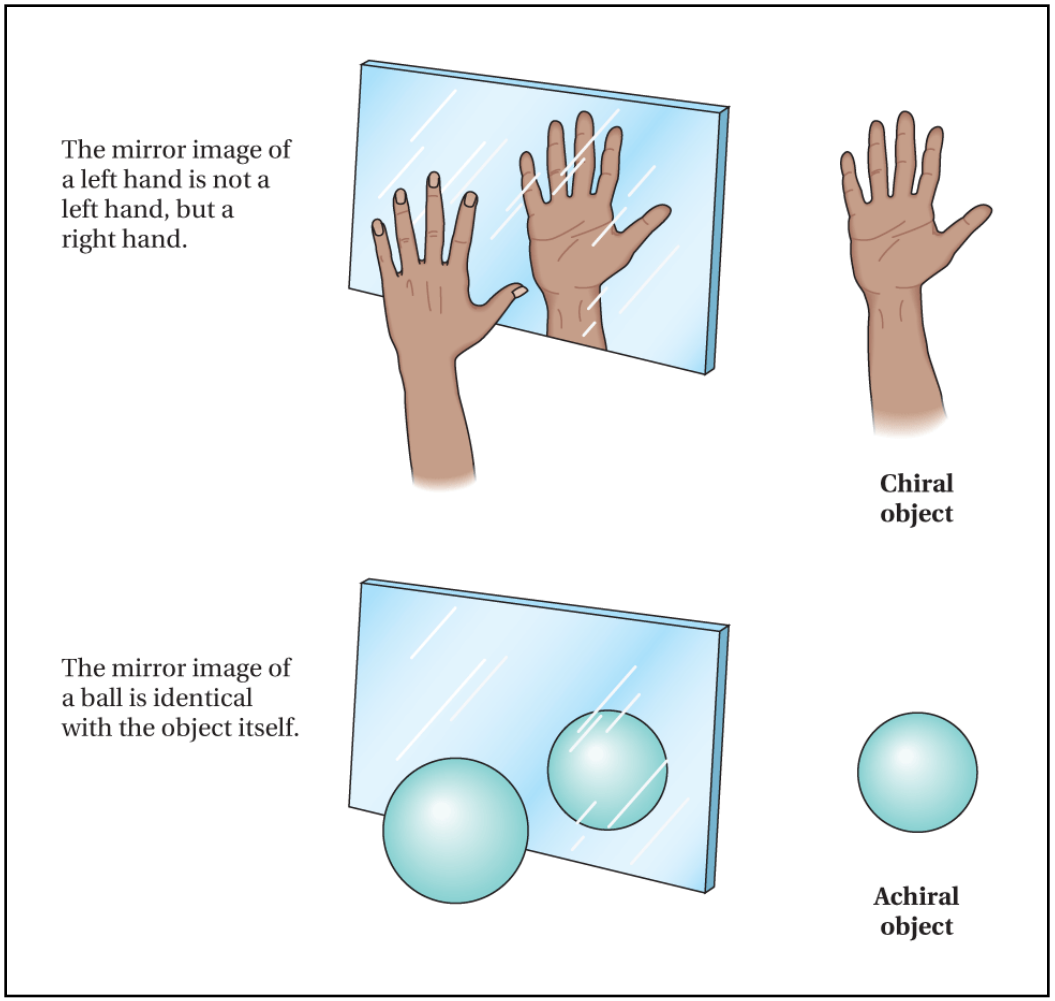
Chapter 5
Stereochemistry

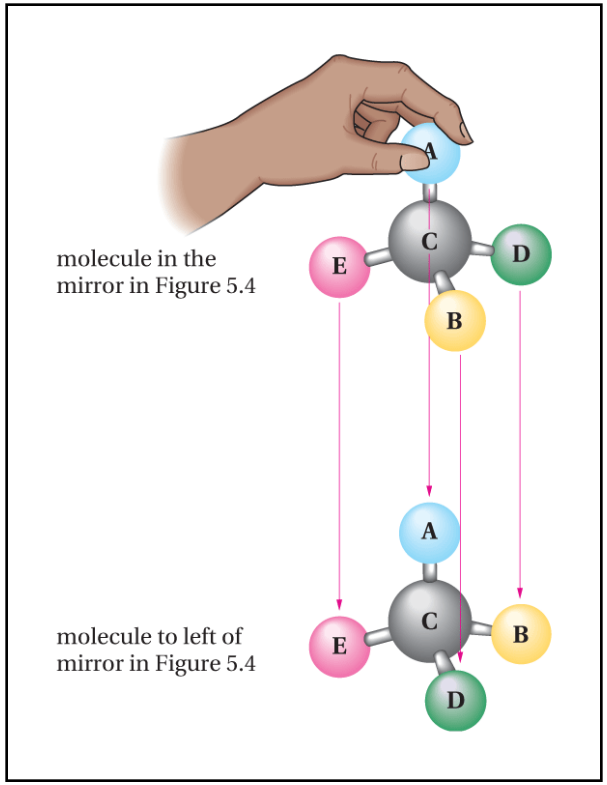
- It is the chemistry science that deals with organic compounds in 3-diminsions.



Organic molecules (including many drugs) have handedness that results from substitution patterns on sp^3 hybridized carbon. We say that the left hand is non-super impossible with the right hand.

- it was known that only one compound of the general formula CH3Y and CH2XY had ever been found.
- However for the general formula CHXYZ, there are more than one compound.

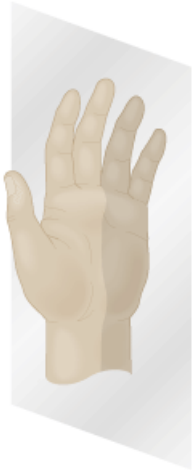
This carbon atom with 4 different groups is called Sterogenic center. As you noticed, 2 isomers exist, and they are non-super impossible on their mirror image



