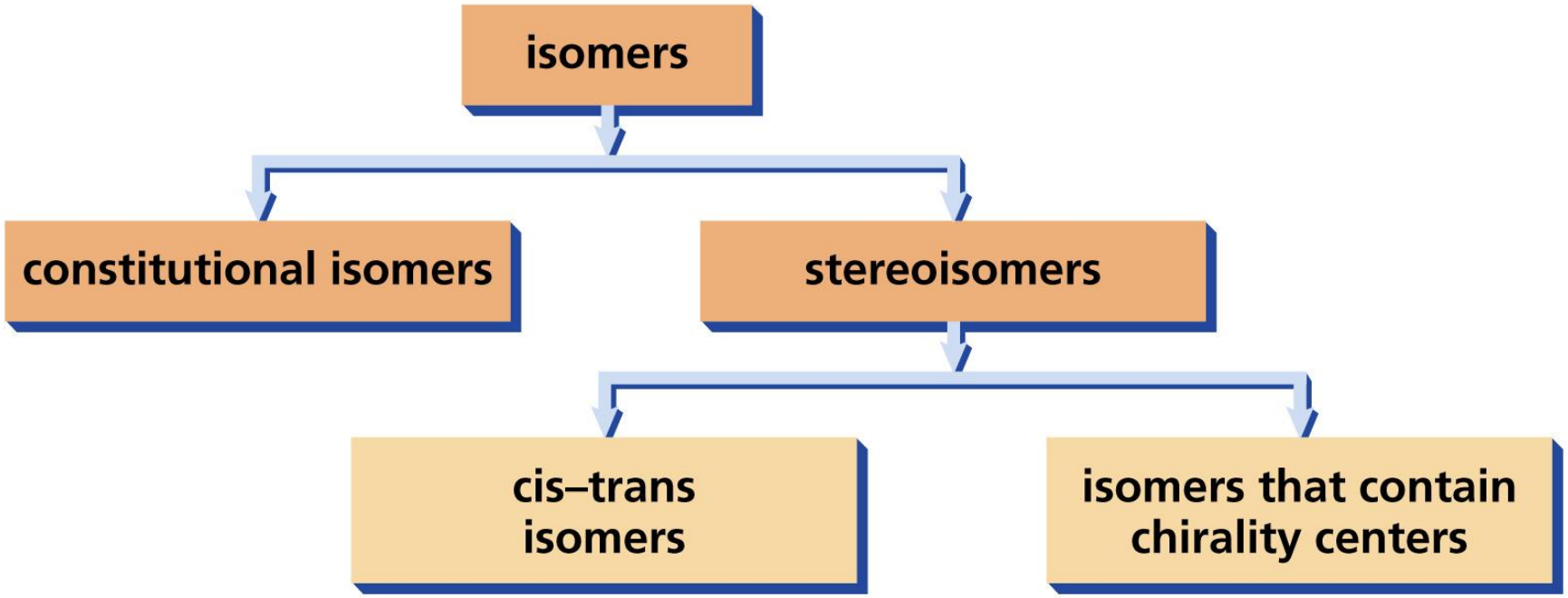
Stereochemistry

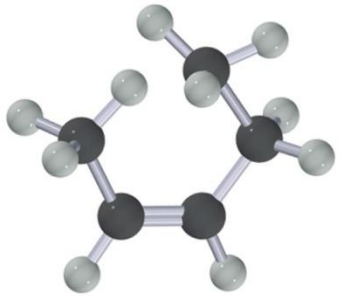
Stereochemistry refers to the 3-dimensional properties and reactions of molecules. It has its own language and terms that need to be learned in order to fully communicate and understand the concepts.

Isomers

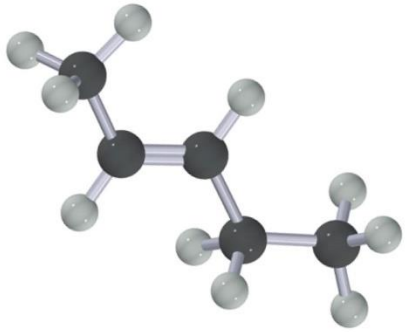
Nonidentical compounds having the same molecular formula



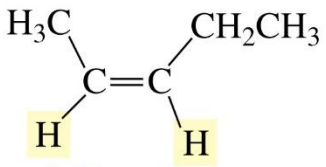
Cis-Trans Isomers



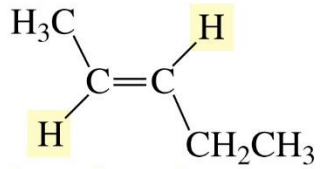
cis-2-pentene



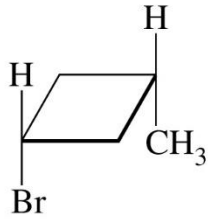
trans-2-pentene



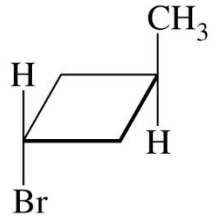
cis-2-pentene



trans-2-pentene



cis-1-bromo-3-methylcyclobutane

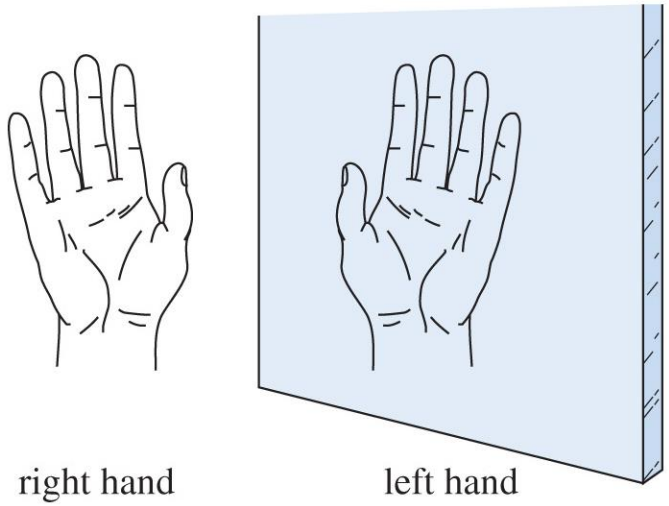


trans-1-bromo-3-methylcyclobutane

- **Stereoisomers** – compounds with the same connectivity, different arrangement in space
- **Enantiomers** – stereoisomers that are non-superimposible mirror images; only properties that differ are direction (+ or -) of optical rotation
- **Diastereomers** – stereoisomers that are not mirror images; different compounds with different physical properties

- **Asymmetric center** – sp^3 carbon with 4 different groups attached
- **Optical activity** – the ability to rotate the plane of plane –polarized light
- **Chiral compound** – a compound that is optically active (achiral compound will not rotate light)
- **Polarimeter** – device that measures the optical rotation of the chiral compound

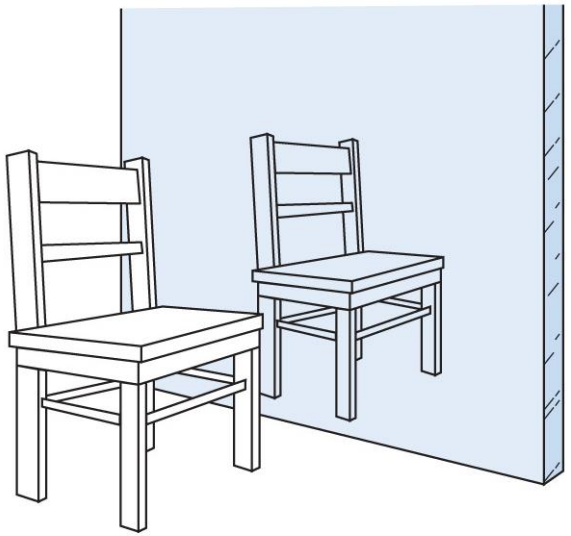
Chirality



- “Handedness”: Right-hand glove does not fit the left hand.
- An object is **chiral** if its mirror image is different from the original object.

