REVIEW OF ISOMERS

- ***Isomerism*** is the phenomenon of two or more compounds having the same number and kind of atoms.

- In ***structural isomers***, the difference between isomers is due to different structural arrangements of the atoms that form the molecules.

- Example:

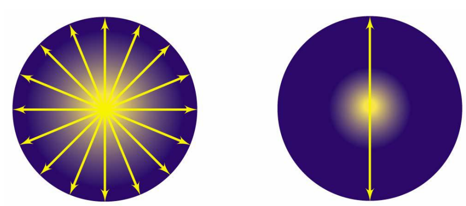
	CH_3
$CH_3CH_2CH_2CH_3$	**CH_3CHCH_3**
Butane	Isobutane

- In ***stereoisomerism***, the isomers have the same structural formula, but differ in spatial arrangement of atoms. These types of isomers are called stereoisomers.

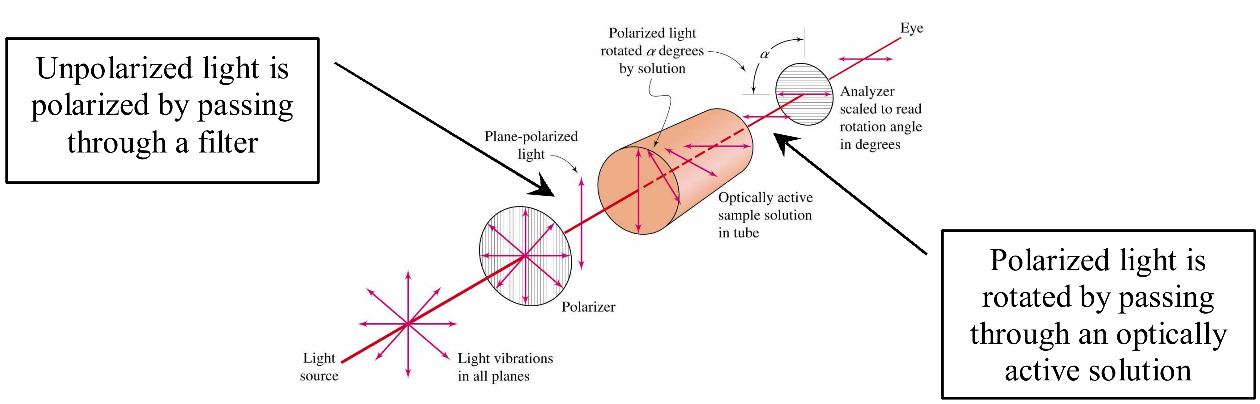
- There are two types of stereoisomers:

  1. *cis-trans isomers* (geometric isomers)
  2. *Optical isomers*

- Optical isomers have the ability to rotate plane-polarized light.
- Plane-polarized light is light that is vibrating only in one plane.
- Ordinary (unpolarized) light consists of electromagnetic waves vibrating in all directions (planes) perpendicular to the direction in which it is traveling.



(a) Ordinary (unpolarized) light (b) Plane-polarized light



OPTICAL ACITVITY

- Many naturally occurring substances are able to rotate the plane of polarized light.
- These substances are called optically active.
- When plane-polarized light passes through an optically active substance, the plane of polarized light is rotated.
- The extent of rotation of light is measured as specific rotation [α] and is an important property of substances.

Specific Rotation of Some Organic Molecules

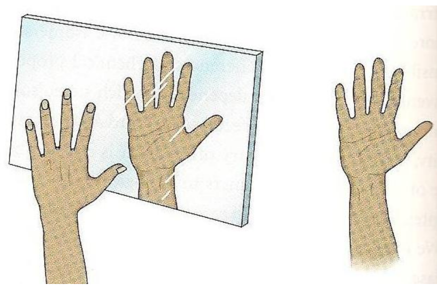
Compound	$[\alpha]_D$	Compound	$[\alpha]_D$
Penicillin V	+233°	Cholesterol	−31.5°
Sucrose	+66.47°	Morphine	−132°
Camphor	+44.26°	Acetic acid	0

- In addition to determining the extent of rotation, the direction of rotation can also be measured.
- From the vantage point of the observer, the rotation can occur:
  - Clockwise (Right) dextrarotatory (D-) (+)
  - Counterclockwise (Left) levorotatory (L-) (–)

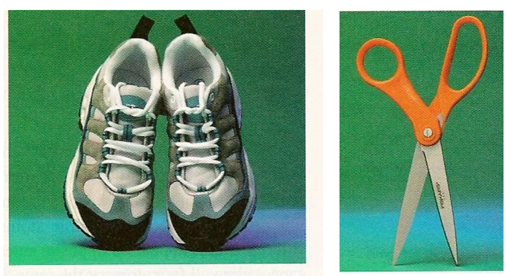
CHIRAL MOLECULES

- The tetrahedral arrangement of single bonds around a carbon atom makes asymmetry (lack of symmetry) possible in organic molecules.

