IN THE NAME OF ALLAH THE SUPEREMLY MERCIFUL AND THE MOST KIND

BASIC CONCEPTS OF ORGANIC CHEMISTRY

SANA JAMSHAID

Preface

There are a lot of books on organic chemistry with very useful information that everyone gets advantage from it. But to understand this information given in them is not so easy for everyone. To understand this information we should have some basic information about organic chemistry.

The intent of this book is to provide the basic concepts of organic chemistry to the students which are new to organic chemistry and the tutors and teachers to provide good material for teaching organic chemistry. This book contains the basic information about the organic compounds and their chemistry.

I have tried to explain these concepts included nomenclature, tautomerism, and stereochemistry of organic compounds as well as reactive intermediates in organic compounds reactions.

With the help of simple examples these concepts are explained very well for the pioneer students as well as new teachers to teach the organic concepts.

Acknowledgements

First of all, I am grateful to The Almighty Allah for establishing me to complete this book.

Though the following dissertation is an individual work, I could never have reached the heights or explored the depths without the help, support, guidance and efforts of a lot of people.

I acknowledge with gratitude to associate professor **Dr. Abdur Rauf Raza** my respective teacher, who always been sincere and helpful in making me understands the different aspects of organic chemistry and conceptual problems in stereochemistry.

A very special thanks to my family and friends for the support they've lent me over the time I take to wrote this book.

I also place on record, my sense of gratitude to one and all who, directly or indirectly, have lent their helping hand in this venture.

I have tried hard and soul together to make this work helpful for students as well as teachers. I don't know how far I am able to do that. Furthermore I don't claim all the information in this book is included perfectly. There may be shortcomings, factual error, mistakes which are all mine and I am responsible for those but I have tried my best to overcome these.

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Chapter: 1

Introduction and nomenclature of organic compounds

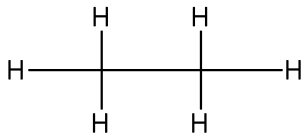
Organic chemistry is that branch of chemistry that deals with the structure, properties, and reactions of compounds that contain carbon .Organic compounds are also called as hydrocarbons as they contain both hydrogen and carbon atoms mainly. Hydrocarbons are classified in to two basic types namely;

a. Saturated Hydrocarbons
b. Unsaturated Hydrocarbons

Saturated Hydrocarbons:-

The term "saturated" is used to refer to a compound in which all carbon-carbon bonds are single bonds and every carbon atom is connected to a different atom. A saturated hydrocarbon will contain all the hydrogen atoms possible according to the alkane general formula C_nH_{2n+2}.

Ethane, C_2H_6, is an example of a saturated hydrocarbon.



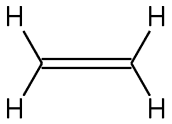
Ethane C_2H_6

Other examples of saturated compounds are octane, C_8H_{18}, and diethyl ether, $C_4H_{10}O$.

Unsaturated Hydrocarbons:-

The term "unsaturated" is used to designate a compound which contains double or triple bonds and therefore not every carbon is bonded to a different atom.

Ethene, C_2H_4, is an example of an unsaturated hydrocarbon.



Ethane C_2H_4

Other examples of unsaturated compounds are benzene, C_6H_6, and acetic acid, $C_2H_4O_2$.

An alkene is a hydrocarbon containing double bonds. The general formula of an alkene is C_nH_{2n}.
An alkyne is a hydrocarbon containing triple bonds. The general formula of an alkyne is C_nH_{2n-2}.

Alkanes are precursor of majority of organic compounds.

Major sources of organic compounds are:

I. Petroleum
II. Bituminous (soft) coal,
III. Natural gas
IV. Plants & Animals.

IUPAC Nomenclature of Organic Compounds

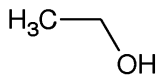
Depending upon the structure of molecule IUPAC nomenclature of organic compounds consists of following:

Longest carbon (parent) chain: Carbon chain which is long and contain the functional group if present.

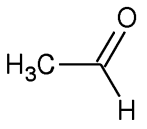
Following is the table showing the name of carbon chain depending upon the number of carbon atoms.

No. of carbon atoms	**Parent name of carbon chain**	**suffix**
1	Meta	en
2	Etha	en
3	Propa	en
4	Buta	en
5	Penta	en
6	Hexa	en
7	Hepta	en
8	Octa	en
9	Nona	en
10	Deca	en
11	Undeca	en
12	Dodeca	en

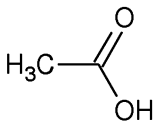
Functional Group: Substituent of high power present on organic compound makes it prior in reactivity. For example



Ethanol



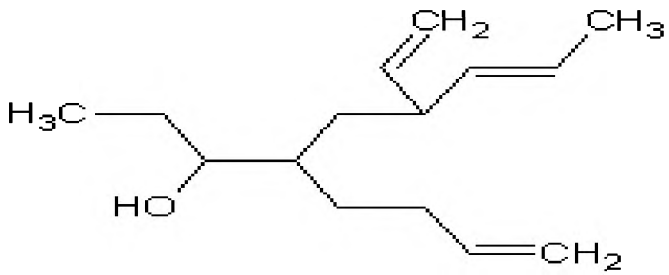
Acetaldehyde



Acetic acid

Function group	Symbol	Suffix
Acid Anhydride	-$(CO)_2O$	----anhydride
Carboxylic Acid	-COOH	----oic acid ----carboxylic acid
Ester	-COOR	----oate
Acid Halides	-COX (X=Br,Cl,I,F)	----oyl halide ----carbonyl halide
Acid Amide	-CONH,-CONHR,-$CONHR_2$	----carboxyamide ----amide
Nitriles	-CN	----nitrile ----carbonitrile
Aldehyde	-COH	----al
Ketone	-COR	----one
Alcohol	-OH	----ol
Thiols	-SH	----thiol
Amines	NH_2, NHR, NHR_2	----amine

Substituent: A substituent is an atom or group of atoms substituted in place of a hydrogen atom on the parent chain of a hydrocarbon. The suffix **-yl** is used to form names of radicals, either separate or chemically bonded parts of molecules (substituent).If substituent have further substitution than that substituent name is written in parentheses. For example



6-ethenyl-4-(prop-2'-enyl) octa-6-en-3-ol

For example propane is written as propyl- , while propene is written as propenyl- .

Presence of double & triple bond: Presence of double and triple bond is also mentioned in the IUPAC name of organic compound. The suffix **–nyl** is used for double and -ynyl is used for triple bond.

The IUPAC systematic name of an organic compound can be constructed based on a series of steps and rules:

- Identification of the principle functional group and substituent.
- Identifications of the longest continuous chain containing the principle functional group.
- Assign **l**ocants (*i.e.* numbering) to the principle functional group and substituent.

The steps and rules are *summarized* below, more details are provided as the cases are encountered.

Principle Functional group	• The principle functional group is used to define the class the compound belongs to *e.g.* an alcohol, ROH • The principle functional group is usually given the lowest locant possible.
Longest chain	• The longest continuous chain containing the principle functional group defines the root name. • Other groups attached to this chain are called substituent. • If there are two chains of equal length, then the choice that gives the simplest substituent is chosen.
Numbering (*i.e.* assigning locants)	• The numbers that define the positions of the principle functional group and substituent are called locants. • Compounds are numbered from one end of the longest continuous chain. • The locants are assigned such that the principle functional group gets the lowest possible locants. • If this result in a "tie" then the first point of difference rule is applied so that the first time a difference in numbering occurs, then the method that gives the lower number at this first difference is used. • In the event that there is no first point of difference then **alphabetization** is used.

The IUPAC name of an organic molecule is assembled from components that describe various features of the molecule.

Functional group suffix

This is added to the end of the name based on the principle functional group.

Root

This defines the number of atoms (usually carbon atoms) in the longest continuous chain that contains the principle functional group.

Substituent prefix

Any group other than the principle functional group are substituent and are added to the beginning of the name in alphabetical order.

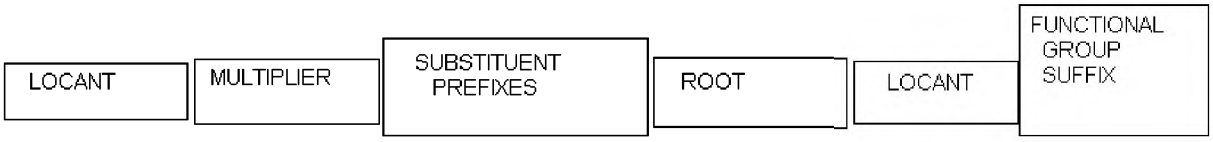
Multiplier

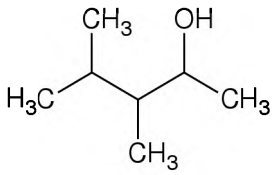
If a group occurs more than once, a simple multiplier (*e.g.* di, tri, tetra, *etc.*) is used to indicate how many times it occurs.

Locants

Locants are numbers (or occasionally letters *e.g.* N-) that define the position of the principle functional group and substituent. Typically there needs to be a locant for each functional groups and each substituent. The 1993 modifications require that the locant for the principle functional group is placed before the functional group suffixes, e.g. pentan-2-ol, see below.

The basic structure of the IUPAC name is shown schematically below:





3,4-dimethylpentan-2-ol

1: The principle functional group is an alcohol, so the suffix -**ol** is required.

2: The longest continuous chain with the -OH attached is C5 and an alkane so we have a **pentane** system.

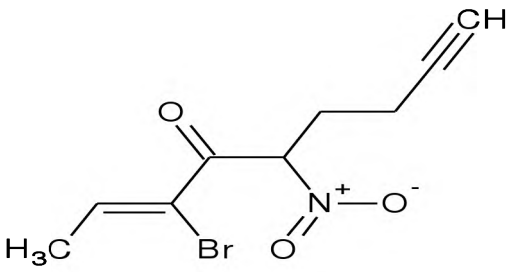
3: There are two substituents. Both are methyl groups, hence **dimethyl.**

4: The -OH is on C2 so we have a **-2-ol.**

5: The methyl groups are on C3 and C4, so we have a **3, 4-dimethyl.**

hence : **3,4-dimethylpentan-2-ol**

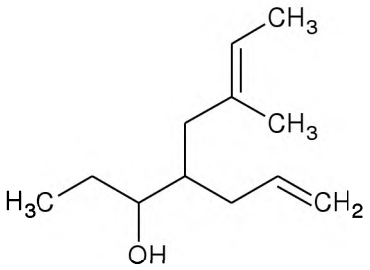
While naming IUPAC nomenclature to organic compounds we should be careful if two vowels came across each other, the first vowel should be ignored and the last one is wrote.



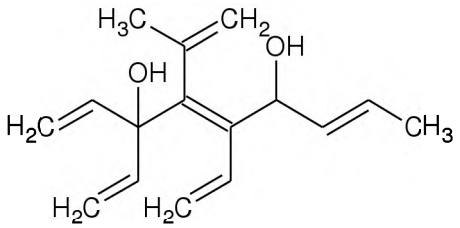
3-Bromo-5-nitronon-2-en-8-yn-4-one

Naming Alcohols:

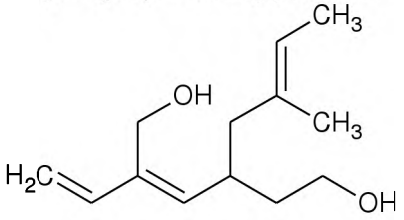
If alcoholic -OH functional group is present than parent name ends with – ol. Also when only one functional group like alcohol is present then mentioning its position if present in centre of long parent chain but if present a side the long parent chain it is not necessary to mention its position because it will be terminal and always one.



6-methyl-4-(prop-2-en-1-yl) oct-6-en-3-ol



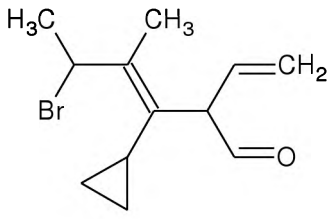
3, 5-diethenyl-4-(prop-1-en-2-yl) nona-1, 4, 7-triene-3, 6-diol



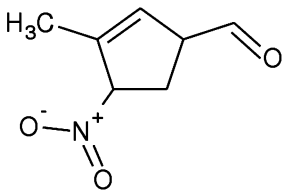
2-ethenyl-4-(2-methylbut-2-en-1-yl) hex-2-ene-1, 6-diol

Naming Aldehydes

If aldehydic COH functional group is present than parent name ends with – ol. Also when only one functional group like aldehyde is present then mentioning its position is not necessary because it will be terminal and always one.



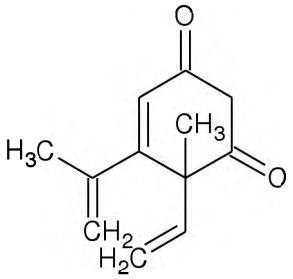
5-bromo-3-cyclopropyl-2-ethenyl-4-methylhex-3-enal



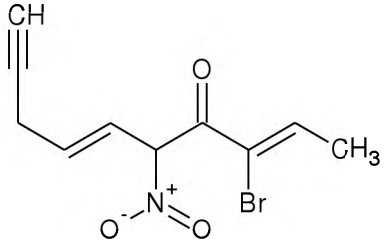
3-methyl-4-nitrocyclopent-2-ene-1-carbaldehyde

Naming Ketones

If ketonic COR functional group is present than parent name ends with – one. Also when only one functional group like ketone is present then mentioning its position is necessary because ketones will never be terminal.



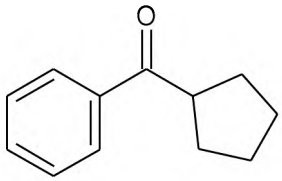
6-ethenyl-6-methyl-5-(prop-1-en-2-yl) cyclohex-4-ene-1, 3-dione



3-bromo-5-nitrodeca-2, 6-dien-9-yn-4-one

Cyclic ketones:

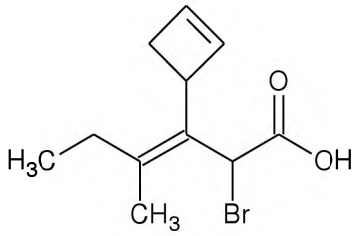
Sometimes the cyclic system is blocked then we cannot number them. In this situation we named them separately. For example



Cyclopentyl (phenyl) methanone

Naming carboxylic acids:

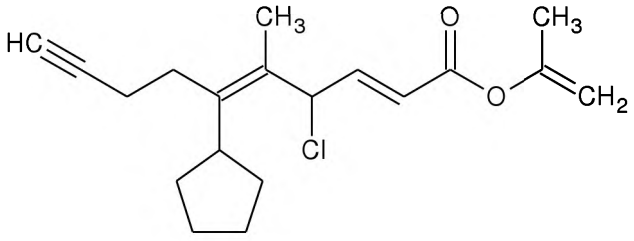
If carboxylic acids COOH functional group is present than parent name ends with –enoic acid. Also when only one functional group like carboxylic acids is present then mentioning its position is not necessary because it will be terminal and always one.



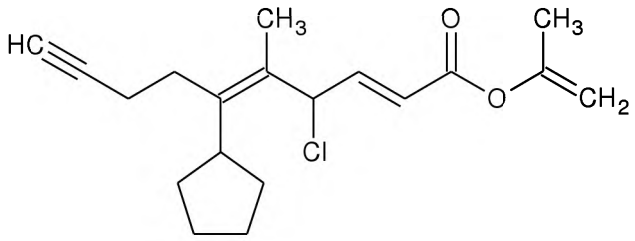
2-bromo-3-(cyclobut-2-en-1-yl)-4-methylhex-3-enoic acid

Naming Esters:

If ester COOR functional group is present than parent name ends with – oate .Also when only one functional group like ester is present then mentioning its position is not necessary because it will be terminal and always one.



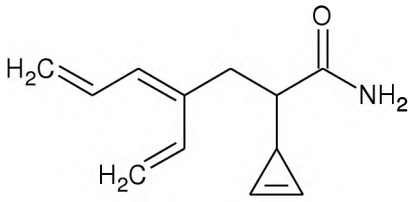
Prop-1-en-2-yl-4-chloro-6-cyclopentyl-5-methyldeca-2, 5-dien-9-ynoate



Prop-1-en-2-yl-4-chloro-6-cyclopentyl-5-methyldeca-2, 5-dien-9-ynoate

Naming Acid amides:

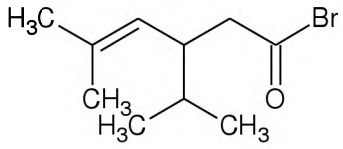
If acid amide CONHR functional group is present than parent name ends with – carboxyamide. Also when only one functional group like acid amide is present then mentioning its position is not necessary because it will be terminal and always one.



2-(cycloprop-2-en-1-yl)-4-ethenylhepta-4, 6-dienamide

Naming Acid halides:

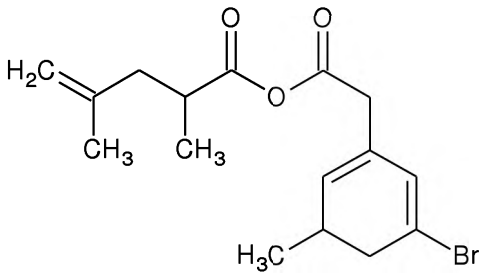
If acid halide COX functional group is present than parent name ends with – carbonyl halide. Also when only one functional group like acid halide is present then mentioning its position is not necessary because it will be terminal and always one.



5-methyl-3-(propan-2-yl) hex-4-enoyl bromide

Naming Acid anhydrides:

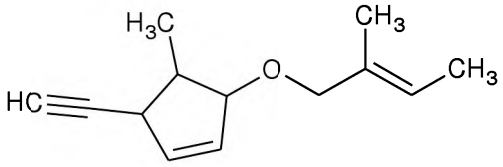
If Acid anhydrides $(CO)_2O$ functional group is present than parent name ends with -oic anhydride. Also when only one functional group like Acid anhydrides is present then mentioning its position is not necessary because it will be terminal and always one.



(5-bromo-3-methylcyclohexa-1, 5-dien-1-yl) acetic-2, 4-dimethylpent-4-enoic anhydride

Naming Ether:

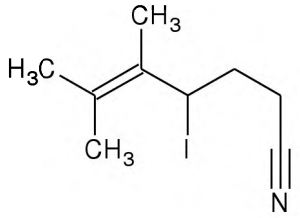
If Ether ROR functional group is present than parent name ends with –ether. Also when only one functional group like Ether is present then mentioning its position is not necessary because it will be terminal and always one.



3-ethynyl-4-methyl-5[(-2-methylbut-2-en-1-yl) oxy] cyclopentene

Naming Nitriles:

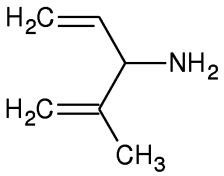
If Nitrile -CN functional group is present than parent name ends with – nitrile.



4-iodo-5, 6-dimethylhept-5-enenitrile

Naming Amines:

If amine –NHR functional group is present than parent name ends with – amine.

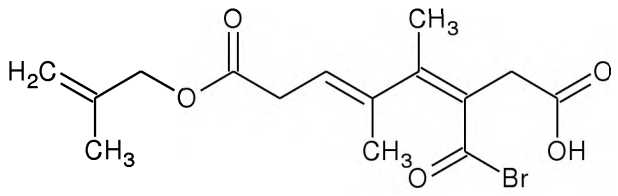


2-methylpenta-1, 4-dien-3-amine

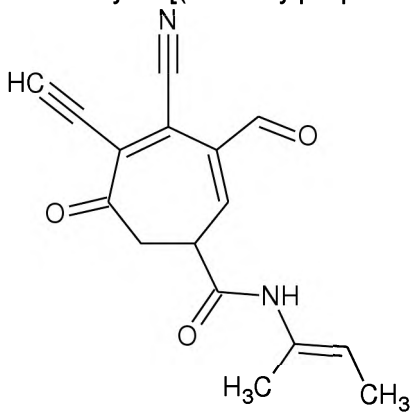
Nomenclature of organic compounds contains multi functional groups

If an organic compound contains more thane one type of functional group than the prior one gat the parent chain name whiles other all are considered as substituent. Following is the table showing the suffixes and prefixes of functional group on priority basis.

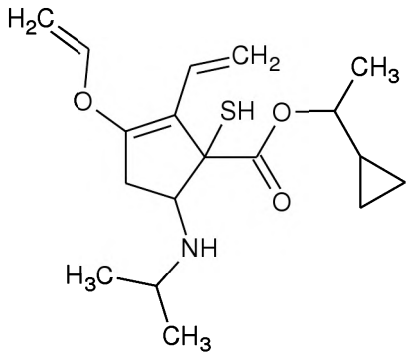
Function group	**Symbol**	**Suffix**	**Prefix** (If substituent)
Acid Anhydride	$-(CO)_2O$	----anhydride	Not yet
Carboxylic Acid	-COOH	----oic acid ----carboxylic acid	Carboxy--
Ester	-COOR	----oate	Alkoxy carbonyl--
Acid Halides	-COX (X=Br,Cl,I,F)	----oyl halide ----carbonyl halide	Halo carbonyl--
Acid Amide	-CONH,-CONHR,-$CONHR_2$	----carboxyamide ----amide	Dialkylamide--
Nitriles	-CN	----nitrile ----carbonitrile	Cyano--
Aldehyde	-COH	----al	Formyl--
Ketone	-COR	----one	Keto/Oxo--
Alcohol	-OH	----ol	Hydroxy--
Thiols	-SH	----thiol	Marcapto--
Amines	NH_2, NHR, NHR_2	----amine	Amino--



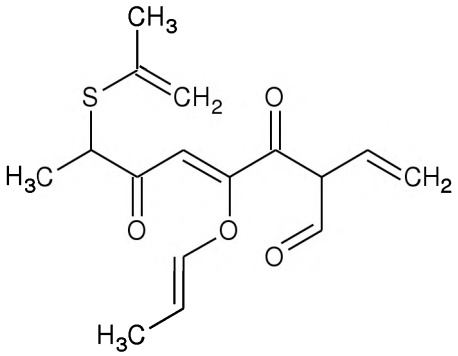
3-(bromocarbonyl)-4, 5-dimethyl-8-[(2-methylprop-2-en-1-yl)oxy]-8-oxoocta-3,5-dienoic acid



N-(-but-2-en-2-yl)-4-cyano-5-ethynyl-3-formyl-6-oxocyclohepta-2, 4-diene-1-carboxamide



1-cyclopropylethyl 2-ethenyl-3-(ethenyloxy)-5-(propan-2-ylamino)-1-sulfanylcyclopent-2-ene-1-carboxylate



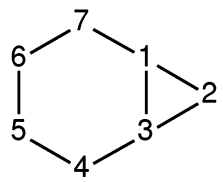
2-ethenyl-3, 6-dioxo-4-[prop-1-en-1-yloxy]-7-(prop-1-en-2-ylsulfanyl) oct-4-enal

Nomenclature of homo and heterocyclic organic compounds

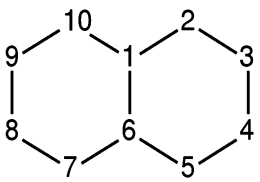
Bicyclic organic molecules nomenclature

A bicyclic molecule is a molecule that features two fused rings. Bicyclic molecules occur widely in organic and inorganic compounds.

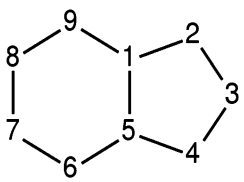
Two rings that share two common atoms are called fused rings. This ring system and the next type called bridged rings share the same designation of ring system. Each of the two common atoms is called a bridgehead atom, and there are three paths between the two bridgehead atoms. In fused rings, the shortest path is always a zero, meaning zero atoms between the two bridgehead atoms. Numbering starts at a bridgehead continues around the largest ring, through the other bridgehead and around the shorter ring.



bicyclo [4.1.0] heptane

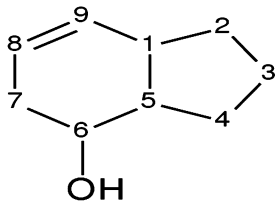


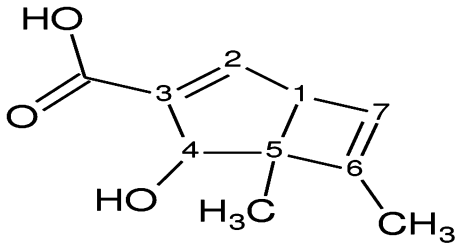
bicyclo [4.4.0] decane



bicyclo [4.3.0] nonane

Substituents and functional groups are indicated in the usual ways. Fused rings systems are always numbered larger before smaller, and numbered in such a way as to give the highest priority functional group the lower position number.



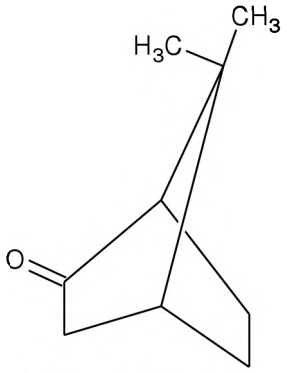


Bicyclo [3.4.0] non-8-en-6-ol

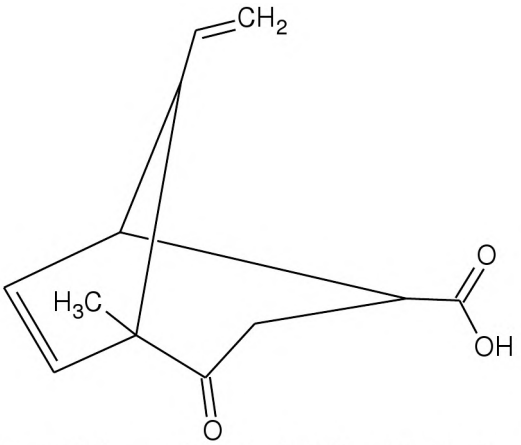
4-hydroxy-5, 6-dimethylbicyclo [3.2.0] hepta-2, 6-diene-3-carboxylic acid

Tricyclic organic molecules nomenclature

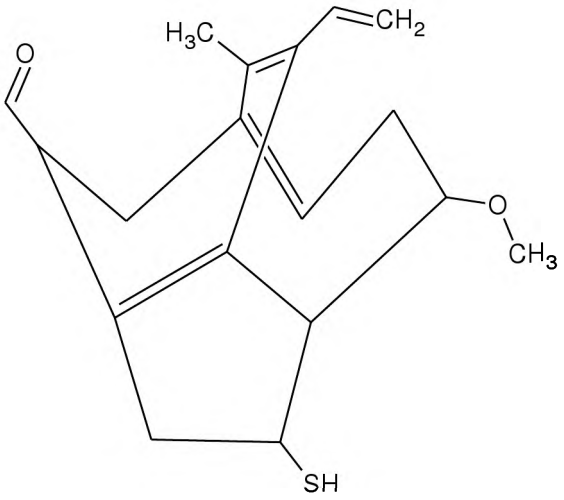
Two rings that share more than two common atoms are called bridged rings. Bridged rings share the same designation of ring system as bycyclic molecules in which there are three paths between the two bridgehead atoms. The longer path is counted first, then the medium, then the shortest. Numbering starts at a bridgehead continues around the largest ring, through the other bridgehead and around the medium path, ending with the shortest path numbered from the original bridgehead atom. Some examples are here as:



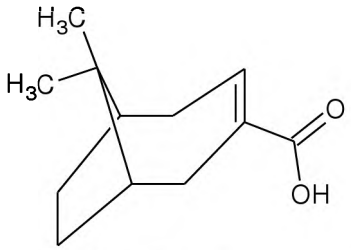
7,7-dimethylbicyclo[2.2.1]heptan-2-one



8-ethenyl-5-methyl-4-oxobicyclo [3.2.1] oct-6-ene-2-carboxylic acid



10-ethenyl-5-methoxy-9-methyl-3-sulfanyltricyclo[6.3.2.0^{4,11}]trideca-1(11),7,9-triene-12-carbaldehyde



9,9-dimethylbicyclo[4.2.1]non-3-ene-3-carboxylic acid

Naming the heterocyclic compounds

A cyclic organic compound containing all carbon atoms in ring formation is referred to as a carboxylic compound. If at least one atom other than carbon forms a part of the ring system then it is designated as a heterocyclic compound. Nitrogen, oxygen and sulfur are the most common heteroatoms but heterocyclic rings containing other hetero atoms are also widely known.

Heterocyclic compounds may be classified into *aliphatic* and *aromatic.* The aliphatic heterocyclic is the cyclic analogues of amines, ethers, thioethers, amides, etc
A heterocyclic ring may comprise of three or more atoms which may be saturated or unsaturated. Also the ring may contain more than one hetero atom which may be similar or disimilar. When different elements O, S, Se, N etc are present then their naming depend upon the following:

1. Size of ring
2. Nature of ring(Saturated or Unsaturated)
3. Element replaced the carbon atom

Here is the table which shows the prefixes of heteroelements.

Elements	Prefixes
O	Oxa
S	Thia

Se	Selina
Te	Tellura
N	Aza
P	Phospha
As	Arsa
Sb	Stiba
Bi	Bismutha
Si	Sila
Ge	Germa
Sn	Stanna
Pb	Plumba
B	Bora
Hg	Mercura

P in 6 membered cyclic structure named as phosphorine and we called it as phosphor and then phosphorine.To minimize confusion we named the phosphorus contain 6 member ring as phosphorine.To.

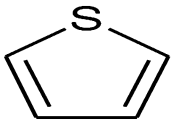
According to this system single three-to-ten-membered rings are named by combining the appropriate *prefix* or *prefixes* (listed in Table).

Ring size	Nitogen Containing		Non Nitrogen Containing	
	Saturated	Unsaturated	Saturated	Unsaturated
3	iridine	irine	irane	irene
4	etidine	ete	etane	ete
5	olidine	ole	olane	ole
6	perhydroine	ine	ane	in
7	perhydroepine	epine	epane	epan
8	perhydrocene	ocene	ocane	ocan
9	perhydronene	onene	onane	onan
10	perhydroecine	ecine	ecane	ecan

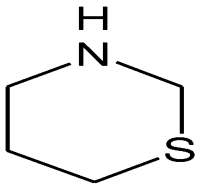
Numbering of the heterocyclic rings becomes essential when substituents are placed on the ring. Conventionally, the hetero atom is assigned position 1 and the substituents are then counted around the ring in a manner so as to give them the lowest possible numbers. While writing the name of the compound, the substituents are placed in an alphabetical order.