The Reason for Handedness: Chirality

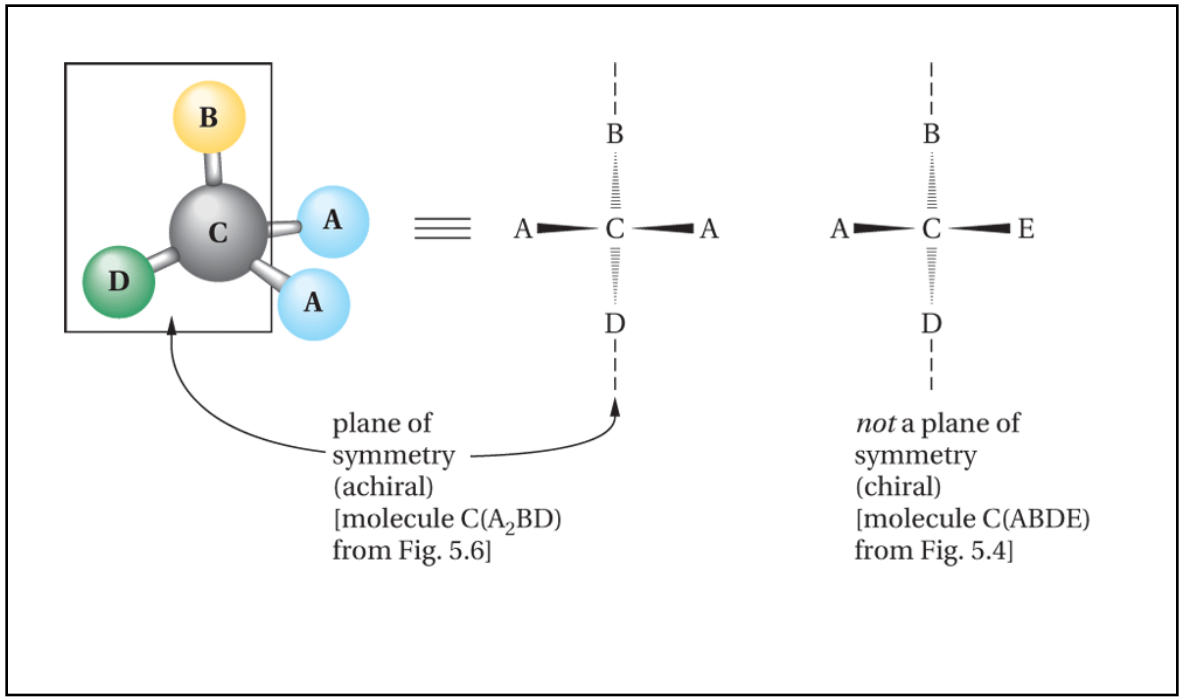
- Molecules that are not superimposable with their mirror images are **chiral** (have handedness)
- A **plane of symmetry** divides an entire molecule into two pieces that are exact mirror images
- A molecule that lack a plane of symmetry is different than its mirror image and is said to be **chiral**
- A molecule with a plane of symmetry is the same as its mirror image and is said to be **achiral**

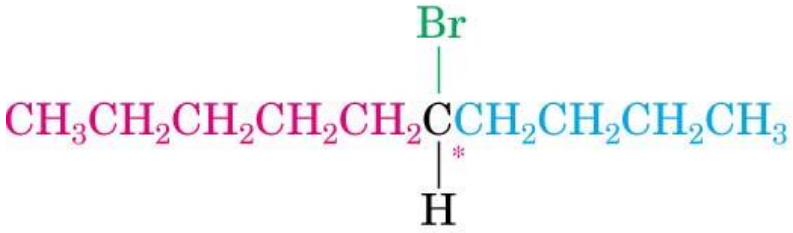
The plane has the same thing on both sides for the flask



There is no mirror plane for a hand

Chirality Centers





5-Bromodecane (chiral)

Substituents on carbon 5

—H

—Br

— $CH_2CH_2CH_2CH_3$ (butyl)

— $CH_2CH_2CH_2CH_2CH_3$ (pentyl)

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*

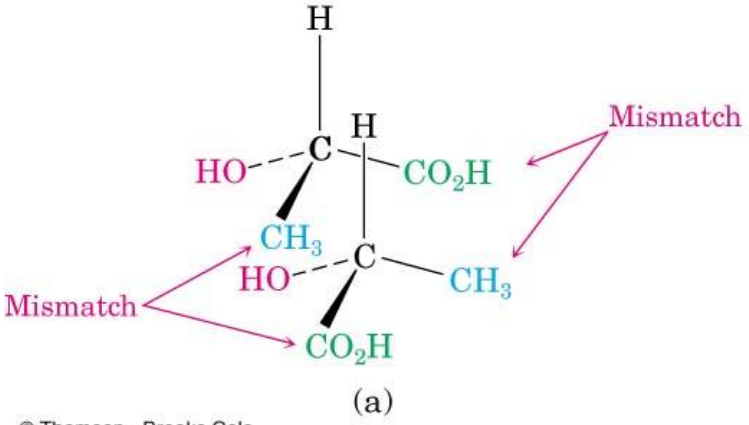
- Plane polarized light is rotated in solutions of optically active compounds
- Measured with **polarimeter**
- Rotation, in degrees, is [α]
- Clockwise rotation is called **dextrorotatory**
- Anti-clockwise is **levorotatory**

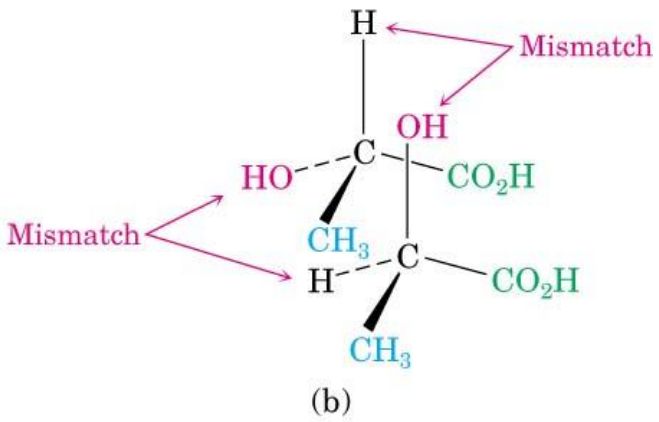
Specific Rotation and Molecules

- 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

Enantiomers and the Tetrahedral Carbon

- **Enantiomers** are molecules that are not the same as their mirror image
- (we test if they are *superimposable*, which is imaginary)
- This is illustrated by enantiomers of lactic acid
- The specific rotation of the enantiomer is equal in magnitude but opposite in sign





