

CHEM 321 Organic Chemistry I - Professor Kathleen Kilway

"Organic Chemistry" by Maitland Jones, 3rd edition

Chapter 4 - 1, 2, 3, 4, 5, 10, 11, 17, 18, 19, 20, 21, 22, 24, 26, 27, 29, 32, 33, 37, 42, 44, 46.

CHAPTER 4: STEREOCHEMISTRY

Section 4.1

I. Preview

A- Stereochemistry

- This is the structural and chemical consequence of the arrangement of atoms in space.
- A molecule is **chiral** if it is not superimposable onto its mirror image.
 - An example of chirality is that your right hand is not superimposable onto your left hand.

Section 4.2

II. Chirality

A- Chirality

- It is the phenomenon of handedness.
- The general rule of thumb for carbon chiral centers is that the carbon must have four different groups attached to it.
- In 3-methylhexane, the third carbon C(3) is chiral because there are four different groups attached to that carbon: hydrogen, methyl, ethyl and a propyl group.
 - The structure and its mirror image are not superimposable even after rotation.
 - Enantiomers** are nonsuperimposable mirror images.

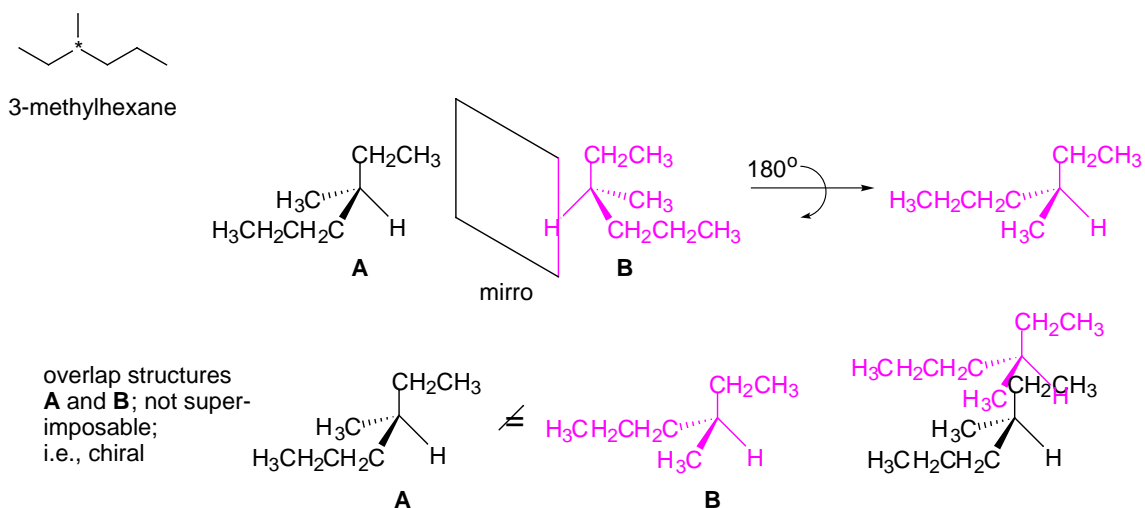


Figure 1

- 4- But in the case of 3-methylpentane, it is not chiral.
- There are **two** ethyl groups attached to that carbon.
 - The structure and its mirror image are superimposable after rotation.
 - Therefore, the molecule is said to be **achiral**.
- 5- See Figure 4.2 on page 153 for an example.

