B.Sc.(H) Chemistry
Semester - II
Core Course - III (CC-III)
Organic Chemistry - I

II. Stereochemistry

5. Physical and Chemical Properties of Stereoisomers

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Syllabus & Coverage

Syllabus

II Stereochemistry:

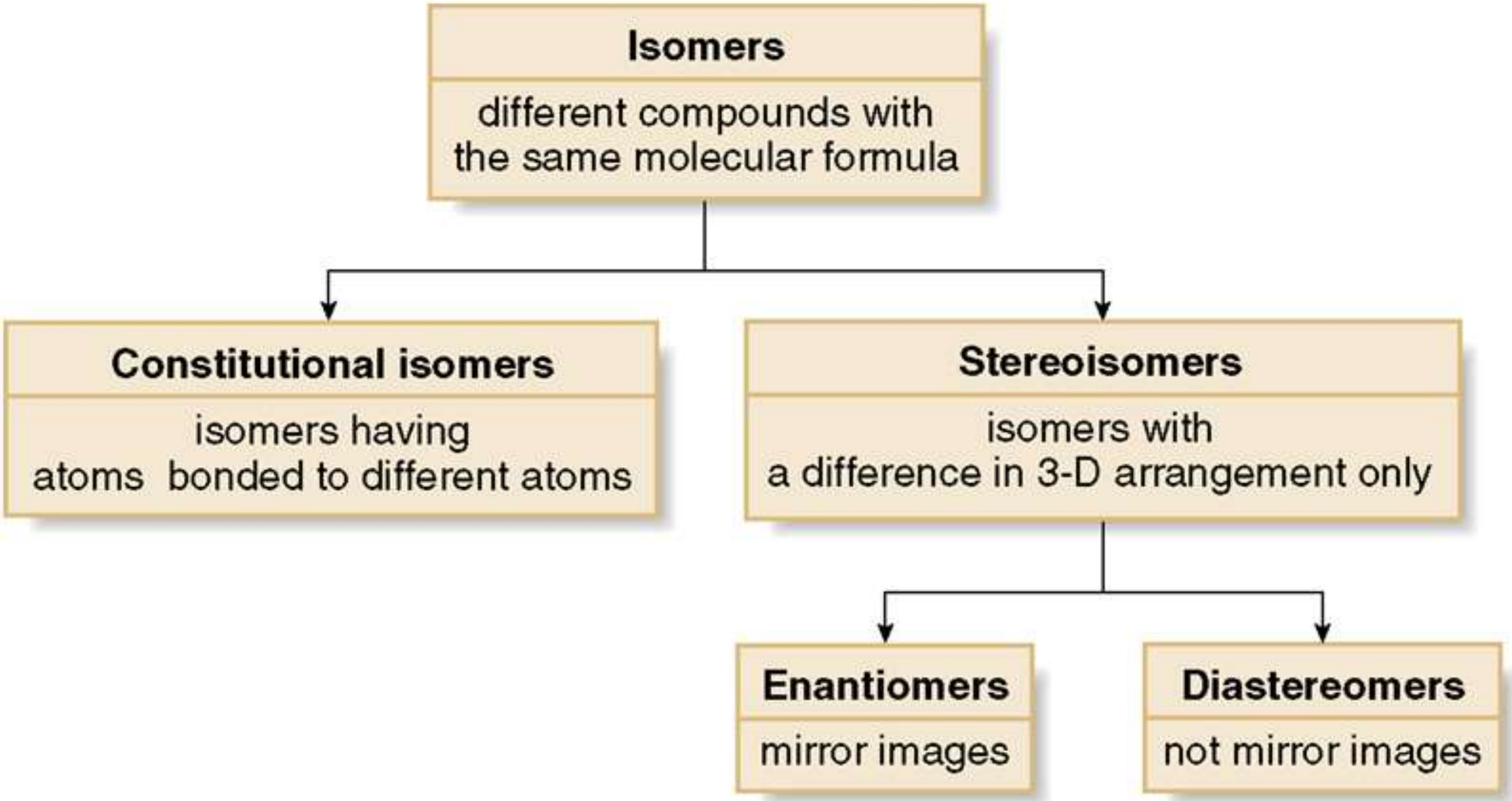
Fischer Projection, Newmann and Sawhorse Projection formulae and their interconversions. Geometrical isomerism: cis–trans and syn-anti isomerism, E/Z notations with Cahn Ingold and Prelog (CIP) rules for determining absolute configuration.

Optical Isomerism: Optical Activity, Specific Rotation, Chirality/Asymmetry, Enantiomers, Molecules with two or more chiral-centres, Distereoisomers, Meso structures, Racemic mixture. Resolution of Racemic mixtures. Relative and absolute configuration: D/L and R/S designations.

