Isomerism

By

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Isomers & Isomerism

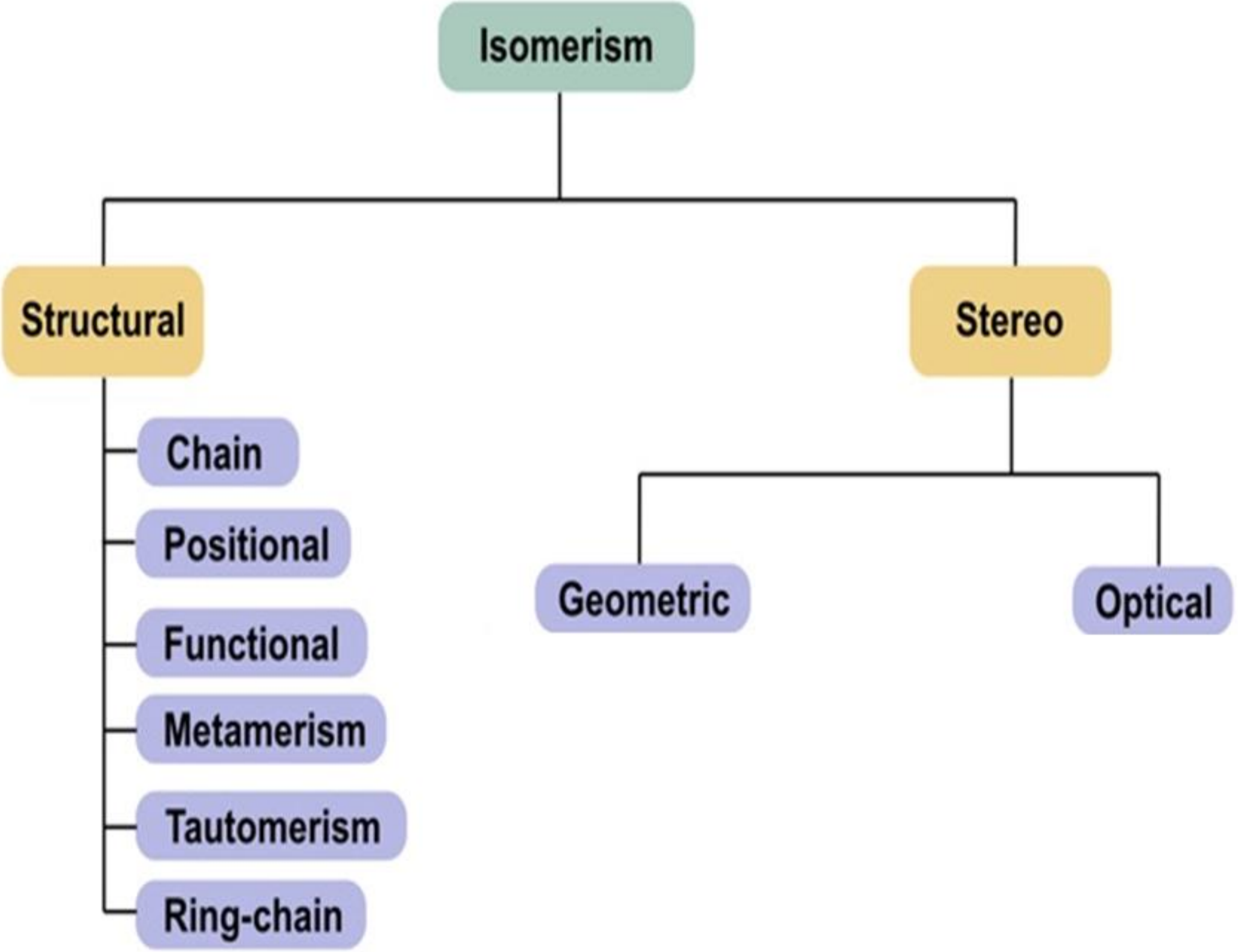
Isomers are molecules with the same molecular formula, but different arrangements of atoms.

The phenomenon of same molecular formula but different arrangement of atoms, causing different physical and chemical properties, is called as Isomerism.

Example

Molecular Formula C_2H_6O

CH_3-O-CH_3	**CH_3CH_2OH**
Dimethyl ether	**Ethyl Alcohol**



Isomerism

Structural

- Chain
- Positional
- Functional
- Metamerism
- Tautomerism
- Ring-chain

Stereo

- Geometric
- Optical

Types of Isomers

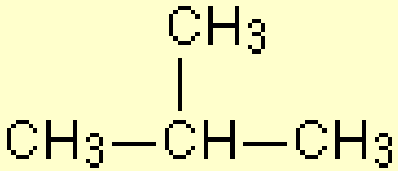
1. Structural Isomers: the atoms are arranged in a completely different order.

Types of structural isomerism

a. Chain isomerism: It occurs when carbon atoms are linked to the main chain in different ways.

$CH_3-CH_2-CH_2-CH_3$

Butane

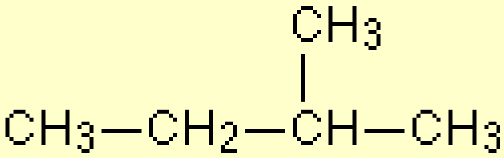


$CH_3-\overset{\overset{\displaystyle CH_3}{|}}{CH}-CH_3$

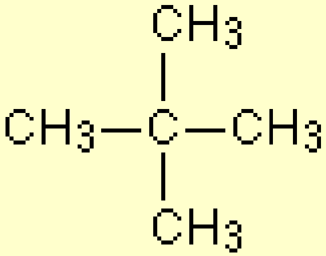
2-methylpropane

C_5H_{12} Pentane

$CH_3-CH_2-CH_2-CH_2-CH_3$



$CH_3-CH_2-\overset{\overset{\displaystyle CH_3}{|}}{CH}-CH_3$

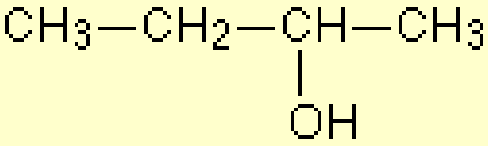


$CH_3-\underset{\underset{\displaystyle CH_3}{|}}{\overset{\overset{\displaystyle CH_3}{|}}{C}}-CH_3$

b. Position Isomers: It occurs when functional groups are attached on different positions on a carbon chain.

$CH_3-CH_2-CH_2-CH_2-OH$

butan-1-ol

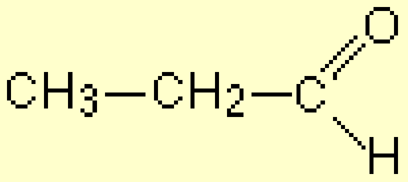


$CH_3-CH_2-\underset{\underset{\displaystyle OH}{|}}{CH}-CH_3$

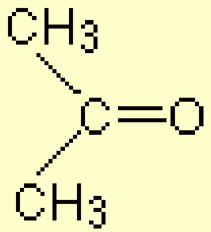
butan-2-ol

c. Functional Group Isomers: due to different arrangements of atoms leading to different functional groups.

(C_3H_6O)

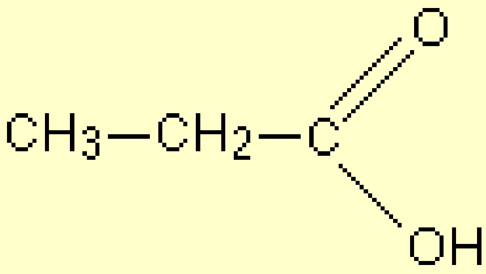


propanal

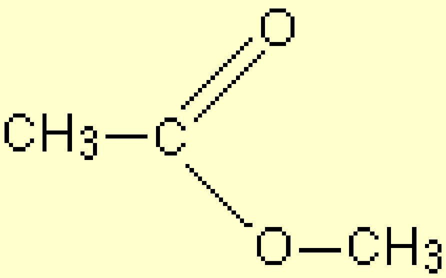


propanone

($C_3H_6O_2$)



propanoic acid



methyl ethanoate

d. Metamerism

This form of isomerism is rare and is limited to molecules having a divalent atom like O or S and alkyl groups around it.

