MODULE

For the syllabus of University of Kalyani

Under

Choice Based Credit System

For

Semester – I

(Honors Course)

Subject: Organic Chemistry – I

(CHEMHT-2)

Chapter: Stereochemistry – I

By

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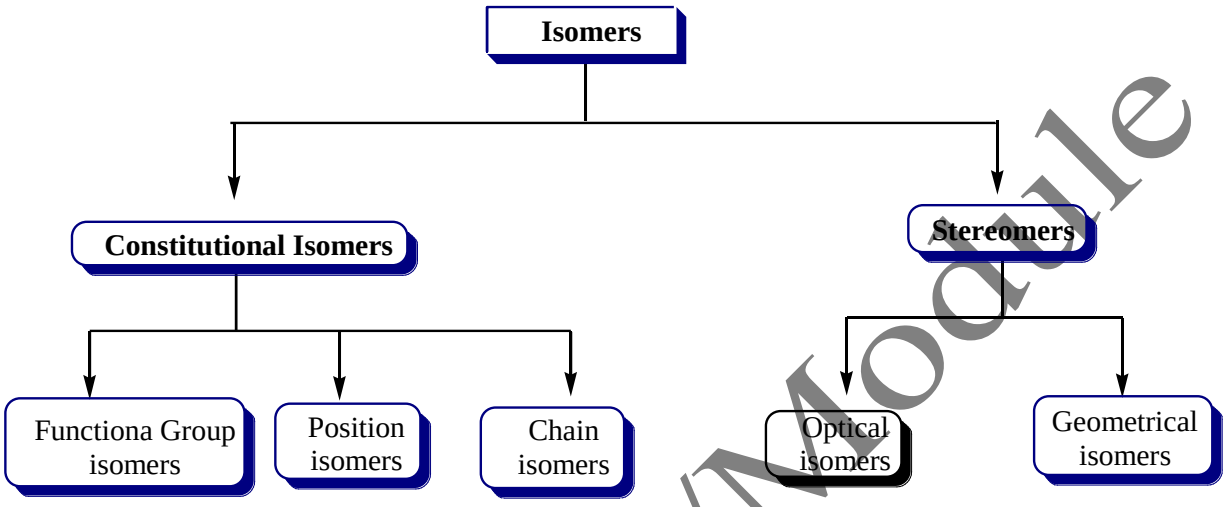
1. Bonding geometries of carbon compounds and representation of molecules:

Isomers: Molecules with same molecular formula but different in structure are known as isomers. They can be classified into the following manner:



Constitutional Isomers: Molecules with same molecular formula but differing in the nature of linkage of atoms regardless of direction in space *i.e.*, bond connectivity are called constitutional isomers or structure isomers. They may be subdivided into the following catagories:

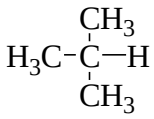
i) Functional group isomers: Differ in nature of functional groups.

e.g., CH_3CH_2OH and CH_3OCH_3.

ii) Position isomers: Differ in position of atoms or functional groups.

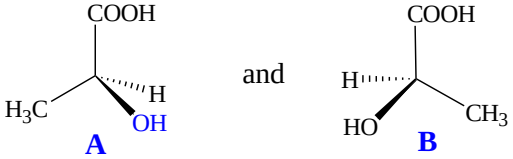
e.g., 1- propanol ($CH_3CH_2CH_2OH$) and 2- propanol ($CH_3CHOHCH_3$)

iii) Chain isomers: Differ in the nature of skeletal structure.

e.g. *n*-butane ($CH_3CH_2CH_2CH_3$) and isobutene 

Stereoisomerism: It arises due to differ only in the relative orientation of atoms and groups in space. Thus molecules having same connectivity of atoms but differing in the relative three dimensional arrangements of atoms or groups are known as stereoisomers.

e.g. Lactic acid



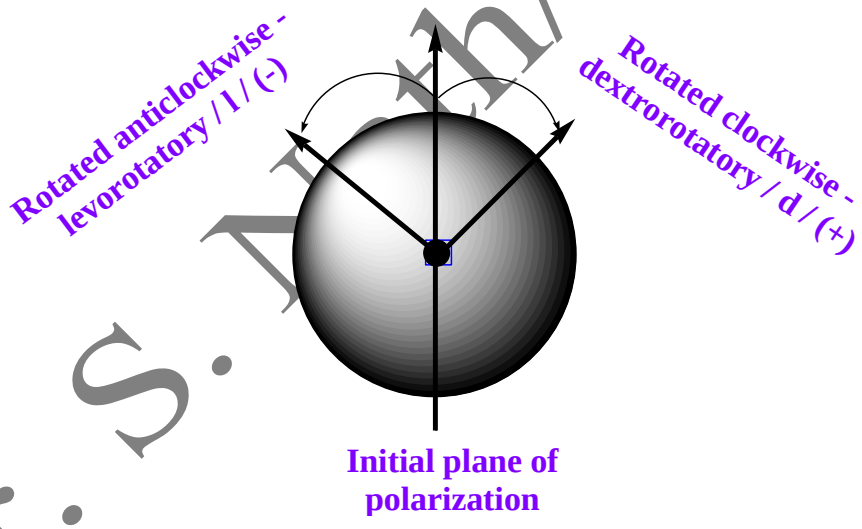
In classical stereochemistry, stereoisomerism are broadly classified as i) Optical isomerism and ii) geometrical isomerism, which is based on the behavior they show towards plane polarized monochromatic light.

Optical isomers: Stereoisomers that are capable of rotating the plane of a plane polarized monochromatic light, when such a light is passed through them are said to be optically active and these stereoisomers are called optical isomers. If the plane is rotated to the right (clockwise) with respect to the initial plane of polarization , the compound is called **dextrorotatory (d or +)** and left (anticlockwise) with respect to the initial plane of polarization , the compound is called **levorotatory (l or -).**

Monochromatic light: Electromagnetic radiation having single wavelength (λ) and whose electric vector (E) is oscillating in a single plane perpendicular to the plane of direction of propagation.

The angle of rotation is expressed in degrees and the optical activity is measured in asimple instrument known as **polarimeter.**

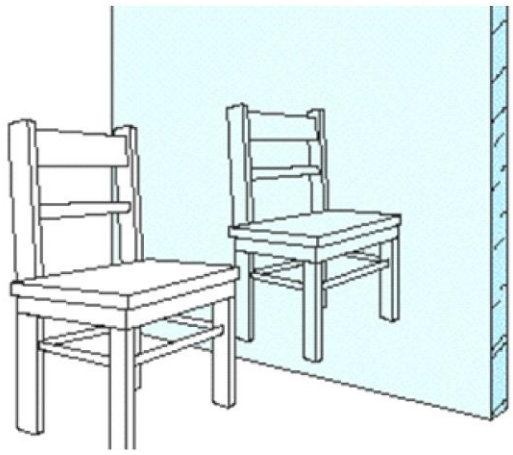
Graphical representation



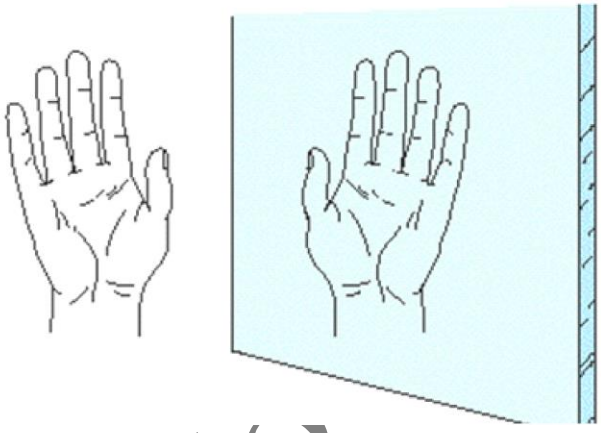
Condition necessary for a molecule to be optically active: Necessary and sufficient condition for a molecule to be optically active is that it is not superimposable on its mirror image or molecule must be dissymmetric *i.e.* molecule must not contain plane of symmetry (σ), centre of symmetry (*i*) and alternating axis of symmetry (Sn).

A molecule (or object) can have only one mirror image. If the image is superposable on the original the molecule is called achiral. On the other hand, if it is not superposable, the molecule and its mirror image form two distinct species called enantiomers giving rise to a type of stereoisomerism known as enantiomerism. Such molecules are called chiral and the two isomers are said to differ in the sense of chirality or handedness in the same way as right hand differs

from the left. *e.g* two forms of lactic acid (A) and (B) which are mirror image of each other but nonsuperposable and thus one is dextrorotatory and other is levorotatory.

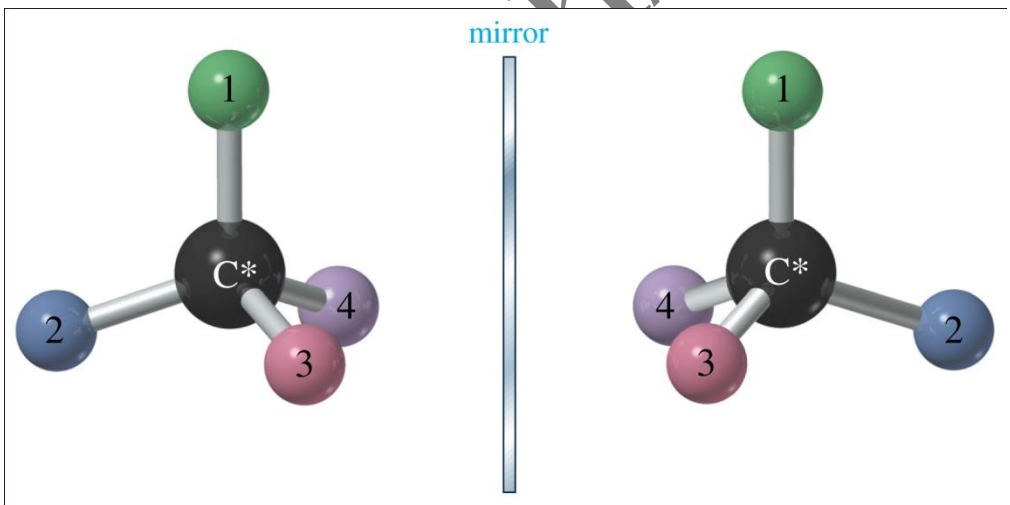


Mirror-image object is same from the original object and are achiral



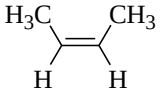
"Handedness": right glove doesn't fit the left hand. Mirror-image object is different from the original object, So are chiral

Chiral carbon: Tetrahedral carbons with 4 different attached groups are chiral. Its mirror image will be a different compound (enantiomer).

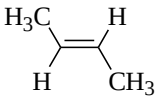


Geometrical isomer or Cis-trans isomer:

It arises due to different arrangement of groups around rigid double bonds like C=C, C=N, N=N etc. This type of isomer is also possible in rigid ring compounds. Also the groups held by each atom in the rigid part should be different from each other. For example, Ca_2=Ca_2 or Cab=Ca_2 type molecule do not show geometrical isomerism, but Cab=Cab type molecule where a≠b, can easily exhibit geometrical isomerism.

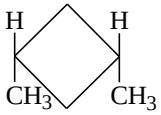


***Cis*-2-butene**

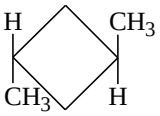


***Trans*-2-butene**

Geometrical isomerism in rigid ring compounds:

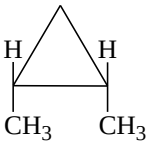


***Cis*-1,3-dimethyl cyclobutane**

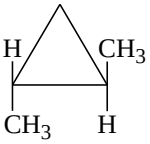


***Trans*-1,3-dimethyl cyclobutane**

Geometrical isomers are usually optically inactive unless there is other site in the molecule giving rise to optical isomers as well. *e.g.* Both *cis*-1,3-dimethyl cyclobutane and *trans*- 1,3-dimethyl cyclobutane are optically inactive, as mirror image are superposable.



***Cis*-1,2-dimethyl cyclopropane**



***Trans*-1,2-dimethyl cyclopropane**

Both *cis*-1,2-dimethyl cyclopropane and *trans*- 1,2-dimethyl cyclopropane are optically active as mirror image does not superimpose.

Representation of a molecule

Since stereochemistry refers to molecules in the three dimensions, appropriate modes of representations of three dimensional molecule on two-dimensional paper is essential. These projection formulas are -

i) Fischer projection formula

ii) Newman projection formula

iii) Sawhorse projection formula

iv) Flying-wedge projection

v) Zigzag projection formula

i) Fischer projection formula:

Fischer Projections use horizontal and vertical lines to represent the 3D state, the horizontal lines represent attachments pointing out of the paper towards us and vertical lines represent attachments pointing out the back of the paper away from us. The intersection represents the central carbon.

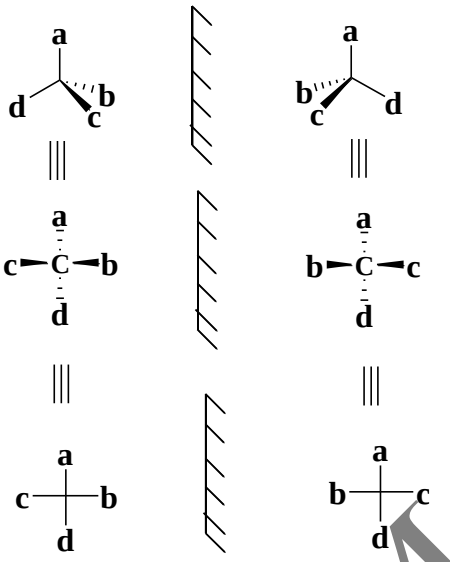
Flat drawing that represents a 3D molecule.

A chiral carbon is at the intersection of horizontal and vertical lines.

Horizontal lines are forward, out-of-plane.

Vertical lines are behind the plane.

Thus Fischer projection may be outlined below:-

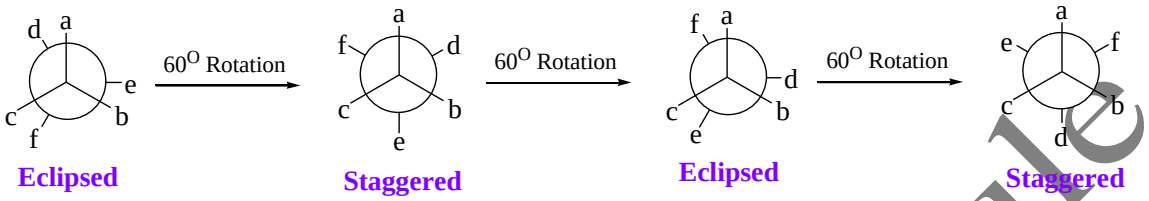


Fischer Rules:

- Carbon chain is on the vertical line.
- Horizontal bonds pointing up with respect to the plane of the paper.
- Vertical bonds pointing down with respect to the plane of the paper.
- Highest oxidized carbon at top.
- Rotation of 180° in plane doesn't change molecule.
- Do not rotate 90°
- Do not turn over out of plane.

