

UNIT-1

Stereochemistry

- stereochemistry is the branch of chemistry dealing with the structures of three-dimensional molecules.
- Compounds having the same molecular formula but differ from each other in physical or chemical properties are called isomers and the phenomenon is called isomerism.

→ There are two main types of isomerism:

- | | |
|--|---|
| ↙ | ↘ |
| <u>constitutional</u> | <u>stereoisomerism</u> |
| <ul style="list-style-type: none"> - Chain isomerism - Position " - functional " - Metamerism " - Tautomerism " | <ul style="list-style-type: none"> - Geometrical isomerism or Cis-Trans " - Optical isomerism |

constitutional isomerism is due to difference in the arrangement of atoms within the molecule. Constitutional isomers are compounds that have the same molecular formula but different structural formulas.

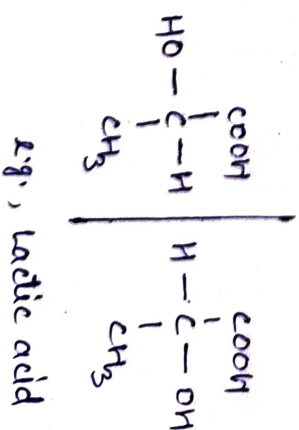
stereoisomerism is caused by different arrangements of atoms or groups in space. The stereoisomers have the same structural formulas but differ in arrangement of atoms in space (configuration).

Optical Isomerism

Optical isomers have same molecular and structural formulae and also have same physical properties, but they differ in their behavior towards light.

Optical isomers are further categorised:

- (i) Enantiomers
- (ii) Diastereomers



Optical Activity

An ordinary light is made up of light waves which vibrate in all planes and when passed through a polarised lens, light waves in one plane only which is known as Plane Polarised Light (PPL).

Optical isomers have the ability to rotate PPL. The compounds exhibiting such behavior are called optically active compounds. The compounds rotating the PPL towards or clockwise is called dextrorotatory, while those rotating PPL towards left or anticlockwise is called levorotatory. The dextrorotatory and levorotatory compounds are denoted by (+) and (-) respectively.

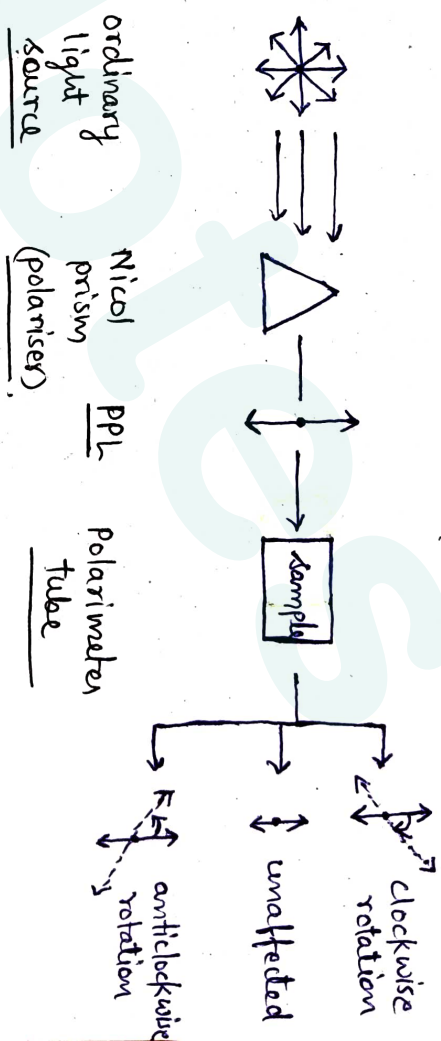


ordinary light



PPL

Determination of optically active compounds

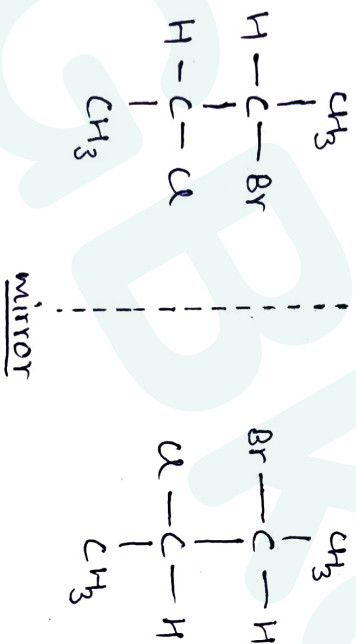


- (i) The Nicol prism make the ordinary light coming from light source into a plane polarised light (PPL).
- (ii) The PPL passes through the polarimeter tube which is filled with the solution of which we have to check optical activity.
- (iii) After passing the polarimeter, if the light goes unaffected or straight, the solution compound is optically inactive. But if the PPL rotate, the compound is optically active.
 - Leavo (-) or dextro (+) depending on the direction of rotation.