$H_3C\text{-}CH_2\text{-}CH_2\text{-}O\text{-}CH_3$

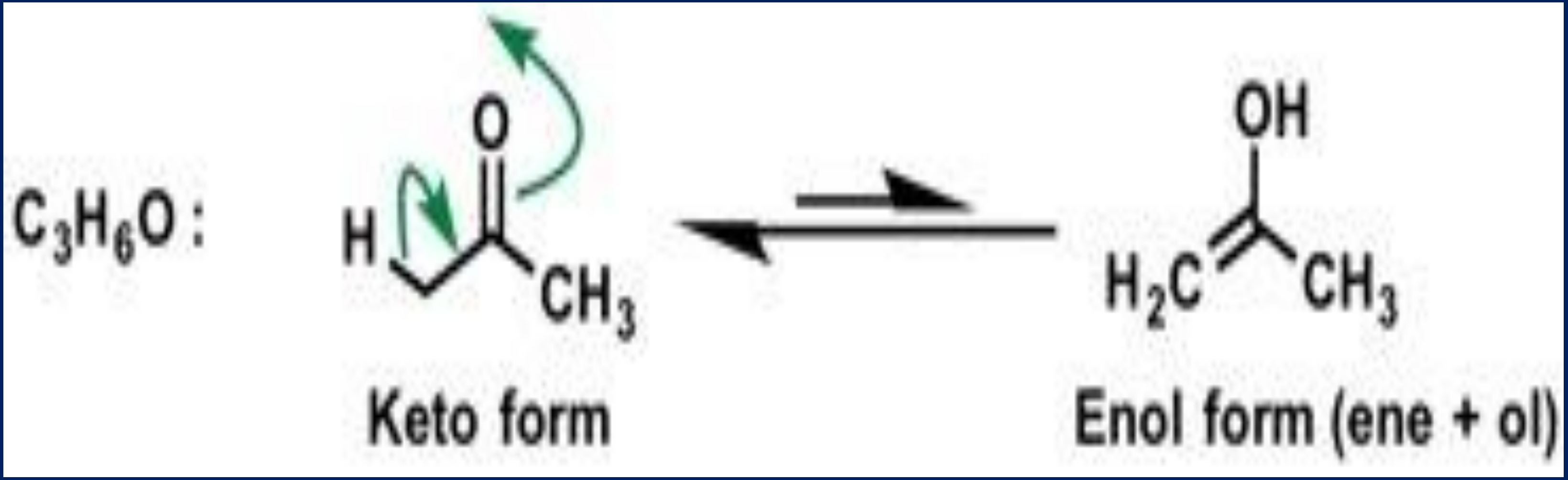
Methoxy Propane

$H_3C\text{-}CH_2\text{-}O\text{-}CH_2\text{-}CH_3$

Ethoxy ethane

e. Tautomerism

This isomerism is due to spontaneous inter conversion of two isomeric forms with different functional groups. For this, the presence of the C=O, and an alpha H atom. The most usual is the ‘keto-enol’ tautomerism,



f. Ring-Chain isomerism

Here one isomer is an open chain molecule and the other a cyclic molecule.

C_3H_6

$CH_3\text{-}CH{=}CH_2$

Propene

Cyclopropane

C_4H_8

$CH_3\text{-}CH_2\text{-}CH{=}CH$

Buteene

Cyclobutane

2. STEREOISOMERISM

Stereo Isomers are molecules that have the same molecular formula, but have a different arrangement of the atoms in space. Stereo isomerism arises due to different spacial arrangement of atoms in a molecule.

Types of stereoisomerism

a. **Optical Isomerism**

b. **Geometrical Isomerism**

a. Optical Isomerism

Optical isomers rotate the plane polarized light clockwise or anticlockwise, this phenomenon is called as optical isomerism. The optical isomers have different behavior towards plane polarized light.

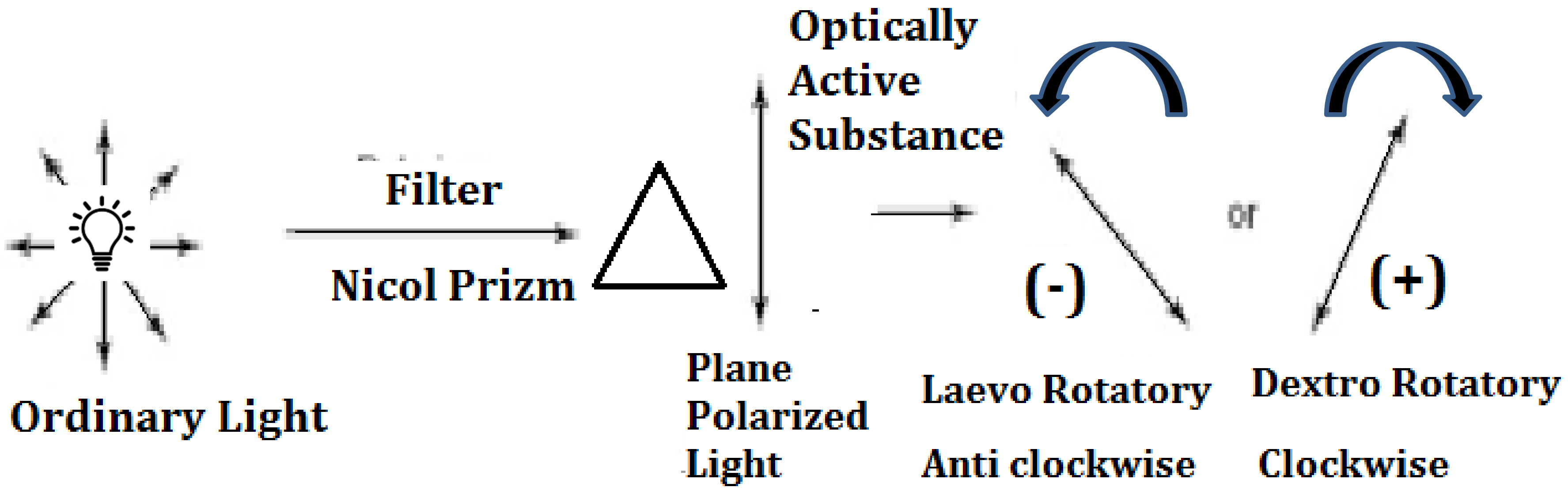
Enantiomers

Simple substances which show optical isomerism exist as two isomers known as **Enantiomers**. There mirror images are non super imposable.

i. Dextro Rotatory (+) Form (rotates clockwise)

ii. Laevo Rotatory (-) Form (rotates anticlockwise)

When a plane polarized light is passed through a compound, the plane of polarization is rotated either clock wise or anticlockwise, this phenomenon is called as Optical activity and the compounds are called as optically active compound (Enantiomers).



Nicol Prizm is type of transparent $CaCO_3$

A **Nicol Prism** is a type of polarizer, an optical device made from calcite crystal (a type of transparent $CaCO_3$) used to produce and analyze plane polarized light.

Dextro Rtatory

The enantiomer which rotates the plane of polarization in a clockwise direction, is known as the **(+)** form or Dextro Rotatory.

Laevo Rotatory

The enantiomer which rotates the plane of polarization in an anti-clockwise direction, is known as the **(-)** form or Leavo Rotatory.

Racemic Mixture

An equimolar mixture (50-50) of dextro and laevo rotatory enantiomers shows no optical activity. This is known as a ***racemic mixture*** or ***racemate***. It has no effect on plane polarized light i.e. **Optically Inactive.**

Optical activity:

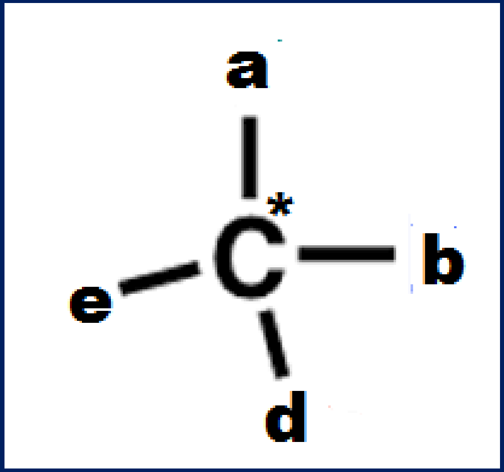
“Optical activity is the property of optically active compounds to rotate the plane of plane-polarized light.”