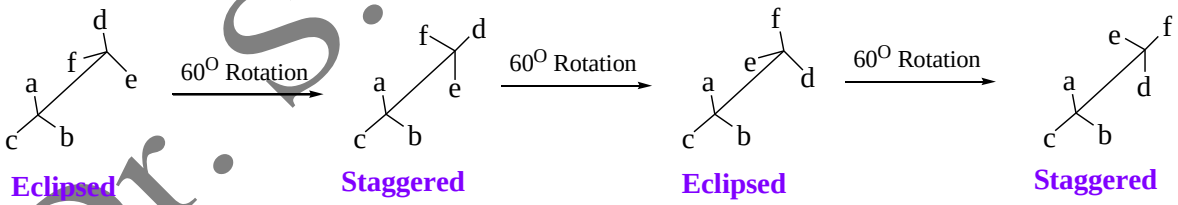
ii) Newman Projections: Three-Dimensional Representations:-

Newman Projections are used mainly for determining conformational relationships. Conformers are molecules that can be converted into one another by a rotation around a single bond. In this notation, the molecue are actually viewing by looking down a particular carbon-carbon bond. The front carbon of this bond is represented by a dot, and the back carbon is represented by a large circle. The three remaining bonds are drawn as *sticks* coming off the dot (or circle), separated by one another by 120 degrees. A **Newman Projection** can be drawn such that the groups on the front carbon are *staggered* (60 degrees apart) or *eclipsed* (directly overlapping) with the groups on the back carbon. Below are two **Newman Projections** of ethane, C_2H_6. The structure on the left is staggered, and the structure on the right is eclipsed. These are the simplest **Newman Projections** because they have only two carbons, and all of the groups on both carbons are identical.



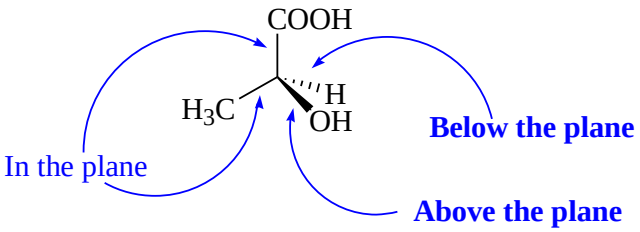
iii) Sawhorse Projections: Three-Dimensional Representations:-

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



iv) Flying-wedge projection:

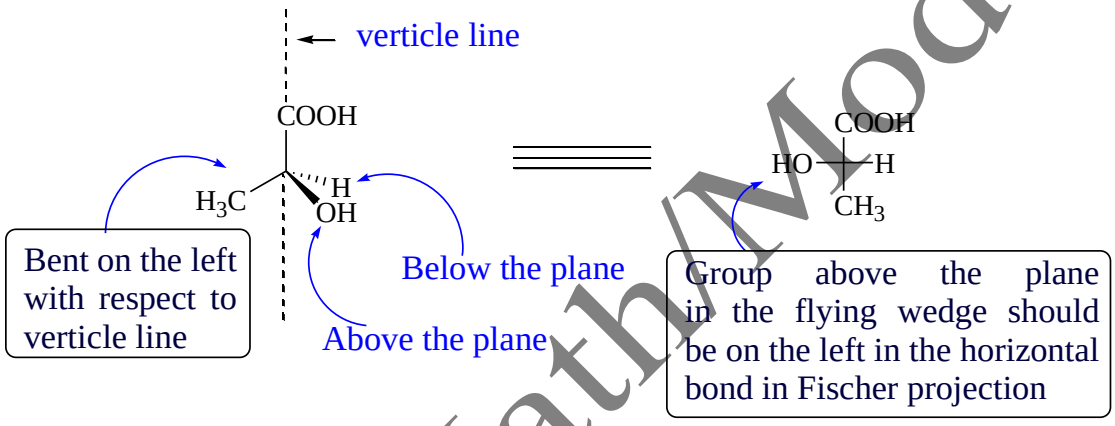
The most commonly-used notation for straight-chain molecules in organic chemistry is the Flying-Wedge Notation. In this notation, two bonds are drawn in the plane of the page (*sticks*), one bond is drawn coming toward us, out of the page (*wedged*), and one bond is drawn going away from us, behind the page (*dashed*).



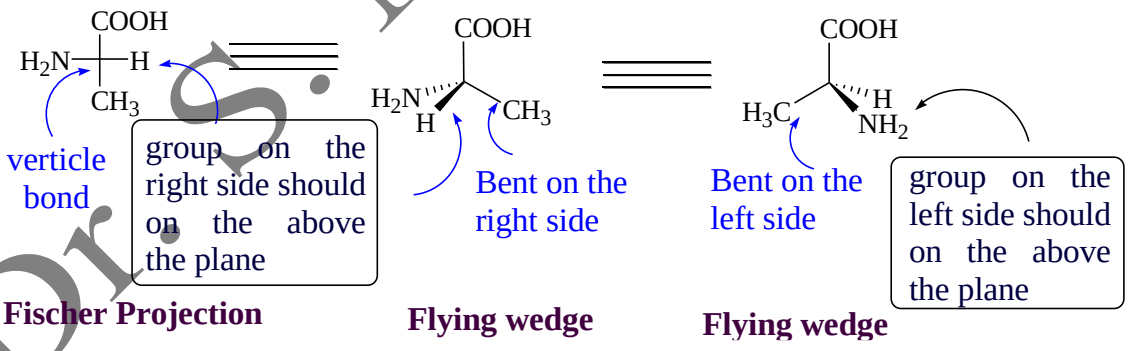
Interconversions of projection formulas

Flying-wedge projection to Fischer projection formula and vice-versa:

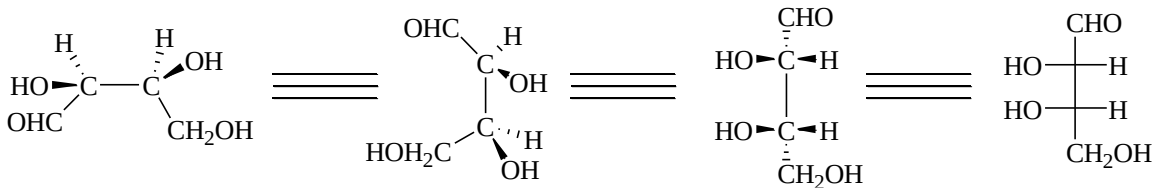
Conversion of flying wedge to Fischer projection may be carried out as follows:



Conversion of Fischer projection to flying wedge may be carried out by the reverse method:

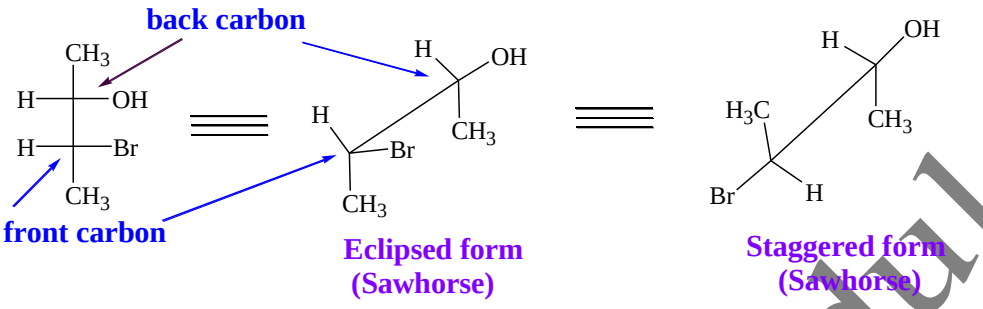


Similarly, for molecules with two chiral centre ⟶

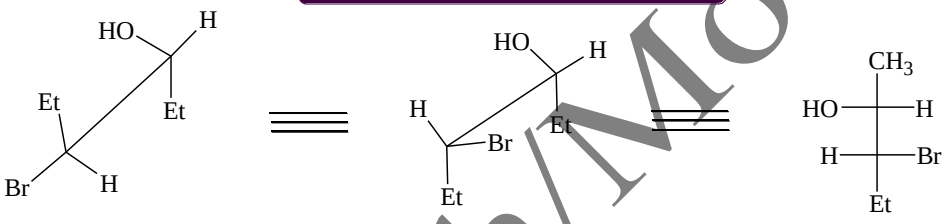


Fischer projection formula to Sawhorse and vice versa:

Fischer projection to Sawhorse

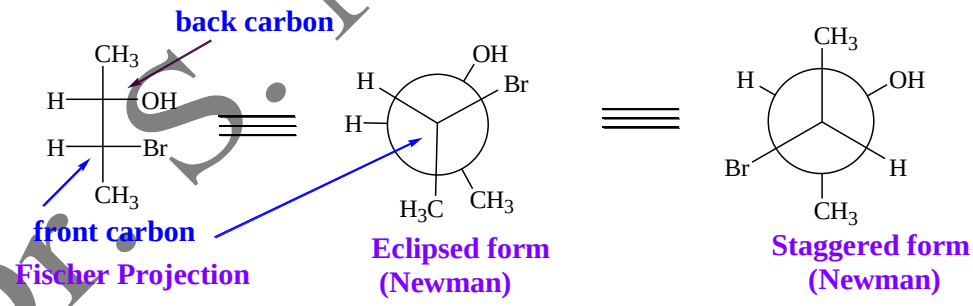


Sawhorse to Fischer projection

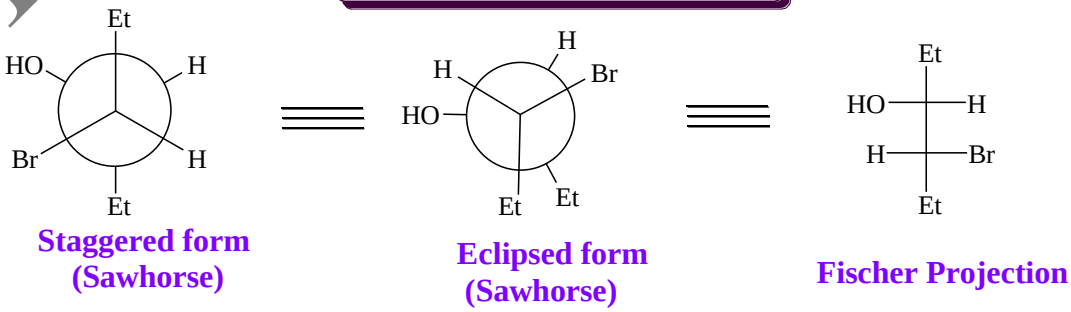


Fischer projection formula to Newman and vice versa:

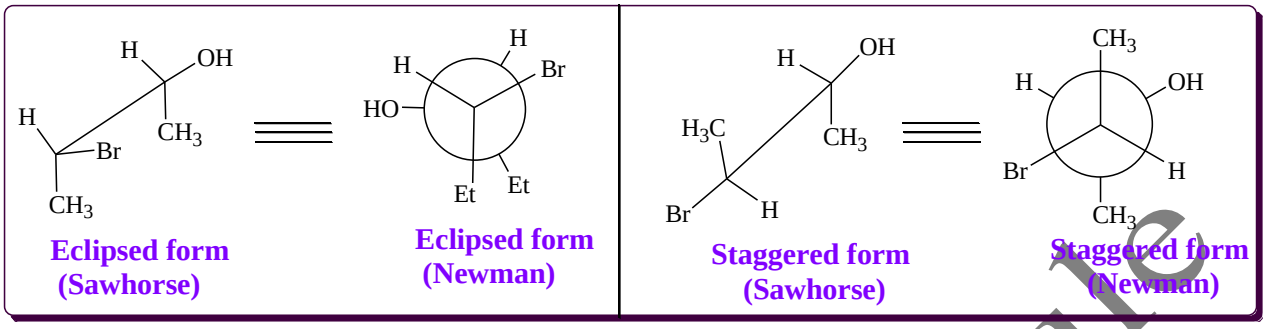
Fischer projection to Newman



Newman toFischer projection



Sawhorse to Newman and vice versa:



Eclipsed form (Sawhorse) | Eclipsed form (Newman) | Staggered form (Sawhorse) | Staggered form (Newman)

2. Concept of Chirality and symmetry:

Symmetry operations and symmetry elements: In order to study the symmetry of a molecule, certain operations such as rotation and reflection are performed and if by so doing an arrangement is obtained which is indistinguishable from the original one, the operation is called a symmetry operation and the molecule is said to possess an element of symmetry.

Four fundamental element of symmetry are present:

i) Simple or proper axis of symmetry (Cn)

ii) Plane of symmetry (σ)

iii) Centre of symmetry (i)

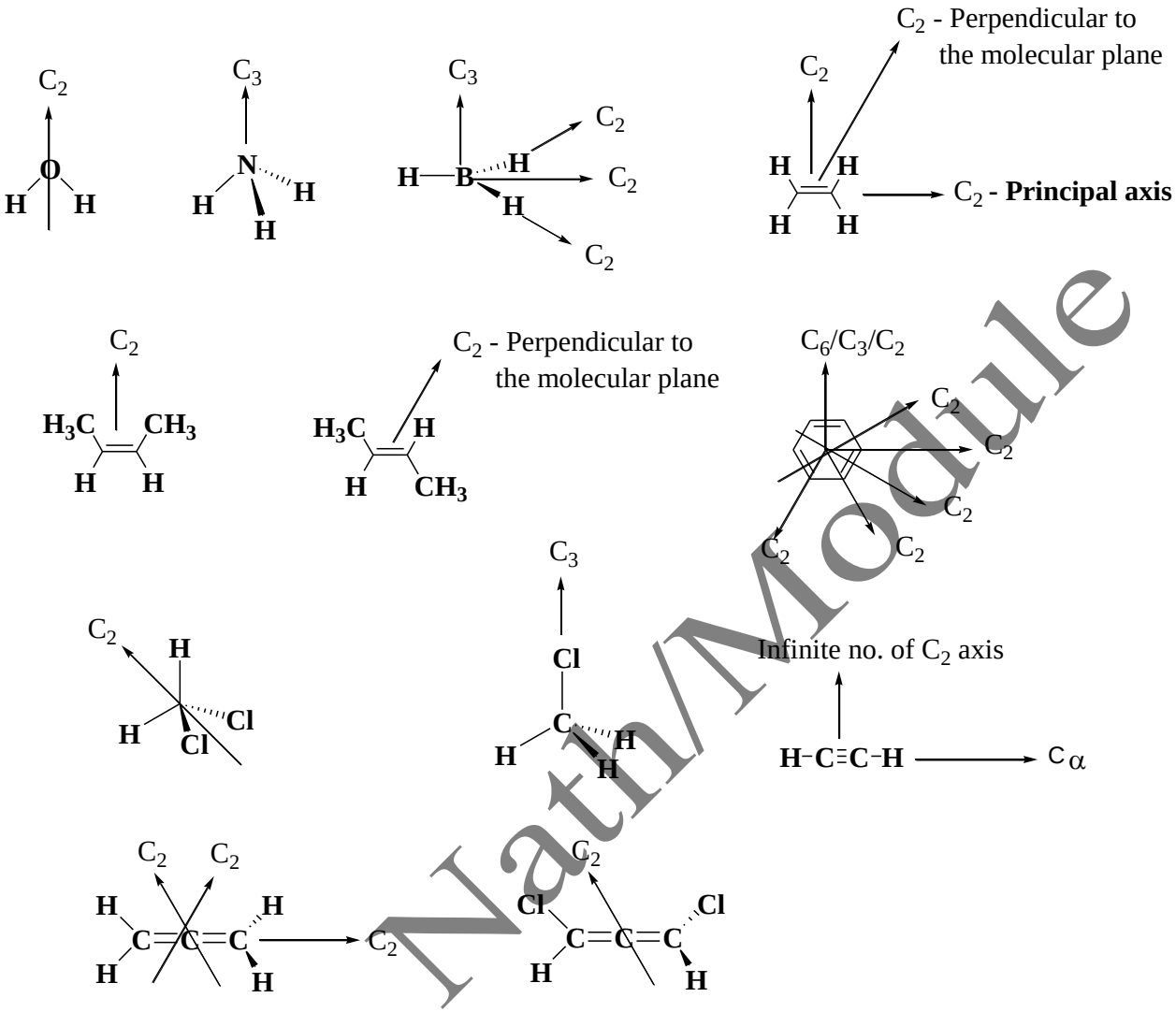
iv) Alternating axis of symmetry (Sn)

There are basically only two symmetry operations - rotation and reflection and there combination thereof. Symmetry based solely on simple rotation is often called symmetry of first kind whereas symmetry based on reflection or rotation-reflection combination is known as symmetry of second kind.

i) Simple or proper axis of symmetry (Cn): If a molecule is rotated around an imaginary axis through an angle of $360^{O}/n$ and an arrangement is obtained which is indistinguishable from the original, the axis is called simple axis of symmetry of order 'n'

The axis is designated as Cn and the operation is called Cn operation. If the operation repeated 'n' times then identical orientation obtained.

