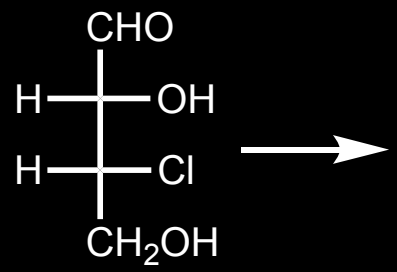
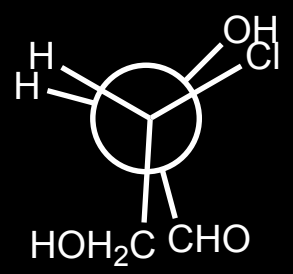
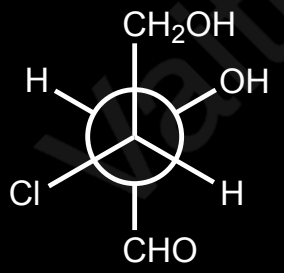
One to Projection another Projection

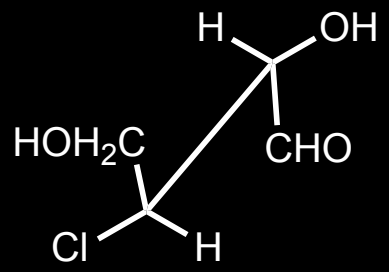
Conversion of Fischer to Newman to Sawhorse Projection



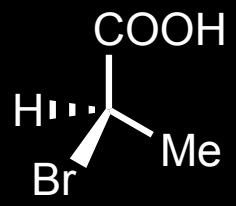


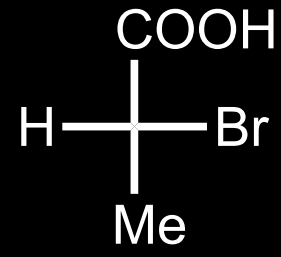
Rotate 180°



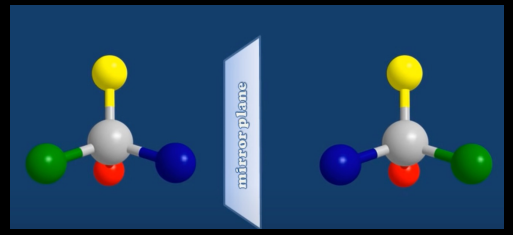


Conversion of Wedge into Fischer Projection



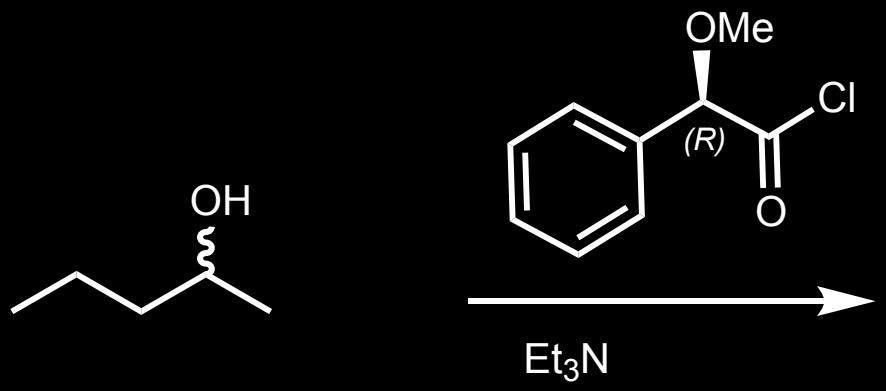


Stereochemistry



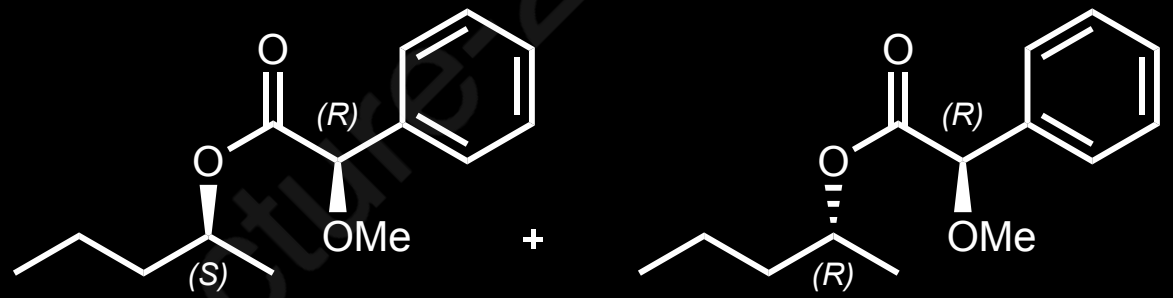
☞ *Achiral environment–*
Enantiomers have identical physical and chemical properties

☞ *Chiral environment (living systems)–*
behave differently with different enantiomers



(±)-2-petanol

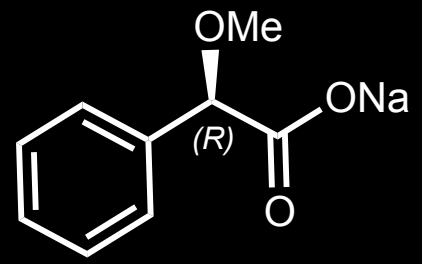
(Racemic mixture)