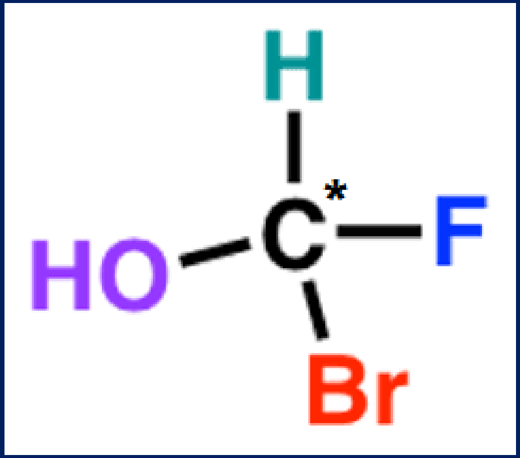
Conditions for Optical activity:

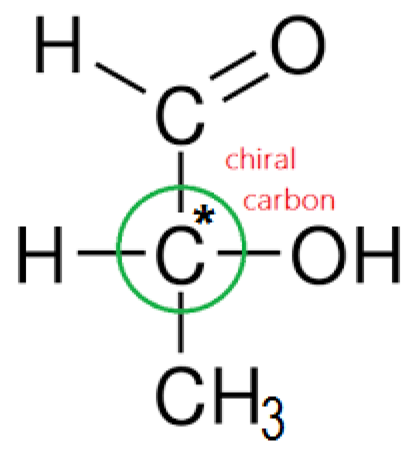
a. There must be an asymmetric carbon atom present in a compound.
b. The compounds should be non-superimposable mirror images of each other.
c. There should not be an element of symmetry in the molecule.
d. The molecule should possess a chiral axis and chiral plane.

Chiral Carbon or Asymmetric Carbon atom

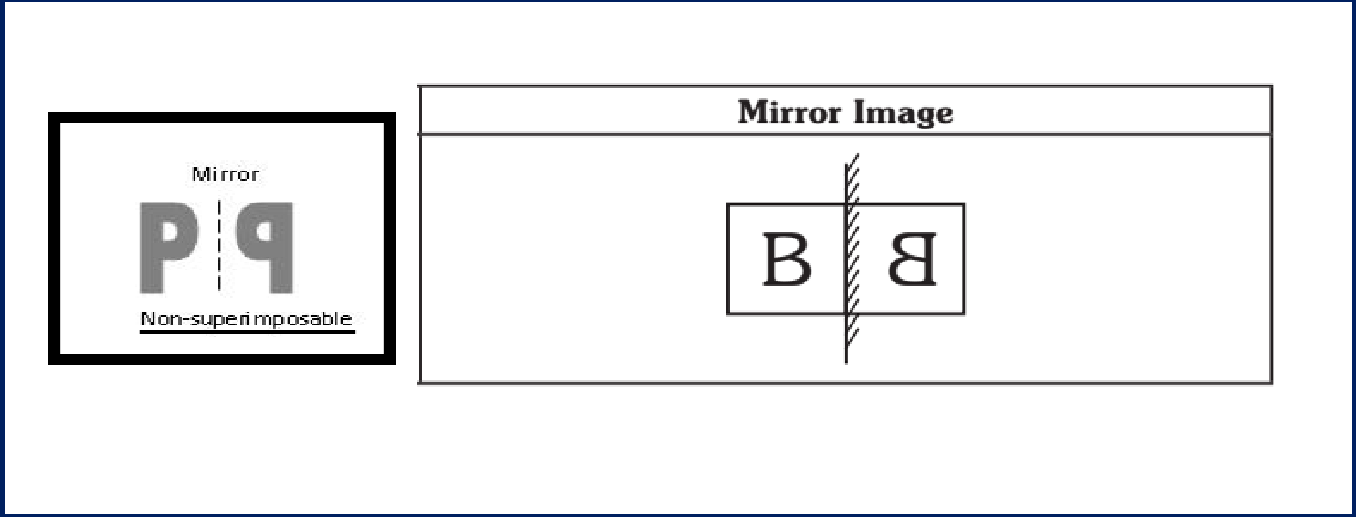
All the four valencies of carbon are satisfied fith four different atoms or groups

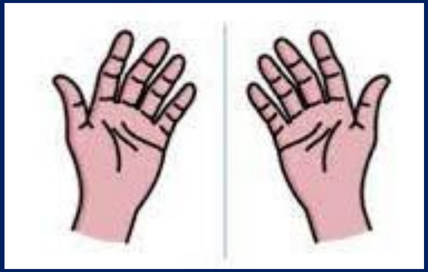


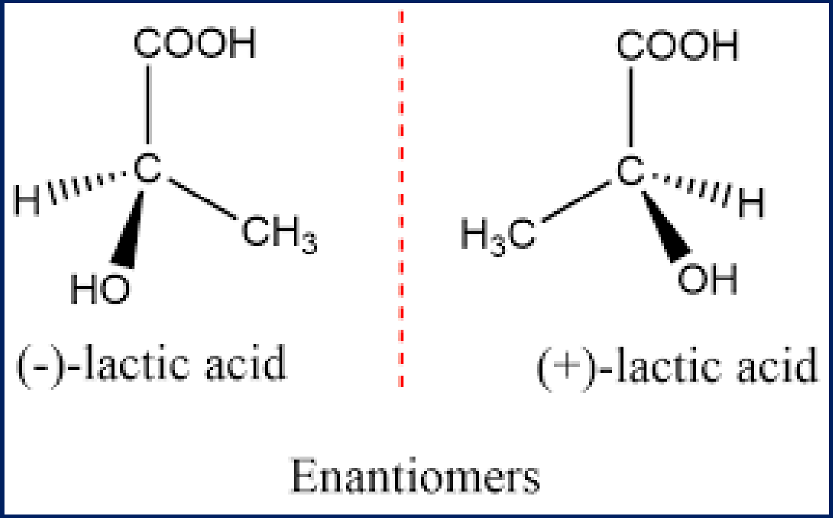




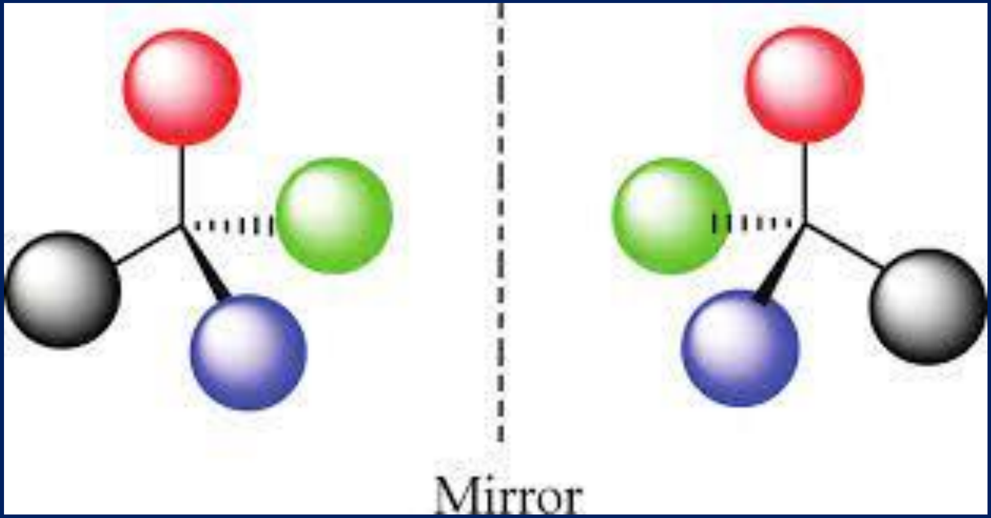
Non Superimposable images (Enantiomers)





