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Stereochemistry

Isomerism was first of all discovered by German chemist leibig and Wohler in 1820. They found that silver fulminate (AgCON) and silver cyanate (AgNCO) have the same atomic composition but their properties are very much different. Similarly Berzalius and Wohler found that molecular formula of ammonium cyanate (NH_4CNO) and urea (NH_2CONH_2) are same as CH_4N_2O but the physical as well as chemical properties of both are not same Gay-Lussac then suggested that the difference in physical and chemical properties in such compounds are due to the mode of attachment of atoms in these compounds.

For example molecular formula C_2H_2O represents two entirely different compounds –

CH₃-OH   CH₃-O-CH₃

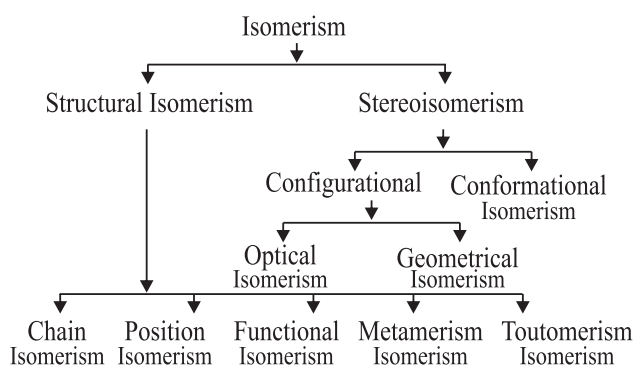(Ethyl alcohol)   (Di methyl ether)

Thus, it becomes clear that a compound cannot be characterized properly on the basis of molecular formula. This phenomenon was introduced by Berzelius then first of all the term, "isomerism".

Thus, "those compounds which have same molecular formula but different molecular structures are called isomers and this phenomenon is called 'isomerism'. These compounds have different physical or chemical or both the properties.

Types of Isomerism :

On the basis of structure and symmetry of the molecules, isomerism ma be classified as shown in the following flow chart :

Isomerism

Structural Isomerism   Stereoisomerism

Configurational   Conformational Isomerism

Optical Isomerism   Geometrical Isomerism

Chain Isomerism   Position Isomerism   Functional Isomerism   Metamerism Isomerism   Toutomerism Isomerism

Stereoisomerism

In structural isomerism the positions of various atoms in the molecules are different so that they show different physical as well as chemical properties. On the other hand the compounds having identical molecular and structural formula as well as the identical positions of bonds but differs only in spatial arrangement of atoms in molecules are called stereo isomers and this phenomenon is known as stereo isomerism.

The spatial arrangement of atoms or groups is also referred to as configuration of the molecule and thus we can say that the stereo isomers have the same structural formula but different configuration.

Stereo isomerism in which isomers differ in the spatial arrangement of atoms or groups can be classified into two classes –

1. Configuration Isomerism

2. Conformational Isomerism

The different molecules have different energies and hence isomers are also separated by different energy barriers. In case of configurational isomers, the energy barrier is above 100kJ. Mol^{-1}, so

that these isomers are quite stable at room temperature and could be isolated. While if the energy barrier is less than 60kJ Mol^{-1} then these stereo isomers can interconvert at ordinary conditions of temperature and pressure and not isolated, such isomers are called conformers and the isomerism is called conformational isomerism.

Configurational isomerism is again two types;

a- Optical Isomerism

b- Geometrical Isomerism

Geometrical Isomerism

If the two carbon atoms are linked together with a single bond then bond can be rotated freely about the bond axis. When two carbon atoms are joined by a double bond this free rotation about the bond is not possible because the atoms or groups attached to the carbon of the double carbon gets restricted.

In 1875, Vant' Hoff and Le Bel recognized geometrical isomerism in organic compounds having two differently substituted atoms attached to each other by means of a double bond, viz, baC=Cab. The isomer having the similar groups on the same sides was called cis (Latin cis- on same side) and the other having similar groups on the opposite sides was called trans (Latis trans – across, over) This phenomenon on the whole was known as cis – trans isomerism. Thus, this type of isomerism was first of all explained on the basis of the failure of rotation about the double bond, which makes the molecule in rigid one and fixes the position of various groups, the isomerism is commonly known as 'geometrical isomerism.'

Geometrical isomerism can be illustrated beautifully by the following board and nail model. When the two boards are joined by a single nail (as shown in fig) the free rotation of either of the two boards is possible and hence the arrange ends of the boards cannot be arranged relative to each other i.e. this type of model cannot exhibit cis – trans isomerism. On the other hand, the boards are joined by two nails in different holes, free rotation is not possible and hence the relative position of the arrange and other ends can be fixed in two definite ways corresponding to cis and trans isomerism.
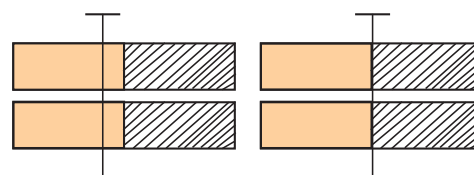
(Free Rotation Possible)
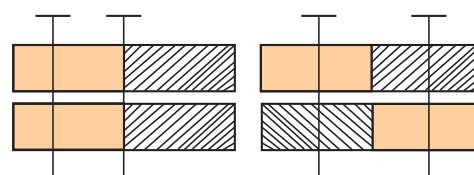
(Free Rotation Not Possible)

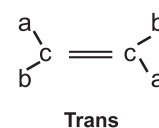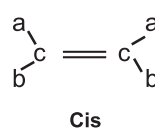This type of isomerism is shown by the following types of compounds:

1- Alkenes

2- Oximes

3- Alicyclic compounds

The following two necessary conditions must be fulfilled by the compounds to show geometrical isomerism:

(i) Rotation restricted bond must be there in the molecule

(ii) Both the substituent must be different to the rotation restricted bond.
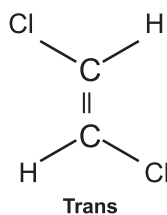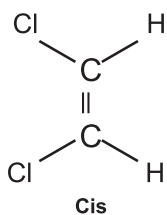
(1) Geometrical Isomerism in Alkenes :

In general, alkene containing identical substituent on one or both doubly bonded carbon atoms does not show geometrical isomerism. Geometrical isomerism results only when each carbon on double bond carries different substituent. Thus, ethane, proper, 1- butane, isobutene etc. do not exhibit geometrical isomerism whereas 2- butane and higher homologues do show geometrical isomerism. As shown in the following examples.
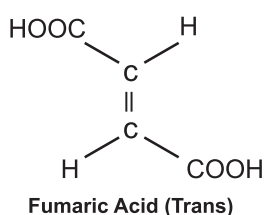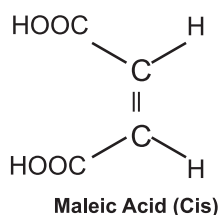

Cis   **Trans**
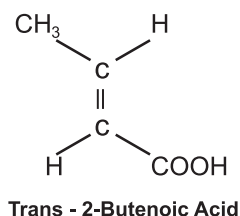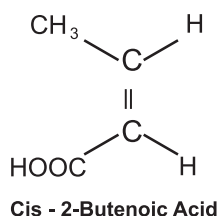
For example, in 2-butene

Cis 2-Butene

Trans 2-Butene

1, 2 - Dichloroethene

Cis
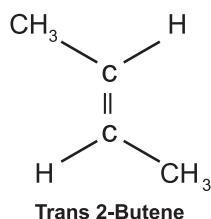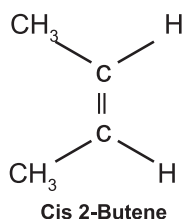
Trans

In maleic and fumaric Acids,

Maleic Acid (Cis)

Fumaric Acid (Trans)

In 2-Butenoic Acid-

Cis - 2-Butenoic Acid

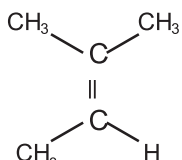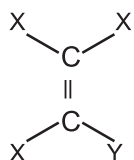**Trans - 2-Butenoic Acid**

It is to be noted that if the both substituent of any of the doubly bonded carbons are same. The compound does not show cis-trans or geometrical isomerism. For example:
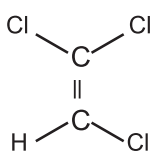
These compounds do not show geometrical isomerism because if the both of substituent of the doubly bonded carbon are exchanged by each other, the configuration of the compound does not change.