(Diastereomers)

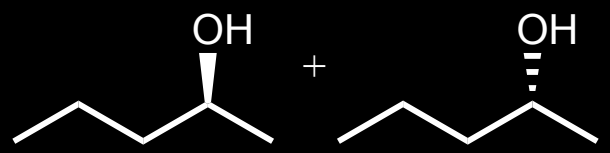
Can be separate by coloumn chormatography

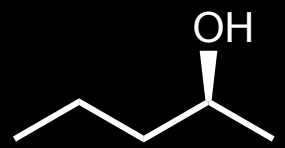
$NaOH/H_2O$



$NaOH/H_2O$

(Racemic mixture = Mixture of two enantiomers)





(*S*)-pentan-2-ol

(*R*)-pentan-2-ol

Stereochemistry

Chiral drugs in Biological System

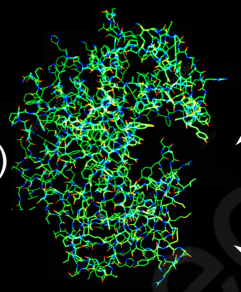
☞ It is appropriate to consider two enantiomers of a given chiral drug as two separate drugs with different properties

Biochemical reactions in body

Reactant

Catalyst (Enzyme)

Product



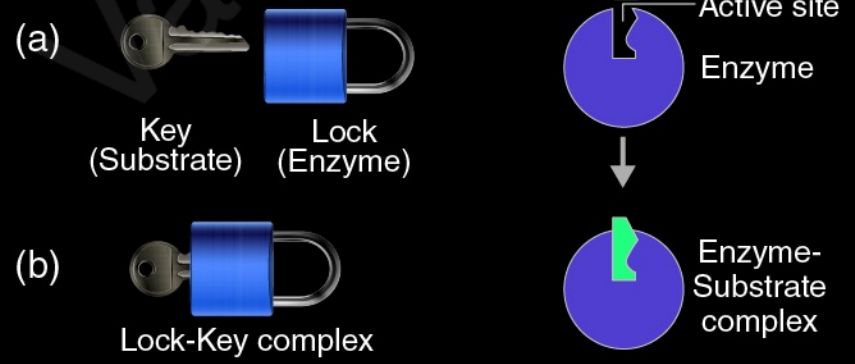
Chiral entity

Enantiomer-A

(Suitable to fit in enzyme)

Enantiomer-B

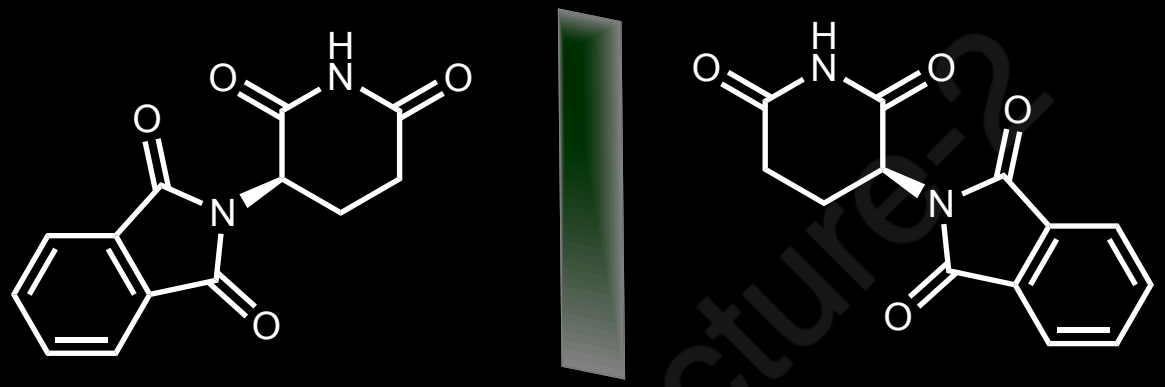
Racemic mixture
(Enantiomer A + Enantiomer B)



**Some of the Pictures taken from the internet

Stereochemistry

What is the importance of Stereochemistry?



anti-nausea drug

teratogen (causes birth defects)