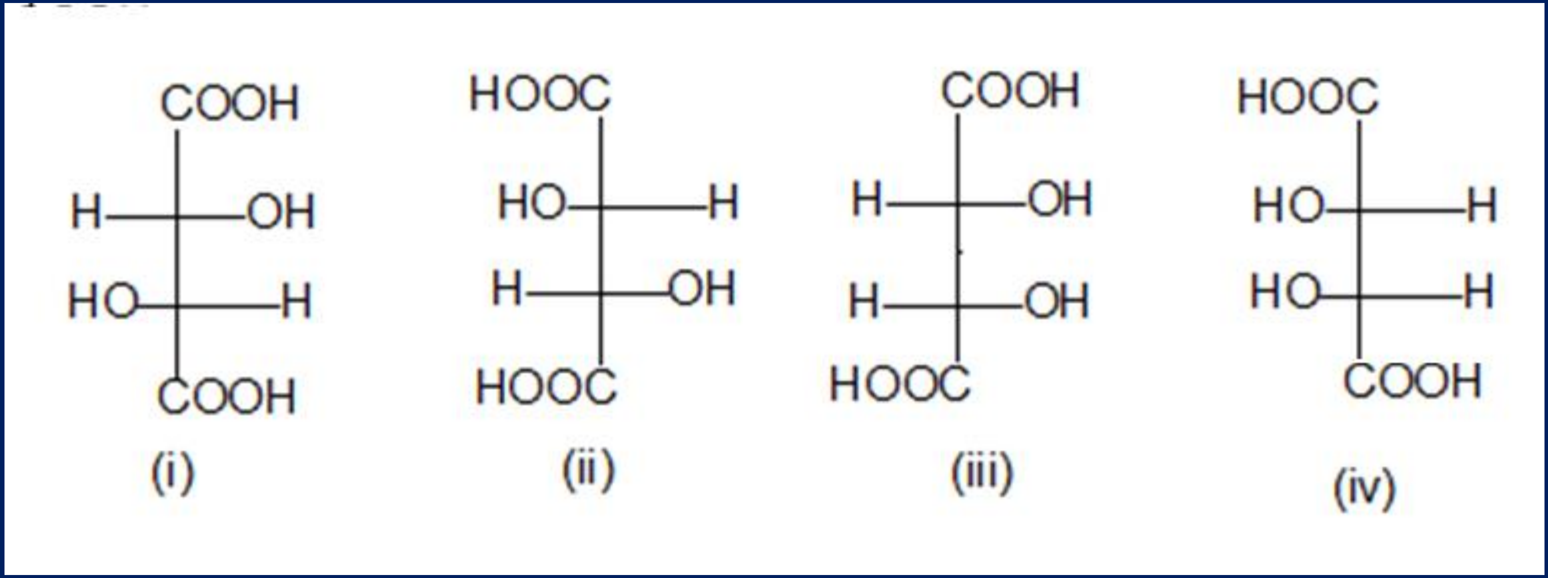


Enantiomers



Diastereomers

Diastereomers are defined as a pair of compounds which have the same molecular formula and sequence of bonded elements but which are non-superimposable, non-mirror images. Diastereoisomerism is found only, in those compounds in which at least two chiral carbon centers are present.

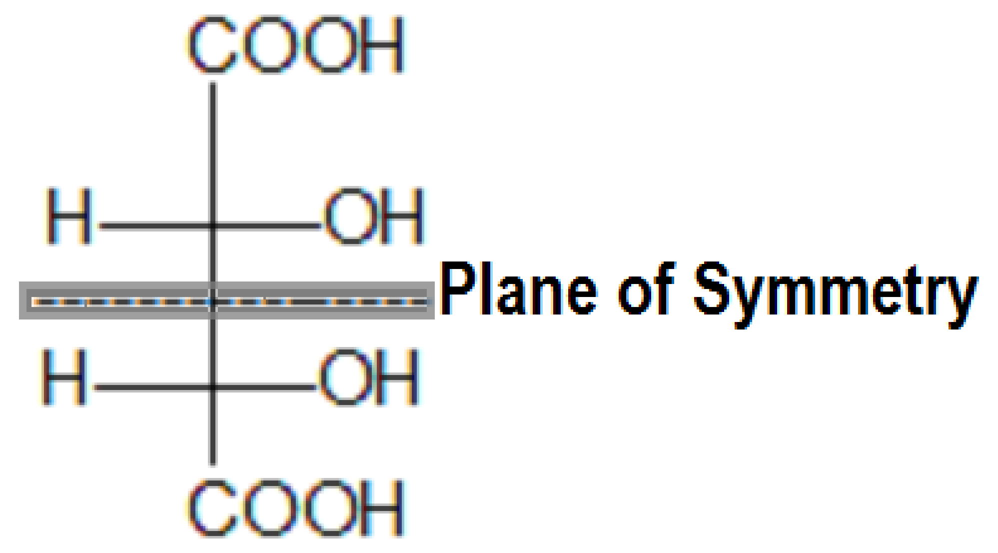


(i) & (iii) and(ii) & (iv) are pair of deiasteroisomers

Total numer of stereoisomrs = 2^n, where n is number of chiral carbon atoms

Meso Compound

An achiral compound with chiral centres is known as a meso compound. Although it has two or more stereocenters, a meso compound has an internal plane of symmetry that makes it superimposable on its mirror image and is optically inactive.



Optical activity in the absence of chiral carbon

Stereoisomerism in organic compounds is usually based on chiral centres acting as stereogenic units.

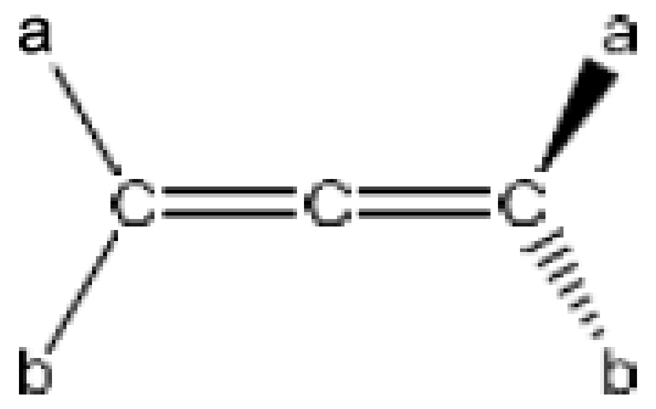
Two other elements of chirality (axes and planes) also behave as stereogenic units.

Hence, compounds such as allenes, hemispiranes, spiranes and biphenyls exhibit optical activity even in the absence of a chiral carbon.

These two elements of chirality are called stereoaxis and stereoplanes.

i. Allenes and Spiranes

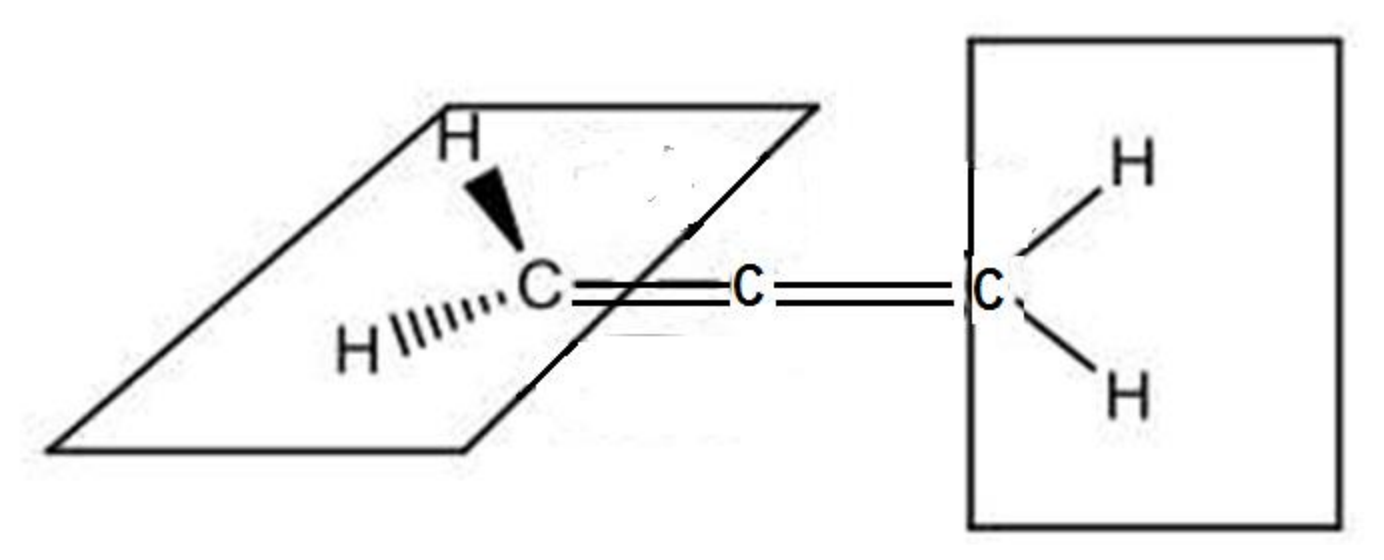
An allene is said to be chiral if the two substituents at each end are different from each other (a≠ b).



