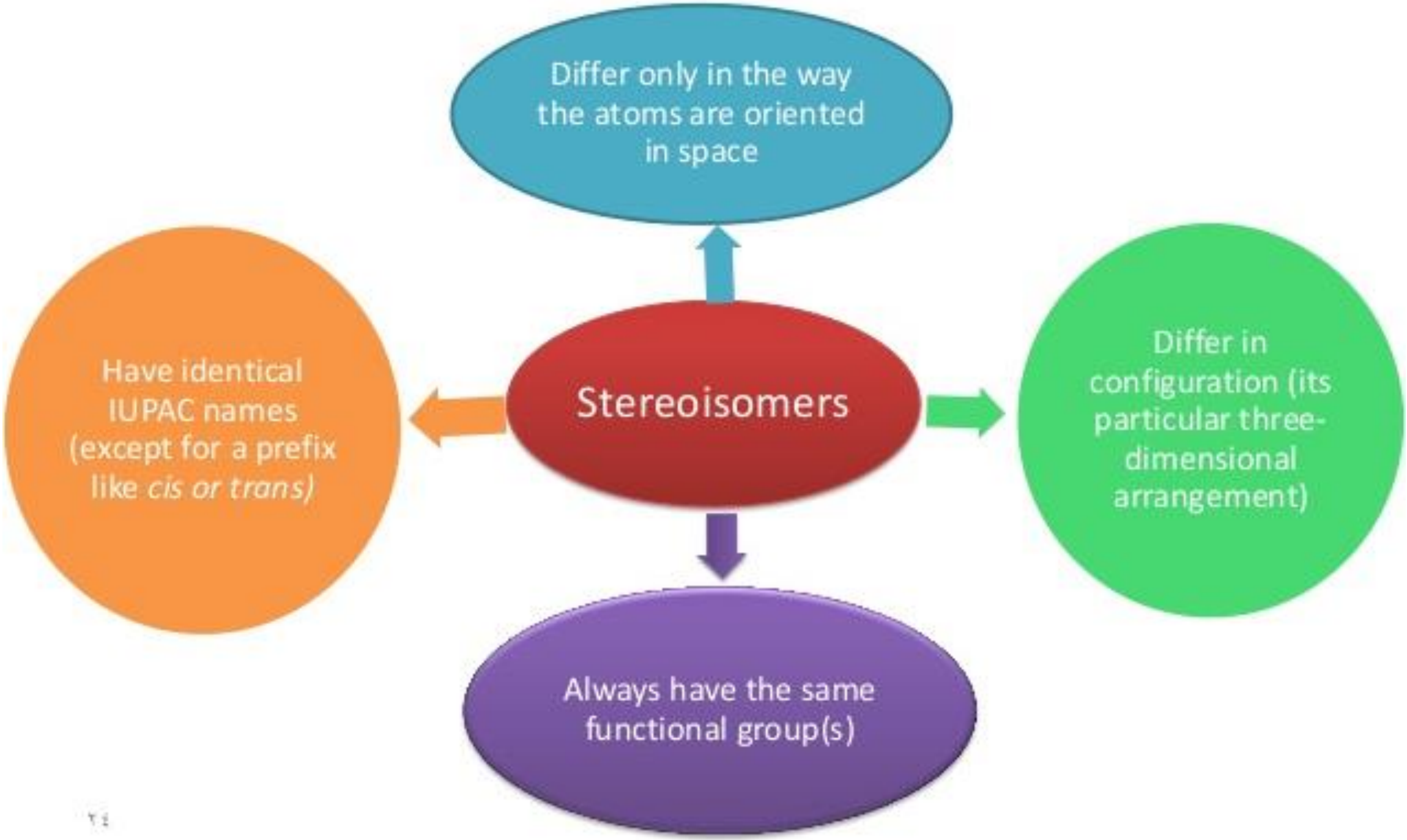
STEREOCHEMISTRY
Part-IV

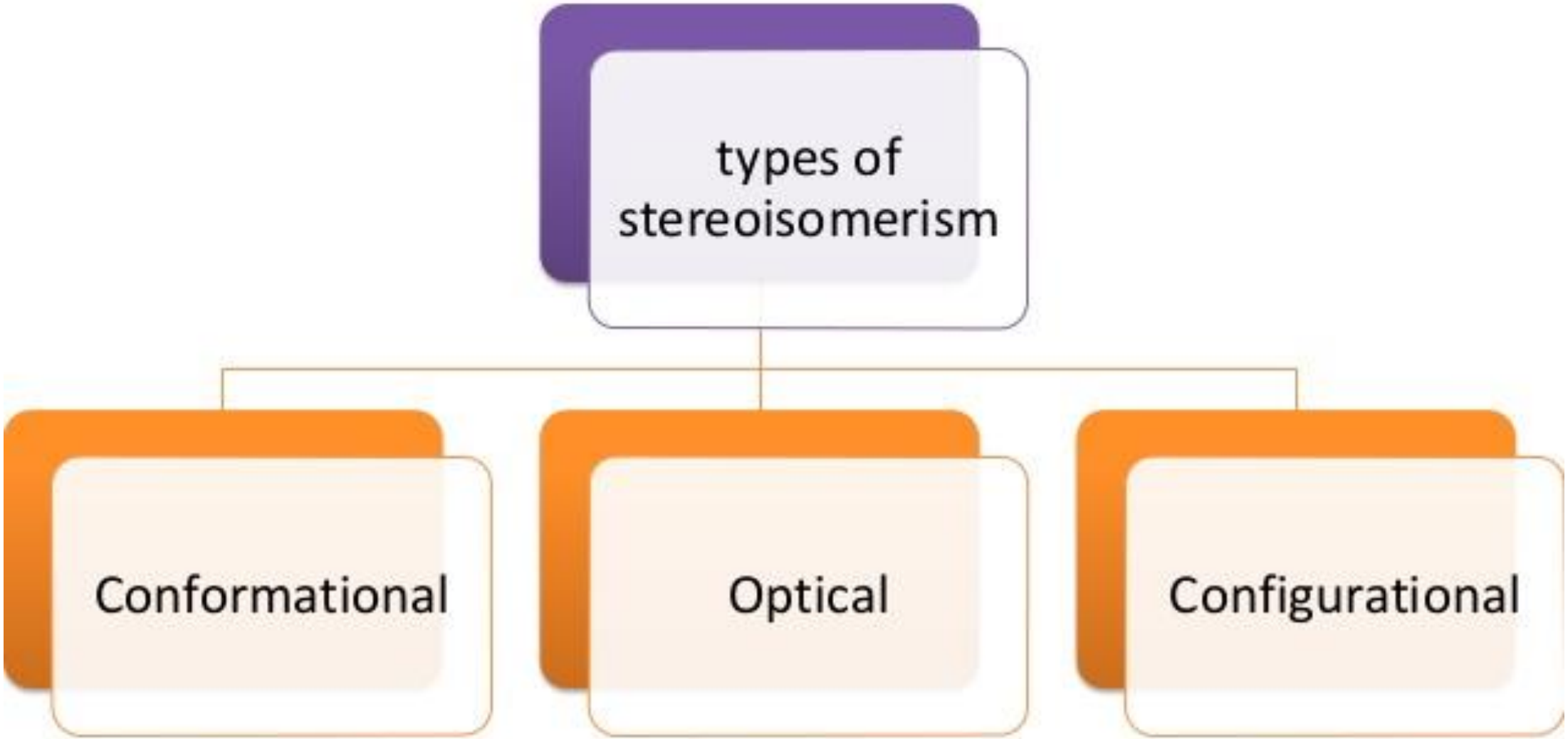
B.Sc Hons (Chemistry)
Sem-I , Paper CC-1

Dr. Indranil Chakraborty

Kharagpur College


Differ only in the way the atoms are oriented in space
Have identical IUPAC names (except for a prefix like *cis or trans)*
Stereoisomers
Differ in configuration (its particular three-dimensional arrangement)
Always have the same functional group(s)

❖**Stereoisomers** have their atoms connected in the same sequence (the same constitution), but they differ in the arrangement of their atoms in space.



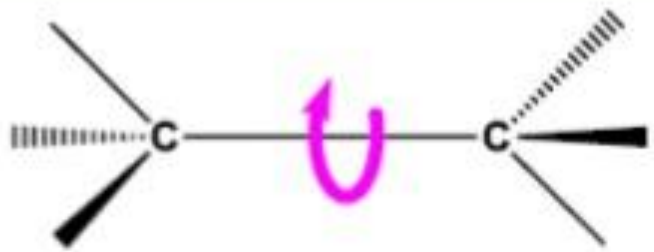
1- Conformational Isomers

❖Isomers have **different spatial orientations of atoms in a molecule** that **result from**

A) Rotations about single bond (alkanes).

B) Ring flipping conformations (cycloalkanes).

❖ The resulting arrangement referred to eclipsed and staggered conformers.



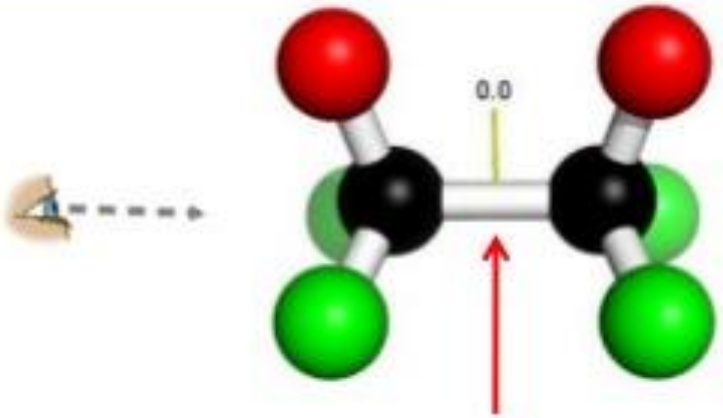
Rotation of C-C single bond

N.B: Rotation occur only in alkane (single bonds) not occur in alkene and alkyne

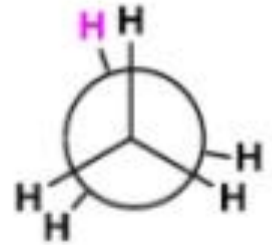
A- Conformational Isomerism in Alkanes

1- Conformation of ethane

❖Conformation isomers are different spatial arrangements of a molecule that are generated by rotation about single bonds.
❖Can be represent by Newman projection



Torsional angle or dihedral angle is 0º

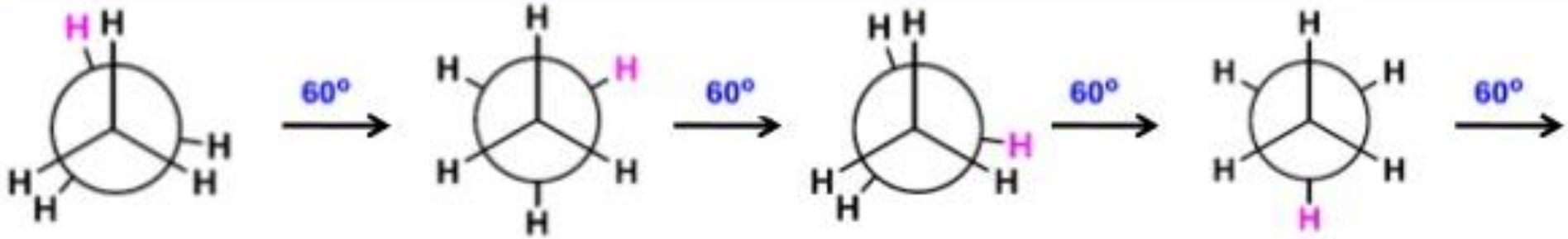


(Eclipsed)
θ H / H = 0°

❖ **Dihedral angle or Torsional angle** (θ) (in degrees) : angle between the plane formed by the first three atoms and the plane formed by the last three atoms.
❖ Rotation can be **clockwise or counterclockwise**.