In case the heterocyclic ring contains more than one hetero atom, the order of preference for numbering is O, S and N. The ring is numbered from the atom of preference in such a way so as to give the smallest possible number to the other hetero atoms in the ring. As a result the position of the substituent plays no part in determining how the ring is numbered in such compounds.

azete

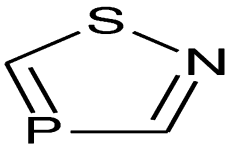


thiophene

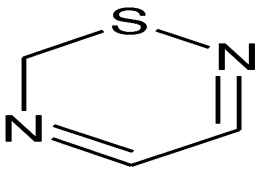


1, 3-thiazinane

If heteroelements are present more than one then priority order should be preffered. As oxygen has the highest priority of all the heteroelements. Besides oxygen sulphur has the second highest priority and nitrogen the third. Priority increases from up to downward in a group and from left to right in periods in periodic table.

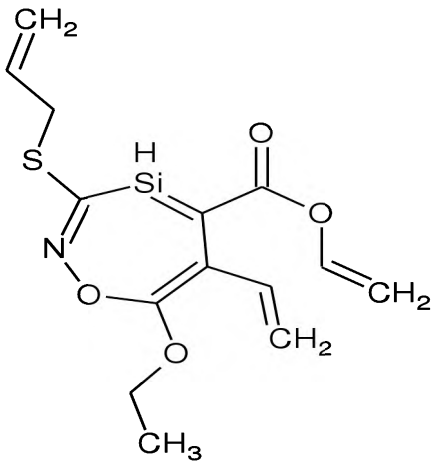


1, 2, 4-thiaazaphosphole



6H-1, 2, 5-thiadiazine

Carboxylic acid and its derivatives and also the nitriles are named as suffix if present on the heterocyclic compounds.



Ethenyl 6-ethyenyl-7-ethoxy-4-methyl-3-(prop-2'-enylthio)-1, 2, 4-oxazasilepine-5-carboxylate

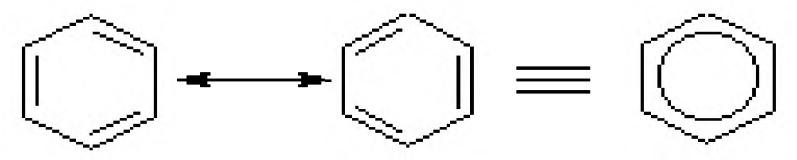
Chapter: 2

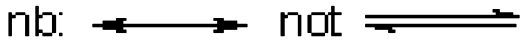
Aromatic compounds

The word aromatic to refer to the class of compounds that contain six membered benzene-like rings with three double bonds.

The fragrant odour of benzene and its derivatives led them to being classed as "aromatic". This classification now has a chemical meaning – "aromaticity" is associated with a special stability resulting from structure.

The aromatic properties of benzene are those that distinguish it from aliphatic hydrocarbons.





General properties of benzene:

- High degree of unsaturation but resistant to addition reactions – generally undergo electrophilic *substitution* (an electrophilic reagent replaces a hydrogen [usually] attached to the ring).
- Unusually stable.
- Pi-Electrons delocalized above and below plane of ring.

Sources of aromatic compounds

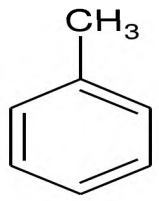
Simple aromatic hydrocarbons come from two main sources: coal and petroleum. Coal is an enormously complex mixture made up primarily of large arrays of benzene-like rings joined together. Thermal breakdown of coal occurs when it is heated to 1000 ℃ in the absence of air, and a mixture of volatile products called *coal tar* boils off. Fractional distillation *at* coal tar yields benzene, toluene, xylene (dimethylbenzene), naphthalene, and a host of other aromatic compounds.

Naming Aromatic compounds

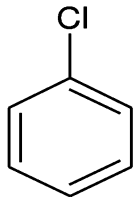
A methyl group, CH_3, can be getting by removing hydrogen from methane, CH_4 and phenyl group, C_6H_5, can be get removing hydrogen from a benzene ring, C_6H_6. Like a methyl or an ethyl group, a phenyl group is always attached to something else.

Aromatic compounds with only one group attached to the benzene ring

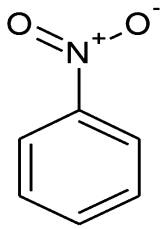
Aromatic compounds containing one substituent end with parent ring name like,



Methylbenzene



Chlorobenzene



Nitrobenzene

Aromatic compounds with more than one group attached to the benzene ring

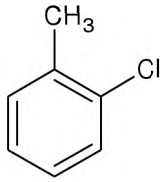
Numbering the ring

Any group already attached to the ring is given the number 1 position. The other ring positions are then numbered from 2 to 6. You can number them either clockwise or anti-clockwise. As with chain compounds, you number the ring so that the name you end up with, which has the smallest possible numbers in it. Examples will make this clear.

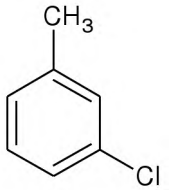
Some simple examples

Substituting chlorine atoms on the ring

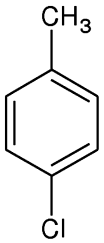
Look at these compounds:



2-Chloromethylbenzene



3-Chloromethylbenzene

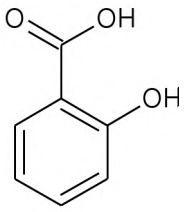


4-Chloromethylbenzene

All of these are based on methylbenzene and so the methyl group is given the number 1 position on the ring. The ring is numbered clockwise in this case because that produces a ***2-*** in the name rather than a ***6-***. 2 is smaller than 6.

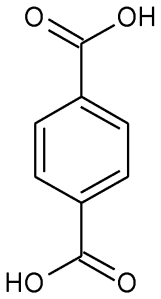
2-hydroxybenzoic acid

This might also be called 2-hydroxybenzenecarboxylic acid. There is a -COOH group attached to the ring and, because the name is based on benzoic acid, that group is assigned the number 1 position. Next door to it in the 2 position is a hydroxyl group, -OH.



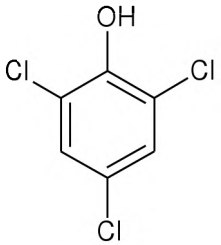
Benzene-1, 4-dicarboxylic acid

The ***di*** shows that there are two carboxylic acid groups, -COOH, one of them in the 1 position and the other opposite it in the 4 position.

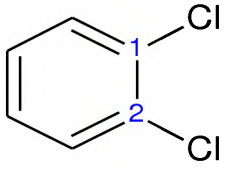


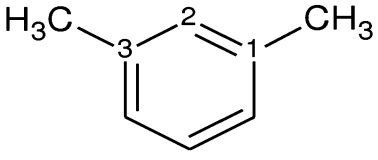
2, 4, 6-trichlorophenol

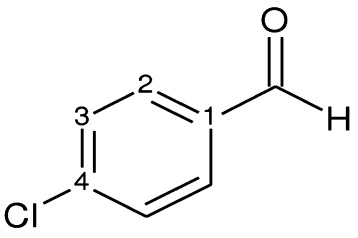
This is based on phenol - with an -OH group attached in the number 1 position on the ring. There are 3 chlorine atoms substituted onto the ring in the 2, 4 and 6 positions.



Disubstituted benzenes are named using one of the prefixes *ortho- (0), meta- (m),* or *para- (p).* An ortho-disubstituted benzene has its two substituents in a 1, 2 relationship on the ring, a meta-disubstituted benzene has it s two substituents in a 1, 3 relationship, and a para-disubstituted benzene has its substituent in a 1, 4 relationship.







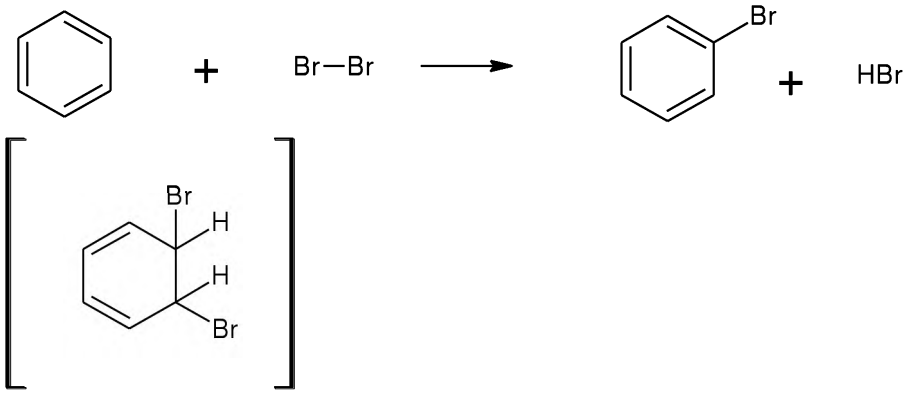
Ortho-Dichlorobenzene
1, 2 disubstituted

meta-Dimethvlbenzene
(meta-xylene)
1, 3 disubstituted

para-chlorobenzaldehyde
1, 4 disubstituted

Stability of Benzene ring:

Although benzene is clearly unsaturated, it is much more stable than typical alkenes and fails to undergo the usual alkenes reactions. Cyclohexene, for instance, reacts rapidly with Br2 and gives the addition product 1,2-dibromocyclohexane, but benzene reacts only slowly with Br2 and gives the *substitution* product C6HsBr. As a result of this substitution, the cyclic conjugation of the benzene ring is retained.



Benzene

Bromobenzene
(Substitution product)

(Addition product)
Not formed

We can get a quantitative idea of benzene's stability by measuring heats of hydrogenation.

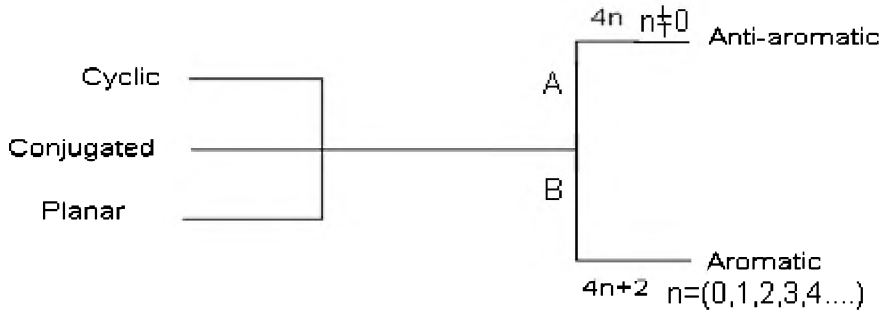
Aromaticity and the Huckel 4n + 2 Rule

Let's list what we've said thus far about benzene and, by extension, about other benzene-like aromatic molecules.

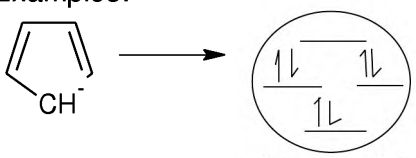
I. Benzene is cyclic and conjugated.
II. Benzene is unusually stable, having a heat o f hydrogenation 150 kl / mol less negative than we might expect for a conjugated cyclictriene.
III. Benzene is planar and has the shape of a regular hexagon. All bond angles are 120°, all carbon atoms are sp2-hybridized, and all carbon-carbon bond lengths are 139 pm.
IV. Benzene undergoes substitution reactions that retain the cyclic conjugation rather than electrophilic addition reactions that would destroy the conjugation.
V. Benzene is a resonance hybrid whose structure is intermediate between two line-bond structures.

This list would seem to provide a good description of benzene and other aromatic molecules, but it isn't enough .Something else, called the Hi.icke14n + 2 rule is needed to complete a description of aromaticity. According to a theory devised by the German physicist Erich Huckel in 1931. a molecule is aromatic only if it h as a planar, monocyclic system of conjugation and contains *a total* of-4/1 + 2 7T *electrons,* where *n* is an integer *(n* = 0, 1,2,3, ...). In o the r words, only *molecules* with 2, 6, 10, 14, and 18 . . . 7Telectrons can be aromatic. Molecules with 4/1 *1T* electrons (4, 8, 12, 16, . . .) *can't* be aromatic, even though they may be cyclic, planar, and apparently conjugated, In fact, planar, conjugated molecules with 4/1 7T electrons are said to be antiaromatic, because delocalization of their 7T electrons would lead to their *destabilization.*

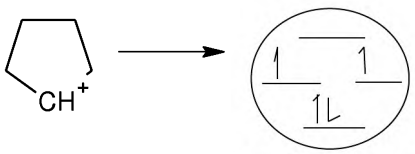
We know that aromaticity provides the benefits of high stability, etc. . . . But what is required for a molecule to *be* aromatic? There are some simple rules:
1) The molecule must be cyclic
2) This cycle must be fully conjugated
3) The cycle must be planar
4) The electrons must be able to "circulate"
5) The conjugated cycle must contain 4n+2 electrons, n = 0, 1,2,3,4...
If the conjugated cycle has only 4n electrons, it is anti-aromatic, and will either be highly
reactive, or will *distort* in order to violate one of the other rules (1-4).
When a compound would fulfill all three conditions than there will be two possibilities for a compound to be aromatic as:



For A:
Here n=can't be zero it should be greater than zero.
For B:
Here n=would be zero or (1, 2, 3, 4….)
4n=4, 8, 12, 16, 20…
4n+2=2, 6, 10, 14, 18 …
In aromatic compounds all the pairs of bonds would lie below the energy level of ground level. For a molecule to be a planar it should be sp2-hybridized or sp-hybridized but the sp3-hybridized compound will never be planar.
Examples:

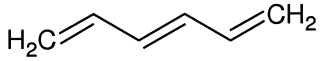


Cyclopenta-2, 4-dienide (stable)
Aromatic (6 π electrons)

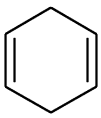


cyclopentylium (unstable)
Anti-aromatic (4 π electrons)

Non-aromatic:
Non-aromatic compounds are those which don't fulfill any of above conditions for aromaticity. For example:

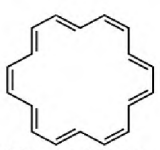


(Not cyclic)

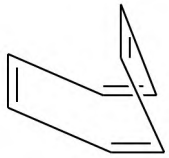


(Not completely conjugated)

(Not planar)
Here are some other examples to understand the phenomenon of aromaticity:



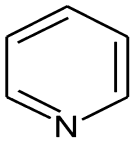
Aromatic (18 π electrons)



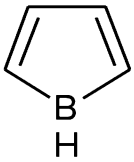
Non-aromatic (Not planar)

Aromaticity in heterocyclic compounds

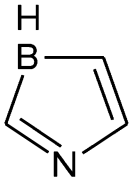
Cyclic compounds whose rings do not only contain carbon atoms may be aromatic, as well. In heterocyclic compounds one or more carbon atoms of the ring are displaced by atoms of other elements, which are then called heteroatoms. Heteroatoms in organic compounds are usually nitrogen, oxygen, or sulfur atoms. In aromatic heterocyclic compounds, it is not only the carbon atoms' orbitals that participate in the formation of the aromatic π system. Orbitals of the heteroatom(s) take part in the π system here too. Pyridine, for example, is such an aromatic heterocyclic compound. Each of the six ring atoms is sp2-hybridized, while the molecule possesses six π electrons. The lone electron pair of pyridine's nitrogen atom occupies an sp2 orbital. These electrons are therefore not π electrons. The remaining two sp2 orbitals of the nitrogen overlap with sp2 orbitals of the adjacent carbons, forming two σ bonds. The π system is the result of the overlapping of the nitrogen's and carbons' p orbitals, which are perpendicular to the ring plane. Here are some examples:



Structure A



Structure B



Structure C

A: - is non-aromatic

- fully conjugated
- planar
- cyclic

B: - is anti-aromatic

- not planar
- not completely conjugated
- cyclic

C: - is non-aromatic

- not fully conjugated
- not planar
- not cyclic

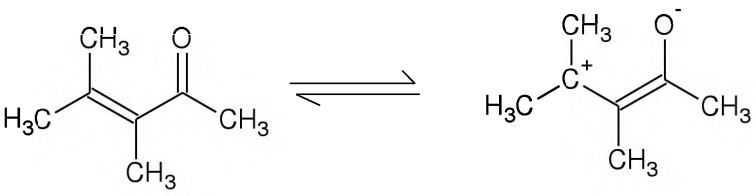
Resonance

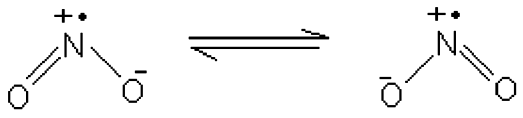
Sometimes all the properties of a molecule can't be represented by a single structure but by two or more structures. These contributing structures are known as canonical forms or resonating structure. The actual molecule is represented by a hybrid of these canonical forms.

Basic rules for resonance structures:

- Electron density only transfer between nuclei.
- Π-electrons can change their density.
- There is no change in σ-bond.

Examples:

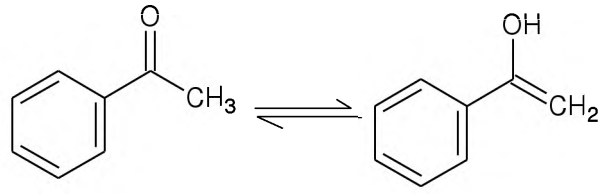




Chapter: 3

Tautomerism

Tautomers are isomers of a compound which differ only in the position of the protons and electrons. The carbon skeleton of the compound is unchanged. A reaction which involves simple proton transfer in an intramolecular fashion is called a tautomerism.

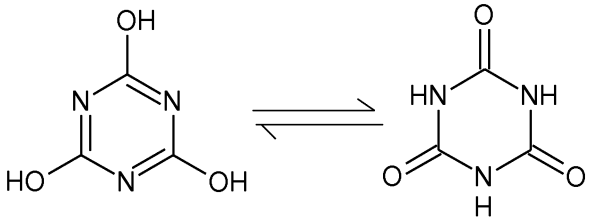


Types of tautomerism:

Following are some types of proton tautomerism as:

Proton tautomerism

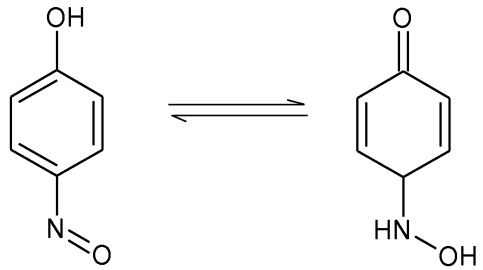
In this type of tautomerism the transfer of proton or hydrogen take place within the molecule.



Proton tautomerism is further classified into following types.

Nitroso-oxime tautomerism:

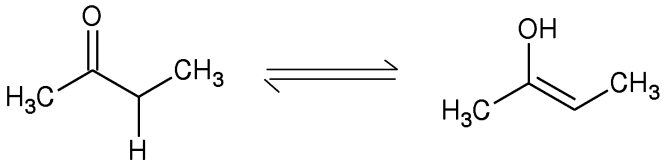
In this tautomerism the nitroso functionality changed into Oxime functionality.



Nitroso Oxime

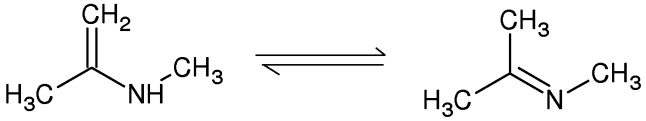
Keto-enol tautomerism:

Keto-enol tautomerism is a very common process, and is acid or base catalyzed. Typically the 'keto' form of the compound is more stable, but in some instances the 'enol' form can be the more stable.



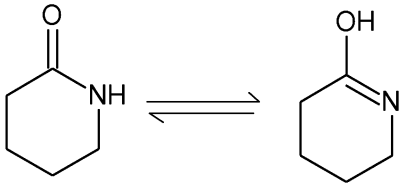
Enamine-Amine tautomerism:

Position of proton from nitrogen of amino group transfers to carbon atom forming double bond at nitrogen.



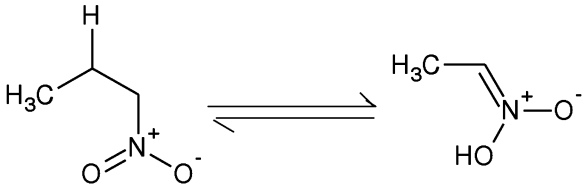
Lactam-Lactin tautomerism:

In this tautomerism hydrogen from amines transfers to carbonyl group to form enol.



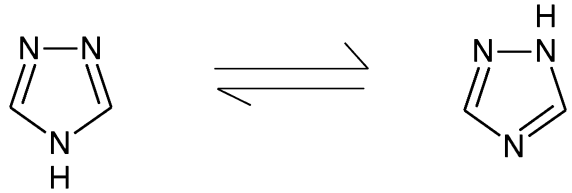
Nitro-acinitro tautomerism:

In this type of tautomerism the hydrogen or proton from carbon is transferred to nitrogen atom.



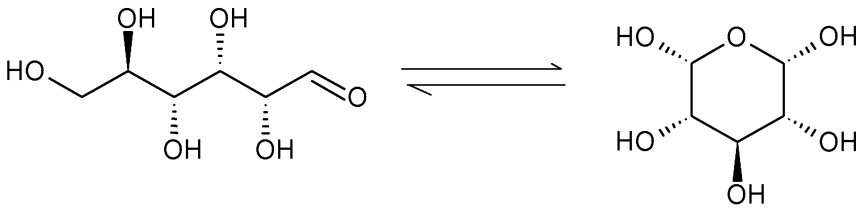
Annular tautomerism:

In this type of tautomerism the transfer of hydrogen take place inside the ring or within the ring structure of the molecule.



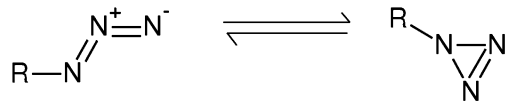
Ring-chain tautomerism:

Open chain form of some organic compounds converted in to cyclic ring due to transfer of proton within the molecule, this phenomenon is called as ring-chain tautomerism.



Valance tautomerism:

In this type of tautomerism there is change in position of nuclei not the hydrogen atom.



Azide Triazirene

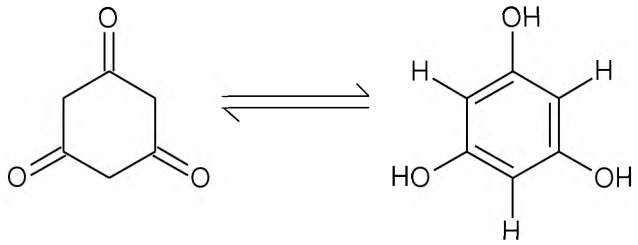
NOTE: The equilibrium arrows above *do not* intend to show the *position* of the equilibrium, only that equilibrium exists between the two forms.

We will further study about Keto-enol tautomerism which is mostly utilizes in organic chemistry and biochemistry. As the enol form of many organic compounds is stable than ketonic one form which is due to presence of proton mobility but not the nuclei of that atom.

Keto-enol tautomerism

A compound containing a carbonyl group (C=O) is normally in rapid equilibrium with an enol tautomer, which contains a pair of doubly bonded carbon atoms adjacent to a hydroxyl (−OH) group, C=C-OH. The keto form predominates at equilibrium for most ketones.

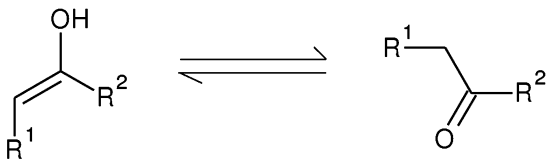
Furthermore, the deprotonated intermediate in the interconversion of the two forms, referred to as an enolate anion, is important in carbonyl chemistry, in large part because it is a strong nucleophile.



Keto form Enol form

Enolization:

The conversion of keto form of any organic compound into its enol form is called as enolization.

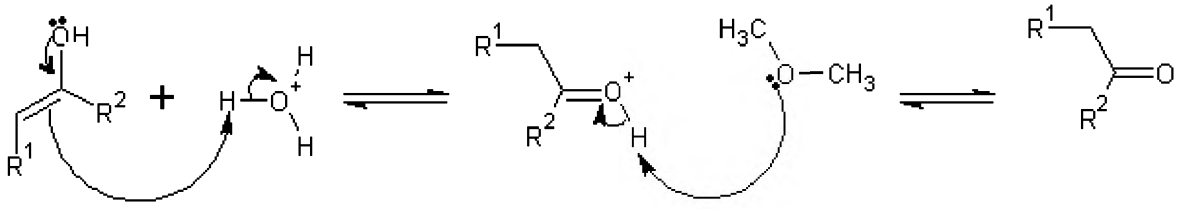


Mechanism

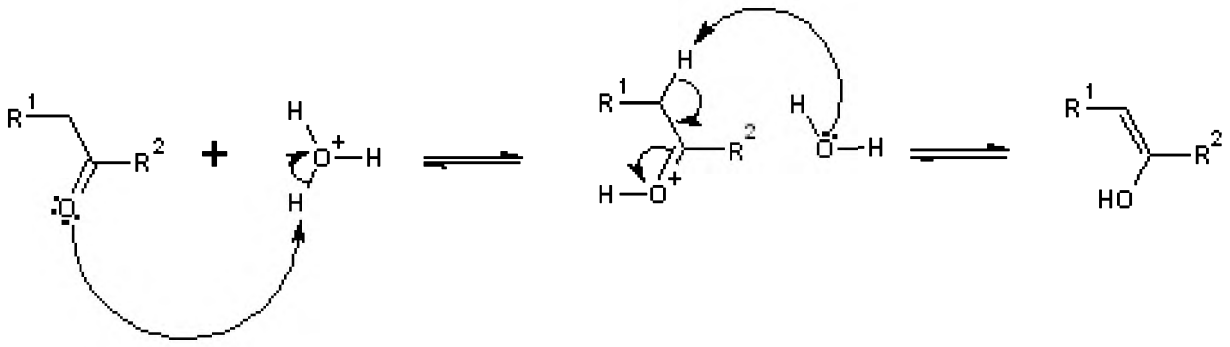
The conversion of an acid catalyzed enol to keto form proceeds by a two step mechanism in an aqueous acidic solution.

First, the exposed electrons of the C=C double bond of the enol are donated to a hydronium ion. This addition follows Markonikov's rule, thus proton is added to the carbon with more hydrogens.This is a concerted step with the oxygen in the hydroxyl group donating electrons to produce the eventual carbonyl group.

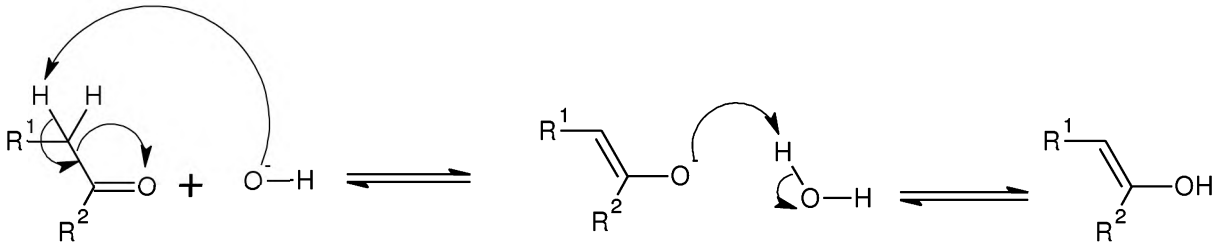
Second, the oxygen in a water molecule donates electrons to the hydrogen in the hydroxyl group, thus relieving the positive charge on the electronegative oxygen atom.



Acid-catalyzed enolization:



Based-catalyzed enolization:



Erlenmeyer rule

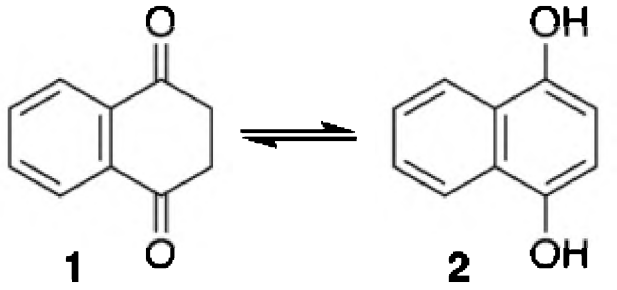
One of the early investigators into keto-enol tautomerism was Richard August Carl Emil Erlenmeyer. His **Erlenmeyer rule** (developed in 1880) states that all alcohols in which the hydroxyl group is attached directly to a double-bonded carbon atom become aldehyde or ketones. This occurs because the keto form is, in general, more stable than its enol tautomer. As the lower energy form, the keto form is favored at equilibrium.

Significance in Biochemistry

Keto-enol tautomerism is important in several areas of biochemistry. The high phosphate-transfer potential of phosphoenolpyruvate results from the fact that the phosphorylated

compound is "trapped" in the less stable enol form, whereas after dephosphorylation it can assume the keto form. Rare enol tautomers of the bases guanine and thymine can lead to mutation because of their altered base-pairing properties.

In certain aromatic compounds such as phenols, the enol is important due to the aromatic character of the enol but not the keto form. Melting the naphthalene derivative 1, 4-dihydroxynaphthalene **1** at 200 °C results in a 2:1 mixture with the keto form **2**. Heating the keto form in benzene at 120°C for three days also affords a mixture (1:1 with first-order reaction kinetics). The keto product is kinetically stable and reverts back to the enol in presence of a base. The keto form can be obtained in a pure form by stirring the keto form in trifluoroacetic acid and toluene (1:9 ratio) followed recrystallisation from isopropyl ether.



When the enol form is complexed with chromium tricarbonyl, complete conversion to the keto form accelerated and occurs even at room temperature in benzene.

DNA

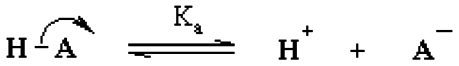
In deoxyribonucleic acids (DNA), the nucleotide bases are in keto form. However, James Watson and Francis Crick first believed them to be in the enol tautomeric form, delaying the solution of the structure for several months.