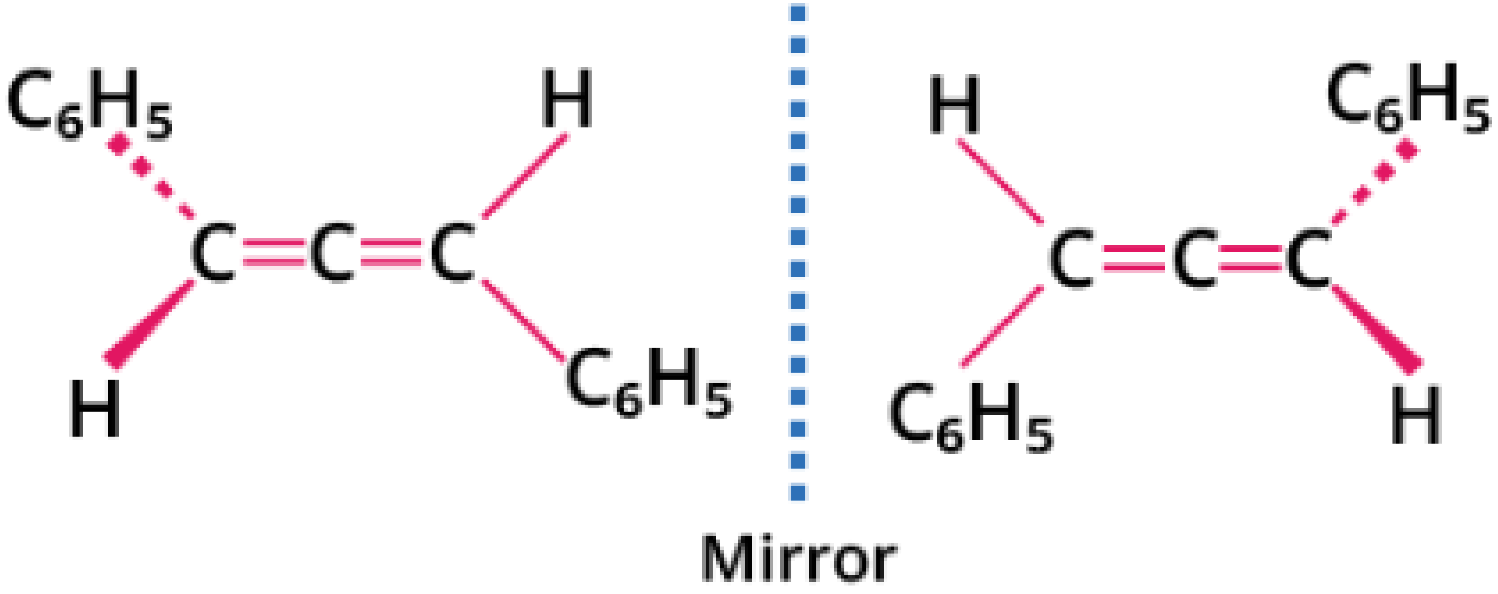
In an allene, the central carbon is sp hybridized and linear and the two other carbon atoms are sp2 hybridized and trigonal.

In allene, the C=C=C is a potential chiral axis.

The two double bonds lie in perpendicular planes. Hence unsymmetrical substituents give chirality to the molecule



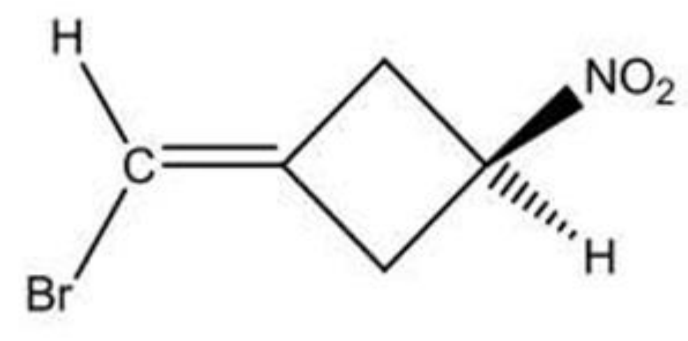
The two methylene groups are perpendicular.



1, 3 - Diphenyl propadiene

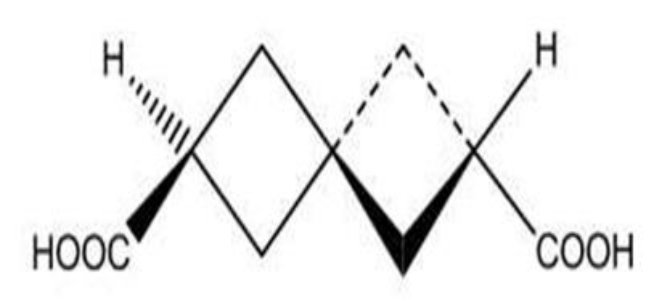
ii. Hemispirane

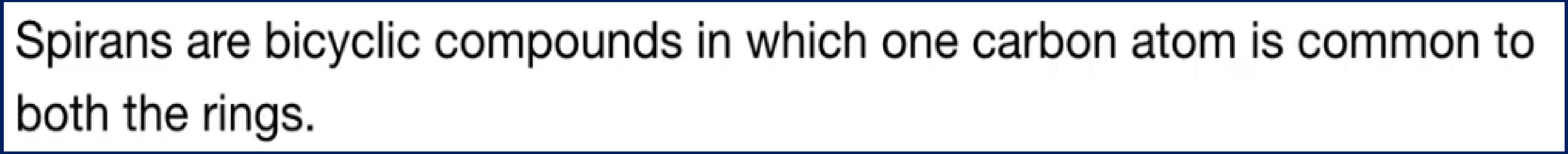
The replacement of one double bond in allene with a ring gives a hemispirane. These type of molecules are also chiral provided the groups at each end are not identical.

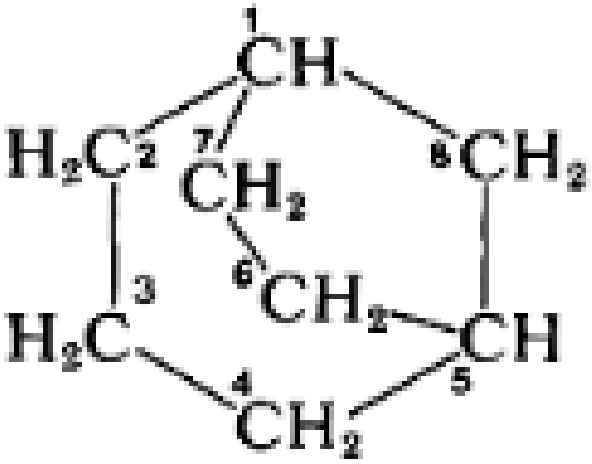


iii. Spirane

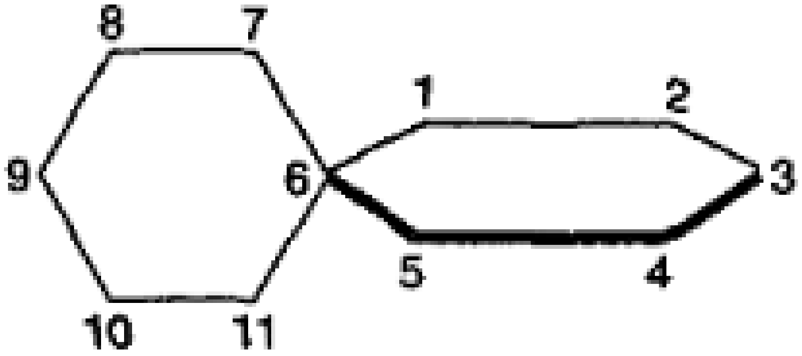
The replacement of both double bonds from alenes by ring systems gives a spirane. Similar rules of optical activity apply here.




Spirans are bicyclic compounds in which one carbon atom is common to both the rings.



bicyclo[3.2.1]octane



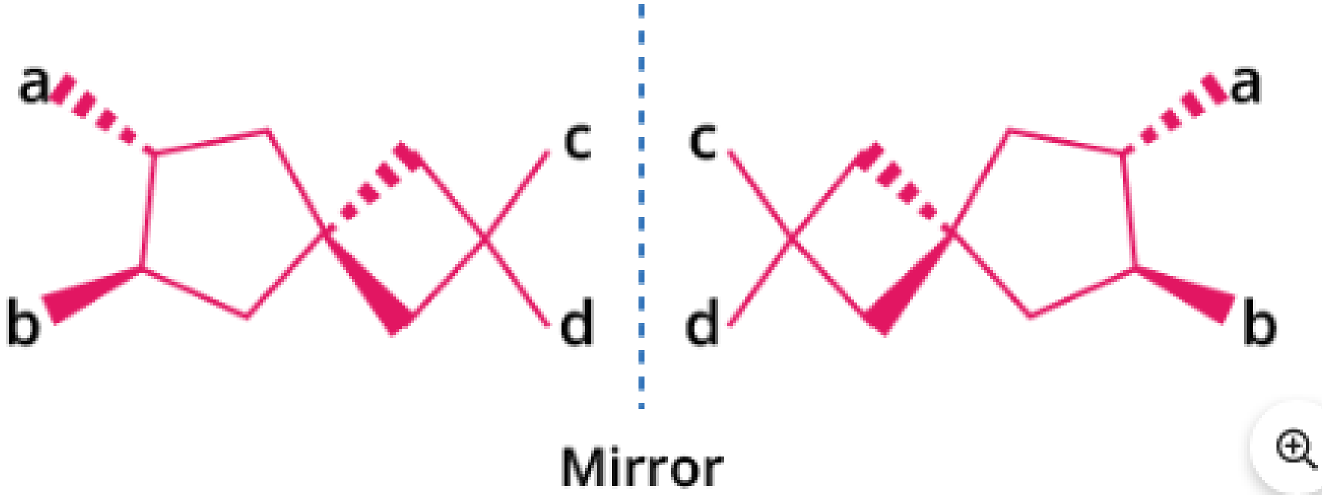
spiro[5.5]undecane

Why spirans are optically active?

