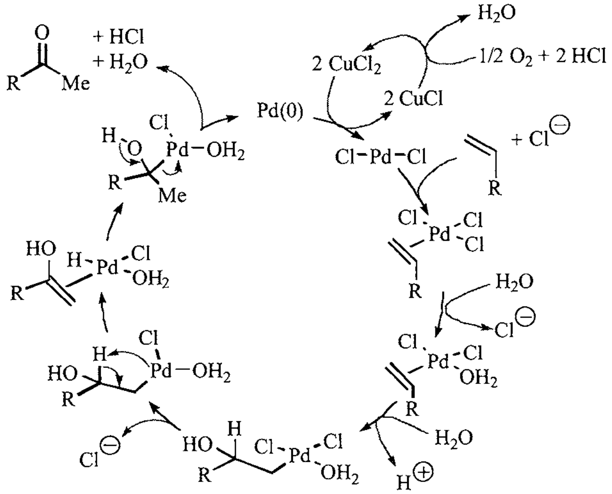
J. F. Bunnett, M. Rauhut, M. D. Knutson, G. E. Bussell, *Journal of the American Chemical Society* **1954**, 76, 5755

Wacker Oxidation Reaction

The Reaction:



Proposed Mechanism:



See O. Hamed, C. Thompson, P.M. Henry, *Journal of Organic Chemistry* **1997**, 62, 7082 for useful mechanistic discussion.

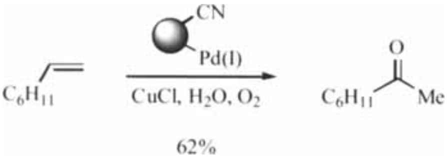
Notes:

Attack of water is always at the more substituted carbon of the alkene. Given competition between a terminal alkene and a more substituted one, preference will be for the terminal bond.

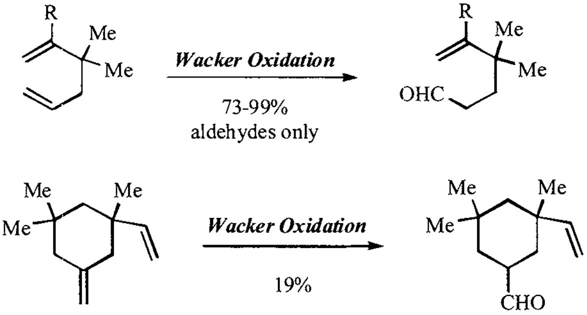
Catalytic Asymmetric Wacker-Type Cyclization

Y. Uozumi, K. Kato, T. Hayashi, *Journal of the American Chemical Society* **1997**, 119, 5063

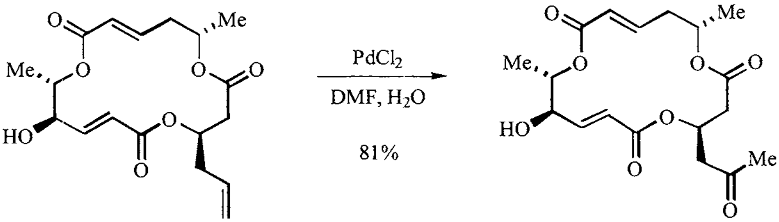
Examples:



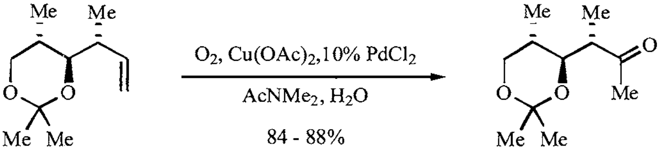
J.-H. Ahn, D. C. Sherrington, *Macromolecules* **1996**, 29, 4164



T.-L. Ho, M. H.Chang, C. Chen, *Tetrahedron Letters* **2003**, 44, 6955



Y. Kobayashi, Y.-G. Wang, *Tetrahedron Letters* **2002**, 43, 4381

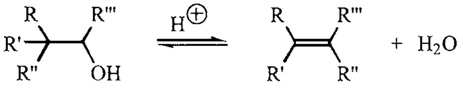


A. B. Smith, III, Y. S. Cho, G. K. Friestad, *Tetrahedron Letters* **1998**, 39, 8765

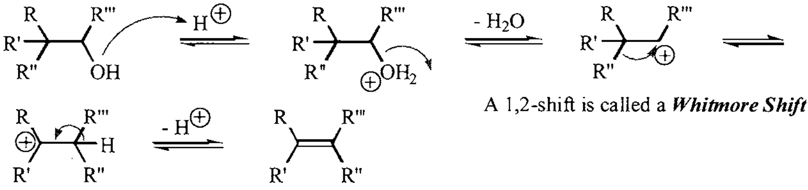
Wagner-Meerwein Rearrangement

See: L. Birladeanu, "The Story of the Wagner-Meerwein Rearrangement", *Journal of Chemical Education* **2000**, 77, 858

The Reaction:



Proposed Mechanism:

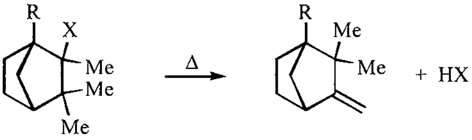


A 1,2-shift is called a ***Whitmore Shift***.

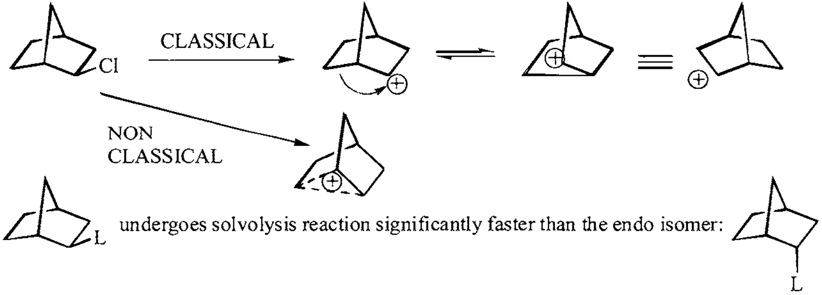
Notes:

M. B. Smith, J. March *in March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1393

The rearrangement of camphene hydrochloride is called the ***Nametkin Rearrangement***

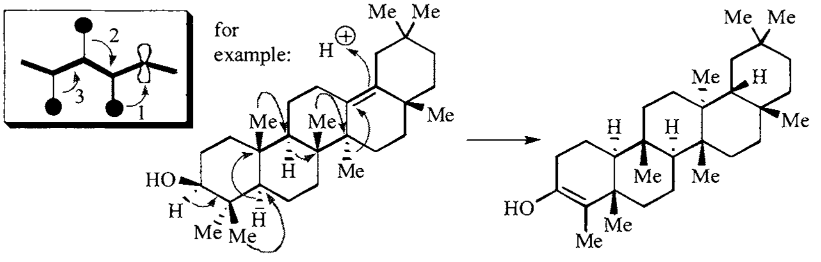


The "classical" - "non-classical" carbocation controversy concerned the ***Wagner-Meerwein rearrangement*** of norbornyl systems:



undergoes solvolysis reaction significantly faster than the endo isomer:

The reaction is also regulated by stereoelectronic factors:



β-Amyrin

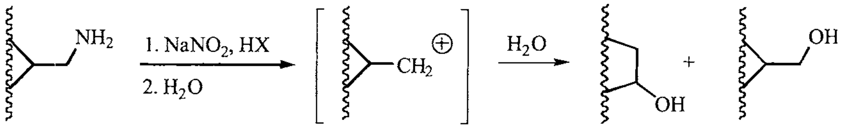
enol of Freidelin

E. J. Corey, J. J. Ursprung, *Journal of the American Chemical Society* **1956**, 78, 5041

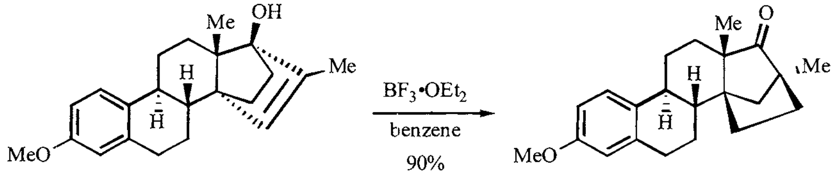
Examples:

Demjanov (Demyanov) Rearrangement

The Reaction:

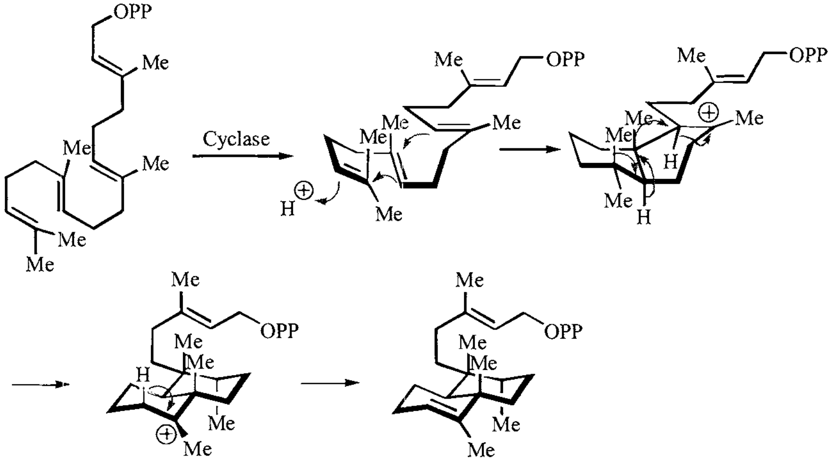


Examples:

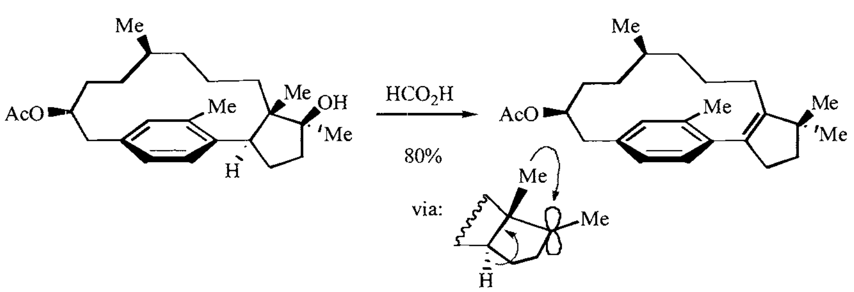


J. R. Bull, K. Bischofberger, R. I. Thomson, J. L. M. Dillen, P. H. Van Rooyen, *Journal of the Chemical Society, Perkin Transactions 1* **1992**, 2545

A detailed biosynthetic pathway analysis:



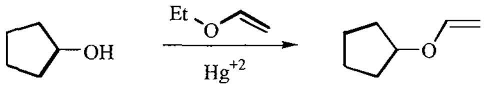
T. Eguchi, Y. Dekishima, Y. Hamano, T. Dairi, H. Seto, K. Kakinuma, *Journal of Organic Chemistry* **2003**, 68, 5433



S. Baeurle, T. Blume, A. Mengel, C. Parchmann, W. Skuballa, S. Baesler, M. Schaefer, D. Suelzle, H.-P. Wrona-Metzinger, *Angewandte Chemie, International Edition in English* **2003**, 42, 3961

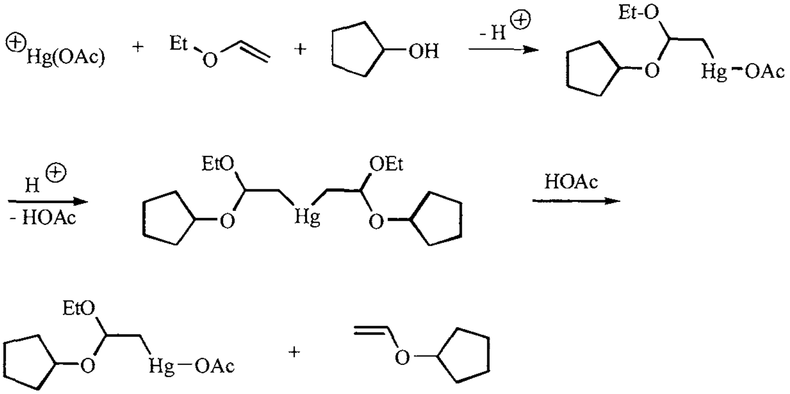
Watanabe-Conlon Transvinylation

The Reaction:



Proposed Mechanism:

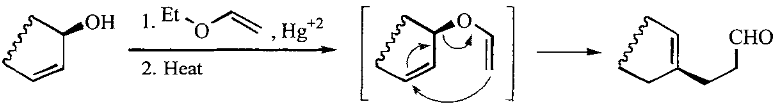
$$Hg(OAc)_2 \rightleftharpoons \overset{\oplus}{Hg(OAc)} + AcO^{\ominus}$$



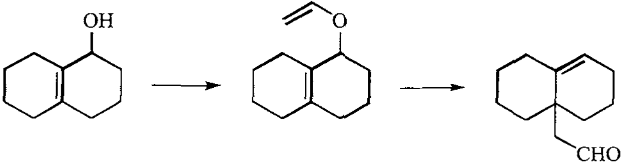
Notes:

This reaction generally uses about 10% molar equivalent of $Hg(OAc)_2$.

This reaction is generally part of a sequence followed by ***Claisen rearrangement*** to generate a remote functional group (aldehyde).

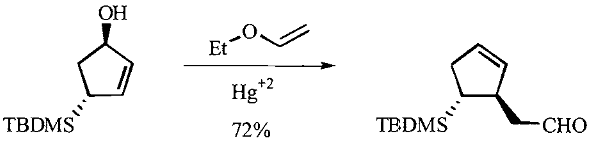


This approach was developed by Burgstahler for:

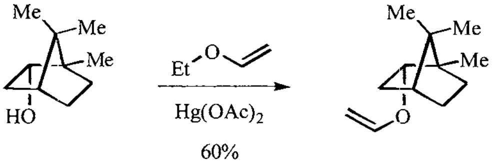


A. W. Burgstahler, I. C. Nordin, *Journal of the American Chemical Society* **1959**, 81, 3151

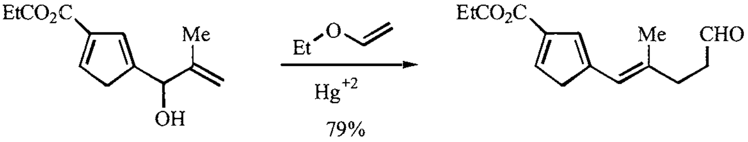
Examples:



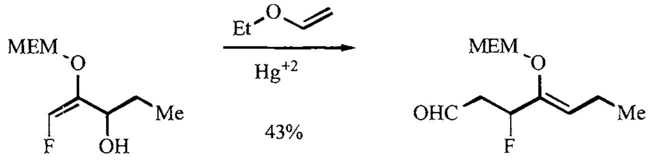
D. L. J. Clive, H. W. Manning, *Journal of the Chemical Society, Chemical Communications*. **1993**, 666



V. Godebout, S. Leconte, F. Levasseur, L. Duhamel, *Tetrahedron Letters* **1996**, 37, 7255



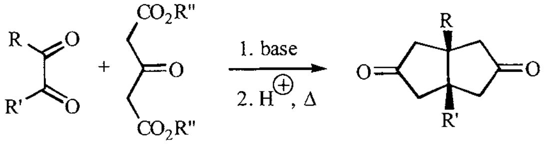
D. H. Williams, D. J. Faulkner, *Tetrahedron* **1996**, 52, 4245



S. T. Patel, J. M. Percy, S. D. Wilkes, *Tetrahedron* **1995**, 51, 11327

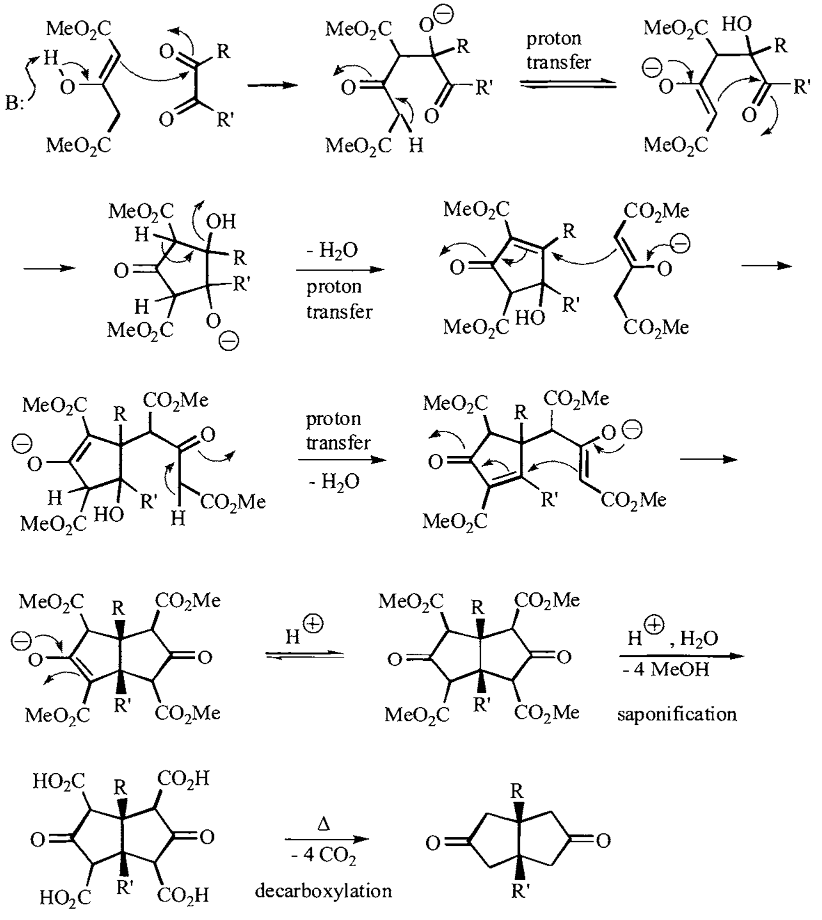
Weiss Reaction

The Reaction:



R's = H, alkyl, aryl or could be a cyclobutane ring or larger

Proposed Mechanism:

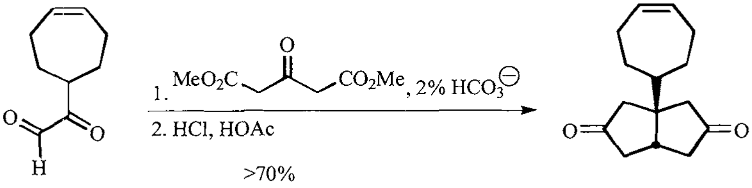


Notes:

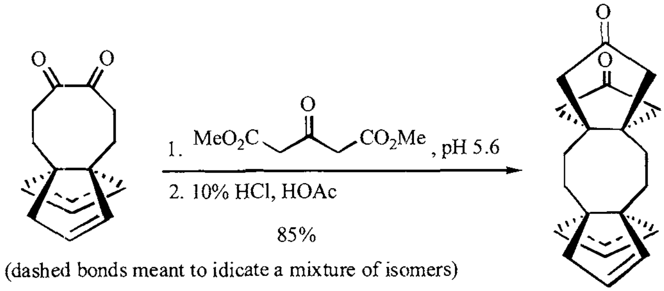
A number of examples are reported in:

U. Weiss, J. M. Edwards, *Tetrahedron Letters* **1968**, 9, 4885

Examples:

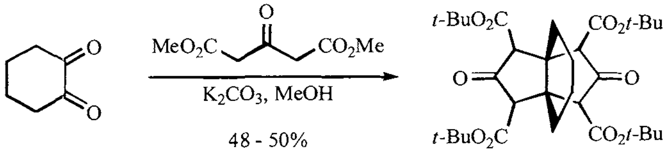


G. Kubiak, X. Fu, K. Bupta, J. M. Cook, *Tetrahedron Letters* **1990**, 31, 4285

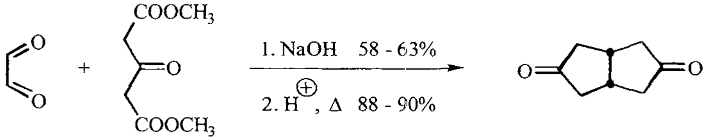


(dashed bonds meant to idicate a mixture of isomers)

L. A. Paquette, M. A. Kesselmayer, G. E. Underiner, S. D. House, R. D. Rogers, K. Meerholz, J. Heinze, *Journal of the American Chemical Society* **1992**, 114, 2652



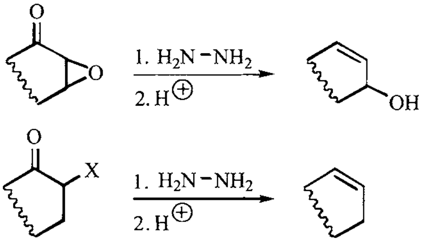
A. K. Gupta, J. M. Cook, U. Weiss, *Tetrahedron Letters* **1988**, 29, 2535



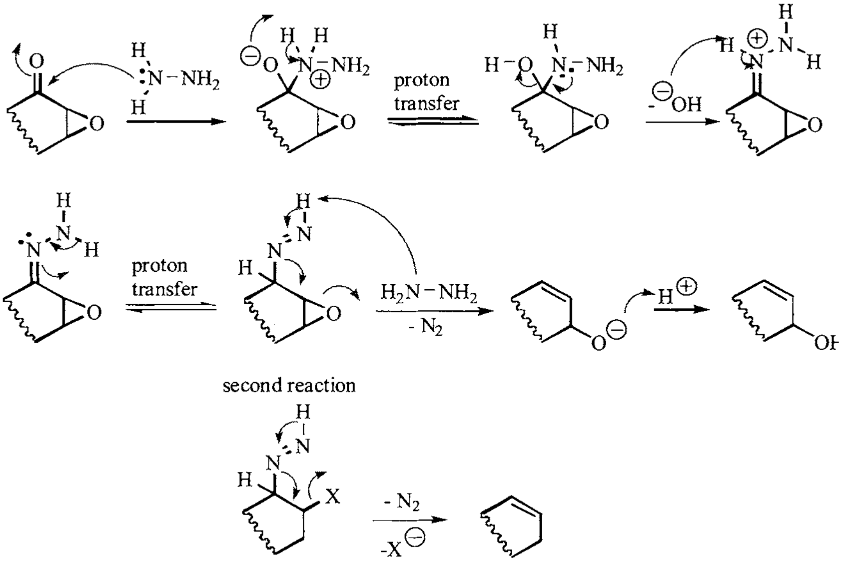
S. H. Bertz, J. M. Cook, A. Gawish, U. Weiss, *Organic Synthesis* CV 7, 50

Wharton Olefination

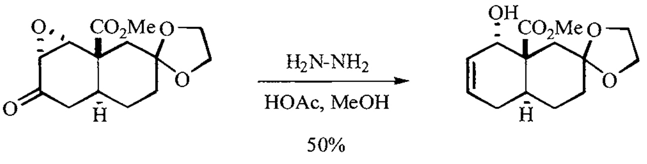
The Reaction:



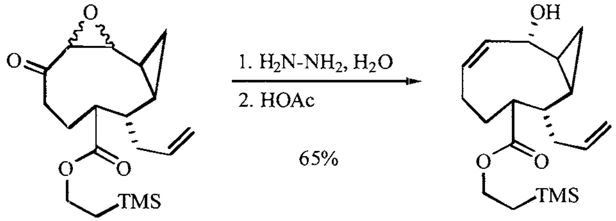
Proposed Mechanism:



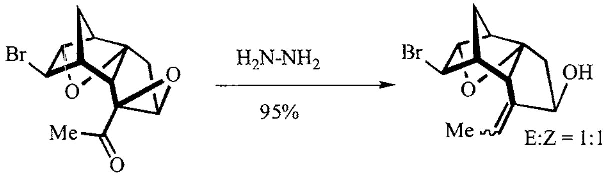
Examples:



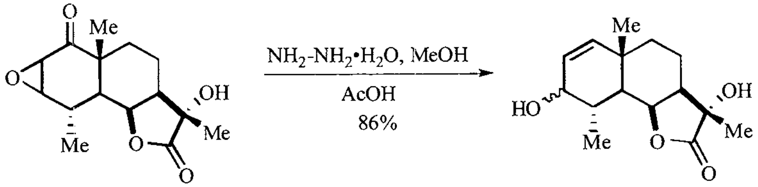
P. A. Zoretic, R. J. Chambers, G. D. Marbury, A. A. Riebiro, *Journal of Organic Chemistry* **1985**, 50, 2981



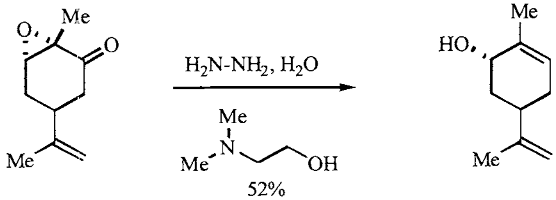
G. Kim, M. Y. Chu-Moyer, S. J. Danishefsky, G. K. Schulte, *Journal of the American Chemical Society* **1993**, 115, 30



T. Sugahara, H. Fukuda, Y. Iwabuchi, *Journal of Organic Chemistry* **2004**, 69, 1744



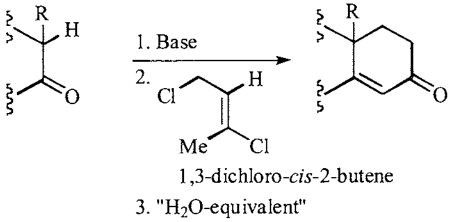
F. J. Moreno-Dorado, F. M. Guerra, F. J. Aladro, J. M. Bustamante, Z. D. Jorge, G. M. Massanet, *Journal of Natural Products* **2000**, 63, 934



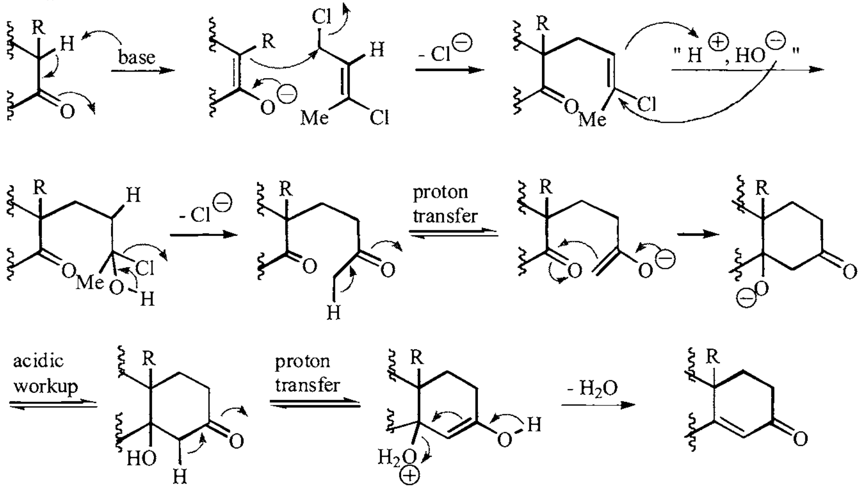
L. Castedo, J. L. Mascarenas. M. Mourino, *Tetrahedron Letters* **1987**, 28, 2099

Wichterle Reaction

The Reaction:



Proposed Mechanism:

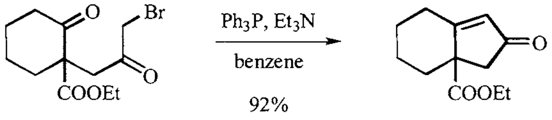


Notes:

This is a modification of the ***Robinson annulation*** in which 1,3-dichloro-*cis*-2-butene is used in place of methyl vinyl ketone.

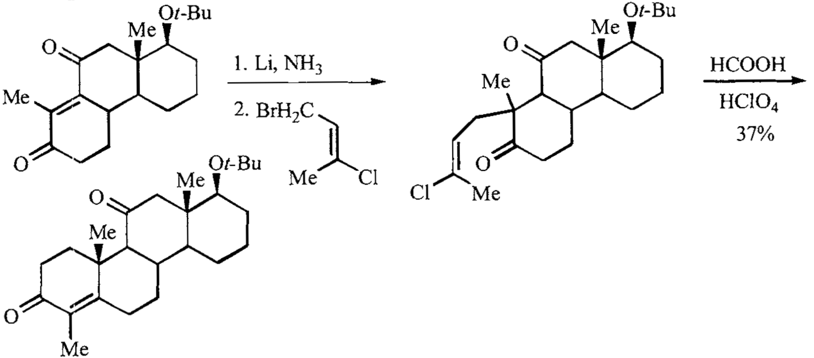
A number of "H^+ OH^- " equivalents are used: ***Oxymercuration*** conditions or formic acid and protic acid, followed by hydrolysis of the formate ester are two common approaches.

A variation of this approach:

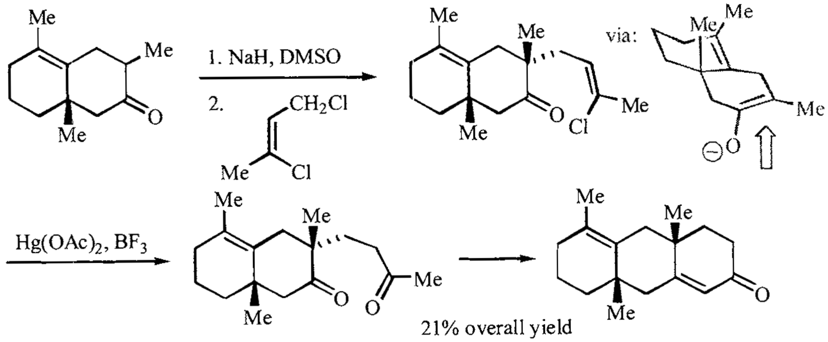


M. P. VanBrunt, R. O. Ambenge, S. W. Weinreb, *Journal of Organic Chemistry* **2003**, 68, 3323

Examples:



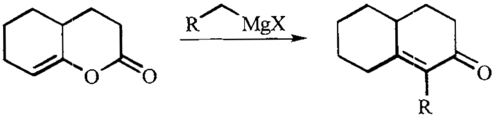
G. Stork, E. W. Logusch, *Journal of the American Chemical Society*, **1980**, 102, 1219



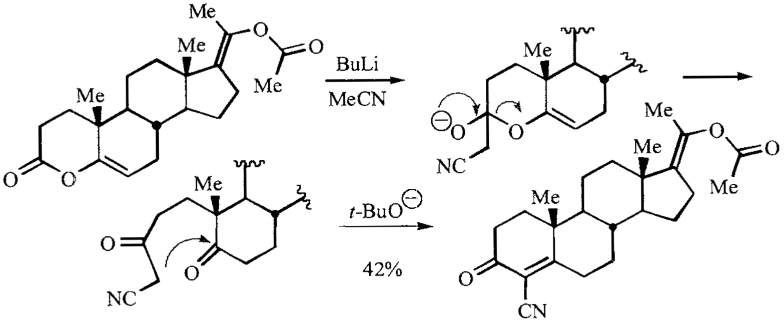
L. A. Paquette, D. T. Belmont, Y.-L. Hsu, *Journal of Organic Chemistry* **1985**, 50, 4667

Fujimoto-Belleau Reaction

The Reaction:



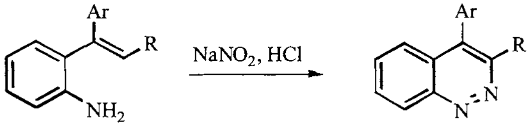
Mechanistic Example:



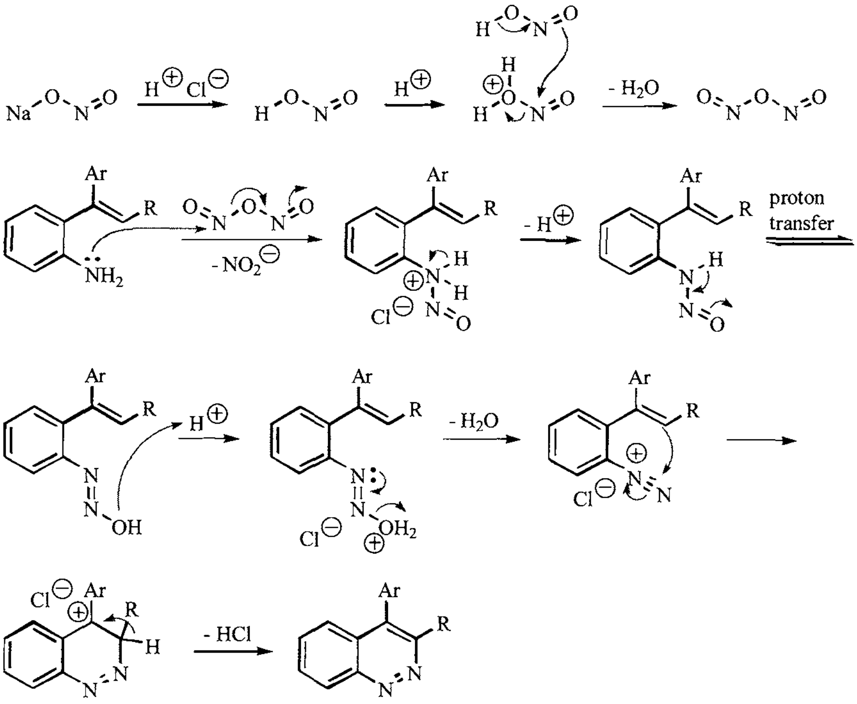
M. Haase-Held, M. Hatzis, J. Mann, *Journal of the Chemical Society Perkin Transactions 1* **1993**, 2907

Widman-Stoermer Synthesis

The Reaction:



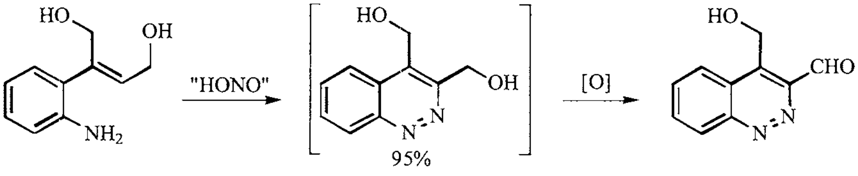
Proposed Mechanism:



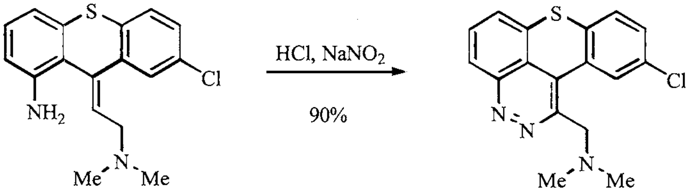
Notes:

See the ***Borsche Cinnoline Synthesis*** and the ***von Richter Cinnoline Synthesis*** for other preparations of cinnolines.

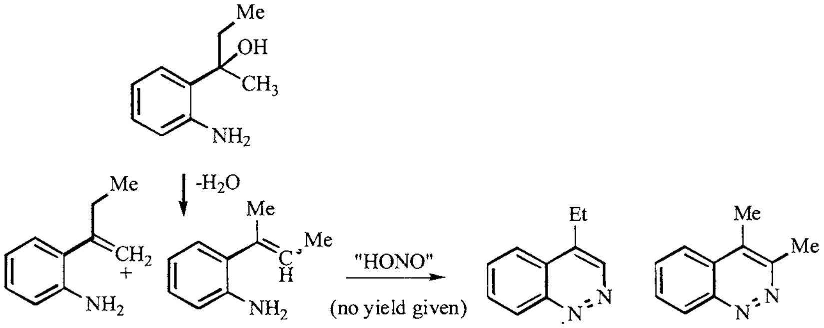
Examples:



J. W. Barton, N. D. Pearson, *Journal of the Chemical Society, Perkin Transactions 1*, **1987**, 1541



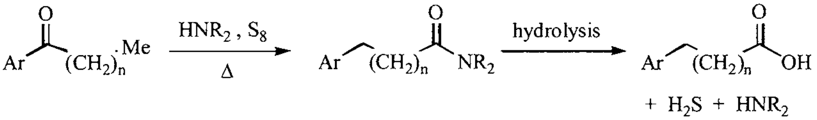
B. S. Ross, R. A. Wiley, *Journal of Medicinal Chemistry* **1985**, 28, 870



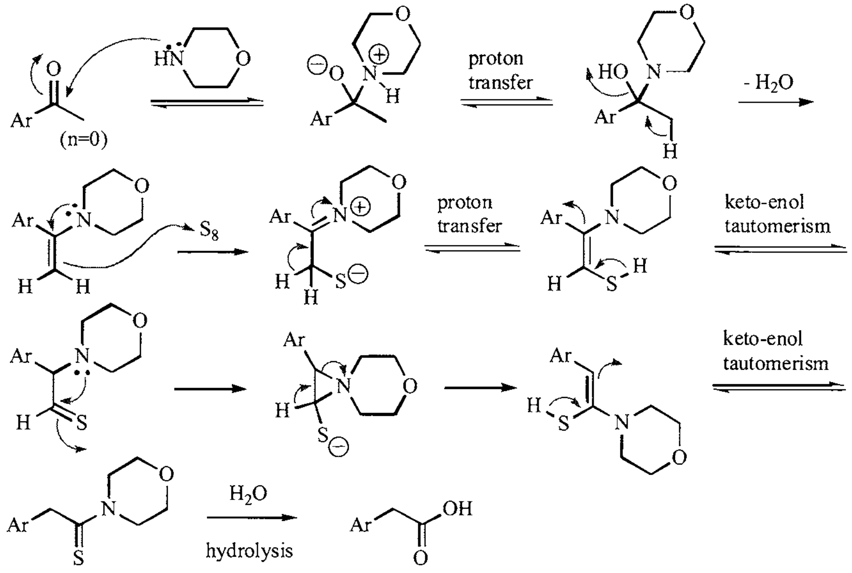
M. H. Palmer, P. S. McIntyre, *Tetrahedron* **1971**, 27, 2913

Willgerodt-Kindler Reaction

The Reaction:



Proposed Mechanism:

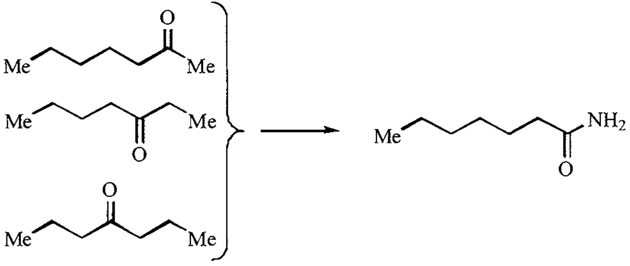


Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1567; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, pp. 267-269.

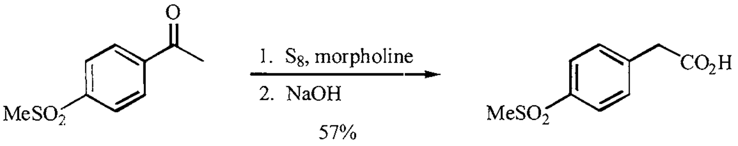
The original ***Willgerodt Reaction*** conditions required high temperature and pressure, with use of ammonium polysulfide $(NH_4)_2S_x$ and H_2O to give either an amide or the ammonium salt of the corresponding acid. ***Kindler's modification***, shown above, eliminated these problems and substituted S_8 and a dry amine, most commonly morpholine.

The reaction will introduce the acid at the terminal carbon, no matter where the carbonyl position is occupied in the starting material:

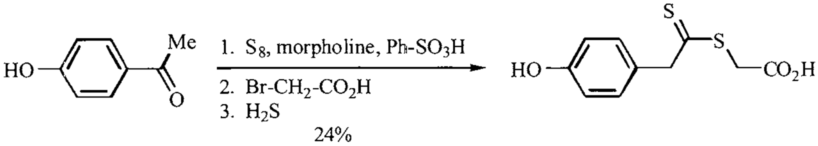


L. Cavalieri, D. B. Pattison, M. Carmack, *Journal of the American Chemical Society* **1945**, 67, 1783

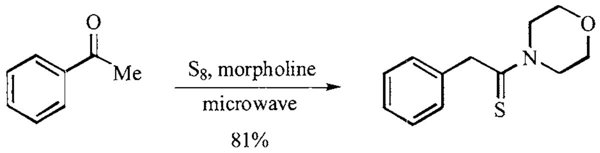
Examples:

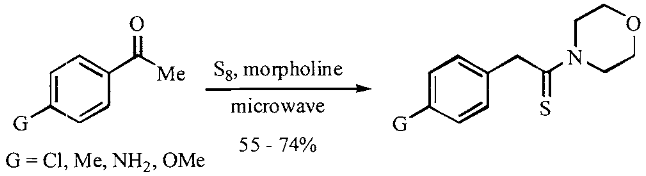


I. W. Davies, J.-F. Marcoux, E. G. Corley, J. Journet, D.-W Cai, M Palucki, J. Su, R. D. Larsen, K. Rossen, P. J. Pye, L. DeMichele, P. Dormer, P. J. Reider, *Journal of Organic Chemistry* **2000**, 65, 8415

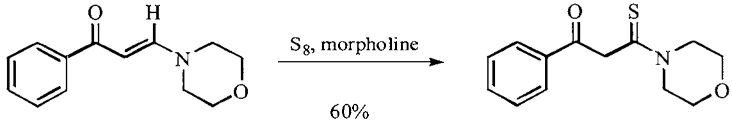


G. Levesque, P. Arsene, V. Fanneau-Bellenger, T.-N. Pham, *Biomacromolecules* **2000**, 1, 387





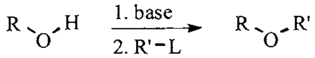
M. Mooshabadi, K. Aghapoor, H. R. Darabi, M. M. Mujtahedi, *Tetrahedron Letters* **1999**, 40, 7549



T. Bacchetti, A. Alemagna, B. Daniel, *Tetrahedron Letters* **1965**, 6, 2001

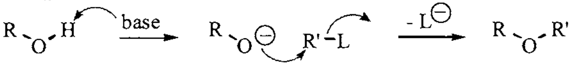
Williamson Ether Synthesis

The Reaction:



L = leaving group = -X, -OTs, -OMs, O-SO_3R'

Proposed Mechanism:

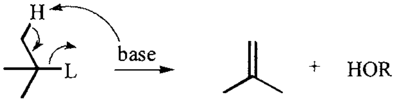


Most ***Williamson Ether Syntheses*** proceed by an S_N2 mechanism. Stereochemical inversions can be expected, where appropriate, as a result.

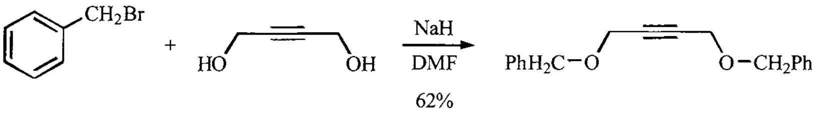
Notes:

Secondary R groups usually give low yields.

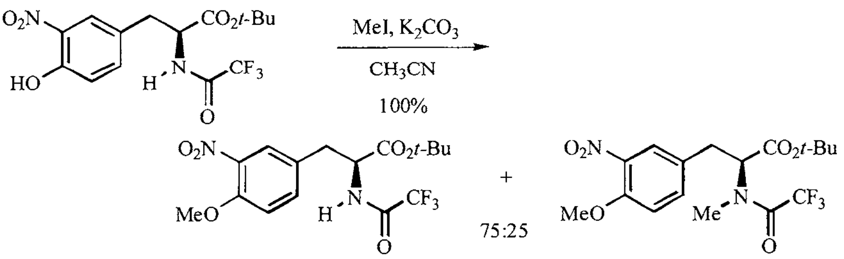
Tertiary R groups are typically not successful due to elimination:



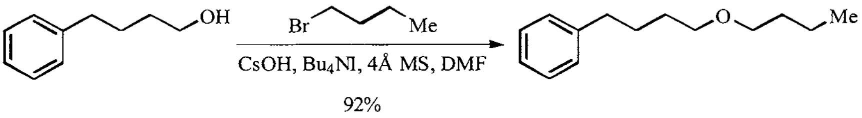
Examples:



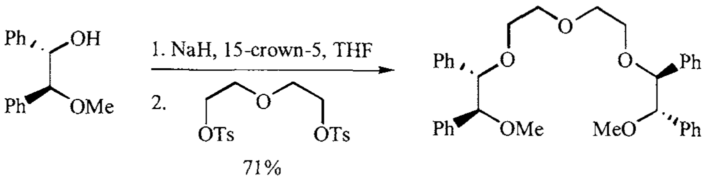
S. Hecht, J. M. Frechet, *Journal of the American Chemical Society* **1999**, 121, 4084



M. Attolini, T. Boxus, S. Biltresse, J. Marchand-Brynaert, *Tetrahedron Letters* **2002**, 43, 1187

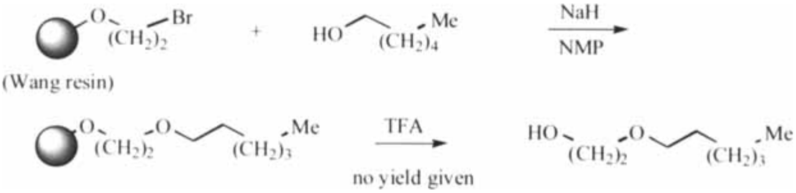


E. E. Dueno, F. Chu, S.-I. Kim, J. W. Jung, *Tetrahedron Letters* **1999**, 40, 1843



H. C. Aspinall, N. Greeves, W.-M. Lee, E. G. McIver, P. M. Smith, *Tetrahedron Letters* **1997**, 38, 4679

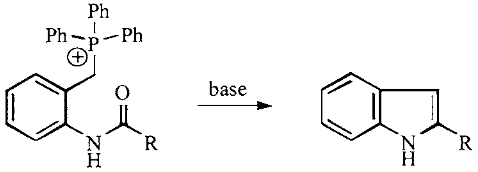
This work discusses the question of substitution vs. elimination, and has useful commentary from a synthetic point of view.



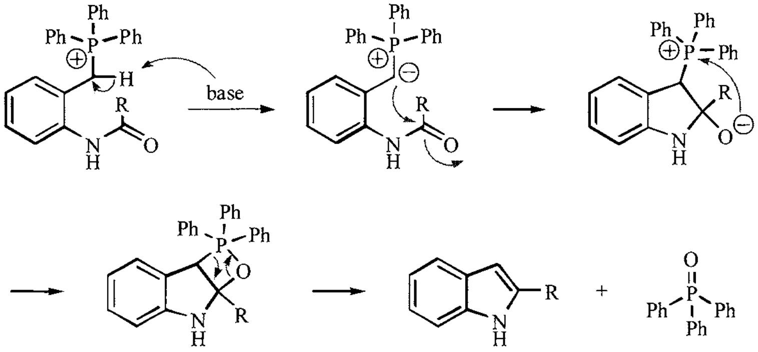
A. Weissberg, A. Dahan, M. Portnoy, *Journal of Combinatorial Chemistry* **2001**, 3, 154

Wittig Indole Synthesis

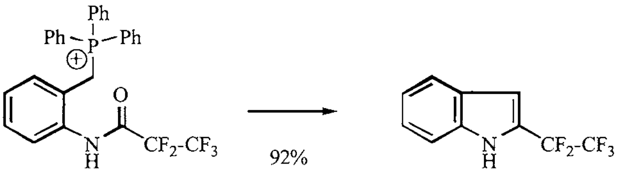
The Reaction:



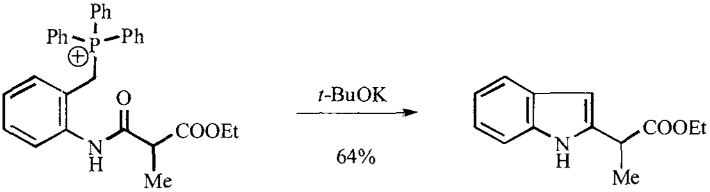
Proposed Mechanism:



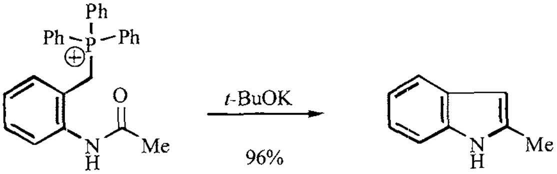
Examples:



K. Miyashita, K. Kondoh, K. Tsuchiya, H. Miyabe, T. Imanishi, *Journal of the Chemical Society: Perkin Transactions 1* **1996**, 1261



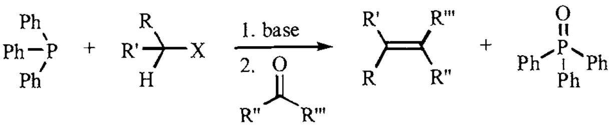
B. Danieli, G. Lesma, G. Palmisano, D. Passarella, A. Silvani, *Tetrahedron* **1994**, 50, 6941



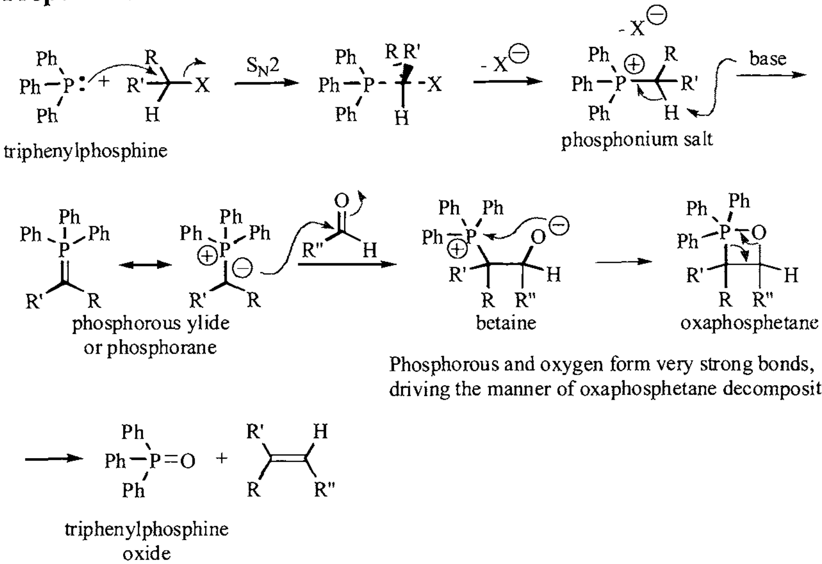
M. Le Corre, Y. Le Stane, A. Hercouet, H. Le Brown, *Tetrahedron* **1985**, 41, 5313

Wittig Reaction (Wittig Olefination Reaction)

The Reaction:



Proposed Mechanism:



Phosphorous and oxygen form very strong bonds, driving the manner of oxaphosphetane decomposition.

Notes:

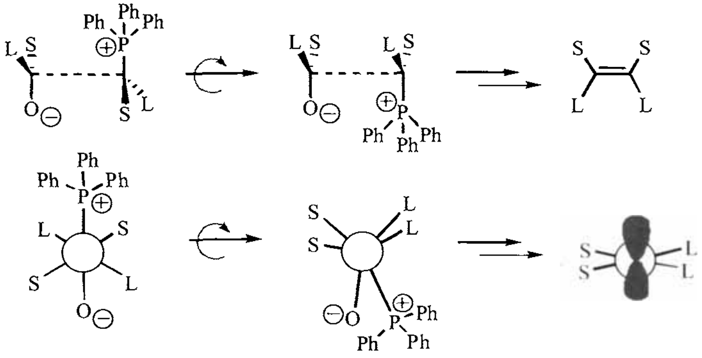
Other phosphines may be used for this reaction, but the choice should not contain a protons that could be abstracted as is the proton on the halide coupling partner, as a mixture of desired and undesired ylides would be formed.

Usually, one uses a strong base such as BuLi, NaNH$_2$ / NH$_3$, NaH or NaOR.

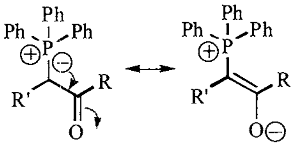
Preferred anti attack of ylide, minimizing steric interactions.

Bond rotation follows to form the betaine.

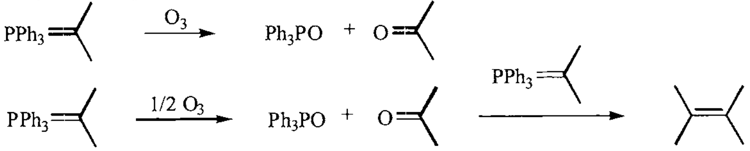
As a result, this reaction often gives the cis / Z - alkene.



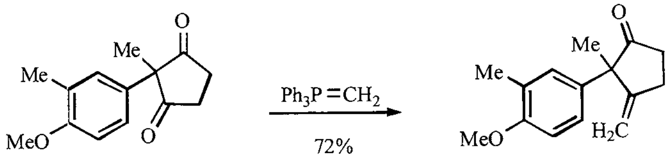
If the halide contains an electron withdrawing group, the negative charge in the ylide is delocalized, decreasing its nucleophilicity and reactivity. Aldehydes may still react, but ketones most likely will not.



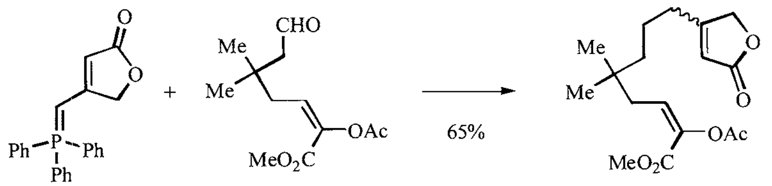
Bestman's Protocol: The intermediate ylide can be cleaved by ozone. By careful addition one can carry out a unique ***Wittig reaction***:



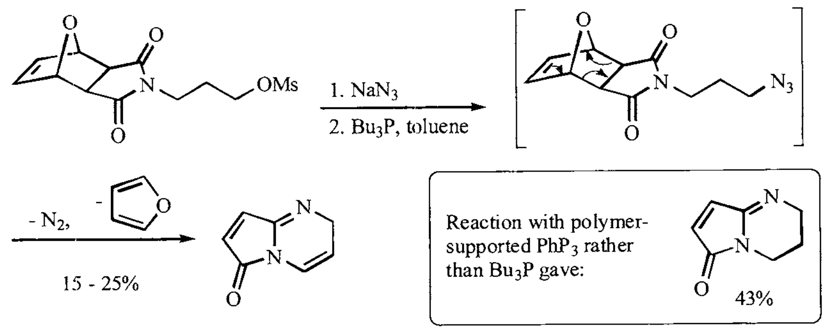
Examples:



S. P. Chavan, R. K. Kharul, R. R. Kale, D. A. Khobragade, *Tetrahedron* **2003**, 59, 2737



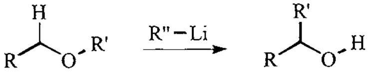
R. K. Boeckman, Jr., T. R. Aless, *Journal of the American Chemical Society* **1982**, 104, 3216



B. J. Neubert, B. B. Snider, *Organic Letters* **2003**, 5, 765

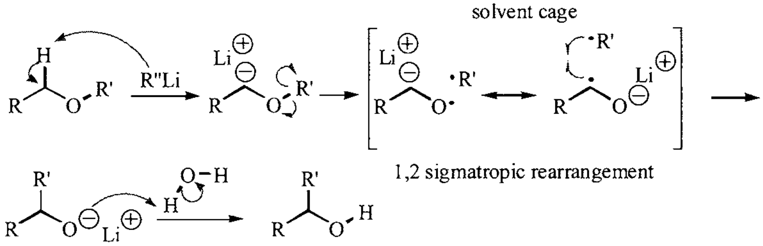
[1,2]-Wittig Rearrangement

The Reaction:



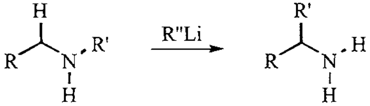
R = H, Alkl, Aryl, Alkenyl, Alkynyl, -COOR, -COOM
R' = Alkyl, Ally, Benzyl, Aryl

Proposed Mechanism:

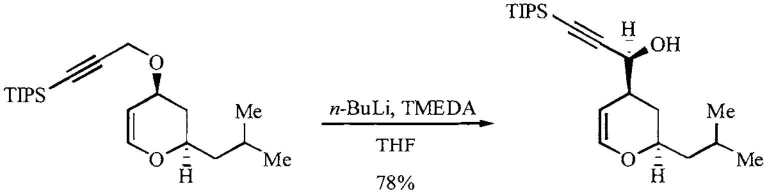


Notes:

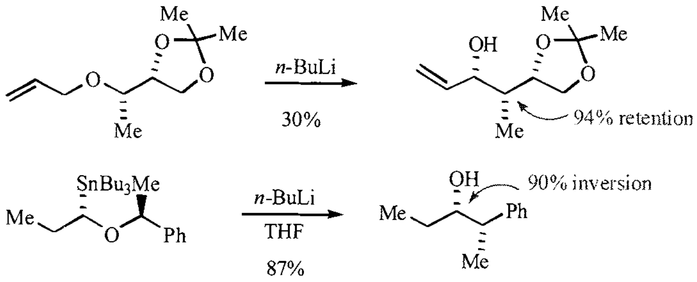
The oxygen can be replaced by nitrogen and then the reaction is known as ***[1,2]-Aza-Wittig Rearrangement***:



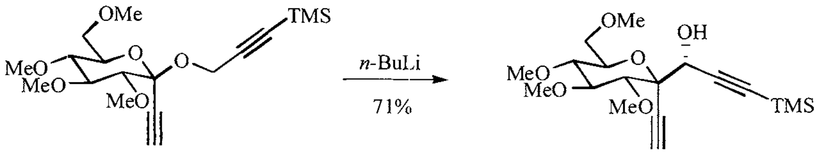
Examples:



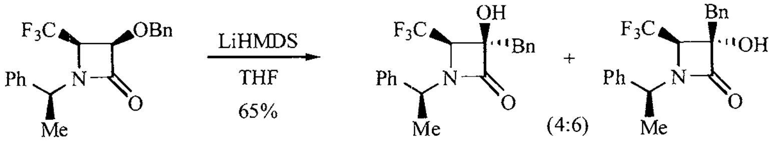
P. Wipf, T. H. Graham, *Journal of Organic Chemistry* **2003**, 68, 8798



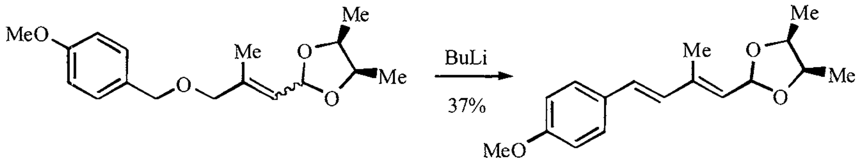
R. E. Maleczka, Jr., F. Geng, *Journal of the American Chemical Society* **1998**, 120, 8551



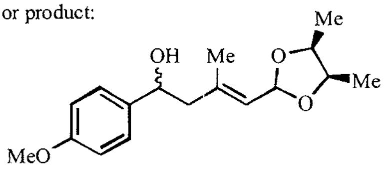
K. Tomooka, H. Yamamoto, T. Nakai, *Journal of the American Chemical Society* **1996**, 118, 3317



A. Garbi, L Allain, F. Chorki, M. Ourevitch, B. Crousse, D. Bonnet-Delpon, T. Nakai, J.-P. Begue, *Organic Lett*ers **2001**, 3, 2529



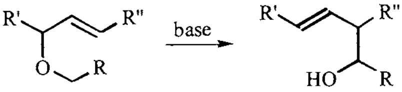
Via dehydration of major product:



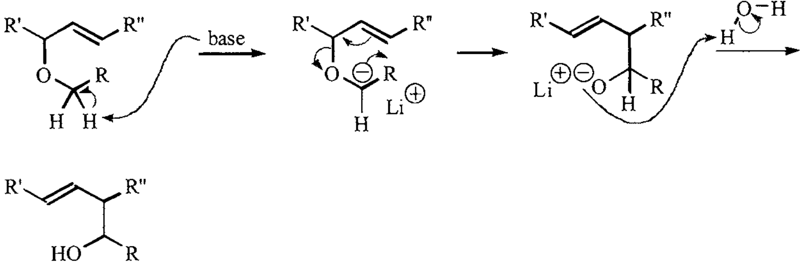
L. Lemiegre, T. Regnier, J.-C. Combret, J. Maddaluno, *Tetrahedron Letters* **2003**, 44, 373

[2,3]-Wittig Rearrangement

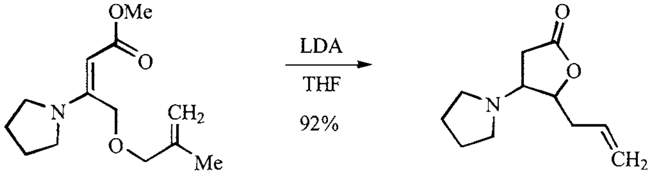
The Reaction:



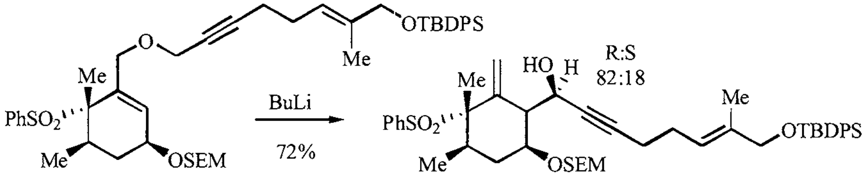
Proposed Mechanism:



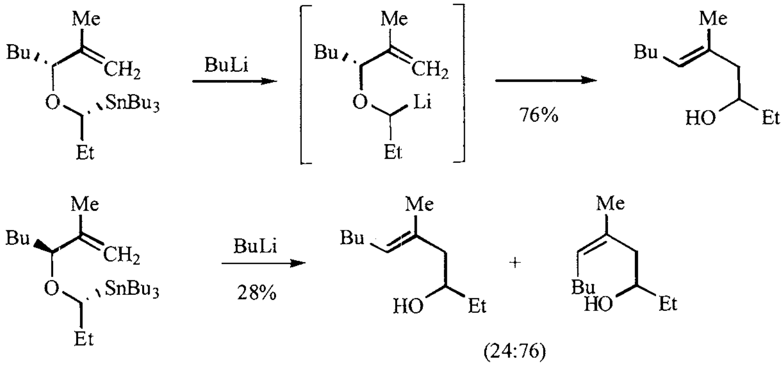
Examples:



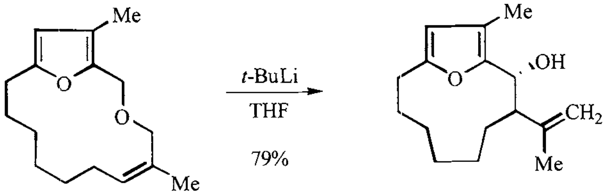
Y. J. Li, P.-T. Lee, C.-M. Yang, Y.-K. Chang, Y.-C. Weng, Y.-H. Liu, *Tetrahedron Letters* **2004**, 45, 1865



A. S. Balnaves, G. McGowan, P. D. P. Shapland, E. J. Thomas, *Tetrahedron Letters* **2003**, 44, 2713



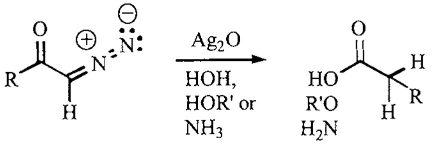
K. Tomooka, T. Igarashi, N. Kishi, T. Nakai, *Tetrahedron Letters* **1999**, 40, 6257



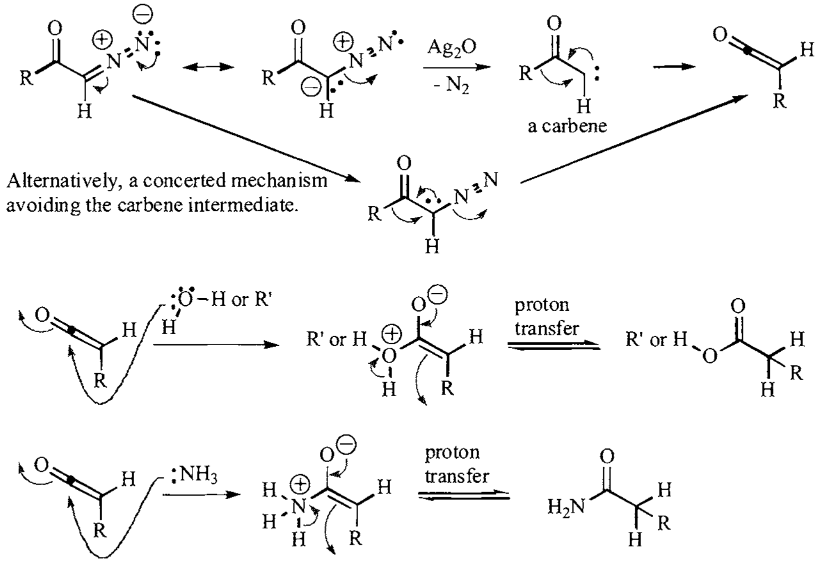
M. Tsubuki, K. Takahashi, T. Honda, *Journal of Organic Chemistry* **2003**, 68, 10183

Wolff Rearrangement

The Reaction:



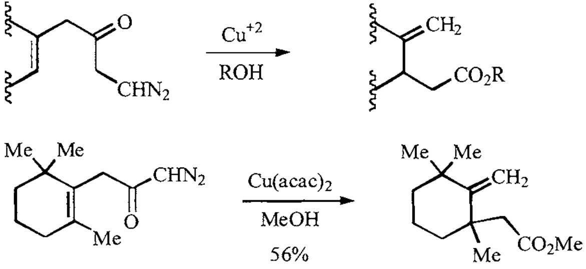
Proposed Mechanism:


Alternatively, a concerted mechanism avoiding the carbene intermediate.