Sequence Rules for Specification of Configuration

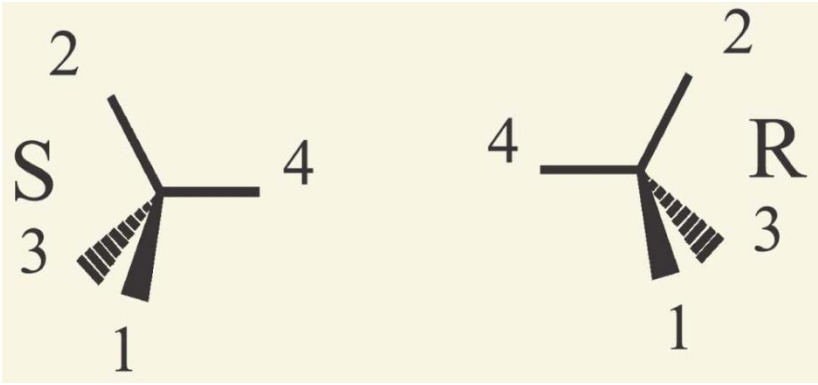
- A general method applies to the configuration at each chirality center (instead of to the the whole molecule)
- The configuration is specified by the relative positions of all the groups with respect to each other at the chirality center
- The groups are ranked in an established priority sequence and compared
- There are 2 ways to draw a chemical structure:

A. Fisher projection: + shape, where horizontal line represent atoms toward you, while vertical line represent atoms pointing away from you.

B. Dashed line bond represent atom away from you while Bold line bond represent atom toward you (of course, atoms with straight line bond represent atoms in the plane)

Sequence Rules (IUPAC)

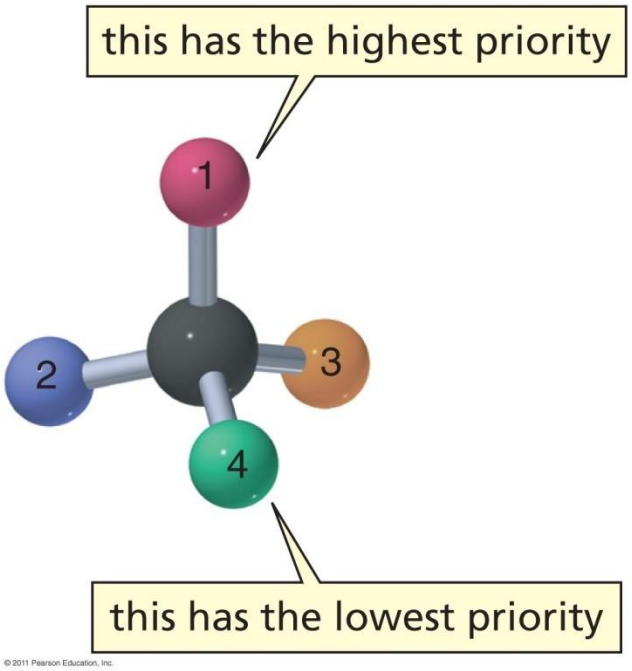
- Assign each group priority according to the Cahn-Ingold-Prelog scheme With the lowest priority group pointing away, look at remaining 3 groups in a plane
- Clockwise is designated R (from Latin for “right”)
- Counterclockwise is designated S (from Latin word for “left”)



Naming Enantiomers

The *R,S* system of nomenclature

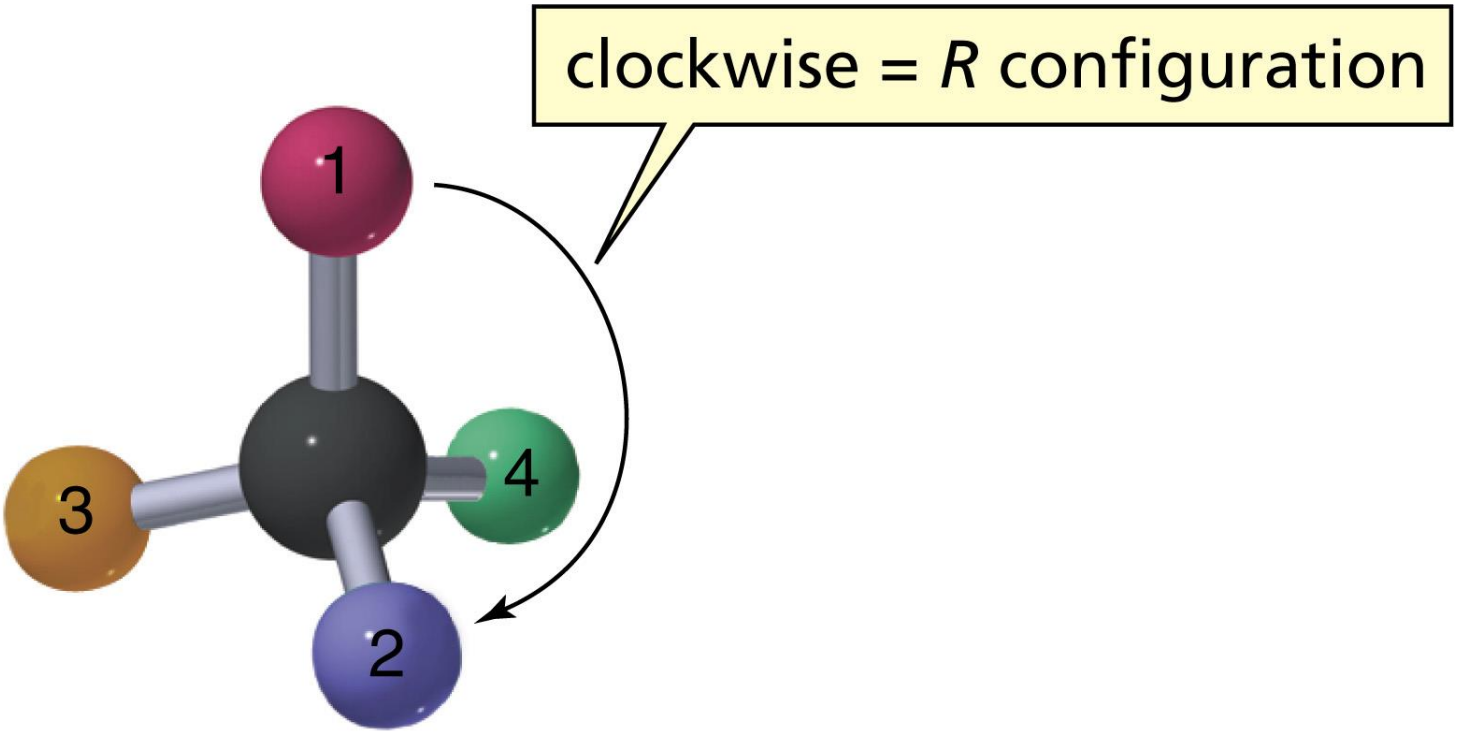
Rank the groups (atoms) bonded to the asymmetric center.