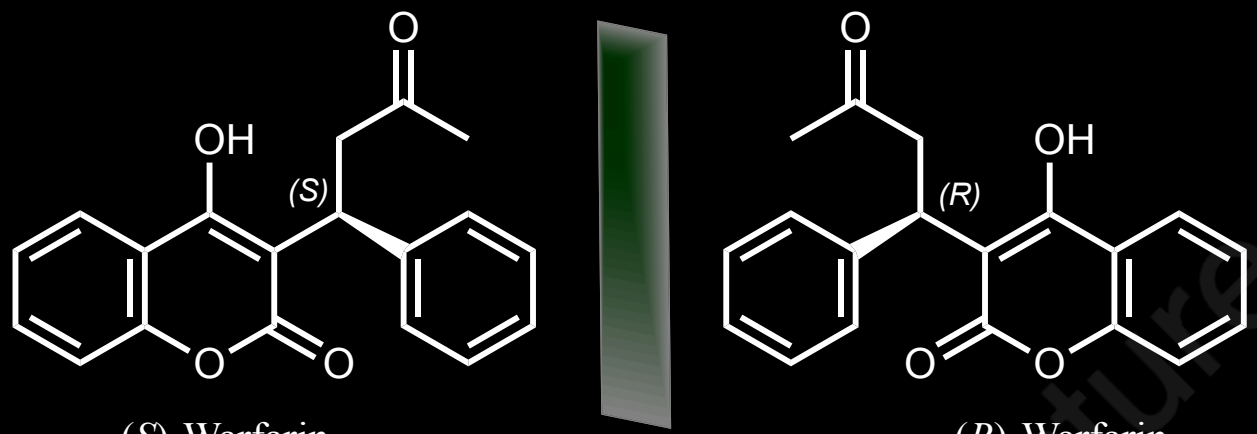
thalidomide

enantiomers

☞ Thalidomide was sold as a mixture of its two enantiomers, and each of these stereo- isomers has a different biological activity.

☞ Although one enantiomer was an effective sedative and anti-nausea drug, the other enantiomer was responsible for thousands of catastrophic birth defects in children born to women who took the drug during pregnancy

Stereochemistry



(*S*)-Warfarin

(*R*)-Warfarin

Warfarin

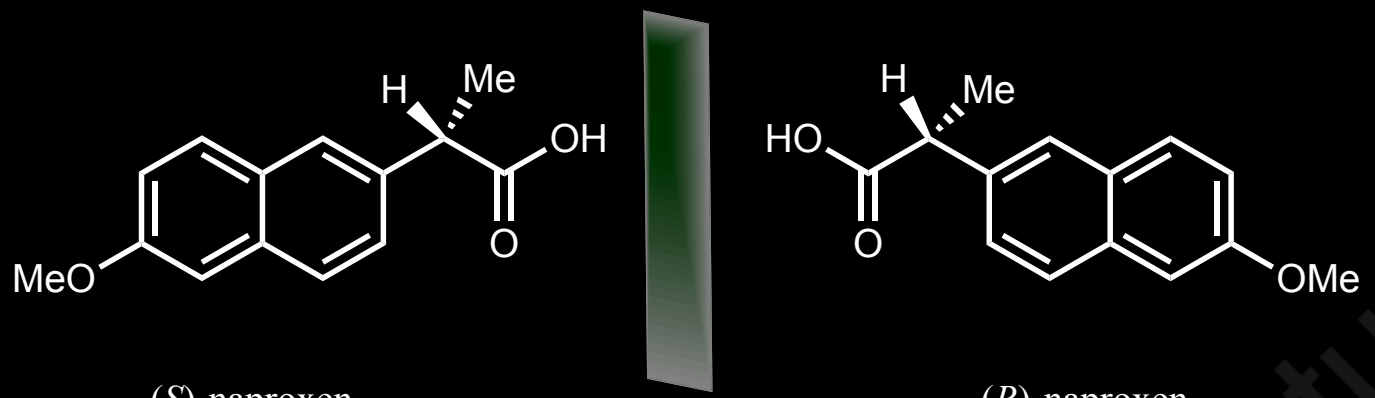
enantiomers

S-warfarin is 2–5 times more potent than the *R*-isomer in producing an anticoagulant response

☞ Although it was initially sold as a rat poison, warfarin is an effective anticoagulant used to prevent blood clots

☞ (*S*)-Warfarin is more extensively bound to albumin than (*R*)-Warfarin

Stereochemistry



(*S*)-naproxen

anti-inflammatroy agent

Naproxen

enantiomers

(*R*)-naproxen

liver toxin

☞ The *S*-enantiomer of **naproxen** is an active anti-inflammatory agent, but the *R*-enantiomer is a harmful liver toxin.

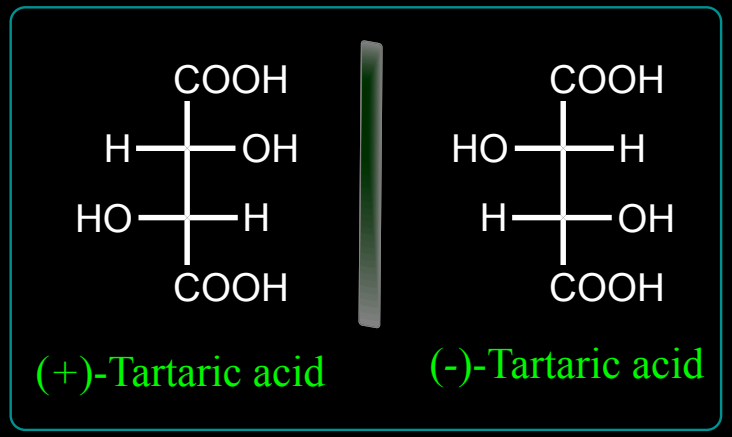
☆ ☆ ☆ If a chiral drug could be sold as a single active enantiomer, it should be possible to use smaller doses with fewer side effects.