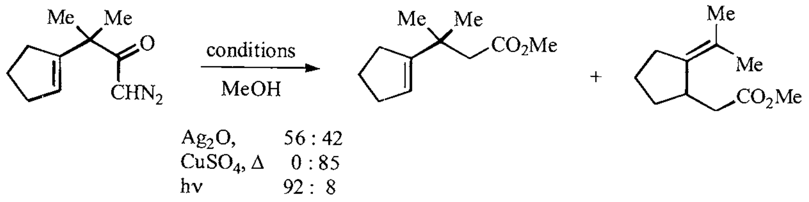
Notes:

M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1405

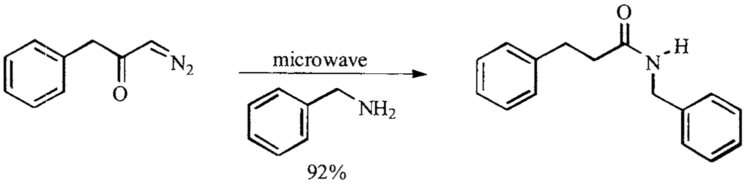
Smith's Vinylogous Wolff Rearrangement:



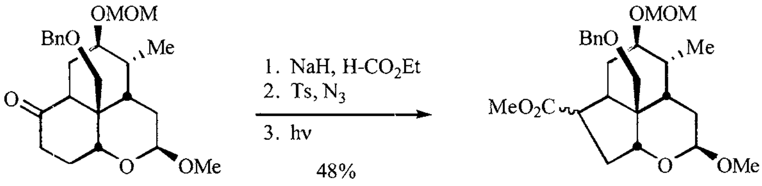
A. B. Smith, III, B. H. Toder, S. J. Branca, *Journal of the American Chemical Society* **1985**, 106, 1995



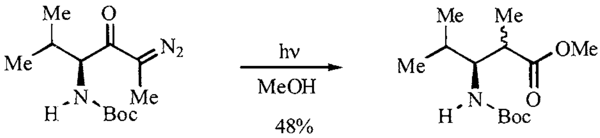
Smith, et. al. (continued)



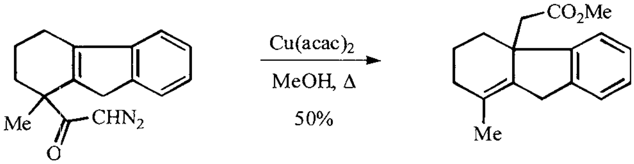
S. G. Sudrik, S. P. Chavan, K. R. S. Chandrakumar, S. Pal, S. K. Date, S. P. Chavan, H. R. Sonawane, *Journal of Organic Chemistry* **2002**, 67, 1574



D. P. Walker, P. A. Grieco, *Journal of the American Chemical Society* **1999**, 121, 9891



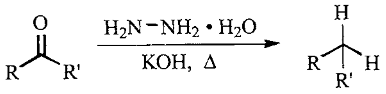
H. Yang, K. Foster, C. R. J. Stephenson, W. Brown, E. Roberts, *Organic Letters* **2000**, 2, 2177



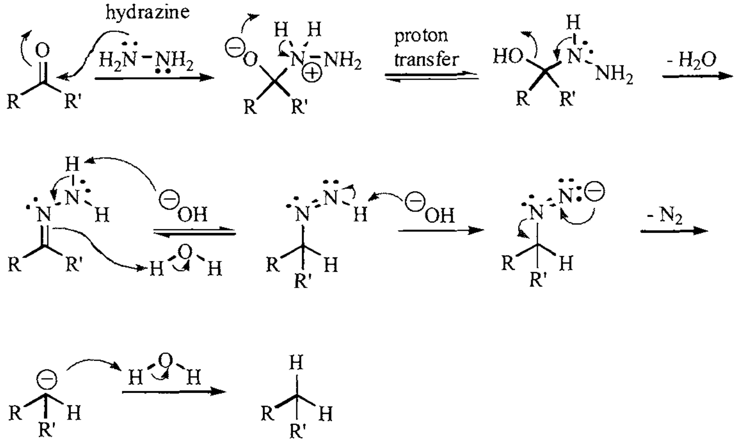
B. Saha, G. Bhattacharjee, U. R.Ghatak, *Tetrahedron Letters* **1986**, 27, 3913

Wolff-Kishner Reduction

The Reaction:



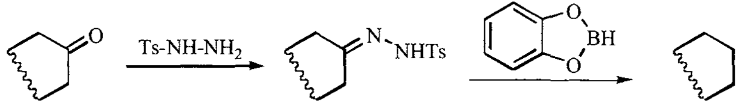
Proposed Mechanism:



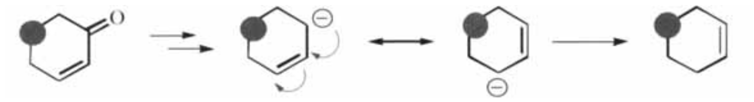
M. B. Smith, J. March in *March's Advanced Organic Chemistry*, 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1548

Notes:

See ***catecholborane*** for a mild and selective alternative to the ***Wolff-Kishner reduction***.

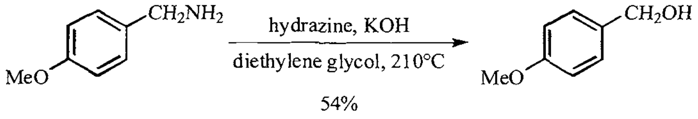


Enone systems can undergo rearrangement



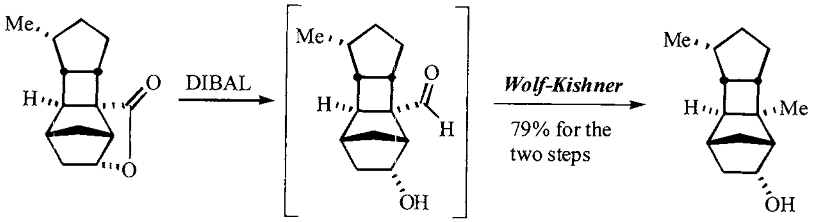
The commonly used approach (above) is better recognized as the ***Huang-Minlon modification***.

Under ***Wolff-Kishner*** conditions, a primary amine can be converted to an alcohol:

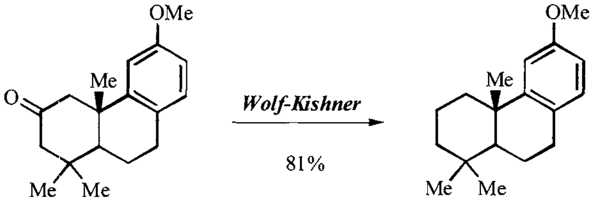


S. M. A. Rahman, H. Ohno, N. Maezaki, C. Iwata, T. Tanaka, *Organic Letters* **2000**, 2, 2893

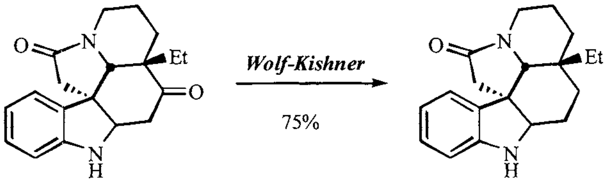
Examples:



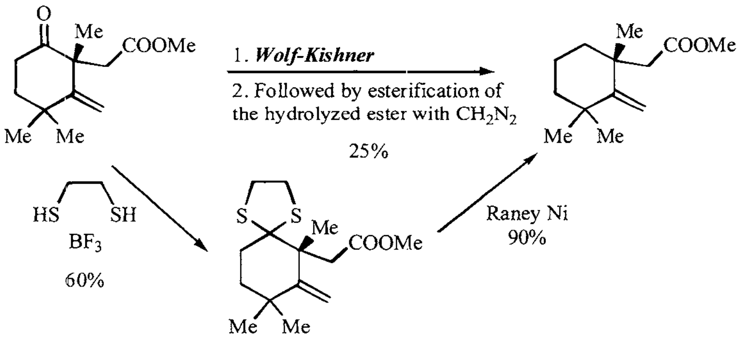
M. Harmata, P. Rashatasakhon, *Organic Letters* **2001**, 3, 2533



H. Nagata, N. Miyazawa, K. Ogasawara, *Organic Letters* **2001**, 3, 1737



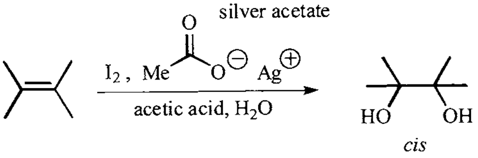
J. P. Marino, M. B. Rubio, G. Cao, A. de Dios, *Journal of the American Chemical Society* **2002**, 124, 13398



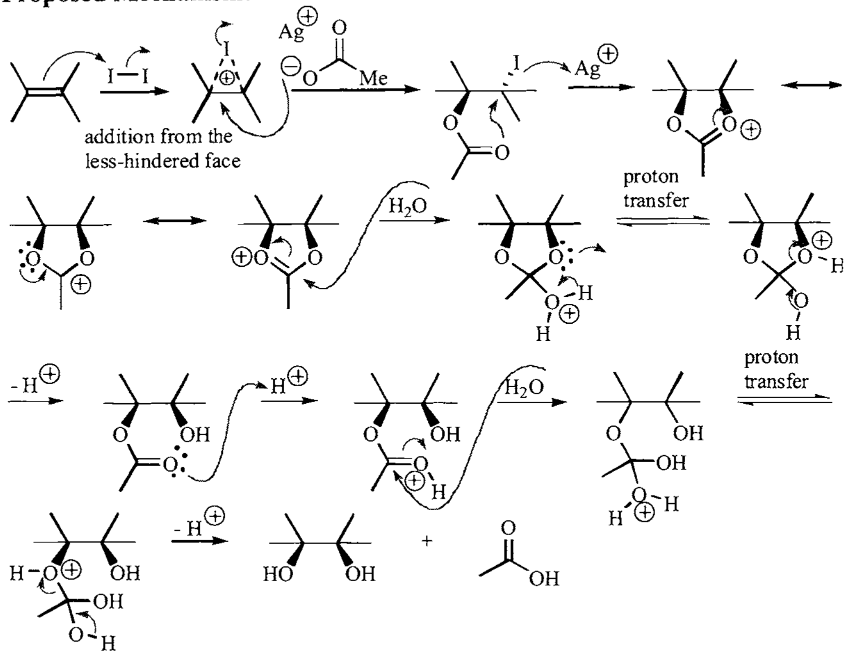
A. Srikrishna, K. Anebouselvy, *Journal of Organic Chemistry* **2001**, 66, 7102

Woodward Modification of the Prevost Reaction

The Reaction:

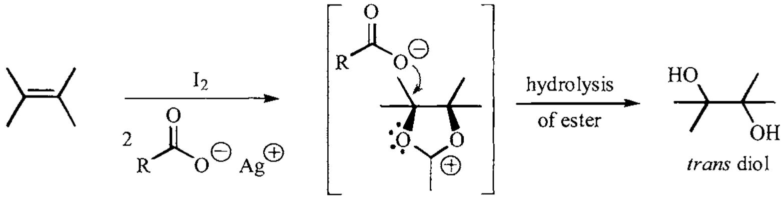


Proposed Mechanism:



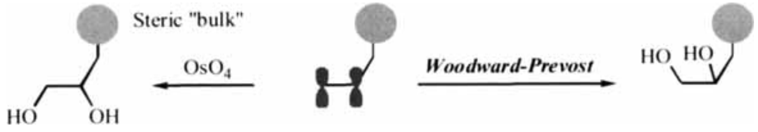
Notes:

The ***Prevost Reaction***:

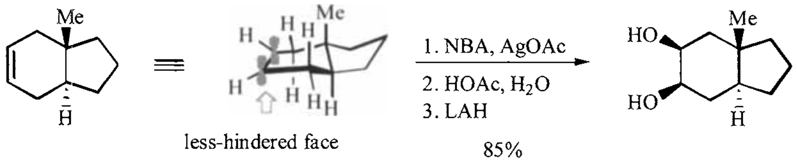


This ***Woodward-Prevost reaction*** provides *cis* diols at the more hindered face. This is due to the first step, the addition of iodine from the less-hindered face.

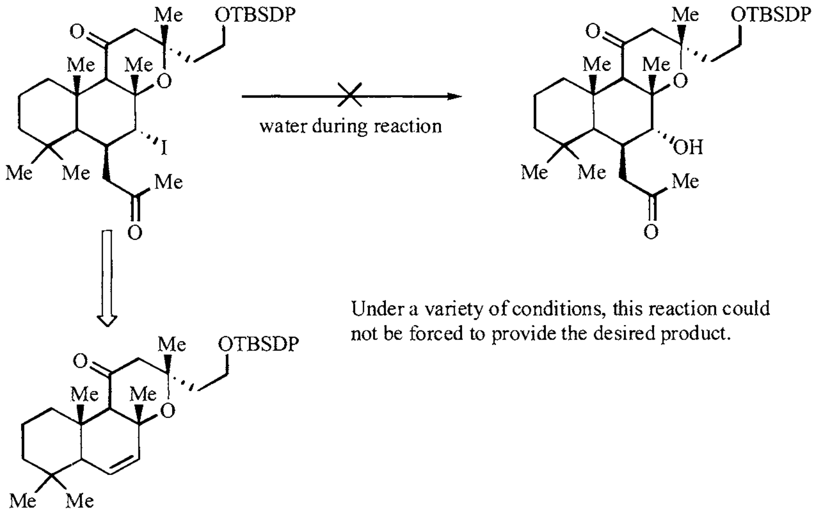
Contrast this reaction with OsO_4 or $MnO_4^{\ominus}$



Examples:



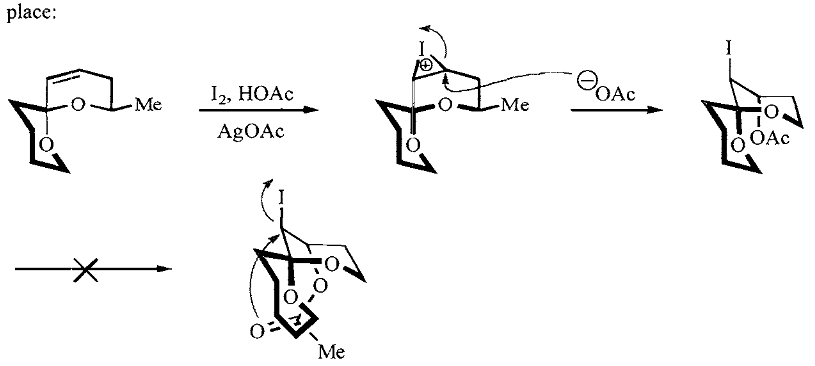
D. Jasserand, J. P. Girard, J. C. Rossi, R. Granger *Tetrahedron Letters* **1976**, 17, 1581



Under a variety of conditions, this reaction could not be forced to provide the desired product.

S. Hamm, L. Hennig. M, Findeisen, D. Muller, P. Weizel, *Tetrahedron* **2000**, 56, 1345

Examples are available to show that show the necessary acetate participation does not always take place:



M. A. Brimble, M. R. Nairn, *Journal of Organic Chemistry* **1996**, 61, 4801

Wurtz (Coupling) Reaction and Related Reactions

In the ***Wurtz Reaction***, both halides are alkyl. For the ***Wurtz-Fittig Reaction***, there is one alkyl and one aryl group, while in the ***Fittig Reaction***, both coupling partners are aryl halides.

Wurtz (Coupling) Reaction:

$$2\ \mathrm{R{-}X} \xrightarrow{2\,\mathrm{Na}} \mathrm{R{-}R} + 2\,\mathrm{NaX}$$

Fittig Reaction

$$2\ \mathrm{Ar{-}X} \xrightarrow{2\,\mathrm{Na}} \mathrm{Ar{-}Ar} + 2\,\mathrm{NaX}$$

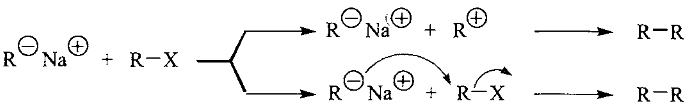
Wurtz-Fittig Reaction

$$\mathrm{Ar{-}X} + \mathrm{R{-}X} \xrightarrow{2\,\mathrm{Na}} \mathrm{Ar{-}R} + 2\,\mathrm{NaX}$$

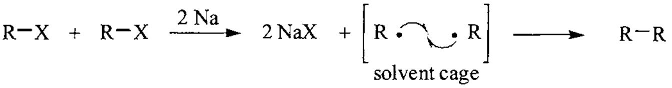
Proposed Mechanism:

Much is not known about the details of the reaction.
It could be a simple S_N1 or S_N2:

$$\mathrm{R{-}X} \xrightarrow{2\,\mathrm{Na}} \mathrm{Na{-}X} + \mathrm{R}^{\ominus}\mathrm{Na}^{\oplus}$$



or a radical pathway could be followed:

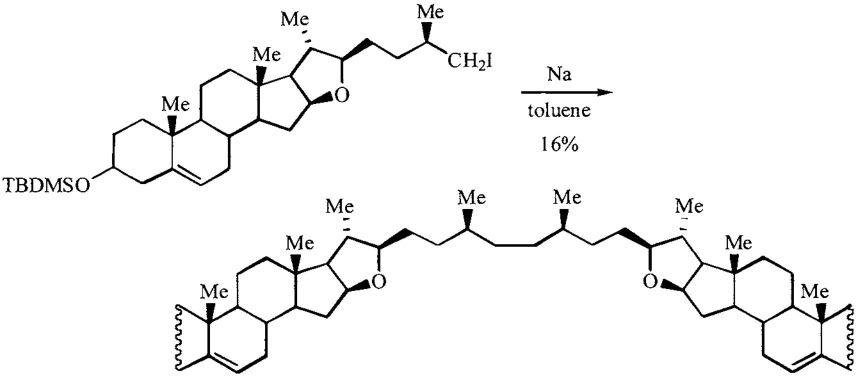


Notes:

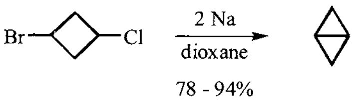
M. B. Smith, J. March in *March's Advanced Organic Chemistry,* 5th ed., John Wiley and Sons, Inc., New York, 2001, p. 1452; T. Laue, A. Plagens, *Named Organic Reactions*, John Wiley and Sons, Inc., New York, 1998, p. 282

See: T. D. Lash, D. Berry, *Journal of Chemical Education* **1985**, 62, 85

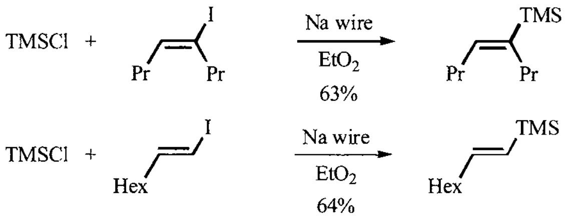
Examples:



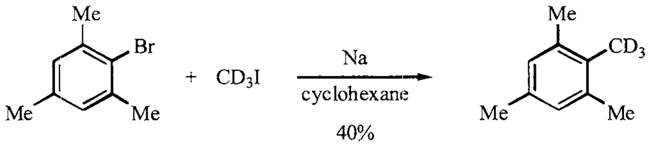
J. W. Morzycki, S. Kalinowski, Z. Lotowski, J. Rabiczko, *Tetrahedron* **1997**, 53, 10579



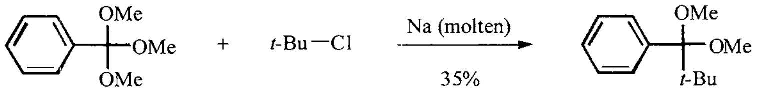
G. M. Lampman, J. C. Aumiller, *Organic Syntheses* CV 6, 133



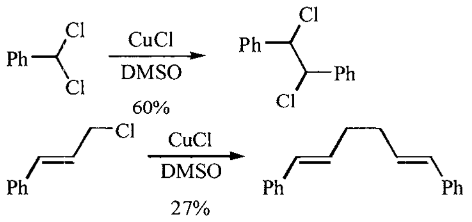
P. F. Hudrlik, A. K. Kulkarni, S. Jain, A. M. Hudrlik, *Tetrahedron* **1983**, 39, 877



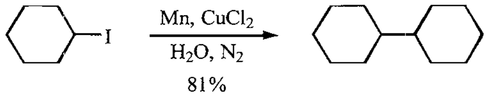
T. L. Kwa, C. Boelhouwer, *Tetrahedron* **1969**, 25, 5771



C. C. Chappelow, Jr., R. L. Elliott, J. T. Goodwin, Jr., *Journal of Organic Chemistry* **1962**, 27, 1409



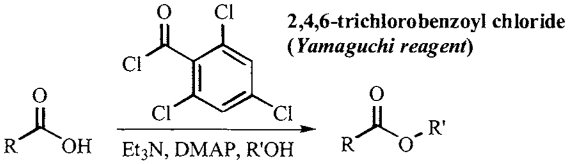
H. Nozaki, T. Shirafuji, Y. Yamamoto, *Tetrahedron* **1969**, 25, 3461



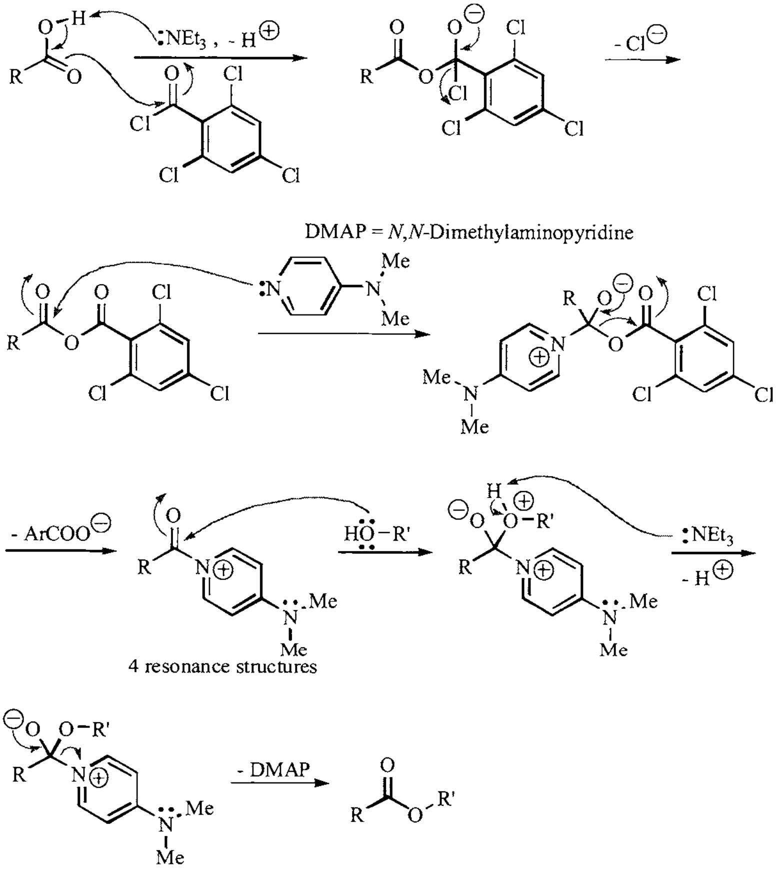
J. Ma, T.-H. Chan, *Tetrahedron Letters* **1998**, 39, 2499

Yamaguchi Esterification / Reagent

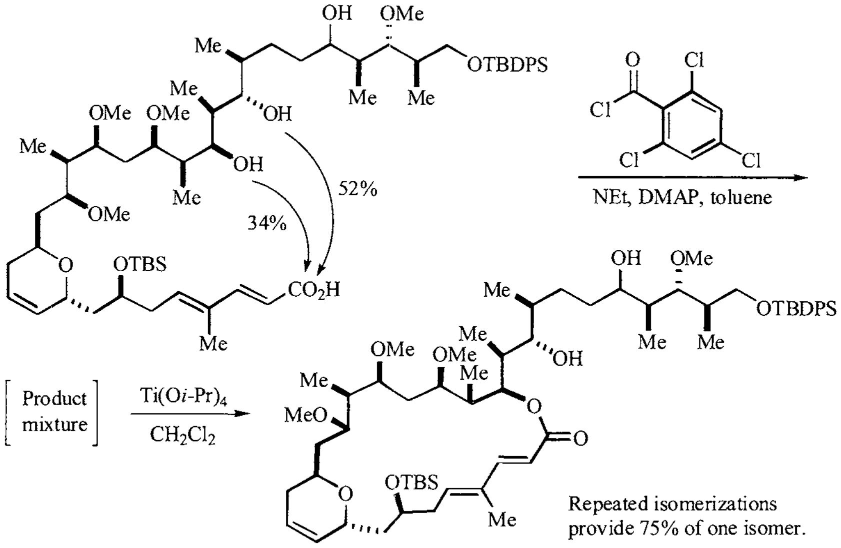
The Reaction:



Proposed Mechanism:

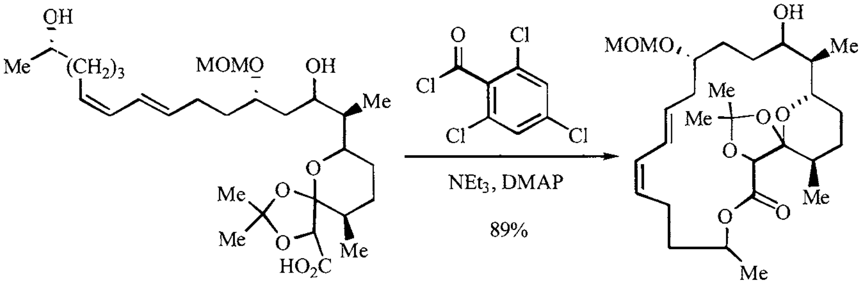


Examples:

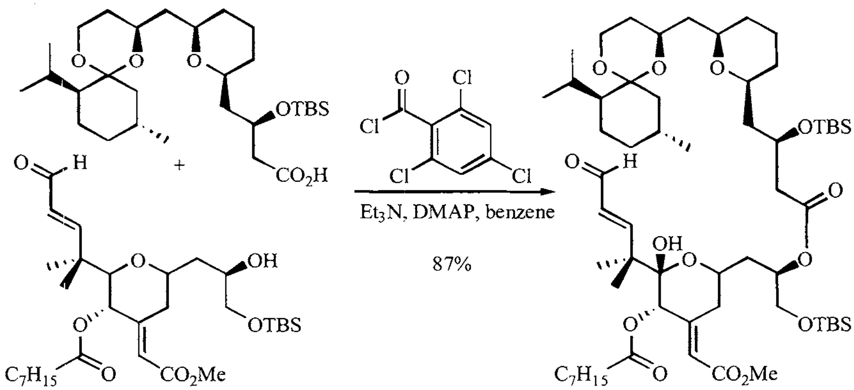


Repeated isomerizations provide 75% of one isomer.

R. Nakamura, K. Tanino, M. Miyashita, *Organic Letters* **2003**, 5, 3583



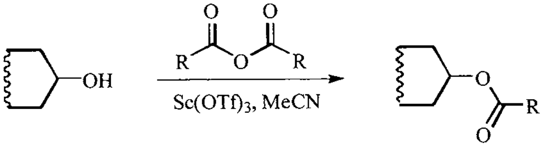
M. Berger, J. Mulzer, *Journal of the American Chemical Society* **1999**, 121, 8393



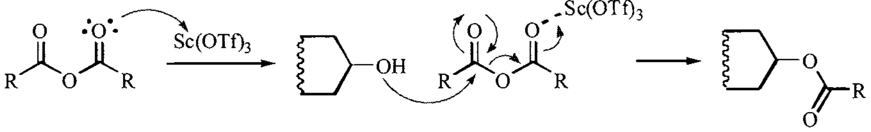
P. A. Wender, J. L. Baryza, C. E. Bennett, F. C. Bi, S. E. Brenner, M. O. Clarke, J. C. Horan, C. Kan, E. Lacôte, B. Lippa, P. G. Nell, T. M. Turner, *Journal of the American Chemical Society* **2001**, 124, 13684

Yamamoto Esterification

The Reaction:

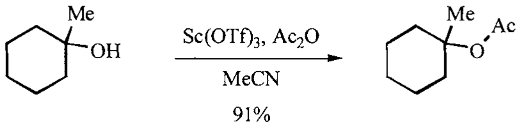


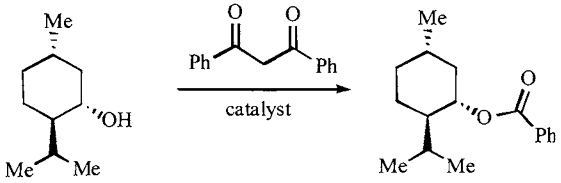
Proposed Mechanism:



Notes:

Sc(OTf)$_3$ is commercially available. This reaction provides good yields and is able to esterify relatively hindered alcohols:



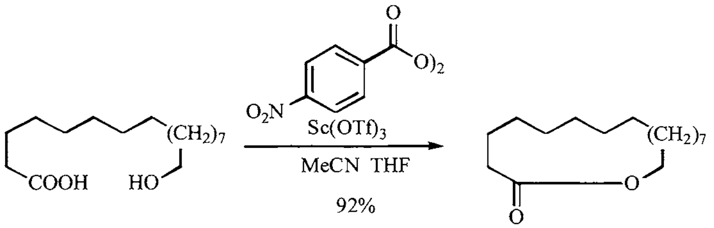


Catalyst	**Yield**
DMAP, Et$_3$N	75%
Sc(OTf)$_3$	> 95%

K. Ishihara, M. Kubota, H. Kurihara, H. Yamamoto, *Journal of Organic Chemistry* **1996**, 61, 4560

Alcohols react preferentially over phenols; an observation not common to other methods.

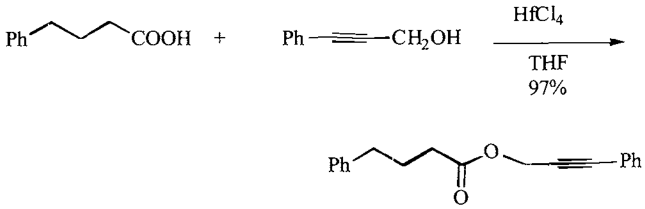
The reaction is readily extended to lactone synthesis:

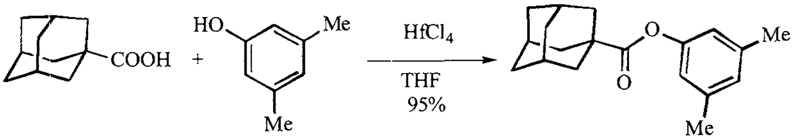


K. Ishihara, M. Kubota, H. Kurihara, H. Yamamoto, *Journal of Organic Chemistry* **1996**, 61, 4560

Examples:

Yamamoto has examined a number of catalyst systems for the reaction. A simple process using $HfCl_4$ in a soxhlet extractor has shown useful characteristics:





K. Ishihara, S. Ohara, H. Yamamoto, *Science* **2000**, 290, 1140

NAME REAGENTS and ACRONYMS

In this section we provide a summary of Name Reagents and Acronyms. A few additional reagents are included. We have tried to provide a simple summary of the chemistry within the format:

Name or Acronym

Structure

Chemical Name

[CAS Number]

Commercially available or Preparation:

Reference to, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **Volume number** page

Notes:

Examples:

Adam's Catalyst

PtO_2

Platinum (IV) Oxide
[1314-15-4]

Commercially available

A. O. King, I. Shinkai, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4162

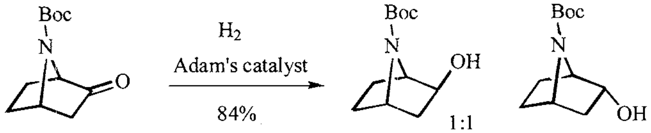
Notes:

1. PtO_2 is a pre-catalyst. In the presence of hydrogen gas and solvent, the oxide is reduced to a fresh platinum surface; the active catalyst.

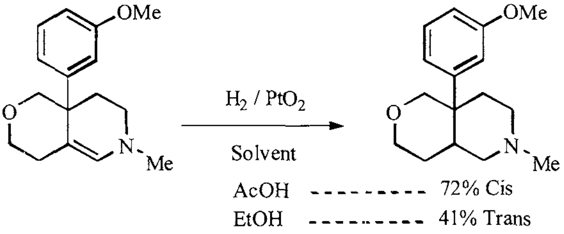
2. The ***Brown procedure***[2] for generating a fresh platinum catalyst uses $NaBH_4$ to reduce the Pt.[1]

Examples:

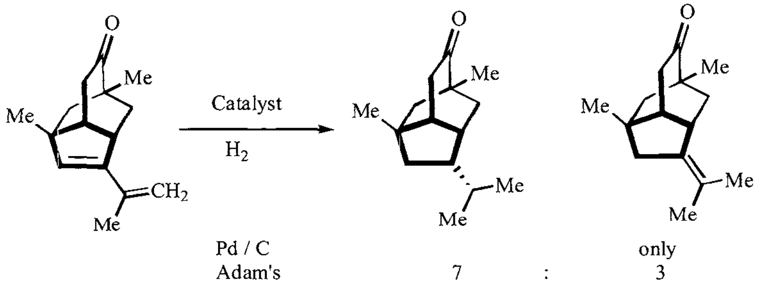
1.[2]



2.[3]



3.[4]



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[1] H. C. Brown, C. A. Brown, *Journal of the American Chemical Society* **1962**, 84, 1493

[2] K. C. V. Ramanaia, N. Zhu, C. Klein-Stevens, M. L. Trudell, *Organic Letters* **1999**, 1, 1439

[3] Reported in: A. O. King, I. Shinkai, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4162

[4] G. A. Schiehser, J. D. White, *Journal of Organic Chemistry* **1980**, 45, 1864

Adams Reagent

$Zn(CN)_2$

Zinc cyanide

[557-21-1]

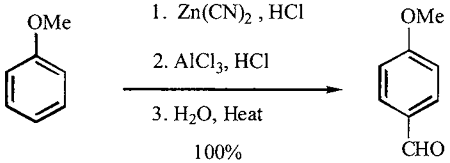
Commercially available

H. Heaney, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **8**, 5564

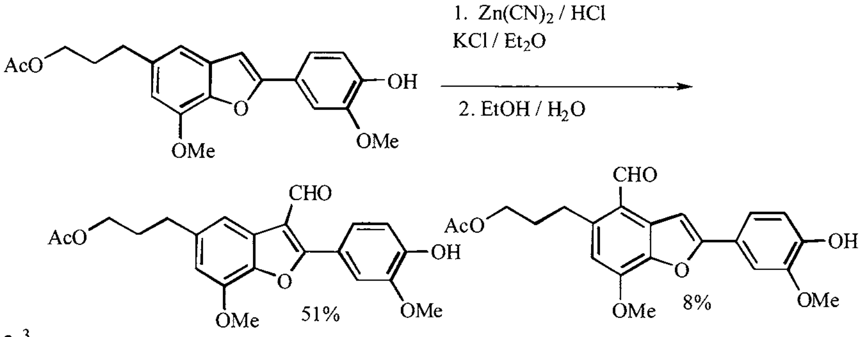
Notes: A useful source of HCN for the ***Gattermann-type formylation*** reaction.

Examples:

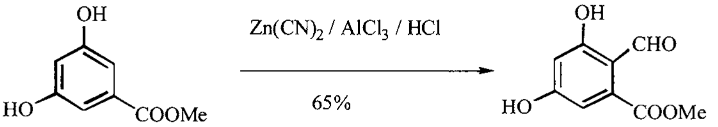
1.[1]



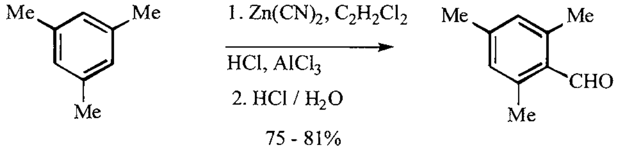
2.[2]



3.[3]



4.[4]



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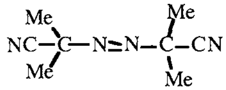
[1] E. Montgomery, *Journal of the American Chemical Society* **1924**, 46, 1518

[2] Z. Yang, H. B. Liu, C. M. Lee, H. Mou Chang, H. N. C. Wong, *Journal of Organic Chemistry* **1992**, 57, 7248

[3] A. V. R. Rao, N. Sreenivasan, D. Reddeppa, N. Reddy, V. H. Deshpande, *Tetrahedron Letters* **1987**, 28, 455

[4] R. C. Fuson, E. C. Horning, S. P. Rowland, M. L. Ward, *Organic Syntheses* CV3, 549

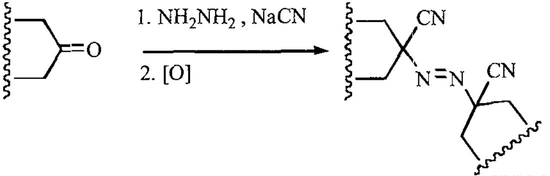
AIBN



$NC-C(Me)_2-N{=}N-C(Me)_2-CN$

2,2'-Azobisisobutyronitrile
[78-67-1]

Commercially available. This and related reagents can be prepared by the general scheme

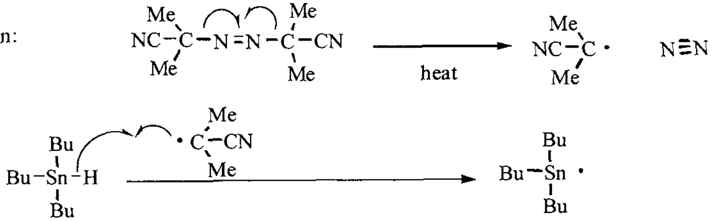


N. S. Simpkins, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 229

Notes:

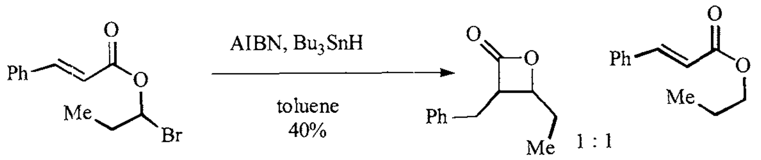
This reagent is useful for initiating radical reactions. Since it is a radical initiator, only small amounts are needed. For reactions at higher temperature, ACN (1,1'-azobis-1-cyclohexanenitrile [2094-98-6]) has been suggested (see Example 2).[1]

Initiation:

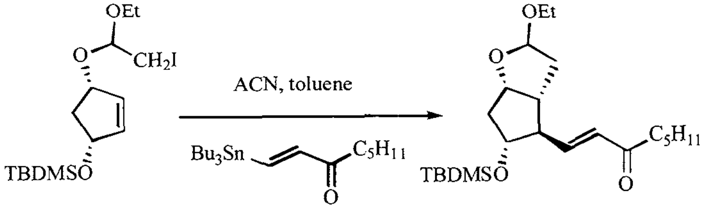


Example

1.[2]



2.[3]



AIBN gave lower yield 72% ACN = Azobiscyclohexylnitrile

---

[1] G. E. Keck, D. A. Burnett, *Journal of Organic Chemistry* **1987**, 52, 2958

[2] K. Castle, C.-S. Hau, J. B. Sweeney, C. Tindall, *Organic Letters* **2003**, 5, 757

[3] G. E. Keck, D. A. Burnett, *Journal of Organic Chemistry* **1987**, 52, 2958

Albright-Goldman Reagent[1]

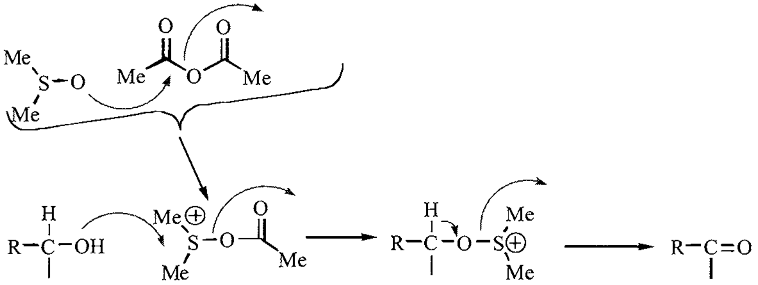
DMSO-Ac_2O

[DMSO] [Acetic anhydride]

Commercially available. Both DMSO and Ac_2O are readily available.

T. T. Tidwell, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 2145

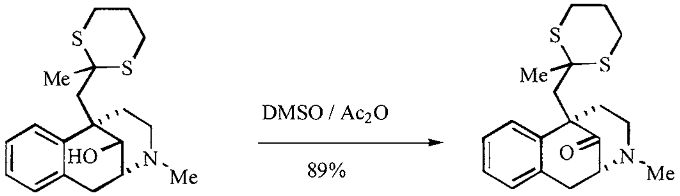
Notes: The mechanism of this oxidation is suggested to be:



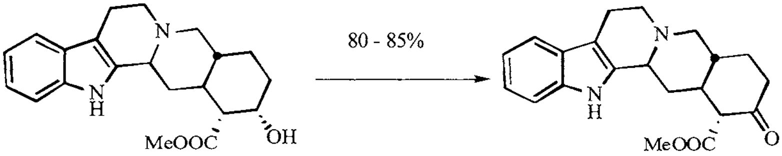
See ***DMSO-based Oxidations***, in ***Aldehyde Syntheses***

Examples:

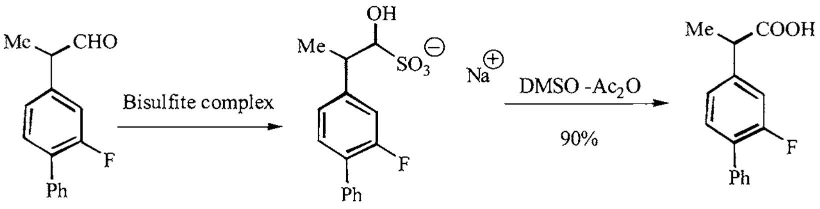
1.[2]



2.[3]



3.[4]



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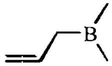
[1] J. D. Albright, L. Goldman, *Journal of the American Chemical Society* **1967**, 89, 2416

[2] E. Montgomery, *Journal of the American Chemical Society* **1924**, 46, 1518

[3] (a) J. D. Albright, L. Goldman, *Journal of American Chemical Society* **1965**, 87, 4214
(b) *Journal of Organic Chemistry* **1965**, 30, 1107

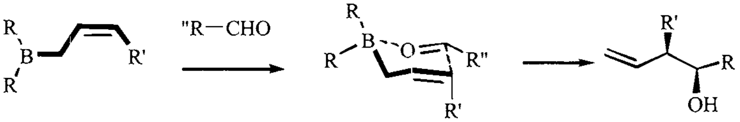
[4] P. G. M. Wuts, C. L. Bergh, *Tetrahedron Letters* **1986**, 27, 3995

Allyl Boron Reagents

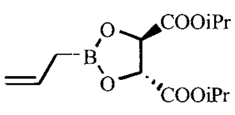


Notes:

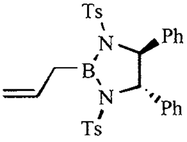
The reagents described are used to generate chiral allyl groups. In reaction with aldehydes:



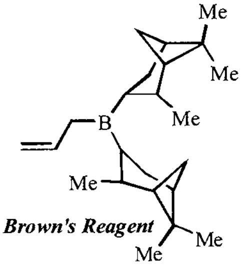
Examples: of chiral allyl-boron reagents:



Rousch Reagent



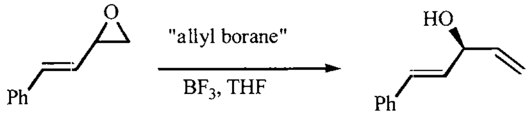
Corey Reagent



Brown's Reagent

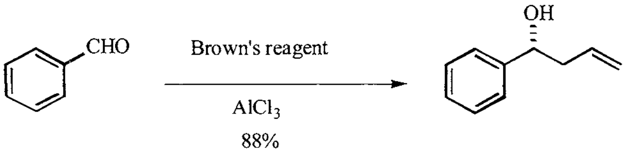
Examples:

1.[1]



	Yield	***Percent ee***
Rousch	70	47
Corey	33	37
Brown	80	96

2.[2]



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[1] M. Lautens, M. L. Madess, E. L. O. Sauer, S. G. Ouellet, *Organic Letters* **2002**, 4, 83

[2] T. Ishiyama, T. Ahiko, N. Miyaura, *Journal of the American Chemical Society* **2002**, 124, 12414

Attenburrow's Oxide[1,2]

MnO_2

Manganese dioxide

[1313-13-9]

Commercially available

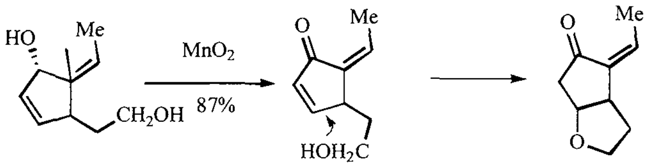
G. Cahiez, M. Alami, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3229

Notes:

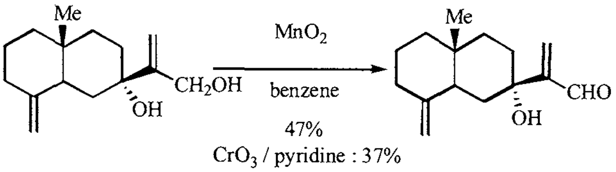
This is a selective oxidizing reagent for sensitive substrates, particularly alcohols adjacent to pi-systems. The preparation of the active reagent is critical to its success.

Examples:

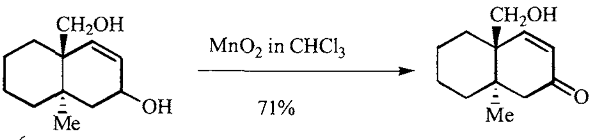
1.[3]



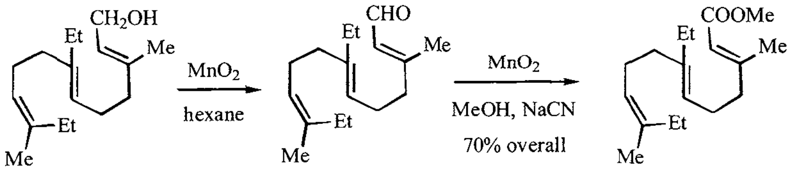
2.[4]



3.[5]



4.[6]



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[1] A. J. Fatiadi, *Synthesis* **1976**, 65, 133

[2] J. Attenburrow, A. F. B. Cameron, J. H. Chapman, R. M. Evans, B. A. Hems, A. B. A. Jansen, T. Walker, *Journal of the Chemical Society* **1952**, 1094

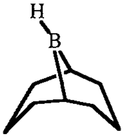
[3] K. M. Brummond, P. C. Still, H. Chen, *Organic Letters* **2004**, 6, 149

[4] J. Cuomo, *Journal of Agricultural and Food Chemistry* **1985**, 33, 717

[5] P. C. Mukharji, A. N. Ganguly, *Tetrahedron* **1969**, 25, 5281

[6] E. J. Corey, J. A. Katzenellenbogen, N. W. Gilman, S. A. Roman, B. W. Erickson, *Journal of the American Chemical Society* **1968**, 90, 5618

9-BBN



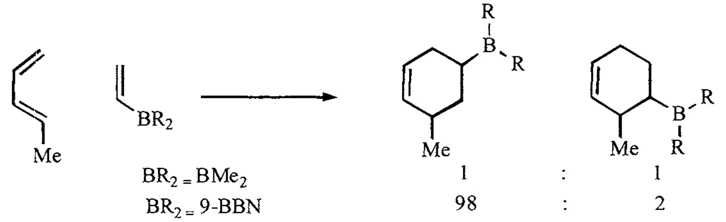
9-Borobicyclo[3.3.1]nonane
[280-64-8]
[21205-91-4] Crystalline dimer

Commercially available. Can be prepared from the reaction of 1,5-cyclooctadiene with diborane.

J. A. Soderquist, A. Negron, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 1, 622

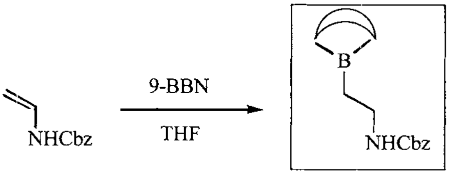
Notes:

As with borane, this reagent exists as a dimer. Unlike diborane, the solid dimer has limited stability to the atmosphere, but should be stored in an inert environment. ***Commercially available solutions should be maintained under inert atmosphere and anhydrous conditions.*** Due to its steric bulk, 9-BBN is seen to be more selective than diborane. This is even observed in reactions where the 9-BBN group is a non-reacting center.[1]



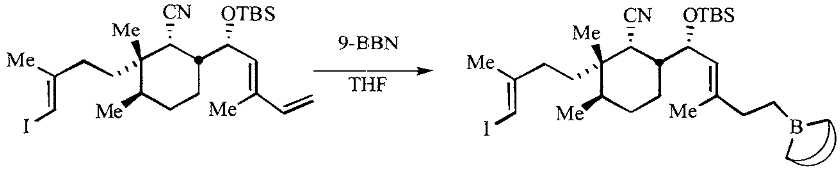
Examples:

1.[2]



This intermediate is taken on to the next step, a ***Suzuki reaction***.

2.[3]



After mild oxidation to form the alcohol (see ***Brown's Hydroboration***) the ***Swern oxidation*** formed the aldehyde in overall 98% yield

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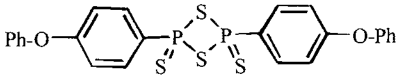
[1] S. C. Pellegrinet, M. A. Silva, J. M. Goodman, *Journal of the American Chemical Society* **2001**, 123, 8832

[2] A. Kamatani, L. E. Overman, *Organic Letters* **2001**, 3, 1229

[3] N. C. Kallan, R. L. Halcomb, *Organic Letters* **2000**, 2, 2687

Belleau's Reagent



1,3,2,4-Dithiadiphosphetane-2,4-bis(4-phenoxyphenyl)-2,4-disulfide
[88816-02-8]

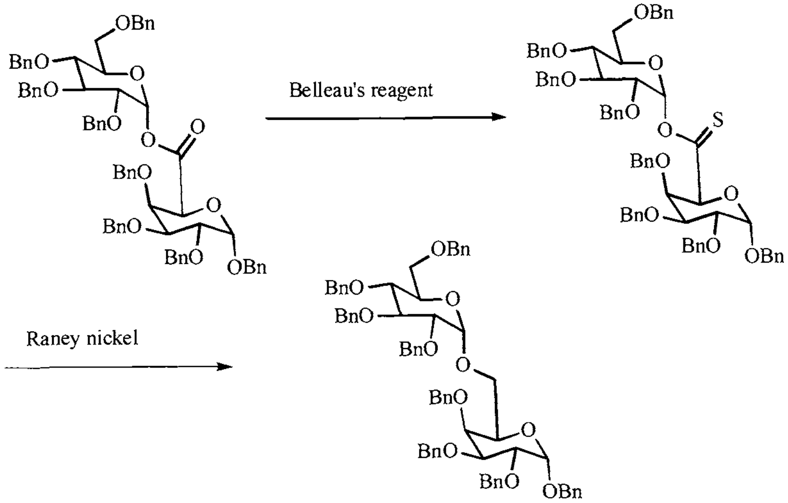
Preparation:[1] Details of the synthesis are not reported except that the procedure followed H. Z. Lecher, R. A. Greenwood, K. C. Whitehouse, T. H. Chao, *Journal of the American Chemical Society* **1956**, 78, 5018

Notes:

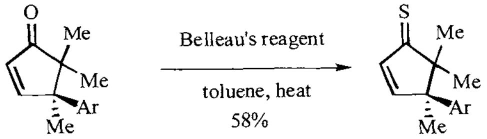
Similar to ***Lawesson's*** and ***Davy's reagents***. Used as a mild thionation reagent for esters and lactones.

Examples:

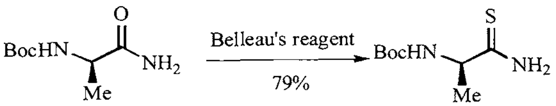
1.[2]



2.[3]



3.[4]



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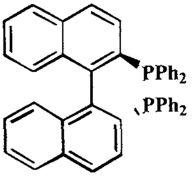
[1] G. Lajoie, F. Lépine, L. Maziak, B. Belleau, *Tetrahedron Letters* **1983**, 24, 3815
[2] A.G. M. Barrett, A. C. Lee, *Journal of Organic Chemistry* **1992**, 57, 2818
[3] A. P. Degnan, A. I. Meyers, *Journal of American Chemical Society* **1999**, 121, 2762
[4] S. V. Ley, A. Priour, C. Heusser, *Organic Letters* **2002**, 4, 711

BINAP



2,2'-Bis(diphenylphosphino)-1,1'-binaphththyl
[76189-55-4] R-(+)
[76189-56-5] S-(-)

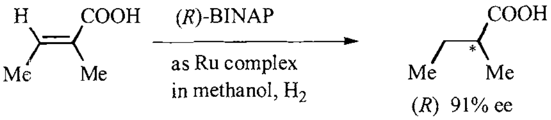
Commercially available

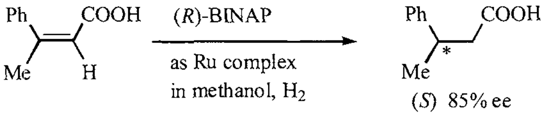
K. Kitamura, R. Noyori, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 509

Notes: A chiral diphosphine ligand to be used with transition metal catalyzed reactions.