Principal axis: Axis of highest order is known as principal axis and is placed vertically to write a molecule. When a molecule has several symmetry axis of same order, the one passing through the greatest number of atoms is taken as the principal axis.

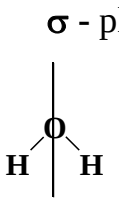


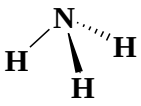
ii) Plane of symmetry (σ): A plane of symmetry is a plane which divide the molecule into two halves which are mirror image of each other or mirror image of one part of the molecule is superposable with that of the other part. The plane is called σ – plane and the operation is called σ – operation. Two σ – operation are equivalent to an identity operation as original molecule is obtained.

σ_h (Horizontal): Plane perpendicular to the principal axis and is unique.

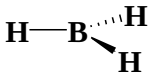
σ_v (Vertical): Plane containing the principal axis, may be greater than one.

σ_d (Diagonal): Plane bisecting the angle between two C_2 axis.

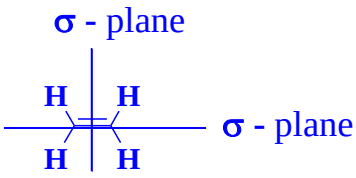




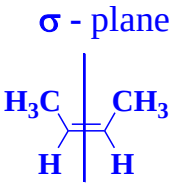
three σ - plane each containing N-H bond



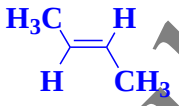
three σ - plane each containing B-H bond and molecular plane



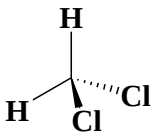
and molecular plane



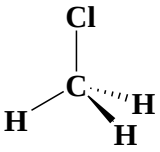
and molecular plane



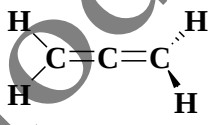
only molecular plane



Two σ - plane, one passing through H-C-H atoms and another through Cl-C-Cl atoms



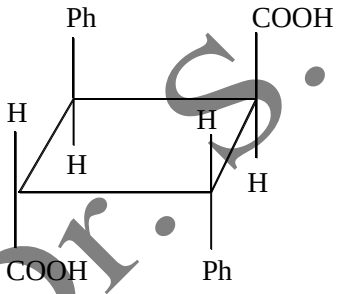
Three σ - plane, each passing through H-C-Cl atoms



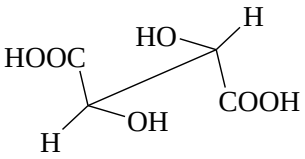
Two σ_d - plane, each passing through H-C-H atoms and are perpendicular to each other

iii) Centre of symmetry or inversion centre (*i*): It is point within a molecule such that if an atom (or point) joined to it and the line extended to an equal distance beyond, it encounters an equivalent atom (or point). It should be noted that all straight lines passing through the centre of inversion (i) must encounters identical atoms on either side of the centre.

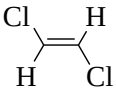
e.g.- the following molecule has inversion centre:



α – truxillic acid



Meso- tartaric acid anti conformation

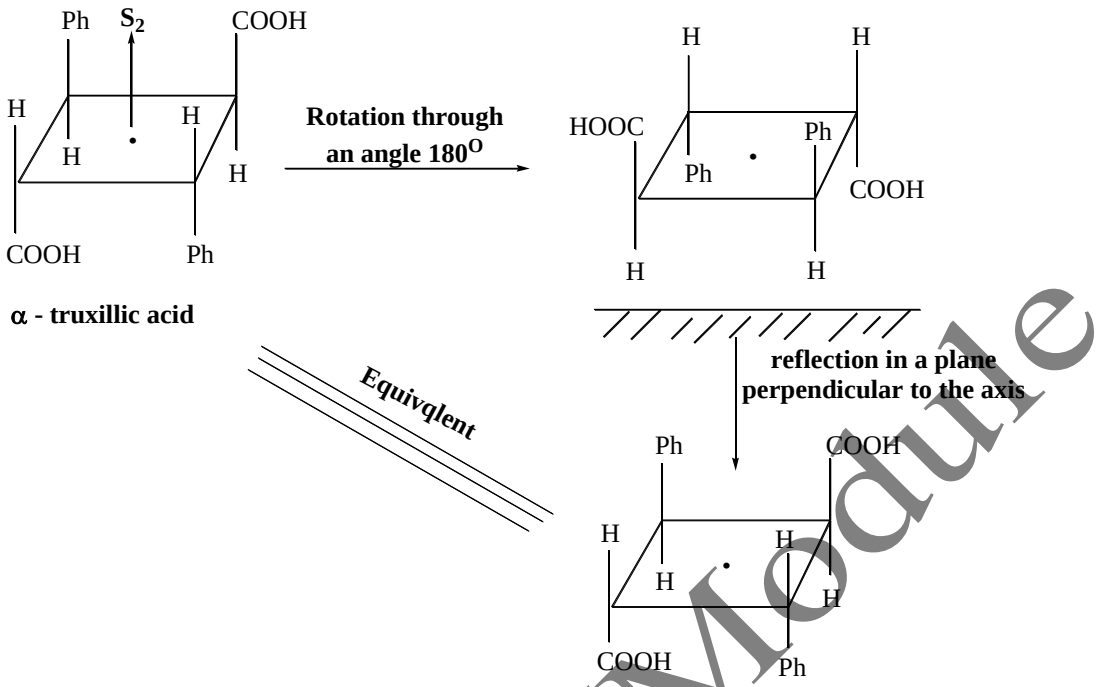


trans dichloro ethylene

(iv) Improper or alternating or rotation reflection axis of symmetry (Sn):

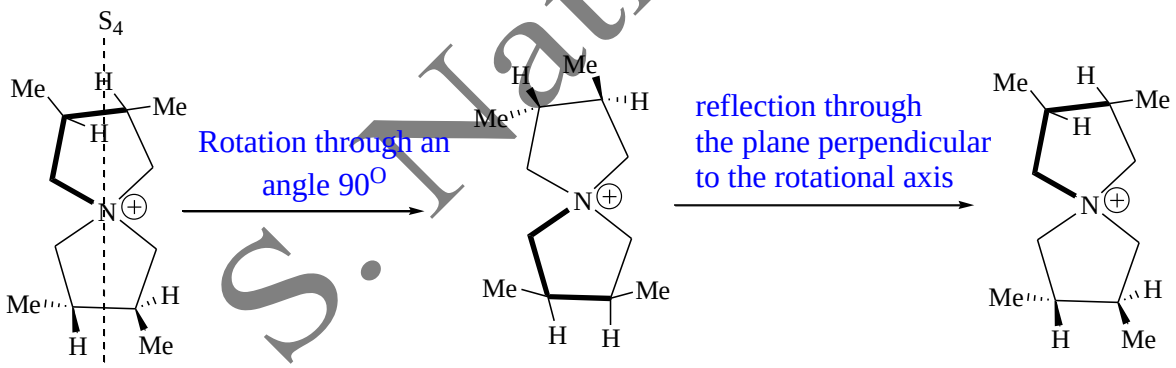
It is an axis of order 'n' if rotation of the molecule about the axis by $360^O/n$ followed by reflection in a plane perpendicular to the axis generates a structure indistinguishable from the original. The order of two operations may be reversed without change in the result.

e.g.- α-truxillic acid has S_2 axis:



S_2 axis is equivalent to an inversion centre and S_1 axis ($C_1+\sigma = \sigma$) is equivalent to σ- operation.

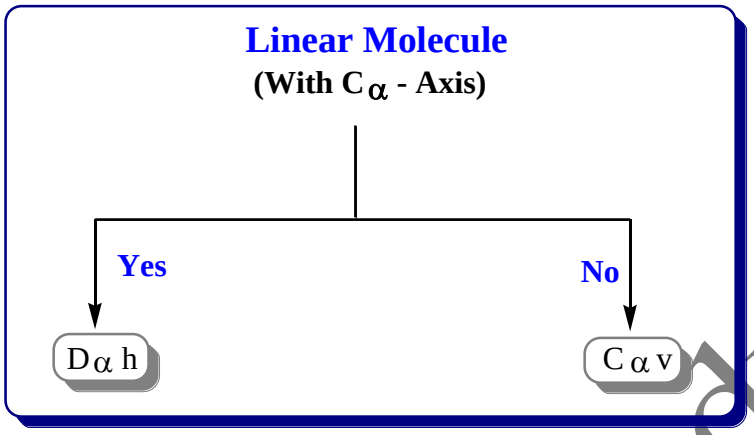
The molecule 3,4,3',4'-tetramethylspiro-(1,11')-dipyrrolidinium ion has only S_4 and do not have σ or inversion centre.



Point Group Classification:

The molecular structure are infinitely varied, but they can be classified into a limited number of symmetry related categories known as **symmetry point group** or **simply point** group on the basis of the symmetry operations that can be performed on them. These symmetry operations or symmetry elements combinedly form a group and since each of the operations leaves the centre of gravity of the molecule unchanged, the group is called a point group.

Diagram - A



Example:

Molecule	Symmetry Elements	Point Group
H—≡≡—H	C_α , $\perp C_2$, σ_h	$D_\alpha h$
O=C=O	C_α , $\perp C_2$, σ_h	$D_\alpha h$
H−C≡N	C_α , σ_v	$C_\alpha v$
H−Cl	C_α , σ_v	α