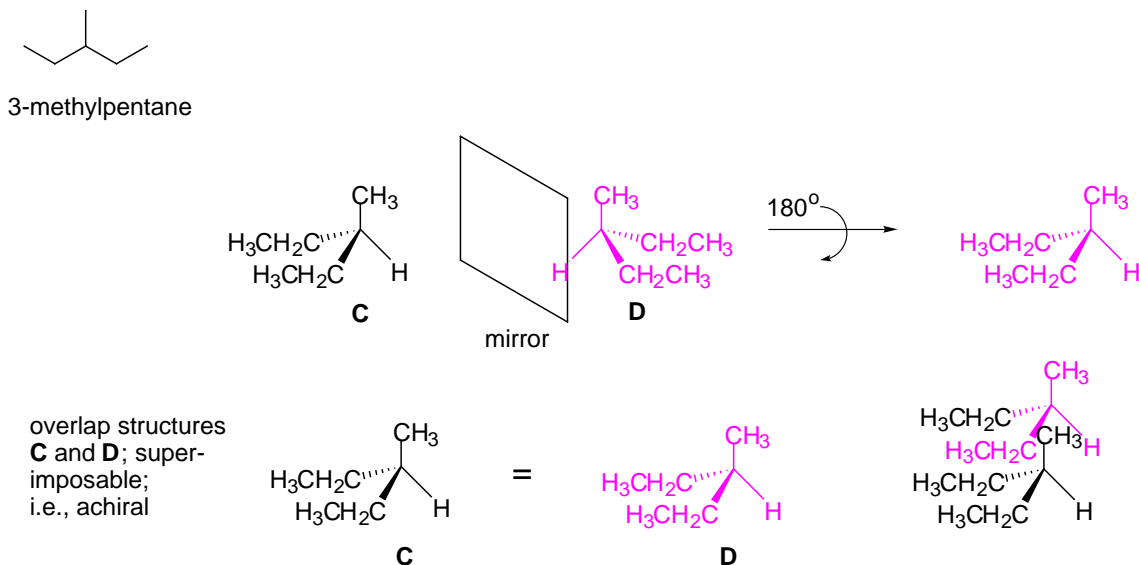


Figure 2

Section 4.3

III. Properties of Enantiomers: Physical Differences

A- Enantiomers have almost all of the same physical properties.

- Boiling points.
- Melting points.
- Densities.
- The exception is the way that they rotate plane-polarized light.

B- Optical activity

- It is the rotation of plane-polarized light (ppl).
- If a molecule rotates ppl, then it is said to be **optically active**.
- Enantiomers rotate light in opposite directions.
 - The clockwise direction is **dextrorotatory** (+).
 - The counterclockwise direction is **levorotatory** (-).
- A 50:50 mixture of the two enantiomers is said to be a **racemic** mixture.
- Sometimes we designate the "chiral" carbon with a *.
- Absolute configuration** is the arrangement in space of the atoms in an enantiomer.

Section 4.4

IV. The (R/S) Convention

A- Stereogenic Center

- 1- It is an atom (usually carbon) of such nature and bearing groups of such nature that it can have two nonequivalent configurations.
- 2- An example is the C(3) of 3-methylhexane.

B- R/S Convention (Cahn-Ingold-Prelog)

- 1- Identify the stereogenic center.
- 2- Each group is given a priority.
 - a- 1 is used for highest; 4 for lowest.
 - b- Atom of lowest atomic number is given the lowest priority (See Figure 4.9 on page 158).
 - c- When atomic numbers are equal, priority is assigned by atomic weights; e.g. $T > D > H$ (See Figure 4.10 on page 158).
 - d- If two carbons are present, look at what is directly attached to each carbon. E.g. methyl vs ethyl, the methyl has 3 hydrogens attached whereas the ethyl one carbon and two hydrogens therefore the methyl carbon has the lowest priority (See Figure 4.12 on page 158).
 - e- If they are still equal, you have to look at groups further along the chain.
- 3- A further complication is multiple bonds.
 - a- The problem is resolved by treating a $C=C$ as $C-C-C-C$ (See Figure 4.14 on page 159).
- 4- Put the lowest priority in the back (See Figure 4.15 on page 160).
- 5- If 1, 2, 3 is clockwise, then **R**; if 1, 2, 3, is counterclockwise, then **S**.
- 6- R configuration changes to the S configuration via a mirror plane and vice versa.
- 7- Models are of great help here.

Section 4.5

V. The Physical Basis of Optical Activity

A- Light has both wave and particle properties.

B- Polarimeter

- 1- It is a device, which measures the net change in the plane of polarization.
 $[\alpha] = \alpha/cl$
 where c = concentration in grams per milliliter (g/mL)
 and l = length of the tube in decimeters (dm).

Section 4.6

VI. Properties of Enantiomers: Chemical Differences

A- Enantiomers

- 1- They have identical chemistries with achiral reagents, but different with chiral reagents.

Section 4.7

VII. Interconversion of Enantiomers by Mobile Equilibria: *Gauche* Butane

A- The *gauche* form of butane is chiral.

- 1- It cannot be superimposed on its mirror image (See Figure 4.30 on page 169).