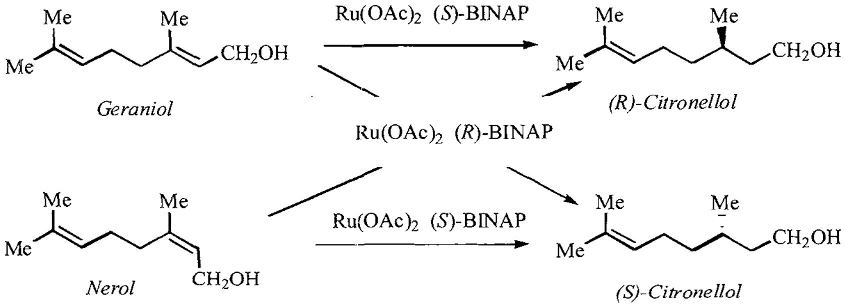
Examples:

1.[1]

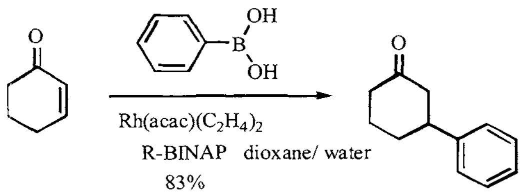




2.[2]



3.[3]



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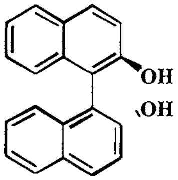
[1] T. Ohta, H. M. Kitamura, K. Nagai, R. Noyori, *Journal of Organic Chemistry* **1987**, 52, 3174

[2] H. Takaya, T. Ohta, S. Inoue, M. Tokunaga, M. Kitamura, R. Noyori, *Organic Syntheses* **1994**, 72, 74

[3] T. Hayashi, M. Takahashi, Y. Takaya, M. Ogasawara, *Organic Syntheses* **2001**, 79, 84

BINOL

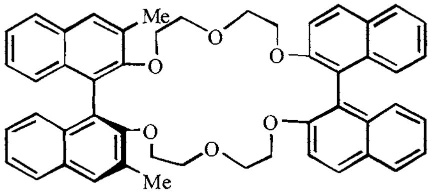


(*R* or *S*)-1,1'-bi-2,2'-naphthol
[18531-94-7]

Commercially available

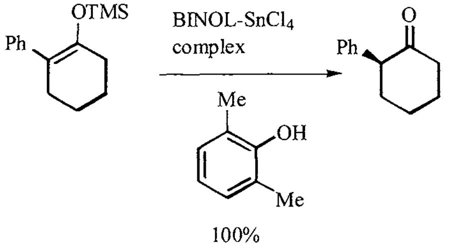
K. Mikama, Y. Motoyama, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 1, 397

Notes: As a reagent for introducing chirality, a BINOL-based crown ether has been reported:[1]

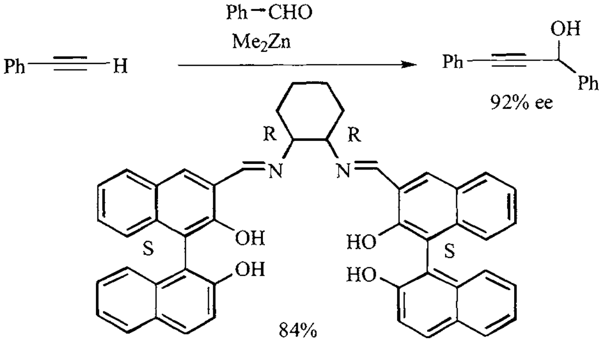


Examples:

1.[2]



2.[3]



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[1] R. C. Helgeson, J. M. Timko, P. Moreau, S. C. Peacock, J. M. Mayer, D. J. Cram, *Journal of the American Chemical Society* **1974**, 96, 6762

[2] K. Ishihara, S. Nakamura, M. Kaneeda, H. Yamamoto, *Journal of the American Chemical Society* **1996**, 118, 12854

[3] Z.-B. Li, L. Pu, *Organic Letters* **2004**, 6, 1065

BITIP

Ti(i-PrO)$_4$ / BINOL

Binol/Titanium isopropoxide

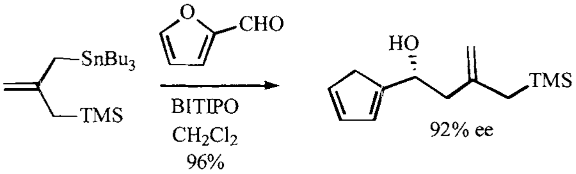
Preparation:[1]

Notes:

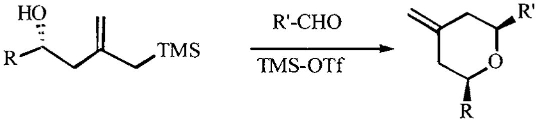
A useful chiral catalyst.

Examples:

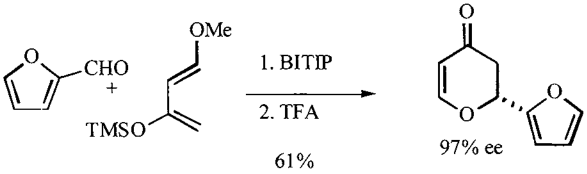
1.[2]



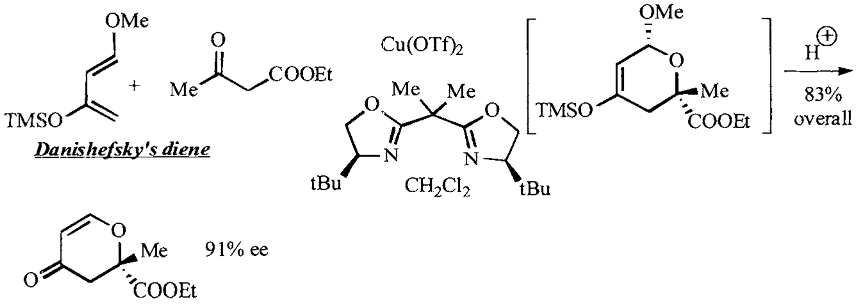
Intermediates of this type are useful for a pyran annulation protocol:



2.[3]



For an example of other uses of chiral Lewis acids (***CLA***) to synthesis:[4]



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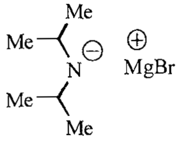
[1] G. E. Keck, K. H. Tarbet, L. S. Geraci, *Journal of the American Chemical Society* **1993**, 115, 8467

[2] G. E. Keck, J. A. Covel, T. Schiff, T. Yu, *Organic Letters* **2002**, 4, 1189[2]

[3] G. E. Keck, X.-Y. Li, D. Khrishnamurthy, *Journal of Organic Chemistry* **1995**, 60, 5998

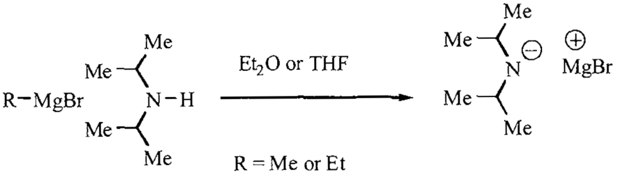
[4] C. Wolf, Z. Fadul, P. A. Hawes, E. C. Volpe, *Tetrahedron Asymmetry* **2004**, 15, 1987

BMDA



Bromomagnesium diisopropylamide
[50715-01-0]

Preparation: From the reaction of RMgX with diisopropylamine.

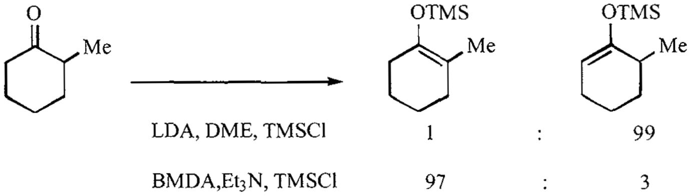


R. H. Erickson, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 740

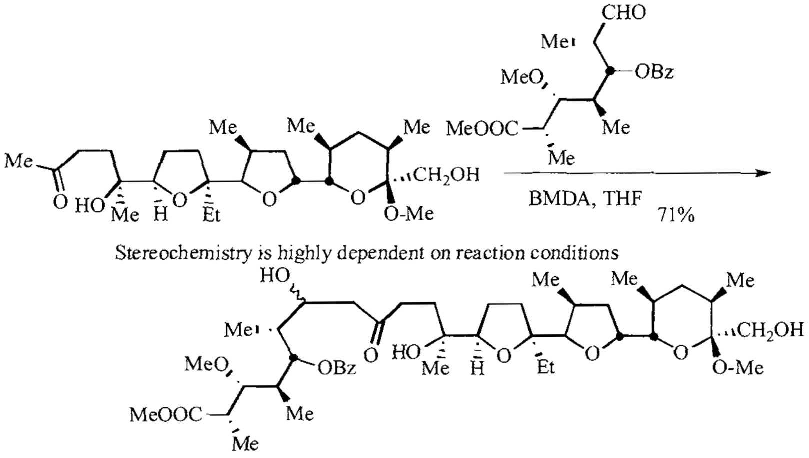
Notes: Shown to be an extremely useful base for generating thermodynamic enolates.[1] Useful for ***aldol condensations***.

Examples:

1.[2]



2.[3]



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[1] M. E. Krafft, R. A. Holton, *Tetrahedron Letters* **1983**, 24, 1345

[2] A. Yanagisawa, T. Watanabe, T. Kikuchi, H. Yamamoto, *Journal of Organic Chemistry* **2000**, 65, 2979

[3] T. Fukuyama, K. Akasaka, D. S. Karanewsky, C.-L. J. Wang, G . Schmid, Y. Kishi, *Journal of the American Chemical Society* **1979**, 101, 262

BMS

BH_3-Me_2S
Borane Dimethylsulfide
[13292-87-0]

Commercially available

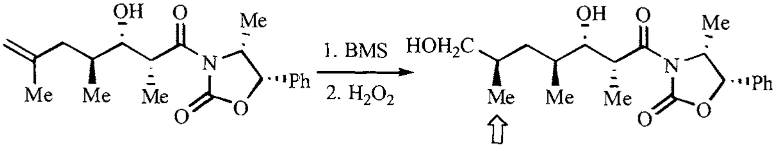
M. Zaidlewics, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 634

Notes: 1. Use as other ***hydroborating reagents***. Its value is in the increased reagent stability and solvent solubility. Like other hydroborating agents, it is stable to an array of functional groups. It is useful for the reduction of ozonides.

2. A recent report describes replacing the dimethyl sulfide with larger alkyl-substituted sulfides to reduce stench.[1]

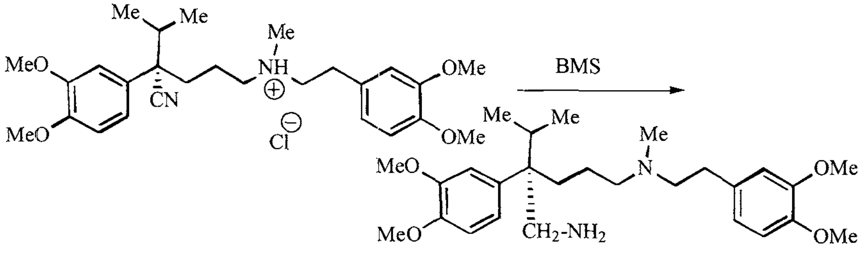
Examples:

1.[2]



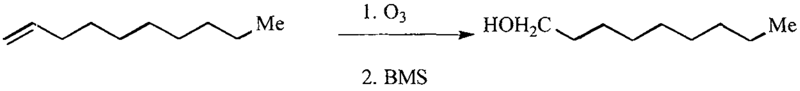
78% with this stereochemistry

2.[3]



73%

3.[4]



100%

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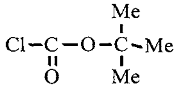
[1] M. Zaidlewicz, J. V. B. Kanth, H. C. Brown, *Journal of Organic Chemistry* **2000**, 65, 6697

[2] D. A. Evans, J. Bartroli, T. Godel, *Tetrahedron Letters* **1982**, 23, 4577

[3] R. M. Bannister, M. H. Brookes, G. R. Evans, R. B. Katz, N. D. Tyrrell, *Organic Process Research & Development* **2000**, 4, 467

[4] L. A. Flippin, D. W. Gallagher, K. Jalali- Araghi, *Journal of Organic Chemistry* **1989**, 54, 1430

Boc-Cl



$$\mathrm{Cl-\underset{\underset{O}{\|}}{C}-O-\overset{Me}{\underset{Me}{C}}-Me}$$

t-Butoxycarbonylchloride
t-Butyl chloroformate
[24608-52-4]

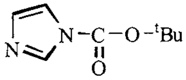
Preparation: Prepared from *t*-butyl alcohol (or K^+ *t*-BuO^-) and phosgene.

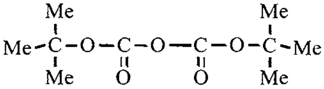
G. Sennyey, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 859

Notes:

Reagent used for the protection of amino groups. Because of the steric influence of the Boc protecting group, it is quite stable to base hydrolysis and catalytic reduction with hydrogen.

See 1-(*t*-butoxycarbonyl)imidazole [49761-82-2] (I. Grapsas, S. Mobashery, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 835) and di-*t*-butyl dicarbonate (Boc_2O) [24424-99-5](M. Wakselman, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1602 for similar roles as providing Boc protecting groups.

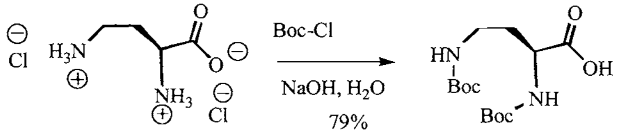




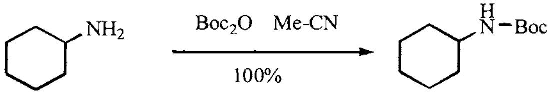
$$\mathrm{Me-\overset{Me}{\underset{Me}{C}}-O-\underset{\underset{O}{\|}}{C}-O-\underset{\underset{O}{\|}}{C}-O-\overset{Me}{\underset{Me}{C}}-Me}$$

Examples:

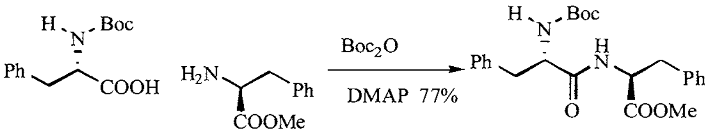
1.[1]



2.[2]



3.[3]



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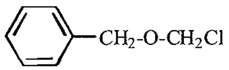
[1] R. C. F. Jones, A. K. Crockett, *Tetrahedron Letters* **1993**, 34, 7459
[2] Y. Basel, A. Hassner, *Journal of Organic Chemistry* **2000**, 65, 6368
[3] D. K. Mohapatra, A. Datta, *Journal of Organic Chemistry* **1999**, 64, 6879

BOMCl



Benzyl chloromethyl ether
Source of the BOM (**Benzyloxymethyl**) protecting group
[3587-60-8]

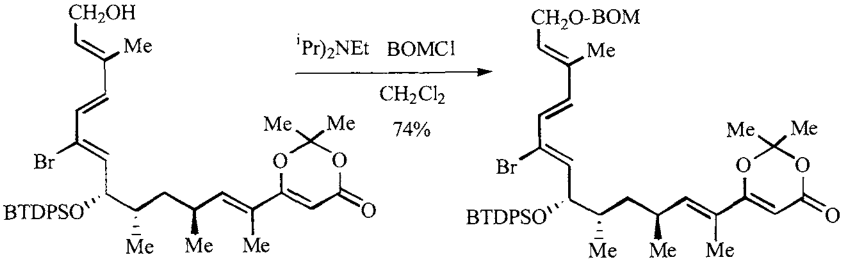
Commercially available

H. W. Pinnick, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 327.

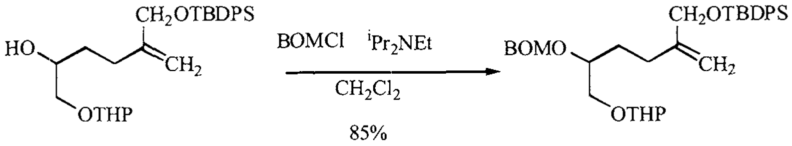
Notes: This is often used as a protecting group for alcohols, where it is observed that primary alcohols form more readily than secondary hydroxy groups, which in turn are more reactive than tertiary alcohols. As with most benzylic ethers, this protecting group can be removed by hydrogenolysis over Pd or by metal-ammonia reduction.[1]

Examples:

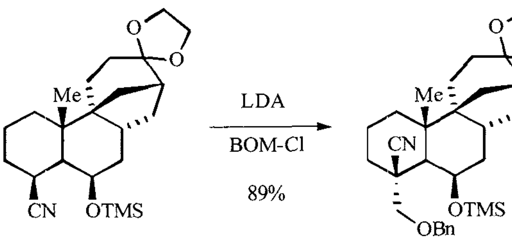
1.[2]



2.[3]



3.[4]



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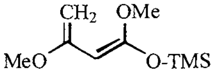
[1] See: T. W. Greene, P. G. M. Wuts, *Protective Groups in Organic Synthesis*, Wiley-Interscience, New York. Third Edition, 1999, p 36

[2] W. R. Roush B. B. Brown, *Journal of Organic Chemistry* **1993**, 58, 2162

[3] K. C. Nicolaou, D. A. Claremon, W. E. Barnette, *Journal of the American Chemical Society* **1980**, 102, 6611

[4] S. M. A. Rahman, H. Ohno, T. Murata, H. Yoshino, N. Satoh, K. Murakami, D. Patra, C. Iwata, N. Maezaki, T. Tanaka, *Organic Letters* **2001**, 3, 619

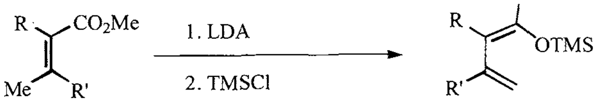
Brassard's Diene



Silan, [(1,3-dimethoxy-1,3-butadienyl)oxy]trimethyl-,(*E*)-
[90857-62-8]

Preparation:[1]

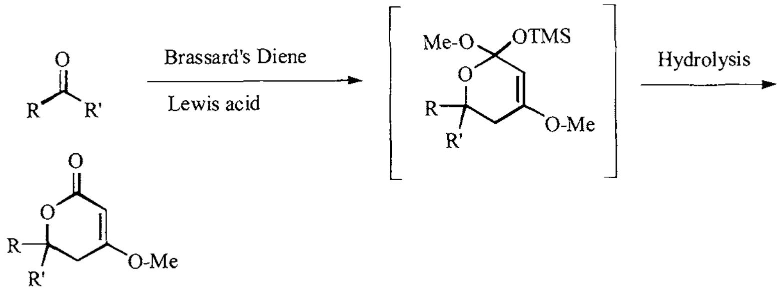
The general preparation was along the lines:



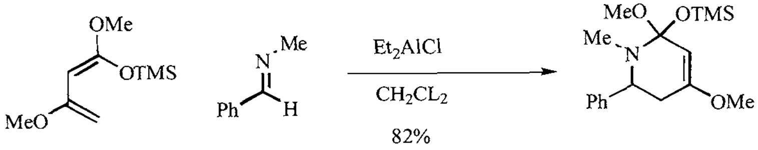
Notes: See similarity with ***Chan's***,[2] ***Danishefsky's*** and ***Rawal's Diene***.
For chemistry of related dienes, see: S. Danishefsky, *Accounts of Chemical Research* **1981**, 14, 400.

Examples:

1.[3]



2.[4]



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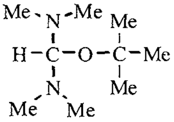
[1] P. Brassard, J. Savard, *Tetrahedron Letters* **1979**, 21, 4911

[2] P. Brownbridge, T. H. Chan, M. A. Brook, G. J. Kang, *Canadian Journal of Chem*istry **1983**, 61, 688

[3] M. M. Midland, R. S. Graham, *Journal of the American Chemical Society* **1984**, 106, 4294

[4] M. M. Midland, J. I. McLaughlin, *Tetrahedron Letters* **1988**, 29, 4653

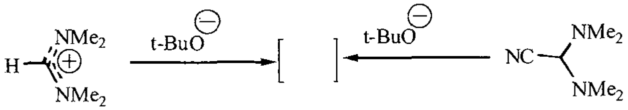
Bredereck's Reagent



$HC(NMe_2)_2{-}O{-}CMe_3$

t-Butoxybis(dimethylamino)methane
[5815-08-7]

Preparation:



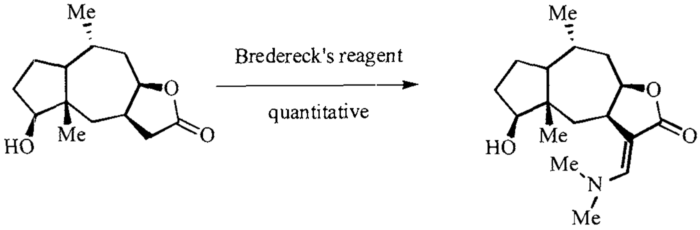
Commercially available

W. Kantlehner, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 828

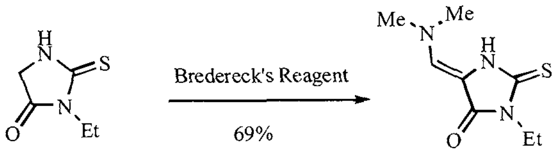
Notes: This reagent places an enamine adjacent to a carbonyl group, in essence, providing a mild formylation protocol.

Examples:

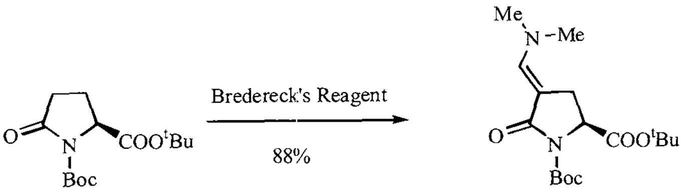
1.[1]



2.[2]



3.[3]



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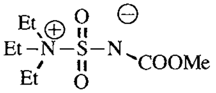
[1] F. E. Ziegler, J.-M. Fang, *Journal of Organic Chemistry* **1981**, 46, 827

[2] R. Jakse, S. Recnik, J. Svete, A. Golobic, L. Golic, B. Stanovnik, *Tetrahedron* **2001**, 57, 839

[3] E. Morera, F. Pinnen, G. Lucente, *Organic Letters* **2002**, 4, 1139

Burgess Reagent



Methyl, *N*-(triethylammoniosulfonyl)carbamate
[29864-56-8]

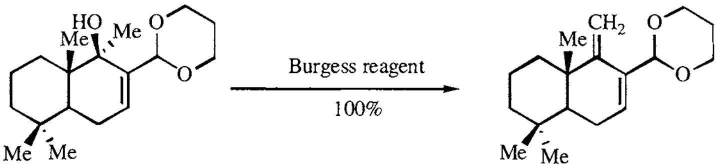
Commercially available

P. Taibi, S. Mobushery, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3345

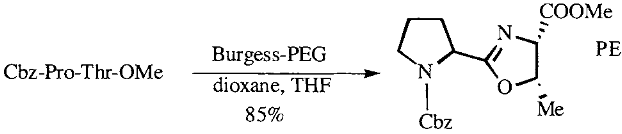
Notes: Efficient catalyst for the stereospecific *cis*-dehydration of 2 and 3 alcohols. Also useful for the preparation of oxazolines, a "***benzyl Burgess reagent***" has been reported[1], as has been a polymer-supported reagent.[2]

Examples:

1.[3]

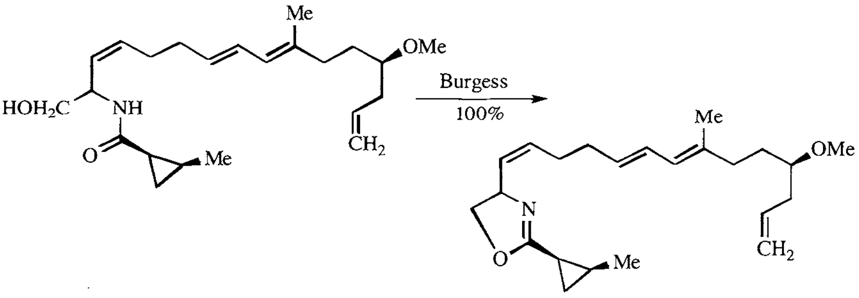


2.[4]



PEG = Polyethylene glycol

3.[5]



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[1] M. R. Wood, J. Y. Kim, K. M. Books, *Tetrahedron Letters* **2002**, 43, 3887

[2] P. Wipf, S. Venkatraman, *Tetrahedron Letters* **1996**, 37, 4659

[3] D. J. Goldsmith, H. S. Kezar, III, *Tetrahedron Letters* **1980**, 21, 3543

[4] P. Wipf, S. Venkatraman, *Tetrahedron Letters* **1996**, 37, 4659

[5] P. Wipf, W. Xu, *Journal of Organic Chemistry* **1996**, 61, 6556

n-Butyl Tin Hydride (TBTH)

$(n\text{-}Bu)_3SnH$
tri-*n*-butylstannane
[688-73-3]

Commercially available

T. V. RajanBabu, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 7, 5016

Notes:

Reactions with TBTH are often initiated with ***AIBN***. Useful for reduction of the C-X bond to C-H.

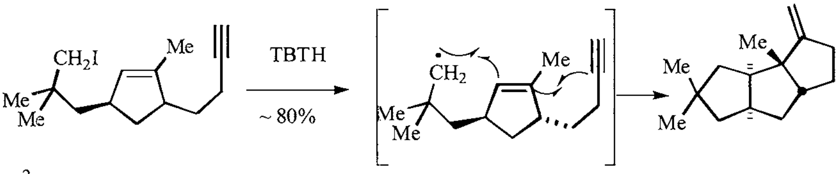
$Bu_3SnH + AIBN \longrightarrow Bu_3Sn$
$Bu_3Sn + R\text{-}X \longrightarrow R + Bu_3SnX$
$R + Bu_3SnH \longrightarrow R\text{-}H + Bu_3Sn$

The reagent will selectively remove I, Br, or Cl in the presence of other functional groups.

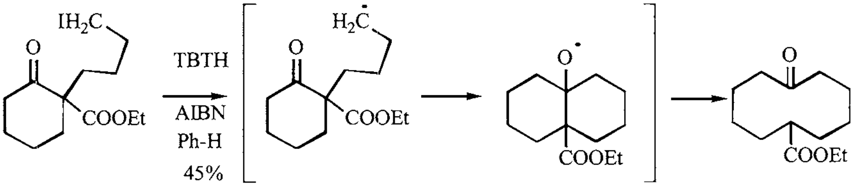
Since this is a source of radicals, the reagent can find use in ***Barton-McCombie Reaction*** and ***Dowd-Beckwith Ring Expansion***, as well as radical cyclization reactions.

Examples:

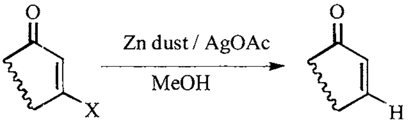
1.[1]



2.[2]



3. Heathcock has found that a Zn-Ag reagent is extremely useful for the conversion:[3]



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[1] D. P. Curran, D. M. Rakiewicz, *Tetrahedron* **1985**, 41, 3943
[2] P. Dowd, S. C. Choi, *Journal of the American Chemical Society* **1987**, 109, 6548
[3] R. D. Clark, C. H. Heathcock, *Journal of Organic Chemistry* **1972**, 88, 3657

CAN

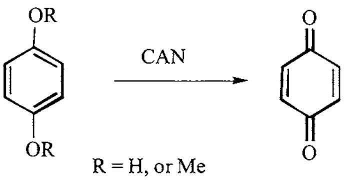
$Ce(NH_4)_2(NO_3)_6$

Cerium(IV) ammonium nitrate, Ceric ammonium nitrate
[16774-21-3]

Commercially available

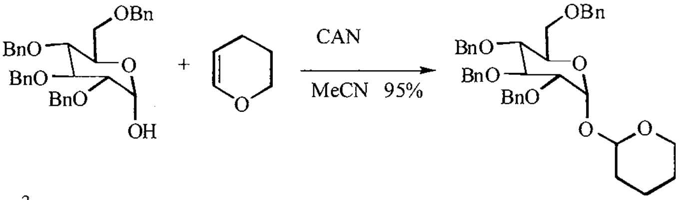
T.-L. Ho, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1029

Notes: A very strong one-electron oxidizing agent. See also *CAS*.

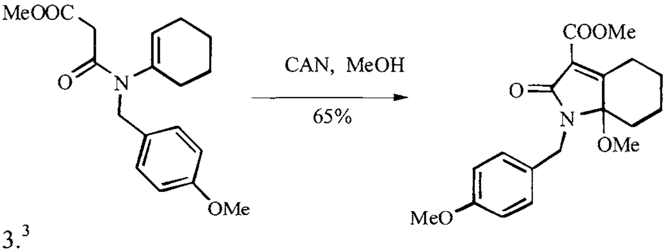


Examples:

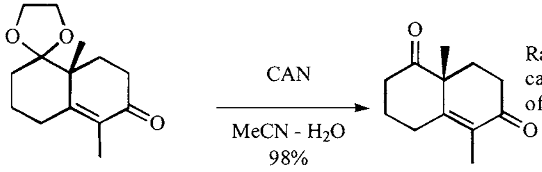
1.[1]



2.[2]



3.[3]



Rapid deproptection, and can be carried out in the presence of a number of other functional groups.

4.[4] Can be used to convert a hydrazone to an ester.

---

[1] K. Pachamuthu, Y. D. Vankar, *Journal of Organic Chemistry* **2001**, 66, 7511

[2] A. J. Clark, C. P. Dell, J. M. McDonagh, J. Geden, P. Mawdsley, *Organic Letters* **2003**, 5, 2063

[3] A. Ates, A. Gautier, B. Leroy, J.-M. Plannencher, Y. Quesnel, I. E. Marko, *Tetrahedron Letters* **1999**, 40, 1799

[4] B. Stefane, M. Kocevar, S. Polanc, *Tetrahedron Letters* **1999**, 40, 4429

CAS

$Ce(NH_4)_4(SO_4)_4$

Cerium(IV) ammonium sulfate
Ceric ammonium sulfate
[7637-03-8] hydrate
[10378-47-9] anhydrous

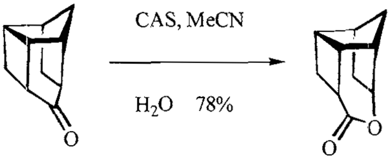
Commercially available

M. Periasamy, U. Radhakrishnan *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1029

Notes: Strong one-electron oxidizing agent. See also CAN.

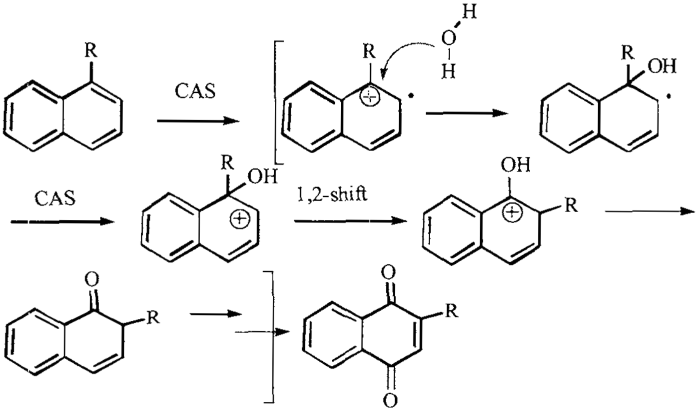
Examples:

1.[1]



Note that the major product from the CAS reaction was the minor product from the peracid-initiated Baeyer-Villiger oxygen insertion.

2.[2]



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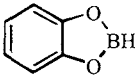
[1] G. Mehta, P. N. Pandeyl, T.-L. Ho, *Journal of Organic Chemistry* **1976**, 41, 953
[2] M. V. Brett, M. Periasany, *Tetrahedron* **1994**, 50, 3515

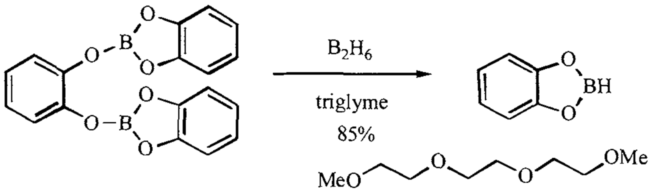
Catecholborane



[274-07-7]

Commercially available

Preparation: A new convenient preparation has been reported.[1]

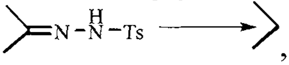


[112-49-2] bp 216
triglyme

M. S. VanNieuwenhze, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 2, 1017

Notes:

A special reducing agent for:[2]

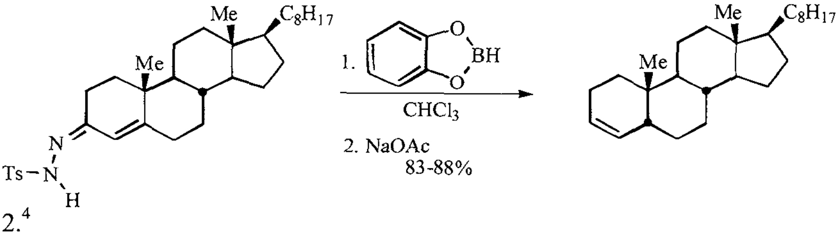


providing an alternative to the ***Wolff-Kishner reduction***.

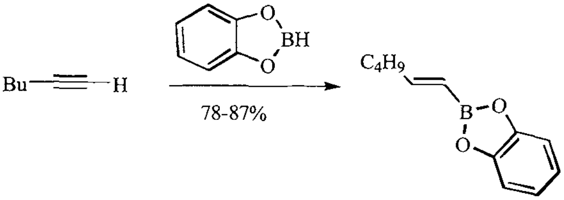
A number of functional groups do not react with catecholborane: These include: organohalogen, alcohols and thiols, ethers, amides, nitro groups, and sulfones. Slowly reducing groups include acid chlorides, esters and nitriles. Aldehydes, ketones, imines, and sulfoxides are reduced. A hydroboraing agent.

Examples:

1.[3]



2.[4]



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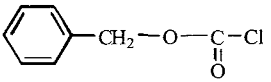
[1] J. V. B. Kanth, M. Periasamy, H. C. Brown, *Organic Process Research & Development* **2000**, 4, 550

[2] G. W. Kabalka, J. D. Baker, Jr., *Journal of Organic Chemistry* **1975**, 40, 1834

[3] G. W. Kabalka, R. Hutchins, N. R. Natale, D. T. C. Yang, V. Broach, *Organic Syntheses* CV6, 293

[4] N. Miyaura, A. Suzuki, *Organic Syntheses* CV8, 532

Cbz-Cl

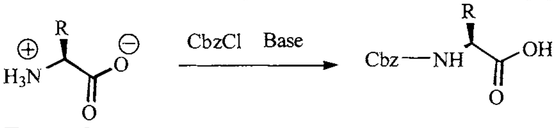


Benzyl chloroformate. source of the carbobenzyloxy (Cbz-) protecting group.
[501-53-1]

Commercially available

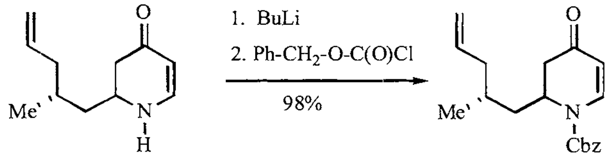
P. Sampson, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 323

Notes: An important functional group for protecting amines as carbamates and alcohols as benzyl carbonates. Notable for the protection of amino acids during peptide synthesis.

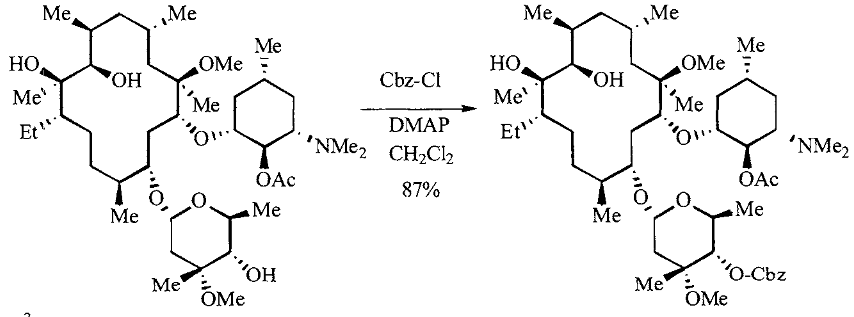


Examples:

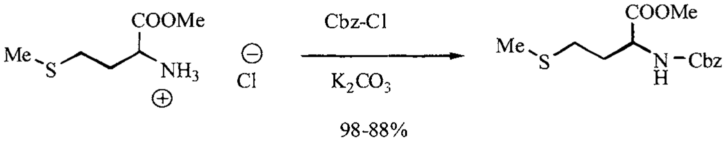
1.[1]



2.[2]



3.[3]



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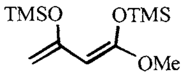
[1] D. L. Comins, C. A. Brooks, R. S. Al-awar, R. R. Goehring, *Organic Letters* **1999**, 1, 229

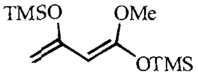
[2] W. R. Baker, J. D. Clark, R. L. Stephens, K. H. Kim, *Journal of Organic Chemistry* **1988**, 53, 2340

[3] M. Carrasco, R. V. Jones, S. Kamel, H. Rapoport, T. Truong, *Organic Syntheses* CV9, 63

Chan's Diene



[81114-98-9]



[74590-73-1]

1,3-Bis-(trimethylsilyloxy)-1-methoxy-buta-1,3-diene
3,7-dioxa-2,6-disilanon-4-ene

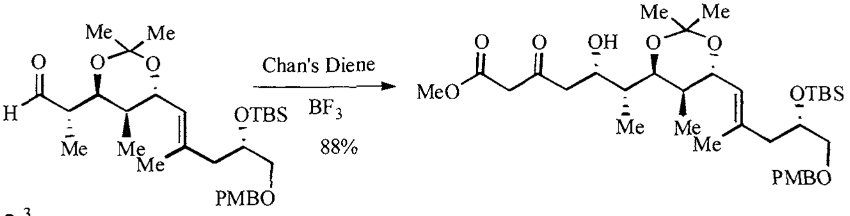
Preparation:[1]

T. Kitahara, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3330

Notes: See ***Brassard's***, ***Danishefsky's*** and ***Rawal's Diene*** and for similar reactions; different substitution patterns.

Examples:

1.[2]



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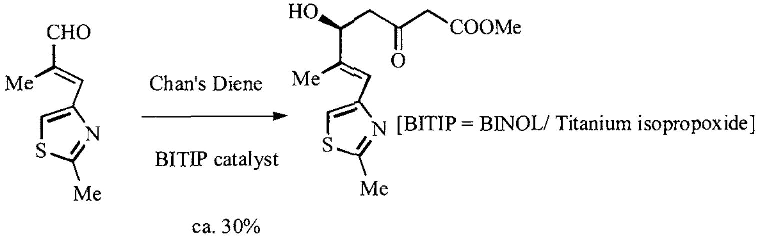
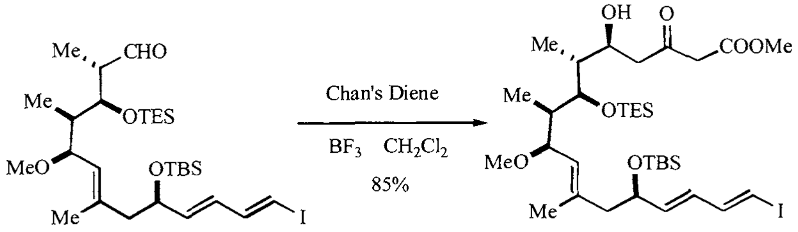


3.[4]



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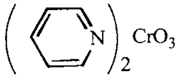
[1] P. Brownbridge, T. H. Chan, *Tetrahedron Letters* **1980**, 21, 3423

[2] D. A. Evans, E. Hu, J. D. Burch, G. Jaeschke, *Journal of the American Chemical Society* **2002**, 124, 5654

[3] G. E. Keck, T. Yu, *Organic Letters* **1999**, 1, 289

[4] I. Paterson, R. D. M. Davies, A. C. Heimann, R. Marquez, A. Meyer, *Organic Letters* **2003**, 5, 4477

Collins and Sarrett Reagents[1]



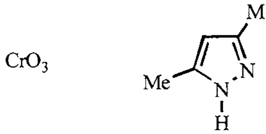
Chromium trioxide bispyridine complex [26412-88-4]
[1333-82-0] [110-86-1]

Preparation: Chromium trioxide is added to pyridine, with cooling. See: *Organic Reactions*, **1998**, 53, 15 for details of preparation. Order of mixing is critical. Addition of pyridine to chromium trioxide may result in fire.

F. Freeman, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **4**, 2272

Notes:

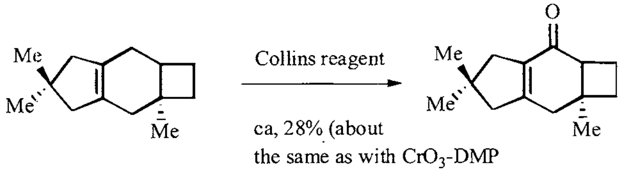
1. A non-acidic oxidizing reagent. It is quite tolerant of other functional groups.
2. Similar to the ***Sarrett Reagent***. The major difference appears that the classical ***Collins Reagent*** is filtered while the ***Sarrett*** is used in pyridine.
3. Allylic oxidations may also be carried out with the related ***Chromium(VI) Oxide-3,5-Dimethylpyrazole*** (DMP) complex.[2]



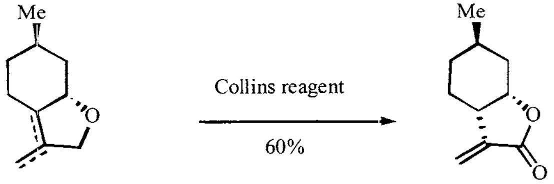
4. The ***Ratcliffe Reagent*** is prepared in situ in dichloromethane.[3]
5. Largely replaced by ***PCC*** and ***PDC***.
6. See ***Chromium-based Oxidizing agents***.

Examples:

1.[4]



2.[5]



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[1] J. C. Collins, W. W. Hess, F. J. Frank, *Tetrahedron Letters* **1968**, 9, 3363

[2] E. J. Corey, G. W. J. Fleet, *Tetrahedron Letters* **1973**, 14, 4459

[3] R. W. Ratcliff, *Organic Syntheses* CV 6, 373

[4] M. Harmata, G. J. Bohnert, *Organic Letters* **2003**, 5, 59

[5] H. M. C. Ferraz, M. V. A. Grazini, C. M. R. Ribeiro, U. Brocksom, T. J. Brocksom, *Journal of Organic Chemistry* **2000**, 65, 2606

Collman's Reagent[1]

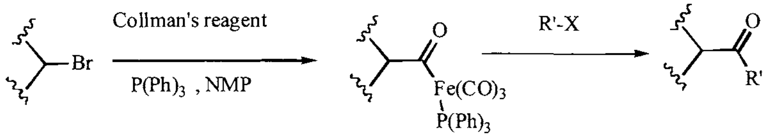
$Na_2Fe(CO)_4$
Disodium tetracarbonylferrate
[14878-31-0]
[59733-73-2] dioxane complex

Commercially available as dioxane complex

R. D. Pike, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **4**, 2299

Notes:

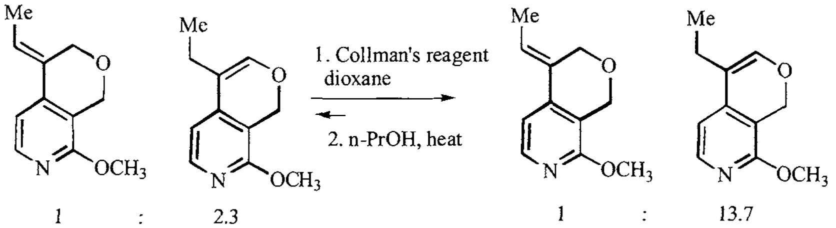
A general scheme:



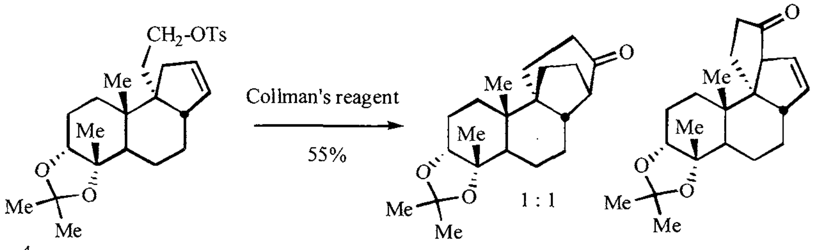
Examples:

Isomerization catalyst

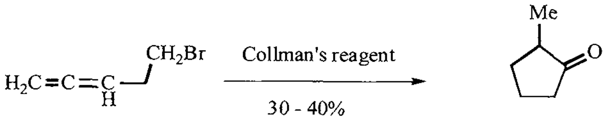
1.[2]



2.[3]



3.[4]



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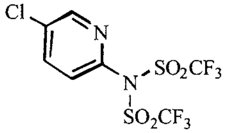
[1] a) J. P. Collman, *Accounts of Chemical Research* **1975**, 8, 342 (b) J. P. Collman, R. G. Finke, J. N. Cawse, J. I. Brauman, *Journal of the American Chemical Society*, **1977**, 99, 2515 (c) J. P. Collman, R. G. Finke, J. N. Cawse, J. I. Brauman, *Journal of the American Chemical Society* **1978**, 100, 4766

[2] D. Bankston, F. Fang, E. Huie, S. Xie, *Journal of Organic Chemistry* **1999**, 64, 3461

[3] J. E. McMurry, A. Andrcjs, G. M. Ksander, J. H. Musser, M. A. Johnson, *Tetrahedron* **1981**, 37, 319

[4] J. Y. Mérour, J. L. Roustan, C. Charrier, J. Benaim, J. Collin, P. Cadiot, *Journal of Organometallic Chemistry* **1979**, 168, 337

Comins' Reagent



2-[*N*,*N*-Bis(trifluoromethylsulfonyl)amino]-5-chloropyridine
[145100-51-2]

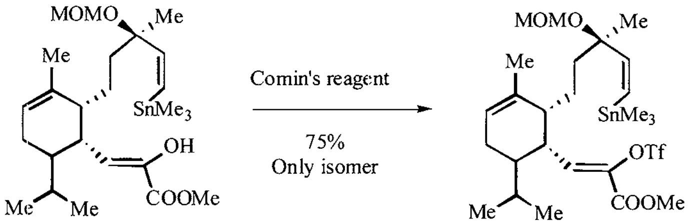
Commercially available

Preparation:[1]

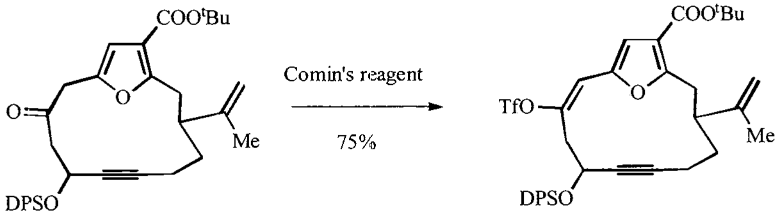
Notes: Reagent used for the conversion of carbonyl groups to –OTf derivatives.

Examples:

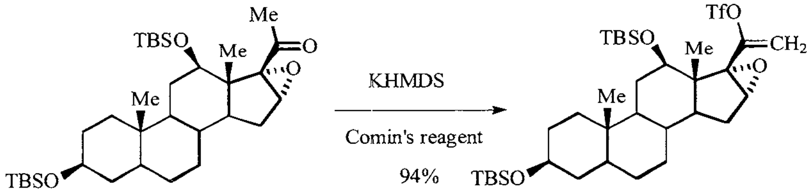
1.[2]



2.[3]



3.[4]



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[1] D. L. Comins, A. Dehgani, C. J. Foti, S. P. Joseph, *Organic Syntheses* CV9, 165

[2] S. M. Ceccarelli, U. Piarulli, J. Telsera, C. Gennaria, *Tetrahedron Letters* **2001**, 42, 7421

[3] J. A. Marshall, E. A. Van Devender, *Journal of Organic Chemistry* **2001**, 66, 8037

[4] K. Yamamoto, C. H. Heathcock, *Organic Letters* **2000**, 2, 1709

Copper-Organometallics

Gilman Cuprates

$$2\ \text{R-Li} \xrightarrow{\text{CuI}} \text{R}_2\text{CuLi}$$

Normant Cuprates

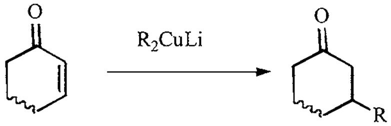
$$2\ \text{R-MgX} \xrightarrow{\text{CuI (cat)}} \text{R}_2\text{CuMgX}$$

Knochel Cuprates

$$2\ \text{R-ZnX} \xrightarrow[\text{LiCl}]{\text{CuCN}} \text{RCu(CN)ZnX}$$

The ***Knochel cuprates*** are able to tolerate a large variety of other functional groups imbedded in "R".

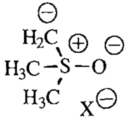
Reactivity differences are readily seen in the 1,4-addition to enones:



The ***Normant variation*** adds the same way. Since the CuI is only catalytic, it becomes obvious that the reagent is much more reactive than the ***Grignard*** starting material.

For the ***Knochel reaction*** an added Lewis acid is needed to enhance the 1,4-addition; otherwise 1,2-addition would take place. A major advantage of the ***Knochel reagent*** is that other functional groups (ester, carbonyl, nitrile, Cl, sulfoxide and terminal alkyne) are possible with the organo-zinc starting material.

Corey-Chaykovsky Reagent[1,2]



Trimethylsulfoxonium iodide
[1774-47-6]

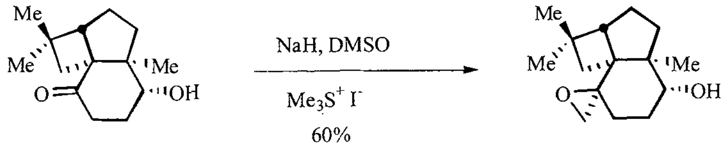
Commercially available. Preparation:[3]

J. S. Ng, C. Liu, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 7, 5335

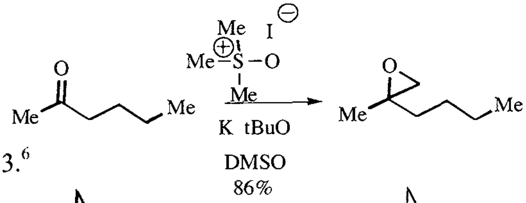
Notes: This reagent finds use in epoxidation of carbonyl groups. Can also cyclopropanate enone systems.

Examples:

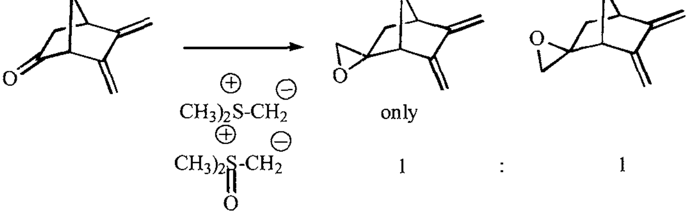
1.[4]



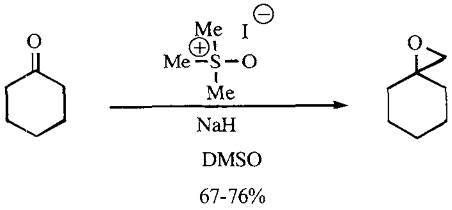
2.[5]



3.[6]



4.[7]



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[1] Review: Y. G. Gololobov, A. N. Nesmeyanov, V. P. Lysenco, I. E. Boldeskul, *Tetrahedron* **1987**, 43, 2609

[2] E. J. Corey, M. Chaykovsky, *Journal of the American Chemical Society* **1962**, 84, 867

[3] Details of the preparation and use of the reagent are provided: E. J. Corey, M. Chaykovsky, *Journal of the American Chemical Society* **1965**, 87, 1350

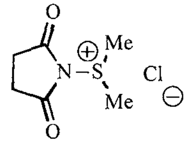
[4] C. F. D. Amigo, I. G. Collado, J. R. Hanson, R. Hernandez-Galan, P. B. Hitchcock, A. J. Macías-Sánchez, D. J. Mobbs, *Journal of Organic Chemistry* **2001**, **66**, 4327

[5] J. S. Ng, *Synthetic Communications* **1990**, 20, 1193

[6] C. Mahaim, L. Schwager, P.-A. Carrupt, P. Vogel, *Tetrahedron Letters* **1983**, 24, 3603

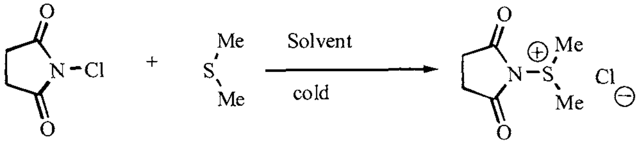
[7] E. J. Corey, M. Chaykovsky, *Organic Syntheses* CV5, 755

Corey-Kim Reagent



N-Chlorosuccinimide-dimethyl sulfide
[39095-38-0]

Preparation: By reaction of NCS with dimethylsulfide. Prepared *in situ* in solvents such as dichloromethane, THF or toluene.

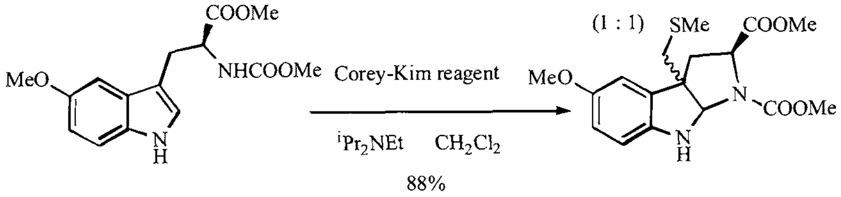


R. C. Kelly, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1208

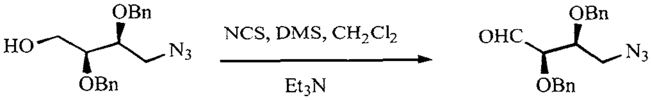
Notes: Mild oxidizing agent (***See DMSO Oxidations in Aldehyde Syntheses***). A source of the S-Me electrophile. For an odorless protocol:[1] Instead of DMSO, dodecyl methyl sulfide is used in the reaction; thus, eliminating the dimethylsulfide by-product.

Examples:

1.[2]

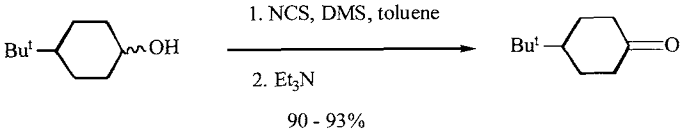


2.[3]



No yield provided; however, it was reported that this process was not as effective as the ***Swern Oxidation***.

3.[4]



In this report a number of additional examples of primary and secondary alcohol oxidations are provided.

---

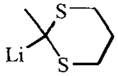
[1] K. Nishide, S. Ohsugi, M. Fudesaka, S. Kodama, M. Node, *Tetrahedron Letters* **2002**, 43, 5177

[2] M. Kawahara, A. Nishida, M. Nakagawa, *Organic Letters* **2000**, 2, 675

[3] J. Z. Ho, R. M. Mohareb, J. H. Ahn, T. B. Sim, H. Rapoport, *Journal of Organic Chemistry* **2003**, 68, 109

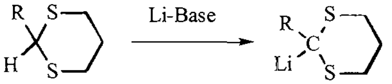
[4] E. J. Corey, C. U. Kim, P. F. Misco, *Organic Syntheses* CV 6, 220

Corey-Seebach Reagent



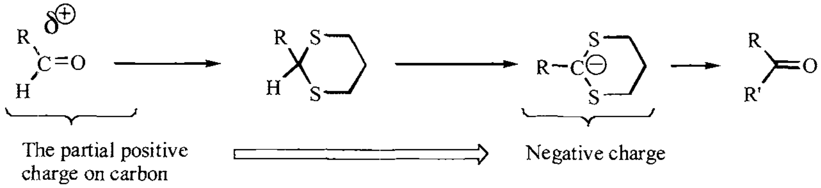
2-Lithio-1,3-dithiane [36049-90-8]

Preparation:



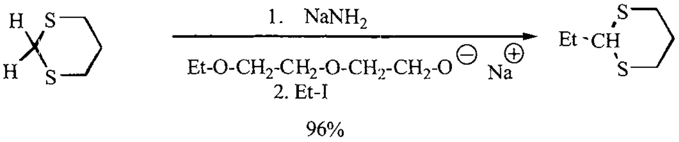
M. Kolb, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 2983

Notes: An "umpolung" reagent.

