Stereochemistry

Department of Pharmaceutical Chemistry

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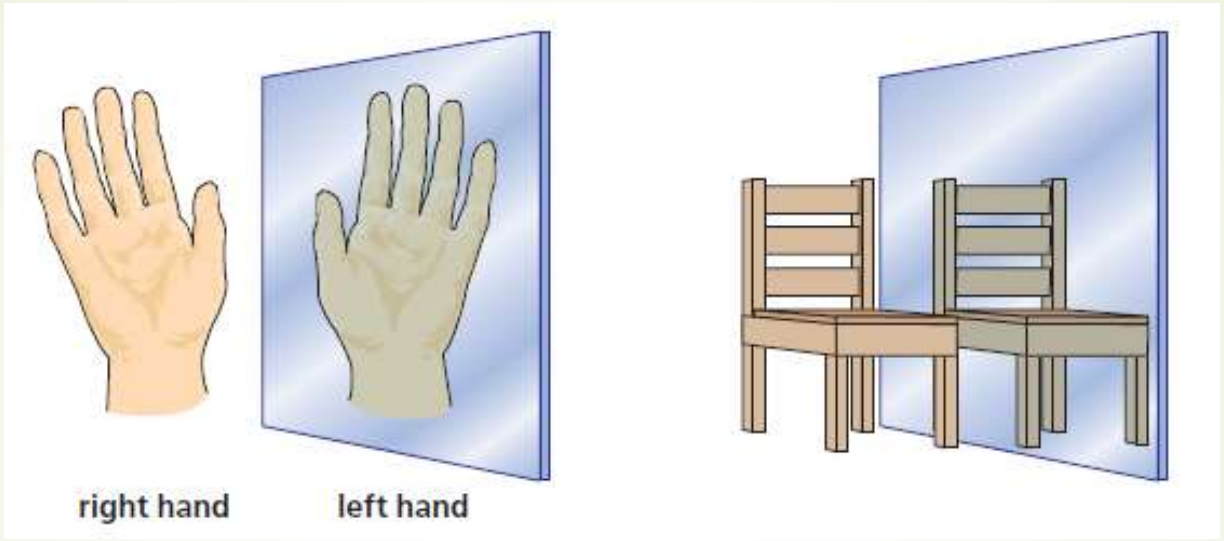
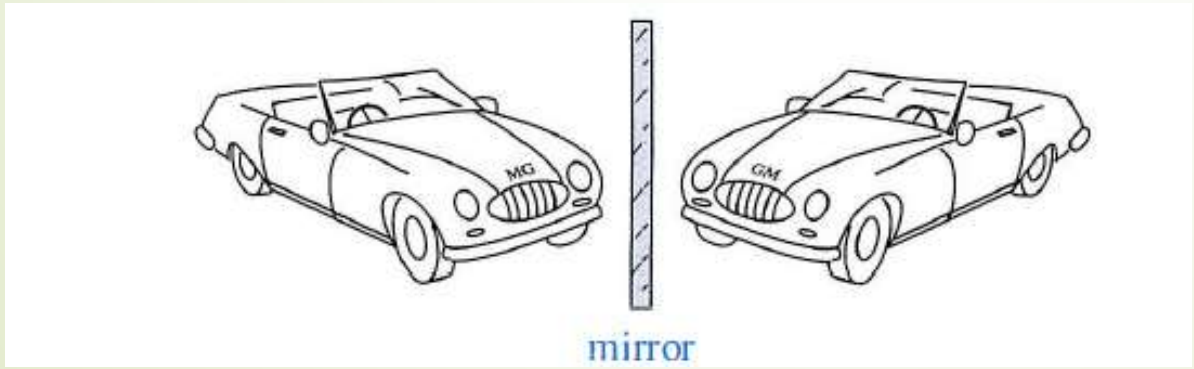
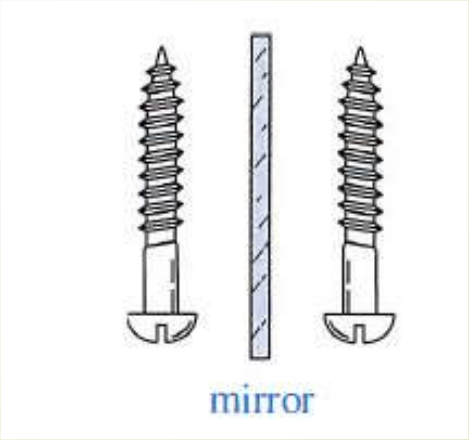
Stereochemistry / Stereoisomers