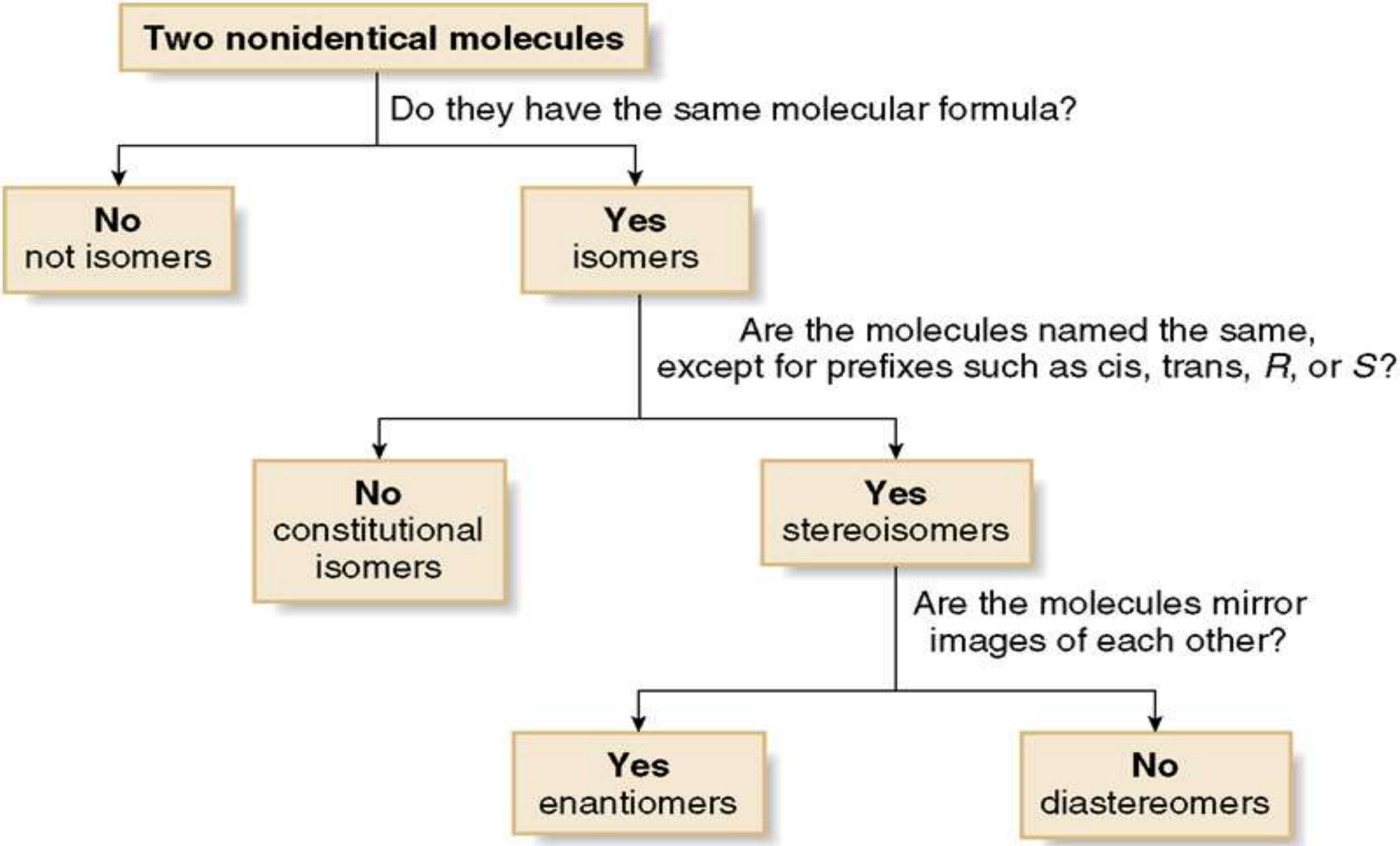
Coverage:

1. Types of Isomers : Comparing Structures
2. Optical Activity
3. Racemic Mixtures : Separation of Racemic Mixtures
4. Enantiomeric Excess and Optical Purity
5. Relative and Absolute Configuration
6. Physical and Chemical Properties of Stereoisomers

Types of Isomers



Determining the Relationship Between Two Non-Identical Molecules



Comparing Structures:

Are the structures connected the same?

yes → **Are they mirror images?**

no → **Constitutional Isomers**

Are they mirror images?

yes → **Enantiomers**
All chiral centers will be opposite between them.

no → **Is there a plane of symmetry?**

Is there a plane of symmetry?

yes → **Meso**
superimposable

no → **Diastereomers**

Optical Activity:

- **The chemical and physical properties of two enantiomers are identical except in their interaction with chiral substances.**

- **The physical property that differs is the behavior when subjected to plane-polarized light (this physical property is often called an optical property).**

- **Plane-polarized (polarized) light is light that has an electric vector that oscillates in a single plane.**

- **Plane-polarized light arises from passing ordinary light through a polarizer.**

Optical Activity:

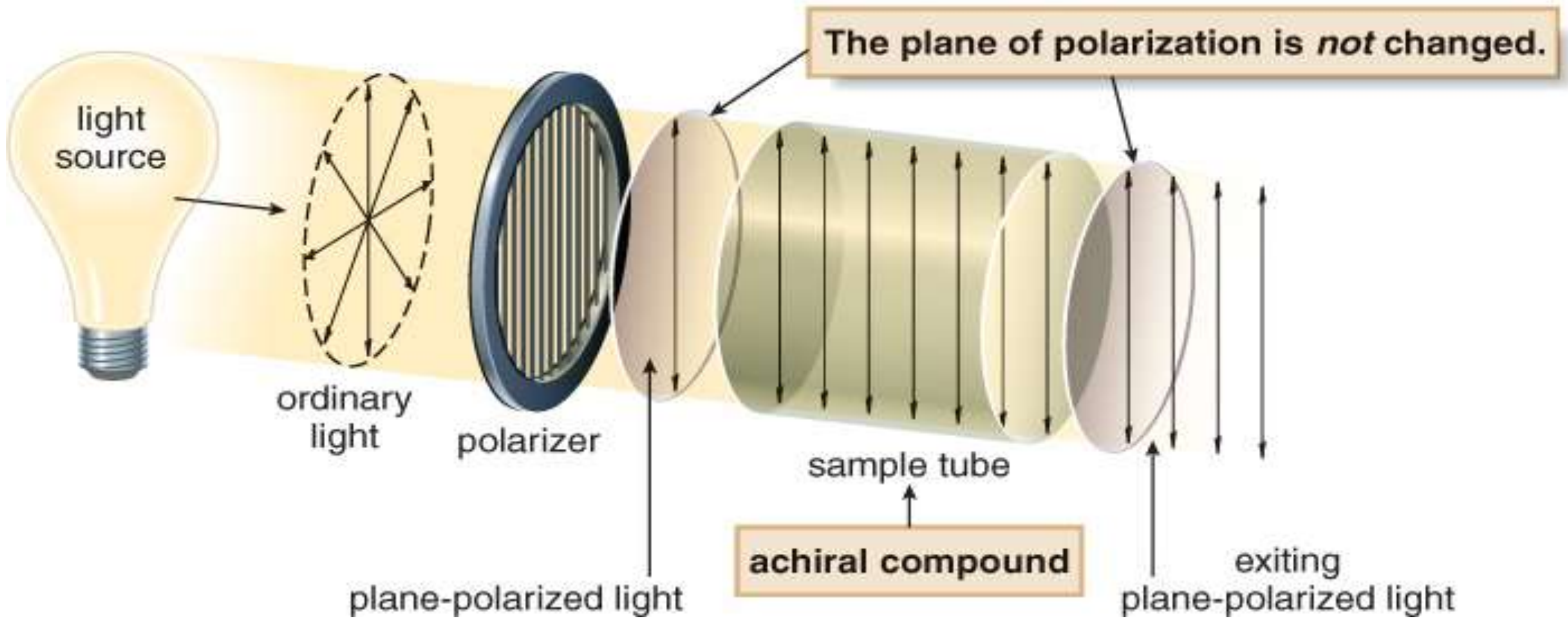
- Originally a natural polarizer, calcite or iceland spar, was used. Today, polarimeters use a polarized lens similar to that used in some sunglasses.

- A polarizer has a very uniform arrangement of molecules such that only those light rays of white light (which is diffuse) that are in the same plane as the polarizer molecules are able to pass through.

- A polarimeter is an instrument that allows polarized light to travel through a sample tube containing an organic compound and permits measurement of the degree to which the light is rotated.

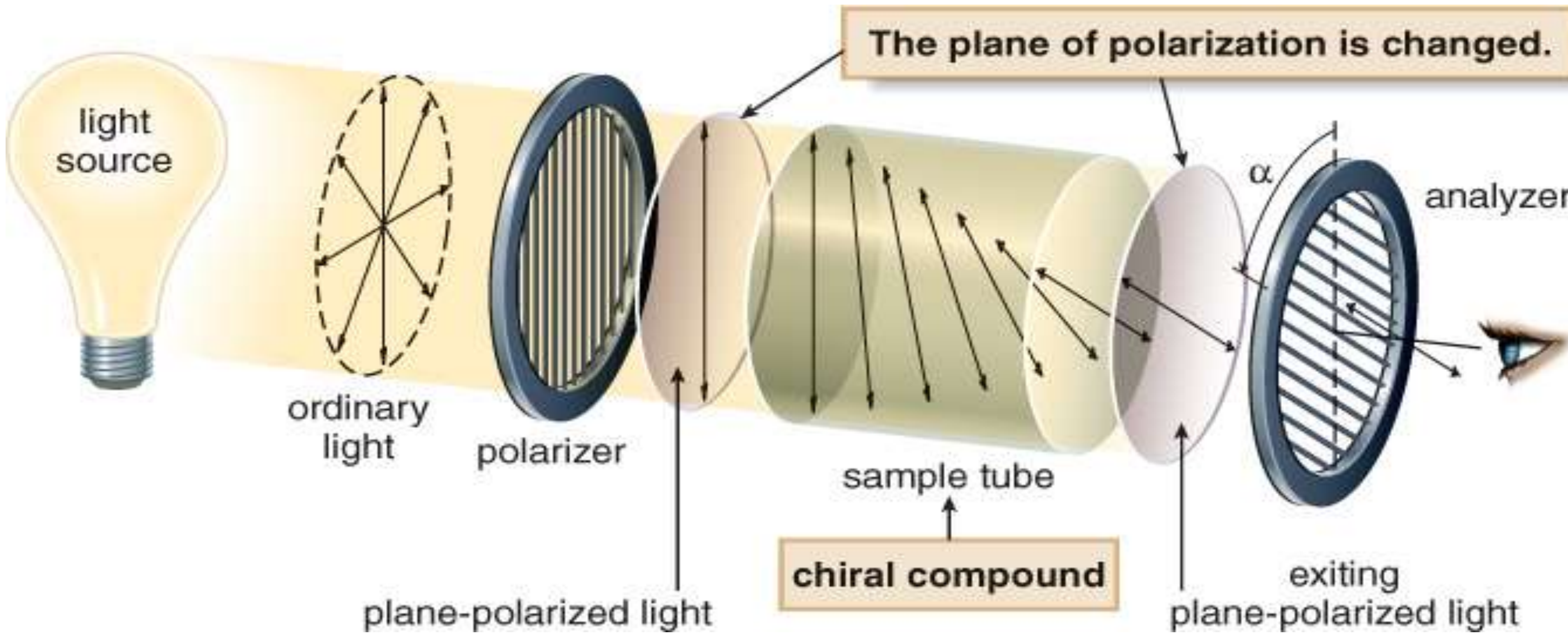
Optical Activity:

- **With achiral compounds, the light that exits the sample tube remains unchanged. A compound that does not change the plane of polarized light is said to be optically inactive.**



Optical Activity:

- **With chiral compounds, the plane of the polarized light is rotated through an angle α. The angle α is measured in degrees (°), and is called the observed rotation. A compound that rotates polarized light is said to be optically active.**



Optical Activity:

- **The rotation of polarized light can be clockwise or counterclockwise.**
- **If the rotation is clockwise (to the right of the noon position), the compound is called dextrorotatory. The rotation is labeled *d* or (+).**
- **If the rotation is counterclockwise, (to the left of noon), the compound is called levorotatory. The rotation is labeled *l* or (-).**
- **Two enantiomers rotate plane-polarized light to an equal extent but in opposite directions. Thus, if enantiomer A rotates polarized light +5°, the same concentration of enantiomer B rotates it –5°.**
- **No relationship exists between *R* and *S* prefixes and the (+) and (-) designations that indicate optical rotation.**

Racemic Mixtures:

- **An equal amount of two enantiomers is called a racemic mixture or a racemate. A racemic mixture is optically inactive. Because two enantiomers rotate plane-polarized light to an equal extent but in opposite directions, the rotations cancel, and no rotation is observed.**

The Physical Properties of Enantiomers A and B Compared to Racemic A+B

Property	A alone	B alone	Racemic A + B
Melting point	identical to **B**	identical to **A**	may be different from **A** and **B**
Boiling point	identical to **B**	identical to **A**	may be different from **A** and **B**
Optical rotation	equal in magnitude but opposite in sign to **B**	equal in magnitude but opposite in sign to **A**	0°

Racemic Mixtures:

- **Specific rotation is a standardized physical constant for the amount that a chiral compound rotates plane-polarized light. Specific rotation is denoted by the symbol [α] and defined using a specific sample tube length (*l*, in dm), concentration (*c* in g/mL), temperature (25^0C) and wavelength (589 nm).**

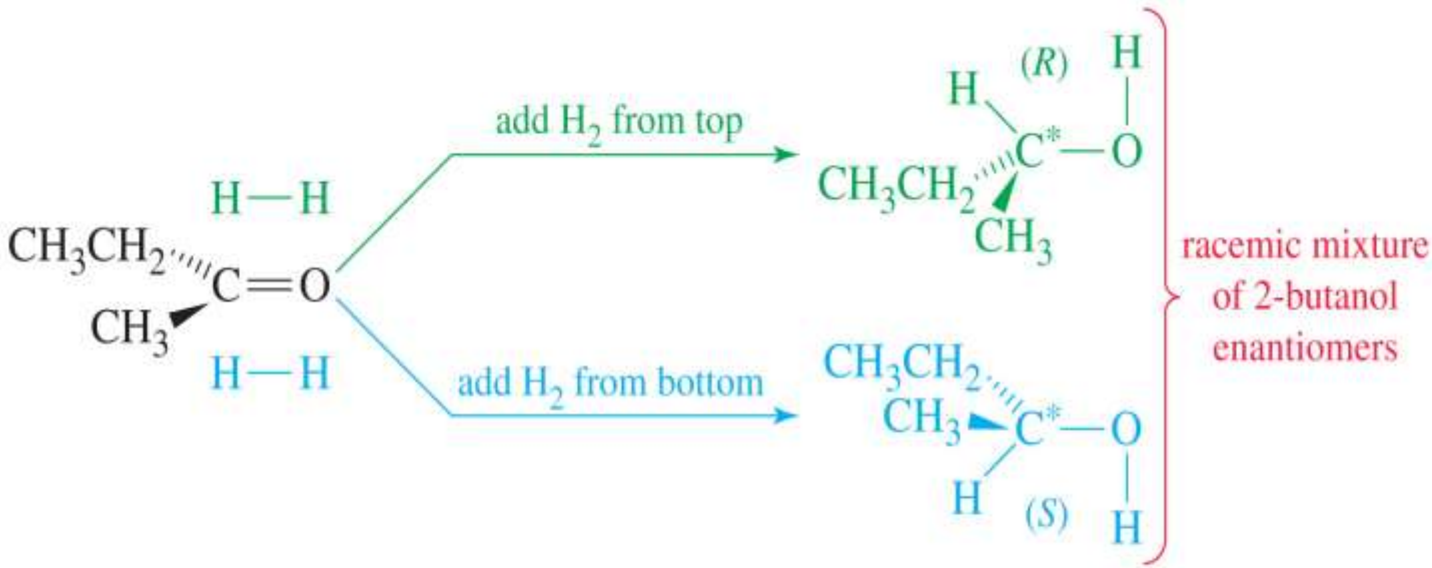
$$\text{specific rotation} = [\alpha] = \frac{\alpha}{l \times c}$$

α = observed rotation (°)
l = length of sample tube (dm)
c = concentration (g/mL)

[dm = decimeter
1 dm = 10 cm]

Racemic Mixtures:

If optically inactive reagents combine to form a chiral molecule, a racemic mixture is formed.



