Stereochemistry

The way atoms (or groups of atoms) are connected to a central atom can create different molecules. The way atoms (or groups of atoms) are arranged around a central atom in space can also create different molecules. These different molecules formed of the same set of atoms are called **isomers**.

Constitutional isomers (or structural isomers)

Molecules with same molecular formula but differing in bonding connectivity are called constitutional isomers (or structural isomers). They are classified as -

(i) Chain isomer
(ii) Functional isomer
(iii) Positional isomer
(iv) Metamer
(v) Tautomer
(vi) Ring - chain isomer

Stereoisomers

The molecules with the same molecular formula but differing in the relative orientation of atoms and groups in space are called **stereoisomers** and the phenomenon is known as **stereo isomerism**. They have the same bonding connectivity but differ in the relative orientation of the atoms and groups in space.

Classification of stereoisomers:

<u>(1) Classification based on symmetric criterion:</u> According to this, stereoisomers are classified into two categories - (i) Enantiomers and (ii) Diastereomers

Enantiomers: If two stereoisomers are related to each other as object and mirror image which are not superimposable then they are called enantiomers and said to exhibit enantiomeric relationship.

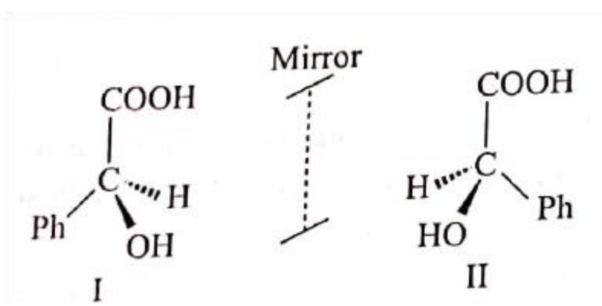


Figure: Two enantiomers of Mandelic acid

Diastereomers: Stereoisomers which are not related to each other as object and mirror image are called diastereomers and said to exhibit a diastereomeric relationship.

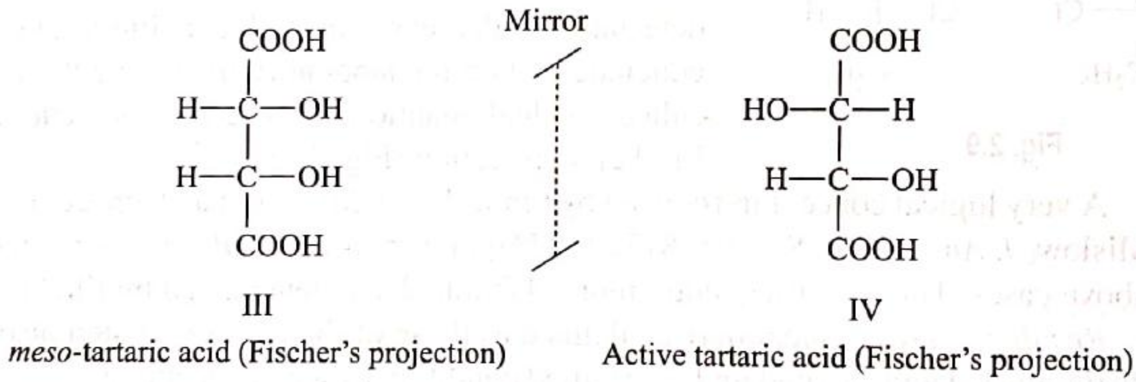


Figure: Two diastereomers of tartaric acid

Racemic modification: When equimolar quantity of the enantiomers of a chiral molecule is mixed together or formed in a reaction, the resultant mixture is called a racemic modification or racemate or simply (±) or (dl) pair. Racemic mixtures differ from the corresponding pure enantiomer in certain physical properties especially in a solid state.

Difference between enantiomers and diastereomers:

(1) Enantiomers being mirror images of each other are related by symmetry elements such as σ-plane, *i* and S_n axis. But diastereomers are not related by any such symmetry element.

