

Stereochemistry

Reading: Wade chapter 5, sections 5-1- 5-7

Study Problems: 5-26, 5-31, 5-32, 5-33, 5-34

Key Concepts and Skills:

- Classify molecules as chiral or achiral, and identify mirror planes of symmetry.
- Identify asymmetric carbon atoms, and name them using the R, S nomenclature.
- Calculate specific rotations from polarimetry data

Lecture Topics:

I. Stereochemistry

Stereochemistry is the study of the three dimensional structure of molecules

Recall that **constitutional isomers** differ in their bonding sequence (pentane, isopentane, and neopentane are constitutional isomers)

Stereoisomers have the same bonding sequence but differ in the spatial orientation of their atoms (example so far: cis- and trans-2-butene). Stereoisomers (like constitutional isomers) have different physical, chemical, and biological properties.

Chirality refers to the relationship between a left and a right hand; they look similar, yet a right-handed glove will not fit a left hand; the two objects are non-superimposable mirror images of each other

Objects that have left-handed and right-handed forms are called **chiral**. A **chiral** object has a non-superimposable mirror image.

Achiral objects have fully superimposable mirror images.

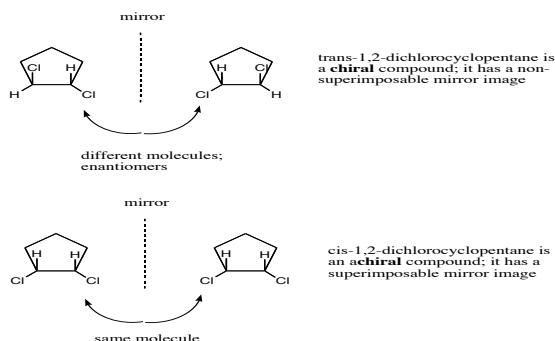
Molecules can be classified as either chiral or achiral.

A **chiral molecule** has a non-superimposable mirror image that is called its **enantiomer**.

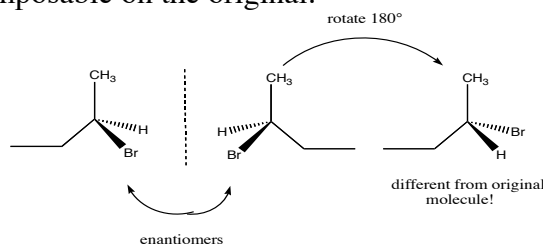
An **achiral molecule** has a mirror image that is completely identical to it and superimposable.

A **chiral compound** always has an enantiomer; and achiral compound always has a mirror image that is the same as the original molecule.

Examples:



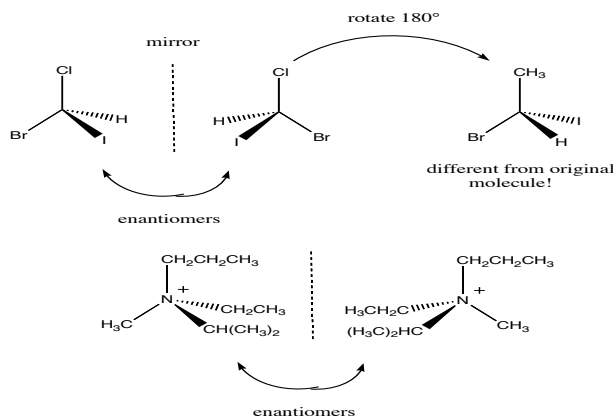
Consider 2-bromobutane: $\text{CH}_3\text{CH}_2\text{CH}(\text{Br})\text{CH}_3$; note that the mirror image of this molecule is not-superimposable on the original:



What defines chirality in this case? The most common (but not the only) feature that lends chirality to a molecule is *a carbon atom that is bonded to four different groups*. Such a carbon atom is called an **asymmetric carbon atom** or a **chiral carbon atom**.

An **asymmetric carbon atom** (a **stereocenter** or **stereogenic carbon atom**) is an atom holding a set of ligands in an arrangement that is non-superimposable on its mirror image.

Examples:



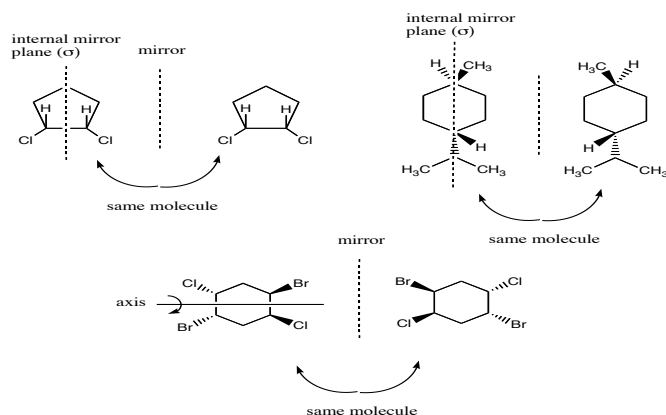
If two groups on a carbon atom are the same, the arrangement is not chiral.