Separation of Racemic Mixtures:
(Resolution of Enantiomers)

React the racemic mixture with a pure chiral compound, such as tartaric acid, to form diastereomers, then separate them.

(*R*)- and (*S*)-2-butanol

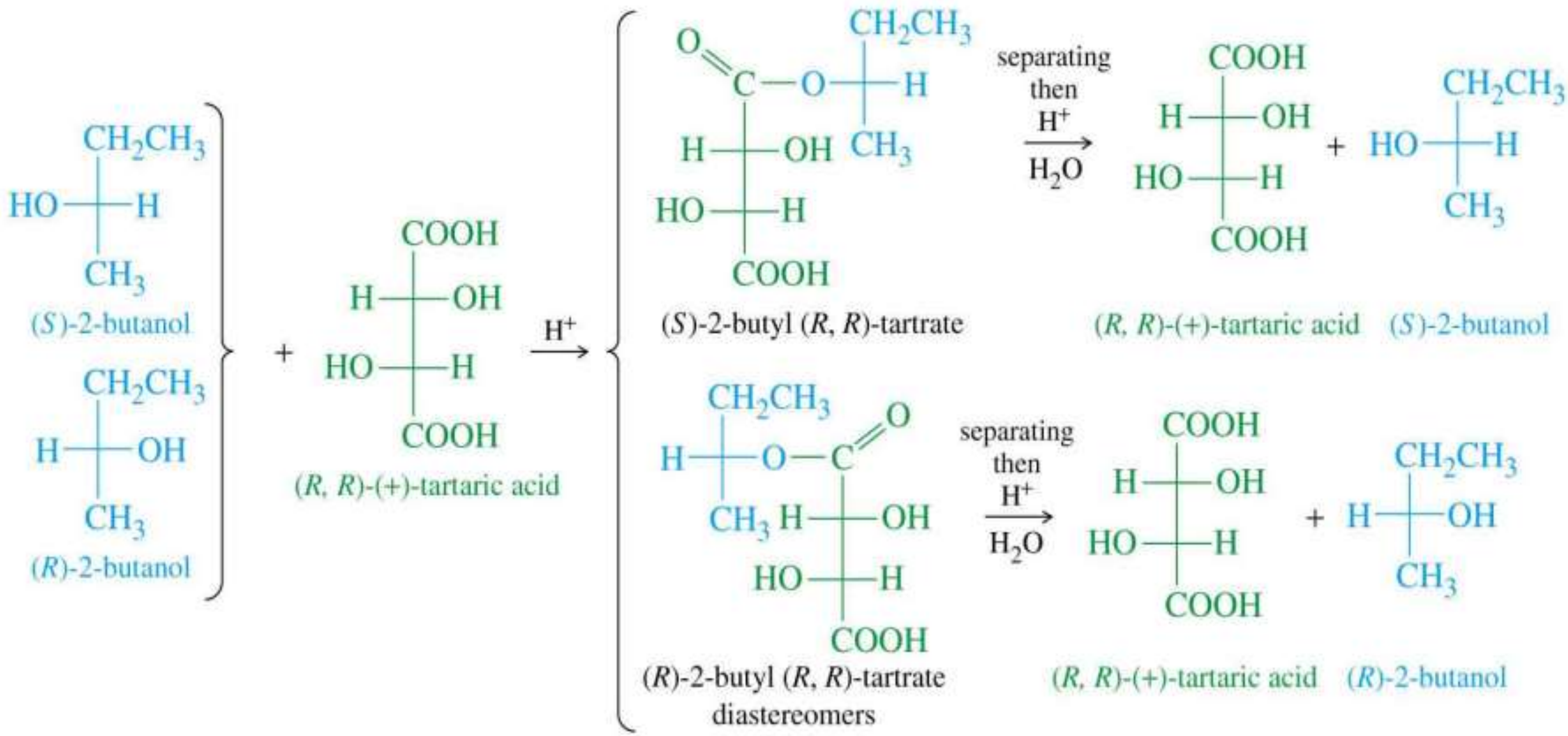
plus

(*R*,*R*)-tartaric acid