Spiranes can be chiral due to its twisted structure.

Examination of formula of spirans shows that the two rings are perpendicular to each other, and hence suitable substitution will produce molecules with no elements of symmetry.

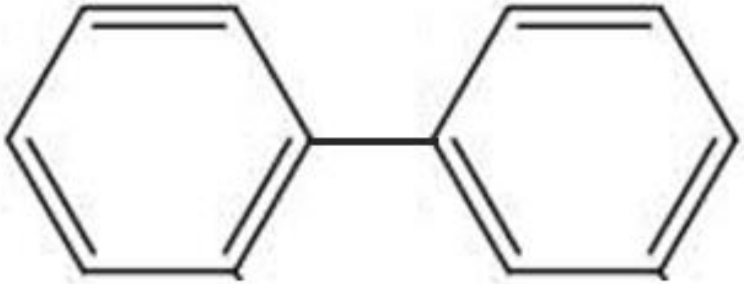
So the optical activity of the spirans are due to the asymmetry of the molecule as a whole, thereby giving rise to optically active forms.



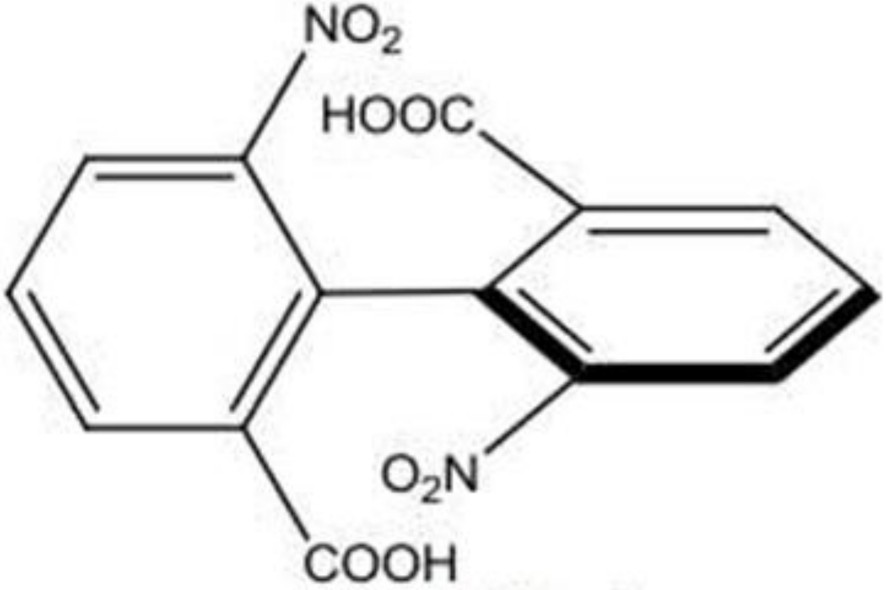
Optical isomerism in unsymmetrical spiro compound

Optical activity in Biphenyls

a. The biphenyl compounds having a proper substitution at the ortho-position of benzene rings resulting in steric hindrance. This steric hindrance makes the biphenyl system non-planar and hence optically active compounds.
b. The two rings lie in different planes which are perpendicular to each other.
c. Chiral biphenyls must contain two different ortho substituents on each ring.
d. In order to display optical activity, the substituents in the ortho position must be large enough to prevent the two rings from becoming coplanar.



Achiral



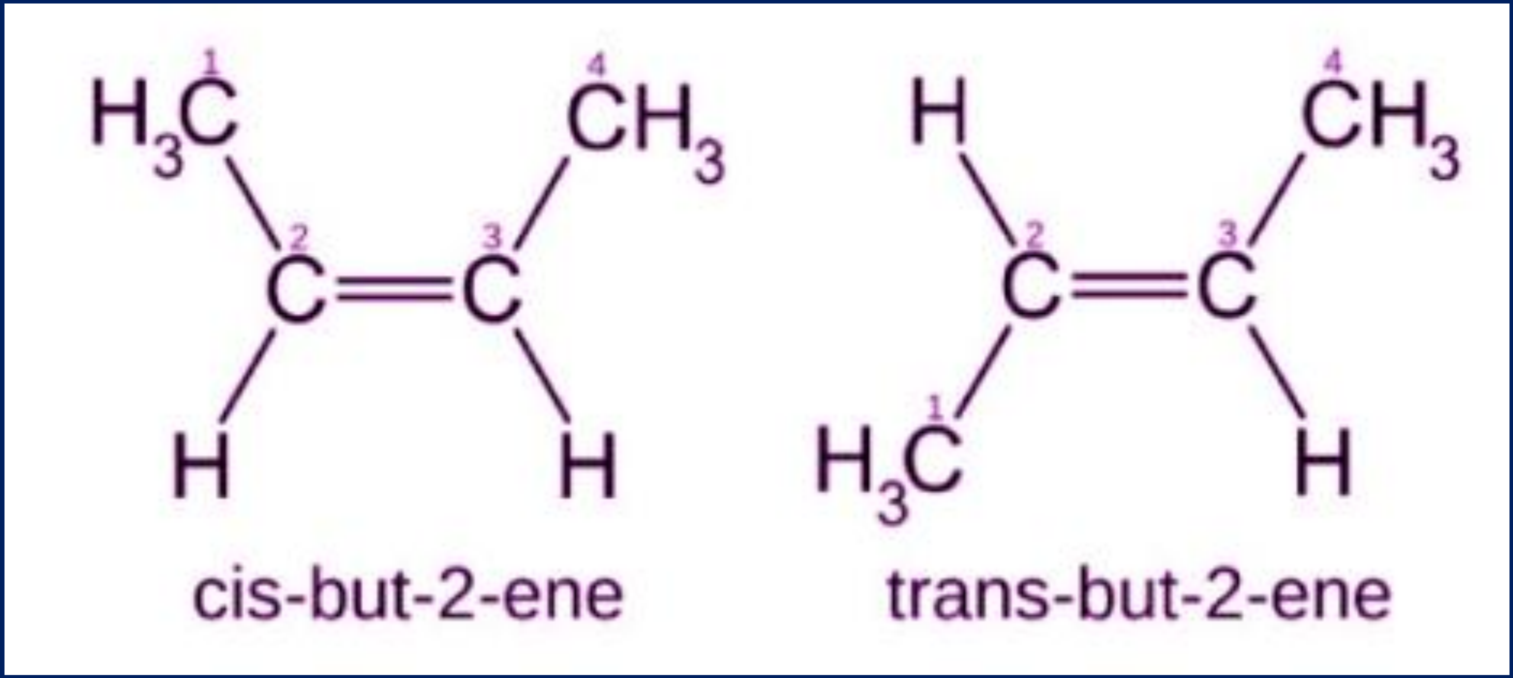
Chiral

Geometric isomerism (also known as cis-trans isomerism or E-Z isomerism)

