

COURSE CODE: SC202 (CHEMISTRY)

COURSE INSTRUCTOR: DR. DEBARATI MITRA &
DR. SANGITA TALUKDAR

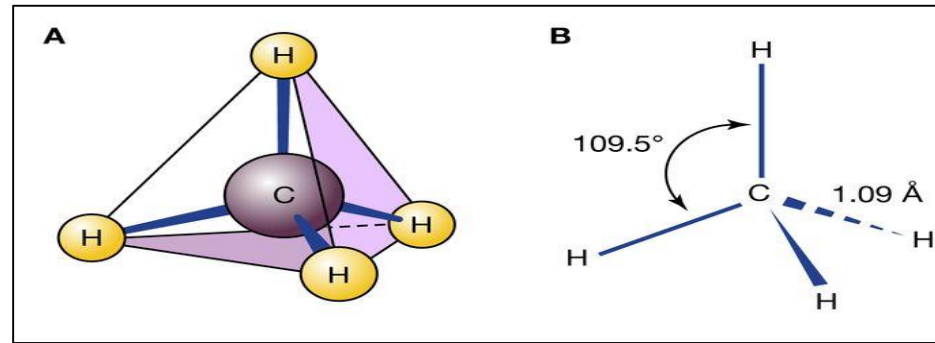
DEPT. OF SCIENCE AND MATHEMATICS
IIITG, GUWAHATI

LECTURE: STEREOCHEMISTRY

DATE: 19.01.23, 24.01.23 & 25.01.23

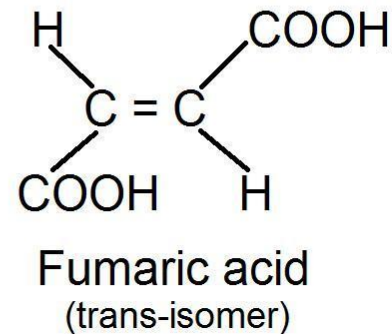
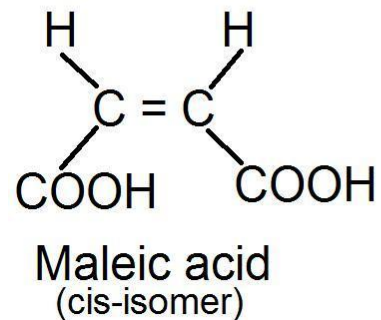
What is Stereochemistry and why is it necessary?

- It is the study of three dimensional structures of molecules.



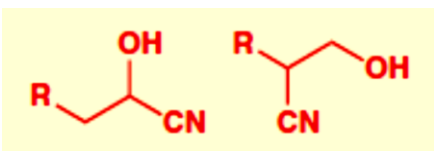
- Cis Butanoic acid (maleic acid) is important for plant and animal, but trans Butanoic acid (fumaric acid) is toxic to the tissue. **So, orientation is important.**

Structures of maleic and fumaric acid

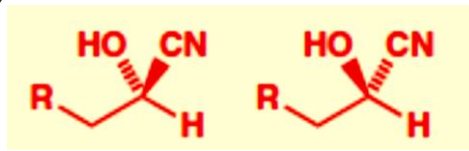


Isomers

- Isomers are different compounds with same molecular formula, they have different arrangement of their atoms.
- Two major classes of isomers are **constitutional isomers** and **stereoisomers**.
- Constitutional isomers** have different IUPAC names, different arrangement of atoms, same or different functional groups, different physical properties and chemical properties.
- Stereoisomers** have same IUPAC names (except prefix like cis and trans), same functional groups, but different arrangement of atoms and bonds in three dimension or space.

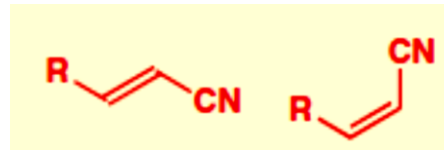


constitutional isomers: the way the atoms are connected up (their *connectivity*) differs



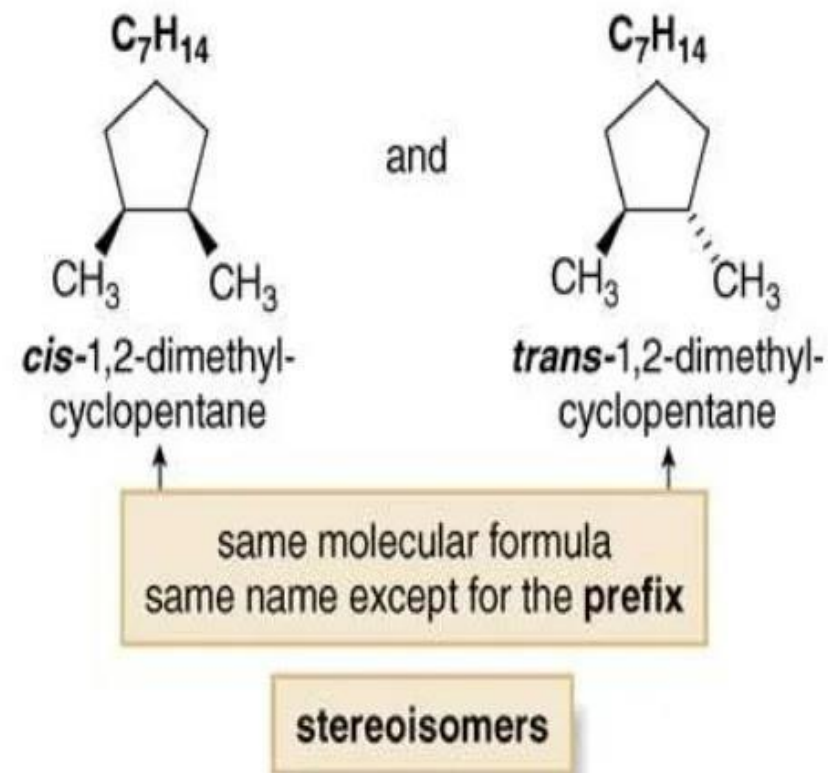
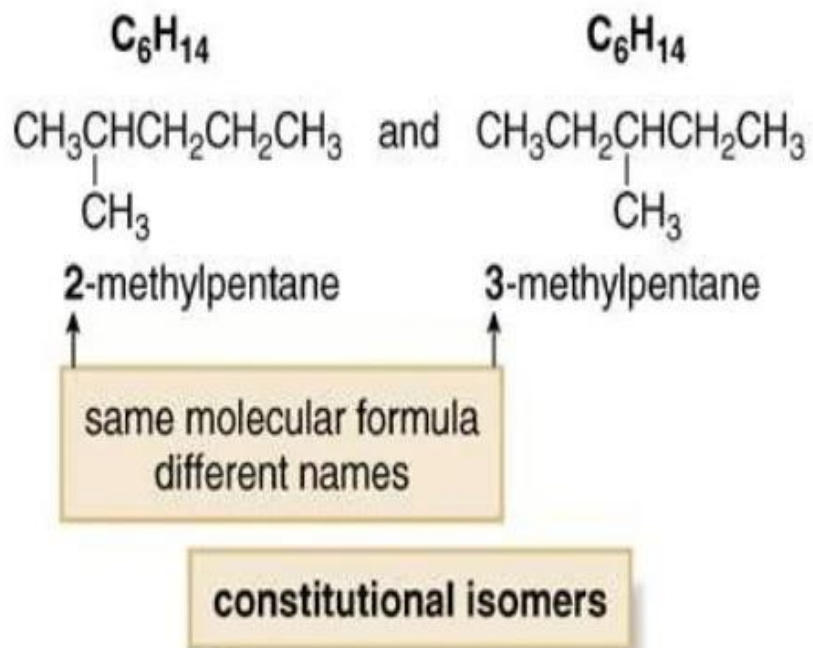
enantiomers

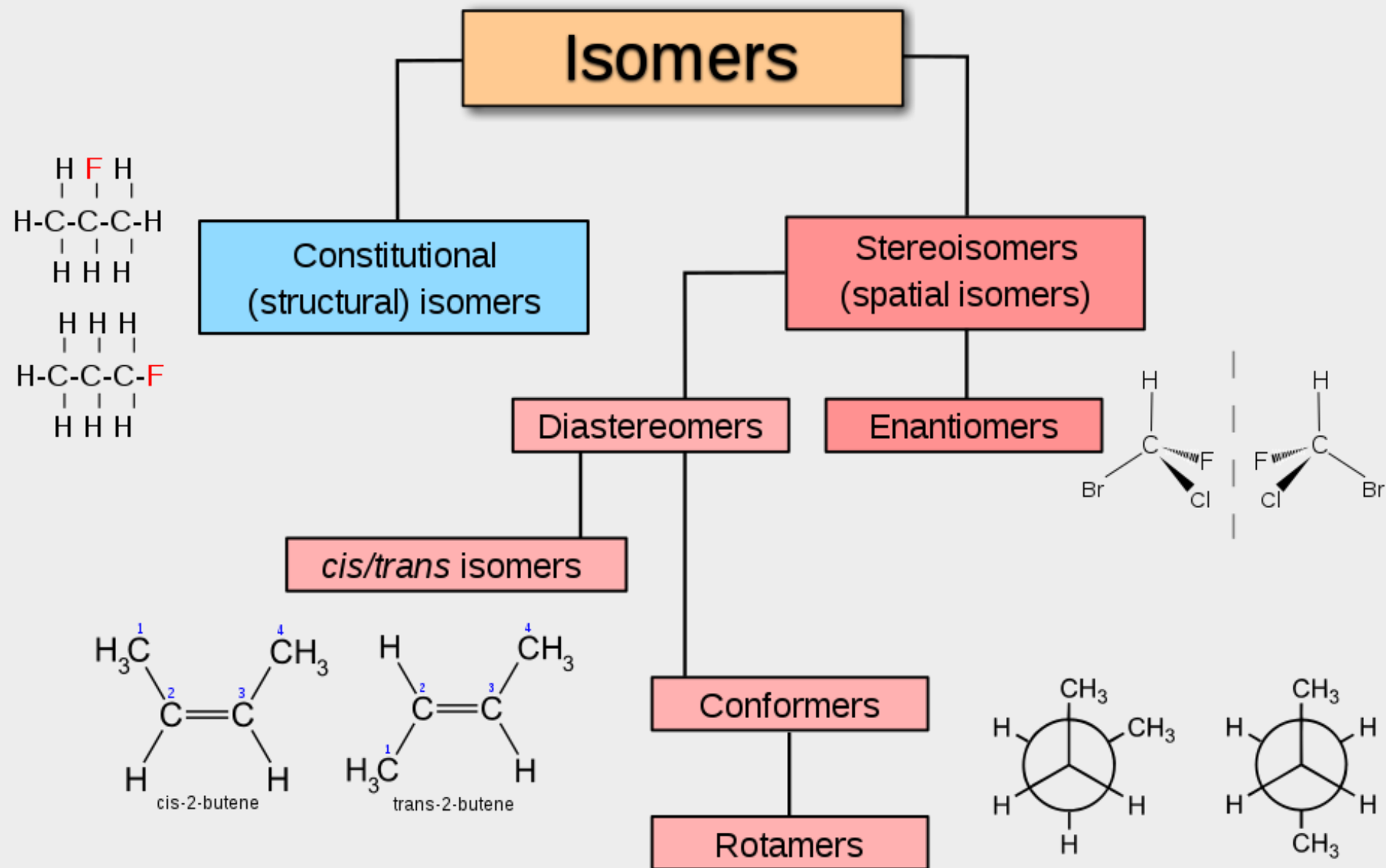
stereoisomers: the atoms have the same connectivity, but are arranged differently

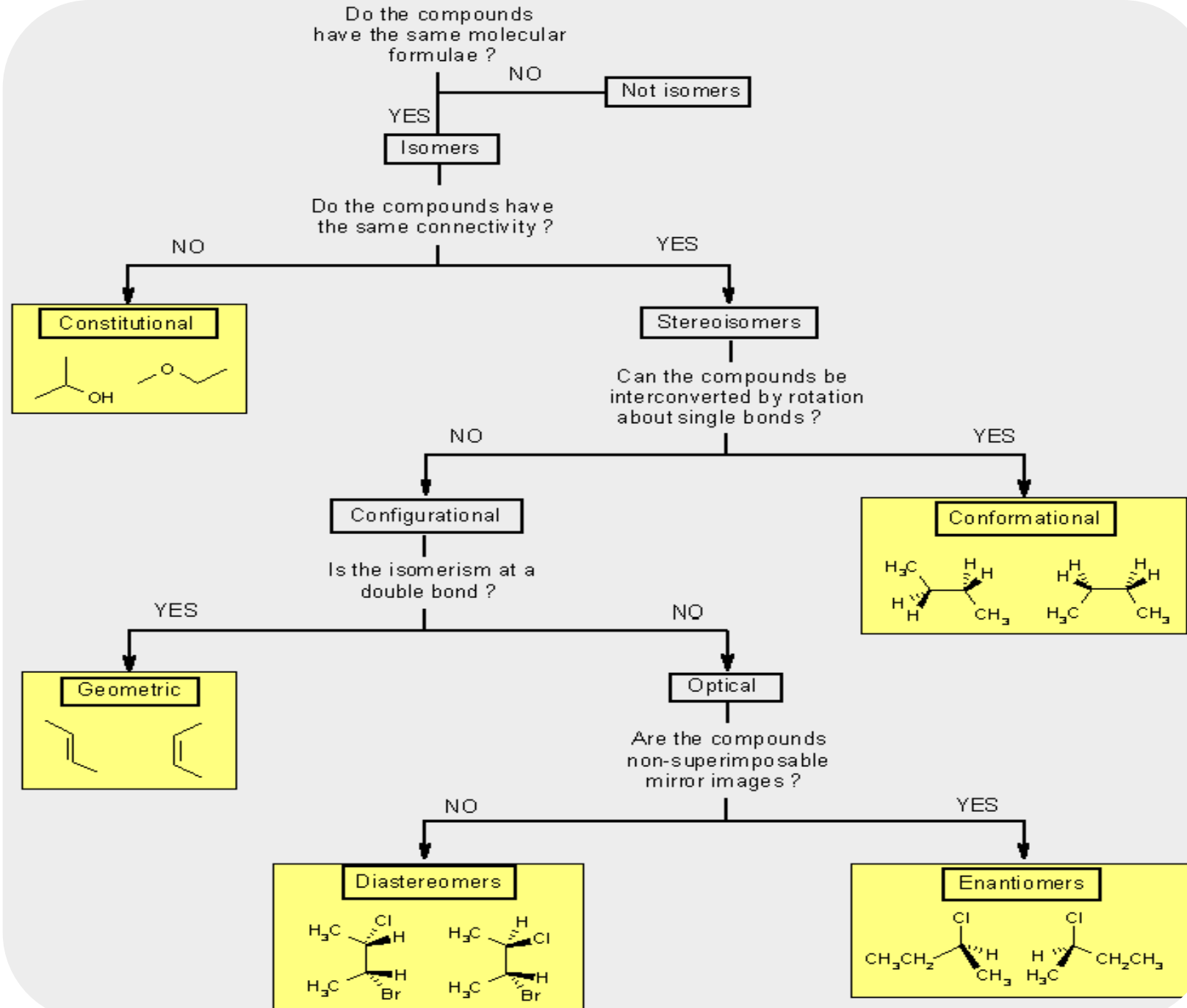


E/Z isomers (double bond isomers)

A comparison of constitutional isomers and stereoisomers.....