Diagram - B

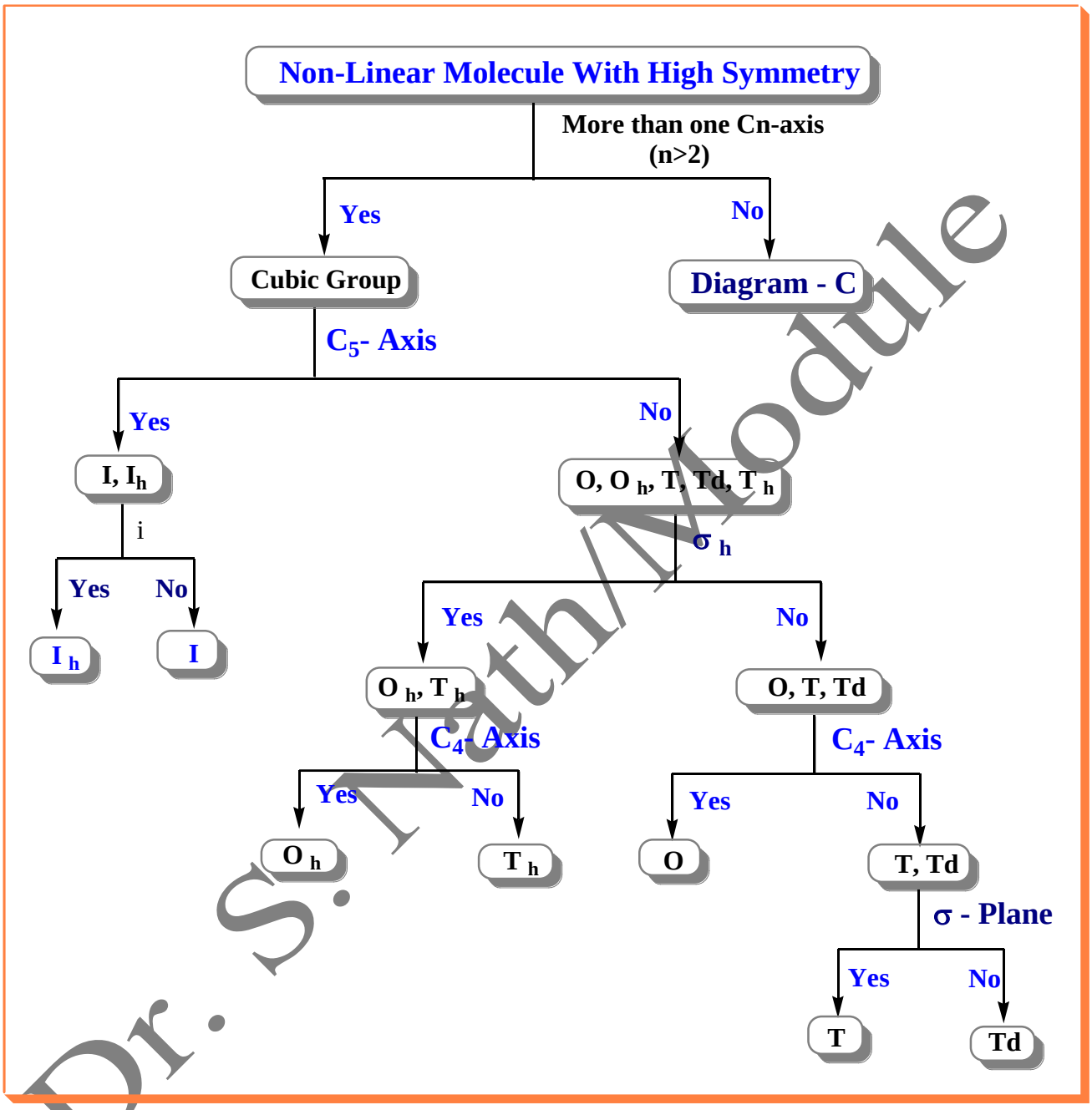


Diagram - C

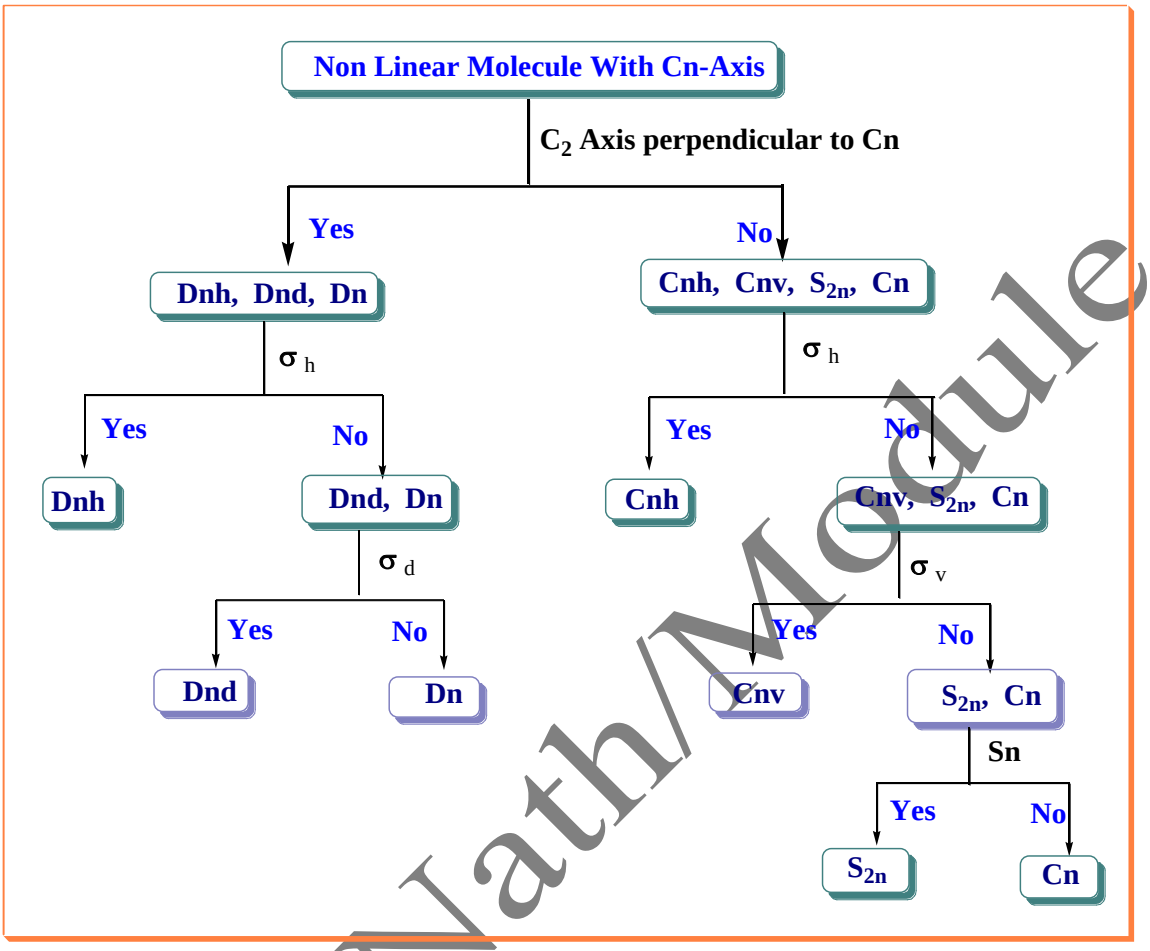
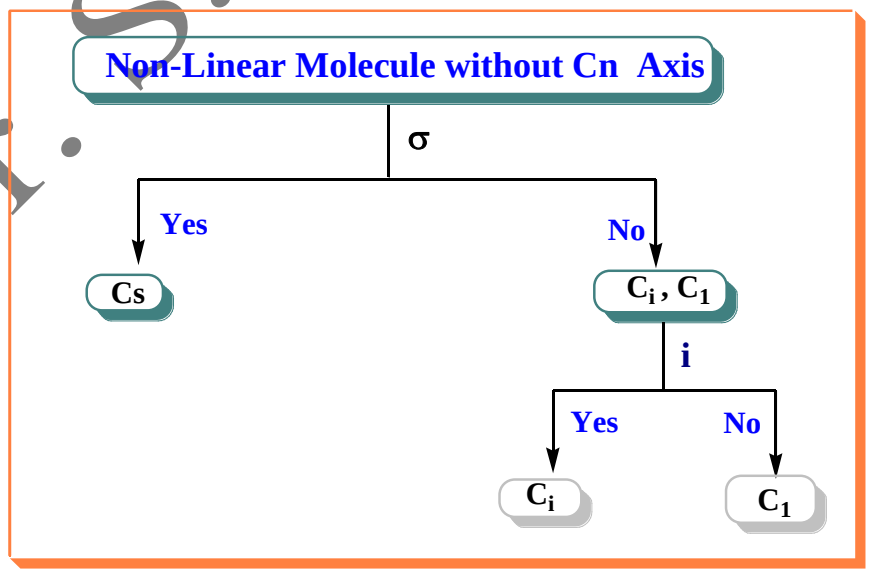
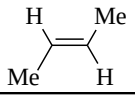
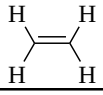
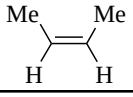
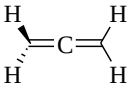
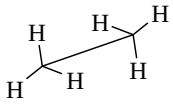
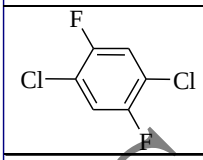
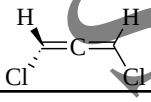
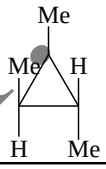
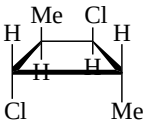
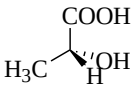
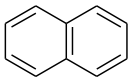
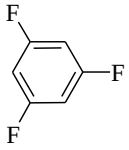
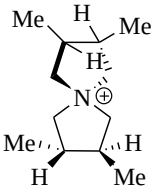


Diagram - D



Example

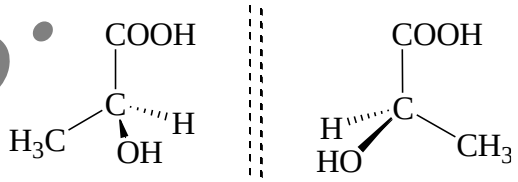
Molecule	Symmetry Elements	Point Group
$CHCl_3$, NH_3	C_3 (Cn), 3 X σ_v	C_{3v}
	C_6 (Cn), ⊥ 6 X C2, σ_h	D_{6h}
	C_2, σ_h	C_{2h}
	C_2, ⊥ C_2, σ_h	D_{2h}
	C_2, σ_v	C_{2v}
	C_2 (Cn), ⊥ 2 X C_2, 2 X σ_d	D_{2d}
BF_3	C_3 (Cn), ⊥ 3 X C2, σ_h	D_{3h}
	C_3 (Cn), ⊥ 3 X C_2, 3 X σ_d	D_{3d}
	C_2, σ_h	C_{2h}
	Only C_2	C_2
	Only σ	C_s
	Only ' *i* '	C_i
	No	C_1

Molecule	Symmetry Elements	Point Group
	C_2 (Cn), ⊥ 2 X C2, σ_h	D_{2h}
	C_2 (Cn), ⊥ 2 X C2, σ_h	D_{2h}
	C_3 (Cn), ⊥ 3 X C2, σ_h	D_{3h}
	C_2, S_4	S_4

All molecules belonging to point groups C_1, C_n and D_n are chiral, while molecules belonging to the rest of the point group are achiral.

Molecular symmetry and chirality:

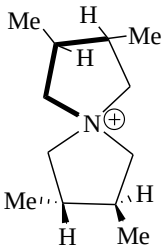
If the mirror image of a molecule is superposable on the original, the molecule is called achiral ie, it is optically inactive. On the other hand, if it is not superposable, the molecule and its mirror image form two distinct species called enantiomers and such molecule are called chiral (optically active)- and two enantiomers are said to differ in the sense chirality. e.g – lactic acid



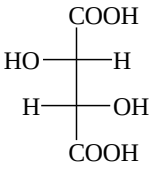
In this molecule four different groups attached to this central carbon atom. This two form of lactic acid are mirror image of each other but non-superposable. So this two are enantiomers. One dextrorotary and other levorotatory. Chirality is necessary and sufficient condition for occurrence of enantiomerism. Chiral molecule is optically active and necessary and sufficient condition for a molecule to be optically active is molecule will be non-superposable on its mirror image.

Condition for mirror image superposable:

If the molecule has plane of symmetry (σ) or centre of symmetry or alternating axis of symmetry (Sn), then it will be superposable on its mirror image. So presence of any one of the element of symmetry among these three leads to a molecule achiral and optically inactive.



Optically inactive due to presence of alternating axis of symmetry (S_4)

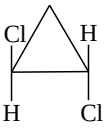


Optically inactive due to presence of plane of symmetry (σ)

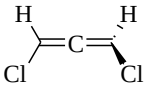
Dissymmetric molecule:

Presence of one or more Cn axes does not interfere with a molecule being chiral and can show optical activity and existing as two enantiomers i.e., mirror image does not superimpose. This type of molecule is called dissymmetric molecule. **These type of molecule belong to the point group Cn and Dn.**

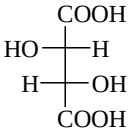
Examples:



trans - 1,2-dichlorocyclopropane (point group- C_2)



1,3-dichloroallene (point group- C_2)

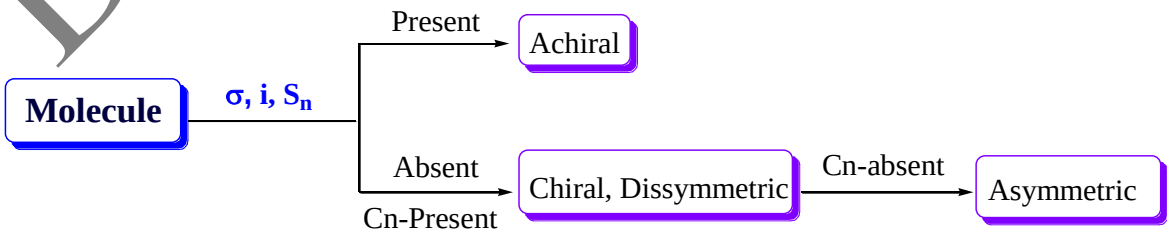


d/l - tartaric acid (point group- C_2)

Asymmetric molecule:

Asymmetric molecule is a chiral molecule, it lacks Cn axis also i.e, all symmetry elements are absent except the trivial C_1 axis. e.g lactic acid.

The following diagram classify the situation:



Enantiomers:

If two stereoisomers are related to each other as object and mirror image which are not superposable they are called enantiomers and said to exhibit enantiomeric relationship. These molecules are chiral and optically active i.e, they turn the plane of a polarized light to an equal degree but in opposite direction. They are called optical isomers. Both asymmetric and dissymmetric molecule (with point group C_1, C_n and D_n only) can exhibit enantiomeric relationship. e.g., lactic acid.

Diastereomers:

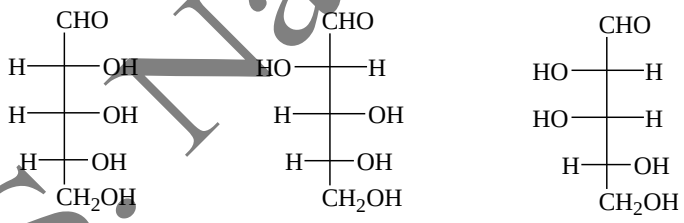
A pair of stereoisomers having no mirror image relationship is known as diastereomers and said to exhibit diastereomeric relationship.

e.g., i) meso tartaric acid and active tartaric acid represents a pair of diastereomers.

ii) Z-but-2-ene and E-but-2-ene represent a pair of diastereomers.

Epimers:

If a molecule contain more than one chiral centre and configurational inversion takes place at one centre only, the product formed is the diastereomer of the original, more specifically, an epimer and the process is called epimerization.

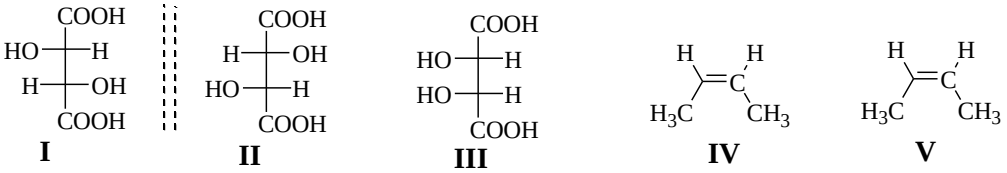


I and II - diastereomer as well as epimer
II and III - diastereomer as well as epimer
I and III - Diastereomer but not epimer

Thus all epimers are diastereomers but all diastereomers may not necessarily be epimers.

Homoers:

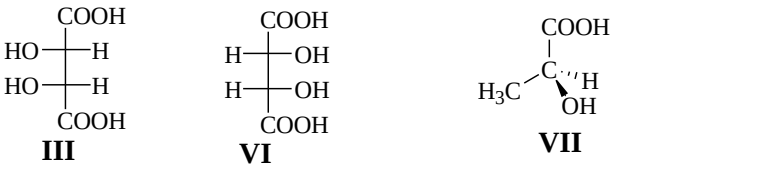
In stereochemistry, another term called homomer is used. Any two structure which are superposable are called homomer.



d/l - tartaric acid meso - tartaric acid

I and II: Enantiomers **II and III:** Disatereomers

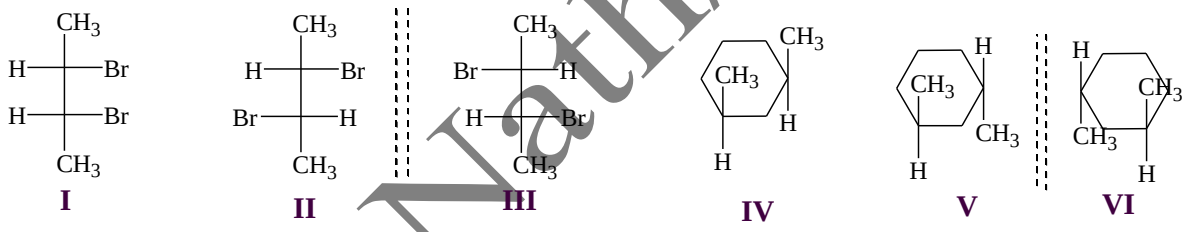
I and III: Disatereomers **IV and V:** Disatereomers



III and VI: Homomer **VII and VIII**: Homomer

Some distinctive features of enantiomers and diastereomers;

Since a molecule can have only one mirror image, enantiomers can exist only in pairs, on the other hand, structural conditions permitting a molecule can have any no. of diastereomers.



I, II and I, III - Diastereomer; II, III - Enantiomer
IV, V and IV, VI - Diastereomer; V, VI - Enantiomer

The two enantiomers are **isometric** two each other and in achiral media, behave in identical fashion, as if they are homomers as they have identical bond connectivity of atoms along with identical relative spatial arrangements of atoms with respect to distance and dihedral angle. Thus enantiomers have the same melting point, boiling point, densities, solubilities, refractive indices, dipolemoment, energy content etc. They also show same reactivity towards achiral reagents. Enantiomers differ in their behavior towards plane polarized monochromatic light.

The diastereimers differ in the spatial relationship of atoms and groups and are therefore **anisometric** relative to each other. They are chemically different and also differ in physical properties like behavior towards plane polarized monochromatic light, melting point, boiling point, densities, solubilities etc. in all other above mentioned properties.

Asymmetric centre or Chiral centre:

A carbon atom that is combined with four different univalent atom or groups and whose affinities are directed toward the vertices of a tetrahedron is asymmetric. The four vertices become distinguishable, all elements of symmetry disappear and the tetrahedron turns into a three dimention four point chiral simplex of C_1 symmetry which is non-superposable with its mirror image.