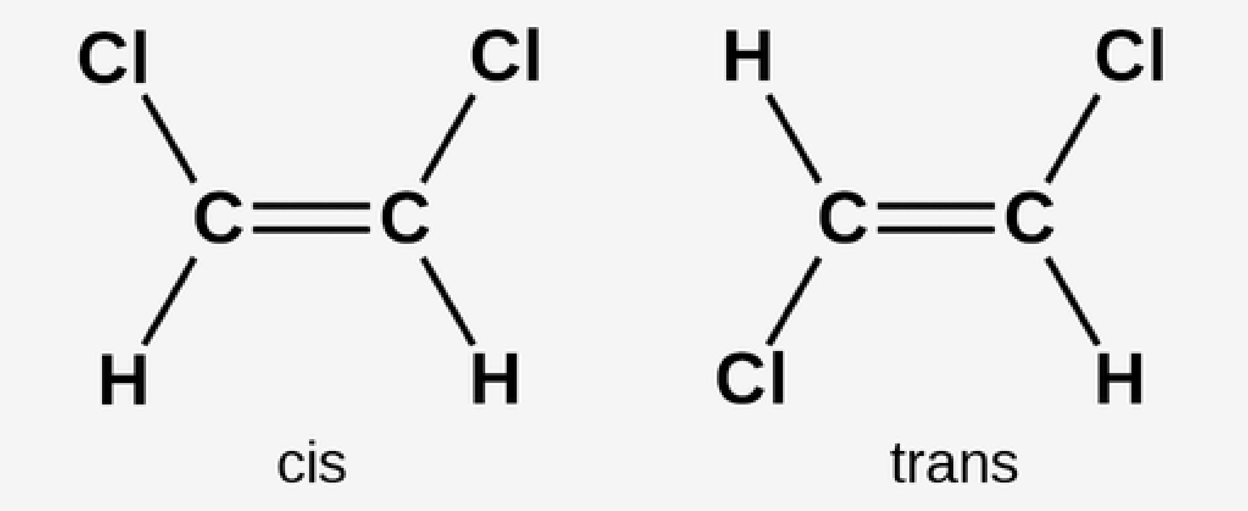
Geometrical isomers occurs as a result of restricted rotation a carbon-carbon bond.

If there is C=C double bond (sp^2 hybridization), the carbon has a σ-bond and a π-bond. The π-bond prevents the rotation about C=C bond. As a result the atoms attached to these carbon are fixed in three dimensional space.

Cis- Similar groups at the same side of C=C bond
Trans- Similar groups at the opposite side of C=C bond

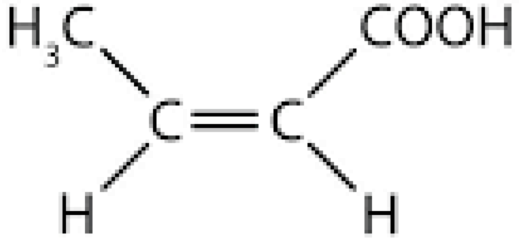


cis-but-2-ene trans-but-2-ene

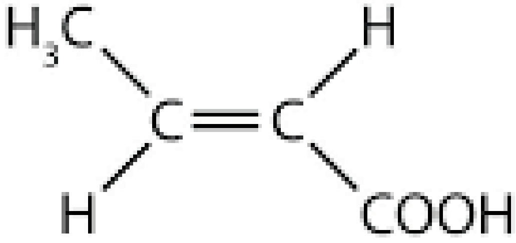


cis trans

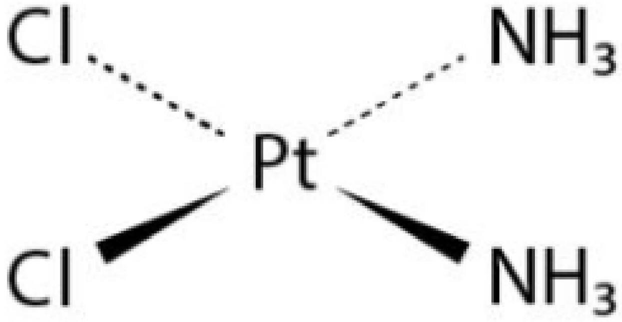
Cis-1,2-dichloroethene **Trans-1,2-dichloroethene**



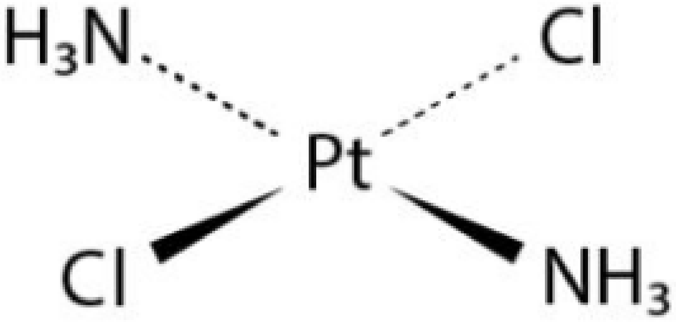
cis



trans



Cis-$[Pt(NH_3)_2Cl_2]$

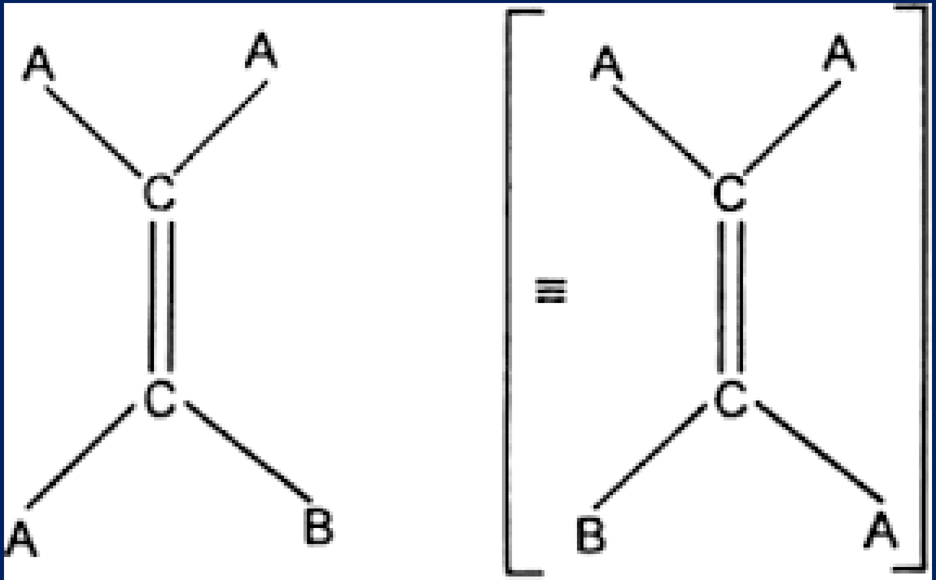


Trans-$[Pt(NH_3)_2Cl_2]$

Note:

Geometrical isomerism is exhibited by alkenes that contain two different groups on each double-bonded carbon atom.

The compound can not show geometrical isomerism in which any of the carbon (of C=C) bonded with same atoms or groups. Following compound will not show cis-Trans isomerism.



E-Z Isomerism

(E comes from the German word, Entgegen, which means opposite. Z comes from a German word, Zusammen, which means together**)**

There are problems as compounds get more complicated. For example, could you name these two isomers using cis and trans?

Because every atom attached to the carbon-carbon double (C=C) bond is different, It can not be assigned "cis" or "trans" to each other. The E-Z notations will be applied here.

Cahn–Ingold–Prelog priority rules(CIP rules) for E-Z notations

However, when a double bond is attached to three or four non-hydrogen substituents, in these situations, the IUPAC system for naming alkene isomers, called the E/Z system, is used. The E/Z system analyzes the two substituents attached to each carbon in the double bond and assigns each either a high or low priority.