(2) Since a molecule can have only one mirror image, enantiomers can only exist in pairs. On the other hand, a molecule can have any number of diastereomers.

(3) In a chiral molecule, the atoms have exactly the same relative positions with respect to interatomic distances and interactions in its enantiomers. In contrast, diastereomers differ in spatial relationship of atom and groups. Thus, enantiomers differ only in their topography. But, diastereomers differ both in geometry and topography. Consequently, enantiomers have the same b.p., m.p., densities, solubilities, refractive indices, dipole moment etc. They show same reactivity towards a chiral reagent. In contrast, diastereomers differ in spatial relationship of atom and groups and therefore, they differ in all above mentioned properties.

(2) Classification based on energy criterion:

(i) **Configurational isomers**: Stereoisomers separated by high energy barrier (> 100 KJ mol^{-1}), are quite stable and at room temperature, are isolable. They are called configurational isomers.

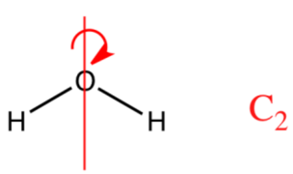
(ii) **Conformational isomers**: Stereoisomers, separated by relatively low energy barrier (< 60 KJ mol^{-1}), easily interconvertible at ambient temperature are known as conformational isomers.

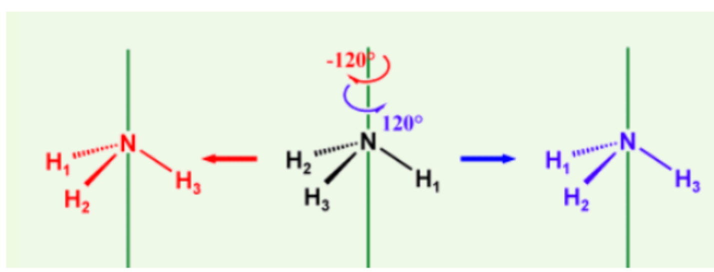
- Changing the configuration of a molecule always means that bonds are broken.
- A different configuration is a different molecule.
- Changing the conformation of a molecule means rotating about bonds, not breaking them.
- Conformations of a molecule are readily interconvertible and all are the same molecule.

Symmetry elements:

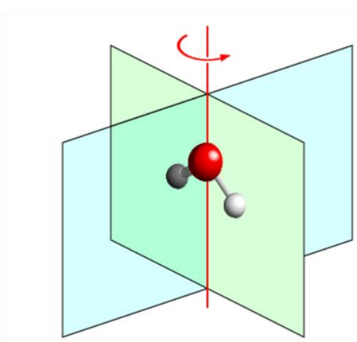
(1) Simple or proper axis of symmetry (C_n): If a molecule is rotated around an imaginary axis by an angle of 360/n and arrives at an arrangement indistinguishable from the original, the axis is called an *n*-fold proper axis of symmetry (C_n) or a simple axis of order '*n*'. The axis is designated by C_n and the corresponding symmetry operation is called C_n operation.

e.g.: H_2O has got a C_2-axis. NH_3 has C_3-axis. C_6H_6 has one C_6 axis and six C_2 axis.





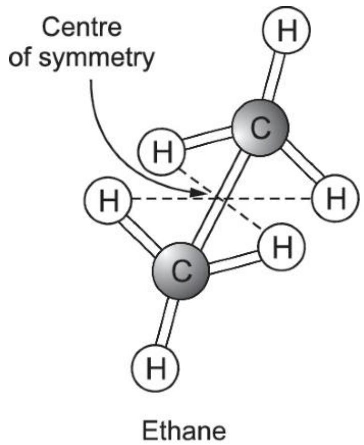
(2) Plane of symmetry (σ): A plane of symmetry is defined as an imaginary plane which divides the molecule into two halves which are mirror images of each other. [1] The plane is designated as σ plane and the operation is called σ operation. e.g.: H_2O has two mutually perpendicular σ-planes. Chloroform has three, benzene has 1-horizontal plane and 6-vertical planes.