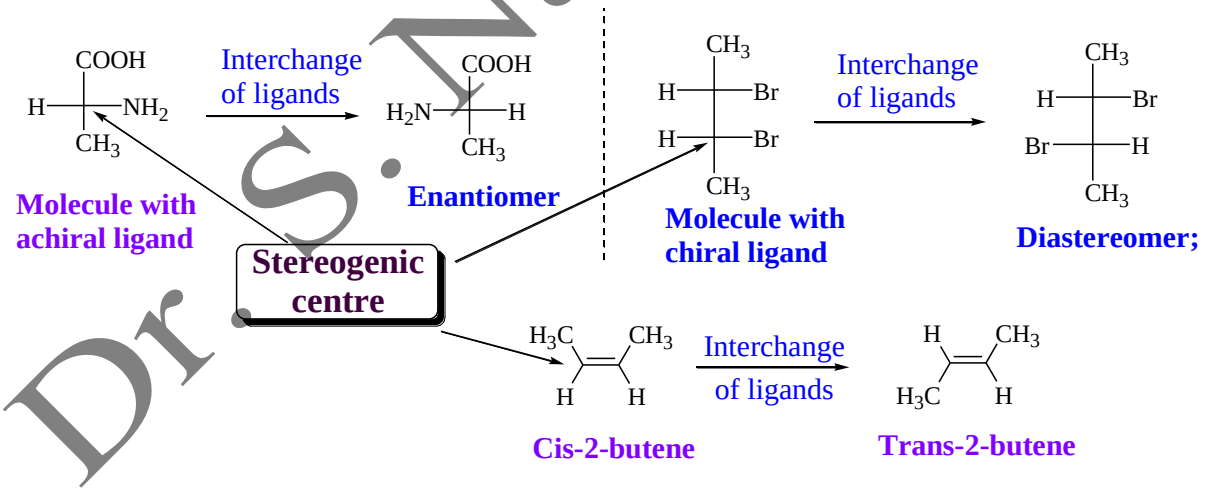
Stereogenic centre:

An atom (usually carbon) of such nature and bearing of groups of such nature that it can have two non-equivalent configurations and mutual exchange of any two groups on that atom generates a new stereoisomers.

The presence of chiral centre usually leads to molecular chirality and one unique feature of this chiral tetrahedral model is that exchange of any two ligands reverses the chirality of the centre giving a new stereoisomer.

If all the ligands are achiral, the transposition leads to an enantiomer, on the other hand if one or more of the ligands are chiral, a diastereomer results. The chiral centre is therefore a stereogenic centre.

Examples: Molecule like Cabcd, C atom is stereogenic. Again C-2 and C-3 of cis- and trans-but-2-ene are stereogenic . In this case axis joining two carbon atom is called stereogenic axis.



Chirotopicity and achirotopicity:

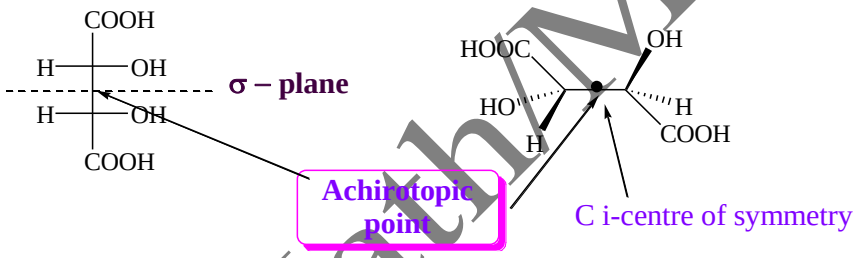
The site symmetry of atoms in molecules are two types – chiral and achiral. Any atom within a molecular framework is said to be **chirotopic** if its site symmetry is chiral i.e, the atom resides in a chiral environment. An atom within a molecular framework is said to be **achirotopic** when its site symmetry is achiral.

All points or atoms in a chiral molecule are chirotopic as chirality is in all inclusive property, as it affects all parts of a chiral molecule.

e.g. In lactic acid, all ligands are chirotopic but in CH_3CH_2COOH, ligands are achirotopic i.e, they do not reside in chiral environment.

Any points or atoms in a chiral molecule is chirotopic, but even in an achiral molecule there may be many chirotopic points or atoms. e.g. in meso-tartaric acid all points are chirotopic, only the centre of symmetry is achirotopic. In general, all points in a model that remain invariant under rotation-reflection operation are achirotopic. Thus all points on a plane of symmetry in a molecule are achirotopic.

Chirotopic and achirotopic point in a molecule may not be a material point coinciding with an atom. An achiral molecule may be divided into two chirotopic segments, then there should be atleast one point in a chiral conformation of the molecule which is achirotopic. The achirotopic point may not contain a atomic nucleus.



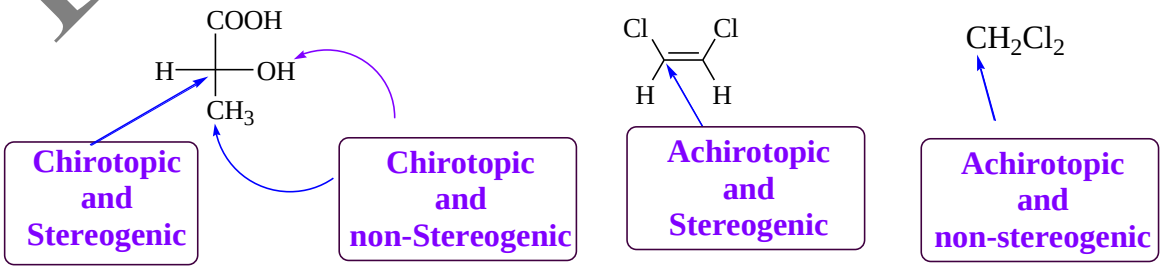
Difference between stereogenicity and chirotopicity:

Stereogenicity is dependent on the disproportion of the bond but chirotopicity is quite independent of it and is only determined by local symmetry. Stereogenicity and chirotopicity may not coincide in many centre.

i) In molecule Cabcd (a ≠ b ≠ c ≠ d) the carbon is stereogenic as well as chirotopic but the ligands are chirotopic but non-stereogenic.

ii) Carbon atoms in 1,2-dichloroethene is stereogenic but achirotopic.

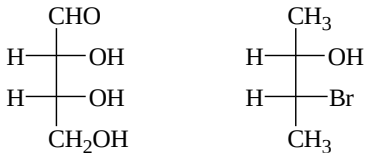
Stereogenic centre may or may not be chiral, but all chiral centre are stereogenic.



Constitutionally unsymmetrical chiral molecule:

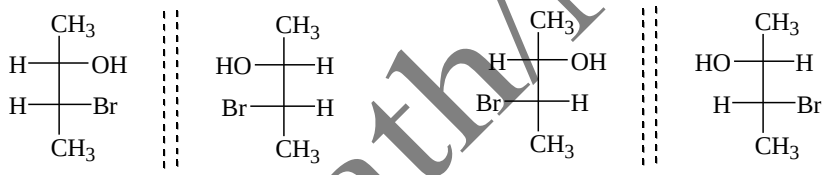
In case of acyclic molecule containing two or more chiral centre is constitutionally unsymmetrical if the two end groups are non-equivalent or if each of the chiral centre is substituted differently.

Examples:



Each chiral centre is capable of existing in two configurations, R and S and the total number of stereoisomers is thus **2^n, n = no. of chiral centre** or no. of stereoisomers is **2^{n-1} (±) pair** as they are enantiomeric. Any stereoisomers in the series will have one enantiomer and **(2^n – 2) diastereomers.**

e.g.- 3-bromo-2-butanol has 2 chiral centre and thus has four stereoisomers or two pair of enantiomers. These are-



Constitutionally symmetrical chiral molecule:

Acyclic molecule containing multiple chiral centre are called constitutionally symmetrical if chiral atoms equidistant from the geometrical centre of the molecule and are identical. The two end groups are equivalent.

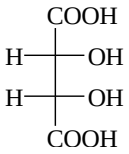
When 'n' even, number of stereoisomers = $2^{n-1} + 2^{\frac{n-2}{2}}$

2^{n-1} = Optically active and $2^{\frac{n-2}{2}}$ = Meso

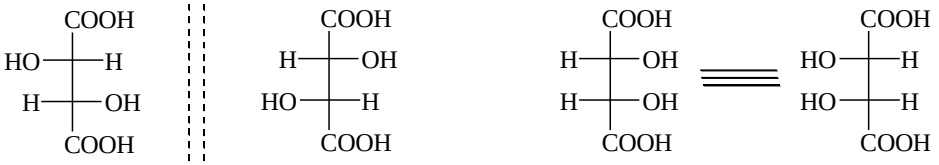
When 'n' even, number of stereoisomers = 2^{n-1}

$2^{n-1} - 2^{\frac{n-1}{2}}$ = Optically active and $2^{\frac{n-1}{2}}$ = Meso

Examples: **(i)** 2,3-dihydroxy succinic acid



No. of chiral centre = 2
Total no. of stereoisomers = 3

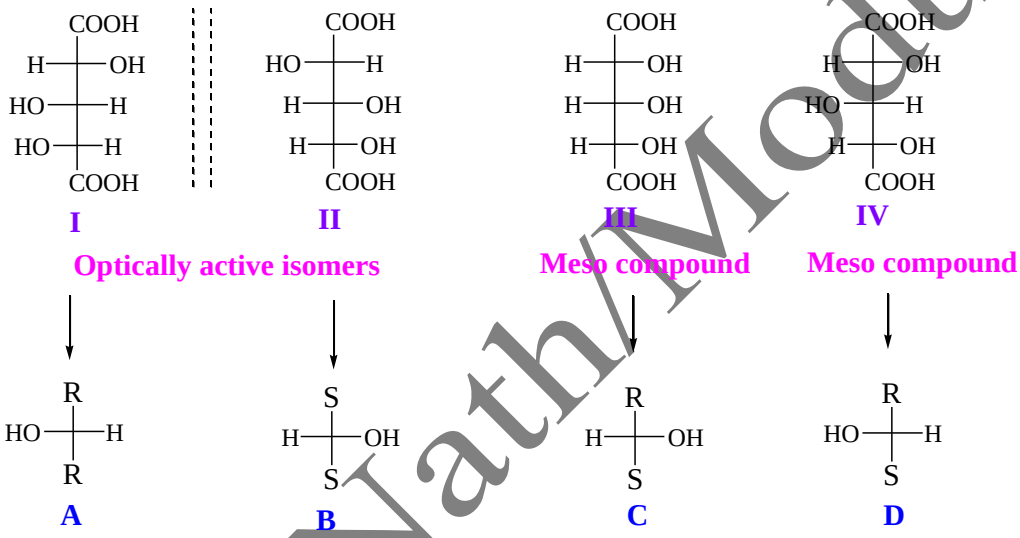


Optically active isomers **Meso compound**

(ii) 2,3,4-trihydroxyglutaric acid; Pseudoasymmetric centre:

It is constitutionally symmetrical molecule and has three chiral centre.

No. of stereoisomers = $2^{3-1} = 4$



Optically active isomers **Meso compound** **Meso compound**

I and II : Enantiomers/optically active
III and IV: Meso

The two carboxylic groups in the two active compound (I) and (II) are non-equivalent and so monoesterification of each gives two (±) pair of diastereomers. Thus total half ester of trihydroxyglutaric acid is eight (2^3) corresponding to a constitutionally unsymmetrical structure with three chiral centre.

The two structure can be abbreviated as A and B by R or S designation of the chiral group. C-3 centre is achiral as the two ligands R, R in (I) and S, S in (II) *i.e*, identical. Configurational assignment can not be given to C-3. C-3 is also **non-stereogenic**, the interchange of H and OH at this centre followed by 180^O rotation keeps the molecule unchanged i.e, (+) form remain (+) and (-) form remain (-). The molecule contain two more chiral centre (C-2 and C-3), which make the molecule chiral as a whole.

C-3 (I) and (II) is **chirotopic but non-stereogenic**. Since R and S descriptor relate to stereogenicity not to chirotopicity, this descriptor are not applicable here.

In case of meso compound (III) and (IV), C-3 in both is chiral, as (III) and (IV) can be abbreviated as (C) and (D) respectively. The centre is also stereogenic, interchange of ligands generates diastereomers. But from local symmetry, C-3 is achirotopic as σ-plane is present. C-3 in both the compounds can be given configurational descriptor 'r' to (III) and 's' to (IV). Lower case use as two molecules are invariant to reflection.

Such an **achirotopic but stereogenic centre is called pseudoasymmetric centre** and is designated as $Ca^{-}a^{+}bc$, a^{+} and a^{-} represents two enantiomorphous ligand.

3. Relative and absolute configuration:

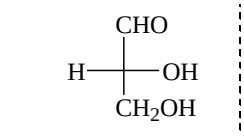
Fischer's D and L nomenclature:

Conventions:

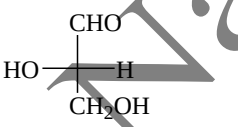
1. As in Fischer's system, the molecule is written with the longest chain vertically

2. The most highly oxidized end of the chain is placed at the top.

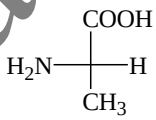
3. If in this projected structure the electronegative group (OH or Cl etc. at the bottom most (highest numbered) chiral centre is on the right hand side, the molecule is given D configuration and if it is on the left, the molecule is given L configuration.



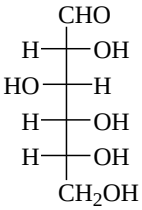
D (+) glyceraldehyde



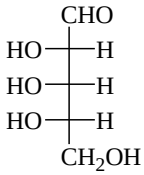
L (+) glyceraldehyde



L (-) Alanine



D (+) Glucose

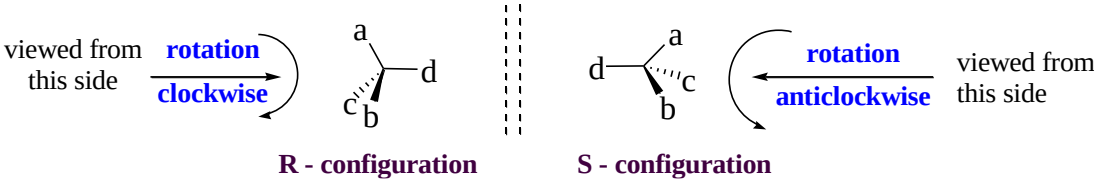


D (+) Ribose

R and S nomenclature:

A self consistent and unambiguous system of cofigurational nomenclature based on three-dimensional structure of molecules by **R: Rectus (right) and S: Sinister (left).**

Assignment of configuration is done by the application of two rules: Sequence rule and Chirality rule. The sequence rule arranges the four ligands of a chiral centre (Cabcd) in a priority sequence (a>b>c>d). The chiral centre is then viewed from the side remote from the lowest ranking group. If from this point of view the arrangement **a → b → c (or 1 → 2 → 3) appears in the clockwise (right handed), the configuration is R and if arrangement appears anticlockwise (left handed) the configuration is S.**



R - configuration **S - configuration**

Sequence rule:

(o) Nearer end of an axis or a plane precedes the farther end (Applicable to axial and planar chirality)

(1) Higher atomoc number precedes the lower atomic number e.g., Br < S < F < O < N < C < H.

(2) Higher atomic mass precedes the lower e.g., T < D < H,

(3) Cis precedes trans and Z precedes E.

(4) Like pair R, R or S, S precedes unlike pair R, S or S, R.

(5) R precedes S.

Sub rule:

(i) Atoms directly attached to the central atom must be sequenced first. If two or more atoms directly attached to the central atom are same then atomic number of the next atom in the ligands are taken into consideration and exploration continues until a decision is reached on the subrule.