Enantiomers

- An enantiomer is a stereoisomer that non-superimposable complete mirror images of each other.
- Molecules must contain at least one chiral centre.
- Enantiomers differ from one another in 3-Dimensional spatial arrangements.
- They have same physical properties.
- Enantiomers are different in rotating PPL.

eg: 2-bromo-3-chlorobutane

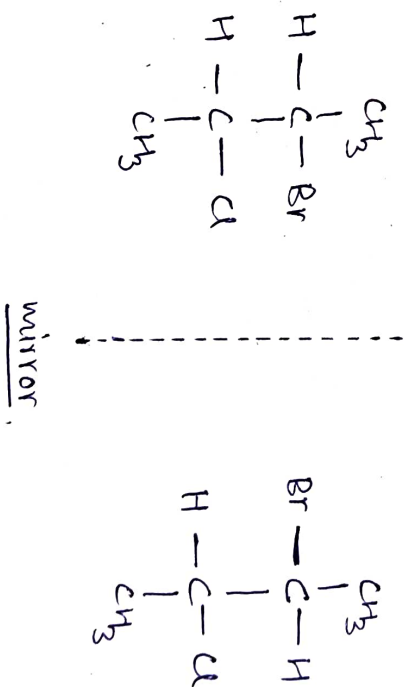


These are complete mirror images but not superimposable.

Diastereomers

- Diastereomers are stereoisomers that are non-mirror images and non-superimposable of each other.
- Molecules must contain more than one chiral center.
- Diastereomers are pair of isomers that have opposite configurations at one or more chiral centres but are not mirror images of each other.

eg: 2-bromo-3-chlorobutane

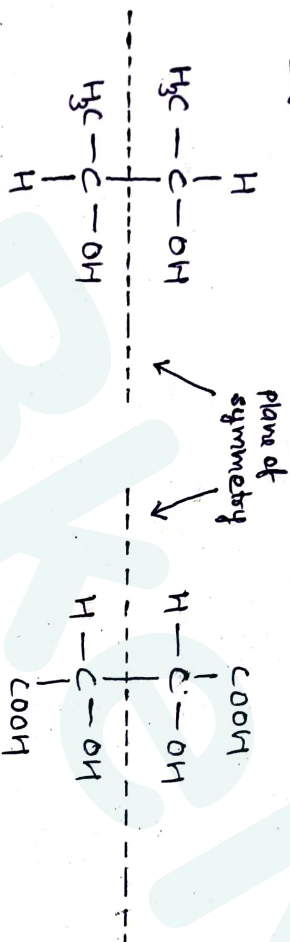


These are neither mirror images nor superimposable of each other.

Meso compounds

- A compound with two or more chiral atoms, but also having a plane of symmetry.
- These molecule have planes of symmetry dividing them midway between the two chiral carbon atoms.
- one half of the molecule is the mirror image of the other half.

e.g.:



meso-2,3-hydroxy butane

meso-tartaric acid.

Elements of Symmetry

Chiral molecules

- mirror images
- non-superimposable
- asymmetric
- optically active

Achiral molecules

- mirror images
- superimposable
- symmetric
- optically inactive.

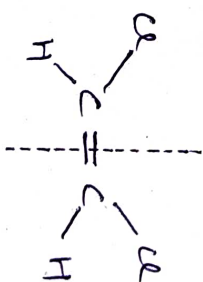
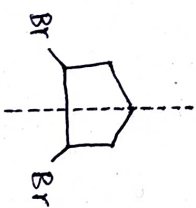
The symmetric molecules (achiral) exhibit any one of the following elements of symmetry.