- 2- There is essentially free rotation at room temperature, which interconverts the two mirror images.
- 3- At very low temperatures, it is possible to "freeze out" the two stereoisomers.
- 4- **Conformational enantiomers** are enantiomers, which are interconvertible through (generally easy) rotations around bonds within a molecule.

Section 4.8

VIII. Diastereomers: Molecules Containing More than One Stereogenic Atom

A- Diastereomers

- 1- **Diastereomers** are "stereoisomers that are not mirror images", which have different physical properties.
- 2- See example below, 2-bromo-3-fluorobutane.
 - a- **A** is the enantiomer of **B**.
 - b- Their stereogenic centers are the opposite when reflected through the mirror plane.
 - c- See also Figure 4.35 on page 172.

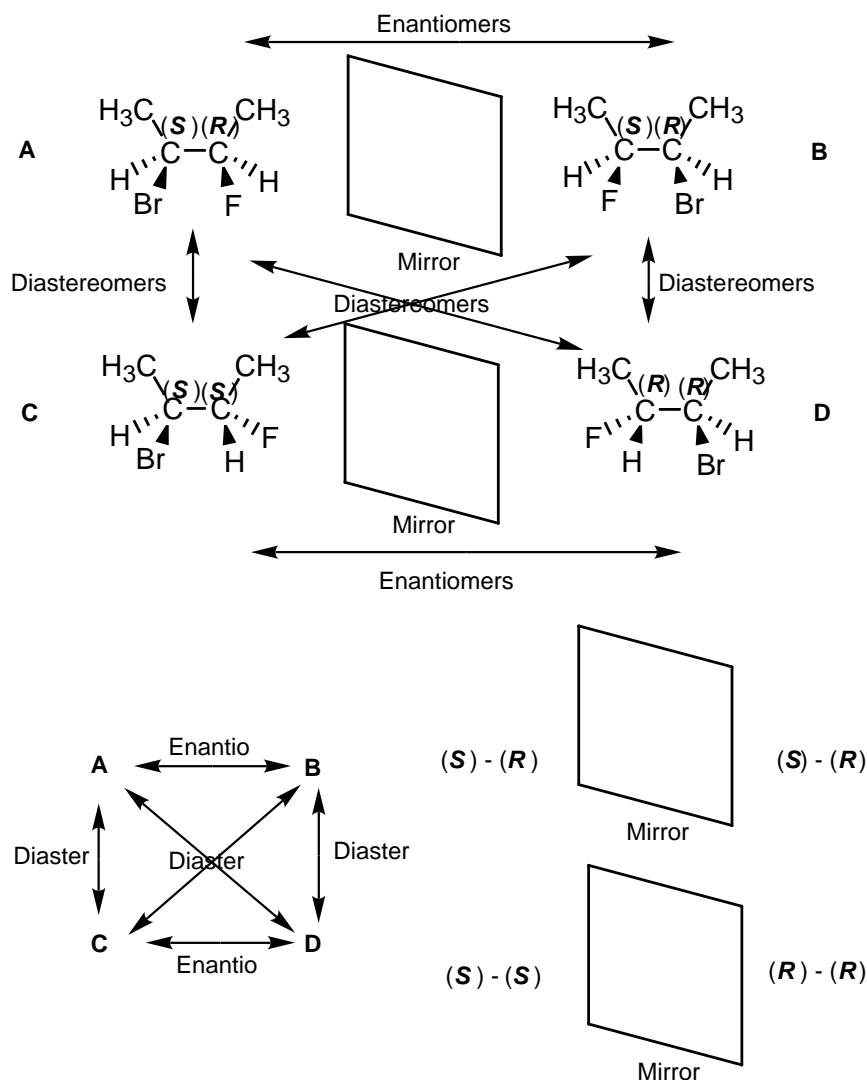


Figure 3

3- Generalization.

- a- For one stereogenic center, there are only two possible stereoisomers, *R* and *S*.
- b- For two stereogenic centers, there are two pairs of enantiomers [(*R*, *S*) and (*S*, *R*); (*S*, *S*) and (*R*, *R*)], or four stereoisomers.
- c- Therefore, we get 2^n isomers, where *n* equals the number of stereogenic centers.

4- What happens in the case of 3,4-dimethylhexane?

