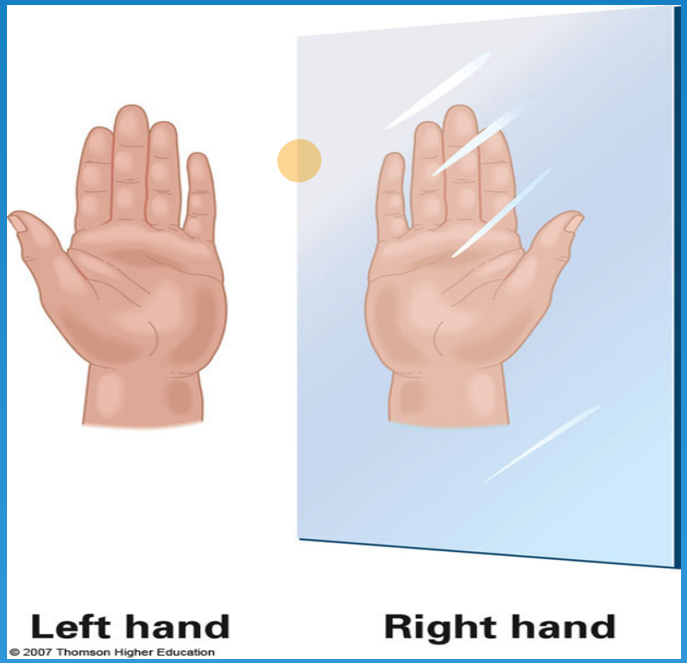
STEREOCHEMISTRY



- what deffernt image
- what sterec chem

reflax

* mirror image

INTRODUCTION

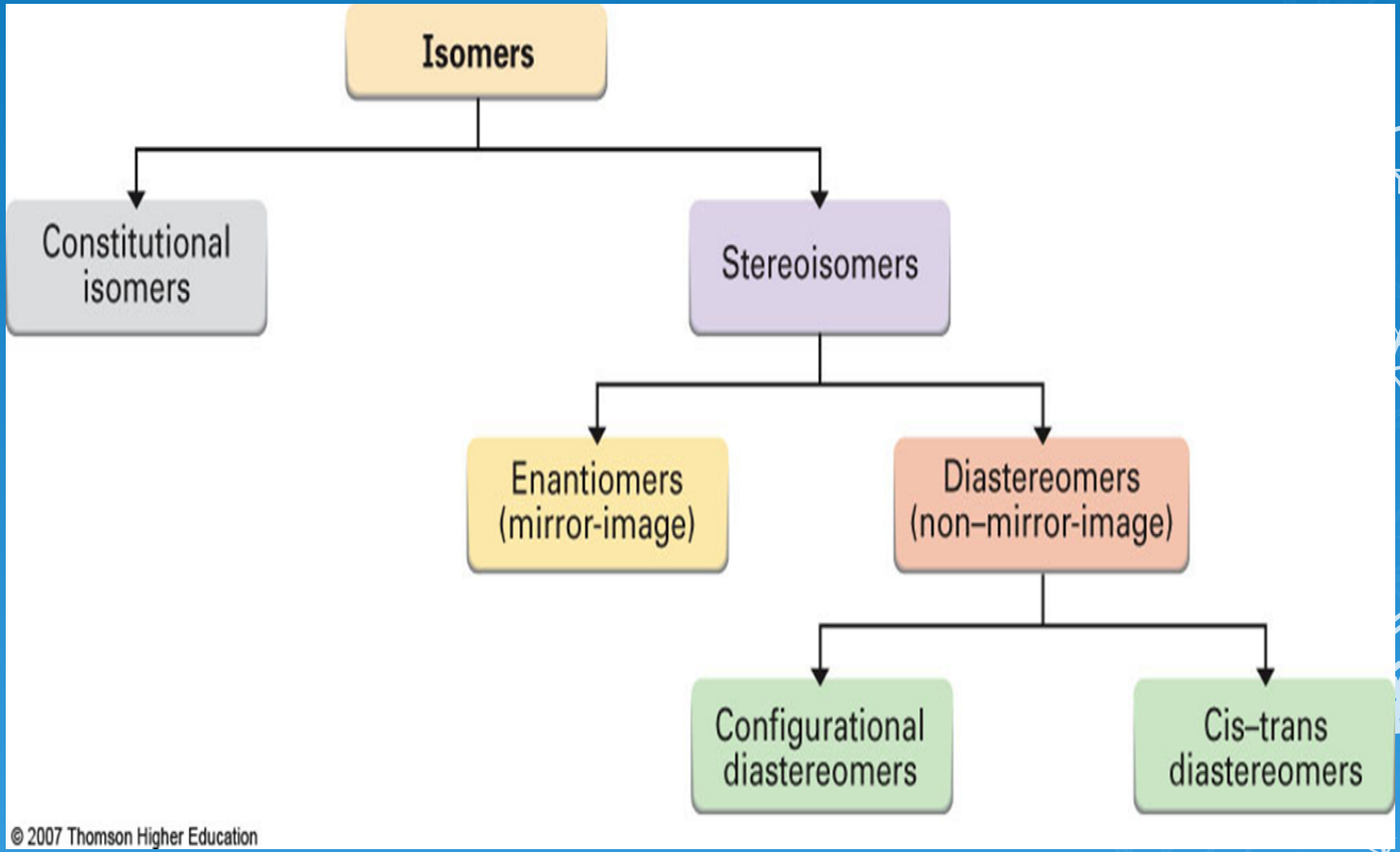
Stereochemistry is the branch of chemistry concerned with the three dimensional structures of molecules.

CHIRALITY or HANDEDNESS:

Stereoisomers have the same atomic connectivity but differ in the spatial arrangement of the constituent atoms.

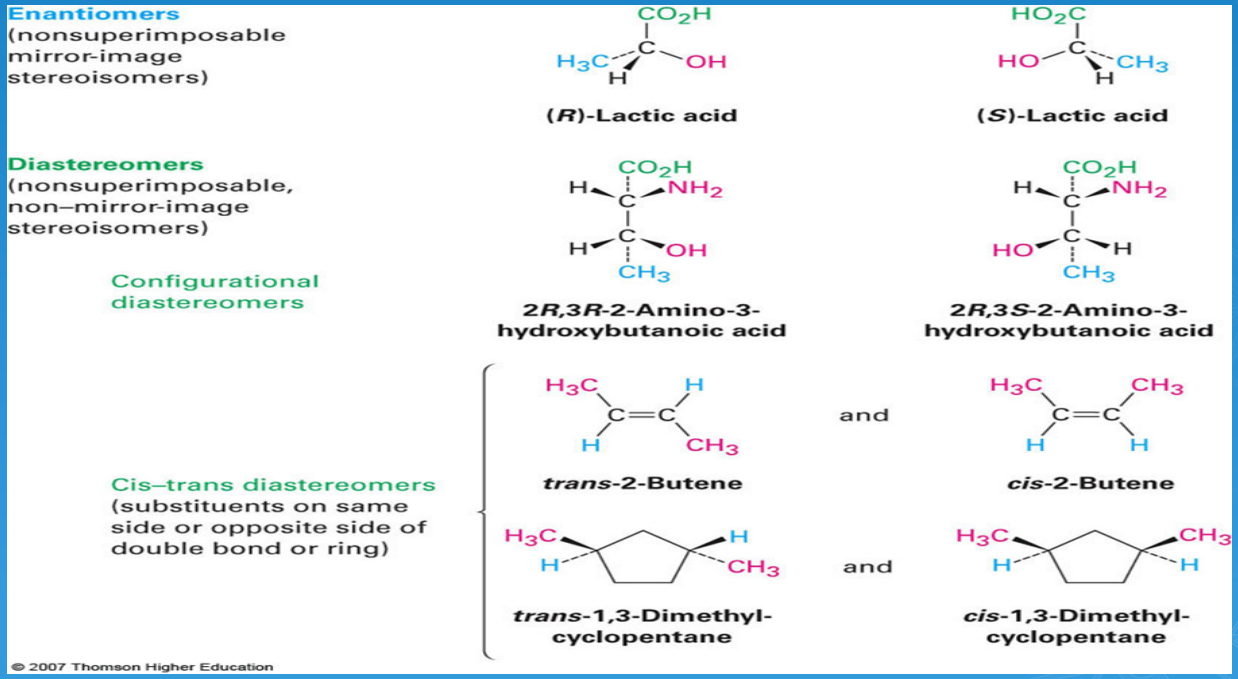
- Handedness is important in organic and biochemistry.
- Molecular handedness makes possible specific interactions between enzymes and substrates—effecting metabolism and pharmaceuticals.

Review Of Isomerism



Stereoisomerism

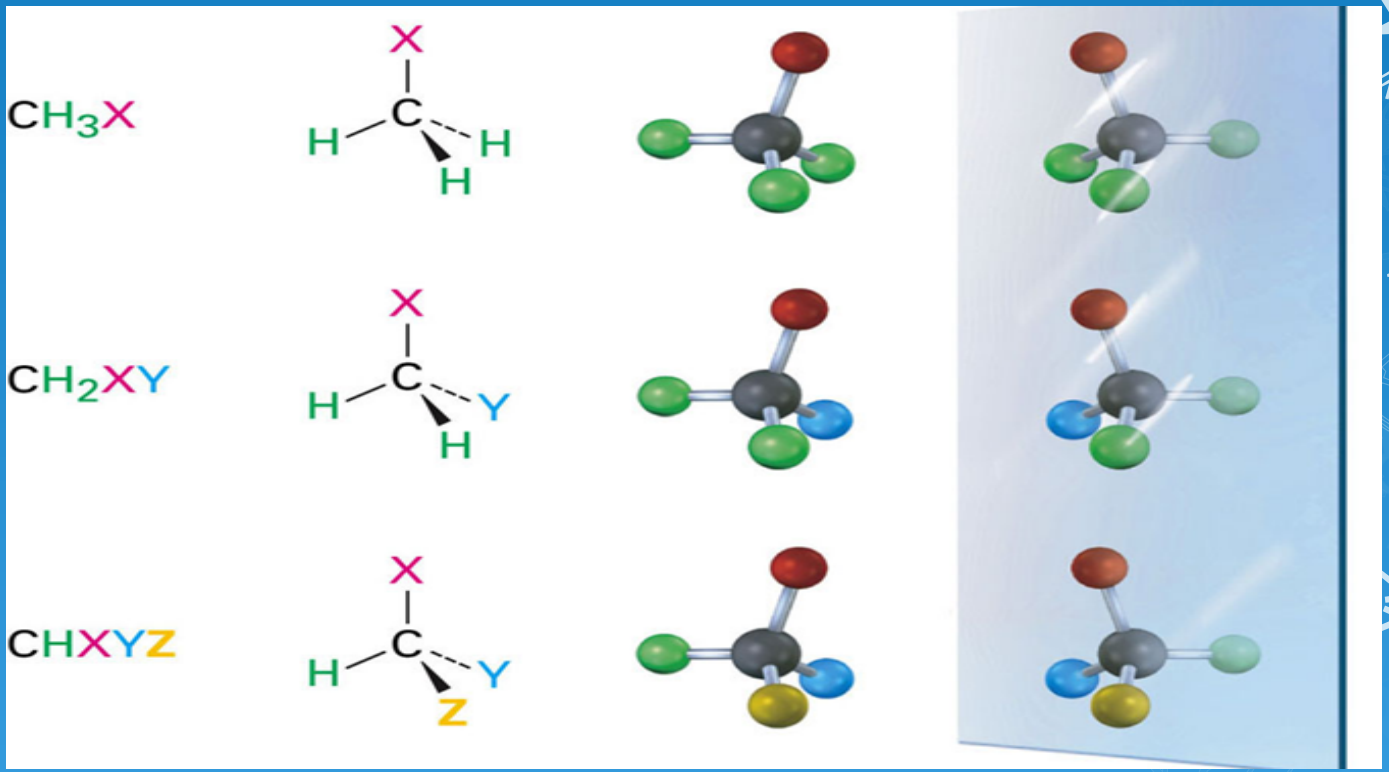
- Same connections, different spatial arrangement of atoms.
- Enantiomers (nonsuperimposable mirror images).
- Diastereomers (all other stereoisomers).
- Includes cis, trans and configurational.



Enantiomers and Tetrahedral Carbon

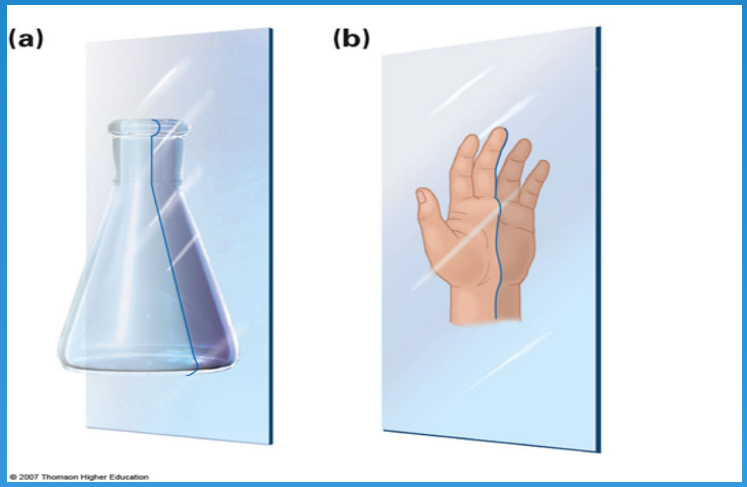
Should have different atom

The tetrahedral carbon must be a chiral carbon.



CHIRAL CENTERS

- A point in a molecule where four different groups (or atoms) are attached to carbon is called a chiral center.
- There are two nonsuperimposable ways that 4 different groups (or atoms) can be attached to one carbon atom.
- If two groups are the same, then there is only one way.
- A chiral molecule usually has at least one chiral center.



Plane of symmetry

Achiral

No plane of summetry

chiral

CHIRALITY

If an object has a plane of symmetry it's the same as its mirror image.

A plane of symmetry divides an entire molecule into two pieces that are exact mirror images .

Achiral means that the object has a plane of symmetry.

Molecules that are not superimposable with their mirror images are chiral (have handedness).

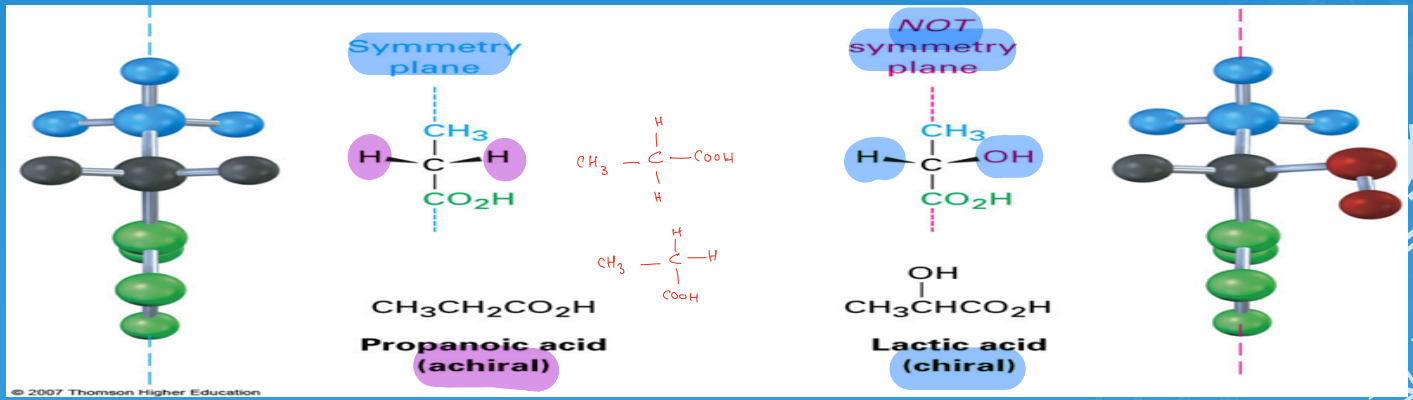
Hands, gloves are prime examples of chiral object.

They have a "left" and a "right" version.

Organic molecules can be Chiral or Achiral.

stereo

no stereo



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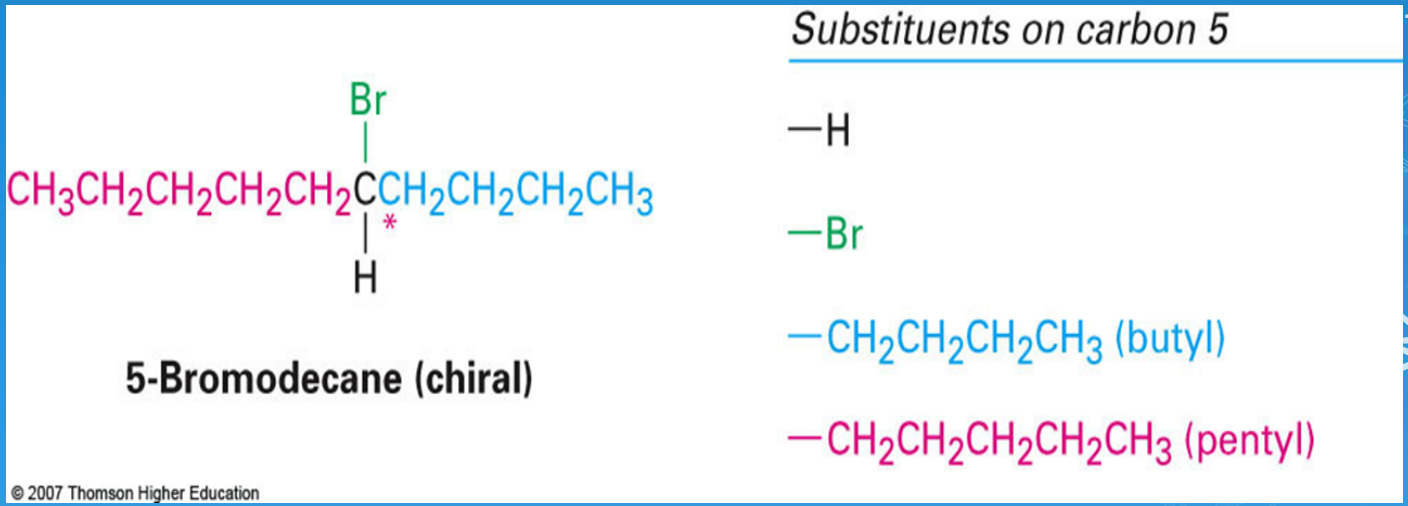
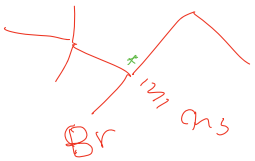


(A) 

Achrail

(B) 

chrial

(C) 

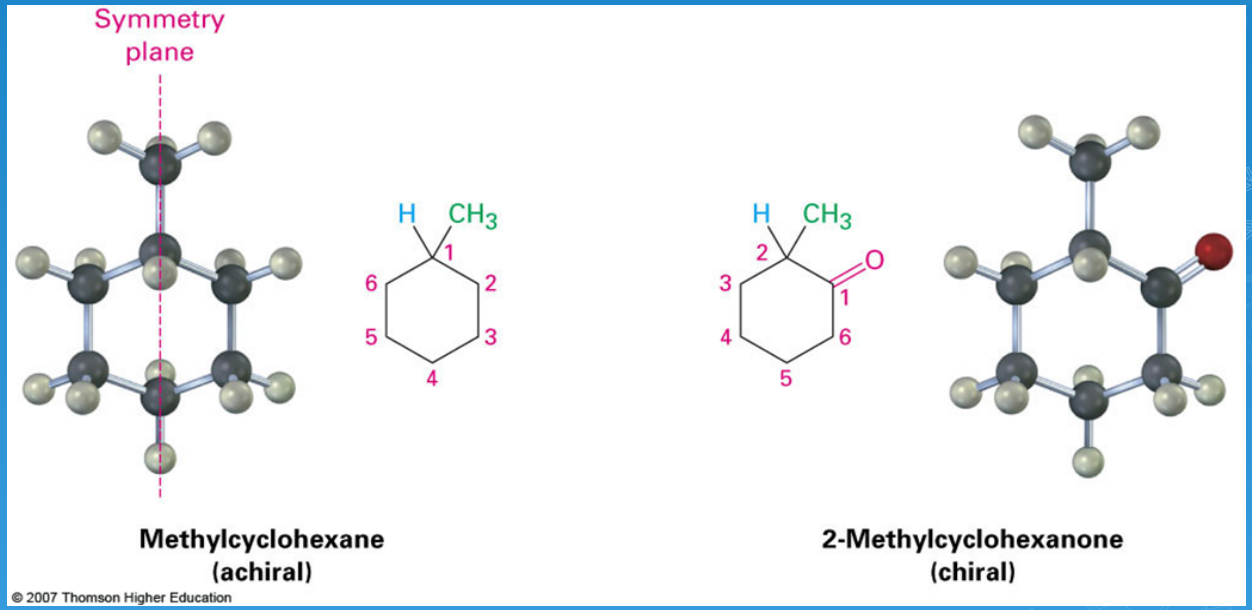
chrial

Chiral Centers in Chiral Molecules

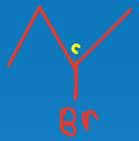
- Groups are considered "different" if there is any structural variation (if the groups could not be superimposed if detached, they are different).
- In cyclic molecules, we compare by following in each direction in a ring.

2^n

Number of isomer possible = chiral centers = 2^n

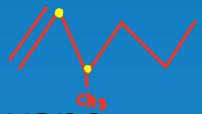


Which of the following molecules are Chiral?



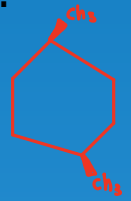
chiral

a. 3-Bromopentane.

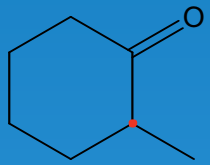


b. 3-Methylhex-1-ene.

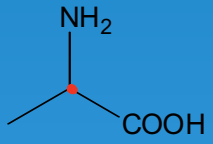
c. Cis-1,4-Dimethylcyclohexane.



d.



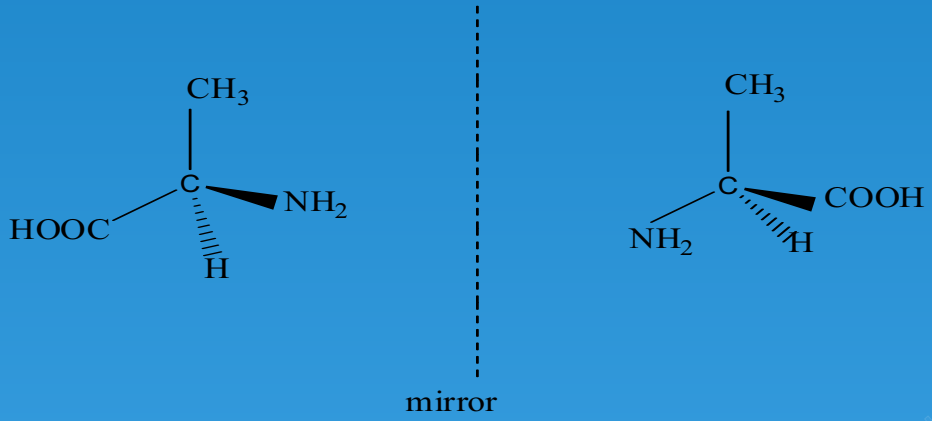
e.



chiral

Enantiomerism

- Molecules exist as three-dimensional objects.
- Molecules that are different than their mirror image .
- These are stereoisomers called enantiomers.
- Molecules that have one carbon with 4 different substituents have a non-superimposable mirror image.
- Enantiomers = non-superimposable mirror image stereoisomers.

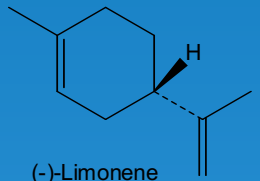


Chirality in Nature and Chiral Drugs

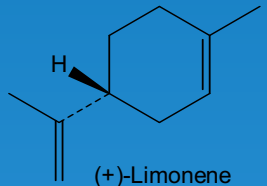
The different enantiomers of a chiral molecule have same physical properties, they almost have different biological properties.

Eg:1 (+)-Limonene has the odor of citrus fruits and

(-)-Limonene has the odor of pine trees.



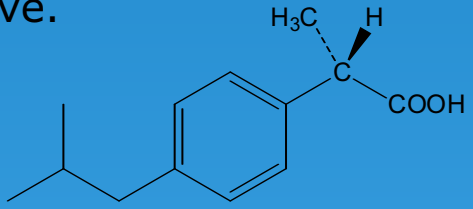
(-)-Limonene



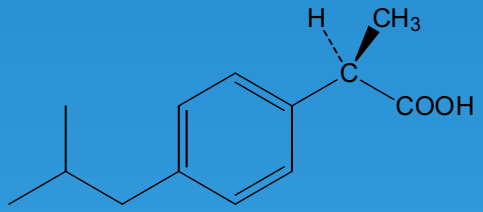
(+)-Limonene

Chiral Drugs:

The S-enantiomer of Ibuprofen is an active analgesic and antipyretic, whereas the R-enantiomer of Ibuprofen in inactive.



(*S*)-Ibuprofen (active)

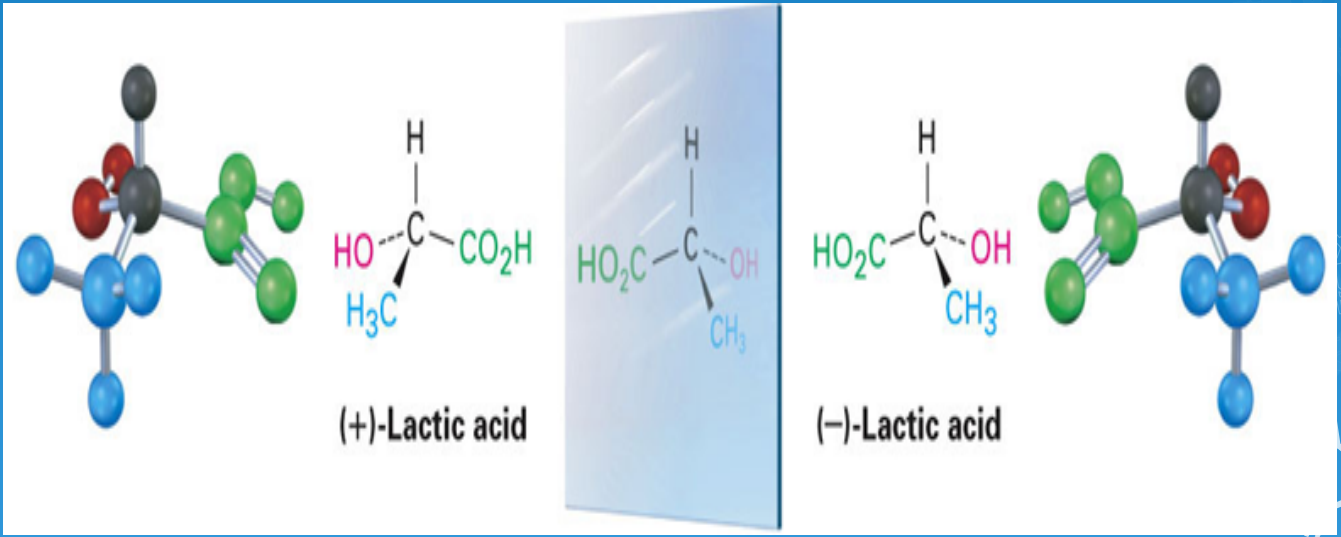


(*R*)-Ibuprofen (inactive)

Enantiomerism

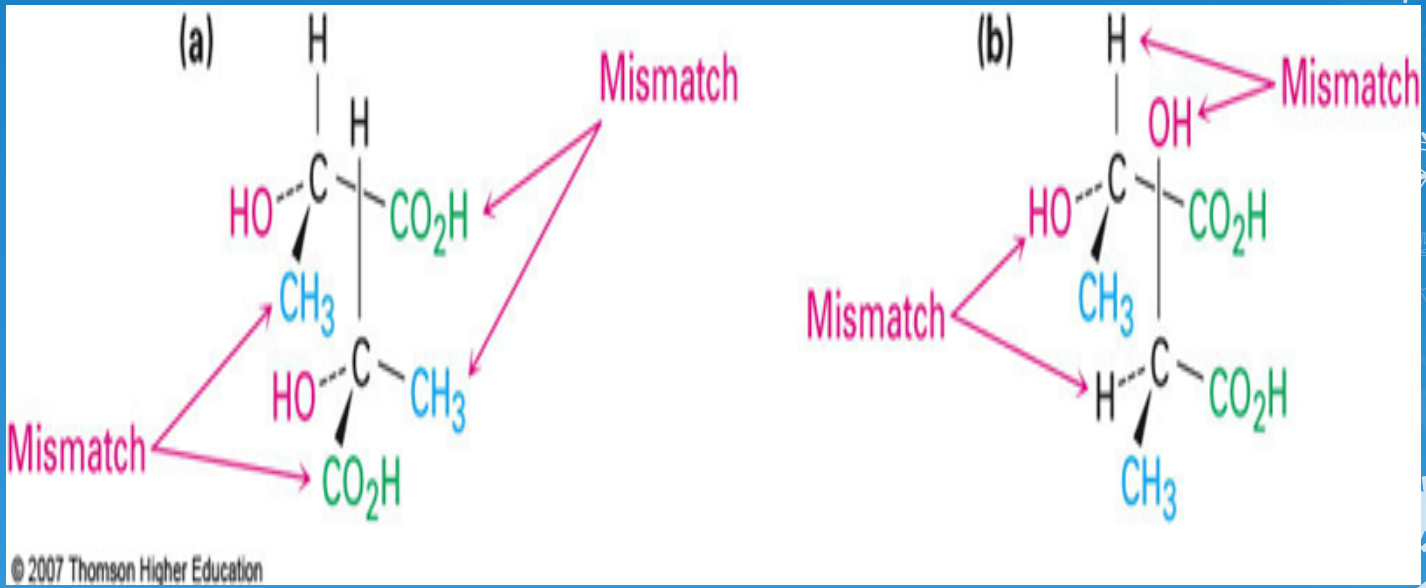
A molecule that is not identical to its mirror image is a kind of stereoisomer called as an enantiomer.

Example: Lactic acid



ENANTIOMERISM

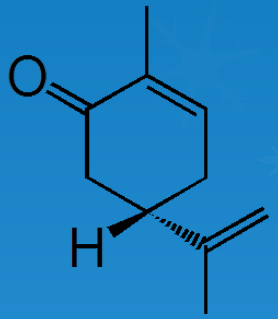
The “right handed” lactic acid can’t be superimposed on top of a molecule of “left-handed “ lactic acid.



Tetrahedral stereogenic centers

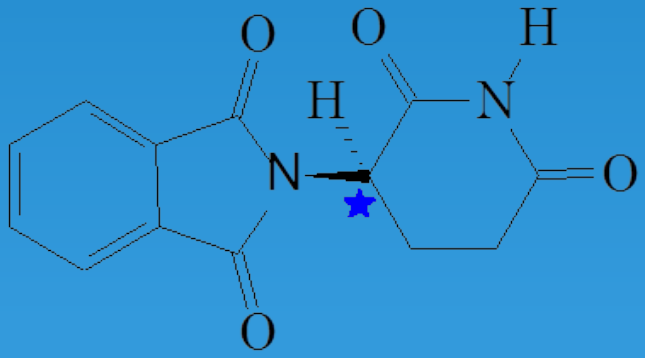
The carbon atom bonded to four different groups is called a tetrahedral stereogenic center asymmetric center, or chirality center OR stereocenter.

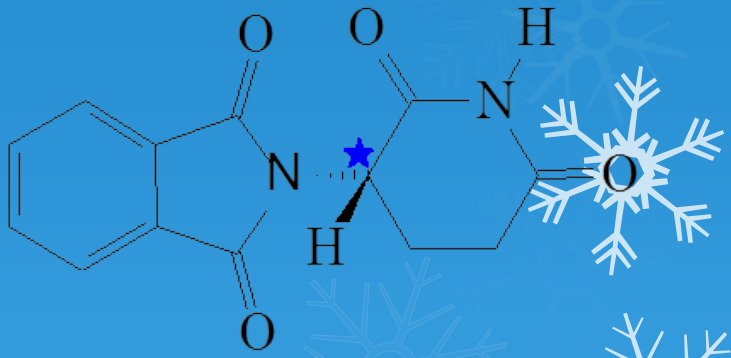
(+)-Carvone is responsible for the odor of caraway seed oil.



(+)-carvone

Thalidomide : Drug



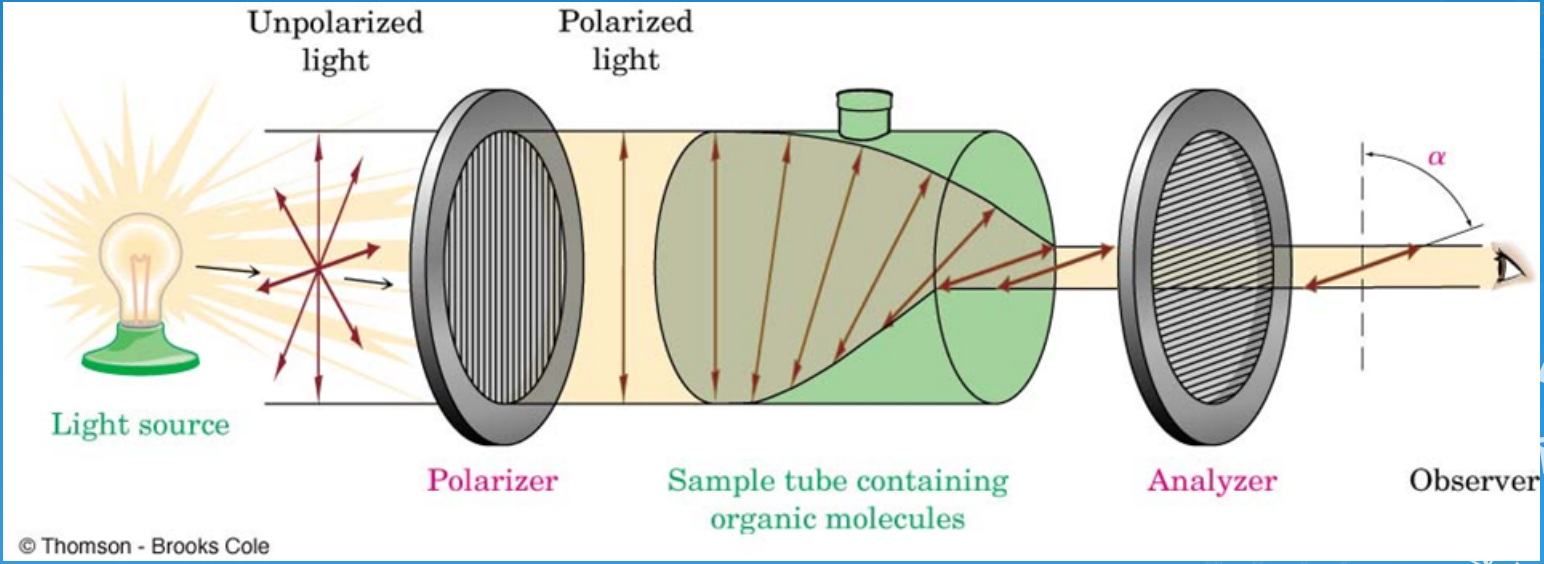


Optical Activity

- Light restricted to pass through a plane is plane-polarized.
- Plane-polarized light that passes through solutions of achiral compounds remains in that plane.
- Solutions of chiral compounds rotate plane-polarized light and the molecules are said to be optically active.
- Light passes through a plane polarizer.
- Plane polarized light is rotated in solutions of optically active compounds.
- Measured with polarimeter.
- Rotation, in degrees, is [□].
- Clockwise rotation is called **dextrorotatory.**
- Anti-clockwise is **levorotatory.**

Measurement of Optical Rotation

- A polarimeter measures the rotation of plane-polarized that has passed through a solution.
- The source passes through a polarizer and then is detected at a second polarizer.
- The angle between the entrance and exit planes is the optical rotation.

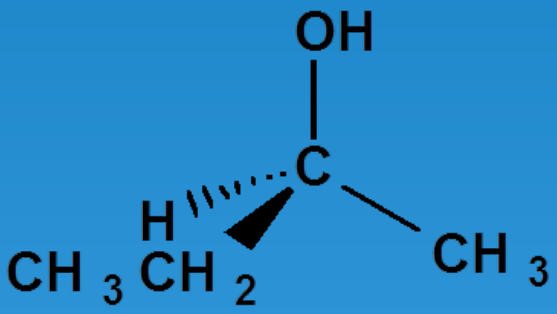


Optical Activity

- Rotation, in degrees, is [α]
- Clockwise (+) = dextrorotatory; Anti-clockwise (-) = levorotatory.
- Plane-polarized light that passes through solutions of achiral compounds remains in that plane ([α] = 0, optically inactive).
- Solutions of chiral compounds rotate plane-polarized light and the molecules are said to be optically active.

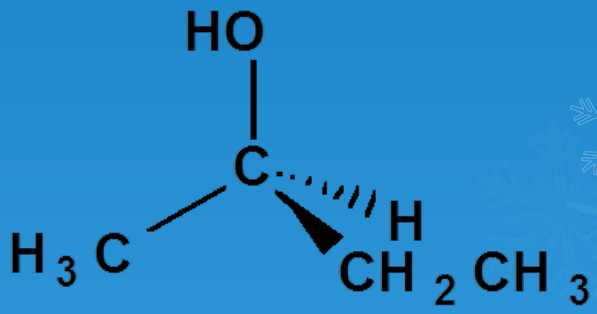
Optical Activity

- Characteristic property of a compound that is optically active – the compound must be chiral.
- The specific rotation of the enantiomer is equal in magnitude but opposite in sign.
- For a pair of enantiomers, the value of the specific rotation of each is the same, but opposite in sign.



(S)-(+)-2-Butanol

$[\alpha]_D^{25}$ +13.52



(R)-(-)-2-Butanol

$[\alpha]_D^{25}$ -13.52

Sequence Rules for Specification of Configuration

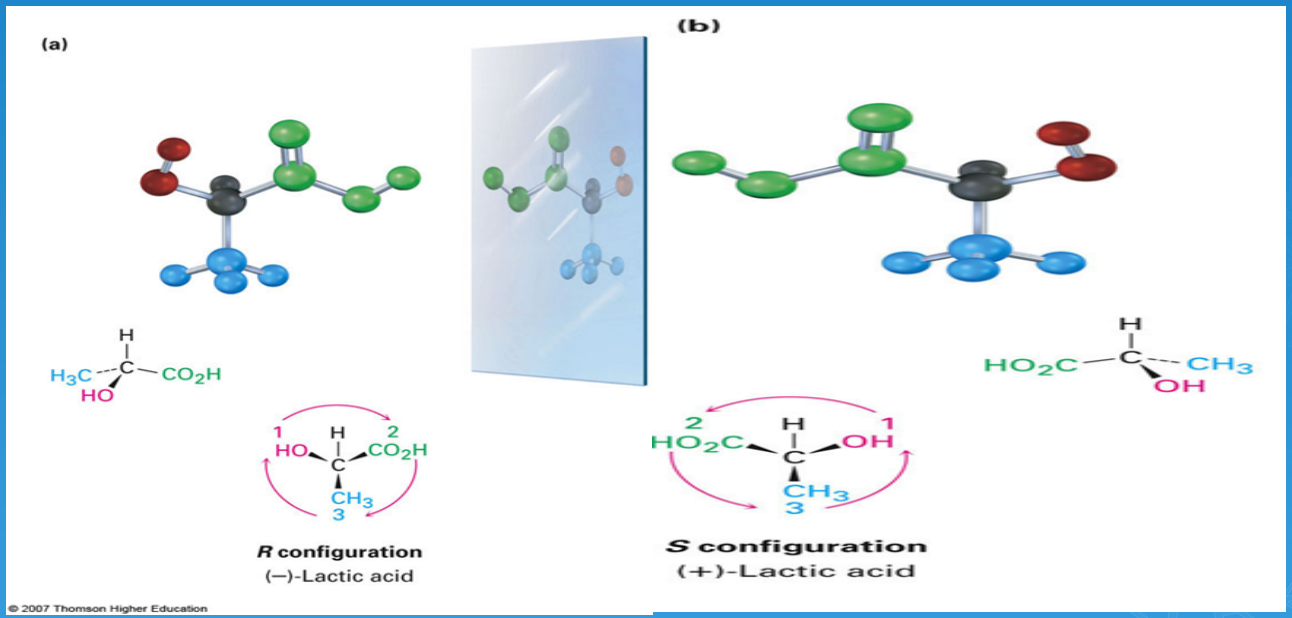
- A general method applies to determining the configuration at each chiral center (instead of to the whole molecule).
- The configuration is specified by the relative positions of all the groups with respect to each other at the chiral center.
- The groups are ranked in an established priority sequence and compared—use the same priority ranking as we did for E/Z names.
- The relationship of the groups in priority order in space determines the label applied to the configuration, according to a rule.

Method:

- Assign each group priority 1-4 according to Cahn-Ingold-Prelog.
- Rotate the assigned molecule until the lowest priority group (4) is in the back, look at remaining 3 groups in a plane.
- Clockwise 1-2-3 movement is designated R (from Latin for "right").
- Counterclockwise is designated S (from Latin word for "left").

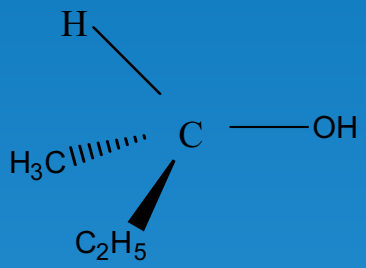
R-S Configuration

- Assign each group priority according to the Cahn-Ingold-Prelog scheme with the lowest priority group pointing away, look at remaining 3 groups in a plane.
- Clockwise is designated R (from Latin for "right").
- Counterclockwise is designated S (from Latin word for "left").

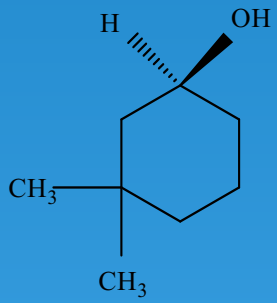


Assign R or S Configuration to each stereocenter.

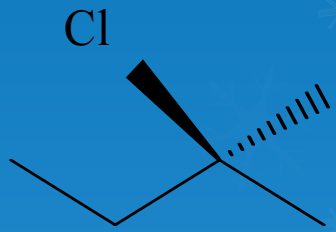
1.



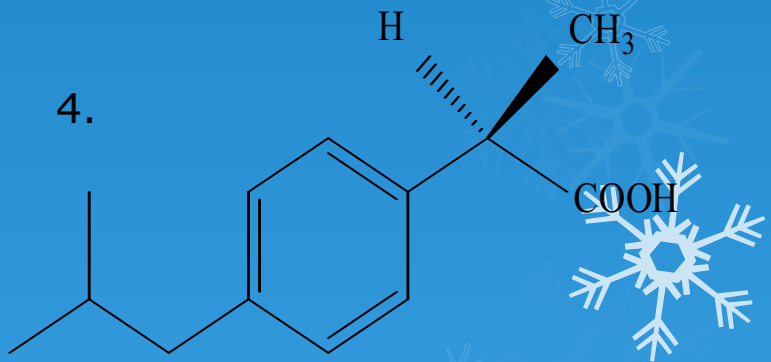
2.



3.



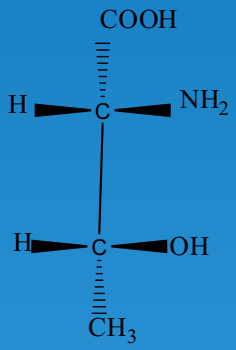
4.



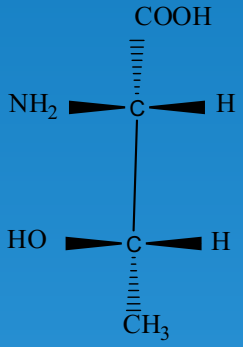
Ibuprofen

DIASTEREOMERS

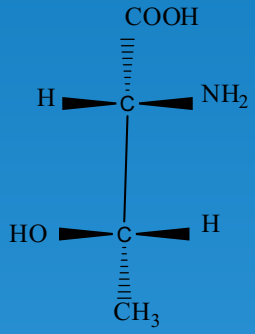
- DIASTEREOMERS ARE STEREOISOMERS THAT ARE NOT ENANTIOMERS.
- They are stereoisomers that are not mirror images of each other.



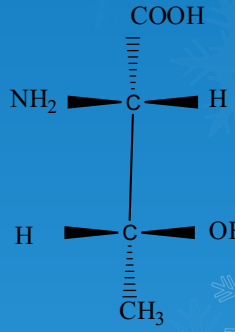
(a)



(b)



(c)

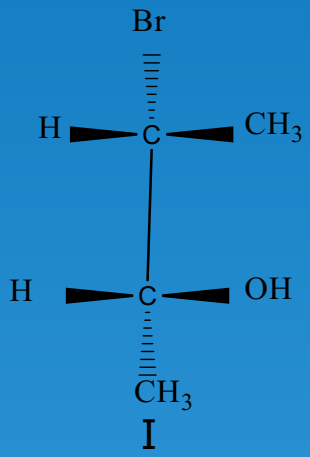


(d)

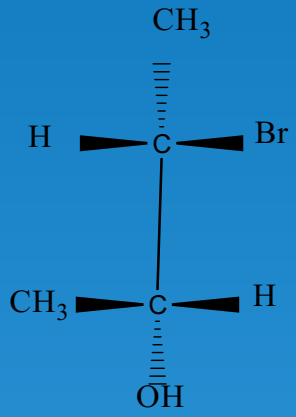
(a) and (b) are enantiomers ; © and (d) are enantiomers

(a) and (c); (a) and (d); (b) and (c); (b) and (d) are diastereomers.

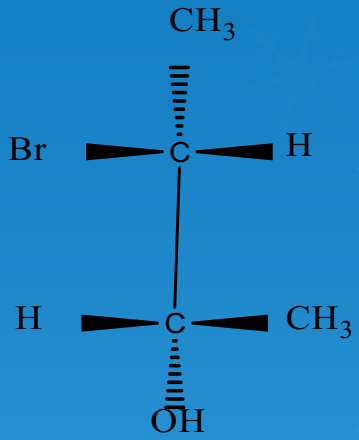
Assign R or S configuration to each stereocenter.



I



II

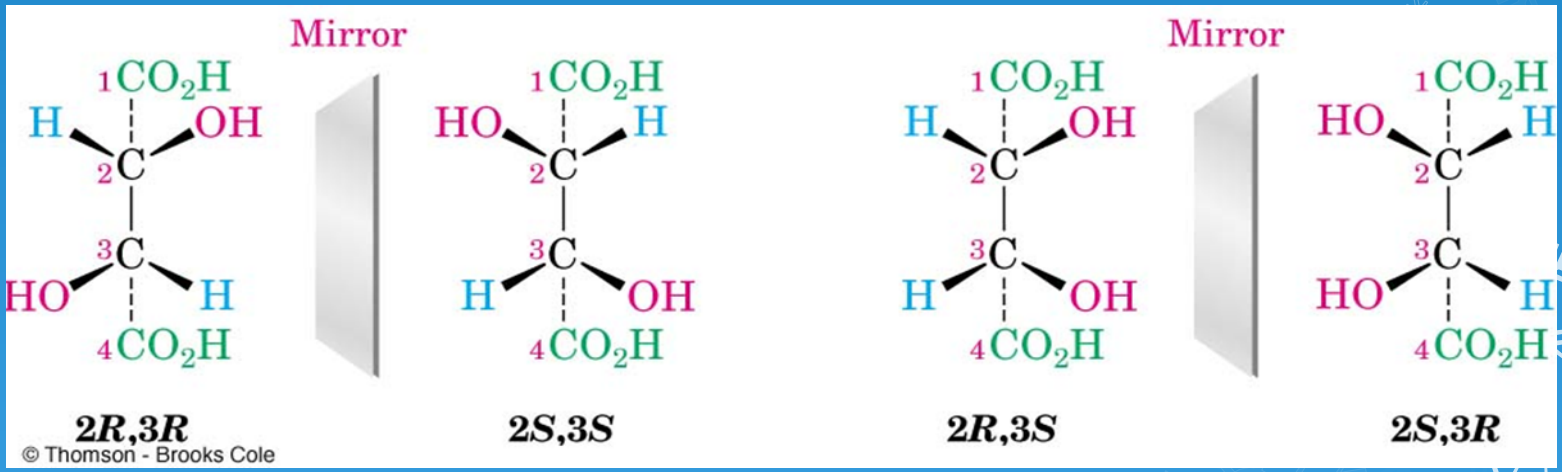


III

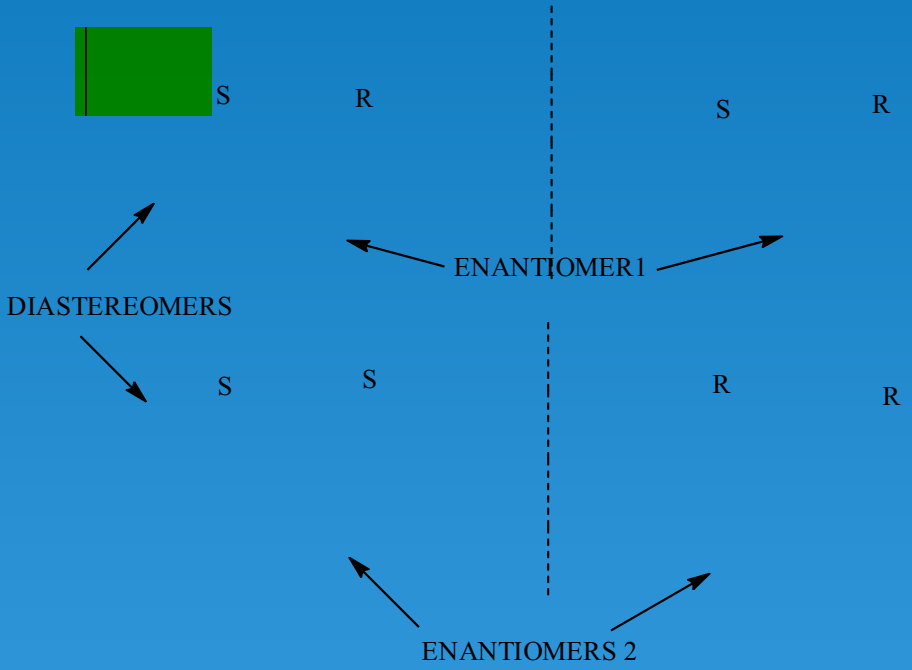
1. (I) and (II) are enantiomers or diastereomers?
2. (I) and (III) are _____.
3. (II) and (III) are _____.

Meso Compounds

- Tartaric acid has two chirality centers and two diastereomeric forms.
- One form is chiral and the other is achiral, but both have two chirality centers.
- An achiral compound with chirality centers is called a meso compound – it has a plane of symmetry.
- The two structures on the right in the figure are identical so the compound (2R, 3S) is achiral.



Assign R/S configuration to each chiral carbon.



RACEMIC MIXTURES

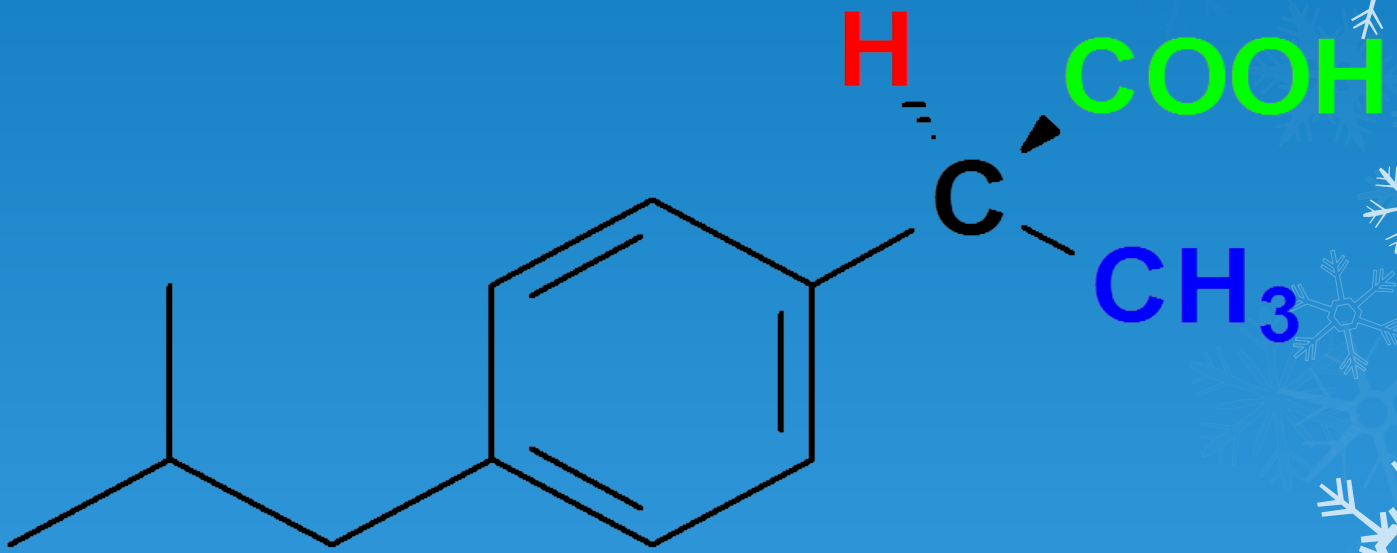
50:50 mixture of enantiomers are termed as racemic mixture or racemate. Such mixtures are optically inactive. Racemates are often denoted by the symbol (+) or (-).

Example: (+) tartaric acid and (-) tartaric acid.

Summary

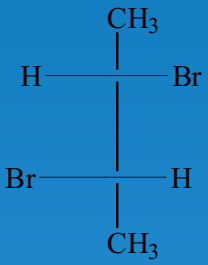
- Optically active describes organic molecules which rotate plane-polarized light.
- A **chiral** molecule does **not** contain **plane of symmetry**.
- **Chirality** is the property of "handedness"; the presence of a tetrahedral carbon atom bonded to four different groups. Also called as a **stereocenter** or **chirality center**.
- **Chiral compounds** can exist as a pair of **mirror image** stereoisomers are called **ENANTIOMERS**.
- **Diastereomers** are stereoisomers that are **not mirror images**.
- **Meso compounds** contain **stereocenters** but are **achiral** and have **plane of symmetry**.
- Chiral compounds rotate the plane of polarized light, if the rotation is in clockwise direction the stereocenter has R configuration and if the rotation is in anticlockwise direction the stereocenter has S configuration. Then the molecule is said to be optically active.
- **Racemates** are **50:50** mixtures of (+) and (-) **enantiomers**.
- **Chiral** molecules are **optically active**.
- **n stereocenters give 2^n stereoisomers**.

The number of stereocenters present in (S)-Ibuprofen.

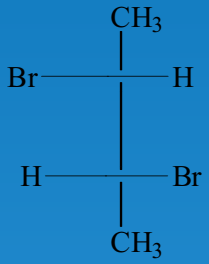


Practice problem

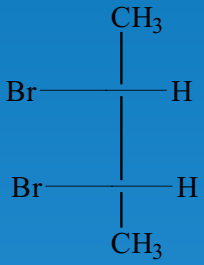
1. In the following Fischer projections, solve the questions given below.



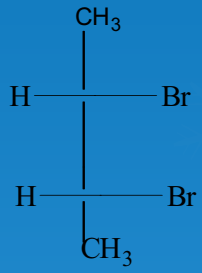
I



II



III



IV

1. The number of stereoisomers for III are _____.
2. The configuration of II and IV stereoisomers is _____.
3. Optically active stereoisomers are _____.
4. The meso compounds are _____.
5. I and III are diastereomers or enantiomers?
6. III and IV are _____.