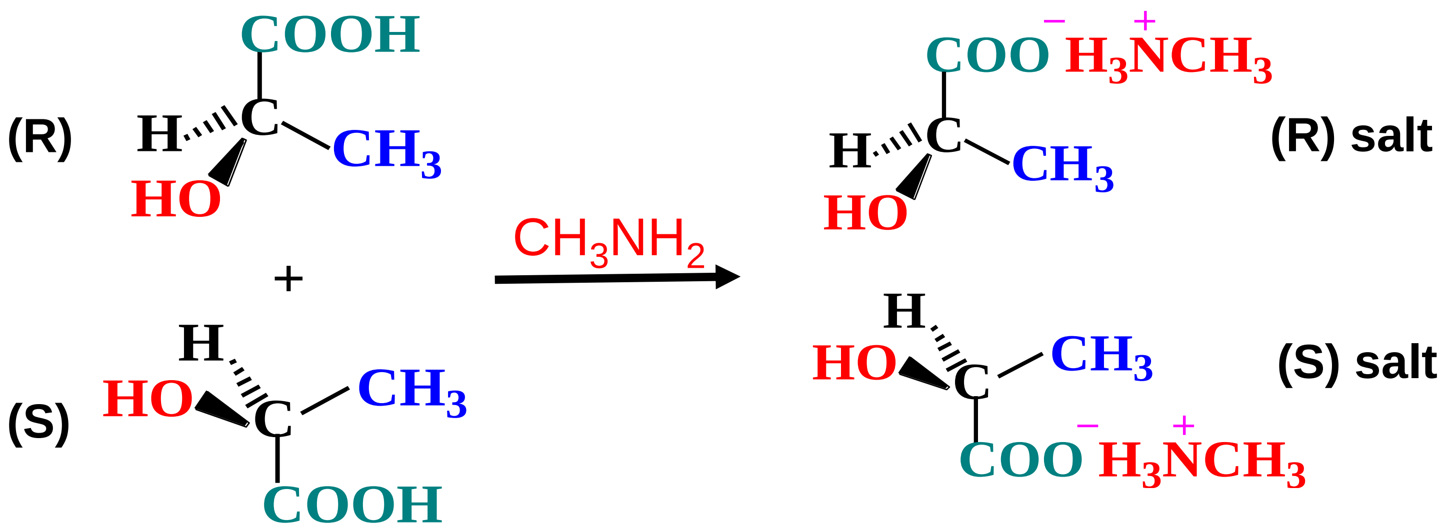
$\xrightarrow{H^+}$ (*R*)-2-butyl (*R*,*R*)-tartrate + (*S*)-2-butyl (*R*,*R*)-tartrate

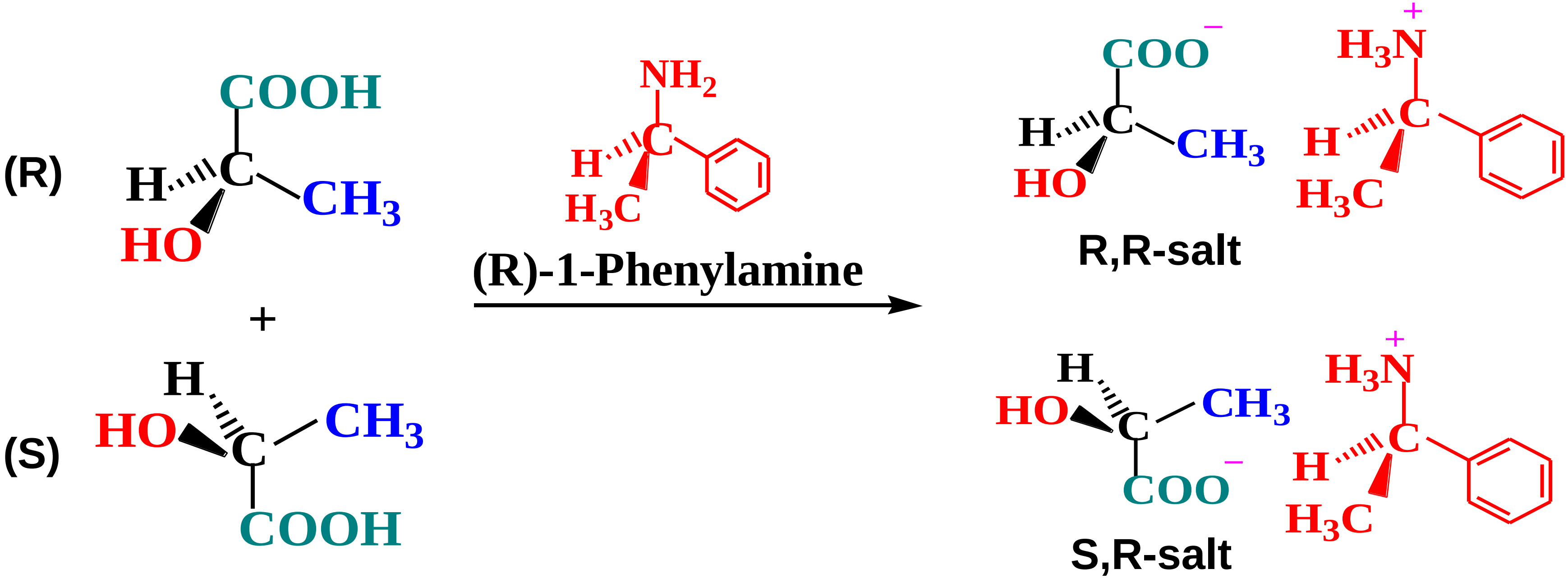
diastereomers, *not* mirror images

React a racemic mixture with a chiral compound to form diastereomers, which can be separated.



