

Module II: Organic Structure and Reactivity

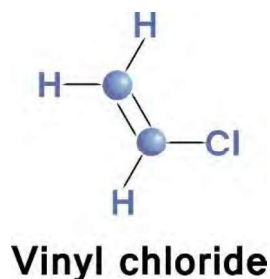
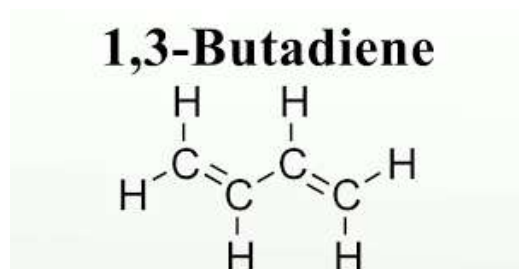
Aromaticity, Geometrical isomerism: cis–trans, E/Z, and syn-anti isomerism; Optical isomerism & Chirality; Wedge, Fischer, Newmann and Sawhorse projection formulae and interconversions; D/L, R/S nomenclature system; Conformational studies of n-butane.

Addition, Elimination, Substitution and Rearrangement reaction.

CONJUGATED MOLECULES

Resonance Effect

If two double bonds in a molecule are separated by a single bond, they are said to be in conjugation and the molecule having such bonds are called conjugated molecules e.g., 1, 3-butadiene.



Another example of conjugation is given by benzene which is a hexagonal ring of carbon atoms with three double bonds in alternate positions. Alternatively, a double bond or a triple bond may also be in conjugation with a lone electron pair e.g., in vinyl chloride. Conjugated molecules do not exhibit the character of pure double bond or triple bond, for example, benzene is expected to be highly reactive since it has three double bonds in the ring but is actually quite stable. In order to explain the difference in the expected and the actual behaviour of the conjugated molecules, Robinson and Ingold stated that such compounds exist in two or more forms none of which can explain all the properties of the molecule under investigation. They called this concept as mesomerism or mesomeric effect. Heisenberg studied the same mathematically.

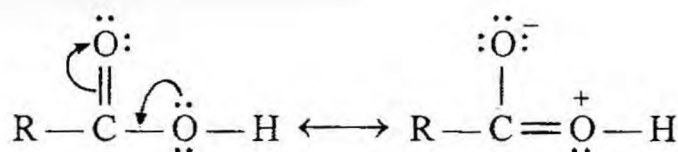
and named it as resonance or resonance effect. According to the concept, If a compound having a certain molecular formula can be represented by different structural formulae which differ only in the arrangement of the electron pairs and not of the atoms, such like structures are called resonating or contributing or canonical structures and the phenomenon is known as resonance. The compound cannot be represented completely by any of the resonating or contributing structures but by a mixture of all of them which is called resonance hybrid (cannot be actually represented). Resonance is indicated by the sign \longleftrightarrow .

It may be noted that the various resonating or contributing structures do not actually exist i. e., they are all hypothetical structures. They have been given simply to explain certain properties of the compounds which cannot be otherwise explained

Examples of Resonance

A common analogy of a resonance hybrid is that of a mule which is a hybrid of horse and donkey.

1. **Monocarboxylic acid.** The acidic character of monocarboxylic acid is explained with the help of resonance. The following contributing structures for the monocarboxylic acid are possible which differ in the position of the electron pairs.

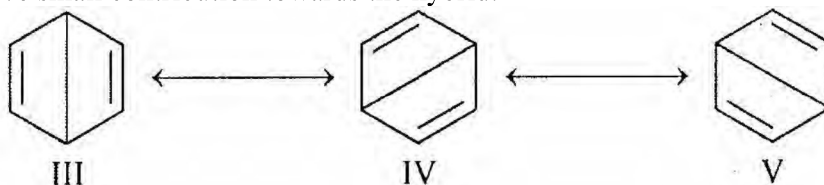


As a result of resonance, the oxygen atom of the O — H group acquires a positive charge i. e., it draws the electron pair towards itself resulting in the release of protons.

2. **Benzene.** Benzene is a hybrid of two equivalent contributing structures (I and II) which differ in the position of the π -electron pairs representing double bonds. These were suggested by Kekule.

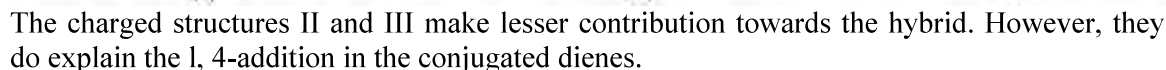


Three more contributing structures (III, IV and V) have been proposed by Dewar. Being less symmetrical they have small contribution towards the hybrid.

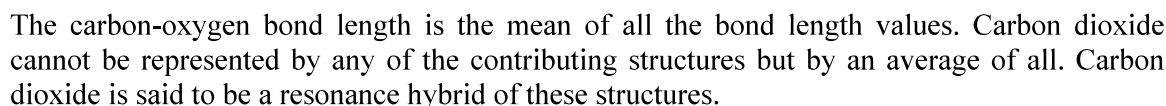


Benzene exists mainly in the form of Kekule structures (I and II). Benzene is, in fact, quite stable and its stability is explained with the help of resonance. As the π -electron charge is distributed over greater area i. e., it gets delocalised.

3. **1, 3 - Butadiene.** The diene can be regarded as the hybrid of the following contributing structures:



4. Carbon dioxide. The structural formula of carbon dioxide (CO_2) molecule is $\text{O} = \text{C} = \text{O}$. The standard $\text{C} = \text{O}$ bond length is 122 pm but the bond length which is obtained for the molecule from spectroscopic studies is 115 pm. The difference in the bond length values can be explained by considering the following structures for carbon dioxide which are known as the resonating structures or contributing structures or canonical structures.



Conditions of resonance:

Wheland has suggested the following conditions for resonance:

- (i) The resonance or the contributing structures must differ only in the position of the electron pairs and not of the atomic nuclei.
- (ii) The resonating structures must have the same number of paired and unpaired electrons.
- (m) The energies of the various resonating structures must be either same or nearly the same.
- (iv) All the contributing or resonating structures do not contribute equally towards the hybrid. The equivalent structures have greater contribution. The contribution of any resonating structure towards the hybrid depends upon the following factors:

- Structures with more covalent bonds are more stable than the structures with less covalent bonds.
- The charged contributing structure is less stable as compared to the structure without any charge.
- Structure with negative charge on more electronegative atom is more stable structure with negative charge on less electronegative atom.

Effects of resonance

Some effects of the resonance are explained as under:

1. **Stability.** As a result of resonance, the energy of the hybrid decreases and its stability therefore increases. Greater the number of contributing structures; greater will be the stability of the hybrid. The stability also depends upon the equivalence of the contributing structures. Moreover, the charged structures have less contribution than the uncharged structures

Resonance energy: The relative stabilities of two different resonance hybrids may be compared in terms of resonance energy. It may be defined as the difference in the energy content of the hybrid and its most stable contributing structure.

2. **Bond length.** The resonance causes a change in bond length values. For example, the standard C — C bond length is 154 pm and C = C bond length is 134 pm. But the value as

determined for benzene is 139 pm, which does not coincide with any of the two values and is intermediate between the two values.

Hückel's molecular orbital theory of conjugated systems

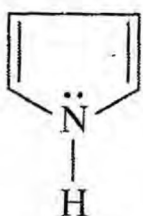
The German chemist Erich Hückel was the first to recognize that an aromatic compound must have an odd number of pairs of pi electrons. In 1931, he described this requirement by what has come to be known as **Hückel's rule**, or the **($4n + 2$) rule**. According to this rule, monocyclic planar systems of trigonally hybridised atoms which contain ($4n + 2$) pi electrons possess considerable stability and hence, aromatic character where 'n' may vary from 0, 1, 2, 3, 4...etc. Thus, cyclic compounds having 2, 6, 10, 14, 18 or 22 pi electrons are expected to show aromatic character. But 'n' does not denote the number of rings in the cyclic compound.

Aromatic character of some cyclic systems:

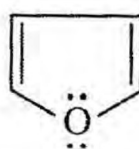
- (1) Monocyclic systems. All the monocyclic compounds shown below have a number of pi electrons in the ring according to the Hückel's rule. i.e., all of them have six pi-electrons in the ring. They are, therefore, aromatic.



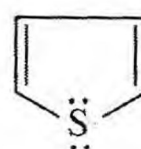
Benzene



Pyrrole

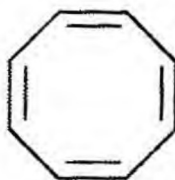


Furan



Thiophene

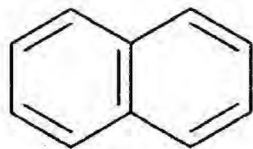
In the heterocyclic compounds pyrrole, furan and thiophene, four pi electrons are contributed by the two double bonds in the ring while two electrons are contributed by the hetero atom. It may be noted that cyclooctatetraene does not show any aromatic character although the ring has four, double bonds in the alternate positions. This is because it does not follow Hückel's rule.



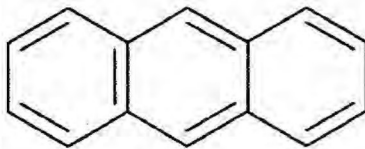
cyclooctatetraene

The number of pi-electrons (8) is not according to Hückel's rule.

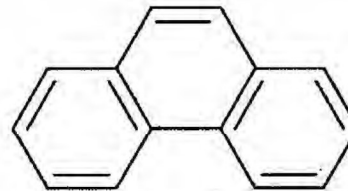
- (ii) Fused ring systems. The polynuclear hydrocarbons such as naphthalene, anthracene and phenanthrene are aromatic in nature according to Hückel's rule (6 and 14 pi electrons).



Naphthalene
(10 π -Electrons)

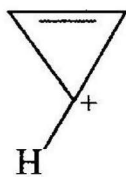


Anthracene
(14 π -Electrons)

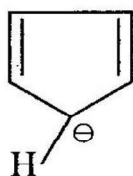


Phenanthrene
(14 π -Electrons)

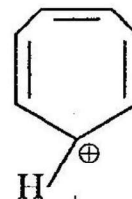
(iii) Aromatic ions system. It may be noted that not only the molecules but even some cyclic ions exhibit aromatic character. A few such ions are listed:



Cyclopropene
cation
(2 π -Electrons)



Cyclopentadiene
anion
(6 π -Electrons)



Cycloheptatriene
cation
(6 π -Electrons)

ISOMERISM

One of the striking features of organic compounds is that they exhibit isomerism. Compounds having the same molecular formula and molecular mass but having different characteristics are called isomers. This phenomenon is called isomerism. The relative position of different atoms or groups in these isomers is different and that causes the difference in properties. Isomerism may be classified into two types:

1. Structural isomerism. In this type of isomerism, the molecules differ in the structural arrangement of the atoms or groups.
2. Stereoisomerism. Here the isomers possess the same structural arrangement but differ with respect to the arrangement of atoms or groups in space.

1. STRUCTURAL ISOMERISM

If two or more compounds differ in the relative arrangement of atoms in the molecule, they are said to be structural isomers and this phenomenon is known as structural isomerism. There are different kinds of structural isomerisms as under:

- (i) Chain isomerism or Nuclear isomerism.
- (ii) Position isomerism.
- (iii) Functional isomerism.
- (iv) Metamerism.
- (v) Tautomerism

Each one of these is discussed as under.

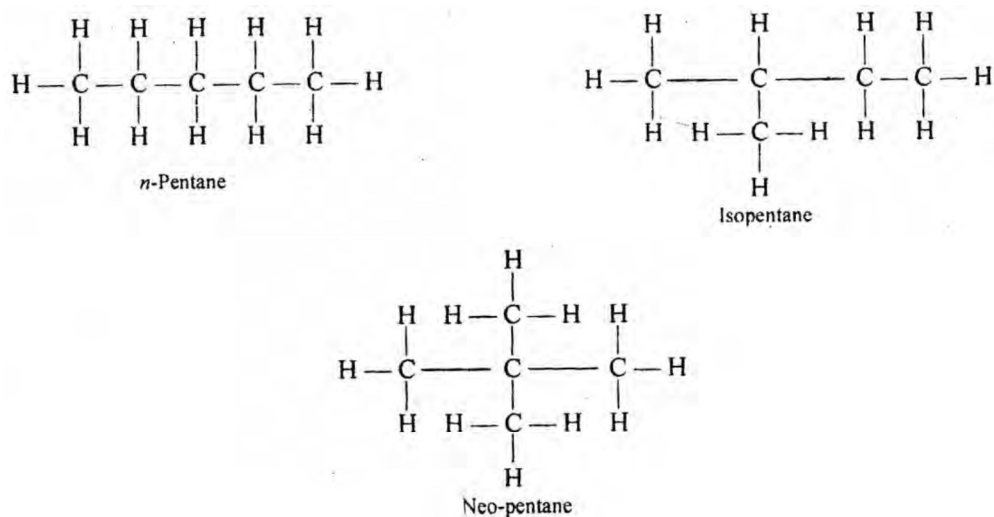
- (i) Chain Isomerism or Nuclear Isomerism

If different compounds of the same class of organic compounds, having the same molecular formula, differ in the structure of carbon chain, they are called chain isomers. Examples of this type of isomerism are:

(a) n-Butane and Isobutane (Mol Formula = C_4H_{10})



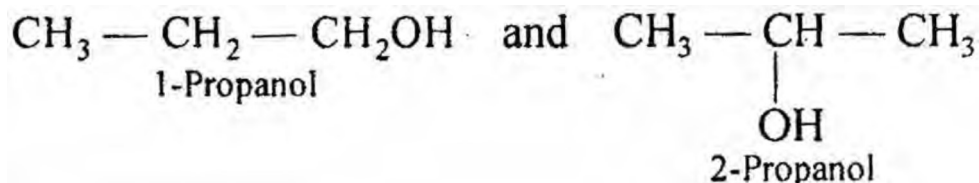
(b) n-Pentane, isopentane and neo pentane (Mol Formula: C_5H_{12})



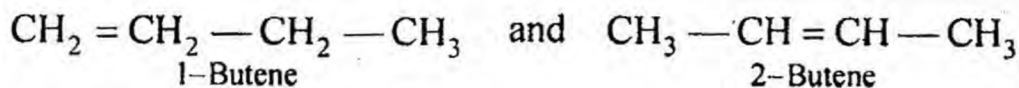
(ii) Position Isomerism

If different compounds, belonging to some homologous series, with same molecular formula have same carbon skeleton but differ in the position of substituent or functional group; these are known as position isomers. Examples of this type of isomers are:

(a) 1-Propanol and 2-propanol (Mol. Formula = C_3H_8O)



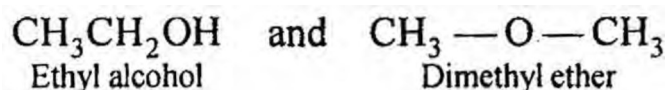
(b) 1-Butene and 2-Butene (Mol. Formula = C₄H₈)



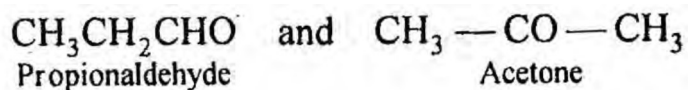
(iii) Functional isomerism

Different compounds, with same molecular formula but different functional groups are known as functional isomers. For example:

(a) Ethyl alcohol and Di methyl ether (Mol. Formula = C₂H₆O)



(b) Propanaldehyde and acetone (Mol. Formula = C₃H₆O)

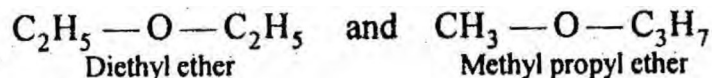


(iv) Metamerism:

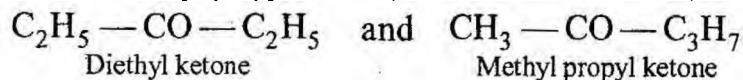
This is a special kind of structural isomerism in which different compounds, with same molecular formula, belong to same homologous series but differ in "the distribution of alkyl groups around a central atom.

Examples are:

(a) Diethyl ether and methyl propyl ether (Mol. Formula = C₄H₁₀O)

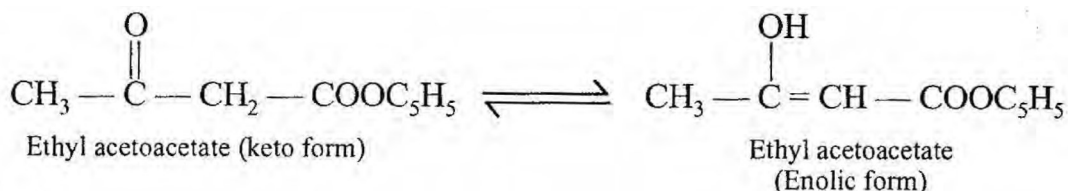


(b) Diethyl ketone and methyl propyl ketone (Mol. Formula = C₅H₁₀O)



(v) Tautomerism :

Compounds whose structures differ in the arrangement of atoms but which exist simultaneously in dynamic equilibrium with each other are called tautomers. This phenomenon is called tautomerism. In most of the cases tautomerism is due to shifting of a hydrogen atom from one carbon (or oxygen or nitrogen) to another with the rearrangement of single or double bonds. For example,



2. STEREOISOMERISM

Compounds having different three-dimensional relative arrangement of atoms in space are called stereoisomers. This phenomenon is called stereoisomerism. These compounds are said to have different configurations. Stereoisomerism is of the following different kinds:

- (i) Geometrical isomerism.
- (ii) Optical isomerism
- (iii) Conformational isomerism

(i) Geometrical isomerism

Two carbon atoms joined by a single bond (sigma bond) are capable of free rotation around each other, but this rotation is hindered in case of compounds containing carbon-carbon double bond. According to molecular orbital theory, carbon atoms involved in double bond formation are sp^2 hybridised so that each carbon atom has three planar sp^2 hybridised orbitals and fourth p orbital having its lobes at right angles to the plane of sp^2 orbitals. The formation of pi bond involves the overlapping of p orbitals. With the formation of a pi bond between C — C along with the sigma bond, which is already existing, there remains no possibility of rotation along C — C axis. Neither of the two doubly bonded carbon atoms can be rotated about double bond without destroying the pi bond, which requires large amount of energy. Thus, at ordinary temperature, the rotation about a carbon - carbon double bond is restricted or hindered and gives rise to a kind of stereoisomerism known as 'Geometrical isomerism'.