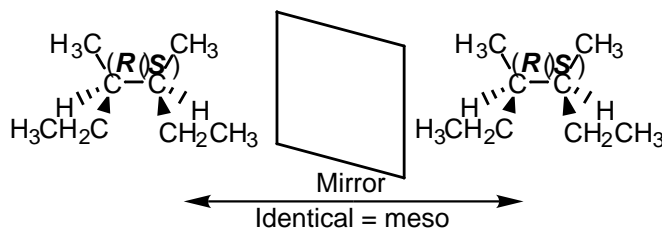


Figure 4

- a- A **meso compound** is a molecule that contains stereogenic centers, but is not chiral.

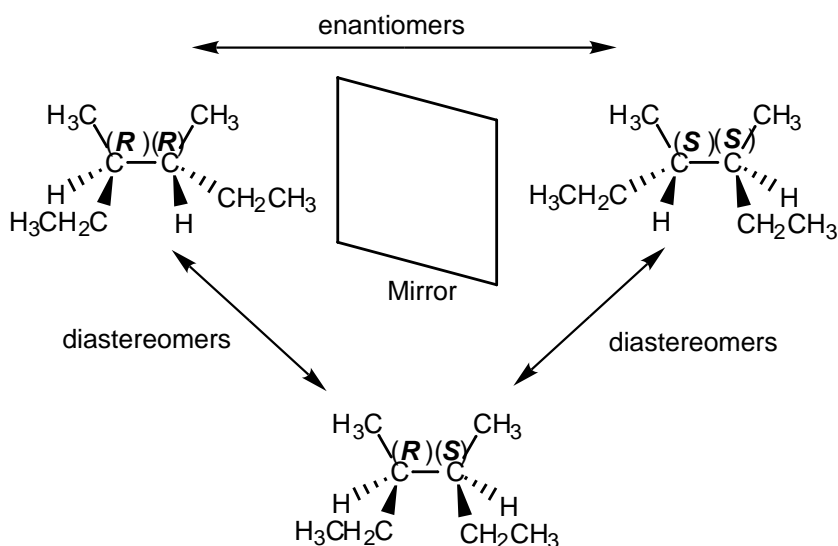


Figure 5

- b- See also Figure 4.39 on page 174.

Section 4.9

IX. Physical Properties of Diastereomers: Optical Resolution

A- Resolution

- 1- It is the separation of enantiomers.
- 2- One general procedure.
 - a- First, allow them to react with a naturally occurring chiral molecule to form a pair of diastereomers either through a covalent bond or an associated bond.

- b- Then, one can separate the diastereomeric pair using crystallization or chromatography because the diastereomeric pairs have different physical properties.

Section 4.10

X. Determination of Absolute Configuration (*R* or *S*)

A- X-ray crystallography

- 1- This is a method, which can determine relative configuration but not absolute configuration.
- 2- You do not know how to do this at this point in time.

Section 4.11

XI. Stereochemical Analysis of Ring Compounds (A Beginning)

A- Review of Isomerism with ring compounds

- 1- **Isomers** have the same molecular formula.
 - a- E.g., 1,1-dichloropropene and 1,1-dichlorocyclopropane.
- 2- **Structural isomers** (constitutional isomers) are molecules of the same formula but with different connectivities among the constituent atoms.
 - a- E.g., 1,1-dichlorocyclopropane and 1,2-dichlorocyclopropane.
- 3- **Stereoisomers** have the same connectivity but different arrangement of their parts in space.
 - a- Diastereomers - *cis*-1,2-dichlorocyclopropane and *trans*-1,2-dichlorocyclopropane.
 - b- Enantiomers - *trans*-(1*R*,2*R*)-dichlorocyclopropane and *trans*-(1*S*,2*S*)-dichlorocyclopropane.
 - c- Therefore, there are four isomers of dichlorocyclopropane.
 - d- See Figure 4.53 on page 182 for an illustration.

Section 4.12

XII. Summary of Isomerism

A- Isomerism

- 1- **Isomers** have the same molecular formula.
- 2- **Structural isomers** (constitutional isomers) are molecules of the same formula but with different connectivities among the constituent atoms.
 - a- Some examples are 1,1-dibromocyclobutane and 1,2-dibromocyclobutane; butane and 2-methylpropane.
- 3- **Stereoisomers** have the same connectivity but different arrangement of their parts in space. Some examples are enantiomers, diastereomers and conformational isomers.
- 4- **Conformational isomers** are enantiomers or diastereomers, which can interconvert through rotations around bonds within the molecule.