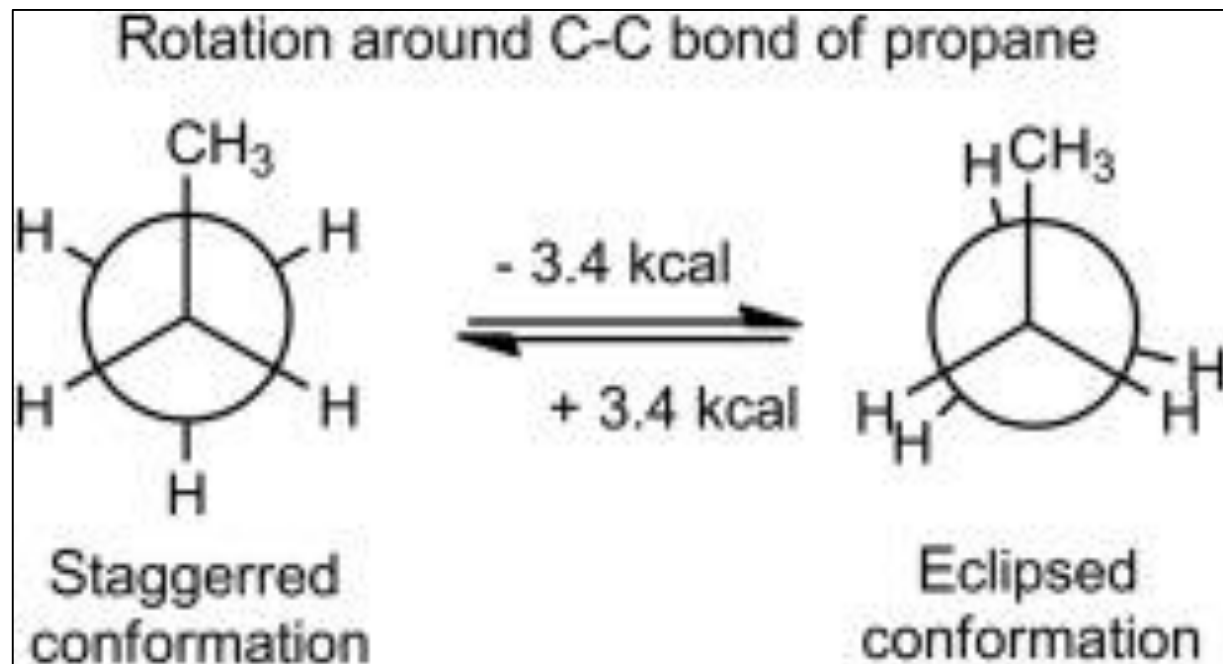






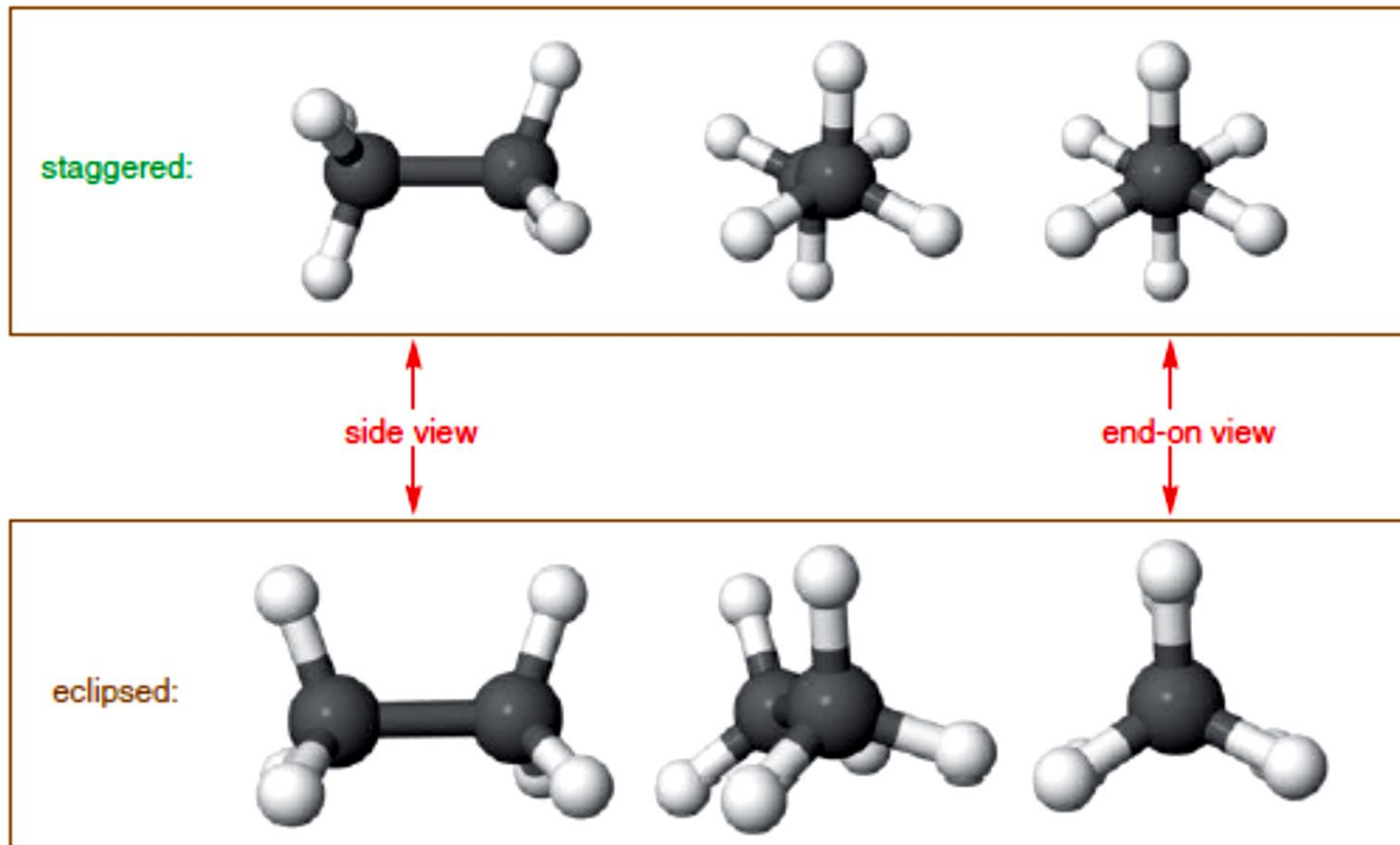
Conformational isomers

- Stereoisomers that are produced by **rotation around single bonds** and are easily **convertible to each other by rotation** at room temperature.
- Energy for rotation is very low.

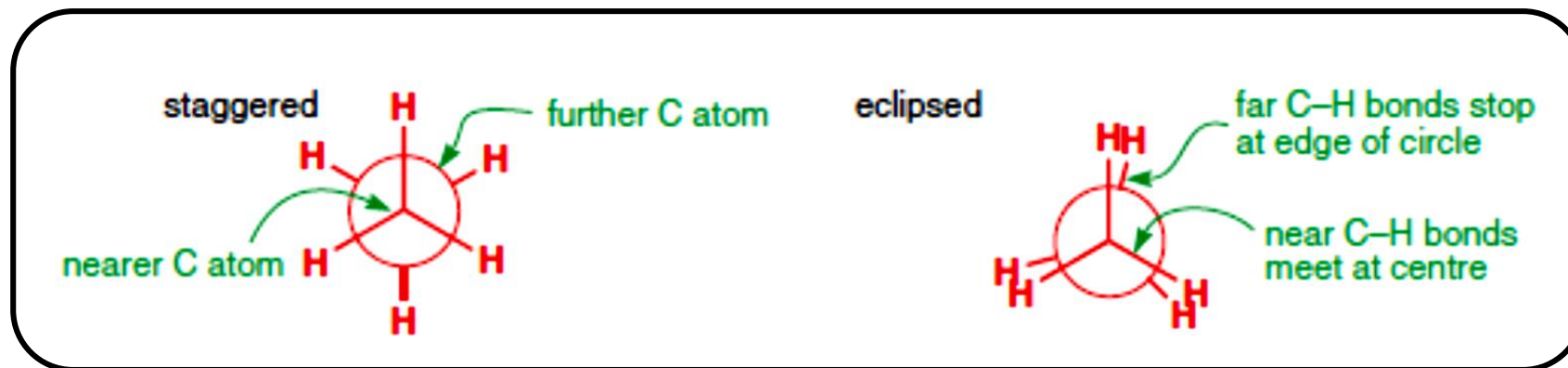


Conformations of ethane

The two extreme conformations of ethane, staggered and eclipsed, each shown from three different viewpoints



Newman projections of the staggered and eclipsed conformations of ethane

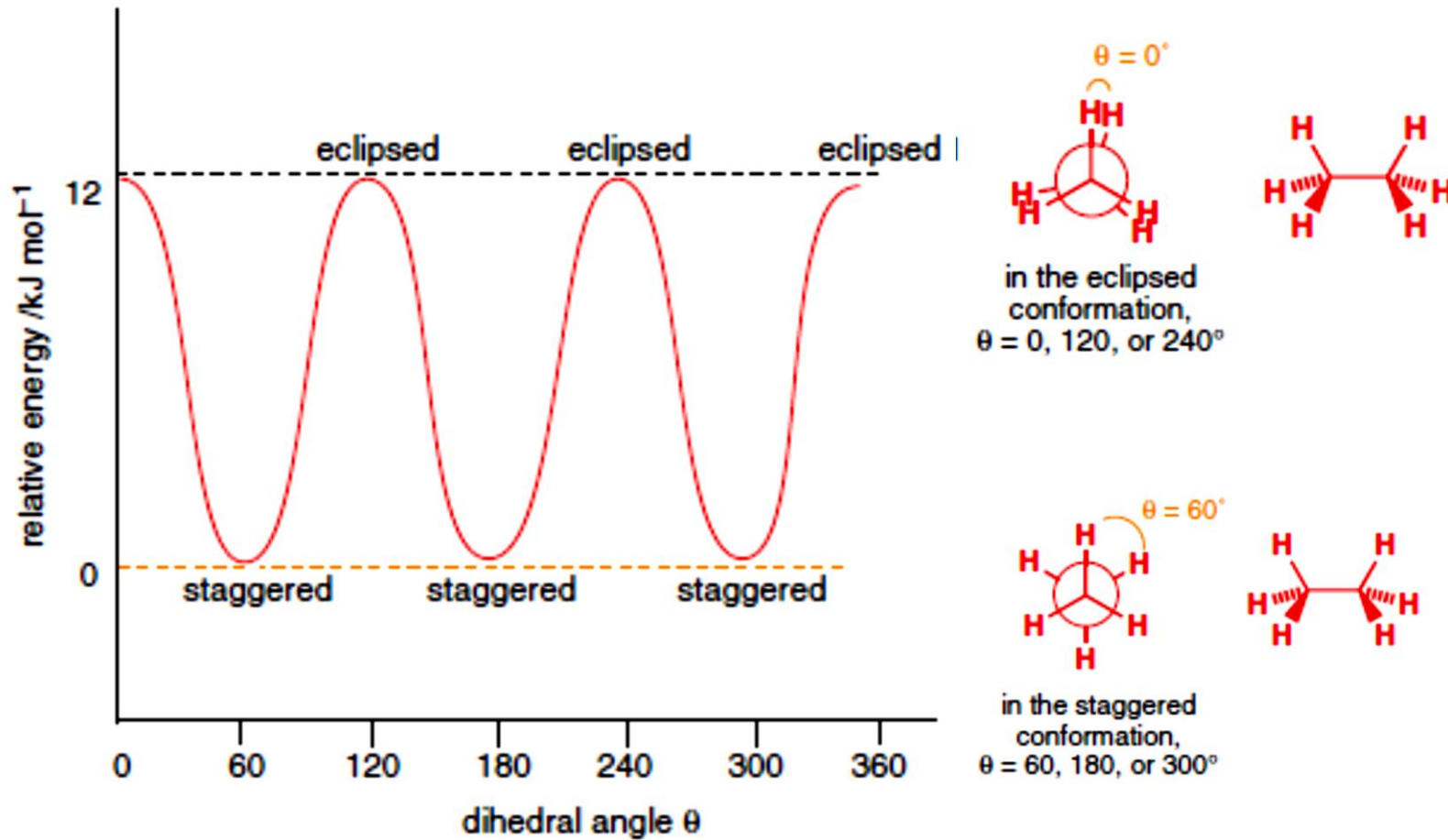


Newman projections are subject to a few conventions:

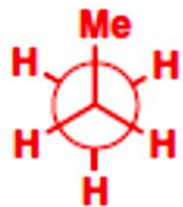
- The carbon atom nearer the viewer is at the junction of the front three bonds.
- The carbon further away (which can't in fact be seen in the end-on view) is represented by a large circle.
- Bonds attached to this further carbon join the *edge* of the circle and do not meet in the centre.
- Eclipsed bonds are drawn slightly displaced for clarity—as though the bond were rotated by a tiny fraction.

The staggered conformation is lower in energy than the eclipsed by 12 kJ mol^{-1} , the value of the rotational barrier.

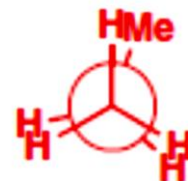
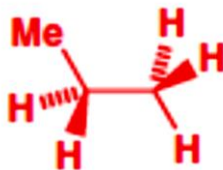
Energy profile diagram of Ethane



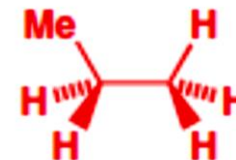
Conformations of propane



the staggered conformation of propane

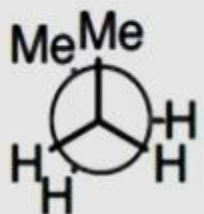


the eclipsed conformation of propane

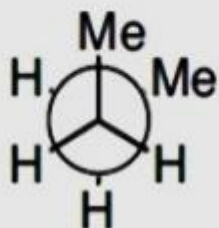


The rotational barrier is now slightly higher than for ethane: 14 kJ mol^{-1} as compared to 12 kJ mol^{-1} .