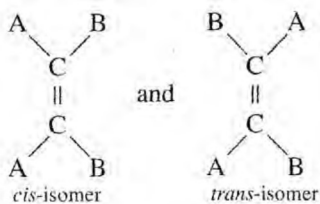
Geometrical Isomerism, also known as cis-trans isomerism takes place in compounds containing carbon-carbon double bond in which each of the two doubly bonded carbon atoms is attached to two different atoms or groups. All the compound with general formula of the type $C_{AB} = C_{DE}$ or $C_{AB} = C_{AB}$ show geometric isomerism. If either of the two carbon atoms carries two identical/groups as in $C_{AB} = C_{AA}$ or $C_{AB} = C_{DD}$, the isomerism does not exist. This isomerism is due to difference in the relative spatial arrangement of the atoms or groups about the doubly bonded carbon atoms.

Conditions to be fulfilled by a compound to exhibit geometrical isomerism

For a compound to show geometrical isomerism the following conditions are necessary:

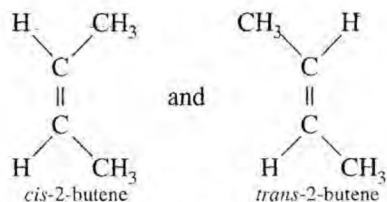
- (i) The molecule must contain a carbon-carbon double bond about which there is no free rotation.
- (ii) Each of the double bonded carbon atoms must be attached to two different atoms or groups.

In case of compounds with formula of the type $C_{AB} = C_{AB}$; if two similar groups are on the same side of double bond, the isomer is known as **cis-** and if two similar groups are on the opposite sides of the double bond the isomer is known as **trans** such as:

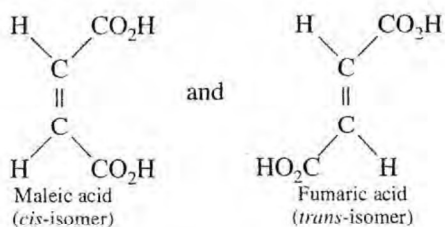


For example,

2-butene exists in two isomeric forms.



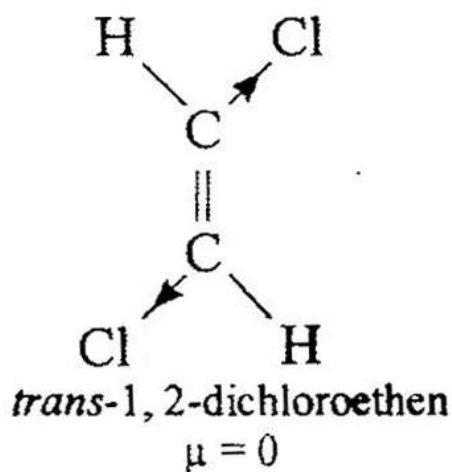
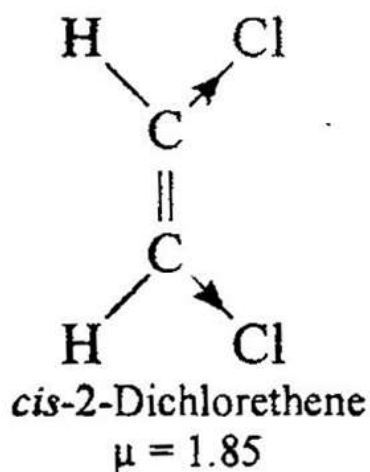
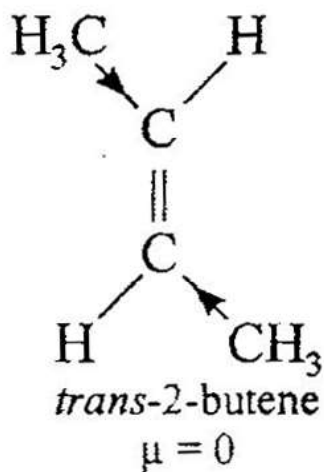
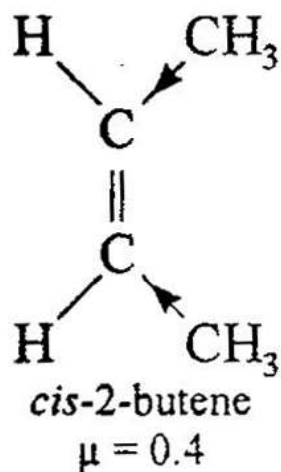
Similarly butene-dioic acid exists in two isomeric forms; *cis*- form is called maleic acid and *trans*- form is called fumaric acid



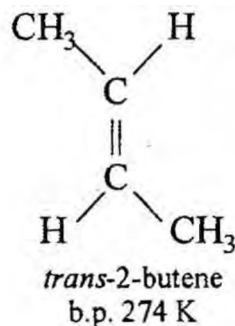
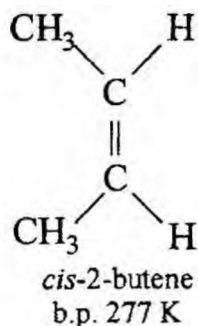
Determination of configuration of a geometrical isomer

Different methods available for determination of configuration of a geometrical isomers are described below;

(i) From Dipole moments. Generally *cis*-isomer has greater dipole moment as compared to *trans*-isomer. In case of *cis*- the similar groups being on the same side, the electronic effects are additive; while in case of *trans*-isomer, the similar groups being on opposite side, the electronic effects cancel each other.



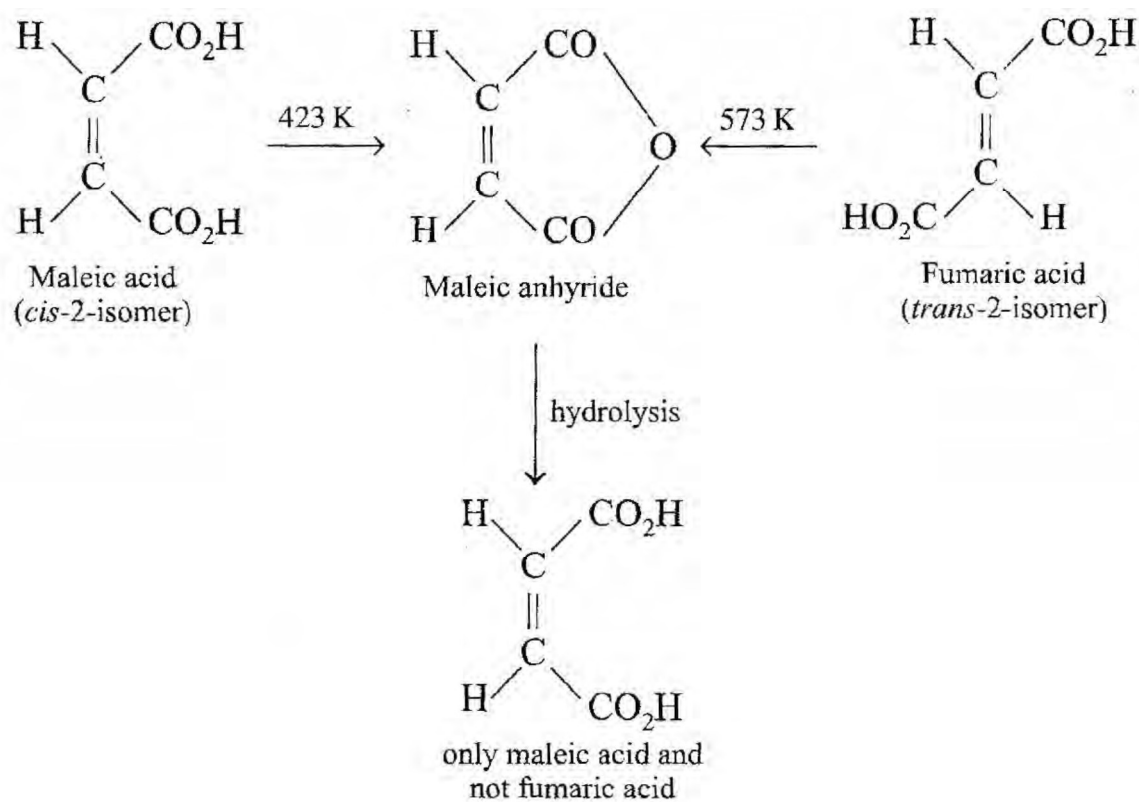
- (ii) From boiling point. Generally speaking, a *cis* isomer has a higher boiling point compared to the *trans* isomer. This is because of higher dipole moment and higher polarity in the molecule which acts as the binding force and is responsible for higher b.p. of the *cis* isomer. Boiling point of *cis*-2-butene is 277 K while the *trans*-2-butene boils at 274 K.



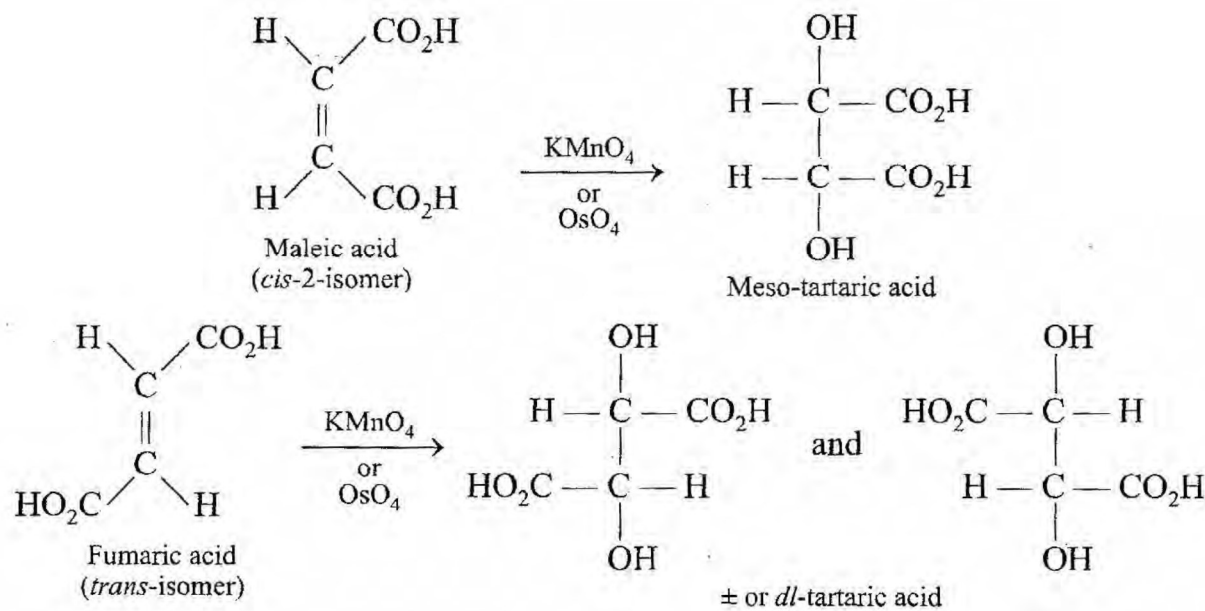
- (iii) From melting point. The isomers show a reverse trend here. The 'U' shape of the *cis* isomer doesn't pack well compared to the straighter *trans* isomer. The poorer packing of the *cis* isomer means that the intermolecular forces are not as effective as they should be

and so less energy is required to melt the cis isomers. Thus, maleic acid melts at 403 K whereas fumaric acid melts at 575 K.

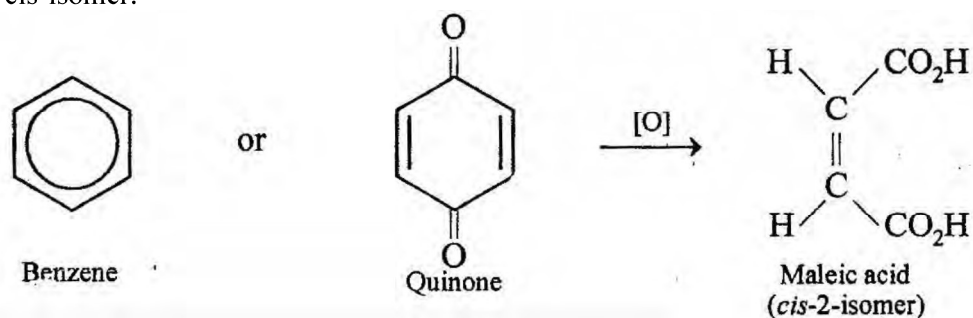
- (iv) From the formation of cyclic compounds. Two geometric isomers (cis and trans) can be distinguished through reactions that lead to formation of ring. Cis-isomer undergoes ring closure more readily than the trans-isomer. For example maleic acid readily loses water when heated to about 423 K, to give an anhydride; while fumaric acid does not give anhydride at this temperature. Rather it must be heated to 573 K to get the same anhydride. Further, hydrolysis of anhydride yields only maleic acid.



- (v) From the formation of the type of optical isomer. Maleic acid and fumaric acid, both on treatment with KMnO_4 or OSO_4 yield optically inactive variety of tartaric acid. Maleic acid yields meso tartaric acid, while fumaric acid yields racemic (\pm or dl) tartaric acid.



- (vi) From the method of preparation. Method of preparation of a compound sometimes leads to its configuration. The isomer obtained by the rupture of a ring must be the *cis*-isomer, e.g., maleic acid can be prepared by the oxidation of benzene or quinone, so it must be a *cis*-isomer.

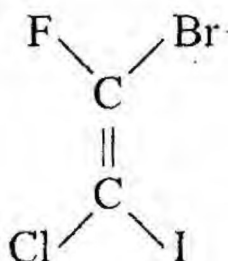


E and Z designations of geometrical isomers

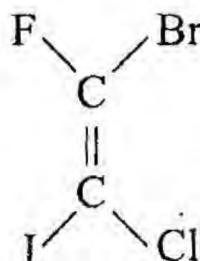
The *cis* and *trans*- designations can be used only for the compounds in which two doubly bonded carbon atoms are having similar atoms or groups e. g., of the type $\text{C}_{\text{AB}}=\text{C}_{\text{AB}}$. But, when the two doubly bonded carbon atoms are having different atoms or groups attached to them e.g., of the type $\text{C}_{\text{AB}}=\text{C}_{\text{DE}}$; it is not possible to assign them *cis* or *trans* configurations. To overcome this difficulty, a more general system for designating the configuration of geometric isomers has been adopted. This system developed by Cahn, Ingold and Prelog originally for the absolute configuration of optical isomers, is known as E and Z system and is based on priority of attached groups. The atoms or groups attached to each carbon of the double bond, are assigned first and second priority. If the atoms or groups having higher priority attached to two carbons are on the same side of double bond the configuration is designated as Z (derived from German word Zusammen meaning together)

and if the atoms or groups of higher priority are on the opposite side of the double bond, the configuration is designated as E (derived from German word -entgegen meaning across or opposite). Priorities of atoms or groups are determined in the same way as for R & S configurations of optical isomers. At. weights or atomic numbers of atoms directly linked with ethylenic carbon atoms are taken into consideration.

Let us consider an example in which two doubly bonded atoms are attached to four different halogens such as $\text{C}_{\text{BrF}} = \text{C}_{\text{ICl}}$. Since Br is having higher priority over F and I is having priority over Cl (due to their higher atomic numbers). The isomer in which Br and I are on the same side of double bond will be called Z and the isomer in which Br and I are on the opposite sides of double bond will be called E.

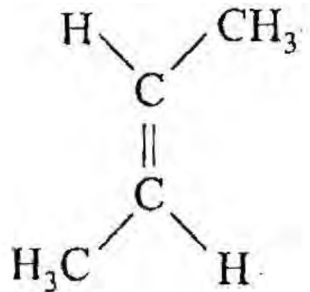
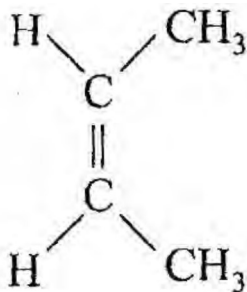


Z-isomer

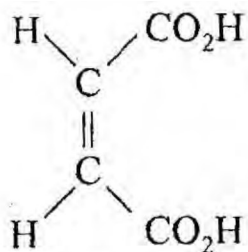


E-isomer

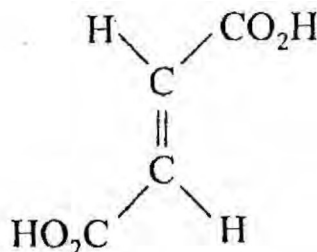
In the same way cis and trans isomers of 2-butene can be called Z and E-2-butenes respectively.



Similarly maleic acid can be specified as Z-isomer and fumaric acid as E-isomer.



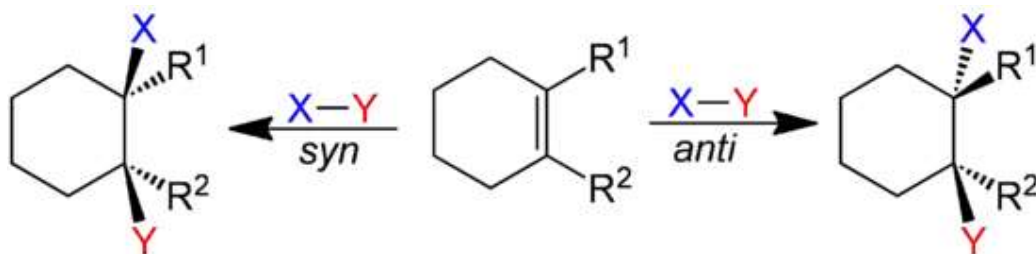
Maleic acid
(*Z-isomer*)



Fumaric acid
(*E-isomer*)

In determining the configuration, we have to select the group of higher priority on one carbon. Similarly we select the group of higher priority on the other carbon atom. If these two groups are on the same side of double bond, the configuration is Z, otherwise it is E.

Syn anti Isomerism



Syn addition is the addition of two substituents to the same side (or *face*) of a double bond or triple bond, resulting in a decrease in bond order but an increase in number of substituents. Generally, the substrate will be an alkene or alkyne. An example of syn addition would be the oxidation of an alkene to a diol via a suitable oxidizing agent such as Osmium tetroxide OsO₄ or Potassium permanganate KMnO₄.

Anti addition is in direct contrast to syn addition. In anti addition, two substituents are added to opposite sides (or *faces*) of a double bond or triple bond, once again resulting in a decrease in bond order and increase in number of substituents. The classical example of this is bromination (any halogenation) of alkenes.

Depending on the substrate double bond, addition can have different effects on the molecule. After addition to a straight-chain alkene such as C₂H₄, the resulting alkane will rapidly and freely rotate around its single sigma bond under normal conditions (i.e. room temperature). Thus whether substituents are added to the same side (syn) or opposite sides (anti) of a double bond can usually be ignored due to free rotation. However, if chirality or the specific absolute orientation of the substituents needs to be taken into account, knowing the type of addition is significant. Unlike straight-chain alkenes, cycloalkene syn addition allows stable addition of substituents to the same side of the ring, where they remain together. The cyclic locked ring structure prevents free rotation.

(ii) Optical isomerism or enantiomerism

Before taking up optical isomerism, let us understand the terms: plane polarised light, optical activity and specific rotation.