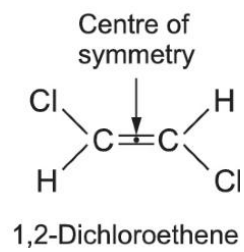


(3) Centre of symmetry (Inversion Centre (*i*):

A centre of symmetry or an inversion centre is a point within a molecule such that if an atom is joined to it by a straight line and the line which is extrapolated to an equal distance beyond it in opposite direction, meets an equivalent atom.

e.g., Staggered ethane, trans-1,2-dichloroethene, each has got one centre of symmetry.





(4) **Improper or alternating axis of symmetry or Rotation-reflection axis of symmetry**:

An improper axis of order 'n' is a (n-fold) axis, such that a rotation of 360/n around it followed by reflection in a plane perpendicular to the axis generate structure which is indistinguishable from the original. e.g. Allene has S_4 axis.

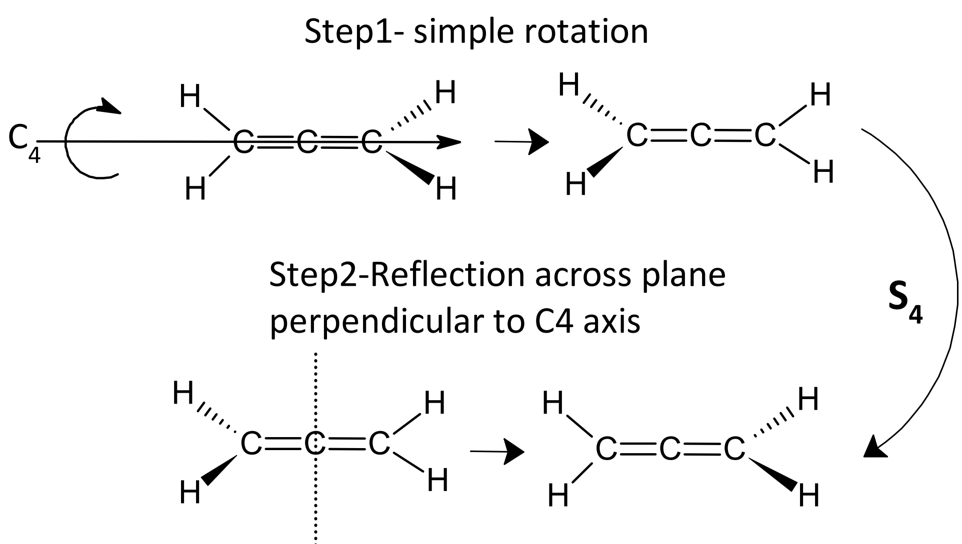
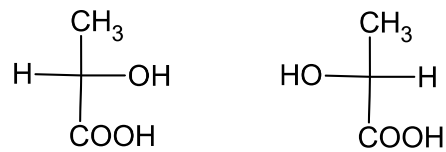


Figure: Allene has an S_4 axis of symmetry

Chirality, optical activity and Molecular symmetry:

A molecule having a mirror image which is superimposable on the original is called **achiral**. A molecule having a mirror image which is not superimposable on the original is called **chiral**. Such molecules have two distinct species each of which are called **enantiomers**, which are related to each other as object and mirror image.

e.g. Lactic acid exists in two forms which are mirror images of each other, but not superimposable.



Two enantiomers of Lactic acid

Chirality is a necessary and sufficient condition for the occurrence of enantiomerism. Any material that rotates the plane of polarized light is said to be **optically active**. Chiral molecules are optically active. Enantiomers rotate the plane of polarized light in the opposite directions though in equal amounts. The isomer which rotates the plane of polarized light towards left is called **laevorotatory** and it is represented as prefix '*l*' or (-). The isomer which rotates the plane of polarized light towards right (clockwise) is called **dextrorotatory** and it is represented by the prefix *d* or (+).