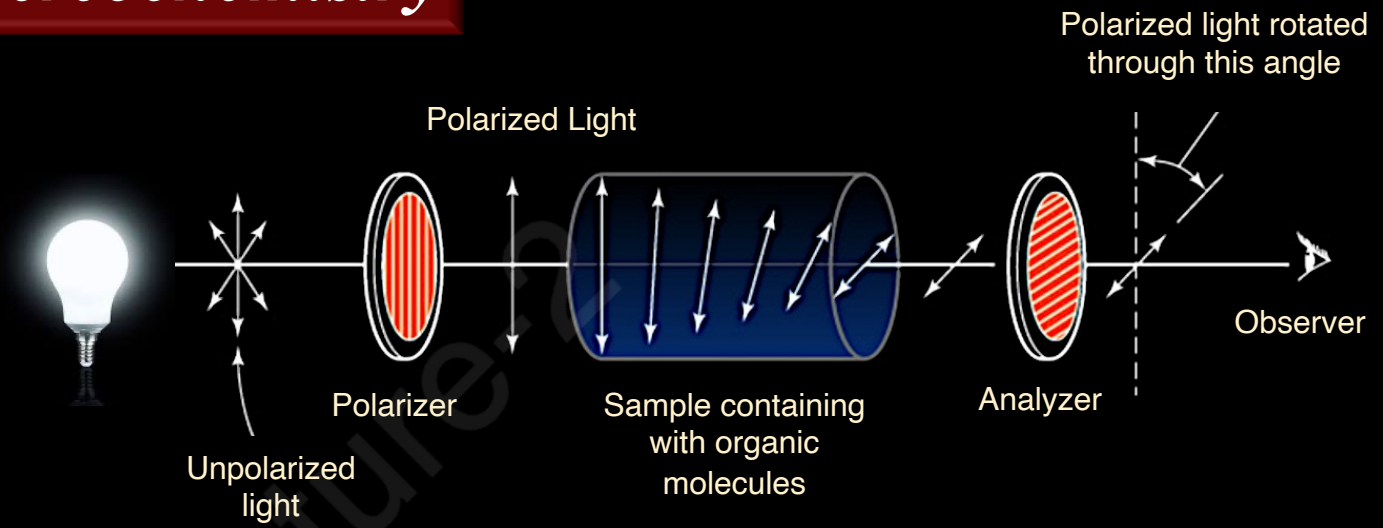
⇧

Optically active compound

Stereochemistry

☆ Optical Activity





☞ The optical activity of a substrate is usually assessed as the optical rotation in degrees.

The degree of rotation of plane-polarized light is measured using a ***polarimeter***.

☞ The source light passes through a polarizer and then is detected at an analyzer.

☞ The angle between the entrance and exit planes is the optical rotation.

☞ A clockwise rotation is called dextrorotatory or (+), while a counterclockwise rotation is levorotatory or (-).

☆ Optical Activity

Stereochemistry

Optical rotation α concentration of the sample x path length

Optical rotation = constant x concentration of the sample x path length

$$\alpha = [\alpha] \times c \times l$$

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

$[\alpha]^{T}_{\lambda}$ = Specific rotation

α = Observed rotation

c = Concentration (g/ ml)

l = length (dm)

☞ The optical rotation a is not very useful for direct comparative purposes since it depends on the path length the light traverses, the concentration of the analyte, the analyte itself and the wavelength of the light.

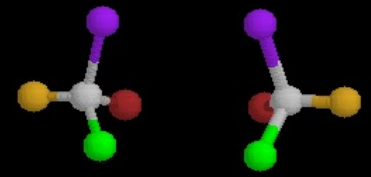
☞ The more useful property is the specific rotation $[\alpha]_D$ that is standardized for concentration and path length.

☆ Question

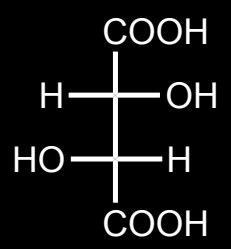
Q: An aqueous solution of pure compound of concentration 0.10 g/ml had observed rotation -30° in a 1.0-dm tube at 589.6 nm and 25°C. Determine the specific rotation

Stereochemistry

☞ Van't Haff and Le Bel related the phenomenon of optical rotation to the presence of asymmetrically substituted carbon atoms (chiral carbon atoms) in the molecules.