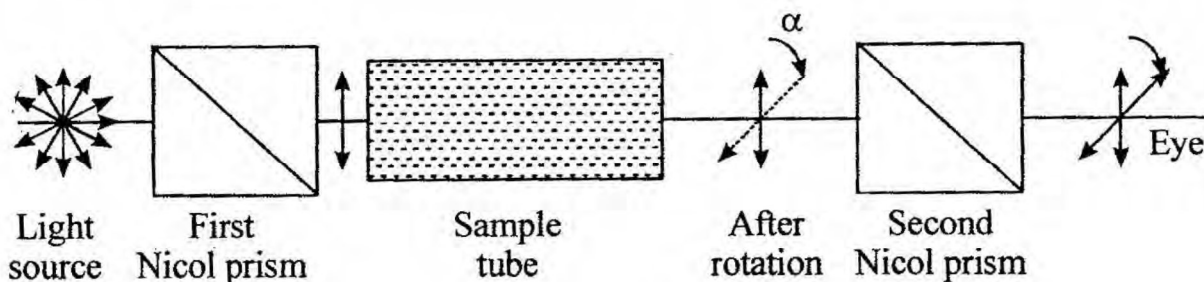
Plane polarised light:

Ordinary light has vibrations taking place at right angles to the direction of propagation of light spread in all the possible planes. If we pass ordinary light through nicol prism, vibrations in all planes except one are cut off. Thus light coming out of nicol prism has vibrations only in one plane. Such a light is called plane polarised light.

Optical activity

Behaviour of certain substances is strange. When a plane polarised light is passed through the solution of such substances, the light coming out of the solution is found to be in a different plane. The plane of polarised light is rotated. Such substances, which rotate the plane of plane polarised light when placed in its path are known as optically active substances and the phenomenon is known as optical activity. The angle of rotation (α) of plane polarised light is known as Optical rotation. The substances which rotate the plane of polarised light to the

clockwise or right direction are known as dextrorotatory or having positive (+) rotation and those which rotate the plane polarised light to the anticlockwise or left direction are known as laevorotatory or having negative (-) rotation. Substances which do not rotate the plane of polarised light are said to be optically inactive. The instrument used for measuring optical rotation is called polarimeter. It consists of a light source, two nicol prisms and in between a tube to hold the solution of organic substance. The schematic representation of a polarimeter is given below:



Specific rotation. The angle of rotation of plane-polarised light or optical rotation (α) of an organic substance depends not only on the kind of molecules but also varies considerably with the number of molecules that light encounters in its path which in turn depends on the concentration of the solution used and the length of polarimeter tube containing it. Besides this, it depends on temperature, wavelength of light and nature of solvent used.

The optical activity of a substance is expressed in terms of *specific rotation*, $[\alpha]_{\lambda}^t$ which is a constant quantity, characteristic of a particular substance,

$$[\alpha]_{\lambda}^t = \frac{\alpha}{l \times c}$$

where, α = observed rotation in degrees

λ = length of polarimeter tube in decimeter

c = concentration of substance in gm per ml of solution

t and λ signify the temperature and wavelength of light used.

When $l = 1$ and $c = 1$, $[\alpha]_{\lambda}^t = \alpha$

Specific rotation is thus defined as the optical rotation produced by a compound when plane polarised light passes through one decimeter length of the solution having concentration one gram per millilitre. Usually the monochromatic light used is D line of sodium ($\lambda = 589 \text{ nm}$). Thus specific rotation of cane sugar can be expressed as

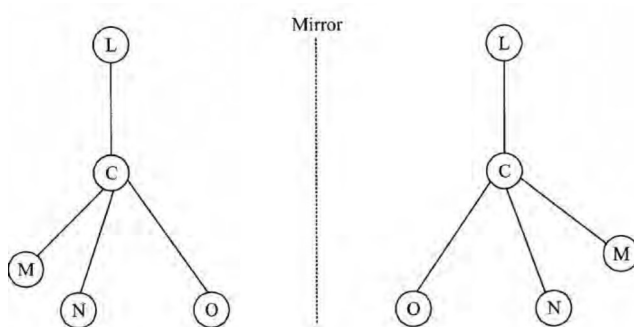
$$[\alpha]_{\text{D}}^{20^{\circ}\text{C}} = +66.5^{\circ} (\text{water})$$

In this expression D stands for D line of sodium, 20°C is temperature of measurement, + sign shows the dextrorotation and water is the solvent used.

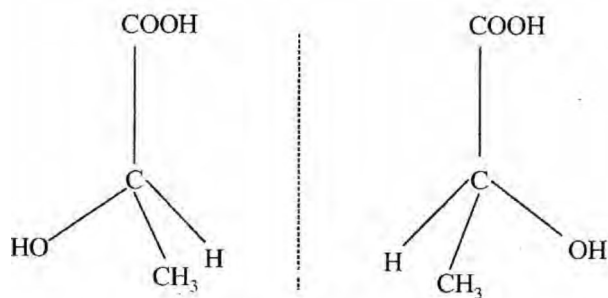
Louis Pasteur, while studying the crystallography of salts of tartaric acid made a peculiar observation. He observed that optically inactive sodium ammonium tartarate existed as a mixture of two different types of crystals which were mirror images of each other. With the help of a hand lens and a pair of forceps, he carefully separated the mixture into two different types of crystals. These crystals were mirror images of each other and were called enantiomorphs and the phenomenon as enantiomorphism. Although the original mixture was optically inactive;

each type of crystals when dissolved in water, were found to be optically active. Moreover the specific rotations of the two solutions were exactly equal but of opposite sign i.e. one solution rotated the plane polarised light to the right or clockwise while the other to the left or anticlockwise and to the same extent. Two types of crystals or solutions were identical in all other physical and chemical properties. Isomers which are non superimposable mirror images of each other are called enantiomers.

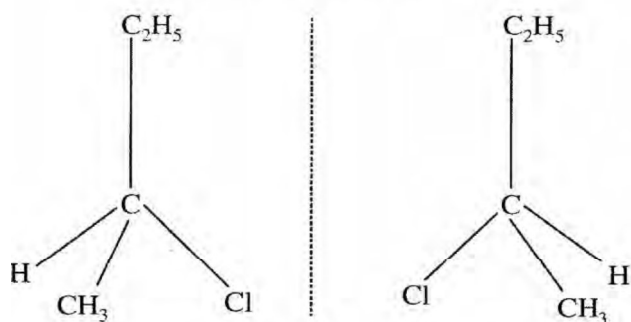
According to La Bell and Van't Hoff the four valencies of a carbon atom are directed towards the four corners of a regular tetrahedron at the centre of which lies the carbon atom. Consider a compound of formula C_{LMNO} having four different groups L, M, N and O - attached to a carbon atom. This compound can be represented by two models which look like mirror images of each other.



It is important to note here that these two molecules cannot be superimposed on each other i.e. they will not coincide in all their parts. We may turn them in as many ways as we like but we find that though two groups of each may coincide, the other two do not. Hence these must represent two isomers of formula C_{LMNO} . Lactic acid $CH_3CHOHCOOH$ and sec-Butyl chloride $C_2H_5CHClCH_3$ exist as two optically active isomers which are enantiomers i.e. mirror images of each other.



Enantiomers of Lactic Acid



Enantiomers of Sec. Butyl Chloride

Mirror images of the two compounds are represented as above. The carbon atom to which four different groups are attached, is known as asymmetric or chiral carbon atom or stereogenic centre. If two of the groups attached to carbon are same, we shall observe that it is possible to superimpose the mirror images on each other. Such a compound will not show optical isomerism or enantiomerism.

Hence non-superimposability of the mirror images is responsible and essential for the type of stereoisomerism known as enantiomerism.

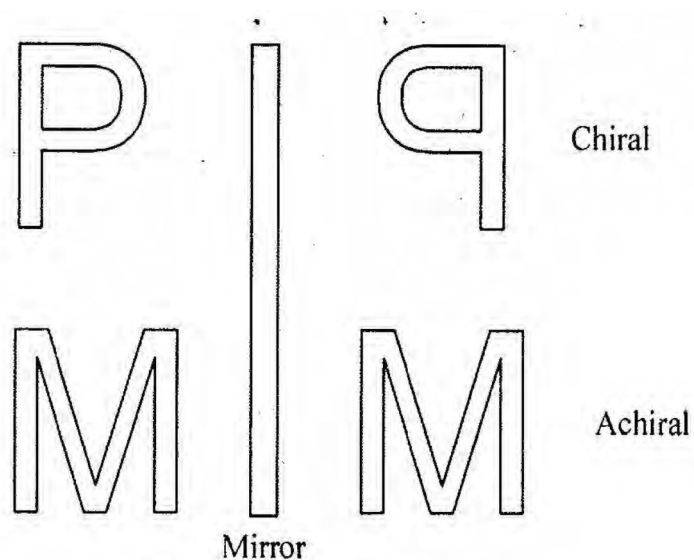
The term optical isomerism is used for the existence of stereoisomers which differ in their behaviour towards the plane polarised light. Thus enantiomeric molecules are always non-superimposable mirror images of each other. The non—superimposability of mirror images arises due to chiral or asymmetric nature of molecule. A molecule is said to be chiral if it has no plane of symmetry and is therefore non-superimposable on its mirror image.

It may be concluded with the remarks that chirality is the fundamental condition of enantiomerism or optical isomerism.

Chirality and dissymetry

An object which is non-superimposable on its mirror image is called chiral object. And an object which is superimposable on its mirror image is called achiral object. Examples of chiral objects including letters from English alphabets are: A pair of hands, shoes, gloves, letters P, F, J etc.

Examples of achiral objects and letters are: Ball, sphere, letters A, O, M, etc.

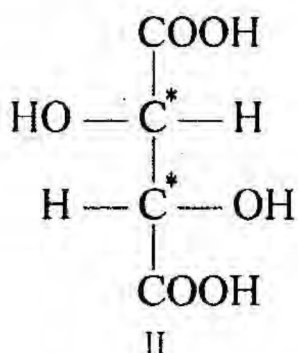
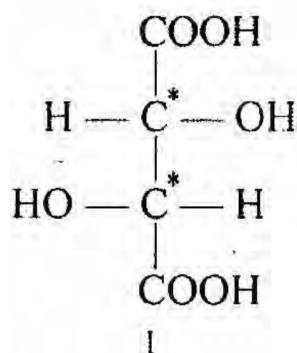


Chiral and achiral Objects

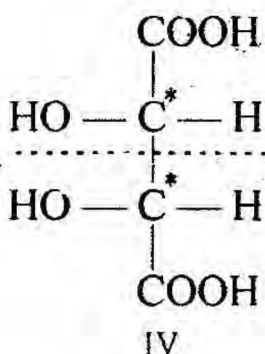
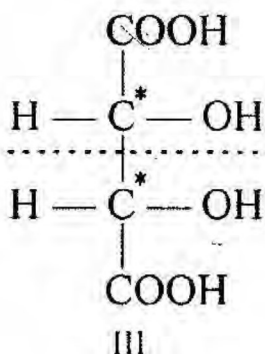
Achiral objects or molecules possess a plane of symmetry that can divide the molecule into two identical halves. Chiral objects or molecules do not possess a plane of symmetry that can divide the molecule into two identical halves. The chirality is also known as dissymmetry while achirality is also known as symmetry.

Thus chirality or dissymmetry is the property associated with certain compounds which do not have a planes of symmetry and are thus non-superimposable on their mirror images. Dissymmetry is an essential condition for optical activity. In the study of enantiomers containing one chiral carbon atom, we find that they do not have a plane of symmetry and hence are dissymmetric in nature, for example, lactic acid, sec-butyl chloride etc. We can thus say that compounds with a chiral carbon atom are optically active in nature.

This is not true, however, for compounds with two or more chiral carbon atoms. Here, one or more isomers may be optically inactive in spite of the presence of chiral carbon atoms. Consider for example, the case of tartaric acid, $\text{CH}(\text{OH})\text{COOHCH}(\text{OH})\text{COOH}$. It has two chiral carbons (stereogenic centres) marked * and thus has four isomers as shown below:



I and II are optically active due to the absence of plane of symmetry

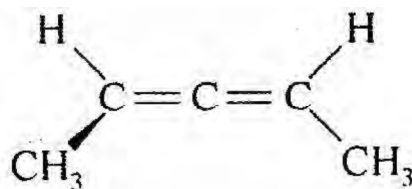
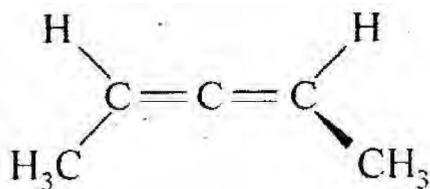


III and IV are optically inactive due to the presence of plane of symmetry (shown by dotted line)

Isomers I and II are non-superimposable mirror images of each other, they are dissymmetric and optically active. But III and IV have a plane of symmetry. Therefore, they are symmetric and optically inactive in nature. In other words, optical activity in organic compounds is due to the presence of dissymmetry and not due to chiral carbon atoms alone.

No. of optical isomers for a compound is given by 2^n where n is the number of chiral carbon atoms.

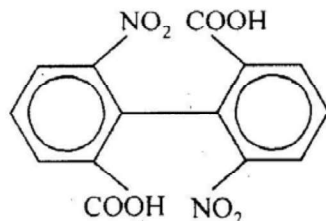
It may be noted that some organic compounds are optically active even though they do not contain chiral atom. For example, **Substituted allenes**. Dienes with double bonds in adjacent positions are called allenes. Substituted allenes may be represented as $\text{RCH} = \text{C} = \text{CHR}$. Pentane —2, 3-diene exists in two optically active forms. This is because the groups linked to one end carbon are in different plane than those linked to the other end carbon.



In allenes, the central carbon is sp hybridized, and the terminal carbons are Sp^2 hybridized. The central carbon forms two $Sp-Sp^2$ sigma bonds. The central carbon also has two p orbitals which are mutually perpendicular. These form pi bonds with the p orbitals on the other carbon atoms. As a result, the substituent at one end of the molecule are in a plane which is perpendicular to

that of the substituents at the other end, so that the compound exists in two forms which are non-superimposable mirror images and are optically active.

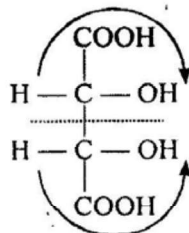
Substituted biphenyl. Benzene rings in substituted biphenyl lie in different planes; hence the compound exhibits optical activity.



We can conclude from the above discussion that the most essential condition for a compound to show optical activity is the presence of dissymmetry and not chirality. However, compounds containing only one chiral carbon are always dissymmetric since they do not have a plane of symmetry.

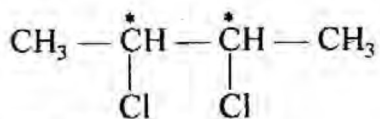
The compounds, with two or more similar chiral carbon atoms which are optically inactive due to the presence of plane of symmetry, are called **meso** compounds.

Consider the following isomer of tartaric acid

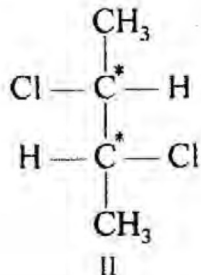
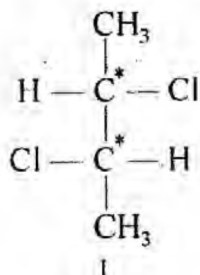


It has a plane of symmetry denoted by the denoted line. The optical rotation of upper half of the molecule is neutralized by that of the lower half as the two rotations are in opposite directions. The net result is that the molecule is optically inactive. Such compounds are known as **meso** compounds.

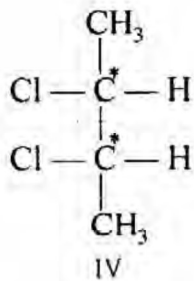
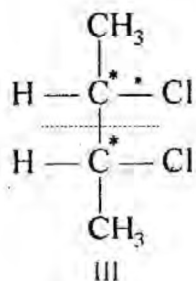
Similarly, we come across meso structures in 2, 3-Dichlorobutane. This compound also possesses two asymmetric carbon atoms (stereogenic centres) marked with *.



The different isomers can be written as



I and II show optical activity due to absence of plane of symmetry (Dissymmetry)



III and IV are optically inactive because of the presence of plane of symmetry

Structures III and IV are meso compounds because the optical activity of the upper half of the molecule is neutralised by that of the lower half.

Properties of enantiomers

(i) They have identical physical properties but differ in direction of rotation of plane polarised light. Though the two enantiomers rotate the plane polarised light in opposite direction, the extent of rotation is the same.

(ii) They have identical chemical properties except towards optically active reagents. The rates of reaction of optically active reagents with two enantiomers differ and sometimes one of the enantiomers does not react at all.

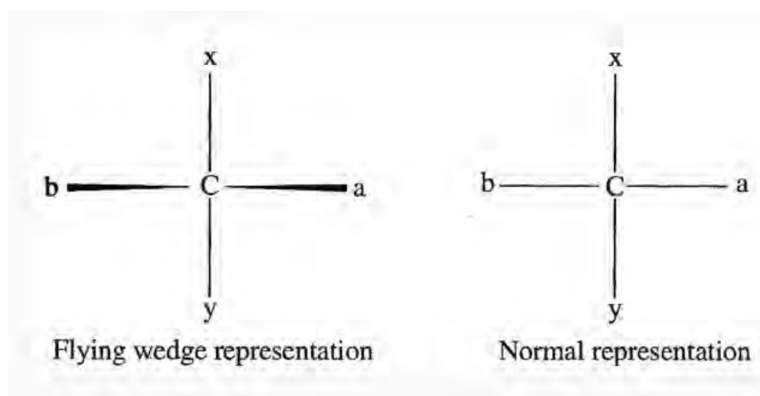
Example: In biological system (-) or l-glucose is neither metabolised by animals nor fermented by yeast whereas (+) or d-glucose undergoes both these processes and plays an important role in animal metabolism and fermentation. Similarly mould *penicillium glaucum* consumes only d-tartaric acid when fed with a mixture of equal quantities of d- and l-tartaric acid.

(iii) When equal amounts of enantiomers are mixed together an optically inactive racemic modification denoted by (±) or dl is obtained.

Fischer's projection formula for planar representation of three dimensional molecules.

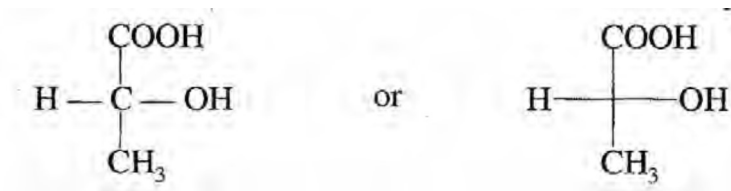
Emil Fischer in 1891 introduced a simple method for representing three dimensional molecules in one plane. It is known as Fischer projection formula. Following points are to be observed for this purpose:

- (i) The chiral molecule is imagined in such a way that two groups point towards the observer and two away from the observer. The groups pointing towards the observer are written along the horizontal line (shown by thick wedge-like bonds) and those pointing away are written along the vertical line. The central carbon is present at the crossing of the horizontal and vertical lines.