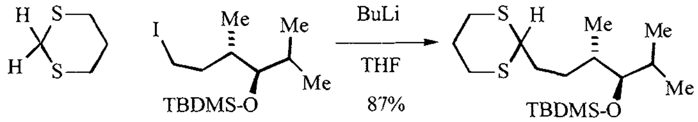


Examples:

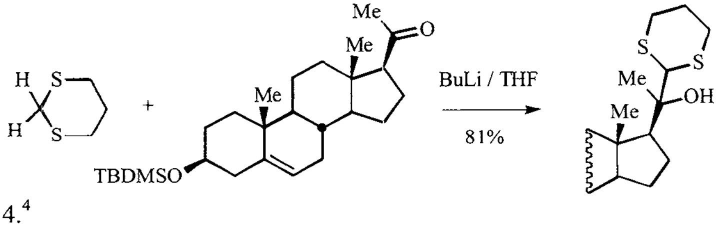
1.[1]



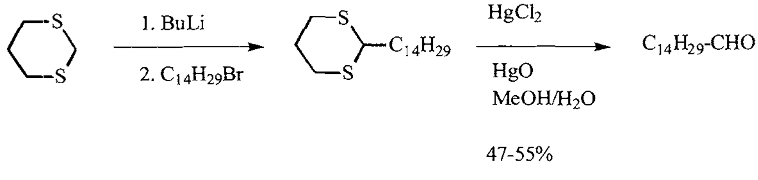
2.[2]



3.[3]



4.[4]



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[1] P. Gros, P. Hansen, P. Caubere, *Tetrahedron* **1996**, 52, 15147

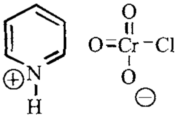
[2] P. G. Steel, E.J. Thomas, *Journal of the Chemical Society, Perkin Transaction 1* **1997**, 371

[3] B. G. Hazra, S. Basu, B. B. Bahule, V. S. Pore, B. N. Vyas, V. M. Ramraj, *Tetrahedron* **1997**, 53, 4909

[4] D. Seebach, A. K. Beck, *Organic Syntheses* CV6, 869

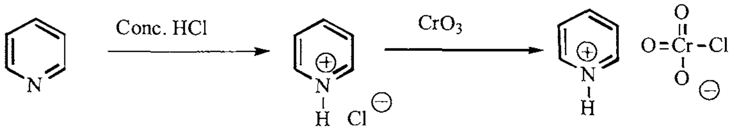
Corey's Reagent

PCC



Pyridinium Chlorochromate
[26299-14-9]

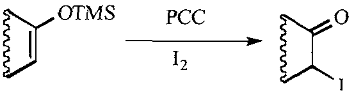
Commercially available. An improved preparation has been reported.[1]



G. Piancatelli, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4356

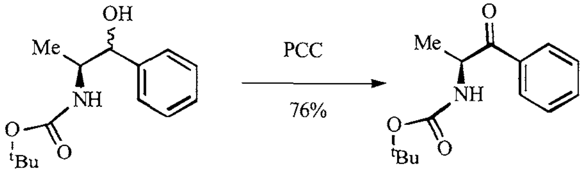
Notes:

PCC can be used under solvent-free conditions.[2] Mechanistic studies.[3]
PCC/I_2 is useful for the conversion:[4]

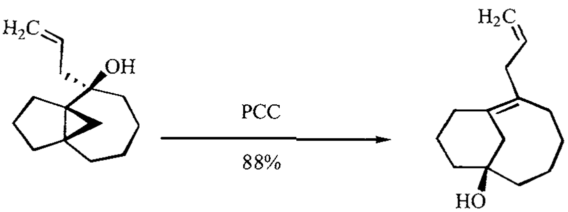


Examples:

1.[5]



2.[6]



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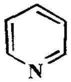
[1] S. Agarwal, H. P. Tiwari, J. P. Sharma, *Tetrahedron* **1990**, 46, 4417
[2] P. Salehi, H. Firouzabadi, A. Farrokhi, M. Gholizadeh, *Synthesis* **2001**, 2237
[3] S. Agarwal, H. P. Tiwari, J. P. Sharma, *Tetrahedron* **1990**, 46, 1963
[4] G. Piancatelli, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4356
[5] G. I. Hwang, J.-H. Chung, W. K. Lee, *Tetrahedron* **1996**, 52, 12111
[6] J. Cossy, S. BouzBouz, M. Laghgar, B. Tabyaoui, *Tetrahedron Letters* **2002**, 43, 823

Cornforth Reagent



CrO_3 H_2O

Chromium trioxide / Pyridine / Water
[110-86-1]
[1333-82-0]

Fieser's Reagent

CrO_3 HOAc

Chromium trioxide	Acetic Acid
[1333-82-0]	[64-19-7]

F. Freeman, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1273

Criegee Reagent

$Pb(OAc)_4$

Lead tetraacetate (LTA)

[546-67-8]

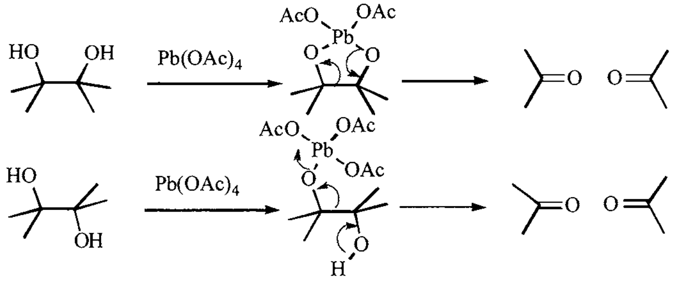
Commercially available

M. L. Mihailovic, Z. Cekovic, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 2949

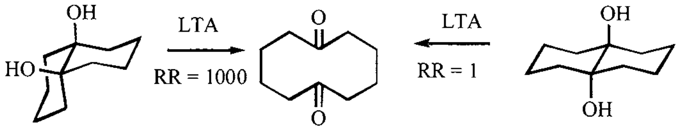
Notes:

The "named reagent" is most closely associated with the cleavage of 1,2-diols.

Cis-diols are cleaved more readily than *trans* diols. Different mechanistic interpretations are invoked for the two processes:

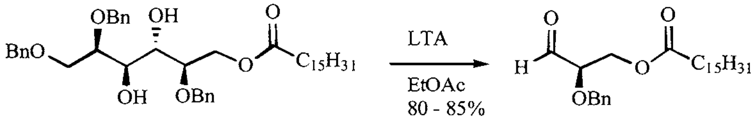


Reported[1]

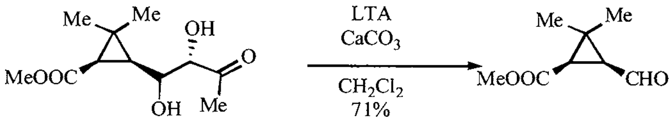


Examples:

1.[2]



2.[3]



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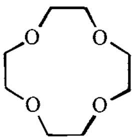
[1] M. L. Mihailovic, Z. Cekovic, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 2949

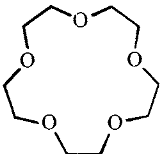
[2] J. Xia, Y.-Z. Hui, *Tetrahedron: Asymmetry* **1997**, 8, 451

[3] M. G. Banwell, G. S. Forman, *Journal of the Chemical Society, Perkin Transactions 1* **1996**, 2565

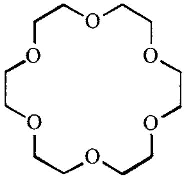
Crown Ether



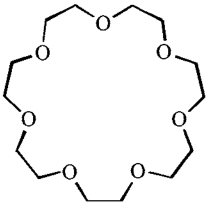
12-Crown-4



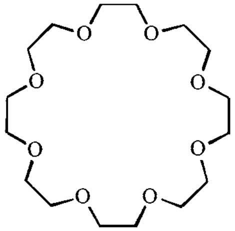
15-Crown-5



18-Crown-6



21-Crown-7



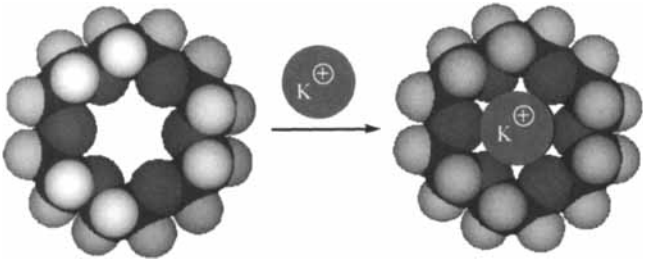
24-Crown-8

n-Crown-m

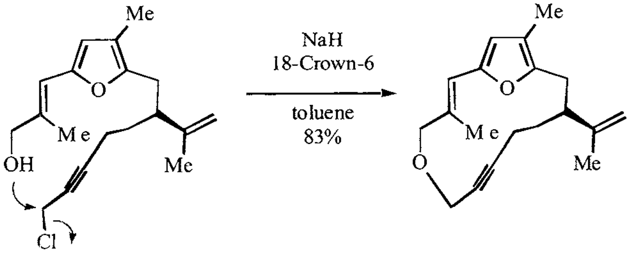
Where **n** gives ring size and **m**- gives number of heteroatoms

Commercially available

These materials, generally used as cosolvents, are useful in holding cations in their cavaties; thus, allowing the anion to be more reactive.



Example: [1]



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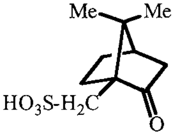
[1] J. A. Marshall, G. S. Bartley, E. M. Wallace, *Journal of Organic Chemistry* **1996**, 61, 5729

CSA



Camphorsulfonic Acid
[5872-08-2]

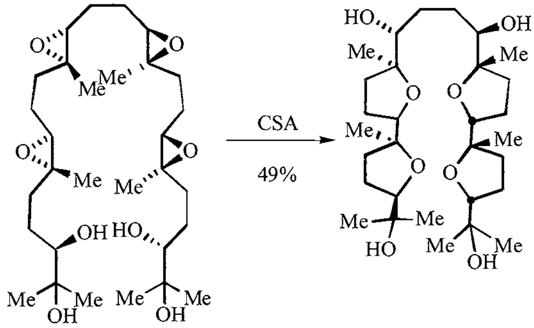
Commercially available

E. M. Leahy, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 969

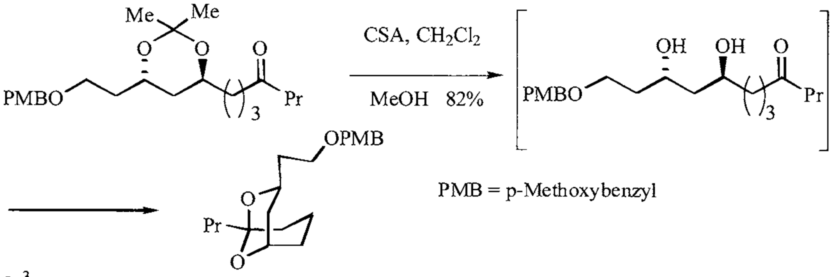
Notes: A useful acid catalyst.

Examples:

1.[1]

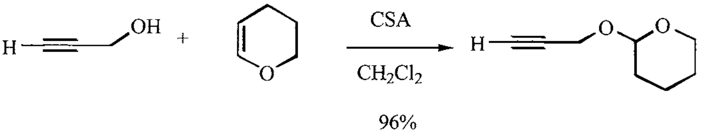


2.[2]



PMB = p-Methoxybenzyl

3.[3]



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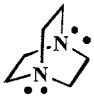
[1] X. Xiong, E. J. Corey, *Journal of the American Chemical Society* **2000**, 122, 9338

[2] J. Aiguade, J. Hao, C. J. Forsyth, *Organic Letters* **2001**, 3, 979

[3] A. G. Myers, B. Zheng, *Organic Syntheses* CV10, 2350

DABCO

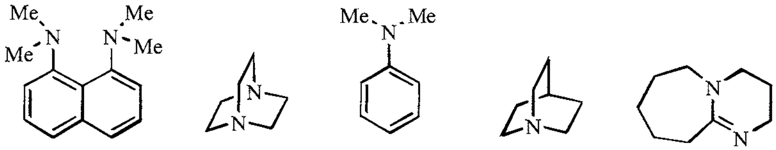


[280-57-9]
1,4-Diazabicylo[2.2.2]octane, triethylenediamine, TED

Commercially available

U. V. Mallavadhani, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1494

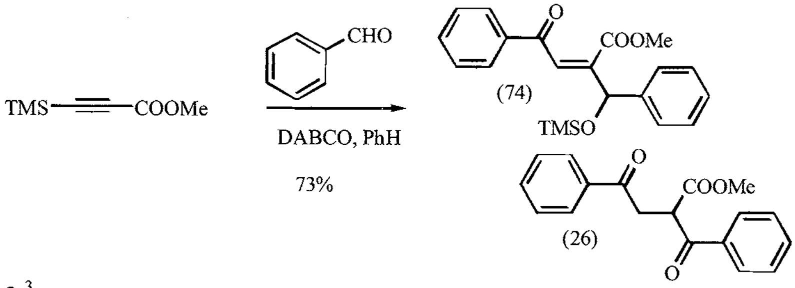
Notes: Useful for organometallic complexation. Selective base used for the ***Bayliss-Hillman reaction***. Has been used for the ***Haller-Bauer*** cleavage reaction. Streitwieser[1] has examined a new scale of amine basicity (K_{ip}), where the *lower* the pK_{ip} values the stronger the base. In this analysis:



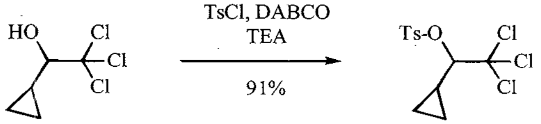
	Proton Sponge	***DABCO***	***DMAP***	Quinuclidine	***DBU***
pK_{ip}	2.15	0.80	0.61	0.15	-3.78

Examples:

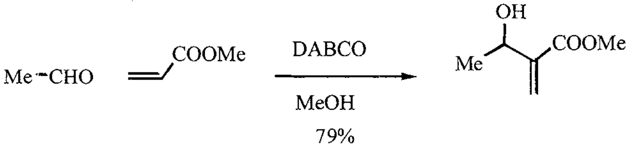
1.[2]



2.[3]



3.[4]



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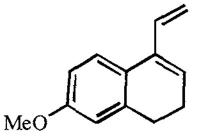
[1] A. Streitieser, Y.-J. Kim, *Journal of the American Chemical Society* **2000**, 48, 11783
[2] Y. Matsuya, K. Hayashi, H. Nemoto, *Journal of the American Chemical Society* **2003**, 125, 646
[3] Z. Wang, S. Campagna, K. Yang, G. Xu, M. E. Pierce, J. M. Fortunak, P. N. Confalone, *Journal of Organic Chemistry* **2000**, 65, 1889
[4] C. Behrens, L. Paquette, *Organic Syntheses* CV10, 2316

Dane's Diene



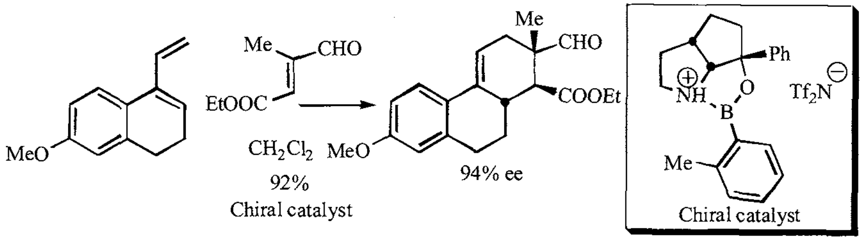
1-Vinyl-6-methoxy-3,4-dihydronaphthalene
[2811-50-9]

Notes:

This is a diene useful for the construction of steroid skeletal.

Examples:

1.[1]



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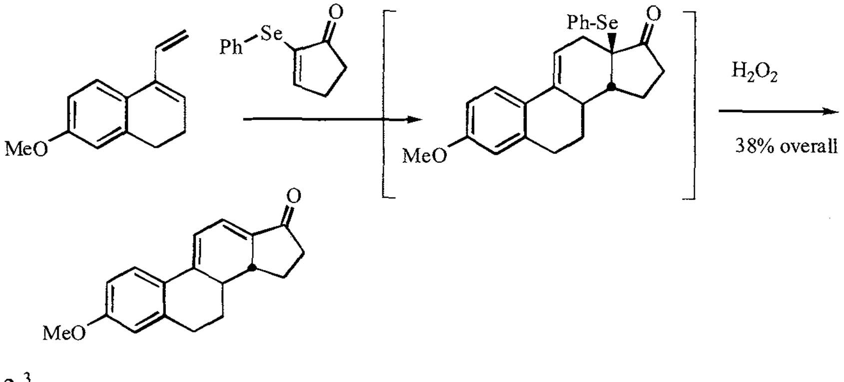
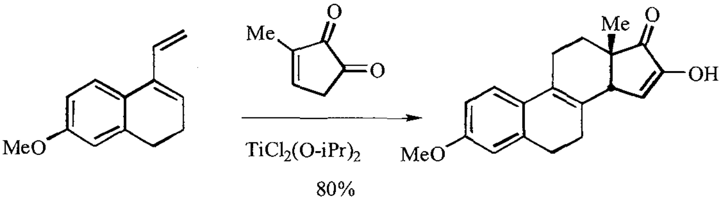


3.[3]



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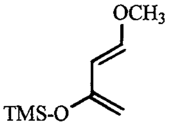
[1] Q.-Y. Hu, P. D. Rege, E. J. Corey, *Journal of the American Chemical Society* **2004**, 126, 5984

[2] S. Woskiand, M. Koreeda, *Journal of Organic Chemistry* **1992**, 57, 5736

[3] G. Quinkert, M. del Grosso, A. Bucher, M. Bauch, W. Döring, J. W. Bats, G. Dürner, *Tetrahedron Letters* **1992**, 33, 3617

Danishefsky's Diene

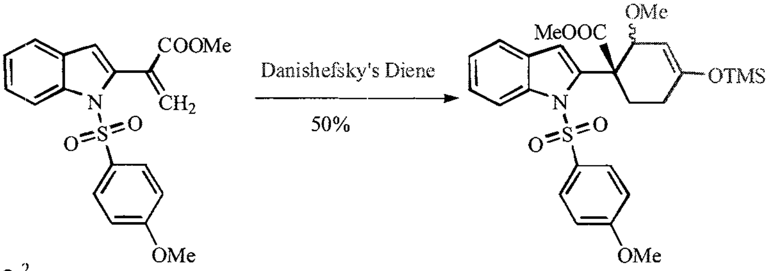


trans-1-methoxy-3-trimethylsiloxy-1,3-butadiene
[59414-23-21]

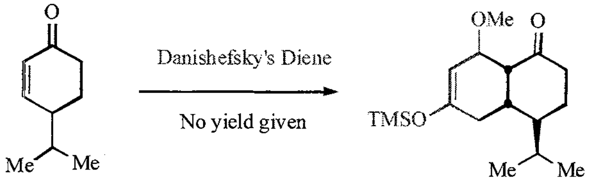
T. Kitahara, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3395

Examples:

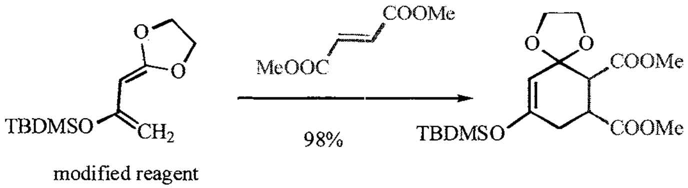
1.[1]



2.[2]



3.[3]



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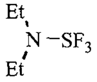
[1] B. Danieli, G. Lesma, M. Luzzani, D. Passarella, A. Silvani, *Tetrahedron* **1996**, 52, 11291
[2] B. Ye, H. Nakamura, A. Murai, *Tetrahedron* **1996**, 52, 6361
[3] J. P. Konopelski, R.A. Kalsar, *Tetrahedron Letters* **1993**, 34, 4587

DAST



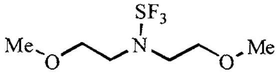
(Diethylamino)sulfur trifluoride
[38078-09-0]

Commercially available

A. H. Fauq, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1787

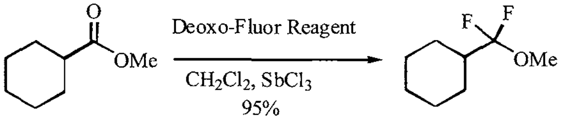
Notes:

A useful fluorinating reagent. Readily converts the –OH group of an alcohol to –F. Deoxy-Fluor Reagent® [bis-(2-methoxyethyl) amino sulfur trifluoride] has been found to be more stable.[1]

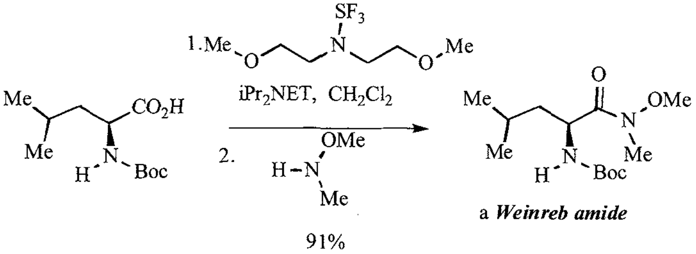


Examples:

1.[1]



2.[2]



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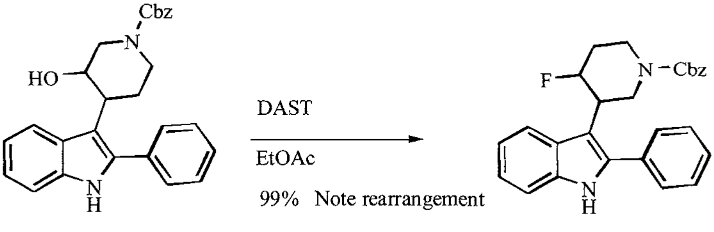
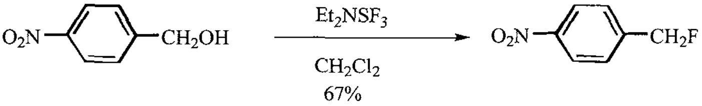


4.[4]



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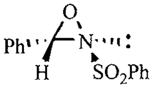
[1] G. S. Lal, E. Lobach, A. Evans, *Journal of Organic Chemistry* **2000**, 65, 4830

[2] A. R. Tunoori, J. M. White, G. I. George, *Organic Letters* **2000**, 2, 4091

[3] D. J. Hallett, U. Gerhard, S. C. Goodacre, L. Hitzel, T. J. Sparey, S. Thomas, M. Rowley, R. G. Ball, *Journal of Organic Chemistry* **2000**, 65, 4984

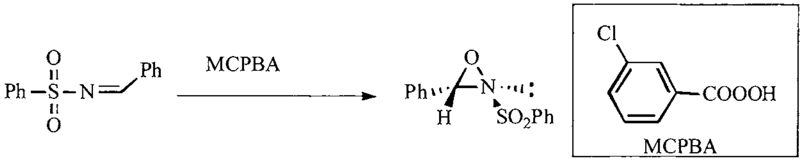
[4] W. J. Middleton, E.M. Bingham, *Organic Syntheses* CV6, 835

Davis's Oxaziridine



2-(phenylsulfonyl)-3-phenyloxaziridine
[63160-13-4]]

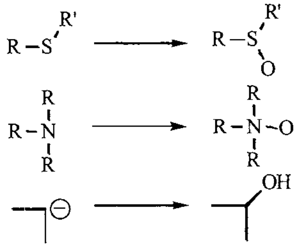
Preparation:



B.-C. Chen, F.A. Davis, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4054

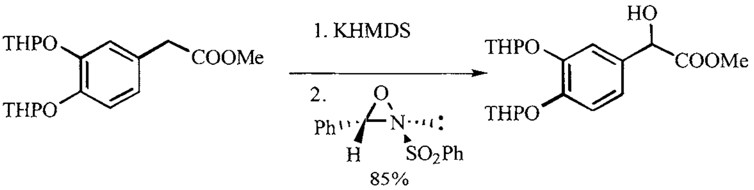
Notes:

A useful oxidizing agent. Will convert organic sulfides to sulfoxides without overoxidation and disubstituted enamines to α-aminoketones. Most useful is the oxidation of carbanions to hydroxyl groups.

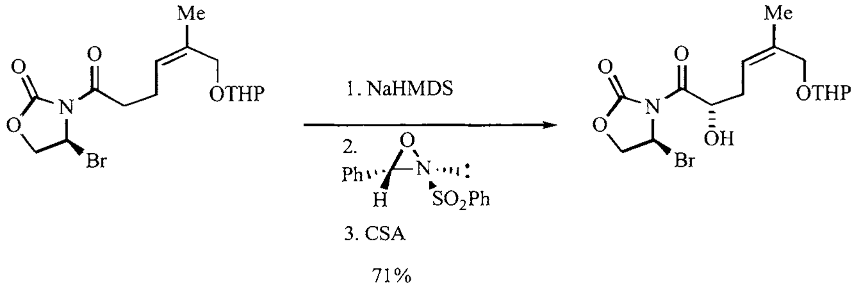


Examples:

1.[1]



2.[2]



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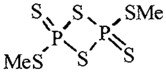
[1] J. Narayanan, Y. Hayakawa, J. Fan, K. L. Kirk, *Bioorganic Chemistry* **2003**, 31, 191

[2] J. D. White, R. G. Carter, K. F. Sundermann, *Journal of Organic Chemistry* **1999**, 64, 684

Davy's Reagent



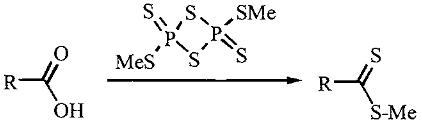
2,4-bis(methylthio)-1,3,2,4-dithiadiphosphetane-2,4-disulfide
[82737-61-9]

Preparation:

J. Voss, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 535

Notes:

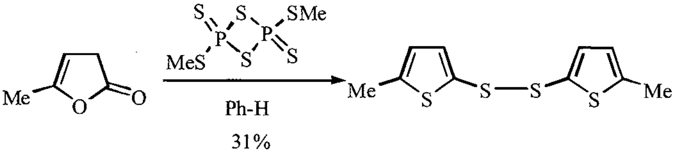
More reactive than ***Lawesson's Reagent***. Can convert a carboxylic acid directly to a dithioester. See also, ***Belleau's Reagent***.



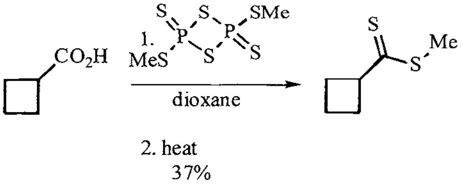
Is also useful for the general conversion of a carbonyl group to a thiacarbonyl.

Examples:

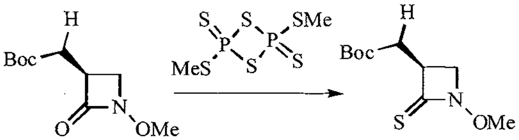
1.[1]



2.[2]



3.[3]



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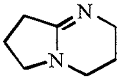
[1] N. M. Yousif, U. Pedersen, B. Yde, S.-O. Lawesson, *Tetrahedron* **1984**, 40, 2663
[2] Y. Vallee, S. Masson, J.-L, Ripoli, *Tetrahedron* **1990**, 46, 3928
[3] J. Nieschalk, E. Schaumann, *Liebigs Annelen* **1996**, 141 (AN 1995: 48264)

DBN



1,5-Diazabicyclo[4.3.0]non-5-ene
[3001-72-7]

Commercially available

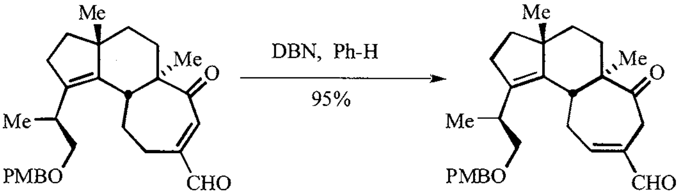
A. C. Savoco, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1491

Notes:

An organic base, soluble in a variety of common organic solvents. Useful for equilibrations and elimination reactions.

Examples:

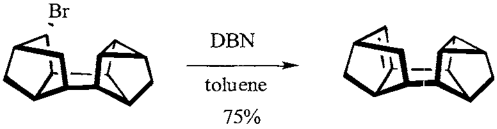
1.[1]



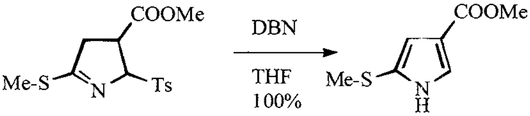
2.[2]

G = H	77	23
G = COOMe	21	79

3.[3]



4.[4]



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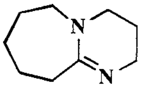
[1] E. Piers, M. Gilbert, K. L. Cook, *Organic Letters* **2000**, 2, 1407
[2] R. C. Mease, J. A. Hirsch, *Journal of Organic Chemistry* **1984**, 49, 2927
[3] G.-C. Wei, T. J. Chow, Y.-P. Yang, Y.-J. Chen, *Tetrahedron* **1993**, 49, 2201
[4] F. Berree, E. Marchand, G. Morel, *Tetrahedron Letters* **1992**, 33, 6155

DBU

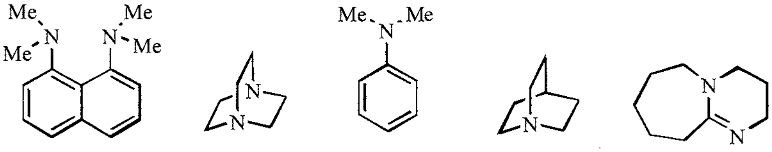


[6674-22-2]
1,5-Diazabicyclo[5.4.0]undec-7-ene

Commercially available

A. C. Savaca, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1497

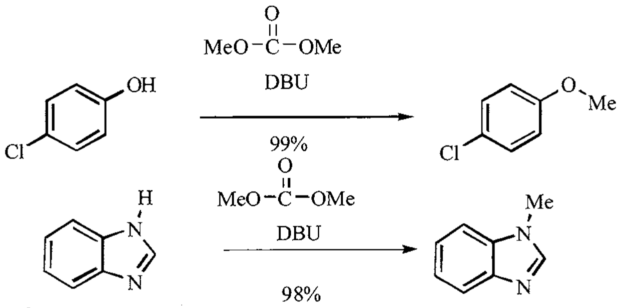
Notes: Streitwieser[1] has examined a new scale of amine basicity (K_{ip}), where the *lower* the pK_{ip} values the stronger the base. In this analysis:



	Proton Sponge	***DABCO***	***DMAP***	Quinuclidine	***DBU***
pK_{ip}	2.15	0.80	0.61	0.15	-3.78

Examples:

1.[2]



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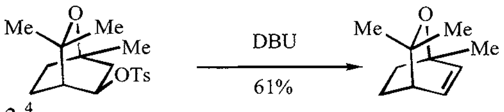

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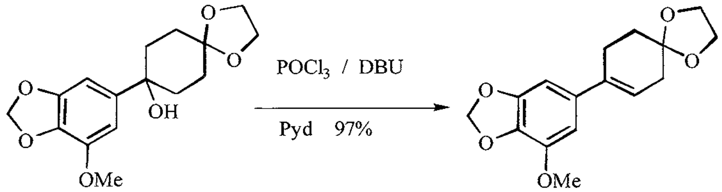

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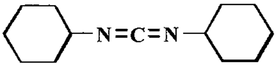
[1] A. Streitieser, Y.-J. Kim, *Journal of the American Chemical Society* **2000**, 48, 11783
[2] W.-C. Shieh, S. Dell, O. Repic, *Organic Letters* **2001**, 3, 4279
[3] F. A. Luzzio, D. Y. Duveau, *Tetrahedron: Asymmetry* **2002**, 13, 117
[4] P. Magnus, I. K. Sebhat, *Tetrahedron* **1998**, 54, 15509

DCC

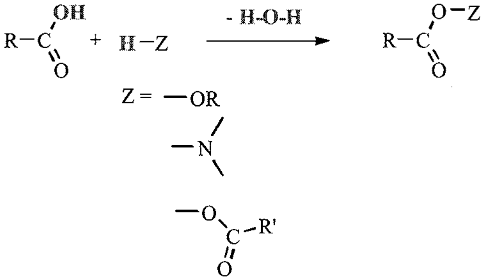


1,3-Dicyclohexylcarbodiimide
[538-75-0]

Commercially available

J. S. Albert, A. D. Hamilton, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1751

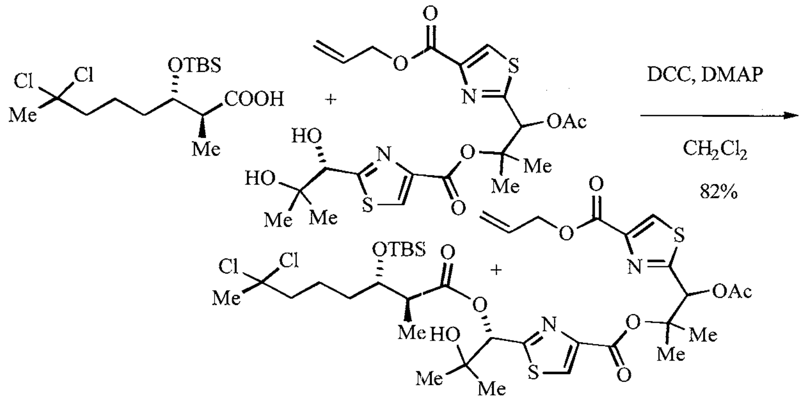
Notes: Dehydrating agent often used to form esters, amides or anhydrides.



With ***DMSO***, provides a mild oxidizing agent (***Pfitzner-Moffatt Oxidation***). The reagent has been useful in forming the peptide linkage from amino acids.
With ***DMAP*** is used for the ***Steglich Esterification***.

Examples:

1.[1]



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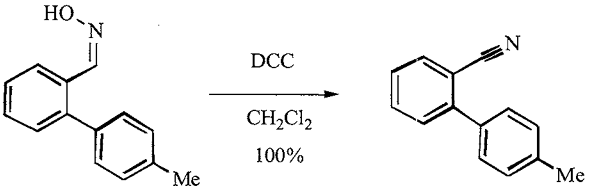

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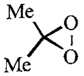
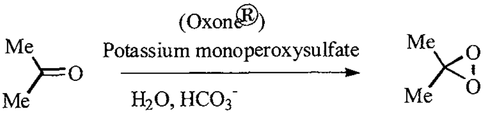
[1] J. R. P. Cetusic, F. R. Greene, III, P. R. Graupner, M. P. Oliver, *Organic Letters* **2002**, 4, 1307
[2] D. Goubet, P. Meric, J.-R. Dormoy, P. Moreau *Journal of Organic Chemistry* **1999**, 64, 4516

DDO



Dimethyldioxirane
[74087-85-7]

Preparation:[1,2]

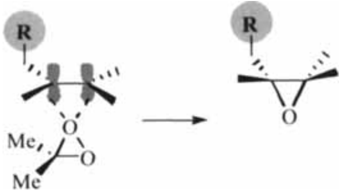


Oxone is commercially available

J. A. Crandall, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 206

Notes:

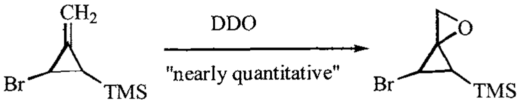
A selective and reactive oxidizing agent. Will epoxidize α,β-unsaturated carbonyl compounds. In epoxidation reactions, there is a strong steric influence directing the facial selectivity:



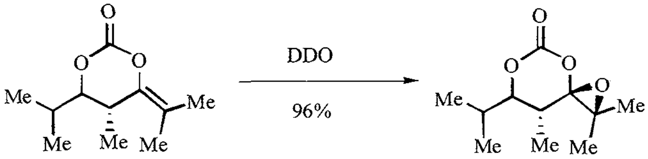
The amount of *trans* isomer increases with increasing steric bulk of the R- group

Examples:

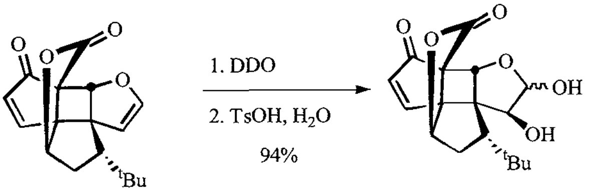
1.[3]



2.[4]



3.[5]



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[1] $2KHSO_3•KHSO_4•K_2SO_4$ is commercially available as ***Oxone***®.

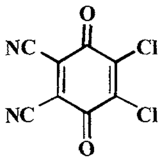
[2] See: R. W. Murray, M. Singh, *Organic Syntheses* CV9, 288 for details of preparation.

[3] W. E. Billups, V. A. Litosh, R. K. Saini, A. D. Daniels, *Organic Letters* **1999**, 1, 115

[4] B. C. Raimundo, C. H. Heathcock, *Organic Letters* **2000**, 2, 27

[5] M. T. Crimmins, J. M. Pace, P. G. Nantermet, A. S. Kim-Meade, J. B. Thomas, S. H. Watterson, A. S. Wagman, *Journal of the American Chemical Society* **1999**, 121, 10249

DDQ



2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
[84-58-2]

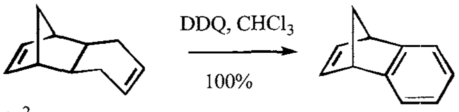
Commercially available

D. R. Buckle, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1699

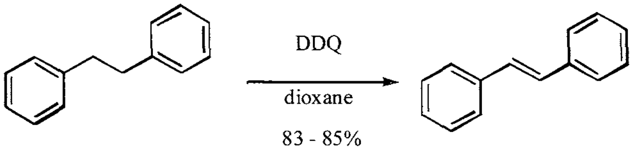
Notes: An oxidizing agent useful for dehydrogenations; particularly those resulting in aromatization, extended conjugation from aromatic systems, and the formation of enones. Oxidation of phenol provides quinones.

Examples:

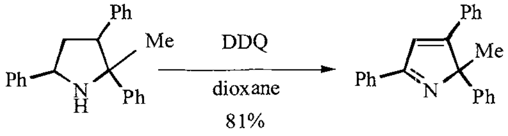
1.[1]



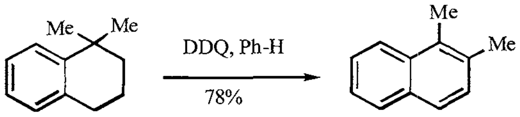
2.[2]



3.[3]



4.[4] Rearrangement may accompany dehydrogenation:



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[1] S. Cossu, O. DeLucchi, *Tetrahedron* **1996**, 52, 14247

[2] J. W. A. Findlay, A. B. Turner, *Organic Syntheses* CV 5, 428

[3] S. R. Cheruka, M. P. Padmanilayam, J. L. Vennerstrom, *Tetrahedron Letters* **2003**, 44, 3701

[4] Reported by D.R. Buckle, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1700 (E. A. Braude, L. M. Jackman, R. P. Linstead, G. Lowe, *Journal of the Chemical Society* **1960**, 3123)

DEAD

EtOOC−N=N−COOEt

Diethyl Azodicarboxylate

[1972-28-7]

Commercially available

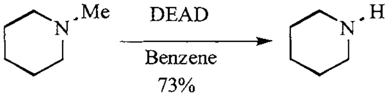
E. J. Stoner, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1790

Notes:

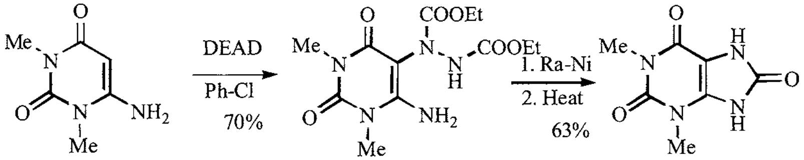
An oxidizing agent. Useful for the dealkylation of amines; and the conversion of pyrimidines to purines. It is most often associated with triphenylphosphine (***TPP***) in the ***Mitsunobu reaction***.

Examples:

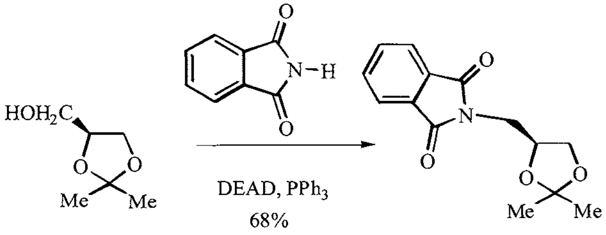
1.[1]



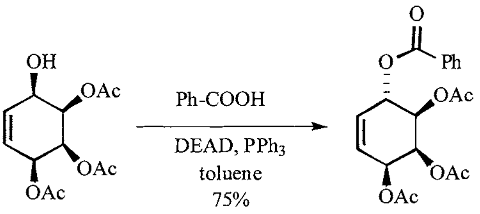
2.[2]



3.[3]



4.[4]



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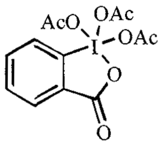
[1] E. M. Smissman, A. Makriyannis, *Journal of Organic Chemistry* **1973**, 38, 1652

[2] E. C. Taylor, F. Sowinski, *Journal of Organic Chemistry* **1974** 39 907

[3] B. B. Lohray, A. S. Reddy, V. Bhushan, *Tetrahedron: Asymmetry* **1996**, 7, 2411

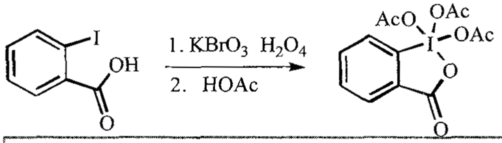
[4] A. Patti, C. SanFilippo, M. Piattelli, G. Nicolosi, *Tetrahedron: Asymmetry* **1996**, 7, 2665

Dess-Martin Reagent



1,1-Triacetoxy-1,1-dihydro-1,2-benziodoxol-3(1H)-one
periodinane
[87413-09-0]

Preparation:

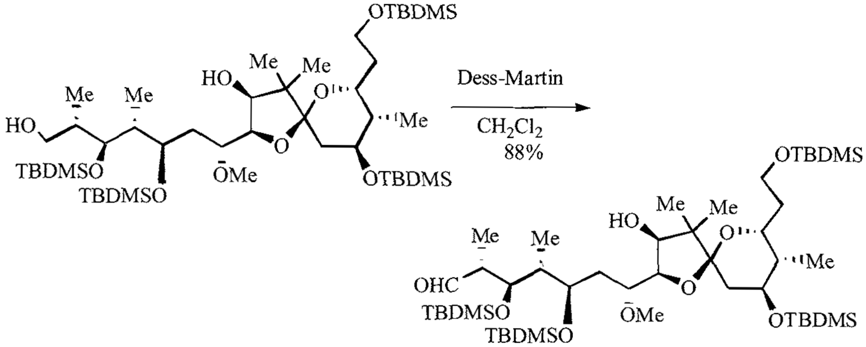


Robert J. Boeckman, Jr., *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 7, 4982

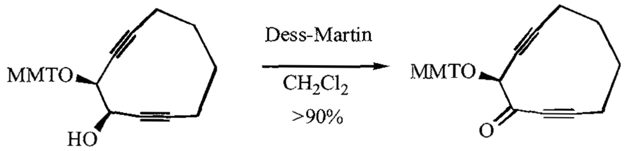
Notes: Selective oxidizing agent. Since a mechanistic requirement of this reagent functioning ability is a complexation with the substrate, it is exceedingly important that only the –OH group binds efficiently. A useful advantage of this oxidation protocol is that it takes place under essentially neutral conditions. See: ***Dess-Martin Oxidation***.

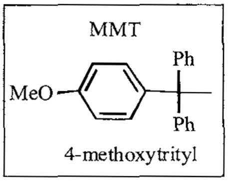
Examples:

1.[1] Note the preferential oxidation of the primary alcohol



2.[2]





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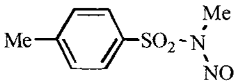
[1] D. A. Evans, J. R. Gage, J. L. Leighton, *Journal of the American Chemical Society* **1992**, 114, 9434

[2] A. G. Myers, P. S. Dragovich, *Journal of the American Chemical Society* **1992**, 114, 5859

Diazald®



N-Methyl-*N*-nitroso-*p*-toluenesulfonamide

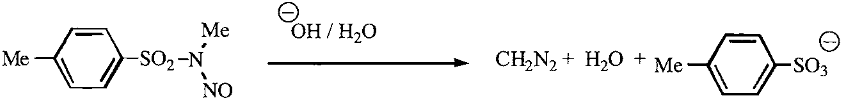
[80-11-5]

Commercially available

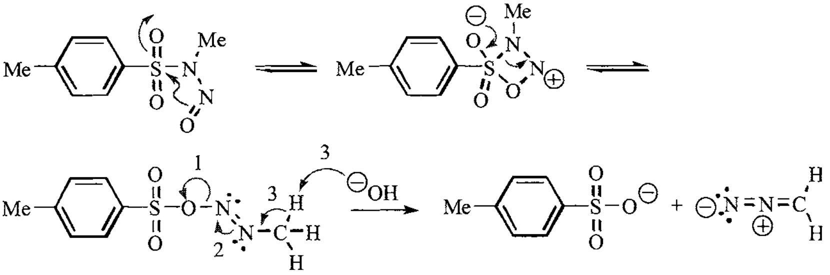
Y. Terao, M. Sekiya, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3555

Notes:

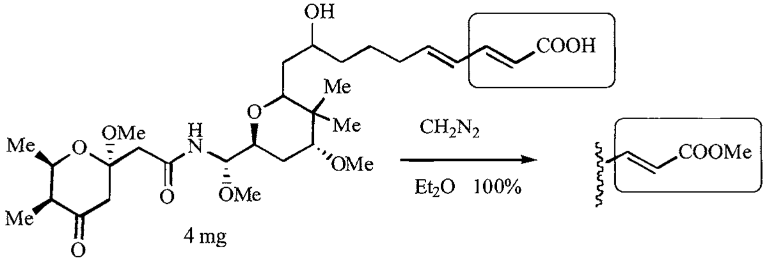
Precursor of diazomethane, a highly toxic and unpredictably explosive gas. Possibly a carcinogen. Read details carefully before preparation. Reactions with and preparation of diazomethane should be carried out in a fume hood and behind a sturdy safety shield. Rough glass surfaces and strong sunlight are known to initiate detonation.



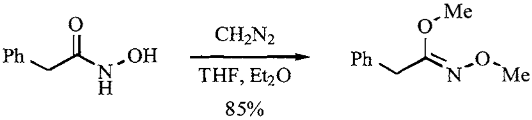
Mechanism



Example of using diazomethane to prepare methyl ester:[1]



Example of using diazomethane to prepare methyl ether:[2]



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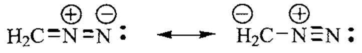
[1] D. Vuong, R. J. Capon, E. Lacey, J. H. Gill, K. Heiland, T. Friedel, *Journal of Natural Products* **2001**, 64, 640

[2] A. Leggio, A. Liguori, A. Napoli, C. Siciliano, G. Sindona, *Journal of Organic Chemistry* **2001**, 66, 2246

Diazomethane

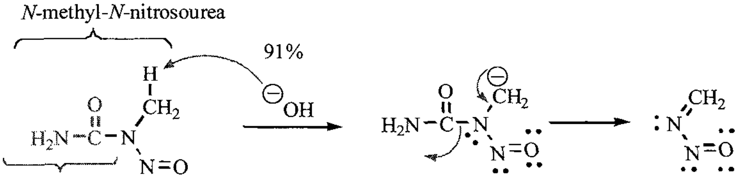


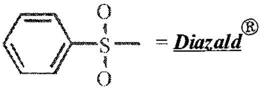
$\overset{\oplus}{}\overset{\ominus}{}\ H_2C{=}N{=}N{:} \longleftrightarrow \overset{\ominus}{}\ \overset{\oplus}{}\ H_2C{-}N{\equiv}N{:}$

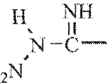
[334-88-3]

Preparation:

Major sources are the basic hydrolysis of *N*-methyl-*N*-nitrosourea (or *N*-methyl-*N*-nitroso-*p*-toluenesulfonamide (***Diazald***®) or 1-methyl-3-nitro-1-nitrosoguanidine (**MNNG**).





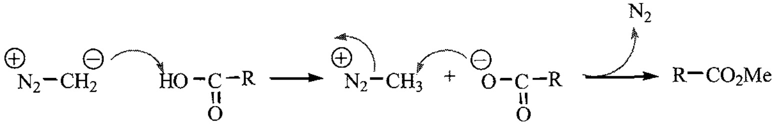


1-Methyl-3-nitro-1-nitrosoguanidine (MNNG)

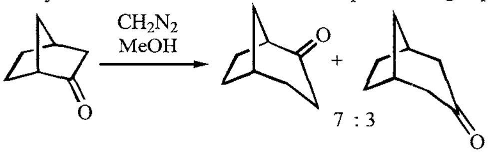
T. Sammakia, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1512

Notes:

Diazomethane is prepared immediately prior to using it. It is a powerful methylating agent, particularly useful for mild preparation of methyl esters of acids.

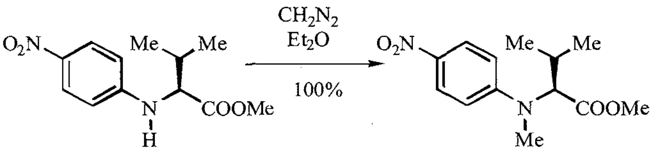


Diazomethane is also useful for cyclopropanation reactions and for reaction with acid chlorides to produce diazo ketones. [***See Wolff Rearrangement***] It can be used to generate methyl ethers and *N*-methylations. Reaction with ketones can provide ring expansions.[1]



Examples:

1.[2]



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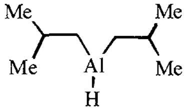
[1] Y. Auberson, R. Mampuya Bimwala, P. Vogel, *Tetrahedron Letters* **1991**, 32, 1637

[2] M. L. Di Gioia, A. Leggio, A. Le Pera, A. Liguori, A. Napoli, C. Siciliano, G. Sindona, *Journal of Organic Chemistry* **2003**, 68, 7416

DIBAL (DIBAL-H, DIBAH)

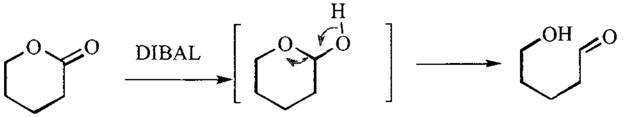


Diisubutylaluminum hydride
[1191-15-7]

Commercially available

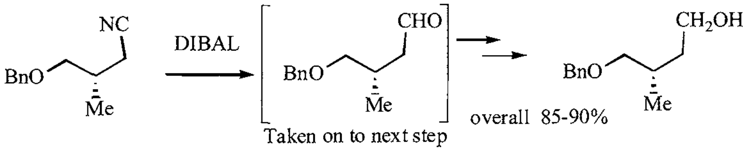
P. Galatsis, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1908

Notes: A reducing agent. Alcohols are generated from aldehydes, ketones, esters and acid chlorides. Nitriles can be converted to aldehydes. Tosylates will be replaced by –H; halides are inert. Amides are reduced to amines. Reduction of lactones can provide a useful synthetic strategy:

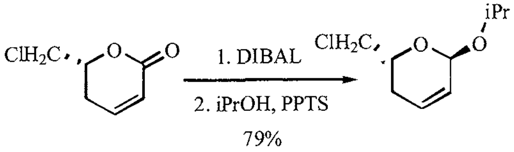


Examples:

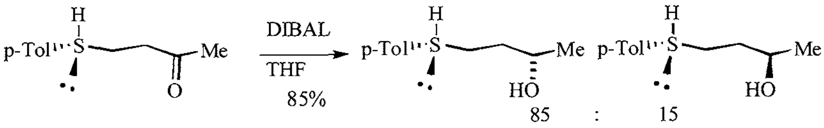
1.[1]



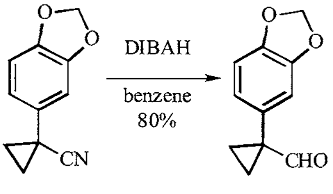
2.[2]



3.[3]



4.[4]



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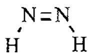
[1] A. K. Ghosh, C. Liu, *Organic Letters* **2001**, 3, 635

[2] J. L. Vicario, A. Job, M. Wolberg, M. Muller, D. Enders, *Organic Letters* **2002**, 4, 1023

[3] G. Solladié, F. Colobert, F. Somny, *Tetrahedron Letters* **1999**, 40, 1227

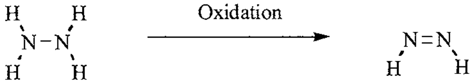
[4] R. V. Stevens, L. E. Dupree, P. L. Lowenstein, *Journal of Organic Chemistry* **1972**, 37, 977

Diimide



[15626-42-3]

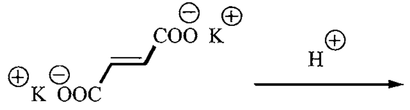
Preparation:

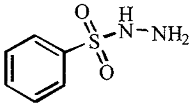


D. J. Pasto, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1892

Notes:

The reagent can be prepared in situ, by the copper-catalyzed oxidation of hydrazine. Hydrogen peroxide or oxygen are often the oxidants. The acid-catalyzed decomposition of potassium azodicarboylate provides a useful source of diimide:

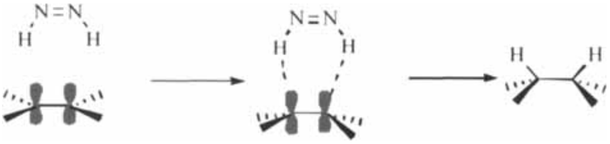




as is the decomposition of sulfonylhydrazines:

This reduction finds unique application because:

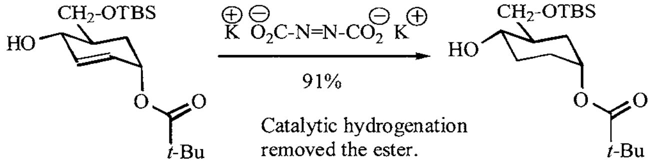
1. The reagent is extremely tolerant of other functional groups.
2. Reduction is *cis*, from the less-hindered face.



3. Reactivity decreases with increasing substitution about the alkene bond
4. Alkynes reduce faster than alkenes
5. Alkenes with electron-withdrawing groups react faster than those with electron-donating groups.
6. Use of deuterium or tritium-labeled diimde affords a method of *cis* reduction without scrambling of label.

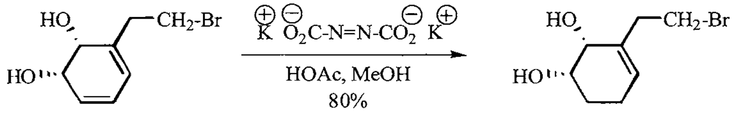
Examples:

1.[1]



Catalytic hydrogenation removed the ester.

2.[2]



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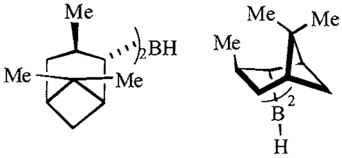
[1] M. H. Haukaas, G. A. O'Doherty, *Organic Letters* **2002**, 4, 1771

[2] D. A. Frey, C. Duan, T. Hudlicky, *Organic Letters* **1999**, 1, 2085

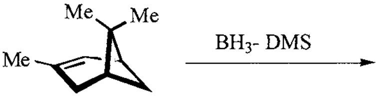
Diisopinocampheylborane

(Ipc_2BH)



[(+) 21947-87-5]
[(-) 21932-54-7]

Preparation:



Either (+) or (-)

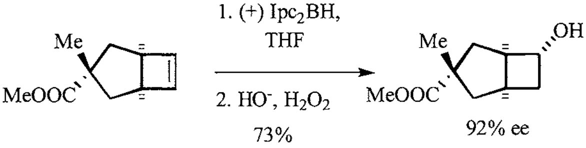
R. K. Dhar, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1914

Notes:

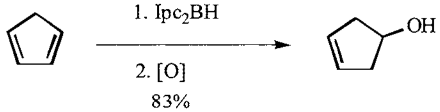
A useful reagent for asymmetric hydroboration. See ***Brown's Hydroboration Reaction***.

Examples:

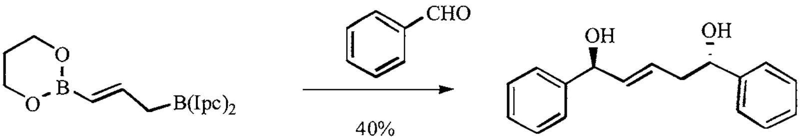
1.[1]



2.[2]



3.[3]



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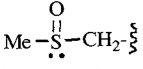
[1] A. E. Greene, M.-J. Luche, A. A. Serra, *Journal of Organic Chemistry* **1985**, 50, 3957

[2] H. M. Hess, H. C. Brown, *Journal of Organic Chemistry* **1967**, 32, 4138

[3] E. M. Flamme, W. R. Roush, *Journal of the American Chemical Society* **2002**, 124, 13644

Dimsylate



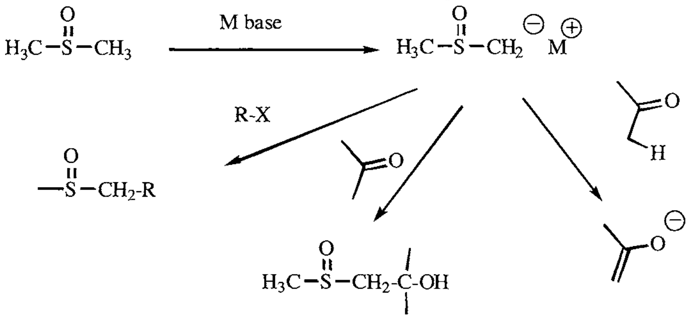
$Me-S(=O)-CH_2-$

Methylsulfinylmethide

Preparation: The "dimsyl anion" is generated from dimethylsulfoxide (DMSO) by use of base. The resulting lithio- or sodio- derivative is generally used in the DMSO solvent.

M. Harmata, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 7, 4596.

Notes: This is generally found as a base or nucleophile.

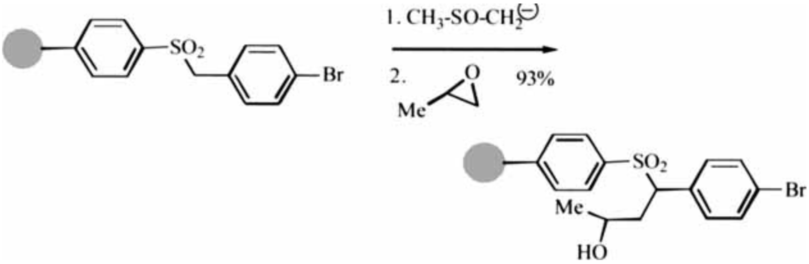


Generally used as M Dimsylate:

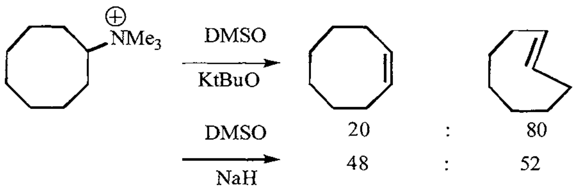
M= Na [15590-23-5]; K [15590-26-8]; Li [57741-62-5]

Harmata suggests that the use of K*t*-BuO/DMSO as a basic mixture most likely involves *t*-BuO as the actual base. This is seen in Example 2, where addition of Crown ether doesn't influence the already high degree of dissociation for the active base, *t*-BuO ⁻.

Examples:



2.[2]



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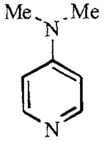
[1] W.-C. Cheng, C.-C. Lin, M. J. Kurth, *Tetrahedron Letters* **2002**, 43, 2967

[2] R. D. Bach, J. W. Knight, *Tetrahedron Letters* **1979**, 20, 3815

DMAP



4-(Dimethylamino)pyridine
[1122-58-3]
[82942-26-5] Polymer-bound

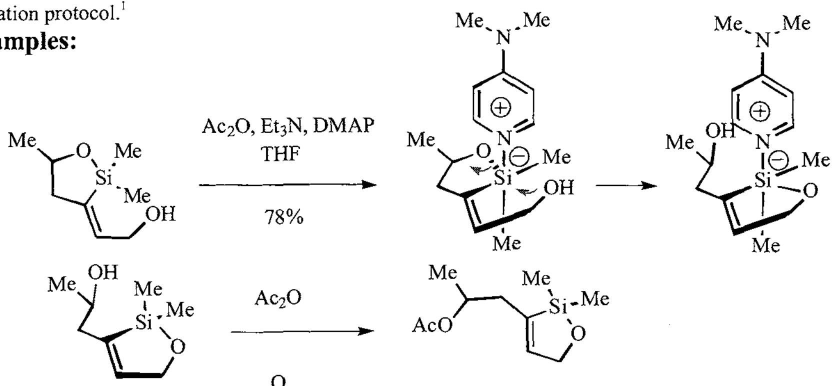
Commercially available

A. Hassner, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 2022

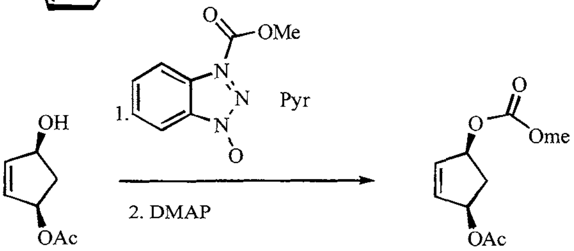
Notes: A basic catalyst for amine and alcohol acylations, (particularly useful for hindered alcohols), macrocyclization, and for ***Steglich esterification***. ***DMAP/PCC*** provides a useful oxidation protocol.[1]

Examples:

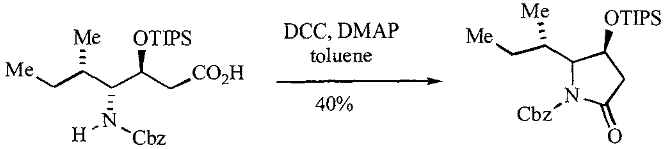
1.[2]



2.[3]



3.[4]



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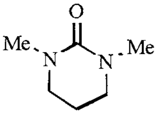
[1] F. S. Guziec, Jr., *Encyclopedia of Reagents for Organic Synthesis,* John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 2024

[2] D. Bonafoux, I. Ojima, *Organic Letters* **2001**, 3, 2333

[3] P. G. M. Wuts, S. W. Ashford, A. M. Anderson, J. R. Atkins, *Organic Letters* **2003**, 5, 1483

[4] B. Liang, D. J. Richard, P. S. Portonovo, M. M. Joullié, *Journal of the American Chemical Society* **2001**, 123, 4469

DMPU



N,N'-Dimethylpropyleneurea
[7226-23-5]

Commercially available

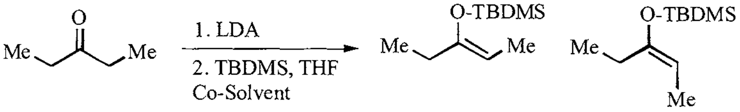
A. K. Beck, D. Seebach, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 2123

Notes:

A co-solvent with properties and reaction enhancements similar to ***HMPA***. It is a dipolar aprotic solvent, miscible in water and most organic solvents. Can be cooled to dry ice temperature.