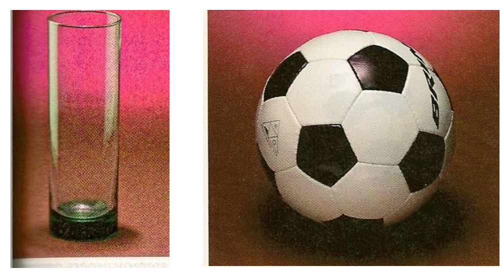
- An ***asymmetric*** object that is not superimposable on its mirror image and is called ***chiral***. The right and left hands are mirror images of one another that are not super-imposable and are therefore chiral.



- A ***symmetric*** object that has a superimposable mirror image is called ***achiral***. Many common objects such as shoes and scissors are chiral, while a glass and soccer ball are examples of achiral objects.

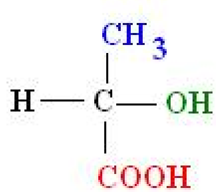


Chiral objects

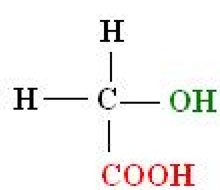


Achiral objects

- A carbon atom that possesses ***four different functional*** groups is called a ***chiral*** carbon and forms non-superimposable mirror images.



Chiral

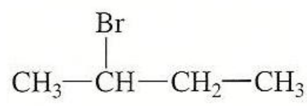


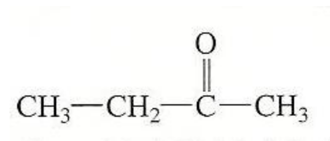
Achiral

CHIRAL MOLECULES

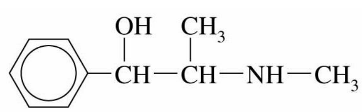
Examples:

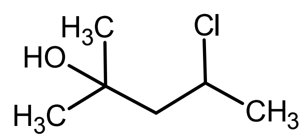
1. Identify each of the following structures as chiral or achiral. If chiral, indicate the chiral carbon.

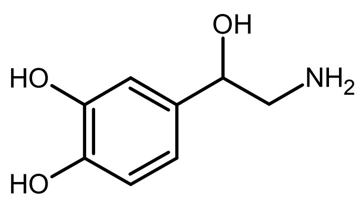
a) 

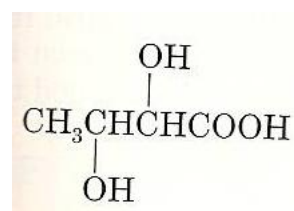
b) 

2. Identify all the chiral carbons in each of the following molecules:

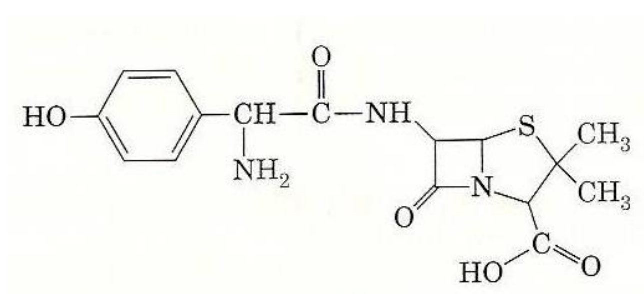
a) 

b) 

c) 

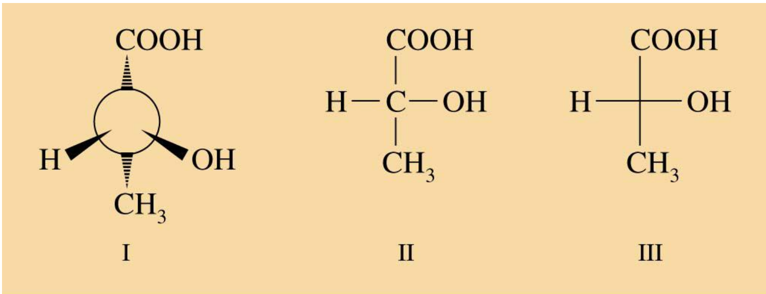
d) 

