بسم الله الرحمن الرحيم

Chelating and medical interest

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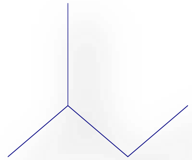
- **Stereo chemistry is the branch of chemistry concerned with the three dimensional aspects of molecules.**

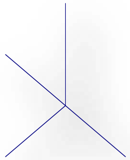
- ***Isomers*: Different compounds that have the same No. & kinds of atoms.**

- **Constitutional Isomers** have same formula but different connections between atoms. They have different physical and chemical properties
- Example: Pentane (C_5H_{12}) has three isomers

n-Pentane

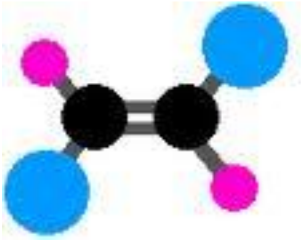


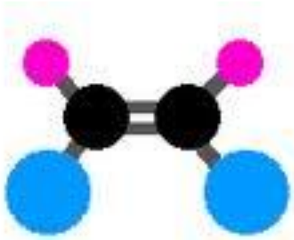
Isopentane

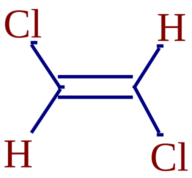


Neopentane

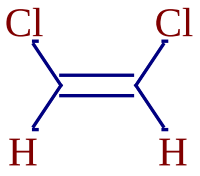
- ***Geometric isomers***: **Are isomers that differ in the arrangements of their atoms in the space. It is specific examples of a large class of isomers called *stereoisomer*.**







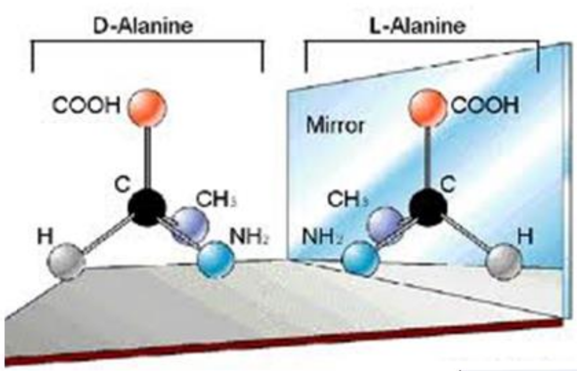
Trans isomer

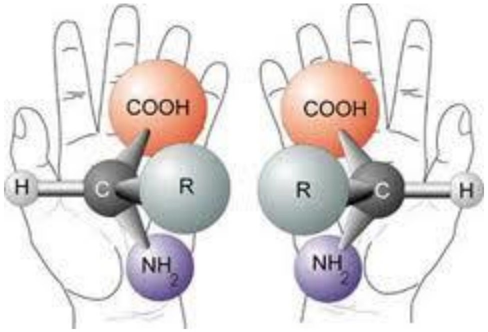


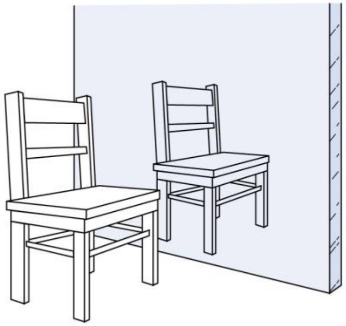
Cis isomer

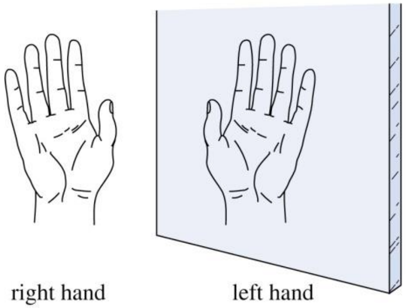
Stereogenic Carbons **are those that have four different groups attached.**

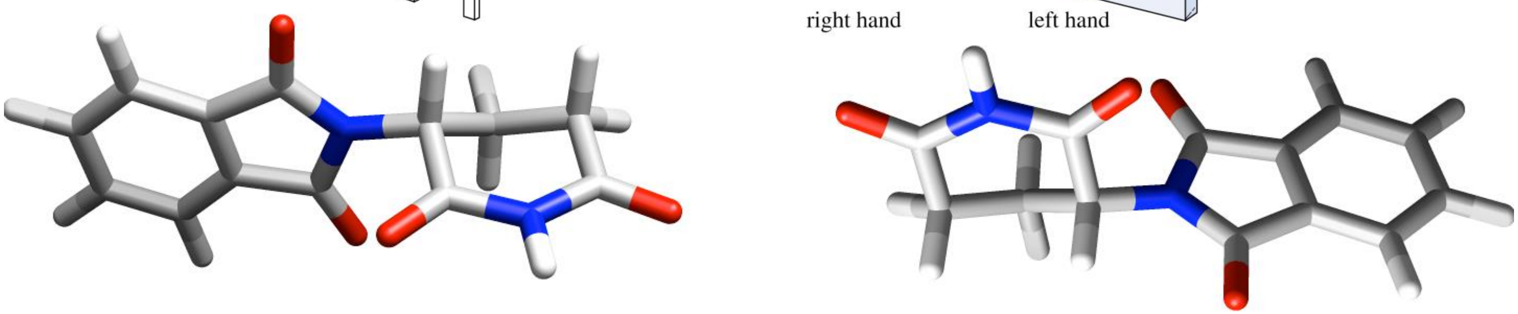
- ***Enantiomers***: **Stereoisomer that are mirror images but cannot be superimposed.**











Mirror image

- **Enantiomers have identical physical properties mp, bp, spectroscopic, absorptions, etc.**

- ***BUT*** **different in biological properties, such as taste, odor and reaction with a chiral receptor in a living system. One enantiomer of a drug could be cure for a disease and another one could be very toxic. Also, enantiomers have same optical activity but opposite optical rotation, one enantiomer rotates plane polarized light to the right and another one to the left.**

ISOMERS
(same number and kind of atoms, but are different molecules)

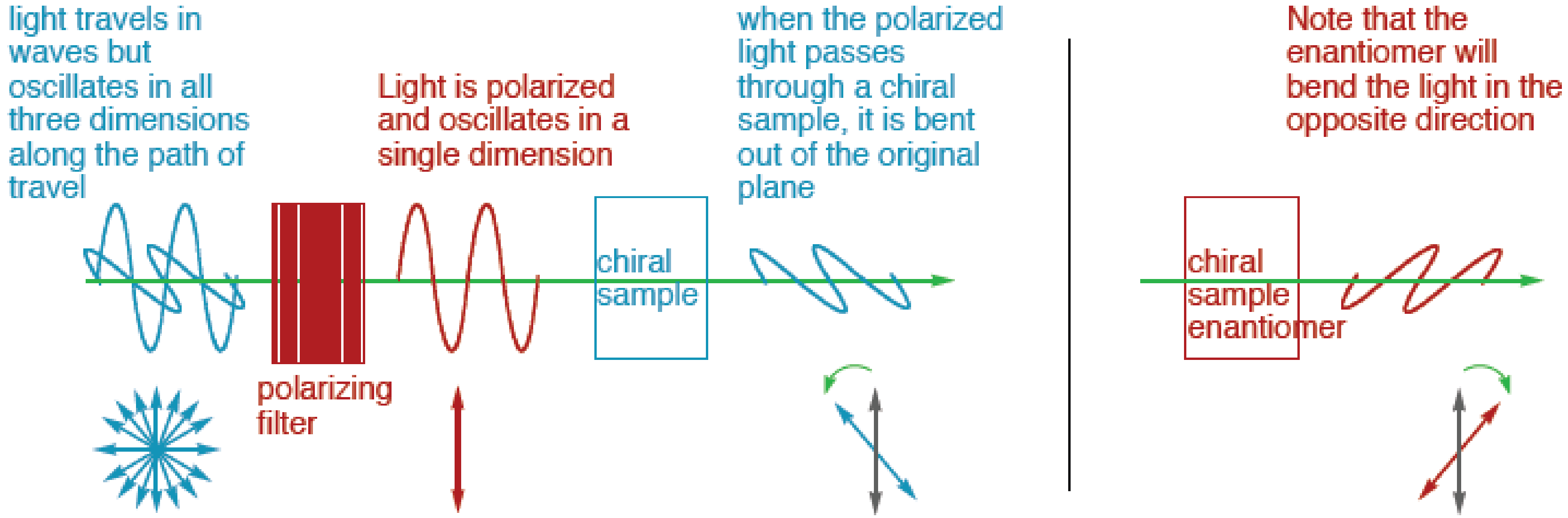
- **Constitutional**
  (bonded differently)
- **Stereoisomers**
  (Only different in 3-dimensional arrangement)
  - **Enantiomers**
    (mirror images)
  - **Diastereomers**
    (not mirror images)
    - **Configurational**
    - **cis/trans**

Jean-Baptiste Biot (1774-1862)

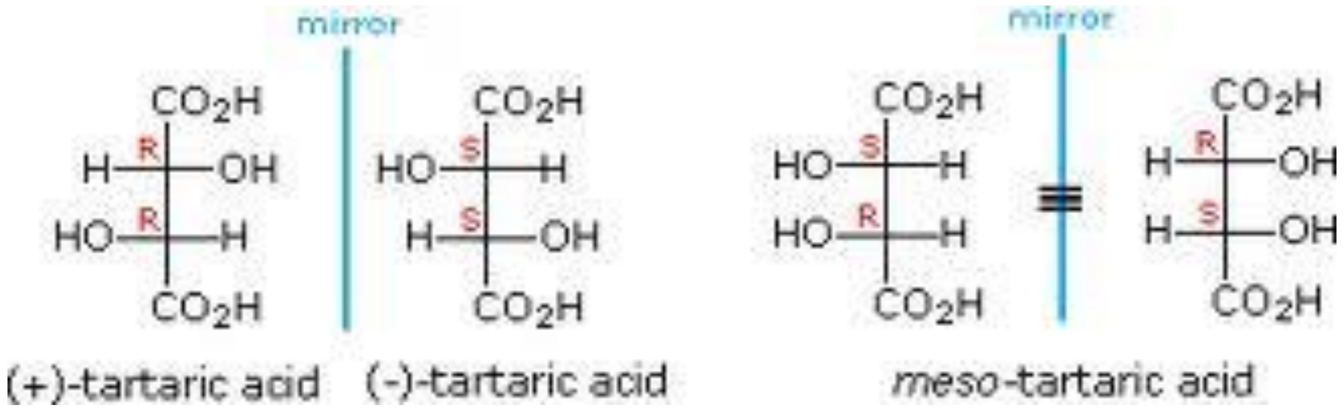
- In 1815 he discovers that certain natural ***organic compounds rotate plane polarized light***.

Polarized light : Light in which all rays vibrate in single plane.

Optically active compound: A compound capable of rotating the plane of polarized light.

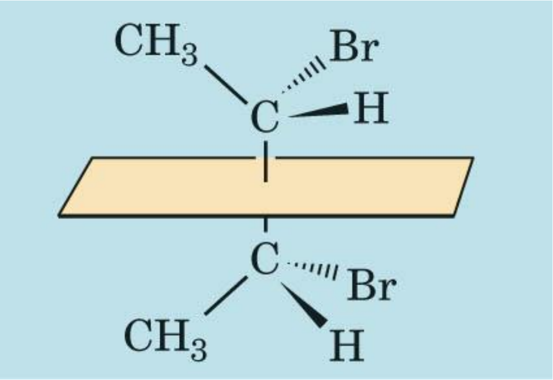


Meso stereoisomer: **A molecule that contains chiral centers but is optically inactive.**



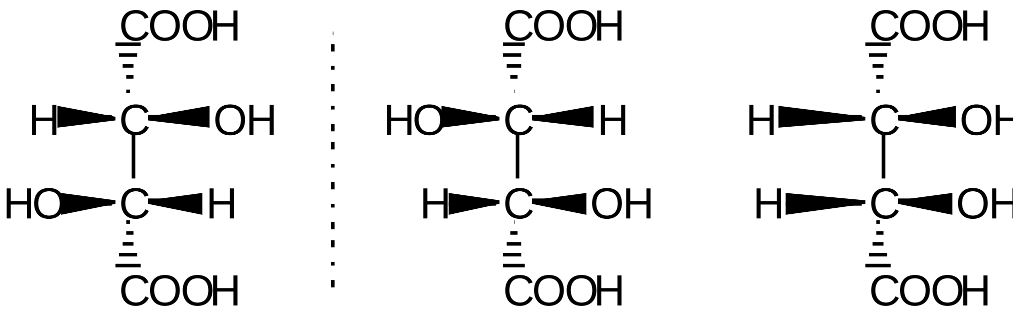
Racemic Mixture- **50/50 mixture of enantiomers. Shows *NO* optical activity.**

- Meso compound: achiral despite the presence of stereogenic centers
  - Not optically active
  - Superposable on its mirror image
  - Has a plane of symmetry



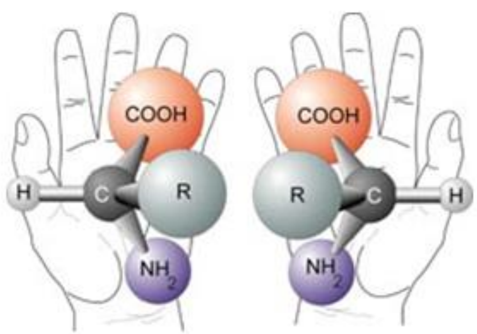
PROPERTIES OF STEREOISOMERS

Properties of the stereoisomers of tartaric acid

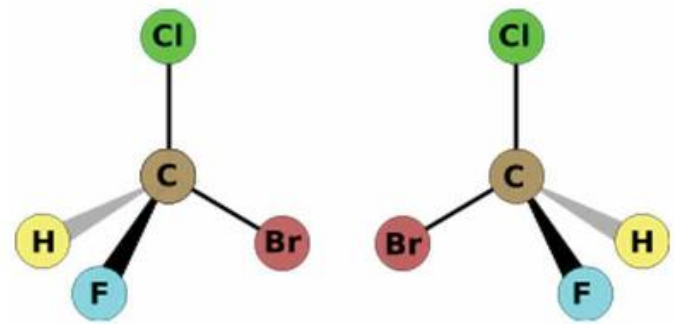


	(*R*,*R*)-Tartaric acid	**(*S*,*S*)-Tartaric acid**	**Meso tartaric acid**
specific rotation	+12.7	-12.7	0
melting point (° C)	171-174	171-174	146-148
density at 20°C (g/cm^3)	1.7598	1.7598	1.660
solubility in water at 20°C (g/100 mL)	139	139	125
pK_1 (25°C)	2.98	2.98	3.23
pK_2 (25°C)	4.34	4.34	4.82

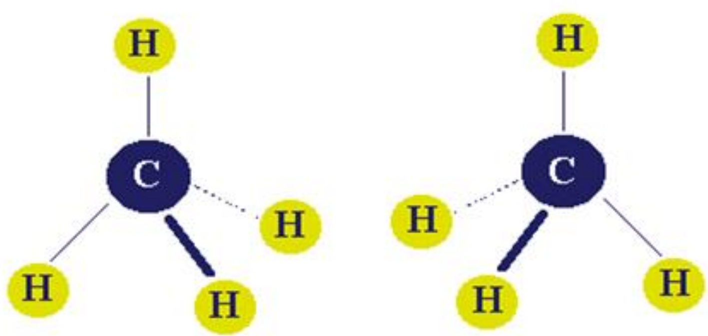
- Molecules that can exist as enantiomers are called ***Chiral Molecules***. While molecules that have a plane of symmetry are not chiral ***(achiral)***.



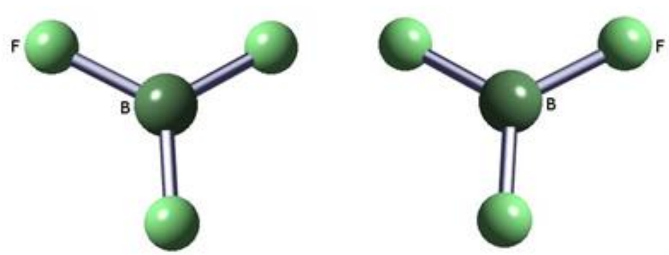
chiral



chiral



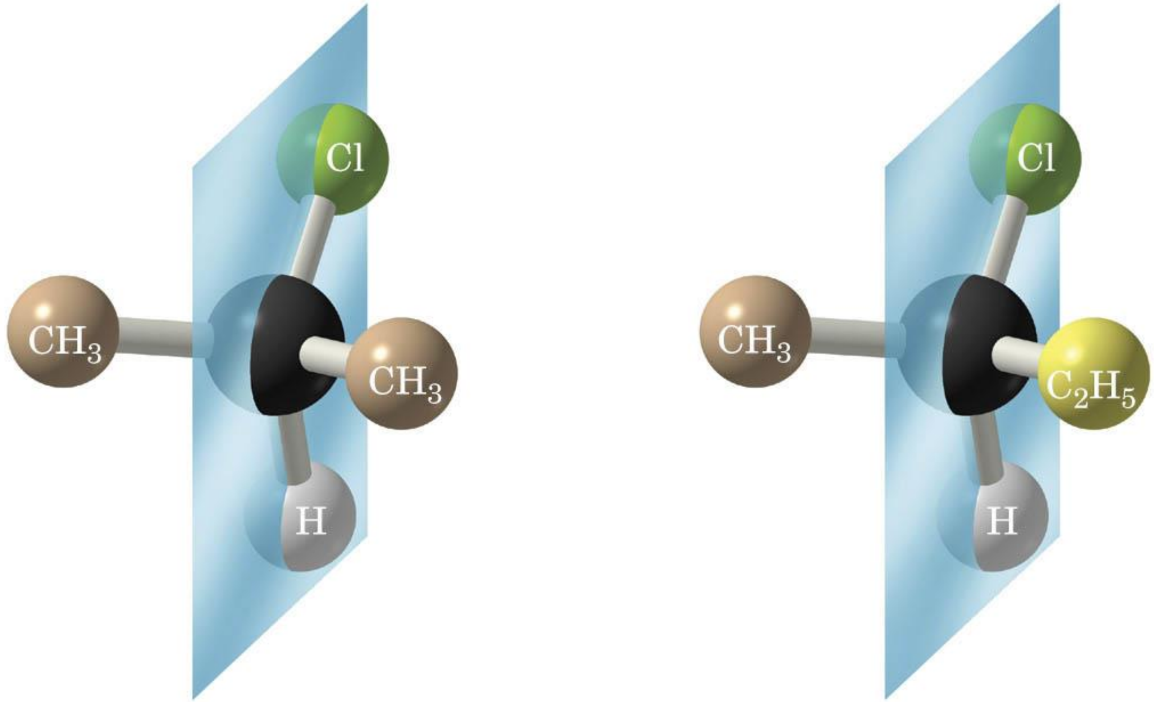
achiral



achiral

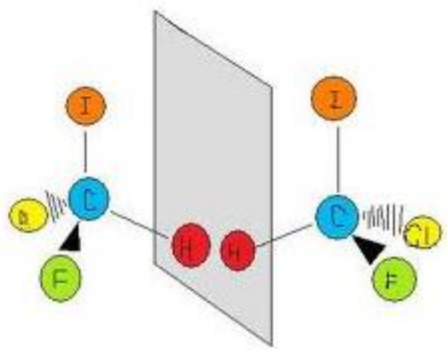
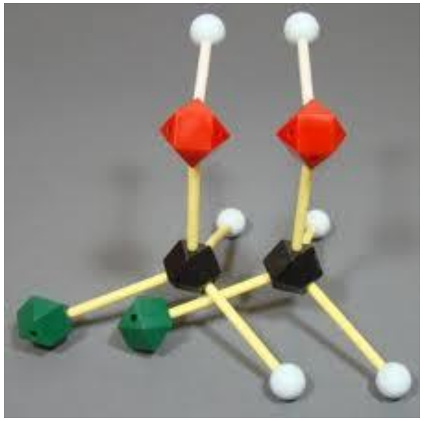
Tests for Chirality: Planes of Symmetry

- Plane of symmetry
  - An imaginary plane that bisects a molecule in such a way that the two halves of the molecule are mirror images of each other
  - A molecule with a plane of symmetry cannot be chiral
- Example
  - 2-Chloropropane (a) has a plane of symmetry but 2-chlorobutane (b) does not



(a) (b)

- ***Chiral carbon***: **If a tetrahedral carbon is connected to 4 different groups, it's called chiral carbon, this molecule has *stereocenter*. The mirror image of a chiral molecule is not same with the original molecule, they are *nonsuperimposable*.**

Achiral molecule: If a molecule and its mirror image are same it's called achiral molecule. Achiral molecule and its mirror image are *Superimposable.*

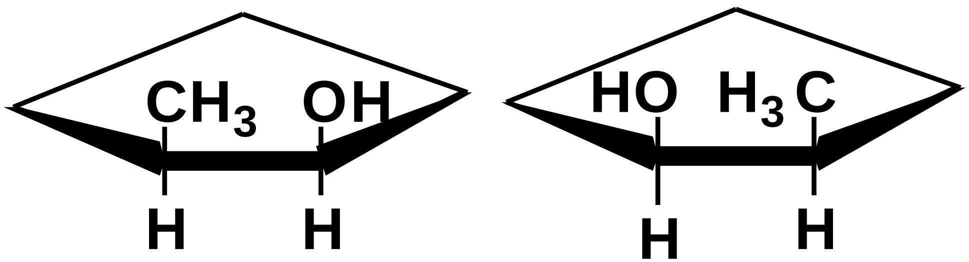
SUBDIVISION OF ISOMERS

ISOMERS
(Different compounds with same molecular formula)

- ***Constitutional isomers***
  (Isomers whose atoms have a different connectivity)
- ***Stereoisomers***
  (Isomers that have the same connectivity but that differ in the arrangement of their atoms in space)
  - ***Enantiomers***
    (Stereoisomers that are nonsuperposable mirror images of each other)
  - ***Diastereomers***
    (Stereoisomers that are not mirror images of each other)

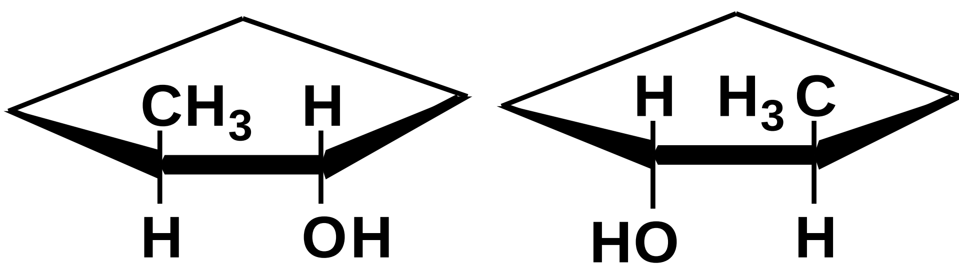
ENANTIOMERS & DIASTEREOMERS

- 2-Methylcyclopentanol



***cis*- 2-Methylcyclopentanol**
(a pair of enantiomers)

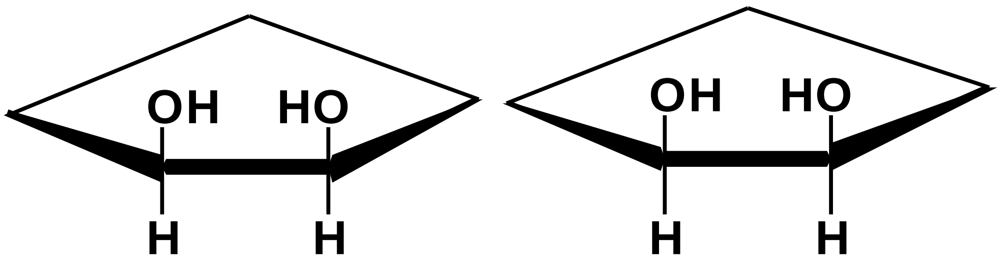
diastereomers



***trans*- 2-Methylcyclopentanol**
(a pair of enantiomers)

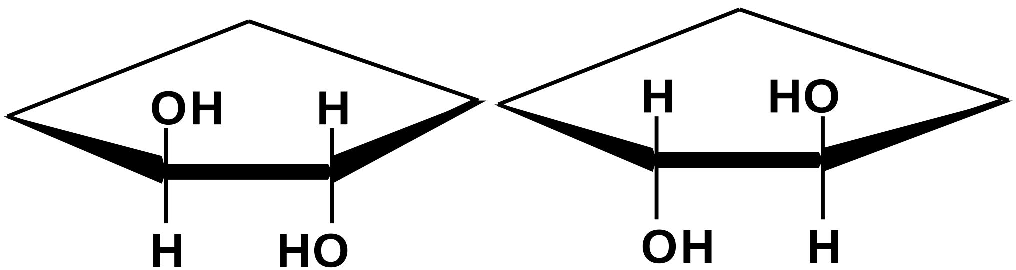
ENANTIOMERS & DIASTEREOMERS

- 1,2-Cyclopentanediol



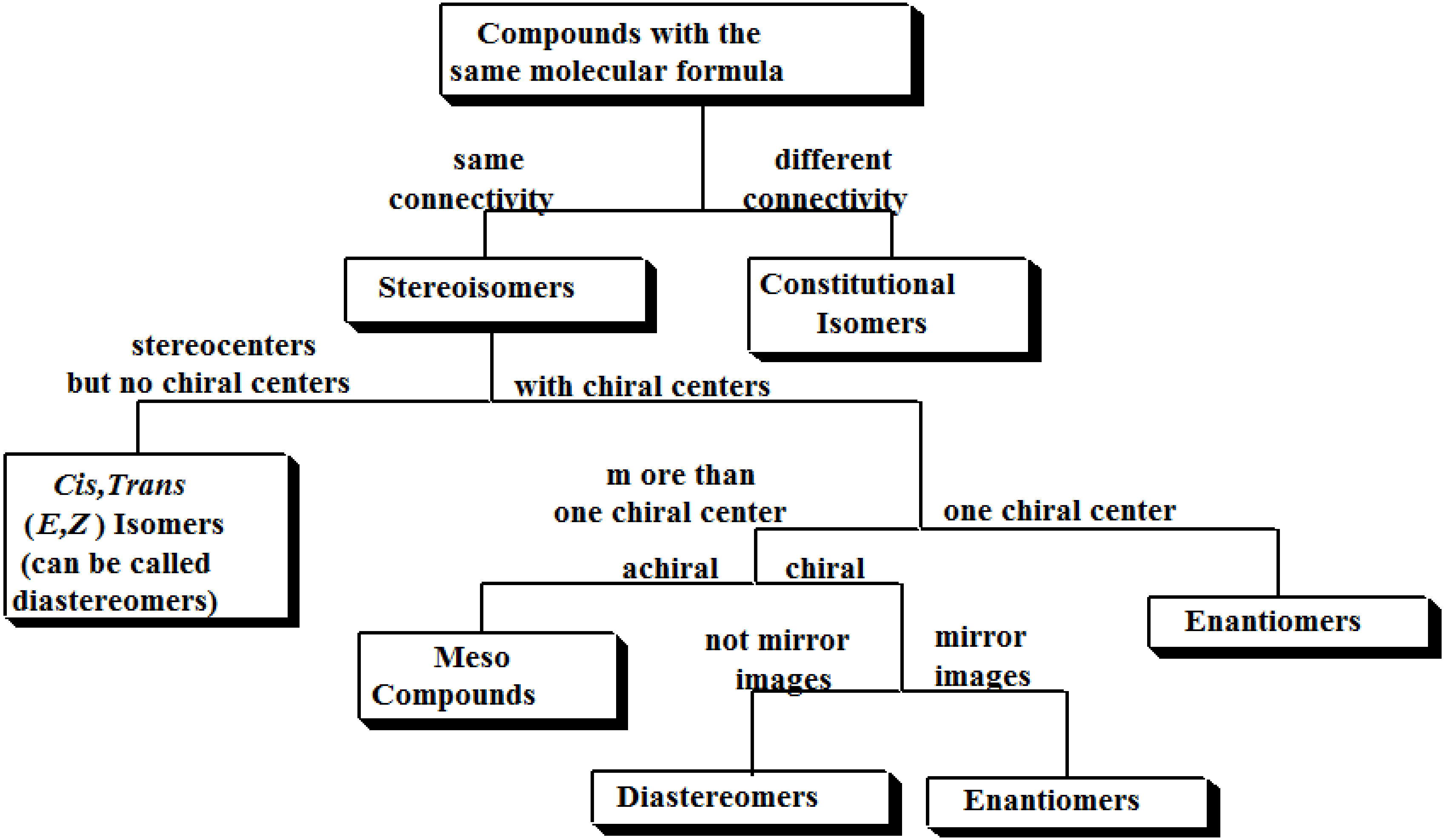
***cis*-1,2-Cyclopentanediol**
(one meso compound)

diastereomers



***trans*-1,2-Cyclopentanediol**
(a pair of enantiomers)

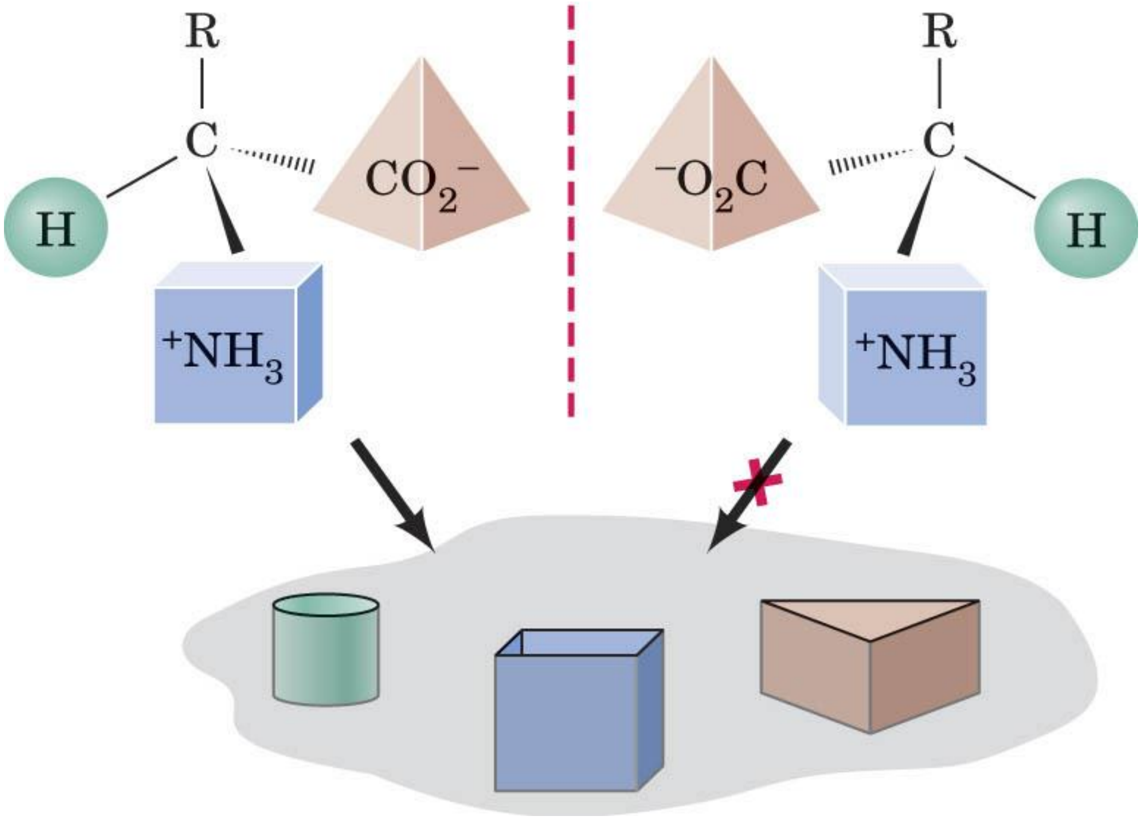
ISOMERS


Compounds with the same molecular formula
same connectivity
different connectivity
Stereoisomers
Constitutional Isomers
stereocenters but no chiral centers
with chiral centers
Cis,Trans (E,Z) Isomers (can be called diastereomers)
m ore than one chiral center
one chiral center
achiral
chiral
Meso Compounds
not mirror images
mirror images
Enantiomers
Diastereomers
Enantiomers

THE IMPORTANCE OF CHIRALITY IN LIVING SYSTEM

- **Most biologically important molecules are chiral. The bioactivity of chiral molecules is specifically associated with specific enantiomers. This resulted from reaction between a chiral molecule and a chiral receptor that only accommodates one enantiomers. This is the key factor in drug design.**

- **Example to the Biological Importance of Chirality The binding specificity of a chiral receptor site for a chiral molecule is usually only favorable in one way**



CHIRALITY IN THE BIOLOGICAL WORLD

- **Except for inorganic salts and a few low molecular weight organic substances, the majority of molecules of living systems are chiral.**

- **Although these molecules can exist as a number of stereoisomers, generally only one is produced and used in a given biological system.**

- **It's a chiral world!**

- **Enzymes are like hands in a handshake.**
  - **The substrate fits into a binding site on the enzyme surface.**
  - **A left-handed molecule, like hands in gloves, will only fit into a left-handed binding site and**
  - **a right-handed molecule will only fit into a right-handed binding site.**
  - **Because of the differences in their interactions with other chiral molecules in living systems, enantiomers have different physiological properties.**

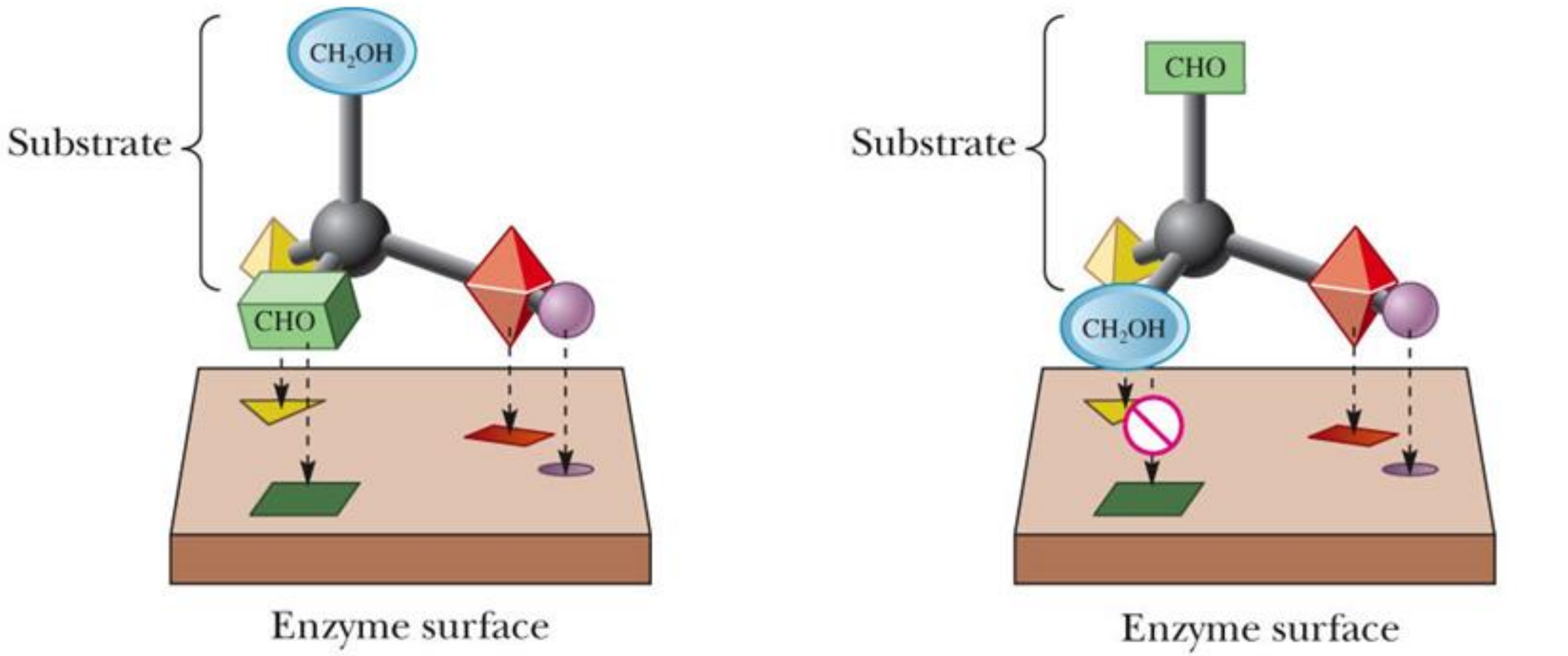
Molecules with More than One Stereocenter

A compound with one stereocenter can exist in two stereoisomeric forms (enantiomers) called (R) and (S). If there are two stereocenters, each center may be (R) or (S). The various stereocenter combinations are shown in the table.

Stereocenters	Possible Combinations	Stereoisomers
1	R S	2
2	RR SS RS SR	4

The maximum number of stereoisomers is 2^n, where n is the number of stereocenters.

- A schematic diagram of an enzyme surface capable of binding with (*R*)-glyceraldehyde but not with (*S*)-glyceraldehyde.

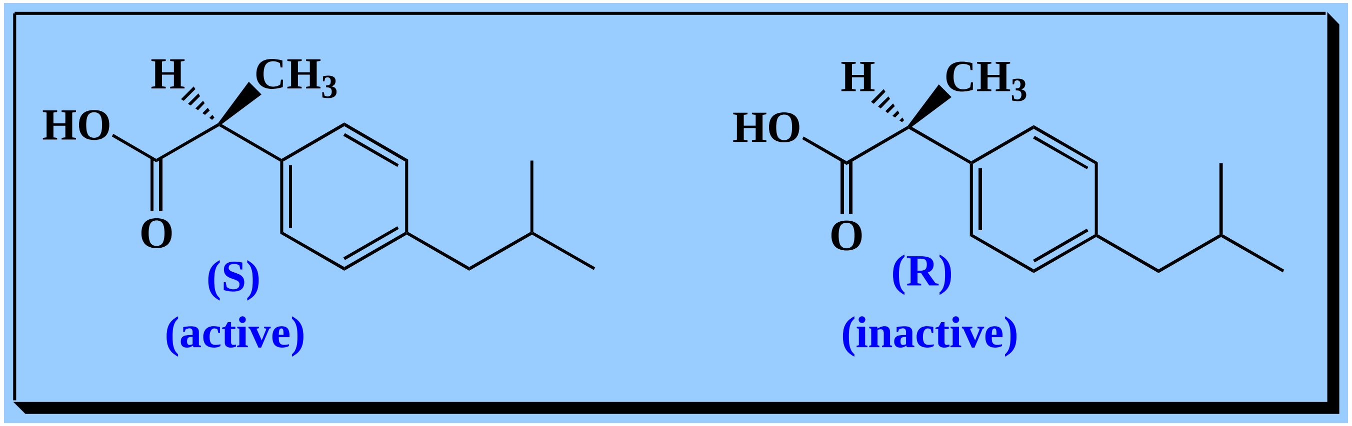


This enantiomer of glyceraldehyde fits the three specific binding sites on the enzyme surface.

This enantiomer of glyceraldehyde does not fit the same binding sites.

Chiral Drugs

The driving force behind the effort to design enantioselective reactions is the pharmaceutical industry. Typically, only one enantiomer of a chiral drug is active. One example is the antiinflammatory drug ibuprofen (sold as advil, motrin, nuprin). The (S) enantiomer is active while the (R) enantiomer is inactive.



THANK YOU