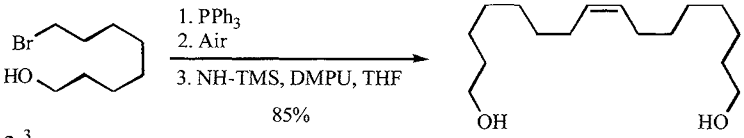
Examples:

1.[1]

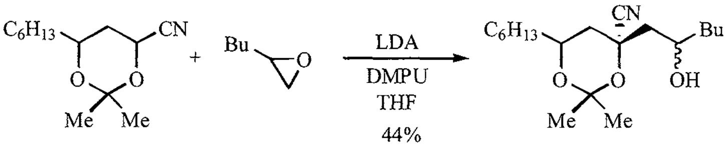


Co-Solvent		**Ratio**	
None	30	:	70
HMPA	95	:	5
DMPU	94	:	6

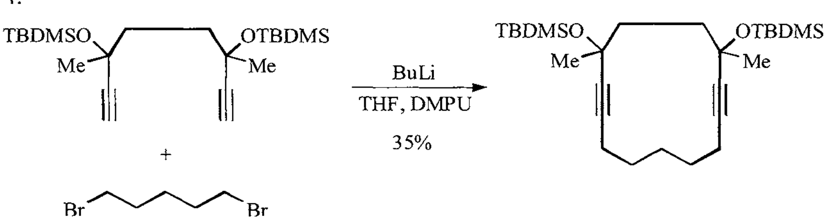
2.[2]



3.[3]



4.[4]



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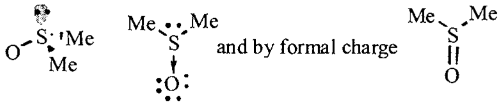
[1] T. Mukhopadhyay, D. Seebach, *Helvetica Chemica Acta,* **1982**, 65, 385; Reported by A. K. Beck, D. Seebach, *Encyclopedia of Reagents for Organic Synthesis, John Wiley and Sons, Inc.*, L. A. Paquette, Ed., New York, 1995, 3, 2123

[2] S. Poulain, N. Nairet, H. Patin, *Tetrahedron Letters* **1996**, 37, 7703

[3] S. D. Rychnovsky, S.S. Swenson, *Journal of Organic Chemistry* **1997**, 62, 1333

[4] C. Boss, R. Keese, *Tetrahedron* **1997**, 53, 3111

DMSO



Dimethylsulfoxide
[67-68-5]

Commercially available

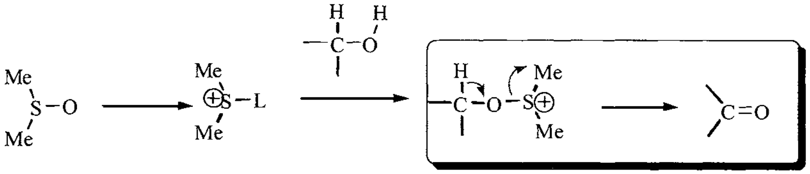
A. P. Krapcho, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 2141

Notes: A polar, aprotic solvent; miscible in water and many organic solvents. Efficiently solvates cations. Can greatly enhance the rates of nucleophilic displacement reactions.

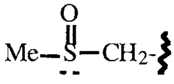
Will reduce the order of reactivity for the halide ions

Protic Solvents	**DMSO**
I > Br > Cl > F	F > Cl > Br > I

A number of alcohol oxidations are based on the general scheme: **See DMSO based Oxidations under *Aldehyde Syntheses***

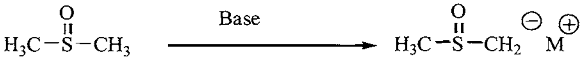


See: Dimsyl group



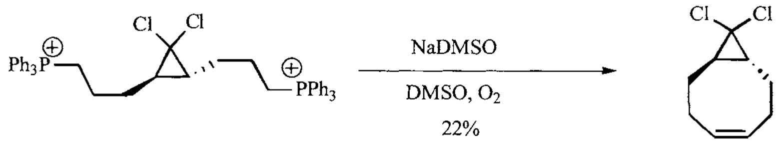
Methylsulfinylmethide

Preparation The "dimsyl anion" is generated from dimethylsulfoxide (DMSO) by use of base. The resulting lithio- or sodio- derivative is generally used in the DMSO solvent.



$$H_3C-\overset{\overset{O}{\|}}{S}-CH_3 \xrightarrow{\text{Base}} H_3C-\overset{\overset{O}{\|}}{S}-\overset{\ominus}{C}H_2\ \overset{\oplus}{M}$$

Sodium dimsylate (M. Harmata, *Encyclopedia of Reagents for Organic Synthesis, John Wiley and Sons, Inc.*, L. A. Paquette, Ed., New York, 1995, 7, 4596.) is often used to initiate ***Wittig reactions***.[1]



See use in the ***Krapcho Dealkoxycarbonylation*** reaction..

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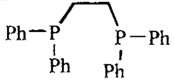
[1] J. A. Deyrup, M. F. Betkouski, *Journal of Organic Chemistry* **1975**, 40, 284

Dppe (DIPHOS)



1,2-Bis(diphenylphosphino)ethane
[1663-45-2]

Commercially available

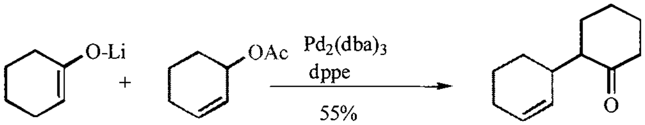
G. T. Whiteker, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 515

Notes: Ligand. Used for Pd-catalyzed nucleophilic reactions at allylic positions. See also, ***Dppp***. With Br_2 forms a useful brominating agent, ***1,2-bis(diphenylphosphino)ethane tetrabromide*** [7726-95-6].[1] This reagent is useful for the conversion:

$$R\text{-}OTHP \longrightarrow R\text{-}Br$$

Examples:

1.[2]



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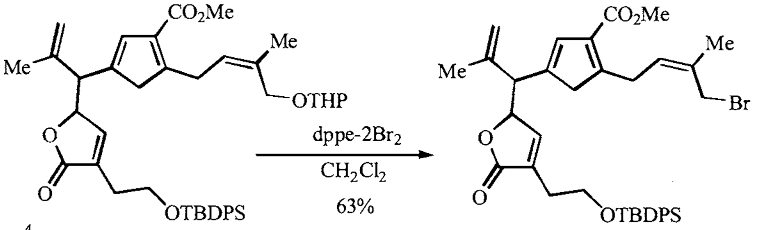
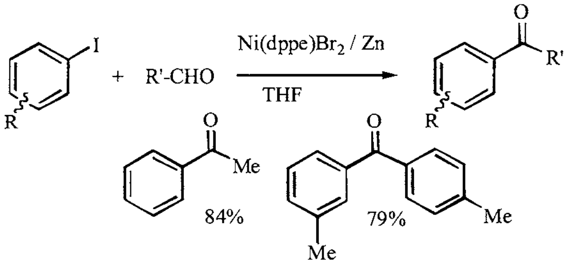


3.[4]



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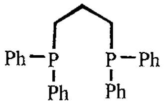
[1] Reported by L. A. Paquette, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 517

[2] J.-C. Fiaud, J.-L. Malleron, *Chemical Communications* **1981**, 1159

[3] C. M. Rayner, P. C. Astles, L. A. Paquette, *Journal of the American Chemical Society* **1992**, 114, 3925

[4] Y.-C. Huang, K. K. Majumdar, C.-H. Cheng, *Journal of Organic Chemistry* **2002**, 67, 1682

Dppp



1,2-Bis(diphenylphosphino)propane
[6737-42-4]

Commercially available

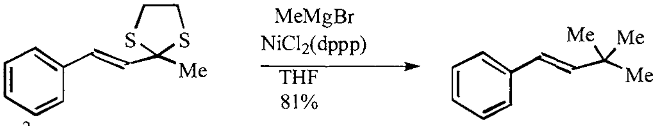
G. T. Whiteker, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 521

Notes:

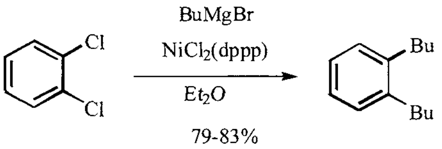
Ligand. Used for Pd-catalyzed reactions of aryl and vinyl halides and triflates. Also for ***Kumuda coupling*** reactions. See ***Dppe*** for a similar reagent.

Examples:

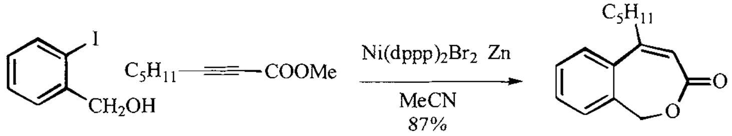
1.[1]



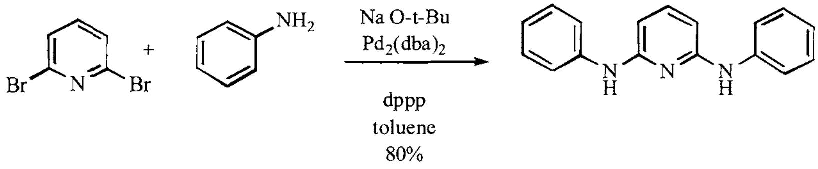
2.[2]



3.[3]



4.[4]



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[1] T.-M. Yuan, T.-Y. Luh, *Organic Syntheses* CV 9, 649

[2] M. Kumada, K. Tamao, K. Sumitani, *Organic Syntheses* CV 6, 407

[3] D. K. Rayabarapu, C.-H. Cheng, *Journal of the American Chemical Society* **2002**, 124, 5630

[4] S. Wagaw, S. L. Buchwald, *Journal of Organic Chemistry* **1996**, 61, 7240

Eaton's Reagent

P_2O_5 / $MeSO_3H$

[39394-84-8]

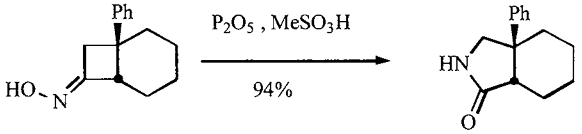
Preparation: Add $MeSO_3H$ to P_2O_5, (10:1, m/m) stir until P_2O_5 is dissolved. **Commercially available**

L. A. Dixon, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4129

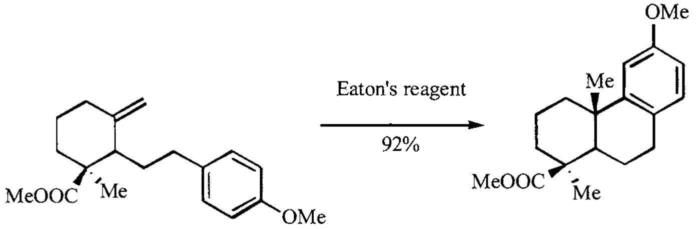
Notes: A useful alternative to PPA (Polyphosphoric acid)

Examples:

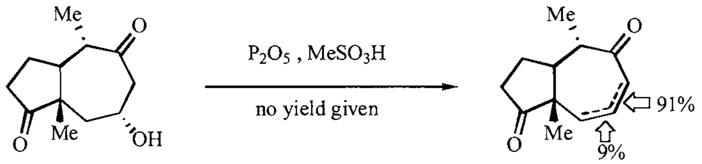
1.[1]



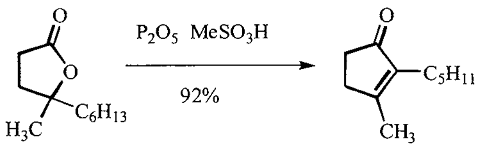
2.[2]



3.[3]



4.[4]



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[1] P. W. Jeffs, G. Molina, N. A. Cortese, P. R. Hauck, J. Wolfram, *Journal of Organic Chemistry* **1982**, 47, 3876

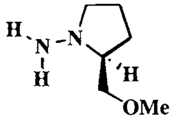
[2] X.-J. Hao, M. Node, K. Fuji, *Journal of the Chemical Society, Perkin Transaction 1* **1992**, 1505

[3] F. E. Ziegler, J.-M. Fang, C. C. Tam, *Journal of the American Chemical Society* **1982**, 104, 7174

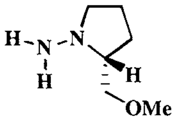
[4] P. E. Eaton, G. R. Carlson, J. T. Lee, *Journal of Organic Chemistry* **1973**, 38, 4071

Ender's Reagent (SAMP, RAMP)

SAMP:
(*S*)-1-Amino-2-methoxymethylpyrrolidine



RAMP:
(*R*)-1-Amino-2-methoxymethylpyrrolidine

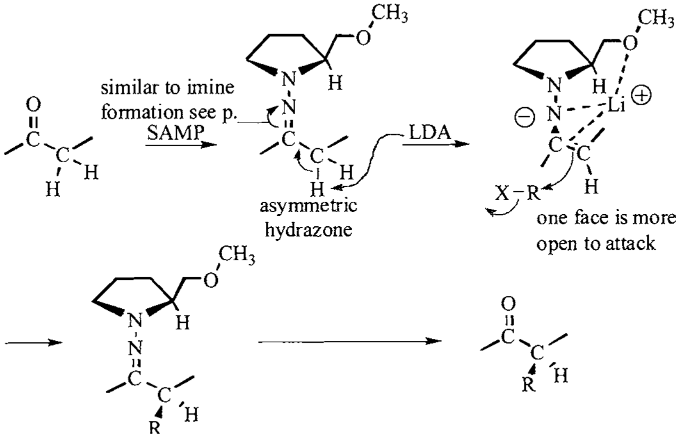


[59983-39-0]

Commercially available

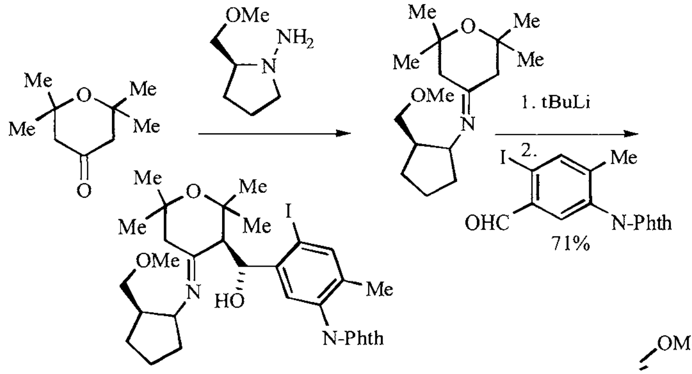
D. Enders, M. Klatt, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 178

Notes: Chiral directing group for alkylation of carbonyl

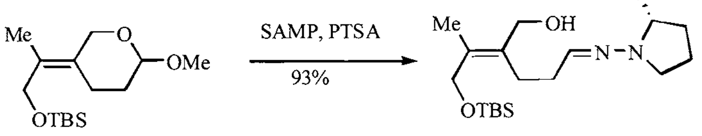


Examples:

1.[1]



2.[2]



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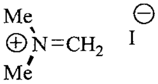
[1] A. B. Smith, III, H. Ishiyama, Y. S. Cho, K. Ohmoto, *Organic Letters* **2001**, 3, 3967

[2] A. Toro, P. Nowak, P. Deslongchamps, *Journal of the American Chemical Society* **2000** 122, 4526

Eschenmoser's Salt



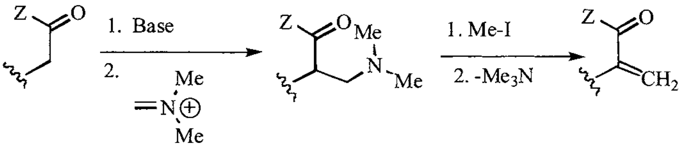
$\mathrm{Me_2N^{\oplus}{=}CH_2\ I^{\ominus}}$

Dimethyl(methylene)ammonium iodide
[33627-00-6]
The chloride salt is known as ***Böhme's salt***

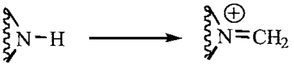
Commercially available

E. F. Kleinman, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 2090

Notes: Useful reagents for ***Mannich reactions*** with active methylene compounds. Particularly useful for the preparation of exo methylene groups.

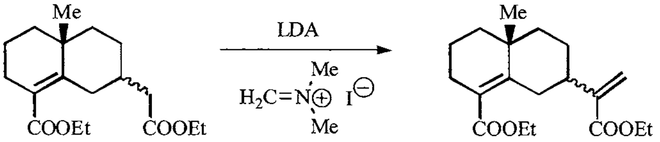


Also for the conversion:

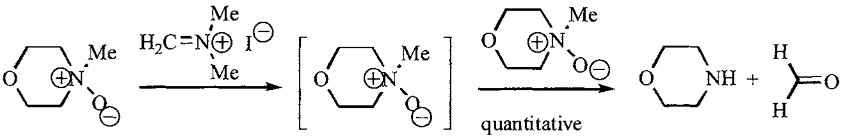


Examples:

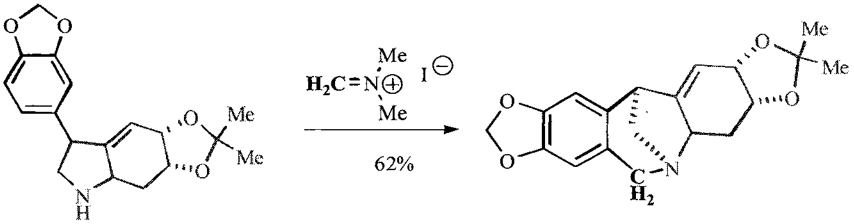
1.[1]



2.[2]



3.[3]



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[1] F. Bohlmann, H. Suding, *Liebigs Annalen der Chemie* **1985**, 1, 160 (AN 1985:166963)

[2] T. Rosenau, A. Potthast, P. Kosma, C.-L. Chen, J. S. Gratzl, *Journal of Organic Chemistry* **1999**, 64, 2166

[3] C.-K. Sha, A-W. Hong, C.-M. Huang, *Organic Letters* **2001**, 3, 2177

Fetizon's Reagent

Ag_2CO_3 / Celite
[534-16-7] / [61790-53-2]

Commercially available

M. Fetizon, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4448

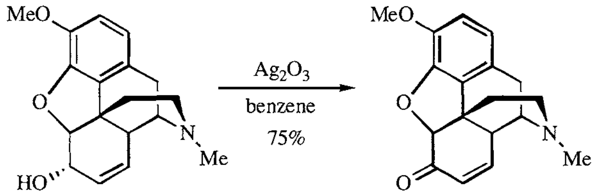
Notes:

Celite™ is a commercially available inorganic material; mostly SiO_2. Generally finds use as a filtering aid.

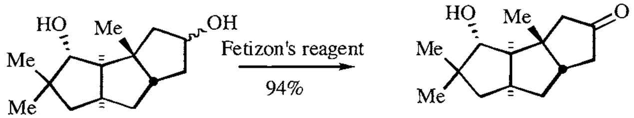
This is a mild oxidizing agent for conversion of primary alcohols to aldehydes and secondary alcohols to ketones.

Examples:

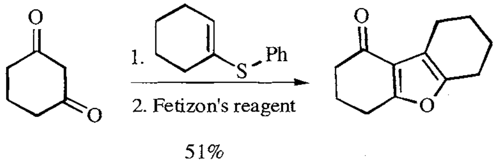
1.[1] One of the earliest reports of using silver as an oxidizing agent:



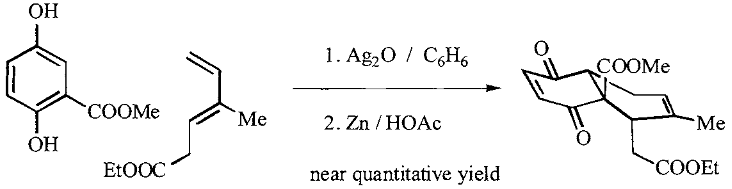
2.[2]



3.[3]



4.[4]



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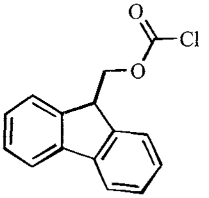
[1] H. Rapoport, H. N. Reist, *Journal of the American Chemical Society* **1955**, 77, 490

[2] R. L. Funk, G. L. Bolton, J. U. Daggett, M. M. Hansen, L. H. M. Horcher, *Tetrahedron* **1985**, 41, 3479

[3] Y. R. Lee, J. Y. Suk, B. S. Kim, *Organic Letters* **2000**, 2, 1387

[4] D. P. Walker, P. A. Grieco, *Journal of the American Chemical Society* **1999**, 121, 9891

Fmoc-Cl



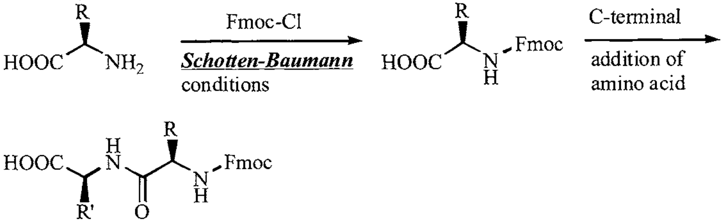
9-Fluorenylmethyl chloroformate
[28920-43-6]

Commercially Available.

R. L. Polt, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **4**, 2545

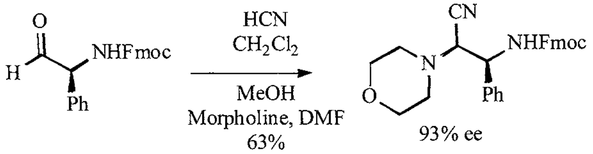
Notes:

A useful protecting group for nitrogen.

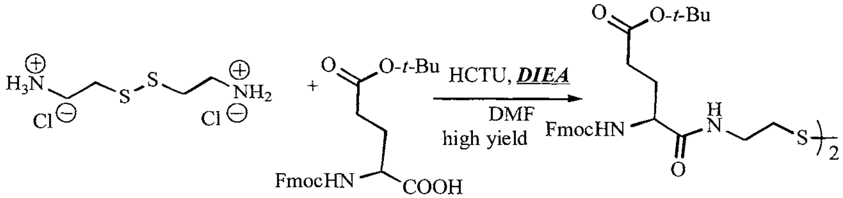


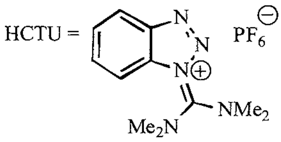
Examples:

1.[1]



2.[2]





[490019-20-0] a strong condensing agent

---

[1] A. G. Myers, B. Zhong, D. W. Kung, M. Movassaghi, B. A. Lanman, S. Kwon, *Organic Letters* **2000**, 2, 3337

[2] A. Ortiz-Acevedo, G. R. Dieckmann, *Tetrahedron Letters* **2004**, 45, 6795

Furukawa's Cyclopropanation reagent[1]

I-CH$_2$ZnEt

Preparation:

Et$_2$Zn + I-CH$_2$-I

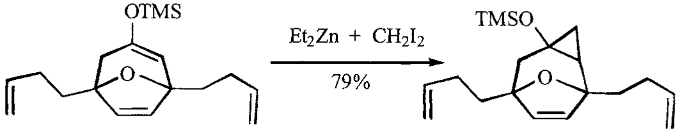
P. Knochel, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1861

Notes:

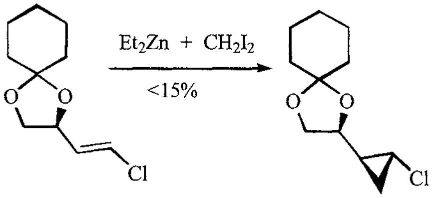
Cyclopropanation reagent. A similar reagent, prepared from EtZnI + CH$_2$I$_2$, [I-CH2-Zn-Et] [33598-72-0] is known as the ***Sawada Reagent***. [P. Knochel, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **4** 2473]
Advantage over ***Simmons-Smith*** is the homogeneity of the reaction; and the high yields with enol ethers. (Not true for ***Sawada Reagent***.)

Examples:

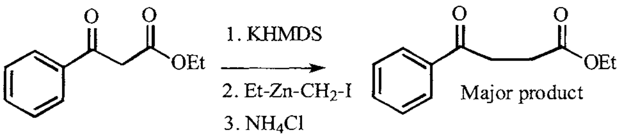
1.[2]



2.[3]



3.[4]



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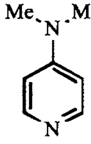
[1] J. Furukawa, N. Kawabata, J. Nishimura, *Tetrahedron Letters* **1968**, 9, 3495
[2] A. J. Blake, A. J. Highton, T. N. Majid, N. S. Simpkins, *Organic Letters* **1999**, 1, 1787
[3] D. A. Evans, J. D. Burch, *Organic Letters* **2001**, 3, 503
[4] R. Hilgenkamp, C. K. Zercher, *Organic Letters* **2001**, 3, 3037

Furukawa's reagent



+ $CH_3\text{-}SO_2Cl$

Mesyl chloride
Methanesulfonyl chloride

DMAP

[124-63-0, 1122-58-3]

Preparation: Stir the alcohol with MsCl, ***DMAP***, H_2O, and CH_2Cl_2 at rt.

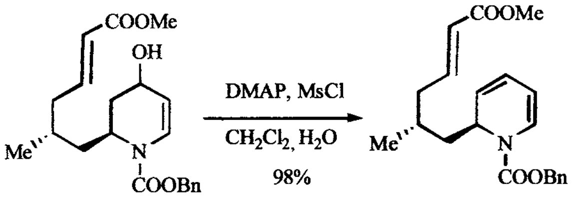
V. Vaillancourt, M. M. Cudahy, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3311

Notes:

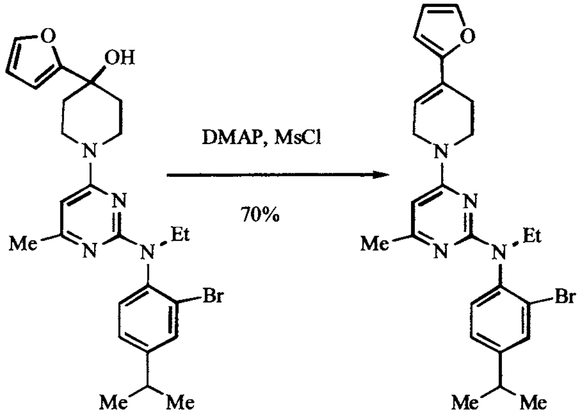
Dehydrating agent

Examples:

1.[1]



2.[2]



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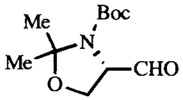
[1] D. L. Comins, C. A. Brooks, R. S. Al-war, R. R. Goehring, *Organic Letters* **1999**, 1, 229

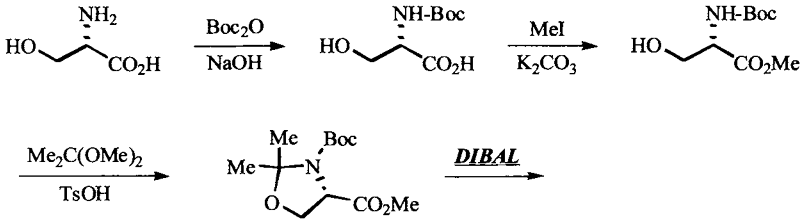
[2] A. Nakazato, T. Kumagai, T. Okubo, H. Tanaka, S. Chaki, S. Okuyama, K. Tomisawa, *Bioorganic & Medicinal Chemistry* **2000**, 8 1183

Garner's Aldehyde



3-(*tert*-butoxycarbonyl)-2,2-dimethyl-4-formyloxazolidin
[102308-32-7]

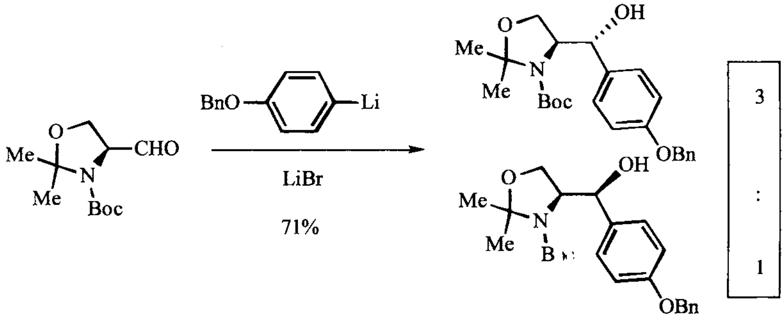
Preparation



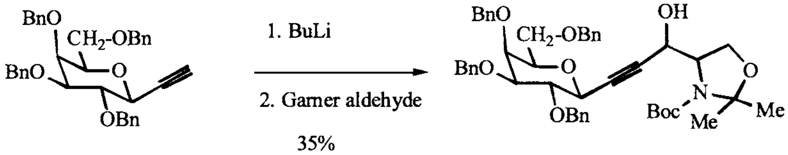
Notes: An extremely useful chiral reagent.

Examples:

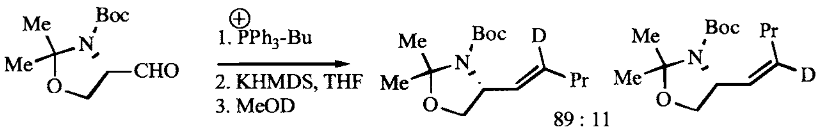
1.[1]



2.[2]



3.[3]



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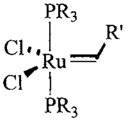
[1] N. Okamoto, O. Hara, K. Makino, Y. Hamada, *Journal of Organic Chemistry* **2002**, 67, 9210

[2] A. Dondoni, G. Mariotti, A. Marra, *Journal of Organic Chemistry* **2002**, 67, 4475

[3] J. S. Oh, B. H. Kim, Y. G. Kim, *Tetrahedron Letters* **2004**, 45, 3925

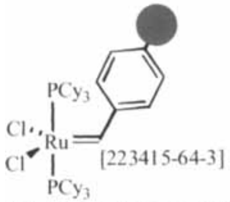
Grubb's Reagent



Commercially Available

Notes:

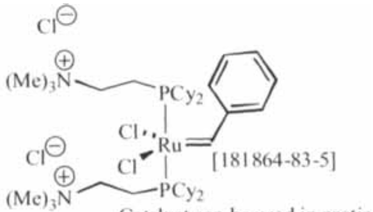
The labs of R.M. Grubbs has prepared and examined a number of catalysts along the general structure shown above. See ***RCM Reaction*** for additional examples. These catalysts continue to evolve, but bear the same general characteristics. The catalysts are generally tolerant to an array of ot\her functional groups. The catalysts are generally more stable than the ***Schrock catalysts***. Examples include:



[223415-64-3]

Catalyst readily recovered for reuse.

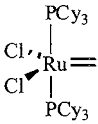
2.



[181864-83-5]

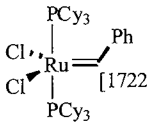
Catalyst can be used in protic solvents, air-sensitive.

3.



[171368-36-8]

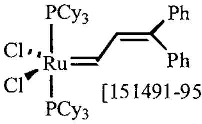
4.



[172222-30-9]

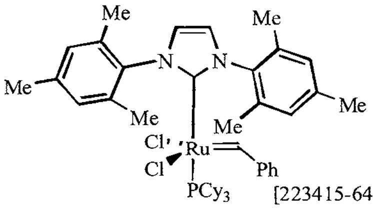
air-sensitive.

5.



[151491-95-1]

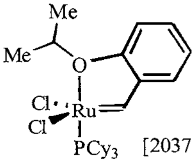
6.



[223415-64-3]

Nolan's Catalyst

7.

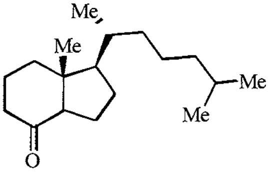


[203714-71-0]

Hoveyda-Grubbs Catalyst

Grundmann's Ketone

Windaus-Grundmann Ketone

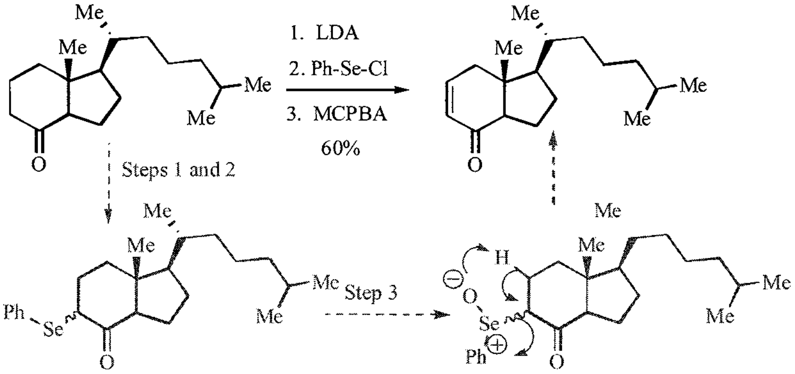


[66251-18-1]

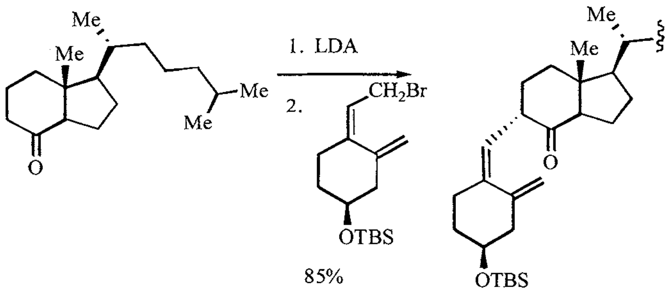
(1*R*,7a*R*)-7a-methyl-1-((*R*)-6-methylheptan-2-yl)-octahydroinden-4-one

Examples:

1.[1]



2.[2]



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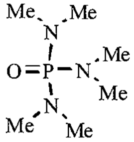
[1] W. H. Okamura, G.-D. Zhu, D. K. Hill, R. J. Thomas, K. Ringe, D. B. Borchard, A. W. Norman, L. J. Mueller *Journal of Organic Chemistry* **2002**, 67, 1637

[2] E. M. Codesido, L. Castedo, J. R. Granja, *Organic Letters* **2001**, 3, 1483

HMPA, HMPT



Hexamethylphosphoric Triamide
[680-31-9]

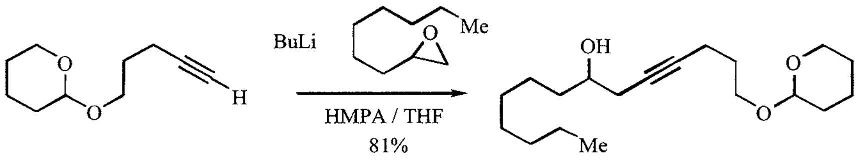
Commercially available.

R. R. Dykstra, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **4**, 2668

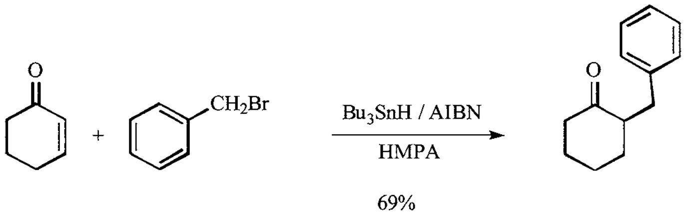
Notes: A powerful Lewis base able to form strong cation complexes. This attribute is often associated with greatly increased reactivities when used in solvent. This is particularly true when used with organolithium reagents. Soluble in most solvents.

Examples:

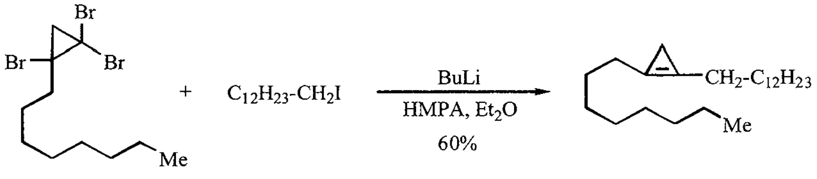
1.[1]



2.[2]



3.[3]



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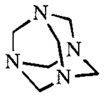
[1] S. SanKaranarayanan, A. Sharma, S. Chattopadhyay, *Tetrahedron: Asymmetry* **1996**, 7, 2639

[2] E. J. Enholm, P. E. Whitley, Y. Xie, *Journal of Organic Chemistry* **1996**, 61, 5384

[3] J. R. Al Dulayymi, M. S. Baird, M. J. Simpson, G. R. Port, *Tetrahedron* **1996**, 52, 12509

HMTA



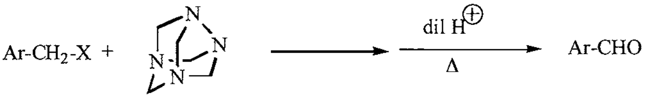
Hexamethylenetetramine
[100-97-0]

Commercially Available

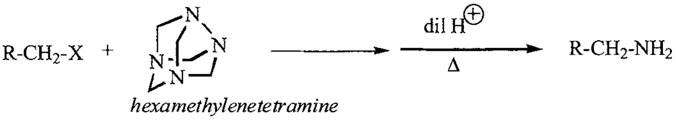
S. N. Kilényi, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **4**, 2666

Notes: HMTA finds use for:

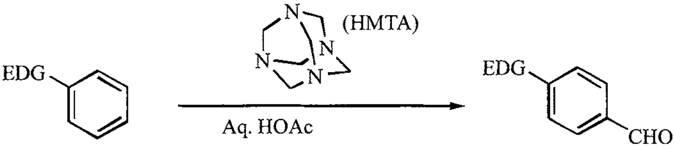
Oxidation of benzylic halides (See: ***Sommelet Reaction***)



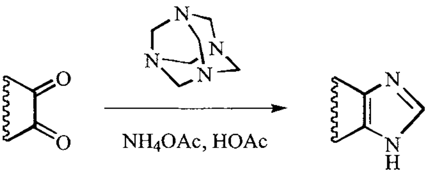
Ammonolysis of alkyl halides (See: ***Delépine Reaction***)



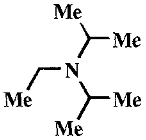
Electrophilic formylation of aromatics (See: ***Duff Reaction***)



Provides imidazoles from 1,2-diketones



Hünig's Base, DIPEA, DIEA



Diisopropylethylamine
[7087-68-5]

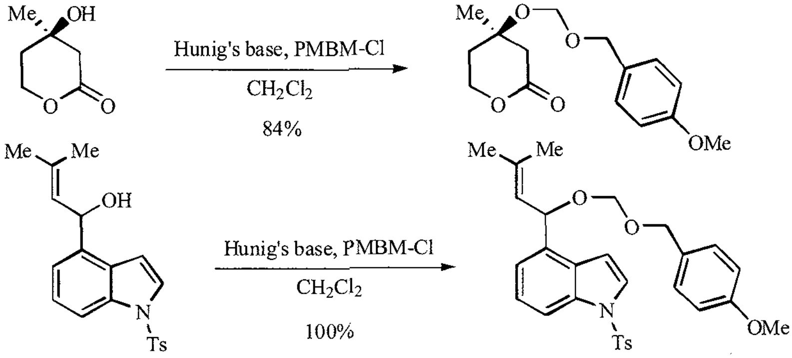
Commercially available

K. L. Sorgi, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L.A. Paquette, Ed., New York, 1955, **3**, 1933

Notes: Because of the severe steric constraints of this amine, it serves well as a proton scavenger and is quite resistant to quaternization.

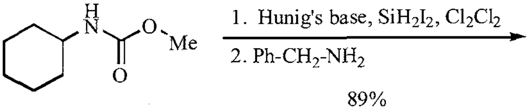
Examples:

1.[1]

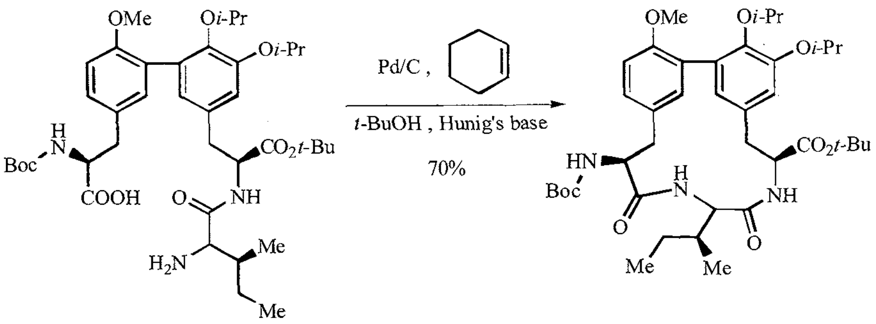


PMBM-Cl = *p*-methoxybenzylchloromethyl ether

2.[2]



3.[3]



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[1] A. P. Kozikowski, J.-P. Wu, *Tetrahedron Letters* **1987**, 28 5125

[2] S. Gastaldi, S. M. Weinreb, D. Stien, *Journal of Organic Chemistry* **2000**, 65, 3239

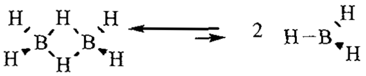
[3] S. Boisnard, A.-C. Carbonnelle, J. Zhu, *Organic Letters* **2001**, 3, 2061

Hydroboration Reagents[1]

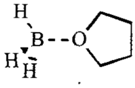
See *Brown's Hydroboration Reaction*

Diborane

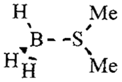
Easily prepared in laboratory quantities by reaction of $NaBH_4$ and BF_3 in THF under dry, inert atmosphere.



In the absence of stabilization boron, borane tends to maintain the dimeric form.



BH_3-THF



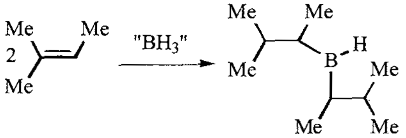
BH_3-DMS

See *BMS*

Alkyl Derivatives:

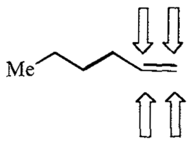
Disiamylborane

Prepared by addition of 2-methyl-2-butene to diborane



A hindered borane providing increased reaction selectivity:

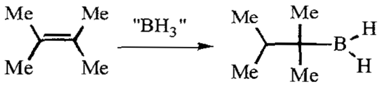
6 94 Borane



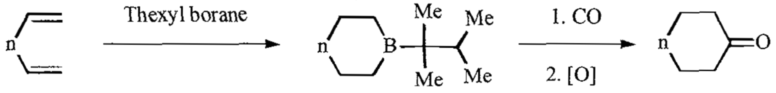
Ref 1, page 282

1 99 Disiamylborane

Thexylborane



A hindered borane particularly useful for reaction with dienes:



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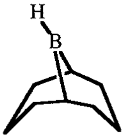
[1] H. C. Brown, *Boranes in Organic Chemistry*, Cornell University Press, Ithaca, 1972. This is a dated but extremely interesting perspective written by the major driving force in the development of the extremely useful chemistry of boron.

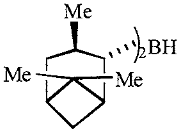
9-BBN

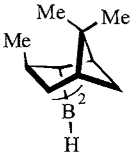
A useful borane derivative



Diisopinocampheylborane (Ipc₂BH)

A chiral hydroborating agent





See also: *Catecholborane*

Hydrogenation Catalysts

Ni

Ni_2B
Nickel Boride

[12007-01-1]

T. J. Caggiano, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3694

Ni Catalysts

[7440-02-0]

C. R. Sarko, M. DiMare, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3701

Raney Nickel

Pd

Pt/BaSO₄
Rosenmund Catalyst

Pd/CaCO₃ / ***Pb-poisoned***
Lindlar Catalyst

Pd/C

[7440-05-3]

A. O. King, I. Shinka, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3867

Pd/Gr (graphite)

[59873-73-3]

E. M. Leahy, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3887

$Pd(OH)_2$
Pearlman's Catalyst

Pt

Pt/Al_2O_3

[7440-06-4]

A. O. King, I. Shinka, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4159

Pt/C

Heyn's Catalyst [7440-06-4]

A. O. King, I. Shinka, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4160

PtO_2

Adam's Catalyst

Rh

Rh/Al_2O_3

[7440-16-6]

S. Siegel, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4405

$Rh(PPh_3)_3Cl$

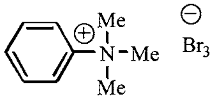
Wilkinson's Catalyst

Ru

Ru Catalysts

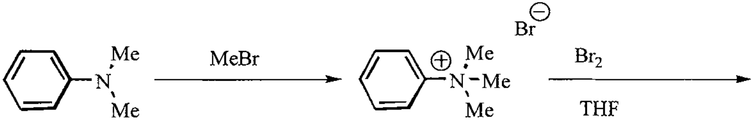
S. Siegel, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4410

Jacques Reagent



Phenyltrimethylammonium perbromide
PTT, PTAB
[4207-56-1]

Preparation:

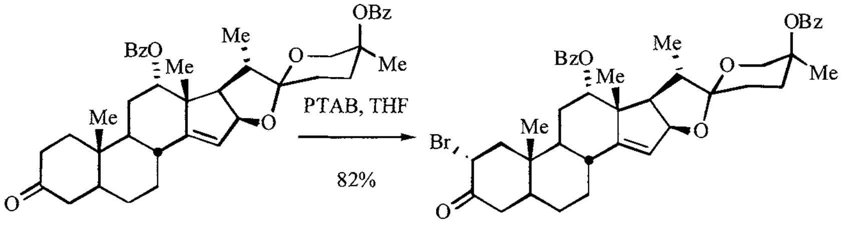


N. DeKimpe, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4098

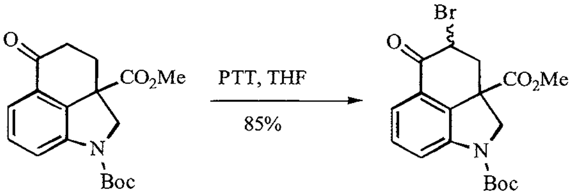
Notes: A brominating agent

Examples:

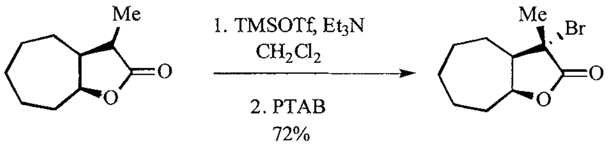
1.[1]



2.[2]



3.[3]



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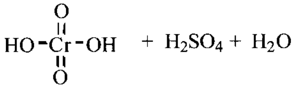
[1] S. Lee, P. L. Fuchs, *Organic Letters* **2002**, 4, 317
[2] S. K. Burt, A. Padwa, *Organic Letters* **2002**, 4, 4135
[3] Y. Higuchi, F. Shimoma, M. Ando, *Journal of Natural Products* **2003**, 66, 810

Jones Reagent



$$HO{-}\overset{O}{\underset{O}{\overset{\|}{\underset{\|}{Cr}}}}{-}OH + H_2SO_4 + H_2O$$

Preparation: CrO_3 + water, then carefully sulfuric acid or CrO_3 + sulfuric acid, then diluted with water to a specific volume. CAUTION: *READ DIRECTIONS FOR PREPARATION*

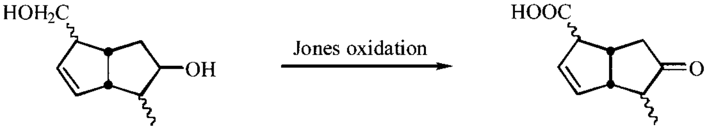
F. Freeman, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1261

Notes: A useful reagent in that one can titrate the oxidation. Primary alcohols are converted to acids; secondary alcohols to ketones; alkenes and alkynes are resistant. Related reagents:

Cornforth Reagent	*Fieser's Reagent*
Pyridine / Chromic acid	Acetic Acid / Chromic Acid

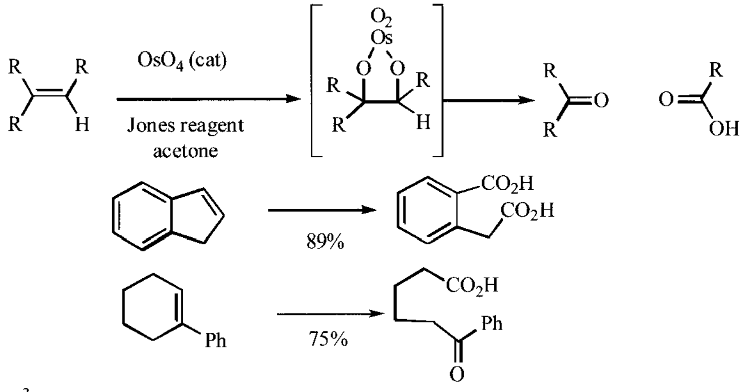
Examples:

1.[1]

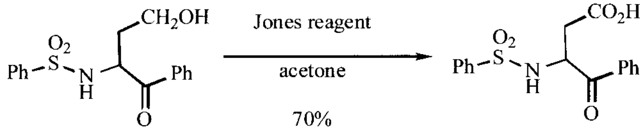


No yield provided; product taken directly to a diazomethane esterification. Overall yield OK.

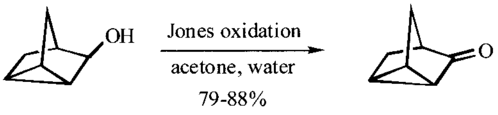
2.[2]



3.[3]



4.[4]



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[1] J.-H. Tai, M.-Y. Chang, A.-Y. Lee, N.-C. Chang, *Journal of Organic Chemistry* **1999**, 64, 659

[2] J. R. Henry, S. M. Weinreb, *Journal of Organic Chemistry* **1993**, 58, 4145

[3] A. K. Sharma, P. J. Hergenrother, *Organic Letters* **2003**, 5, 2107

[4] J. Meinwald, J. Crandall, W. E. Hymans, *Organic Syntheses* CV5, 866

KHMDS

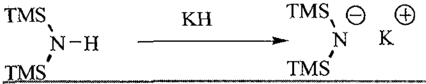
$KN(SiMe_3)_2$

Potassium hexamethyldisilazide, potassium bis(trimethylsilyl)amide

[40949-94-8]

Commercially available

Can be prepared from hexamethyldisilane and potassium hydride:



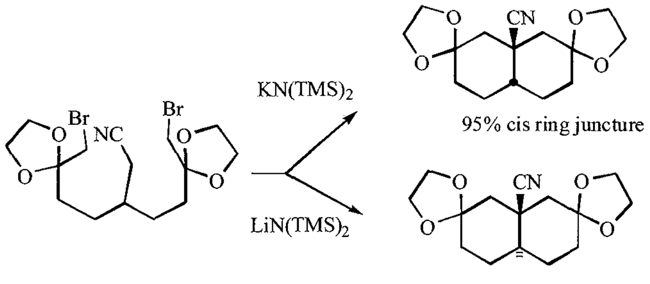
B. T. Watson, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4234

Notes:

A strong, sterically demanding, base useful for preparation of kinetic enolates. Soluble in THF, ether and toluene.

Examples:

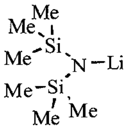
1.[1]



95% cis ring juncture

95% trans ring juncture

LHMDS



[4039-32-1]

Lithium hexamethyldisilazide, LiHMDS

Preparation:

M. Gray, V. Snieckus, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L.A. Paquette, Ed., New York, 1995, 5, 3127

Notes: For preparation of kinetic enolates.

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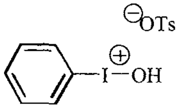
[1] (a) G. Stork, J. O. Gardner, R. K. Boeckman, Jr., K. A. Parker, *Journal of the American Chemical Society* **1973**, 95, 2014 (b) G. Stork, R. K. Boeckman, Jr. *Journal of the American Chemical Society* **1973**, 95, 2016

Koser's Reagent



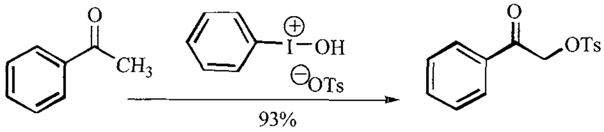
HTIB Hydroxy(tosyloxy)iodobenzene
[12415-97-5]

Commercially available

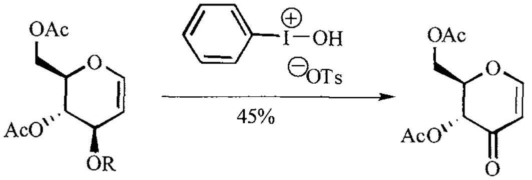
G. F. Koser , *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 4, 2782

Examples:

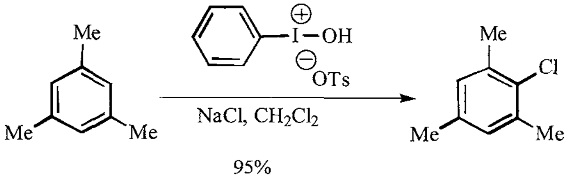
1.[1]



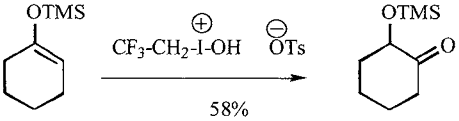
2.[2]



3.[3]



4.[4]



A fluoro analog of the ***Koser's reagent.***

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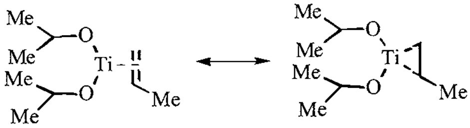
[1] T. Nabana, H. Togo, *Journal of Organic Chemistry* **2002**, 67, 4362

[2] A. Kirschning, *Journal of Organic Chemistry* **1995**, 60, 1228

[3] P. Bovonsombat, E. Djuardi, E. McNelis, *Tetrahedron Letters* **1994**, 35, 2841

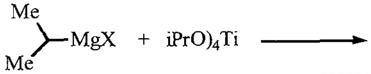
[4] V. V. Zhdankin, C.J. Kuehl, A. J. Simonsen, *Journal of Organic Chemistry* **1996**, 61, 8272

Kulinkovich Reagent



Bis(2-propanolato)[(1,2-h)-1-propene]titanium
[169123-69-7]

Preparation:

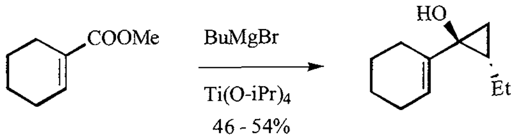


A. J. Phillips, *e-Encyclopedia of Reagents for Organic Synthesis*, L.A. Paquette, Ed., John Wiley & Sons, Inc., online reference available at *http://www.interscience.wiley.com.*

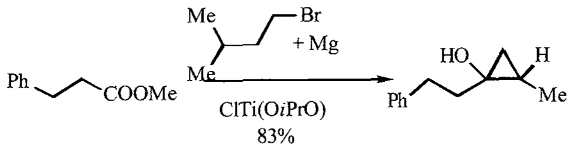
Notes: A reagent that allows for a unique preparation of cyclopropanol derivatives.

Examples:

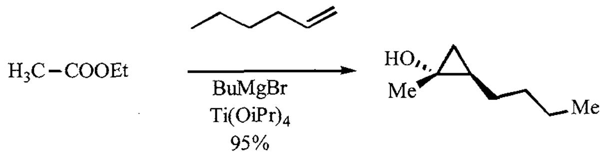
1.[1]



2.[2]



3.[3]



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[1] J. Lee, H. Kim, J. K. Cha, *Journal of the American Chemical Society* **1995**, 117, 9919
[2] E. J. Corey, S. A. Rao, M. C. Noe, *Journal of the American Chemical Society* **1994**, 116, 9345
[3] J. Lee, H. Kim, J. K. Cha, *Journal of the American Chemical Society* **1996**, 118, 4198

L-Selectride®

LiBH(*s*-Bu)3

Lithium Tri-*s*-butylborohydride
[38721-52-7]

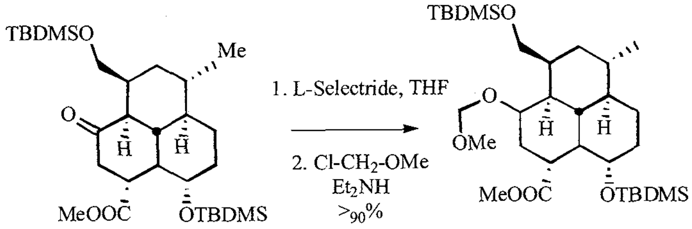
Commercially available

J. L. Hubbard , *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3172

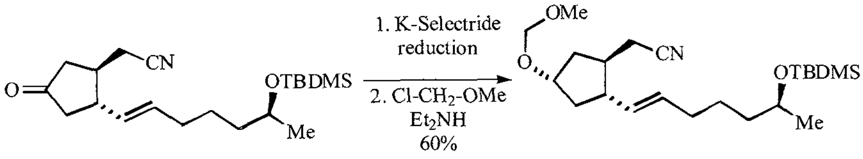
Notes: Selective reducing agent. The potassium and sodium Selectrides are also available. Will convert C-X to C-H, with I>Br>Cl.

Examples:

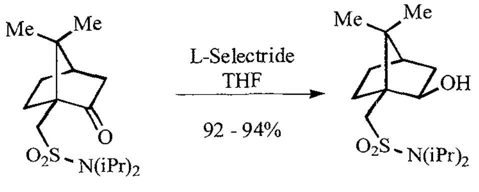
1.[1]



2.[2]



3.[3]



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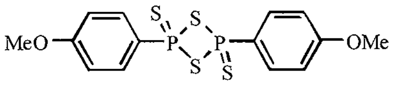
[1] E. Piers, M. A. Romero, *Tetrahedron* **1993**, 49, 5791

[2] J. Nokami, M. Ohkura, Y. Dan-Oh,Y. Sakamoto, *Tetrahedron Letters* **1991**, 32, 2409

[3] W. Oppolzer, C. Chapuis, G. Bernardinelli, *Tetrahedron Letters* **1984**, 25, 5885

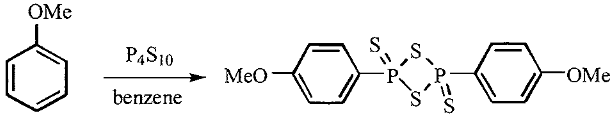
Lawesson's Reagent



2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide [19172-47-5]

Commercially available

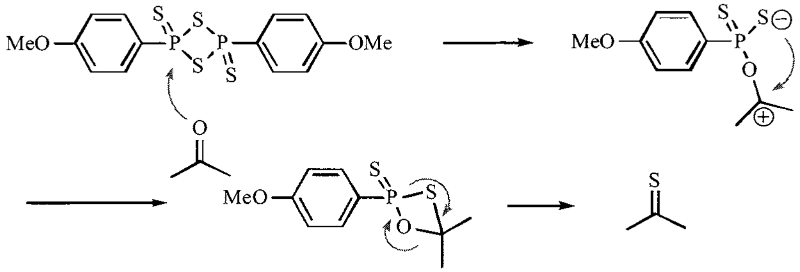
Preparation:



J. Voss, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 530

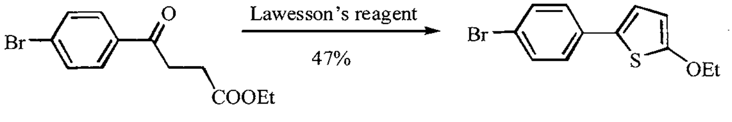
Notes: A combination of phosphorus pentasulfide and hexamethyldisiloxane can be used to prepare thionoesters and thionolactones in comparable yields and with a simplified workup.[1] A solvent-free conversion of ketones, lactones, esters and amides, to the corresponding thio analogs with ***Lawesson's Reagent***.[2]

See also: ***Belleau's*** and ***Davy's Reagents***.

