Chapter 9: Stereochemistry

Some objects have right-handed and left-handed versions

Handed objects are mirror images of each other. If the mirror images are superimposable, the object can be used with either hand.

9.1 Enantiomers and the tetrahedral carbon

A tetrahedral carbon where 2 or 3 of the groups are the same can be rotated to be the same as its mirror image.

A tetrahedral carbon with 4 different groups is not superimposable with its mirror image.

Two non-superimposable mirror image molecules are enantiomers of each other.

(+) - lactic acid and (-) - lactic acid are mirror images that cannot superimpose - they are enantiomers.
9.2 The reason for handedness in molecules: chirality

An object that is not identical to its mirror image is **chiral** - (every chiral object has an enantiomer).

An object is **achiral** (not chiral) if it has an **internal plane of symmetry** (internal mirror plane) - a plane that divides the object into two identical halves.

Tetrahedral carbon as a chirality center

A carbon bonded to four different groups is a **chirality center** because it causes the molecule to be chiral.

If there's **any** (even minor) **difference** between the groups, they are considered different.

Mark the chirality centers with a star:
Solutions of certain organic molecules (like sugar or camphor) will cause plane-polarized light to rotate - these are **optically active** substances.

The direction of rotation, if known, can be used in a chemical name. (-)-Morphine rotates light counterclockwise, while (+)-sucrose rotates light clockwise. The specific rotation, \([\alpha]_D\), is a standardized rotation that corrects for path length and concentration.

<table>
<thead>
<tr>
<th>Compound</th>
<th>([\alpha]_D)</th>
<th>Compound</th>
<th>([\alpha]_D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin V</td>
<td>+233</td>
<td>Cholesterol</td>
<td>−31.5</td>
</tr>
<tr>
<td>Sucrose</td>
<td>+66.47</td>
<td>Morphine</td>
<td>−132</td>
</tr>
<tr>
<td>Camphor</td>
<td>+44.26</td>
<td>Cocaine</td>
<td>−16</td>
</tr>
<tr>
<td>Chloroform</td>
<td>0</td>
<td>Acetic acid</td>
<td>0</td>
</tr>
</tbody>
</table>

Pasteur discovered in 1848 that two different crystals of sodium ammonium tartarate can crystallize and can be carefully separated from each other (with a microscope and tweezers).

A solution of an equal mixture of the crystals shows **no optical activity**, but solutions of each of the two crystal types alone rotate light by **equal and opposite angles**.

Pasteur hypothesized that there was asymmetry within the molecules, long before the structures of the molecules were known.

Later it was confirmed that Pasteur was looking at the two **enantiomers** of sodium ammonium tartarate.
9.5 Sequence rules for specifying configuration

The Cahn-Ingold-Prelog sequence rules (the same as for $E/Z$) can be used to assign a stereochemical designation for the **configuration** of a chirality center.

1. Look at each atom attached to the carbon. The highest atomic number is 1, the lowest is 4.
2. If two atoms are the same, continue along the chain until there is a difference.
3. A double bond counts as two single bonds.

With group #4 (usually an H) pointed away from you, if an arrow drawn from 1 to 2 to 3 is **clockwise**, the configuration is $R$ (like a right turn on a steering wheel). If the arrow is **counterclockwise**, the configuration is $S$.

If group 4 is pointed toward you, do the same analysis but **reverse the result**.

Assigning configuration

If group 4 is in the plane of the paper, be very careful. Imagine yourself in the paper looking down the C-H bond and consider whether the rotation is $R$ or $S$. 
9.6 Diastereomers

When a molecule only has one chirality center that's either \((R)\) or \((S)\), there are two enantiomers. Those are the only stereoisomers.

A molecule with \(n\) chirality centers can have up to \(2^n\) stereoisomers. There are 4 stereoisomers of 2-amino-3-hydroxybutanoic acid:

In a pair of molecules, if ALL the chirality centers have the opposite configurations, the molecules are mirror images and enantiomers.

If only SOME of the chirality centers are opposite, the molecules are diastereomers.

9.7 Meso compounds

There are four combinations of chirality centers in tartaric acid:

But, the last two are actually the same. We can keep them flat on the paper and rotate \(180^\circ\) to superimpose.

The structures are identical because of the internal symmetry plane which makes the molecule achiral.

Meso: achiral molecule which contains chirality centers.

\((+), (-), (\text{meso})\) tartaric acid
Properties of stereoisomers

Are any of the compounds below meso?

Enantiomers have all the same physical properties, except the direction of rotation of plane-polarized light, and biological properties (smell, toxicity, drug effectiveness, etc).

Diastereomers are completely different compounds that have all different physical properties.

9.8 Racemic mixtures and the resolution of enantiomers

Pasteur's original mixture of (+)- and (-)-tartaric acid did not rotate plane-polarized light because it was an equal mixture of two enantiomers. One enantiomer cancels the other's rotation of light.

Racemic mixtures are denoted as (±). If a chiral molecule is drawn flat, it is assumed it's a racemic mixture.

Meso-tartaric acid contains only one isomer - it's achiral. (±)-Tartaric acid contains a racemic mixture of two chiral enantiomers in equal amount.

Racemic mixtures can be resolved - usually by reacting them with a single chiral reagent. The result is two diastereomers which can be separated.
9.9 A review of isomerism

When a new chirality center is formed from achiral reactants, a racemic mixture will always be formed. The symmetrical, flat carbocation can be approached equally well from either face. (The two transition states are mirror images).

9.10 Addition of \( \text{H}_2\text{O} \) to an **achiral** alkene

When a new chirality center is formed from achiral reactants, a racemic mixture will always be formed.
9.11 Addition of H₂O to a chiral alkene

When chiral and achiral reactants create a new chirality center, the result is an unequal mixture of two diastereomers.

\[ \text{(R)-4-Methyl-1-hexene (chiral)} \rightarrow \rightarrow \text{4-Methyl-2-hexanol (chiral)} \]

The carbocation is no longer symmetrical. One side is more approachable than the other.

\[ \text{Chiral alkene} \]

\[ \text{Chiral carbocation} \]

 unequal amounts

\[ \text{2 faces are different!} \]