Conformation of ethane (Newman projection of ethane)

❖ When **one of the carbon atom (front) is kept fixed and other is rotated about C - C bond an infinite numbers of isomers are possible by rotation about single bonds**

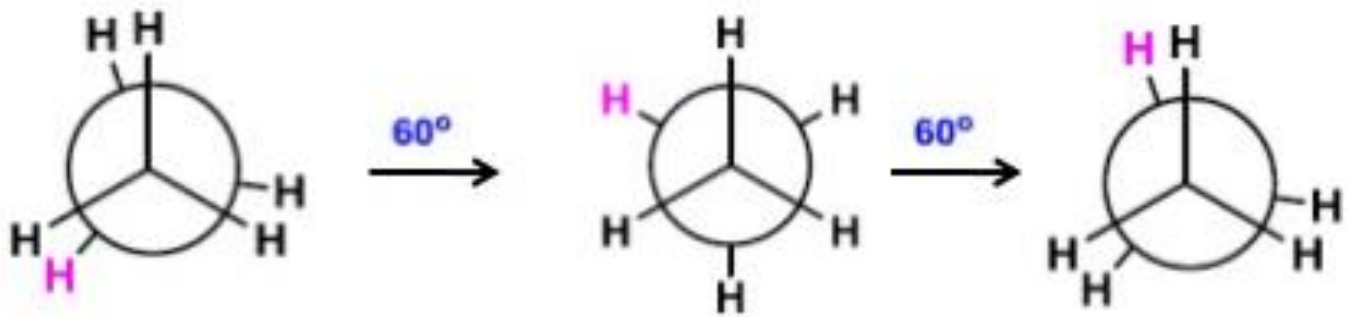


(Eclipsed) θ H / H = 0°

(Gauche) θ H / H = 60°

(Eclipsed) θ H / H = 120°

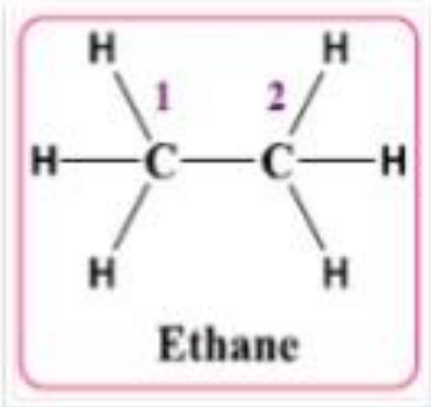
(Gauche) θ H / H = 180°



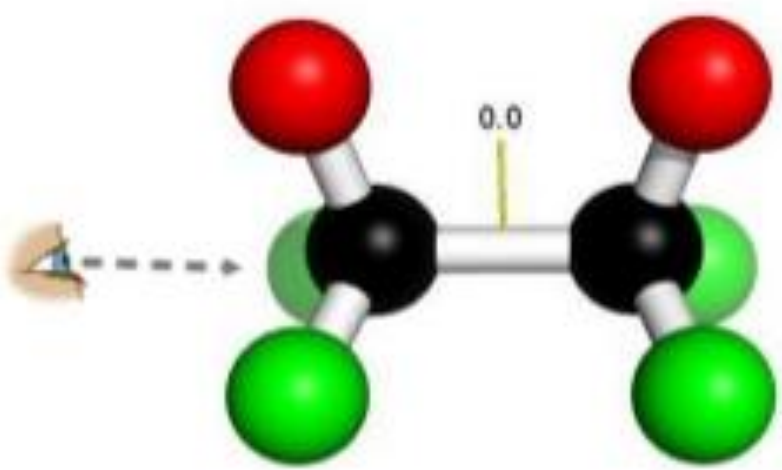
(Eclipsed) θ H / H = 240°

(Gauche) θ H / H = 300°

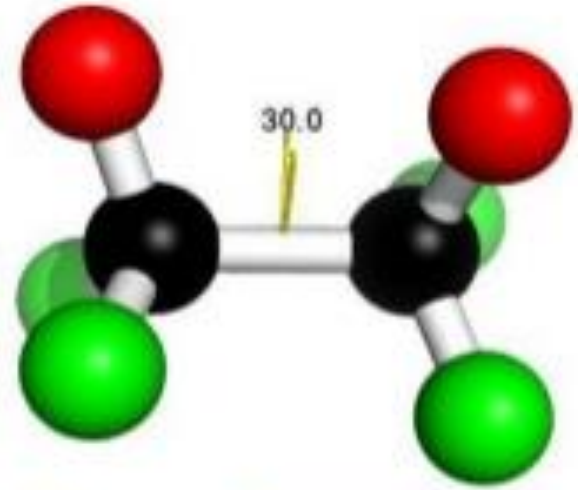
(Eclipsed) θ H / H = 360°



N.B. All structures consider as conformers



30



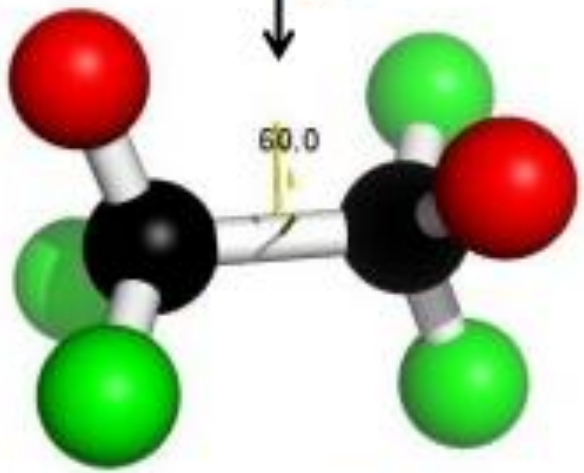
Eclipsed form

$(\theta = 0)$

Skew conformation

$(\theta = 30)$

30



Staggered form

$(\theta = 60)$

- Any conformations between eclipsed and staggered are called **skew conformations**.
- **Skew conformation of ethane is rapid at room temperature, and is sometimes described as free rotation.**
- It is clear from that **eclipse conformation is of highest energy, skewed conformation is of intermediate energy, and staggered (gauche) conformation is the most stable**

2- Configurational Isomers

❖**Configurational Isomers** are stereoisomers that cannot be converted into one another by rotation around a single bond.

❖It is classified into:

➢Optical isomers

➢Geometrical isomers

A- Geometrical isomers

❖ **Geometrical isomers :** compounds with the **same** connectivity, **different** arrangement of atoms in space.

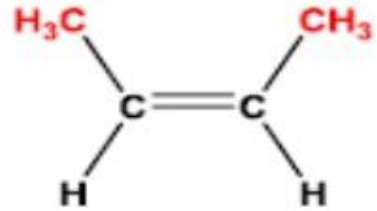
❖ Two system used to **describing** the orientation of substituents within a molecule **(configuration at double bond and configuration of cyclic compound),** known as **cis/trans** or **E/Z** system.

❖ **Stereoisomers** about **double bond** and **ring structure** arise **because rotation about the double bond is restricted.**

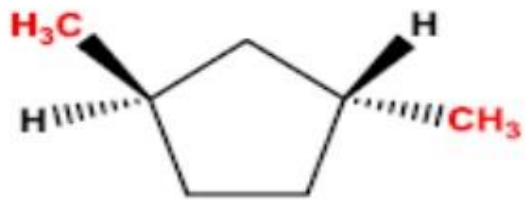
❖ **Substituents** on the **same side** (**cis**, latin word) or **opposite side** (**trans**) of double bond or ring.

❖ When **two groups** are the **same** to use the ***cis/trans system*** *of naming, if you have* **four different** groups on a double bond use the ***E/Z system.***

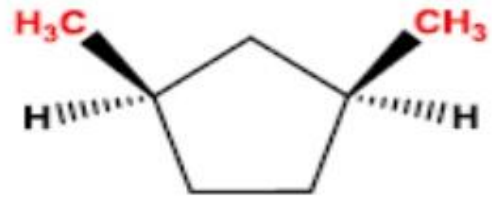
Trans-but-2-ene



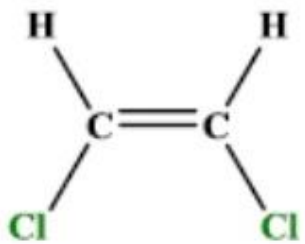
Cis-but-2-ene



Trans-1,3-dimethylcyclopentane

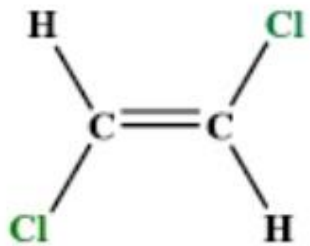


Cis-1,3-dimethylcyclopentane



Boiling point = 47.5 ^{0}C

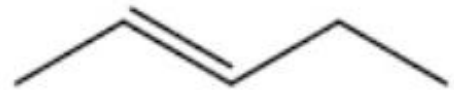
Cis-1,2-dichloroethene



Boiling point = 60.3 ^{0}C

Trans-1,2-dichloroethene

Cis–2-pentene



Trans-2-pentene

❖ The **chemical properties** of geometrical isomers tend to be **similar** but their **physical properties are different**

❖ **E/Z isomers** is used when there are **more than two different substituents** on a double bond.

➢ **Z** (from the German zusammen) **means "together"** and corresponds to the term **cis.**

➢**E** (from the German entgegen) **means "opposite"** and corresponds to **trans.**

❖ For each of the atoms attached to each carbon of the double bond it is necessary to determine which has the **higher priority**

❖ **Rank** the atoms directly attached to double bond according to their **atomic numbers.**

➢**High priority** is given to the atom with **higher atomic number**

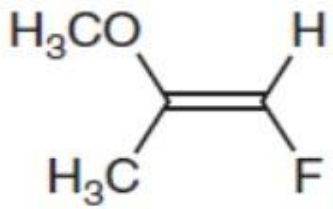
➢**{ H–(1) < C– (6)< N–(7) < O–(8) < F–(9) < Cl–(17) < Br–(35) < I–(53) }**

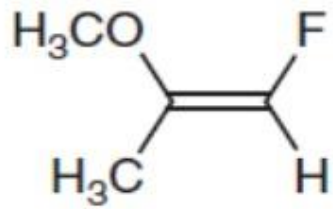
❖If **isotopes** of same element are present, the **higher priority** is given to the isotope with **higher atomic mass (mass number)**.