Separation of Racemic Lactic Acid:





Enantiomeric excess and Optical purity: *ee* and *op*

- **Enantiomeric excess (*ee*) is a measurement of the excess of one enantiomer over the racemic mixture.**

  ***ee* = % of one enantiomer - % of the other enantiomer.**

- **Consider the following example: If a mixture contains 75% of one enantiomer and 25% of the other, the enantiomeric excess is 75% - 25% = 50%. Thus, there is a 50% excess of one enantiomer over the racemic mixture.**
- ***ee* is numerically equal to Optical Purity.**
- **The optical purity can be calculated if the specific rotation [α] of a mixture and the specific rotation [α] of a pure enantiomer are known.**

op = ([α] mixture/[α] pure enantiomer) x 100.

Stereochemistry

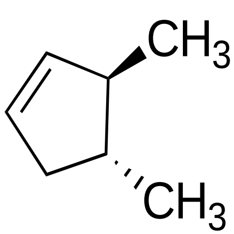
An optically pure substance consists exclusively of a single enantiomer.

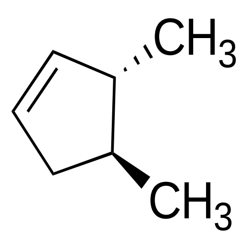
Optical purity of a optically active substance is expressed as the Enantiomeric Excess = % One Enantiomer – % Other Enantiomer

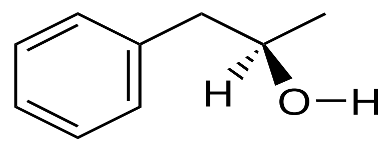
Absolute and Relative Configuration

Absolute configuration is the precise three-dimensional arrangement of atoms in space.

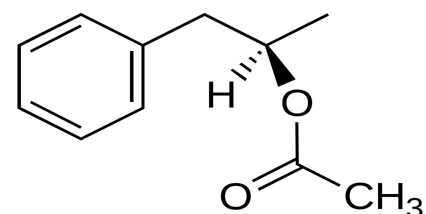
Relative configuration compares the three-dimensional arrangement of atoms in space of one compound with those of another compound.







$[\alpha]_D = +33.0$



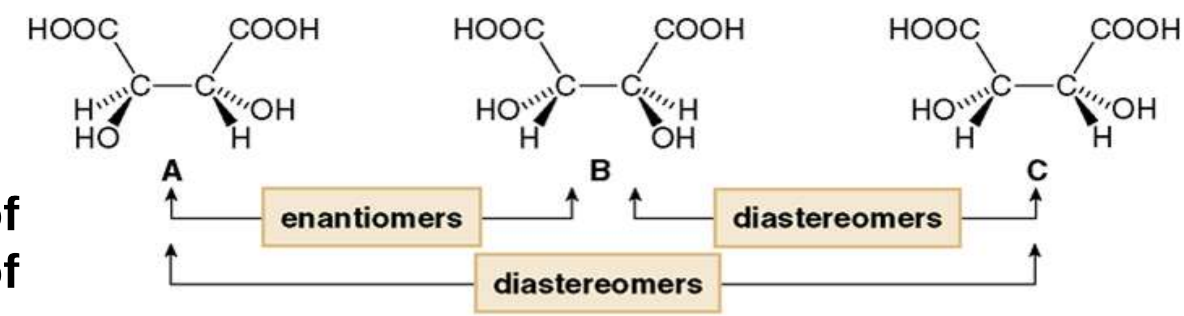
$[\alpha]_D = -7.0$

There is NO correlation between the sign of the optical rotation and the three-dimensional arrangement of atoms.

Physical Properties of Stereoisomers:

- **Since enantiomers have identical physical properties, they cannot be separated by common physical techniques like distillation.**
- **Diastereomers and constitutional isomers have different physical properties, and therefore can be separated by common physical techniques.**

The physical properties of the three stereoisomers of tartaric acid.

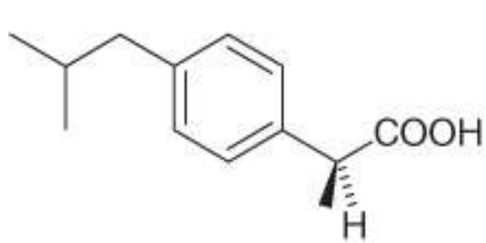


Property	A	B	C	A + B (1:1)
melting point (°C)	171	171	146	206
solubility (g/100 mL H_2O)	139	139	125	139
[α]	+13	−13	0	0
R,*S* designation	*R*,*R*	*S*,*S*	*R*,*S*	—
d,*l* designation	*d*	*l*	none	*d*,*l*

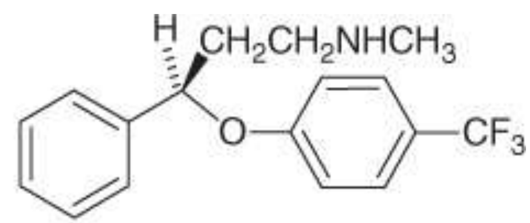
- The physical properties of **A** and **B** differ from their diastereomer **C.**
- The physical properties of a racemic mixture of **A** and **B** (last column) can also differ from either enantiomer and diastereomer **C.**
- **C** is an achiral meso compound, so it is optically inactive; [α] = 0.