General Rules

1. If a compound has no asymmetric carbon it is usually (but not always) achiral.
2. If a compound has just one asymmetric carbon atom, it is chiral
3. if a compound has more than one asymmetric carbon atom, it may or may not be chiral

II. Mirror Planes of Symmetry

1,2- cis-dichlorocyclopentane is achiral despite having two asymmetric carbon atoms. The reason for this is that any molecule with an internal mirror plane of symmetry cannot be chiral, even though it may contain chiral carbon atoms. The internal mirror plane indicates that a molecule's mirror image is the same as the original molecule. Similarly, if there is an axis in the molecule about which a 180° turn will yield the mirror image, the molecule is achiral.

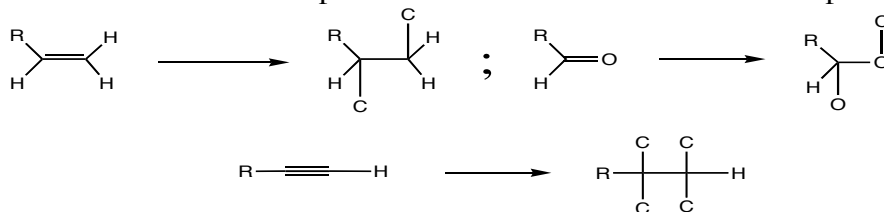


Carbon atoms with two of the same substituents have an internal mirror plane and are thus not centers of chirality (not stereocenters or chiral carbon atoms)

III. Nomenclature of Asymmetric Carbon Atoms

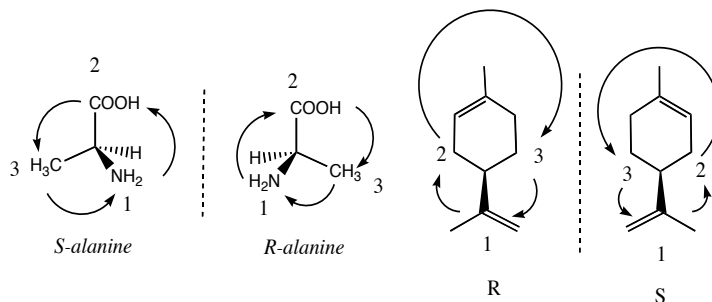
Cahn-Ingold-Prelog rules for assigning the configuration of chirality centers: each asymmetric center is assigned either *R* or *S* configuration.

1. Assign priorities to the four substituents about the carbon atom
 - a. atoms with higher atomic numbers receive higher priority:
 $I > Br > Cl > S > F > O > N > ^{13}C > ^{12}C > Li > ^3H > ^2H > ^1H$
 - b. In the case of two substituents with equal priority, use the next atoms along the chain to assign priority; one high priority atom takes priority over any number of lower priority atoms:
 $CH_2Br > CHCl_2 > C(CH_3)_3 > CH(CH_3)(CH_2Br)$
 - c. Treat double and triple bonds as if each were a bond to a separate atom:



2. Put the fourth (lowest) priority group in back and view the molecule along the bond from the asymmetric carbon atom to the low priority group. Draw an arrow from the first through the second to the third group. If the arrow is pointing clockwise, the asymmetric carbon atom is called “*R*”; if the arrow is pointing counterclockwise, the asymmetric carbon atom is called “*S*”

Examples:



IV. How to Distinguish Enantiomers

Since the physical properties of enantiomers are almost identical, we can use their optical properties to distinguish them: light interacts with chiral molecules in different ways

- Plane polarized light can be rotated in opposite directions by enantiomers.
 - When plane-polarized light passes through a solution containing a chiral compound, the chiral compound causes the plane of vibration to rotate, and the compound is said to be **optically active**.
 - Enantiomeric compounds rotate the plane of polarized light by exactly the same amount, but in opposite directions.* If pure (R) rotates light 30° clockwise, pure (S) will rotate light 30° counterclockwise; if pure (R) rotates light 5° counterclockwise, pure (S) will rotate light 5° clockwise.
- Note:* we cannot predict the direction in which a particular enantiomer will rotate the plane of polarized light!

- A **Polarimeter** measures the rotation of plane-polarized light by a solution. The wavelength of light commonly used is that of the yellow sodium D line (chiral compounds rotate different wavelengths of light to different extents, so it is best to work with a single common wavelength for all measurements)

- Compounds that rotate plane polarized light toward the right (clockwise) are called dextrorotatory (d), and the direction of rotation is signified by a (+) sign: *example-* (+)-2-butanol or (d)-2-butanol

- Compounds that rotate plane polarized light toward the left (counterclockwise) are called levorotatory (l), and the direction of rotation is signified by a (-) sign: *example-* (-)-2-butanol or (l)-2-butanol

- We define a compound's specific rotation $[\alpha]$ as the rotation found using a 10 cm (1 dm) sample cell and a concentration of 1 g/ml:

$$[\alpha]_D^{25} = \alpha(\text{observed})/c \cdot l$$

Where $\alpha(\text{observed})$ = rotation observed in the polarimeter

c=concentration in g/mL

l=pathlength in dm

For $[\alpha]_D^{25}$, the superscript denotes the temperature, the D subscript denotes the wavelength: the sodium D line.