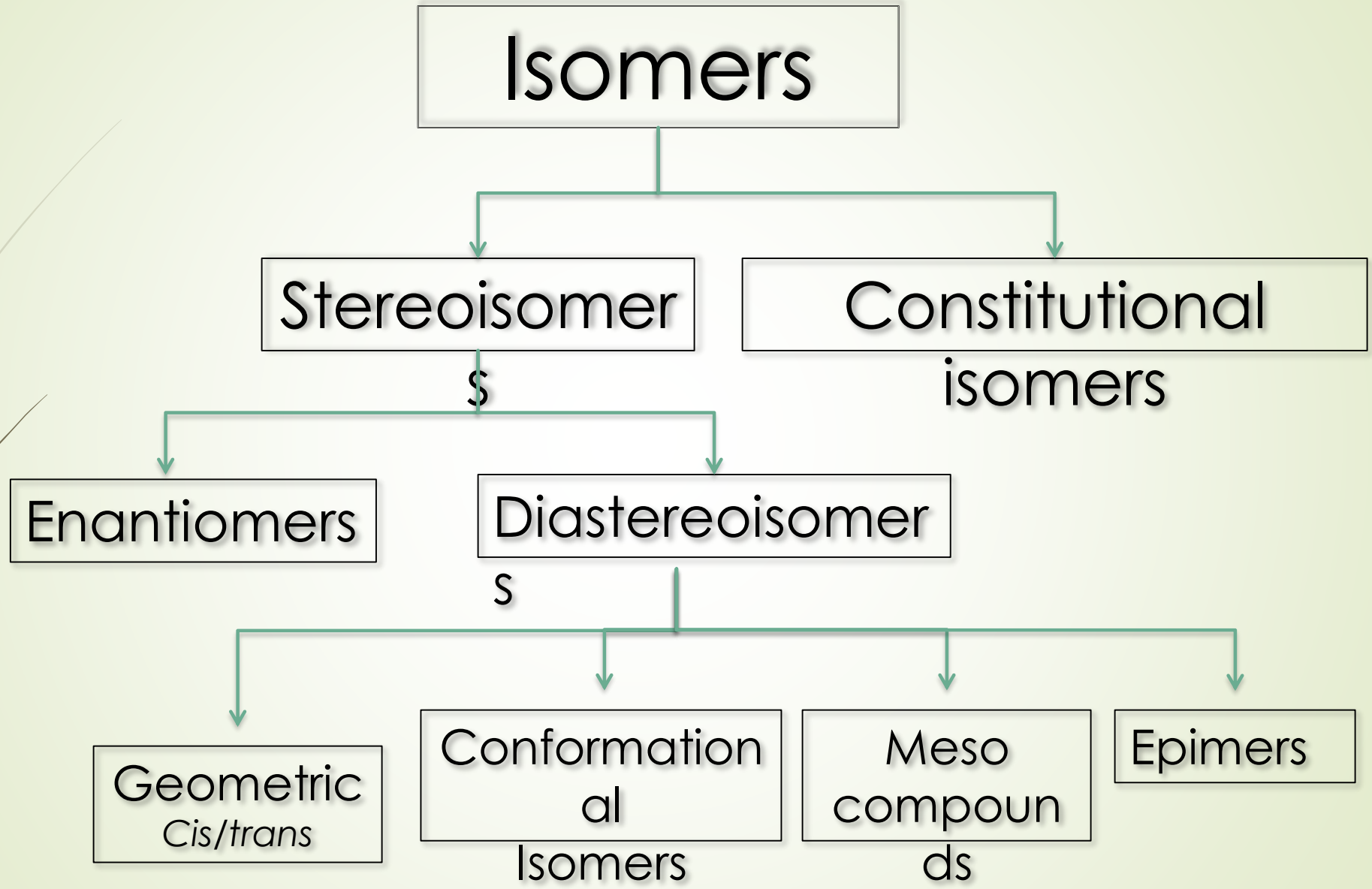
- The study of the three dimensional structure of molecules.

Chirality








Isomers
Stereoisomers
Constitutional isomers
Enantiomers
Diastereoisomers
Geometric
Cis/trans
Conformational Isomers
Meso compounds
Epimers

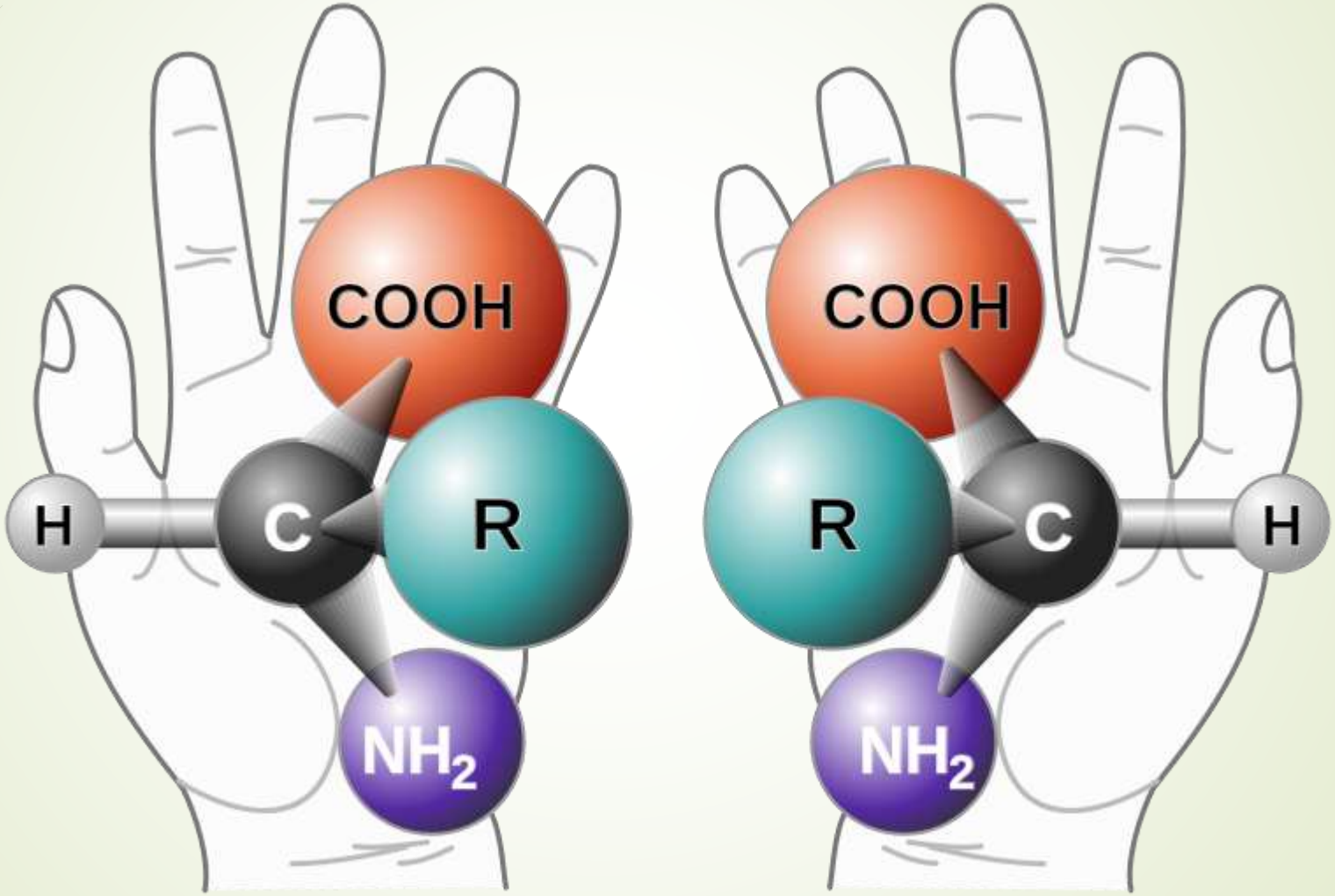
Constitutional/Structural Isomers:

- Are **compounds** have same molecular formula but different structural formula

Stereoisomers:

- Are compounds have same molecular formula but different arrangement of atoms in space

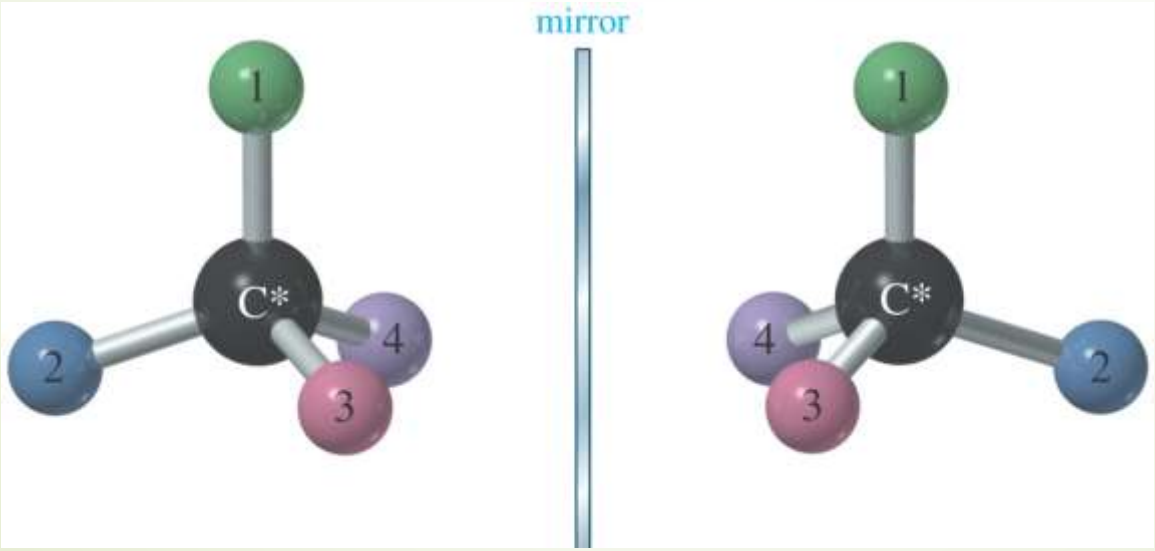
Chirality



Chirality

How about molecules?

- Chemical substances can be **handed**
- Handed substances are said to be **chiral**
- Molecules, that are **chiral** are nonsuperimposable on their mirror image

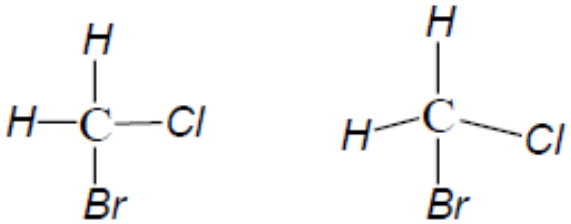


Stereochemistry of Tetrahedral Carbons

We need:

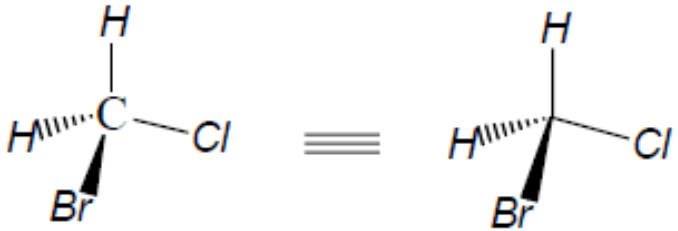
- ***one Carbon sp^3-hybridized, at least***
- ***to represent molecules as 3D objects***

For example:



2D drawing

Not appropriate for Stereochem



3D drawing

Appropriate for Stereochem

Thus, we can define……

- ***Stereoisomers**: isomers that have same formula and connectivity <u>but</u> differ in the position of the atoms in space*

- ***Stereochemistry**: chemistry that studies the properties of stereoisomers*

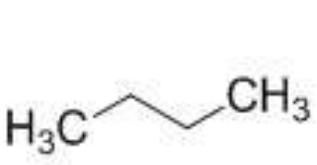
Chirality in Molecules

- Mirror-image isomers are called ***enantiomers***. Since they differ from one another only in the way the atoms are oriented in space, enantiomers belong to the general class called ***stereoisomers***.