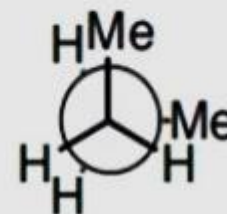
Conformations of butane



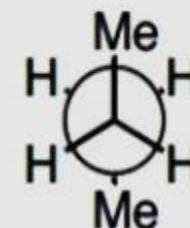
fully eclipsed
(eclipsed)
 $\theta_{\text{Me/Me}} = 0^\circ$



gauche
(staggered)
 $\theta_{\text{Me/Me}} = 60^\circ$



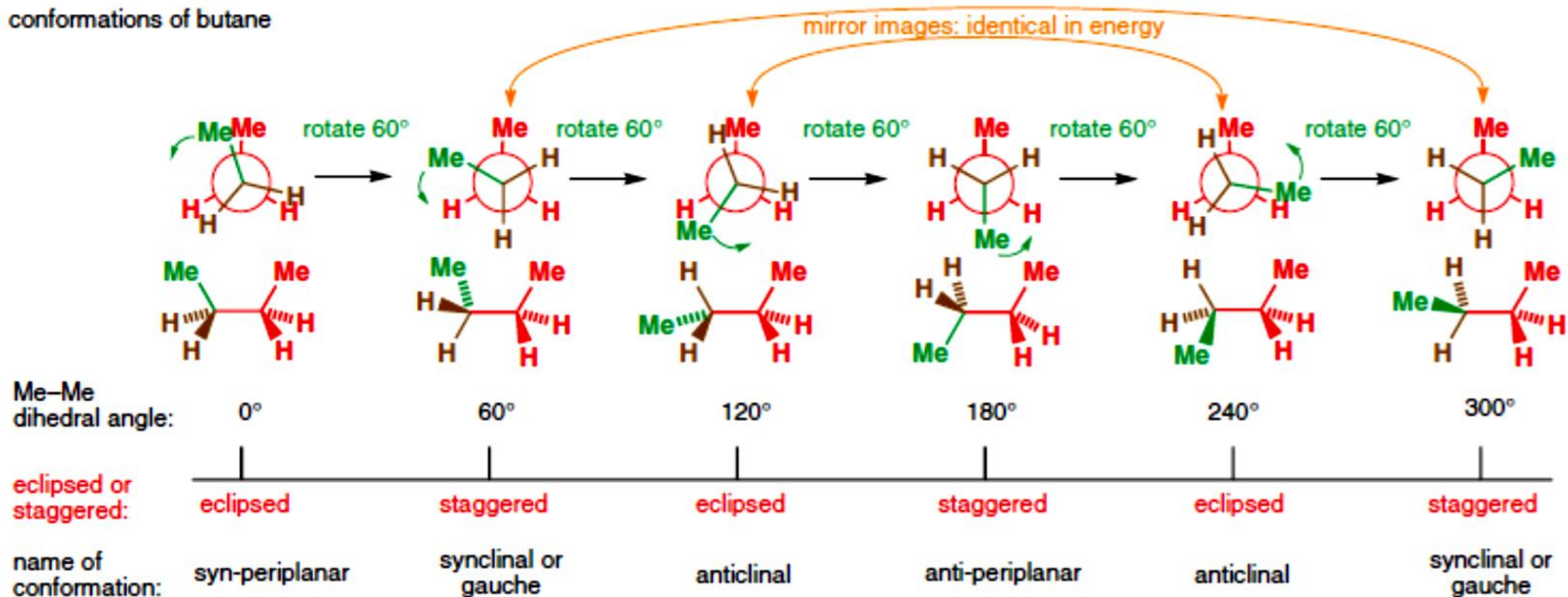
eclipsed
(eclipsed)
 $\theta_{\text{Me/Me}} = 120^\circ$



anti
(staggered)
 $\theta_{\text{Me/Me}} = 180^\circ$

The rotational barrier is only 20 kJ mol^{-1} .

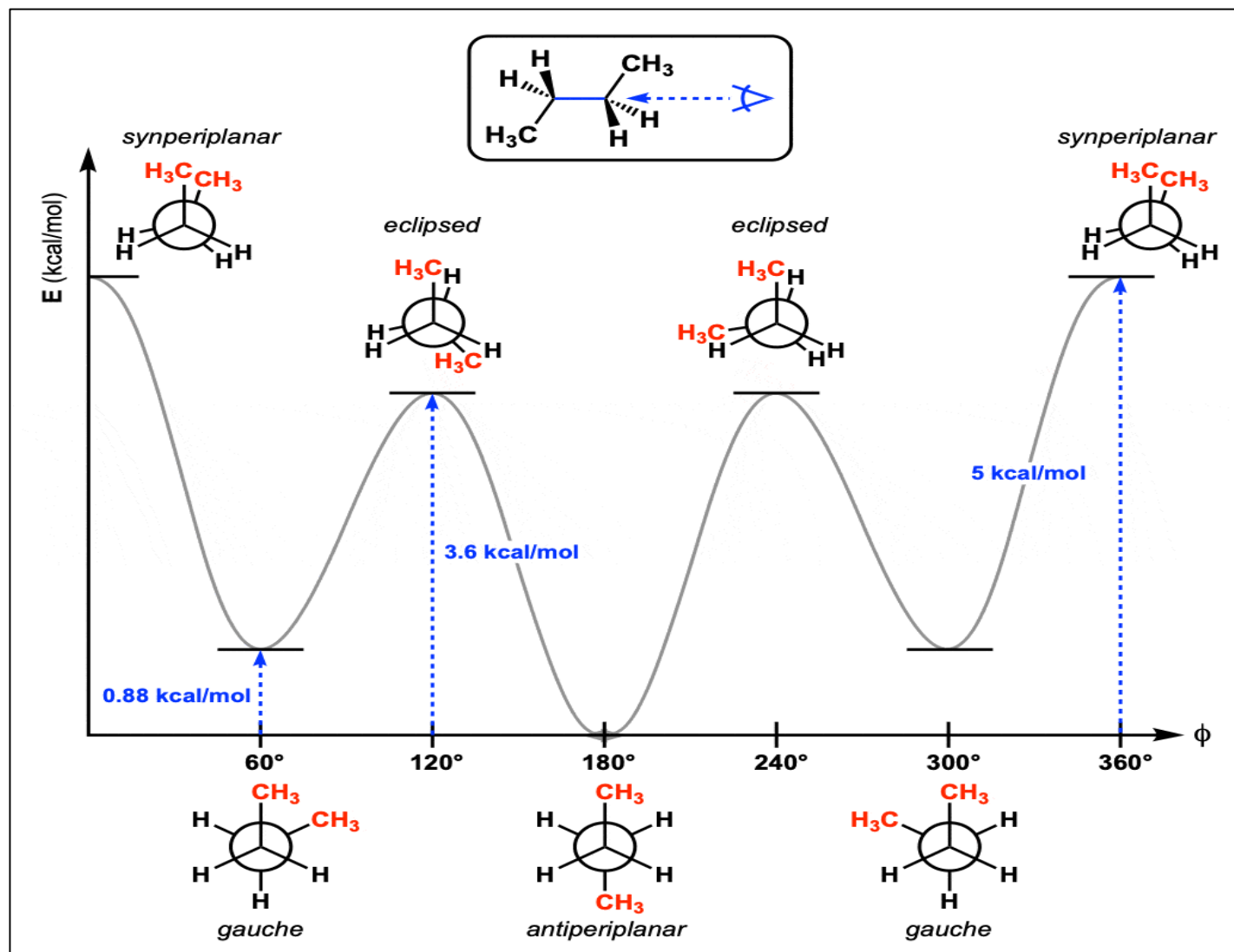
conformations of butane



Conformations and conformers

Butane can exist in an infinite number of conformations (we have chosen to show only the six most significant) but has only three conformers (potential energy minima)—the two synclinal (gauche) conformations and the anti-periplanar conformation.

Energy profile diagram of n-Butane

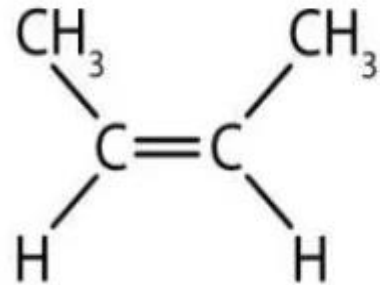


Configurational isomers

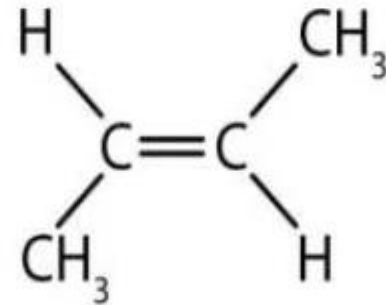
- Stereoisomers which are not readily inter-convertible even by rotation, can only be converted to each other by **breaking or making the bond**.
- They are of two types: Geometrical isomers and optical isomers.

Geometrical isomers

- Geometrical isomer arises from **restriction in rotation** around double bond or because of a ring system.



cis-2-butene



trans-2-butene

Compounds with double bonds:

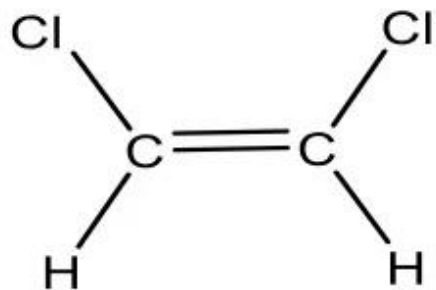
Cis isomer – have same substituents on the same side of the double bond (*Z-zusammen (together)* with more complex molecules having high priority groups on the same side).

Trans isomer – have the same substituents on the opposite side of the double bond (*E - entgegen (opposite)* with more complex molecules having high priority groups on opposite sides).

Compounds with bonds in a ring:

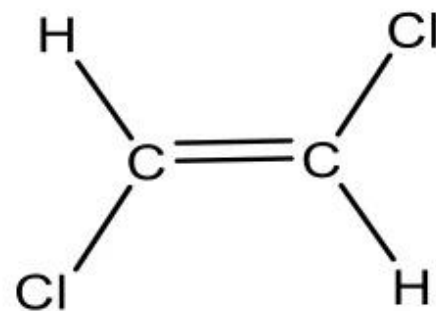
Cis isomer – have the same substituents on the same side of the ring.

Trans isomer - have the same substituents on the opposite side of the ring.



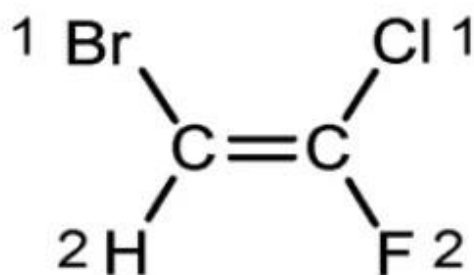
cis-1,2-dichloroethene

(*Z*)-1,2-dichloroethene



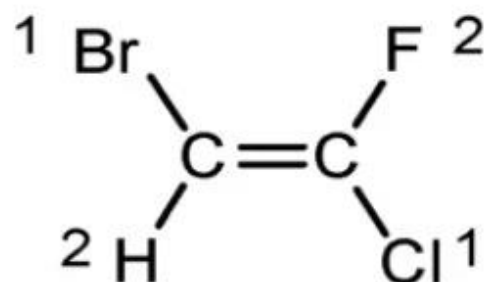
trans-1,2-dichloroethene

(*E*)-1,2-dichloroethene



groups with higher priority
on the same side

***Z*-isomer**



groups with higher priority
on opposite side

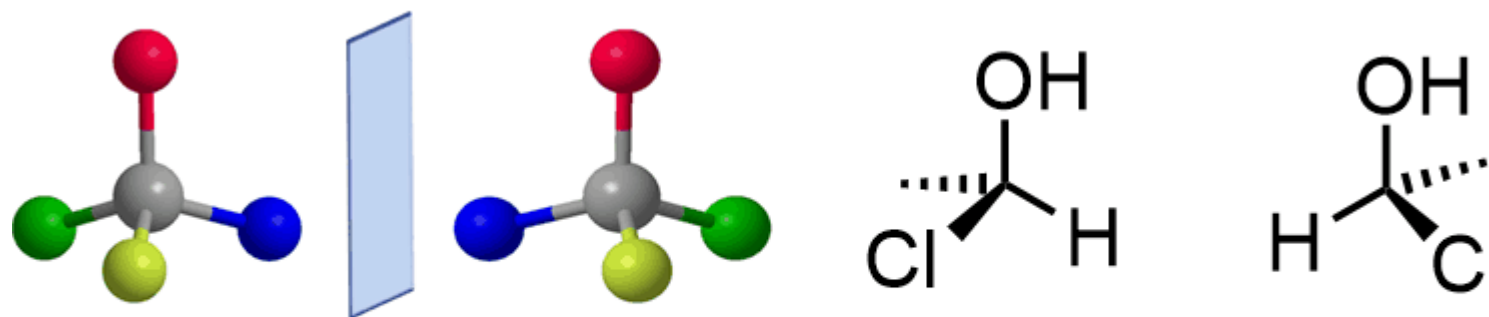
***E*-isomer**

Optical isomers

- **Optical isomerism** occurs mainly in substances that have the same molecular and structural formula, but they cannot be **superimposed** on each other.
- Optical isomers are of two types: Enantiomers and Diastereoisomers or Diastereomers.

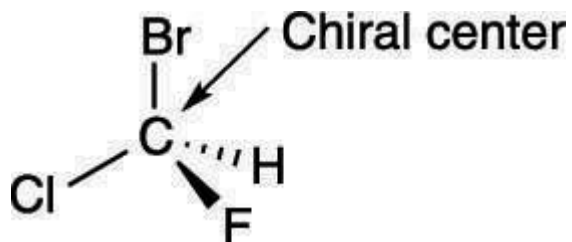
Enantiomers

- Enantiomers are a pair of molecules that exist in two forms that are **mirror images** of one another but cannot be superimposed one upon the other.
- Enantiomers have identical physical properties (m.p., b.p., density, solubility) and chemical properties (except towards optically active reagent).

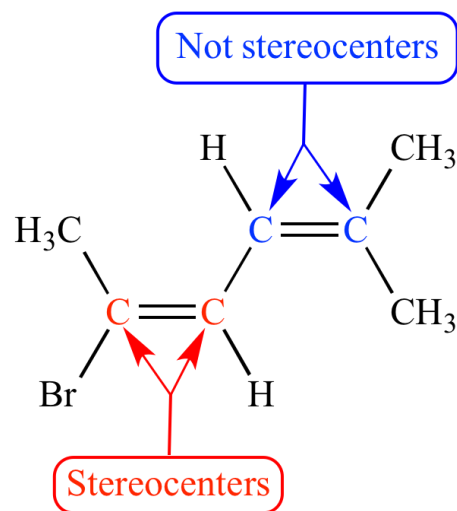


Enantiomers - mirror images

- A molecule that can exist as a pair of enantiomers has the property of **chirality**.
- **Chiral centre** is defined as a carbon bearing four different atoms/groups.