(1) Plane of symmetry

It is that element of symmetry in which the molecule when divided into two equal halves, then gives one half as mirror of the other half.
e.g. meso-tartaric acid

2) Centre of symmetry → of a line drawn from

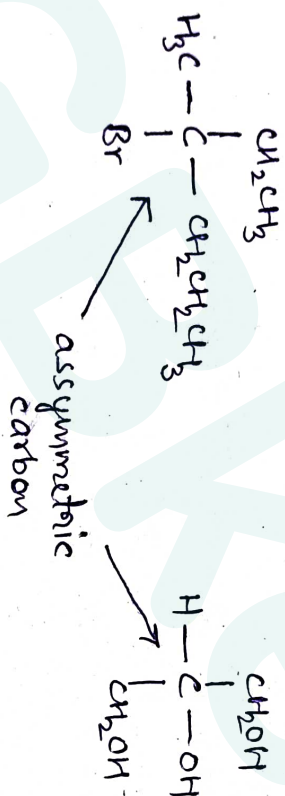
any group of a molecule, passes through the centre of molecule meets an identical group, when extended to an equal distance, is termed as the centre of symmetry.



Concept of chirality

- A molecule is chiral if its two forms are mirror images of each other but are non-superimposable.
- Presence of an asymmetric carbon atom is most important feature for chirality in molecules.
- The chiral carbon atom is the one which is attached to four different types of atoms or groups of atoms, resulting in asymmetry.

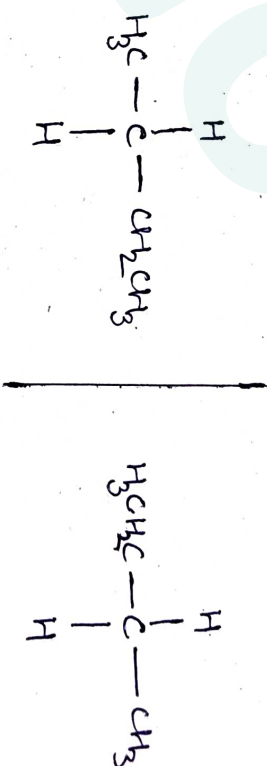
Examples,



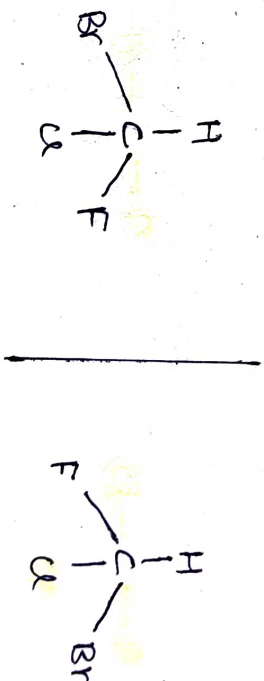
An asymmetric carbon atom only means that a carbon atom is bonded to four different groups and which means that a molecule lacks a plane of symmetry.

If the number of chiral carbon atoms in a compound is 'n', the maximum number of stereoisomers existing will be 2^n .

Achiral Molecules → is the one which is superimposable on its mirror image. They have a plane of symmetry.



Achiral molecule: mirror images are superimposable



chiral molecule: mirror images are non-superimposable

Nomenclature of Optical Isomers

DL system of Nomenclature

The DL system was developed by Fisher.

This method is used for optically active compounds.

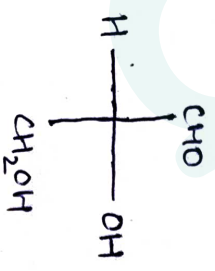
Hence, 'D' represents the compounds which rotate clockwise or in right hand side.

→ D(+) Dextrorotatory.

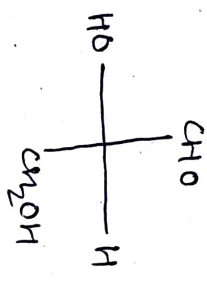
L represents compounds which rotate anticlockwise or in left hand side.

→ L(-) Levorotatory

The D and L configuration is used for amino acids and carbohydrates. In this configuration, 'Glyceraldehyde' is used as a reference compound.



D(+)-glyceraldehyde

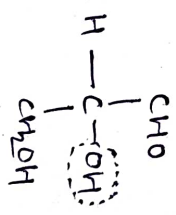


L(-)-glyceraldehyde

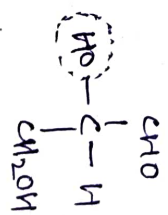
Rules

- (i) Draw proper fisher projection formulae of molecules.
- (ii) Highest oxidised group must be on top.
- (iii) Observe bottommost chiral asymmetric carbon, if it contain -OH/-NH₂ at right, then 'D'; if at left, then 'L'.
- (iv) Longest chain should be on vertical line.
- (v) If -OH and -NH₂, both are present, then D/L are decided by -NH₂ group.