➢**ordinary hydrogen** is written **1H1**, **deuterium** is **2H1**, and **tritium** is **3H1**.

Nomenclature of Z/E Isomers

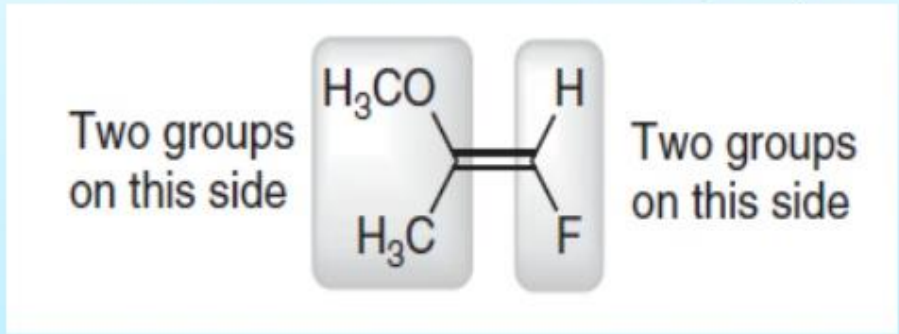
e.g. 1



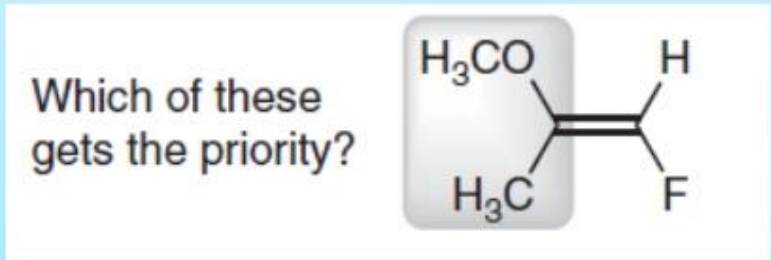


1- Determine the **position** of double bond.

2- **Look at both sides** of the double bond; each side has two groups:



3- We begin with one side (let's start with the left), and we **ask which of the two groups on the left has priority:**

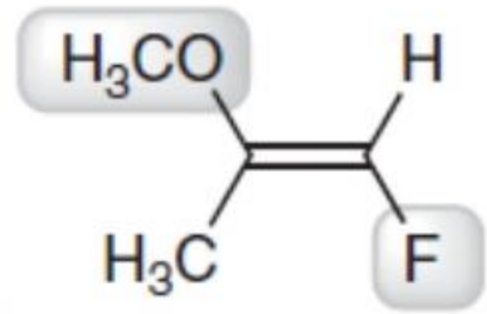


➢**The oxygen atom gets priority over the carbon atom, based on atomic number**

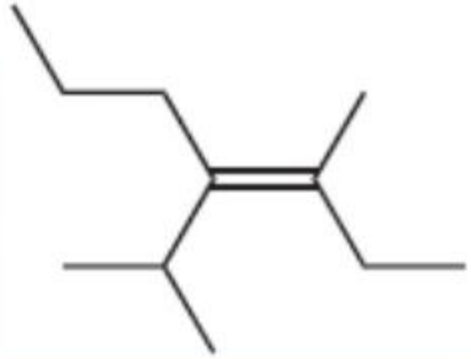
4- Comparing the two groups on the right side, the **fluorine atom gets priority over the hydrogen atom**, again based on **atomic numbers.**

➢So now we know which group gets the priority on each side:

5- The **two groups** become in **opposite** direction, So the Compound called **E.**



e.g. 2



➢In this example, we have to compare carbon atoms to each other.

➢The groups are all different, so we need to find a way to assign priorities. To do so, we follow this rules: **If the atoms are the same on one side, then just move farther out and analyze again.**

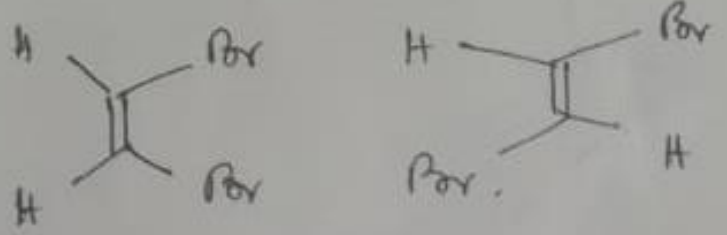
➢we compare the two groups on the **left side**, the first atom in two groups is carbon but the **carbon** atom in the **above** groups is attached to **C,H,H**, While the **carbon** atom in the **below** groups is attached to **C,C,H, So the below group gets priority over the above group.**

➢When comparing the two groups on the **right side**, the first atom in two groups is carbon but the **carbon** atom in the **above** groups is attached to **H,H,H,** While the **carbon** atom in the **below** groups is attached to **C,H,H, So the below group gets priority over the above group.**

➢The **two groups** become in **same** direction, So the Compound called **Z.**

Nomenclature of- cis-trans isomers

* If an alkene contains similar substituent on each Carbon on the same side of- the double bond, the isomer is called cis-isomer. When similar substituents are on opposite side of- the double bond, they are called trans isomers.



Cis-1,2-dibromo ethene

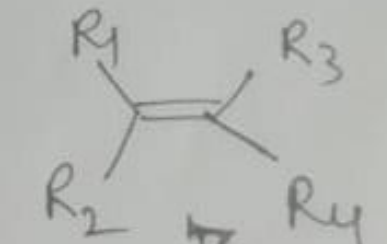
Trans-1,2-dibromo ethene.

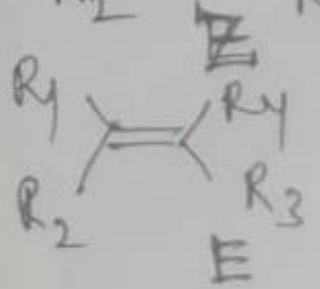
* When all the four groups on SP^2 carbon are different a different type of- nomenclature other than cis-trans is required and this is called **E-Z** nomenclature.

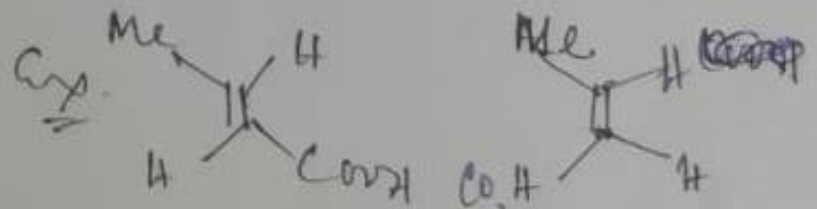
Let, we have a compound $R_1R_2C=CR_3R_4$. The first job is to make an order of precedence of the groups R_1 & R_2 and R_3 & R_4 as per CIP rule & sequence let us also consider that $R_1 > R_2$ and $R_3 > R_4$. Now the isomer where, R_1 and R_3 are on the same side & the double bond, is known as Z isomer and where R_1 and R_3 are on the opposite side is called E isomer. (Z = cis like; E = trans like)

Z ⇒ German. ZUSAMMEN = Together

E ⇒ German. ENTGEGEN = Opposite



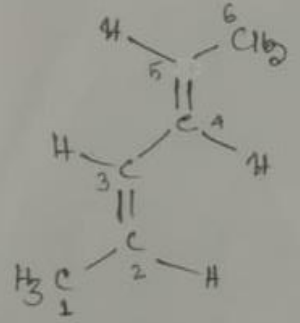




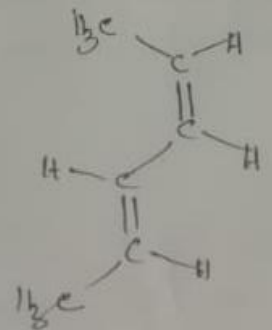
(E)-2 Butenoic acid : (Z)-2 Butenoic acid.

Me > H; CO_2H > H.

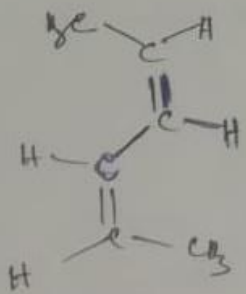
When cis-trans isomers contain more than one double bonds nomenclature is done specifying the configuration of each double bond.



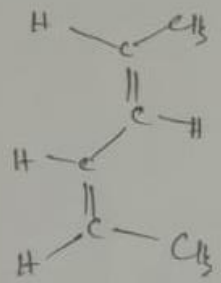
2E, 4E



2E, 4Z



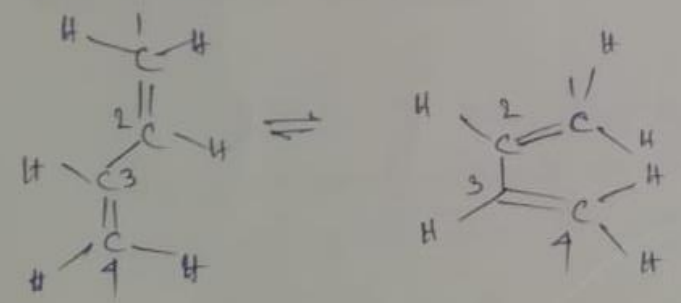
2Z, 4Z,



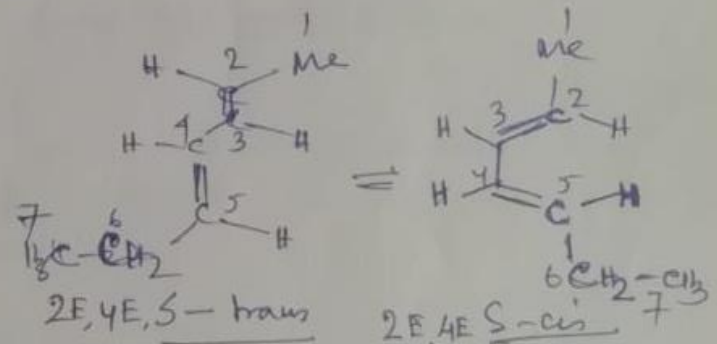
2Z, 4E

Hexa-2,4-diene.

Acyclic conjugated dienes can be written in different conformations by rotating the C–C single bond that joins the two double bonds.



1,3 Butadiene (S-trans) 1,3 Butadiene (S-cis)



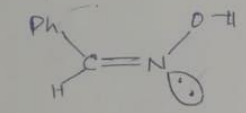
2E, 4E, S – trans

2E, 4E S-cis

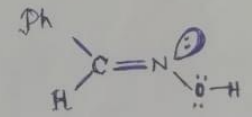
Stereochemical nomenclature of oximes

Compounds containing C=N or N=N can also show cis-trans isomerism. In oxime chemistry the terms cis and trans is replaced by the terms syn and anti respectively.