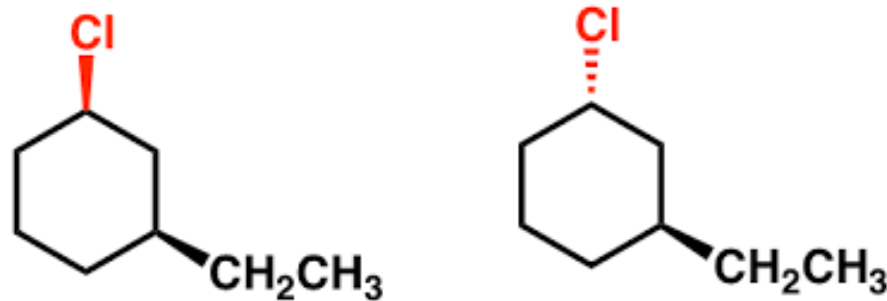


- A **stereocenter** or **stereogenic center** is an atom bearing groups such that an interchanging of any two groups leads to a stereoisomer.



Diastereomer

- Diastereomers (sometimes called diastereoisomers) are a type of a stereoisomer. Diastereomers are defined as non-mirror image non-identical stereoisomers.
- Diastereomers have different physical (m.p., b.p., density, solubility) and chemical properties which help them to be separated easily.



Configuration

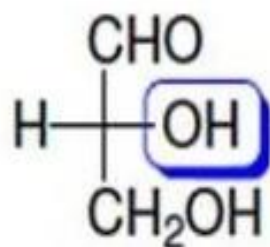
The arrangement of atoms that characterizes a particular stereomer is called its configuration.

The following methods are used to assign configuration.

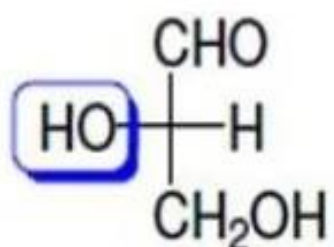
- A. Absolute configuration [R and S system]
- B. Relative configuration [D and L system]

Fischer projection and D/L notation

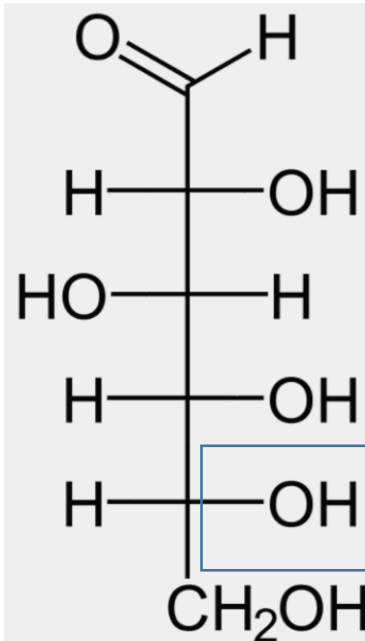
- Fischer first developed a method for drawing carbohydrates in two dimensions and a convention with respect to orientation; so as to indicate their three dimensional structures known as Fischer projection.
- Fischer and Rosanoff then devised a notation for designating the configurations of carbohydrates as D or L.
- In carbohydrates, if the –OH group attached to the penultimate carbon atom (from the bottom, the first chiral centre) lies in the left hand side then it is L, else D.



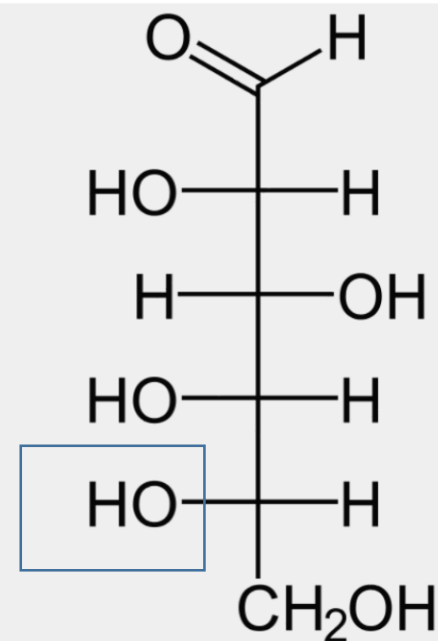
D-(+)-glyceraldehyde
Fischer projection



L-(-)-glyceraldehyde
Fischer projection



D-Glucose

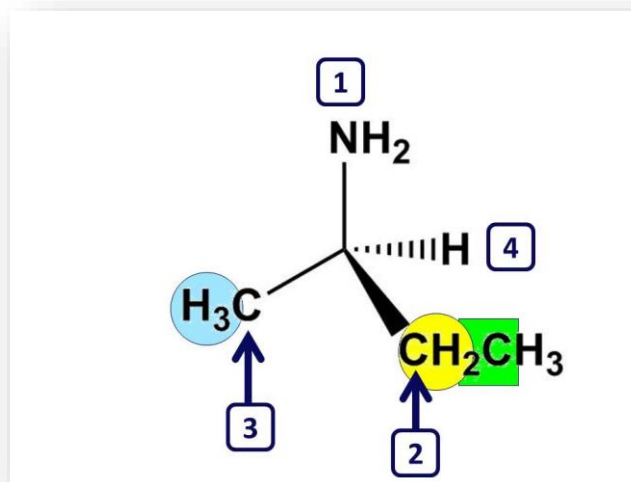


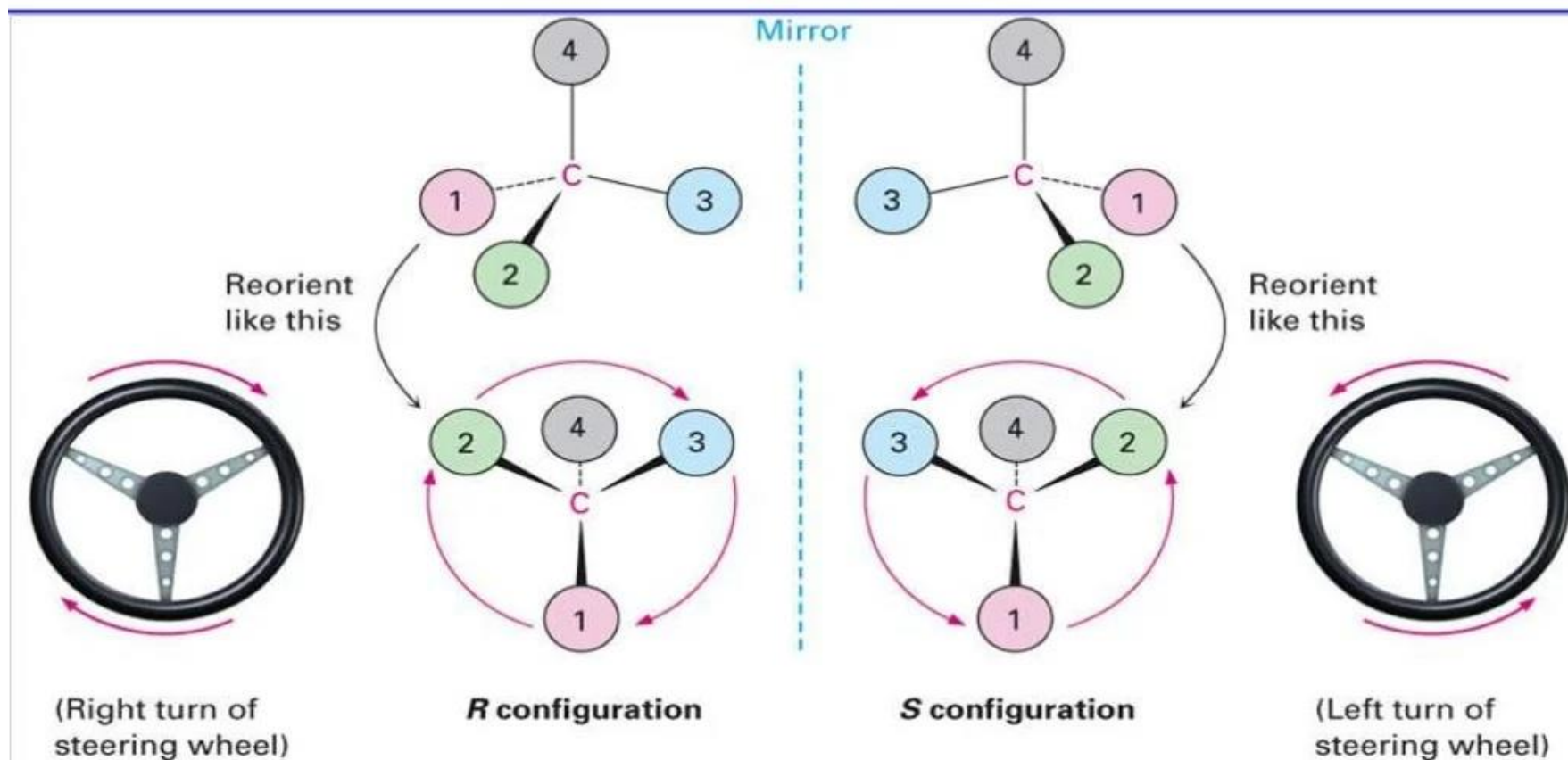
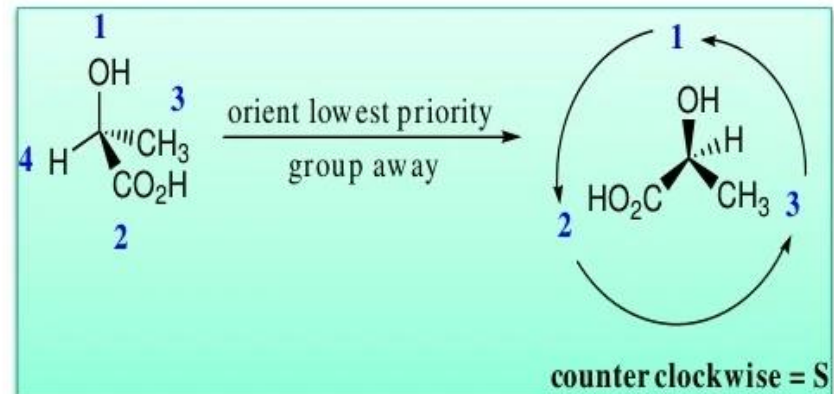
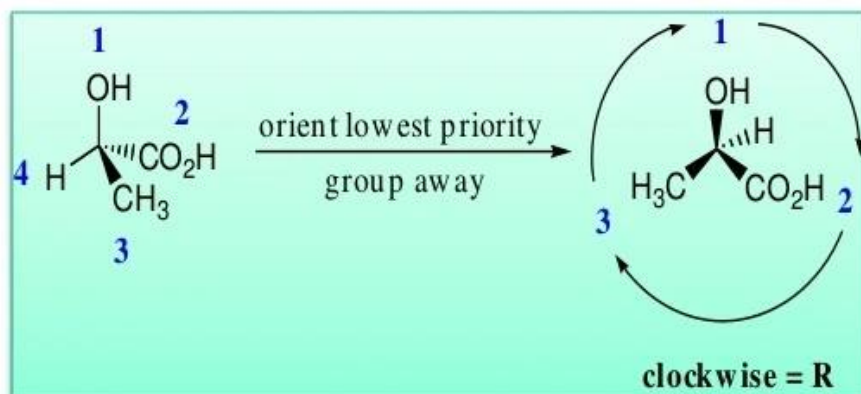
L-Glucose

Cahn-Ingold-Prelog (CIP) sequence rules/R-S notation

Assigning the absolute configuration

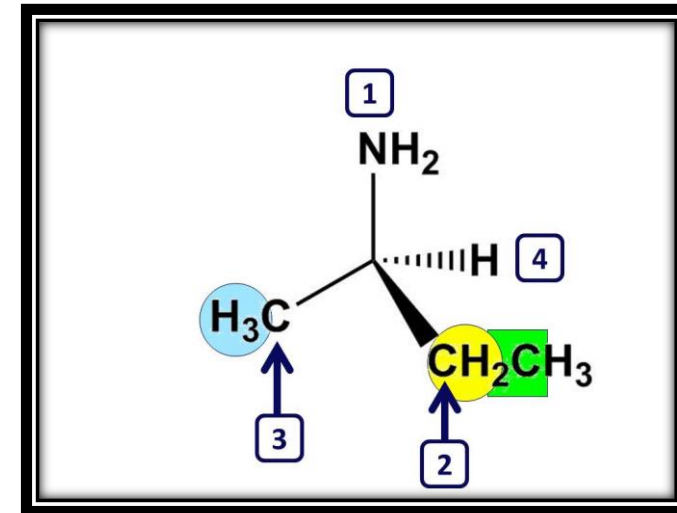
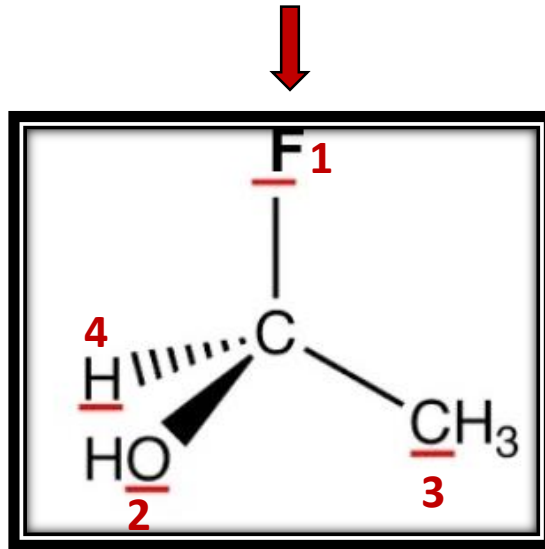
1. Use the CIP priority rules to assign priority to the four groups on the chiral atom.
2. Orient the molecule so that the lowest priority atom is in the back (away from you). Look at the remaining three groups of priority 1-3. if the remaining three groups are arranged so that priorities 1→2→3 are in a **clockwise** fashion, then that chiral centre should be assigned as **R** (Rectus or right) ; if follows **anti-clock wise** rotation, then it will be designated as **S** (Sinister or left).





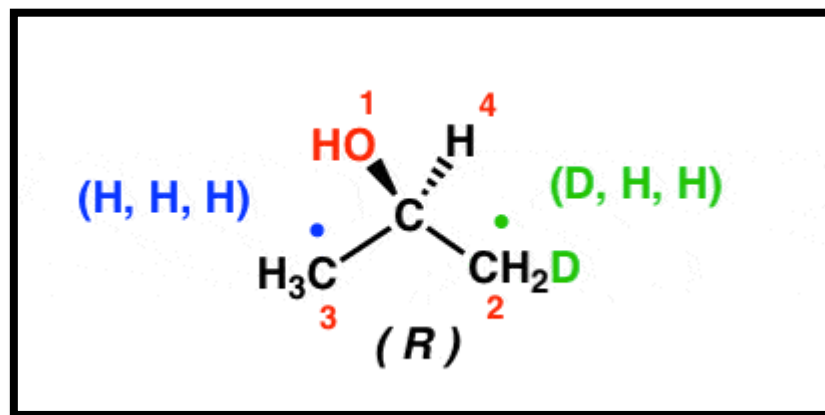
CIP sequence rule

Rule-1: Among the four different atoms attached to the chiral carbon, **higher the atomic number higher will be the priority**. In the following example, the atomic number sequence is $F > O > C > H$, hence the priority.