3. Label the 4 chiral carbons in amoxicillin, an antibiotic in the family of penicillins.



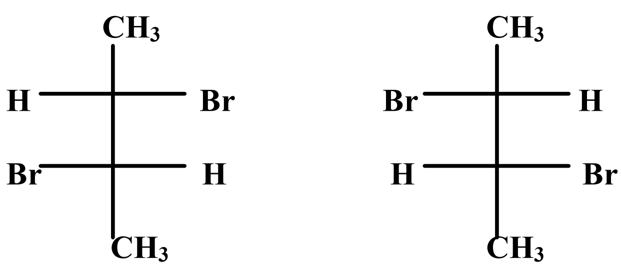
FISHER PROJECTIONS

- Chemists use **Fisher projections** to show the bonds to a chiral atom.
- In these diagrams, the bonds to the chiral atom are drawn as intersecting lines, with the chiral carbon being at the center of the intersecting lines.
- The horizontal lines represent the bonds that come forward in the three-dimensional structure (bold wedges), and the vertical lines represent the bonds that that point away (dash lines).



Fisher projections

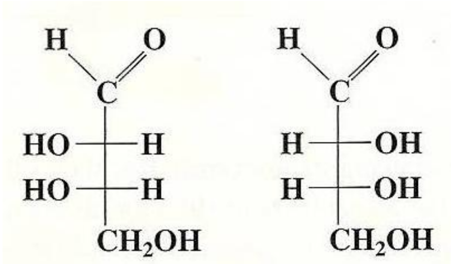
- Fisher projections can also be written for larger compounds that have two or more chiral carbons. For example, the two mirror images shown below are different. Each chiral carbon is bonded to four different groups.



- Note that when drawing Fisher projections for mirror images, the position of the substituents on the horizontal line are reversed while the groups on the vertical lines are left unchanged.

FISHER PROJECTIONS

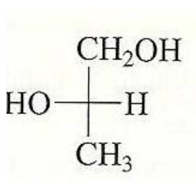
- Similarly the two isomers of the carbohydrate erythrose can be drawn as shown below. Note that each molecule has two chiral carbons.

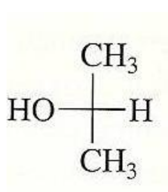


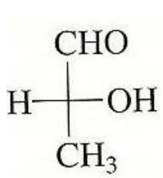
L-erythrose D-erythrose

- By convention, Fisher projections are written with the most highly oxidized carbon (carbonyl) written on top. The L isomer is assigned to the left-handed stereoisomer (with —OH on the left side of the chiral carbon), and D isomer is assigned to the right-handed stereoisomer (with —OH on the right side of the chiral carbon).

Examples:
Determine if each Fisher projection shown below is a chiral compound. If so, identify it as the D or L isomer, and draw the mirror image.

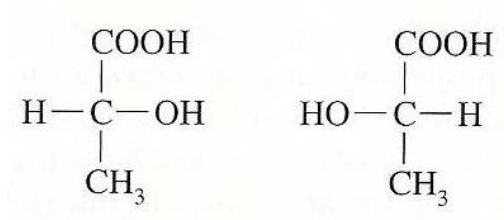
1) 

2) 

3) 

ENANTIOMERS

- Chiral molecules that are non-superimposable mirror images of each other are stereoisomers and are called ***enantiomers***. Enantiomers are related to one another as a right hand is related to a left hand.



Enantiomers of lactic acid

- Enantiomers possess similar chemical and physical properties (except for rotation of light). They rotate plane-polarized light to the same degree but in different direction.

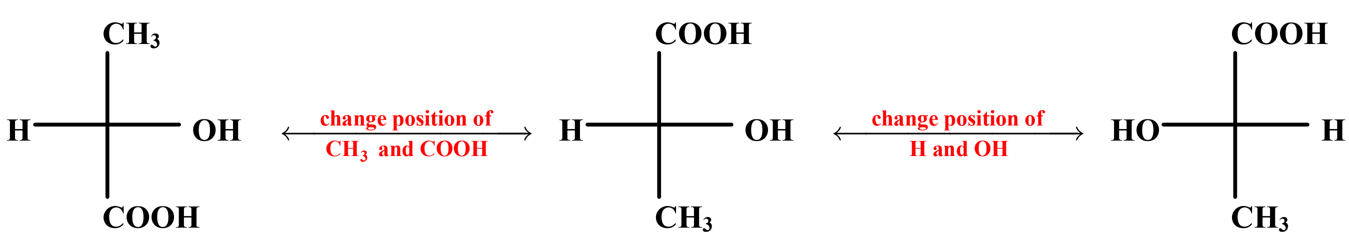
- Enantiomers possess different biochemical properties. For example:

  - (+)-Glucose ("blood sugar") is used for metabolic energy whereas (-)-glucose is not.