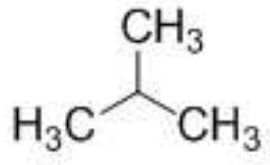
- One enantiomeric form of limonene smells like oranges, while its mirror image smells like lemons.

- Most molecules in the plant and animal world are **chiral** and usually only one form of them enantiomer is found.

- Nineteen of the twenty known amino acids are **chiral**

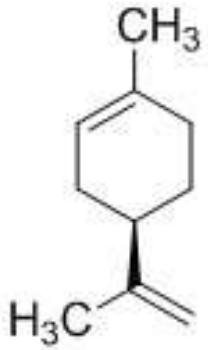


n-butane



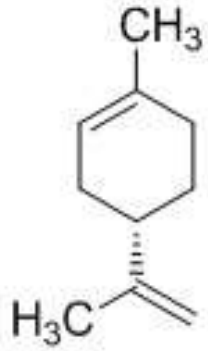
isobutane

structural isomers



(+)-limonene

"orangy taste"



(-)- limonene

"lemony taste"

Stereochemical isomers

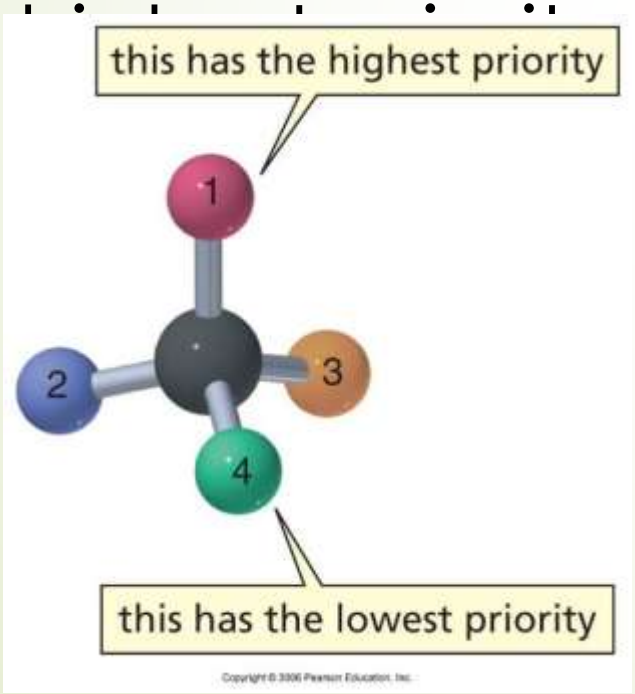
(*R*), (*S*) Nomenclature(Absolute Configuration)

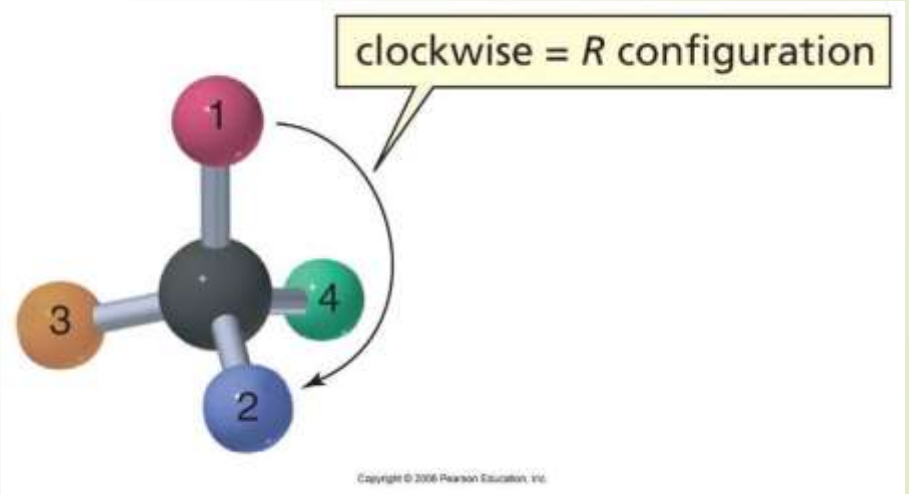
➢Arrangement of atoms that characterizes a particular stereoisomer is called its ***configuration***

- Called the **Cahn-Ingold-Prelog** convention
- Different molecules (**enantiomers**) must have different names.
- Usually only one **enantiomer** will be biologically active.
- Configuration around the chiral carbon is specified with (***R***) and (***S***).

Cahn-Ingold-Prelog Rules

- Assign a priority number to each group attached to the **chiral** carbon.
- Atom with highest atomic number assigned the
  1. and so on



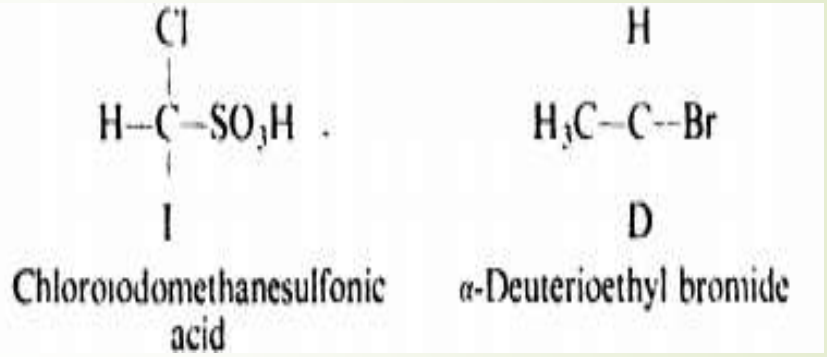


Assign (*R*) or (*S*)

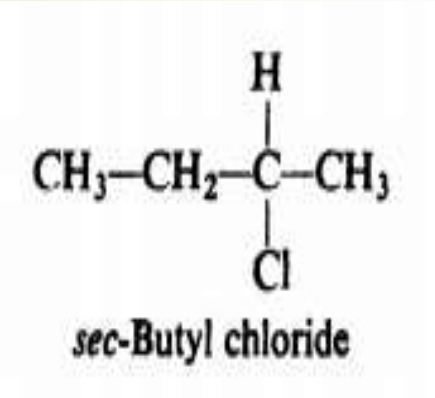
- Working in 3D, rotate molecule so that lowest priority group is in back.
- Draw an arrow from highest to lowest priority group.
- Clockwise = (*R*), Counterclockwise = (*S*)

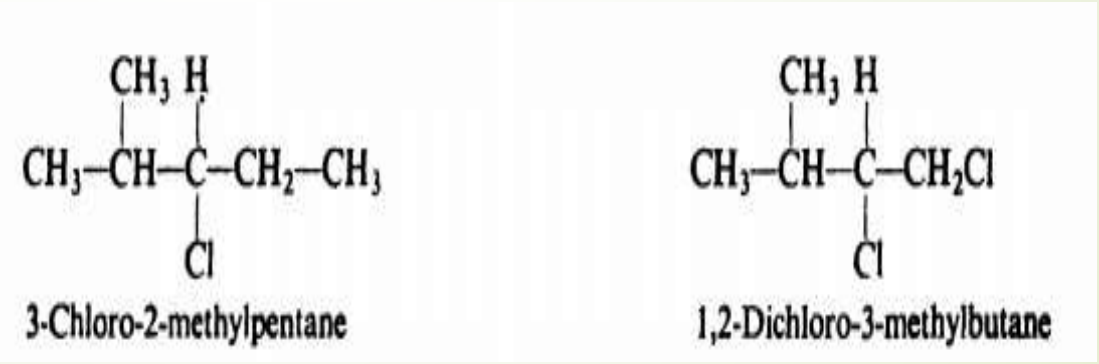
Sequence rules

Sequence Rule 1. If the four atoms attached to the chiral center are all different



Sequence Rule 2. If the relative priority of two groups cannot be decided by Rule I

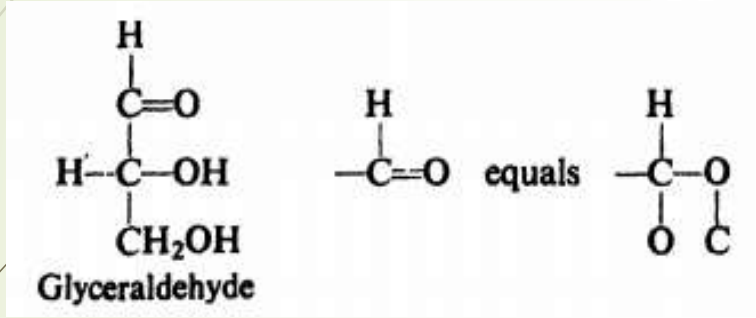




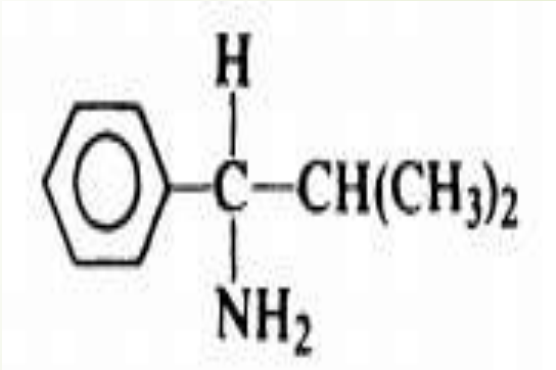
$CH_{3=}$ H, H, H// $C_2H_{5=}$ C, H, H

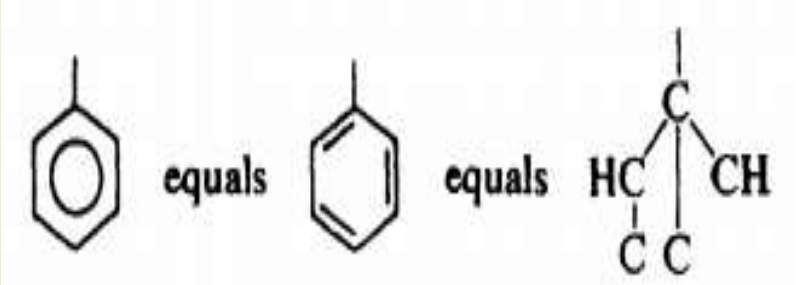
Sequence Rule 3: Where there is a double or triple bond, both atoms are considered to be duplicated or triplicated.

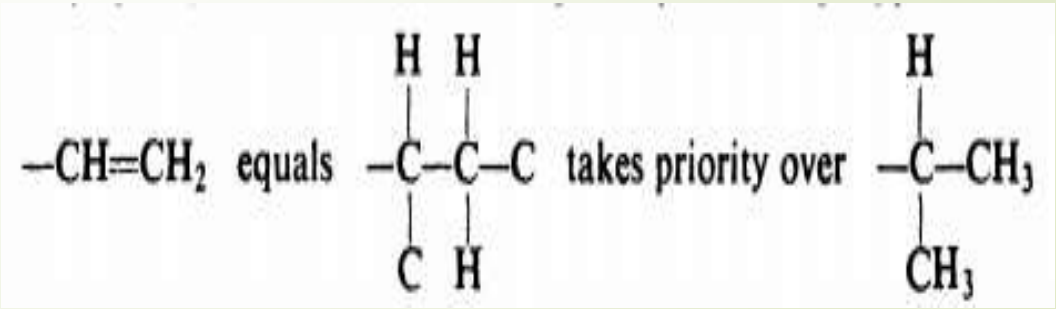
For example



The phenyl group

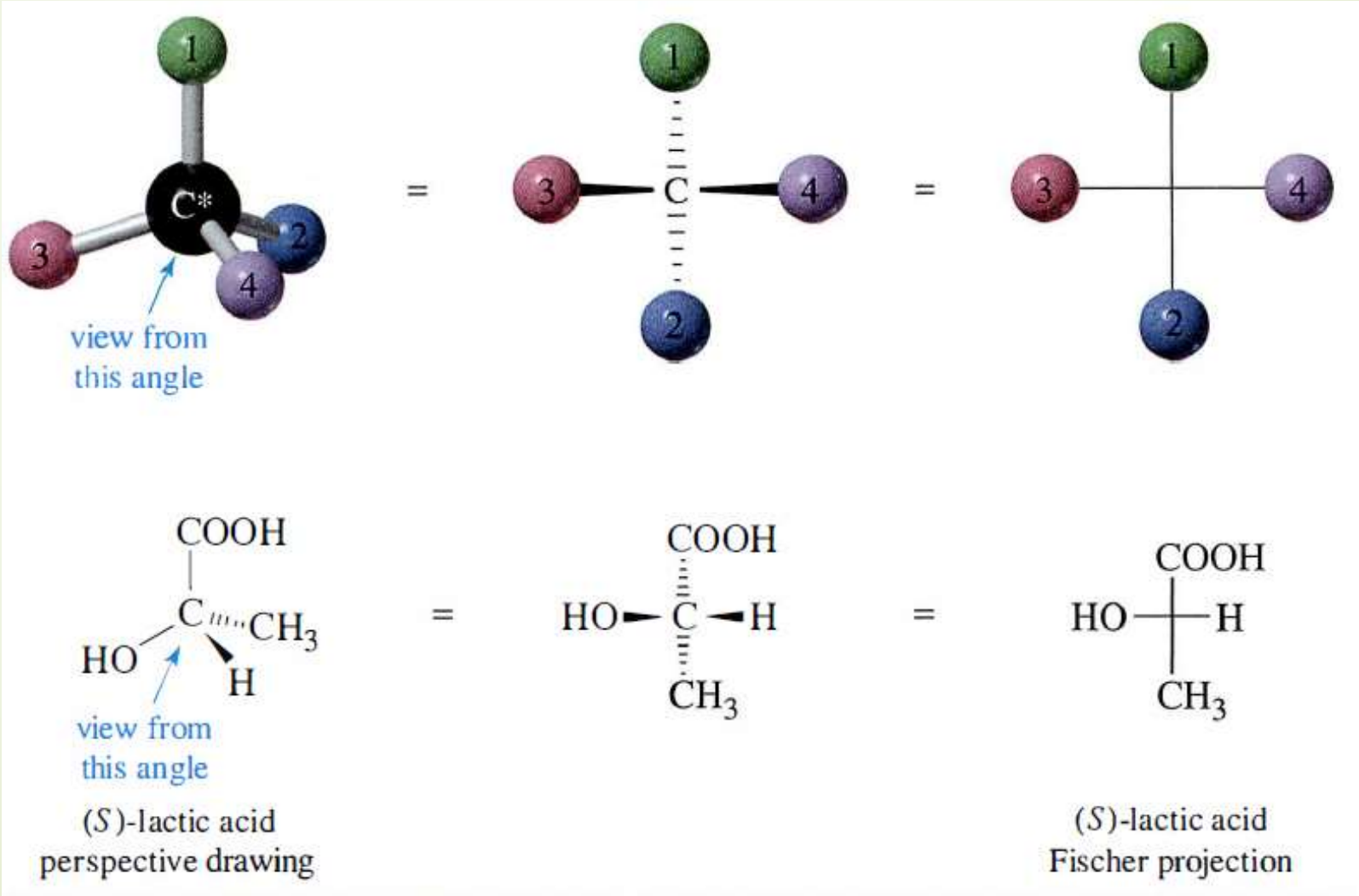




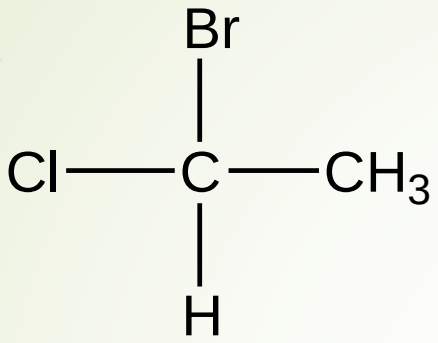


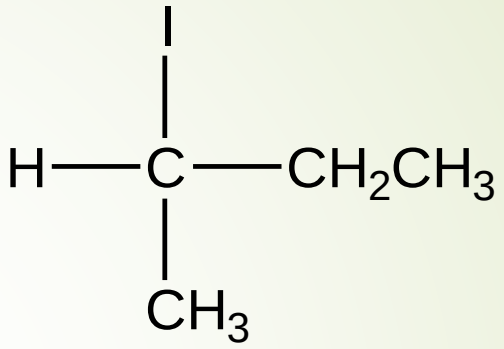
The chiral center

- All the chiral molecules there is a carbon (C*) that holds four different groups



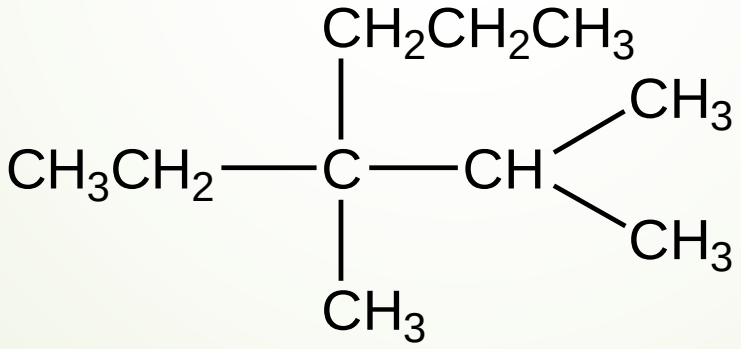
Identify as *R*, *S*, or achiral.



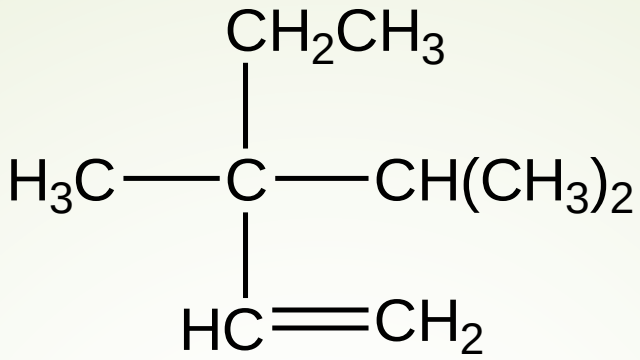


Br > Cl > CH_3 > H

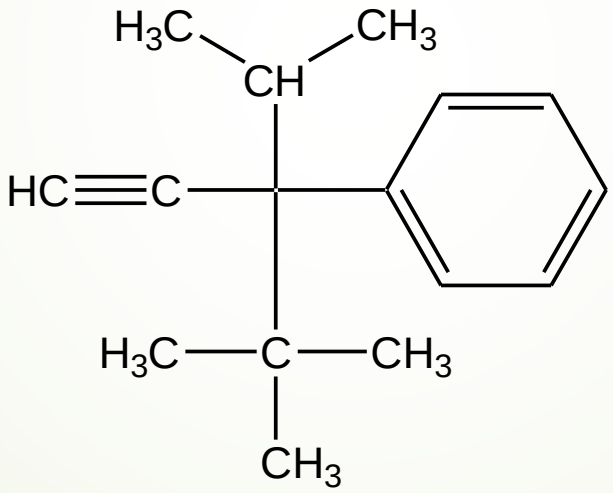
I > CH_3CH_2 > CH_3 > H



$CH(CH_3)_2$ > $CH_2CH_2CH_3$ > CH_2CH_3 > CH_3

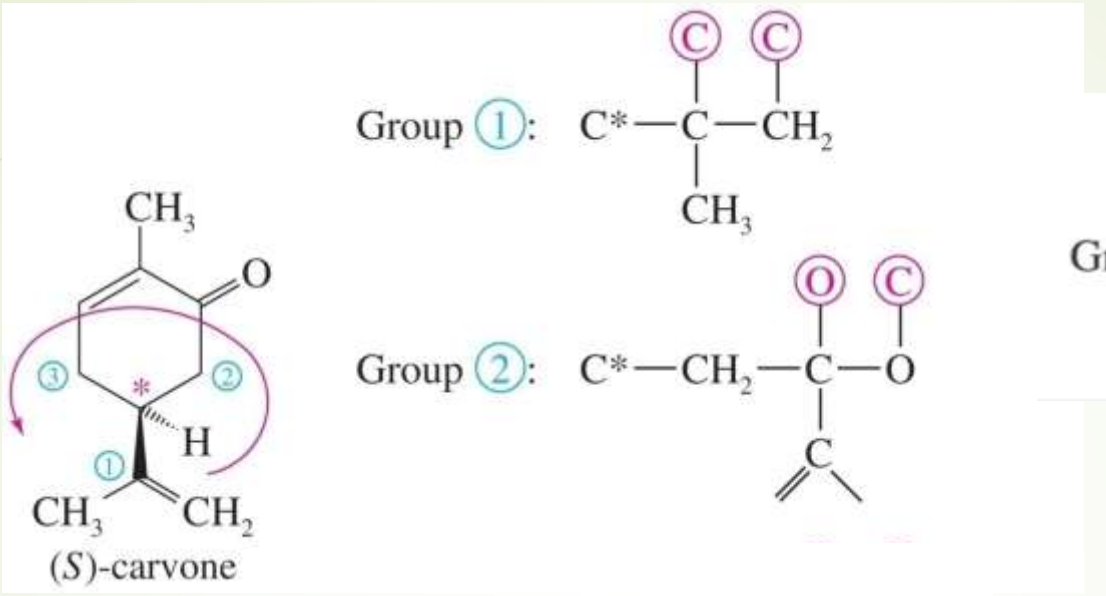


$CH{=}CH_2 > CH(CH_3)_2 > CH_2CH_3 > CH_3$

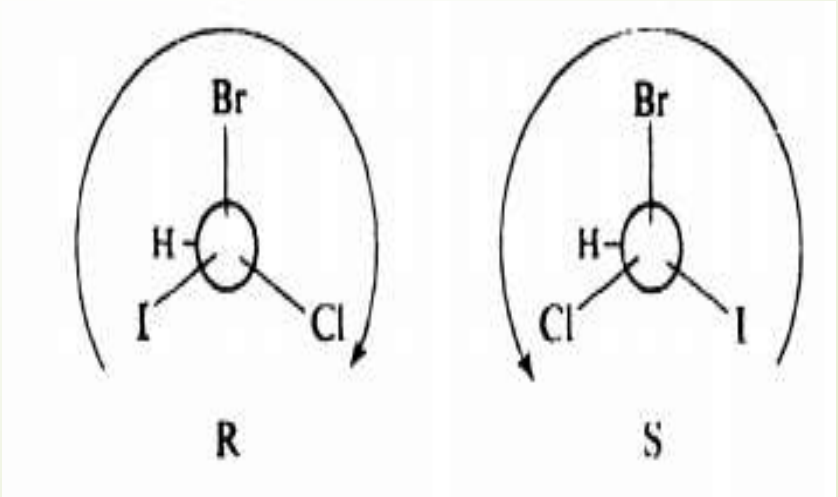


$C_6H_5 > HC{\equiv}C > C(CH_3)_3 > CH(CH_3)_2$

Configuration in Cyclic Compounds

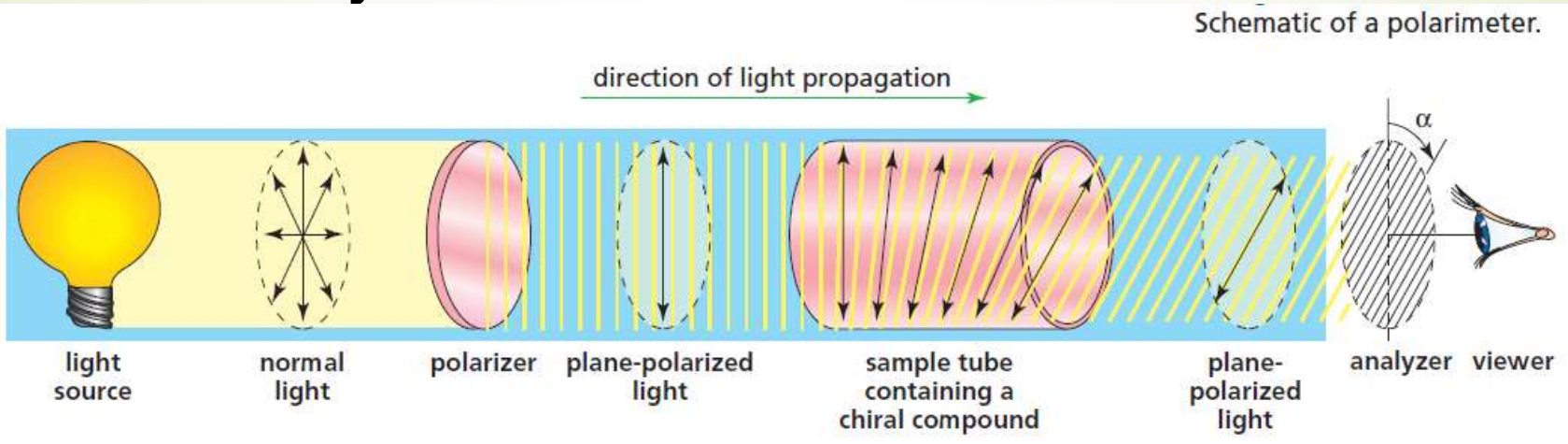


The most generally useful way yet suggested is the use of the prefixes R and S. According to a procedure proposed by R. S. Cahn



Polarimetry

- Light restricted to pass through a plane is *plane-polarized*
- A **polarimeter** measures the rotation of plane-polarized light that has passed through a solution
- Rotation, in degrees, is [α]
- Clockwise (+) = **dextrorotatory**; counterclockwise (-) = **levorotatory**



- Not related to (**R**) and (**S**)
- Plane-polarized light that passes through solutions of **achiral** compounds remains in that plane ([a] = 0, ***optically inactive***)
- Solutions of chiral compounds rotate plane-polarized light and the molecules are said to be ***optically active***

Racemic Mixtures

- Equal quantities of *d*- and *l*- enantiomers a 50/50 mixture.
- Notation: (*d,l*) or (±)
- No optical activity.

Specific Rotation

- Observed rotation depends on the length of the cell and concentration, as well as the strength of optical activity, temperature, and wavelength of light.

$$[\alpha] = \frac{\alpha(\text{observed})}{C * l}$$

- Where α (observed) is the rotation observed in the polarimeter, *c* is concentration in g/ml, and *l* is length of sample cell in decimeters.

Solved Problem 2

- When one of the enantiomers of 2-butanol is placed in a polarimeter, the observed rotation is 4.05° counterclockwise. The solution was made by diluting 6 g of 2-butanol to polarimeter tube for the measurement. Determine the specific rotation for this a total of 40 ml, and the solution was placed into a 200 mm enantiomer of 2-butanol.

Solution

Since it is levorotatory, this must be (–)-2-butanol The concentration is 6 g per 40 ml = 0.15 g/mL, and the path length is 200 mm = 2 dm. The specific rotation is

$$[\alpha]_D^{25} = \frac{-4.05^\circ}{(0.15)(2)} = -13.5^\circ$$

Calculate % Composition

The specific rotation of (*S*)-2-iodobutane is +15.90°. Determine the % composition of a mixture of (*R*)- and (*S*)-2-iodobutane if the specific rotation of the mixture is -3.18°.

Sign is from the enantiomer in excess: levorotatory.

$$\text{o.p.} = \frac{\text{observed rotation}}{\text{rotation of pure enantiomer}} \times 100$$

$$\text{o.p.} = \frac{3.18}{15.90} \times 100 = 20\%$$

l = 60% *d* = 40%

Properties of Enantiomers

- Same boiling point, melting point, density
- Same refractive index
- Different direction of rotation in polarimeter
- Different interaction with other chiral molecules
  - Enzymes
  - Taste buds, scent