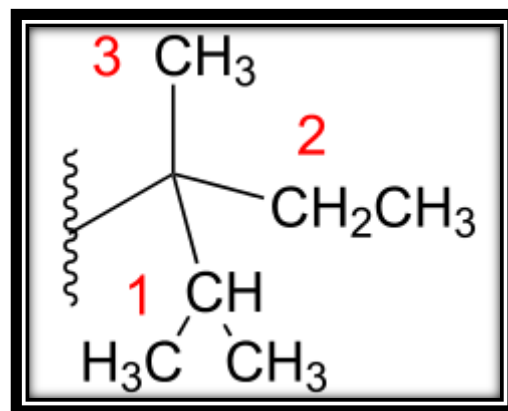


Rule-2: If there is a **tie** between two or more atoms, we must consider atoms at a **two-bond** distance from the stereocenter to break the tie. If there is still a tie, then we must consider atoms at a three-bond distance from the stereocenter until the tie is broken.

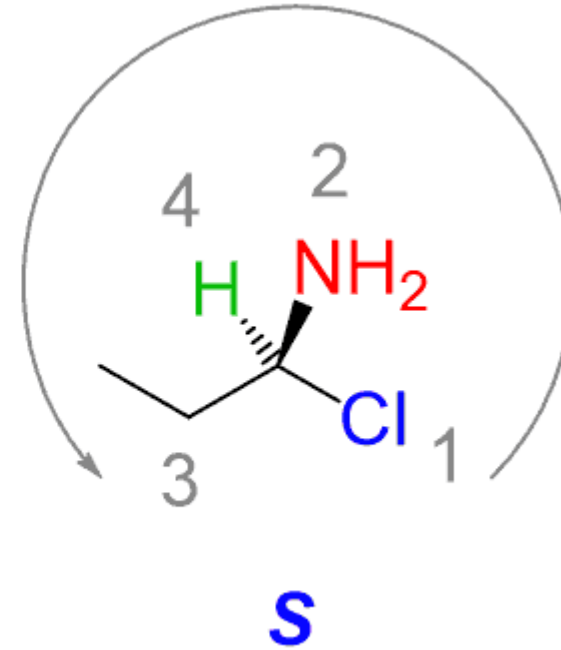
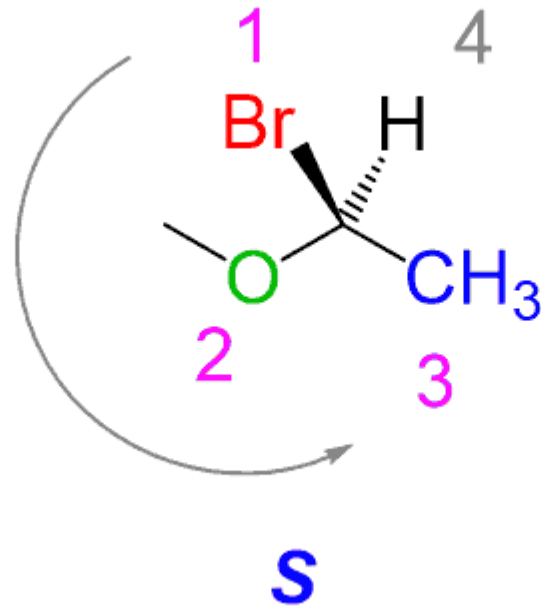
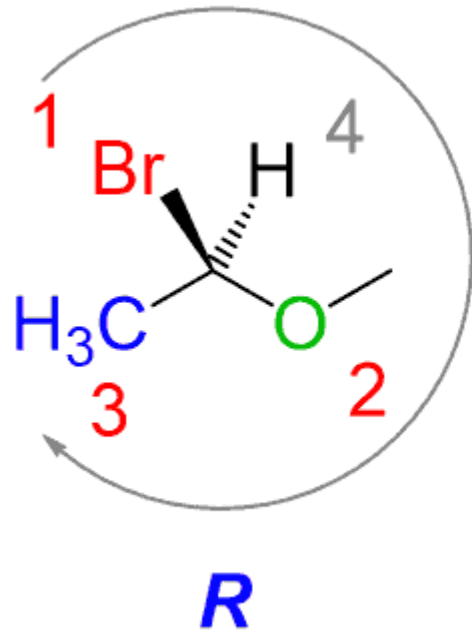
Rule-3: If two atoms attached to the chiral centre are **isotopes**, then **isotope with higher mass number** will precede the lower.



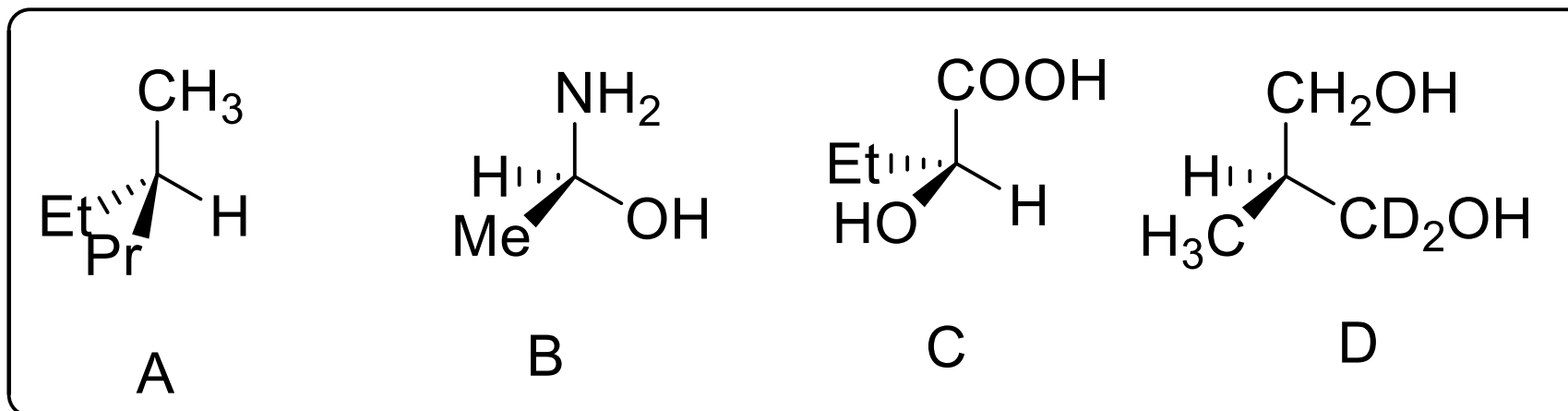
Rule-4: The priority sequence of **tertiary carbon > secondary carbon > primary carbon**, attached to the stereogenic centre.



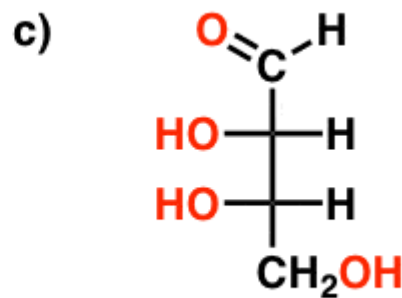
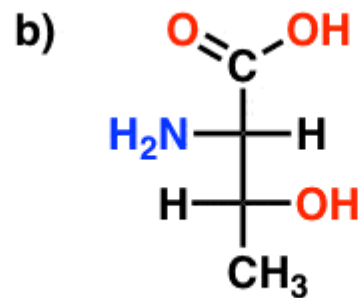
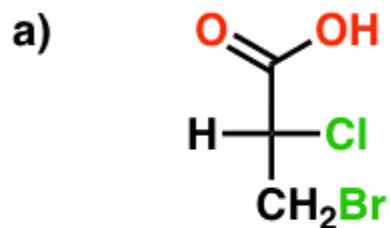
Examples



1. Predict the absolute configuration of the following molecules.

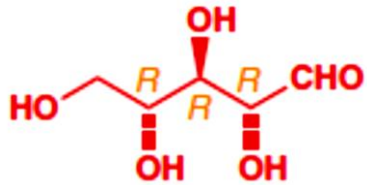


2. Determine R/S for all chiral centres in the following molecules.

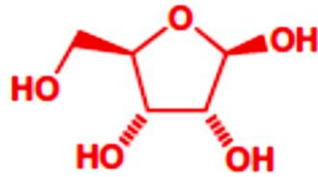


Predicting the number of stereoisomers

- For a molecule with 1 chiral center, $2^1 = 2$ stereoisomers are possible
- For a molecule with 2 chiral centers, a maximum of $2^2 = 4$ stereoisomers are possible
- For a molecule with n chiral centers, a maximum of 2^n stereoisomers are possible.
- These stereoisomers consist of 2^{n-1} diastereoisomers, each of which has a pair of enantiomers.

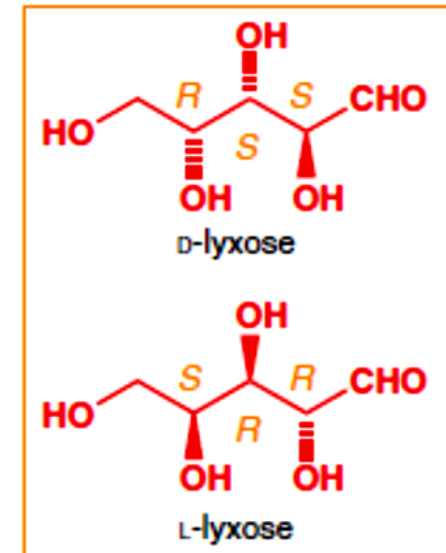
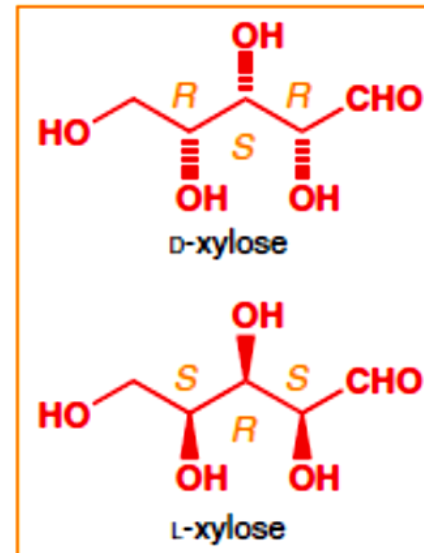
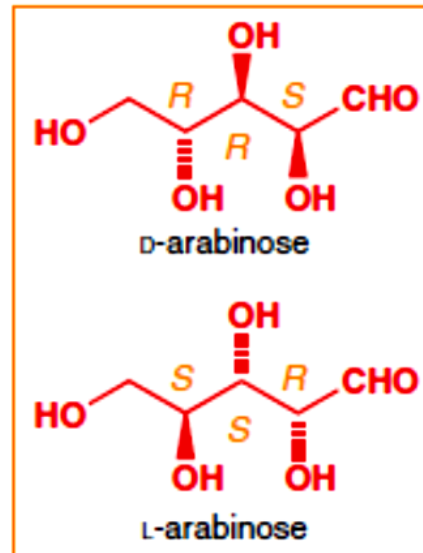
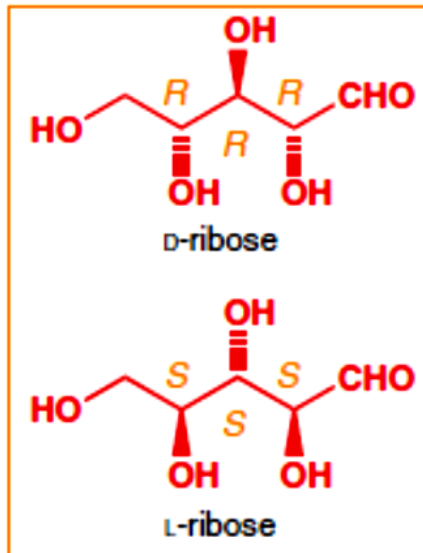


D-ribose,
open-chain form

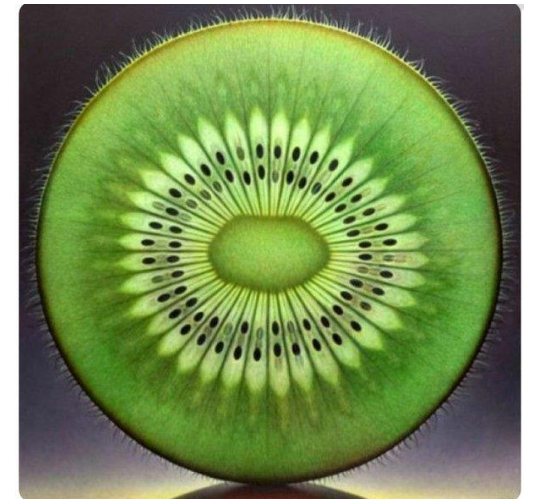
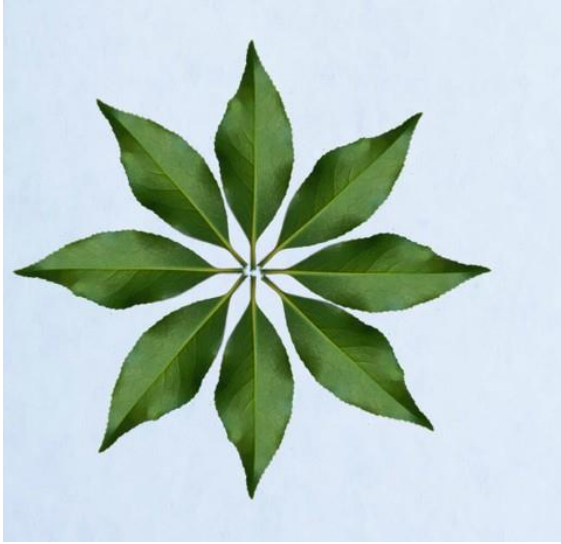


D-ribose,
cyclic hemiacetal form

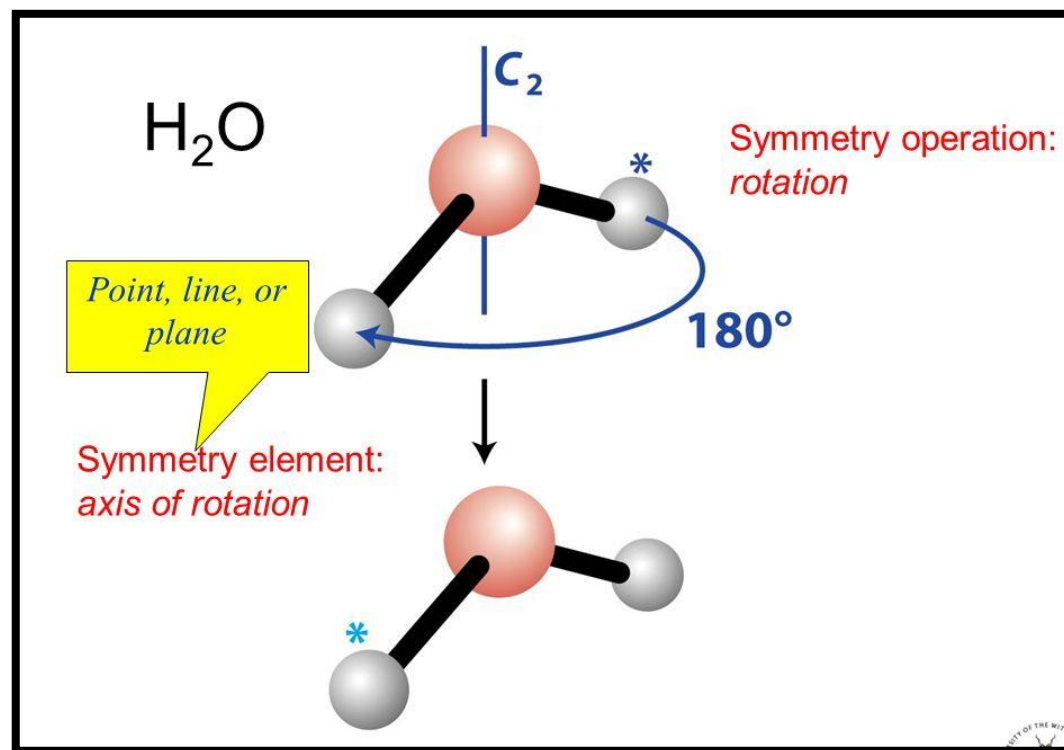
As there are 3 stereogenic centres so there are $8 (= 2^3)$ ways of arranging R s and S s.