In aldoximes. The isomer where the hydrogen atom and the hydroxyl groups are on the same side of the double bond is called SYN, and the anti form is the isomer that containing OH gr and H atom on opposite side of the double bond.

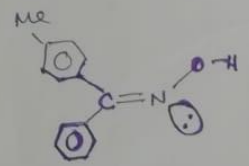


Anti-Benzaldoxime

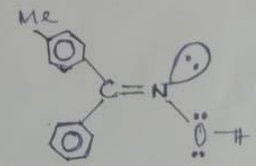


Syn-Benzaldoxime

In ketoximes the prefix syn or anti indicates the configurational relationship between the first group mentioned and the OH group.

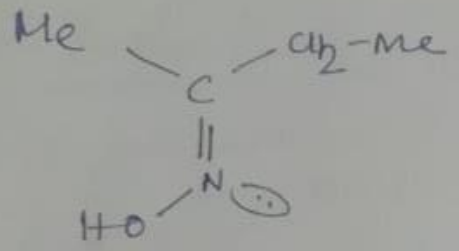


Syn-p-tolyl phenyl ketoxime
or
anti-phenyl p-tolyl ketoxime
or
Z-phenyl-p-tolyl ketoxime

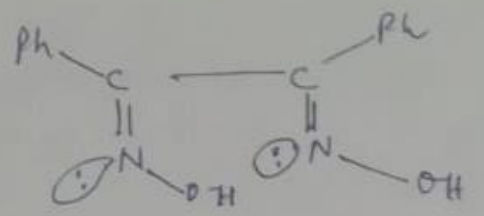


syn-phenyl-p-tolyl ketoxime
or
anti-p-tolyl-phenyl ketoxime
or
E-phenyl-p-tolyl ketoxime

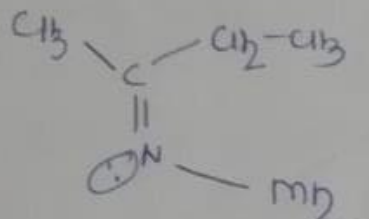
[In E-Z nomenclature in fact the p-tolyl gr has greater priority over phenyl and OH gr has priority over lone pair. Thus oximes can also be named as E/Z-]



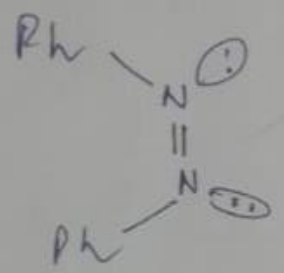
(E) - Butanone oxime



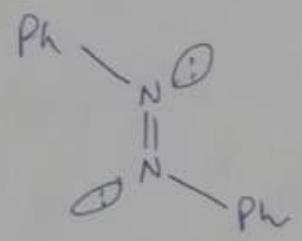
(Z, E) - Benzildioxime



(Z)



Syn or Z Azobenzene



anti azobenzene or E - Azobenzene.

B- Optical isomers

❖ Some organic molecules has the **ability** to rotate the plane polarized light (PPL). These compounds were termed **optically active compounds.**

❖ When the compound rotate the PPL to **right** "clockwise", it is termed **(+)** or Dextrorotatory **(d)** but when the compound rotate the PPL to **left** "anti-clockwise", it is termed **(-)** or levorotatory **(l)**

❖ The organic molecules that not **able** to rotate the plane polarized light (PPL) called **optically Inactive compounds.**

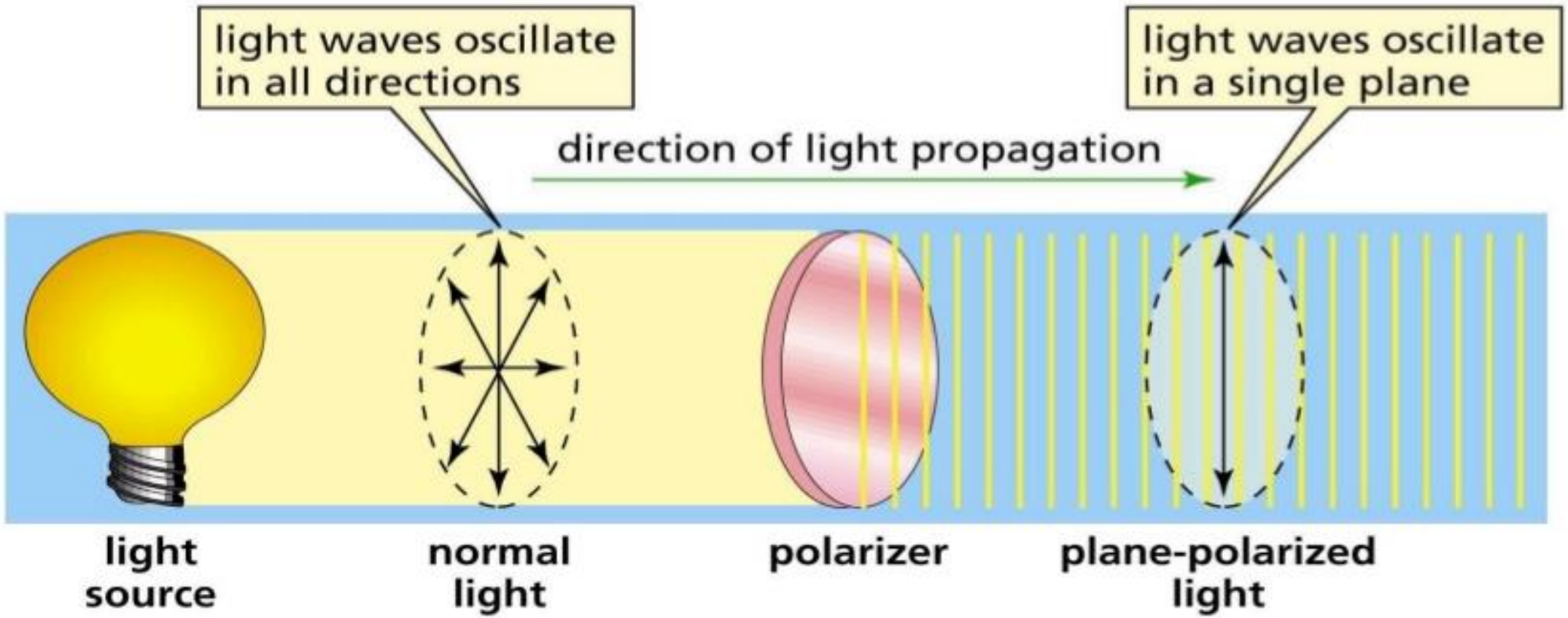
Polarimeter

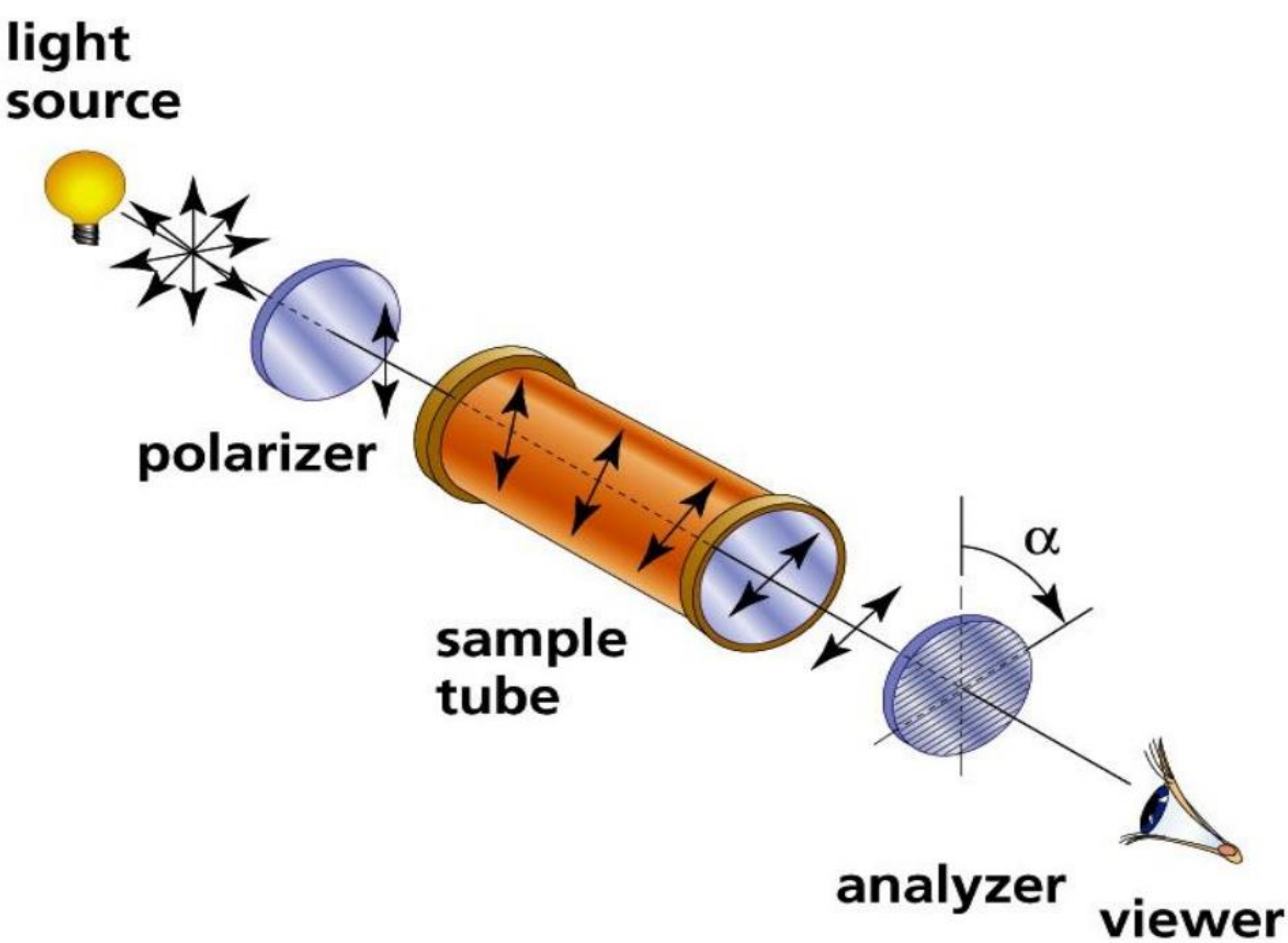
➢**Polarimeter** is an **instrument used to** determine the **optical activity** of optically active compounds.