Examples:

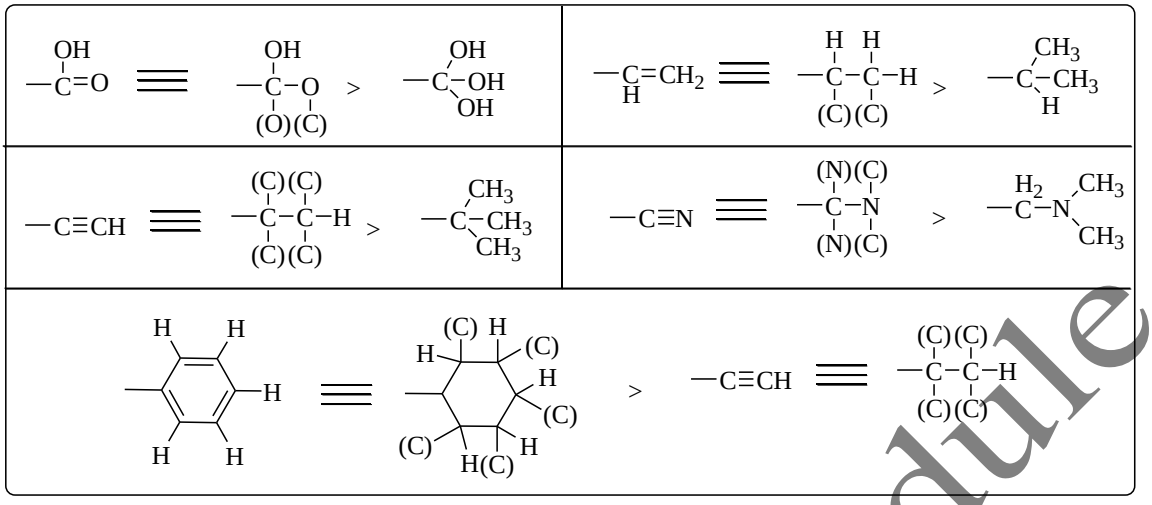
i) $-CH_2CH_3 > -CH_3$ ii) $-CH_2OH > -CH_2NH_2$ iii) $-CH_2CHFBr > -CH_2CHFCl$

iv) $-CH_2CH_2CH_3 > -CD_2CH_3$ v) $-CH_2CD_2CH_3 > -CH_2CH_2CH_3$

Priority rule (2) must not be used until priority rule (1) is completely exhausted.

(ii)

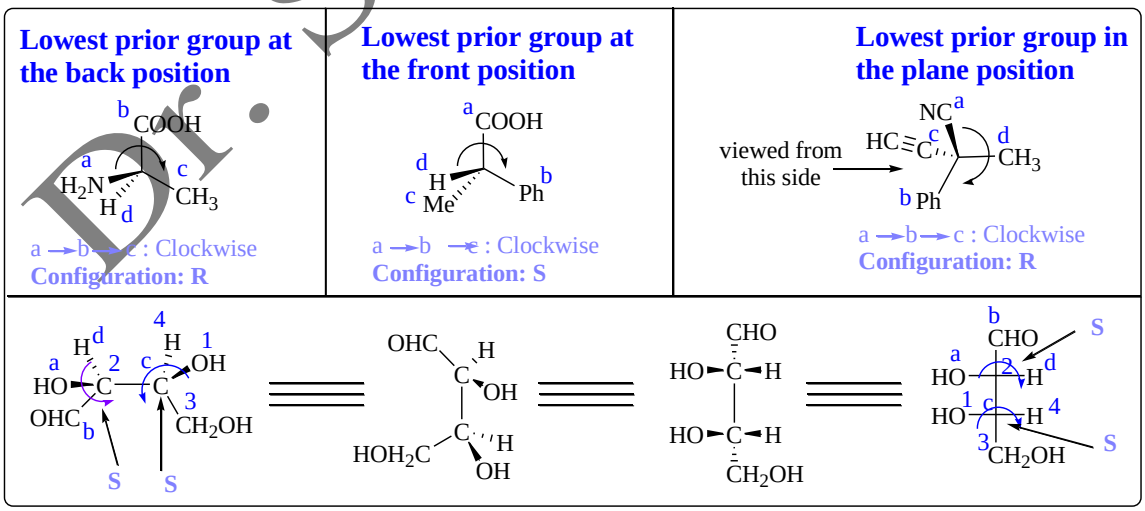
(iii) In case of atoms with double or triple bond, the atom to which they are multiple bonded must be duplicated or triplicated as the case may be at both ends of the multiple bonds.

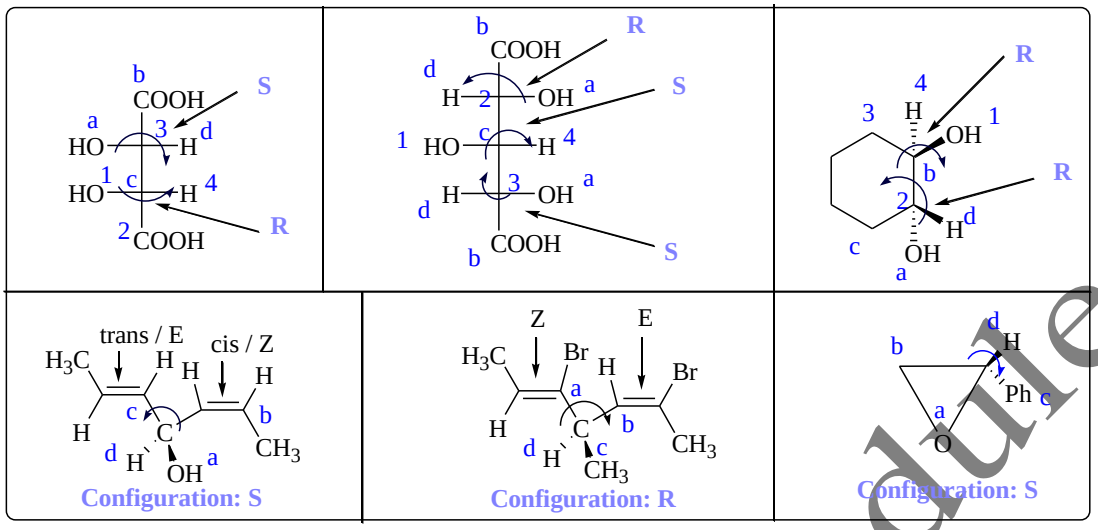


R/S – Nomenclature in Fischer Projection formula:

In Fischer Projection formula the lowest prior group should be at the vertical position. If it remains in the horizontal position then it should be transferred to the vertical position. Otherwise apply **'very good'** method. It consists of two operations: fixing up the priority order of the ligands and tracing a semicircle joining a→b→c ignoring 'd', the lowest priority group. If 'd' is on the vertical line in the Fischer projection (it does not matter whether it is at the top or at the bottom), the sequence give correct descriptor (**i.e, the sequence a→b→c: Clockwise then descriptor should be R and the sequence a→b→c: Anticlockwise then descriptor should be S).** If on the other hand 'd' is on the horizontal line, the sequence gives the wrong answer and the descriptor assigned on this basis should be reversed. (**i.e, the sequence a→b→c: Clockwise then descriptor should be S and the sequence a→b→c: Anticlockwise then descriptor should be R).**

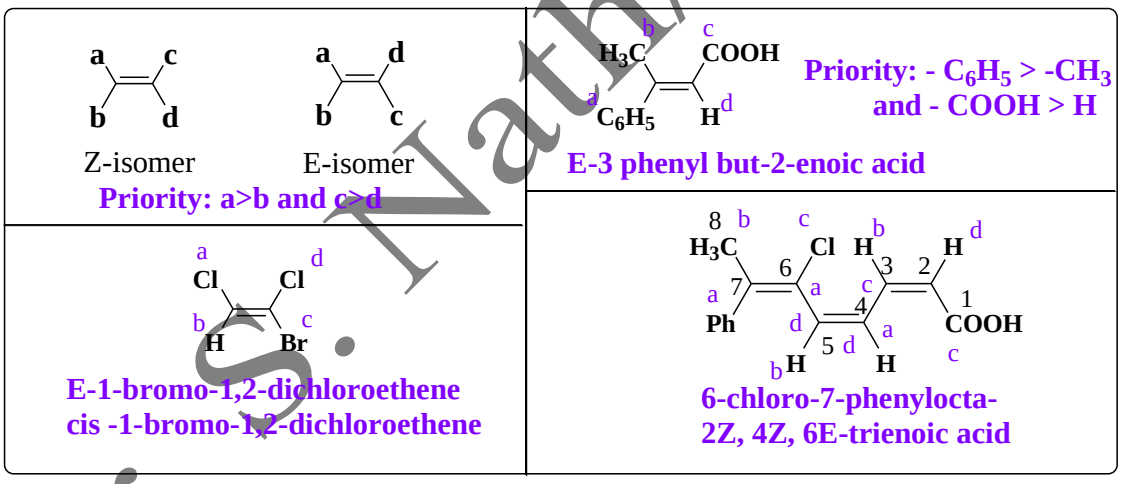
Examples:





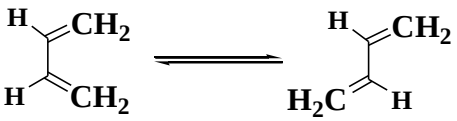
E and Z nomenclature:

This is applicable for molecules of general type Cab=Ccd. If priority of a>b and c>d and 'a' and 'c' remain in the same side of the double bond then it will be Z isomer and 'a' and 'c' in opposite side of the double bond then it will be E.



Cisoid (S-Cis) and Transoid (S-trans) nomenclature:

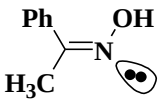
Cis and trans isomerism with respect to a single bond.



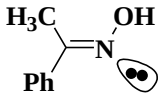
Cisoid or s-cis transoid or s-trans

Syn – anti nomenclature:

It is applicable in case of geometrical isomerism containing double bonded trivalent atom having non-linear structure.



Syn / Z

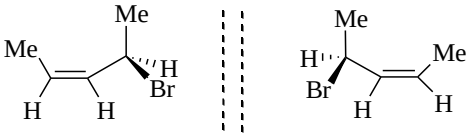


Anti / E

Priority: Ph > CH_3
and -OH > lone pair

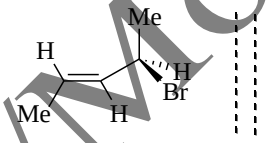
Problem: Write down all the possible stereoisomers of MeCH=CH-CHMeBr

Answer: There should be four stereoisomer. The molecule contains one chiral centre which can have R and S configuration and one double bond which can have E and Z configuration. Hence four stereoisomers are possible with configuration RE, SE, RZ and SZ.

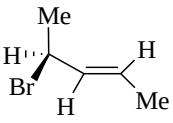


R/Z

S/Z



R/E

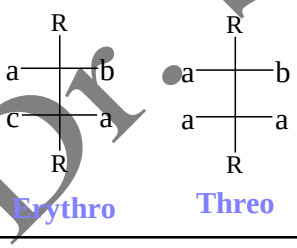


S/E

Molecules with two or more chiral centres:

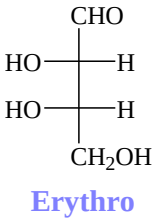
Threo and erythro nomenclature:

Threo and erythro prefixes are used to specify stereoisomers of molecules of the type RCab-CacR having two adjacent chiral centre and exhibiting enentiomerism. The diastereomer in which two like (or similar) groups are on the same side of the Fischer Projection is called the erythro form, whereas threo-isomer is that stereoisomer in which similar or like groups are on the opposite sides of the vertical carbon chain in Fischer Projection.

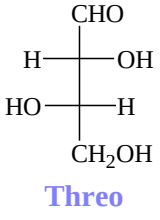


Erythro

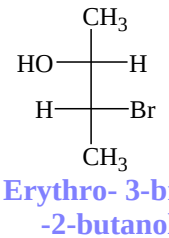
Threo



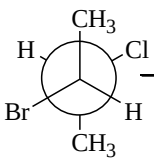
Erythro

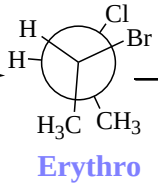


Threo

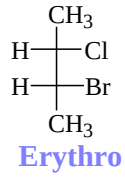


Erythro- 3-bromo -2-butanol

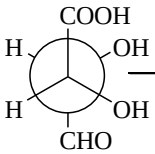


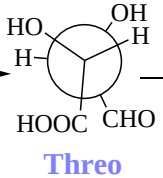


Erythro

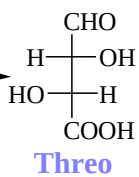


Erythro





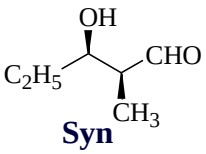
Threo



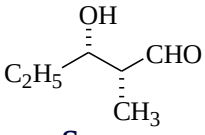
Threo

Syn-Anti nomenclatures for aldol:

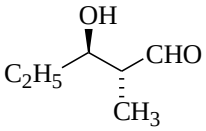
Syn and anti nomenclature is a simple system of nomenclature for aldol type of compounds containing multiple chiral centre. The longest carbon chain is written in a zigzag fashion. If two substituents (usually alkyl and hydroxyl) on the adjacent chiral centres are on the same side of the plane, the prefix syn is used; if they are on opposite sides, the prefix anti is used.



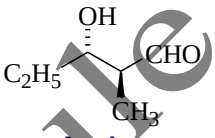
Syn



Syn



Anti



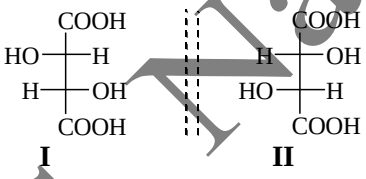
Anti

Meso-Compound:

When in a set of diastereomers, a non-linear diastereomer is found to be optically inactive inspite of the presence of multiple chiral centre. Meso compound is found to have different physical and chemical properties than its optically active isomers.

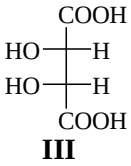
According to IUPAC - A compound is termed meso-when its individual molecule contain equal numbers of enantiomeric groups, identically linked, but contain no other chiral group.

A set of stereoisomers in which the meso compound belongs must contain atleast one chiral stereoisomers. e.g, tartaric acid have the following isomers-



I **II**

d/l - tartaric acid



III

meso - tartaric acid

III : Optically inactive (due to presence of σ or i) – meso

I and II : Optically active – d/l pair

Meso-tartaric acid can also exist in chiral conformations having no elements of symmetry. Under normal state each chiral conformation can have equal number of its mirror image conformation through internal rotation. As a result statistically we get an equimolecular mixture of a pair of conformational enantiomers and therefore it is optically inactive and show no optical rotation. In fact meso-tartaric acid may be considered as a residual stetreoisomer that we can isolate as achiral molecule under the experimental time frame.

4. Optical Activity of Chiral Compounds:

Optical Rotation:

A plane-polarized light being constituted of two oppositely circularly polarized components provides a chiral medium and two enantiomers interact differently, rotating the plane of the polarized light either in a clockwise or in an anticlockwise direction. If rotates clockwise then it is dextrorotatory (d or +) enantiomer and if rotates anticlockwise then levorotatory (l or -) enantiomer.

The chiral sample usually taken in a tube of definite length (l in dm) as a solution of an achiral solvent of definite conc. (or as a neat liquid) then according to Biot's law

Angle of rotation, $\alpha = [\alpha].l.c$

$[\alpha]$ = proportionality constant called **specific rotation**

l = Path length in dm

c = Concentration in g/ml

Angle of rotation depends on –

i) Nature of the substances

ii) Distance through which plane polarized light passed in

iii) Concentration of the optically active compound

Further it also depends on

iv) Temperature (T)

v) Wavelength (λ) of monochromatic light

vi) Solvent

It is customary to denote the rotation of an optically active compound in terms of its specific rotation and it is expressed as

$$[\alpha]_{\lambda}^{T}\ (\ \uparrow\ ) = \frac{\alpha}{l.c}$$

Solvent

Specific rotation may then be defined as optical rotation of an optically active compound when it is taking in a cell of 1 dm length and its conc. is 1 g/ml.