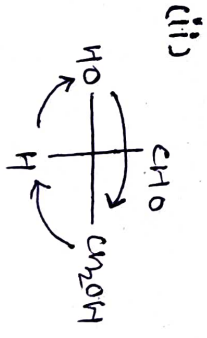
Examples



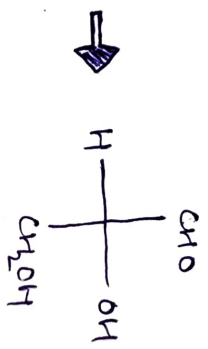
-OH group is on right side
so, D(+)

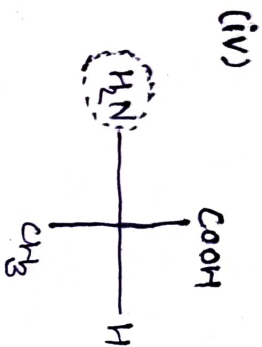
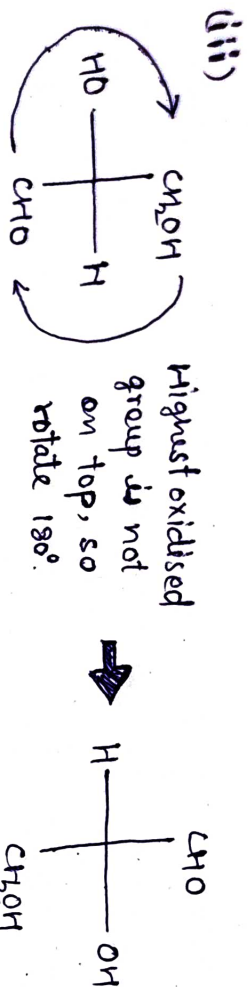


-OH group is on left side
so, L(-)

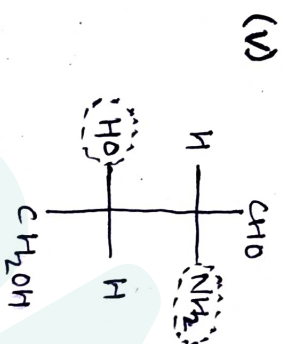


longest chain is not on the vertical line, so rotate it clockwise





$-\text{NH}_2$ on left,
so $\text{L}(-)$



both $-\text{OH}$ & $-\text{NH}_2$ are present,
 $-\text{NH}_2$ will decide, so $\text{D}(+)$.

R and S Nomenclature

This is absolute configuration, which is used for optically active compounds.

\Rightarrow R \rightarrow Rectus (Right), which rotate PPL clockwise

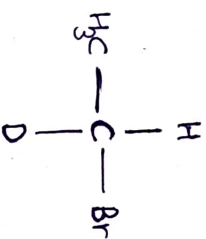
\Rightarrow S \rightarrow Sinister (Left), which rotate PPL anticlockwise

This configuration given by R.S. Cahn, Christopher Ingold and V. Prelog.

Sequence rules

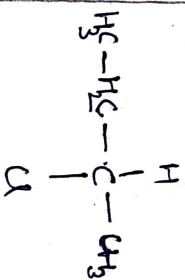
Rule-1 \rightarrow If the atoms attached to the chiral centre are all different, then the highest atomic number containing molecule gets the first priority. If the two atoms are isotopes of the same element, then the priority is given to the atom of highest mass number.

For example \rightarrow for α -deuterioethyl bromide, it is Br, C, D, H.



'D' and 'H' are isotopes of hydrogen but 'D' has the higher mass.

Rule-2 \rightarrow If the two or more atoms of a group attached to the center are same, then give priority according to the next atom of the group. e.g.

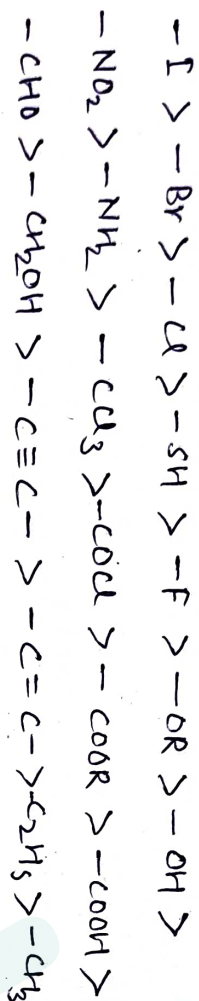


sec-butyl chloride

two same atoms attached on carbon. In CH_3 , next atoms are H, H, H. In CH_2Cl , next atoms are H, H, C. So, 'C' has the higher atomic number, priority will be given to CH_2Cl .

Rule-3 → The lowest priority atom or group must be on bottom of vertical line.

Functional groups with their priority order:



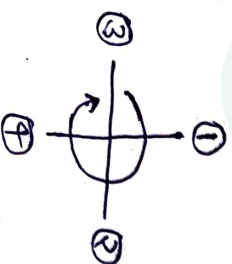
Rules for R and S configuration

1) The atoms or groups attached with a chiral centre are assigned with a number according to sequence rules.

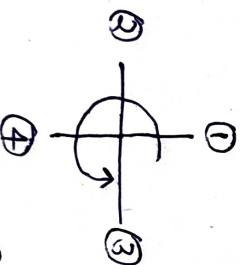
2) If the lowest priority group is on vertical line then,

- Rotation of (1) → (2) → (3) in clockwise, configuration will be 'R'.

- Rotation of (1) → (2) → (3) in anticlockwise, configuration will be 'S'.



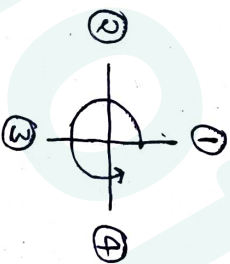
R-configuration



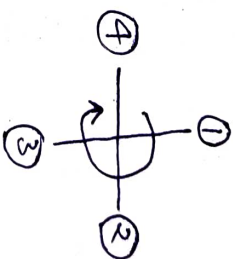
S-configuration

3) But if the lowest priority group is on horizontal line, the configuration becomes just opposite.

- (1) → (2) → (3) in clockwise, configuration is 'S'.
- (1) → (2) → (3) in anticlockwise, configuration is 'R'.



R-configuration



S-configuration

Reactions of chiral molecules

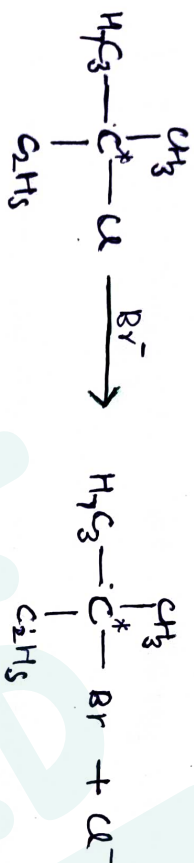
Chiral molecules undergoes three major reactions:

- Retention
- Inversion
- Racemisation

1. Retention

Bond at chiral carbon do not break after the reaction.
Configuration of substrate and product remains same.

'R' isomer \rightarrow 'R' isomer
'S' isomer \rightarrow 'S' isomer



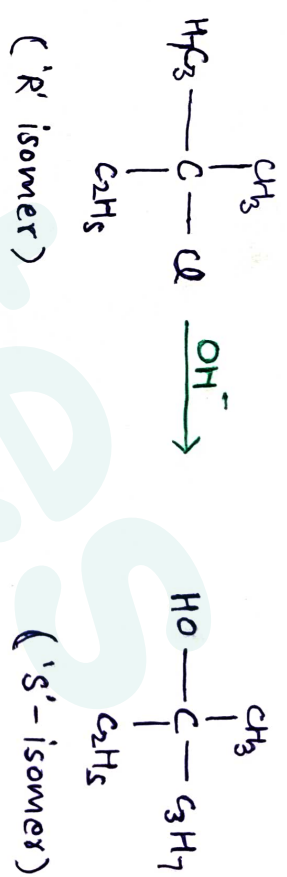
('S' isomer)

('S' isomer)

2. Inversion

Isomer gets converted to other form after reaction. It follows $\text{S}_\text{N}2$ mechanism.

'R' isomer \rightarrow 'S' isomer
'S' isomer \rightarrow 'R' isomer



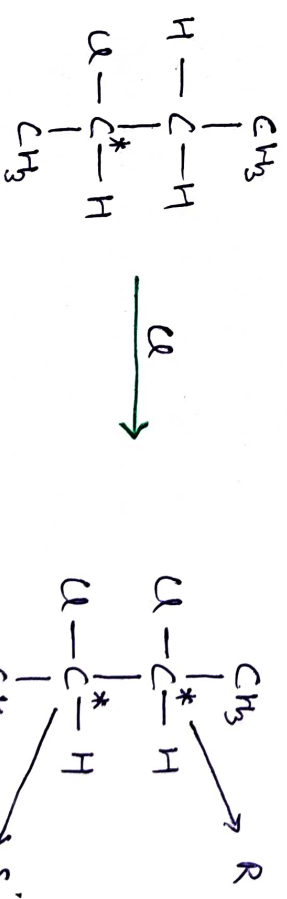
('R' isomer)

('S' isomer)

3. Racemisation

Optically active compound is converted into optically inactive compound after the reaction. Second chiral center forms diastereomer.