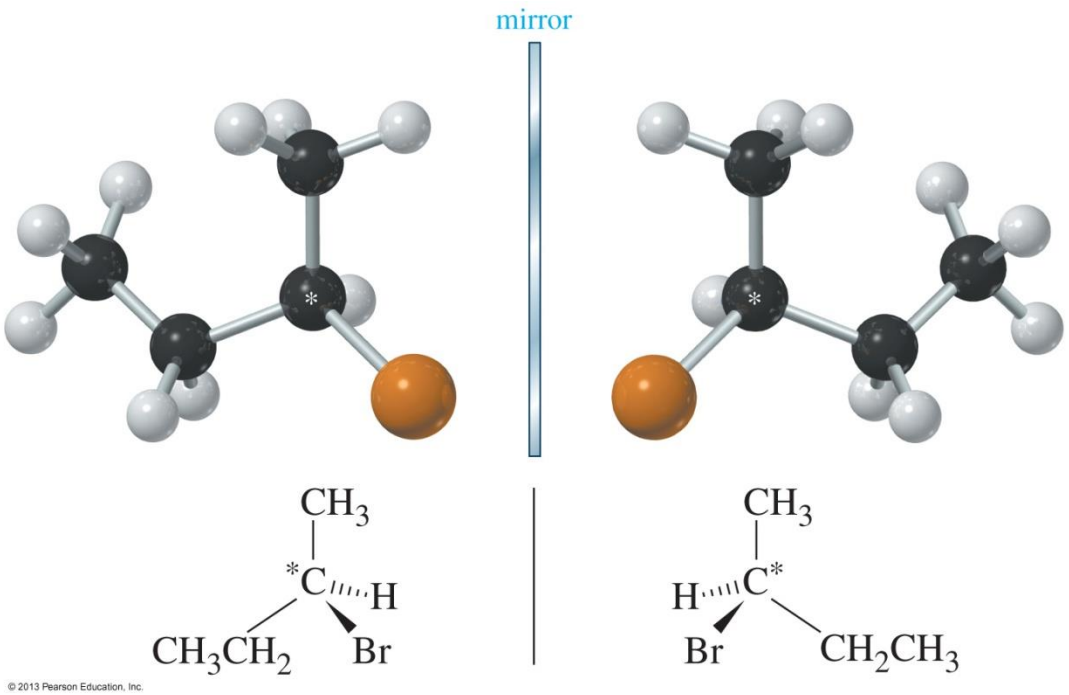
Achiral

- Mirror images that can be superposed are ***achiral*** (not chiral).



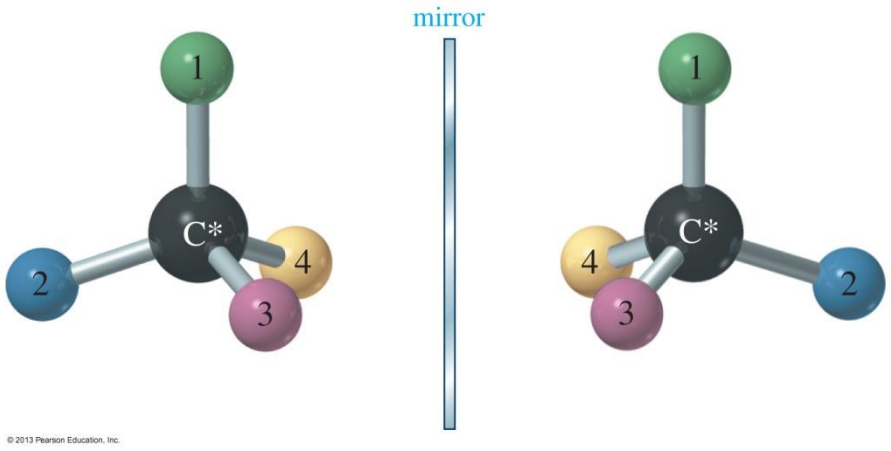
Stereoisomers

Enantiomers: Compounds that are nonsuperimposable mirror images. Any molecule that is chiral must have an enantiomer.



Chiral Carbon Atom

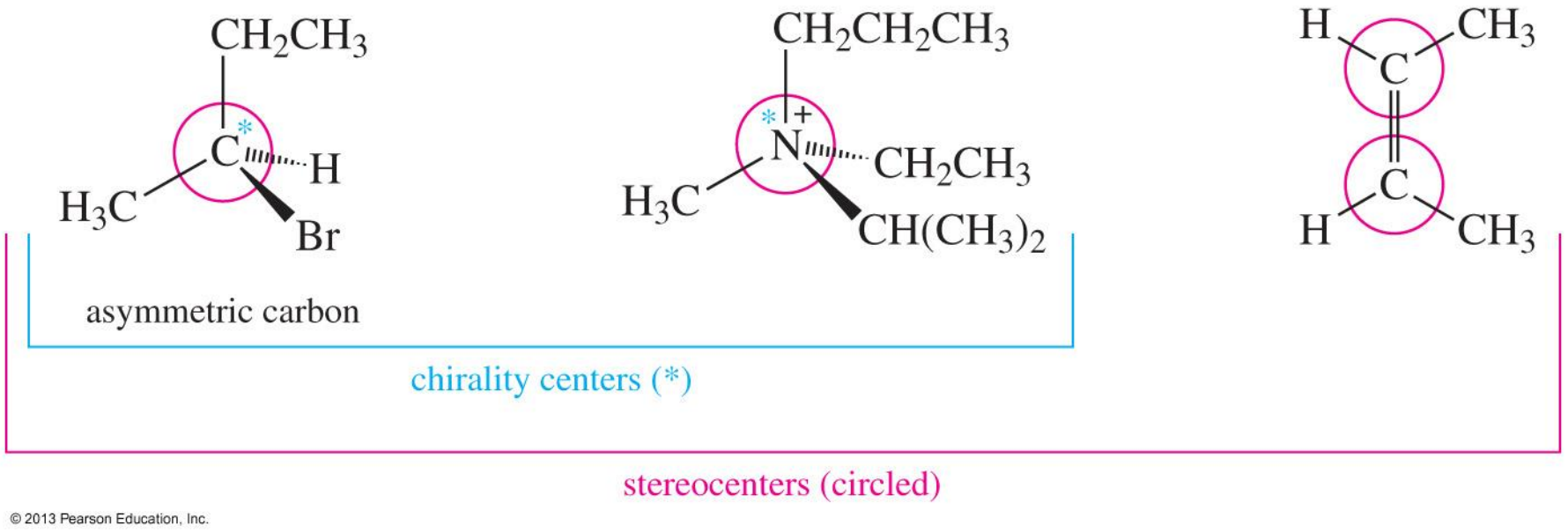
- Also called *asymmetric carbon* atom.
- Carbon atom that is bonded to four different groups is chiral.
- Its mirror image will be a different compound (enantiomer).