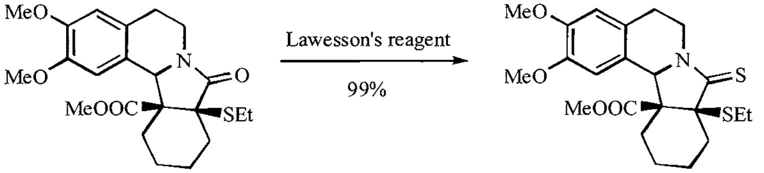


Examples:

1.[3]



2.[4]



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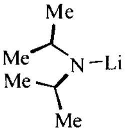
[1] T. J. Curphey, *Tetrahedron Letters* **2002**, 43, 371

[2] R. S. Varma, D. Kumar, *Organic Letters* **1999**, 1, 697

[3] V. M. Sonpatki, M. R. Herbert, L. M. Sandvoss, A. J. Seed, *Journal of Organic Chemistry* **2001**, 66, 7283

[4] A. Padwa, M. D. Danca, *Organic Letters* **2002**, 4, 715

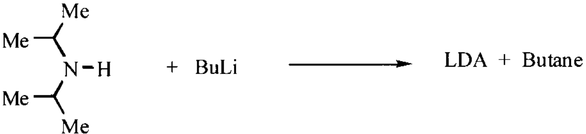
LDA



Lithium Diisopropylamide
[4111-54-0]

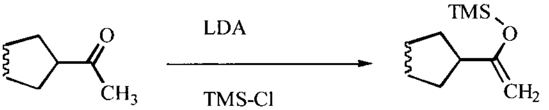
Commercially available

Preparation:

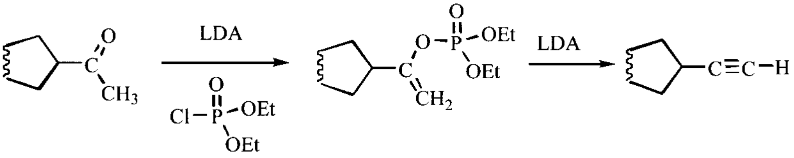


W. I. Iwema Bakker, P. L. Wong & V. Snieckus, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3096

Notes: An extremely common and widely used base. Often used to remove an acidic proton leading to a "kinetic enolate". When carried out with TMS-Cl, the process allows for the isolation of a kinetic silyl enol ether.

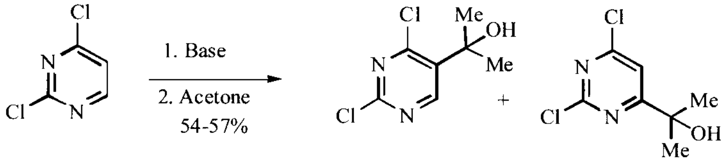


Trapping the kinetic enolate of a methyl ketone with diethyl phosphochloridate provides an enol phosphate, that can, in turn, be converted to an alkyne:



The reagent is extremely useful for the preparation of cross-conjugated enolates of α,β-unsaturated systems:

Example:[1]



Base	Ratio	
LDA	100	0
LTMP	35	65

---

[1] N. Plé, A. Turck, P. Martin, S. Barbey, G. Quéguiner, *Tetrahedron Letters* **1993**, 34, 1605

Lemieux-Johnson Reagent

$NaIO_4$-OsO_4

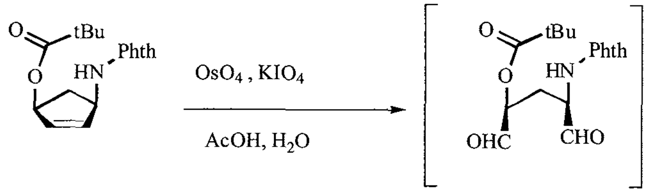
[7790-28-5, 20816-12-0]

Preparation:

A. G. Wee, B. Liu, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 7, 4616

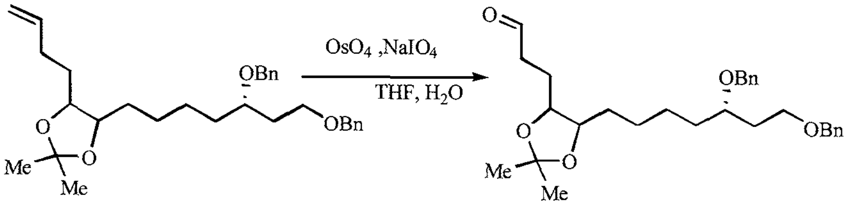
Examples:

1.[1]



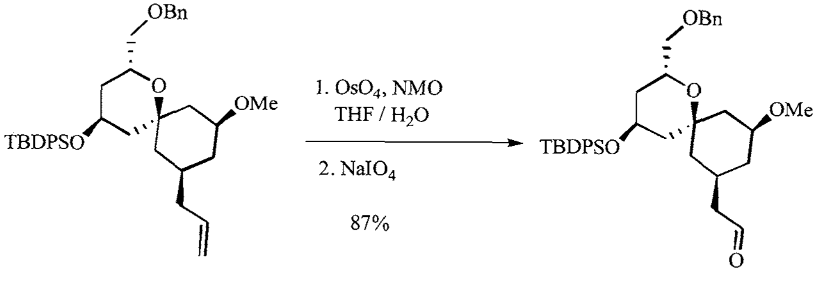
Not isolated; carried on to next step.

2.[2]



Taken directly to the next step

3.[3]



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[1] F. A. Luzzio, A. V. Mayrov, W. D. Figg, *Tetrahedron Letters* **2000**, 41, 2275

[2] S. Takahashi, A. Kubota, T. Nakata, *Organic Letters* **2003**, 5, 1353

[3] D. Zuev, L. A. Paquette, *Organic Letters* **2000**, 2, 679

Lemieux-von Rudloff Reagent

$NaIO_4$ / $KMnO_4$

[7790-28-5, 7722-64-7]

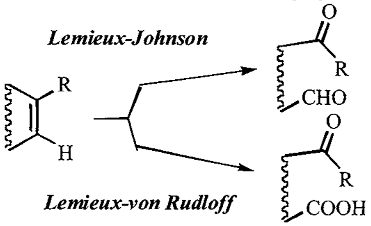
Preparation:

An aqueous solution (often with a miscible organic cosolvent) of $NaIO_4$ and $KMnO_4$ with strong stirring.

A. G. Wee, B. Liu, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **7**, 4620

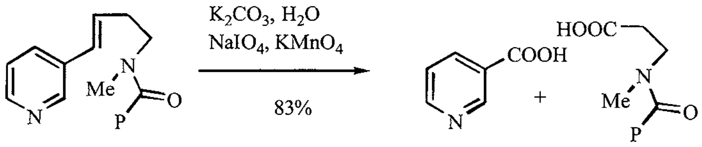
Notes:

Since $KMnO_4$ is a strong oxidizing agent, one expects the following reaction generalization:

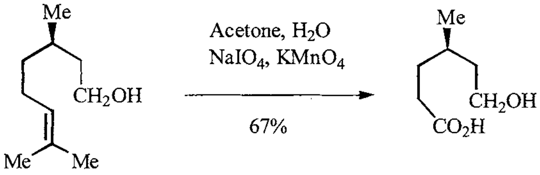


Examples:

1.[1]



2.[2]



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[1] A. A. Liebman, B. P. Mundy, H. Rapoport, *Journal of the American Chemical Society* **1967**, 89, 664

[2] C. G. Overberger, H. Kayel, *Journal of the American Chemical Society* **1967**, 89, 5640

Lindlar's Catalyst

$Pd / CaCO_3 / PbO$

[7440-05-3], [471-34-1], [1317-36-8]

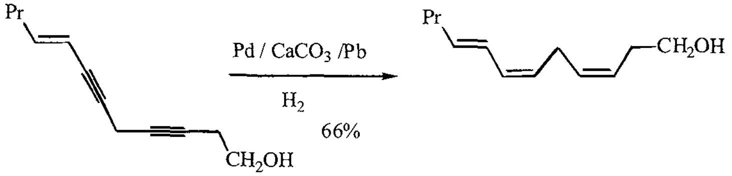
Preparation:

A. O. King, I. Shinkai, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3866

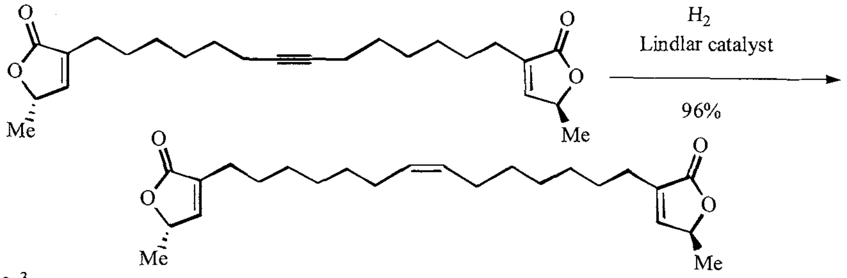
Notes: Major use is the *cis* reduction of an alkyne to an alkene.

Examples:

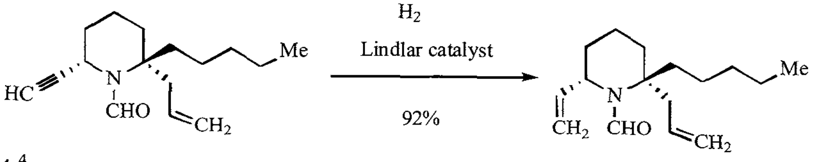
1.[1]



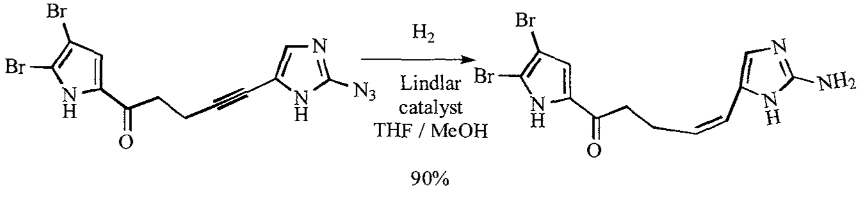
2.[2]



3.[3]



4.[4]



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[1] A. Tai, F. Matsumura, H. C. Coppel, *Journal of Organic Chemistry* **1969**, 34, 2180

[2] A. Fulrstner, T. Dierkes, *Organic Letters* **2000**, 2, 2463 Quinoline was added to the reduction mixture

[3] T. Itoh, N. Yamazaki, C. Kibayashi, *Organic Letters* **2002**, 4, 2469

[4] T. Lindel, M. Hochgörtel, *Journal of Organic Chemistry* **2000**, 65, 2806

Lombardo Reagent
CH_2Br_2, $TiCl_4$, Zn

Preparation:

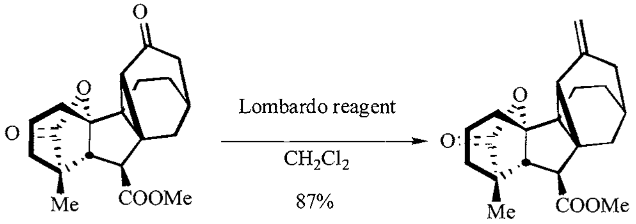
$$\text{Zn dust} \xrightarrow[\text{slowly add TiCl}_4]{\text{CH}_2\text{Br}_2\text{, THF}}$$

N. A. Petasis, J. P. Staszewshi, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1565

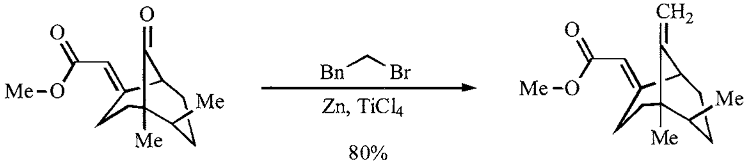
Notes: Original report: L. Lombardo, *Tetrahedron Letters* **1982**, 23, 4293 Sometimes called the ***Oshima-Lombardo Reagent.***

Examples:

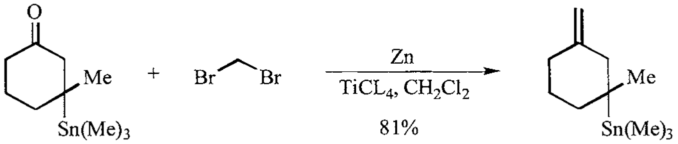
1.[1]



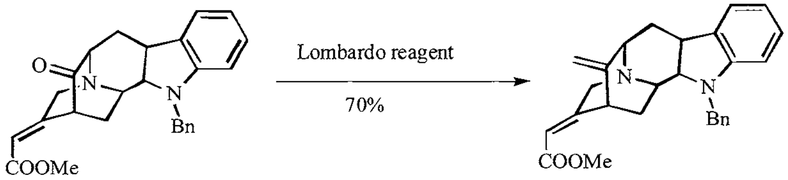
2.[2]



3.[3]



4.[4]



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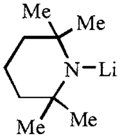
[1] M. Furber, L. N. Mander, *Journal of the American Chemical Society* **1988**, 110, 4084

[2] H. Huang, C. J. Forsyth, *Journal of Organic Chemistry* **1995**, 60, 5746

[3] L. Plamondon, J. D. Wuest, *Journal of Organic Chemistry* **1991**, 56, 2066

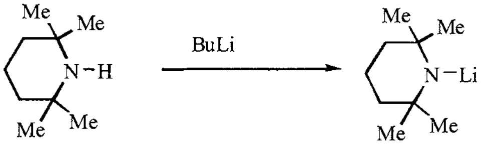
[4] P. Magnus, B. Mugrage, M. DeLuca, G. A. Cain, *Journal of the American Chemical Society* **1989**, 111, 786

LTMP (LiTMP)



Lithium 2,2,6,6-tetramethylpiperidide
[38227-87-1]

Preparation:

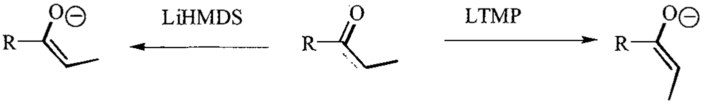


M. Campbell, V. Snieckus, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3166

Notes: Hindered base with low nucleophilicity. Is stable with TMS-Cl; thus reactions can be carried out under equilibrium-controlled conditions, where substrate, TMS-Cl and ***LTMP*** are present at the same time.

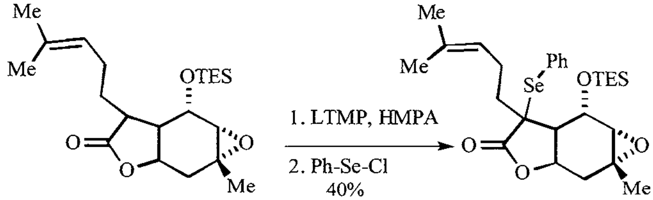
See also: ***LDA***, ***NHMDS***, ***KHMDS***, ***LHMDS*** for other strong bases

As a generalization,



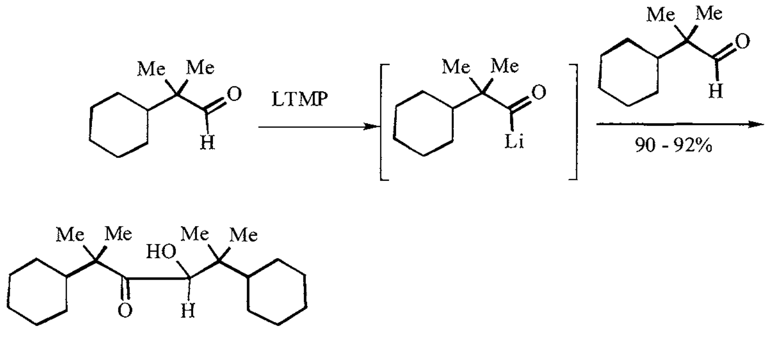
Examples:

1.[1]



Reaction failed with LDA

2.[2]



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[1] A. B. Smith, III, R. E. Richmond, *Journal of Organic Chemistry* **1981**, 46, 4814

[2] C. S. Shiner, A. H. Berks, A. M. Fisher, *Journal of the American Chemical Society* **1988**, 110, 957

Luche Reagent[1]

$NaBH_4 + CeCl_3$

[1191-15-7]

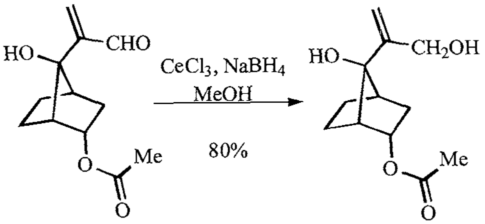
Preparation: Equal amounts of $NaBH_4$ and $CeCl_3$ (7 H_2O) in methanol

L. A. Paquette, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1031

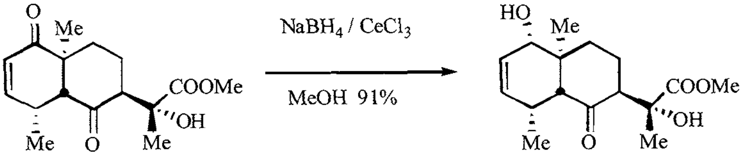
Notes: Specifically reduces enones to allylic alcohols via 1,2-addition. Sometimes stereochemistry is different from $NaBH_4$ alone.

Examples:

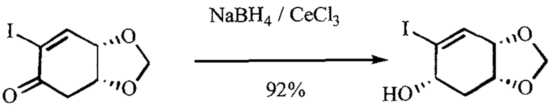
1.[2]



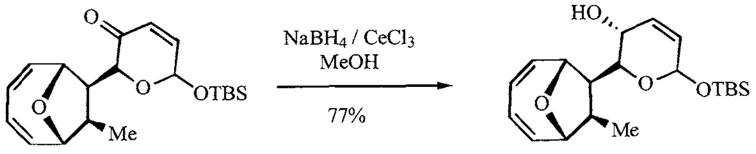
2.[3]



3.[4]



4.[5]



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[1] J.-L. Luche, A. L. Gemal, *Journal of the Chemical Society, Chemical Communications* **1978**, 976

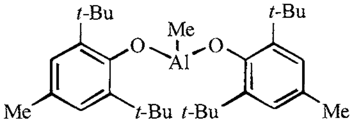
[2] D. L. J. Clive, S. Sun, V. Gagliardini, M. K. Sano, *Tetrahedron Letters* **2000**, 41, 6259

[3] F. J. Moreno-Dorado, F. M. Guerra, F. J. Aladro, J. M. Bustamanta, Z. D. Jorge, G. M. Massanet, *Tetrahedron* **1999**, 55, 6997

[4] C.-K. Sha, A.-W. Hong, C.-M. Huang, *Organic Letters* **2001**, 3, 2177

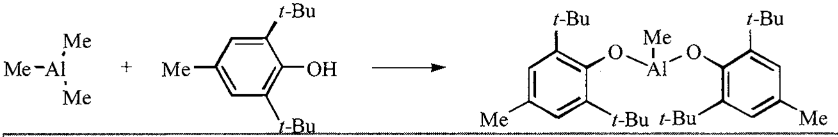
[5] K. Takao, G. Watanabe, Y. Yasui, K. Tadano, *Organic Letters* **2002**, 4, 2941

MAD



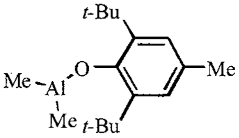
Methylaluminum bis(2,6-di-*t*-butyl-4-methylphenoxide)
[65260-44-8]

Preparation:[1] prepared by reaction of trimethylaluminum with 2 equiv of 2,6-di-*t*-butyl-4-methylphenol in toluene or CH_2Cl_2.



K. Maruoka, H. Yamamoto, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3415

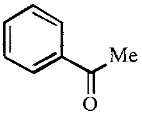
Notes: For a similar reagent, see **DAD** (Dimethylaluminum 2,6-Di-*t*-butyl-4-methylphenoxide) [86803-85-2]

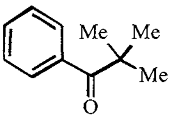


MAD is a bulky Lewis acid used to complex with functional groups to provide a steric discrimination to a number of organic transformations.

Examples:

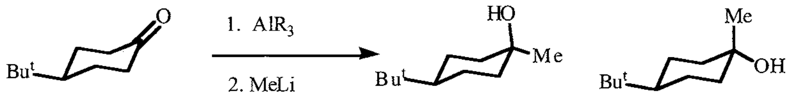
1.[2] **Selectivity in carbonyl reaction.** Here we see that sterically less-hindered ketones are preferentially complexed, leaving the more-hindered ketone to react.





Ratio of Reduction	1	16 with 2 equiv. of MAD

2.[1] Increased carbonyl discrimination:

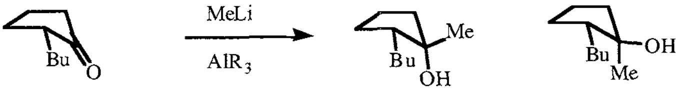


AlR_3	Ratio
None	79 : 21
MAD	1 : 99

---

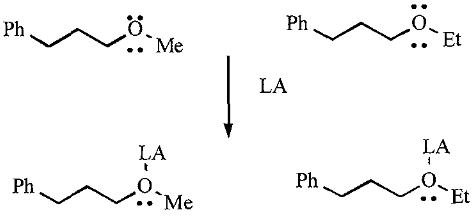
[1] K. Maruoka, T. Itoh, M. Sakurai, K. Nonoshita, H. Yamamoto, *Journal of the American Chemical Society* **1988**, 110, 3588. This article provides a wealth of tabulated data for a number of cyclic systems.

[2] K. Maruoka, Y. Araki, H. Yamamoto, *Journal of the American Chemical Society* **1988**, 110, 2650



AlR$_3$	Yield	Ratio
None	77%	75 : 25
MAD	82%	1 : 99

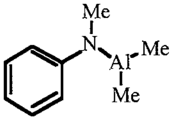
2. [1] **Oxygen Complexation.** Here we see that sterically less-hindered ethers are preferentially complexed.

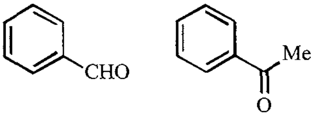


Lewis Acid	Rel. Complexation		
BF_3 etherate	NONE		
$SnCl_4$	2	:	1
MAD	99	:	1

3.[2]

A reagent has been developed that will preferentially complex with aldehydes, so that a ketone can be reacted in the presence of an aldehyde.





MAD / MeMgI	9	:	1
$Me_2AlNMePh$ / MeLi	1	:	6

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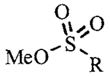
[1] S. Sato, H. Yamamoto, *Journal of the Chemical Society, Chemical Communications* **1997**, 1585

[2] K. Maruoka, Y. Araki, H. Yamamoto, *Tetrahedron Letters* **1988**, 29, 3101

Magic Methyl and Related Reagents



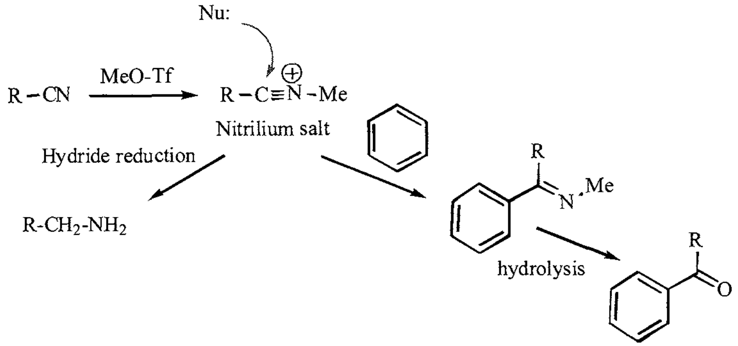
Methyl fluorosulfonate, R = F
Methyl triflate, R = CF_3

Commercially available

R.W. Alder, J.G.E. Phillips, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3617

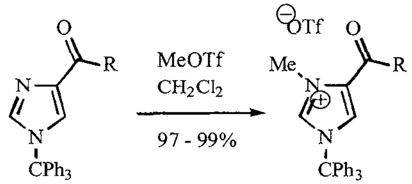
Notes:

Both reagents are powerful methylating agents, reacting with O, N, and S. Read precautions carefully. The ***Methyl fluorosulfonate (Magic Methyl)*** is no longer commercially available. Methyl triflate is extremely (sometimes violently) reactive towards amines. Except for extremely hindered or unactivated amines, not generally required for the task.

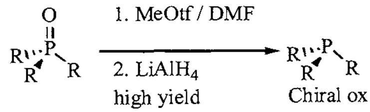


Examples:

1.[1]



2.[2]



Chiral oxides are reduced with inversion at P.

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[1] B.-C. Chen, A. P. Skoumbourdis, J. E. Sundeen, G. C. Rovnyak, S. C. Traeger, *Organic Process Research & Development* **2000**, 4, 613

[2] T. Imamoto, S. Kikuchi, T. Miura, Y. Wada, *Organic Letters*, **2001**, 3, 87

Mander's Reagent

NC-COOMe

[17640-15-2]

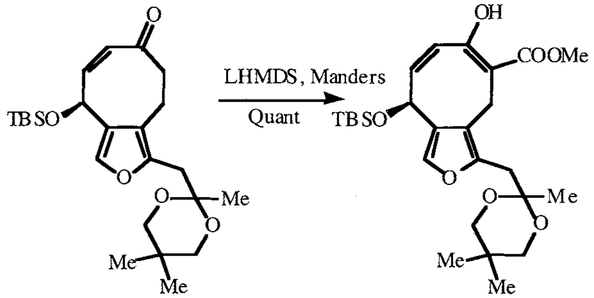
Commercially available.

L. N. Mander, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3466

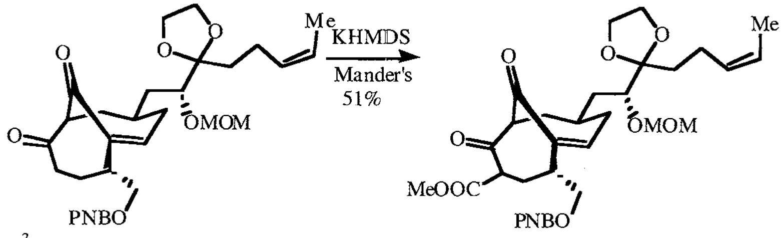
Notes: Used for the α-carbomethoxylation of carbonyl compounds.

Examples:

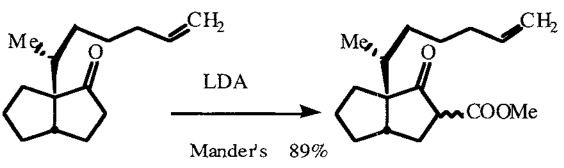
1.[1]



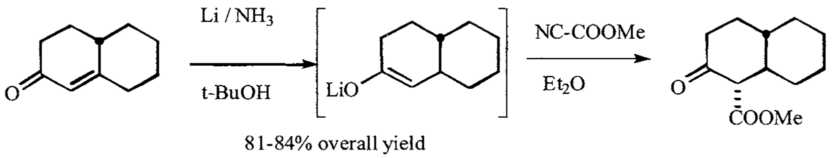
2.[2]



3.[3]



4.[4]



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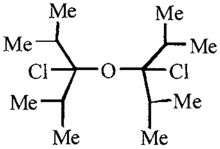
[1] I. Efremov, L. A. Paquette, *Journal of the American Chemical Society* **2000**, 122, 9324

[2] C. Chen, M.E. Layton, S. M. Sheehan, M. D. Shair, *Journal of the American Chemical Society* **2000**, 122, 7424.

[3] J. D. Winkler, M. B. Rouse, M. F. Greaney, S. J. Harrison, Y. T. Jeon, *Journal of the American Chemical Society* **2002**, 124, 9726

[4] S. R. Crabtree, L. N. Mander, S. P. Sethi, *Organic Syntheses* CV9, 619

Markiewicz Reagent

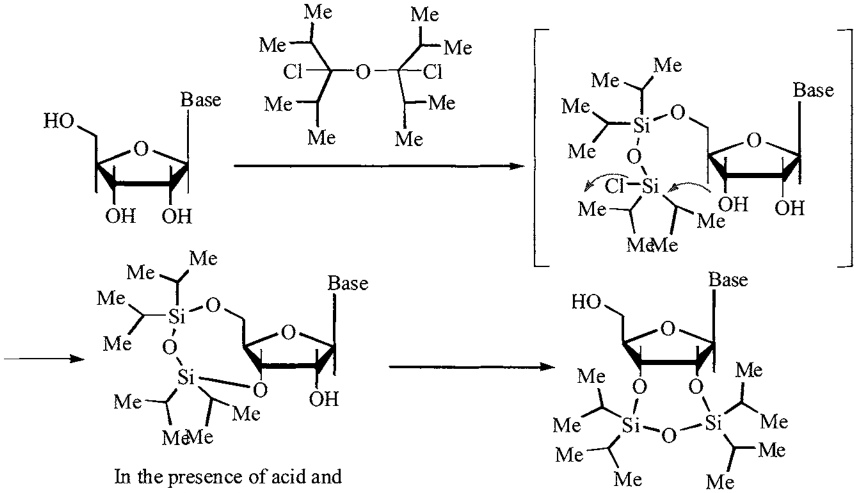


1,3-dichloro-1,1,3,3-tetraisopropyl disiloxane [TIPSCl]
[69304-37-6]

Commercially available

J. Slade, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1730.

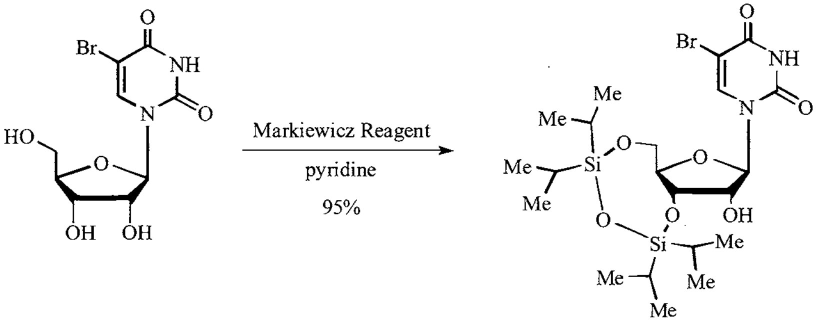
Notes: A useful protecting group; primary alcohols react about 10^3 faster than secondary alcohols.



In the presence of acid and DMF this can isomerize.

Examples:

1.[1]



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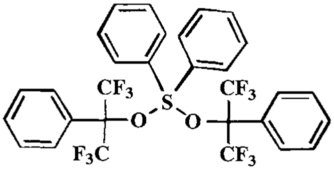
[1] S.C. Holmes, A.A. Arzumanov, M.J. Gait, *Nucleic Acid Research* **2003**, 31, 2759.

Martin sulfurane



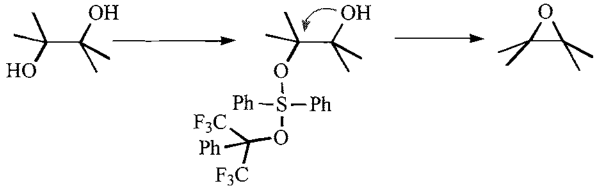
[32133-82-7]
Diphenylbis(1,1,1,3,3,3-hexafluoro-2-phenyl-2-propoxy)sulfurane

Commercially available

B. A. Rodin, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **4**, 2201

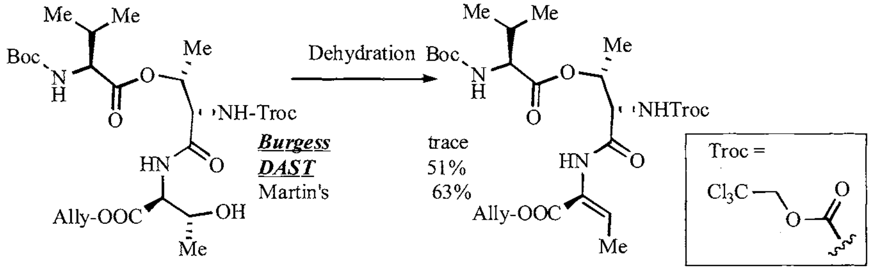
Notes:

Dehydrating agent; tertiary alcohols react instantly. Primary alcohols are often unreactive. Pinacols are often converted to epoxidea:



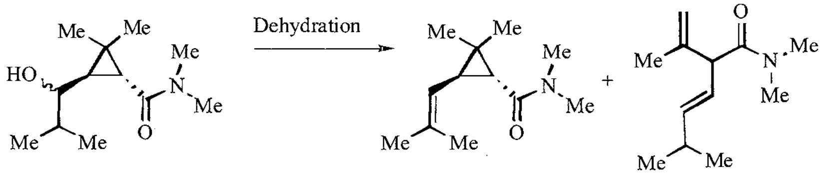
Examples:

1[1].



Burgess	trace
DAST	51%
Martin's	63%

2.[2]



Burgess	No yield given	1	:	4
Martin		92%		

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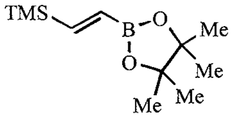
[1] F. Yokokawa, T. Shioiri, *Tetrahedron Letters* **2002**, 43, 8673
[2] M. Majewski, V. Snieckus, *Tetrahedron Letters* **1982**, 23, 1343

Matteson's Reagent

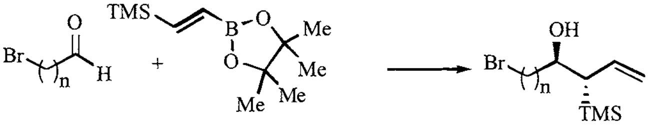


Pinacol *E*-1-trimethylsilyl-1-propene-3-boronate
[126688-99-1]

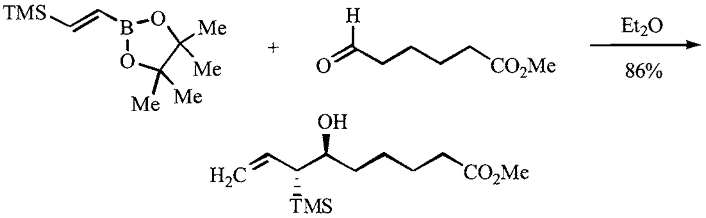
Preparation: D. J. S. Tsai, D. S. Matteson, *Tetrahedron Letters* **1981**, 22, 2751

Examples:

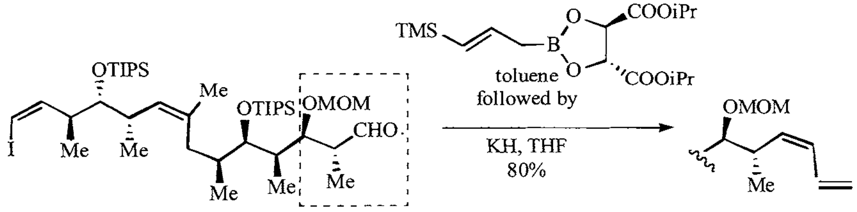
1.[1]



2.[2]



3.[3]



This sequence does not use the Matteson boronate intermediate; however, was referenced as the method for the conversion.

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[1] B. P. Hoag, D. L. Gin, *Macromolecules* **2000**, 33, 8549

[2] D. A. Smith, K. N. Houk, *Tetrahedron Letters* **1991**, 32, 1549

[3] S. S. Harried, C. P. Lee, G. Yang, T. I. H. Lee, D. C. Myles, *Journal of Organic Chemistry* **2003**, 68, 6646

McMurry's Reagent[1]

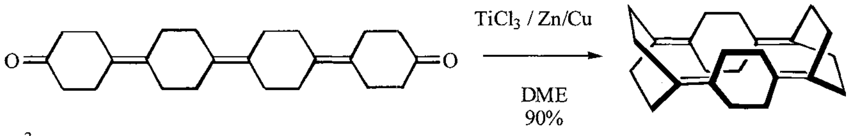
$TiCl_4$ / reducing agent

Preparation: Essentially this reaction involves the preparation of a low-valent titanium reagent that then couples carbonyl groups, including esters to aldehydes/ketones. Generally, $TiCl_4$ is reduced with some reducing agent ($LiAlH_4$, Zn, Mg).

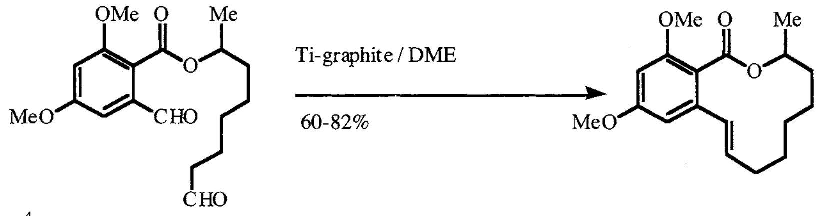
Notes: See ***McMurry Olefination***.

Examples:

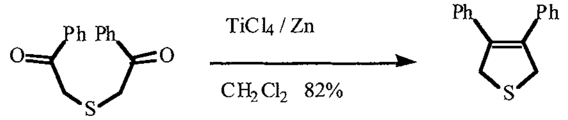
1.[2]



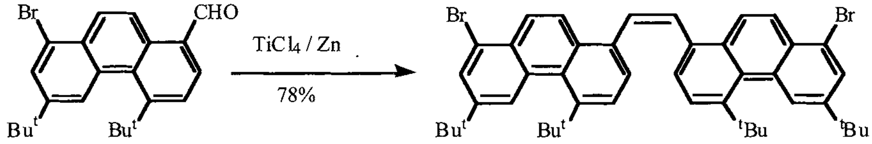
2.[3]



3.[4]



4.[5]



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[1] J. E. McMurry, T. Lectka, J. G. Rico, *Journal of Organic Chemistry* **1989**, 54, 3748

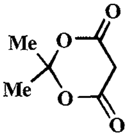
[2] J. E. McMurry, G. J. Haley, J. R. Matz, J. C. Clardy, J. Mitchell, *Journal of the American Chemical Society* **1986**, 108, 515

[3] A. Fürstner, O. R. Thiel, N. Kindler, B. Bartkowska, *Journal of Organic Chemisty* **2000**, 65, 7990

[4] J. Nakayama, H. Machida, R. Satio, M. Hoshino, *Tetrahedron Letters* **1985**, 26, 1983

[5] F. B. Mallory, K. E. Butler, A. Bérubé, E. D. Luzik, Jr., C. W. Mallory, E. J. Brondyke, R. Hiremath, P. Ngo, P. Carroll, *Tetrahedron* **2001**, 57, 3715

Meldrum's Lactone



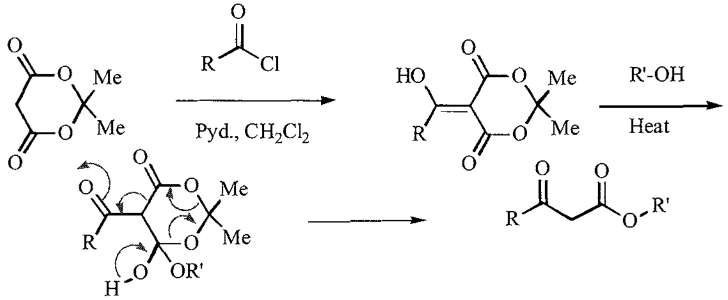
2,2-Dimethyl-1,3-dioxane-4,6-dione
[2033-24-1]

Commercially available

O. Yonemitsu, K. Hirao, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 2056

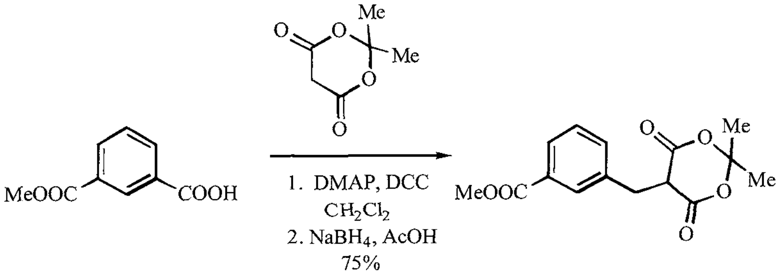
Notes:

Useful for the general preparation of β-keto esters[1]

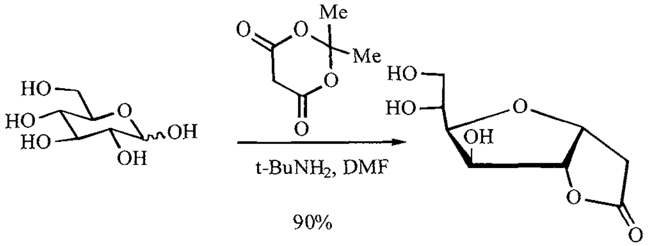


Examples:

1.[2]



2.[3]



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[1] Y. Oikawa, K. Sugano, O. Yonemitsu, *Journal of Organic Chemistry* **1978**, 43, 2087
[2] B. Hin, P. Majer, T. Tsukamoto, *Journal of Organic Chemistry* **2002**, 67, 7365
[3] R. Bruns, A. Wernicke, P. Köll, *Tetrahedron* **1999**, 55, 9793

MEMCl

Source of the 2-methoxyethylmethyl (MEM) group
2-Methoxyethoxymethyl chloride
[3970-21-6]

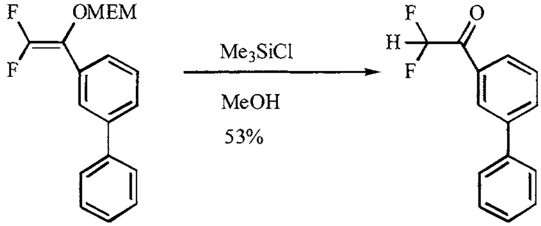
Commercially available

P. G. M. Wuts, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3351

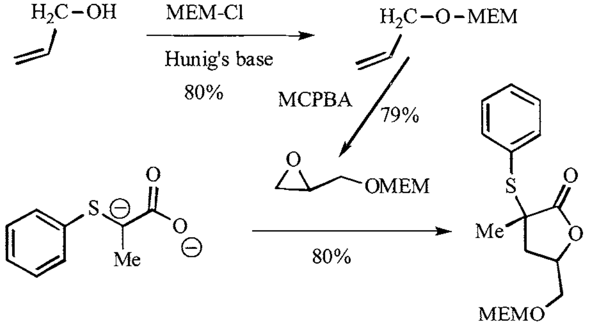
Notes: This alcohol protecting is easily attached and readily removed by Lewis acids such as zinc bromide and titanium tetrachloride. Phenols can be protected (reaction of the sodium salt with MEMCl) and deprotected with TFA. More easily removed than the MOM group.

Examples:

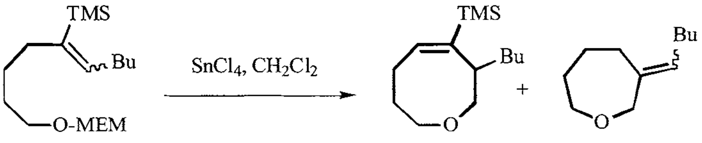
1.[1] Example of a removal of an enol-MEM group



2.[2]



3.[3]



An analysis of how product ratios depended on the stereochemistry in the starting material.

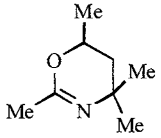
---

[1] G. A. DeBoos, J. J. Fullbrook, J. M. Percy, *Organic Letters* **2001**, 3, 2859

[2] J. R. Donaubauer, T.C. McMorris, *Tetrahedron Letters* **1980**, 21, 2771

[3] T. A. Blumenkopf, G. C. Look, L. E. Overman *Journal of the American Chemical Society*, **1990**, 112, 4399

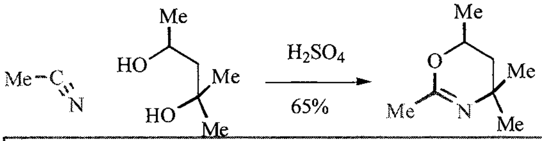
Meyer's Reagent



5,6-Dihydro-2,4,4,6-tetramethyl-1,3(4*H*)-oxazine
[26939-18-4]

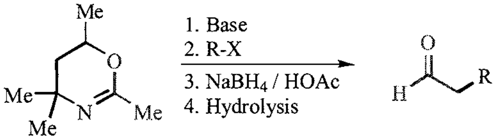
Commercially available

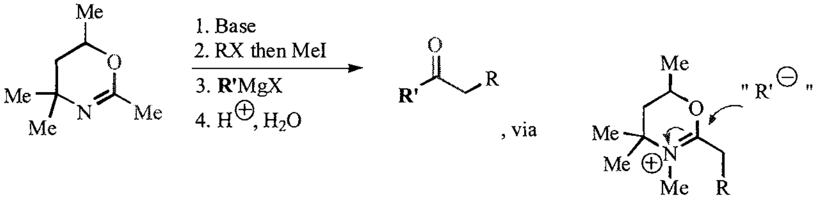
Preparation: ***Ritter reaction***



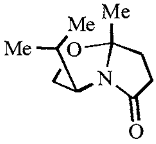
T. D. Nelson, A.I. Meyers, *Encyclopedia of Reagents for Organic Synthesis,* John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 888

Notes: Useful reagent for the preparation of aldehydes and ketones





Meyer's Reagent

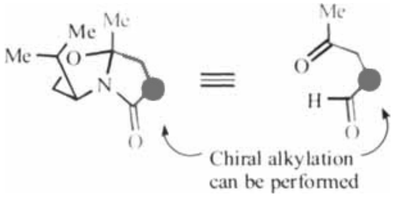


Tetrahydro-3-isopropyl-7a-methylpyrrolol[2,1-b]-5(6*H*)-one
(3*S*,*cis*) [98203-44-2]; (3*R*,*cis*) [123808-97-9]

Commercially available

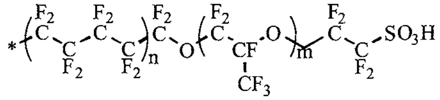
T. D. Nelson, A.I. Meyers, *Encyclopedia of Reagents for Organic Synthesis,* John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **7**, 4756

Notes:



Nafion-H

Reagent



Nafion-H
[63937-00-8]

Commercially available

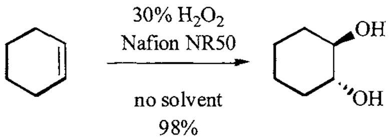
Y. El-Kattan, J. McAtee, *Encyclopedia of Reagents for Organic Synthesis,* John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3677

Notes:

An extremely useful acid catalyst with the acidity of concentrated sulfuric acid. Has been proposed as a replacement for mineral acids in the instructional organic laboratory for dehydration and esterification reactions.[1]

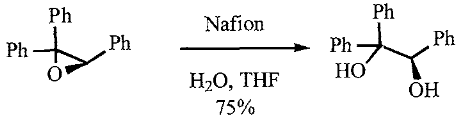
Examples:

1.[2]

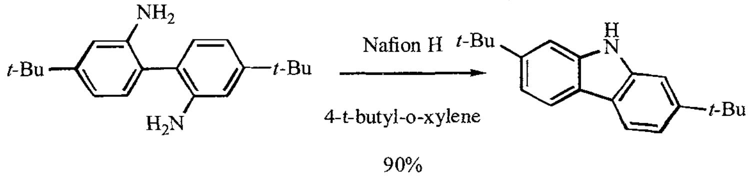


The resin could be reused; after 10 cycles almost no loss in yield.

2.[3]



3.[4]



90%

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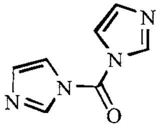
[1] M. P. Doyle, B. F. Plummer, *Journal of Chemical Education* **1993**, 70, 493

[2] Y. Usui, K. Sato, M. Tanaka, *Angewandte Chemie International Edition in English* **2003**, 42, 5623

[3] B. D. Brandes, E. N. Jacobsen, *Journal of Organic Chemistry* **1994**, 59, 4378

[4] T. Yamato, C. Hideshima, K. Suehiro, M. Tashiro, G. K. S. Prokash, G. A. Olah, *Journal of Organic Chemistry* **1991**, 56, 6248

N,N'-Carbonyldiimidazole
CDI



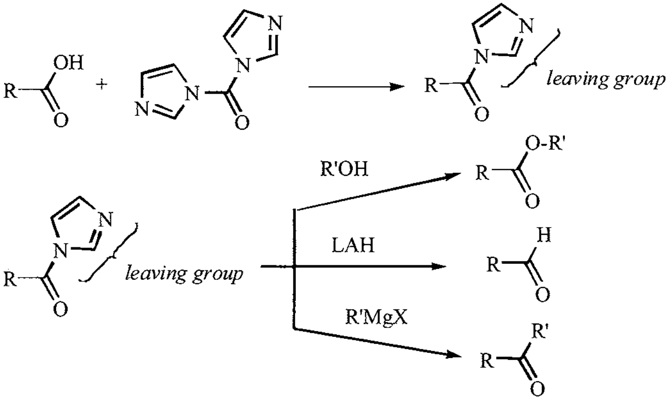
[530-62-1]

Commercially available

A. Armstrong, *Encyclopedia of Reagents for Organic Synthesis,* John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1006

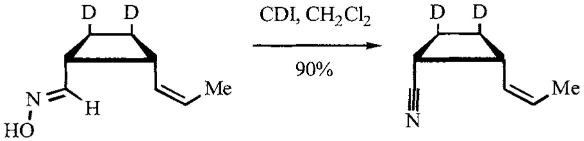
Notes:

Useful for activation of carboxylic acids..

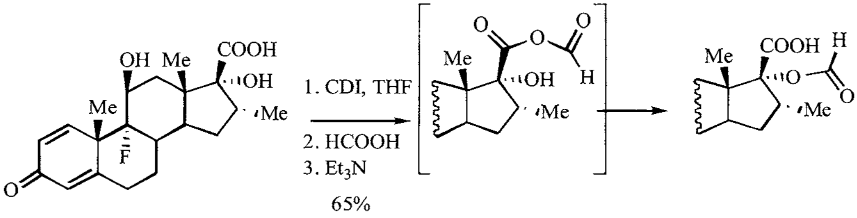


Examples:

1.[1]



2[2]



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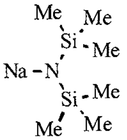
[1] R. E. Conrow, G. W. Dillow, L. Baker, L. Xue, O. Papadopoulou, J. K. Baker, B. S. Scott, *Journal of Organic Chemistry* **2002**, 67, 6835

[2] W. von E. Doering, X. Cheng, K. Lee, Z. Lin, *Journal of the American Chemical Society* **2002**, 124, 11642

NaHMDS, $NaN(SiMe_3)_2$



Sodium Hexamethyldisilazide, NaHMDS
[1070-89-9]

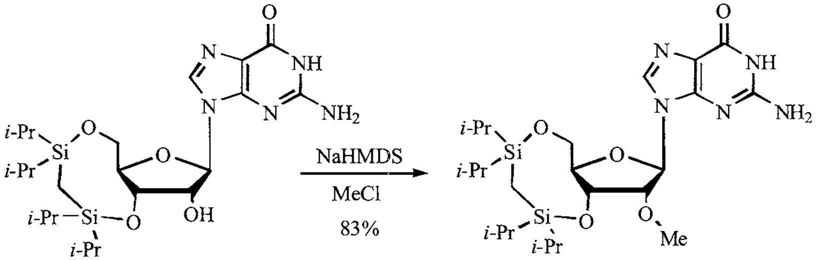
Commercially available

B. T. Watson, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 7, 4564

Notes: Strong, sterically-hindered base, soluble in THF, ether, and toluene. The Li and K analogs are also available. The reagent also can act as a nucleophile under certain conditions.

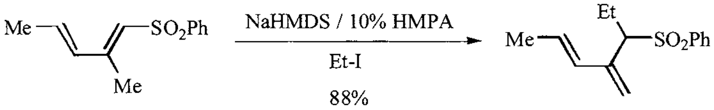
Example

1.[1]

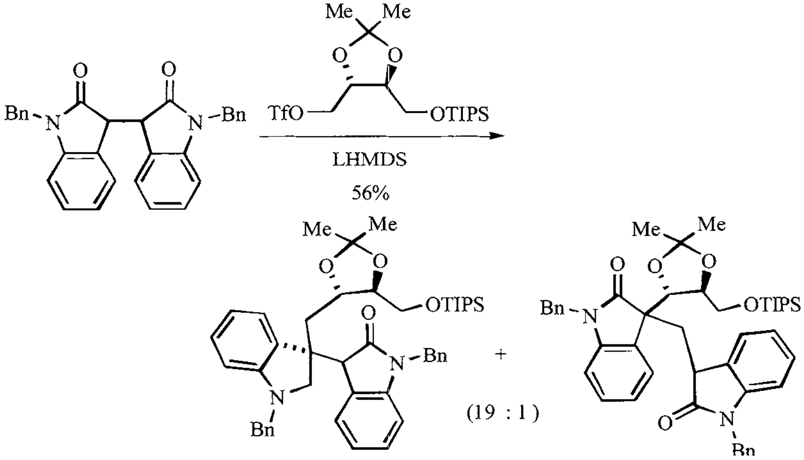


Use of NaH resulted in significant *N*-alkylation.

2.[2]



3.[3] The lithio reagent serves much the same function:



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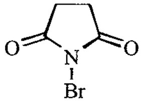
[1] S. Chow, K. Wen, Y. S. Sanghvib, E. A. Theodorakisa, *Bioorganic & Medicinal Chemistry Letters* **2002**, 13, 1631

[2] X. Li, D. Lantrip, P. L. Fuchs, *Journal of the American Chemical Society* **2003**, 125, 14262

[3] S. B. Hoyt, L. E. Overman, *Organic Letters* **2000**, 2, 3241

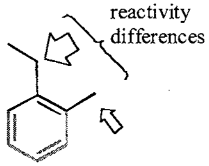
NBS



N-Bromosuccinimide
[128-08-5]

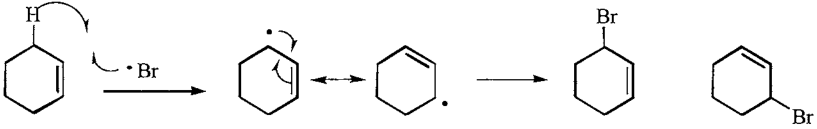
Commercially available

S. C. Virgil, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 768



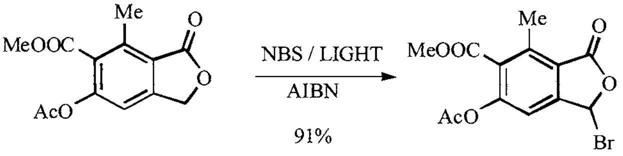
Notes: Used for allylic and benzylic brominations (***Wohl-Ziegler Reaction***). With moist DMSO the reagent is useful for bromohydrin formation, providing trans addition of bromine and water. Can brominate alpha to carbonyl in carbonyl (carboxyl)-containing compounds. With DMF useful for aromatic bromination of activated aromatic rings, such as phenols, aromatic ethers, aniline derivatives and activated heterocyclic compounds. For similar chemistry, see also ***NBA*, *N-Bromoacetamide***.

In allylic bromination, the radical nature of the reaction can lead to rearranged products.

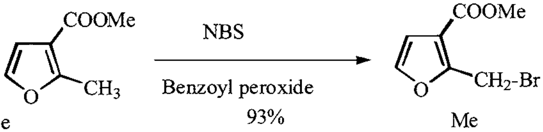


Examples:

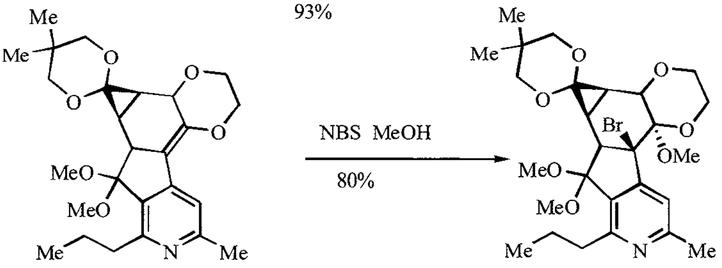
1.[1]



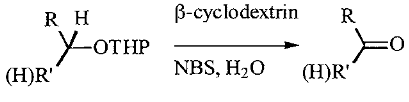
2.[2]



3.[3]



4.[4] Useful for the conversion:



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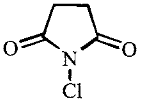
[1] T. R. Kelly, D. Xu, G. Martınez, H. Wang, *Organic Letters* **2002**, 4, 1527
[2] H. Khatuya, *Tetrahedron Letters* **2002**, 42, 2643
[3] D. L. Boger, S. Ichikawa, H. Jiang, *Journal of the American Chemical Society* **2000**, 122, 12169
[4] M. Narender, M. S. Reddy, K. R. Rao, *Synthesis* **2004**, 1741

NCS

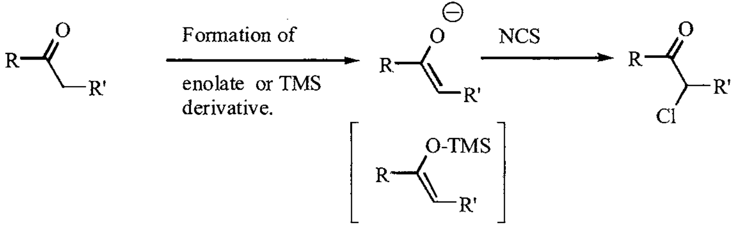


N-Chlorosuccinimide
[128-09-6]

Commercially available

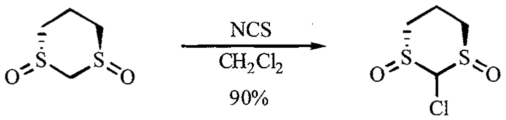
S. C. Virgil, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1205

Notes: Used for the a-chlorination of carbonyl compounds, sulfoxides and sulfides (See: ***Ramberg-Bäcklund rearrangement***). Also used for preparing *N*-chloroamines.

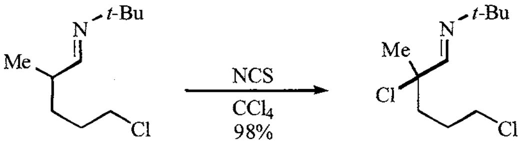


Examples:

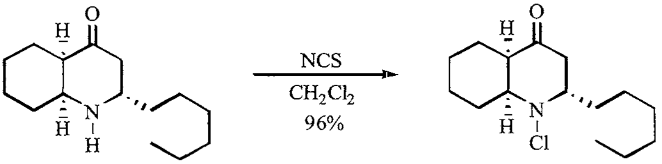
1.[1]



2.[2]



3.[3]



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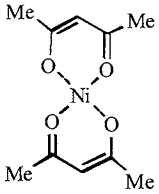
[1] V. K. Aggarwal, G. Boccardo, J. M. Worrall, H. Adams, R. Alexander, *Journal of the Chemical Society Perkin Transactions 1* **1997**, 11

[2] N. DeKimpe, C. Stevens, M. Virag, *Tetrahedron* **1996**, 52, 3303

[3] B. B. Snider, T. Liu, *Journal of Organic Chemistry* **1997**, 62, 5630

$Ni(acac)_2$



Nickel(II) acetylacetonate
[3264-82-2] .

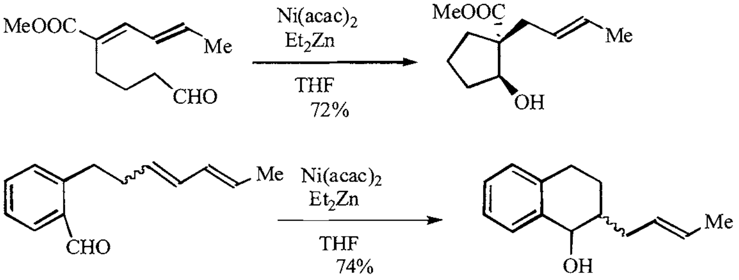
Commercially available

J. Doyon, *Encyclopedia of Reagents for Organic Synthesis,* John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3689

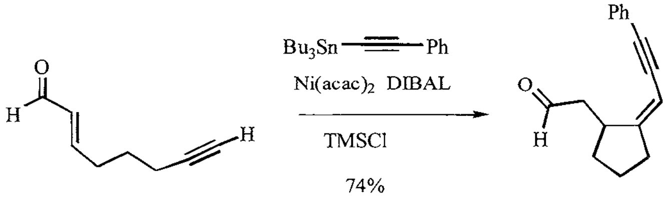
Notes: Catalyst for polymerization and dimerization of alkynes and alkenes. Has been used for catalyzing conjugate additions to enones. Useful as a Lewis acid.

Examples:

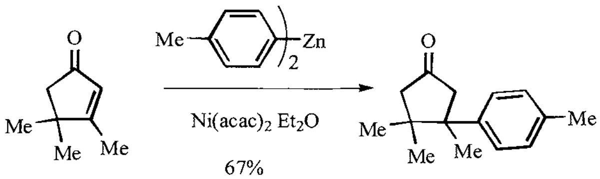
1.[1]



2.[2]



3.[3]



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[1] K. Shibata, M. Kimura, M. Shimizu, Y. Tamaru, *Organic Letters* **2001**, 3, 2181
[2] M. Lozanov, J. Montgomery, *Journal of the American Chemical Society* **2002**, 124, 2106
[3] A. E. Greene, J. P. Lansard, J. L. Luche, C. Petrier, *Journal of Organic Chemistry* **1984**, 49, 931

Ni(cod)$_2$

Bis(1,5-cyclooctadiene)nickel
[1295-35-8]

Commercially available

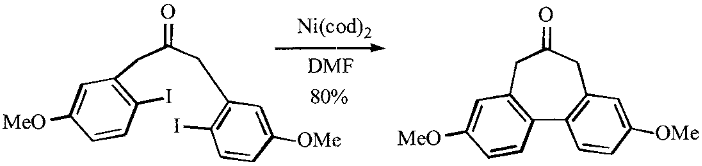
P. A. Wender, T.E. Smith, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 1, 450

Notes:

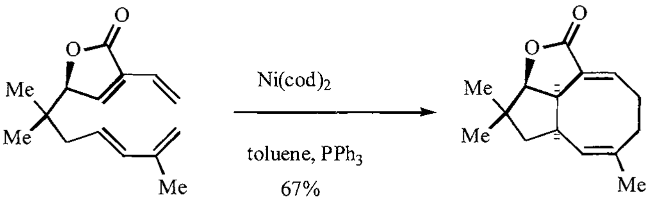
Useful source of nickel(0).

Examples:

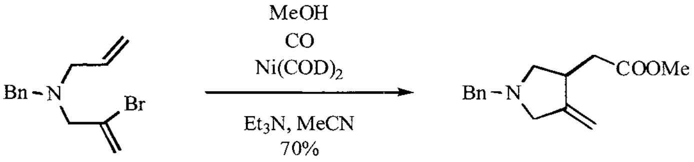
1.[1]



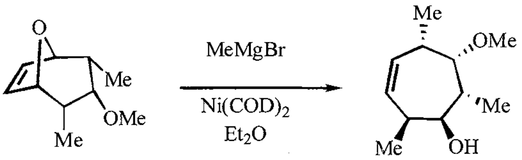
2.[2]



3.[3]



4.[4]



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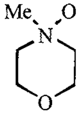
[1] M. F. Semmelhack, L.S. Ryono, *Journal of the American Chemical Society* **1975**, 97, 3873

[2] P. A. Wender, N. C. Ihle, C. R. D. Correia, *Journal of the American Chemical Society* **1988**, 110, 5904

[3] S. Arai, K.Tokumaru, T. Aoyama, *Tetrahedron Letters* **2004**, 45, 1845

[4] M. Lautens, S. Ma, *Journal of Organic Chemistry* **1996**, 61, 7246

NMO

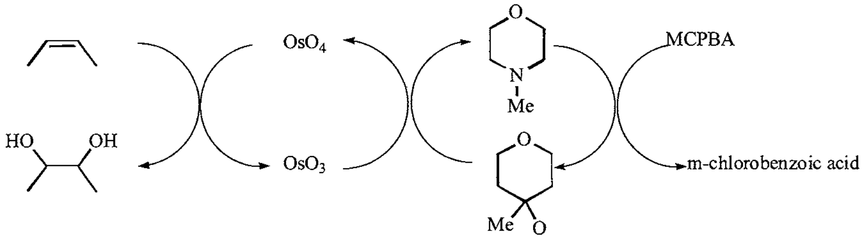


N-Methlymorpholine-*N*-oxide [7529-22-8]

Commercially available

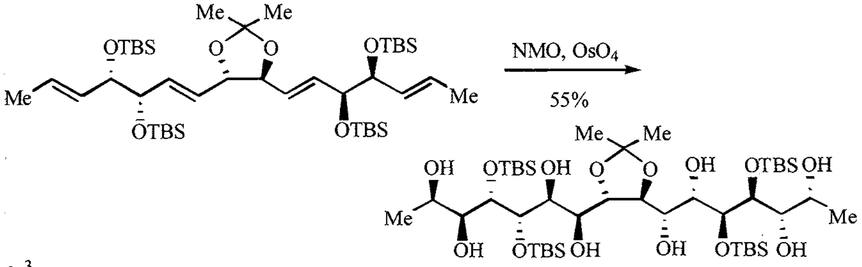
M. R. Sivik, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3545

Notes: A useful and relatively mild oxidizing agent. Most current use attempts to use catalytic amounts.of OsO_4; thus NMO is used as a co-oxidant with OsO_4 for hydroxylation of alkenes. A method has been developed that allows catalytic amounts of NMM (*N*-methylmorpholine) to be used.[1]



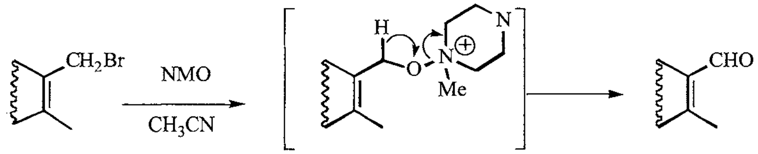
Examples:

1.[2]

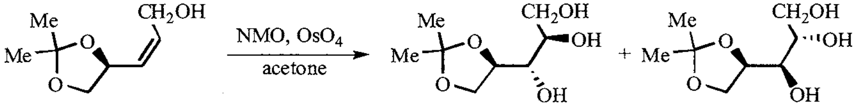


2.[3]

NMO can carry out the conversion of an activated halogen compound to an aldehyde



3.[4]



(6 : 1)

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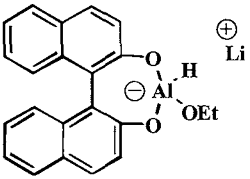
[1] K. Bergstad, J. J. N. Piet, J. E. Backvall, *Journal of Organic Chemistry* **1999**, 64, 2545

2.J. A. Marshall, S. Beaudoin, K. Lewinskit, *Journal of Organic Chemistry* **1993**, 58, 5876

[3] W. P. Griffith, J. M. Jolliffe, S. V. Ley, K. F. Springhorn, P. D. Tiffin, *Synthetic Communications* **1992**, 22, 1967 (AN 1992:489712)

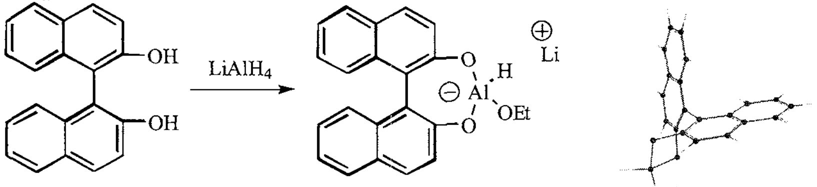
[4] J. K. Cha, W. J. Christ, Y. Kishi, *Tetrahedron Letters* **1983**, 24, 3943

Noyori's Reagent



[16853-85-3] ·Lithium aluminum hydride-2,2′-dihydroxy-1,1′-binaphthyl ((*R*)-BINAL)
[18531-94-7] ·Lithium aluminum hydride-2,2′-dihydroxy-1,1′-binaphthyl ((*S*)-BINAL)

Preparation:

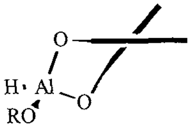


BINOL

Commercially available

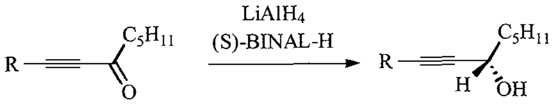
A. S. Gopalan, H. K. Jacobs, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons,
L. A. Paquette, Ed., New York, 1995, **5**, 3022

Notes: Used for enantioselective reduction of carbonyl groups. The reducing agent (for the appropriate enantiomer) can be designated in carton style to show the twist in the ring systems as:



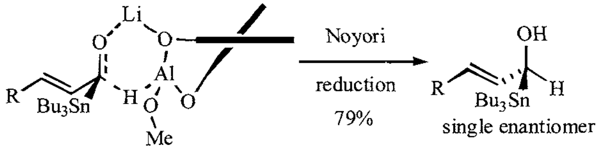
Examples:

1.[1]



R = H 84%
R = C_4H_9 90%

2.[2]



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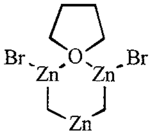
[1] M. Nishizawa, M. Yamada, R. Noyori, *Tetrahedron Letters* **1981**, 22, 247
[2] J. A. Marshall, W. Y. Gung, *Tetrahedron Letters* **1998**, 29, 1657

Nystead Reagent



[41114-59-4]
Most likely a complex mixture
resulting from Schlenk equilibrium.

I-Zn-CH_2-Zn-I

Bis(iodozincio) methane
[31729-70-1]
Similar reagent

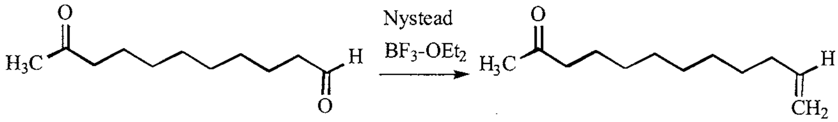
Commercially available

S. Matsubara, *e-Encyclopedia of Reagents for Organic Synthesis*, L.A. Paquette, Ed.,, John Wiley & Sons, Inc., online reference available at *http://www.interscience.wiley.com.*

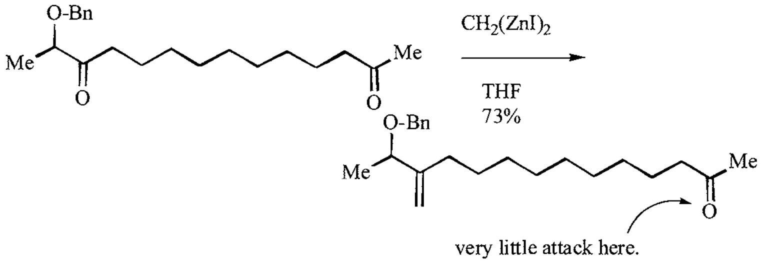
Notes: The bromo- variation, due to poor solubility is of limited use. Useful for the BF_3-catalyzed methylenation of aldehydes in the presence of ketones.

Examples:

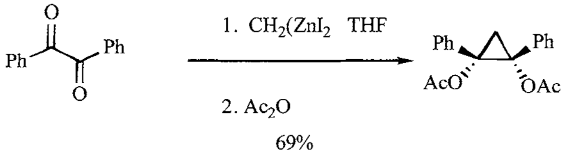
1.[1]



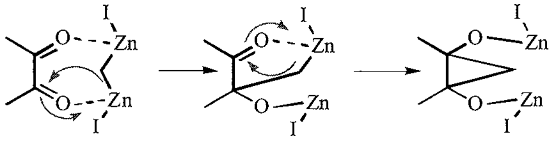
2.[2]



3.[3]



via:



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[1] S. Sugihara, M. Utimoto, *Synlett*, **1998**, 313; from S. Matsubara, *e-Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Ltd., 2003

[2] K. Ukai, A. Arioka, H. Yoshino, H. Fushimi, K. Oshima, K. Utimoto, S. Matsubara, *Synlett* **2001**, 513; from S. Matsubara, *e-Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Ltd., 2003

[3] S. Matsubara, K. Ukai, H. Fushimi, Y. Yokota, H. Yoshino, K. Oshima, K. Omoto, A. Ogawa, Y. Hiokib, H. Fujimotob, *Tetrahedron* **2002**, 58, 8255

Osmium tetroxide

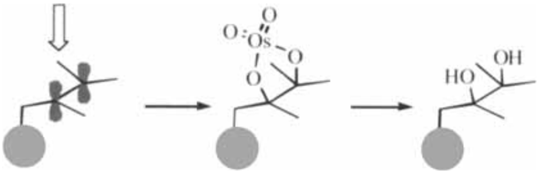
OsO_4

[20816-12-0]

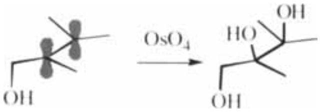
Commercially available

Y. Gao, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette,
York, 1995, **6**, 3801

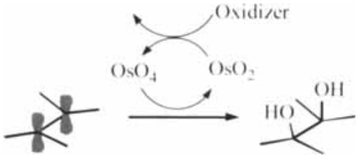
Notes: Useful for the *cis*-dihydroxylation of alkenes. Attacks alkenes from the less-hindered face.



In examples containing an allylic hydroxyl (or alkoxy) group, the newly formed *cis*-diol will be anti to the existing group. This appears to override other steric factors (see footnote 1).



Early experiments used OsO_4 in stoichiometric amounts, more modern use reoxides the OsO_2 formed in the reaction: Common reagents for this include ***TBHP*** and ***NMO***

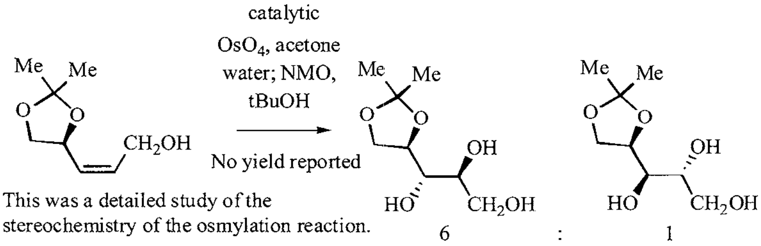


For studies on a polymer-bound OsO_4 reagent, see: S. Kobayashi, M. Endo, S. Nagayama, *Journal of the American Chemical Society* **1999**, 121, 11229

A recoverable, microencapsulated OsO_4 has been described: S. Nagayama, M. Endo, S. Kobayashi, *Journal of Organic Chemistry* **1998**, 63, 6094

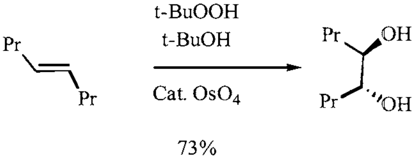
Examples:

1.[1]



This was a detailed study of the stereochemistry of the osmylation reaction.

2.[2]



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[1] J. K. Cha, W. J. Christ, Y. Kishi, *Tetrahedron* **1984**, 40, 2247

[2] K. B. Sharpless, K. Akashi, *Journal of the American Chemical Society* **1976**, 98, 1986

Oxone®[1]

($2KHSO_5.KHSO_4.K_2SO_4$)

A "triple salt", providing a convenient souce of
potassium monoperoxysulfate (potassium hydrogen persulfate)
[37222-66-5]

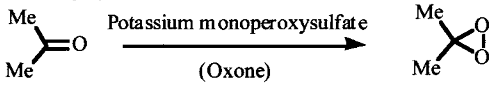
Commercially available

J. M. Crandall, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4265

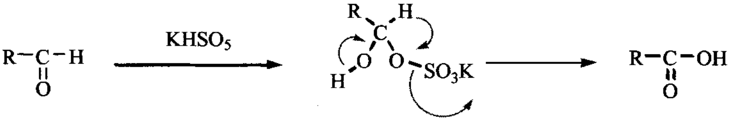
Notes: This reagent is a useful oxidizing agent.

The reagent can provide for ***Baeyer-Villiger*** conditions and reacts with nitrogen and sulfur to form *N*-oxides and sulfones, respectively.

As a reagent, it is commonly found in the preparation of dimethyldioxirane (***DDO***), itself a useful oxidizing agent.



The oxidation of aldehydes to acids might follow the following mechanism:

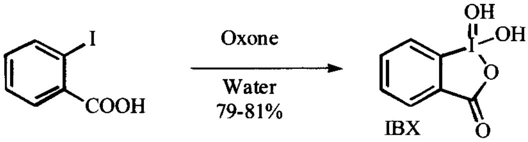


Examples:

1.[2]

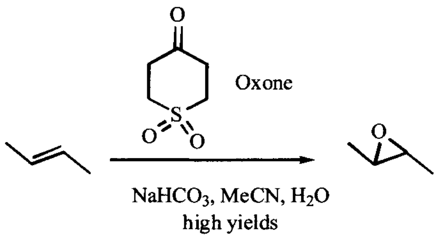
$$R{-}CHO \xrightarrow[\text{General high yield}]{\text{Oxone}} R{-}COOH$$

2.[3]



3.[4] Use of Oxone for conversion of C-B to C-OH bonds in the hydroboration reaction.

4.[5]



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[1] Also commercially available as Curox® and Caroat®

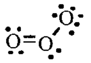
[2] B. R. Travis, M. Sivakumar, G. O. Hollist, B. Borhan, *Organic Letters* **2003**, 5, 1031

[3] M. Frigerio, M. Santagostino, S. Sputore, *Journal of Organic Chemistry* **1999**, 64, 4537

[4] D. H. B. Ripin, W. Cai, S. J. Brenek, *Tetrahedron Letters* **2000**, 41, 5817

[5] D. Yang, Y.-C. Yip, G.-S. Jiao, M.-K. Wong, *Journal of Organic Chemistry* **1998**, 63, 8952

Ozone



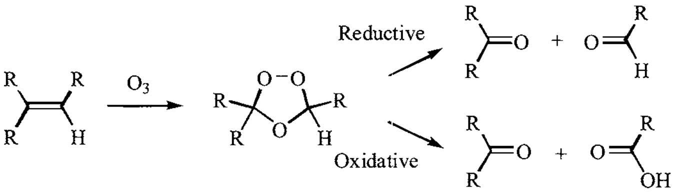
O_3

[10028-15-6]

Preparation: generated by passing dry oxygen through two electrodes connected to AC.

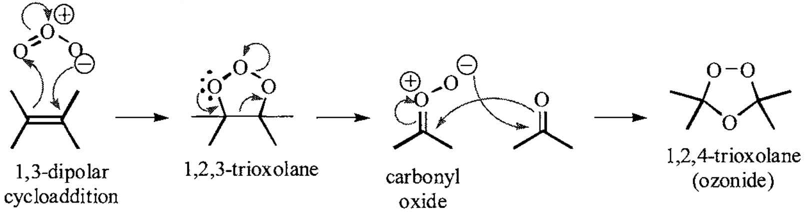
R. A. Berglund, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3837

Notes: For organic chemists the major use of this oxidizing agent is in the cleavage of alkene bonds. This can be followed by either oxidative or reductive workups. The reaction can be run in a number of ***common solvents***.

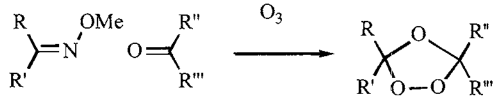


Among the reducing agents for the reductive workup, Me_2S is one of the most common. Hydrogen peroxide is a common oxidative workup.

Criegee Mechanism for Ozonolysis

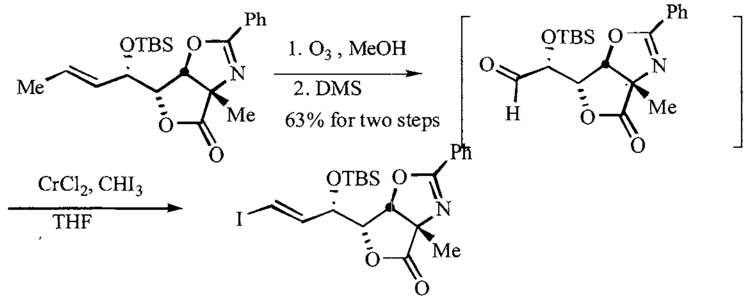


Griesbaum Coozonoysis Reaction[1]



Examples:

1.[2]



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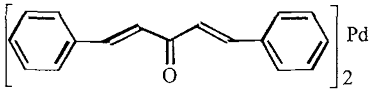
[1] Y. Tang, Y. Dong, J. M. Karle, C.A. DiTusa, J. L. Vennerstrom, *Journal of Organic Chemistry* **2004**, 69, 6470

[2] P. H. Dussault, J. M. Raible, *Organic Letters* **2000**, 2, 3377.

Pd(dba)$_2$



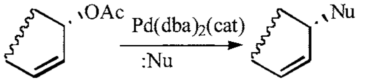
Bis(dibenzylideneacetone)palladium(0)
[32005-36-0]

Commercially available

J. R. Stille, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 482

Notes:

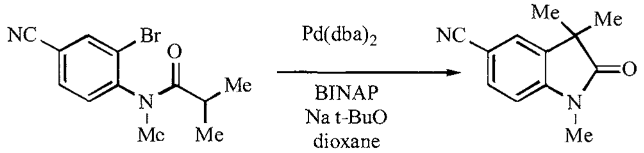
Catalytic amounts of Pd(dba)$_2$ will activate allylic acetates to nucleophilic attack.



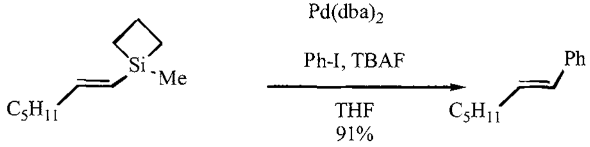
Triphenylphosphine or ***1,2-bis(diphenylphosphino)ethane (dppe)*** are often part of the reaction mixture.

Examples:

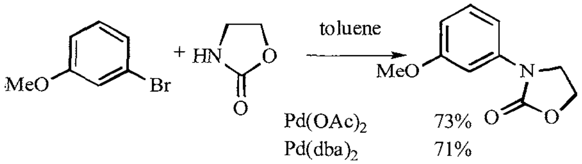
1.[1]



2.[2]



3.[3]



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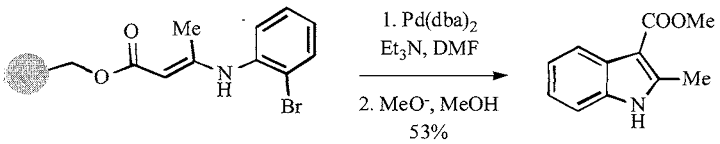

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[1] K. H. Shaughnessy, B. C. Harmann, J. F. Hartwig, *Journal of Organic Chemistry* **1998**, 63, 6546

[2] S. E. Denmark, J. Y. Choi, *Journal of the American Chemical Society* **1999**, 121, 5821

[3] S. Cacchi, G. Fabrizi, A. Goggiamani, G. Zappia, *Organic Letters* **2001**, 3, 2539

[4] K. Yamazaki, Y. Kondo, *Journal of Combinatorial Chemistry* **2002**, 4, 191

Pearlman's Catalyst

$Pd(OH)_2$ / C

Palladium(II) hydroxide on carbon
[7440-05-3]

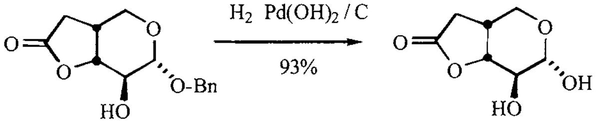
Commercially available

A. O. King, I. Shinkai, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3888

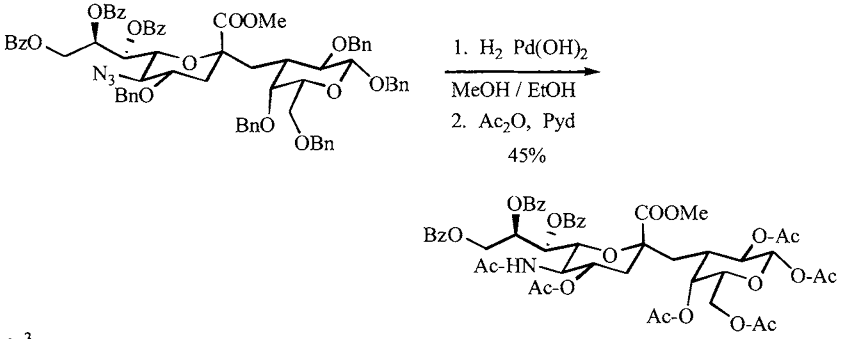
Uses: A catalyst that finds use in the removal of benyzyl groups under hydrogenolysis conditions.

Examples:

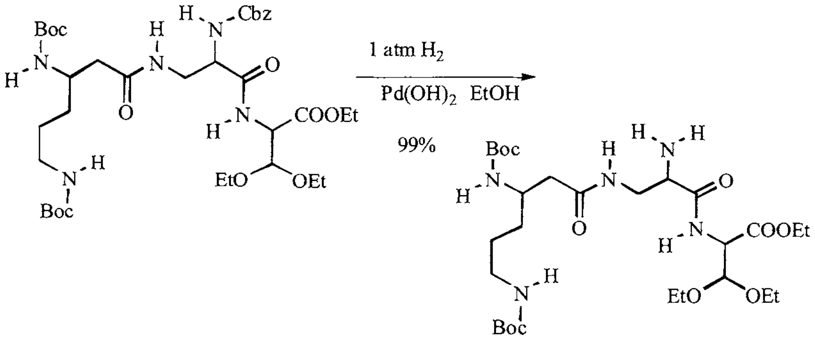
1.[1]



2.[2]



3.[3]



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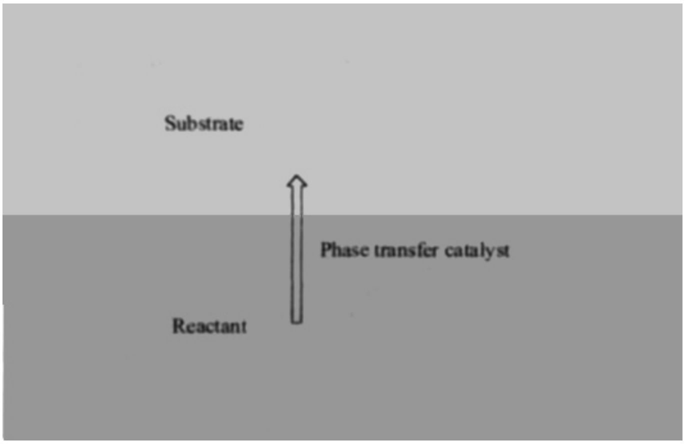
[1] Y. Al-Abed, N. Naz, D. Mootoo, W. Voelter, *Tetrahedron Letters* **1996**, 37, 8641
[2] W. Notz, C. Hartel, B. Waldscheck, R. R. Schmidt, *Journal of Organic Chemistry* **2001**, 66, 4250
[3] D. E. DeMong, R. M. Williams, *Journal of the American Chemical Society* **2003** 125, 8561

Phase-transfer Catalysts

Commercially available

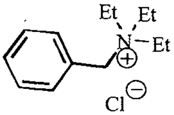
Notes: A phase transfer reagent is a compound soluble in both an aqueous and organic phase.



Generally the phase transfer catalyst will be either a salt (ex, KMnO4, NaOCl, etc) where the anion portion of the reactant is transported to the substrate by way of a cationic material with solubility in both phases.

We also include crown ethers as phase transfer reagents. In these case the cation of the reactant is most likely coordinated.

Examples:



Triethylbenzylammonium bromide ***[TEBA]***

[56-37-1], P.B. Savage, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 376

$Bu_4N^+ Br^-$

Tetrabutylammonium bromide

[1643-19-2], A.B. Charette, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **7**, 3632

$(Me(CH_2)_7]_3N\text{-}Me)^+ Cl^-$

Methyltrioctylammonium chloride [Aliquat]®

[5137-55-3]. M.E. Bos, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **7**, 3632

PPA

Unspecified structure

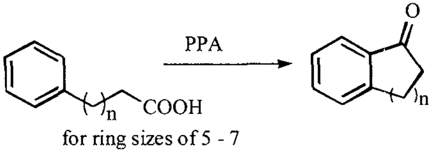
Polyphosphoric acid
[8017-16-1]

Commercially available

J. H. Dodd, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4169

Notes: A strong mineral acid of unspecified structure. It contains a mixture of phosphoric acids and derivatives, with a high content of P_2O_5. Does chemistry similar to that found with ***Eaton's reagent***.

Useful for ***Friedel-Crafts acylation*** reactions:



Examples:

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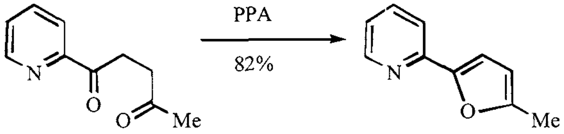
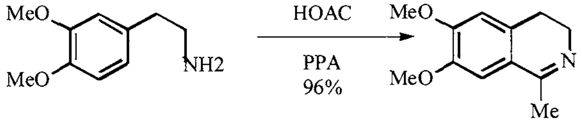
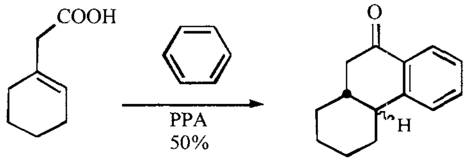


2.[2]



3.[3]



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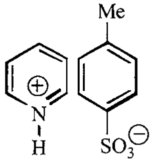
[1] A. Jones, P. U. Civcir, *Tetrahedron* **1997**, 53, 11529

[2] A. P. Venkov, I. I. Ivanov, *Tetrahedron* **1996**, 52, 12299

[3] M. M. Ramana, P. V. Potnis, *Synthesis* **1996**, 1090

PPTS

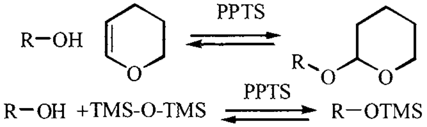


Pyridinium *p*-toluenesulfonate
[24057-28-1]

Commercially available

A. A. Galan, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4375

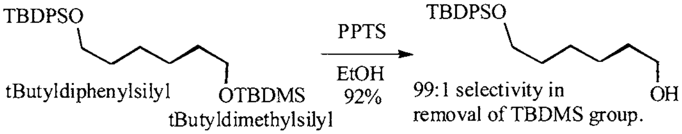
Notes: A weak acid, useful for substrates with acid-sensitive functional groups. Has been used to place and remove alcohol protecting groups:



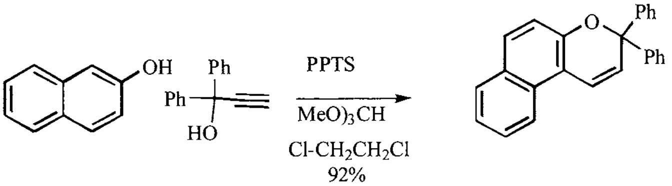
Examples:

1.[1]

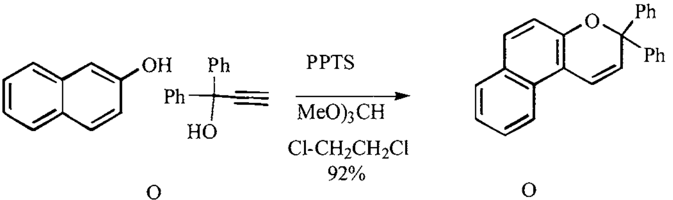
Selective removal of protecting groups:



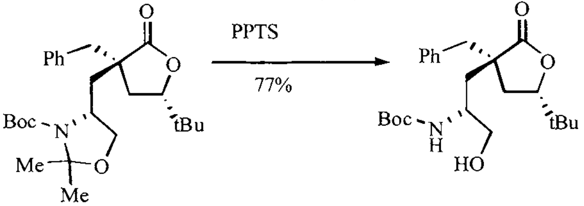
2.[2]



3.[3]



4.[4]



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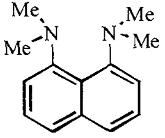
[1] C. Prakash, S. Saleh, I. A. Blair, *Tetrahedron Letters* **1989**, 30, 19
[2] W. Zhao, E. M. Carreira, *Organic Letters* **2003** 5, 4153
[3] H. Choo, Y. Chong, C. K. Chu, *Organic Letters* **2001**, 3, 1471
[4] K. Nakamura, T. J. Baker, M. Goodman, *Organic Letters* **2000**, 2, 2967

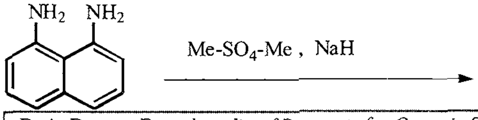
Proton Sponge

Proton Sponge



[20734-58-1]
1,8-bis(dimethylamino)naphthalene

Commercially available. Can be prepared:[1]

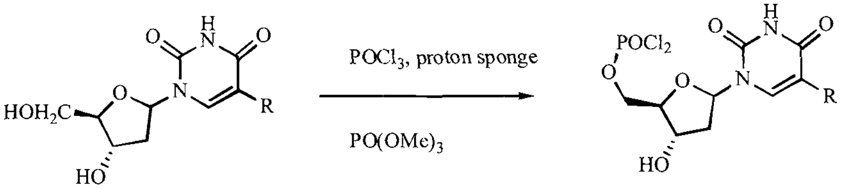


B. A. Barner, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 1, 494

Notes: A very strong base (pKa = 21.1) with poor nucleophilicity due to steric effects. This makes it a useful organic base for reactions sensitive to most other Lewis bases.

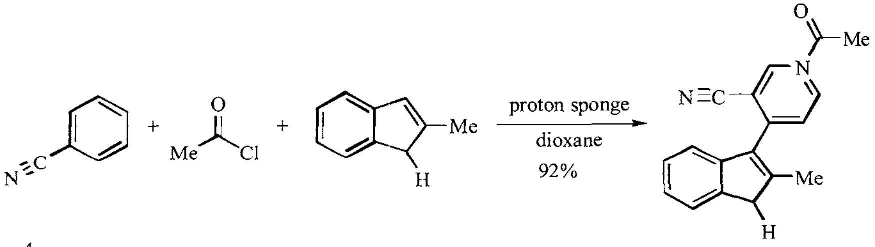
Examples:

1.[2]

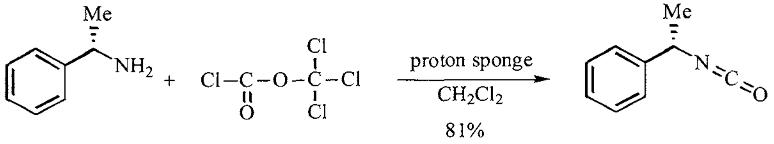


Other organic bases were not effective

2.[3]



3.[4]



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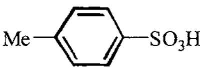
[1] H. Quast, W. Risler, G. Döllscher, *Synthesis* **1972**, 558

[2] T. Kovács, L. Ötvös, *Tetrahedron Letters* **1988**, 29, 4525

[3] R. Lavilla, T. Gotsens, M. Guerrero, J. Bosch, *Synthesis* **1995**, 382

[4] S. T. Sigurdsson. B. Seeger, U. Kutzke, F. Eckstein, *Journal of Organic Chemistry* **1996**, 61, 3883

PTSA



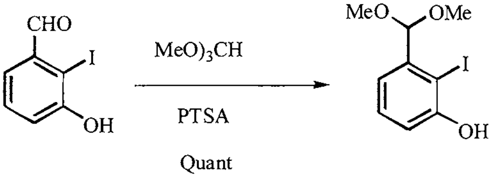
[104-15-4]
Tosic Acid

Commercially available.

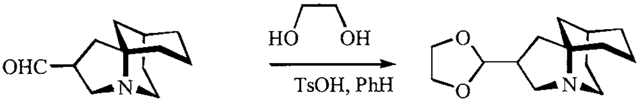
G. S. Hamilton, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **7**, 4941.

Examples:

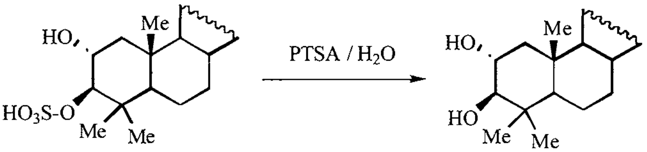
1.[1]



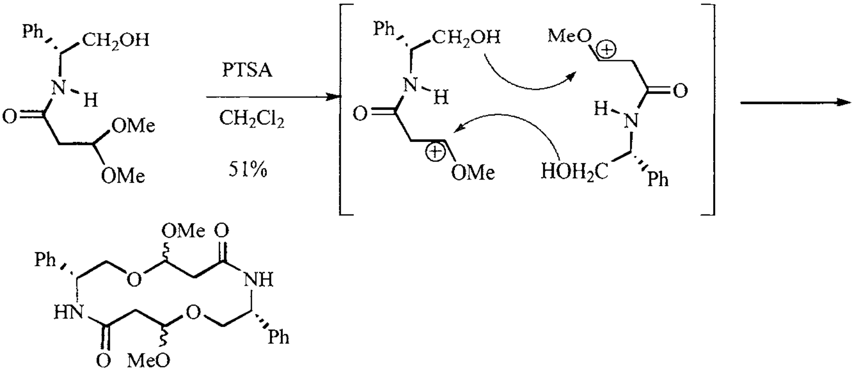
2.[2]



3.[3]



4.[4]



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[1] G. A. Kraus, I. Kim, *Organic Letters* **2003**, 5, 1191

[2] K. M. Brummond, J. Lu, *Organic Letters* **2001**, 3, 1347

[3] S. B. Singh, *Tetrahedron Letters* **2000** 41, 6973

[4] D. Dugat, A. Chiaroni, C. Riche, J. Royer, H.-P. Husson, *Tetrahedron Letters* **1997**, 38, 5801

Raney Nickel

Ni-Al

[106-51-4]

Commercially Available

T.-K. Yang, D.-S. Lee, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4401

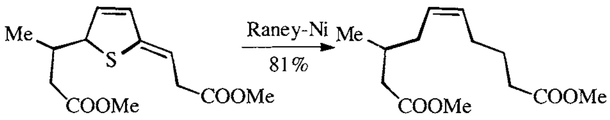
Notes:

1.Many forms, based on ratio of NaOH to aluminum

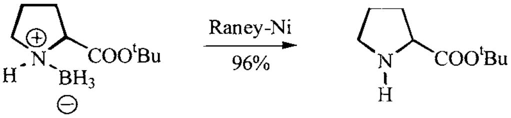
2.Particularly useful for reducing C-S bonds.[1]

Examples:

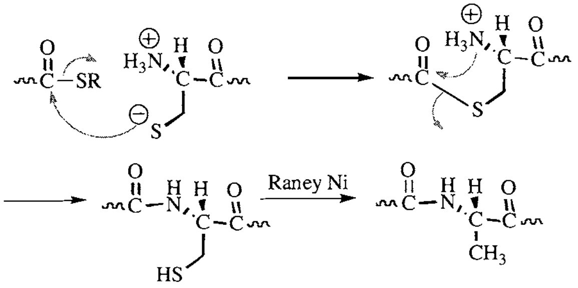
1.[2]



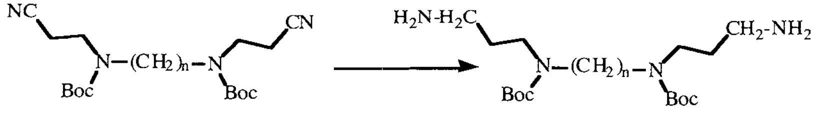
2.[3]



3.[4] A method for making peptides:



5.[5]



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[1] See:H. Atkins, *Organic Reactions*, Vol 8, Chapter 1; G . R. Pettit, E. E. vanTamelen, *Organic Reactions*, Vol 12, Chapter 5.

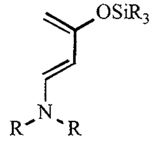
[2] S.-M. Yang, S. K. Nandy, A. R. Selvakumar, J.-M. Fang, *Organic Letters* **2000**, 2, 3719

[3] M. Couturier, J. L. Tucker, B. M. Andresen, P. Dubé, J. T. Negri, *Organic Letters* **2001**, 3, 465

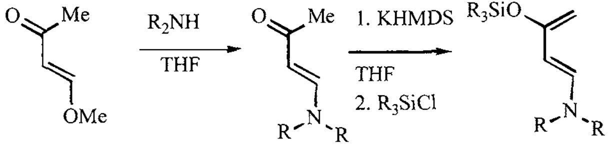
[4] Z. Y. Liang, P. E. Dawson, *Journal of the American Chemical Society* **2001**, 123, 526

[5] B. Klenke, I. H. Gilbert, *Journal of Organic Chemistry* **2001**, 66, 2480

Rawal's Diene



Preparation:[1]



Notes:

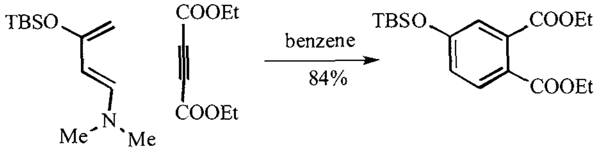
See: Brassard's, Chan's, and ***Danishefsky's dienes***.

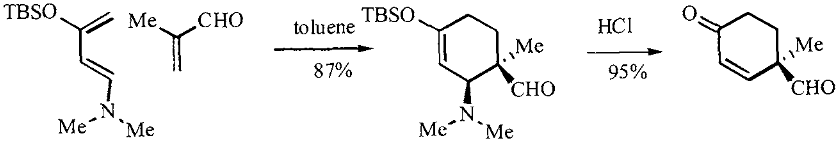
Rawal's diene has been shown to be about 25 times more reactive than ***Danishefsky's diene***.[1]

See: ***Diels-Alder Reaction***.

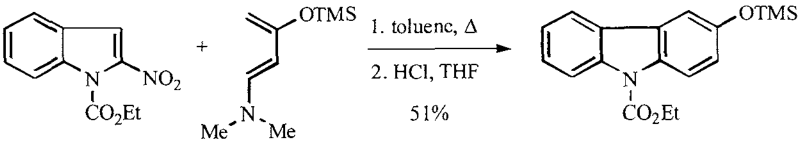
Examples:

1.[1]





2.[2]



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[1] S. A. Kozmin, V. H. Rawal, *Journal of Organic Chemistry* **1997**, 62, 5252

[2] T. L. S. Kishbaugh, G. W. Gribble, *Tetrahedron Letters* **2001**, 42, 4783

Rosenmund Catalyst

Pd / $BaSO_4$

[7440-05-3]

Commercially available

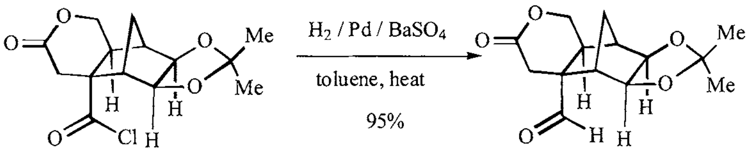
S. Siegel,*Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995 **6**, 3861

Notes: Used for the conversion of an acid chloride to an aldehyde. Quinoline is often added to further reduce catalyst activity. See: ***Rosenmund Reduction***.

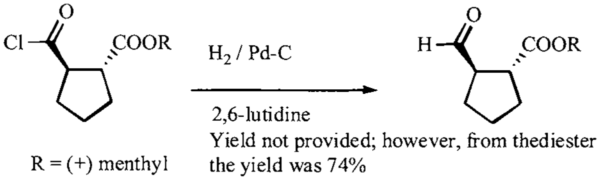
An improved procedure uses THF as solvent with 2,6-dimethylpyridine as base.[1]

Examples:

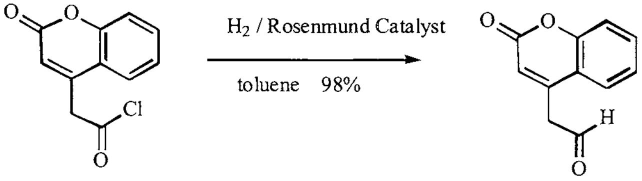
1.[2]



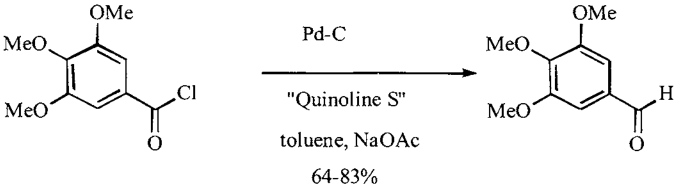
2.[3]



3.[4]



4.[5] A modified ***Rosenmund Reduction***:



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[1] A. W. Burgstahler, L. O. Weigel, C. G. Shaefer, *Synthesis* **1976**, 767

[2] S. Danishefsky, M. Hirama, K. Gombatz, T. Harayama, E. Berman, P.F. Schuda, *Journal of the American Chemical Society* **1979**, 101, 7020

[3] M. O. Duffey, A. LeTiran, J. P. Morken, *Journal of the American Chemical Society* **2003**, 125, 1458

[4] S. Chimichi, M. Boccalini, B. Cosimelli, *Tetrahedron* **2002**, 58, 4851

[5] A. I. Rachlin, H. Gurien, D. P. Wagner, *Organic Syntheses* CV6, 1007

Schlosser's Base

(Sometimes referred to as the *Lochmann-Schlosser Base*)

n-BuLi / t-BuO$^-$ K$^+$

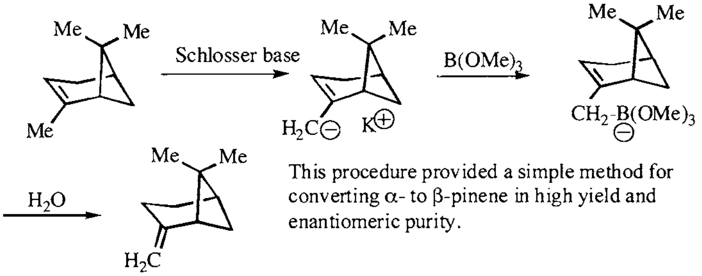
Preparation: BuLi, after removal of hexane, is taken up in cooled (-90 C) THF. At reduced temperature, (-50 C) is added the t-BuOK and material from which a proton is to be abstracted.[1, 2]

X. Xia, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L.A.Paquette, Ed., New York, 1995, **2**, 923

Notes: The combination of n-BuLi / K$^+$$t$-BuO$^-$ is considerably more basic than n-BuLi alone. It can exchange C-H bonds of pK$_a$ 35-50.[3]

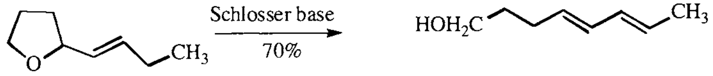
Examples:

1.[4] After removal of an allylic proton, a useful contathermodynamic isomerization:

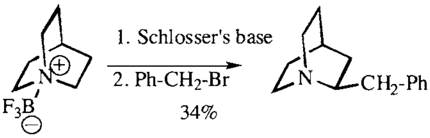


This procedure provided a simple method for converting α- to β-pinene in high yield and enantiomeric purity.

2.[5]



3.[6]



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[1] a.) M. Schlosser (Editor), in *Organometallics in Synthesis. A Manual*, John Wiley and Sons, New York, 1994, Chapter 1.; b.) See M. Schlosser, O. Desponds, R. Lehmann, E. Moret, G. Rauchschwalbe, *Tetrahedron* **1993**, 49, 10175.

[2] Y. Naruse, Y. Ito, S. Inagaki, *Journal of Organic Chemistry* **1999**, 64, 639 examine a number of different base combinations in a study on ethylations.

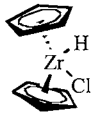
[3] M. Schlosser, S. Strunk, *Tetrahedron Letters* **1984**, 25, 741

[4] H. C. Brown, M. Zaidlewicz, K. S. Bhat, *Journal of Organic Chemistry* **1989**, 54, 1764

[5] F. Cominetti, A. Deagostino, C. Prandi, P. Venturello, *Tetrahedron* **1998**, 54, 14603

[6] S. V. Kessar, P. Singh, K. N. Singh, S. K. Singh, *Chemical Communications* **1999**, 1927

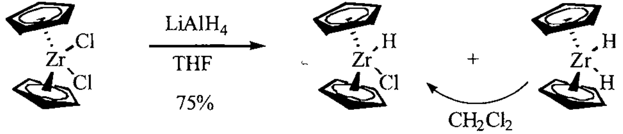
Schwartz Reagent



Chlorobis(cyclopentadienyl)hydridozirconium
[37342-97-5]

Commercially available

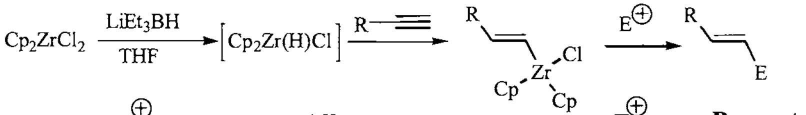
Preparation:[1]

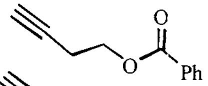
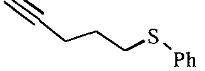


T. Takahashi, N. Suzuki, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc, New York, edited by L.A. Paquette, 1995, **2**, 1082

Notes:

Lipshutz[2] notes that the shelf-life of the reagent suggests that a simple in-situ preparation serves well:

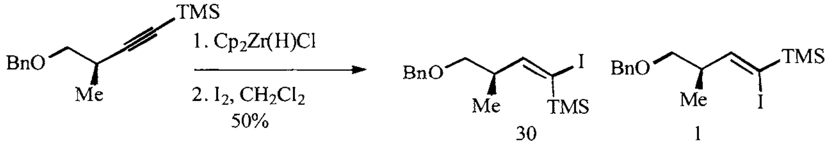


$E^{\oplus}$ source	Alkyne	$E^{\oplus}$	Percent
I_2		I	80
H_2O		H	88

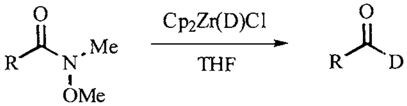
The hydrozirconation of alkenes will generally result in positional isomerization of the Zr to the least-hindered position. The Zr-intermediate can be replaced with Br (Br_2, NBS), I (I_2), Cl (*NCS*), OH (MCPBA, or basic aq. hydrogen peroxide).

Examples:

1.[3]



2.[4] Also converts ***Weinreb amides*** to aldehydes



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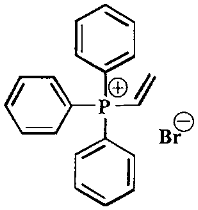
[1] S. L. Buchwald, S. J. LaMaire, R. B. Nielsen, B. T. Watson, S. M. King, *Organic Syntheses* CV9, 162

[2] B. H. Lipshutz, R. Keil, E. L. Ellsworth, *Tetrahedron Letters* **1990**, 31, 7257

[3] A. Arefolov, N. F. Langille, J. S. Panek, *Organic Letters* **2001**, 3, 3281

[4] J. T. Spletstoser, J. M. White, G. I. George, *Tetrahedron Letters* **2004**, 45, 2787

Schweizer's Reagent

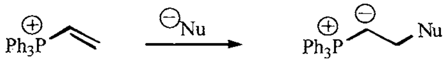


Vinyltriphenylphosphonium bromide
[5044-52-0]

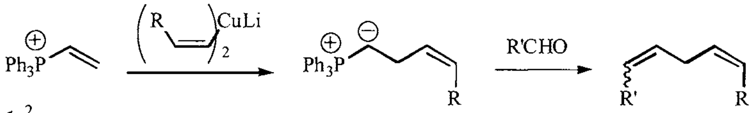
Commercially available

Edward E. Schweizer, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc, New York, edited by L.A. Paquette, 1995, 7, 5508

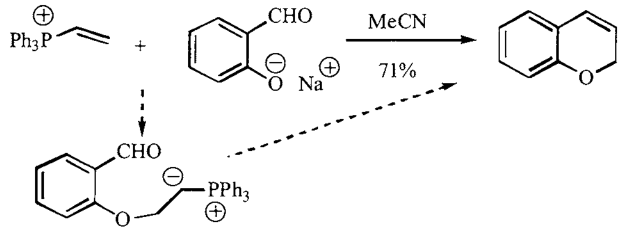
Notes: Useful reagent for generating functionalized ***Wittig intermediates***.



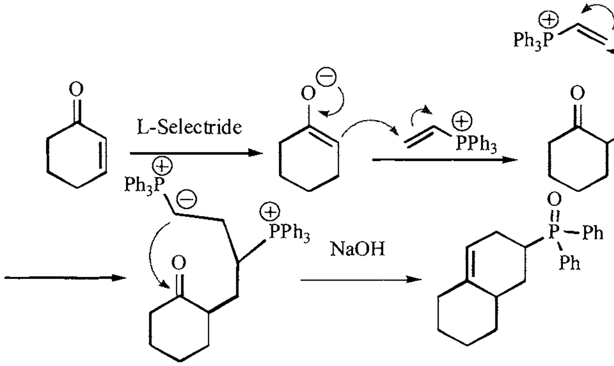
Unique application for non-conjugated dienes[1]



1.[2]



2.[3]



Overall yield for this three-component, one step reaction was 70%

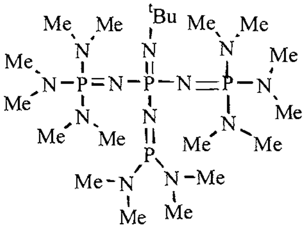
---

[1] B. O'Connor, G. Just, *Tetrahedron Letters* **1985**, 26, 1799.

[2] E. E. Schweizer, *Journal of the American Chemical Society* **1964**, 86, 2744

[3] H. H. Posner, S. B. Lu, *Journal of the American Chemical Society* **1985**, 107, 1424

Schwesinger P4 base



Phosphorimidic triamide, (1,1-dimethylethyl)tris[tris(dimethylamino)phosphoranylidene]
Phosphazene Base P4-*t*-Bu
[111324-04-0]

Commercially available

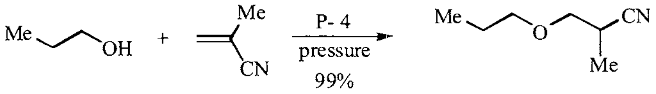
Reinhard Schwesinger, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc, New York, edited by L.A. Paquette, 1995, **6**, 4110

Notes:

Extremely strong base. Has excellent soublizing properties, and complex cation so that the anion is more reactive.

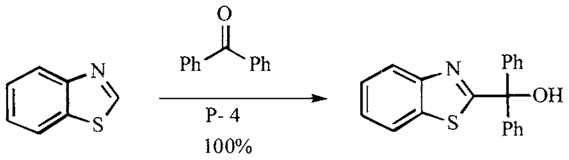
Examples:

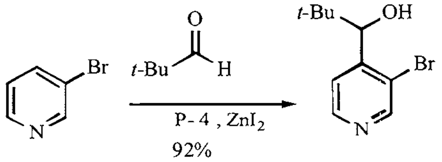
1.[1]



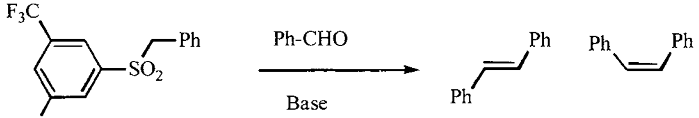
No conversion found with NaOH, ***DABCO***, ***DMAP***, ***DBU***.

2.[2]





3.[3]



KHMDS	20%	1	99
P - 4/ THF	78%	5	95

---

[1] G. Jenner, *Tetrahedron* **2002**, 58, 4311

[2] T. Imahorl, Y. Kondo, *Journal of the American Chemical Society* **2003**, 125, 8082

[3] D. A. Alonso, C. Najera, M. Varea, *Tetrahedron Letters* **2004**, 45, 573

Selenium Dioxide

SeO_2

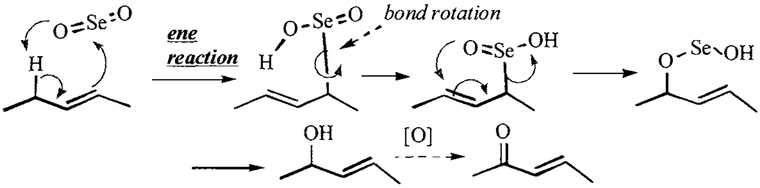
Selenium (IV) Oxide
[7446-08-4]

Commercially available

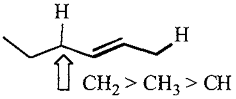
William J. Hoekstra, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 4437

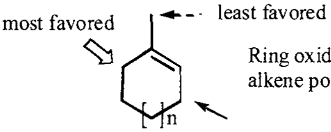
Notes:

Primarily noted for its ability to oxidize (hydroxylate) saturated allylic, propargylic or cabon atom alpha to a carbonyl group.



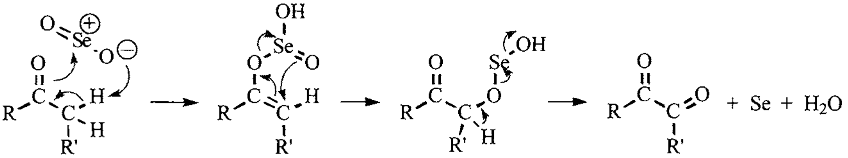
General observations: See reference 2 for additional comments.





Ring oxidation preferred; and α to the more substituted alkene position.

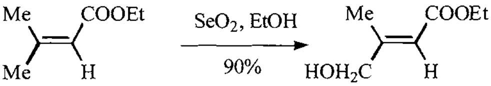
Oxidation α to a carbonyl group is called a ***Riley oxidation***.



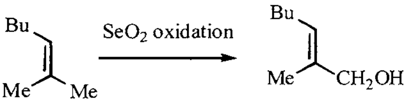
For mechanistic studies see: E. J. Corey, J. P. Schaefer, *Journal of the American Chemical Society* **1960**, 82, 918

Examples:

2.[1]



3.[2]



>98% this isomer

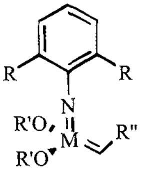
This was a detailed study of the regiochemistry of SeO_2 allylic oxidation.

---

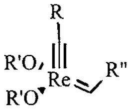
[1] R. W. Curley, Jr., C. J. Ticoras, *Journal of Organic Chemistry* **1986**, 51, 256

[2] H. Rapoport, U. T. Bhalerao, *Journal of the American Chemical Society* **1971**, 93, 4835

Schrock's Catalyst



M = Mo or W



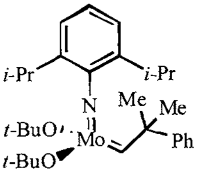
These catalysts generally contain W, Mo or Re, and have a general structure:

Commercially available

Notes:

The Schrock catalysts are very reactive and subtle changes in substitution can modify reactivity. The catalysts are generally tolerant to other functional groups. Tend to be less stable to air, water or heat than ***Grubbs catalysts***. Useful for ***RCM reactions***.

