CHAPTER 05: STEREOCHEMISTRY

I. Chirality and Stereocenters

We have already seen constitutional (different connectivity) and geometric (cis/trans) isomers.

In this chapter we will look at:

- **Stereoisomers** are molecules that have the same bonding sequence, but they differ in orientation in space.
  - Stereoisomers can often have drastically different physical, chemical, and biological properties:

**Chirality (Handedness)**

- Your right and left hands are mirror images that are not superimposable are known as enantiomers.

- **Enantiomers** are non-superimposable mirror images.
  - A molecule can only have one enantiomer (enantiomers exist as pairs, like right and left hands).

- Chiral objects are not superimposable on their mirror images.

- Achiral objects are superimposable on their mirror images.
There are two ways to determine if a molecule is chiral.

1. Ultimate test → Test to see if mirror images are superimposable.
   Example 1: Are these molecules stereoisomers?

Example 2: Are these molecules stereoisomers?

2. Quick Test → Look for a mirror plane of symmetry (aka mirror plane). This is a plane that divides an object into two equal halves that are mirror images.

**CASE #1**

**CASE #2**

   Scenario A:

   Scenario B:

**Summary:**
II. R/S Nomenclature for Configurations of Stereocenters (Cahn-Ingold-Prelog System)

A. Assigning Group Priorities for R/S Nomenclature Rules

1. Assign Priority to each group attached to the asymmetric carbon. (1 = high, 4 = low)
   a. Atoms with higher atomic numbers receive higher priorities.
      
      I > Br > Cl > S > F > O > N > $^{13}$C > $^{12}$C > Li > etc...
      53 > 35 > 17 > 16 > 9 > 8 > 7 > 13 > 12 > 3 > etc...
      ($^{13}$C is larger than $^{12}$C)

2. In case of ties, go to the 2$^{nd}$ atom and then the 3$^{rd}$ etc..until the first difference is found.

3. Treat double and triple bonds as if each were a bond to a separate atom. (listed in order from low to high….)

4. Place lowest priority (4) group in the back. Connect 1, 2, 3 and if:
   i. Clockwise = “R”
   ii. Counterclockwise = “S”
What if a molecule has more than one stereocenter?

- In general, a molecule with “n” number of stereocenters can exist as a maximum of $2^n$ stereoisomers.
- It can have fewer than the maximum because of MESO compounds, which will be stereoisomers of the molecule but are not chiral as we shall see shortly…

### III. Stereoisomers and Fischer Projections

**Drawing Fischer Projections:**

**Important**

- Horizontal lines are ________________________________.
- Vertical lines are ________________________________.

**More complicated Examples**

1) Rotate the longest carbon chain so that it is eclipsed along every bond.

2) Put the longest carbon chain vertically with carbon 1 at the top.
   - (C#1 is the most highly oxidized form of carbon)
   - In general...COOH>CHO>CH$_2$OH>CH$_3$
3) Look at the molecule from the bottom of the U-shaped bonds (from the “spine”). Imagine stretching the chain out flat and “smashing” flat onto plane of the paper.

4) Draw the longest carbon chain as a line, use crossing lines for every stereocenter. Do not write a “C” atom label at the crosses.

Example:

Rules for Comparing Fischer Projections:
Example:

IV. Other Types of Steroisomers

- **Diastereomers**: Stereoisomers that are not enantiomers.

1. **Meso Compounds**

   *A molecule with a mirror plane of symmetry will not be chiral even if it has stereocenters.*

   **Example:**
2. Molecules with Double Bonds (Cis-trans isomers)

3. Cycloalkanes and Other Rings (Cis-trans isomers)

4. Molecules with Multiple Stereocenters

A molecule with two or more stereocenters will be chiral if it does not have a mirror plane of symmetry.

Example:

5. It is possible for a molecule to be chiral even if it does not have a stereocenter. These are usually molecules that have twisted or helical structures or that have restricted rotation.
6. Conformations, Symmetry, and Chirality

Sometimes, a molecule can appear to be chiral because of its conformation. If you can rotate around the bond or ring flip, then it is just a conformational isomer.

V. Optical Rotation and Optical Activity

A. Plane-Polarized Light

- Light is made of waves of electricity and magnetism…

- In a regular beam of light, the electric wave of an individual photon can oscillate in any direction.

- This gives the beam of light, which is composed of many photons, the appearance of simultaneously oscillating in all possible directions (all possible orientations)
- A polarizing “filter” can be used to **align** photons that are not oscillating in a specific planar orientation into a specific direction.

- Photons that are oscillating at 90° to the filter are effectively eliminated.

- The resulting beam has photons that are vibrating in only one specific direction.
  - This is called ________________________________.

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**Polarizing filters can have interesting effects on light:**

Two polarized filters with their axes parallel.

Two polarized filters with their axes perpendicular.

Two polarizers, 1 and 2 with perpendicular axes, and third polarizer between them, axis at 45° to the other two.
B. Optical Rotation

- **Chiral molecules rotate plane-polarized light.** If a beam of polarized light is passed through a sample of a chiral molecule, the plane of its oscillation will be rotated so that it oscillates in a different direction:

  ![Optical Rotation Diagram]

  - The *observed rotation* \( \alpha_{\text{obs}} \) is the angle that the light is rotated by a given sample.

  - **Specific rotation** \( [\alpha]_D \): the angle that light is rotated by a pure single enantiomer of a substance at a standard concentration, cell length, and wavelength:

    \[
    \alpha_{\text{obs}} = \text{specific rotation} \times \text{cell length} \times \text{wavelength}.
    \]

- When a sample has a mixture of the two enantiomers of a compound, \( \alpha_{\text{obs}} \) will be less than the maximum possible rotation \( [\alpha]_D \).

- A **racemic mixture** is a mixture that contains the two enantiomers of a chiral compound in equal amounts.
  - A 50:50 mixture of enantiomers = \( \alpha_{\text{obs}} \) of 0°:
  - A racemic mixture is sometimes indicated by (±) in front of the name.
VI. Stereochemical Consequences of Radical Halogenation

- When a stereocenter is produced at a carbon that is planar in either the reactant or intermediates, a mixture of configurations will be produced.

EXAMPLE:

<table>
<thead>
<tr>
<th>Properties of Enantiomers and Diastereomers:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enantiomers</td>
</tr>
<tr>
<td>- Similar Physical Properties</td>
</tr>
<tr>
<td>MP, BP, Refractive Index, Density</td>
</tr>
<tr>
<td>One difference = rotation of polarized light (+/-)</td>
</tr>
<tr>
<td>- Have to use chemical means to separate</td>
</tr>
<tr>
<td>Different interactions with other chiral molecules</td>
</tr>
</tbody>
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