(2) Geometrical Isomerism in Oximes :

When aldehydes or ketones reacts which hydoxyl amine, the aldoxime or ketoximes are produced respectively as follows:

(R^1 = H means Aldehyde)   **(Oxime)**
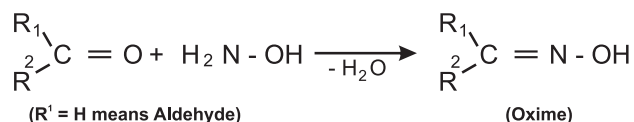
Since oximes are compounds containing C=N in which both C and N atoms are sp^2 hybridized, the third sp^2 orbital of nitrogen is occupied by a lone pair of electrons. Thus, in analogy to alkene, oximes are coplanar and there is restricted rotation around C=N double bond. Hence oximes also exhibit geometrical isomerism which are called 'syn' and 'anti' isomers. The isomer, in which OH group on nitrogen and H or smaller group of the carbon appears on the same side, is called 'syn', where if they are on the opposite sides, it is called 'anti' isomer. Examples are :

In acetaldoxime : ($CH_3CH=NOH$)

(Syn)

(Anti)
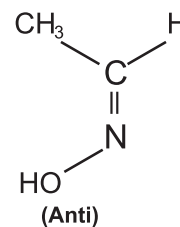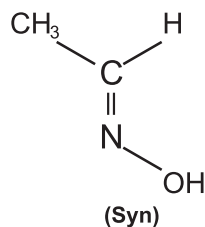
In banzaldoxime : ($C_6H_5CH=NOH$)

(Syn)

(Anti)
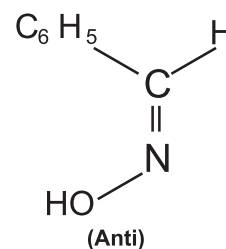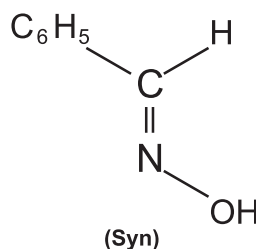
Similarly in acetophenone :

(Syn)

(Anti)

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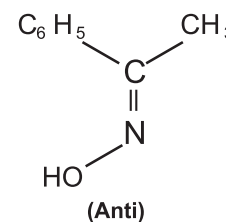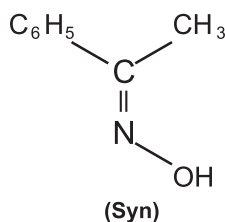
(3) Geometrical Isomerism in Alicyclic Compounds :

A compound to exhibit geometrical isomerism there should be restricted rotation about a bond. Thus, disubstituted cycloalkanes like cyclopropane, cyclo butane, cyclopentane etc. also exhibit geometrical or cis – trans isomerism. If both of the same substituent (or prime, as sequence rule) are in the same side, the alicyclic compound is called cis isomer and if they are in opposite side, the compound is trans isomer. Some examples are here -

1. Dimethyl cyclopropane :

2. 1, 3 – Dichlorocyclo butane :

3. 1,2 – Dimethylcyclo pentane :
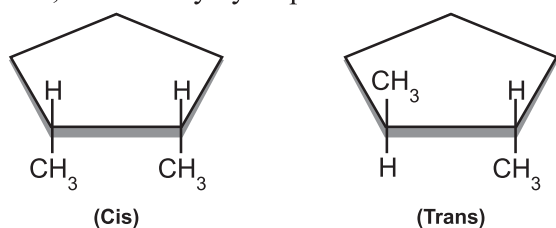
Some Properties of Geometrical Isomers :

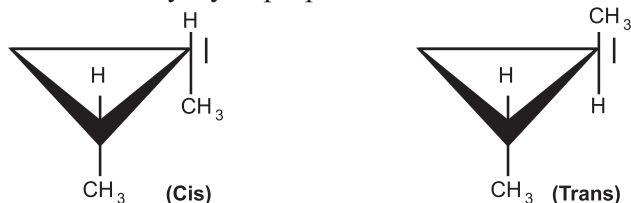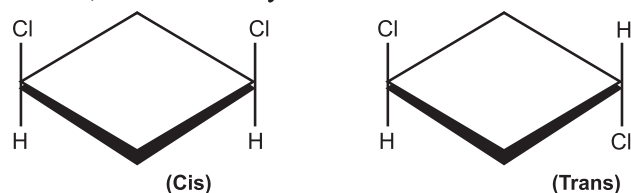The stereo – configuration of geometrical isomers are different, thus, their physical or chemical or both of the properties are found different. Some such important properties are as follows:

(1) Dipole Moment :

If the substituent on both of doubly bonded carbon exerts the equal electronic effect, then the trans isomers have zero dipole moment. In this case the both groups compensate the electronic effects and the resultant effect becomes zero. For example in trans 2-butene, in trans 1,2-dichloroethene etc. the dipole moment in zero while their cis isomers are polar and show definite amount of dipole moment. As show below –

$\mu = 1.85D$ $\mu = 0.0 D$

and
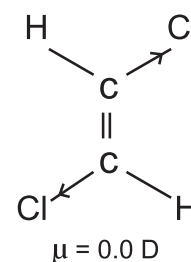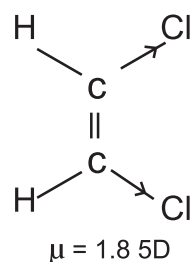
(Cis) $\mu = 0.40 D$ (Trans) $\mu = 0.0 D$
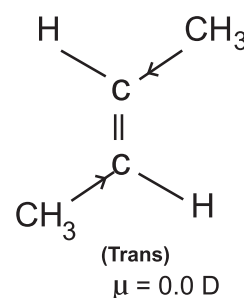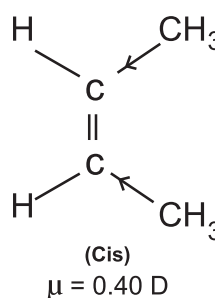
In the geometrical isomers having substituent with opposite electronic effect then the cis isomer show lower dipole moment than the trans isomer. For example 1-chloropropene:

(Cis) $\mu = 1.71D$ (Trans) $\mu = 1.77D$
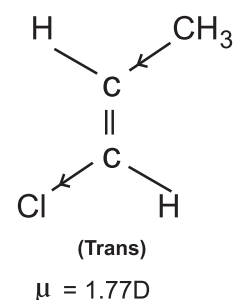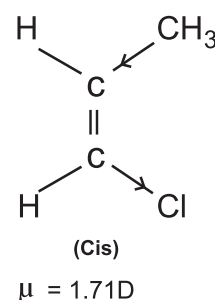
(2) Melting and boiling point :

The melting and boiling points are also highly affected by geometrical isomerism. The Van der Waal's forces of attractions are more in trans isomers than that of the cis isomers. It is because the molecules in trans isomers can come close to each other and exerts strong Van der Waal's forces between them. For example:

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Maleic Acid
M.Pt. = 130^{0}C

Fumaric Acid
M.Pt. = 287^{0}C

and

Alocinnamic Acid
M.Pt. = 68^{0}C

Cinnamic Acid
M.Pt. = 133^{0}C
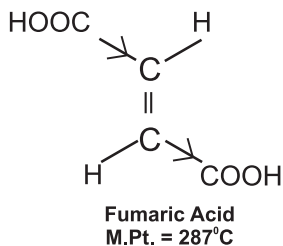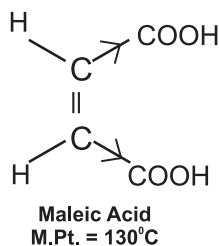
It is to be noted that this effect on melting and boiling points reverts, if there are the attached substituent have exact opposite electronic effect, crotonic acid (trans) has lower than the isocrotonic acid (cis) form

Isocrotonic Acid
M.Pt. = 150^{0}C

Crotonic Acid
M.Pt. = 72^{0}C
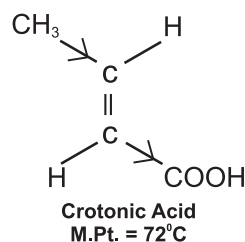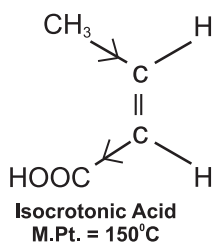
(3)   Chemical Properties :

Chemical properties of cis-trans isomers are different, for example in maleic acid, there are two – COOH groups in same side (i.e. cis form) will form anhydride at 140^{0}C while in fumaric acid these both are in opposite side (trans), will forms anhydride at 275^{0}C. It is shown as follows:

(Meleic Acid) $\xrightarrow[\text{(-H}_2\text{O)}]{140^0 \text{ C}}$ (Meleic Anhydride)

(Fumaric Acid) $\xrightarrow[\text{(-H}_2\text{O)}]{270^0 \text{ C}}$
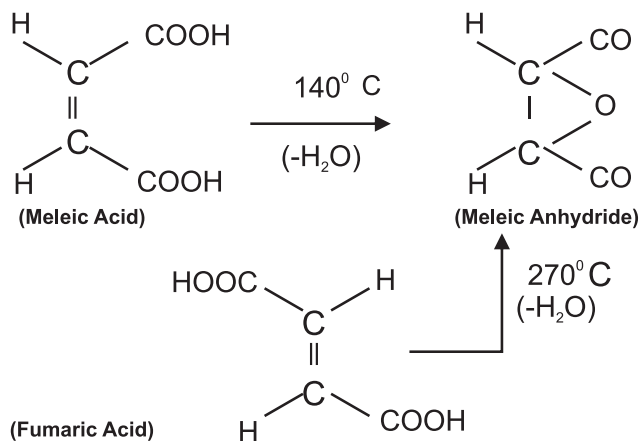
(4)   Hydrogen Bonding :

In some cis-rtans isomers, the hydrogen bonding changes the physical properties of compounds. For example in 1, 4-butanedioic acid the cis isomer shows intra molecular hydrogen bonding while trans isomer shows inter molecular hydrogen bonding. Due to this hydrogen bonding their melting points are very different as shown below –

(Intramolecular H-bonding)
M.Pt. = 130^{0}C

(Intermolecular H-bonding)
M.Pt. = 287^{0}C
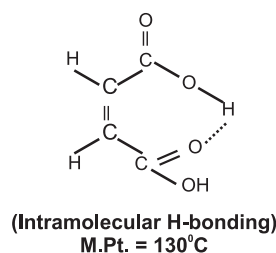
Reason : Weak van der Waal's forces   Reason : Strong van der Waal's forces
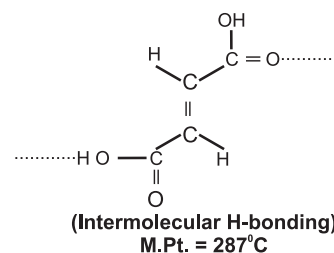
Optical Isomerism

The concept of optical isomerism was introduced by French chemist 'Louis Pasteur' in 1848. He observed that there were two different types of crystals of a single compound sodium ammonium tartrate, which were mirror images of each other.

$$\overset{+}{Na}\overset{-}{O}OC - \underset{\underset{OH}{|}}{C}H - \underset{\underset{OH}{|}}{C}H - CO\overset{-}{O}\overset{+}{N}H_4$$
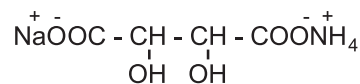
Sodium ammonium tartrate

He picked up the two sets of crystals and later on after x-ray analysis it has observed that each of sets – rotated the plane polarised light. As the crystals sets are mirror images of each other, so that they are not superimposable to each other and called stereo isomers. Thus, stereo isomers which are not super imposable on each other are called optical isomers and this phenomenon is known as 'optical isomerism'.
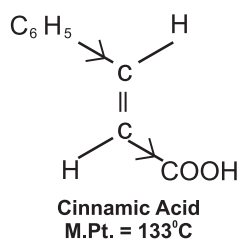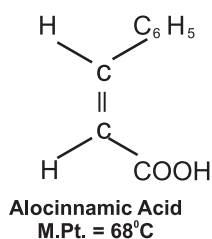
The compounds which rotate the plane polarized light in equal and opposite direction are also called enantiomers. Enantiomer which rotates the plane polarized light in clock wise direction is called 'dextrorotatory' [Latin, dexter, right] and denoted by the prefix d or (+) before the name of the compound. On the other hand the enantiomer with rotates the plane polarized light in anti clock wise

direction is called 'Laevorotatory' [Latin, lavus, left] and is denoted by the prefix l or (-) before the name of the compound.

Plane Polarised Light :

As we know that the light is concerned a as a wave phenomenon in which the vibrations occur at right angles to the direction in which the light travels i.e. the light is a transverse wave in nature. There are infinite number of planes passing through the line of propagation, and the ordinary light vibrates in all these planes. Plane polarized light is light whose vibrations take place only in one of these possible planes. Ordinary light is turned into plane – polarized light by passing it through a Nicole prism, as shown below:

Slit — **Plane Monochromic Light**

Nicol Prism — **Plane Polarized Light**
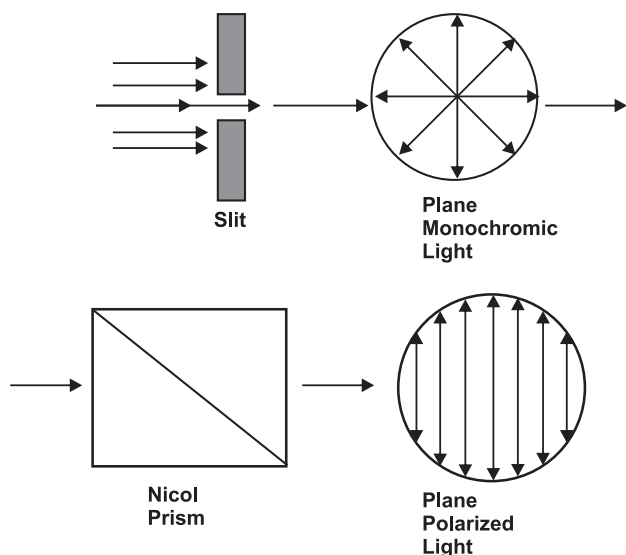
Optical activity can be detected as well as measured by polarimeter in which polar light pass through an optically active compound where the plane of polar light is rotated at right or left. If it is rotated towards right, the compound is dextro rotatory (d) and if it is rotated towards left it is laevorotatory (l). The angle at which the polar light rotates in left or right is called the 'angle of rotation.

The mechanism of polarimeter is shown in the following figure. It consists of a light source, two Nicole prisms and sample tube to hold the substance. The prism is placed near the source of light is known as polarizer while the other is placed near the eye is known as analyzer.

Specific Rotation :

The extent of rotation, observed in a polarimeter depends upon the number of optical active molecules that encounter the light beam. If more molecules encounter to the light the larger is the observed rotation. 'The specific rotation of a compound is defined as the number of degrees of rotation observed by 1.0 gm of sample in 1.0 ml of its solution in a tube with path length 1.0 decimeter using light of specific wavelength.'

Slit — **Monochromic Light** — **Nickol Prism** — **Plane Polarised Light**

Observation Tube — **Left Side Rotaion** — या — **Right Side Rotaion**
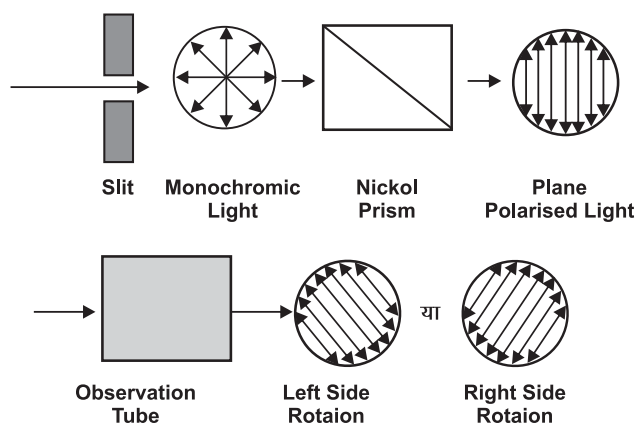
Specific rotation can be expressed as:

$$\text{Specific Rotation} = [\alpha]_\lambda^t = \frac{\alpha}{l \cdot C}$$

Where $\alpha =$ Observed angle of rotation

$l =$ Length of observation tube in decimeter

$C =$ Concentration of solution

$t =$ temperature of the sample

$\lambda =$ wave length of light

If the specific rotation of the compound is multiplied by its molecular weight then it is known as molecular rotation.

$$\text{Molecular rotation (M)} = [\alpha]_\lambda^t \times \text{molecular weight}$$

The change in rotation angle can be measured directly from the polarimeter. Thus optical activity of any compound is purely a experimentally observed property.

Elements of Symmetry :

The phenomenon of rotation of plane polarized light by some compounds is known as

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optical activity. An optically active molecule is known as chiral molecule (or asymmetric molecule). The term chiral is derived from the Greek word cheer meaning hands and it is used as both of our hands are mirror images of each other and not super imposable to each other. Thus, the chirality is is due to molecular asymmetry. Generally an asymmetric carbon shows optical activity.

To determine whether the molecule is chiral or achiral is to be made by certain features related to molecular symmetry. The major symmetry features are as follows :

1. Plane of Symmetry
2. Axis of Symmetry
3. Centre of Symmetry

(1) Plan of Symmetry:

If 'a molecule possess such a plane in it, that it divides the molecule in two parts in such a way that half the molecule is mirror image of rest half part. Such a plan is said to be plane of symmetry and any molecule having such plane of symmetry does not show optical activity. The mirror image of such molecule is superimposable. For example the following letters of English:
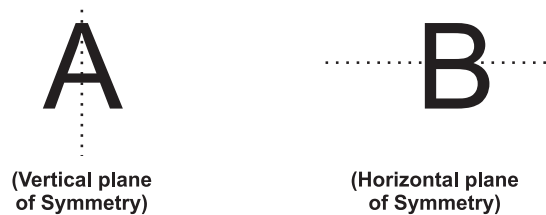

(Vertical plane of Symmetry)   (Horizontal plane of Symmetry)

There are various molecular examples, which have plane of symmetry and due to which they do not show any optical activity. For example prop ionic acid have a vertical plane of symmetry and meso- tartaric acid have horizontal plane of

Propanoic Acid
Plane of Symmetry

meso-tartaric Acid
Plane of Symmetry
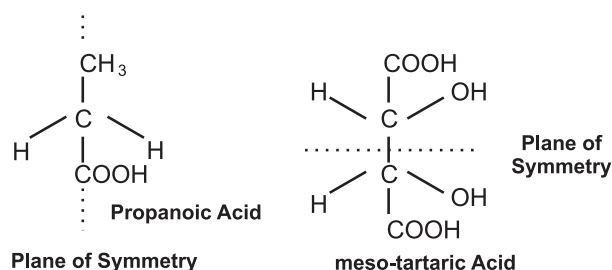
symmetry in it. As shown below:

(2) Axis of Symmetry :

A molecule is said to possess an n-fold of axis of symmetry if, it is rotated through an angle $3600/n$ about this axis and an identical structure is obtained. For example the H_2O molecule :

C_2 - Axis of Symmetry C_2 - Axis of Symmetry

It has C_2 or two fold axis of symmetry because by rotating the H_2O molecule by $360/2 = 180$, about this axis will result into indistinguishable configration of water molecule. Similarly the NH_3 molecule has three fold axis of symmetry (C_3). Molecules having such axis of symmetry are optically inactive.

(3) Centre of Symmetry :

An imaginary point in the centre of molecule where the lines are drawn from any directions on both of the sides of molecule, they reach at equal distances from the centre. For example the latter S.

Centre of Symmetry

Molecular example ethene, benzene etc have a centre of symmetry as shown below. Any molecule which has a centre of symmetry does not show optical activity.

(Ethene)   (Benzene)
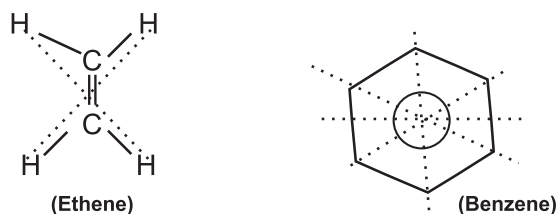
Chirality and Chiral Molecule :

A molecule which does not have any of the elements of symmetry is to be said an asymmetric molecule and all the asymmetric molecules are optically active. Such molecules are said to be chiral molecule and this characteristic is known as

chirality. Thus, we can say that the terms chiral and chirality are used in reference to compounds whose mirror images are not superimposable. Such molecules are capable to rotate the plane of polarised light, either in right (d) or in left (l).

If all the four valences of a carbon is substituted by different groups, it shows chirality because its mirror image does not superimpose to it. Thus, such organic molecules show optical activities but there also must not exist any element of symmetry in the molecule. For example lactic acid is optically active, because it has a chiral carbon, as shown below:
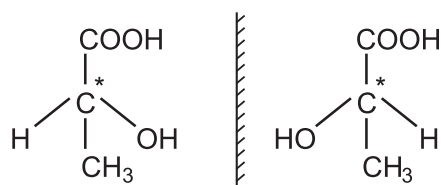
(Enantiomers of Lactic Acid)

The staric carbon is chiral centre. This molecule is optically active because it is chiral and does not have any element of symmetry. Both of the mirror images are optical isomers because if one of above is dextro rotatory then the other will definitely be laevorotatory. Again the staric carbon is also known as 'stereogenic centre', because this is chiral centre which causes the optical activity in the molecule. Some other examples are given here with stereogenic centre.

It is important to note that the physical and chemical properties of optical isomers are same, only and only the optical properties are found different. Due to this reason it is very difficult to resolve or separate these both isomers. The optical isomer which rotate the polar light in clock wise direction is called dextrorotatory and denoted by d or (+), while if rotate in anti clock wise di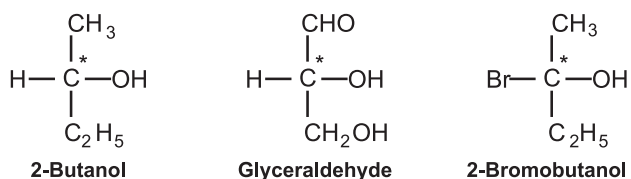rection it is called laevorotatory and denoted by l or (-). 'The optical isomers which are mirror images to each other are called enantiomers whereas the molecules of same compound are optically active but not mirror images of each other are called distereo mers.'

Compounds with two Stereogenic Centres :

There may be two or more stereogenic centers in a single compound. These compounds with two stereogenic centers are again divided into two types –

1. Compounds containing two dissimilar chiral centers

2. Compounds containing two identical chiral centers

(1) Compounds Containing Two Dissimilar Chiral Centers:

The number of optical isomers will be 2^n, where n is the number of chiral centers in a molecule. For example there are two stereogenic or chiral centers in 2, 3 – dichlorobutanoic acid, so the number of optical isomers will be $2^2 = 4$. As shown below-
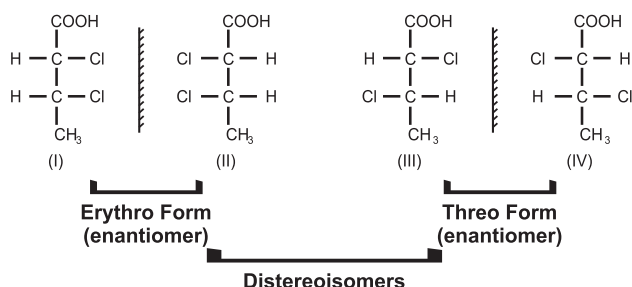
Since the structures I & II as well as III & IV are non – super imposable mirror images, so that they are enantiomer pairs. But the structure I & III, I & IV, II & III, III & IV are not mirror images to each other of the same compound, although they all are stereo isomers. " Such stereo isomers which are not mirror images of each other are called diastereo isomers" As we know that all the physical and chemical properties of enantiomers are same, but in contrast the diastereo isomers exhibit different physical and chemical properties. Due to this reason it is very easy to resolve or separate out the diastereo isomers by various physical or chemical methods.

If the identical groups on both chiral centers are on the same side, it is called "erythro form" while if they are in opposite to each other, it is called "threo form". The name erythro and threos are taken from the erythros and threos carbohydrates as shown below:

$$
\begin{array}{cc}
\text{CHO} & \text{CHO} \\
\text{H}-\text{C}-\text{OH} & \text{H}-\text{C}-\text{OH} \\
\text{H}-\text{C}-\text{OH} & \text{OH}-\text{C}-\text{H} \\
\text{CH}_2\text{-OH} & \text{CH}_2\text{-OH} \\
\textbf{Erythros} & \textbf{Threos}
\end{array}
$$
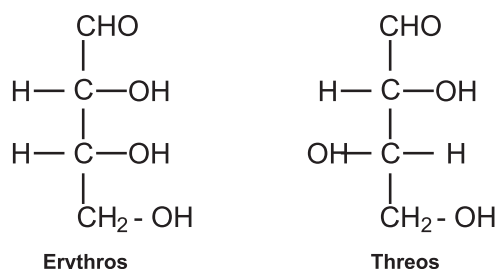
(2) Compounds Containing Two Identical Chiral Centers :

One of the classic example of this series is the tartaric acid :

$$
\text{HOOC - } \overset{*}{\text{CH}} \text{ - } \overset{*}{\text{CH}} \text{ - COOH}
$$
$$
\qquad\quad | \qquad |
$$
$$
\qquad\quad \text{OH} \quad \text{OH}
$$
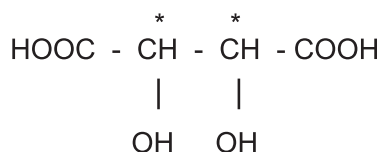
There are two stereogenic or chiral centers in this compound, so the $2^2 = 4$ optical isomers must be there in molecule as shown below :

$$
\begin{array}{cccc}
\text{COOH} & \text{COOH} & \text{COOH} & \text{COOH} \\
\text{H}-\text{C}-\text{OH} & \text{HO}-\text{C}-\text{H} & \text{H}-\text{C}-\text{OH} & \text{HO}-\text{C}-\text{H} \\
\text{HO}-\text{C}-\text{H} & \text{H}-\text{C}-\text{OH} & \text{H}-\text{C}-\text{OH} & \text{HO}-\text{C}-\text{H} \\
\text{COOH} & \text{COOH} & \text{COOH} & \text{COOH} \\
\text{(I)} & \text{(II)} & \text{(III)} & \text{(IV)}
\end{array}
$$

सममिति तल

Threo   **Erythro**

The structure I and II are enantiomers which are threo forms of tartaic acid. Similarly the structure III and IV are mirror images to each other but they are not enantiomers 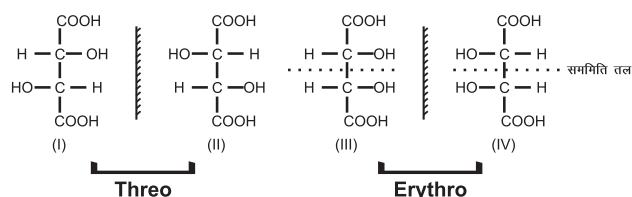or optically active compounds because a plane of symmetry is present in both of the molecule. This plane of symmetry makes the molecules optically inactive. Thus, the tartaric acid have two stereogenic centers but have only two optical isomers (I & II).

The structure III and IV are known as meso tartaric acid which are optically inactive. Since this compound possess a plane of symmetry, the optical rotation due to the half part of the molecule is cancelled by exactly equal and opposite optical rotation in other half of the molecule. Thus, they are optically inactive due to "in internal compensation." Such compounds which possess chiral centers, but are optically inactive due to internal compensation are called 'meso compounds.'

As we know that the basic requirement for a compound to be optically active is its nonsuper impossibility of its mirror image. Although the largest number of known optically active compounds are optically active due to the presence of chiral atom. On the other hand, many compounds are also known which do not possess any chiral carbon atom, but on the whole their molecules are chiral, hence they are optically active. Such a type of chirality is called as 'molecular chirality.' Various compounds like allenes, biphenyls etc. are optically active due to molecular chirality while there is no any chiral carbon in these compounds.

Fisher Projection Formulae :

We have learnt that, stereochemistry is concerned with three dimensional structures of molecule. There is a need to write three dimensional structures of molecule on two dimensional paper or board. To solve this problem Emyl Fisher suggested a technique to draw the structure of molecules on paper or board and which is known as "Fisher Projection Formulae"

To write a Fisher Projection Formulae, the following rules are to be followed :

(i) Two mutually perpendicular lines are to be drawn on paper, one of them is vertical and the other is horizontal, as shown below. The point where these lines cut to each other is known as the chiral centre of the molecule.

$$
\begin{array}{c}
\text{c} \\
\text{a} - | - \text{b} \quad \leftarrow \text{Chiral Center} \\
\text{d}
\end{array}
$$
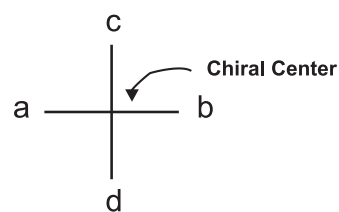
(ii) The vertical line possess the longest carbon chain of the molecule in such a manner that C_1 carbon remains at the top of this vertical line.

(iii) Remaining two groups are placed at two ends of the horizontal line.

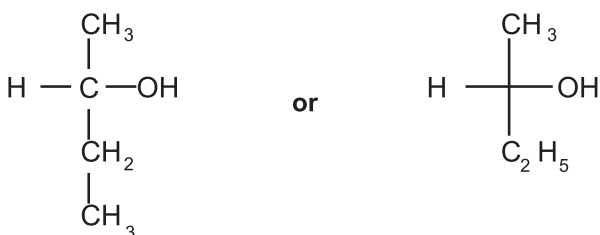(iv) The horizontal line represents the groups lifted above the plane of paper and the vertical line shows the groups behind the plane of paper. In other words horizontal bonds point towards the viewer and vertical bonds point away from the viewer.
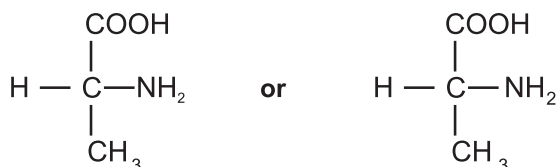
It is to be cleared by the following examples:

1. The lactic acid, CH_3-CH (OH) - COOH

2. In butanol, CH_3-CH_2– CH(OH) – CH_3


3. In alanine, CH_3-CH (NH_2) - COOH

It is important to remember following points while writing the Fisher Projection Formulae:

(i) The projection plane should not be lifted out or rotated in the plane.

(ii) Rotation of 90^0 and 270^0 in the plane is not allowed as it will change the position of the horizontal substituent to vertical and vice-versa and hence the configuration of the molecule.

(iii) The projection plane can however be rotated in the plane through 180^0 or 360^0 which keeps the horizontal substituent as horizontal, and the vertical substituent as vertical. For example :
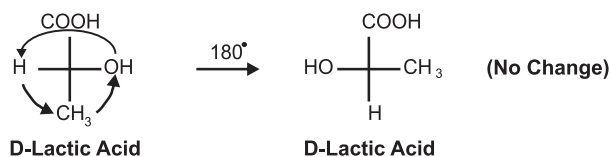
(iv) The configuration of molecule does not change by exchanging two pairs of substituent; for example
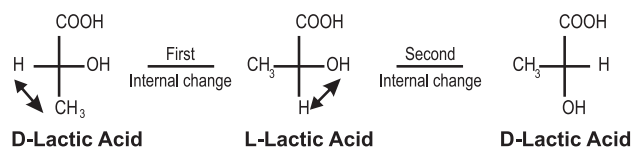
Relative and Absolute Configuration :

So far we have learnt that an asymmetric molecule have two optical isomers, where one of them rotates the polar light in clock wise (d) and other is anti clock wise (l). Thus the 'd' and 'l' isomerism is totally based on optical properties. Now there was a need of an approach to express the actual configuration or any relative configuration of such molecules to their three dimensional arrangement of substituent. An attempt was established by Emyl Fisher in 1890, while he was working on sugars and amino acid. He assigned the three dimensional formulae of molecules by Fisher Projection Formulae as discussed above.

A configuration of glyceraldehydes was arbitrary assigned as D–glyceraldehydes by Rosanoff in 1906. He arranged the glyceraldehydes molecule as Fisher Projection Formulae and said that if the –OH group is right side the configuration is accepted as D configuration. On the other hand if –OH group is placed in the left hand side, it is to be considered as L- glyceraldehydes. It is clear from this discussion that D and L configurations are not related to their d and l characteristics, however the compounds are of course optically active. Here also the D is placed for dextrorotatory and L is for laevo rotatory but these symbols are used to see the structure by viewer. If the eye of viewer goes to clock wise to see the –OH group in the structure of glyceraldehydes, it is called its D-configuration and vice-versa, as shown below:

CHO
|
H — C*—OH
|
CH₂OH

D–glyceraldehyde

CHO
|
HO— C — H
|
CH₂ - OH
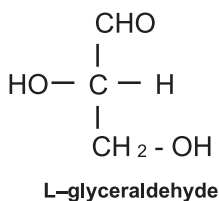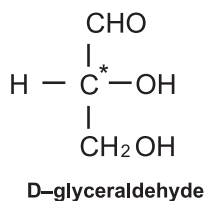
L–glyceraldehyde

On this basis sugars are given D or L as the configuration of last chiral carbon of them as shown below:

|
H — C —OH
|
CH₂OH

(D-sugar)

|
HO— C — H
|
CH₂OH
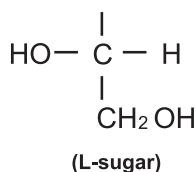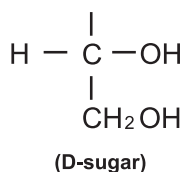
(L-sugar)

This attempt was very useful to study the sugars and amino acids. The configurations of other substances can be related to D or L – glyceraldehydes. This is called relative configuration. All those compounds which are obtained or converted into D – glyceraldehydes are also called D – configurations of those compounds. For example in following series of reaction, these all are D – configuration:

CHO
|
H — C —OH
|
CH₂OH

D-glyceraldehyde

$\xrightarrow[\text{HgO}]{\text{[O]}}$

COOH
|
H — C —OH
|
CH₂OH

D-glyceric acid

$\xrightarrow{\text{Pbr}_5}$

COOH
|
H — C —OH
|
CH₂Br

$\xrightarrow[\text{-HB}]{\text{2 H}}$

COOH
|
H — C —OH
|
CH₃

D-lactic acid
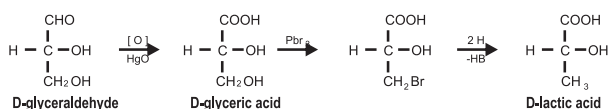
Similarly those compounds are converted into D-glyceraldehydes by reactions, are also have D-configurations:

COOH
|
H — C —OH
|
CH₂NH₂

D-Isocerine

$\xrightarrow[\text{[O]}]{\text{HNO}_3}$

COOH
|
H — C —OH
|
CH₂OH

D-glyceric acid

$\xrightarrow[\text{- H}_2\text{O}]{\text{2 H}}$

CHO
|
H — C —OH
|
CH₂OH₂

D-glyceraldehyde

It should be kept in mind that there is no direct relation between d/l and D/L.

In 1950, when x-ray crystallography technique became available, Bijvoet determined the actual configuration of D-glyceraldehydes and coincidently it was found to be exactly identical as proposed by Rosanoff and Fisher. Configuration which shows the actual orientation of atoms or 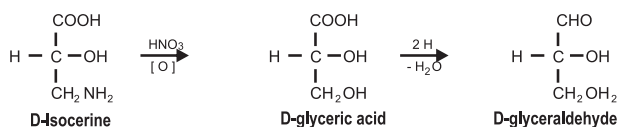groups of a molecule in a particular stereo isomer is termed as absolute configuration. While the configuration of other optically active compounds has been subsequently established relative to both of the configurations of glyceraldehydes are
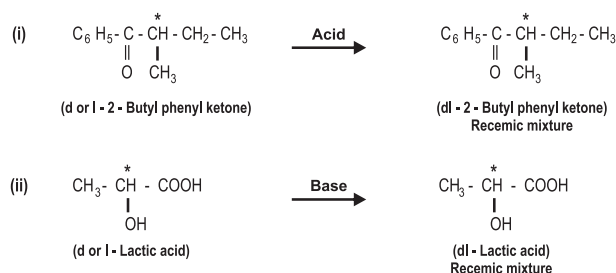
referred as 'relative configurations.'

D and L have the same meaning as d and l, but D and L give the view of viewer as shown below :

COOH
|
H — C —OH
|
CH₃

D-Lactic

COOH
|
HO— C — H
|
CH₃

L-Lactic acid

Right **Left**
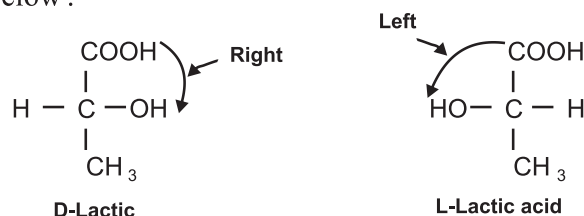
Racemisation and Racemic Mixture :

In a mixture of 50% is dextro rotatory and 50% of laevo rotator are taken, it is called racemic mixture of the optically active compound. Since the two enentiomers have equal and opposite optical rotations, the resulting mixture becomes optically inactive by the phenomenon called external compensation.' In such mixture, the optical rotation of one enentiomer is cancelled by the equal but opposite optical rotation of the other enentiomer. Such mixture is represented by placing Dl- before the name of optically active compound, for example the racemic mixture of lactic acid is shown by dl – lactic acid.

For example, racemic mixture is produced in the following reactions:

(i)   C₆H₅- C - *CH - CH₂- CH₃ $\xrightarrow{\text{Acid}}$ C₆H₅- C - *CH - CH₂- CH₃
               ‖ | ‖ |
               O   CH₃   O   CH₃

(d or l - 2 - Butyl phenyl ketone)   **(dl - 2 - Butyl phenyl ketone)**
                                              Recemic mixture

(ii)   CH₃- *CH - COOH $\xrightarrow{\text{Base}}$ CH₃- *CH - COOH
                 | |
                 OH   OH

(d or l - Lactic acid)   **(dl - Lactic acid)**
                                  Recemic mixture

The processes by which the d or l enantiomers are converted to their racemic mixtures (dl), is called 'racemisation, for example, the above reactions are the processes of racemisation of their enantiomers.

The reaction proceeds by 'Sɴ1' mechanism involves two steps. In the first step the carbocation intermediate is formed which has planar geometry. Hence in second step the attacking nucleophile can attack the carbocation from either side resulting in equal ratio of enantiomeric mixture (dl) For example the alkaline hydrolysis of 2-

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chloropropanoic acid give dl – racemic mixture of lactic acid:

Example, racemic mixture produces in the following reactions:

(Carbocation) 50% (d) 50% (l)

(dl-Lactic acid)
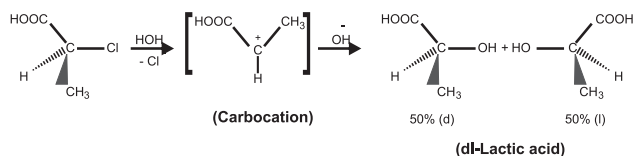
Resolution of Racemic Mixture :

The asymmetric synthesis from a symmetric compound, generally gives a racemic mixture (dl). Generally the naturally occurring asymmetric compounds are found either d or l enantiomer. Most of naturally occurring enantiomer is d. As we know that except optical rotation, all the physical as well as the chemical properties of enantiomers are same. Thus, it is very difficult to separate the dl-racemic mixture as d and l isomers. Therefore special methods are used for their separation or resolution and some of them are as follows:
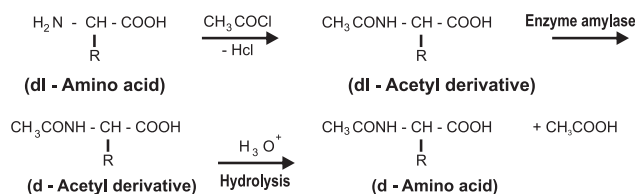
(1) Mechanical Resolution:

This method is of historical importance only because it was first used by Pasteur for the resolution of sodium ammoniumtartar ate which crystallizes out in the form of racemic mixture at 27^0C. Here, the crystals formed have two different forms with different shapes, being mirror images of each other. Pasteur has separated these with the help of a magnifying lens and a small forceps. This is laborious method and applicable only to racemic mixture of crystalline substances.

(2) Biochemical Method:

The principle of this method is that the certain micro organisms like bacteria, yeast, fungi etc. selectively destroy one of the enantiomer of the racemic mixture, leaving behind the other enantiomer. For example when penicillium glaucum mould was slowed to grow in racemic mixture (dl) of ammonium tartarate, the d-enantiomer was destroyed and l-ammonium tartrate is obtained.'

Similarly dl-amino acids can also be separated by such a method. First of all the dl-amino acid is acetylated to protect the amino group.

Then the racemic mixture of acetyl derivative is kept with enzyme amylase, which selectively destroyed the l-derivative by hydrolysis. The d-acetyl derivative is then hydrolyzed and d-amino acid is obtained. As shown below -

H_2N - CH - COOH $\xrightarrow[- Hcl]{CH_3COCl}$ CH_3CONH - CH - COOH $\xrightarrow{Enzyme\ amylase}$
|R |R
(dl - Amino acid)   **(dl - Acetyl derivative)**

CH_3CONH - CH - COOH $\xrightarrow[Hydrolysis]{H_3O^+}$ CH_3CONH - CH - COOH $+ CH_3COOH$
|R |R
(d - Acetyl derivative)   **(d - Amino acid)**

These methods are not more applicable due to –

1. It is impracticable to find an appropriate micro–organism to resolve a given racemic mixture.

2. Since dilute solutions are generally used to develop the micro – organism, so that the yields are very poor.

3. One enantiomer is always destroyed; hence it is a costly method.

(3) Column Chromatographic Method :

Now – a- day it is also an excellent method for resolution of a racemic mixture of enantiomers. If a racemic mixture solution is allowed to pass through a column of an optically active substance, one of the enantiomers selectively adsorbs quickly on an adsorbent of the column whereas the other enantiomer gets eluted smoothly. Thus, both of the enantiomers come out from the column one by one so they can be separated easily is pure form.

(4) Chemical Methods :

These are most widely used methods for the resolution of racemic mixtures. These methods are based on the principle that enantiomers have same physical as well as chemical properties but the diastereoisomers have different physical or chemical properties. Thus enantiomers in a racemic mixture are first converted into diastereo isomeric mixtures by self formation processes. The diastereo isomeric mixture is then separated by physical techniques like crystallization, distillation, fractional distillation, solubility, etc. The pure enantiomers are regenerated again by hydrolysis.

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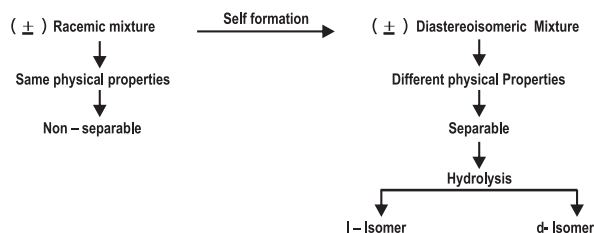
As follows:

Conformational Isomerism :

As we know that carbon-carbon double bond restricts the rotation and shows cis-trans or geometrical isomerism, where as carbon-carbon single bond is easily rotates at room temperature. The energy required for rotation about this single bond is about 3-15 k.Cal. per mole and it is easily available at room temperature in the environment. Thus by rotation of single bond the different arrangements of atoms/groups that can be converted in to one another. This phenomenon is known as conformational isomerism and the various structures of the molecule are called conformers. These conformers are generally non-separable at room temperature and are also known as rotamers. The study of physical and chemical properties of these conformers like stability, energy etc. is called 'conformational analysis.'
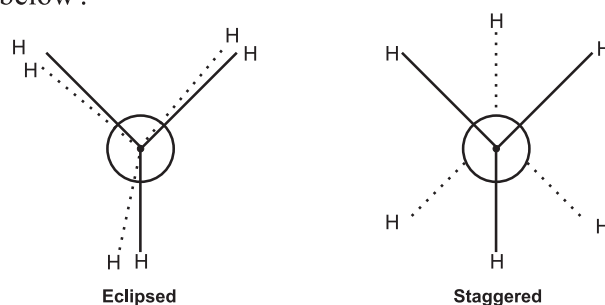
(I)   Conformations of Ethane:

In the ethane molecule there are only two sp3 carbons bonded by a single sigma bond which is free to rotate via this bond. Various conformation may be possible out of which there are two extreme orientations or conformations namely 'staggered and eclipsed' forms. In the staggered conformations, each hydrogen on the front carbon is placed between each of the hydrogen on the back carbon i.e. all hydrogen atoms are most for apart. In the eclipsed conformation, hydrogen on the front carbon are placed directly in front of hydrogen on the back carbon so that all hydrogen are nearest possible. Thus, the staggered conformation is most stable whereas eclipsed form is most unstable.

There are two methods to represent the conformations in molecules :

(i)   Newman Projection

(ii) Sawhorse Projection

In Newman projection method, the two carbon atoms of ethane are represented by two circles, one behind the other so that only front carbon is seen. While in Sawhorse projection we view carbon-carbon bond from an oblique angle and indicate spatial arrangement by showing the entire C-H bond. Both projections are show as below :

Both the extreme conformations of ethane are differing in their relative stability. The staggered conformations have minimum repulsion between the H-atoms attached tetrahederally to the two carbons. On the other hand the eclipsed conformation has maximum force of repulsion between H-atoms. Thus the staggered is more stable than eclipsed conformation and the energy difference between both is only 3 K.Cal.per mole. It is very low energy gap between the both conformations, which is easily available in atmosphere at room temperature. Thus, these conformations are interconvertible and not separable at room temperature.

Conformations in ethane can also be represnted by Sawhorse Projection formula, as follows :
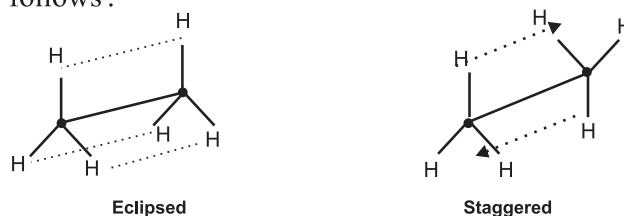
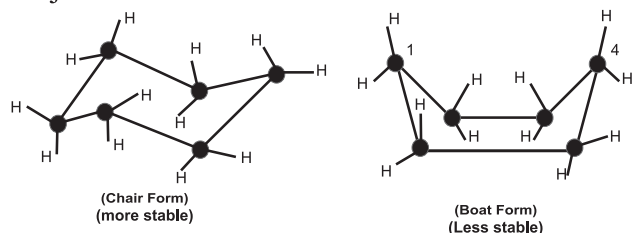### (II)   Conformations in Ring System: Cyclohexane :-

In cyclohexane, all the six carbons are sp^3 hybrid and angle between them should be $109^0 28'$. Thus it may not be a hexagonal planar. Mohr (1918) showed that cyclohexane shows two types of

conformations as chair and boat from. The energy difference between the forms is nearly 5-6 K.Cal. per mole, so that they can be easily interconvertible and hence it is difficult to separate them at room temperature. Chair form is formed by staggered conformation while the boat type is formed due to its eclipsed conformations. Thus chair form of cyclohexane is most stable and boat is the least stable.

In the cyclohexane both of the conformations are shown below by Newman Projection :

(Chair Form)
(more stable)

(Boat Form)
(Less stable)
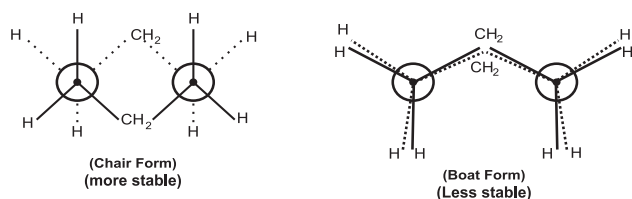
These conformations are shown by Sawhorse Projection formulae as follows :

(Chair Form)
(more stable)
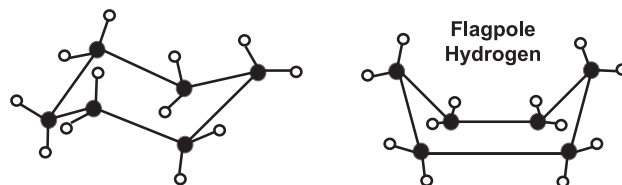
(Boat Form)
(Less stable)

The chair form (staggered conformation) has no torsional strain. The hydrogen atoms at the opposite corners of the ring, i.e. at C_1 and C_4 have maximum separation and there is no repulsion. The boat form (eclipsed conformation) is also free of angle strain, but the hydrogen at C_1 and C_4 are close enough to cause ven dar Waal repulsion and are called "Flagpole hydrogen."

Axial and Equatorial Hydrogen :

The 12 H in the chair form of cyclohexane are arranged in two sets. Hydrogen atoms which lie above and below the plane of the molecule alternatively and are parallel to the axis of the cyclohexane ring are known as 'axial hydrogen' atoms. The other set of six hydrogen atoms lie along the equator of the cyclohexane ring are called equatorial hydrogen atoms and bonds holding them are called as equatorial bonds as shown in the following figure :

(Axial Hydrogens)   (Equatorial Hydrogens)
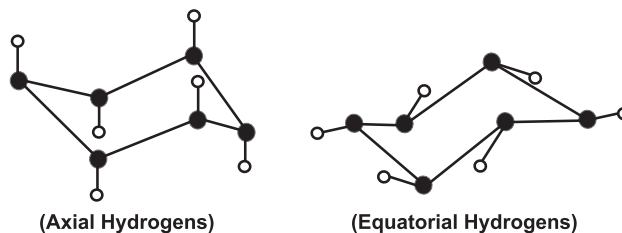
All the 12H are shown as follows :

Flagpole
Hydrogen

In boat form, the hydrogens at C_1 and C_4 look like flagpole of boat so that these are called flagpole hydrogen.

Importance of Stereochemistry :

In various organic compounds the molecular formulae as well as the structural formulae are same but the spatial arrangements of their substituent groups are different. Stereochemical study helps us to understand the actual three dimensional picture of molecule in our brain which cannot be drawn on paper or board. These studies are also helpful to understand the mechanism of organic reactions and organic synthesis. The knowledge of stereo structures induces the research work in this area to make better understanding of the subject as well as mechanisms and new synthetic methods in organic or molecular chemistry.

Practice Questions

Multiple Choice Questions :

1. Which of the following is not considered as stereo isomerism?

   (a) Geometrical isomerism

   (b) Conformational isomerism

   (c) Functional group isomerism

   (d) Optical isomerism

2. Which of the following does not show

geometrical isomerism?

(a) $CH_3 - CH = CH - CH_3$

(b) $Cl - CH = CH - Cl$

(c) $CH_3 - C(OH) = CH(OH) - CH_3$

(d) $(CH_3)_2 C = CH - CH_3$

3. Which of the following statement is true for optical isomerism?

(a) Axis of symmetry must be present in the molecule.

(b) Plane of symmetry must be present in the molecule.

(c) Centre of symmetry must be present in the molecule.

(d) None of above.

4. Meso tartaric acid does not show optical activity, because –

(a) It has two chiral centers

(b) It has external compensation

(c) It has a plane of symmetry

(d) It has erythro form

5. Which of the following compound does not show optical isomerism?

(a) Ethyl alcohol

(b) 2 – Butanol

(c) 2 – chloro propane

(d) Lactic acid

6. Which of the following statements is not true for to draw Fisher Projection Formulae?

(a) Two perpendicular lines are drawn which cut to each other.

(b) Number one carbon is placed at left side.

(c) Groups of horizontal are projected upward.

(d) Molecule must be rotate about 180^0

7. Which of the following is taken as reference to represent the relative configuration?

(a) Lactic acid

(b) Tartaric acid

(c) Glyceraldehyde

(d) Sodium potassium tartrate

8. Which of the following methods is not used in resolution of a racemic mixture?

(a) Biochemical method

(b) Mechanical method

(c) Fractional distillation method

(d) Column chromatography method

9. Which of the following statement is not true for conformational isomerism?

(a) Represented by Newman and Sawhorse projection formulae

(b) There are infinite number of conformational isomers

(c) Eclipsed conformation is most stable

(d) Ring systems also show conformational isomers

10. Which of the following statements is not true for diastereoisomers?

(a) They show optical activity

(b) These isomers have different physical properties

(c) They show internal compensation

(d) They scatter the plane polar light

Ans. : 1(c), 2(d), 3(d), 4(c), 5(a)

6(b), 7(c), 8(c), 9(c), 10(d).

Very Short Answer Questions :

1. Define the isomerism.

2. What do you mean by stereo isomerism?

3. What is optical activity?

4. What is the necessary condition for optical isomerism?

5. State about the element of symmetry.

6. Why the meso tartaric acid is optically inactive?

7. What is racemisation?

Short Answer Questions :

1. Define the optical activity. Explain with example that the optical activity is found in which type of molecule?

2. Butanol does not show optical activity while

2-butanol shows; why ?

3. What are the necessary conditions for optical activity? Give some examples of optical active molecules.

4. Discuss the optical activity of lactic acid.

5. Explain racemisation with a suitable example

6. Explain the erythro and threo forms with suitable example.

7. What do you mean by absolute configuration?

8. Explain the difference between conformation and configuration necessary condition for geometrical isomerism.

9. What is meaning of geometrical isomerism? Write the necessary condition for geometrical isomerism.

10. Discuss the stereo isomerism shown by oximes.

11. What is conformation? Draw the Newman projection of ethane.

12. Discuss the salt formation method of resolution of enantiomers.

Long Answer Questions :

1. Discuss the optical isomerism of tartaric acid.

2. Discuss enantiomerism and diastereoiso-merism with suitable examples.

3. Explain the stereo isomerism. Discuss the stereo isomerism tartaric acid and draw it's all structures. Explain that when tartaric acid is synthesized, there we get optically inactive tartaric acid?

4. What do you mean by optical isomerism? Discuss the optical isomerism of compound with two similar stereogenic carbons.

5. Explain the stereo isomerism of tartaric acid. How many optical isomers are present in tartaric acid? What are the differences between meso tartaric acid and racemic tartaric acid?

6. Physical properties of geometrical isomers are different but the physical properties of optical isomers are same. Explain.