Chapter: 4

Acidity and Basicity

Acidity and basicity are the based on the same chemical reaction, just looking at it from opposite sides.

First, consider the general equation of a simple acid reaction:



The more stable the conjugate base, $\mathbf{A^-}$, is then the more the equilibrium favors the product side.....
The more the equilibrium favors products, the more $\mathbf{H^+}$ there is....
The more $\mathbf{H^+}$ there is then the stronger **H-A** is as an acid....
So looking for factors that stabilize the conjugate base, $\mathbf{A^-}$, gives us a "tool" for assessing acidity.

Key Factors that affect the stability of **the conjugate base, $\mathbf{A^-}$**,

$\mathbf{HF > H_2O > NH_3 > CH_4}$	**Electronegativity:** When comparing atoms within the same row of the periodic table, the more electronegative the anionic atom in the conjugate base, the better it is at accepting the negative charge.
HI > HBr > HCl > HF	**Size:** When comparing atoms within the same group of the periodic table, the larger the atom the weaker the **H-X** bond and the easier it is to accommodate negative charge (lower charge density)
$\mathbf{RCO_2H > ROH}$	**Resonance:** In the carboxylate ion, $\mathbf{RCO_2^-}$ the negative charge is delocalized across 2 electronegative atoms which make it more stable than being localized on a specific atom as in the alkoxide, $\mathbf{RO^-}$.

A convenient way to look at basicity is based on electron pair availability.... the more available the electrons, the more readily they can be donated to form a new bond to the proton and, and therefore the stronger base.

Key Factors that affect electron pair availability in a **base, B**

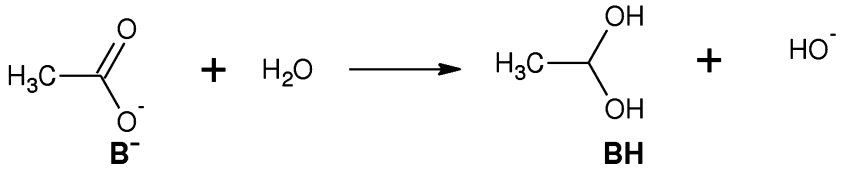
$\mathbf{CH_3^- > NH_2^- > HO^- > F^-}$	**Electronegativity:** When comparing atoms within the same row of the periodic table, the more electronegative the atom donating the electrons is, the less willing it is to share those electrons with a proton, so the weaker the base.
$\mathbf{F^- > Cl^- > Br^- > I^-}$	**Size:** When comparing atoms within the same group of the

periodic table, the larger the atom the weaker the **H-X** bond and the lower the electron density making it a weaker base.

$RO^- > RCO_2^-$

Resonance: In the carboxylate ion, RCO_2^- the negative charge is delocalized across 2 electronegative atoms which make it the electrons less available than when they localized on a specific atom as in the alkoxide, RO^-.

Given an acid donating a proton to water:



B⁻ **BH**

The extent of that reaction at equilibrium is quantitated by the Ka:

$$K_a = \frac{[A^-][H_3O^+]}{[HA]}$$

•Since the products of the reaction are in the numerator, larger Ka values are observed for stronger acids.
Also, since pKa = -log Ka, smaller pKa values are observed for stronger acids.

Given a base accepting a proton from water:

The extent of that reaction at equilibrium is quantitated by the Kb:

$$K_b = \frac{[HB][OH^-]}{[B]}$$

Since the products of the reaction are in the numerator, larger Kb values are observed for stronger bases.
Also, since pKb = -log Kb, smaller pKb values are observed for stronger bases.

Acidity of organic acids

Lower the value of pKa larger will the acidity of an acid, while larger the value of pKa lower will the acidity of an acid.
Here are some acids with there pKa values showing there acidic strength.

Acids	pKa values
Hydroiodic acid	-10
Hydrochloric acid	-7
Sulphuric acid	-3
Hydrogen sulphate	2
Acetic acid	4.8
Hydrogen sulphide	7

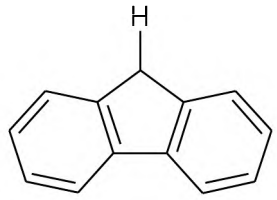
Ammonium ion	9.2
Phenol	10
Methanol	15.5
Acetone	20
Ethyne	25
Ammonia	33
Benzene	43
Methane	48

Water, H2O, is the base of the hydronium ion, H3O+, pKa -1.74. This value is greater than the pKa of HCl, -7. This means that HCl will give up its protons to water essentially completely to form the H3O+ cation. We call HCl a strong acid in water. One can assume that all of the HCl in a water solution is 100 percent dissociated meaning that both the hydronium ion concentration and the chloride ion concentration correspond directly to the amount of added HCl.

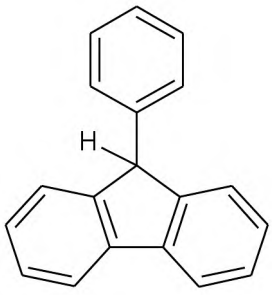
On other hand Ammonia, NH3, is the base of the ammonium ion, NH4+, pKa 9.24. This value is higher than the pKa of acetic acid, 4.75. This means that acetic acid will give up its protons to ammonia essentially completely to form the NH4+ cation. We call acetic acid a strong acid in ammonia.
One can assume that all of the acetic acid in an ammonia solution is 100 percent dissociated meaning that both the ammonium ion concentration and the acetate ion concentration correspond directly to the amount of added acetic acid.
Factors affecting the acidity of organic acids:

- Inductive effect:
- Stability of anion
- Resonance or Mesomeric effect

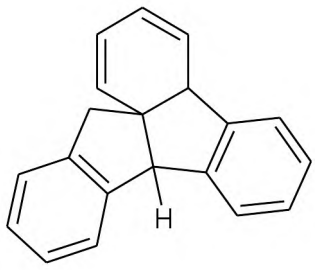
To understand the effect of these three factors on acidity of organic acids let's take an example as follow:



pKa = 22.8



pKa = 18.5

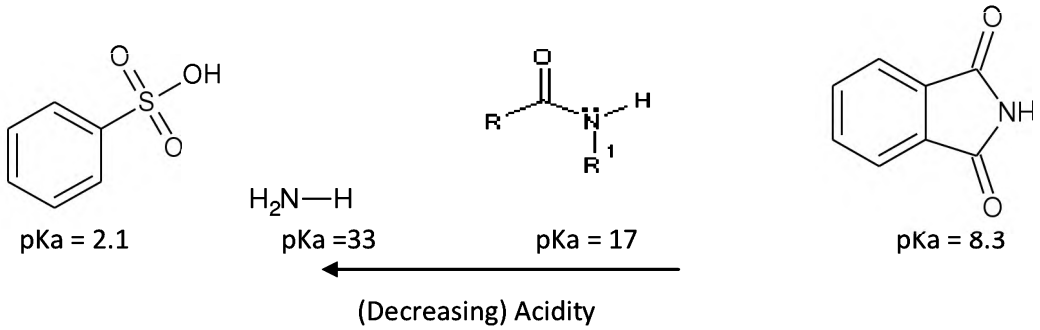


pKa = 11

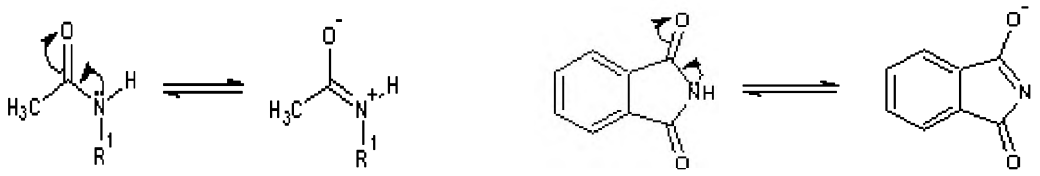
Inductive effect has most contribution in increasing the acidity of these three organic compounds. If all these three structure loses there hydrogen they will get the negative charge. The negative charge of 3rd structure resonates on 5 rings than the 1st and 2nd one. So the 3rd structure is more stable and will be more acidic as its pKa value shows. The rest of two have lesser resonance contributing structures than 3rd one. The dominant factor here is the stability of anion.

It is an important general rule of thumb that Anion Stability usually exerts the strongest effect upon acidity, i.e., is dominant over bond strength effects. The one special type of *exception* will be considered shortly. Anion stability, in turn is affected by (1)

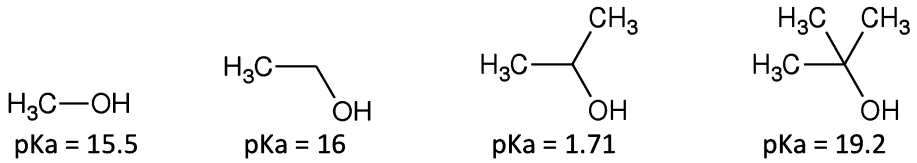
resonance stabilization, (2) inductive effects, (3) hybridization effects and (4) Electronegativity effects.



The electron withdrawing group like carbonyl and lone pair cause resonance and thus more resonance contributing structure are formed.



With the help of pKa values we can compare different functionalities as:



A more electronegative substituent X will increase the acidity of an oxy (or hydroxy) acid XO-H by greater withdrawal of electron density from the oxygen-hydrogen bond. This both weakens the O-H bond and increases the positive charge on hydrogen. Polarity of hydrogen oxygen bond in above organic compounds decreases by increasing the number of methyl groups.

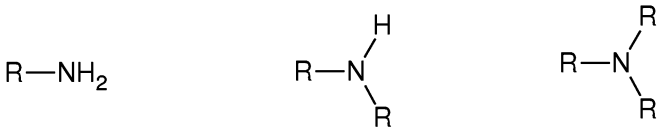
pKa values	R_1	R_2	R_3
48	H	H	H
10	NO_2	H	H
4	NO_2	NO_2	H
0	NO_2	NO_2	NO_2

Electron withdrawing and electron with donating group attached to organic compound also affect the acidity. When electron with donating group is present then polarity increases by donation of electron density while when electron withdrawing group is present than polarity is decreases by drifting of electron density towards electron withdrawing group. In this condition the stability of organic compound is increases and then lesser will the pKa value. From left to right in periodic table the Electronegativity increases. If we move down the group acidity is increasing and pKa value is decreasing. If polarity is decreasing than the pKa value should increase. Moving down the group a shell is increasing and effective nuclear charge increases. The Electronegativity is decreasing down the group .Halogens acids have covalent bond but have ionic character also.

Halogen acids	HF	HCL	HBr	HI
pKa values	3	- 7	-9	-10

Basicity of organic bases

In organic chemistry mostly we deal with nitrogen containing bases. Nitrogen is a trivalent element and 95% of organic bases are nitrogen containing.



Tertiary amine contains bulky groups and has maximum sterric effect. While secondary amines have minimum sterric effect. Primary amines have no sterric effect.
Following are the values of some organic bases as:

R	R-NH	R_2N-H	R_3N
Methyl	10.6	10.8	9.8
Ethyl	10.7	11.0	10.8
Propyl	10.7	11.0	10.3
Butyl	10.7	11.0	9.9

The decreasing order of basicity of primary, secondary and tertiary amines are as follow:

2°>1°>3°

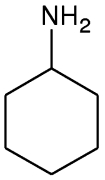
If alkyl group attached with amines are sp^2 hybridized than there pKb values are different than chain of alkyl group attached. Also the hydrogen bonding in amines also affect there pKb values. Sterric factor in tertiary amines is responsible for the lower pKb values. Electron withdrawing groups increase the availability of nitrogen's lone pair and, as a result, also increase the basicity of amines; alkyl amines are more basic than ammonia.
Electron-withdrawing groups decrease the availability of the non-bonding electron pair and decrease basicity; amides are much less basic than ammonia.

Here X=Cl, F.

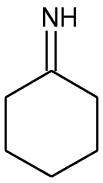
For ''Cl'' pKa = 5.5 pKa = 9.65

For ''F'' pKa = 5.7 pKa = 8.7

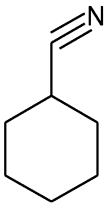
In first structure three electron withdrawing groups are directly attached with carbon attached with nitrogen while in second structure three electron withdrawing groups are attached with 2nd carbon which has no direct link with nitrogen. So here the inductive effect affects the basicity of these two bases. And inductive effect basically decreases the basicity.
Basicity of nitrogen containing compounds also depends upon the hybridization of nitrogen.



sp3



sp2



sp

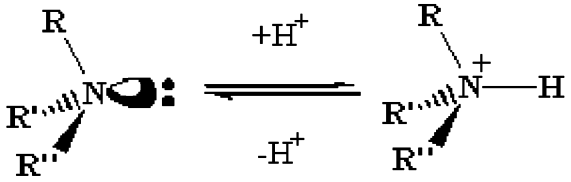
Hybridization effect the basicity of nitrogen thus there trend is like

sp3 > sp2 > sp

Or it can be say as

Amines > Imines > Nitriles

The reactivity of amine is dependent upon the lone pair of electrons and this feature enables the amine nitrogen to behave as either a Bronsted base or a nucleophile. The majority of simple amines yield alkaline aqueous solutions (if soluble) and aliphatic possess pK_a values ~ 9 and when the pK_a value exceeds 9 the majority of the amine will exist in a protonated state.

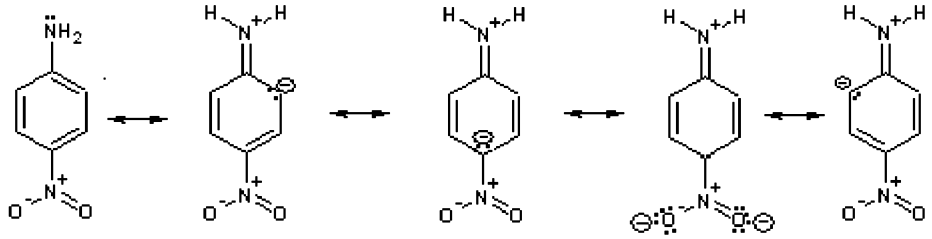


.

Amine	Structure	pK_a
Ammonia	NH_3	9.26
Triethylamine	Et_3N	10.64
Ethylamine	$EtNH_2$	10.75
Diethylamine	Et_2NH	10.98
Piperidine		11.20
Aniline	$PhNH_2$	4.58
Pyridine		5.23

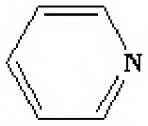
It is clear from the above table that electron-donating groups stabilize the positive charge of the ammonium nitrogen and therefore enable the above equilibrium to lie further to the right hand side. Consequently, the association constant is reduced and the pK_a is subsequently raised. This is clearly evident by consideration of ethylamine and diethylamine (*note* that sterric effects actually serve to decrease the basicity of the nitrogen in triethylamine). The basicity of the nitrogen atoms in amines such as aniline and pyridine are dramatically affected by aromaticity and the ability to form numerous canonical forms *via* resonance of the amines' lone pair of electrons with the benzene p-system.

A similar electron pair delocalization is responsible for the very low basicity (and nucleophilic reactivity) of amide nitrogen atoms (last green shaded structure). This feature was instrumental in moderating the influence of amine substituents on aromatic ring substitution, and will be discussed further in the section devoted to carboxylic acid derivatives.

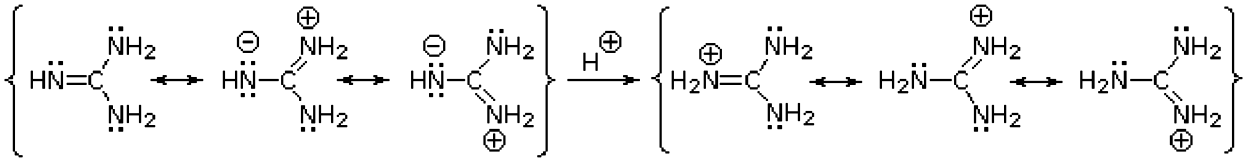


Reduced Basicity of para-Nitroaniline due to Electron Pair Delocalization

The influence of a conjugated amine group on the basicity of an existing amine will be displayed. Although 4-dimethylaminopyridine (DMAP) might appear to be a base similar in strength to pyridine or N,N-dimethylaniline, it is actually more than ten thousand times stronger, thanks to charge delocalization in its conjugate acid. The structure in the gray box shows the locations over which positive charge (colored red) is delocalized in the conjugate acid. This compound is often used as a catalyst for acyl transfer reactions.

	Loss of conjugation of the nitrogen lone pair with the phenyl ring occurs if the amine nitrogen becomes protonated. Consequently, aniline is less basic.
	Enhanced *s*-character for the sp^2 hybridized nitrogen render it more electronegative in comparison to a normal sp^3 nitrogen and therefore decreasing its ability to become positively charged.

Although resonance delocalization generally reduces the basicity of amines, a dramatic example of the reverse effect is found in the compound guanidine (pK_a = 13.6). Here, as shown below, resonance stabilization of the base is small, due to charge separation, while the conjugate acid is stabilized strongly by charge delocalization. Consequently, aqueous solutions of guanidine are nearly as basic as are solutions of sodium hydroxide.



guanidine base
small stabilization

guanidinium conjugate acid
large stabilization

So its clear now from above discussion that acidity and basicity are just inverse of each other. Therefore, both are affected by the same factors.

σ-value and Hammet equation

A more accurate prediction of pKa, but for a small class of compounds, may be made using Hammett equations. In 1940, L.P. Hammett demonstrated that the effects on pKa of meta- and para- substituted aromatic compounds (benzoic acids) were linear and additive.

$$\sigma = \log K/ K_o = \Delta pKa$$

where $\mathbf{K_o}$ is the acid dissociation constant for the ionization of benzoic acid and K is the acid dissociation constant for the ionization of a substituted benzoic acid with a given substituent at a given position on the aromatic ring. Since **log K_o** is directly related to the standard free energy change accompanying the ionization of benzoic acid (*via* $DG° = -2.303RT\log K_o$), and log K is directly related to the standard free energy change accompanying the ionization of the substituted benzoic acid, the substituent constant is actually related to DDG°, the difference in the free energy changes for the two ionization processes, i.e., a measure of the substituent effect expressed in terms of a free energy quantity.

Since the **K's** depend somewhat upon the temperature and critically upon the nature of the solvent, **s** is defined specifically for water at **25 °C.** Also, since the magnitude of the substituent effect depends upon the position of the substituent upon the aromatic ring, there are different substituent constants for *para*, *meta*, and *ortho* substituents. Typically, these are distinguished as $\mathbf{s_p}$, $\mathbf{s_m}$, and $\mathbf{s_o}$. If the ratio **(K/ K_o) >1,** i.e., the substituent has increased the acidity of the benzoic acid, is positive. Such a substituent is considered to be an *electron-withdrawing group* (EWG), because electron density is increased at the reaction site in the product benzoate anion, and an EWG will favor this change by withdrawing electron density away from the reaction site. Groups such as **m-Cl, p-Cl, m-NO_2, p-NO_2,** etc. which have relatively large dipole moments oriented with the positive end directed toward the reaction site are EWG's. On the other hand, electron donating groups (groups which tend to increase the electron density near the reaction site) disfavor the ionization to a negatively charged ion and have **K/K_o<1**. These groups have negative sigma values.

These include alkyl groups (at both the *meta* and *para*-positions), *para* alkoxy groups, and *p*-amino groups. The Hammett substituent constants for many hundreds of substituent groups have been measured and tabulated. It should be noted that, by definition, Hammett substituent constants are relative to hydrogen as a basis of comparison. That is to say, $\mathbf{s_H}$ **= 0.0.**

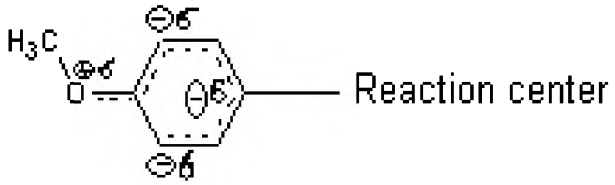
HAMMET SUBSTITUENT CONSTANTS

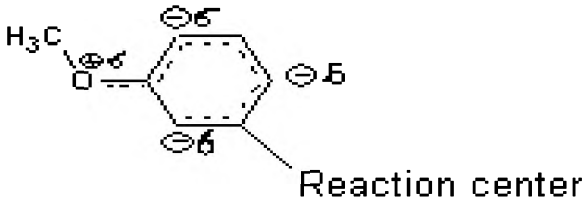
Hammett constants are based upon the acid dissociation of benzoic acid and m- and p-substituted benzoic acids in water at 25 °C. The K_a's of some of these acids are given in the table below:

Substituent (X)	K_a	pK_a	s_p	EWG or EDG
p-OCH_3	$3.5x10^{-5}$	4.46	-0.27	EDG

p-CH_3	$4.3x10^{-5}$	4.34	-0.17	EDG
H	$6.46x10^{-5}$	4.19	0.00	Standard
p-Cl	$1.10x10^{-4}$	3.96	0.23	EWG
p-NO_2	$3.90x10^{-4}$	3.41	0.78	EWG

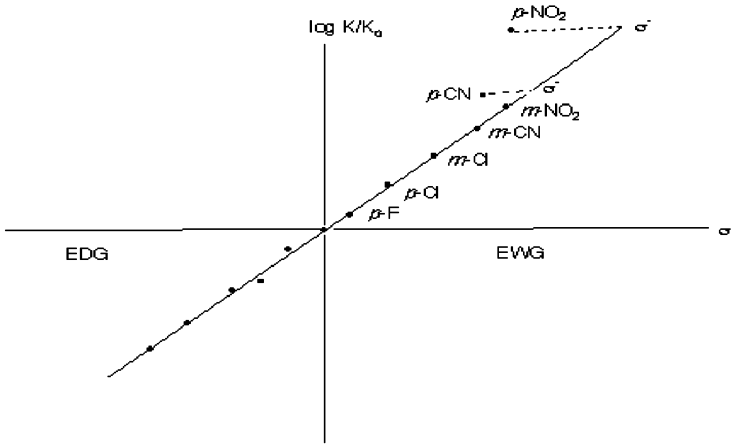
As an example, the *meta* sigma value of chlorine is 0.37, while the *para* sigma is only 0.22, i.e., both substituents are EWG, but the *meta* one is more strongly so. Note that the inductive effect is dominant for the halogens, in part because they are poorer electron donors via the resonance effect than is oxygen. Also, the *meta* sigma of methoxy is +0.11 (it is EWG), while the *para* sigma is –0.27 (it is EDG). Strong evidence exists that the inductive effects in the *meta* and *para* positions are very similar. So for *para* methoxy, the resonance effect is dominant over the inductive effect, but both are significant. For an amino group, the electron donating power is even greater. Note also that the sigma for *p*-SCH_3 (0.00) is less negative than that for *p*-methoxy, even though the inductive effect of sulfur is surely less than that of oxygen. This is apparently because of an orbital mismatch; that is, the larger 3p AO of sulfur overlaps less efficiently with the smaller 2p AO of the attached ring carbon, resulting in a much smaller resonance effect in the case of sulfur substituents. For the same reason, a *p*-fluoro substituent (+0.06) is less strongly electron withdrawing than a *p*-Cl) +0.23) or Br substituent.





Hammett further observed that if log (K/K_o) for the ionization of other acids was plotted versus these sigma values, reasonably linear plots were obtained. For example, if the log (K/K_o) data for the ionization of *meta* and *para* substituted phenylacetic acids in water at 25 °C was plotted versus his sigma values a linear plot of slope 0.489 was obtained. Similarly, if the data for ionization of substituted phenylpropionic acids was plotted vs. sigma, a linear plot of slope 0.212 was obtained.

A typical Hammet plot for the dissociation of phenols is shown below. The regression line is defined by all of the resonance-electron-donating groups and by meta groups whether they are EDG or EWG. Only the *para* resonance-EWG groups such as nitro, Cyano, and carboethoxy deviate, and their deviations are quite large. Whereas the sigma value for *p*-nitro is 0.78, the s^- value is 1.27! On the other hand, the sigma value for *meta* nitro does not require any change, i.e., the s^-value is the same as the s value.



Chapter: 5

Reactive Intermediates

Reactivity and stability are inversely proportional to each other. Highly reactive specie is less stable while highly stable specie is less reactive.

Depending upon the enthalpy of the reaction and gibbs free energy compounds can be differentiating as stable and reactive.

Special conditions are applied for highly reactive compound. As **Na** is highly reactive thus can't used at ordinary temperature. If gold is placed in water no reaction will occur whatever the time duration it took while Na immediately react with water to form hydrogen gas.

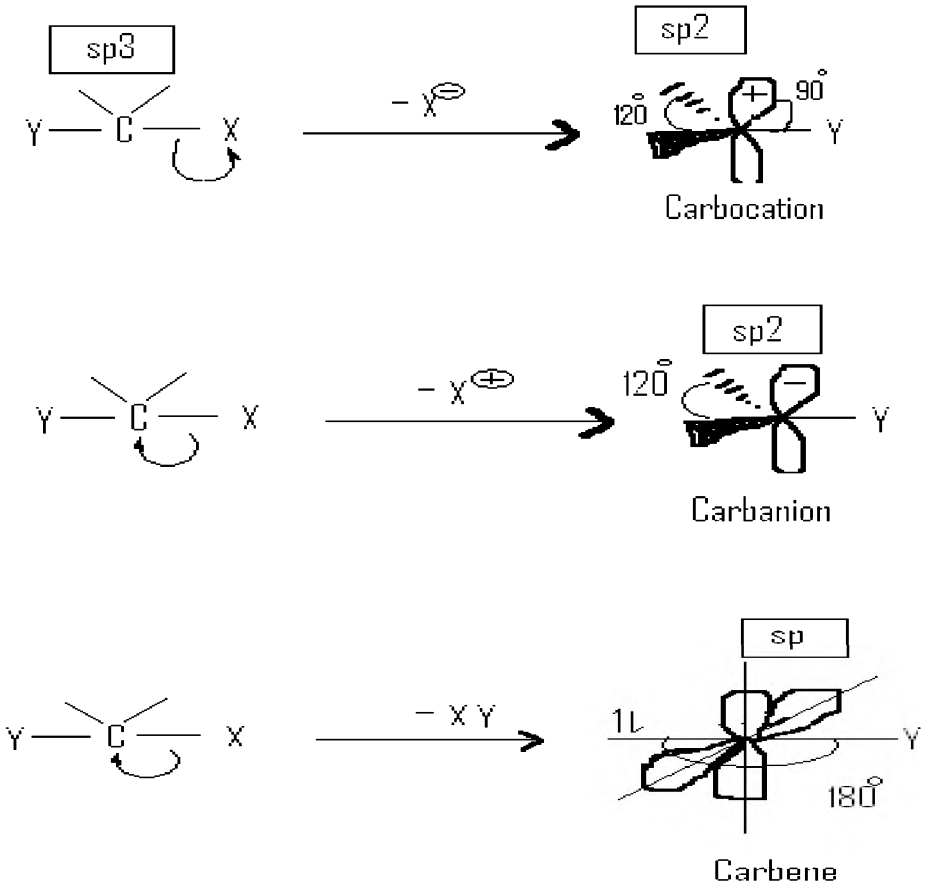
Some metals are more reactive some are moderate and someone has very low reactivity.

Benzene and aromatic compounds have moderate reactivity, thus we provide heat to cross the energy barrier or to gives active energy to the reaction. As benzene is highly stable and is less reactive and made reactive by heating.

All carboxylic acids and its derivatives are moderate reactive. The highly reactive compounds have very small life measured in nanometer. They can't exist in Free State.

Transition elements are difficult to isolate, but some of them can be isolated. We have some reactive intermediate species as carbene, nitrenes and benzyne.These reactive intermediates are highly reactive so can't exists in Free State.

Carbon containing specie's existence has three possibilities.



Carbocation: Bearing positive charge.

Carbanion: Bearing negative charge.

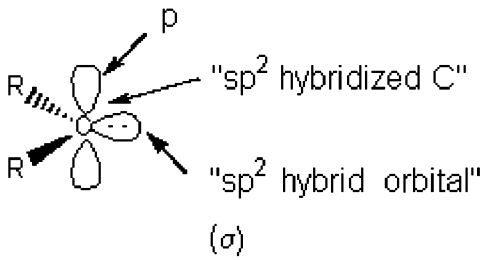
Carbene: Having empty orbital.

Carbenes:

Carbenes are a family of organic molecules composed of neutral divalent carbon atom with a sixest of electrons and two substituents. These reactive intermediate specie has two pi-bonds. Carbene contains 2 orbitals, one has electron pair and other is empty. Carbene have carbon bearing non-bonding electron pair.

Structure of carbenes:

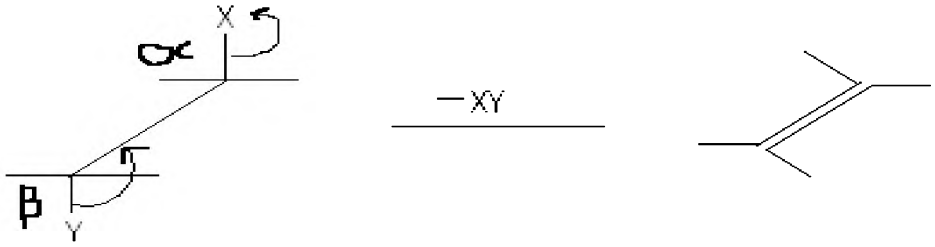
If carbene is sp hybridized than the angle between two hydrogen should be 180°.When different carbenes are analyzed by X-ray diffraction, different angles has been observed ranging 100-150°.The characteristic angle for sp2 hybridized carbene is 120°.Thus it shows that one of the orbital is empty. The structure of carbene is as:



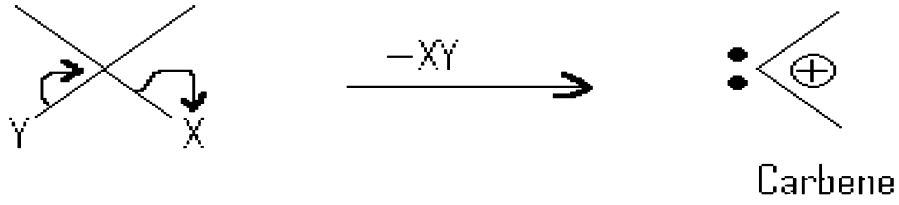
Generation of carbenes:

Carbene can be generated by different mechanism. But the old one mechanism is α-elimination.