Ranking Rules:

1. **Consider the atomic number of the atoms bonded directly to the asymmetric carbon.**
2. **If there is a tie, consider the atoms attached to the tied atoms.**
3. **Multiple bonds are treated as attachment of multiple single bonds using "divide-duplicate."**
4. **Rank the priorities by mass number in isotopes.**

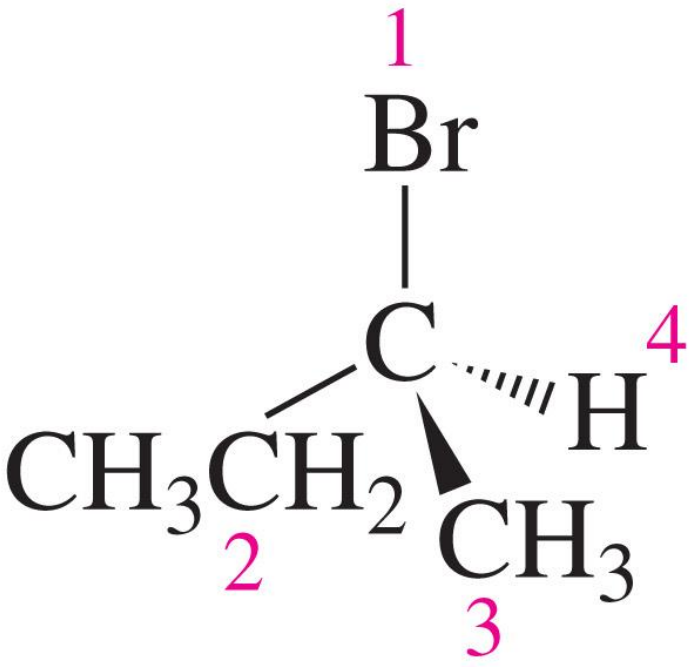
Orient the lowest priority (4) away from you