Stereocenters

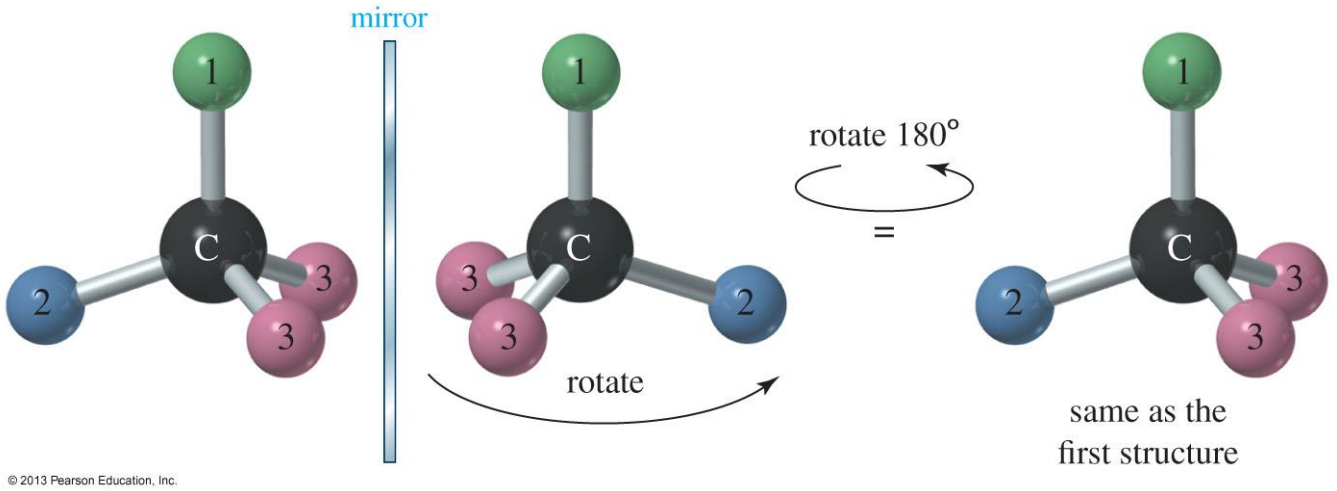
- An asymmetric carbon atom is the most common example of a **chirality center.**
- Chirality centers belong to an even broader group called *stereocenters.* A ***stereocenter*** *(*or *stereogenic atom)* is any atom *at* which the interchange of two groups gives a stereoisomer.
- Asymmetric carbons and the double-bonded carbon atoms in *cis-trans* isomers are the most common types of stereocenters.

Examples of Chirality Centers



Asymmetric carbon atoms are examples of chirality centers, which are examples of stereocenters.

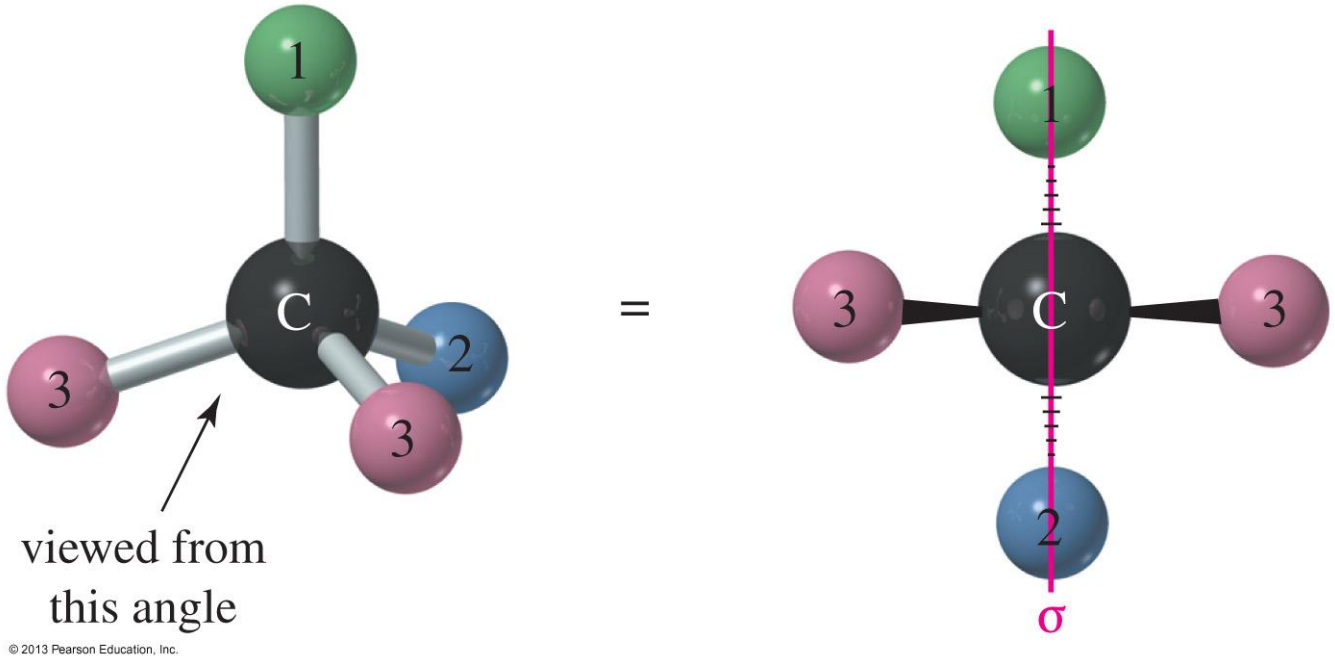
Achiral Compounds



Take this mirror image and try to superimpose it on the one to the left matching all the atoms. Everything will match.

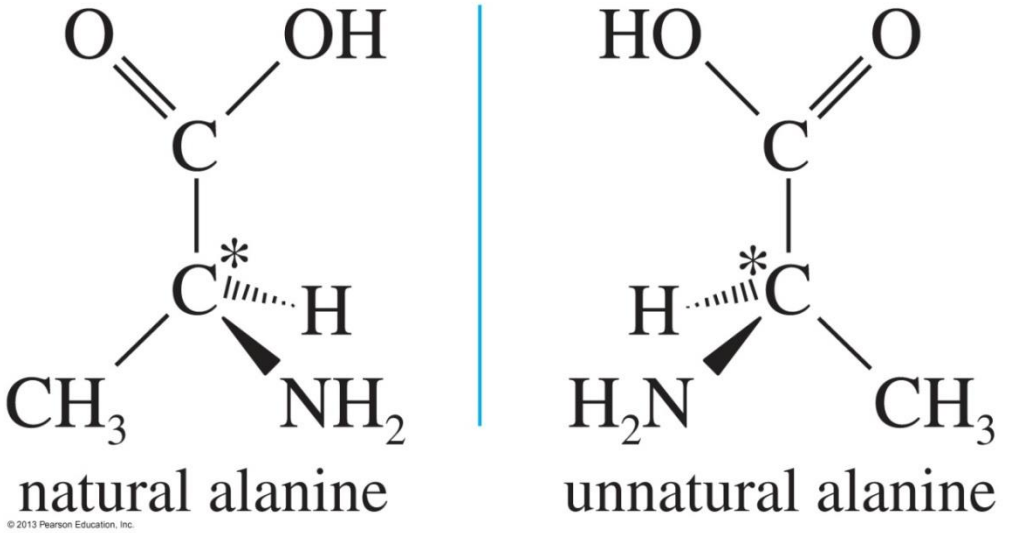
When the images can be superposed, the compound is ***achiral***.

Planes of Symmetry



- A molecule that has a plane of symmetry is ***achiral***.

(*R*) and (*S*) Configuration



natural alanine unnatural alanine

- Both enantiomers of alanine receive the same name in the IUPAC system: 2-aminopropanoic acid.
- Only one enantiomer is biologically active. In alanine only the enantiomer on the left can be metabolized by the enzyme.
- A way to distinguish between them is to use stereochemical modifiers (R) and (S).

Cahn–Ingold–Prelog Priority System

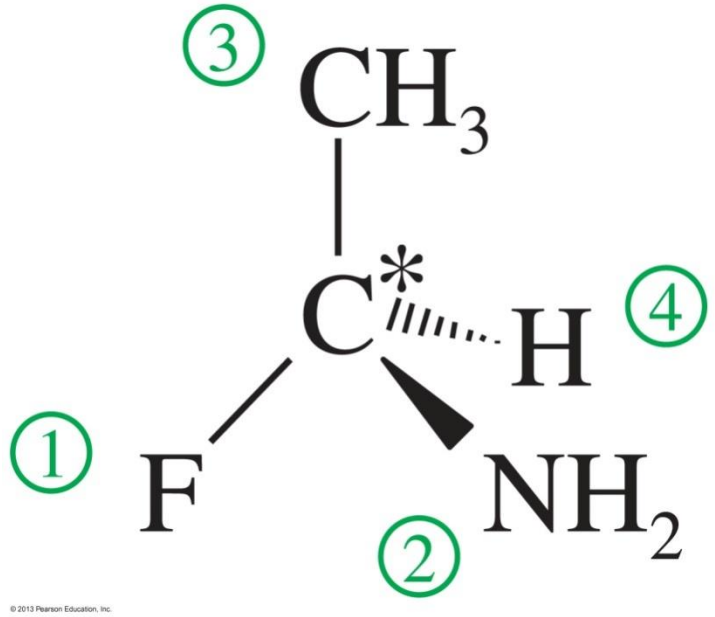
- Enantiomers have different spatial arrangements of the four groups attached to the asymmetric carbon.
- The two possible spatial arrangements are called **configurations**.
- Each asymmetric carbon atom is assigned a letter (*R*) or (*S*) based on its three-dimensional configuration.
- **Cahn–Ingold–Prelog** convention is the most widely accepted system for naming the configurations of chirality centers.

(*R*) and (*S*) Configuration: Step 1 Assign Priority

- Assign a relative “priority” to each group bonded to the asymmetric carbon. Group 1 would have the highest priority, group 2 second, etc.
- Atoms with higher atomic numbers receive higher priorities.

$I > Br > Cl > S > F > O > N > {}^{13}C > {}^{12}C > {}^{2}H > {}^{1}H$

Assign Priorities

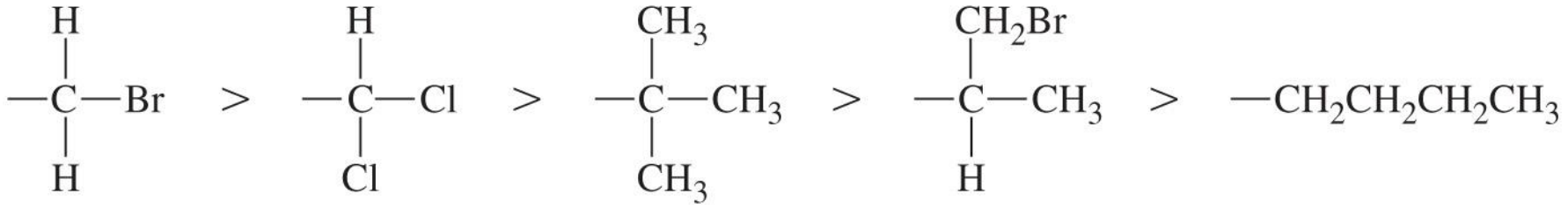


Atomic number: F > N > C > H

(R) and (S) Configuration: Breaking Ties

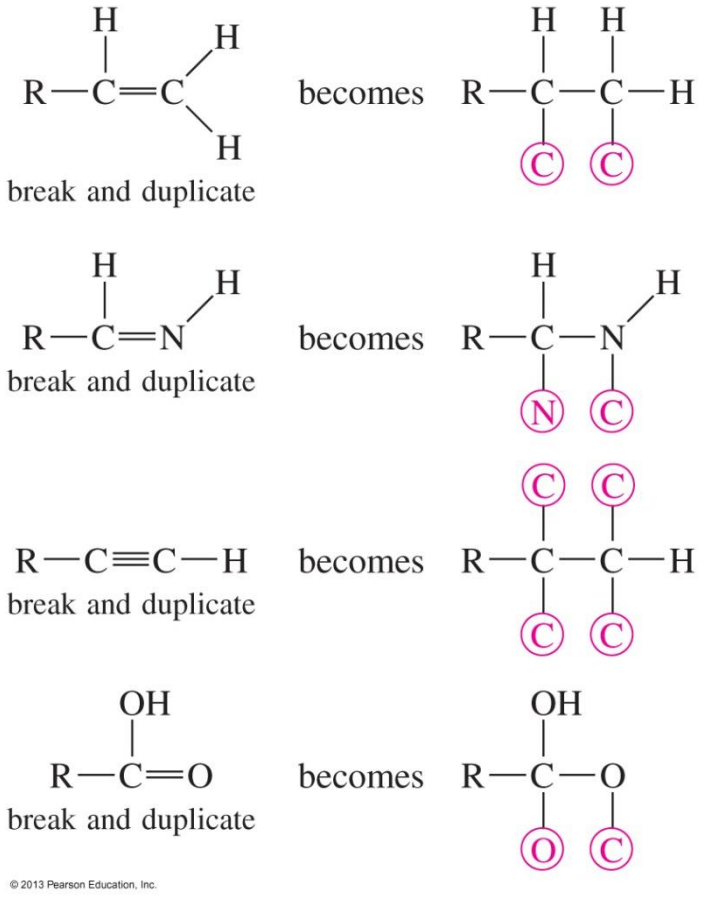
In case of ties, use the next atoms along the chain of each group as tiebreakers.

Examples



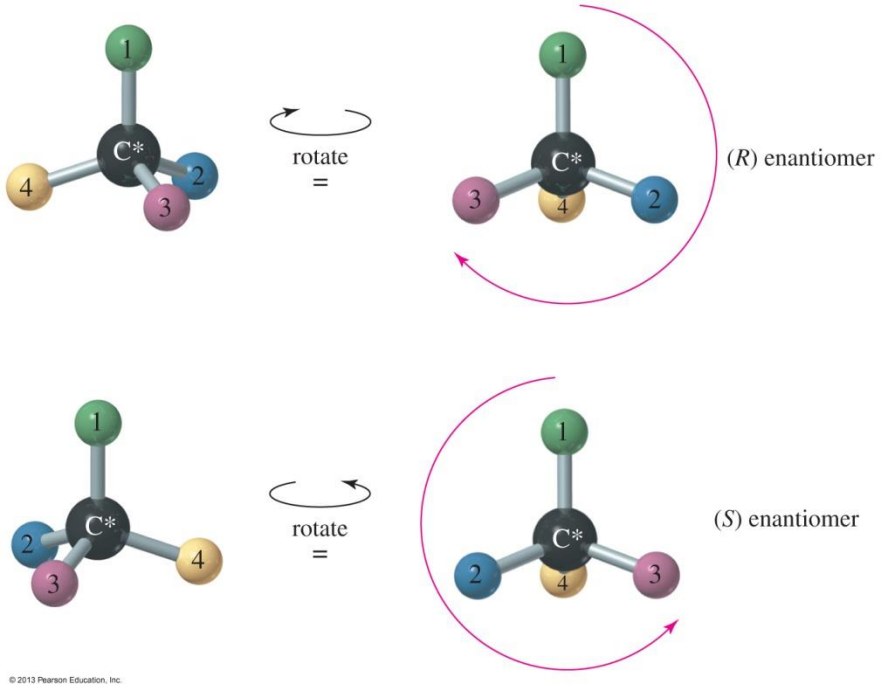
(R) and (S) Configuration: Multiple Bonds

Treat double and triple bonds as if each were a bond to a separate atom.

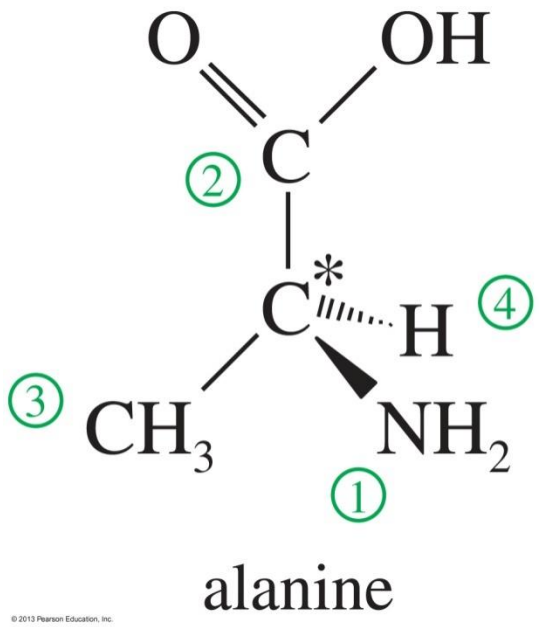


(R) and (S) Configuration: Step 2

- Working in 3-D, rotate the molecule so that the lowest priority group is in back.
- Draw an arrow from highest (1) to second highest (2) to lowest (3) priority group.
- Clockwise = (*R*), Counterclockwise = (*S*)



Assign Priorities



alanine

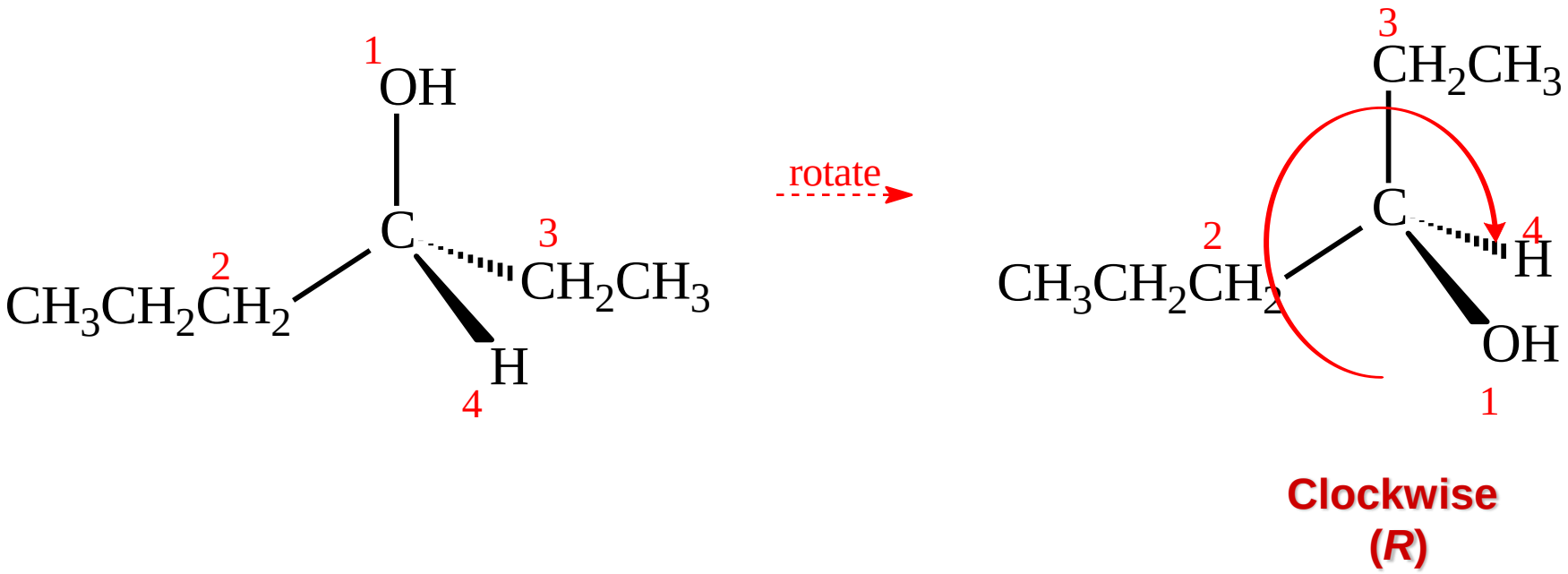
Counterclockwise

(*S*)

Draw an arrow from Group 1 to Group 2 to Group 3 and back to Group 1. Ignore Group 4.

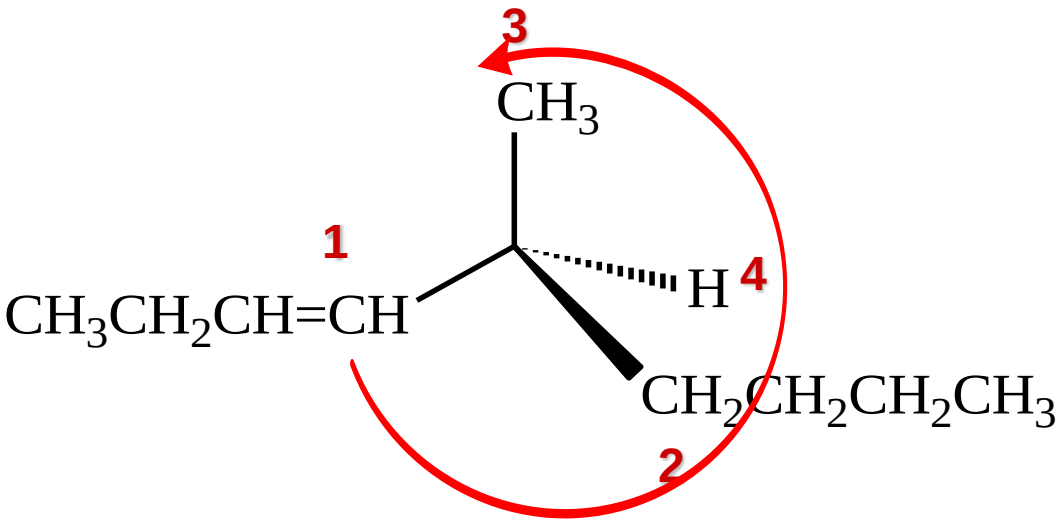
Clockwise = (*R*) and Counterclockwise = (*S*)

Example



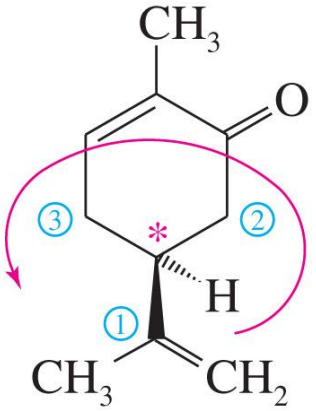
When rotating to put the lowest priority group in the back, keep one group in place and rotate the other three.

Example



Counterclockwise
(*S*)

Configuration in Cyclic Compounds



(*S*)-carvone

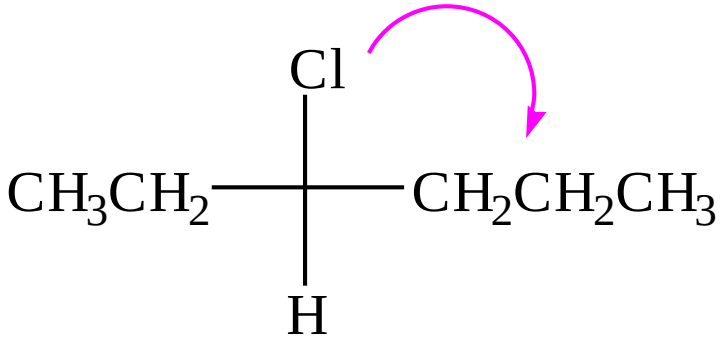
Group 1: C* — C(C)(C)(CH3) — CH2

Group 2: C* — CH2 — C(O)(C) — O — C

Group 3: C* — CH2 — C(C)(H) — C(C)(CH3) — C(=O)

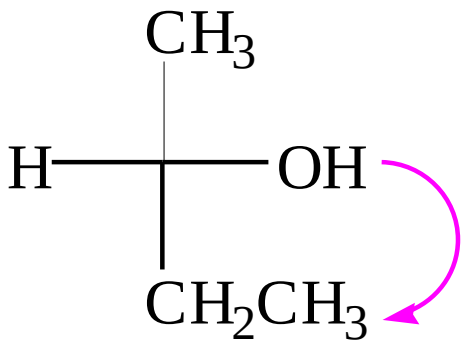
Naming from the Fischer Projection

1. Rank the groups (or atom) that are bonded to the asymmetric carbon and draw an arrow with the highest priority to the lowest priority



(*R*)-3-chlorohexane

2. If the lowest priority is on a horizontal bond, the naming is opposite to the direction of the arrow



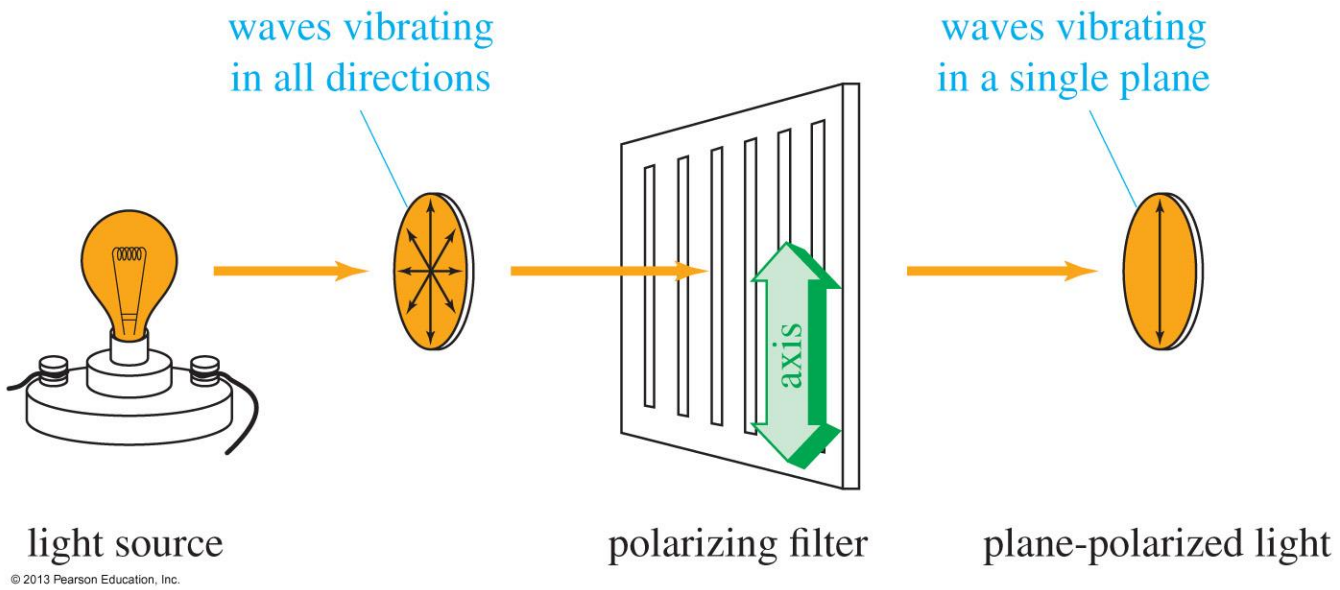
(*S*)-2-butanol

Properties of Enantiomers

- Same boiling point, melting point, and density.
- Same refractive index.
- Rotate the plane of polarized light in the same magnitude, but in opposite directions.
- Different interaction with other chiral molecules:
  - Active site of enzymes is selective for a specific enantiomer.
  - Taste buds and scent receptors are also chiral. Enantiomers may have different smells.

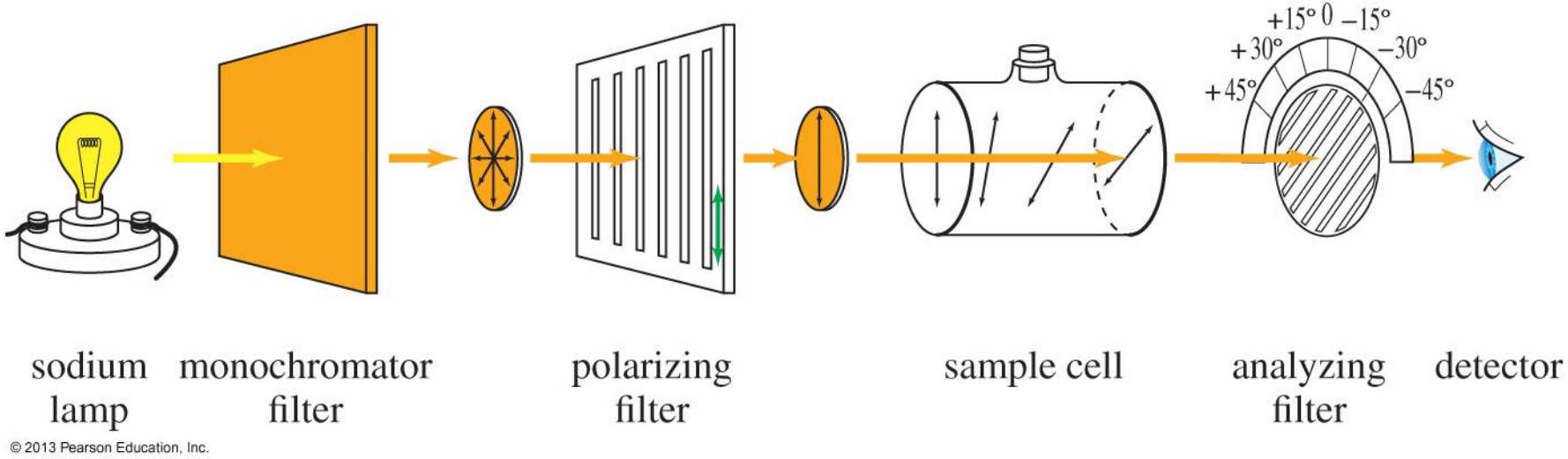
Polarized Light

Plane-polarized light is composed of waves that vibrate in only one plane.