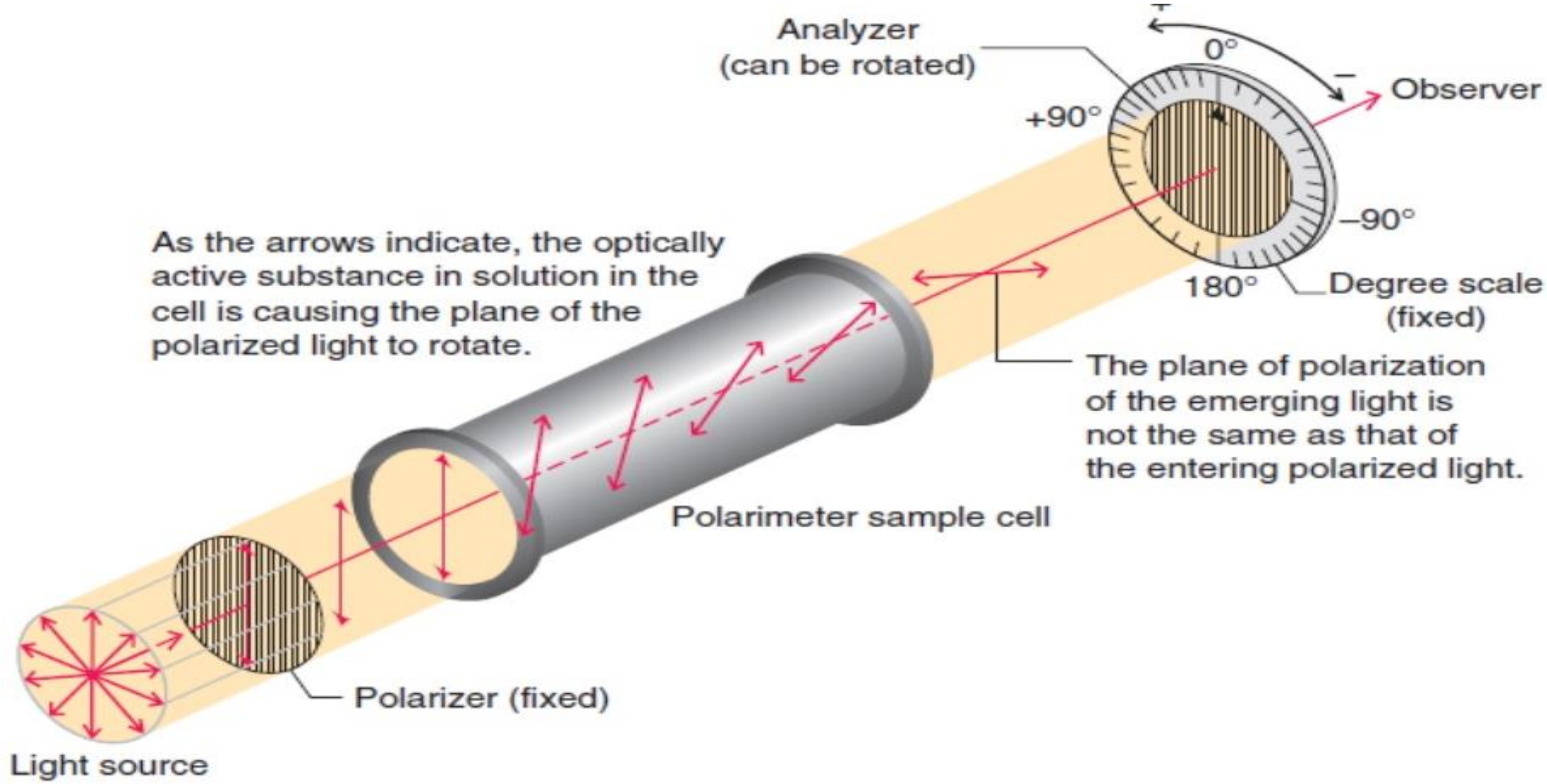
➢**The simplest polaramiter is composed of:**

1) **light source** (usually sodium lamp).
2) **polarizer**: it can convert a **beam of light of mixed polarization into a beam with well-defined polarization e.g.**(Nickel prism).
3) **tube for holding the sample.**
4) **Analyzer**
5) **Measuring scale** to determine the number of degrees of rotation.

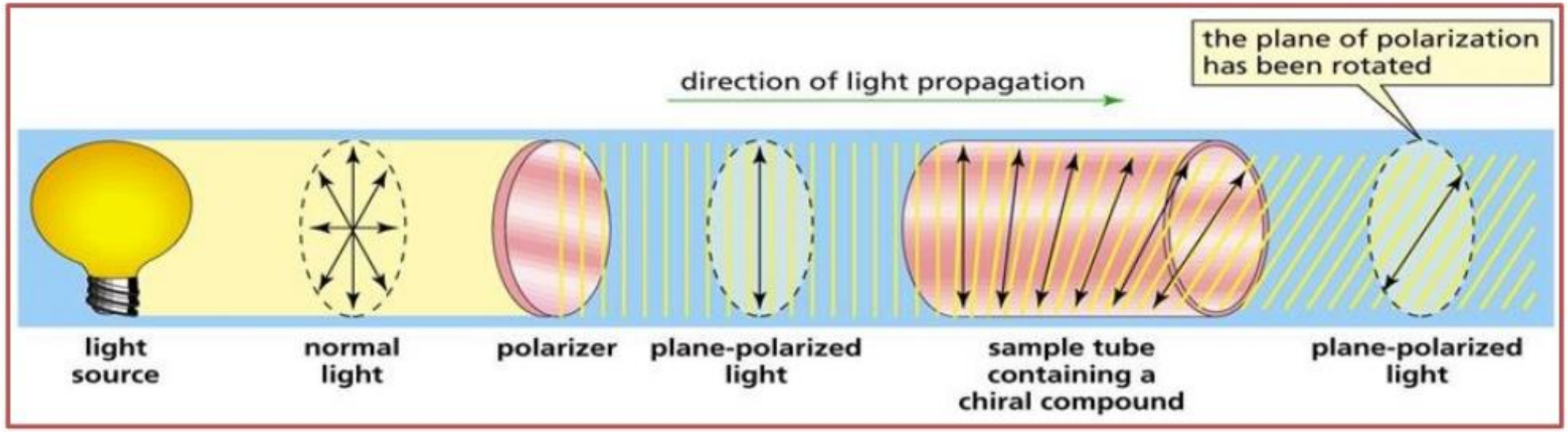
Plane-Polarized Light



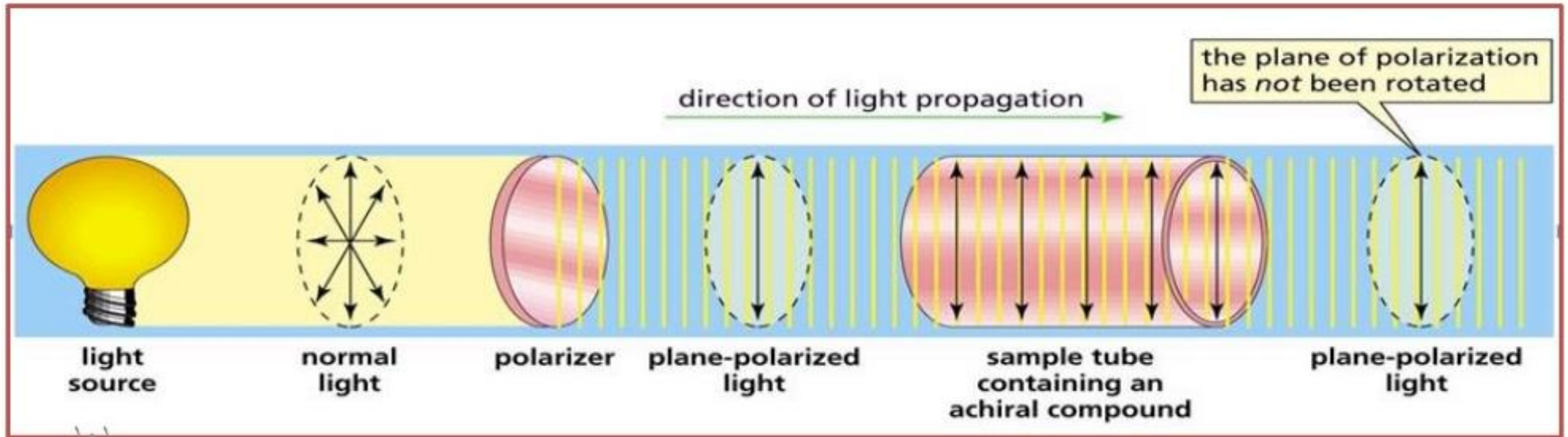

light
source
polarizer
sample
tube
α
analyzer
viewer


Analyzer
(can be rotated)
0°
+
–
Observer
+90°
–90°
180°
Degree scale
(fixed)
As the arrows indicate, the optically active substance in solution in the cell is causing the plane of the polarized light to rotate.
The plane of polarization of the emerging light is not the same as that of the entering polarized light.
Polarimeter sample cell
Polarizer (fixed)
Light source

Plane-Polarized Light through chiral Compound



Plane-Polarized Light through an Achiral Compound



Specific rotation

➢**The number of degrees that the plane of polarized light is rotated as the light passes through a solution of enantiomers** depends on the number of **chiral molecules in sample.** This of course, depends also on the **length** of the tube and the **concentration** of the enantiomers.

➢**Enantiomers** are stereoisomers that are **non super-imposable** on its **mirror image**.

➢**Enantiomers** rotate the plane of polarized light by exactly **the same number of degrees but in opposite directions**

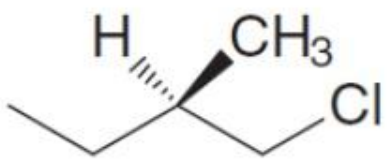
➢Specific rotation [α] can be calculated by the following equation: **[α] = α /cl**

α = observed rotation

c = concentration in g/mL

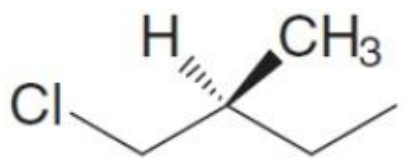
l = length of tube in dm

➢**Specific rotation is defined as** the rotation produced by a solution of unit concentration (1g/ml) and unit length (10 cm).



(*R*)-(−)-1-Chloro-2-methylbutane

$[\alpha]_D^{25} = -1.64$



(*S*)-(+)-1-Chloro-2-methylbutane

$[\alpha]_D^{25} = +1.64$

Types of optical activity

Dextrorotatory

new	older
(+)-	d-

do not confuse with D

- Rotates the plane of polarized light to the **right** (clockwise)

Levorotatory

new	older
(-)-	l-

do not confuse with L

- Rotates the plane of polarized light to the **left** (counterclockwise)

Meso compound

linked, but contain no other chiral group. Chiral groups that are mirror images to each other are called *enantiomeric* groups.

A set of stereoisomers in which the *meso* compound belongs must contain at least one *chiral* stereoisomer. For example, tartaric acid, $CO_2HC^*HOH\text{-}C^*HOHCO_2H$ has two chiral centres (asterisked) and have the following stereoisomers (shown in Fischer projections).