Symmetry



- A **symmetry element** is a geometrical entity such as a line, a plane or a point about which one can perform an operation of **rotation, reflection or inversion**.
- A **symmetry operation** is a movement of a molecule/object about a **symmetry element** such that the resulting configuration is **indistinguishable** from the original.
- A symmetry operation will transform a molecule into an **equivalent or identical** configuration.



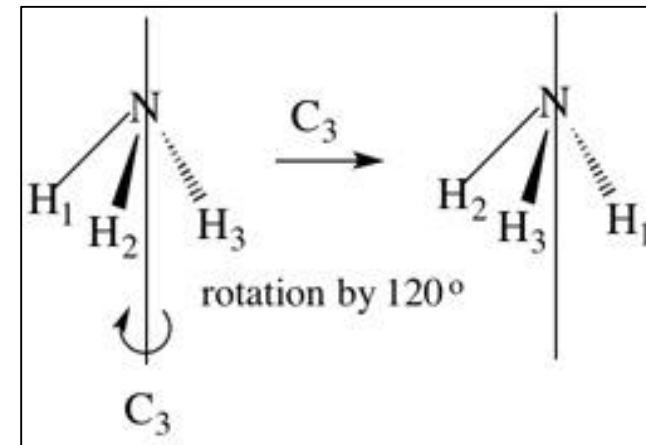
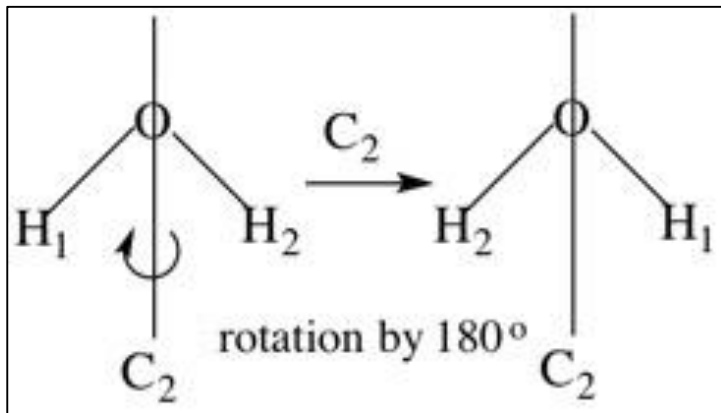
Symmetry elements	Symmetry operations
1. Identity [E]	Doing nothing
2. Proper rotation axis or axis of symmetry [C_n]	Rotation about the axis through some angle
3. Mirror plane or plane of symmetry [σ]	Reflection about the plane
4. Inversion centre or centre of symmetry [i]	Inversion [reflection about a point]
5. Improper rotation axis or Rotation-reflection axis [S_n]	Rotation about an axis through some angle followed by a reflection in a plane

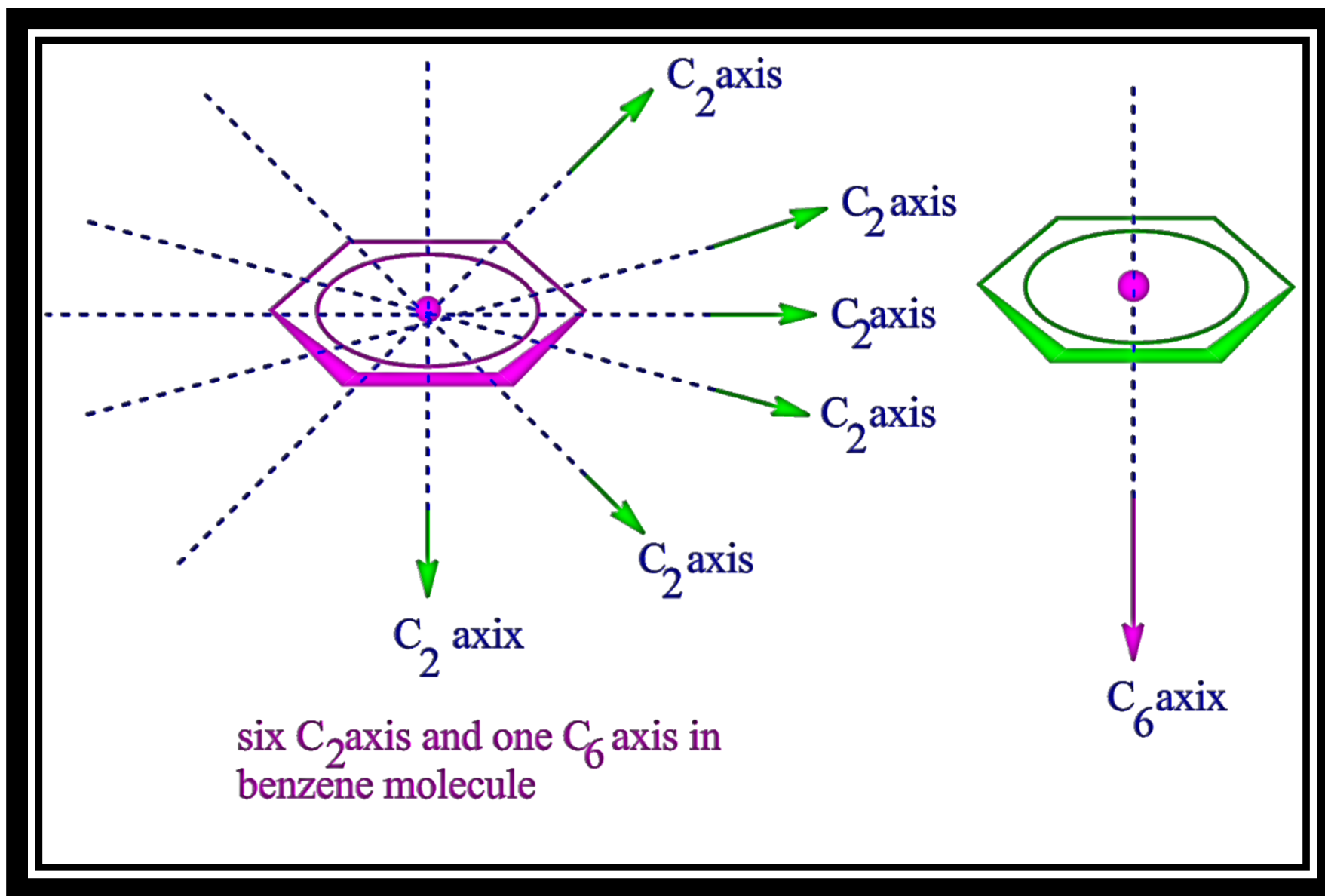
1. Identity (E)

- This is an operation which brings molecule back to its original orientation.
- This operation **does nothing**. It is simplest of all symmetry elements.
- It is the only element/operation possessed by all molecules.
- It is denoted by E.

2. Axis of symmetry (C_n)

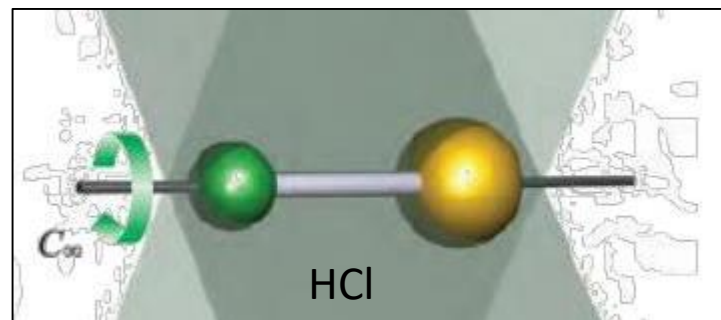
- It is called n-fold rotational axis.
- If the rotation of a molecule **about an axis through some angle** results in a configuration which is **indistinguishable from the original structure**, then the molecule is said to possess a proper rotational axis or axis of symmetry.
- It is denoted as C_n .
- n is known as the order of rotation.
- The angle of rotation is $360^\circ/n$.





Principal and subsidiary axis

- In molecules with more than one axis of symmetry, the axis with the **highest fold symmetry** (highest n in C_n) is called the **principal axis**. The other axes are called **subsidiary axes**. For benzene, the principal axis is thus C_6 .
- In case, there are more than one axes of same order, the axis **passing through maximum number of atoms** is the principal axis.
- The axis of symmetry can be C_∞ (e.g., HCl).



Symbol of the proper rotation axis	Order of rotation axis	$360^\circ / n$
1. $C_2 (= C_6^3)$	2	180
2. $C_3 (= C_6^2)$	3	120
3. C_4	4	90
4. C_5	5	72
5. C_6	6	60

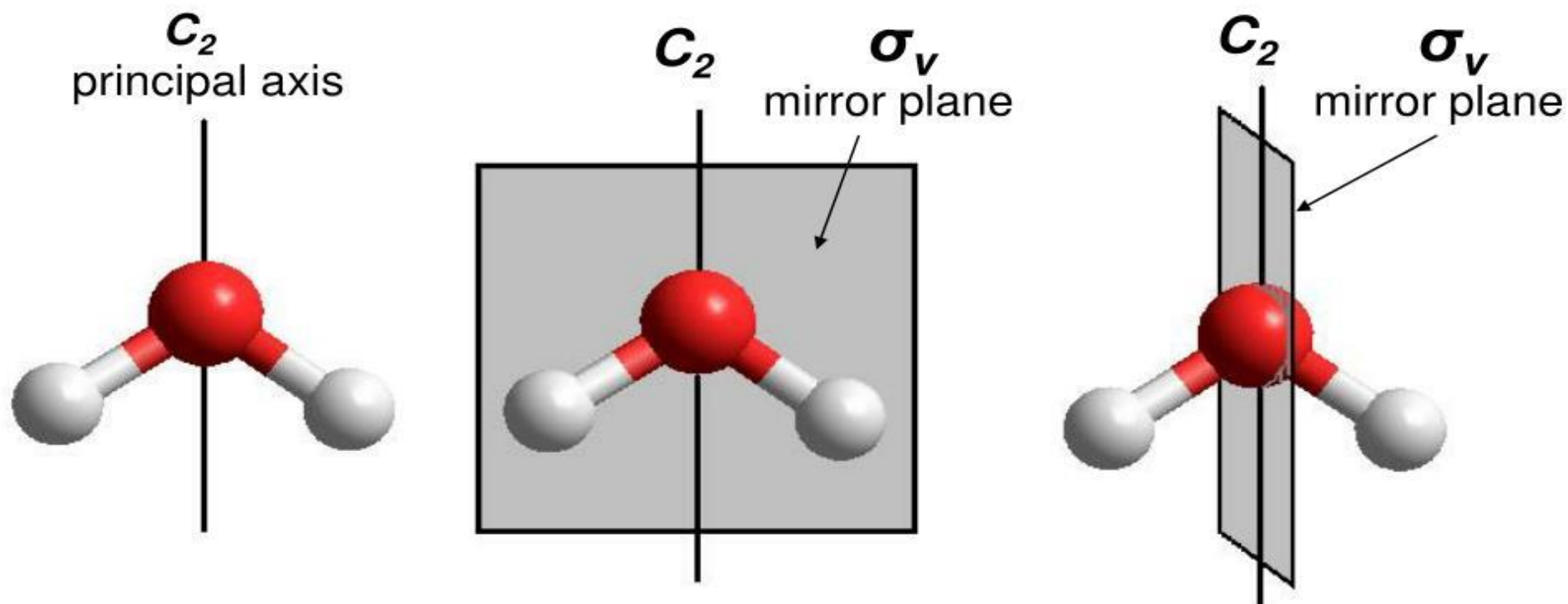
3. Plane of symmetry (σ)

- A mirror plane is an **imaginary plane** which divides a molecule into two equal halves such that one half is the exact **mirror image** of the other.
- It is denoted by σ .

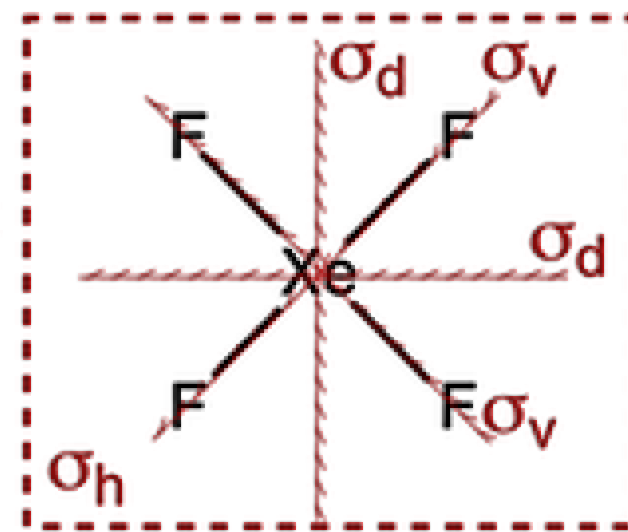
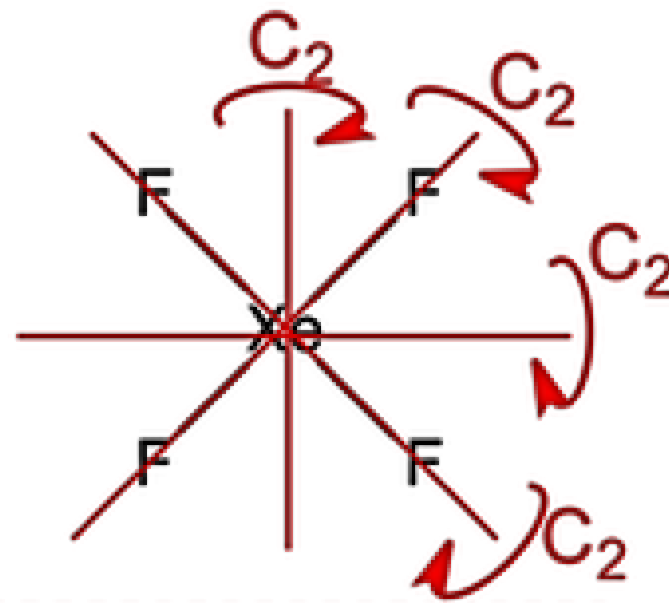
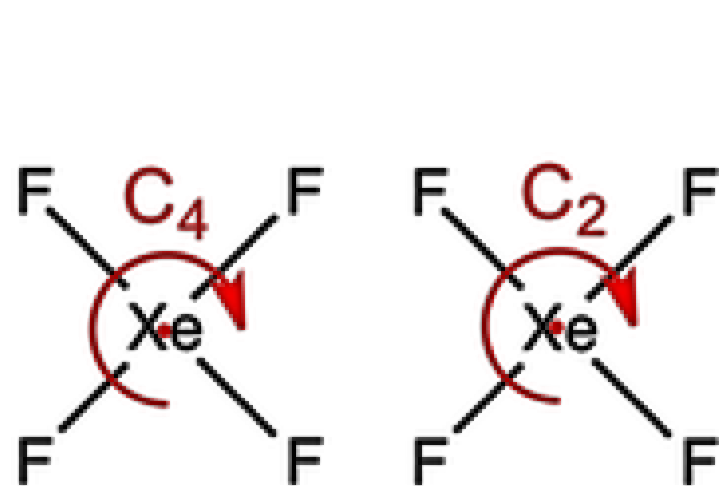
Classification of mirror plane:

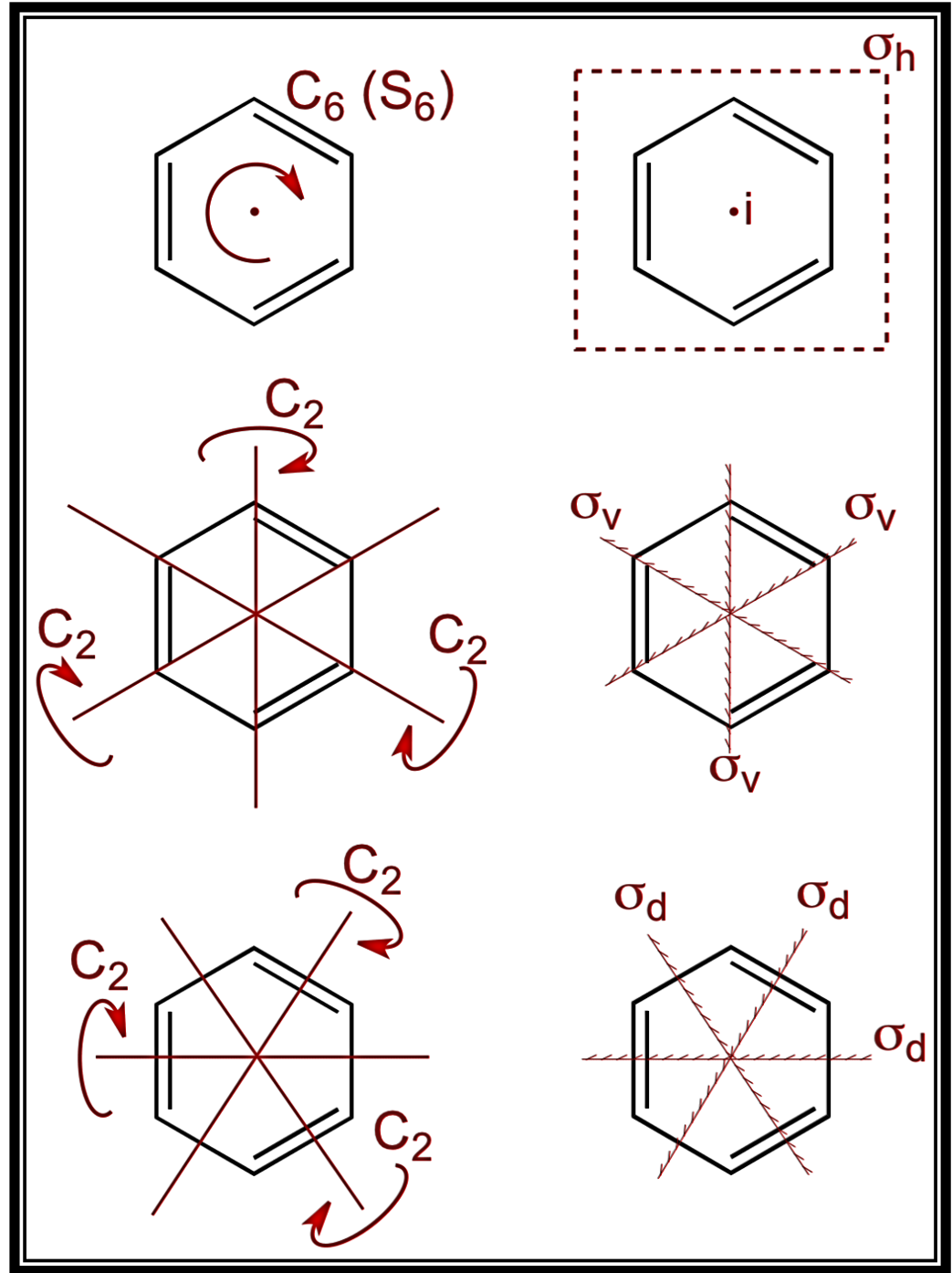
- Vertical plane of symmetry (σ_v): The principal axis **lies on** this plane.
- Horizontal plane of symmetry (σ_h): The principal axis is **perpendicular** to this plane.
- Diagonal plane of symmetry (σ_d): This plane **passes through the principal axis** but **bisects the angle** between two subsidiary axes.

Rotational axes and mirror planes of the water molecule:



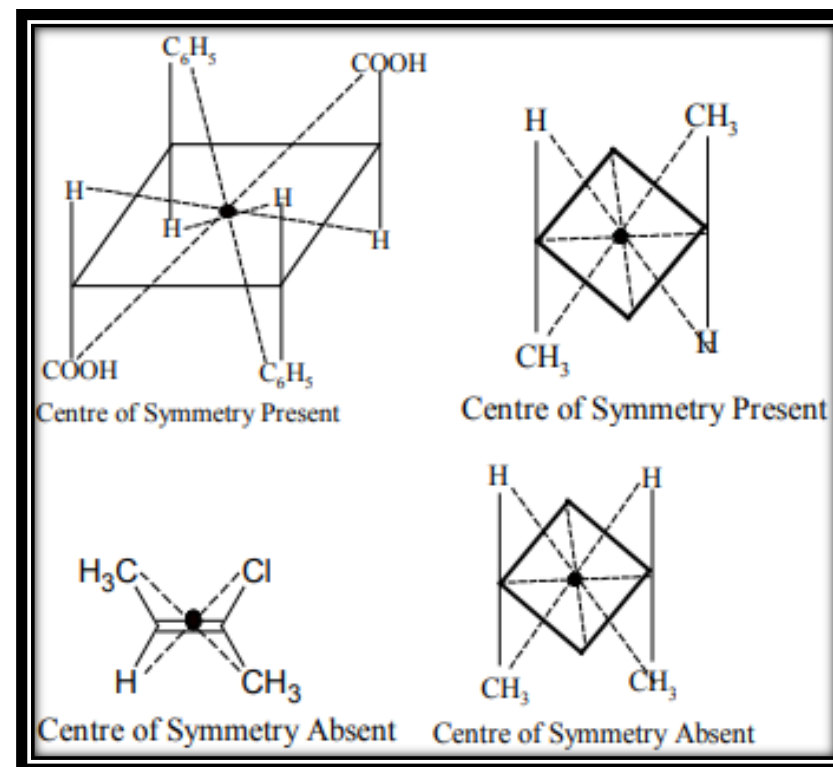
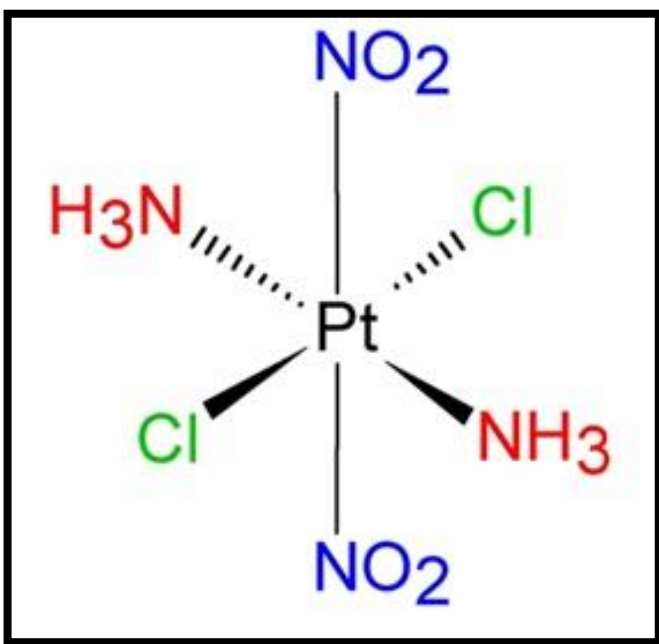
The water molecule has only one rotational axis, its C_2 axis, which is also its principal axis. It has two mirror planes that contain the principal axis, which are therefore σ_v planes. It has no σ_h mirror plane, and no center of symmetry.





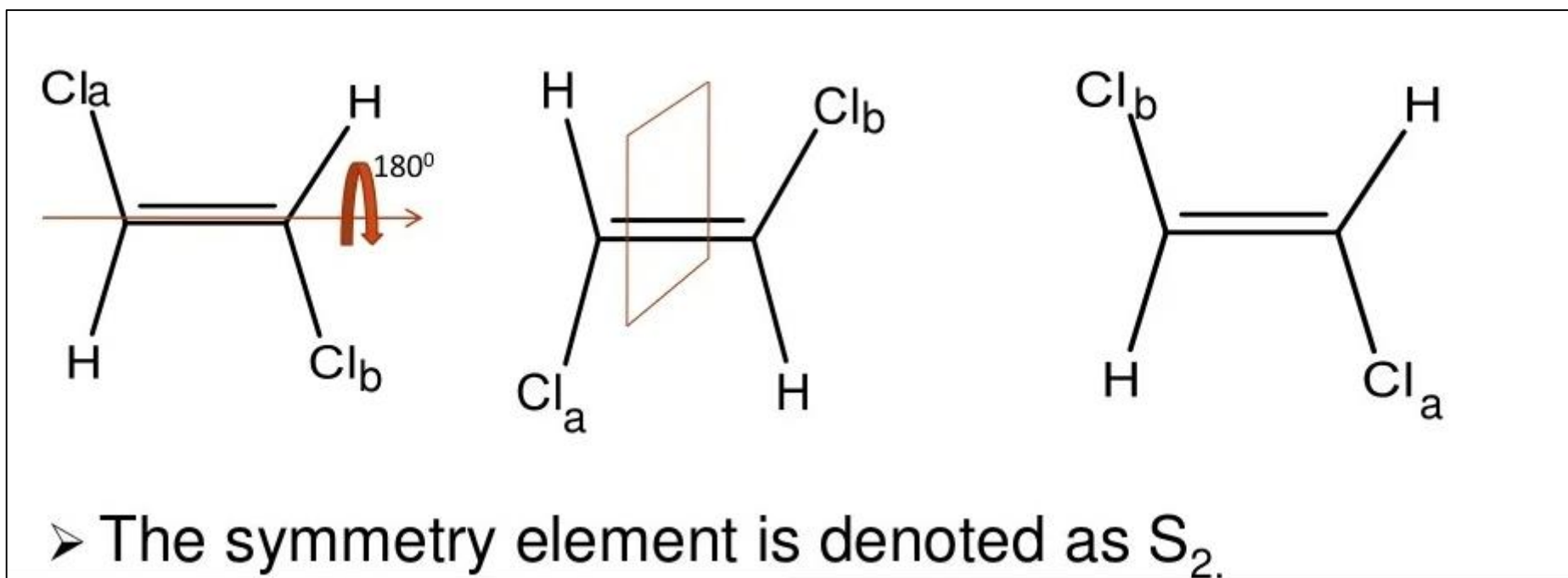
4. centre of symmetry (i)

- If a line, drawn through a point within a molecule and upon extending an equal distance on the other side, encounters same atom/group, then that point is called centre of symmetry or centre of inversion.
- It is denoted as 'i'.



5. Improper axis of symmetry/ Rotation-reflection axis/ Alternate axis of symmetry (S_n)

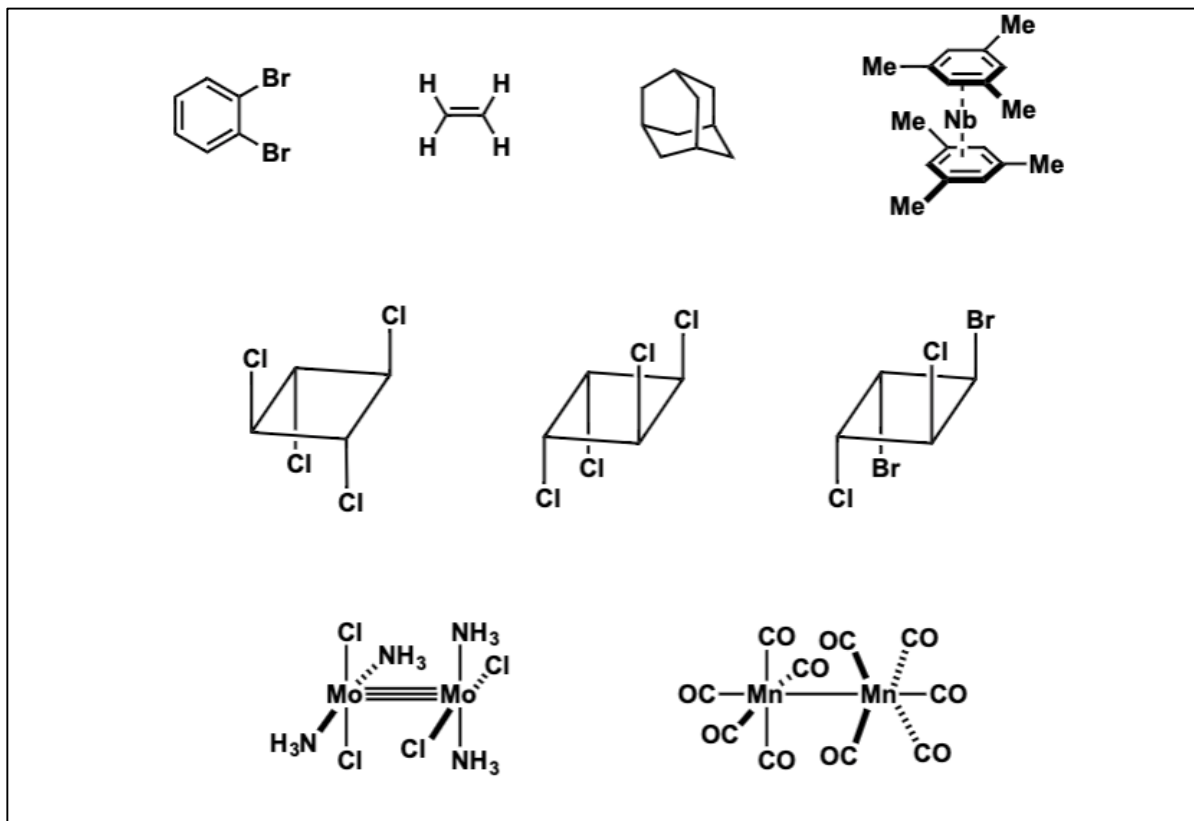
- If a molecule undergoes **rotation about an axis through some angle followed by reflection through a plane perpendicular to the axis**, giving rise to an indistinguishable structure from the original one; then the molecule is known to have improper axis.
- It is denoted by S_n .



1. Draw the structures and find the symmetry elements in the following molecules.

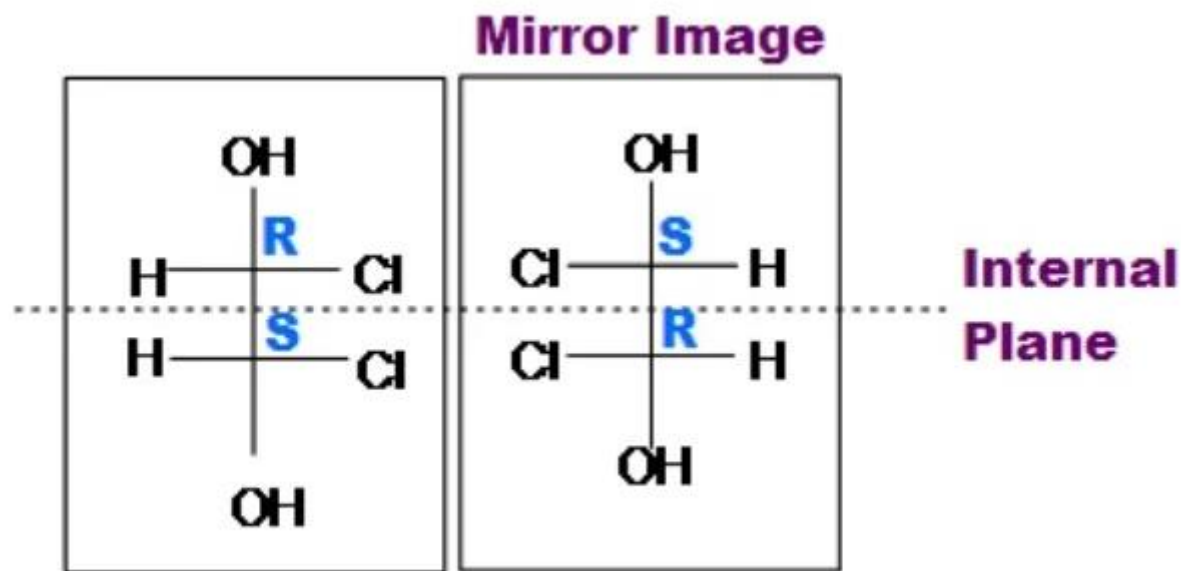
BF_3 , NH_3 , CCl_4 , CHCl_3 , C_2H_2 , C_2H_4 , cis 1,2-dichloro ethane, trans 1,2-dichloro ethene.

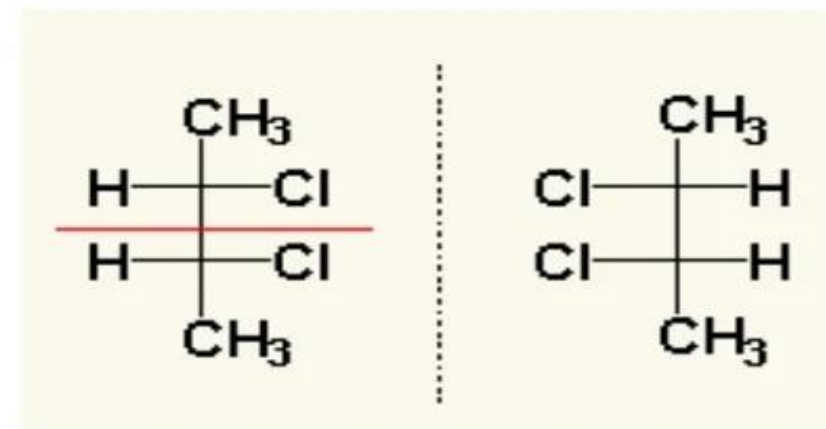
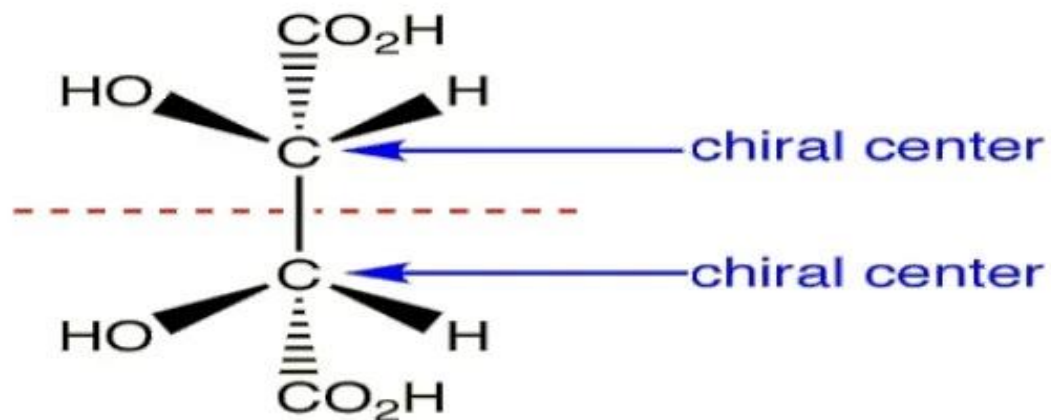
2. Find the symmetry elements in the following molecules.



MESO compounds

- A meso compound is a molecule with multiple stereocentres that is superimposable on its mirror image.
- Meso compounds are **achiral compounds** that has multiple chiral centres.
- Meso compounds are **optically inactive**.
- It has an internal symmetry plane that divides the compound in half.



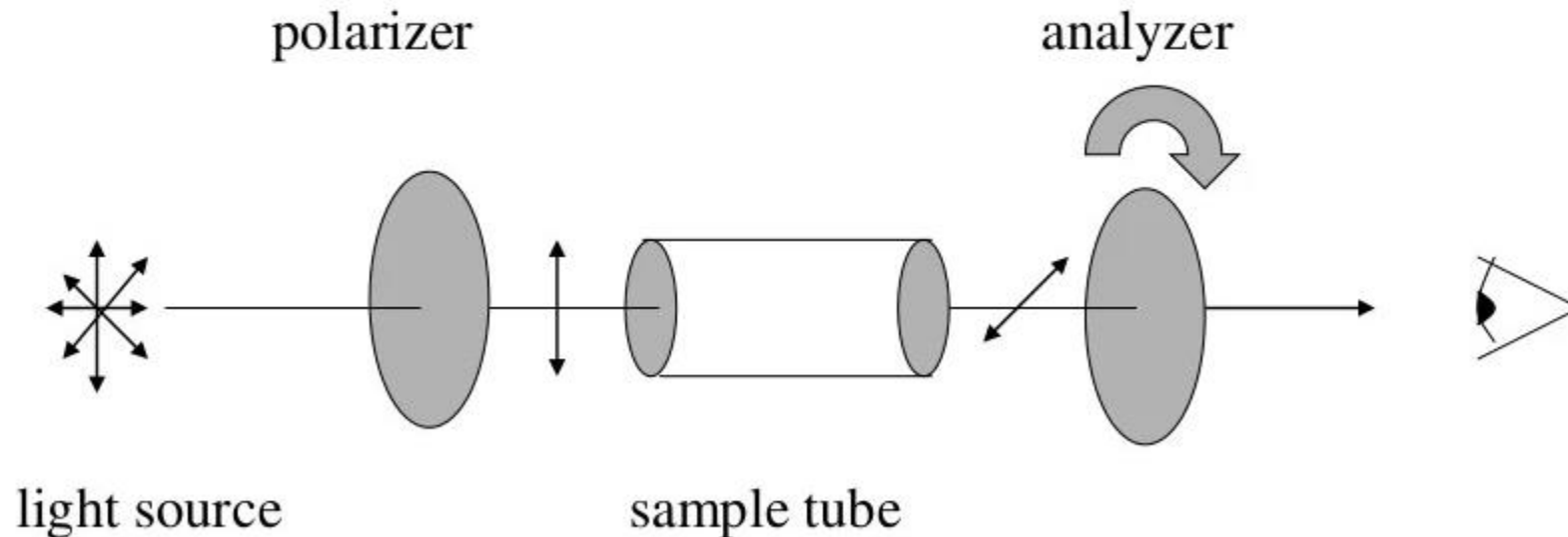


A meso compound should contain two or more identical substituted stereocentres. Also, it has an **internal symmetry plane** that divides the compound in two halves. These two halves reflect each other by the internal mirror. The optical rotation by one half is equal and opposite that of by the other half, resulting in an **optically inactive compound**. That is why, the meso compound is said to be **internally compensated**.

Optical activity

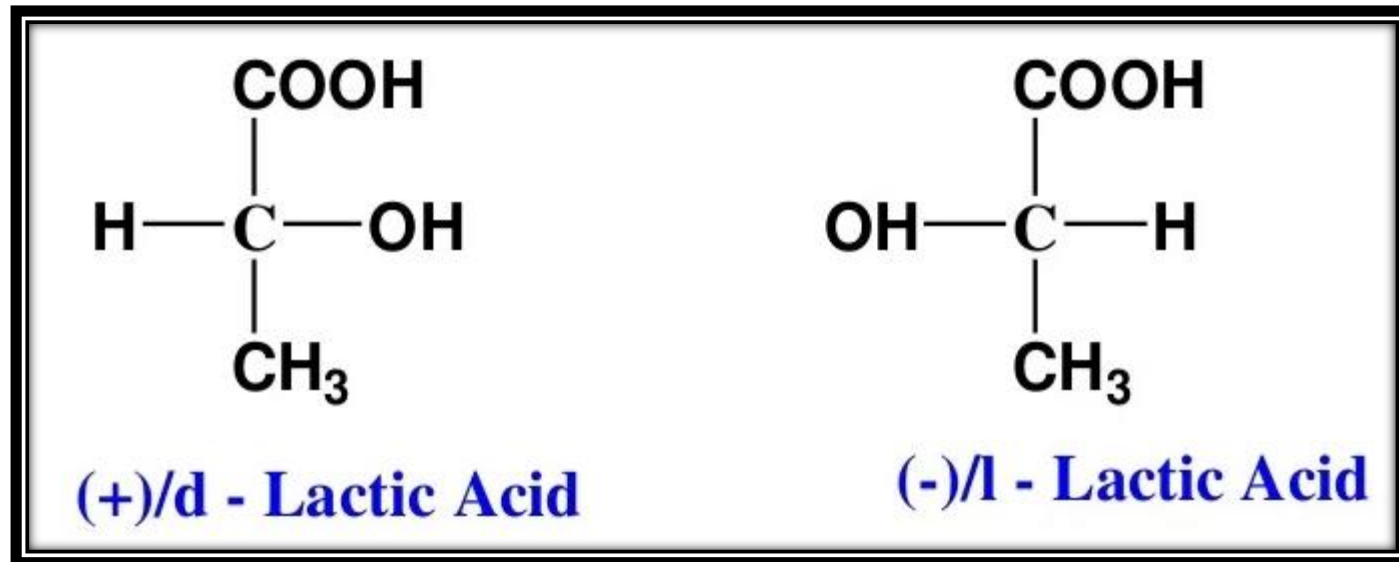
Optical activity is the ability of a chiral molecule to rotate the plane of plane-polarised light using a polarimeter.

A simple polarimeter consists of a light source, polarising lens, sample tube and analysing lens.



Dextrorotatory: Compound that rotate the plane polarised light towards **clockwise direction**. It is denoted by (+) or d.

Laevorotatory: Compound that rotate the plane polarised light towards **anti-clockwise direction**. It is denoted by (-) or l.



Specific rotation: The angle of rotation in degrees of the plane of polarization of a ray of monochromatic light that passes through a tube 1 decimetre long, containing the substance in solution or fused state at a concentration of 1 gram per milliliter in a polarimeter.

The diagram shows the formula for specific rotation, $[\alpha]_D^t (\text{Solvent}) = \frac{\alpha}{lc}$, enclosed in a black rectangular box. Red arrows point from descriptive text to parts of the formula: 'temperature' points to the superscript t ; 'wavelength of monochromatic light D = Na 'D' line 589 nm' points to the subscript D ; 'observed rotation (degrees)' points to the numerator α ; 'concentration (g ml)⁻¹' points to the denominator c ; 'length of sample tube (decimeters)' points to the denominator l ; and 'Solvent used must be quoted: rotation is solvent dependent' points to the '(Solvent)' part of the formula. The text 'Specific rotation' is also present on the left side of the box.

temperature

Specific rotation

wavelength of monochromatic light
D = Na 'D' line 589 nm

$[\alpha]_D^t (\text{Solvent}) = \frac{\alpha}{lc}$

observed rotation (degrees)

concentration (g ml)⁻¹

length of sample tube (decimeters)

Solvent used must be quoted:
rotation is solvent dependent

Specific Rotation

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

Example: A sample of 2 g in 10 mL of solution
measured in a 25 cm long cell
gives an observed α of $+134^\circ$
The specific rotation is?

$$[\alpha]_{\lambda}^t = \frac{(+134^\circ)}{2.5 \text{ (0.2)}}$$

$$[\alpha]_{\lambda}^t = +268^\circ \quad (\text{actually deg/cc}^2\text{g}^{-1})$$

Racemic mixture

- ❖ A mixture having equal amounts of enantiomers is called **racemic mixture** or **racemic modification**.
- ❖ A racemic mixture or **racemate** is one that has equal amounts of enantiomers of a chiral molecule.
- ❖ A racemic mixture is denoted by the prefix **(±)** or dl, also by **RS** or **SR**.

Resolution

- The process of separation of racemic form into individual enantiomers is called **resolution**.
- The following methods are used for this process:
Mechanical method, Biochemical method, Chemical method and Chromatographic method.

References