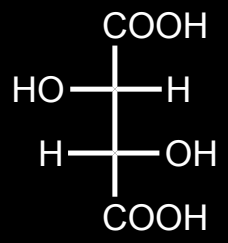


Optical activity of molecules containing chiral centers



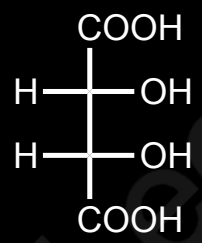
(+)-Tartaric acid

$[\alpha]_D$ = +12°



(-)-Tartaric acid

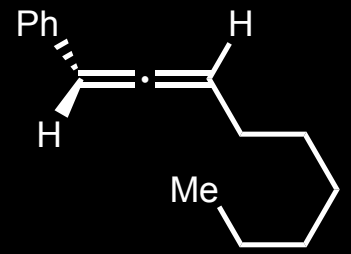
$[\alpha]_D$ = -12°



meso Tartaric acid

No optical activity

Optical activity of molecules containing without chiral centers

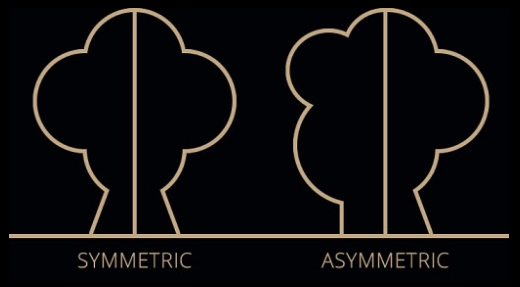


allene derivative

$[\alpha]_D$ = -248.4°

ref: OL, 2013, 15, 2254

An object or molecule or crystal can be superimposable on its mirror image when it has any one of the following elements of symmetry:



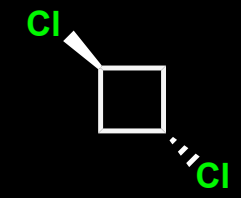
1) Plane of Symmetry
2) Centre of Symmetry
3) Alternating axis of Symmetry

☞ In order to show a molecule for optical activity, it must not contain these symmetry elements

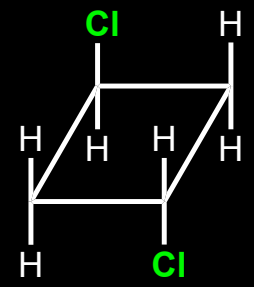
Stereochemistry

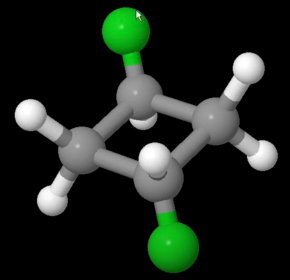
Plane of Symmetry:(σ)

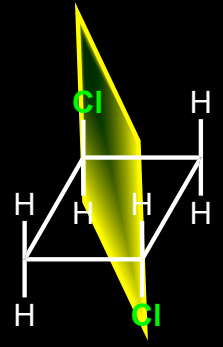
☞ imaginary plane passing through the centre of molecule can divide it into two parts such that one is the exact mirror image of the other.