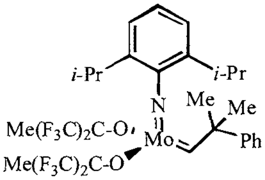
1.



[126949-65-3]

Reactions need to carried out in Schlenk lines.

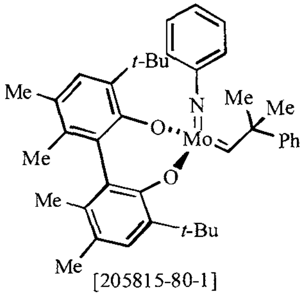
2.



[136070-71-8]

Reactions need to carried out in Schlenk lines.

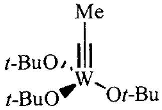
3.



[205815-80-1]

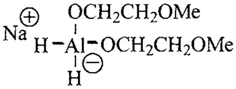
Schrock-Hoveyda catalyst

4.



[78234-36-3]

SMEAH



$Na^{\oplus}\ [H_2Al(OCH_2CH_2OMe)_2]^{\ominus}$

Sodium bis(2-methoxyethoxy)aluminum hydride
[22722-98-1]

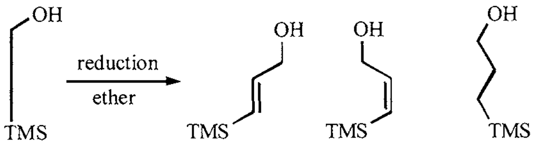
Commercially available.

M. Gugelchuk, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 7, 4518

Notes: Selective reducing agent.

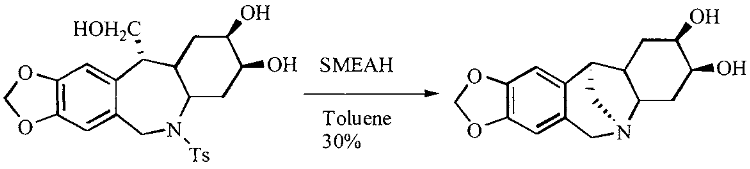
Examples:

1.[1]

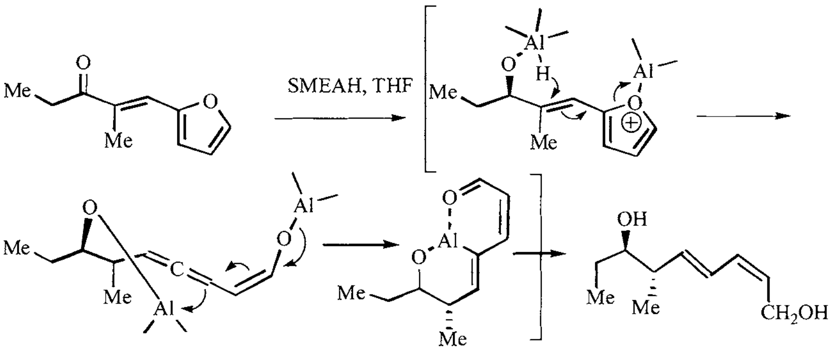


$LiAlH_4$	19	49	32
SMEAH	100	0	0

2.[2]



3.[3]



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[1] S. E. Denmark, T. K. Jones, *Journal of Organic Chemistry* **1982**, 47, 4595

[2] M. Ishizaki, O. Hoshino, Y. Iitaka, *Journal of Organic Chemistry* **1992**, 57, 7285

[3] R. B. Gammill, L. T. Bell, S. A. Mizsak, *Tetrahedron Letters* **1990**, 31, 5301

Sodium Nitrite

$NaNO_2$

[6732-00-0]

Commercially available. Less expensive than Li or K counterparts; thus more commonly used.

K. J. McCullough, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 7 4604

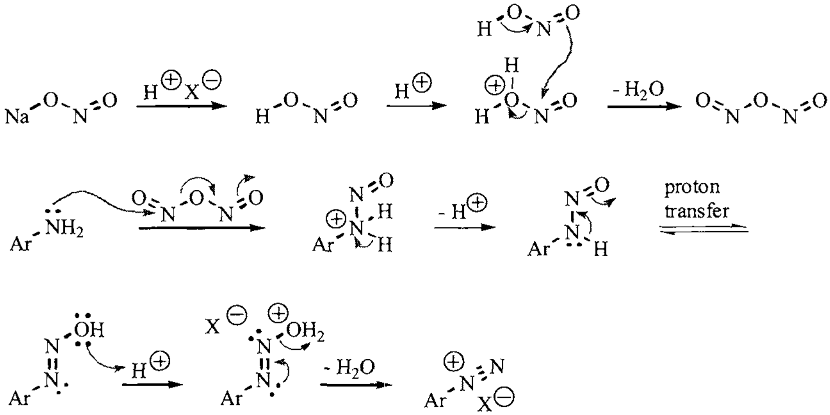
Notes:

General source of the unstable nitrous acid; most often formed *in-situ*.

For synthetic organic chemistry the reagent finds use for preparing diazo compounds:

$ArNH_2 + NaNO_2 + 2\,HX \longrightarrow ArN_2^+X^- + NaX + 2\,H_2O$

Proposed Mechanism:



Other variations of the reaction:

Griess (Diazotization) Reaction

$2\,ArNH_2 + N_2O_3 + 2\,HNO_3 + H_2O \longrightarrow 2\,ArN_2^+NO_3^- + 4\,H_2O$

Knoevenagel (Diazotization) Method

$ArNH_2 + RONO + HX \longrightarrow ArN_2^+X^- + ROH + H_2O$

Witt (Diazotization) Method

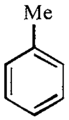
$2\,ArNH_2 + Na_2S_2O_5 + 4\,HNO_3 \longrightarrow 2\,ArN_2^+NO_3^- + Na_2S_2O_7 + 4\,H_2O$

A selection of reactions using this general approach include:

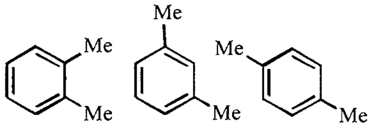
Bart Reaction; Borsche (Cinnoline) Synthesis; Demjanov Rearrangment; Diazo Reaction; Gattermann Reaction; Gattermann Method; Pschorr Arylation; Sandmeyer Reaction; Schiemann Reaction (Balz-Schiemann Rxn); Tiffeneau-Demjanov Reaction; Widman-Stoermer (Cinnoline) Synthesis

Solvents

Benzene-based solvents

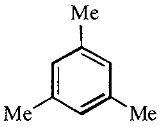


Toluene

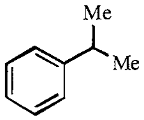


Xylenes

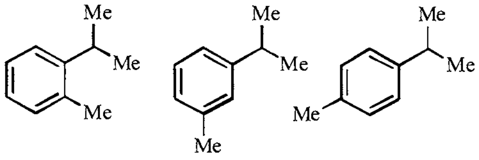
o- m- p-



Mesitylene



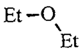
Cumene



Cymene

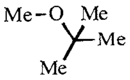
o- m- p-

Ether-based solvents



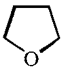
Et₂O

Diethyl ether



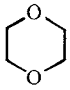
MTBE

Methyl *t*-butyl ether

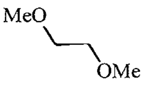


THF

Tetrahydrofuran



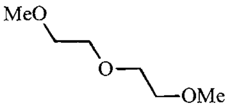
Dioxane



Glyme

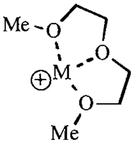
DME

Dimethoxyethane

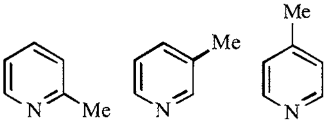


Diglyme

Ethers can stabilize cations; diglyme can provide properties similar to those found in ***crown ethers***.



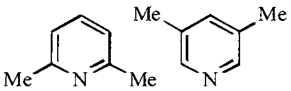
Pyridine-based solvents



Picolines

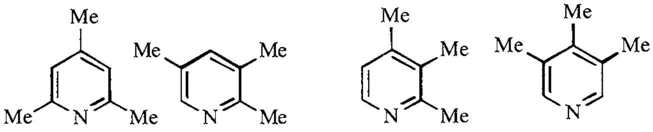
2-, 3-, and 4- picoline

2-, 3-, and 4-methylpyridine



Lutidine **Lupetidine**

2,6-

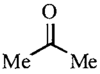


Collidines

2,4,6- **2,3,5-** **2,3,4-** **3,4,5-**

Additional Common Solvents and Additives

Acetone:



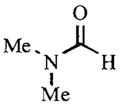
Acetonitrile: MeCN

Carbon tetrachloride: CCl_4

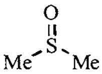
Chloroform: $CHCl_3$

Dichloromethane: CH_2Cl_2

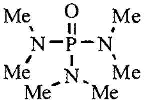
Dimethylformamide, DMF:



Dimethylsulfoxide, *DMSO*:



Hexamethylphosphoramide, *HMPA*, *HMPT*:



Stiles Reagent

$MeOMgOCO_2Me$

Methyl magnesium carbonate (MMC)

[4861-79-4]

Preparation: Bubble carbon dioxide into a solution of magnesium methoxide. Upon heating, a series of equilibrium reactions forms the reagent:

$$CO_2 + Mg(OMe)_2 \rightleftharpoons MeO\text{-}MgO\text{-}CO_2Me \;\; x\,CO_2 \rightleftharpoons (MeO\text{-}CO_2^-)_2Mg$$

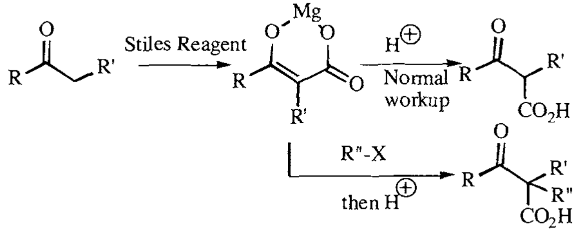
Magnesium methoxide [109-88-6]

D. Caine, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3204

L. N. Mander, *e-Encyclopedia of Reagents for Organic Synthesis* L.A. Paquette, Ed.,, John Wiley & Sons, Inc., online reference available at *http://www.interscience.wiley.com.*

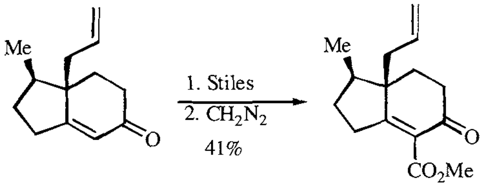
Notes:

1. Used for placing a carboxyl group adjacent to an existing carbonyl.
2. A useful method of incorporating an alkyl group with the carboxylation has been reported.[1]

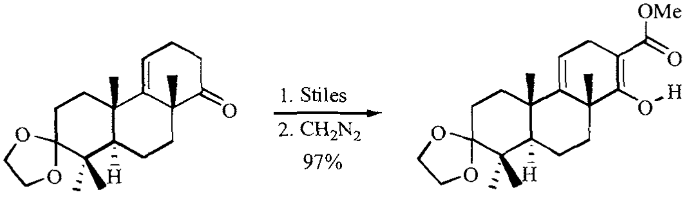


Examples:

1.[2]



2.[3]



3.[4]

$$Me\text{-}NO_2 \xrightarrow[\text{Reagent}]{\text{Stiles}} MeOOC\text{-}CH_2\text{-}NO_2$$

---

[1] E. S. Hand, S. C. Johnson, D. C. Baker, *Journal of Organic Chemistry* **1997**, 62, 1348

[2] A. S. Kende, J. Chen, *Journal of the American Chemical Society* **1985**, 107, 7184

[3] F. G. Favaloro, Jr., T. Honda, Y. Honda, G. W. Gribble, N. Suh, R. Risingsong, M. B. Sporn, *Journal of Medicinal Chemistry* **2002**, 45, 4801

[4] Reported in K. B. G. Torssell, K.V. Gothelf, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A.Paquette, Ed., New York, 1995, **6**, 3745

Stryker's Reagent

$(Ph_3PCuH)_6$

hexa-*m*-hydrohexakis(triphenylphosphine)hexacopper

[33636-93-0]

Commercially available:

Preparation: An expedient preparation of ***Stryker's reagent.***[1]

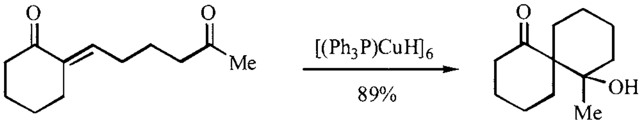
J. F. Daeuble, J. M. Stryker, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **4**, 2651

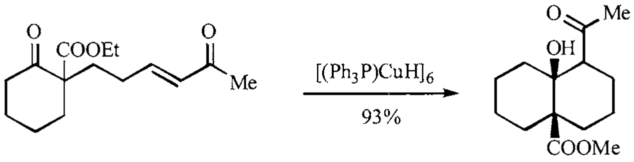
Notes:

Conjugate addition of hydride. The reagent will not react with isolated double bonds, carbonyl groups. Many functional groups resistant to reaction.

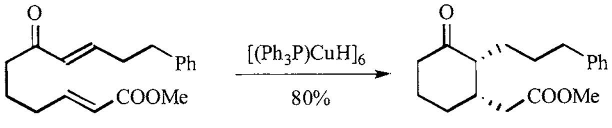
Examples:

1.[2]

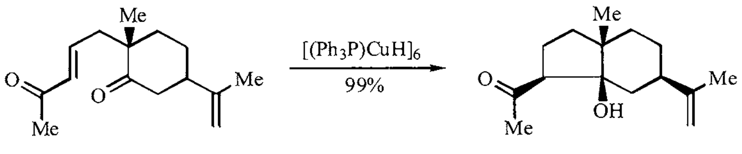




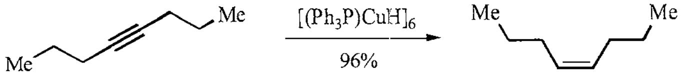
2.[3]



3.[4]



4.[5]



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[1] P. Chiu, Z. Li, K. C. M. Fung *Tetrahedron Letters*, **2003**, 44, 455.

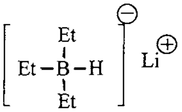
[2] P. Chiu, C.-P. Szeto, Z. Geng, K.-F. Cheng, *Organic Letters*, **2001**, 3, 1901

[3] T. M. Kamenecka, L. E. Overman, S. K. Ly Sakata, *Organic Letters* **2002**, 4, 79

[4] P. Chiu, C. P. Szeto, Z. Geng, K. F. Cheng, *Tetrahedron Letters* **2001**, 42, 4091

[5] J. F. Daeuble, C. McGettigan, J.M. Stryker, *Tetrahedron Letters* **1990**, 31, 2397

Super hydride



$$\left[\begin{array}{c} \mathrm{Et} \\ \mathrm{Et{-}B{-}H} \\ \mathrm{Et} \end{array}\right]^{\ominus} \mathrm{Li}^{\oplus}$$

Lithium triethylborohydride
[*22560-16-3*]

Commercially available

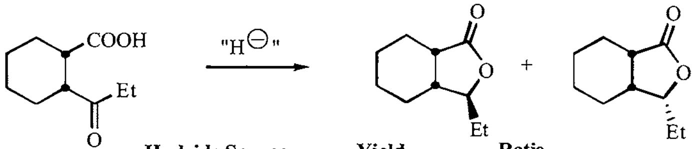
M. Zaidlewicz, H. C. Brown, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **5**, 3180

Notes: An extremely powerful source of hydride. If one assigns a relative value of 1 for the nucleophilic character of hydride from $NaBH_4$, the hydride from $LiAlH_4$ is about 250 times more reactive and that from Super hydride is about 10,000 times more reactive.

The reagent is particularly useful for the reaction C-X -> C-H, where X = I > Br > Cl > F. The replacement of tosylate and mesylate are also readily carried out.

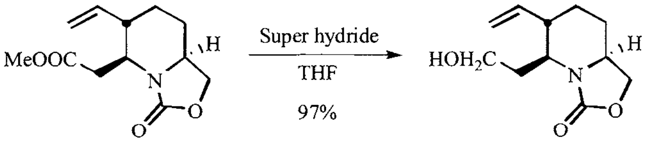
Examples:

1.[1]

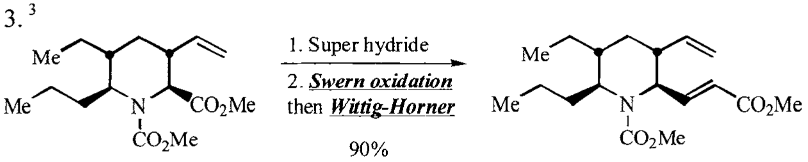


Hydride Source	Yield	Ratio		
DIBAL	64	25	:	75
Super hydride	83	85	:	15
L-Selectride	65	75	:	25

2.[2]



3.[3]



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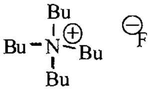
[1] E. A. Bercot, D. E. Kindrachuk, T. Rovis, *Organic Letters* **200X**, XX, XXX; see a similar study: N. Pourahmady, E. J. Eisenbraun *Journal of Organic Chemistry* **1983**, 48, 3067

[2] Naoki Toyooka, Maiko Okumura, Hideo Nemoto, *Journal of Organic Chemistry* **2002**, 67, 6078

[3] N. Toyooka, A. Fukutome, H. Nemoto, J. W. Daly, T. F. Spande, H. M. Garraffo, T. Kaneko, *Organic Letters* **2002**, 4, 1715

TBAF



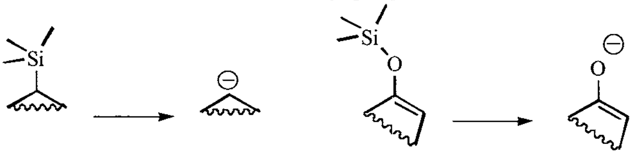
$\mathrm{Bu{-}\overset{Bu}{\underset{Bu}{N^{\oplus}}}{-}Bu}\quad F^{\ominus}$

Tetrabutylammonium fluoride
[100-85-6]

Commercially available

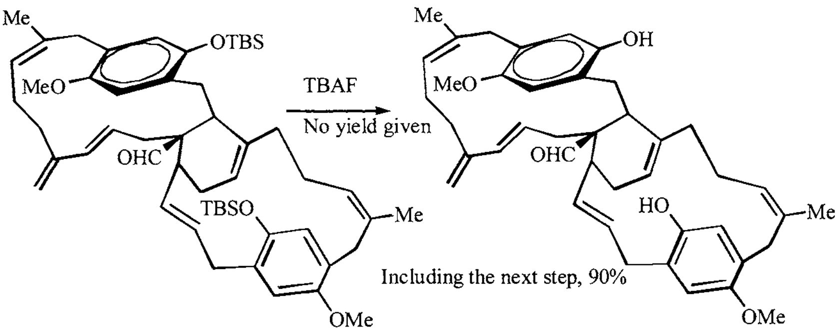
H.-Y. Li, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 7, 4728

Notes: Useful for the removal of silyl groups:



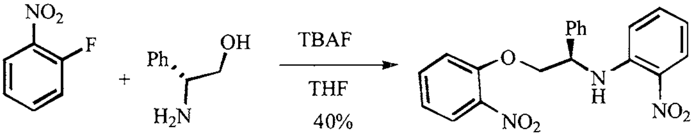
Examples:

1.[1]

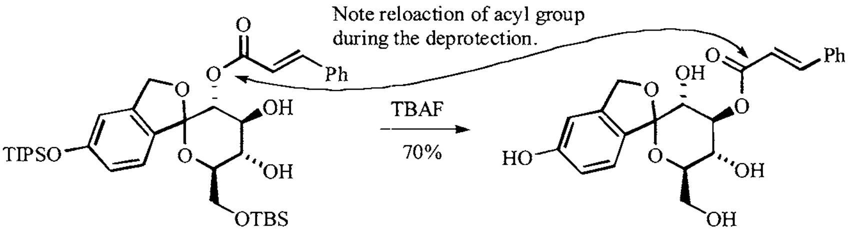


2.[2]

Promotion of S_NAr reactions:



3.[3]



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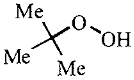
[1] M. E. Layton, C. A. Morales, M. D. Shair, *Journal of the American Chemical Society* **2002**, 124, 773

[2] T. Temal-Laib, J. Chastanet, J. Zhu, *Journal of the American Chemical Society* **2002**, 124, 583

[3] C. Hamdouchia, C. Jaramillo, J. Lopez-Pradosb, A. Rubioa, *Tetrahedron Letters* **2002**, 43, 3875

TBHP



t-Butyl hydroperoxide
[75-91-2]

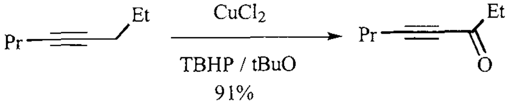
Commercially available.

K. Jones, T. E. Wilson, S. S. Nikam, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 880

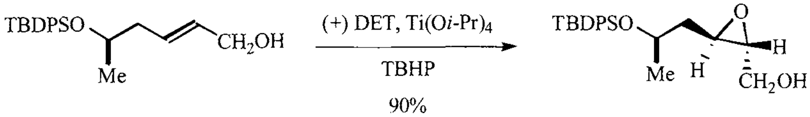
Notes: Oxidizing agent. See also ***THP*** (triphenylmethyl hydroperoxide), [4198-93-0]. Is useful with OsO_4 for catalytic hydroxylation reactions,

Examples:

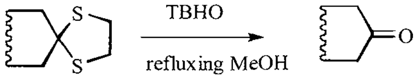
1.[1]



2.[2]



3.[3] A method for removing thioketals:



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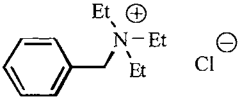
[1] P. Li, W. M. Fong, L. C. F. Chao, S. H. C. Fung, I. D. Williams, *Journal of Organic Chemistry* **2001**, 66, 4087

[2] R. M. Garbaccio, S. J. Stachel, D. K. Baeschlin, S. J. Danishefsky, *Journal of the American Chemical Society* **2001**, 123, 10903

[3] N. B. Barhate, P. D. Shinde, V. A. Mahajan, R. D. Wakharkar, *Tetrahedron Letters* **2002**, 43, 6031

TEBA (TEBAC)



Benzyltriethylammonium chloride
[56-37-1]

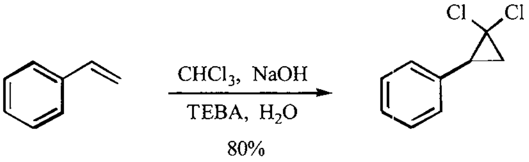
Commercially available

P. B. Savage, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 376

Notes: Useful phase transfer reagent.

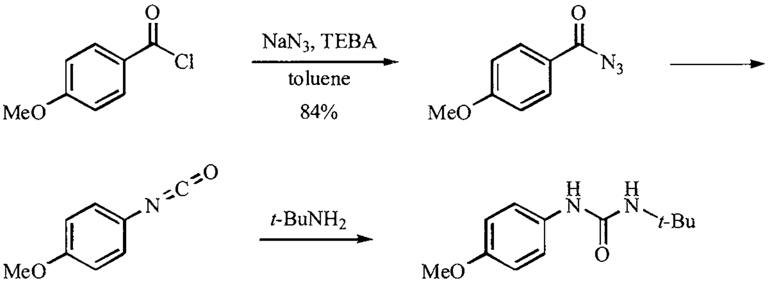
Examples:

1.[1]



2.[2]

A phase transfer approach to substituted ureas via a ***Curtius Rearrangement***



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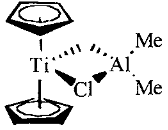
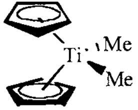
[1] M. Makosza, M. Wawrzyniewicz, *Tetrahedron Letters* **1969**, 10, 4659

[2] G. Groszek, *Organic Process Research & Development* **2002**, 6, 759

Tebbe Reagent



[67719-69-1]



See: The ***Petasis modification*** of the ***Tebbe Reagent.***[1] N. A. Petasis, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995 **1**, 470
[1271-66-5]

Commercially available

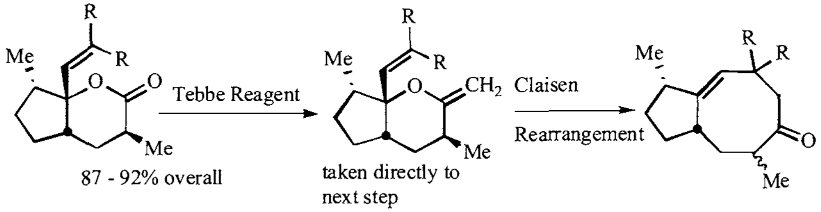
D. A. Strauss, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1078

Notes:

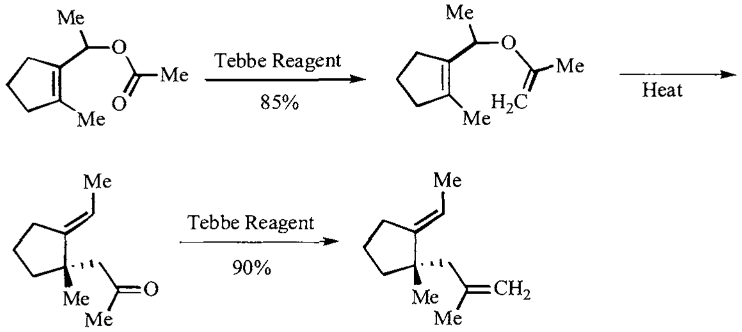
1. Particularly useful for conversion of lactones and esters to enol ethers
2. Can serve as alternative to Wittig reagent for the methylenation of hindered ketones.
3. See ***Tebbe Reaction***.

Examples:

1.[2]



2.[3]



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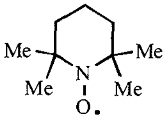
[1] This reagent is useful due to its low acidity and basicity, allowing it to be used in the presence of easily enolizable carbonyl compounds. The reagent will selectively react with a simple carbonyl in the presence of a carboxyl-type carbonyl group.

[2] W. A. Kinney, M. J. Coghlan, L. A. Paquette, *Journal of the American Chemical Society* **1986**, 106, 6868

[3] J. W. S. Stevenson, T. A. Bryson, *Tetrahedron Letters* **1982**, 23, 3143

TEMPO

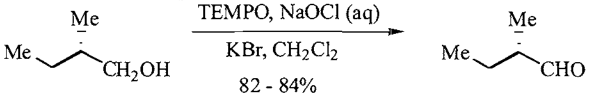


[2564-83-2]
2,2,6,6-Tetramethylpiperidin-1-oxyl

Commercially available

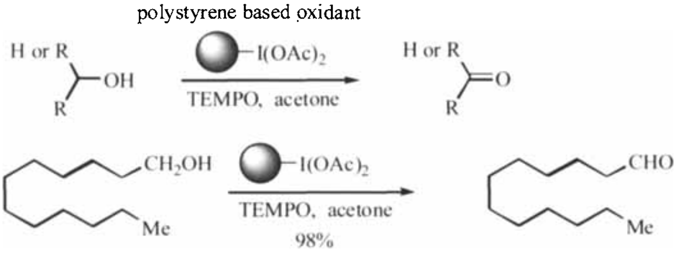
F. Montanari, S. Quici, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 7, 4821

Notes: In conjunction with other oxidizing agents, this reagent provides mild conditions for oxidations, for example:[1]

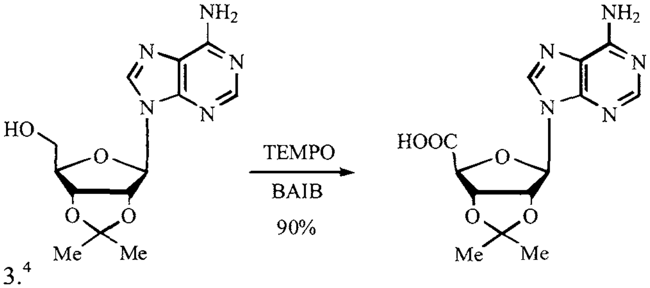


Examples:

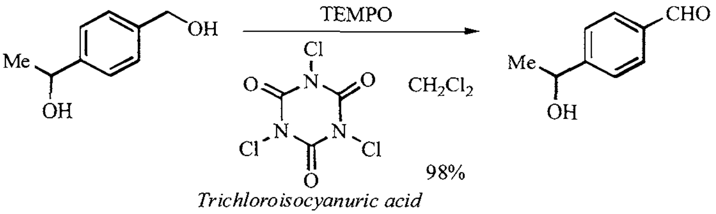
1.[2]



2.[3]



3.[4]



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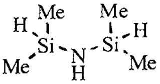
[1] P. L. Anelli, F. Montanari, S. Quici, *Organic Syntheses* CV8, 367. A number of other primary alcohol oxidations are reported.

[2] K. Sakuratani, H. Toga, *Synthesis* **2003**, 21

[3] Jeffrey B. Epp, Theodore S. Widlanski, *Journal of Organic Chemistry* **1999**, 64, 293

[4] L. De Luca, G. Giacomelli, A. Porcheddu, *Organic Letters* **2001**, 3, 3041

1,1,3,3-Tetramethyldisilazane



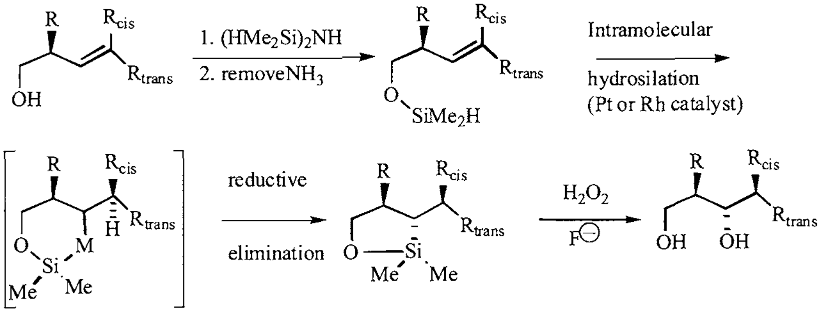
[15933-59-2]

Commercially available

K. Tamao, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, **1995**, **7**, 4809

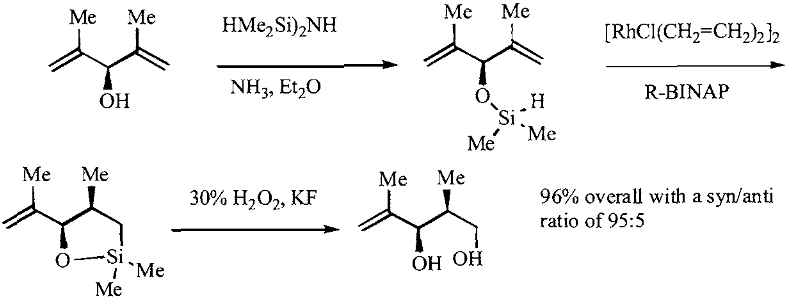
Notes:

Tamoa notes how this is particularly useful for polyol synthesis:



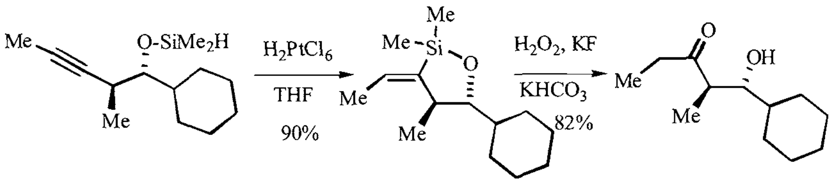
Examples

1.[1]



96% overall with a syn/anti ratio of 95:5

2.[2]



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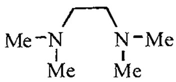
[1] K. Tamao, T. Tanaka, T. Nakajima, R. Sumiya, H. Arai, Y. Ito, *Tetrahedron Letters* **1990**, 31,7333

[2] J. A. Marshall, M. M. Yanik, *Organic Letters* **2000**, 2, 2173

TMEDA



N,N,N',N'-Tetramethylethylenediamine
[110-18-9]

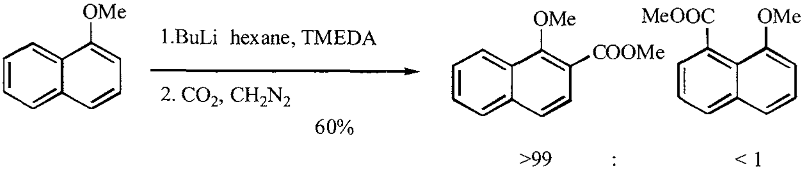
Commercially available

R. K. Haynes, S. C. Vonwiller, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **7**, 4811

Notes:

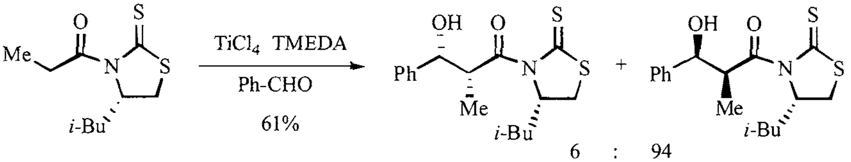
Enhances reactivity of organolithium reagents.

Note the influence of TMEDA on the lithiation of naphthyl methyl ether: (D.A. Shirley, C.F. Cheng, *Journal of Organometallic Chemistry* **1969**, 20, 251.)

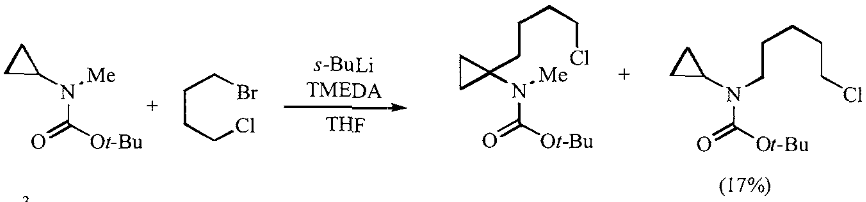


Examples:

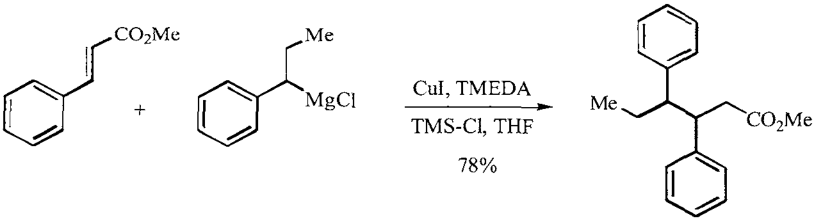
1.[1]



2.[2]



3.[3]



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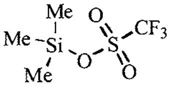
[1] M. T. Crimmins, K. Chaudhary, *Organic Letters* **2000**, 2, 775

[2] Y. S. Park, P. Beak, *Tetrahedron*, **1996**, 52, 12333

[3] P. S. Van Heerden, B. C. B. Bezuidenhoudt, D. Ferreira, *Tetrahedron* **1996**, 52, 12313

TMSOTf

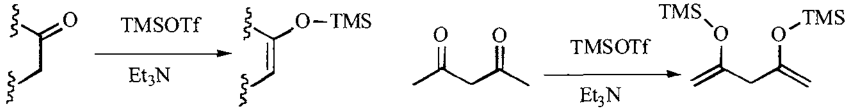


Trimethylsilyl trifluoromethanesulfonate
[88248-68-4]

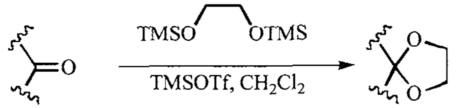
Commercially available

JJ. Sweeny, G. Perkins, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 7, 5315

Notes: A very efficient Lewis acid. Useful for the conversion of ketones to their corresponding TMS enol ethers:



Can serve as catalyst for the selective ketalization of multicarbonyl-containing compounds. Sterically-hindered or conjugated carbonyl groups will react much more slowly to the reaction:



Examples:

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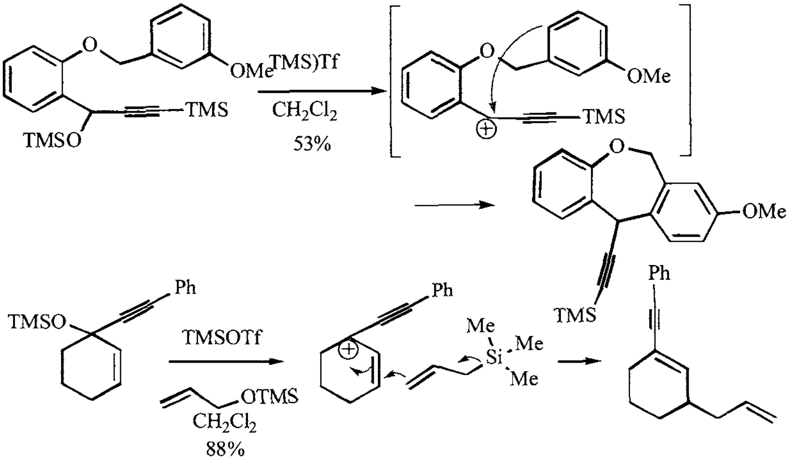
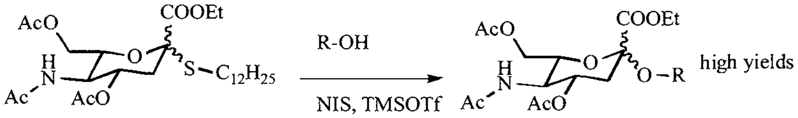


2.[2]



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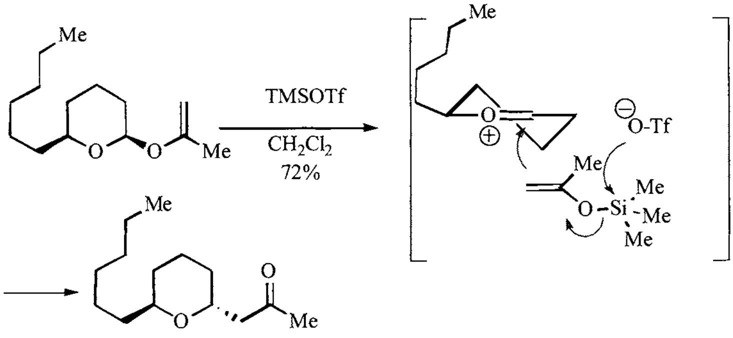
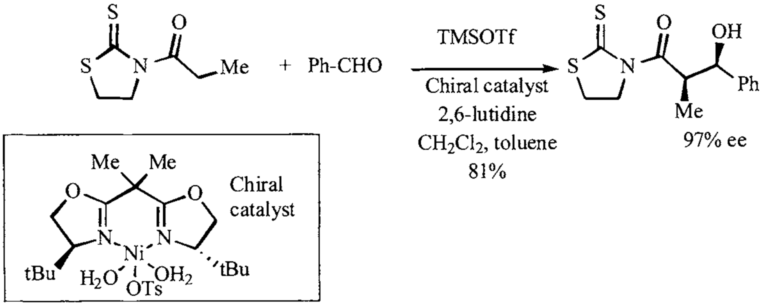
[1] T. Ishikawa, M. Okano, T. Aikawa, S. Saito, *Journal of Organic Chemistry* **2001**, 66, 4635

[2] K. Matsuoka, T. Onaga ,T. Mori, J.-I. Sakamoto,T. Koyama N. Sakairi, K. Hatanoa, D. Terunuma, *Tetrahedron Letters* **2004**, 45, 9384

3.[1]



4.[2]



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[1] D. J. Dixon, S. V. Ley, E. W. Tate, *Journal of the Chemical Society, Perkin Transaction 1* **1999**, 2665

[2] D. A. Evans, C. W. Downey, J. L. Hubbs, *Journal of the American Chemical Society* **2003**, 125, 8706

TPAP

$Pr_4N^+RuO_4^-$

Tetra-*n*-propylammonium perruthenate

[114615-82-6]

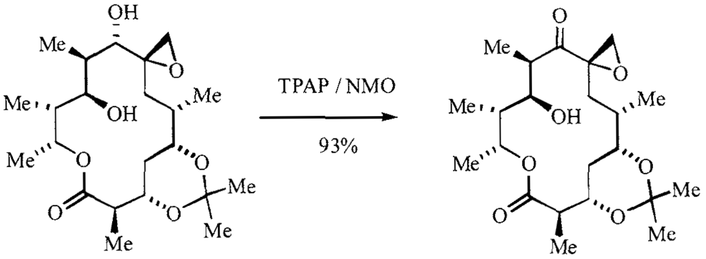
Commercially available

S. V. Ley, J. Norman, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, 7, 4827

Notes: Mild oxidizing agent. Generally carried out in the presence of a co-oxidant, often ***NMO***.

Examples:

1.[1]



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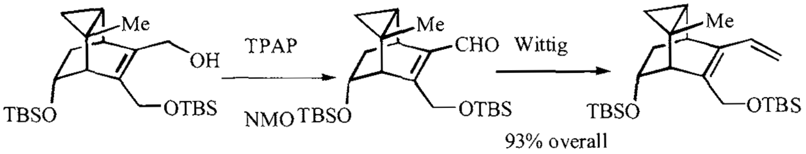

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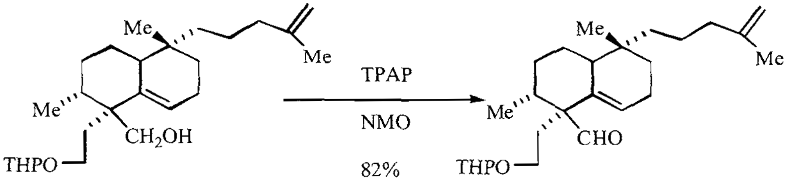

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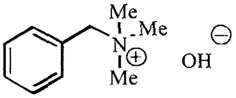
[1] T. Hu, N. Takanaka, J. S. Panek, *Journal of the American Chemical Society* **1999**, 121, 9229

[2] L. A. Paquette, H.-J. Kang, C. S. Ra, *Journal of the American Chemical Society* **1992**, 114, 7387

[3] H. Miyaoka, M. Yamanishi, Y. Kajiwara, Y. Yamada, *Journal of Organic Chemistry* **2003**, 68, 3476

Triton-B



Benzyltriethylammonium hydroxide
[100-85-6]

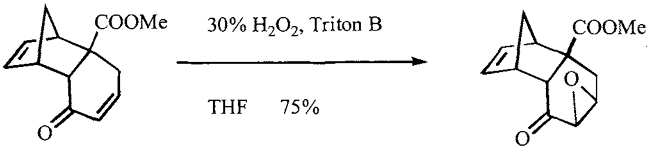
Commercially available

M. E. Bos, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **1**, 382

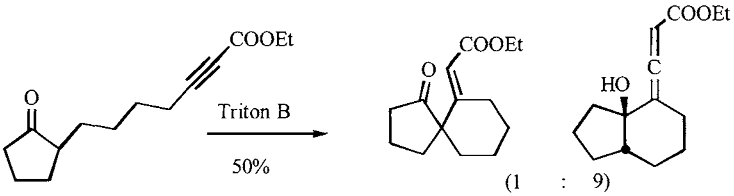
Notes: This reagent (see structural similarity with ***TEBA***) serves as a phase transfer catalyst and a base.

Examples:

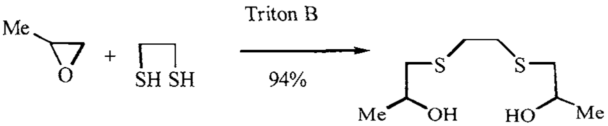
1.[1]



2.[2]



3.[3]



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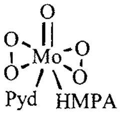
[1] N. Yoshida, K. Ogasawara, *Organic Letters* **2000**, 2, 1461

[2] F. Wendling, M. Miesch, *Organic Letters* **2001**, 3, 2689

[3] M. R. Younes, M. M. Chaabounib, A. Bakloutia, *Tetrahedron Letters* **2001**, 42, 3167

Vedejs Reagent

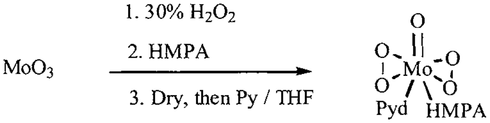


MoOPH

[23319-63-3]

Oxodiperoxymolybdenum(pyridine)(hexamethyphospotriamide)

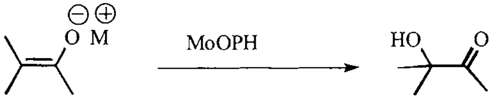
Preparation:[1]



E. Vedejs, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **6**, 3825

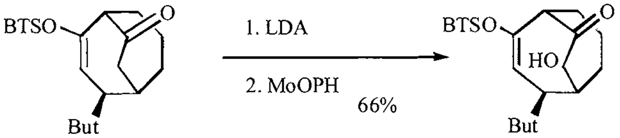
Notes:

The reagent is useful for the hydroxylation of enolate anions.

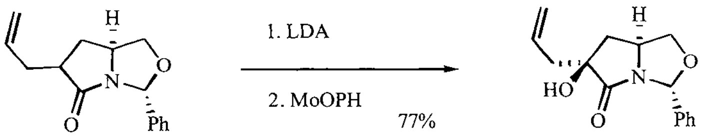


Examples:

1.[2]



2.[3]



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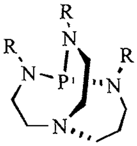
[1] E. Vedejs, S. Larsen, *Organic Synthesis* **1985**, 64, 127

[2] K.Takeda, Y. Sawada, K. Sumi, *Organic Letters* **2002**, 4, 1031

[3] S. Makino, K. Shintani, T. Yamatake, O. Hara, K. Hatano, Y. Hamata, *Tetrahedron* **2002**, 58, 9737

Verkade's Superbase



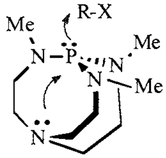
2,8,9-trialkyl-2,5,8,9-tetraaza-1-phosphabicyclo[3.3.3]undecane
R = Me, *i*-Pr, *i* -Bu

Commercially available

Notes:

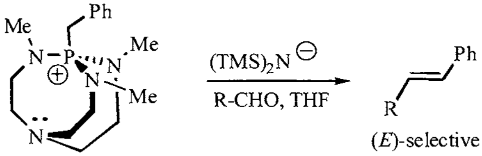
A strong base, with calculated pKa of 29.[1]
See: ***Schwesinger P4 base*** for similar non-ionic bases.

Ready reaction on P due to:[2]



Examples:

1.[2]



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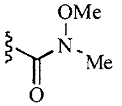
[1] B. Kovacevic, D. Baric, Z. B. Maksic, *New Journal of Chemistry* **2004**, 28, 284 (AN 2004:87563)
[2] Z. Wang, J. G. Varkade, *Tetrahedron Letters* **1998**, 39, 9331

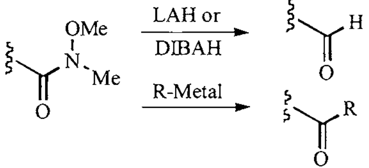
Weinreb Amide[1]



Preparation: These intermediates are readily prepared from an activated acid (acid chloride) and the methoxymethyl amine.

Notes:

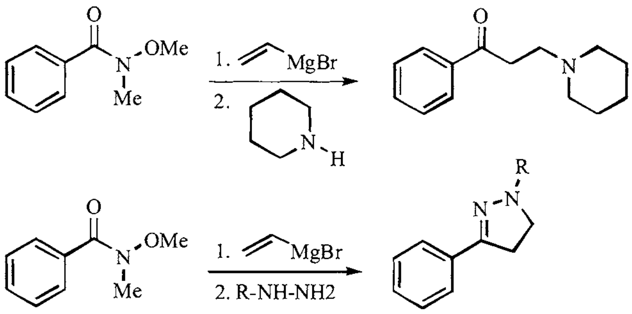
1. This useful functional group is particularly well-suited to react with hydride or organometallic reagents.



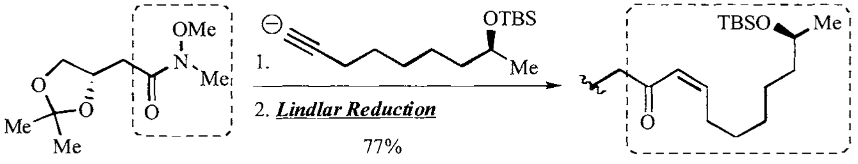
2. For application on solid support.[2]

Examples:

1.[3]



2.[4]



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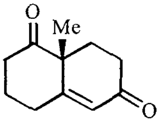
[1] S. Nahm, S. M. Weinreb, *Tetrahedron Letters* **1981**, 22, 3815

[2] T. Q. Dinh, R. W. Armstrong, *Tetrahedron Letters* **1996**, 37, 1161

[3] A. Gomtsyan, R.J. Koenig, C.-H. Lee, *Journal of Organic Chemistry* **2001**, 66, 3613

[4] Y.-G Suh, J.-K. Jung, S.-Y. Seo, K.-H. Min, D.-Y. Shin, Y.-S. Lee, S.-H. Kim, H.-J. Park, *Journal of Organic Chemistry* **2002**, 67, 4127

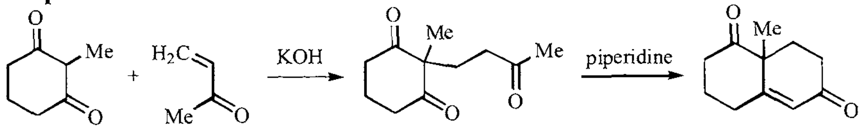
Wieland-Miescher Ketone



8a-Methyl-3,3,8,8a-tetrahydro-2*H*,7*H*-naphthalene-1,6-dione
[20007-72-1]

Commercially available

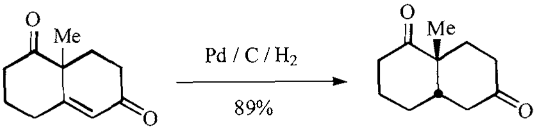
Preparation:[1]



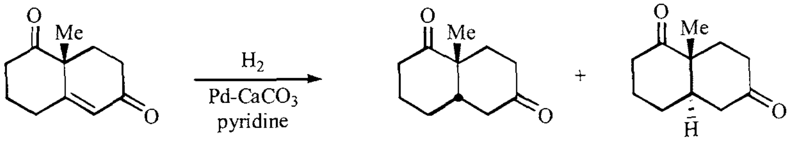
Notes: Chiral preparations include the proline-catalyzed reactions[2] and recently an aldolase antibody 38C2 method has been reported.[3] See also:[4]

Examples:

1.[5]



2.[6]



73%

13%

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[1] S. Ramachandran, M. S. Newman, *Organic Syntheses*, CV5, 486

[2] G. Zhong, T. Hoffmann, R. A. Lerner, S. Danishefsky, C. F. Barbas, III, *Journal of the American Chemical Society* **1997**, 119, 8131

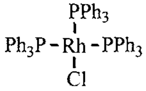
[3] B. List, R. A. Lerner, C. F. Barbas III, *Organic Letters* **1999**, 1, 59

[4] D. Rajagopal, R. Narayanan, S. Swaminathan, *Tetrahedron Letters* **2001**, 42, 4887

[5] S. Karimi, *Journal of Natural Products* **2001**, 64, 406

[6] K. Park, W. J. Scott, D. F. Wiemer, *Journal of Organic Chemistry* **1994**, 59, 6313

Wilkinson’s Catalyst



$$\begin{array}{c} PPh_3 \\ | \\ Ph_3P-Rh-PPh_3 \\ | \\ Cl \end{array}$$

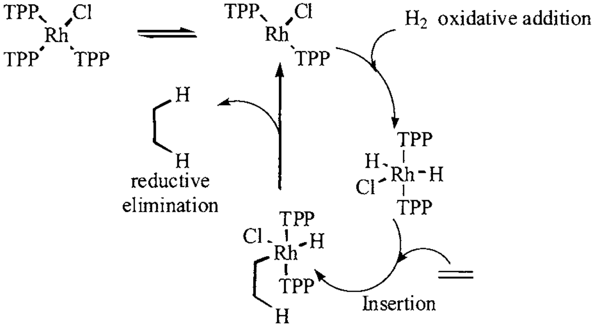
Chlorotris(triphenylphosphine)rhodium (I)
[14694-95-2]

Commercially available

K. Burgess, W. A. van derDonk, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **2**, 1253

Notes:

Useful for homogeneous reduction of alkenes. As a consequence of the reagent bulk, it is understandable that the reactivity of alkene reduction is dependent on substitution; the less-substituted alkenes react faster. Also, reduction occurs from the less-hindered face in a *cis*-stereochemistry. Many other functional groups are tolerated by conditions.



Examples:

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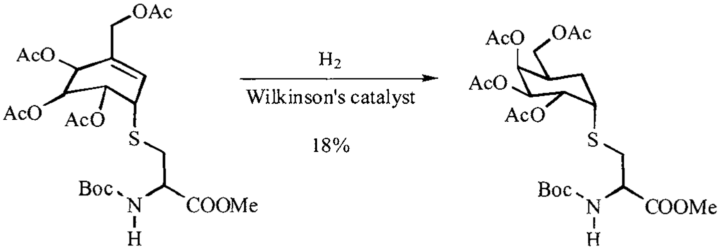

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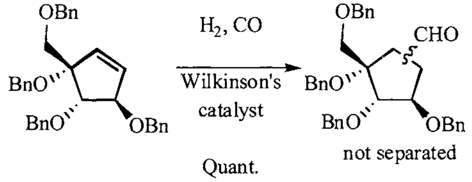
[1] L. J. Whalen, R. L. Halcomb, *Organic Letters* **2004**, 6, 3221

2.[1] Use in hydroformylation:



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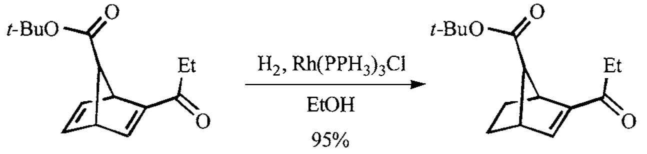

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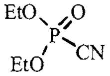
[1] M. Seepersauda, M. Kettunenb, A. S. Abu-Surrahc, T. Repob, W. Voelterd, Y. Al-Abed, *Tetrahedron Letters* **2002**, 43, 1793

[2] H. M. L. Davies, E. Saikali, N. J. S. Huby, V. J. Gilliatt, J. J. Matasi, T. Sexton, S. R. Childers, *Journal of Medicinal Chemistry* **1994**, 37, 1262

Yamada's Reagent

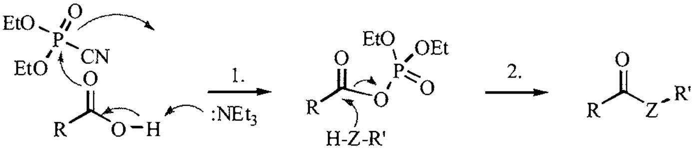


DEPC, diethyl phosphorocyanidate, diethyl phosphoryl cyanide, diethyl cyanophosphonate [2942-58-7]

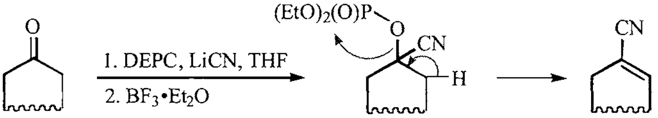
Commercially available. Prepared by the reaction of triethylphosphite with cyanogen bromide

H. H. Patel, *Encyclopedia of Reagents for Organic Synthesis*, John Wiley and Sons, Inc., L. A. Paquette, Ed., New York, 1995, **3**, 1851

Notes: Useful for carboxylic acids activation towards the preparations of esters, thioesters and amides:



The reagent also finds application in the conversion:



Examples:

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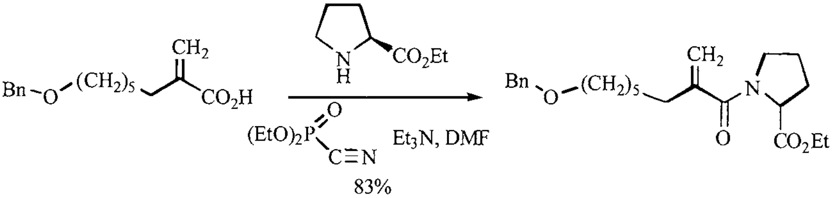
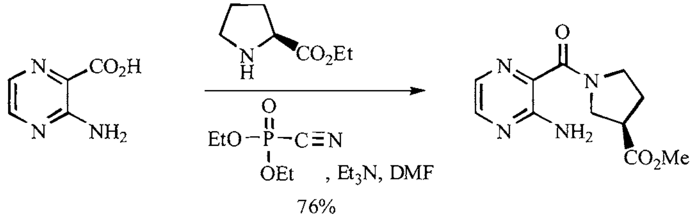


2.[2]



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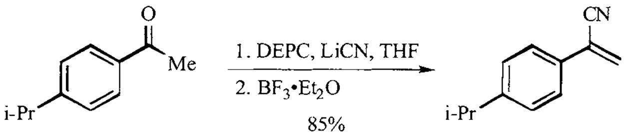

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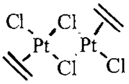
[1] J. Jew, J. Kim, B. Jeong. H. Park, *Tetrahedron: Asymmetry* **1997**, 8, 1187

[2] T. Okawa, S. Eguchi, *Tetrahedron Letters* **1996**, 37, 81

[3] S. Harusawa, R. Yoneda, T. Kurihara, Y. Hamada, T. Shioin, *Tetrahedron Letters* **1984**, 25, 427

Zeise's Dimer



Di-μ-chlorodichlorobis(η2-ethene) diplatinum
[12073-36-8]

Commercially available

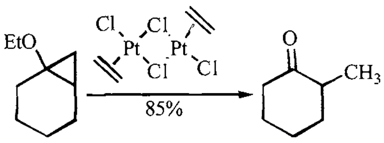
A. J. Phillips, *e-Encyclopedia of Reagents for Organic Synthesis*, L.A. Paquette, Ed.,, John Wiley & Sons, Inc., online reference available at *http://www.interscience.wiley.com.*

Notes:

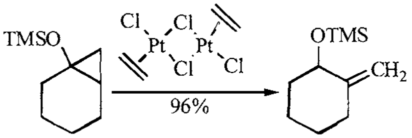
Useful for opening cyclopropane rings and hydrating alkynes.

Examples:

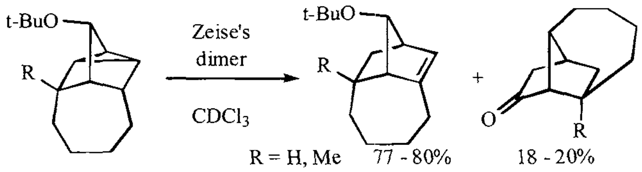
1.[1]



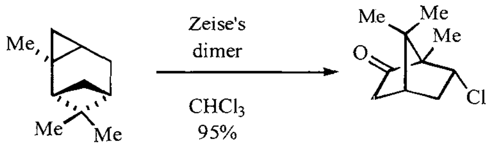
2.[2]



3.[3]



4.[4]



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[1] J. Beyer, P. R.Skaanderup, R. Madsen, *Journal of the American Chemical Society* **2000**, 122, 9575
[2] K. Ikura, I. Ryu, N. Kambe, N. Sonoda, *Journal of the American Chemical Society* **1992**, 114, 1520
[3] Y. Chen, J. K. Snyder, *Journal of Organic Chemistry* **2001**, 66, 6943
[4] Z. Ye, M. Dimke, P. W. Jennings, *Organometallics* **1993**, 12, 1026

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