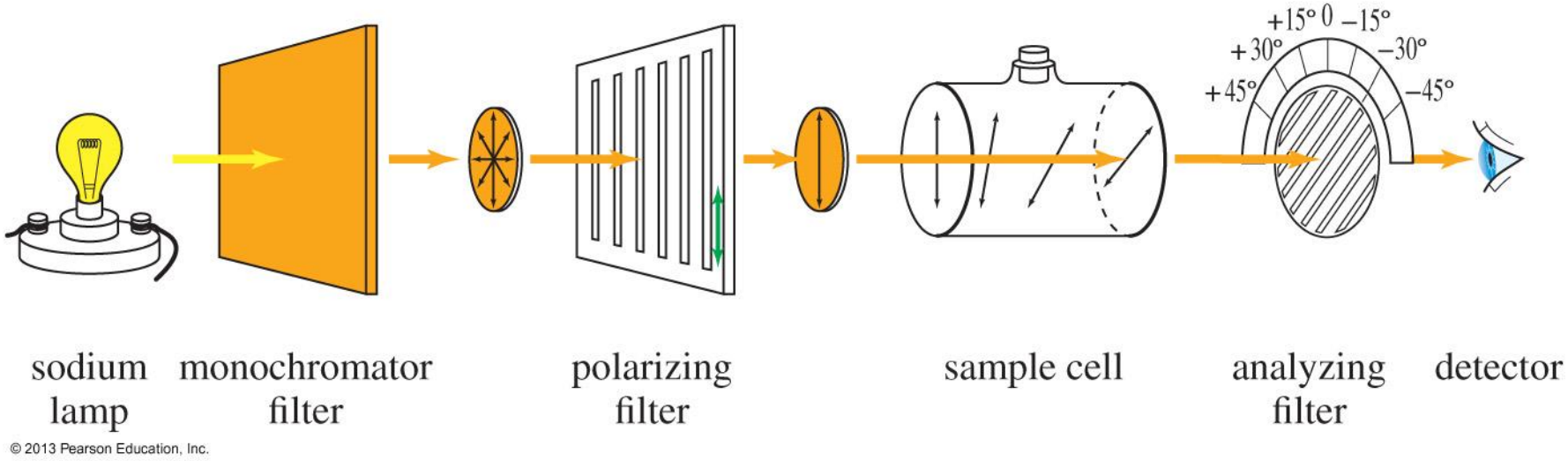


Optical Activity

- Enantiomers rotate the plane of polarized light in opposite directions, but same number of degrees.



Polarimeter



Clockwise

Dextrorotatory (+)

Counterclockwise

Levorotatory (-)

Not related to (*R*) and (*S*)

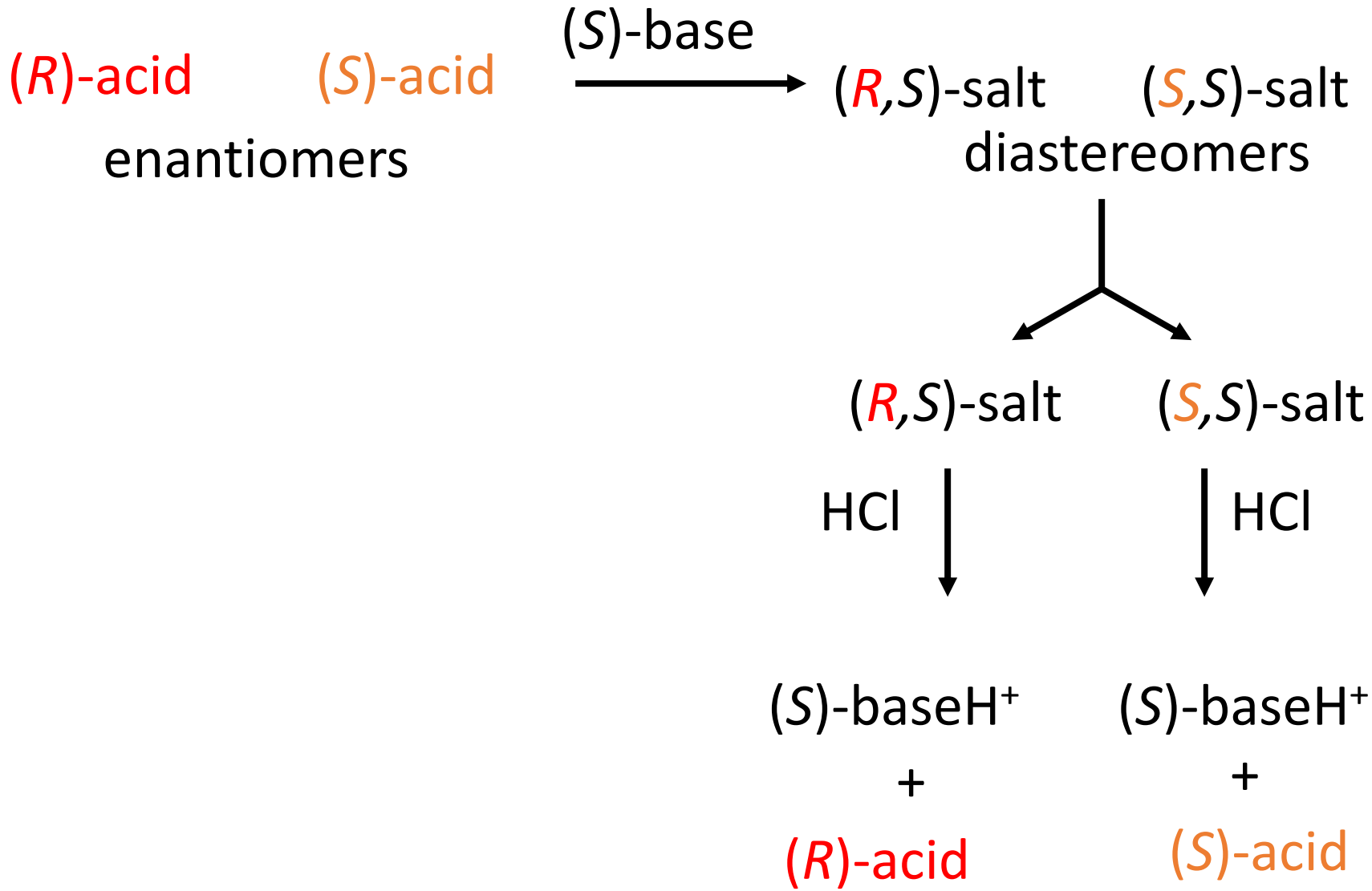
Specific Rotation

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

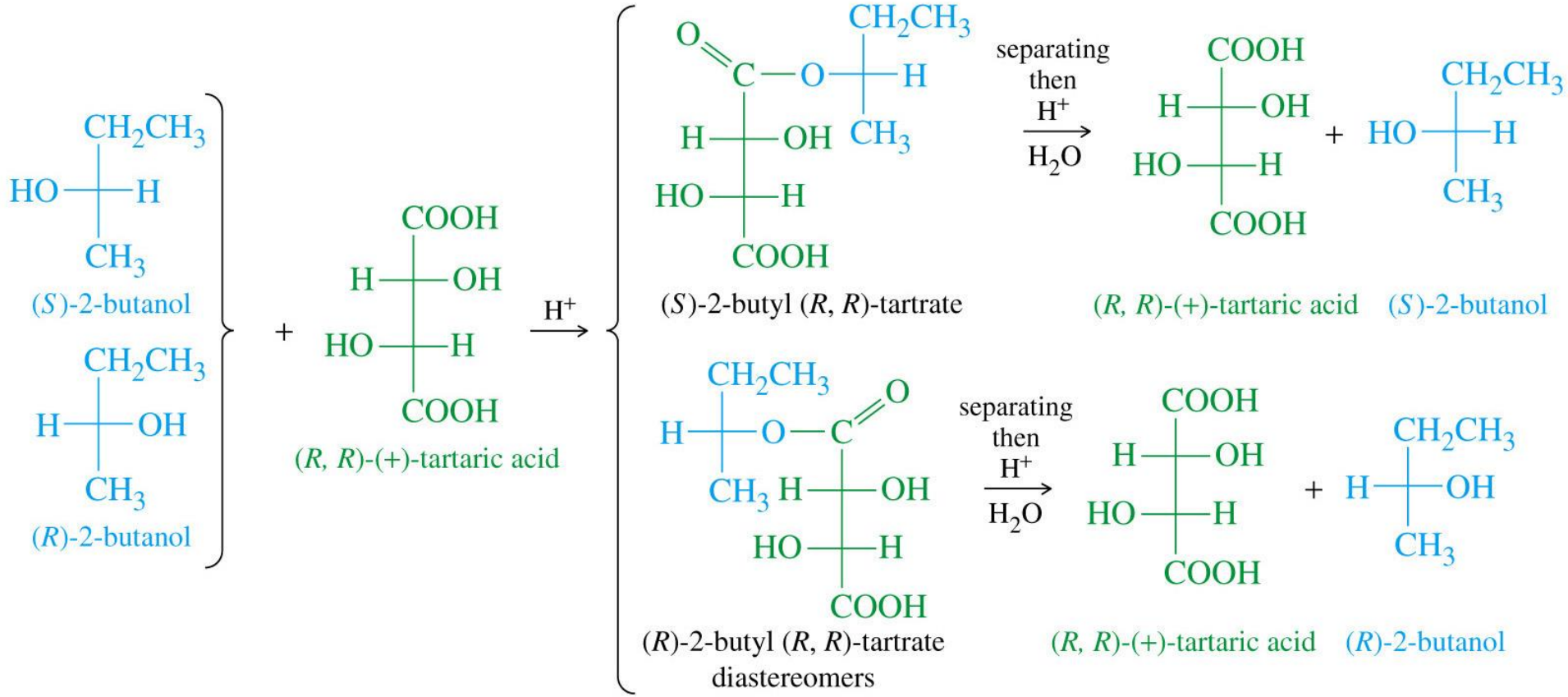
$$[\alpha] = \frac{\alpha \text{ (observed)}}{c \bullet l}$$