Chemical Properties of Enantiomers:

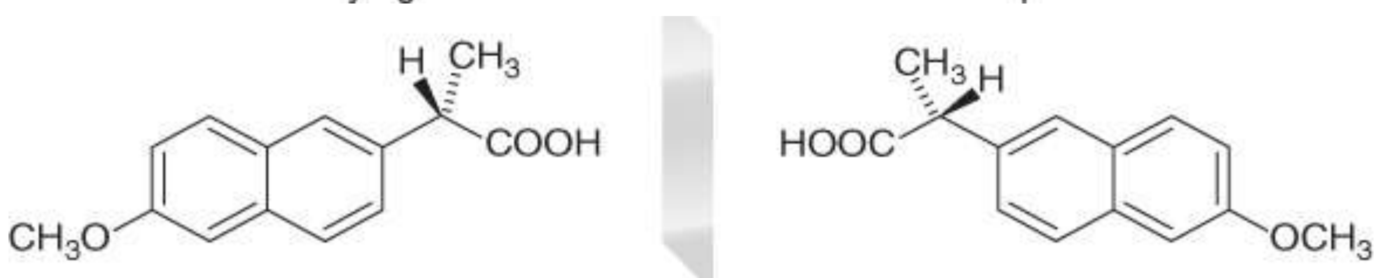
- **Two enantiomers have exactly the same chemical properties except for their reaction with chiral non-racemic reagents.**
- **Many drugs are chiral and often must react with a chiral receptor or chiral enzyme to be effective. One enantiomer of a drug may effectively treat a disease whereas its mirror image may be ineffective or toxic.**



(*S*)-ibuprofen
anti-inflammatory agent



(*R*)-fluoxetine
antidepressant

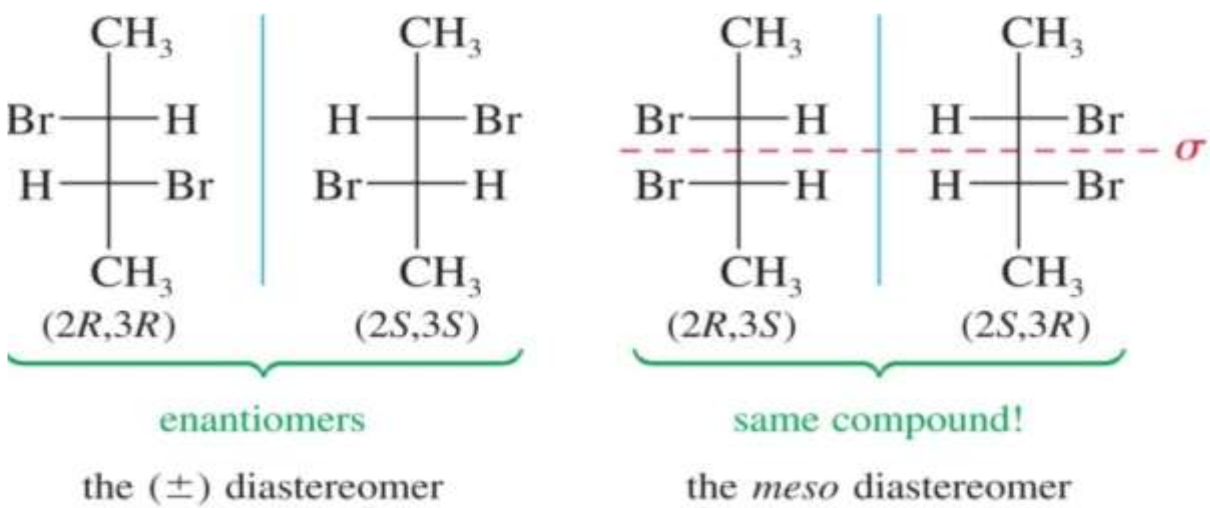


(*S*)-naproxen
anti-inflammatory agent

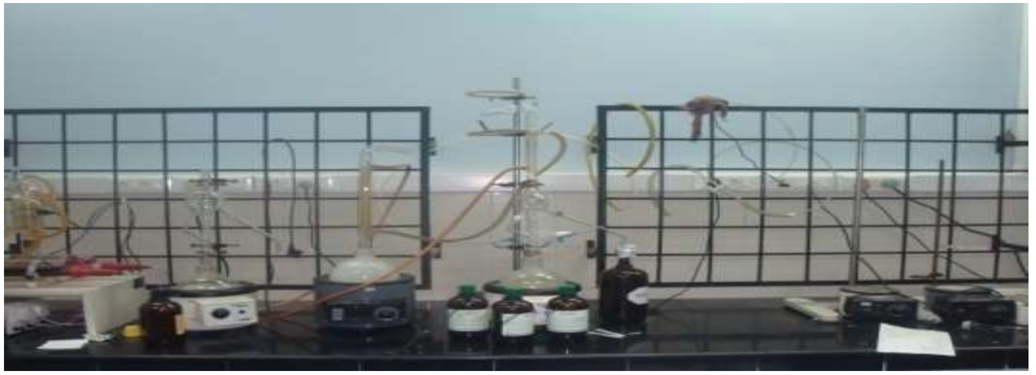
(*R*)-naproxen
liver toxin

Properties of Diastereomers

- **Diastereomers have different physical properties, so they can be easily separated.**
- **Enantiomers differ only in reaction with other chiral molecules and the direction in which polarized light is rotated.**
- **Enantiomers are difficult to separate.**
- **Convert enantiomers into diastereomers to be able to separate them.**



Thank You



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