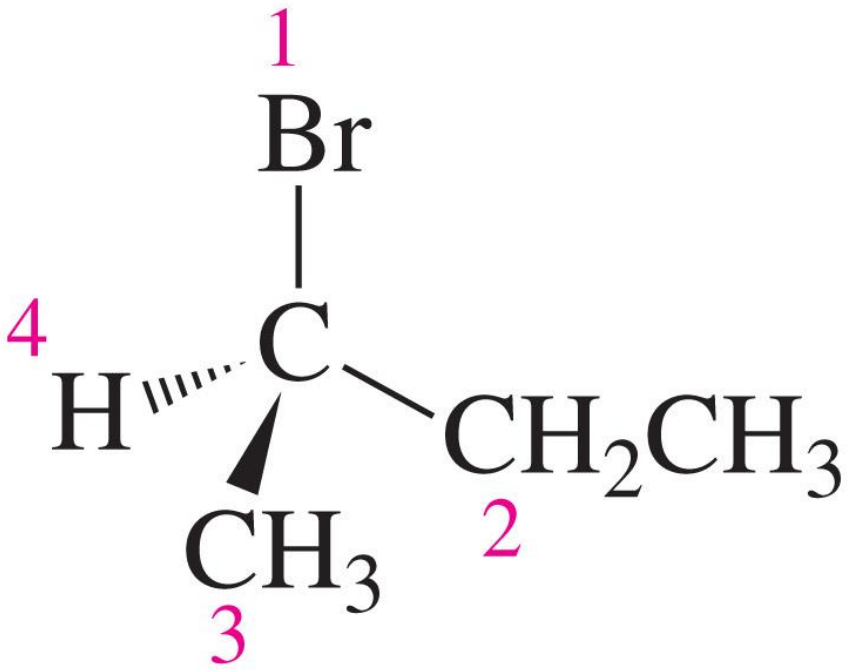


Clockwise = *R* configuration Counterclockwise = *S* configuration

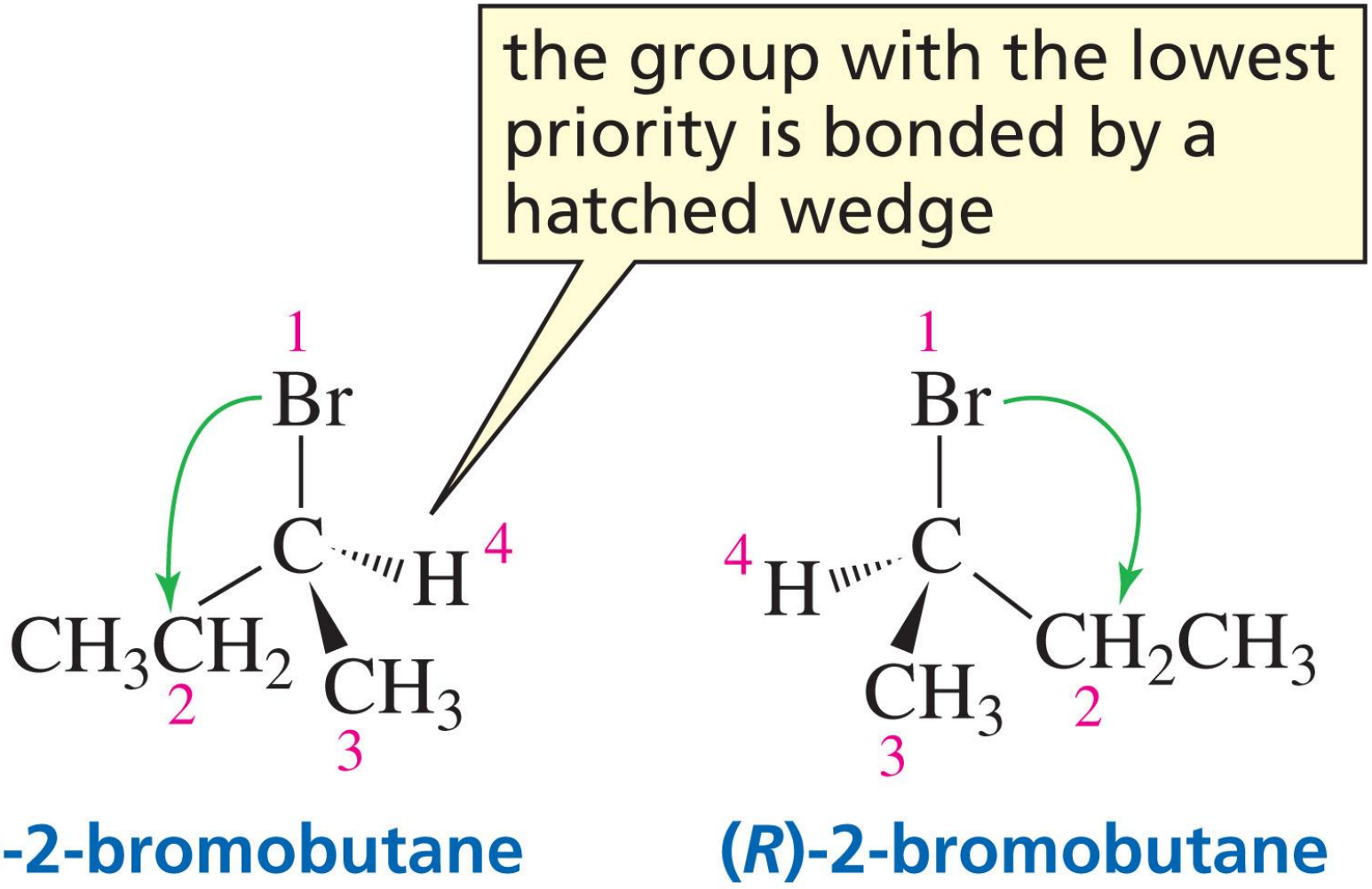
Naming from the Perspective Formula

1. Rank the groups bonded to the asymmetric center

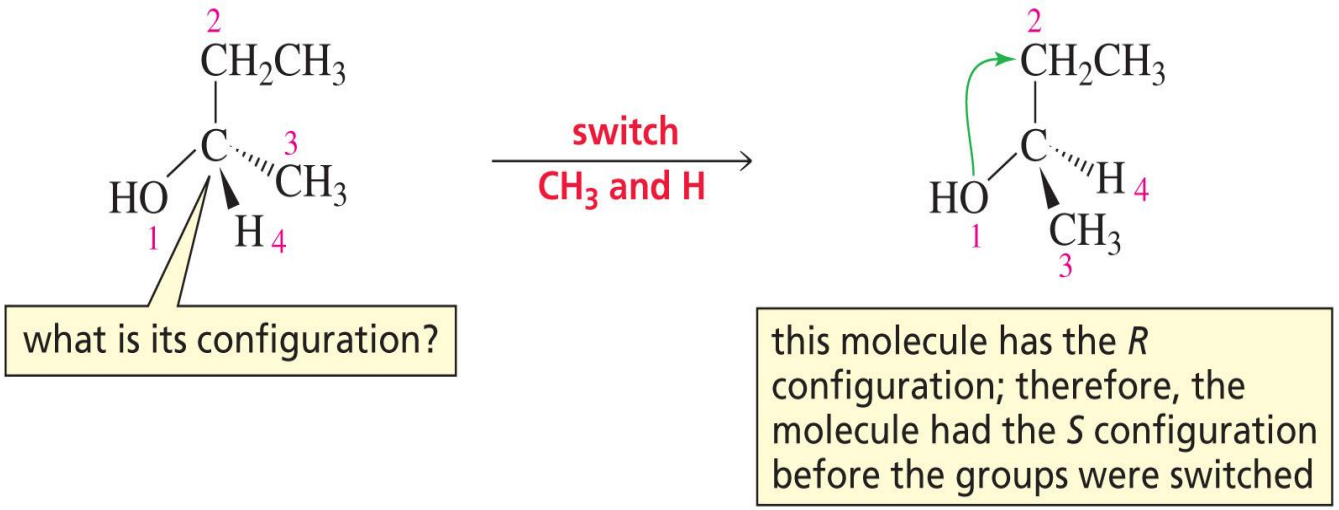




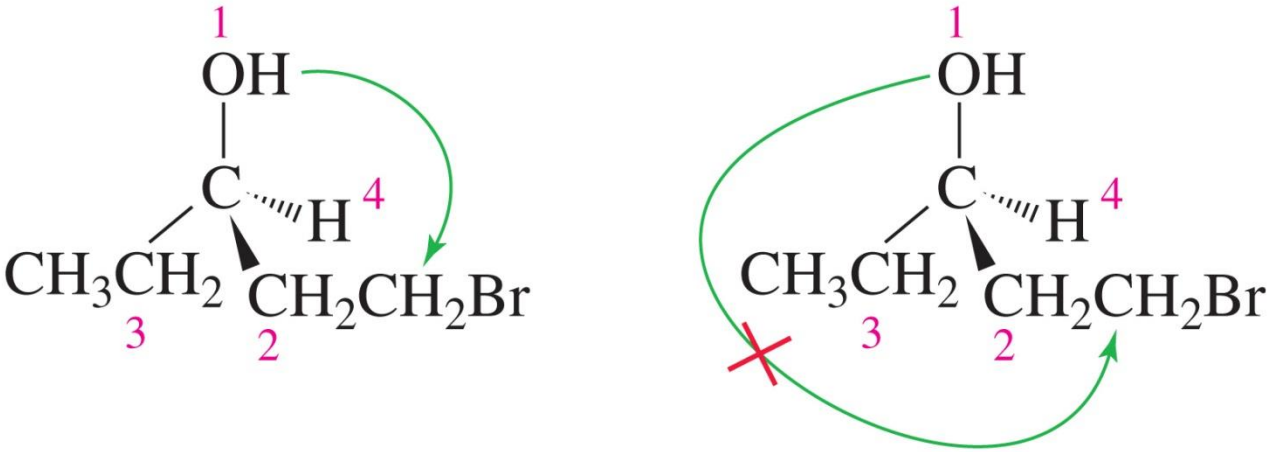
2. If the group (or atom) with the lowest priority is bonded by hatched wedge



3. If necessary, rotate the molecule so that the lowest priority group (or atom) is bonded by a hatched wedge



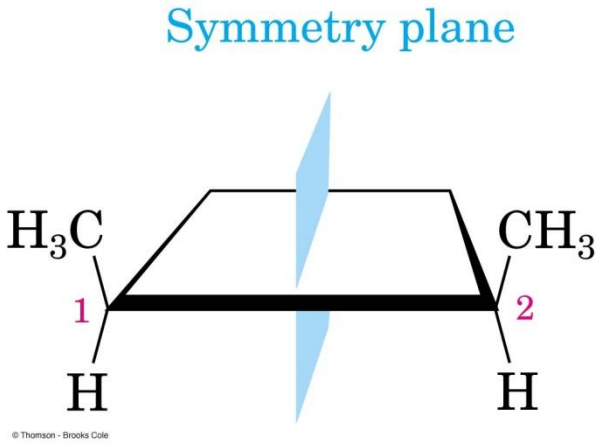
4. You can draw group 1 to group 2, passing group 4, but never group 3