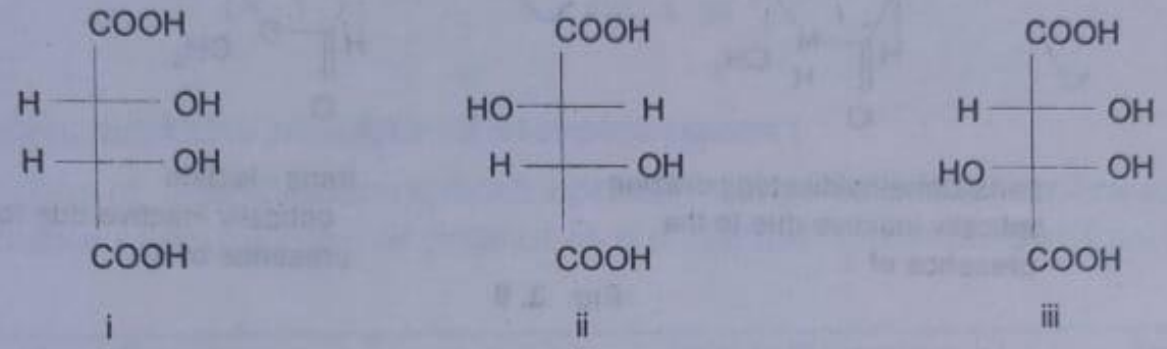
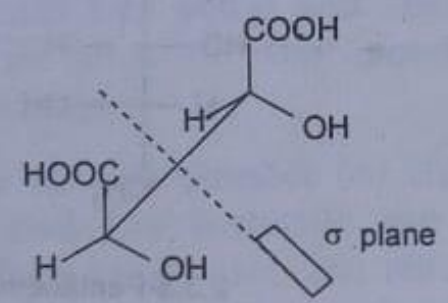
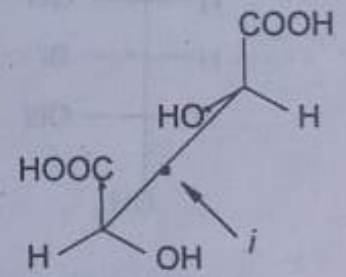


Fig. 3. 7

Of these, (i) is optically inactive and (ii), (iii) are optically active. The compound (i) is called *meso*-tartaric acid. Its inactivity is said to be due to the presence of plane of symmetry (in *eclipsed* conformation) or due to the presence of centre of symmetry (in *staggered* conformation). These are shown below in sawhorse projections. The active isomer of any compound cannot pass through an achiral conformation.



meso - tartaric acid
(eclipsed sawhorse)



meso - tartaric acid
(staggered sawhorse)

Fig. 3. 8

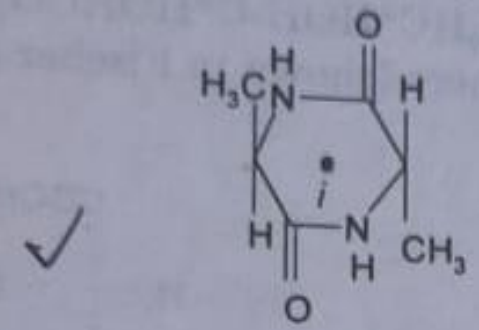
The isomers (ii) and (iii) are optically active because they cannot be transformed into such a conformation in which symmetry elements σ, i or S_n (n=even) are possible.

In this case, one noticeable fact is that *meso*-tartaric acid can also exist in *chiral* conformations having no elements of symmetry. In these forms, if frozen, (free rotation about C-2–C-3 σ– bond is prevented), *meso*-tartaric acid should exhibit optical activity. Under normal state, each chiral conformation can have equal amount of its mirror image-conformation through internal rotation (conformational change). As a result of which statistically we get an equimolecular mixture of a pair of conformational enantiomers (conglomerate) and, therefore, it is optically inactive. In fact *meso*-tartaric acid may be considered as a *residual stereoisomer* that we can isolate as achiral molecule under the experimental time-frame.

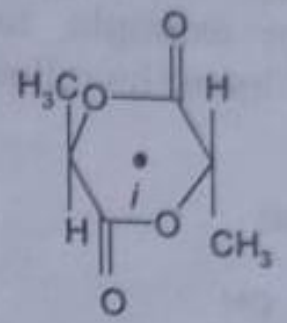
Thus *meso*-tartaric acid is optically inactive due to the presence of elements of symmetry (σ, i, S_n), *it is said to be internally compensated* molecule. The sense of internal compensation is

that the (+)-rotation of one part of the molecule is being nullified by the (–)-rotation of the other part within the same molecule.

A few more examples of *meso*- compounds are given below .



trans-Dimethyldiketopiperazine
optically inactive due to the
presence of *i*

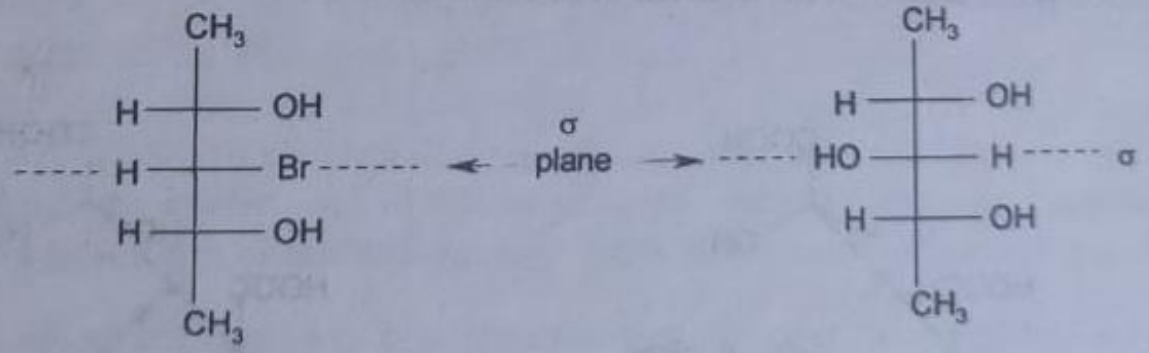


trans - lactide
optically inactive due to the
presence of *i*

Fig. 3. 9

The term *meso* is normally used for acyclic stereoisomers having possibilities of conformational variation. In the above case we have a cyclic rigid system but the compound contains chiral centres (asterisked). Inactivity is due to the presence of symmetry element *i*. Therefore, this type of stereoisomers may also be called *meso* compounds. In case of each of the above structure, *cis*-isomer is *chiral* stereoisomer.

The term *meso* is normally used for acyclic stereoisomers having possibilities of conformational variation. In the above case we have a cyclic rigid system but the compound contains chiral centres (asterisked). Inactivity is due to the presence of symmetry element *i*. Therefore, this type of stereoisomers may also be called *meso* compounds. In case of each of the above structure, *cis*-isomer is *chiral* stereoisomer.



3-Bromo-2,4-pentanediol
(inactive due to σ plane)

Fig. 3. 10

2,3,5-Pentanetriol
(inactive due to σ plane)

Fig. 3. 11

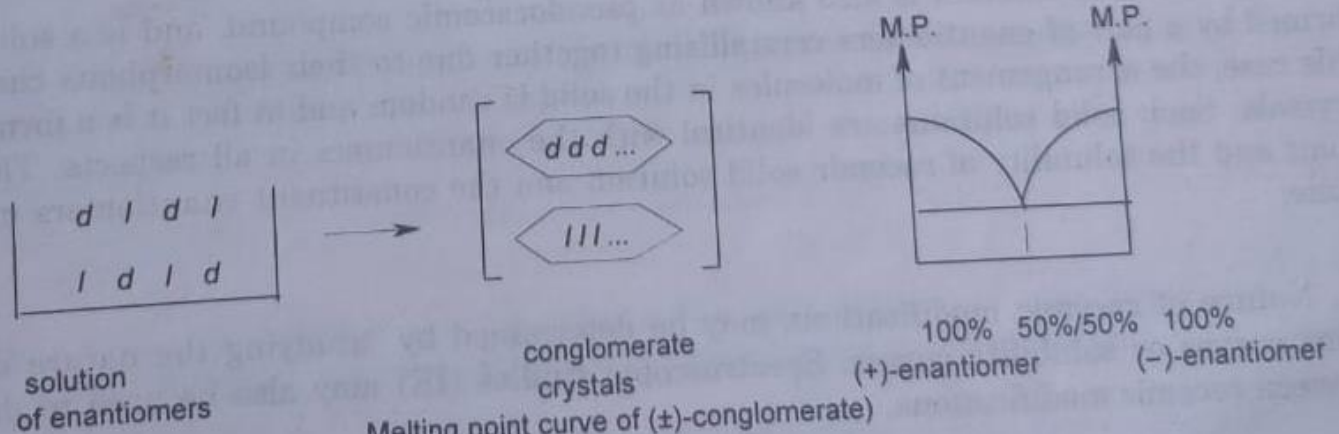
In the compound like 1,3-disubstituted cyclobutane (assuming planer structure) , two diastereoisomers are possible. Both of these are achiral due to the presence of plane of symmetry, although each of the substituted carbon atoms may be considered as *chiral* centre. These carbon centres are *stereogenic* but *achirotopic* (since the local or site symmetry is achiral). These diastereoisomers *cannot* be called *meso*-compounds because, the set does not have any *chiral* stereoisomer.

Racemic modification

The *racemic modification* is an *equimolecular* mixture of a pair of enantiomers independent of whether it is crystalline, liquid or gaseous. The racemic modification is optically inactive due to *external compensation*, i.e., (+)-rotation of one enantiomer is compensated by the (–)-rotation of the other. Since racemic modification is a mixture, it can be separated into pure enantiomers. The process is known as *resolution*. *meso*-compounds cannot be resolved. The racemic modification may exist in three different forms in the solid state.

(i) racemic mixture or (±) - conglomerate :

It is a mechanical mixture of two types of crystals, the (+)- and (-)-forms. The mixture contains as many crystals of (+)-form as (–)-form (separate solid phase) and that is why its resultant optical activity is nil. A mixture of two crystalline types necessarily has a melting point different from each of the types, which gives a means of distinguishing enantiomers and the racemic mixture, simply by a examining the melting points. The conglomerate is a true eutectic mixture, and its melting point is necessarily lower than that of each of its pure enantiomers. The melting point curve of conglomerate can be represented as follows. Other physical properties of the racemic mixture are mainly the same as those of the constituent enantiomers.



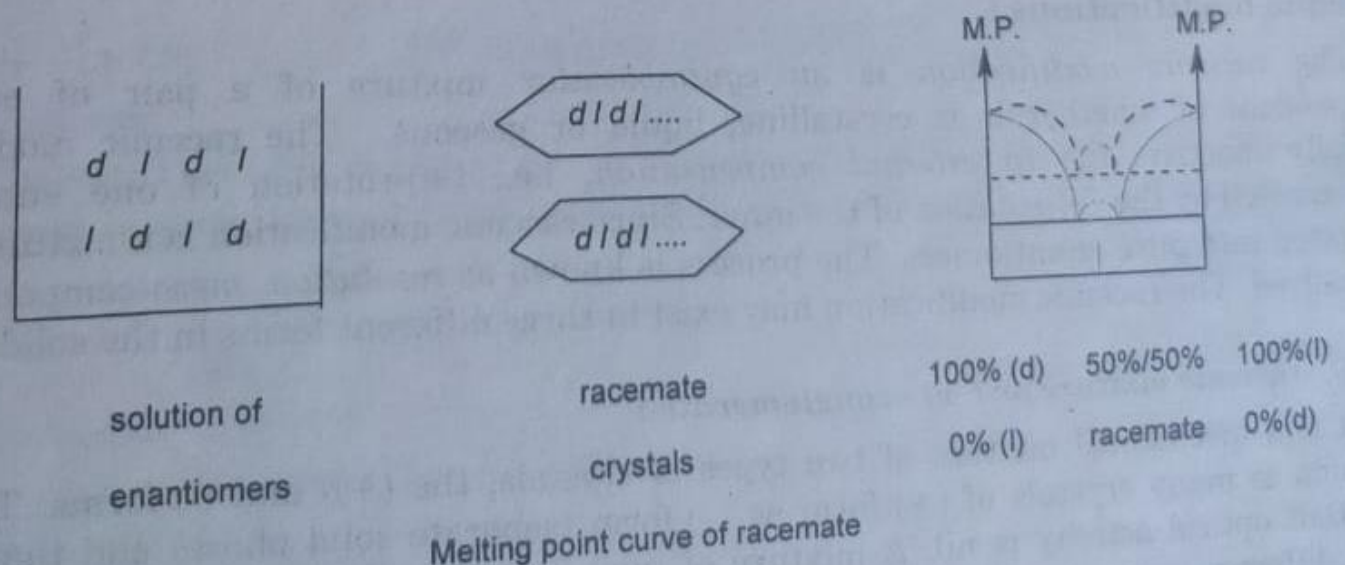
Melting point curve of (±)-conglomerate)

Fig. 3.16

Racemic compound

(ii) ***Racemic compound or Racemate*** :

This consists of a pair of enantiomers as a molecular compound, that is, the crystalline lattice incorporate both enantiomers in equal numbers. A new compound has, therefore, been formed in the solid state. When dissolved, it decomposes, liberating its constituents in equimolecular ratio. The physical properties of a racemate are different from those of the constituent enantiomers. The melting point of the racemate may be either lower or higher than that of its constituents. The melting point of a racemate is illustrated, by the following curve. Racemate may exist in any form of homogeneous phase.



Racemic solid solution

(iii) ***Racemic solid solution*** **:**

Racemic solid solution is also known as pseudoracemic compound, and is a solid solution formed by a pair of enantiomers crystallising together due to their isomorphous character. In this case, the arrangement of molecules in the solid is random and in fact it is a form of mixed crystals. Such solid solutions are identical with the enantiomers in all respects. The melting point and the solubility of racemic solid solution and the constituent enantiomers may be the same.

Nature of racemic modifications may be determined by studying the nature of melting point curves or solubility curves. Spectroscopic studies (IR) may also be used to distinguish between racemic modifications.

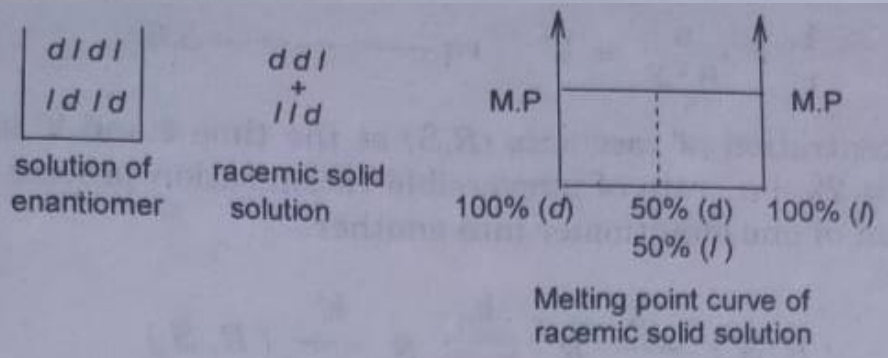


Fig. 3. 18

It is to be noted that pure enantiomer may be converted into a racemic modification by several chemicals methods. The process is called *racemisation*. Separation of racemic modification into pure enantiomers is called *resolution*. These methods have been discussed below in short.

Racemisation

Racemisation(*Discovered by Pasteur in 1853*)is the process of producing a racemic modification starting from either of the pure enantiomers. Racemates have the same constitutions as the pure enantiomers.

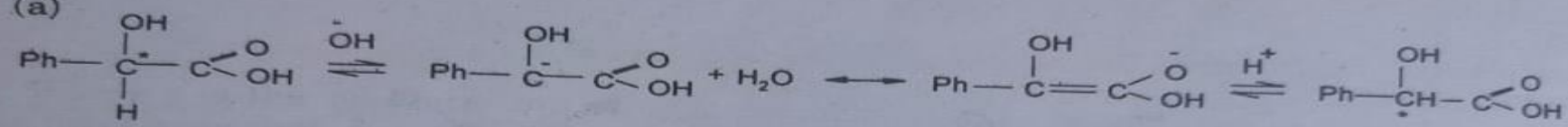
From thermodynamic standpoint, racemisation is a spontaneous process. A racemic modification is a mixture of two different molecular species and, therefore, possesses an entropy of mixing, ΔS. The is calculated to be around 6 J mol^{-1}. Since ΔS is a positive quantity, ΔG in the expression $\Delta G = \Delta H - T\Delta S$ is negative (assuming ΔH constant). At 27°C (300K), ΔG change is -1.8 $kJmol^{-1}$. Therefore, racemisation is a thermodynamically favourable process. Driving Force for racemisation is entirely entropic.

Racemisation is an irreversible process arising from an reversible interconversion of enantiomers. It is always associated with the disappearance of optical activity. Although racemisation is thermodynamically favourable, it is generally quite slow unless a suitable pathway is available. In the process of racemisation, the configurations of all the chiral centres get inverted. Although optical activity also changes gradually, it is not always possible easily to measure the rate of change of optical activity directly.

(ii) By anion formation : (Base catalysed Process):

If an acidic hydrogen is bonded to a chiral centre then racemisation may be achieved through carbanion formation. The hydrogen is lost as proton, being promoted by base. Carbanion should undergo delocalisation with an adjacent π-electron system so that parent chiral carbon can become planar at an intermediate form. Recombination of the achiral intermediate with the proton then gives racemic modification. A few examples are given below.

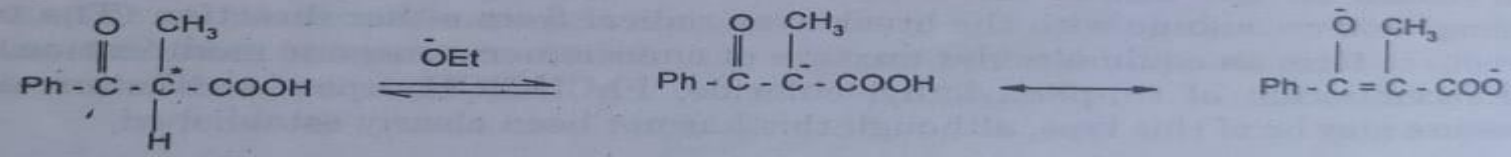
(a)



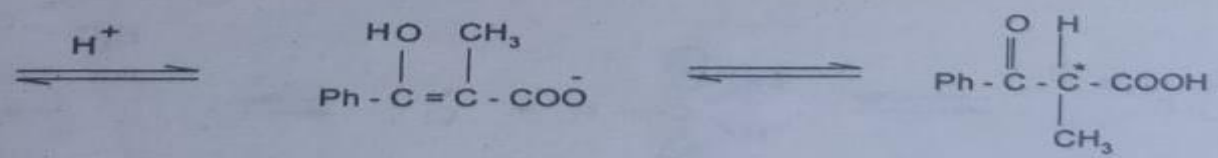
(+)-Mandelic acid — carbanion intermediate — At equilibrium, racemic modification is obtained.

Fig. 3. 23

(b)



(+)-2-Benzoylpropanoic acid



(-)-isomer

(iii) By cation formation :(Acid - catalysed Process) :

Racemisation can be achieved through the formation of a planar carbocation (achiral) by the heterolytic cleavage of a ligand attached to the chiral carbon. A few examples are given below :

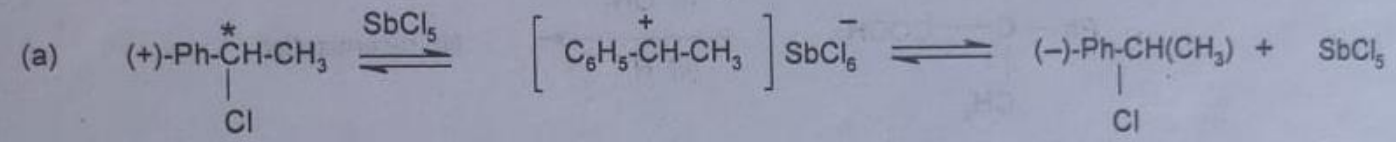


Fig. 3. 29

Carbocation formation is facilitated because benzylic carbocation is very much resonance stabilised. Since carbon atom of carbocation is sp^2 hybridised, it is planar and can recombine with the ligand from either of the two faces of the planer carbocation with equal probability to form both the enantiomers in equal quantities. There are however cases where partial retention of configuration of the chiral centre occurs due to asymmetric nature of the salvation of the intermediate carbocation (see Chapter Six). These may lead to the formation of unequal amount of enantiomers.

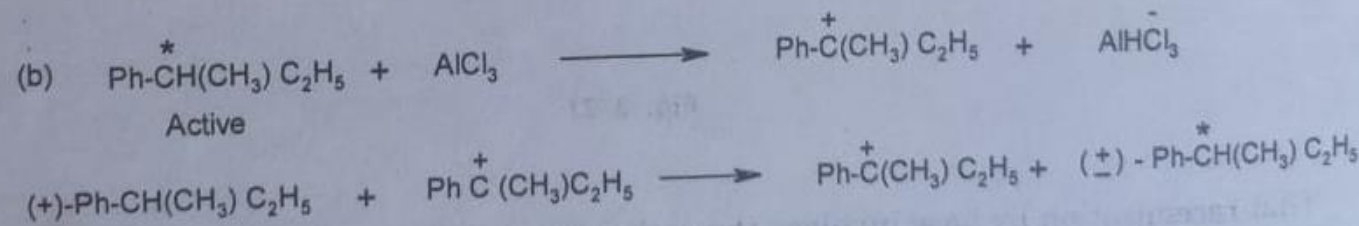


Fig. 3. 30

Usually this type of racemisation is possible when the carbocation is resonance stabilised. The reaction is normally catalysed by Lewis acids like $SbCl_5$, $AlCl_3$, $HgCl_2$, $SnCl_2$, $ZnCl_2$, etc.

Resolution of racemic modification :

Resolution is the method of separation of racemic modification into its pure enantiomers. In practice the separation is not always quantitative and the form separated may not be optically pure, i.e., it may consist of the (+)- and (−)- forms in unequal amounts. A large number of methods for resolution have now been developed and different nature of compounds needs different methods.

Mechanical separation :

This involves the manual separation of *racemic conglomerate*. A *racemic conglomerate* contains enantiomorphous crystals in equal quantities. Pasteur introduced this method in 1848 and separated (+)- and (−) -forms of tartaric acid using sodium ammonium tartrate. It should

be noted that *racemic compound* cannot be separated mechanically. Method of mechanical separation has limited use because it requires longer time and racemic conglomerates are rarely obtained. This manual separation of enantiomorphous crystals from a racemic conglomerate crystals leading to dextro-rotatory and laevo-rotatory solutions is called *triage*.

(ii) ***Preferential crystallisation by inoculation*** :

In this process a supersaturated solution of the racemic modification is treated with a crystal of a pure enantiomer (seeding) or an isomorphous substance, whereupon this form is preferentially precipitated. The resolution of (±)-glutamic acid by inoculation has been perfected for industrial use. The method works better with racemic conglomerate .Usually, method requires a transition temperature depending on the nature of the racemic compound.

(iii) ***Biochemical separation*** :

This method is based on the fact that certain bacteria and moulds, when they grow in a dilute solution of a racemic modification, destroy one enantiomer preferentially leaving behind the other. For example, *Pencillium glaucum* (mould) destroys the (+) - forms when grown in a dilute solution of racemic ammonium tartrate. The (–)-enantiomer remains unaffected. The main disadvantages are (i) only one enanantiomer can be isolated and (ii) selective micro organisms are difficult to isolate.

main disadvantages are (i) only one enanantiomer can be isolated and (ii) selective micro organisms are difficult to isolate.

(iv) ***The Chemical method : Resolution through the formation of diastereoisomers :***

This is the best method of resolution of a racemic modification. The basis of chemical method of separation consists in converting the enantiomers of a racemic modification into a pair of diastereoisomers. The racemic modification is treated with an optically active substance and the diastereoisomers thereby formed are separated by fractional crystallisation. The separated diastereoisomers are then individually treated with suitable reagent to regenerate the pure enantiomer.

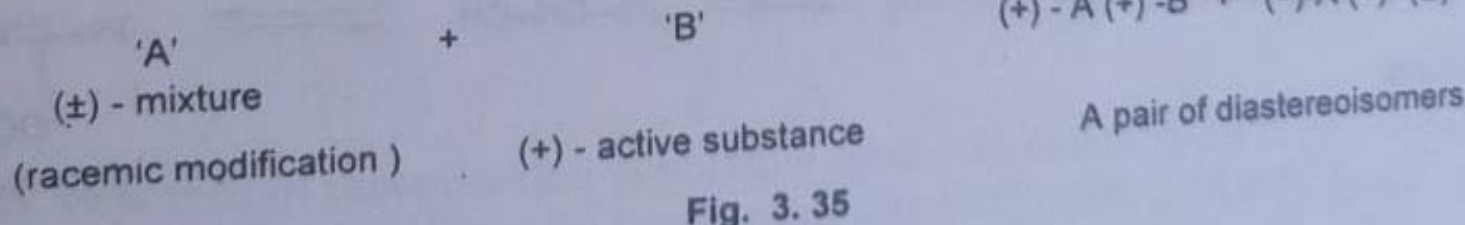


Fig. 3. 35

Resolution by means of diastereoisomer formation may be used on a variety of compounds. A few examples are given below.

(i) *Resolution of acids :*

Racemic modification of acids is resolved using optically active bases. Usually naturally occurring alkaloids like brucine, strychnine, ephedrine, quinidine, cinchonine, cinchonidine and [illegible] are used to resolve optically active acids. Certain synthetic bases like (–)-phenylethylamine and amphetamine are also used.

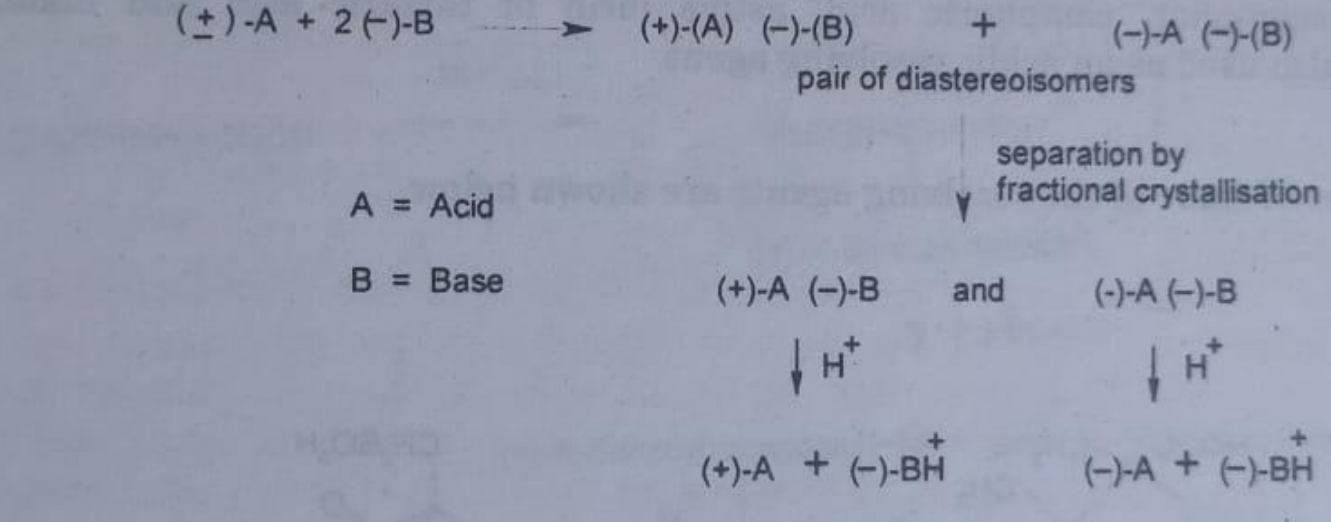
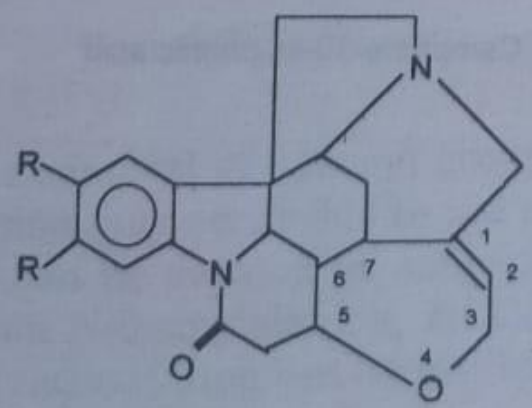
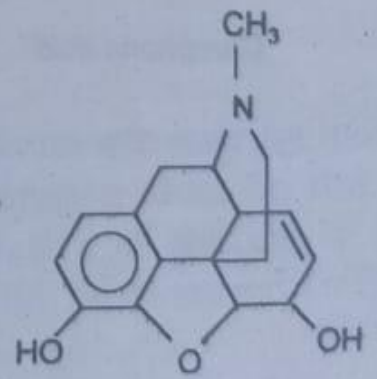


Fig. 3. 36

Structures of some of active bases used are given below.



R= H, Strychnine
Brucine



Morphine

Enantiomeric Excess & Optical purity

Optical purity of a enantiomeric mixture means the excess of one enantiomer over the *d,l* pair in a *d,l* - mixture. Optical purity is expressed as fraction or percentage optical purity. For example, if one enantiomeric mixture is 30% optically pure with respect to *d*-form, then the rest 70% is a racemic modification. That is, % composition of this mixture is *d*-isomer, (30+ 35) = 65% and *l*-isomer, 35%. Optical purity is also called *enantiomeric excess* (*ee*).

% Optical purity is related to optical activity of enantiomers by the following expression.

$$\% \text{ Optical Purity} = \frac{\text{specific rotation of enantiomeric mixture}}{\text{specific rotation of pure enantiomer}} \times 100 = \frac{[\alpha]_{obs}}{[\alpha]_{max}} \times 100$$

$[\alpha]_{max}$ indicates the specific rotation of enantiomerically pure(ep) sample.

For example, let the specific rotation of an enantiomeric mixture is (+)-25° and that of pure enantiomer is (+)-50°, then the % optical purity of the enantiomeric mixtureis equal to

$$\frac{(+) - 25}{(+) - 50} \times 100 = 50\ \%$$ with respect of (+)-enantiomer.

This means that in the enantiomeric mixture, the excess of (+) -enantiomer is 50% and rest 50% exists as racemic modification. Thus, the composition of enantiomeric mixture is, (+)-enantiomer (25 + 50) = 75% and (-)-enantiomer 25%.

This means that in the enantiomeric mixture, the excess of (+) -enantiomer is 50% and rest 50% exists as racemic modification. Thus, the composition of enantiomeric mixture is, (+)-enantiomer (25 + 50) = 75% and (-)-enantiomer 25%.

On the other hand, if the % of major or minor enantiomer that is present in the mixture is known, optical purity can be calculated as follows :

$$\%\ \text{optical purity} = 2(\%\ \text{of the major enantiomer}) - 100\%, \quad \text{or}$$

$$\%\ \text{optical purity} = 100\% - 2\ (\%\ \text{of the minor enantiomer}).$$

It is to be noted that optical purity is expressed on the basis of the enantiomer which is the major component in the enantiomeric mixture. Optical purity of racemic modification is *zero*.

Enantiomer excess (ee):

Enantiomer excess is considered to be the same as optical purity. *ee* can also be calculated from the expression :

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

where $[d]$ and $[l]$ represents the mole fractions of the individual enantiomers d and l.

From the above equation it follows,

$$\%\ \text{of } d \text{ or } l = \frac{ee + 100}{2}, \text{ for the major component}$$

$$\%\ \text{of } d \text{ or } l = \frac{100 - ee}{2}, \text{ for the minor component}$$

Optical activity can be measured in a mixture of enantiomers if these are present in unequal amounts. Using the value of the measured rotation, one can calculate the composition of such a mixture. For example, if a solution of (+) alanine from a fossal displays an $[\alpha]$ of only 4.25 (*i.e.* one-half of the value for the pure enantiomer), one can conclude that 50% of the sample is pure (+)-isomer while the other 50% is racemic. It is said to have 50% enantiomer excess. Because the racemic portion consists of equal amounts of (+) and (–), the actual composition of the sample is 75% (+) and 25% (–). The 25% (–) enantiomer cancels the rotation of a corresponding amount of the (+) enantiomer. This mixture is called 50% (*i.e.*, 75%–25%) optically pure. The observed optical rotation is one-half that of the pure dextrorotatory enantiomer. Optical purity can be found from the following relationship:

$$\% \text{ Optical purity} = \left(\frac{[\alpha]_{\text{observed}}}{[\alpha]} . 100 \right) = \text{Enantiomer excess}$$

The enantiomeric excess can also be determined from NMR spectroscopy (see, schemes 1.152 and 1.154).