

STEREOCHEMISTRY

Stereochemistry is a unique part of chemistry concerned with the study of the spatial arrangement of atoms and molecules in the compound, its effect on chemical reaction and relations to the properties of compounds. It is also known as 3D chemistry. Different enantiomers have different selectivity for biological targets and have different biological actions. Hence, stereochemistry have great importance in pharmaceutical industry.



Stereoisomers

The isomers that are different from each other only in the way the atoms are oriented in space are called stereoisomers.

Absolute Configuration (R and S system of nomenclature)

In order to designate absolute configurations a system of nomenclature called *Cahn-Ingold-Prelog system* has been developed.

- Assign priority to the groups attached. Higher atomic number will get higher priority.
- The H atom or group of lowest priority is brought vertically in Fischer projection.

Enantiomers

Stereoisomers having non superimposable mirror images are optically active and these are called enantiomers.

d-enantiomer
Rotates the plane
polarised light

towards right.

l-enantiomer
Rotates the plane
polarised light
towards left.

Meso form

If plane of symmetry is present in the molecule then, one of the isomer will be optically inactive due to internal compensation because half of the molecule will rotate the plane polarised light towards right and another half towards left. So, total rotation of plane polarised light will be zero.

R-configuration

HO
$$\stackrel{\overset{\leftarrow}{\longleftarrow}}{\underset{H}{\longleftarrow}}$$
 CH₂OH

Move the arrow in order of decreasing priority. If it rotates clockwise, configuration is *R* (*rectus*) configuration.

Diastereomers

Stereoisomers that are not mirror images of each other are called diastereomers.

Number of stereoisomers

The number of stereoisomers depends on structure and number of asymmetric carbon atoms present in the molecule.

In unsymmetrical molecule

Number of enantiomers = 2^n

Meso forms = 0

Total optical isomers = 2^n where, n = number of chiral or asymmetric carbon atoms.

In symmetrical molecule

- When n is odd, Number of enantiomers $= 2^{(n-1)} - 2^{(0.5n - 0.5)}$ Meso forms = $2^{(0.5n - 0.5)}$ Total optical isomers = $2^{(n-1)}$
- When *n* is even, Number of enantiomers = $2^{(n-1)}$ Meso forms = $2^{(n/2-1)}$ Total optical isomers = $2^{(n-1)} + 2^{(n/2-1)}$

S-configuration

HOH₂C
$$\stackrel{\stackrel{?}{\leftarrow}}{\stackrel{\circ}{\leftarrow}}$$
 OH

Move the arrow in order of decreasing priority. If it rotates anticlockwise, then the configuration is S (sinister) configuration.

Racemic mixture

If both d and l enantiomers present in equal amount (50-50%) then the mixture is optically inactive due to external compensation, the mixture is known as racemic mixture.

Resolution of racemic mixture

The process of separation of a racemic mixture into *d*- and *l*-forms is called *resolution*.

Following are the methods by which a racemic mixture can be resolved:

- Mechanical separation
- Biochemical separation
- Chemical separation
- Chromatographic method
- Selective adsorption method

Racemisation

Conversion of (+) or (-) isomer into its racemic mixture (±) is known as racemisation. It is reverse of resolution and can be carried out either by heat, light or use of chemical reagents, etc.