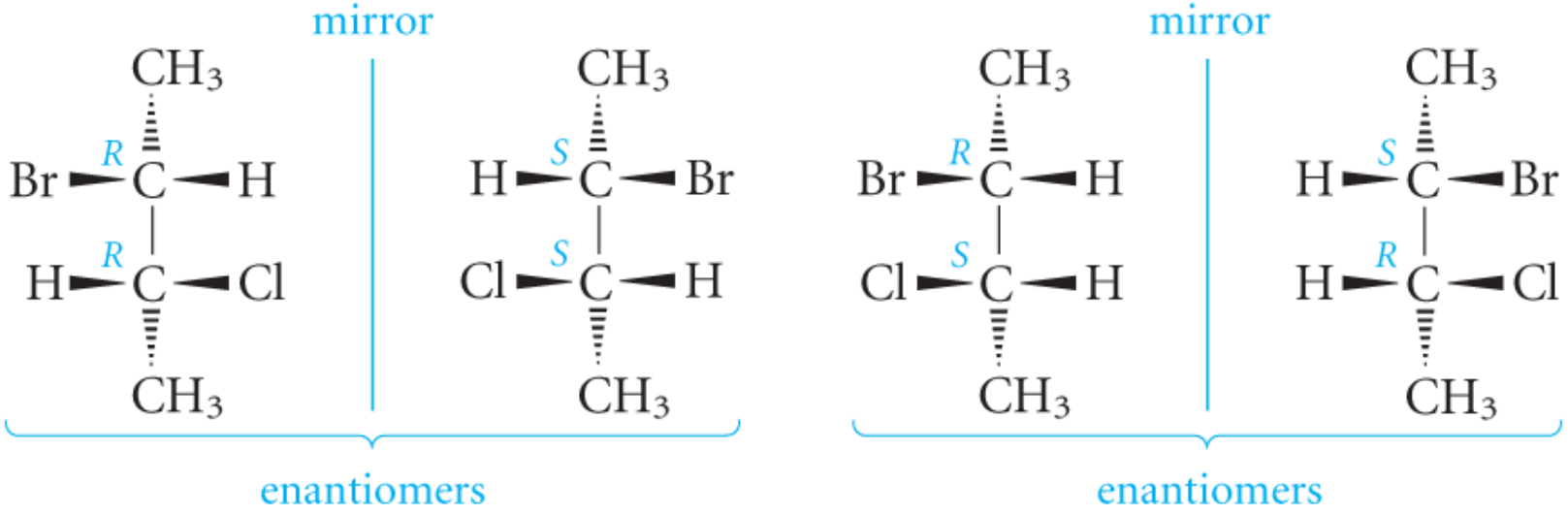
Molecules with More Than Two Chirality Centers

- Molecules can have very many chirality centers
- Each point has two possible permanent arrangements *(**R*** or ***S**)*, generating two possible stereoisomers
- So the maximum number of possible stereoisomers with n chirality centers is 2^n

- If plane of symetry exsist then the number of possible stereoisomers with n chirality centers is $2^n - 1$



Enantiomers

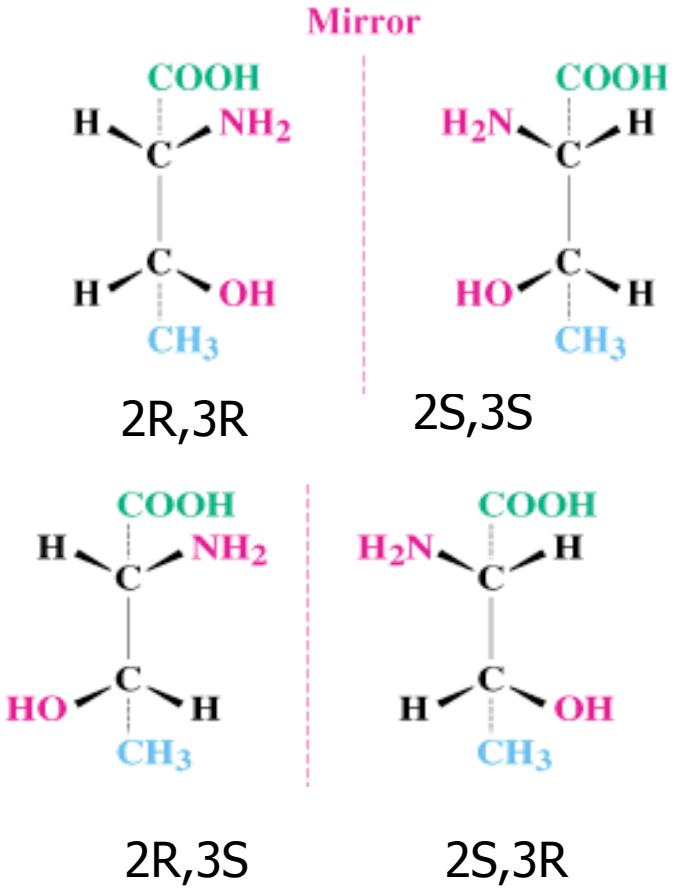


Enantiomers have identical physical and chemical properties (i.e density, solubility, melting point, boiling point) except for the direction of rotation of plane polarized light.

Diastereomers

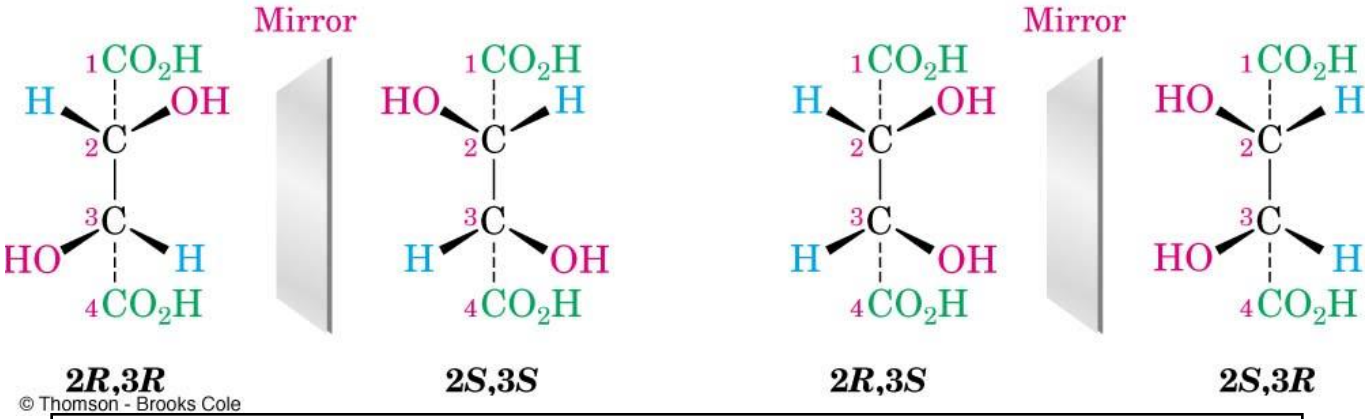
Diasteromers are completely different compounds and thus have completely different physical and chemical properties.

