IV Stereochemistry

**Remember Isomers:** Different compounds with the same molecular formula

**Remember cis and trans and E/Z**

**Drawing in 3D:**
- The solid wedges represent bonds that point out of the plane of the paper towards the viewer
- The hatched wedges represent bonds that point back from the plane of the paper away from the viewer

*Example of two different compounds:*

*Example of two identical structures:*
4.1 Chirality

**Plane of Symmetry:** If you have a mirror plane in a molecule it has a plane of symmetry

- *If a molecule and its mirror image exactly match, they are superimposable*
- *If they don't match, they are nonsuperimposable*

*Examples:*
⇒ An object (molecule) that is NOT superimposable (nonsuperimposable) on its mirror image is CHIRAL

⇒ An object that is superimposable on its mirror image is ACHIRAL

Examples:

Q1: Identify chiral carbon centers in Epinephrine and Carvone

Chiral Carbon Atom: A Carbon with four different bonded groups
Configuration: The orientation of groups around a chiral carbon center (also called stereocenter or stereogenic center)

Enantiomers: Stereoisomers that are mirror images (each individual enantiomer is chiral)
Racemic Mixture: A 50/50 mixture of enantiomers
4.1.1 3D Expression of Enantiomers

Four different possibilities:

Example:

Q2: Why are enantiomers important?
4.1.2 Physical Properties of Enantiomers

**Identical Properties:** Density, melting point, boiling point, molecular weight

**Different Properties:** They differ in their rotation of polarized light

**Plane Polarized Light:** Light oscillating in only one plane

*Example:*

**Polarimeter:** Instrument used to measure the rotation of plane-polarized light

*Schematic Representation:*
Optically Active Compound: A Compound that ROTATES plane-polarized light; such compounds are not superimposable on their images

⇒ Chiral compounds are optically active

Specific Rotation: Calculated degree of rotation of an optically active compound

\[ \alpha = \frac{\text{observed rotation (degrees)}}{\text{length of sample tube, dm \times concentration of sample, g/cm}^3} \]

Dextrorotatory: Rotation of plane polarized light to the right (d or +)
Levorotatory: Rotation of plane polarized light to the left (l or -)

Examples:
- Menthol: \( \alpha = -50^\circ \)
- Cholesterol: \( \alpha = -31.5^\circ \)
- \( \alpha \)-D-Glucose: \( \alpha = +112.2^\circ \)
- Sucrose: \( \alpha = +66.5^\circ \)
- Vitamin C: \( \alpha = +21.5^\circ \)
- Nicotine: \( \alpha = -169^\circ \)
Examples:

4.1.3 Stereoisomers with Two or More Chiral Carbon Atoms

van't Hoff Rule: The maximum number of stereoisomers possible for a compound is $2^n$, where $n$ is the number of chiral carbon atoms.

Consider 2-deoxyribose:

- Two chiral carbon atoms
- Maximum number of stereoisomers $= 2^2 = 4$
- Two pair or mirror images:
These four combinations are NOT related as mirror images. They are called **Diastereomers**

**Diastereomers:** Stereoisomers that are NOT mirror images
⇒ They can differ in a number of physical properties including melting points, boiling points and densities

**Meso Compounds:** Stereoisomers that are superimposable on their images
⇒ Meso compounds are achiral

*Example:*

- Cyclic compounds can also have *cis/trans* stereoisomers
*Example:*
4.2 Specification of Configuration

How to describe the chiral center and the chiral compound?

Cahn, Ingold, Prelog Designation (R,S)

R,S  Terms used to describe the configurations of chiral compounds

Step 1: Each group connected to the chiral carbon is assigned a priority

Step 2: The molecule is viewed such that the group of lowest priority is directed AWAY from the viewer. The remaining three groups are in a plane and projected towards the observer

Step 3: If the eye moves clockwise as it goes from the highest priority to the second highest and the third highest priority, the configuration is assigned R (Rectus, Latin for right)
If the eye moves counter clockwise as it goes from the highest priority to the second highest and the third highest priority, the configuration is assigned S (Sinister, Latin for left)

Generic Example:
4.2.1 Determination of Group Priorities

**Rule 1:** If all four atoms directly attached to the chiral compound are different, priority depends on the atomic number. The higher the atomic number, the higher the priority.

I > Br > Cl > S > F > O > N > C > H

**Rule 2:** If two or more of these atoms directly bonded to the chiral carbon are identical, the priority of these groups is determined by comparing the next atoms of the groups and so on.

**Rule 3:** If a double or triple bond must be considered, the involved atoms are treated as duplicated or triplicated, respectively.

*Example:*
4.2.2 Determining R and S Configuration

Generic Example:

First Step: Assign Priorities

Second Step: Put the group of the lowest priority to the back

Third Step: Determine if the priorities are arranged in a clockwise fashion ⇒ R
Counterclockwise ⇒ S

If you have more than one chiral center in a molecule, you MUST determine the configuration for each chiral center

Examples:
4.3 Resolution of Enantiomers

*How do you separate enantiomers?*
(remember, enantiomers have beside optical activity the same physical properties)

⇒ Make Diastereomers out of them

**Resolution through Diastereomers:** A Method for separating Enantiomers

How it works:

- You react your inseparable enantiomers with a single optically active enantiomer

- The result is a pair of diastereomers ⇒ Different physical properties

- Separate the physically and do a chemical reconversion

⇒ Enzymes do the same in your body
4.4 Synthesis of Stereoisomers

- Generation of a MESO compound

- Generation of a pair of ENANTIOMERS

- Generation of a pair of DIASTEREOMERS
4.5 Enantiotopic Hydrogens and Prochiral Centers

- If a carbon is bonded to two hydrogens and two different groups, the two hydrogens are called **enantiotopic hydrogens**
  ⇒ replacing one of the hydrogens will result in an enantiomer
  ⇒ You would create a chiral center

- If the chiral center would be R, the hydrogen is called **pro-R-Hydrogen**

- If the chiral center would be S, the hydrogen is called **pro-S-Hydrogen**

The carbon to which enantiotopic hydrogens are attached is called **prochiral center**  ⇒ after replacing one hydrogen, the center would be chiral

*Examples:*
Summary of Chapter 4:

- Chirality
  - Superimposable
  - Nonsuperimposable
  - Chiral Centers
  - Enantiomers
  - Racemates
- Properties of Enantiomers
  - Optical activity
- van't Hoff Rule
  - Diastereomers
  - Meso Compounds
- Absolute Configuration
  - R, S
  - Determination of Priority Groups
- Resolution of Enantiomers
- Synthesis of Enantiomers
- Enantiotopic Hydrogens
- Prochirality