'R' isomer \rightarrow RR, RS isomer
'S' isomer \rightarrow RS, SS isomer



['S' 2-chlorobutane]

['R,S' -optically inactive]

In this reaction, 'H' is replaced by 'Cl' and forms a meso-compound.

Racemic Modification and Resolution of Racemic Mixture

- Racemic mixture is an equimolar (equal moles) mixture of two enantiomers (dextro and levo forms).
- The net optical rotation of a racemic mixture is zero because equals number of moles of dextrorotatory and levorotatory molecules are present in the mixture.
- The racemic mixture may be represented as (±) or (DL) or (RS).
- Conversion of an optically active compound into a racemic modification is called racemisation.
- Racemisation can be done by following:
 - (i) Action of heat
 - (ii) Auto-racemisation (kept at room temperature)
 - (iii) Use of chemical reagents

Resolution

Separation of enantiomers from a racemic mixture is described as resolution.

Following methods are used for the resolution of racemic mixture:

- (i) Mechanical separation
 - (ii) Biochemical separation
 - (iii) Chemical method (via diastereomers)
 - (iv) Chromatography
- 1) Mechanical separation
 - If the 'D' and 'L' forms of a substance exist in well defined crystalline forms. The separation can be done by hand-picking with the help of magnifying lens and a pair of tweezers. For example, sodium ammonium tartrate
 - The method has very limited application and applies to only few crystalline constituents.
 - 2) Biochemical separation
 - In this method, the resolution is done by use of microorganisms.

→ When certain bacteria or moulds are added to racemic mixture, they decompose one of the optically active forms more rapidly than the other.

→ For example, when the mould is added to the solution of racemic ammonium tartrate, this would completely decompose the 'd' form, while 'l' form is left practically unaffected.

→ The main drawback of the method is that half of the material is destroyed during resolution.

3) Chemical separation

This is the best method of resolution. The racemic mixture is made to combine with another optically active compound and enantiomers are converted to diastereomers. Diastereomers are separated on the basis of their different physical properties by fractional distillation.

4) Chromatography

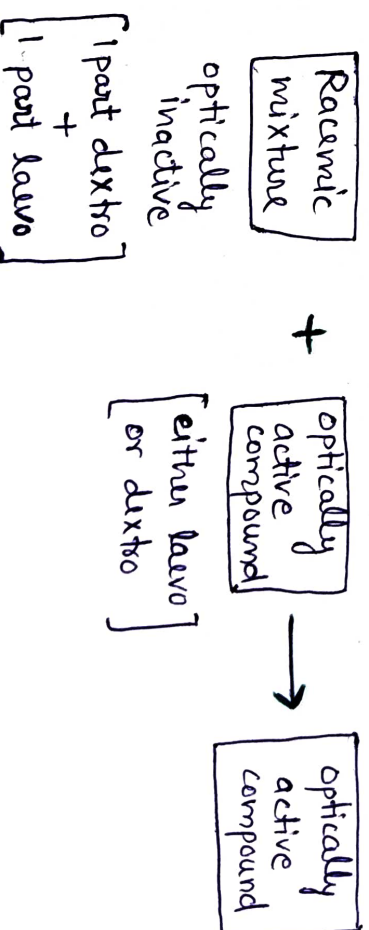
→ In this process, the racemic mixture is run through a column which is filled with an optically active adsorbent (a chiral substance)

→ In this, optically active substance are selectively adsorbed by optically active adsorbent on the basis of their affinity.

→ The enantiomers with interact differently with the chiral substance and elute at different rates.

Asymmetric Synthesis

In this method, an optically active compound is directly prepared from an optically inactive compound under the influence of some other optically active substance.



Generally, inactive compounds are symmetric and active compounds are asymmetric. So, it can be said that symmetric molecules are converted into asymmetric molecules,

Types of asymmetric synthesis:

- (i) Partial asymmetric synthesis
- (ii) Absolute asymmetric synthesis.

1) Partial

→ In this, both enantiomers [(+) and (-)] are formed but one of the two is obtained in larger amount than the other.

2) Absolute

In absolute asymmetric synthesis, the racemic mixture is completely converted to any of the two forms of enantiomer. Only one enantiomer can be obtained completely [either (+) or (-)].