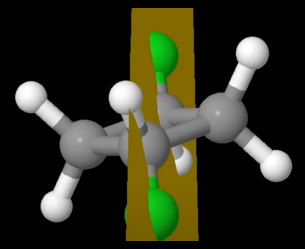


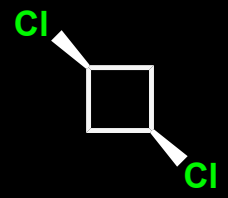
achiral



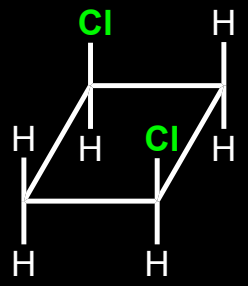


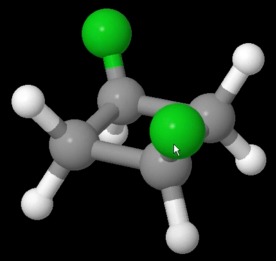


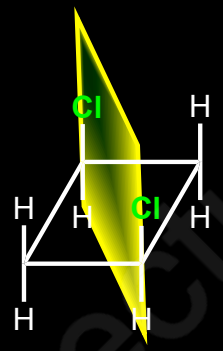


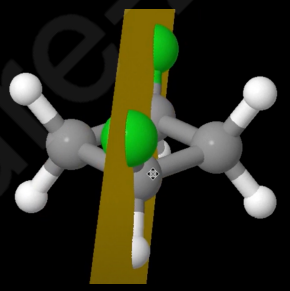


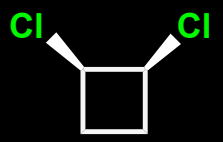
achiral



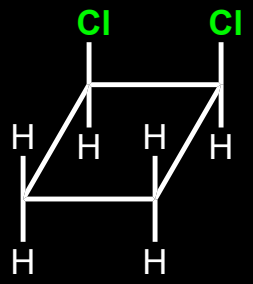


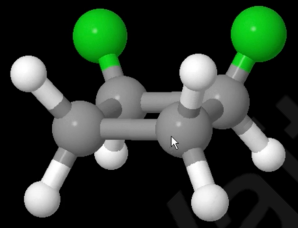


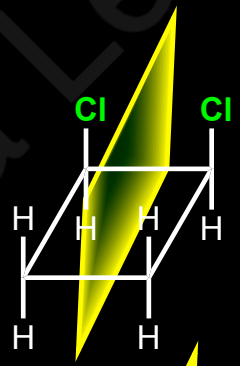


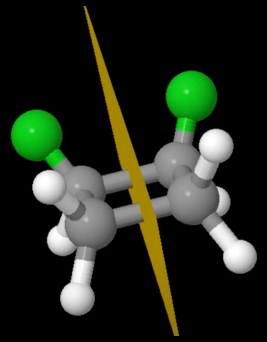


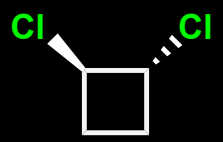
achiral



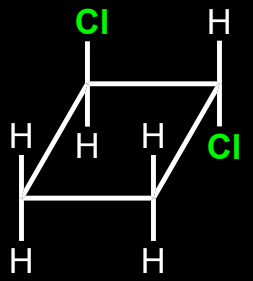


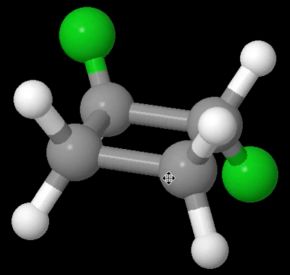


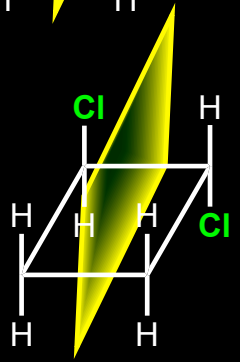


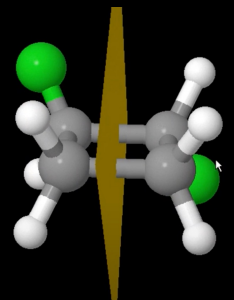


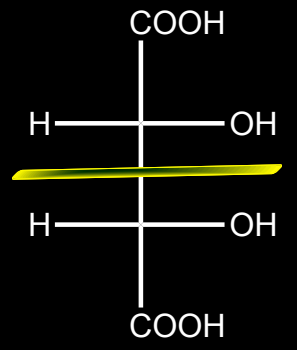
chiral

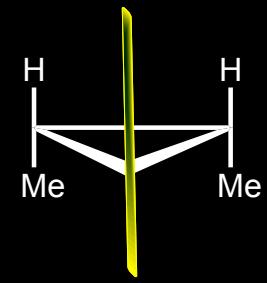


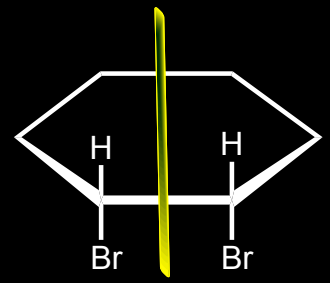






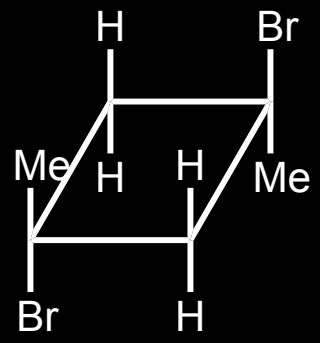


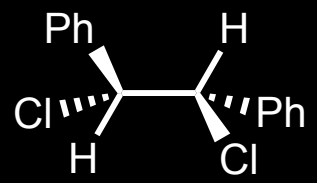


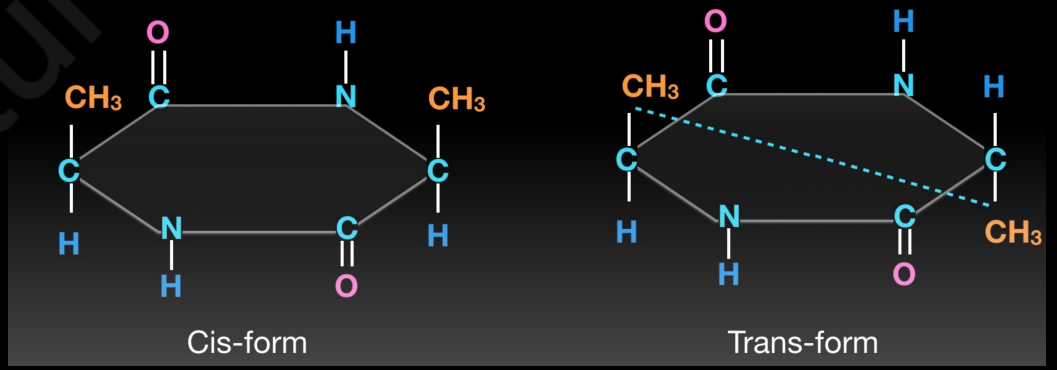


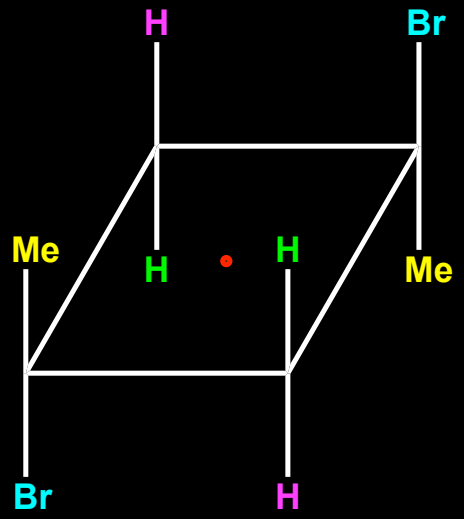
B) Center of Symmetry:(i)