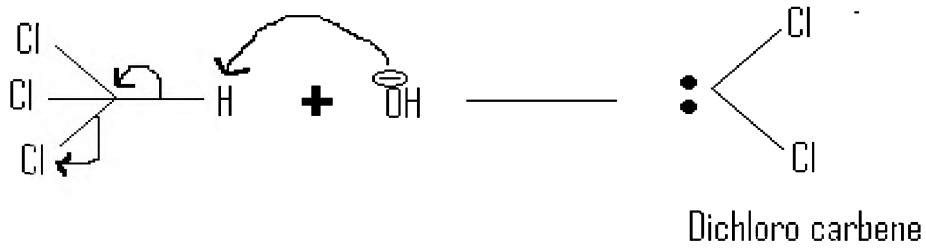
α -elimination: Generation of carbene by this mechanism is first reported when the scientist react chloroform with sodium hydroxide. Two groups are eliminated from two adjacent carbons and results C-C bond.



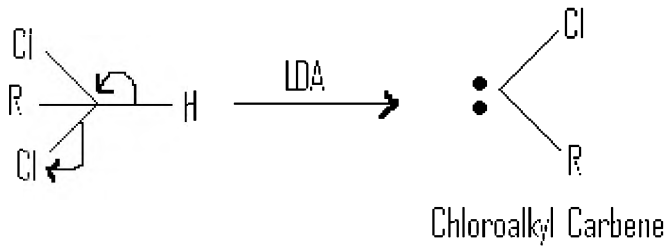
In α-elimination both groups leave from the same carbon, both with there electron pairs.



For three chloro groups we use the stronger base like sodium hydroxide as:

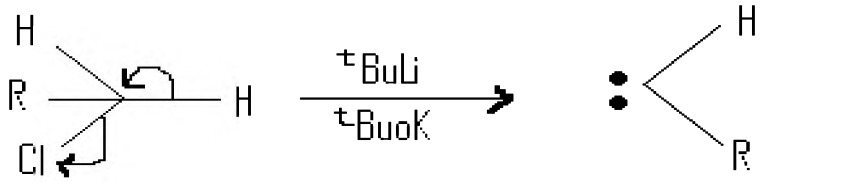


For two chloro groups we use the stronger base than sodium hydroxide as:



Chloroalkyl Carbene

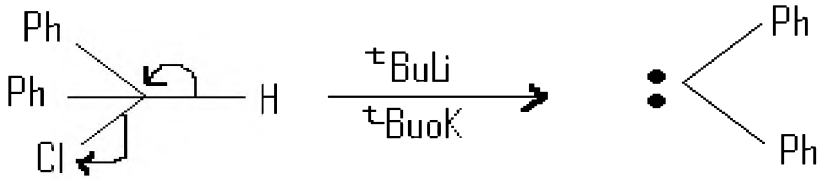
For one chloro group we use super base having pKa over 35 like potassium tertiary butoxide+butyl lithium (schlosier's base).



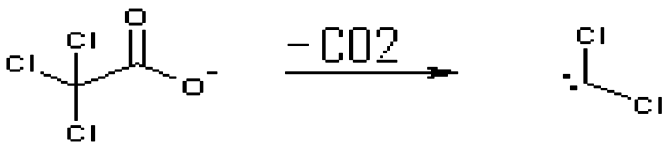
Alkyl Carbene

As carbenes are highly reactive speice,it is very difficult to isolate them from any mixture due to there short life.

When we have both phenyl groups with one chloro group as follow:



Diphenyl carbenes can be isolated. It is electron deficient and both phenyl groups are stablizied.Different bases are used for in different carbenes's generation. Like for carboxylic acids and there salts as:

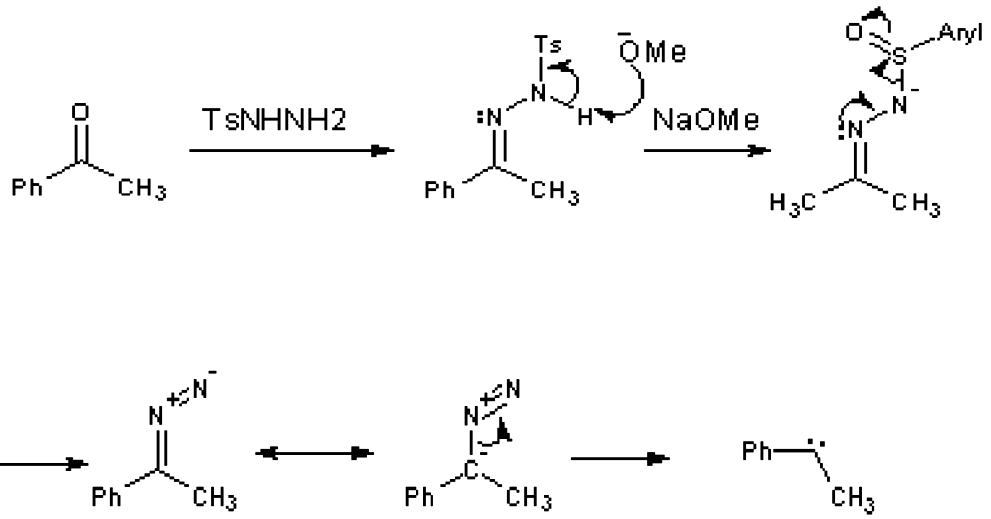


It is also an α-elimination.

From aliphatic diazo compounds:

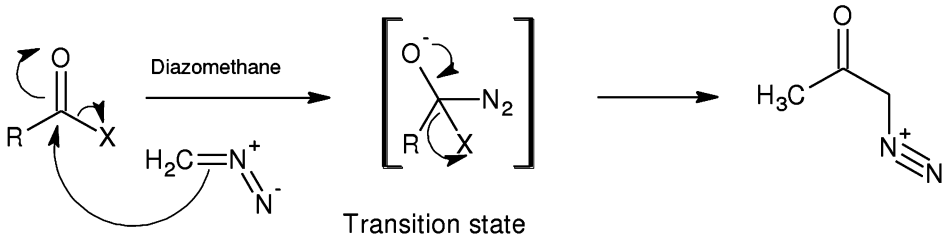
Aliphatic diazo compounds can be decomposed either photolytically or thermally to generate carbenes.

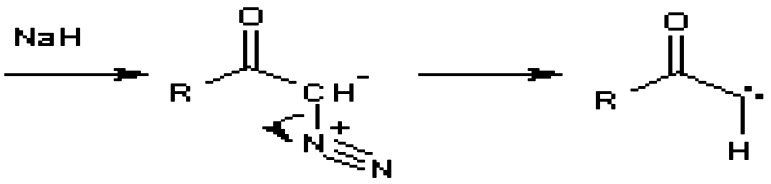
By ketones and aldehydes:



The carbene produced by this method is more stable than produced by α-elimination.

By acid halides:





Types of carbenes:

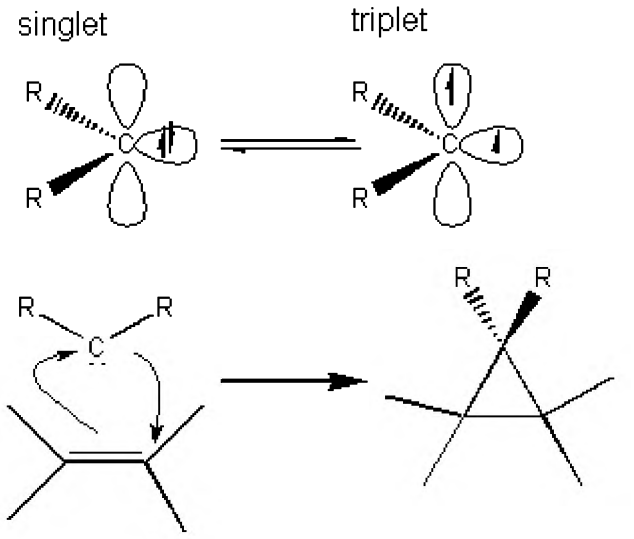
Carbene exists in two forms.

- Singlet
- Triplet

A singlet carbene contains two electrons in a **sp2** hybridized orbital and a vacant **p** orbital. The reaction with alkenes is thought to be concerted, whereas a triplet carbene has two unpaired electrons and would go through a stepwise mechanism. In the stepwise mechanism there would be free rotation about C-C single bonds and thus not stereospecific.

The triplet state is more stable then the singlet one. It is thought that only in the singlet state the carbene is added stereospecific. That is because it has an electrophillic character which allows transition state of free centers. In the triplet state the two electrons which don't take part at reaction are assigned each one to one of the free orbitals.

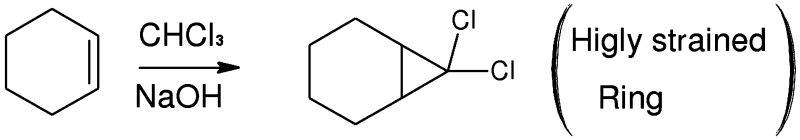
The conclusion is that is a theory that says that in singlet state if the carbene is a trans form results a trans form and if is a cis form results a cis form. If is in triplet state result both cis and trans.



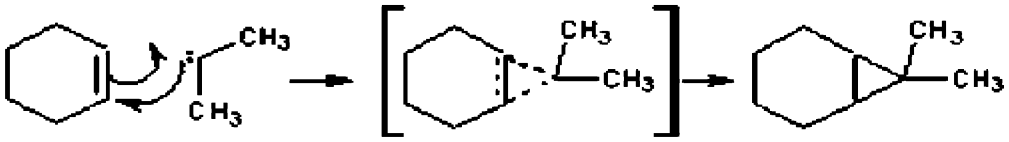
Applications or reactions of carbenes:

Carbenes can be isolated if it contain stable substituent. Mostly carbenes are short-lived due to unstability. Carbenes are electron deficient (contain a lone pair of electron).In organic chemistry carbenes is the only specie which carbon bearing lone electron pair is present.

Generation of singlet carbene:



Mechanism:

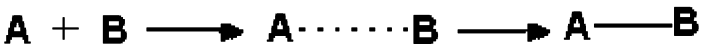


Transition state

Singlet and triplet carbenes react in different ways. So we have two types of mechanisms in organic chemistry which tells the procedure of a reaction.

1: Concerted Mechanism (One step mechanism)

In these types of reactions bond formation and bond breakdown take place simultaneously.

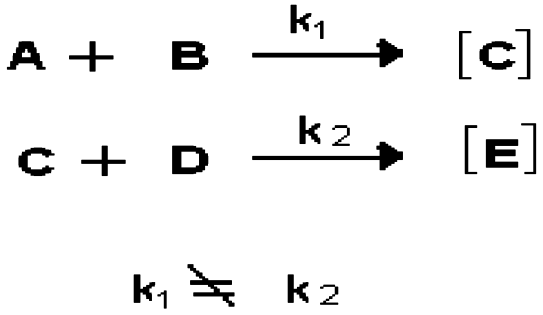


Transition state

Example: SN2 Mechanism (as above reaction of formation of carbene).

2: Step-wise Mechanism (involve more than one step)

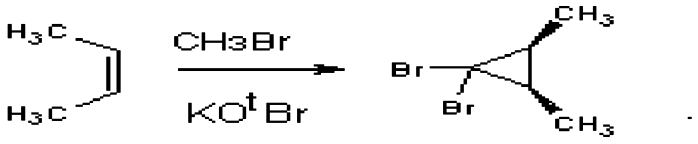
In these types of reactions bond formation and bond breaking take place in step wise.



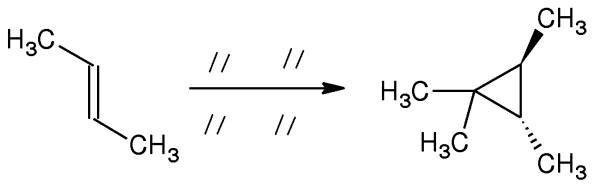
If k1 step is faster and k2 is slower than k2 shows the rate mechanism while if k2 is faster than k1 than k1 is slower and is rate determining step.

Example: SN1 Mechanisms

Cis-Butene:



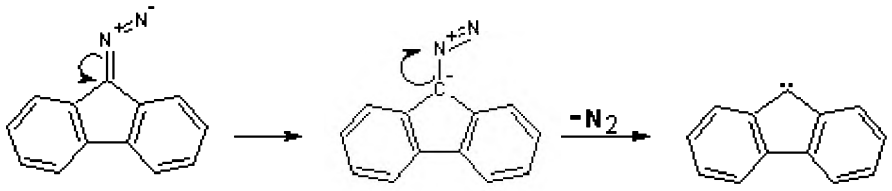
Trans-Butene:



If a singlet carbene is generated than by same reactants of Cis or Trans we will get the same product only substituent position is changed (in or out of the plane).

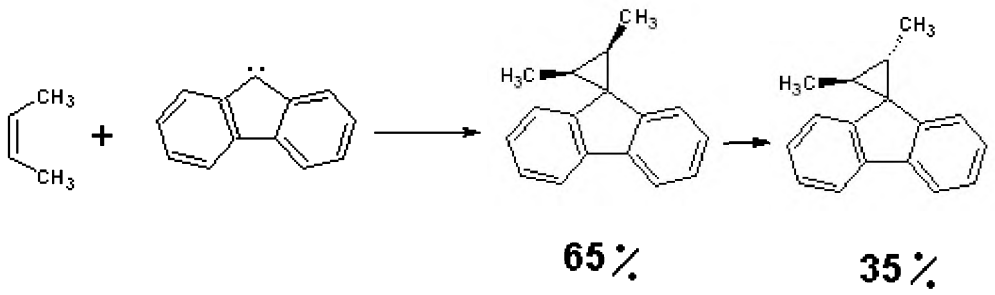
Generation of triplet carbene (diaryl carbene):

From Diazo Compounds:



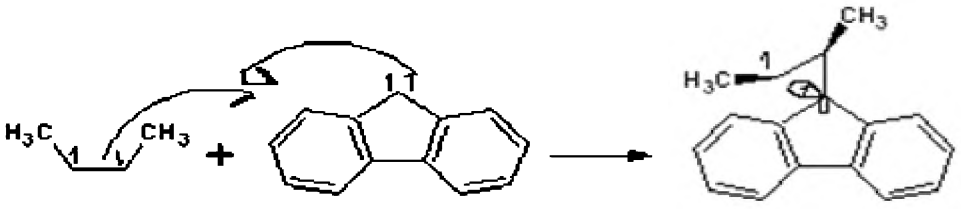
Reactions of triplet carbene:

Triplet carbene react with Cis-butene and gives two products. One is cis-product and 2nd is trans-product but percentage is different. Cis-product is 65% and trans-product is 35%.

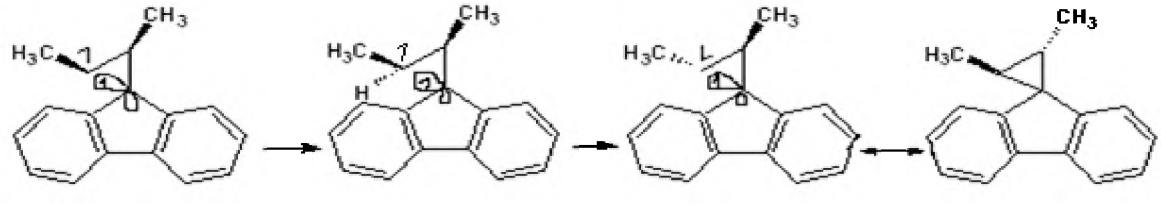


Mechanism:

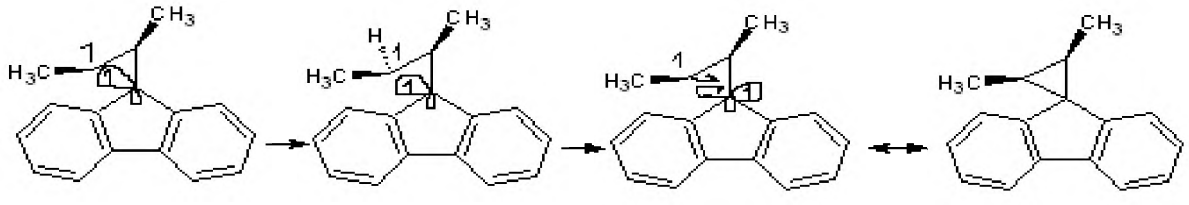
Single single electron of opposite spins from both reactants reacts to form a covalent bond.



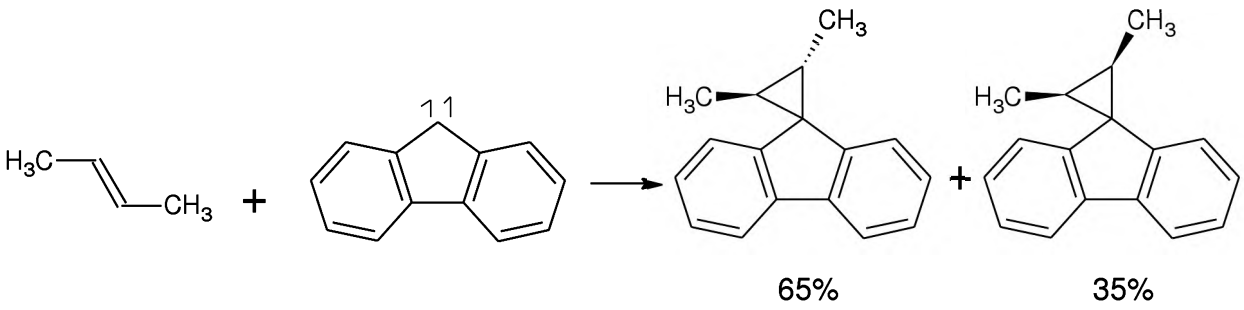
Now the electrons of same spins on the product react in two ways. First possibility is the electron not directly attached with carbene flipped and thus its spin will be changed then it will react with the electron directly attached to carbene to form a covalent bond. And Trans product is formed.



In 2nd possibility the electron directly attached with carbene flipped and thus its spin will be changed then it will react with the electron not directly attached to carbene to form a covalent bond. And Cis product is formed.

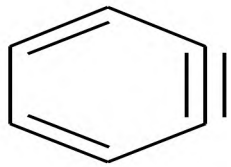


Triplet carbene react with Trans-butene is same way with different mechanism. But in this case percentage of cis and trans-products will be different or opposite. Like cis-product will be 35% and trans-product will be 65%.

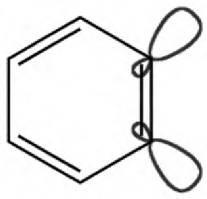


Benzynes

It has a simple structure having C-C two double bonds and C-C one triple bond. It have bond lengths not identical. One bond has short length than others.



If each triply bonded carbon atom in a benzyne molecule is sp-hybridized, as is typical of triply bonded carbon atoms, there would be severe angle strain in the molecule. It is more likely that each triply bonded carbon atom in a benzyne molecule is sp2-hybridized, in which case two sp2-hybridized orbitals that are not parallel to each other overlap laterally to form the pi bond that is not part of the loop of pi electrons **(2)**.

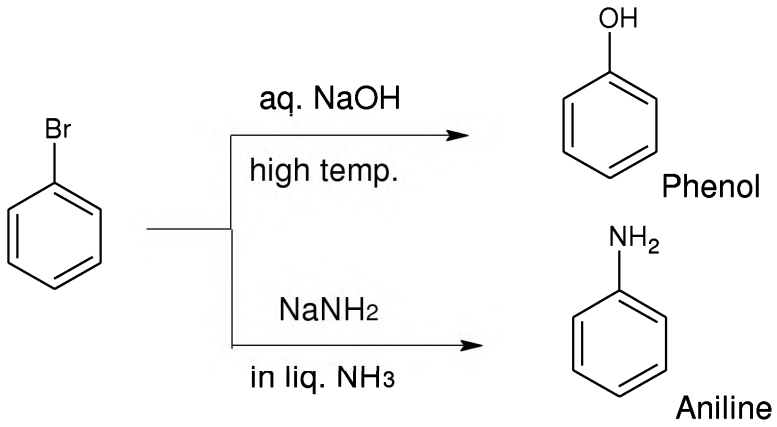


2

In either case, the pi bond in a benzyne molecule that is not part of the loop of pi electrons would be very weak, which is consistent with the observation that, despite being aromatic, benzynes are extremely unstable and reactive.

Preparation of Benzynes

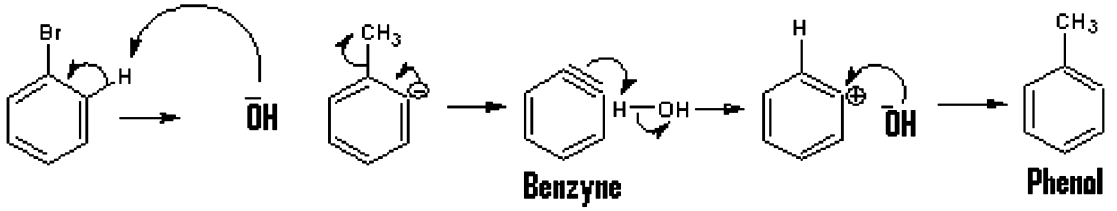
From Bromobenzene:



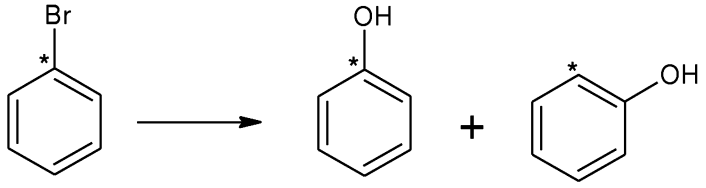
The high temperature of reaction shows that it is substitution reaction.

Mechanism:

It is not take place by simple substitution. Spectroscopy evidence also tells us existence of intermediate.

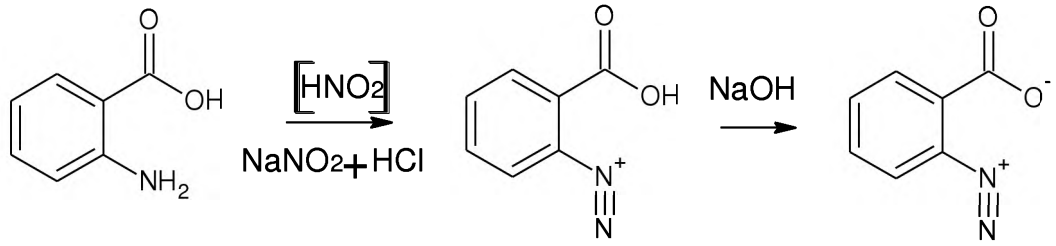


If isotopic carbon is present in benzyne ring than possibilities of two products are there.

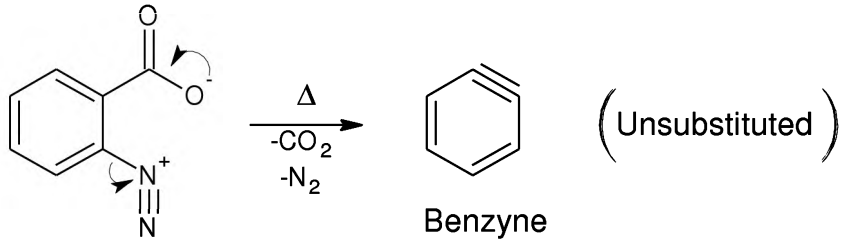


The mechanism of above reaction shows the existence of intermediate stage. Thus there are many evidences that benzynes are produced in these reactions as intermediate.

From 2-Amino benzoic acid (Anthranilic acid):

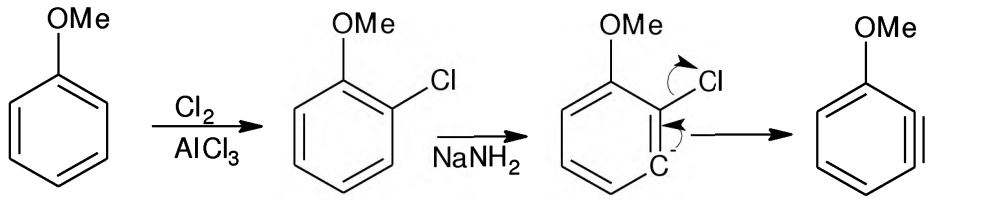


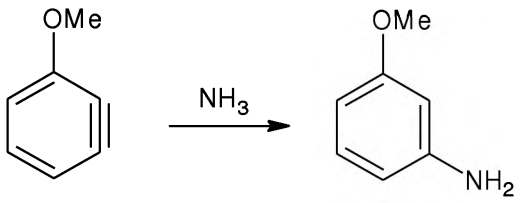
This process takes place in H_2O thus products are formed in the form of ions.



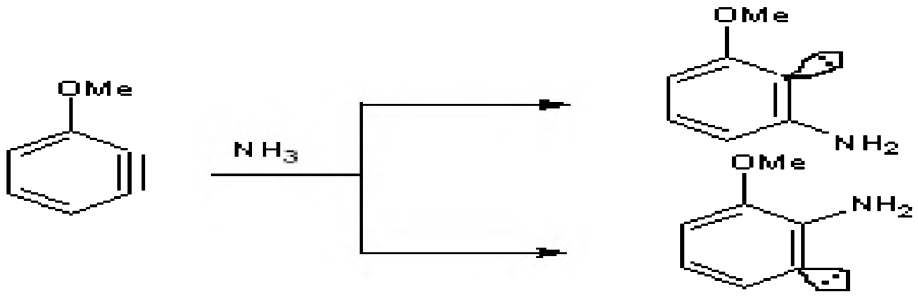
Generation of Substituted benzyne

By Freidal crafts Alkylation or Acylation:





The reaction of methoxy benzyne with ammonia gives evidence of two different intermediate stages which have different properties.

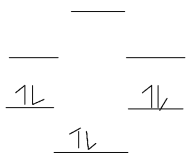


The intermediate product have negative charge between two substituent stabilized both neighbor's carbon and show resonance while other can't do this.

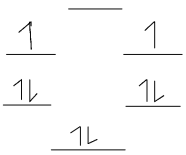
Structure of Benzyne:

By X-ray crystallography benzyne has two C-C double bonds and one C-C triple bond.

Configuration of benzyne compared to benzene:

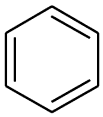


Benzene



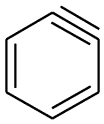
Benzyne (Antiaromatic)

ESR (Electron spin resonance) for free radicals is a technique and, thus benzyne shows positive ESR or able to detect.



C_6H_6

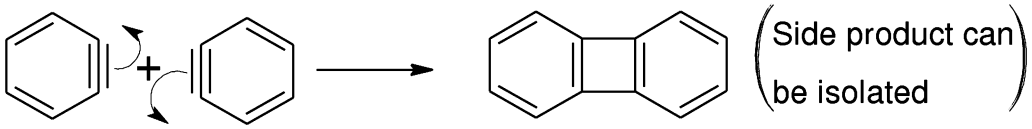
Atomic mass=78amv



C_6H_4

Atomic mass=76amv

Fusion of Benzyne atoms:



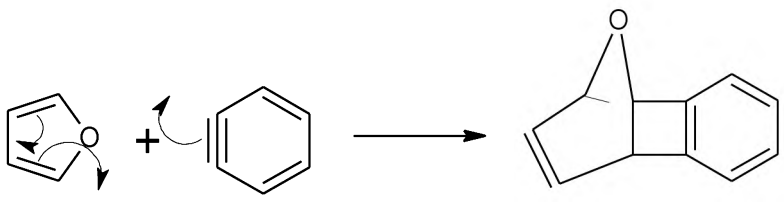
Atomic mass=152amv

This is the evidence by mass spectroscopy (MS) as benzyne has high electric potential.

Reaction of Benzyne:

Benzyne undergoes pericyclic reactions like Diel-Alder's reaction. Lots of natural products can be synthesized by addition of this six-membered molecule. One of example is as follow:

Diel-Alder's reaction (pericyclic reaction):

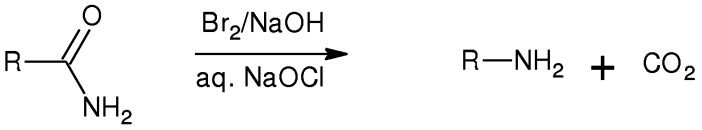


Furan Benzyne Bicyclo-Diel-Alder's Addict

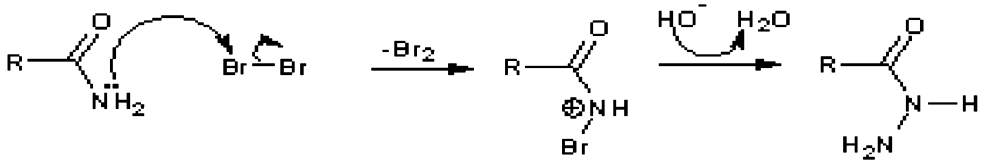
Nitrenes:

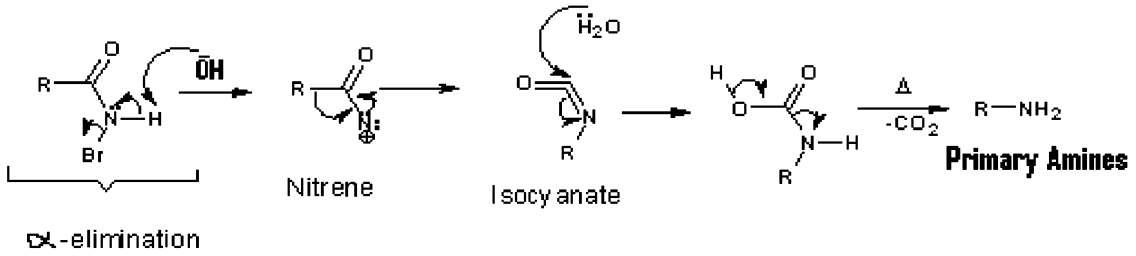
If nitrogen has electron pair (lone pair) likes carbene than it is called as nitrene. German chemist first generates nitrenes in Hoffmann Re-arrangement. Nitrogen bearing electron pair (non-bonding) is highly reactive and unstable.

Generation of Nitrenes:



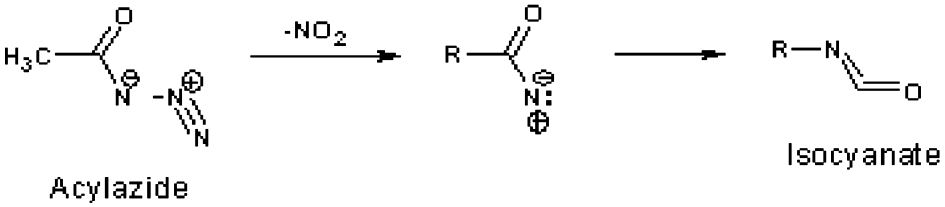
Mechanism:



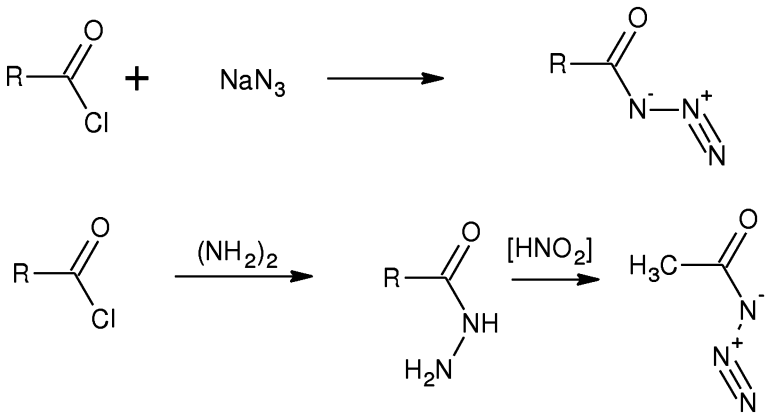


Nitrene is very electronegative than carbene. Nitrenes are reactive intermediate and have very poor stability. Purpose of generating carbene is to react it with further species. It can be trapped. But in case of nitrene, it is very difficult to trapped nitrene as it's very unstable and thus amine group migrate and formed primary amines.

Primary amines are not easy to prepare. It can be generate by reacting any alkyl group containing compound with ammonia. That's why separation of primary and secondary amines from a mixture is very difficult. There is some following other methods to generate nitrenes.



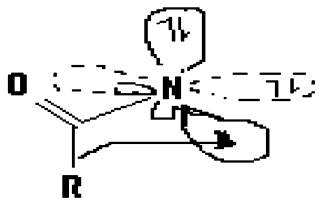
Preparation of Acylazide:



Acylazide upon heating evolves nitrogen gas and nitrenes.

Structure of Nitrene:

Its structure resembles with carbene's structure.



Chapter: 6

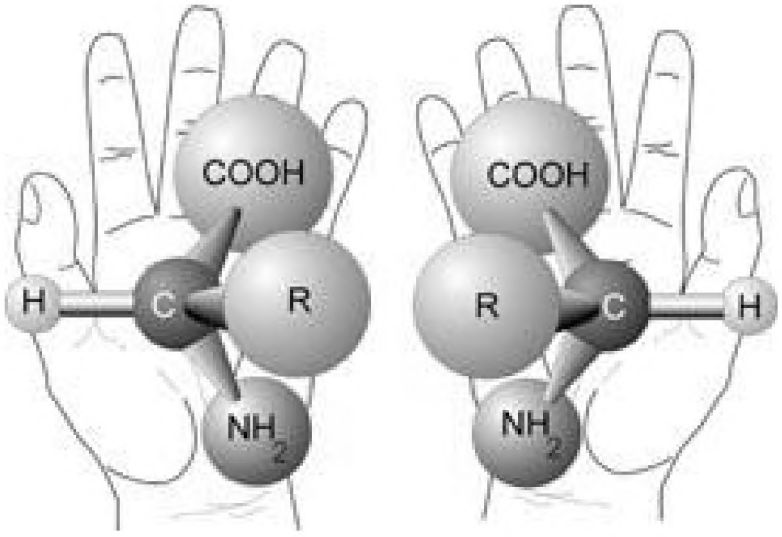
Stereochemistry

Stereochemistry, a sub discipline of chemistry, involves the study of the relative spatial arrangement of atoms within molecules. An important branch of stereochemistry is the study of chiral molecules.

Nature produces many compounds which show chirality. All amino acids except glycerine produced by nature are all chiral. Majority of medicine produced by nature are isolated from plants are all chiral compounds. Starch, glucose, cellulose, glycogen all are polymers of glucose, and glucose is a chiral molecule.

Chirality:

The term "chiral" (from the Greek for "hand") is applied to molecular systems whose asymmetry results in handedness; that is, the existence of a pair of nonsuperimposable mirror-image shapes (as illustrated by the relationship between one's right and left hands). The term **chiral** in general is used to describe an object that is non-superimposable on its mirror image. **Achiral** (not chiral) objects are objects that are identical to their mirror image. Human hands are perhaps the most universally recognized example of chirality: The left hand is a non-superimposable mirror image of the right hand. Many macroscopic examples of handed systems exist, including any object that features an inherent spiral or twist that can exhibit a left

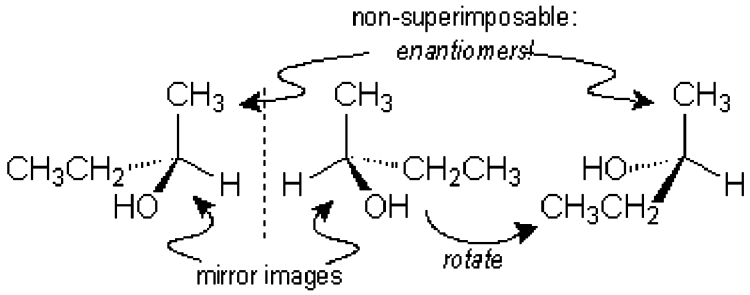


and right-handed form: scissors, spiral staircases, screw threads, gloves, and shoes.

In chemistry, chirality usually refers to molecules. Two mirror images of a chiral molecule are called enantiomers or optical isomers. Pairs of enantiomers are often designated as "right-" and "left-handed."

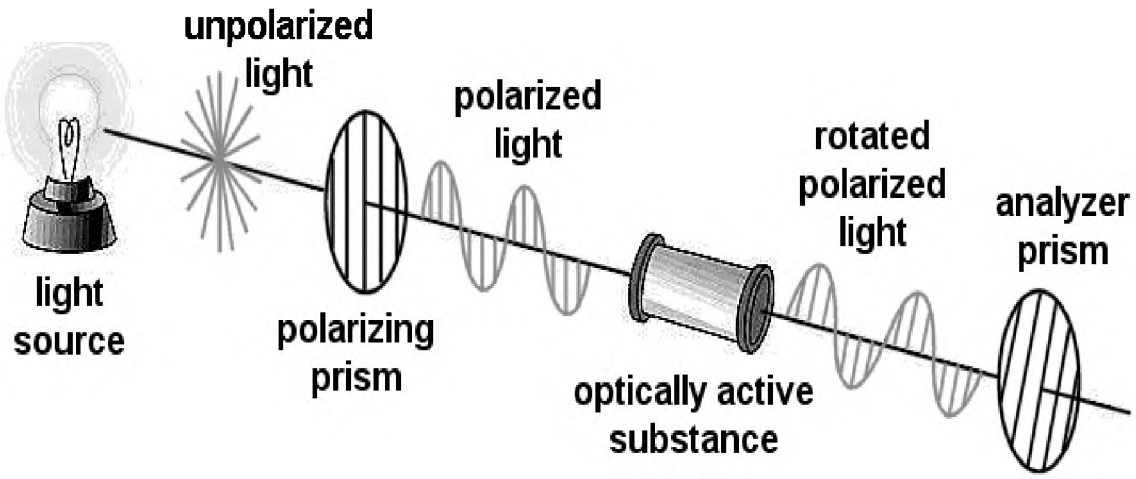
The two enantiomers of 2-butanol are shown at right. The mirror image of the first molecule can be rotated such that the -H and -CH_3 groups are in the same positions as in the original molecule. The -OH and -CH_2CH_3 groups are in the reverse positions, so the

mirror image is a different molecule: 2-butanol contains a chiral centre and exists as two enantiomers.

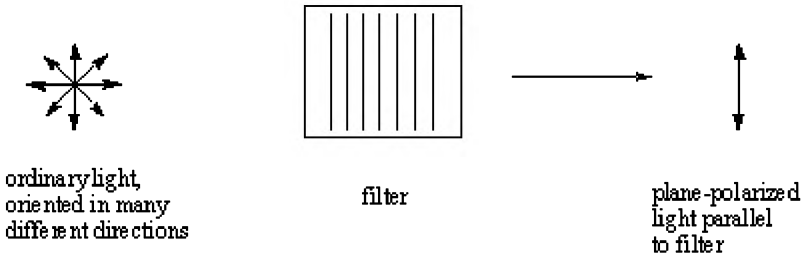


Optical Activity of Enantiomers

Plane-polarized light is also chiral, due to the relative orientations of the electrical and magnetic field oscillations. As a result, a solution of a chiral molecule can interact with such light, rotating the plane of polarization, a property called *optical activity*.

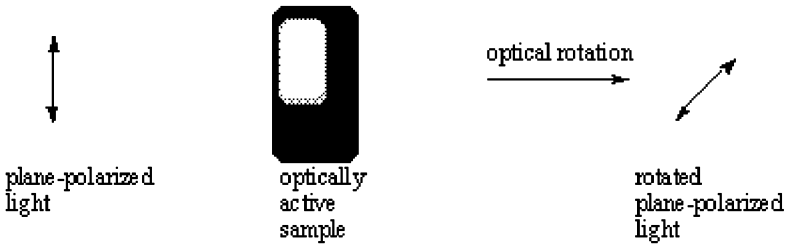


The light that we typically see is unpolarized; that is, it consists of waves that are oriented in every possible direction in an even distribution. We can pass unpolarized light through a polarizing filter to obtain plane-polarized light, which consists of light waves oriented in only a single direction.



Plane-polarized light

Solutions of chiral compounds have the property of rotating plane-polarized light passed through them. That is, the angle of the light plane is tilted to the right or to the left after emerging from the sample. Achiral compounds do not have this property. The ability of a solution to rotate plane-polarized light in this fashion is called optical activity, and solutions which have this ability are said to be optically active.



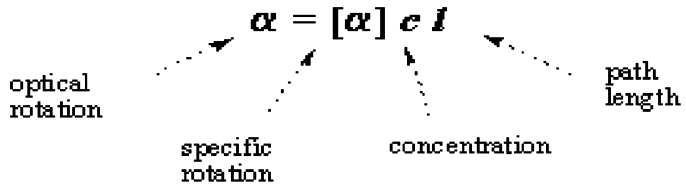
Rotation of plane-polarized light by optically active compounds

Using a technique called polarimetry; optical activity is measured by a device called a polarimeter. Monochromatic light (light containing a single color) is filtered through a polarizer to produce plane-polarized light, and it is passed through the sample. A second filter is placed with its slits parallel to those of the first filter, and then the sample is rotated until light is transmitted through the second filter. The number of degrees the sample is rotated is called the optical rotation of the sample. If rotation occurs to the right (clockwise), the optical rotation is given a + sign and the sample is considered dextrorotary. If rotation occurs to the left (counter-clockwise), the optical rotation is assigned a--sign and the sample is levorotary.

- The **d** or **(+)** optical isomer rotates the light plane clockwise (*dextro*rotary)
- The **l** or **(-)** optical isomer rotates the light plane counter-clockwise (*levo*rotary)

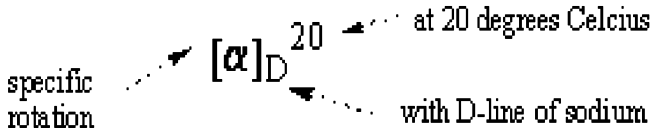
Wavelength of Na-lamp is represented by D, it has two values D1 and D2 but mostly used in D1. Na-lamp is a standard lamp is used mostly in optical activity having wavelength 589.3nm.

The optical rotation of a given sample varies with its concentration and the light's path length:



Dependency of the optical rotation on concentration and path length

The proportionality constant [α] is *characteristic* of a particular chiral compound for fixed wavelengths of light and fixed temperatures. The constant is called the specific rotation of the compound. Chemists have compiled a large volume of specific rotation data, using as standard conditions the D-line of sodium as the light source and a temperature of 20 degrees Celsius. Specific rotations are usually reported in this manner:



A chiral compound has a specific rotation that is equal in magnitude but opposite in direction from its enantiomer. This type of symmetry is expected given that enantiomers are mirror images. For instance, one enantiomer of 2- butanol has a specific rotation of +13.5 degrees while the other enantiomer of 2-butanol has a specific rotation of -13.5 degrees. The pair can be designated as (+)-2-butanol and (-)-2-butanol or (d)-2-butanol and (l)-2-butanol, where (d) and (l) correspond to dextrorotary and levorotary, accordingly. Note, however, that *designations of optical activity do not correlate with absolute (R)/(S) configurations.* A (+) compound might have an (R) or (S) configuration. It is impossible to tell the absolute configuration of a substance from its specific rotation. This holds for the reverse process as well: it is difficult to predict the specific rotation of a compound given its absolute configuration

Dependence of optical rotation:

1. Concentration of solution (c)
2. Path length (ℓ)
3. Solvent
4. Temperature
5. Wavelength of radiation (λ)

Concentration and path length effects hugely on optical rotation while solvent, temperature and wavelength of radiations affect a small difference on optical rotation.

Conc. α θ α

C α α (θ)

More concentration more the value of “α”

Path length α α

α α ℓ

More the path length more the value of α

α α c

α α ℓ

α α c ℓ

α = [α] c ℓ

$$[\alpha]^{T}_{\lambda} = \frac{\alpha}{c\,l}$$

For sodium-lamp

$$[\alpha]^{T}_{D} = \frac{\alpha}{c\,l}$$

Temperature is reported in degree celcius "°C"

Units:

Unit of path length in SI system is "dm". While unit of concentration when organic compound is in liquid state is "g/cm³" and if organic compound is in solid state than its units will be "g/100ml".

So for liquids optical rotation have formula as:

$$[\alpha]^{T}_{D} = \frac{100\,\alpha}{d.l}$$

So for solids optical rotation have formula as:

$$[\alpha]^{T}_{D} = \frac{100\,\alpha}{c\,l}$$

Normally path length is "1" or l = 1 so

$$[\alpha]^{T}_{D} = \frac{100\,\alpha}{c}$$

Calculation of concentration:

Molar rotation = Molecular mass × Specific rotation / 100

Or

$$[M]^{20}_{D} = \frac{M \times [\alpha]^{20}_{D}}{100}$$

Or

$$[M]_D^{20} = \frac{M \times 100\alpha}{c \cdot 100}$$

Example:

m = 28 mg = 0.028g

V = 1ml

1ml = 0.028g

100ml = 0.028 X 100 = 2.8g/100ml

C = 0.028 g/ml

Solvent = Ethanol

l = 10 cm = 1 dm

Molar mass of acid = M = 152 amv

α = - 4.35°

T = 20℃

$$[\alpha]_D^{20} = \frac{(-4.35)100}{0.028 \times 1}$$

$$[\alpha]_D^{20} = -155.4^{\circ}$$

-155.4° represents the specific rotation.

For molar rotation,

$$[M]_D^{20} = \frac{152\ (-155.4^{\circ})}{100}$$

$$[M]_D^{20} = -236$$

Chirality is the property of organic compounds which show optical rotation in optical activity.

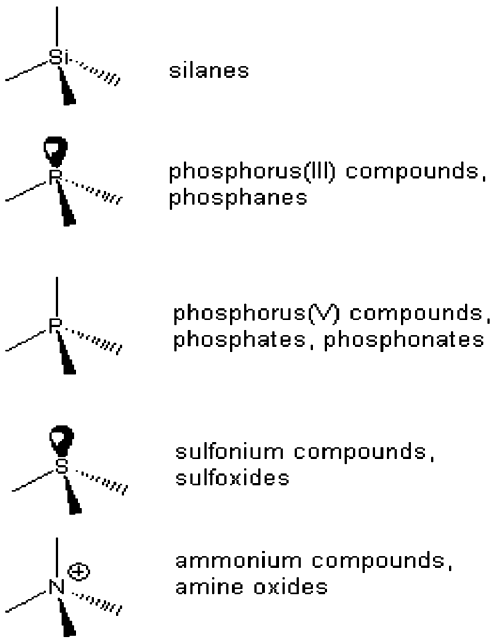
Elements of chirality:

- Centre of chirality
- Axis of chirality
- Plane of chirality
- Helicity of chirality

Centre of chirality:

Each atom that carries four different substituents in a tetrahedral arrangement is a chirality center.

Silicon and germanium are, like carbon, elements of the fourth main group and appear as chirality centers in chiral compounds. Nitrogen, as an element of the fifth main group, possesses a special characteristic. In amines, it carries three substituents and a lone electron pair. Including the lone electron pair, it is tetrahedrally surrounded by four "substituents" and is sp^3-hybridized. In amines, nitrogen could therefore appear as a chirality center. A molecule with four substituents (a, b and c, d) arranged in pairs around an axis are chiral if these pairs don't lie in the same plane and each pair consists of two different substituents.



Axis of chirality:

A molecule with four substituents (a, b and c, d) arranged in pairs around an axis is chiral if these pairs do not lie in the same plane and each pair consists of two different substituents (that is, a is unequal b and c is unequal d).

This type of chirality is illustrated by certain molecules with cumulated double bonds.

In the alkenes 1, 3-dichloropropadiene, for instance, two planes are defined by carbon C1 and its substituents hydrogen and chlorine, as well as C3 and its substituents hydrogen and chlorine. These planes are perpendicular. The molecule shows D_2 point symmetry. The main C_2 symmetry axis of the D_2 point group lies along the cumulated double bonds. In the case of chiral molecules, this is called **chirality axis**. The two C_2 axes of the D_2 point group are perpendicular to the main C_2 axis, lie within the planes of the formerly mentioned molecule, and pass through carbon C2. A prerequisite of the chirality of alkenes, such as 1, 3-

dichloropropadiene, is the prevention of the rotation of carbon-carbon double bonds. 1, 3-Dichloropropadiene contains no asymmetric carbon atom. However, it is chiral.

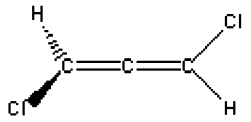


Figure 1

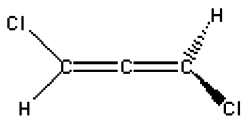


Figure 2

Plane of chirality:

Chirality does not result only from a chirality center or chirality axis, but may also arise from another chirality element, namely a **chirality plane**. A chirality plane is the plane of a structural fragment in a chiral molecule that cannot lie in a symmetry plane because of restricted rotation or structural requirements. The enantiomers of such a chiral molecule differ in the spatial arrangement of the remaining atoms of the molecule with respect to the chirality plane.

13-Bromo-1, 10-dioxa [8] paracyclophane is an example of a chiral and optically active ansa compound. The chirality plane lies inside the plane of the aromatic ring. The rotation of the aromatic ring is restricted by sterric interactions between the aliphatic bridge and the bromine at the aromatic ring.

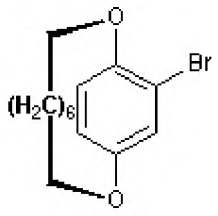


Figure 3

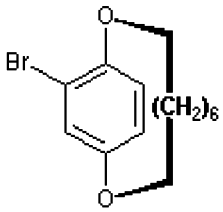


Figure 4

Helicity of chirality:

A special case of **chirality axis** appears in molecules with a **helical** shape. Helices are chiral objects that look like screws and can therefore be right or left-handed respectively. In nature, this type of chirality is frequently found, for example, in mussel or snail shells. A helically shaped molecule, that is of great interest for chemists and biologists, is deoxyribonucleic acid (DNA), which appears in two right-handed (A- and B-helix) and one left-handed (Z-helix) types of helices. The DNA backbone is winded around the chirality axis. A helix's rotational sense, or **helicity**, can be ascertained by following the chirality axis from the end of the helix. It does not matter from which end of the helix the molecule is viewed, because the result of ascertaining the helicity of a particular molecule is always the same.

Hexahelicene is a well-known helically-shaped molecule (view animation). Hexahelicene is chiral and its enantiomers do not easily interconvert. Therefore, it is optically active and the

enantiomers can be separated from each other. One enantiomer forms a right-handed helix, while the other enantiomer forms a left-handed one. The helical shape of hexahelicene is forced by the sterric interaction of the overlapping terminal aromatic rings.

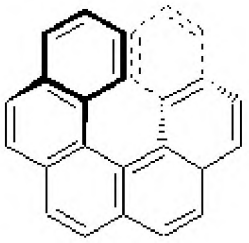


Figure 5

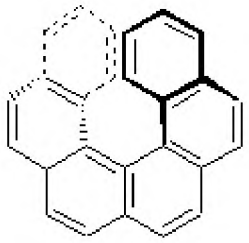


Figure 6

These elements of chirality when present in an organic compound, there presence in chiral compounds is shown by different symbols. Like as follow,

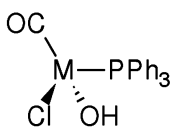
Centre of chirality is shown by **R & S** symbols.

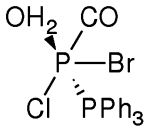
Axis of chirality is shown by **aR & aS** symbols.

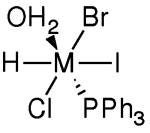
Plane of chirality is shown by **pR & pS** symbols.

Helicity of chirality is shown by **M & P** symbols.

In organic chemistry we deal with carbon containing compounds, so being carbon is tetravalent we prefer the four substituents. But if central atom contain more than four substituents than that would be chiral. Metals are penta or hexavalent; these metals contain more than four substituents and thus show chirality.







It is not essential for a compound to show chirality, it should have four substituent. It could be more than four. But minimum criteria for chirality are, the chiral compound should have four substituent.

Symmetry:

The symmetry of a molecule is determined by the existence of **symmetry operations** performed with respect to **symmetry elements**. A symmetry element is a line, a plane or a point in or through an object, about which a rotation or reflection leaves the object in an orientation indistinguishable from the original.

Elements of symmetry:

The presence of a single chiral center indicates chirality of a molecule. Another way to recognize chirality is to detect the presence of some symmetry elements.

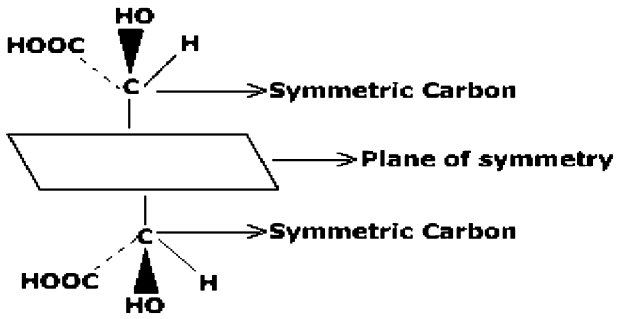
A molecule will not be chiral if it possesses:

1. a plane of symmetry (δ)
2. a center of symmetry (S)
3. An n fold alternating axis of symmetry (S_n or C_n) where n is an even number.

These three are called elements of symmetry.

Plane of symmetry:

A plane that divides an object into two identical halves is called plane of symmetry. Its also called mirror plane as it cuts a molecule into two parts, where one is the mirror image of the other. Molecules having such a plane are always inactive due to internal compensation. For e.g., meso tartaric acid has a plane of symmetry.



Mesotartaric acid

There are two symmetric carbon atoms and they are therefore achiral. Hence meso tartaric acid is optically inactive. Plane of symmetry is of two types: vertically (δv) and horizontally (δh).

CH_4:

If we pass a plane from centre of the molecule vertically than both h will be mirror image of each other. Thus it have plane of symmetry with value 9δv and have no δh.

CH_3CL: Only have 3δv and no δh.

CH_2Cl_2 have 3δv and no δh.

$CHCl_3$ have 3δv and no δh.

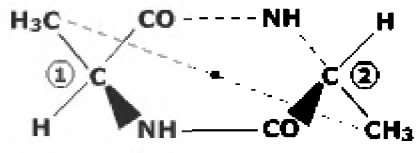
CCl_4 have 9δv and no δh.

In tetrahedral molecule we never ever get Sh because if we cut tetrahedral structure horizontally both halves will not mirror image of each other.

Center of symmetry:

The center of symmetry is an imaginary point in the molecule. If a line is drawn from an atom or a group of the molecule to this imaginary point and then extended to an equal distance

beyond the point, it meets the mirror image of the atom or group. For e.g., trans-1, 4-dimethyl-diketopiperazine has a center of symmetry and therefore optically inactive.



Trans - Dimethyl - Diketopiperazine

If a line is drawn from methyl group on carbon 1 to the center of symmetry and extended beyond this point by an equal distance it meets the methyl group at carbon 4, therefore it is optically inactive.

Ethane: The value of centre of symmetry for ethane is S_2.

Axis of symmetry:

When a structure is rotated through an angle of 2p/n about an imaginary axis and then reflected across a plane perpendicular to the axis, an identical structure results.

If we pass an imaginary line through an axis of an object (may be organic or inorganic molecule) it rotates the angle n =360°/θ .If we rotate the axis at 90° we get undistinguishable form of molecule. Θ = 120° (by rotating the molecule of CH_4 we get the undistinguishable form with angle of 120°).

n = 360/120 =3 so C_4 is present in methane. And we can say that axis of CH_4;

C_4 = Θ = 90°, C_3 = Θ = 120°, C_2 = Θ = 180°

$4C_3$ called point group or symmetrical groups.

Where "4" indicates that there are four number of axis in CH_4.

For CH_3CL:

If we rotate this molecule at 120° we get distinguishable form, only one axis is along x-axis and thus it have only $1C_3$ in chloromethane. If we pass the axis between the bonds than we get the undistinguishable form by rotating 180°.And thus we get $4C_2$ is also present in CH_4 molecule.

CH_2Cl_2:

In this molecule rotation at all axis gives distinguishable form. Only two axis in CH_2Cl_2 which are undistinguishable and have $2C_2$ (between hydrogen and chlorine atoms).

$CHCl_3$:

Only one axis (carbon-hydrogen bond) which is undistinguishable and get only C_3 .No C_2 is present.

CCl_4:

Along all halogen bond carbon shows undistinguishable form and have $4C_2$ and $4C_3$.

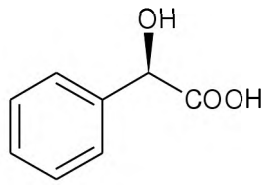
CH_4 and CCl_4 have same axis of symmetry or have similar behavior.

CH_3Cl and $CHCl_3$ shows similar behavior.

CH_2Cl_2 shows exceptional behavior.

From all these elements of symmetry we can tell which molecule or compound show symmetry or chirality. To understand this phenomena lets took example of some organic compounds as follow:

Mandelic acid:

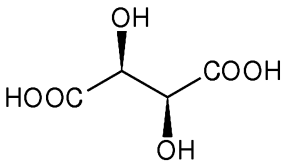


- It have no axis of symmetry (if we rotate this molecule from any side we get distinguishable form).
- It have no plane of symmetry as well.
- It have no centre of symmetry.

Mandelic acid have no symmetry and thus called as unsymmetrical molecule but it still shows chirality (rotate the polarized light).

It is not compulsory that compounds show chirality should be symmetrical or unsymmetrical. But we can say that asymmetrical molecules show chirality. As there are 90% molecules which are asymmetrical and shows chirality but there are also some exceptions that symmetrical molecules also shows chirality.

Tartaric acid:

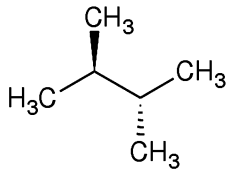


- No axis of symmetry as when we rotate this molecule from any side we get distinguishable form.
- If we bisect this molecule vertically we get the mirror images.
- It shows centre of symmetry.

This molecule is symmetrical so it is not chiral or achiral.

Presence of asymmetrical centers (carbon) does not mean that it is chiral. We should measure the elements of symmetry in that molecule. Asymmetric centre in which central atom attached to four different substituents or more than it, while asymmetrical is that in which elements of symmetry are present. The molecule have asymmetric centre or carbon even be chiral.

Isomer of tartaric acid:



C_n : C_2

δn : 0δv = no

Sn : 0Sn = no

This is symmetrical molecule but it shows chirality (as if we place polarized light in its path it will rotate the light).

Conclusion:

Tartaric acid is itself an achiral molecule but its isomer shows chirality because the two substituents attached with it, one is above the plane other is below the plane.

Symmetrical: If all elements of symmetry or one and two elements are present.

Asymmetrical: If no elements of symmetry are present.

Dissymmetrical: If only axis of symmetry is present and other two are absent.

Isomerism

Compounds having the same molecular formula, but differing in physical and chemical properties are known as isomers. This phenomenon is known as isomerism.

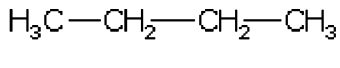
Isomers may be classified into two types viz,

- Regioisomers (structural isomers)
- Stereoisomers

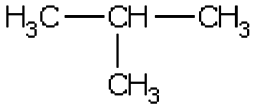
Regioisomers:

Structural isomerism arises due to the difference in the arrangement of atom in the molecule i.e., the isomers have different structure. There are five different ways in which the structural isomerism arises. These are:

Skeletal isomers: This type of isomerism arises from the difference in the nature, structure of the carbon chain. For example, for butane (C_4H_{10}), the following arrangements are possible.



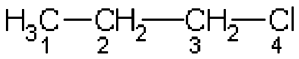
n-butane (butane)
(straight chain)



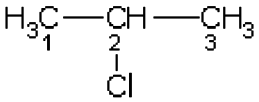
iso-butane (2-methylpropane)
(branched chain)

Positional isomers: This isomerism arises due to the difference in the position of the same functional group or the same substituent while the arrangement of carbon atoms remains same. For example,

Chloropropane (C_3H_7Cl) can have two positional isomers given below.



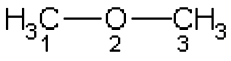
(n-propyl chloride)
(1-chloropropane)



(iso-propyl chloride)
(2-chloropropane)

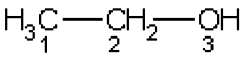
Functional isomers: The compounds having the same molecular formula but different functional groups are said to exhibit functional isomerism. Such compounds are termed functional isomers. For example, there are two compounds having the molecular formula C2H6O viz,

Ether



(methoxymethane) dimethyl ether

Alcohol



(ethanol) ethyl alcohol

Stereoisomers:

Stereoisomers have the same structure and bond order but their atoms and groups of atoms are arranged differently in space. They have different *spatial arrangements* and their molecules are not *superimposable*. There are two types:

- Configurational isomers (due to configuration of atoms)
- Conformational isomers

Configurational isomers:

The three-dimensional arrangement of atoms or groups attached to a chiral centre is called the configuration. Isomers with chiral centers are normally asymmetric molecules that do not have a plane or centre of symmetry. Achiral molecules are symmetrical molecules that have

a plane or centre of symmetry. Configurational isomers are further classified in to three types viz,

- Enantiomers
- Diasteroisomers
- Epimers

Conformational isomers:

In chemistry, **conformational isomerism** is a form of stereoisomerism in which the isomers can be interconverted exclusively by rotations about formally single bonds.

Example: Atropisomers

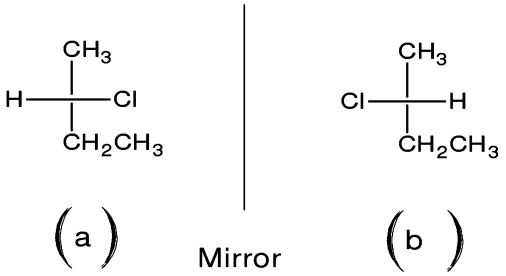
Enantiomers: Organic compounds that contain an asymmetric (*chiral*) Carbon usually have two non-superimposable structures. These two structures are mirror images of each other and are, thus, commonly called enantiomers.

Examples: Lactic acid

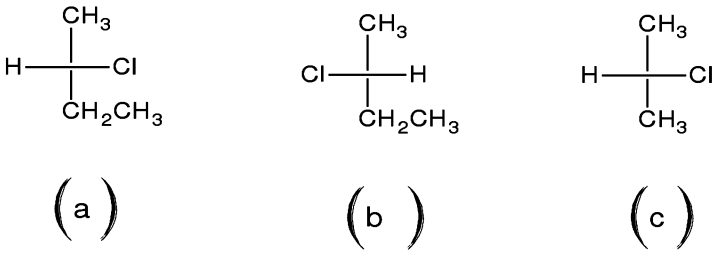
Diasteroisomers: Diastereomers are stereoisomers that are not enantiomers (mirror images) of each other. Due to their different shape, diastereomers can have different physical and chemical properties. This is perhaps especially true of diastereomers involved in biological systems.

Examples: D-Threose

An organic compound which shows isomerism has different isomeric forms some of them are enantiomers of each other and some are diastereomers. To understand this phenomenon lets take an example of 2-chlorobutane.



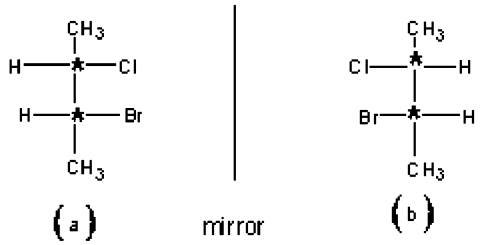
Rotating structure (b) 180° in the plane of the paper, the only allowable rotation, does not lead to a form that is superimposable on structure (a). Rotations of less than or more than 180° are not allowed because in a two-dimensional projection, it is impossible to see the difference in the position of atoms that are located in front of or behind the plane.



0° rotation 180° rotation of (b)

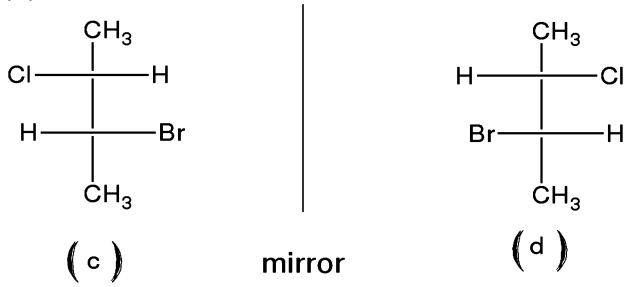
Structures (a) and (b) are the only pair of enantiomers for 2-chlorobutane.

The compound 2-chloro-3-bromobutane has two stereogenic centers and a maximum of four enantiomers. Compare these two Fischer projections.



***Steriogenic centre**

Structure (*b*) cannot be superimposed on structure (*a*) by rotating it in the plane of the page, so structures (*a*) and (*b*) are enantiomers. The additional two enantiomers are created by allowing rotation about one of the stereogenic centers while restricting rotation about the other. Structure (*c*) is created by allowing rotation about the upper stereogenic center (carbon 2) of structure (*a*).

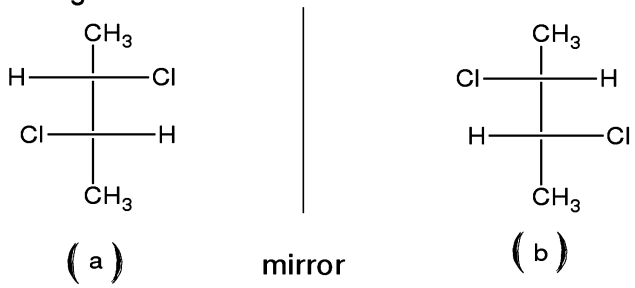


Notice that structure (*c*) has a different configuration from structures (*a*) and (*b*). Structure (*d*), the mirror image of (*c*), cannot be superimposed on structure (*c*) by rotating it in the plane of the page. Therefore, structures (*c*) and (*d*) are enantiomers. Any further rotation about the stereogenic centers creates a structure that is already drawn. For example,

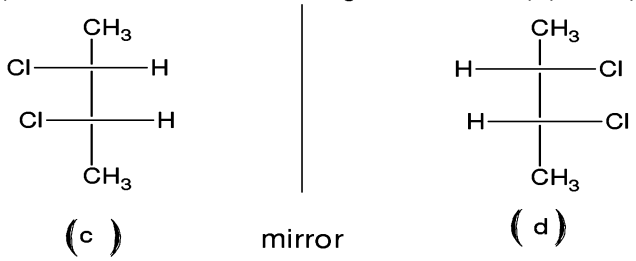
starting with structure (*a*) and allowing rotation about the lower stereogenic center (carbon 3) generates structure (*d*) again. This situation agrees with the maximum number of enantiomers predicted by the van't Hoff rule: $2^n = 2^2 = 4$.

The relationship between the enantiomers of separate enantiomorphic pairs is called **diastereoisomerism.** For example, while structures (*a*) and (*b*), and (*c*) and (*d*), are enantiomers, the relationship of (*a*) to (*c*) is one of diastereoisomerism. They are not mirror images, so structure (*a*) is a **diastereomer** of structures (*c*) and (*d*). Likewise, structure (*b*) is a diastereomers of structures (*c*) and (*d*). In the same fashion, structures (*c*) and (*d*) are diastereomers of (*a*) and (*b*). **Enantiomers** have opposite configurations at all stereogenic centers, while **diastereomers** have the same configuration at one or more stereogenic centers but opposite configurations at others.

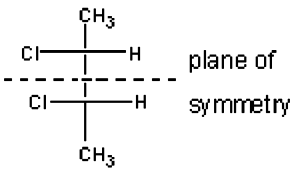
Optically inactive stereogenic centers (meso forms). Some molecules are optically inactive even though they contain stereogenic centers. These compounds normally contain a **plane of symmetry.** The compound 2, 3-dichlorobutane should have four enantiomers because it has two stereogenic centers.



Structure (*b*) cannot be superimposed on structure (*a*) by rotating it in the plane of the page; thus, structures (*a*) and (*b*) are enantiomers. Rotation about the upper stereogenic center leads to structure (*c*), which is a different configuration from (*a*) and (*b*).



Structure (*d*) is the mirror image of (*c*). It can be superimposed on (*c*) by rotating it 180°. Because these two structures are superimposable mirror images, they are not optically active, even though they contain two stereogenic centers. The reason for this lack of optical activity is the plane of symmetry through the center of the molecule.

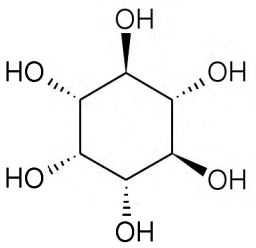


These types of molecules are called *meso* forms. In ***meso* forms,** the stereogenic centers are optically active, but due to the molecular symmetry, they rotate plane-polarized light to the same degree but in opposite directions. This phenomenon results in an internal cancellation of optical activity.

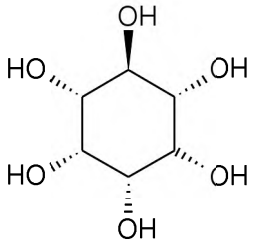
Epimers: In chemistry, **epimers** are diastereomers that differ in configuration of only one stereogenic center. Diastereomers are a class of stereoisomers that are non-superposable, non-mirror images of one another. In chemical nomenclature, one of the epimeric pairs is given the prefix **epi-** for example in inositol and *epi-inositol.*

Examples: Epi-inositol

Inositol and epi-inositol are epimers of each other and have six asymmetric centers have opposite configuration at one centre and rest five are similar.

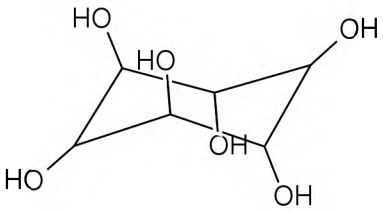


Inositol



Epi-inositol

Inositol naturally exists in chair form. Epi-inositol looking have plane of symmetry so should be achiral, but in actual have no plane of symmetry and thus is chiral.



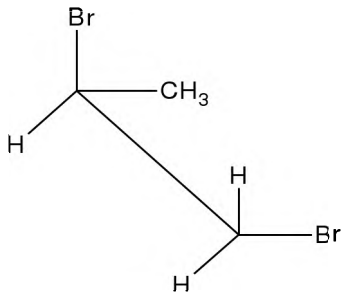
Drawing three dimensional structure on two dimensional paper

There are three methods of drawing three dimensional structures on two dimensional paper, which are follow as;

1. Sawhorse projections
2. Newman projections
3. Fischer projections

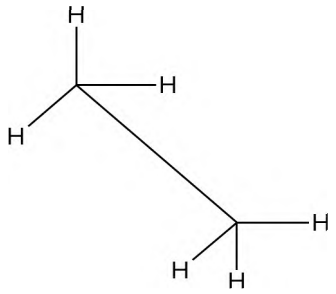
Sawhorse projections: A perspective formula indicating the spatial arrangement of bonds on two adjacent carbon atoms. The bond between the two atoms is represented by a

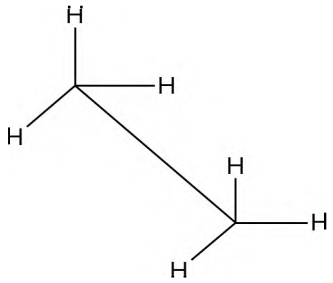
diagonal line, the left-hand bottom end of which locates the atom nearer the observer and the right-hand top end the atom that is further away.



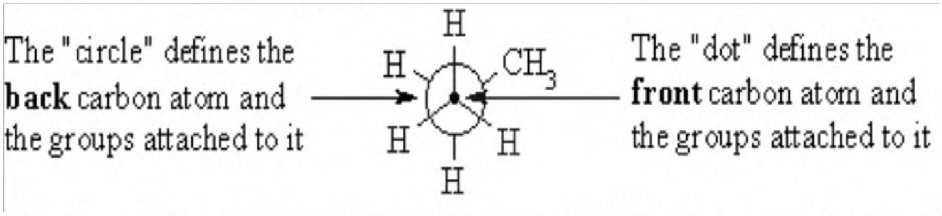
Sawhorse Projections are very similar to Newman Projections, but are used more often because the carbon-carbon bond that is compressed in a Newman Projection is fully drawn out in a Sawhorse Projection. When properly laid-out, Sawhorse Projections are useful for determining enantiomeric or diasteromeric relationships between two molecules, because the mirror image or superimposibility relationships are clearer.

Like with Newman Projections, a Sawhorse Projection is a view of a molecule down a particular carbon-carbon bond, and groups connected to both the front and back carbons are drawn using *sticks* at 120 degree angles. Sawhorse Projections can also be drawn so that the groups on the front carbon are *staggered* (60 degrees apart) or *eclipsed* (directly overlapping) with the groups on the back carbon. Below are two Sawhorse Projections of ethane. The structure on the left is staggered, and the structure on the right is eclipsed. These are the simplest Sawhorse Projections because they have only two carbons, and all of the groups on the front and back carbons are identical.



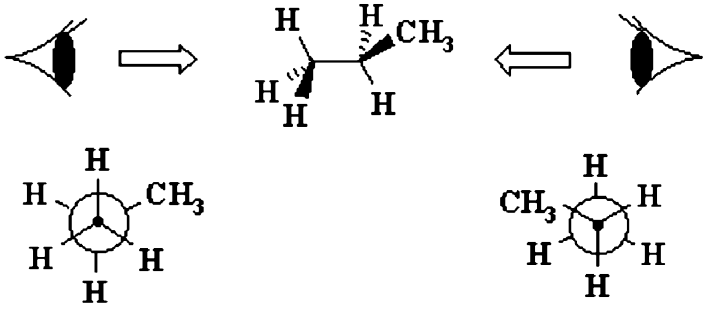


Newman projections: These projections are drawn by looking directly along a particular bond in the system (here a C-C bond) and arranging the substituents symmetrically around the atoms at each end of that bond. The protocol requires that the atoms within the central bond are defined as shown below:



In order to draw a Newman projection from a wedge-dash diagram, it is useful to imagine putting your "eye" in line with the central bond in order to look along it. Let's work through an example, consider drawing a Newman projection by looking at the following

wedge-dash diagram from the left hand side.
• First draw the dot and circle to represent the front and back C respectively.
• Since the front carbon atom has an H atom in the plane of the page pointing up we can add that first.
• The back carbon atom has an H atom in the plane of the page pointing down.
• Now add the other bonds to each C so that it is symmetrical.
• The groups / bonds (blue) that were forward of the plane of the page in the original wedge-dash diagram are now to our right.
• Those behind (green) the plane are now to our left.

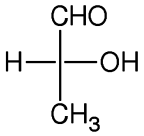


- Try the same thing, but looking from the right to generate the other Newman Projection.

Limitations of sawhorse and newman projections

To draw 3D structure on 2D paper by these two methods there should be two asymmetric carbon centers. Sawhorse and newman projections are failed to draw structure of enantiomers contain one asymmetric center and more than two asymmetric centers. So for drawing the structure of compounds with one and more than two asymmetric centre an other method have been introduced called as Fischer projection.

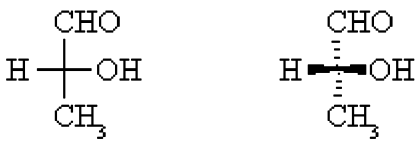
Fischer projections: Fischer Projections are abbreviated structural forms that allow one to convey valuable stereochemical information to a chemist without them having to draw a 3D structural representation of a molecule. These representations are only used for molecules that contain chirality centers, which are then represented as simple crosses.



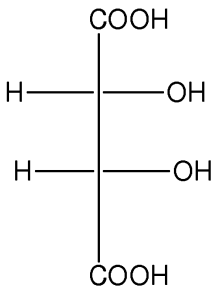
They can be derived by considering the more accurate 3D representation using wedges and assuming the convention that horizontal lines represent bonds coming out of the plane of the paper and vertical lines represent bonds going behind the plane of the paper.

Example:

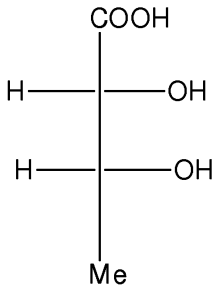
High oxidation state element is represented on the top and low is below. None of the bond is on the plane two are above the plane horizontal) and two are below the plane (vertical).



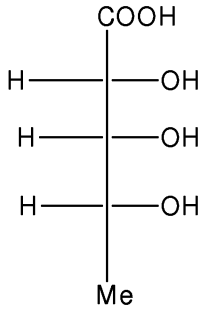
Where oxidation state is no of electron removed by element. In case of two asymmetric carbon the long carbon parent chain is parallel to the plane. It can be drawn as;



Or



In case of more than two asymmetric centre we can draw them in same manner as in case of one and two asymmetric centers.



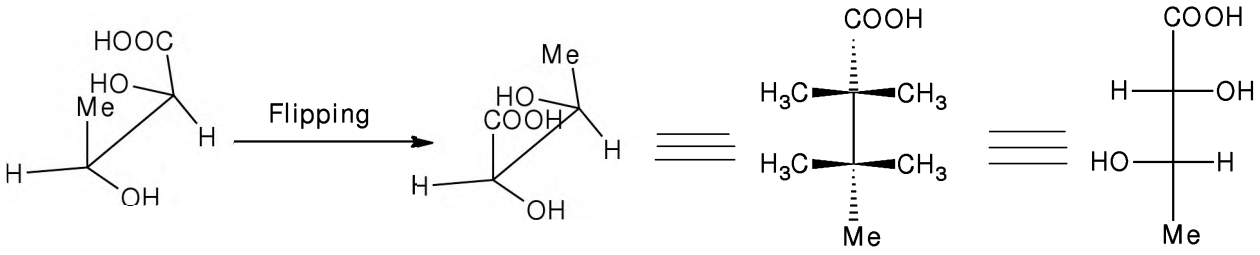
If we change or replace one substituent than the configuration will changed and if we replaced two exact substituents than the configuration will retained.

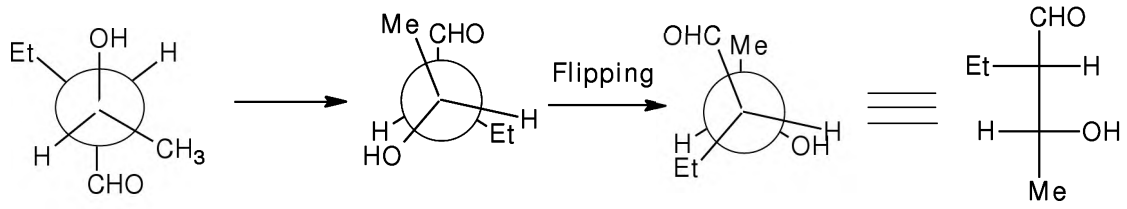
Conversion of sawhorse and newman projections into Fischer projections

By follow these rules we easily convert sawhorse and newman projections into fischer projections;

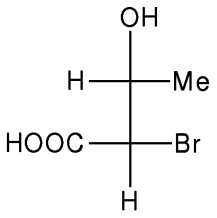
1:-The molecule of any chiral compound containing the chiral carbon is viewed in such a way that the two groups or bonds attached to this carbon are horizontal and point towards the observer while the other two are vertical and point away from the observer.
2:-The various atoms or groups attached to the chiral carbon are then projected on the plane of the paper in form of a cross. by convention the chiral carbon is not shown but it is believed to lie at the intersection of horizontal and vertical line.
3:-If the chiral molecule contains two or more chiral carbons, each carbon must be viewed individually in the same manner described above.
4:-As far as possible the vertical part of the projection formula thus obtained should represent the longest chain of carbon atoms with the most oxidized carbon (-COOH in lactic acid, -CHO in glyceraldehydes, -CH2OH in 2-methyl-1-butanol) at the top.

This carbon is then numbered according to IUPAC nomenclature. To derive a three dimensional structure of a molecule from its Fischer projection, we simply reverse the process described above.

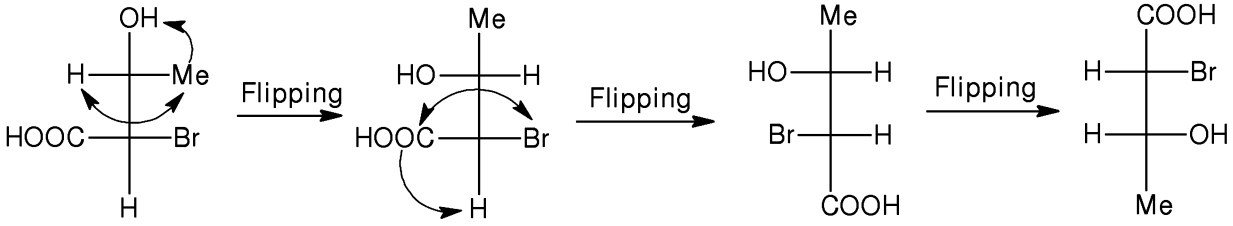




Non-True Fischer projection: Sometimes the fischer projection may not be true of some compounds. In these structures the groups of high priority are arranged in random manner. For example,



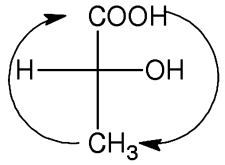
It is not a true fischer projection. To convert it into true fischer projection we should change its two consecutive carbon atoms. We suppose to change two changes to make it true fischer projection.



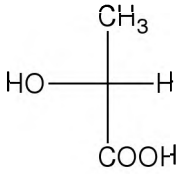
We changed the configuration in conformational isomers. Relative position of substituent will change but the bond doesn't change. They will interchange in X-way to give true fischer projections.

ALLOWED MOTIONS FOR FISCHER PROJECTION:

1. **180° rotation** (not 90° or 270°):

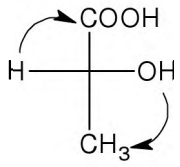


Same as

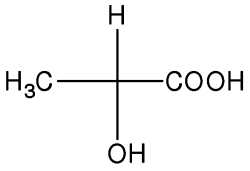


–COOH and –CH3 go into plane of paper in both projections;
–H and –OH come out of plane of paper in both projections.

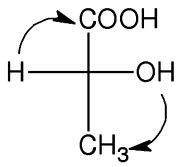
2. **90° rotation:** Rotation of a Fischer projection by 90° inverts its meaning.



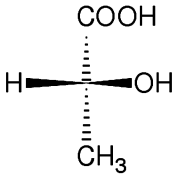
Not same as



–COOH and –CH3 go into plane of paper in one projection
but come out of plane of paper in other projection.

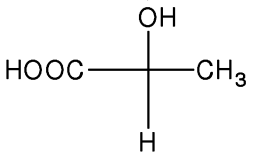


Same as

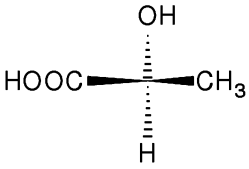


(R)-Lactic acid

90° rotation

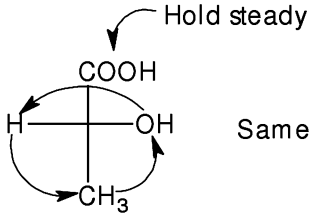


Same as

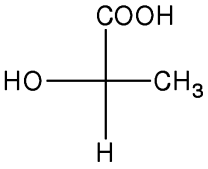


(S)-Lactic acid

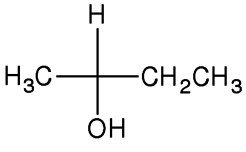
4. One group hold steady and the other three can rotate:



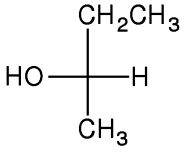
Same as



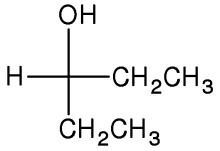
4. Differentiate different Fischer projections:



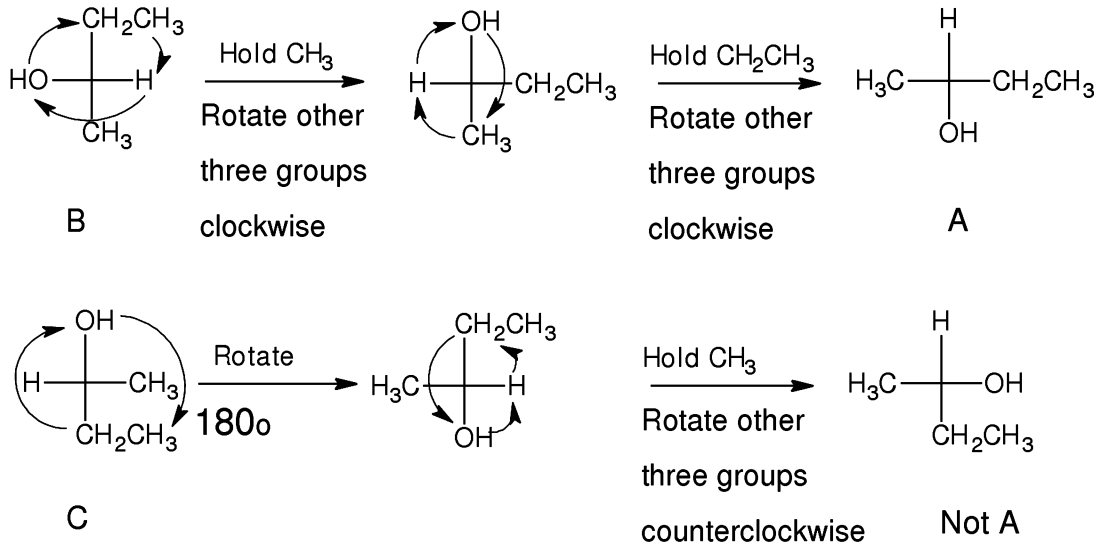
A



B



C



Nomenclature of chiral compounds (CIP rule):

The D, L (dextrorotatory and levorotatory) system, proposed by M. A. Rosanoff in 1906, is still used for naming amino acids and carbohydrates but it is not unequivocal in all cases and cannot easily be applied to all families of compounds. Therefore, an unequivocal and generally applicable nomenclature is necessary to distinguish between stereoisomers, differing only in their absolute configuration. For instance, the simplest chiral alcohol, 2-butanol, forms two different enantiomers, which are not distinguishable by the name 2-butanol.

In the early sixties, ***R. S. Cahn*** (England), ***C. K. Ingold*** (England), and ***V. Prelog*** (Switzerland) introduced the unequivocal and generally applicable (*R, S*) system (also called Cahn-Ingold-Prelog or CIP system) for naming the absolute configuration of chirality centers. Modified (*R, S*) systems can also be applied to chirality axes and planes. The CIP sequencing rules are the basis of the (*R, S*) system.

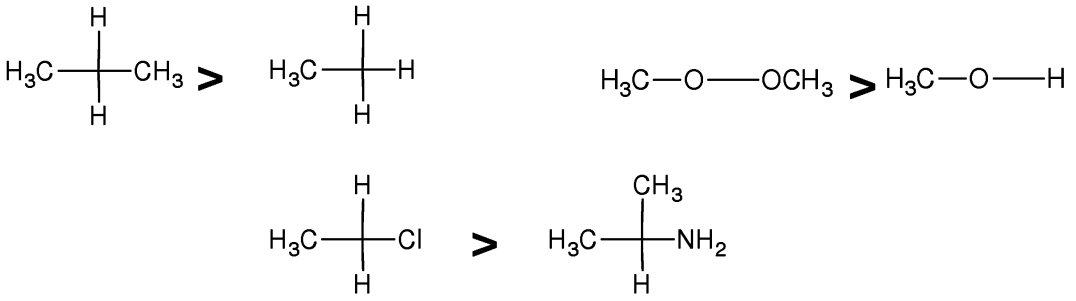
Rules for assigning R S Configuration:

1:- According to the CIP sequencing rules, the four substituents of a tetrahedral chirality center are ranked in order of decreasing atomic number of the atoms directly bonded to the chirality center. Isotopes of the same chemical element are listed in order of decreasing atomic mass.

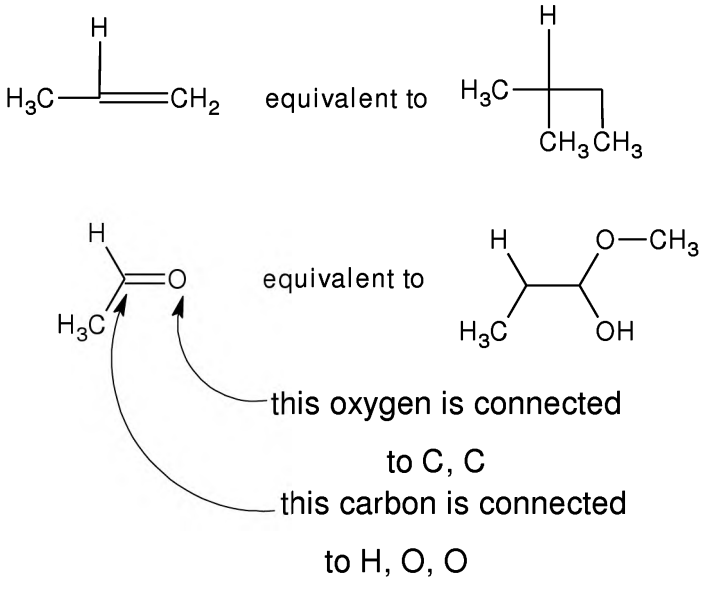
H < D < C < N < O < F < Cl < I

Priority ranking in order of decreasing atomic number

2:- Where two or more atoms bonded to the chirality center have the same atomic number, the second atoms are used to rank the substituents. If the second atoms are also the same, the third are used, and so on. In the illustration, this is explained by different distance spheres around the chirality center of 2-butanol. Atoms directly bonded to the asymmetric carbon are inside the innermost square and so on. In this case, the CIP sequence of the atoms directly bonded to the chirality center C2 is: O > C1 = C3 > H. According to the first rule, carbon atoms C1 and C3 cannot be distinguished. In the second sphere, C1 is connected to three hydrogens, while C3 is connected to two hydrogens and one carbon. Therefore, C3 precedes C1 and the final CIP sequence is: O > C3 > C1 > H.



3:- Multiple bonds are counted as the corresponding number of single bonds. A double-bonded atom is counted twice, a triple-bonded atom three times, and so on. For instance, according to the CIP rules the carbon of a keto group is equated with a carbon carrying two single-bonded oxygens.