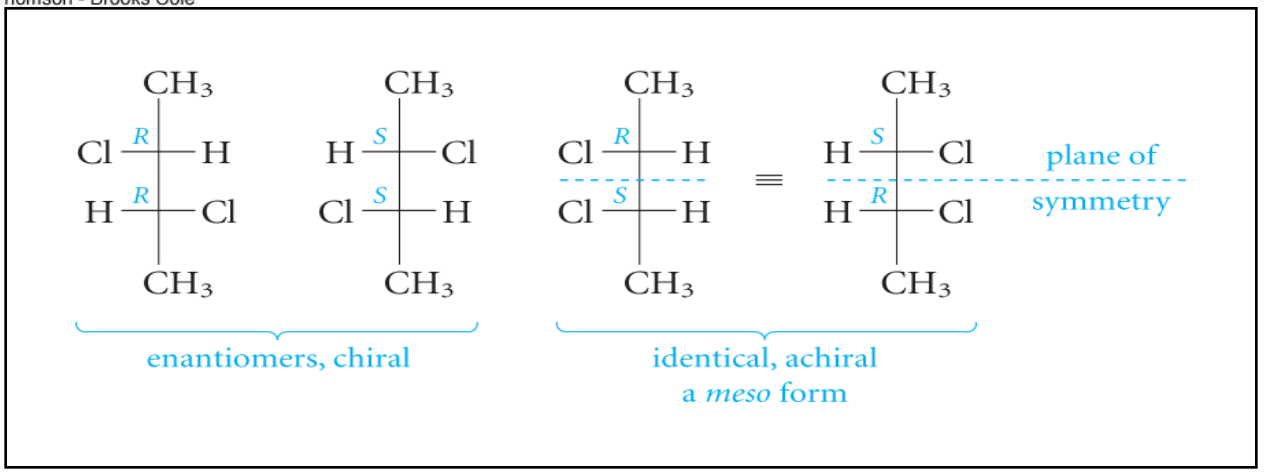
- Molecules with more than one chirality center have mirror image stereoisomers that are enantiomers
- In addition they can have stereoisomeric forms that are not mirror images, called **diastereomers**



Meso Compounds

- 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



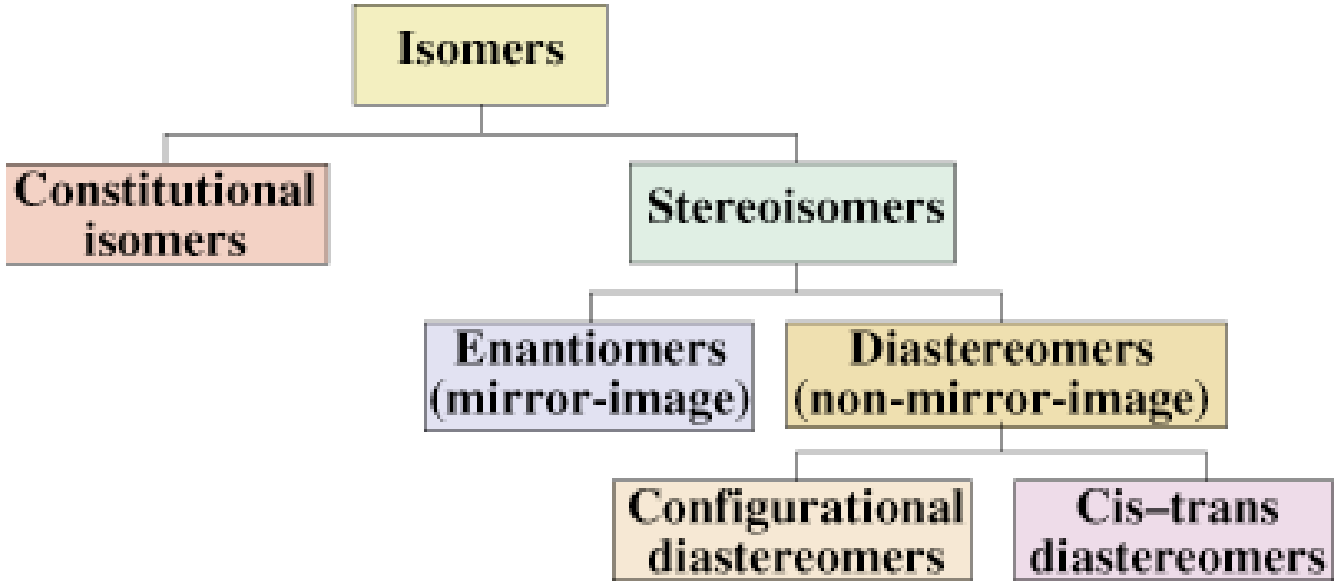


Racemic Mixtures and Their Resolution

- A 50:50 mixture of two chiral compounds that are mirror images does not rotate light – called a **racemic mixture**
- The pure compounds need to be separated or **resolved** from the mixture (called a racemate)
- This gives diastereomers that are separated by their differing solubility