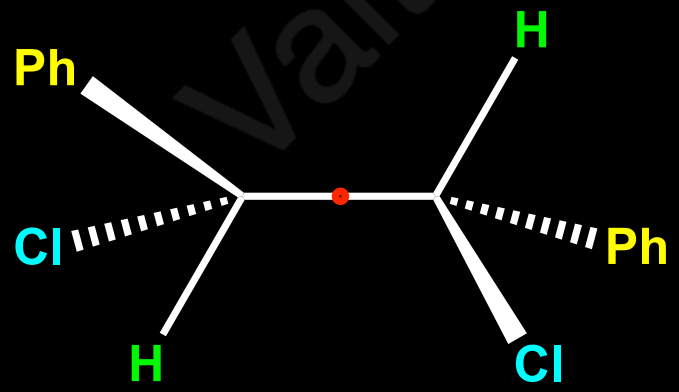
☞ It is an imaginary point in the molecule from which the similar groups are at equidistant.





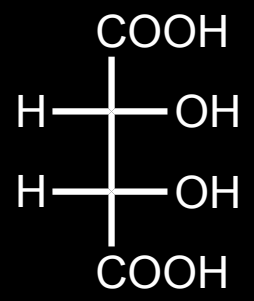




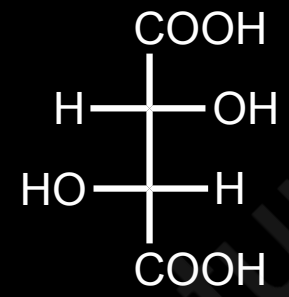


Relative configuration

The position of atoms or groups in space in relation to (i.e., relative to) something else in the molecule.



Both OH *are Same side*

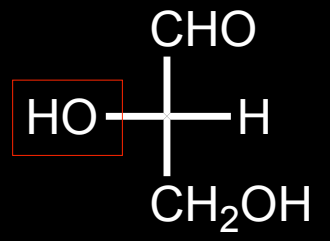


Both OH *are Opposite side*

Compare the arrangement of atoms in space –one compound with another

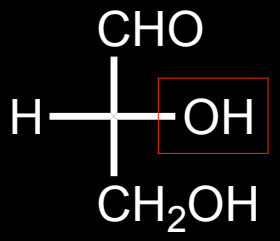
Fischer's guess

Fischer drew two enantiomers of glyceraldehyde as Fischer projection



L-glyceraldehyde

(-)-enantiomer

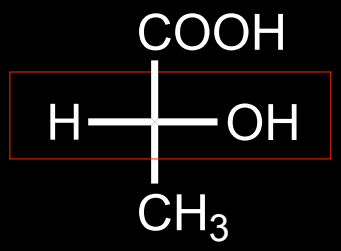


D-glyceraldehyde

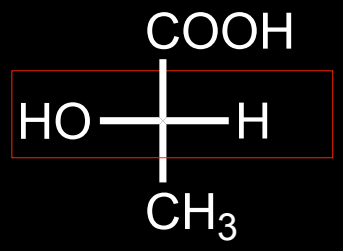
(+)-enantiomer

D,L- Nomenclature

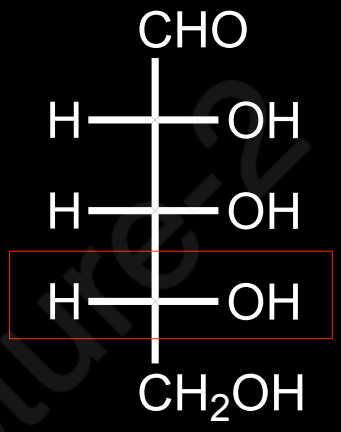
Sugars has -OH group of the bottom chiral carbon on left is L-family of sugars and Right is D-family of sugars



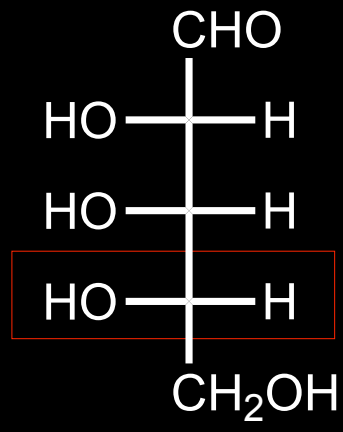
D-lactic acid



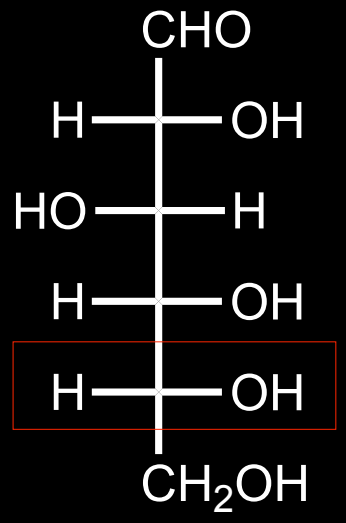
L-lactic acid



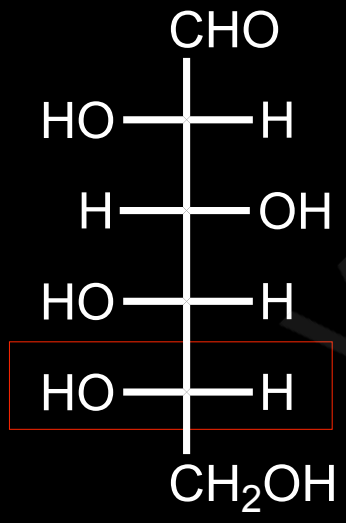
D-ribose



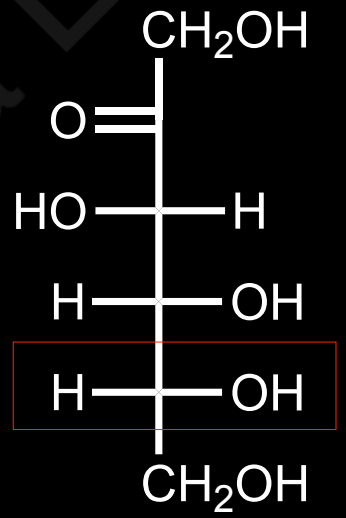
L-ribose



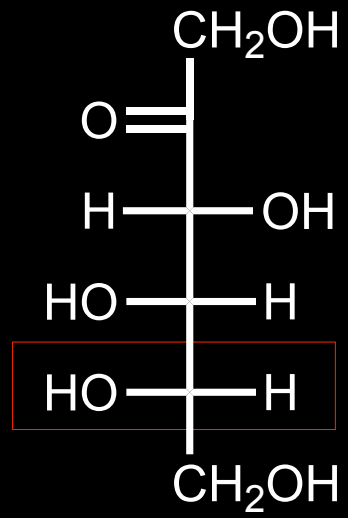
D-glucose



L-glucose



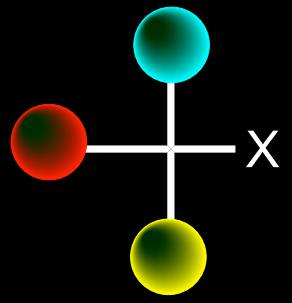
D-fructose



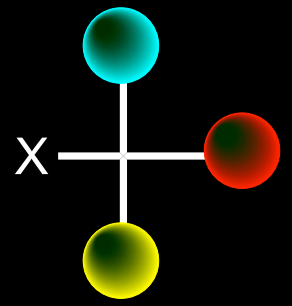
L-fructose

D,L- Nomenclature

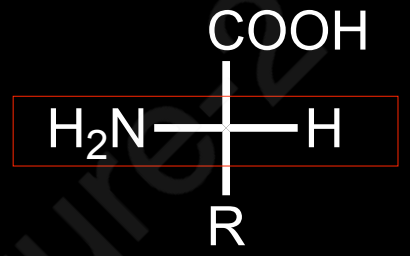
Rosanoff theory:



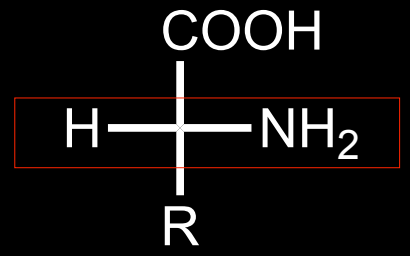
D-configuration



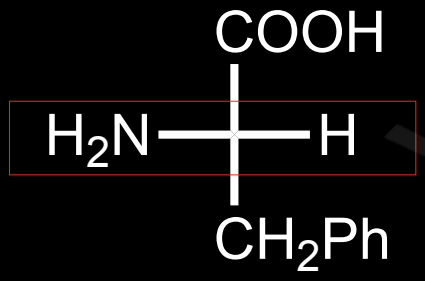
L-configuration



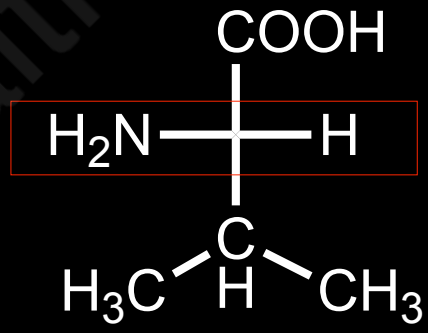
L-amino acid



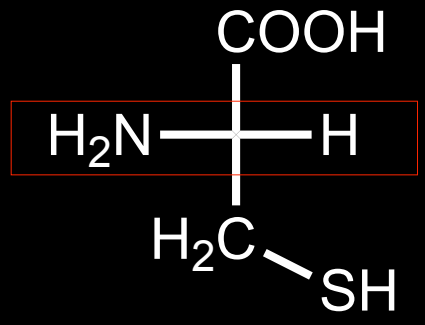
D-amino acid



L-Phenylalanine



L-Valine



L-Cysteine