  - (+)-Lactic acid is produced by reactions occurring in muscle tissue, and (-)-lactic acid is produced by the lactic acid bacteria in the souring of milk.

- In compounds with only one chiral carbon, the relationship between enantiomers is such that if we change the position of any two groups attached to a chiral carbon, we obtain the structure of its enantiomer (Isomers I and II).

- If we make a second change, the structure of the original isomer is obtained (Isomers I and III).



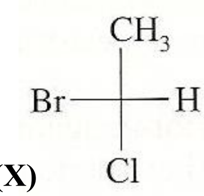
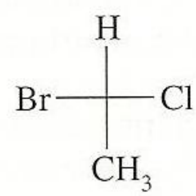
Isomer I **Isomer II** **Isomer III**

ENANTIOMERS

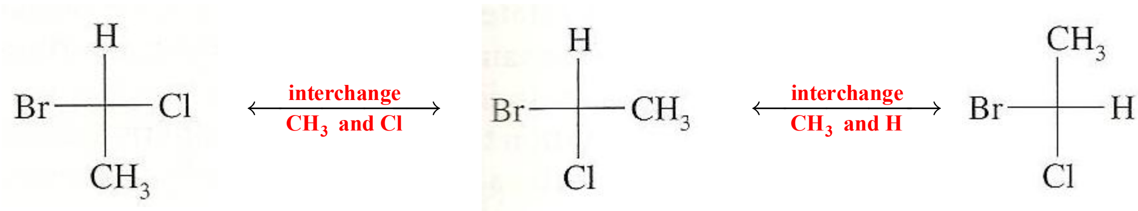
- When evaluating different Fisher projections,

    1. Compare the two structures.
    2. Make successive changes until the formulas are identical.
    3. If an odd number of changes are made, the two original formulas are enantiomers. If an even number of changes are made, the two original formulas are identical.

For example:

(X)   **(Y)**

Are these structures enantiomers or the same?

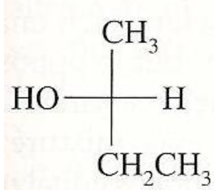
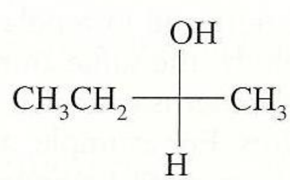


(Y) **(X)**

- Since two changes were made to convert Y into X, the two structures are the same.

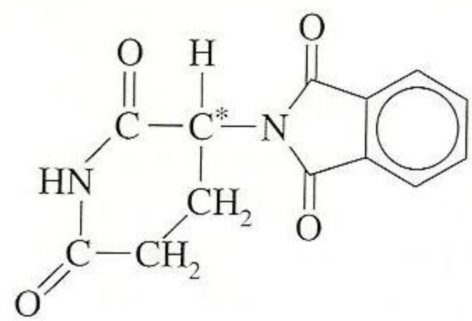
Examples:

1. Determine if the structures shown below are enantiomers or identical.

(A)   **(B)**

RACEMIC MIXTURES

- A mixture containing equal amounts of a pair of enantiomers is known as a ***racemic mixture***.
- Such a mixture is optically inactive and shows no rotation of polarized light.
- Each enantiomer rotates the plane of polarized light by the same amount, but in opposite directions. Thus, the rotation by each isomer is canceled.
- Many pharmaceutical compounds are prepared as racemic mixtures, since organic synthesis reaction are often not ***stereospecific***. Unfortunately, often only one enantiomer of these mixtures has biological activity because many biological molecules are stereospecific.
- Furthermore, the inactive enantiomer may cause adverse affects. The most famous example of such effect is the racemic mixture of the drug thalidomide. While one isomer is effective at suppressing immune responses, the other isomer causes birth defects.



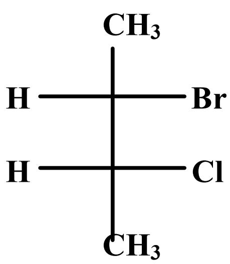
Thalidomide

DIASTEREOMERS & MESO COMPOUNDS

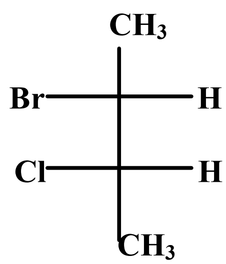
- The number of stereoisomers increases as the number of chiral atoms in a molecule increases. The maximum number of stereoisomers for a given compound is given by the formula ***2^n***, where ***n*** is the ***number of chiral carbons*** in a molecule.