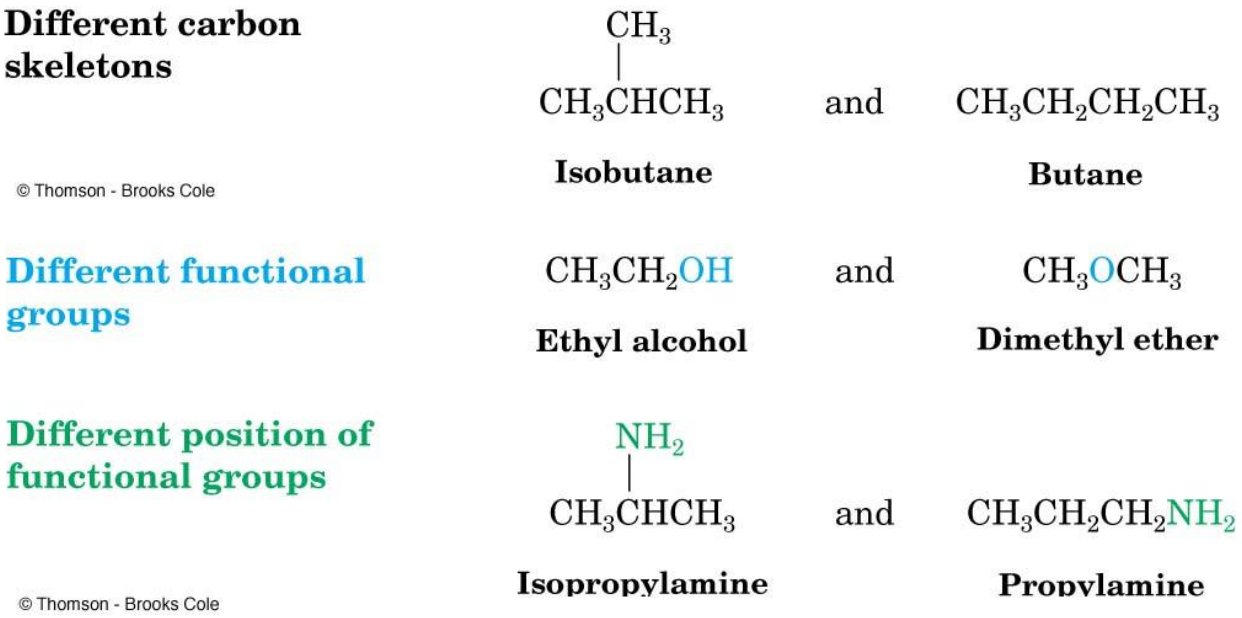
A Brief Review of Isomerism

- The flowchart summarizes the types of isomers we have seen



Constitutional Isomers

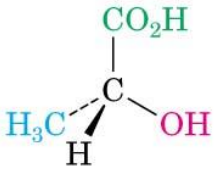
- Different order of connections gives different carbon backbone and/or different functional groups



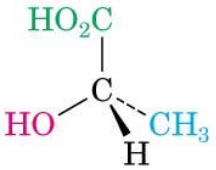
Stereoisomers

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

Enantiomers (nonsuperimposable mirror-image stereoisomers)



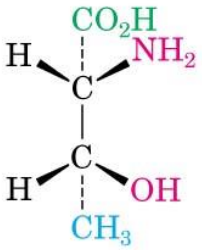
(*R*)-Lactic acid



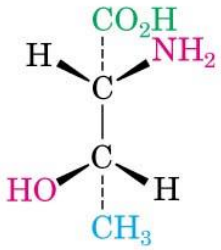
(*S*)-Lactic acid

Diastereomers (nonsuperimposable, non–mirror-image stereoisomers)

Configurational diastereomers



2*R*,3*R*-2-Amino-3-hydroxybutanoic acid



2*R*,3*S*-2-Amino-3-hydroxybutanoic acid

Practice Problems

1. Chiral molecules that have nonsuperimposable mirror images are called:

a.** enantiomers **b.**diastereomers **c.meso* compounds **d.**stereogenic

2. A 50:50 mixture of enantiomers

a. is a *meso* form. **b.**is a pair of diastereomers.

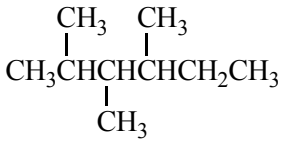
b. ***c.**is a racemic mixture. **d.**rotates plane polarized light.

3. The terms that best describe the isomeric relationship between staggered and eclipsed ethane are

a.configurational, achiral, diastereomers. **b.**conformational, chiral, enantiomers.

***c.**conformational, achiral, diastereomers. **d.**configurational, chiral, enantiomers.

4. How many stereogenic centers are present in the following molecule?



a. 1 ***b.**2 **c.**3 **d.**4

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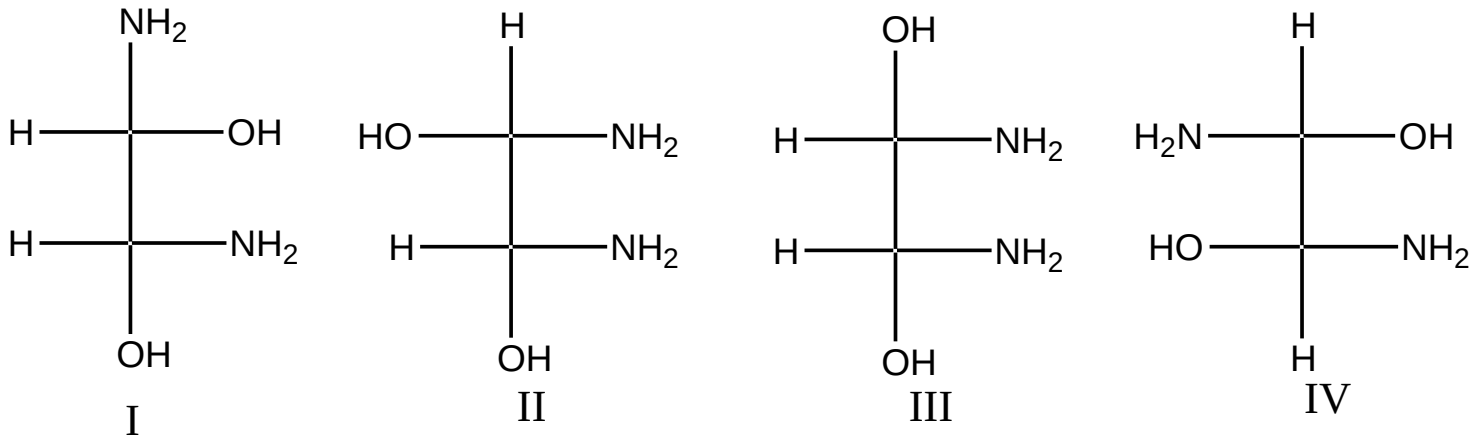
- **Looking to the following Fisher projection and answer questions 5-8**



5. The pair of enantiomer

A. I and II B. II and III C. I and IV D. III and IV

6. The pair of diasteromer

A. I and IV B. II and III C. I and II D. II and IV

7. The Meso compound is

A. I B. II C. III D. IV

8. The pair of identical

A. I and II B. I and IV C. III and IV D. II and III

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