Molecular Rotation:

For compounds undergo association in solution, the solvent and conc. affects the specific rotation. It becomes sometimes necessary to compare the rotating powers of analogous compounds of different molecular weights (M) and in such cases, the comparison is more meaningful if molecular rotation [M] or [φ] are used instead of specific rotation.

$$[M] = [\phi] = \frac{[\alpha].M}{100} = \frac{\alpha.M}{l.c.100} = \frac{\alpha}{l(dm).c.100/M}$$

$$= \frac{\alpha}{l(dm).c\ (mole/100\ ml)}$$

The ability to rotate the plane of plane polarized light is also exhibited by certain crystal like in organic substance like quartz (SiO_2). But optical activity of an organic compound revels itself not only in the crystalline state, but also in liquid state , in solution and in vapour. So optical activity is an **intrinsic property** of their molecules and is not associated with the state of crystalline lattice.

Problem: A solution of 22 mg of an optically active compound in 1cc methanol showed an optical rotation of -4.4^O in a 10 cm long polarimeter cell. What is the specific rotation?

Solution:

We know, specific rotation, $[\alpha] = \frac{\alpha}{l.c}$

α = Optical rotation = -4.4^O

l = Path length = 10 cm = 1 dm

c = Conc. = 22 mg/cc = 0.022 g/ml

Then, $[\alpha] = \frac{\alpha}{l.c} = \frac{-4.4^O.}{1X0.022} = -200^O$

Racemic Modification:

When an equimolecular quantities of two enantiomers of a chiral molecule are mixed together or formed in a reaction, the resultant mixture is called racemic modification or a racemate or (±) pair. Racemic modification do not show any optical rotation due to external compensation i.e., (+) rotation of one enantiomer is compensated by (-) rotation of the other.

Classification of racemic modification:

On the basis of the difference in the nature of packing in the crystal lattice, racemic modifications are divided into three classes:

i) Racemic mixture or conglomerate:

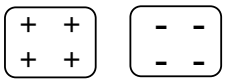
If the crystal lattice are formed entirely from enantiomers of like chirality then it is called conglomerate. It is mechanical mixture of two types of crystal (+) and (-) forms.

ii) Racemic compound or racemate:

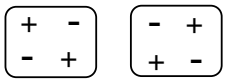
If each unit crystal consists equal number of (+) and (-) enatiomers, then it is called Racemic compound or racemate.

iii) Pseudoracemate:

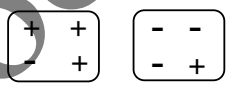
Unit crystals are formed indiscriminately from both the enantiomers and the lattice energy becomes independent of the configuration of the constituent enantiomers.



Racemic mixture or conglomerate



Racemic compound or racemate



Pseudoracemate

Racemisation:

Racemisation is a process of producing racemic modification starting from either of the pure enantiomers. Racemisation is a thermodynamically favourable process as it leads to an increase in entropy and would proceed spontaneously if a convenient pathway is available for the interconversion of the enantiomers.

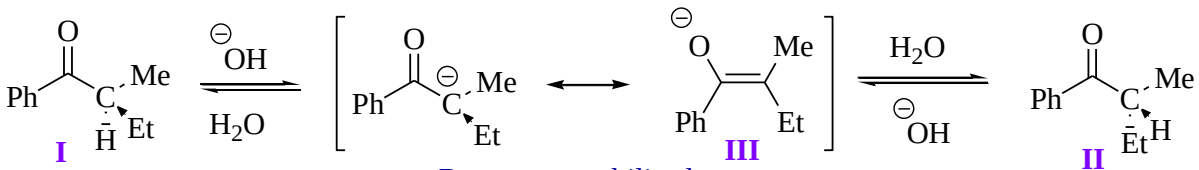
Mechanism of racemisation:

When racemisation is carried out by a chemical reaction, the enantiomers usually has to pass through a symmetrical species (can be transition state or intermediate). So then when the molecule is reformed, the two enantiomers are produced with quqal facility and in equal amoumts.

i) Mechanism involving carbanions:

If a ligand at a tetrahedral chiral centre is removed by heterolytic cleavage (generally proton removed by base) a carbanion is formed. Carbanion should undergo delocalization with an adjacent π-electron system, so that parent carbon become planner at an intermediate form. When ligand recombines then it can do so either from the same side it left (retention) of from the opposite side (inversion). Two approaches are enantiomorphic and so equally facile giving a product which is racemic.

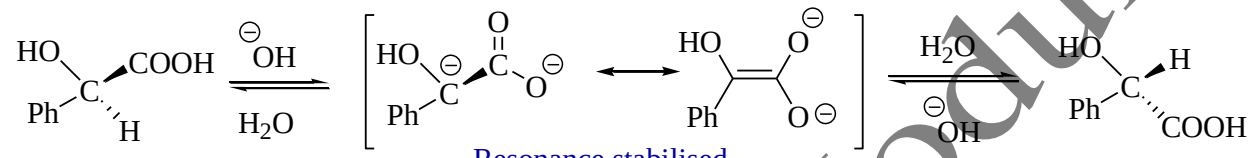
Example: Phenyl sec-butyl ketone undergoes easy racemisation on treatment with aq. NaOH.



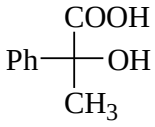
S - Configuration — Resonance stabilised symmetrical intermediate — R - Configuration

When Phenyl sec-butyl ketone I (or II) was treated with NaOH, it forms a resonance stabilized symmetrical intermediate enolate ion III, which when recombine it forms equal amount of I and II and a racemic mixture was obtained.

Similarly, mandelic acid undergoes easy racemisation on treatment with aq. NaOH.



R - Configuration — Resonance stabilised symmetrical intermediate — S - Configuration



atrolactic acid

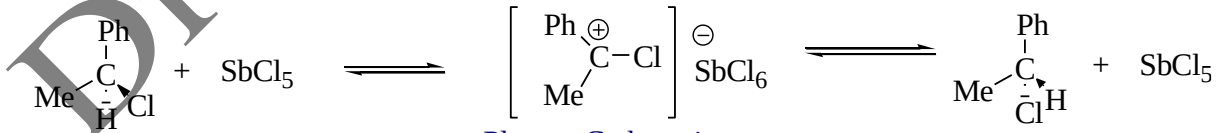
For atrolactic acid no racemisation takes upon similar treatment as there is no enolisable hydrogen atom

ii) <u>Mechanism involving carbonium ions:</u>

Racemisation can be achieved through the formation of a planner carbonium ion by heterolytic cleavage of a ligand attached to the chiral carbon. The planar carbocation can recombines with the ligand from either of the two faces with equal probability to form both the enantiomers in equal quantities. The mechanism operates when the substrate is capable of giving rise to a stable carbocation- benzylic, allylic or tertiary. The reagents applied for these transformations are generally SbF_5, $AlCl_3$, $ZnCl_2$ or mineral acid.

e.g., α-chloro ethyl benzene undergoes easy racemisation upon treatment with $SbCl_5$.

α-chloro ethyl benzene form stable benzylic type carbocation on treatment with $SbCl_5$, which when recombine with chloride form both the enantiomer to form racemic mixture.

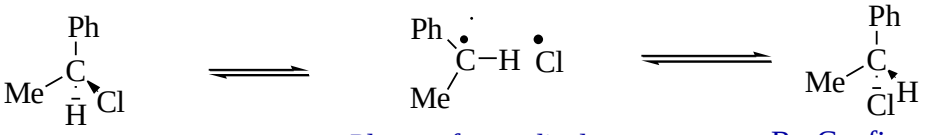


S - Configuration if (+) or d — Planner Carbocation (symmetrical) intermediate — R - Configuration it will be (-) or l

iii) <u>Mechanism involving free radical:</u>

A free radical has a near planner structure and if a chiral centre is converted into a free radical pair by hemolytic cleavage of a bond, the recombination of the pair would lead to a racemic

product. Substrates which produce resonance stabilized radicals allilylic, benzylic may undergo racemisation by this mechanism under the influence of light and heat.
e.g.- α-chloro ethyl benzene in enantiomerically pure form when distilled under normal pressure undergoes extensive racemisation.

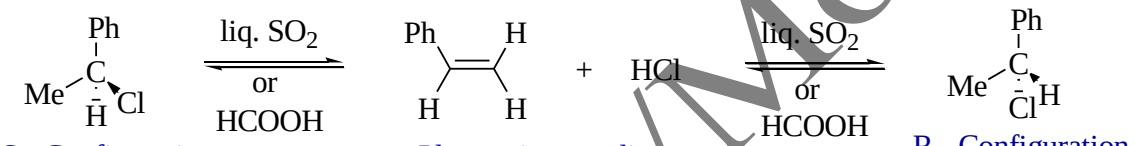


S - Configuration if (+) or d | Planner free radical (symmetrical) | R - Configuration it will be (-) or l

iv) <u>Mechanism involving stable symmetrical intermediate:</u>

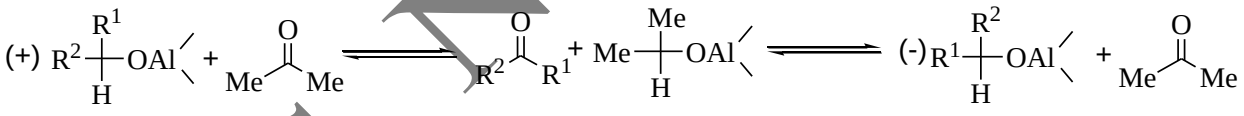
Sometimes racemisation is possible through the reversible formation of stable optically inactive intermediates.

Example 1. α-chloro ethyl benzene under racemisation on treatment with liquid SO_2 or HCOOH



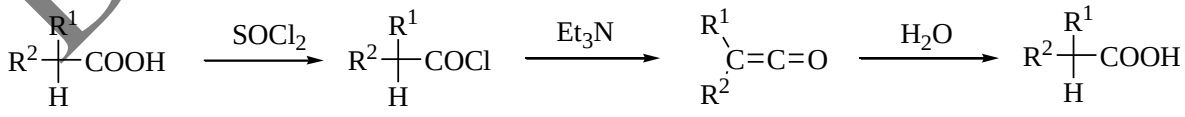
S - Configuration if (+) or d | Planner intermediate (symmetrical) | R - Configuration it will be (-) or l

Example 2. In Meerwein-Ponndorf- Verley (MPV) reduction / Oppenauer oxidation procedure in which a secondary alcohol in the form of its aluminum derivative (aliminium alkoxide) is heated with a trace of ketone.



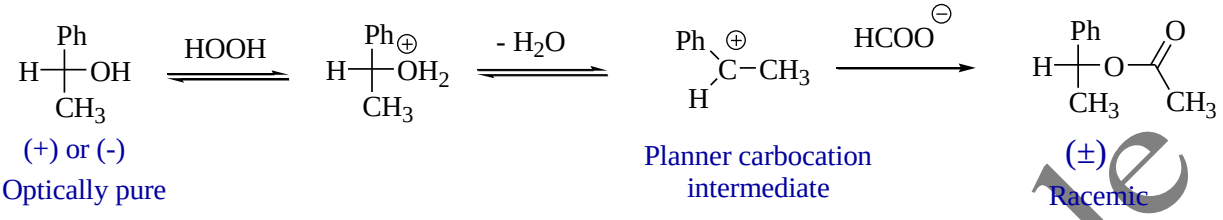
The ketone initiates a reversible oxidation reduction sequence and an equilibrium is established between enantiomers (leading to racemisation) or between diastereomers (leading to epimerization).

Example 3. Sometimes, the acid chloride of an optically active carboxylic acid, during reaction in the presence of a tertiary amine, undergoes racemisation through a ketene.



(+) or (-) Optically pure | Symmetrical ketene intermediate | (±) Racemic

During some reaction an optically active substrate can give racemised product having equimolecular amount of enantiomers. This reaction can not be treated as a case of racemisation as the reactant and the product have different constitutions.



(+) or (-)
Optically pure

Planner carbocation intermediate

(±)
Racemic

Resolution:

When a racemic modification is separated into its pure enantiomer, the process is called reolution. In this process optical rotation is enhanced, called optical activation and equals to that of a pure enantiomer in the case of complete resolution.

Method of resolution:

Enantiomeric discrimination can be achieved by using chiral reagents or a chiral medium through the establishment of diastereomeric relationships. Unlike racemisation, resolution is not a thermodynamically favourable process and is not expected to occur spontaneously under ordinary circumstances. Most of the natural products, food stuffs, drugs, flavouring agents, perfumes and other biologically active material usually show their desirable or beneficial effects in one enantiomeric form only. It is necessary therefore that the chiral compounds be available in the desired enantiomeric forms. This is possible in two ways: i) Asymmeric synthesis and

ii) Resolution of racemic modifications synthesized in the laboratory.

Resolution through the formation of diastereomers:

The formation of diastereomeric salts and their fractional crystallization, is best method for resolution and is applicable to a much wider range of compounds. The principle is illustrated here in the resolution of a racemic acid (±) A with an optically pure base, (+) B which combines with the racemic acid giving two diastereomeric salts.

$$(\pm)\ A + (+)\ B \longrightarrow (+)\ A.\ (+)\ B + (-)\ A.\ (+)\ B$$

Being diastereomeric, the two salts differ in properties such as solubility, boiling point and adsorption coefficient. When crystallized from a solvent, one of them [say (+) A.(+) B] would separate first and after several crystallization be available in pure state as judged by the melting point and optical rotation which would attain constant values. Decomposition of the salt with mineral acids would furnish (+) A in enantiomerically pure form.

The substrate and the resolving agent must have suitable functional groups capable of interacting with each other. It is essential that the configuration of the chiral centres remain unchanged during the formation of the diastereomers as well as during the regeneration of the enantiomers. Salt formation, for this reason, is the most desired reaction. Other reactions involve formation of esters, urethane derivative, molecular adducts etc. depending on the nature of the substrate.

Resolution of organic acids:

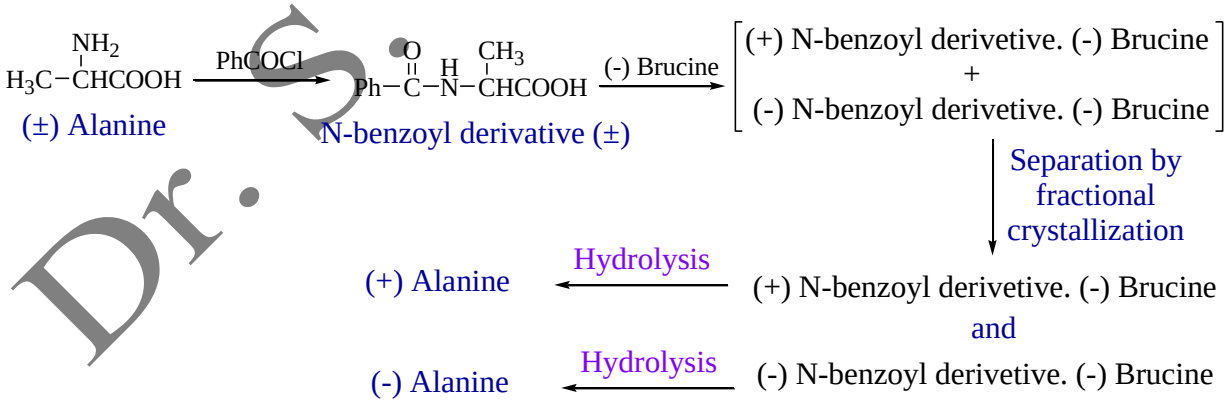
Organic acids are by far the most important groups of compounds which are resolved directly by this method. Organic bases are used as resolving agents are the naturally occurring alkaloids such as quinine, brucine, strychnine, ephedrine, cinchonine and cinchonidine. A large number of racemic acids have been successfully resolved with quinine and brucine alone.

Resolution of organic bases:

Organic bases can also be resolved by the above method. The number of enantiomerically pure naturally occurring acids is few. Tartaric acid and its derivatives such as dibenzoyl, diacetyl are used for the resolution of amines. Some optically active acids have been prepared from terpenoid ketones and alcohols such as 3-, 9-, 10- camphorsulphonic acids and menthyloxy and bornyloxyacetic acid.

Resolution of amino acids:

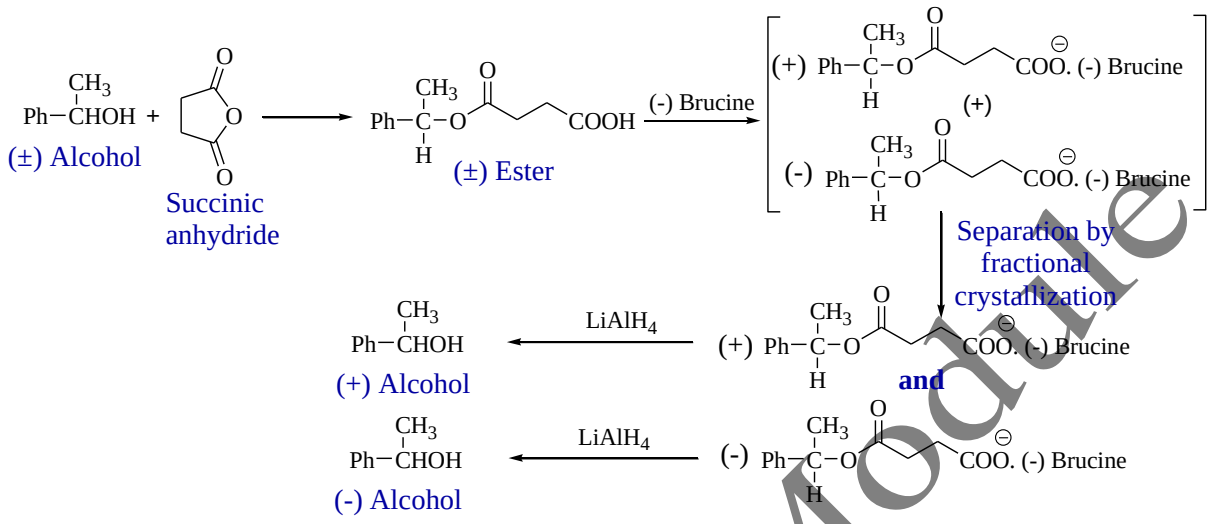
Amino acids exist in zwitterionic structure and before resolution, either the amino or the carboxyl group should be derivatised. The usual method os to formylate the amino group and then convert the product into diastereomeric salts with optically active bases. The formyl group can be removed under mild hydrolysis condition and no racemisation usually occurs.



Resolution of alcohols:

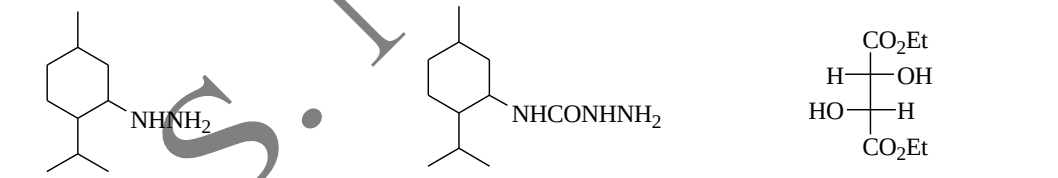
The alcohol is first converted into a half ester of succinic acid or phthalic acid by heating with succinic anhydride or with phthalic anhydride respectively. The half esters may then be treated

as typical acids and resolved using optically active bases. The resolved half ester is finally hydrolysed or reduced with LiAlH4 to set the alcohol free.



Resolution of alaldehydes and ketones:

For the resolution of aldehydes and ketones derivatisation reagents in optically active form may be used. Some of the resolving reagents are the hydrazide of (+) mandelic acid, amidohydrazide of (+) tartaric acid, tartaric acid derivative, menthylsemicarbazide, menthyl hydrazine etc. Ketones can also be converted into ketals or dithioketals using optically active 2,3-butanediol or 2,3-butanedithiol. In the latter case, after purification by fractional crystallization, the thioketal can be directly desulphurised by treatment with raney nickel to the ketone.



Optical purity and enantiomeric excess:

Enantiomeric excess express the enantiomeric composition of enantiomeric mixture.

$$\% \text{ Optical Purity} = \frac{\text{Specific rotation of enantiomeric mixture}}{\text{Specific rotation of pure enantiomer}} \times 100 = \frac{\alpha_{obs}}{\alpha_{pure\ or\ max}} \times 100$$

= enantiomeric exess

On the other hand

Enantiomeric Exess (ee) = $\frac{[d] - [l]}{[d] + [l]}$ X 100

[d] and [l] is the mole fraction of the individual enantiomer dextro (d) and levo (l) So, [d] + [l] = 1

$[l] = 1 - [d]$

$ee = \frac{[d] - [l]}{[d] + [l]}$ X 100

$= \frac{[d] - (1 - [d])}{1}$ X 100

$= (2[d] - 1)$ X 100

$[d] = \frac{100 + ee}{2 X100}$

% of d or major comonent = $\frac{100 + ee}{2}$

$[d] = 1 - [l]$

$ee = \frac{[d] - [l]}{[d] + [l]}$ X 100

$= \frac{(1-[l]) - [l]}{1}$ X 100

$= (1 - 2[l])$ X 100

$[l] = \frac{100 - ee}{2 X100}$

% of l or minor comonent = $\frac{100 - ee}{2}$

Problem – 1: A sample mixture of an optically active compound exhibits $[\alpha]_D$ = + 15° but the specific rotation of the pure compound is 60°. What is the stereoisomeric composition of the sample mixture?

Answer:

enantiomeric exess (ee) = $\frac{\alpha_{obs}}{\alpha_{pure\ or\ max}}$ X 100 = $\frac{15}{60}$ X 100 = 25

As the mixture has specific rotation (+) 15^O so major component is dextrorotatory

% of d or major comonent = $\frac{100 + ee}{2}$ = $\frac{100 + 25}{2}$ = 75

% of l or minor comonent = $\frac{100 - ee}{2}$ = $\frac{100 - 25}{2}$ = 25

Problem - 2: Calculate the specific rotation of a mixture of R- and S- acid with 33% ee (with respect to R-isomer). Given specific rotation of S-acid is + 24^0

Answer:

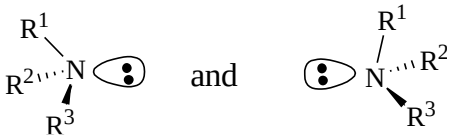
enantiomeric exess (ee) = $\frac{\alpha_{obs}}{\alpha_{pure\ or\ max}}$ X 100 So, 33 = $\frac{\alpha_{obs}}{24^O}$ X 100

$\alpha_{obs} = \frac{33 X 24^O}{100} = 7.92^O$

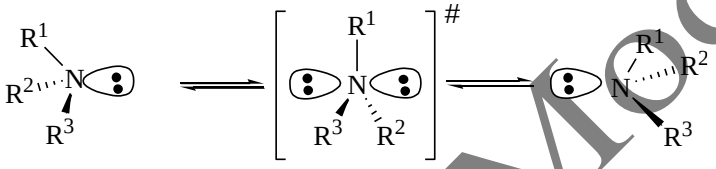
Specific rotation of the mixture should be (-) 7.92^O as pure S-acid is dextro and enantiomeric exess levo as it is with respect to R-isomer.

Invertomerism of chiral trialkyl amine:

Tertiary amine having pyramidal configuration containing three different groups of the following type should exist in two resolvable enantiomeric forms which are-



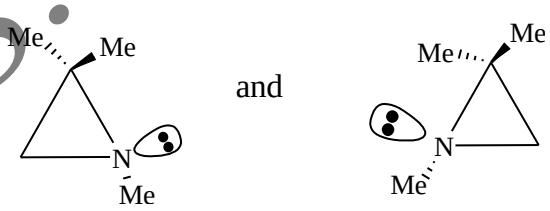
Here one apex of tetrahedral arrangement is occupied by a pair of electron. But such tertiary amine is not resolvable in two enantiomeric forms as the two forms are readily interconvertible via flipping through a transition state in which the nitrogen atom is SP^2 hybridised.



Transition state

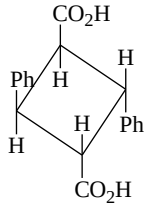
These two forms are often called **invertomers**. Inversion of nitrogen compounds is normally facile and resolution does not possible for these type of tertiary amines and gives conformers known as invertomers.

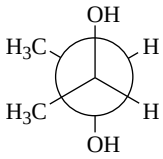
Flipping can be stopped in the amines in which nitrogen atom is a part of small ring. Highly strained small ring compound can not arrive at the bond angle 120^O in the transition state necessary for the nitrogen inversion. Thus properly substituted aziridines should be resolvable into two enantiomeric forms. Thus the following compound is resolvable into two enantiomeric forms:



Model Questions

1. Depict the symmetry element present in the following molecules (*any two*):

i) 

ii) 

iii) *Trans*-1,3-dichlorocyclobutane

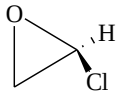
iv) *E* - 1,2 - dichloroethene

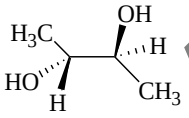
v) 2- Chloro propane

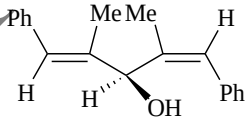
2. Draw the Newman projection formula of

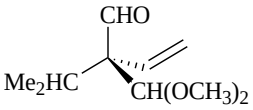
(i) Threo -3-bromo-2-butanol
(ii) (3R, 4S)- 3-chloro – 4 - methyl hexane

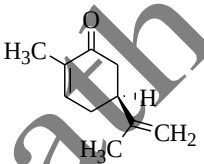
3. Designate R/S configuration of the chiral centers of the following compounds:

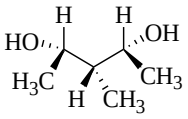
(i) 

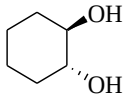
(ii) 

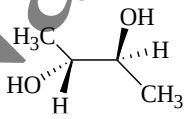
(iii) 

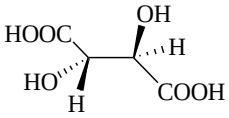
(iv) 

(v) 

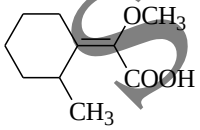
(vi) 

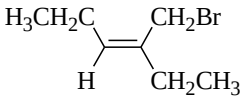
(vii) 

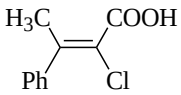
(viii) 

(ix) 

4. . Designate E/Z configuration of the following compounds:

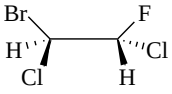
i) 

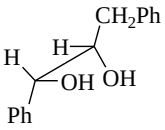
ii) 

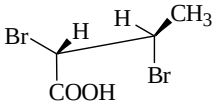
iii) 

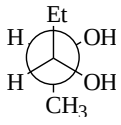
5. Write down all the possible stereoisomers of MeCH=CH-CHMeBr.

6. Designate the following compound as erythro and threo:

i) 

ii) 

iii) 

iv) 

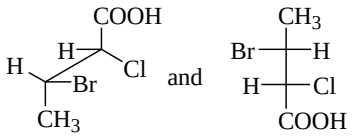
7. What is meant by enantiomeric excess?

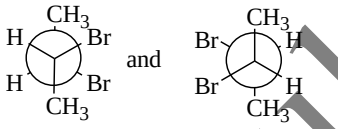
8. What do you mean by pseudoassymmetric centre.

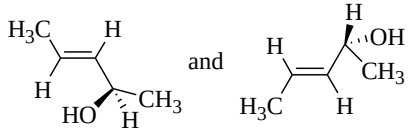
9. Give one example each of the following:

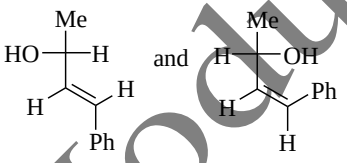
i) An optically active compound possessing a C_2 axis.
ii) A meso compound having three chiral centres.

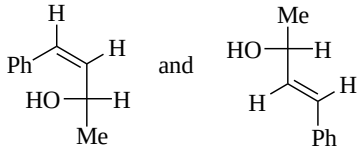
10. Label the following as homomers, enantiomers or diastereomers or constitutional isomer:

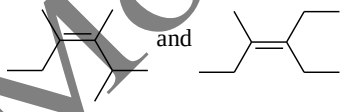
i) 

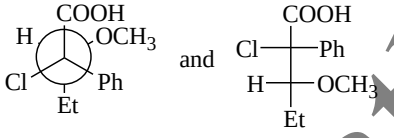
ii) 

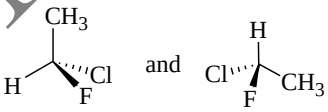
iii) 

iv) 

v) 

vi) 

vii) 

viii) 

11. Calculate the specific rotation of a mixture of R- and S- acid with 30% enantiomeric excess (with respect to R isomer). Given- specific rotation of the S-acid is + 24^O.

12. A sample mixture of an optically active compound exhibits $[\alpha]_D$ = + 15° but the specific rotation of the pure compound is 60°. What is the stereoisomeric composition of the sample mixture?

13. The concentration of a substance dissolved in chloroform is 6.15 g per 100 ml. A portion of this solution in a 10 cm polarimeter tube exhibits a rotation of 2.4º. Calculate the specific rotation.

14. All chiral centres are stereogenic but all stereogenic centres are not chiral. Explain.

15. Predict whether the following statements are true or false:

(i) It a compound has diastereomer it must be chiral
(ii) A meso compound must have two or more chiral centres.

16. Justify the following statements:

(i) S_2 and *i* are equivalent operations.

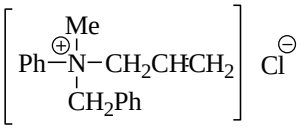
(ii) One fold alternating axis of symmetry is equivalent to a plane of symmetry.
(iii) Meso tartaric acid is optically inactive due to presence of '*i*'.

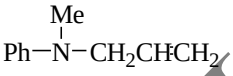
17. Draw the Fischer projection formula for all the possible stereoisomers of 2,3,4 – trihydroxyglutaric acid. Comment on the stereogenicity and chirotopicity of C-3 centre in the active and meso forms.

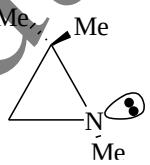
18. Describe a method for resolution of i) Racemic alcohol ii) Racemic amino acid.

19. S-2-bromobutane undergoes racemization when treated with chlorine in presence of sunlight- Explain.

20. Which of the compound is resolvable and which not and explain why?

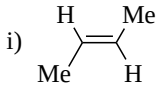
i) 

ii) 

iii) 

21. All the epimers are diastereomers but the reverse is not true. Explain.

22. Find out the point group of the following molecule-

i) 

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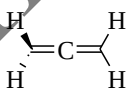
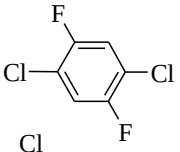
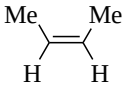
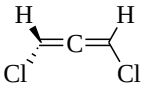
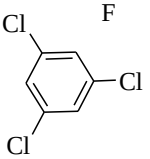
iii) 

iv) 

v) 

vi) 

vii) 

viii) 

ix) 2- Chloro propane x) *Trans*-1,3-dichlorocyclobutane

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