  2^n = Maximum number of stereoisomers for a given chiral compound.
  n = Number of chiral carbon atoms in a molecule.

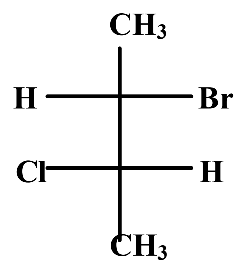
- As an example, 2-bromo-3-chlorobutane has 2 chiral carbons and therefore four possible stereoisomers (structures I-IV shown below).



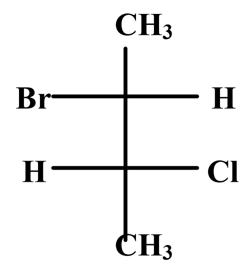
(I)



(II)



(III)



(IV)

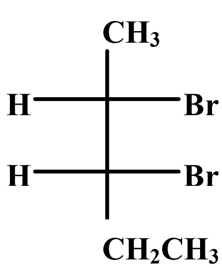
enantiomers **enantiomers**

- Note that isomes I and II are enantiomers and isomers III and IV are also enantiomers. All four compounds are optically active, however properties of I and II differ from properties of III and IV, because they are not mirror images of each another.

- Stereoisomers that are ***not enantiomers*** (mirror images of each other) are called ***diastereomers***.

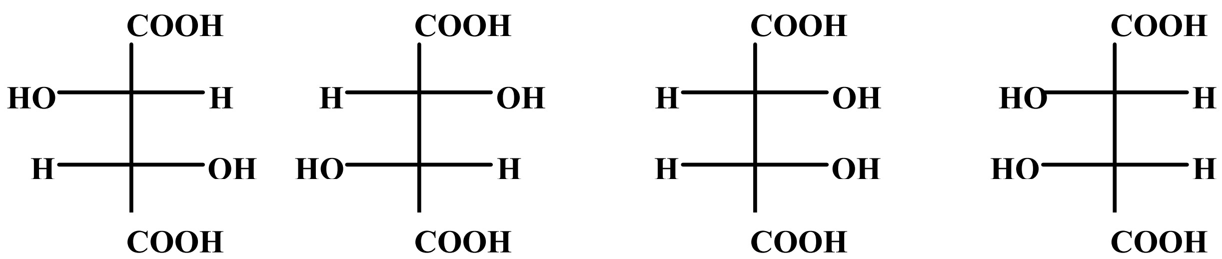
<u>Examples:</u>

1. How many stereoisomers can exist for the compound shown below? Draw their structures and label any pairs of enantiomers and diastereomers.



DIASTEREOMERS & MESO COMPOUNDS

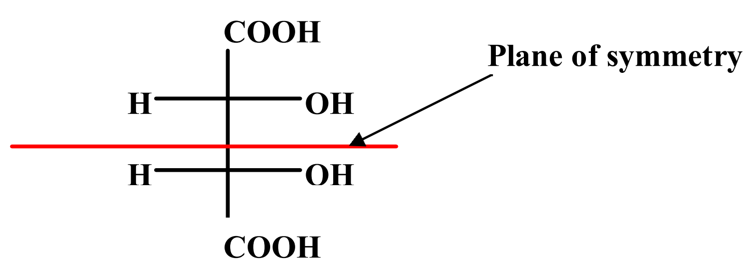
- Tartaric acid has two chiral carbons and can therefore have four stereoisomers shown below.



(A) **(B)** **(C)** **(D)**

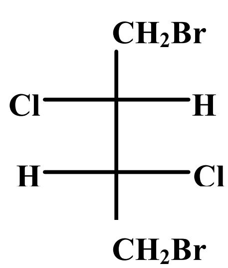
- ***Isomers A and B*** are non-superimposable mirror images, and are therefore ***enantiomers***. Close examination of isomers C and D indicates that they are superimposable, and therefore are the same compound.

- ***Stereoisomers*** that contain chiral carbons and are ***superimposable*** on their mirror images are called ***meso comounds***. Due to the plane of symmetry of these molecules, the rotation of light in one direction by half of the molecule is cancelled by rotation in the opposite direction by the other half of the molecule. Therefore, all meso compounds are optically inactive.



Examples:

1. How many stereoisomers can exist for the compound shown below? Draw their structures and label any pairs of enantiomers and meso compounds.



SUMMARY OF ISOMERISM