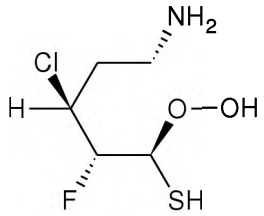


4:- Position the lowest priority group *away from you* as if you were looking along the C-(4) s bond. If you are using a model, grasp the group in your fist.

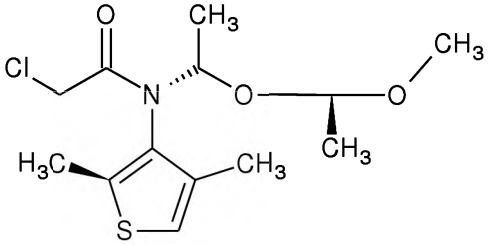
5:- For the other 3 groups, determine the direction of high to low priority (1 to 3).

6:- If this is clockwise, then the center is R (Latin: *rectus* = right).But if this is counter clockwise, then it is S (Latin: *sinister* = left).

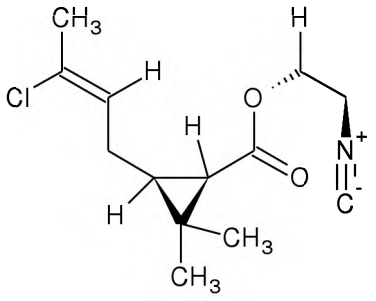
Examples:



(1*S*,2*S*,3*S*)-5-amino-3-chloro-2-fluoro-1-hydroperoxypentane-1-thiol



2-chloro-*N*-(2,4-dimethylthiophen-3-yl)-*N*-{(1*S*)-1-[(1*R*)-1-methoxyethoxy]ethyl}acetamide

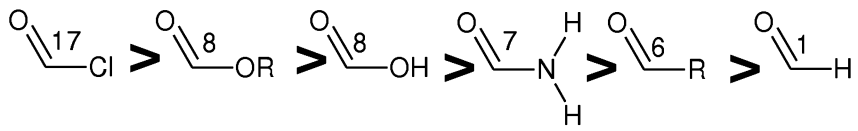


2-isocyanoethyl (1*S*,3*S*)-3-[(2*Z*)-3-chlorobut-2-en-1-yl]-2,2-dimethylcyclopropanecarboxylate

ASSIGNING *R, S* CONFIGURATIONS TO FISCHER PROJECTIONS:

1. Procedures for assigning *R, S* designations:
1) Assign priorities to the four substituents.

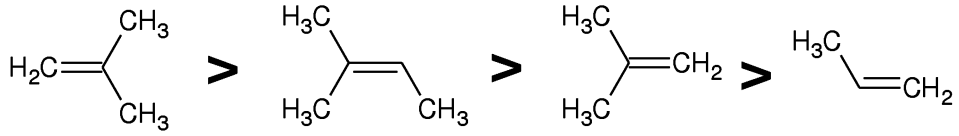
Atomic number priority:



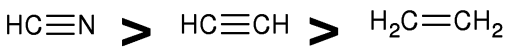
In case of amides:

Di substituted amide > Monosubstituted amides > Unsubstituted amides

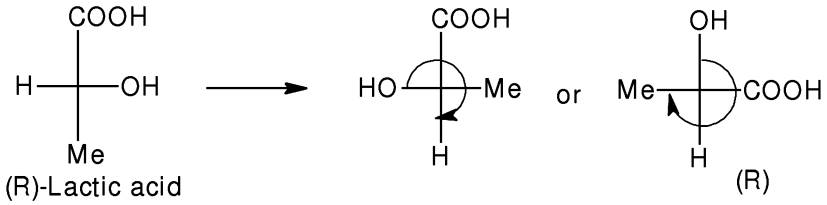
In case of alkenes:



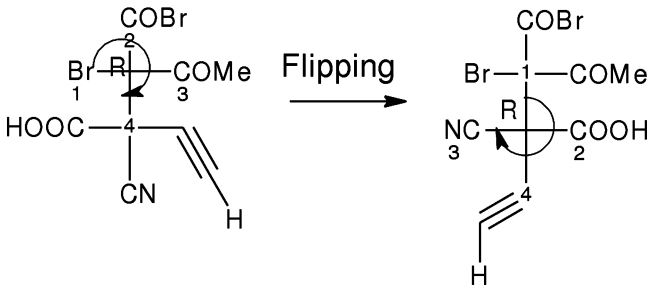
According to nature of bond:



2) Perform one of the two allowed motions to place the group of lowest (fourth) Priority at the top of the Fischer projection.



3) Determine the direction of rotation in going from priority 1 to 2 to 3, and assign **R** or **S** configuration.



CONFIGURATION

Exact arrangement of atoms or group of atoms to asymmetric center in 3 dimensional spaces is called **configuration**.

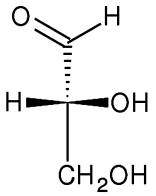
The sequence of arrangement of atoms or group of atoms to asymmetric center in 3 dimensional spaces is called **Absolute configuration**.

Relative and absolute configurations:

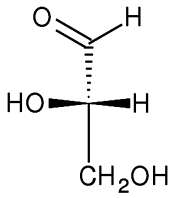
1. Before 1951 only relative configuration of chiral molecules were known.
1) No one prior to that time had been able to demonstrate with certainty what actual spatial arrangement of groups was in any chiral molecule.

2. **Chemical correlation:** configuration of chiral molecules were related to each other through reactions of known stereochemistry.

3. **Glyceraldehyde**: the standard compound for chemical correlation of configuration.



and



(R)-Glyceraldeyhde (S)-Glyceraldeyhde

D-Glyceraldeyhde L-Glyceraldeyhde

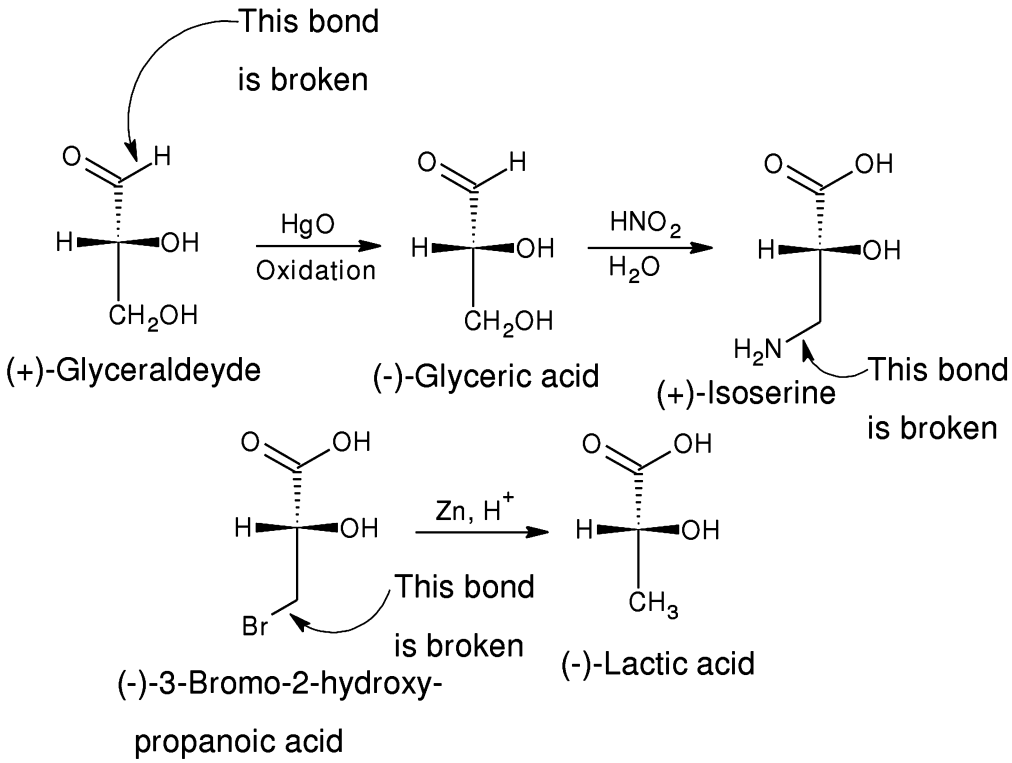
1) One glyceraldehydes is dextrorotatory (+) and the other is levorotatory (–).

2) Before 1951 no one could be sure which configuration belonged to which enantiomer.

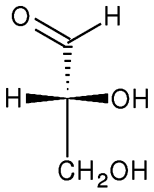
3) Emil Fischer arbitrarily assigned the (*R*) configuration to the (+)-enantiomer.

4) The configurations of other compounds were related to glyceraldehydes through reactions of known stereochemistry.

4. The configuration of (–)-lactic acid can be related to (+)-glyceraldehyde through the following sequence of reactions:

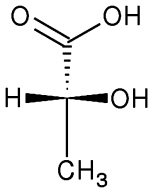


i) If the configuration of (+)-glyceraldehyde is as follows:



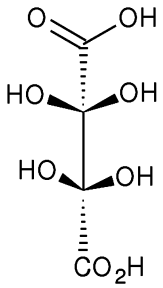
(R)-(+)-Glyceraldehyde

ii) Then the configuration of (–)-lactic acid is:



(R)-(-)-Lactic acid

5. The configuration of (–)-glyceraldehyde was related through reactions of known stereochemistry to (+)-tartaric acid.



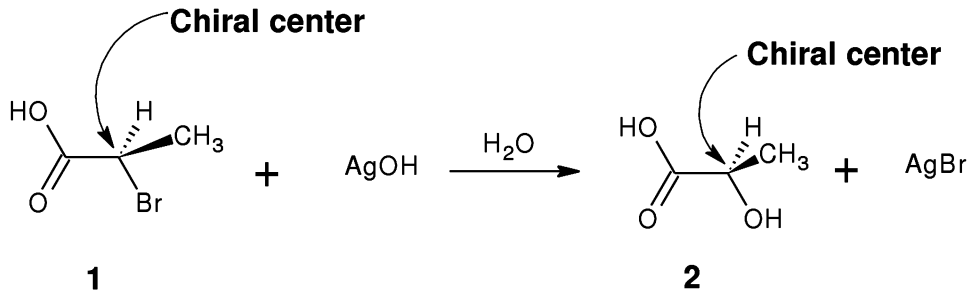
(+)-Tataric acid

i) In 1951 J. M. Bijvoet, the director of the van't Hoff Laboratory of the University of Utrecht in the Netherlands, using X-ray diffraction, demonstrated conclusively that (+)-tartaric acid had the **absolute configuration** shown above.

6. The original arbitrary assignment of configurations of (+) - and (–) -glyceraldehyde was correct.
i) The configurations of all of the compounds that had been related to one glyceraldehyde enantiomer or the other were known with certainty and were now **absolute configurations**.

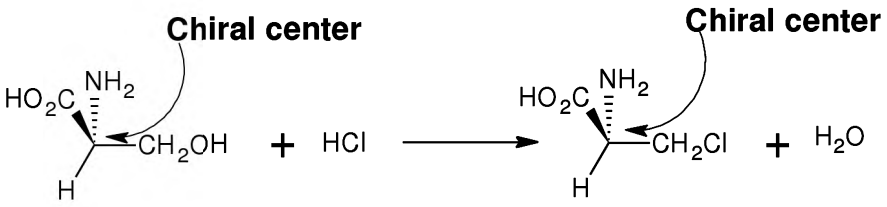
Retention of Configuration:

If the net change in a reaction is the replacement of a ligand on a chiral center in a reactant molecule, and, if in the product the replacement ligand occupies the same site on the chiral center as the replaced ligand did in the reactant, the reaction is said to occur with retention of configuration.



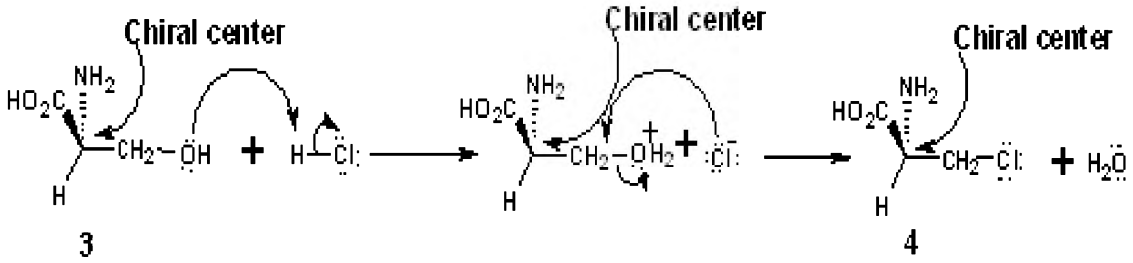
1 **2**

The net reaction is the replacement of bromine atom on the chiral center in **1** with an alcohol group. In the product **(2)** the alcohol group occupies the same site on the chiral center as the bromine atom in **1**. Therefore, the reaction occurs with retention of configuration (see neighboring group participation for mechanism.)



3 **4**

The net reaction is the replacement of hydroxymethyl group (—CH2OH) on the chiral center in **3** with a chloromethyl group (—CH2Cl). In the product **(4)**, the chloromethyl group occupies the same site on the chiral center as the hydroxymethyl group in **3**. Therefore, the reaction occurs with retention of configuration. Retention of configuration in this reaction is a result of the chiral center in the reactant not participating in the reaction. The net reaction is the replacement of hydroxymethyl group (—CH2OH) on the chiral center in **3** with a chloromethyl group (—CH2Cl). In the product **(4)**, the chloromethyl group occupies the same site on the chiral center as the hydroxymethyl group in **3**. Therefore, the reaction occurs with retention of configuration. Retention of configuration in this reaction is a result of the chiral center in the reactant not participating in the reaction.

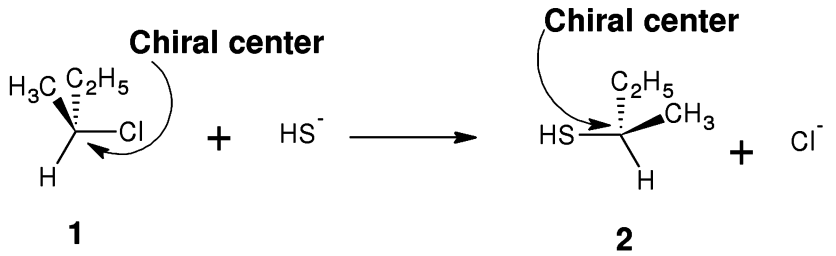


3 4

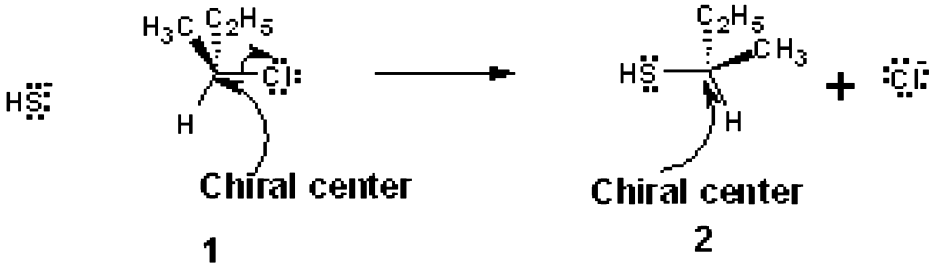
Inversion of configuration:

The inversion of configuration, observed during an SN2 reaction of a substrate in which the carbon atom bearing the leaving group is chiral, is known as Walden inversion.

If the net change of a reaction is the replacement of a ligand on a chiral center in a reactant and if, in the product, the replacement ligand occupies the site opposite to that occupied by the replaced ligand in the reactant, the reaction is said to occur with inversion of configuration.



The net reaction is the replacement of chlorine atom in **1** with a thiol group. In the product **(2)**, the thiol group occupies, on the chiral center, the site opposite to that occupied by the chlorine atom in **1**. Therefore, the reaction occurs with inversion of configuration. Inversion of configuration in this reaction is a result of the reaction being an SN2 reaction, which requires the nucleophile $^{-}$SH to approach the chiral atom from the side opposite to the side of the chlorine atom.



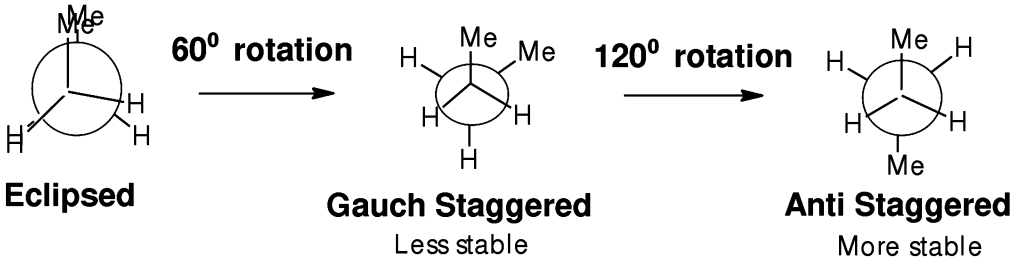
CONFORMATION

Conformation generally means structural arrangement and may refer to as "the three-dimensional shape of compound, chemical conformation, the spatial arrangement of atoms and chemical bonds in a molecule".

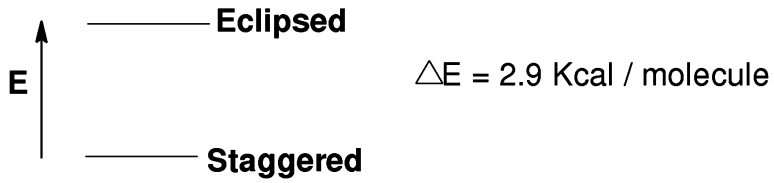
The existence of more than one conformation, usually with different energies, arises from hindered rotation about bonds. Butane has three rotamers: two gauche conformers, which are enantiomeric and an anti conformer, where the four carbon centers are coplanar. The three eclipsed conformations with dihedral angles of 0°,120° and 240° are not considered to be rotamers, but are instead transition states.

Some important examples of conformational isomerism include:

- **<u>Linear alkane conformations with staggered, eclipsed and gauche conformations:-</u>**



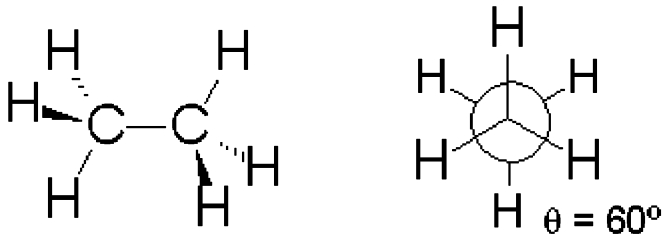
When two bulky groups are at 60°, the conformation is called as Gauch staggered conformation. While when two bulky groups are at 180°, then there is no repulsion between these groups so the conformation is called as Anti staggered. So the overall energy difference between eclipsed and staggered conformations is as:



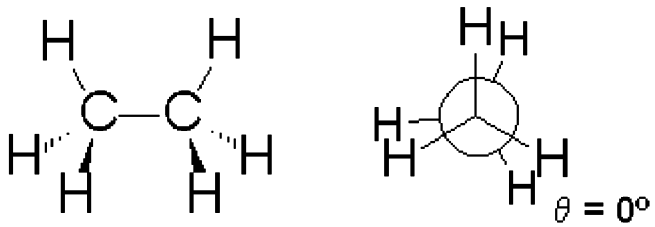
We measure the energy difference per molecule as 3(H-H).

Ethane C_2H_6:

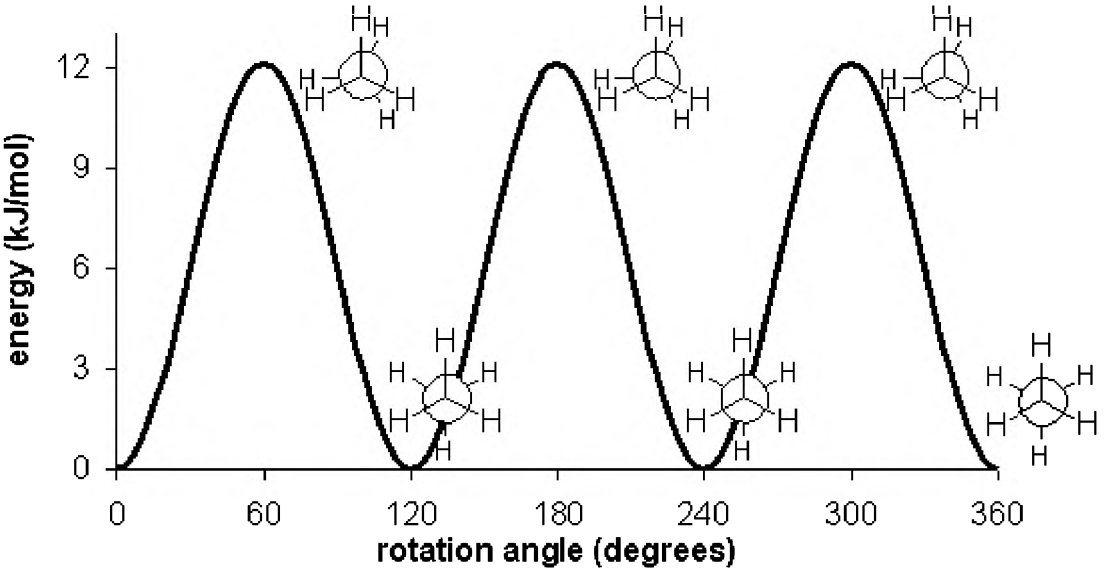
This conformation of ethane is the **staggered** form. The various hydrogen atoms on the two carbons form a dihedral angle of 60º.



This conformation of ethane is the **eclipsed** form. The hydrogen atoms have a dihedral angle of 0º.



The staggered conformation of ethane is more stable than the eclipsed form by 12.1 kJ/mol, so that as one methyl group rotates 360º relative to the other, the compound passes through three stable staggered conformers via three unstable eclipsed forms.



Energy calculation:

3(H-H) =2.9

1(H-H) = 2.9/3 =0.97 Kcal/molecule

Hydrogen-Hydrogen eclipsing is called as **torsional strain.** While methyl-hydrogen eclipsing is called as staggered strain. At methyl there could be another atom but not the hydrogen.

3.40 Kcal/molecule = (Me / H) + 2 (H / H)

(Me / H) = 3.40 – 2(0.97)

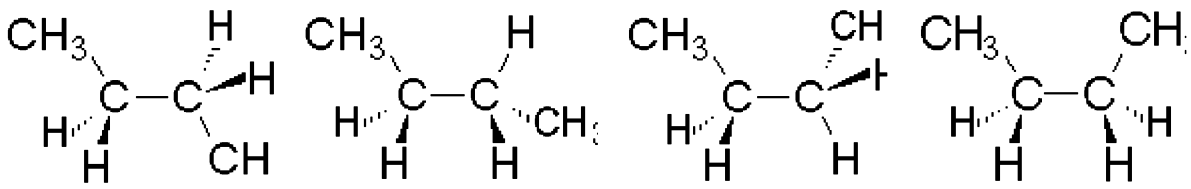
= 1.47 Kcal/molecule

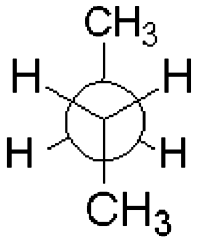
Where 3.40 Kcal/molecule is the whole energy of ethane molecule.

Butane:

Butane has not only eclipsed and staggered conformations, but also forms that vary in the relative orientation of the methyl groups.

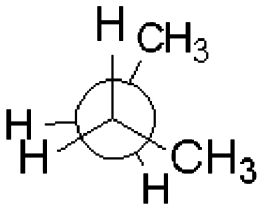
anti **eclipsed** **gauche** **fully eclipsed**





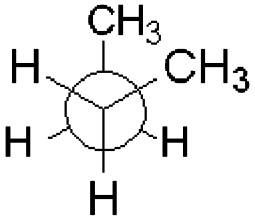
Relative energy: 0 kJ/mol

anti



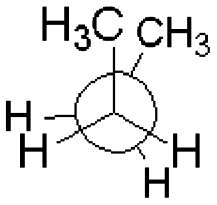
+15.9 kJ/mol

eclipsed



+3.8 kJ/mol

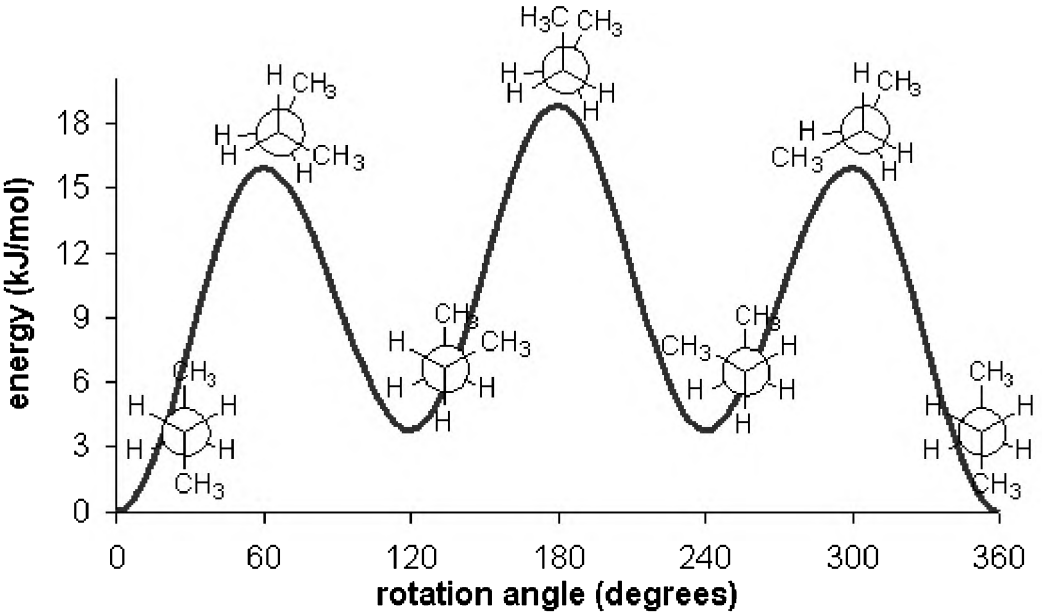
gauche



+18.8 kJ/mol

fully eclipsed

As with ethane, the eclipsed conformations are higher energy than the staggered. The staggered conformation where the two methyl groups are as far away from one another as possible (with a dihedral angle of 180º, seen in the Newman projection) is called anti conformation, and is the lowest-energy arrangement. The two staggered forms with the methyl groups in closer proximity (60º) are the *gauche* conformations. Direct interconversion of one
gauche form to the other requires passing through the highest-energy eclipsed form, where the two methyl groups are next to each other. A space-filling representation of this conformation shows that the methyl groups are physically touching, leading to the high energy.



When size of molecule increases the energy will also increases automatically.

- **<u>Ring conformation:-</u>**

  - Cyclohexane conformations with chair and boat conformations.
  - Carbohydrate Conformation

Tetrahedral molecules have angle of 109.46°.Due to angle strain this value some times increase or decrease simultaneously. In ring form the angle between the carbon bonds due to angle strain will change following table tell us the change in angles of cyclic system.

RING	ANGLES	ANGLE STRAIN
3	60°	49.5°
4	90°	19.5°
5	108°	1.5°
6	120°	-10.5°
7	128.5°	-19°
8	135°	-25.5°

The carbon atoms in cycloalkanes are *sp*3 hybridized and are therefore a deviation from the ideal tetrahedral bond angles of 109°28'. This causes an increase in potential energy and an overall destabilizing effect. Eclipsing of hydrogen atoms is an important destabilizing effect, as well. The **strain energy** of a cycloalkane is the theoretical increase in energy caused by the compound's geometry, and is calculated by comparing the experimental combustion of the cycloalkane with the value calculated using average bond energies.

Hydrocarbons	$-\Delta H_{Combustin}$	**Difference in energy**
C_2H_4	1560	-
C_3H_8	2220	660
C_4H_{10}	2877	657
C_5H_{12}	3536	659
C_6H_{14}	4194	658
C_7H_{16}	4853	659
C_8H_{18}	5511	658
C_9H_{20}	6171	660

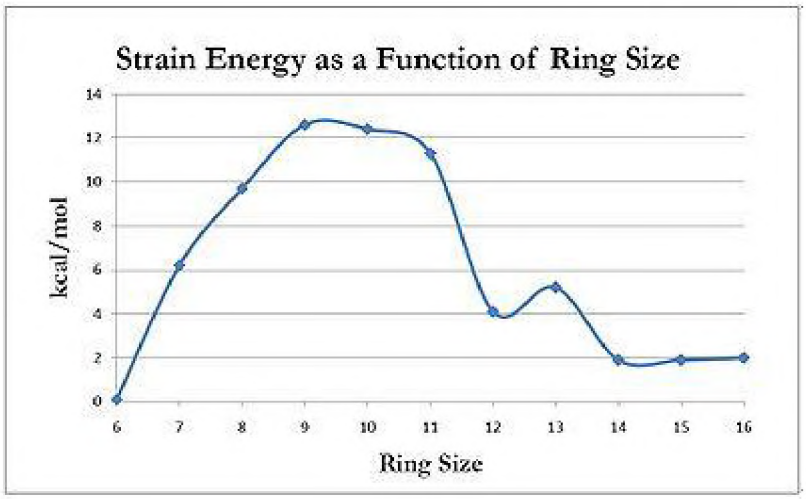
Ring strain is highest for cyclopropane, in which the carbon atoms form a triangle and therefore have 60 degree C-C-C bond angles. There are also three pairs of eclipsed hydrogens. The ring strain is calculated to be around 120 kJ/mol.

Cyclobutane has the carbon atoms in a puckered square with approximately 90-degree bond angles; "puckering" reduces the eclipsing interactions between hydrogen atoms. Its ring strain is therefore slightly less, at around 110 kJ/mol.

For a theoretical planar cyclopentane the C-C-C bond angles would be 108 degrees, very close to the measure of the tetrahedral angle. Actual cyclopentane molecules are puckered, but this changes only the bond angles slightly so that angle strain is relatively small. The eclipsing interactions are also reduced, leaving a ring strain of about 25 kJ/mol.

In cyclohexane the ring strain and eclipsing interactions are negligible because the puckering of the ring allows ideal tetrahedral bond angles to be achieved. As well, in the most stable *chair form* of cyclohexane, axial hydrogens on adjacent carbon atoms are pointed in opposite directions, virtually eliminating eclipsing strain.

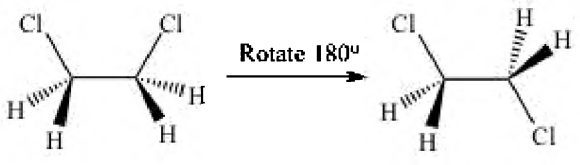
After cyclohexane, the molecules are unable to take a structure with no ring strain, resulting in an increase in strain energy, which peaks at 9 carbons (around 50 kJ/mol). After that, strain energy slowly decreases until 12 carbon atoms, where it drops significantly; at 14, another significant drop occurs and the strain is on a level comparable with 10 kJ/mol. After 14 carbon atoms, sources disagree on what happens to ring strain, some indicating that it increases steadily, others saying that it disappears entirely. Generally speaking though, bond angle strain and eclipsing strain are only an issue for smaller rings.



- **<u>Folding of molecules</u>:-** where some shapes are stable and functional, but others are not.

Besides angle strain cycloalkanes also have torsional strain.

Torsional strain: Strain caused by van der Waals repulsion which can be reduced or eliminated by rotation around a single bond.



Strain between the eclipsed chlorine atoms can be reduced by rotation around the carbon-carbon bond

Puckered theory:

Cyclic system can not be rotate (as by rotating bond will be break).So cyclic system have torsional strain as well as angle strain. To minimize the torsional strain effect cycloalkane change there shapes as staggered and eclipsed conformations. lets see how these cyclic systems change there conformation.

4-membered ring:

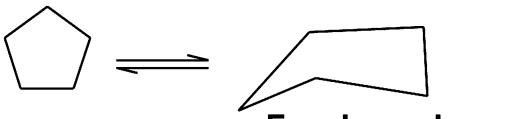
Normally 4-memmbered cycloalkanes exist in square form like,

This form is not perfectly eclipsed to staggered. This molecule has angle strain. It bends and acquire a Glider shape and have dihedral angle (hydrogen adjacent to each other) also called as wing shape.

Glider shape

5-membered ring:

It has 10 torsional strains as well as angle strain which is equally to zero approximately. This molecule is also bend and minimized the four torsional strains and six will remain. This molecule has decrease its torsional strain by puckering (or bending).

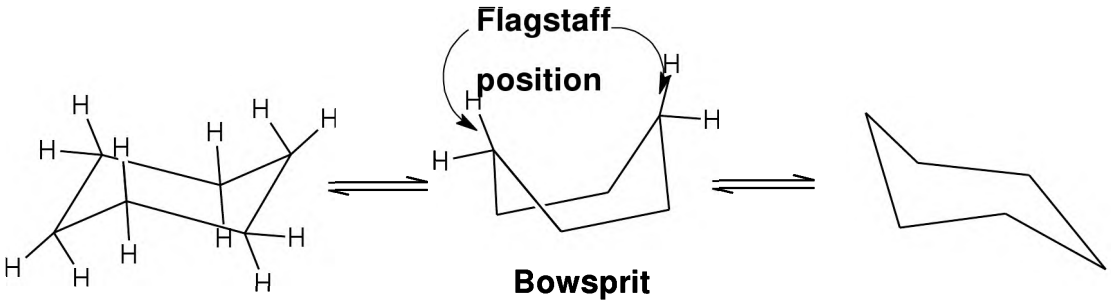


Envelope shape

This shape is also called envelope shape but 5-memmbered ring doesn't exist normally in shape which is totally eclipse or completely staggered. It is half eclipsed and half staggered.

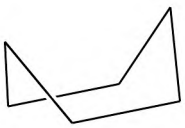
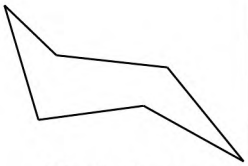
6-memmbered ring:

Its all dihedral angles are at 60°.It have chair conformation. Each carbon has 2 two hydrogen atom, one on axial and other one is on equatorial position. When chair conformation is converted in boat conformation it has 4 torsional strains. While chair conformation have no torsional strain. Hydrogen pointing above in boat conformation possesses repulsion and thus is called as flagstaff position and by repulsion increase the energy of the system. While the hydrogen pointing away are called as Bowsprit.

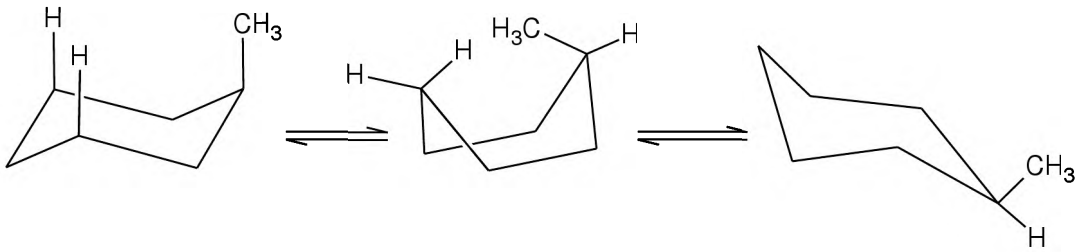


One chair convert to boat and boat convert into another chair conformation but the position will changed. Angle strain is minimized by puckering in 6-memmbered cyclic ring (cyclohexane).

Cyclohexane is difficult to exist in planar form .so it is mostly exist in chair and boat form. Because energy will be higher of planer form than the boat and chair form.

	 Planar form	 Boat form	 Chair form
Torsional strain energy	~12Kcal/mole	4Kcal/mole	0
Angle bending	-10.5^0	0	-1.1^0

If one methyl group is present on chair form then, the methyl group close to hydrogen cause repulsion and effect is called as sterric strain.

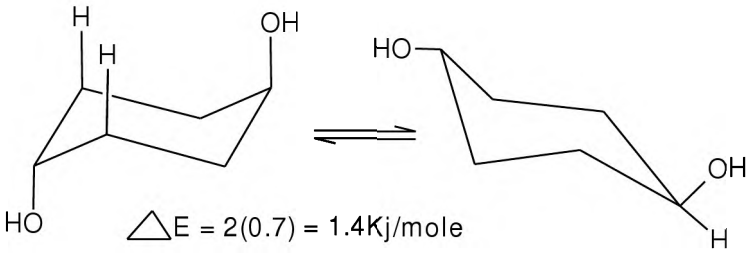


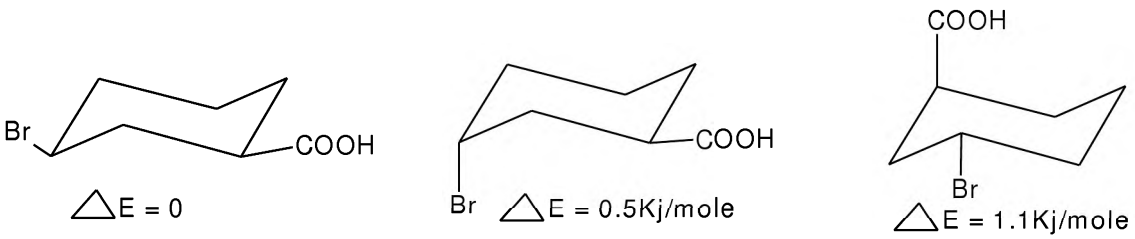
When methyl group is at axial position it cause sterric strain and thus energy of the system will increase but if methyl group is present on equatorial position it cause no effect on the system (as no change in the energy of the system). Different substituents have different effect on energy of the system. Following table shows the effect of substituent on energy of cyclohexane.

Substituents	Energy Kj/mol
CH_3	1.7
C_2H_5	1.8
Tertiary butyl	>>>>
Phenol	3.1
OH/OMe	0.7
Cl/Br/I	0.5
COOH/R	1.1
CN	0.2

These values have calculated at NTP (normal temperature and pressure).In case of two substituents are present;

Now let's see substituent on which position gives stability to the system:

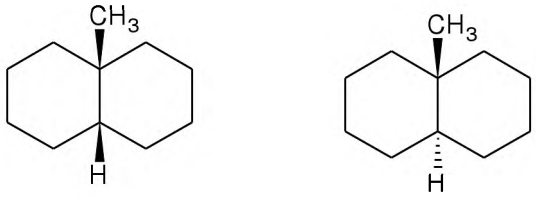




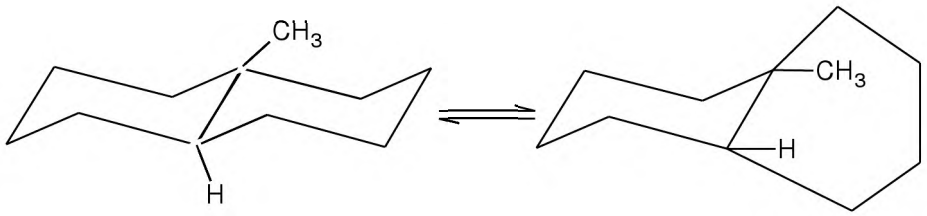
The groups as substituent which cause highly sterric hindrance are called as locking group.

Example: Tertiary butyl

Trans-decane junction can never be flipped due to locking by substituent.

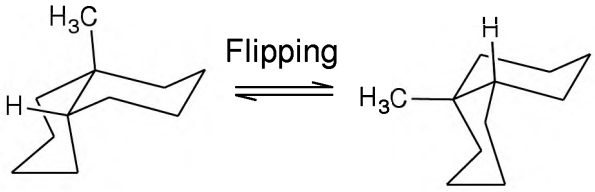


More stable conformation of trans-decane is as;



It has less sterric hindrance at equatorial position.

If cis-decane containing methyl group is flipped the hydrogen on equatorial position goes to axial position and methyl at axial goes to equatorial position.



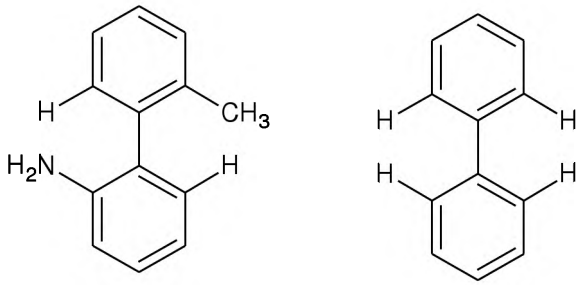
While trans-decane has Trans linked junction so can not be flipped.

- **<u>Atropisomerism:-</u>** due to restricted rotation about a bond, a molecule can become chiral.

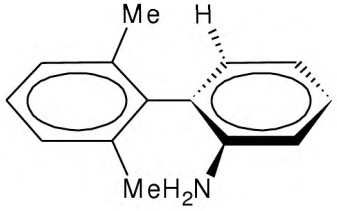
In some cases free rotation is restricted. Like here is an example of atropisomers,

Biphenyls:

The methyl group and hydrogen is sterrically very closed and cause repulsion. After rotation of 2nd ring the methyl and hydrogen are far away from each other due to sterric repulsion free rotation is restricted as by rotation methyl and H_2N groups came close to each other cause too much repulsion. The bond between two phenyl rings is sigma bond and we concern with it not inside the ring. Sigma bond is restricted for free rotation due to sterric repulsion. It has conformational isomers only. Free rotation of C-C bond is restricted. It has no any asymmetric center. It has only two atoms attached rings. These are Sp^2-hybridized ring. The isomers which have opposite configuration as **R** and **S** are called as atropisomers.

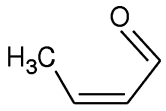


Elements of four types present on a compound have axis of symmetry. Conformation is locked in cyclic system on conformation is totally different from each other.

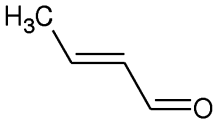


Modified CIP rule:

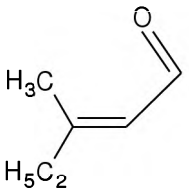
According to this rule configuration name is given to conformational isomers. It is a sequence rule. It is a modified **E** and **Z** nomenclature of stereo compounds.



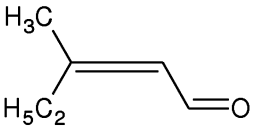
Cis (Z)



Trans (E)

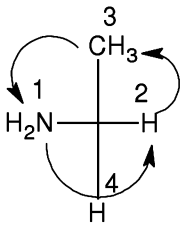


E (trans)

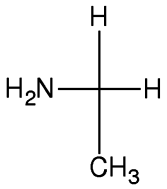


Z (cis)

When four different elements present on C-C double bond highly preference elements on same side then called as Cis or Z and different or opposite as Trans or E.



aS



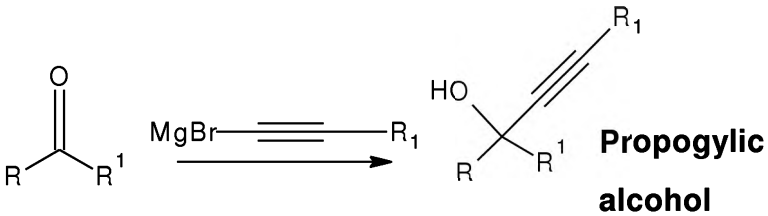
aR

Where "a" represents the axis of chirality.

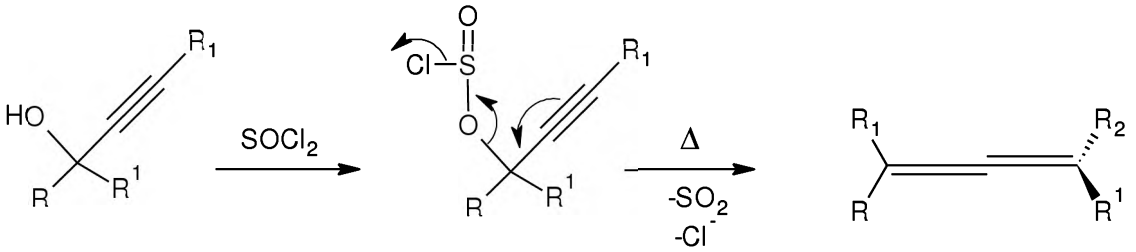
Substituent present on horizontal line will get 1st and 2nd priority. While vertical line would get the 3rd priority.

Allenes: are compounds in which one carbon atom has double bonds with each of its two adjacent carbons.

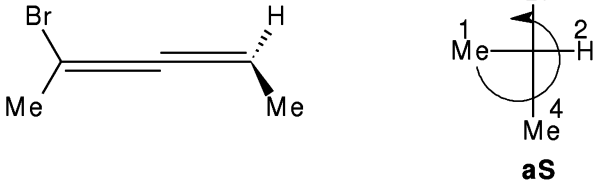
Preparation of allenes:



Propogylic alcohol



Sulphur-chlorine bond is not stable; sulphur-nitrogen bond is also not stable. It has no plane of symmetry and no asymmetric center. But it is still chiral due t axis of chirality present in it.



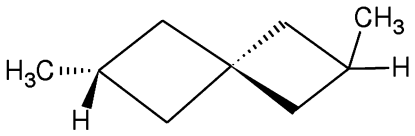
aS

Where "a" represents the axis of chirality.

One configuration has several conformations, but one conformation has no more than one configuration.

Spirenes: have one carbon common in two rings fused in each other.

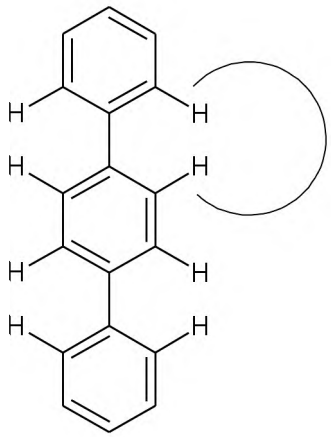
Example:



2,6-dimethylspiro[3.3]heptane

This compound have axis of symmetry so it is chiral.

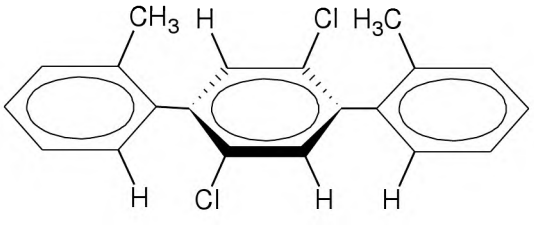
Terphenyls: consist of a central benzene ring substituted with two phenyl groups.



Causing sterric hinderance

Terphenyl

Terphenyls also have axis of chirality. These elements can't assign absolute configuration and can't flipped. These have specific configuration, there conformation is locked and three rings can't be in one plane.



GLOSSARY

acetic acid (CH_3CO_2H): trivial name for ethanoic acid, formed by the oxidation of ethanal or ethanol with $KMnO_4$.
acetone (CH_3COCH_3 or $(CH_3)_2CO$): trivial name for propanone, formed by the oxidation of 2-propanol with $KMnO_4$.
achiral molecule: a molecule that does not contain a stereogenic carbon; an achiral molecule has a plane of symmetry and is superimposable on its mirror image.
acid (carboxylic acid) (RCO_2H): a compound containing the carboxyl group.
acid anhydride ($(RCO)_2O$): a reactive derivative of a carboxylic acid; in the aspirin lab, acetic anhydride is used to convert salicylic acid to aspirin.
acid/base reaction: a reaction in which an acidic H atom is transferred from one molecule to another.
addition reaction: a reaction where a reagent is added across a double or triple bond in an organic compound to produce the corresponding saturated compound.
alcohol (R-OH): a compound which has a hydroxyl group bonded to an R group, where R is a hydrocarbon.
aldehyde (RCHO): a compound that contains a carbonyl group (C=O) at the end of the carbon chain, or that has the CHO attached to a ring.
aliphatic: a compound which does not contain a benzene ring; pentane and cyclohexane are aliphatic compounds.
alkali metal (a metal in Group IA on the periodic table): active metals which may be used to react with an alcohol to produce the corresponding metal alkoxide and hydrogen gas.
alkane: a hydrocarbon which contains only carbon-carbon single bonds; also classified as a saturated hydrocarbon. Straight or branched-chain alkanes have the general formula C_nH_{2n+2}.
alkene: a hydrocarbon which contains at least one carbon-carbon double bond; also classified as an unsaturated hydrocarbon. Straight or branched-chain alkenes have the general formula C_nH_{2n}.
alkoxide (RO^-): an ion containing a negative charge on oxygen; formed by the reaction of an alcohol with an active metal.
alkoxy group (RO-): a substituent containing an alkyl group linked to an oxygen.
alkyl benzene (C_6H_5-R): a benzene ring that has one alkyl group attached; the alkyl group (except quaternary alkyl groups) is susceptible to oxidation with hot $KMnO_4$ to yield benzoic acid ($C_6H_5CO_2H$).
alkyl group (R-): a substituent formed by removing one hydrogen atom from an alkane.
alkyl halide (R-X): a compound which contains at least one halogen atom.
alkyne: a hydrocarbon which contains at least one carbon-carbon triple bond; also classified as an unsaturated hydrocarbon. Straight or branched-chain alkynes have the general formula C_nH_{2n-2}.
amide ($RCONR_2$): the least reactive derivative of a carboxylic acid; it contains a carbonyl group (C=O) that is singly bonded to a nitrogen atom; the condensation product of a carboxylic acid with ammonia or an amine.
amine (RNR_2): a hydrocarbon derivative of ammonia (NH_3); primary, secondary, and tertiary amines have, respectively, one, two and three of the NH_3 hydrogen atoms replaced by hydrocarbon groups.
amino acid: a compound with a carboxyl group and an amino group. In an alpha amino acid, the amino group is on the carbon atom adjacent to the carboxyl group.
amino group: the $-NH_2$ group.
aniline ($C_6H_5NH_2$): a primary (1°) amine in which the NH_2 group is bonded directly to a benzene ring.
aromatic: a compound which contains a benzene ring.

aspirin: trivial name for the compound acetylsalicylic acid; formed by treating salicylic acid with acetic anhydride.
asymmetric carbon atom: a carbon atom with four different substituents; a stereogenic carbon.
benzaldehyde (C_6H_5CHO): simplest **aromatic aldehyde**, formed by the controlled oxidation of benzyl alcohol; vigorous oxidation yields benzoic acid.
benzene: an aromatic cyclic hydrocarbon of formula C_6H_6.
benzoic acid ($C_6H_5CO_2H$): simplest aromatic carboxylic acid, formed by the vigorous oxidation of alkyl benzene, benzyl alcohol, and benzaldehyde.
carbonyl group (R-**CO**-R): a carbon atom which is connected to an oxygen atom with a double bond; the functional groups of aldehydes, ketones, carboxylic acids, esters and amides all contain a carbonyl group.
carboxy group (-CO_2H or -COOH): a carbonyl group to which a hydroxyl group is attached; carboxylic acids have this functional group.
catalyst: a substance which changes the rate of a chemical reaction but is unchanged at the end of the reaction; an example would be the Pt used in the hydrogenation of alkenes.
chirality: the ability of an object or a compound to exist in right and left-handed forms; a chiral compound will rotate the plane of plane-polarized light.
cis: a geometric form of a substituted alkene or a cyclic compound in which two substituents are on the same side of the carbon-carbon double bond or the ring.
constitutional isomers: see structural isomerism
cyclic compound: a molecule which has the two ends of the carbon chain connected together to form a ring.
cyclo: prefix used to indicate the presence of a ring.
dehydration: an elimination reaction in which an alcohol reacts with concentrated acid to yield an alkene plus water.
diene: a hydrocarbon with two double bonds.
diol: a compound with two alcohol groups.
double bond: a group in which two pairs of electrons are shared between two atoms (C=C,C=O, C=N); a double bond is made up of a sigma bond and a pi bond.
enantiomers: stereoisomers which are mirror images; they can be considered to be right and left-handed molecules as they are not superimposable on each other.
ester (R-CO_2-R): also called a carboxylic ester; a molecule which contains a carbonyl group (C=O) that is singly bonded to another oxygen atom which is bonded to another carbon atom (-O-R); produced by the condensation reaction between a carboxylic acid and an alcohol.
ether (C-O-C): a molecule which contains a carbon-oxygen-carbon linkage.
ethoxide (CH_3CH_2O-): anion formed by treating ethanol with an alkali metal.
ethoxy group (CH_3CH_2O-): a two carbon alkoxy susbtituent.
ethyl alcohol (CH_3CH_2OH): trivial name for ethanol.
ethyl group (CH_3CH_2-): a two carbon alkyl substituent.
formaldehyde (CH_2O): trivial name for methanal.
formic acid (HCO_2H): trivial name for methanoic acid.
functional group: a specific collection of atoms that reacts in a characteristic way, used as a means of classifying organic compounds into families; each functional group in a compound behaves independently,
thus the reactivity of even complex molecules can be predicted.
functional isomers: compounds which have the same molecular formula that possess different functional groups.
geometric isomers: stereoisomers which differ in the geometry around either a carbon-carbon double bond or ring.
halo group (X-): substituent which is one of the four halogens; fluoro (F), chloro (Cl), bromo (Br), or iodo (I).

halogenation: the addition of a halogen molecule (only Cl_2 or Br_2) to an alkene to produce an alkyl dihalide or alkyne to produce an alkyl tetrahalide.
heteroatoms: elements other than carbon and hydrogen that are commonly found in organic molecules, such as nitrogen, oxygen and the halogens.
homologous series: compounds which differ only by the number of CH_2 units present; CH_3CH_2Cl, $CH_3CH_2CH_2Cl$, and $CH_3CH_2CH_2CH_2Cl$, all belong to the same homologous series (1° alkyl chlorides).
hydration: the addition of a molecule of water to the carbon-carbon double bond of an alkene to form an alcohol; the reaction follows Markovnikov's rule and requires a mineral acid catalyst (H^+).
hydrocarbons: compounds which contain only carbon and hydrogen.
hydrohalogenation: the addition of a molecule of HCl or HBr to an alkene to form an alkyl halide, or to an alkyne to form a geminal alkyl dihalide, the addition follows Markovnikov's rule.
hydrolysis: a substitution reaction in which a molecule of water replaces a leaving group in a compound; examples would include the hydrolysis of ester or amides to the corresponding carboxylic acids.
hydroxyl group (-OH): the functional group present in an alcohol.
isobutyl: the $(CH_3)_2CH\text{-}CH_2\text{-}$ group, the trivial name for the 2-methylpropyl group.
isopropyl: the $(CH_3)_2CH\text{-}$ group, the trivial name for the 1-methylethyl group.
isomers: compounds which have the same molecular formulas but different structures; they may be sub-classified as functional, geometric, optical, positional, skeletal, stereo, or structural.
IUPAC (International Union of Pure and Applied Chemistry): the organization that establishes the system of nomenclature for organic and inorganic compounds using prefixes and suffixes, developed in the late 19th century.
ketone (RCOR)**:** a compound which contains a carbonyl group (C=O) attached to two carbon atoms.
Markovnikov's rule: organic reaction in which the major product is the one predicted to form by adding a hydrogen atom to the carbon atom of a double bond which contains the greater number of hydrogen atoms.
meta-(*m*-): prefix used to describe disubstituted benzenes in which the two groups are in positions 1 and 3.
methoxy group ($CH_3O\text{-}$): the simplest alkoxy substituent.
methyl alcohol (CH_3OH): trivial name for methanol.
methyl group ($CH_3\text{-}$): the simplest alkyl substituent.
nomenclature: a method of systematically naming organic compounds using prefixes and suffixes.
olefin: another name for an alkene.
optical activity: refers to the ability of a compound to interact with plane polarized light; such a compound is said to be optically active and it will not be superimposable on its mirror image.
optical isomers: this refers to compounds which will rotate the plane of polarized light by the same amount, but in opposite directions; also called enantiomers (i.e. non-superimposable mirror images).
ortho- (*o*-): prefix used to describe disubstituted benzenes in which the two groups are in positions 1 and 2.
oxidation: a reaction in which electrons are lost by a species or molecule e.g. $2Cl^- \rightarrow Cl_2$; also the gain of carbon-oxygen bonds, and/or loss of carbon-hydrogen bonds e.g. 1-butanol → butanal → butanoic acid.
para- (*p*-): prefix used to describe disubstituted benzenes in which the two groups are in positions 1 and 4.
phenol: a compound containing an OH group attached to an aromatic ring; an aromatic alcohol (e.g. C_6H_5OH).

phenyl group (C_6H_5- or Ph-): the group formed by removing one hydrogen atom from benzene.
plane of symmetry: an imaginary surface which divides an object (or molecule) into two equal halves which are mirror images of each other.
polarimeter: an instrument used to measure the optical activity of a compound.
positional isomers: compounds which differ only in the position of a functional group; 2-pentanol and 3-pentanol are positional isomers.
primary (1°): general term used to describe a specific structural arrangement in which a carbon atom is attached to one other carbon atom.
primary alcohol (RCH_2OH): alcohol in which the OH group is bonded to a carbon bonded to one alkyl group.
primary amine (RNH_2): amine in which the N atom is bonded to one alkyl group.
propoxy group ($CH_3CH_2CH_2O$-): a straight chain three carbon alkoxy substituent.
propyl group ($CH_3CH_2CH_2$-): a straight chain three carbon alkyl substituent.
quaternary (4°) carbon: a carbon that is bonded to four carbon atoms.
reduction: a reaction in which a substance gains electrons, or loses O atoms, or gains H atoms; examples would be: Cl_2 H 2Cl-, and the conversion of 2-butanone to 2-butanol.
saturated: a compound which does not contain any double or triple bonds.
secondary (2°): general term used to describe a specific structural arrangement in which a carbon atom that is attached to two other carbon atoms.
secondary alcohol (R_2CH-OH): alcohol in which the OH group is bonded to a carbon atom bonded to two alkyl groups.
secondary amine (R_2NH): amine in which the N atom is bonded to two alkyl groups.
side chain: a chain of atoms which is attached to a longer chain of atoms; examples of side chains would be methyl, ethyl, propyl groups (among others).
skeletal isomers: isomers which differ in the length of the carbon chain; examples are pentane and dimethylpropane.
stereochemistry: the branch of organic chemistry that deals with the three-dimensional structure of molecules.
stereogenic carbon (asymmetric carbon): a carbon atom which is bonded to four different groups or atoms; a chiral molecule must contain a stereogenic carbon, and therefore has no plane of symmetry and is not superimposable on its mirror image.
stereoisomers: isomers which have the same bonding connectivity but have a different three-dimensional structure; examples would be cis-2-butene and trans-2-butene (geometric isomers), and the left and right handed forms of 2-butanol (enantiomers).
structural formula: a convention used to represent the structures of organic molecules in which not all the valence electrons of the atoms are shown.
structural isomerism: relation between two compounds which have the same molecular formula, but different structures; they may be further classified as functional, positional, or skeletal isomers. This relation is also called constitutional isomerism.
substituent: an atom or group of atoms that is attached to a group of atoms; examples would be Cl- (chloro), NO_2- (nitro), CH_3CH_2- (ethyl), etc...
substitution reaction: process in which one group or atom in a molecule is replaced by another group or atom.
tert (*t*-): prefix used to indicate that the carbon atom connected to the main chain of a molecule is itself bonded to three carbon atoms: $(CH_3)_3C$- is the *t*-butyl group. This prefix is not counted for alphabetization purposes.
tert-butyl (*t*-butyl): trivial name for the 1,1-dimethylethyl group.
tertiary (3°): general term used to describe a specific structural arrangement.

tertiary alcohol (R_3C-OH): an alcohol in which the OH group is bonded to a carbon atom bonded to three alkyl groups.
tertiary amine (R_3N): an amine in which the N atom is bonded to three carbon atoms.
toluene ($C_6H_5CH_3$): trivial name for methylbenzene
trans: geometric form of a substituted alkene or cyclic compound in which two substituents are on opposite side of the carbon-carbon double bond or the ring.
triple bond: a group in which three pairs of electrons are shared between two atoms; carbon-carbon (CαC) and carbon-nitrogen (CαN) triple bonds are very common in organic compounds; a triple bond is made up of a sigma bond and two pi bonds.
trivial name: common name which has been used for a long period of time for a simple compound, or a simple common name for a very complicated structure. The structural formula cannot be deduced from the name using a set of rules.
unit of unsaturation: also called the index of hydrogen deficiency (IHD).
unsaturated: refers to a compound which contains at least one double or triple bond; addition of excess hydrogen to such a molecule will produce a saturated compound.

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