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.

Resolution of a Racemic Mixture



Resolution of Enantiomers

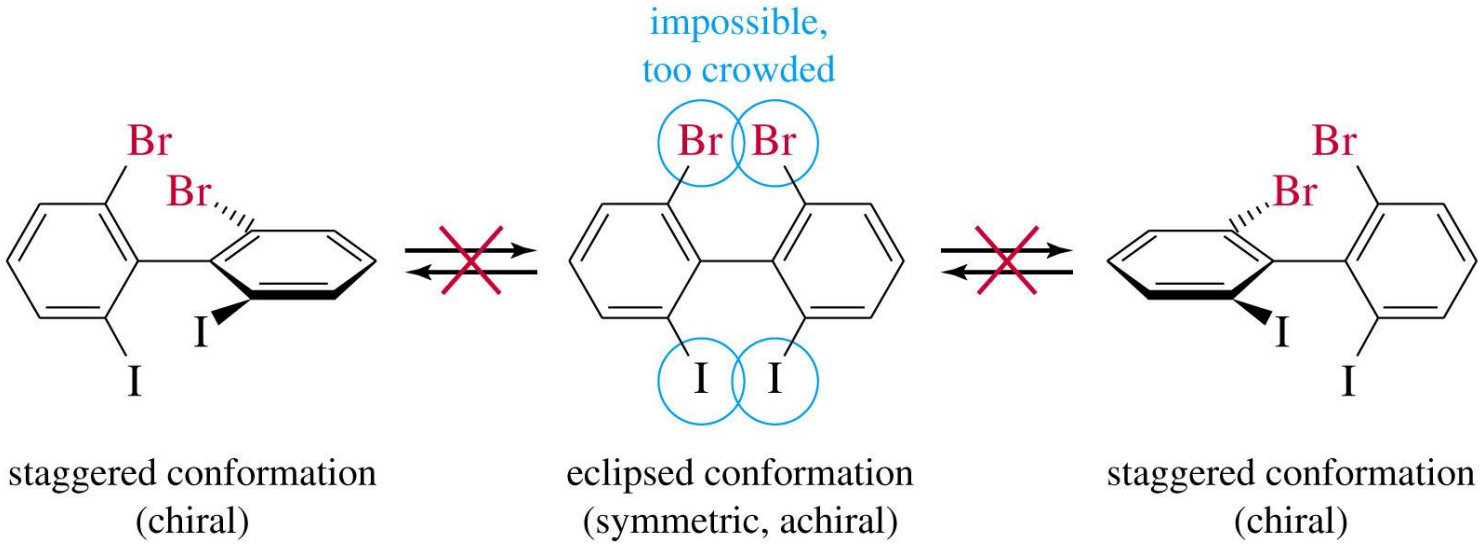


Resolution of Enantiomers

- Chromatographic resolution of enantiomers:
  - Prepare column containing stationary phase coated with a chiral compound
  - Enantiomers form diastereomeric complexes with the chiral stationary phase
  - Separate the diastereomeric complexes based on differences in affinity for stationary phase
    - strongly complexed: elutes slowly
    - weakly complexed: elutes more quickly

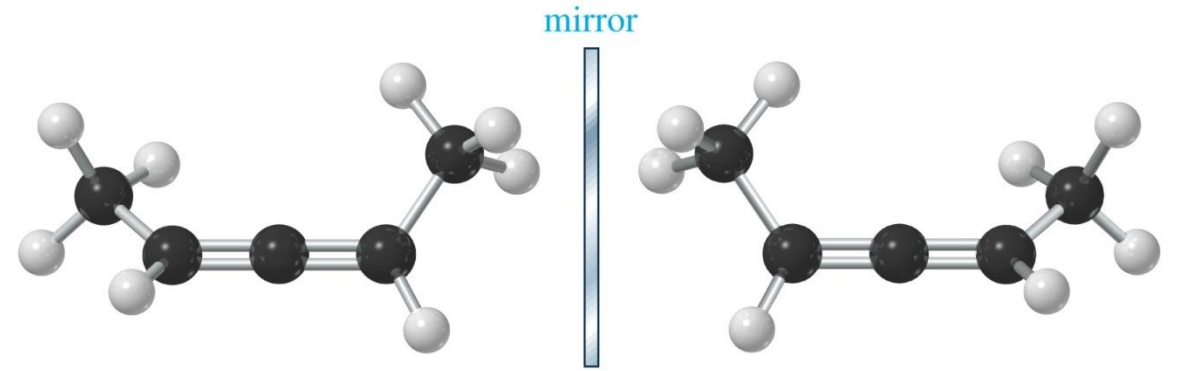
Chiral Compounds w/o Asymmetric Atoms

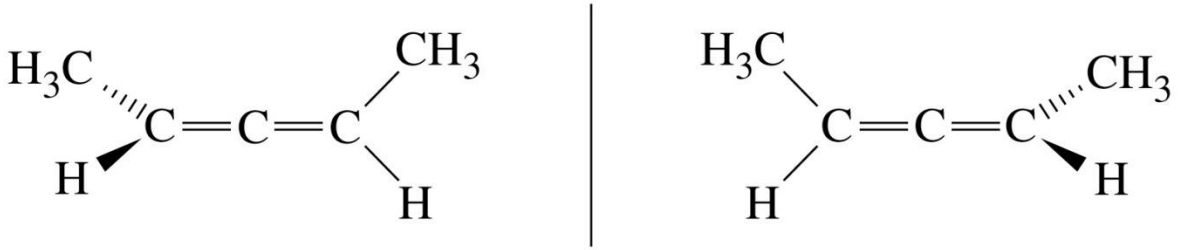
- Conformational enantiomers:
  - compounds that are so bulky or so highly strained that they cannot easily confert from one chiral conformation to the mirror-image conformation
    - "locked" into one conformation



Chiral Compounds w/o Asymmetric Atoms

- Allenes:
  - compounds containing a C=C=C unit
    - central carbon is sp hybridized
      - linear





enantiomers of 2,3-pentadiene