Z Configuration

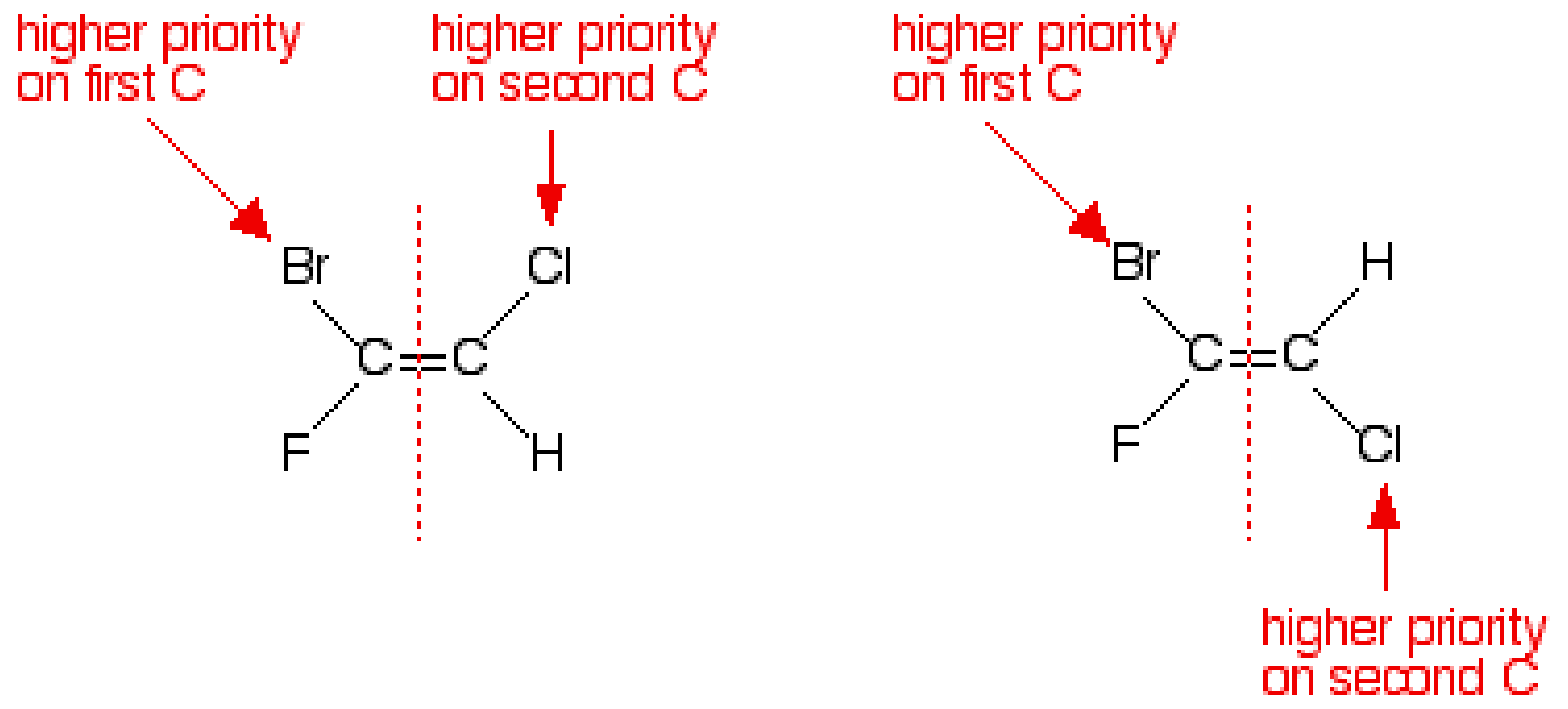
High priority substituents are on the same side of the double bond

E Configuration

High priority substituents are on opposide sides of the double bond

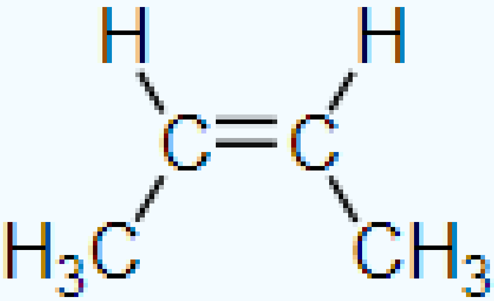
Rule-1:	The substituent whose atom has a higher atomic number takes priority over the substituent whose atom has a lower atomic number.
Rule-2:	If the first atom on both substituent are the identical, then proceed for next atom.

In the given example, at the left-hand end of the bond, it turns out that bromine has a higher priority than fluorine. And on the right-hand end, it turns out that chlorine has a higher priority than hydrogen.

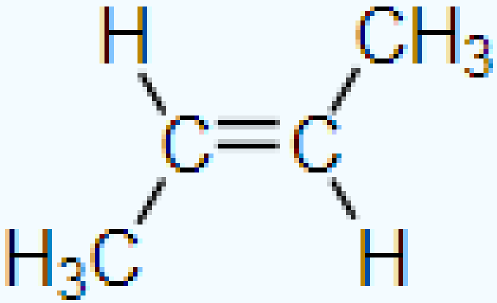


a. If the two groups with the higher priorities are on opposite sides of the double bond, then this is the (E)- isomer.

b. If the two groups with the higher priorities are on the same side of the double bond, that is described as the (Z)- isomer.



cis-2-butene
(*Z*)-2-butene

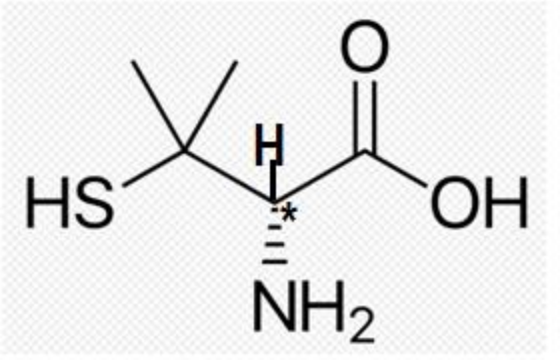


trans-2-butene
(*E*)-2-butene

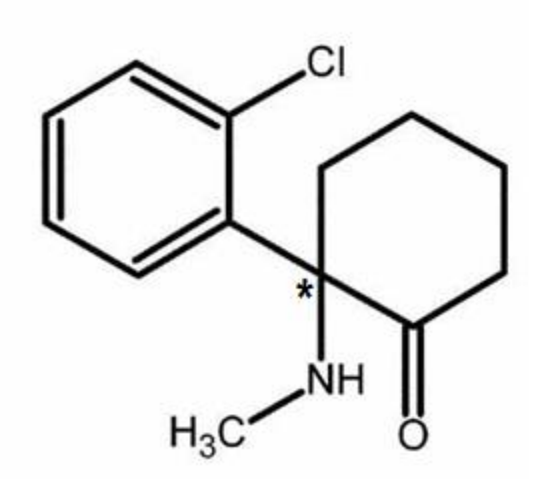
Chiral Drugs

Chemical compounds that come as mirror-image pairs are referred to as chiral compounds. Each pair is called an enantiomer. Drugs that exhibit chirality are referred to as **chiral drugs**. Chiral drugs that are equimolar (1:1) mixture of enantiomers are called racemic drugs or Racemates

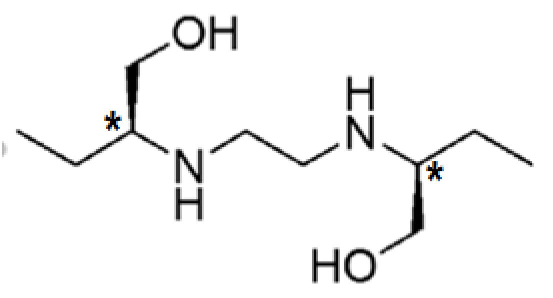
1. Penicillamine - a chiral drug with one chiral center and exists as a pair of enantiomers. Used to treat wilson's disease. Trade name Cuprimine



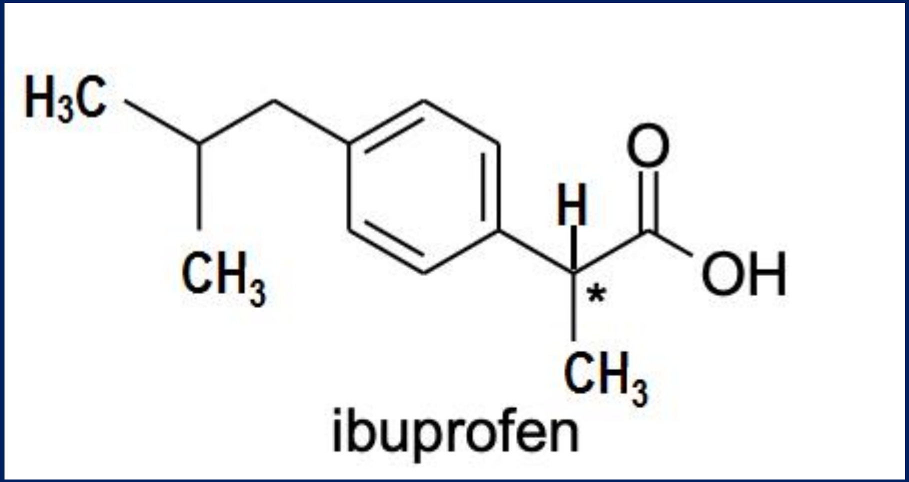
2. Ketamine - a widely used anaesthetic agent. It is a chiral molecule that is administered as a racemate.



3. Ethambutol - The antitubercular agent



4. **Ibuprofen is a widely used chiral drug**. It can be used as either analgesic or antipyretic.



Role of Chirality in drugs

1. Individual stereoisomers exhibit marked differences in pharmacoligical properties.

2. One enantiomer of a chiral drug may be a medicine for particular disease whereas; another enantiomer of the molecule may be not only inactive but can also be toxic. Hence Chirality plays an essential role in drugs.

3. Chirality support the binding affinity and interactions between the drug and its target.

4. In clinical environments, enantiomers of chiral drugs can have reduced harmful effects.