For a molecule to be optically active (chiral) it must be **dissymmetric**. A molecule is dissymmetric if it does not possess an Sn axis. A molecule is said to be **asymmetric** if all the symmetry elements are absent except for the trivial C1-axis. Asymmetry is a sufficient condition for a molecule to be optically active, but it is not a necessary condition. The necessary and sufficient condition for a molecule to be optically active is that it must be dissymmetric. A molecule will be achiral if it has got σ-plane (= S_1-axis) and a centre of symmetry (= S_2-axis).

Chiral centre and Chirality: The property of non-superposability of a molecule (as object) on its mirror image is called chirality. A tetracoordinate atom at the centre of a tetrahedron to which four different ligands are bonded is called an asymmetric centre (or a chiral centre). An asymmetric C atom is a C-atom which is connected to four different groups. It is denoted by C*. This is also known as **chiral centre**.

A molecule that contains just one chiral centre (or one chiral carbon) is always chiral and hence optically active. However, the presence of chiral centre is neither a necessary nor a sufficient condition for optical activity. Optical activity may be present in molecules with no chiral centre;

such types of chirality are known as axial chirality and planar chirality. Some molecules, despite having two or more chiral centres, are found to be optically inactive due to internal compensation.

Specific notation: The amount of rotation (α) is not a constant for a given enantiomer. It depends on the length of the sample vessel, temperature of the solvent, concentration of the solution of the stereoisomer, and the wavelength of the light. Therefore, Specific rotation [α] is defined as-

$$[\alpha]_{\lambda}^{T} = \frac{\alpha}{l \times c} \ for\ solution$$

$$[\alpha]_{\lambda}^{T} = \frac{\alpha}{l \times d} \ for\ pure\ liquids$$

where, α is the observed rotation, *l* is the length of the sample cell in *dm*, c is the concentration in g/mL, d is the density in g/mL

Prob: The observed rotation of 2.0 g of a compound in 10 mL of solution in a polarimeter tube 25 cm long is +134°. What is the specific rotation of the compound?

Sol^{n}: Specific rotation is given by

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

α → observed rotation

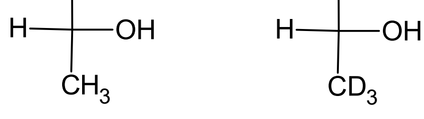
l → length of polarimeter tube (dm)

c → concentration of solution (g/mL)

Here, α = +134°, c = 2.0 / 10 g/mL= 0.2 g/mL, *l* = 25 cm = 2.5 dm

$$[\alpha]_{\lambda}^{T} = \frac{134^{0} \times 10}{2.5 \times 2.0} = 268^{0}$$

Cryptochirality: This refers to the phenomenon where a small change in a molecule (like isotopic substitution) leads to the creation of chirality. Propanol-2 is not chiral. However, replacement of H in one CH_3 by the isotope D imparts chirality to the molecule. Thus, the deuterated isopropanol shows a specific rotation of 0.27°. Such phenomenon of imparting chirality to a molecule by very small structural difference is called "crypto chirality".



Not chiral Chiral, specific rotation=0.27∘

Questions:

1. Define the following terms with examples:
   (a) Stereoisomer
   (b) Enantiomer
   (c) Diastereomer
   (d) Racemic modification
   (e) Laevorotatory
   (f) Dextrorotatory
   (g) Dissymetric molecule
   (h) Asymmetric molecule
   (i) Chiral centre
   (j) Specific rotation
2. Differentiate the following:
   (a) Enantiomer and diastereomer
   (b) Configurational isomer and conformational isomer
   (c) Asymmetry and dissymmetry
   (d) Meso compound and racemic modification
3. What is cryptochirality? Discuss with an example.
4. ‘Asymmetry is a sufficient condition for a molecule to be optically active but it is not a necessary condition.’ Justify the statement.
5. “Dissymmetry is the necessary and sufficient condition for a molecule to be optically active.” Justify the statement.
6. “The presence of chiral centre is neither a necessary nor a sufficient condition for optical activity.” Justify the statement.