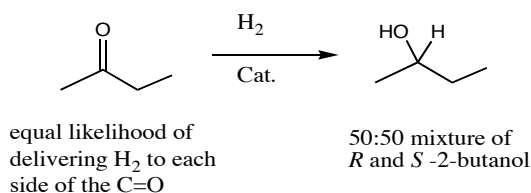
- Note: the (+) or (-) designation is the laboratory measured direction of rotation of light and has nothing to do with the configurations R and S.*

V. Racemic Mixtures

•A **racemic mixture** or **racemate** is a solution of equal amounts of two enantiomers, so that the mixture is optically inactive. E.g., a 50:50 mixture of (+)-2-butanol (+13.5°) and (-)-2-butanol (-13.5°) has a rotation of 0°.

This mixture is referred to as a (±) pair or a (d,l) pair: (±)-2-butanol is a racemic mixture of *R*- and *S*-2-butanol.

•Many chemical reactions lead to racemic mixtures → **When an achiral molecule is converted into a chiral molecule, a reaction that uses optically inactive reactants and reagents/catalysts cannot produce a product that is optically active.**



•In dealing with mixtures that are neither optically pure nor racemic, we can specify the **optical purity** (o.p.) of the system:

$$\text{o.p.} = (\text{observed rotation/rotation of pure enantiomer}) \times 100\%$$

•The **enantiomeric excess (e.e.)** (which equals the optical purity for pure compounds) can be calculated from the excess of the predominant enantiomer as a percentage of the entire mixture:

$$\text{e.e.} = (d-l/d+l) \times 100\% = (\text{excess of major over minor/entire mixture}) \times 100\%$$

Suppose you have a mixture of 6 g of (+)-2-butanol and 4 g of (-)-2-butanol. Calculate the e.e. and the expected observed rotation of the racemate.

$$6\text{g}-4\text{g}/6\text{g}+4\text{g} = 0.2 \times 100\% = 20\% \text{ ee}$$

Which means you have 80% racemic, 20% pure material.

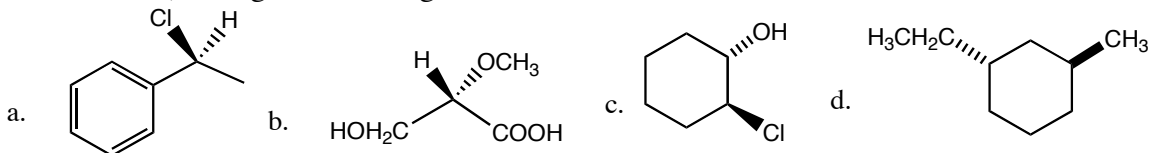
$$\text{Since o.p.} = \text{e.e.} = (\text{observed rotation/rotation of pure enantiomer}) \times 100\%$$

$$(\text{e.e.}/100\%)(\text{rotation of pure enantiomer}) = \text{observed rotation of racemate}$$

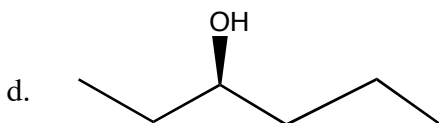
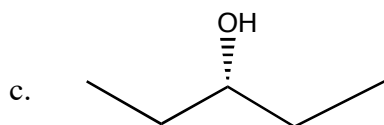
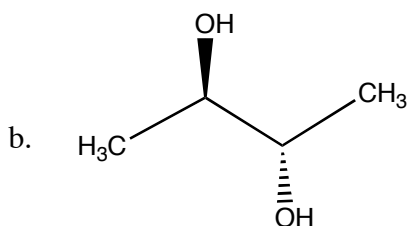
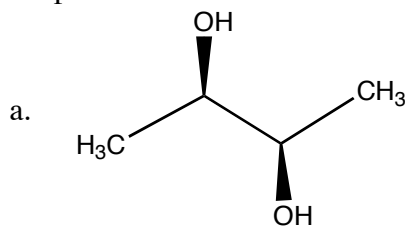
$$(0.2)(+13.5) = +2.7^\circ$$

Additional Problems for practice:

1.) Assign R, S configurations to each chiral center in these molecules:



2.) Draw the mirror image of each of the following compounds, and state whether the mirror image is an enantiomer or is another view of the same compound



3. Identify all the chiral centers in the following molecules:

