

I. CHIRALITY: A chiral carbon atom is defined by *all of the following* criteria:

- A. Only sp^3 carbon atoms can be chiral (not sp^2 or sp . Other atoms like N and S can be chiral).
- B. The sp^3 hybridized carbon atom must be bonded to 4 unique substituents.
- C. A chiral molecule is one that has no "plane of symmetry".
- D. The site of the chiral atom is referred to as a "chiral center"

II. ENANTIOMERS AND DIASTEREOMERS

Configurational stereoisomers have exactly the same molecular formula, the same skeletal structure, the same position of substituents and functional groups and the same functional groups. They differ only in the three-dimensional orientation of substituents around a chiral carbon atom.

A. ENANTIOMERS

Enantiomers are non-superimposable mirror image isomers that arise due to the chirality of an atom or of the overall molecule.

1. "Non-superimposable" means that two enantiomers are structurally identical but cannot be laid on top of each other and have all their bonds overlap.
2. Enantiomers typically have at least one chiral carbon atom, but may have more than one
3. An enantiomeric relationship can be identified by comparing the chiral center configurations of one isomer with the chiral center configurations of a second isomer. *If all chiral centers are inverted in one structure compared to the other, then the two isomers are enantiomers*
4. **PHYSICAL PROPERTIES:** Enantiomers have identical physical properties (i.e., energy, boiling point, melting point, densities, etc.) except that they rotate the plane of polarized light in different directions.
5. **OPTICAL ISOMERS:** Enantiomers are often referred to as "optical isomers" since a single enantiomer will rotate a plane of polarized light in one direction or another. **THE DIRECTION OF ROTATION (i.e., positive or negative) DOES NOT INDICATE ANYTHING ABOUT THE STRUCTURE OF THE ENANTIOMER.**
 - a. **DEXTROROTATORY:** (+, d-) A dextrorotatory enantiomer rotates a plane of polarized light to the right or in a positive direction.
 - b. **LEVOROTATORY:** (-, l-) A levorotatory enantiomer rotates a plane of polarized light to the left or in a negative direction.
 - c. A 1:1 mixture of enantiomers is referred to as a "racemic" mixture.

B. DIASTEREOMERS

Diastereomers are non-superimposable, non-mirror image stereoisomers.

1. Diastereomers arise in molecules with more than one chiral center.
2. A diastereomeric relationship can be identified by comparing the chiral center configurations of one isomer with the chiral center configurations of a second isomer. *If some but not all chiral centers are inverted in one structure compared to the other, then the two isomers are diastereomers.*
3. **PHYSICAL PROPERTIES:** Diastereomers have different physical properties including optical rotation.
4. **MESO COMPOUNDS:** A meso compound contains at least two chiral centers and a plane of symmetry. While it may appear that a meso compound has two enantiomers, the two "enantiomers" are actually the same exact compound.

III. DESIGNATING STEREOCHEMISTRY: There are three commonly accepted methods for designating stereoisomers.

A. OPTICAL ROTATION METHOD ((+)d-, (-)l-)

Enantiomers are often referred to as "optical isomers" since a single enantiomer will rotate a plane of polarized light in one direction or another. **THE DIRECTION OF ROTATION (i.e., positive or negative) DOES NOT INDICATE ANYTHING ABOUT THE STRUCTURE OF THE ENANTIOMER.**

1. **DEXTROROTATORY:** (+, d-) A dextrorotatory enantiomer rotates a plane of polarized light to the right or in a positive direction.
2. **LEVOROTATORY:** (-, l-) A levorotatory enantiomer rotates a plane of polarized light to the left or in a negative direction.

B. CAHN-INGOLD-PRELOG (CIP) METHOD (R-, S-)

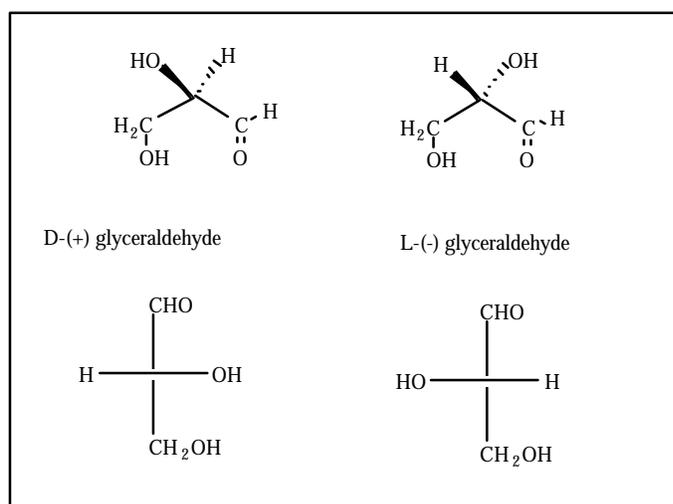
The Cahn-Ingold-Prelog method is used to designate absolute configuration of a chiral center. The following rules are used to designate the absolute configuration of a chiral center using the CIP method.

1. Locate the chiral center.
2. Using sequence or priority rules, rank the four substituents bonded to the chiral carbon atom (1 = highest priority, 4 = lowest priority).
3. Rotate the molecule so that the substituent of lowest priority is directed back.
4. Draw a curved arrow starting at the substituent of highest priority and move it in order of decreasing priority.
5. If the arrow rotates CLOCKWISE, then the configuration of that chiral center is "R".
6. If the arrow rotates COUNTERCLOCKWISE, then the configuration of the chiral center is "S".
7. For a molecule with more than one chiral center, the total possible number of sets of enantiomers is 2^{n-1} .

C. FISHER METHOD (D-, L-)

The Fisher convention relates the configuration of a chiral center to D- or L-glyceraldehyde.

1. (+)-Glyceraldehyde has an absolute configuration of "D".
2. (-)-Glyceraldehyde has an absolute configuration of "L". (See structures)



3. Only molecules sufficiently similar to glyceraldehydes can use the Fisher Method for stereochemical designation
The configuration of a chiral center is designated "D-" or "L-" depending on whether it is analogous to glyceraldehyde or L-glyceraldehyde
4. Fisher projections are used to make the comparison. The Fisher projection is oriented so that the most highly oxidized carbon atom of the main chain is at the top position.
5. The Fisher convention is used most commonly with sugars and amino acids that contain chiral centers.
6. NOTE: There is no simple relationship between d- or (+)- and D-. For example, L-alanine has a (+) optical rotation.

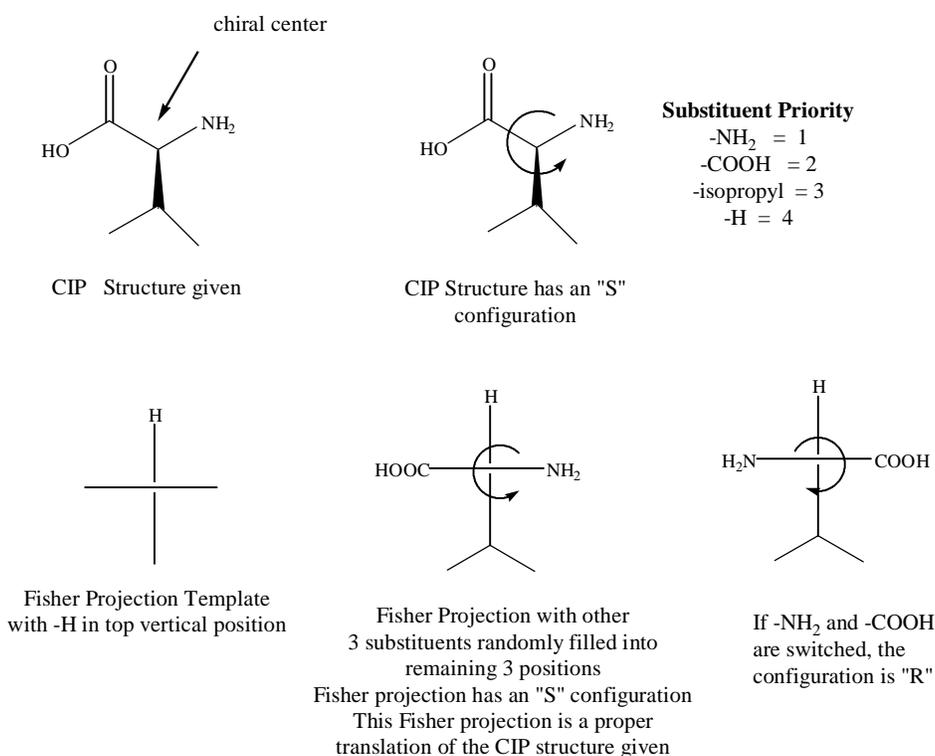
IV. FISHER PROJECTIONS: Fisher projections are representations which are used to depict molecules which contain chiral centers. The following rules can be used for drawing Fisher projections.

- A. Horizontal lines depict bonds coming out of the plane. Vertical lines depict bonds going back into the plane. The point of intersection of two lines represents the chiral center.
- B. Rotation of the entire Fisher projection by 180° in the plane does not alter the configuration of the chiral center. (Rotation by 90° alters the configuration.)
- C. Rotation of three of the four substituents in a clockwise or counterclockwise direction either by 90° or 180° while keeping the fourth substituent stationary does not alter the configuration of the chiral center.
- D. Determining absolute configuration of chiral centers represented by Fisher projections.
 1. Rank the four substituents using the sequence rules.
 2. Move the substituent of lowest priority to the top vertical position using the allowed rules for moving substituents in Fisher projections.
 3. With the remaining three substituents, determine the direction of rotation using the curved arrow. CLOCKWISE = "R" CONFIGURATON, COUNTERCLOCKWISE = "S" CONFIGURATION.

V. CONVERTING BETWEEN CIP STRUCTURES AND FISHER PROJECTIONS

A. Converting a CIP structure to a Fisher Projection

1. Determine the absolute configuration of the chiral center (i.e., R- or S-)
2. Draw a template for a Fisher projection. Fill in the substituent of lowest priority bonded to the chiral center into the top vertical position.
3. Randomly fill in the remaining three substituent onto the Fisher projection.
4. Determine the absolute configuration of the Fisher projection you drew.
5. If the two structures have the same configuration, then the Fisher projection you drew is an accurate translation of the CIP structure
6. If the configuration of the Fisher projection you drew is different from the original CIP configuration, draw a second Fisher projection template.
7. Fill in the four substituents around the chiral center, switching the position of any two groups in this second Fisher projection, relative to the first.



B. Converting a Fisher Projection to a CIP Structure

1. Determine the absolute configuration of the chiral center (i.e., R- or S-)
2. Draw a template for a CIP structure. Fill in the substituent of lowest priority bonded to the chiral center onto the back position (dotted line).
3. Randomly fill in the remaining three substituent onto the CIP structure template.
4. Determine the absolute configuration of the CIP structure you drew.
5. If the two structures have the same configuration, then the CIP structure you drew is an accurate translation of the Fisher projection
6. If the configuration of the CIP structure you drew is different from the original Fisher projection, draw a second CIP template.
7. Fill in the four substituents around the chiral center, switching the position of any two groups in this second CIP structure, relative to the first.