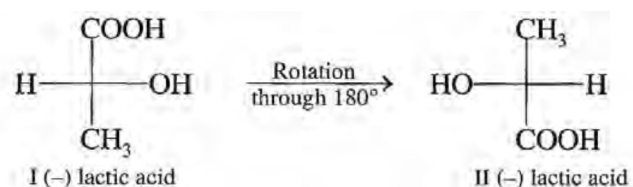


Thus if a, b, x and y are four groups attached to a carbon, the molecule will be represented by the projection formula as above. Here a and b groups point towards the observer (or above the plane) and groups x and y are away from the observer (or below the plane).

- (ii) The longest chain of carbon atoms in the molecule should be represented along the vertical line. Lactic acid, therefore, according to the above conventions will be represented as

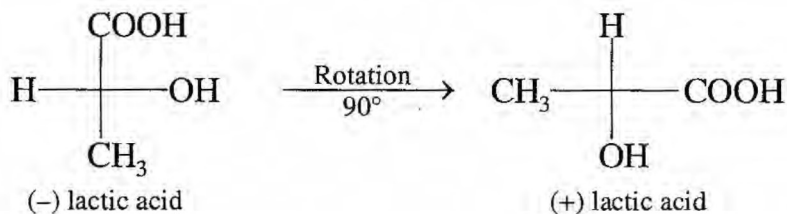


- (iii) We can avoid writing carbon at the crossing of the vertical and horizontal lines. A crossing automatically means the presence of a carbon.
- (iv) If necessary, planar formula may be imagined to be rotated from end to end without lifting it from the plane of the paper. Rotation by 180° in the plane of the paper does not create any change in the configuration of the molecule.

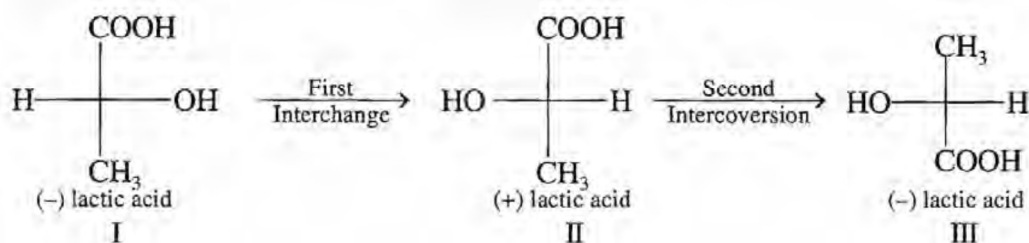


In the above rotation by 180° , II has been obtained from I. There has been no change in configuration of the molecule. I and II are in fact the same thing.

- (v) Rotation by 90° or 270° brings about a change in configuration of the molecule. Consider the following rotation.



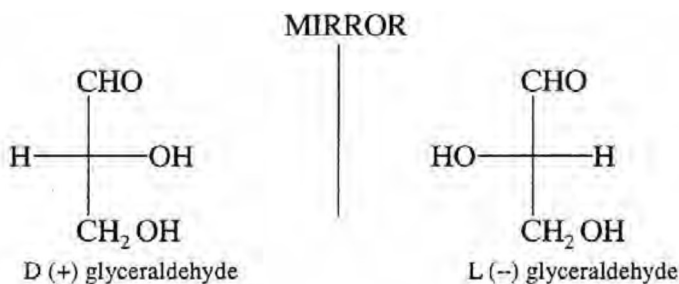
- (vi) If the positions of two groups across the chiral atom are interchanged, it leads to inversion of configuration. Two consecutive such changes neutralise the effect.



Structure III and I are the same because as per rule (iv) above, III on rotation through 180° will give I.

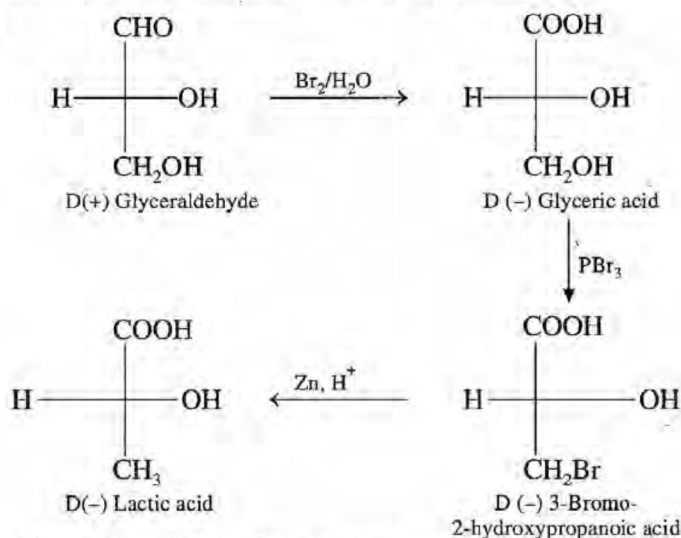
Absolute configuration of optical isomers

In the earlier days, as the modern techniques of finding out configuration were not available, Fischer assigned the following configurations to the (+) and (-) enantiomers of glyceraldehyde arbitrarily and denoted them by capital letters D and L respectively. Small letters d and l represent sign of rotation, While capital letters D and L represent configuration.



The relative configurations of a number of other optically active compounds have been established by correlating them with D(+) or L(-) glyceraldehyde. All those optically active compounds, which are obtained from D(+) glyceraldehyde through a sequence of reactions *without breaking the bonds of asymmetric carbon atom*, are designated as D configuration irrespective of their sign of rotation and the other enantiomer as L configuration.

For example,



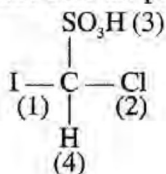
In all the D configurations, —OH attached to asymmetric carbon atom is written on the right hand side of Fischer projection formula. Similarly, in all the L-configurations, —OH attached to the lowest asymmetric carbon atom is written on the left hand side in the Fisher's projection formula.

R and S specification for the configuration of an optically active compound

Cahn, Ingold and Prelog developed a method which can be used to designate the configuration of all the molecules containing asymmetric carbon atom (chiral centre). This system is known as *Cahn-Ingold-Prelog system* or R and S system and involves two steps.

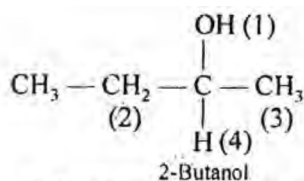
Step I. The four different atoms or groups of atoms attached to chiral carbon atom are assigned a sequence of priority according to the following set of sequence rules.

Sequence Rule 1. If the four atoms, directly attached to asymmetric carbon atom, are all different, the priority depends on their atomic number. The atom of higher atomic number gets higher priority. For example, in chloriodomethane sulphonic acid the priority sequence is I, Cl, SO₃H, H

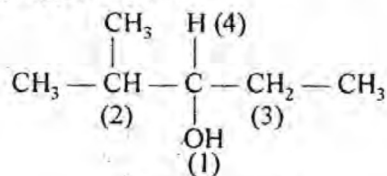


We consider the atom of the group which is directly linked to the central carbon.

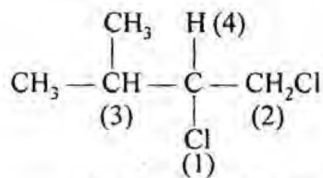
Sequence Rule 2. If Rule 1 fails to decide the relative priority of two groups it is determined by similar comparison of next atoms in the group and so on. In other words, if two atoms directly attached to chiral centre are same, the next atoms attached to each of these atoms, are compared. For example in 2-butanol two of the atoms directly attached to chiral centre are carbon themselves. To decide the priority between the two groups —CH₃ and —CH₂CH₃, we proceed like this. Methyl carbon is further linked to H, H and H. The sum of atomic numbers of three H is 3. The methylene carbon of the ethyl group is linked to two hydrogens and one carbon directly. The sum of at. no. of two H and one C is 8. Thus ethyl group gets the priority over methyl. Hence the priority sequence is OH, C₂H₅, CH₃, H.



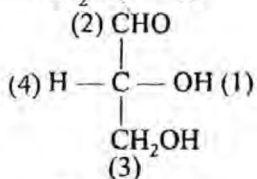
In 2-methyl - 3-pentanol, the C, C, H of isopropyl gets priority over the C, H, H of ethyl, so the priority sequence is OH, isopropyl, ethyl, H.



In 1, 2-dichloro-3-methylbutane the Cl, H, H of CH₂ Cl gets priority over the C, C, H of isopropyl due to atomic number of Cl being higher than that of C. So the priority sequence is Cl, CH₂Cl, isopropyl, H.

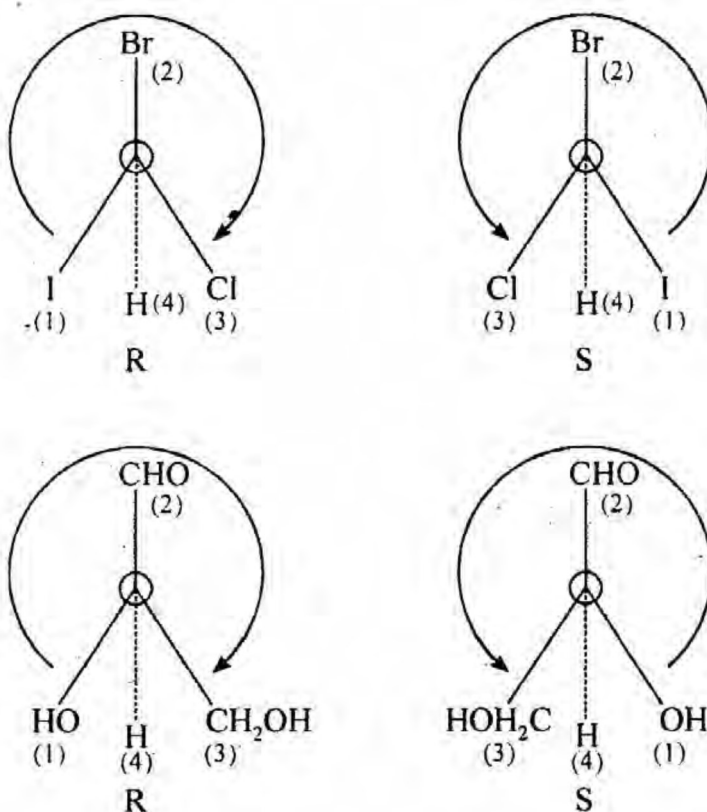


Sequence Rule 3. A doubly or triply bonded atom is considered equivalent to two or three such atoms; but two or three atoms, if attached actually, get priority over doubly or triply bonded atom. In glyceraldehyde, O, O, H of —CHO gets priority over the O, H, H of —CH₂OH; so the priority sequence is —OH, —CHO —CH₂OH —H.



Step II. After deciding the sequence of priority for four atoms or groups attached to asymmetric carbon atom; the molecule is visualised in such a way that the atom or group of lowest or last (*i.e.* fourth) priority is directed away from us, while the remaining three atoms or groups are pointing towards us. Now if on looking at these three groups (pointing towards us) in the order of their decreasing priority, our eye moves in clockwise direction, the configuration is specified as R (from Latin word *rectus* meaning right) and on the other hand if our eye moves in anticlockwise direction the configuration is specified as S (from Latin word *sinister* meaning left).

The following examples illustrate the above method for specification of configurations of R and S to molecules of compounds containing an asymmetric or chiral carbon atom.

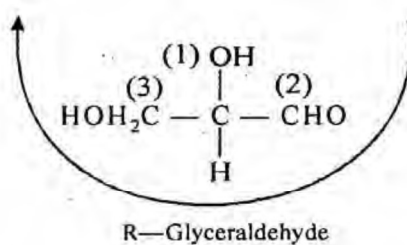


Configuration on the basis of projection formula

When a compound is represented by the Fischer projection formula, the configuration can be easily determined without constructing the model. To determine whether the eye travels clockwise or anticlockwise, we have to place the group or atom of the lowest priority at the bottom of the Fischer projection formula. The following four situations arise:

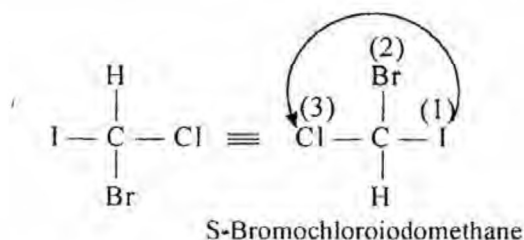
(i) The atom/group of lowest priority is at the bottom. In such a case, simply rotate the eye in the order of decreasing priorities. The configuration is R if the eye travels in clockwise direction and S if the eye travels in anticlockwise direction.

For example, Glyceraldehyde, represented by the following projection formula has R configuration:

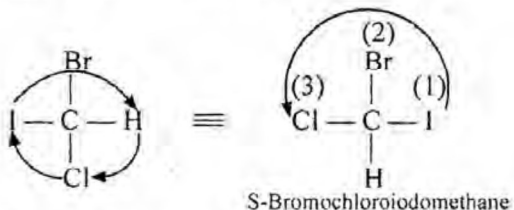


(ii) The atom/group of lowest priority is at the top. In such case, rotate the molecule by 180° so as to bring atom/group of lowest priority at the bottom. This can be done by reversing the

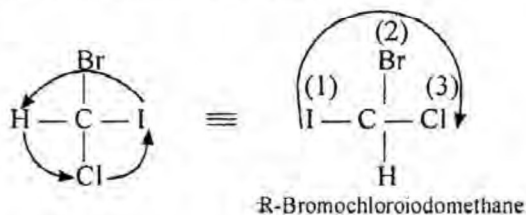
position of all the atoms or groups. Then find the direction in the order of decreasing priorities. For example, the compound CHBrClI , represented by following projection formula, has S configuration:



(iii) The atom/group of lowest priority is at the right hand side of the horizontal line. In such case, change the position of atoms or groups in clockwise direction so that atom/group of the lowest priority comes at the bottom but do not change the position of the atom/group at the top of the vertical end. Then find the direction in the order of decreasing priorities. For example, CHBrClI , represented by following projection formula, has S configuration.



(iv) The atom/group of lowest priority is at the left hand side of the horizontal line. In such case, without changing the position of atom/group at the top of the vertical end, change the position of other atoms/groups in the anticlockwise direction so that atom/group of lowest priority comes at the bottom. Then find the direction in the order of decreasing priorities. For example, CHBrClI , represented by following projection formula, has R configuration.



Racemic modifications

Racemic modification is the term used for a mixture of equal amounts of enantiomers. A racemic mixture is optically inactive because of external compensation. The optical activity caused by one enantiomer is neutralised by the activity of the other enantiomer. The notation for a racemic modification or mixture is \pm or dl. A racemic mixture may also be denoted by the letters R and S. For examples RS-sec. butyl chloride.

Methods for the resolution of racemic mixtures

The separation of racemic modification into enantiomers is called resolution. Since the two enantiomers in a racemic mixture have identical physical and chemical properties, These

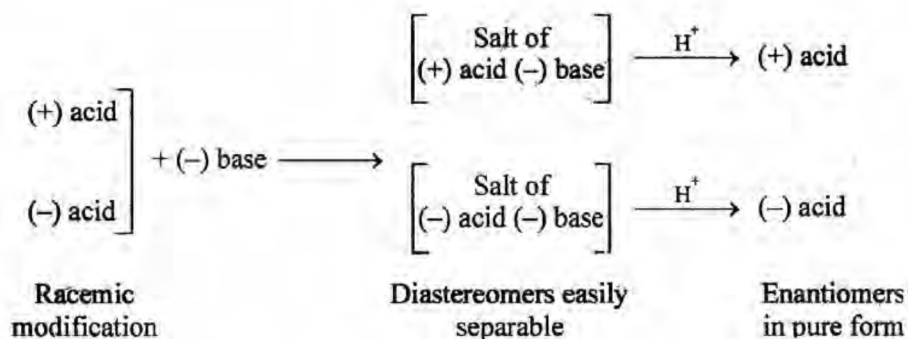
cannot be separated by usual methods of fractional distillation or fractional crystallisation. Special methods are adopted for their separation as given below:

(i) Mechanical separation. This method was first adopted by Pasteur for separating the enantiomers of ammonium tartarate. When racemic modification is crystallized from a solution, two types of crystals are obtained. These are mirror images of each other consisting of (+) and (-) forms which can be separated by hand picking with the help of a pair of tweezers and a powerful lens. This is a very laborious method and can be applied only to those compounds which give well defined distinguishable crystals of enantiomers.

(ii) Biochemical method. Certain micro-organisms grow in a racemic mixture, consuming only one of the enantiomers while leaving the other unaffected. Thus penicillium glaucum when placed in (+) tartaric acid, consumes only (+) tartaric acid and leaves (-) tartaric acid unused. The major disadvantage of this method is that one of the enantiomers get destroyed.

(iii) Chemical method. This method is mostly used for the resolution of racemic modification. In this method the racemic modification is treated with an optically active reagent to get a pair of diastereomers. Since diastereomers differ in their physical properties, it is possible to separate them by physical methods such as fractional crystallisation, fractional distillation etc. The pure diastereomers are then decomposed, into a mixture of optically active reagent and corresponding enantiomer, which can be separated.

Suppose the racemic modification is an (\pm) acid. When it is treated with an optically active, say ($-$) base, it gives a mixture of two salts, one of (+) acid (-) base, the other of (-) acid (-) base. These salts are neither superimposable nor mirror images; so these are diastereomers having different physical properties and can be separated by fractional crystallisation. After separation the optically active acids can be recovered in pure forms by adding a mineral acid.



The commonly used optically active bases for the purpose are naturally occurring alkaloids such as (-) brucine, (-) quinine, (-) strychnine and (+) cinchonine.

Similarly, the resolution of racemic bases can be carried out using a naturally occurring optically active acid such as (-) malic acid. Alcohols can be resolved in a similar way by ester formation using an optically active acid.

CONFORMATIONAL ISOMERISM

Carbon-carbon single bond in alkanes is a sigma bond formed by the overlapping of sp^3 hybrid atomic orbitals along the inter-nuclear axis. The electron distribution in such a bond is symmetrical around internuclear axis; so that free rotation of one carbon against the other is possible without breaking sigma or single covalent bond. Consequently such compound can have different arrangements of atoms in space, which can be converted into one another simply by rotation around single bond, without breaking it. These different arrangements are known as *Conformational Isomers* or *Rotational Isomers* or *Conformers*. Since the potential energy barrier for their inter-conversion is very low, it is not possible to isolate them at room temperature. At least 60-85 kJ/mole must be the energy difference between two conformers to make them isolatable at room temperature.

Hence, conformations can be defined as different arrangements of the atoms which can be converted into one another by rotation around single bonds.

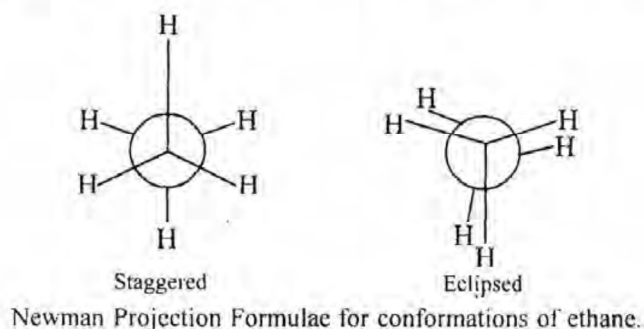
Newman and Sawhorse representations for the conformations of ethane

Alkanes can have an infinite number of conformations by rotation around carbon-carbon single bonds. In ethane two carbon atoms are linked by a single bond and each carbon atom is further linked with three hydrogen atoms. If one of the carbon atoms is allowed to rotate about carbon-carbon single bond keeping the other carbon stationary, an infinite number of arrangements of the hydrogens of one carbon, with respect to those of the other, are obtained. All these arrangements are called conformations (Bond angles and bond lengths remain the same).

Newman representation

This can be easily understood with the help of Newman Projection formulae. The molecule is viewed from front to back in the direction of carbon-carbon single bond. The carbon nearer to the eye is represented by a point and three hydrogen attached to it are shown by three lines at an angle of 120° to one another. The carbon atom away from the eye is represented by a circle and three hydrogens attached to it are shown by shorter lines at an angle of 120° to each other.

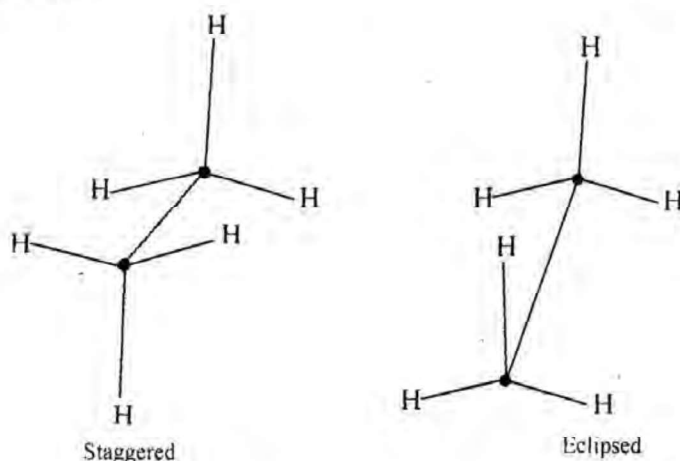
Out of infinite number of conformations, Newman Projection formulae for two extreme cases are as shown below:



The conformation in which the H atoms of two carbons are as far apart as possible, is known as *Staggered conformation* and the conformation in which the H atoms of back carbon are just behind those of the front carbon is known as *Eclipsed conformation*. These are converted into one another by rotation of one carbon against the other through 60° . The other conformations, in between these two, are known as *skew conformations*.

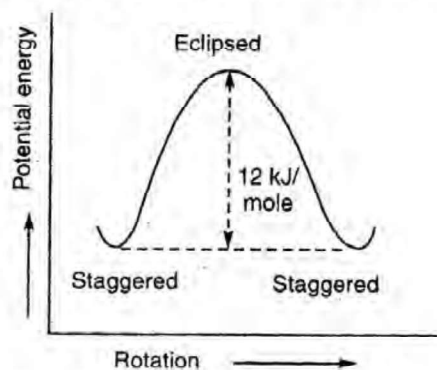
Sawhorse representation

In this representation, the molecule is visualised slightly from above and from the right and then projected on the paper. The bond between two carbons is drawn diagonally and is a bit longer for the sake of clarity. The lower left hand carbon is taken as front carbon and the upper right hand carbon is taken as back carbon. The Sawhorse representation of staggered and eclipsed conformations of ethane are given below :



Sawhorse representation for conformations of ethane

Pitzer in 1936 found that the rotation is not completely free. Rather there exists a potential energy barrier which restricts the free rotations. It means that the molecule spends most of its time in the most stable staggered conformation and it spends least time in the least stable eclipsed conformation; the energy difference being 12 kJ/mole in the case of ethane.



Rotational or torsional energy of ethane

The energy required to rotate the molecule about carbon-carbon bond is called rotational or torsional energy.

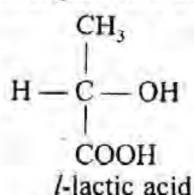
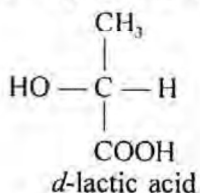
Difference between conformation and configuration

Conformation

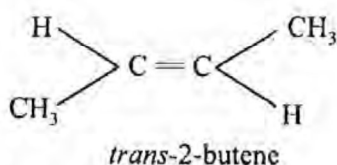
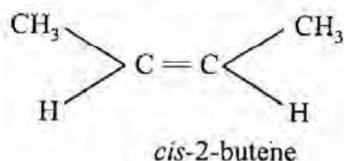
Structures containing different arrangement of atoms of a molecule in space which can arise by rotation about a single bond are called *conformers*. For example ethane exists in different conformations called staggered, eclipsed and skew conformations. The energy difference between different conformers is rather small. This phenomenon is called conformation. The property of conformation is also exhibited by *n*-butane, cyclohexane, stilbene dichloride etc.

Configuration

Structures of a compound differing in the arrangement of atoms or groups around a particular atom in space are called *configurations*. Enantiomers, diastereomers and geometrical isomers come under this category. For example *d*- and *l*-lactic acids are configurations of lactic acid.



cis and *trans* butenes are configuration of butene



Factors affecting relative stability of conformations

The following factors play a vital role in the stability of conformations.

1. **Angle strain.** Every atom has the tendency to have the bond angles that match those of its bonding orbitals. If there is any deviation from this normal bond angle, the molecule suffers from *angle strain*. Conformations suffering from angle strain are found to be less stable.

2. **Torsional strain.** There is a tendency on the part of two carbons linked to each other to have their bonds staggered. That is why the staggered form of any molecule like ethane, *n*-butane is most stable. As the bonds of two connected carbons move towards eclipsed state, a *torsional strain* is set up in the molecule thus raising its energy. Thus the staggered conformations have the least and eclipsed the highest torsional strain. The energy required to rotate the molecule around the carbon-carbon bond is called *torsional energy*.

3. **Steric strain (van der Waals' Strain).** Groups attached to two linked carbons can interact in different ways depending upon their size and polarity. These interactions can be attractive or repulsive. If the distance between the groups or atoms is just equal to the sum of their van der Waals' radii, there will be attractive interactions between them. And if these atom or groups are brought closer than this distance, there will be repulsions leading to *van der Waals' strain* or *steric strain* in the molecule.

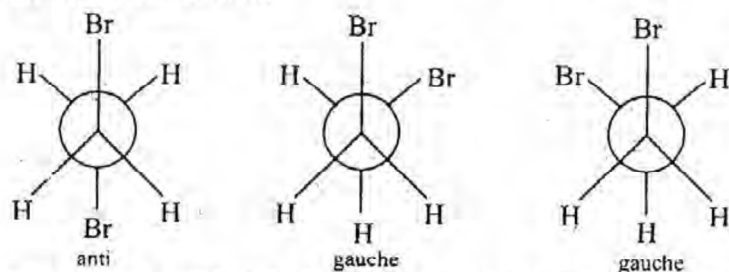
4. **Dipole-dipole Interactions.** Atoms or groups attached to bonded carbons orient or position themselves to have favourable dipole-dipole interactions. It will be their tendency to have maximum dipole-dipole attractions. Hydrogen bond is a particular case of powerful dipole-dipole attractions.

The stability of a conformer is determined by the net effect of all the above factors.

Conformations and change in dipole-moment of 1, 2-dibromoethane with temperature

The conformations of 1, 2 dibromoethane have been extensively studied by dipole-moment measurement. The conformations are depicted as under :

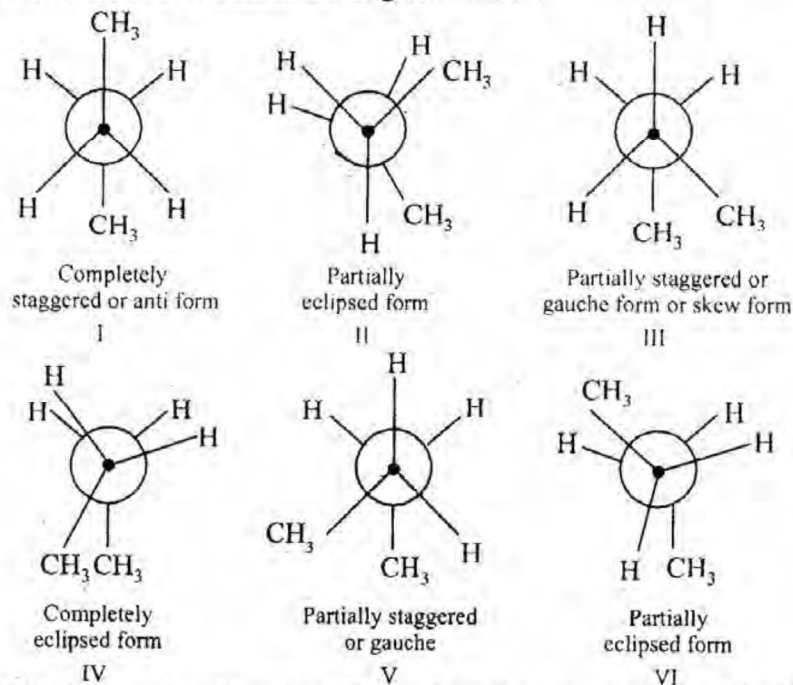
In the liquid state, the percentage of anti forms is 65 corresponding to conformational free energy of 3.5 kJ mol^{-1} in favour of *anti*.



stability of *anti*-form is due to combined effects of steric factor and dipole-dipole interactions. It goes in favour of formation of *anti*- conformer. Dipole movement increases with increase of temperature.

Conformations of butane

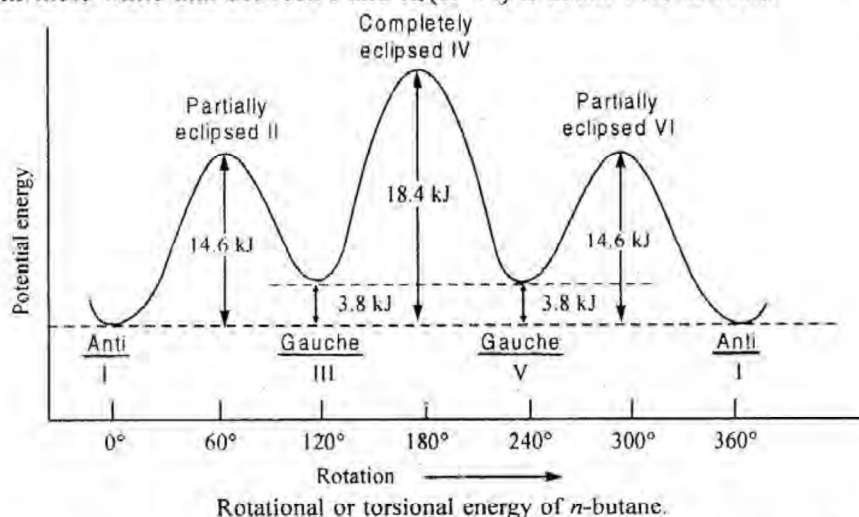
n-butane is an alkane with four carbon atoms, which can be considered to be derived from ethane by replacing one hydrogen on each carbon with a methyl group. If we consider the rotation about the central carbon-carbon bond ($\text{C}_2 - \text{C}_3$), the situation is somewhat similar to ethane; but *n*-butane has more than one staggered and eclipsed conformations (unlike ethane which has only one staggered and one eclipsed conformation). Newman Projection formulae for various staggered and eclipsed conformations of *n*-butane are as given below :



The *completely staggered* conformation, (I) also known as *anti* form, is having the methyl groups as far apart at possible. Let us see how these forms have been obtained. Let us start from structure I. Holding the back carbon (represented by circle) fixed along with its groups, — H, — H and — CH_3 , rotate the front carbon (shown by a dot) in clockwise direction by an angle of 60° . Groups attached to it will also move. *Partially eclipsed* form (II) is obtained. In this conformation (II), methyl group of one carbon is at the back of hydrogen of the other carbon. Further rotation of 60° leads of a *partially staggered* conformation (III), also known as *gauche* form, in which the two methyl groups are at an angle of 60° . Rotation by another 60° gives rise to a *fully eclipsed* form (IV) having two methyl groups at the back of each other. Further rotation of 60° , again leads to *partially staggered or gauche* form (V) having methyl groups at an angle of 60° (as in III). Still further rotation of 60° leads to

partially eclipsed form (VI), having methyl group of one carbon at the back of hydrogen of the other (as in II). If a further rotation of 60° is operated (completing the rotation of 360°), again form I is obtained. Of course, there will be an infinite number of other conformations in between these six conformations (I to VI). (*Gauche* form is also known as skew form).

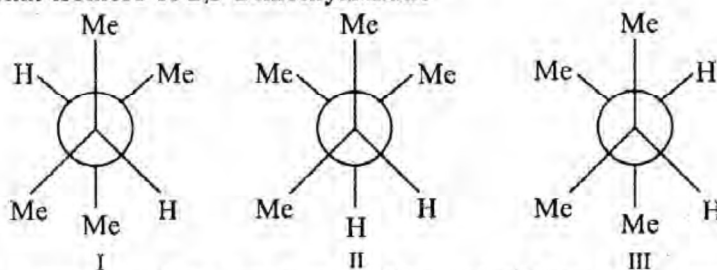
Out of these six conformations, the *completely staggered* or *anti* conformation (I) is most stable and *partially staggered* or *gauche* conformation (III or V) is slightly less stable: the energy difference being only 3.8 kJ/mole. On the other hand the *completely eclipsed* conformation (IV) is least stable and *partially eclipsed* conformation (II or VI) is slightly more stable, again the energy difference being 3.8 kJ/mole. (This is due to presence of steric strain between two methyl groups). The energy difference between most stable conformation (I) and least stable conformation (IV) is about 18.4 kJ/mole while that between I and II (or VI) is about 14.6 kJ/mole.



Thus at ordinary temperature, *n*-butane molecule exists predominantly in *anti* form with some *gauche* forms.

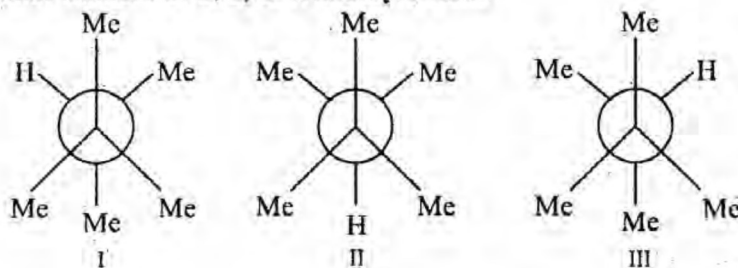
Conformational enantiomers of 2, 3-Dimethylbutane and 2, 2, 3-Trimethylbutane

Conformational isomers of 2,3-Dimethylbutane



Structure I is supposed to have maximum stability out of these three isomers, II and III are conformational enantiomers (mirror-images) also. This can be visualized after rotation of III as a whole.

Conformational isomers of 2, 2, 3-Trimethylbutane

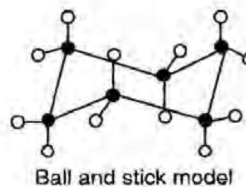
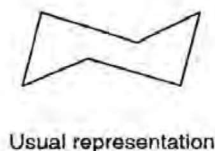
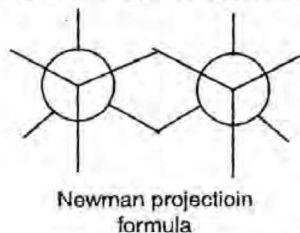


All these structures have the same stability and the compound may be assumed to occur in one conformation only.

Conformations of cyclohexane

Chair conformation

Chair conformation of cyclohexane is represented below :

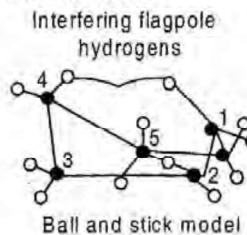
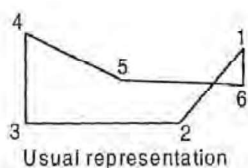
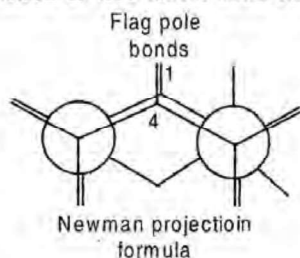


Chair conformation of *n*-butane.

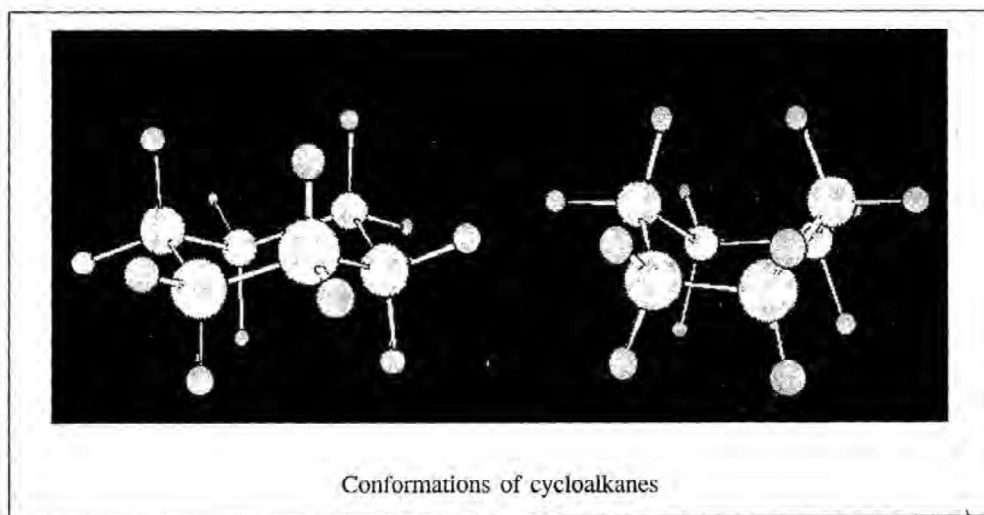
This is the most stable conformation of cyclohexane. In this conformation, all the bond angles are tetrahedral and the C — H bonds on adjacent carbons are in a staggered position. This conformation has no strain and has minimum energy.

Boat Conformation

There is no angle strain in the molecule as all the angles are tetrahedral. But hydrogens on four carbon atoms (C_2 and C_3 , C_5 and C_6) are eclipsed. As a result, there is considerable torsional strain. Also, two hydrogens pointing towards each other at C_1 and C_4 (called flagpole hydrogens) are very close to each other. This brings in van der Waals strain in the molecule. Due to these reasons boat conformation is less stable than chair conformation by an amount 28.8 kJ/mole.

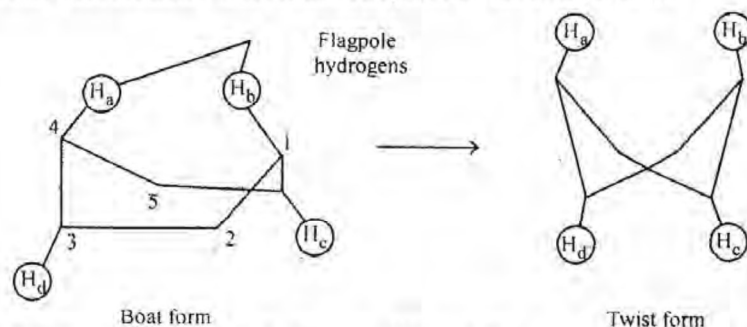


Boat conformation of cyclohexane



Twist conformation of cyclohexane. Sequence of changes in going from chair form to boat form

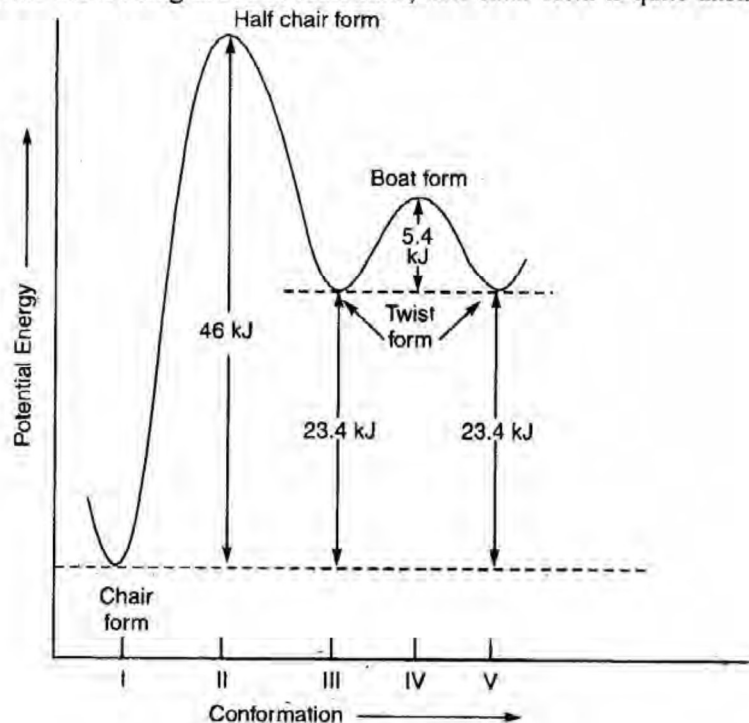
Besides chair and boat conformation, cyclohexane can have several other possible conformations. Consider model of boat conformation of cyclohexane. Hold $C_2 - C_3$ bond in one hand and $C_5 - C_6$ in the other and twist the model so that C_2 and C_5 come upwards and C_3 and C_6 go downwards. We will get another conformation known as *twist form* or *skew boat form*.

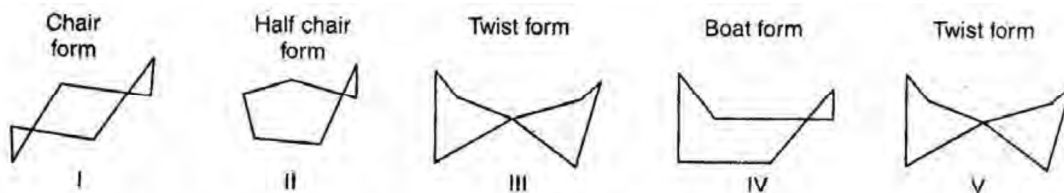


During this twisting, the flagpole hydrogens (H_a and H_b) move apart while the hydrogens H_c and H_d move closer. If this motion is continued another boat form will be obtained in which H_c and H_d become the flagpole hydrogens.

In twist forms the distance between H_a and H_b is equal to that of H_c and H_d and the steric strain is minimum; also the torsional strain of $C_2 - C_3$ and $C_5 - C_6$ (due to their being eclipsed) is partly relieved. Thus the twist form is more stable than boat form by about 5.4 kJ/mole, but it is much less stable than chair form by 23.4 kJ/mole.

If we want to convert the chair form into boat form it will have to pass through a half chair form having considerable angle strain and torsional strain. The energy difference between chair form and half chair form being about 46 kJ/mole, half chair form is quite unstable.

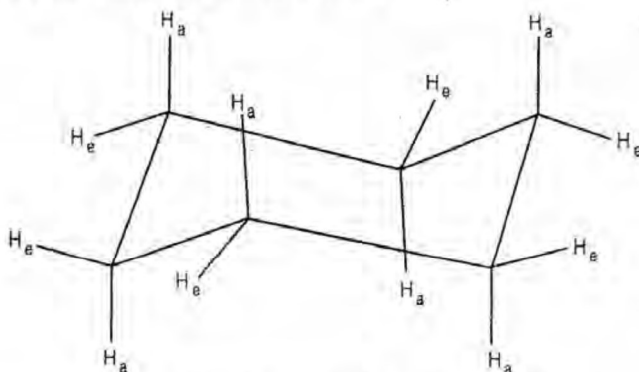




Equatorial and axial bonds in cyclohexane

Consider the structure of chair form of cyclohexane as given below :

Although, the cyclohexane ring is not planar completely, but for approximation, we can take it as planar. Consider the position of various hydrogens in the chair conformation. There are two distinct kinds of hydrogens, Six of the hydrogens which are marked H_e are almost oriented within the plane of cyclohexane ring. These are called **Equatorial hydrogen atoms**. The bonds by which these are held to the ring are called **Equatorial bonds**.



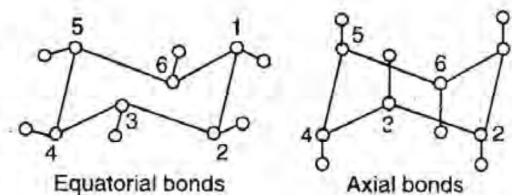
Equatorial and axial bonds in cyclohexane.

We again observe that six hydrogen atoms which are shown as H_a in the figure above are oriented perpendicular to the cyclohexane ring. These are called **Axial hydrogen atoms** and the bonds by which they are held to the ring are called **Axial bonds**.

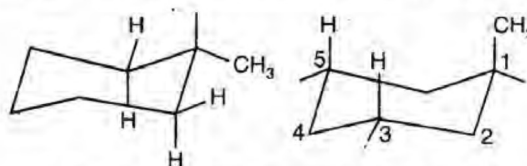
It may be noted that there is one axial and one equatorial hydrogen on each carbon in the chair conformation of cyclohexane.

1, 3-diaxial interaction

Consider the chair model of cyclohexane. Looking at the molecule, we find that six hydrogens lie in the plane while six lie above or below the plane. Six bonds holding hydrogens in the plane are called *equatorial bonds* and six bonds holding hydrogens above or below the plane are called axial bonds. By and large, there is no stress in the molecule and it is as stable as staggered ethane.



If a hydrogen is replaced by a larger group or atom, then crowding occurs. Atoms linked by axial bonds on the same side face severe crowding. This interaction is called 1, 3-diaxial interaction. Generally speaking, atoms or groups have more free space in equatorial position than in axial position.



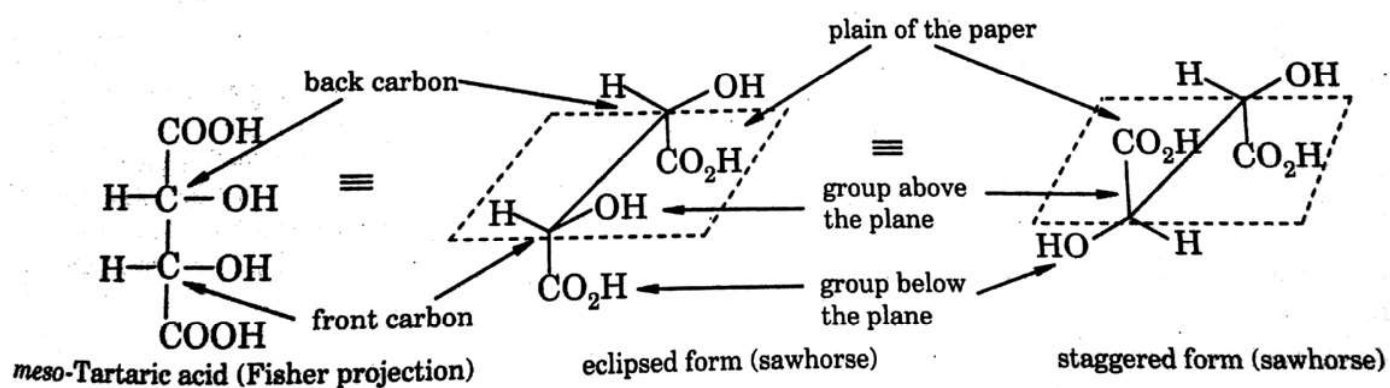
1, 3-diaxial interactions in methyl cyclohexane

There are two possible chair conformations of methyl cyclohexane one with $-\text{CH}_3$ in equatorial position and the other with $-\text{CH}_3$ in axial position.

It is observed that $-\text{CH}_3$ in equatorial position faces less crowding by hydrogens compared to $-\text{CH}_3$ in the axial position. Methyl group in the axial position is approached more closely by axial hydrogens on C – 3 and C – 5. This is called *1, 3-diaxial interaction*.

Wedge, Fischer, Newmann and Sawhorse Projection interconversions

• **Fischer projection to Sawhorse and vice -versa:**



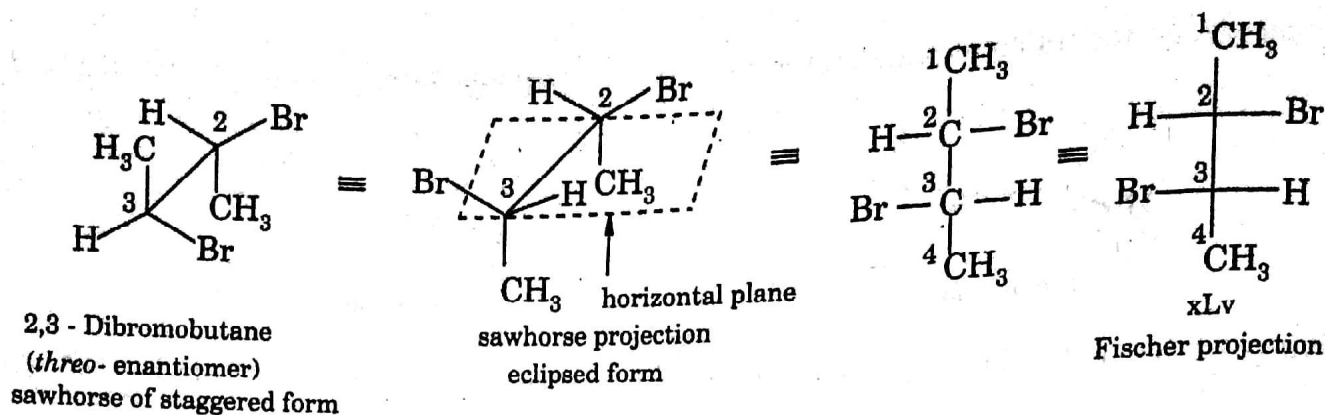


Fig. 2. 66

It is evident from the above examples that conversions of Fischer to sawhorse and *vice-versa* can be easily carried out through eclipsed form of sawhorse with proper numbering of carbon atoms, otherwise transformation may lead to a mirror image (other enantiomer). In conversions, the last chiral centre in Fischer projection (counting from the top) may be considered as the front carbon in sawhorse formula. In transposing chiral centres of eclipsed sawhorse to Fischer, if we write the front carbon as back and *vice-versa* then we will actually get the mirror image of the original configuration.

For example, in case of 2,3-dibromobutane (as shown in the above example, xLv) if the sawhorse form is written as C-2 in front and C-3 as back carbon, then the eclipsed form becomes (xLvi) and its Fischer projection will be as shown by structure (xLvii). (xLvii) is in fact the mirror image of (xLv). Therefore, we are getting the mirror image configuration of the original stereoisomer (xLv).

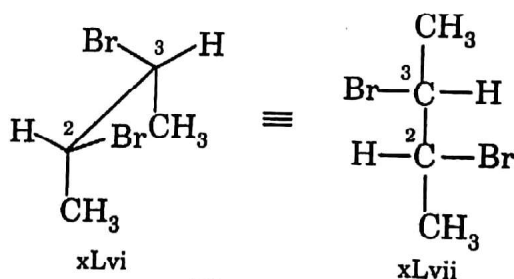


Fig. 2. 67

• **Sawhorse to Newman to Fischer and vice-versa:**

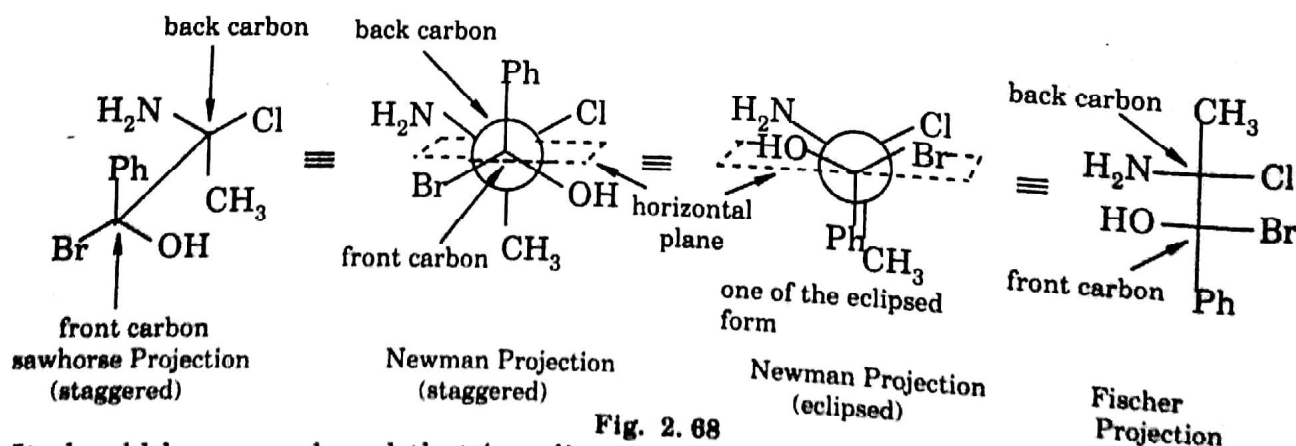


Fig. 2. 68

It should be remembered that in eclipsed form of Newman projection, the vertical bonds shown by dotted line, and transformation to Fischer projection is then carried out keeping front chiral atom as the lowest chiral centre in the Fischer projection (counting from the top).

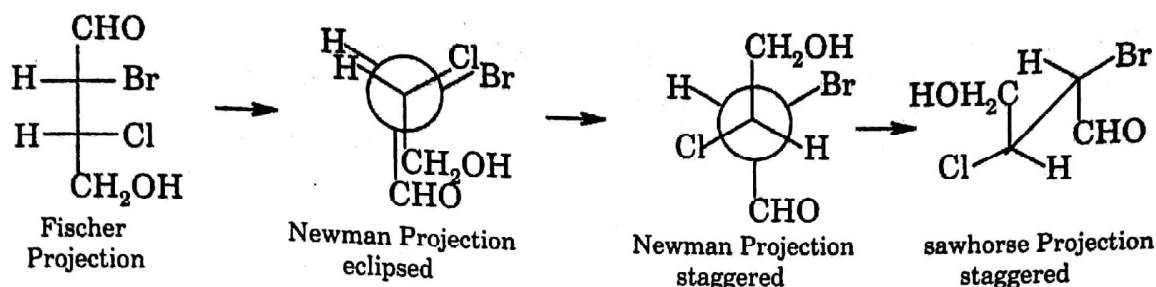


Fig. 2.69

• **Fischer Projection to Flying wedge and vice-versa:**

Conversion of Fischer projections to flying wedge and *vice-versa* may be carried out as follows.

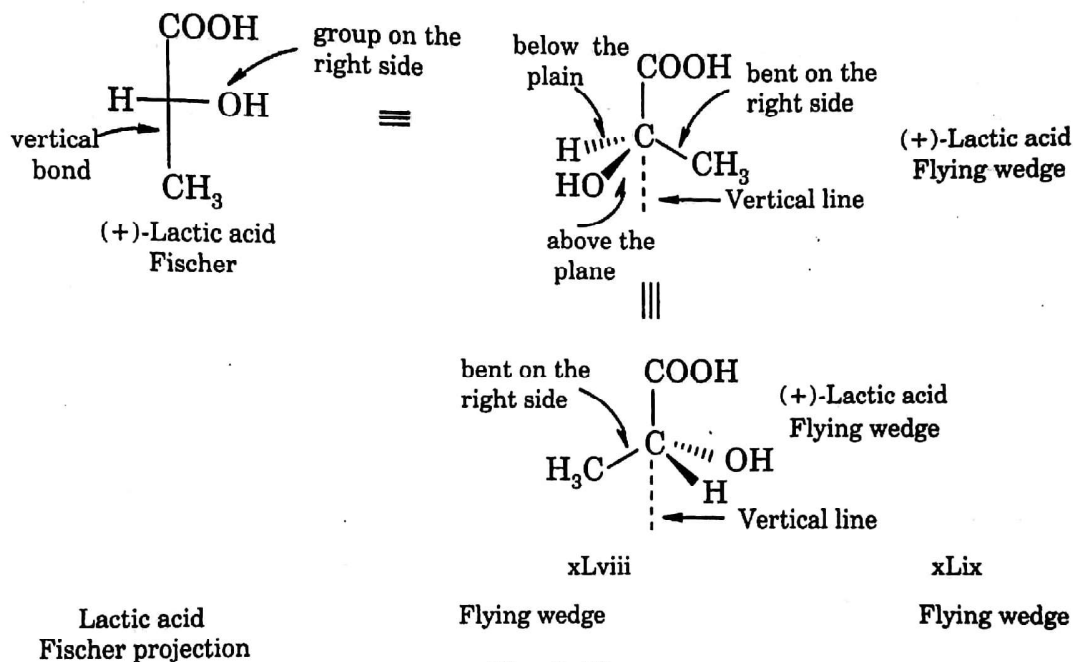


Fig. 2.70

In the above example (Fig. 2.70) Fischer projection of one of the stereoisomers of lactic acid is converted into flying wedge (xLviii, xLix) forms. In doing so, vertical bonds in Fischer projection are considered to be in the plane of the paper and horizontal bonds are to be above and below the plane.

Note that when lower vertical bond linked to $-\text{CH}_3$ group in Fischer projection is bent on the right side in xLviii, the group ($-\text{OH}$) on the right side in the horizontal bond in Fischer projection should be written above the plane of the paper (represented by solid wedge, (—)), the H atom, therefore, should be placed below the plane (represented by hashed wedge, (.....)), If the lower bond linked to CH_3 group in Fischer projection is bent on the left side (as in xLix), the group on the left side in the horizontal bond in Fischer projection is to be placed above (—) the plane of the paper and group on the right side (H) should be placed below (.....) the plane. Thus, both xLviii and xLix represent the flying wedge forms of Fischer projection of same isomer of lactic acid, shown above.

The reverse method may be followed to convert a flying wedge representation to Fischer projection. An example is given below (Fig. 2.71).

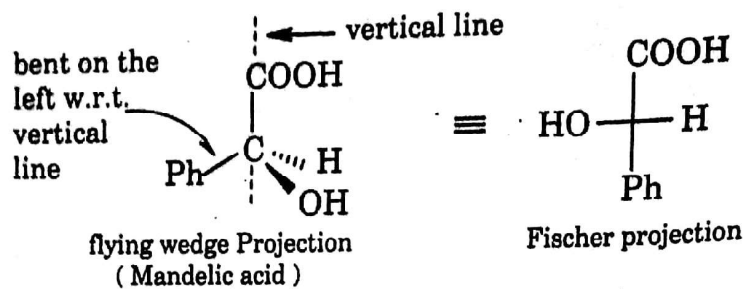


Fig. 2. 71

In the above example, CO_2H and Ph groups are in the plane of the paper in flying wedge representation. In transforming into Fischer projection, the OH group, which is above the plane in flying wedge structure, is put on the left in horizontal bond in Fischer projection, because Ph group in flying wedge projection is bent on the left side with respect to the vertical lines in Fischer projection.

A few more conversions of different flying wedge forms to Fischer projections are given below (Fig. 2.72- 75)

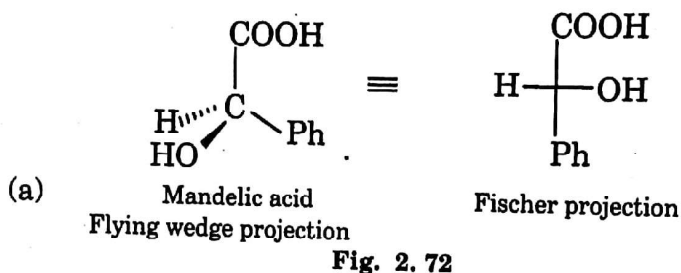


Fig. 2. 72

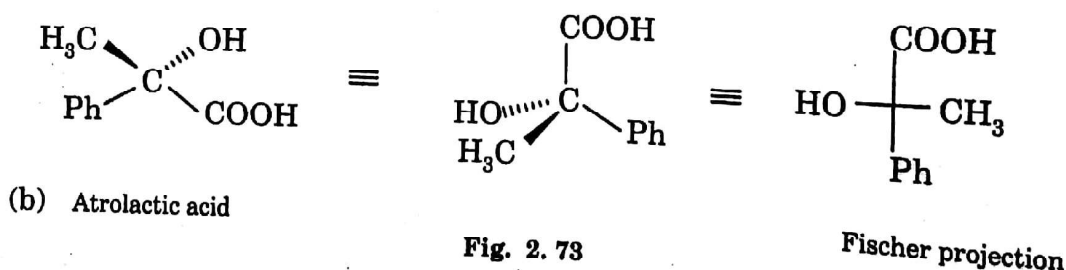


Fig. 2. 73

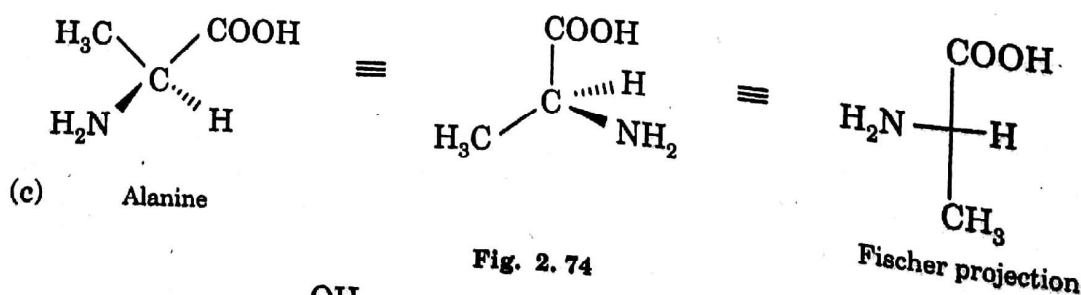


Fig. 2. 74

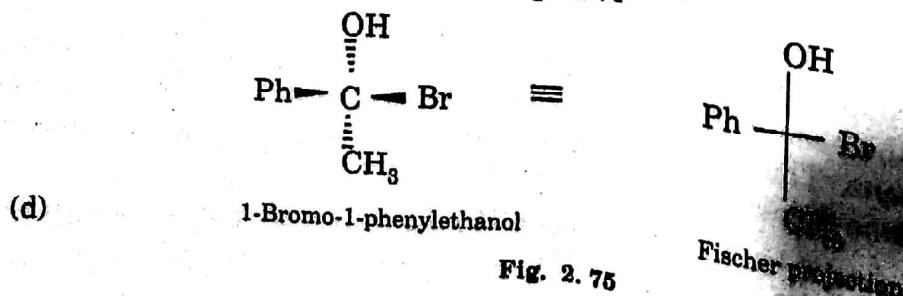


Fig. 2. 75

In the above example (d), horizontal bonds are shown above the plane and vertical bonds below the plane and these are in accordance with the Fischer convention. Therefore, in Fischer projection, the positions of atoms and groups are retained as they were in the form showing by solid and broken bonds.

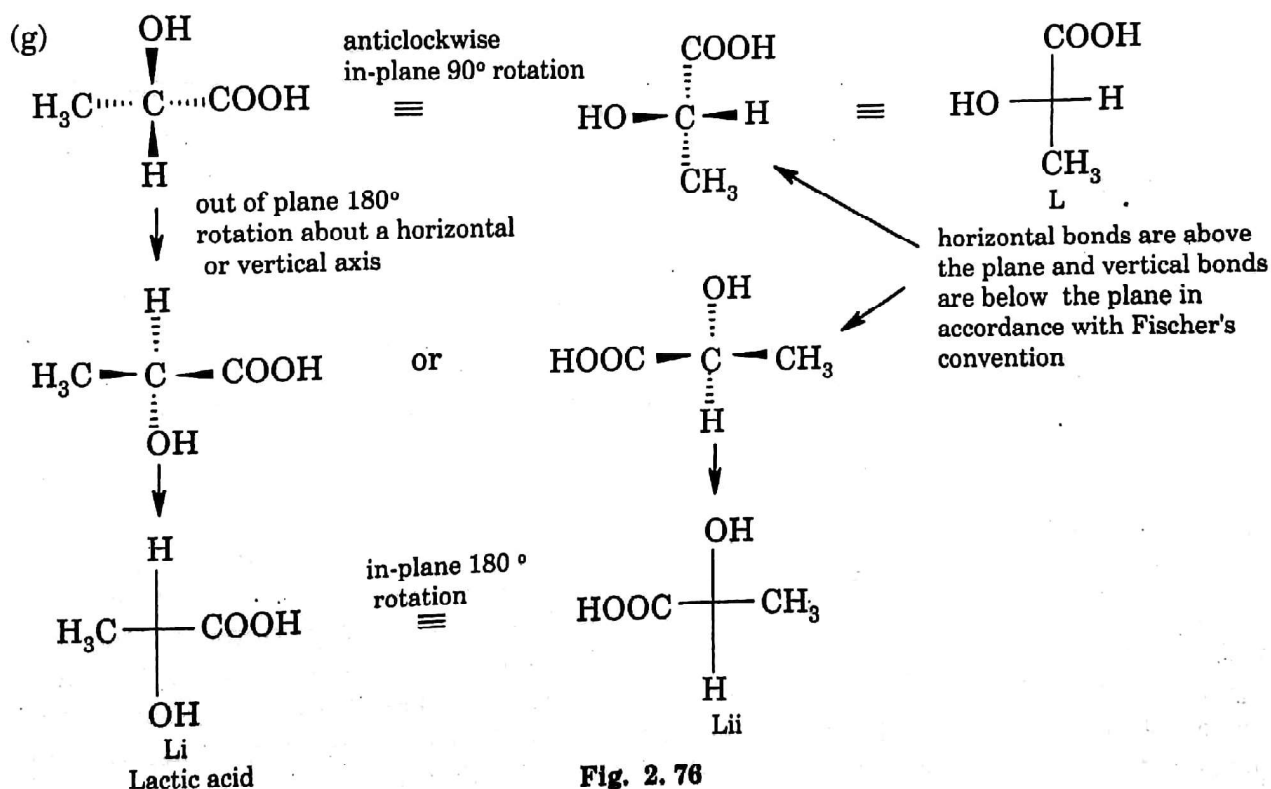
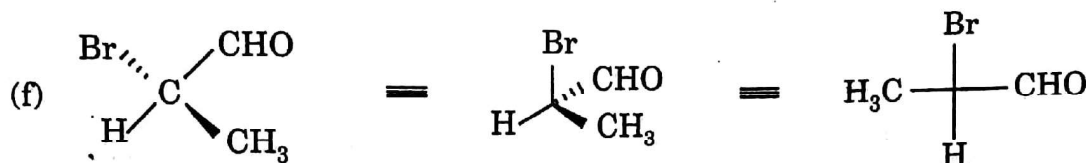
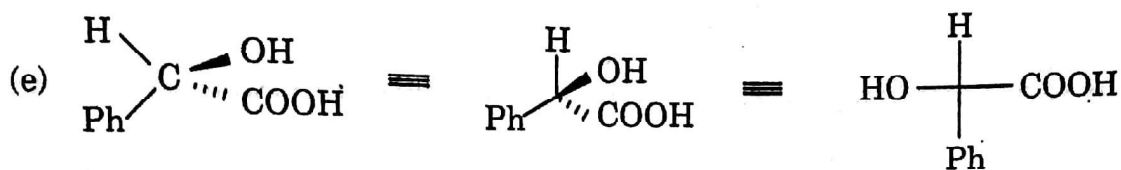


Fig. 2. 76

In example (g), the given structure is not the correct representation in accordance with the Fischer projection, because vertical substituent are shown above the plane and horizontal substituent are shown below. This is in contrary to Fisher's convention. Therefore, the given structure is rotated in-plain by 90° or out of- plane by 180° . These operations give the correct representation of the lactic acid according to the Fisher's convention. The structures (L), (Li) and (Lii) are identical configurations and represent the same isomer of the lactic acid.

The structure (f) is another way of representing three-dimensional form of a stereoisomer. It can also be easily transformed into Fischer projection in the way shown below.

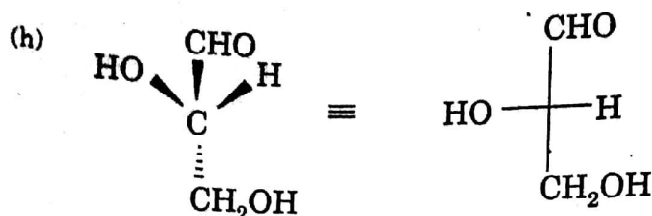


Fig. 2.77

• **Flying wedge containing more than one chiral centre to Fisher projection and vice versa:**

Flying wedge structures of stereoisomers containing two stereocentres can similarly be converted into Fischer projection and *vice-versa*. A few examples are given below in Fig. 2.78 and 2.79.

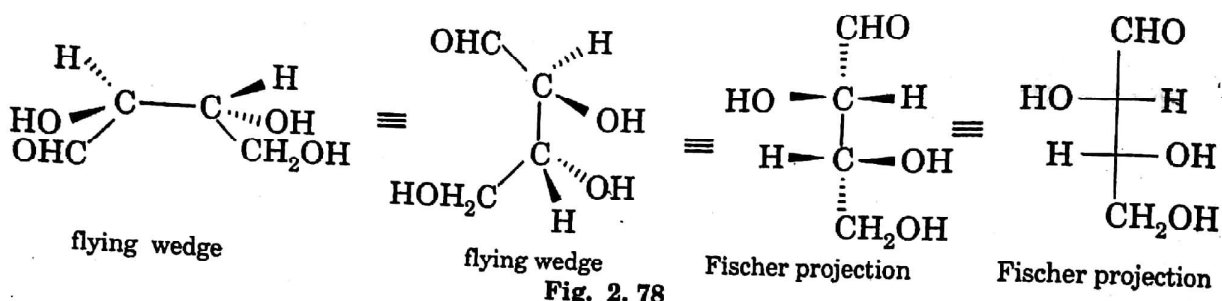


Fig. 2.78

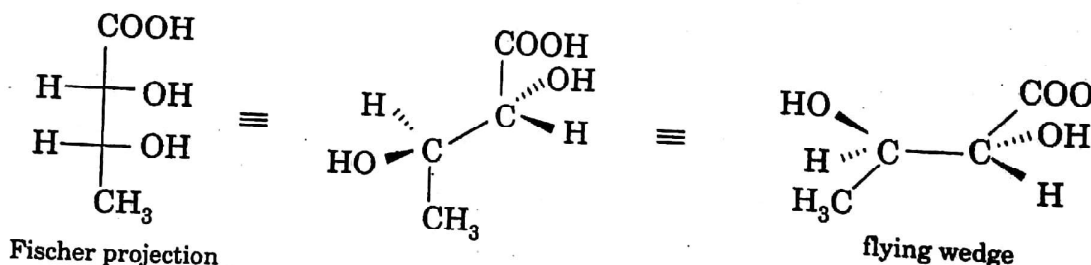
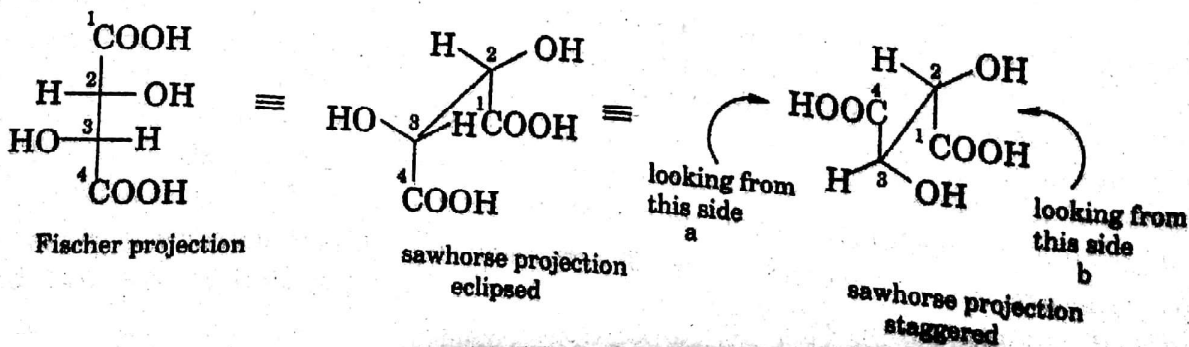
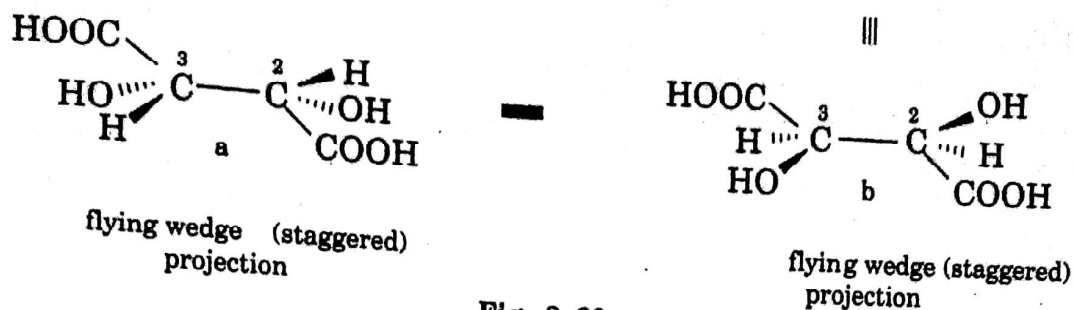


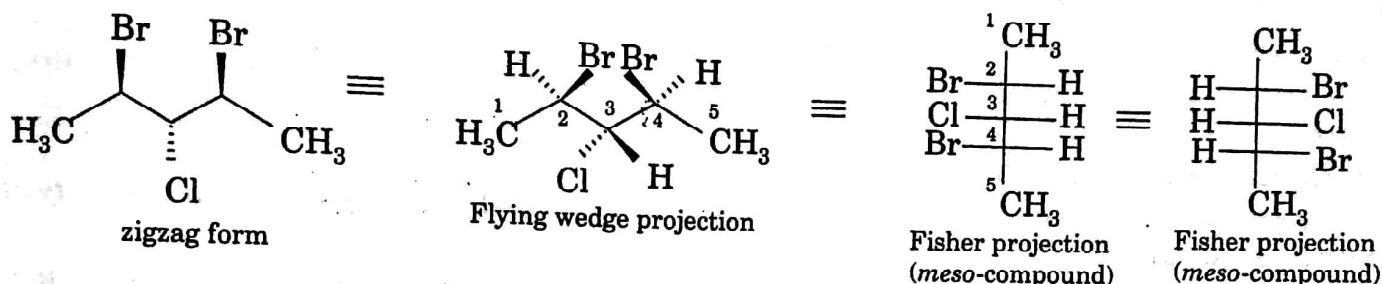
Fig. 2.79

Fischer projection can be transformed into sawhorse form and then to flying wedge structure. An example is shown below (Fig. 2.80). It must be remembered that the same stereoisomer can be represented by eighteen different Fischer projections. In the example below, one Fischer projection of *threo*-tartaric acid (active) is first transformed into sawhorse in eclipsed conformation and then converted into desired staggered form. The same structure can be written in other eclipsed and staggered forms also. Then the staggered form is transferred into flying wedge looking from two directions (a) and (b).



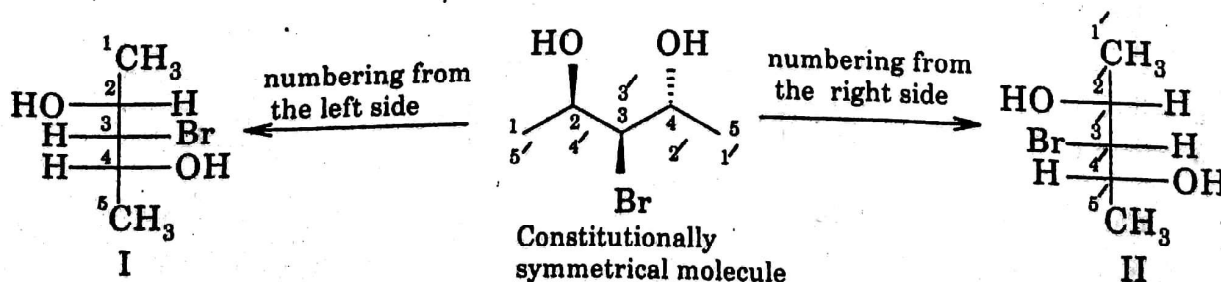


• **Zigzag form to Fischer Projection:**



In the above zigzag structure, H atoms, according to convention, are not drawn. Therefore, zigzag form is first converted in to flying wedge projection by inserting H atoms above and below the plain of the carbon-backbone as the structure demands. It is then converted into Fisher projection by applying the technique discussed earlier

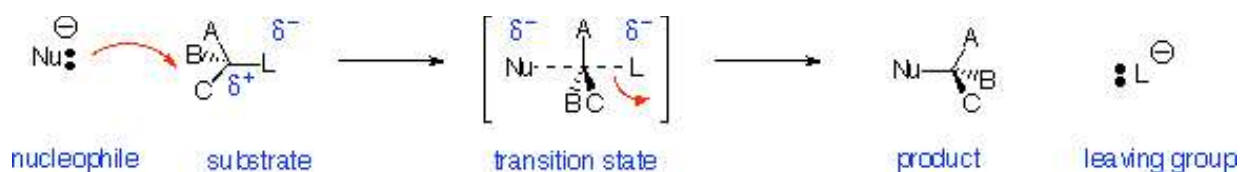
It is to be noted that in the above example, carbon-backbone is numbered from the left side and C-1 is placed at the top in the Fisher projection. Since the compound is symmetrical, the structure can also be numbered from the right side, when we can get the mirror- image Fisher projection of the previous Fisher projection of the same compound. However, in this particular case both are same *meso*-compound (superimposable). In case of a symmetrical molecule, numbering can be done from either end of the carbon chain leading to two apparently different Fisher projections but they are homomers. In unambiguous case numbering should follow IUPAC rules. Two more examples are given below for more illustrations.



Substitution (SN2 , SN1) and Elimination Reactions (E2 , & E1):

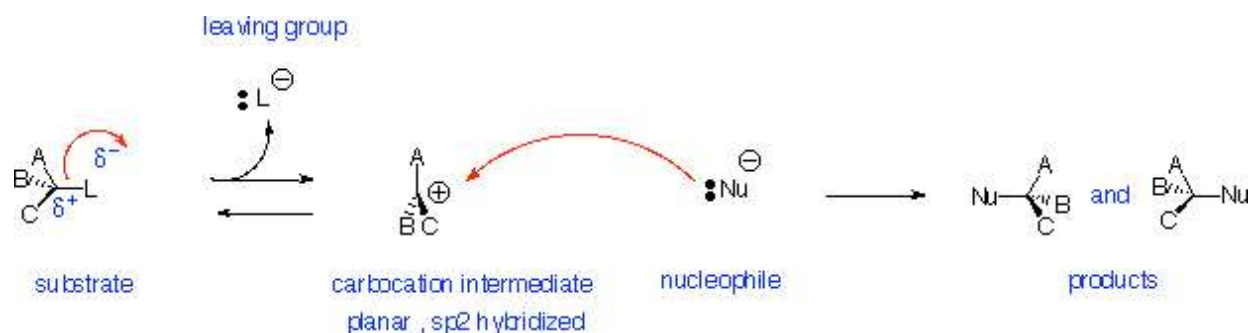
- Nucleophilic Substitution Reactions (SN2 and SN1) replace a leaving group with a nucleophile (Nu: or Nu: -)
- Elimination Reactions (E2 and E1) generate a double bond by loss of " A+ " and " B: - "
- They may compete with each other

Nucleophilic Substitution Reactions - SN2 Reaction:



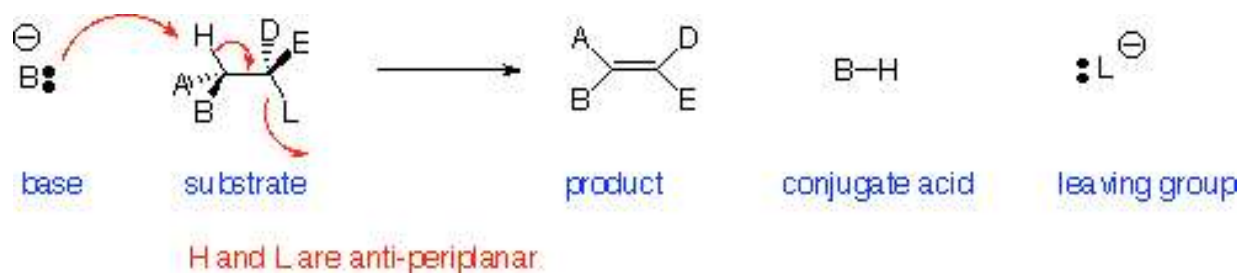
- **Reaction is:**
 - Stereospecific (Walden Inversion of configuration)
 - Concerted - all bonds form and break at same time
 - Bimolecular - rate depends on concentration of both nucleophile and substrate
 - **Substrate:**
 - Best if **primary** (one substituent on carbon bearing leaving group)
 - works if secondary, fails if tertiary
 - **Nucleophile:**
 - Best if more reactive (i.e. more anionic or more basic)
 - **Leaving Group:** Best if more stable (i.e. can support negative charge well):
 - TsO- (very good) > I- > Br- > Cl- > F- (poor)
 - RF , ROH , ROR , RNH₂ are NEVER Substrates for SN2 reactions
 - Leaving Groups on double-bonded carbons are never replaced by SN2 reactions
 - **Solvent:** Polar Aprotic (i.e. no OH) is best.
 - For example dimethylsulfoxide (CH₃SOCH₃), dimethylformamide (HCON(CH₃)₂), acetonitrile (CH₃CN).
 - Protic solvents (e.g. H₂O or ROH) deactivate nucleophile by hydrogen bonding but can be used in some case
-

Nucleophilic Substitution Reactions – SN1 Reaction:



- **Reaction is:**
 - Non-stereospecific (attack by nucleophile occurs from both sides)
 - Non-concerted - has carbocation intermediate
 - Unimolecular - rate depends on concentration of only the substrate
 - **Substrate:**
 - Best if tertiary or conjugated (benzylic or allylic) carbocation can be formed as leaving group departs
 - never primary
 - **Nucleophile:**
 - Best if more reactive (i.e. more anionic or more basic)
 - **Leaving Group:**
 - Same as SN2
 - best if more stable (i.e. can support negative charge well)
 - Examples: TsO^- (very good) $> I^- > Br^- > Cl^- > F^-$ (poor)
 - However, tertiary or allylic ROH or ROR' can be reactive under strongly acidic conditions to replace OH or OR
 - **Solvent:**
 - Same as SN2
 - Polar Aprotic (i.e. no OH) is best
 - Examples: dimethylsulfoxide (CH_3SOCH_3), dimethylformamide ($HCON(CH_3)_2$), acetonitrile (CH_3CN).
 - Protic solvents (e.g. H_2O or ROH) deactivate but can be used in some cases
-

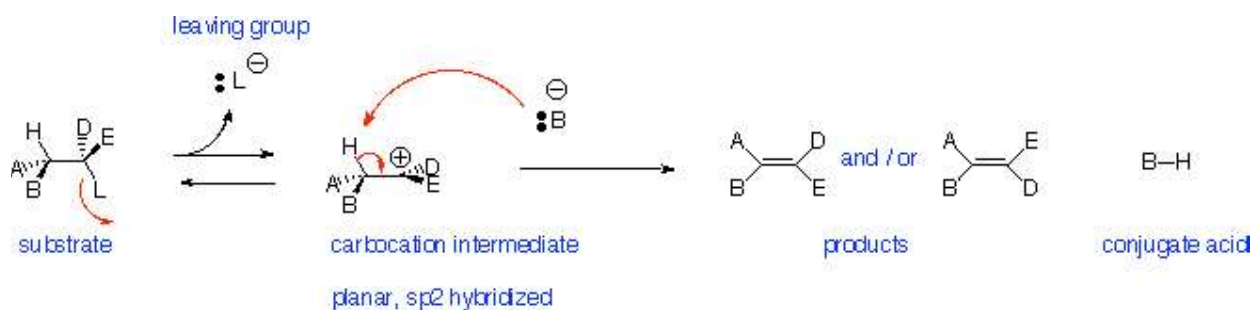
Elimination Reactions - E2 Reaction:



- **Reaction is:**

- Stereospecific (Anti-periplanar geometry preferred, Syn-periplanar geometry possible)
- Concerted - all bonds form and break at same time
- Bimolecular - rate depends on concentration of both base and substrate
- Favoured by strong bases

Elimination Reactions – E1 Reaction:



- **Reaction is:**

- Non-stereospecific- follows Zaitsev (Saytseff) Rule
 - Non-concerted - has carbocation intermediate - favoured for tertiary leaving groups
 - Unimolecular - rate depends on concentration of only the substrate
 - Does NOT occur with primary alkyl halides (leaving groups)
 - Strong acid can promote loss of OH as H_2O or OR as HOR if tertiary or conjugated carbocation can be formed
-

Rearrangement reaction:

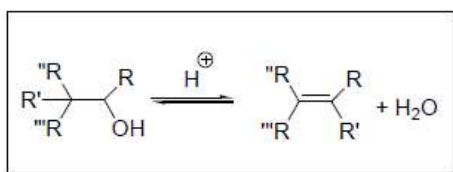
Types of Rearrangements

Rearrangements are divided into intramolecular and intermolecular processes. In intramolecular process, the group that migrates is not completely detached from the system in which rearrangement is taking place. In contrast, in intermolecular process, the migrating group is first detached and later re-attached at another site.

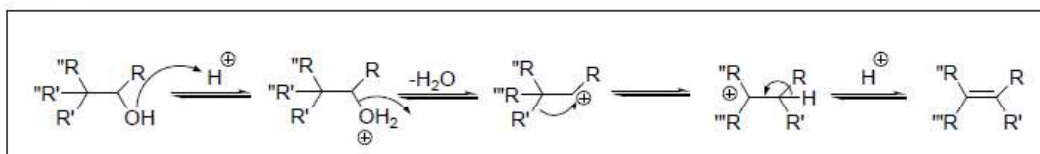
Rearrangement to Electron Deficient Carbon These reactions are classified according to the nature of group that migrates.

Carbon Migration

Wagner-Meerwein Rearrangement It is one of the simplest systems where an alkyl group migrates, with its bonding pair, to an electron-deficient carbon atom.



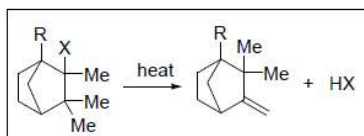
Mechanism



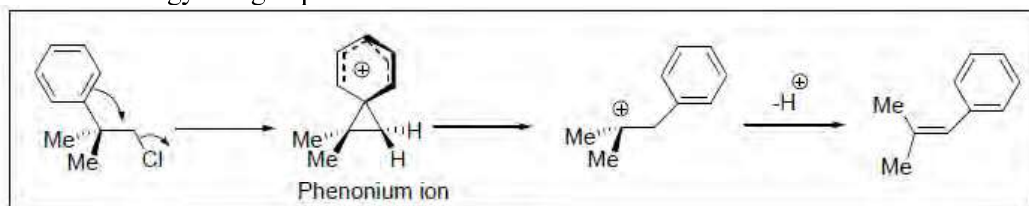
The driving force for the rearrangement resides in the greater stability of a tertiary carbocation compared to that of primary carbocation.

Features of this migration

- The carbocation may be produced by a variety of ways.
- Hydrogen can also migrate in this system.

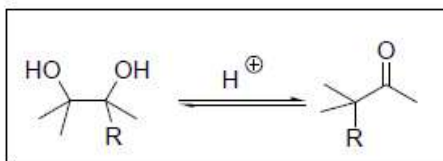


- Aryl groups have a greater migratory aptitude than alkyl group or hydrogen due to the formation of lower-energy bridged phenonium ion.

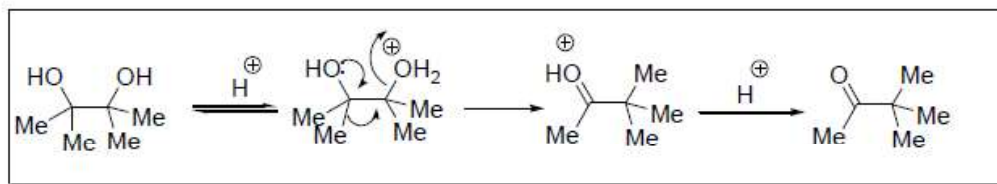


Pinacol Rearrangement

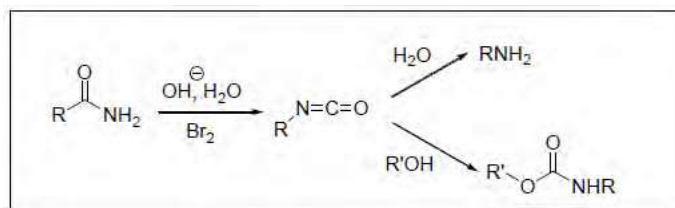
Treatment of 1,2-diols (pinacol) with acid lead to rearrangement to give ketone. Although this rearrangement fundamentally is similar to the above described Wagner-Meerwein rearrangement, but differs in that the rearranged ion, the conjugate acid of ketone, is relatively more stable than the rearranged carbocation formed in Wagner-Meerwein rearrangement. Thus, the driving force for pinacol is greater compared to Wagner-Meerwein rearrangement. However, the characteristics of the Wagner-Meerwein apply to the pinacol rearrangement.



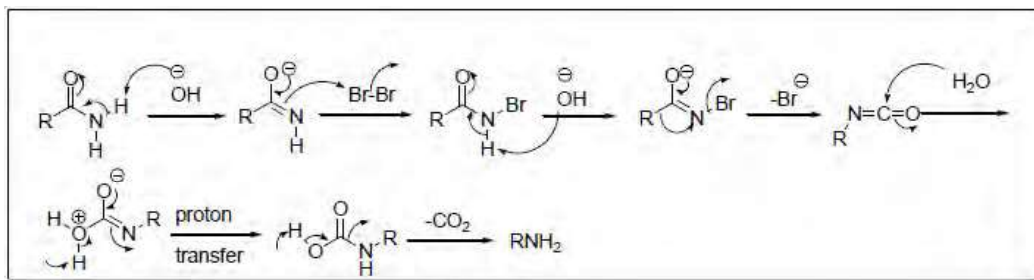
Mechanism



Hofmann Rearrangement This rearrangement provides an effective method for the synthesis of primary aliphatic and aromatic amines from primary amides (Scheme 1).

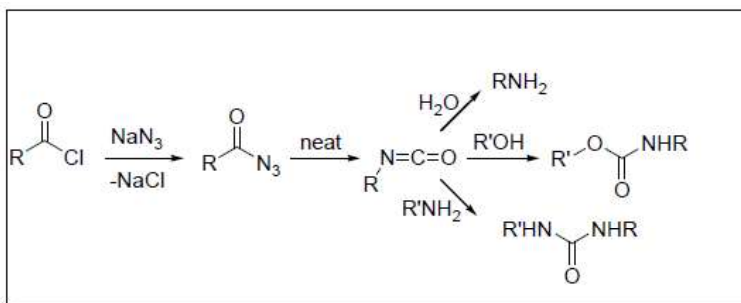


Mechanism Treatment of amide with sodium hypobromite gives *N*-bromo-amide which reacts with base to afford a conjugate base within which rearrangement takes place to give isocyanate. The formed isocyanate may be isolated in anhydrous conditions or it can be converted into amine by aqueous workup (Scheme 2).

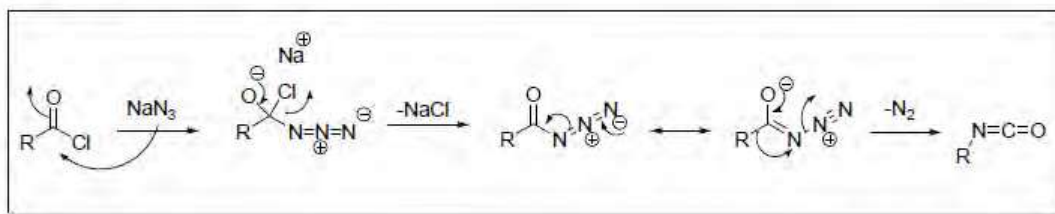


Scheme 2

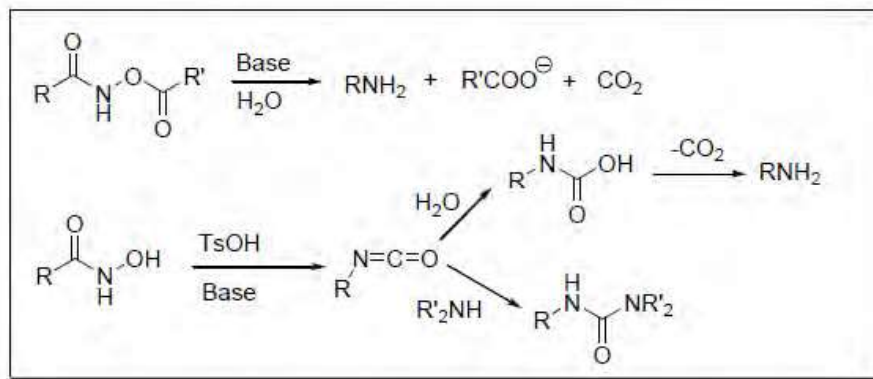
Curtius Rearrangement This rearrangement describes the transformation of acyl azide into isocyanate by decomposition on heating and its application for the synthesis of primary amines, urethanes and ureas as presented in Hofmann rearrangement.



Mechanism



Lossen Rearrangement Ester of hydroxamic acid reacts with base to give isocyanate that could be converted into amine as shown in Hofmann rearrangement.



Mechanism