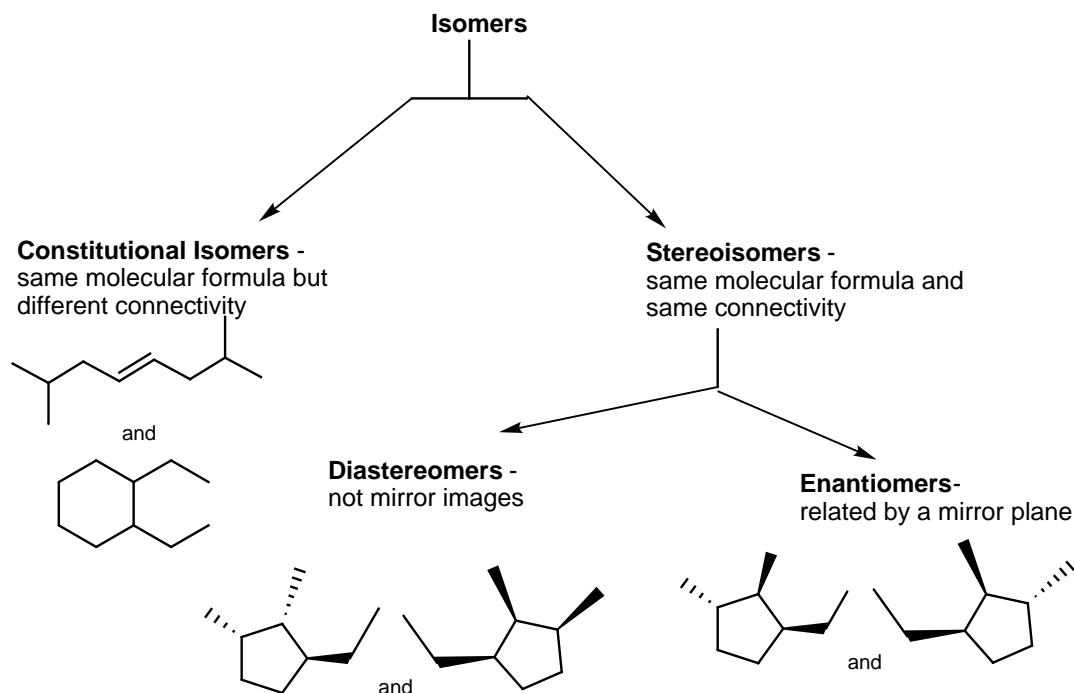


Figure 6

Section 4.13

XIII. Special Topic: Chirality Without "Four Different Groups Attached to One Carbon"

(* = chiral compounds without stereogenic centers)

A- Allenes*

- 1- They are compounds with two double bonds, which are connected directly together.

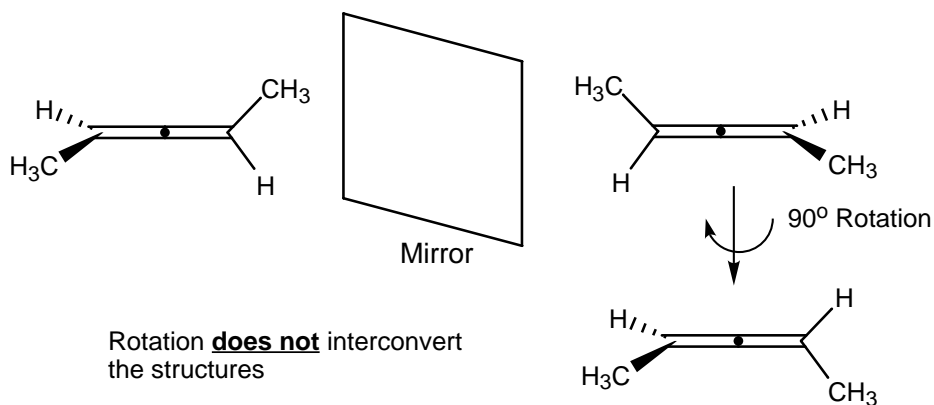


Figure 7

B- Substituted Biphenyl*

- 1- They are compounds with two benzene rings joined by a "single" bond.
- 2- See Figure 4.61 on page 186 of biphenyl.

C- Hexahelicene*

- 1- They consist of six fused benzene rings attached in a curved fashion.
- 2- See Figure 4.63 on page 186 for an example.

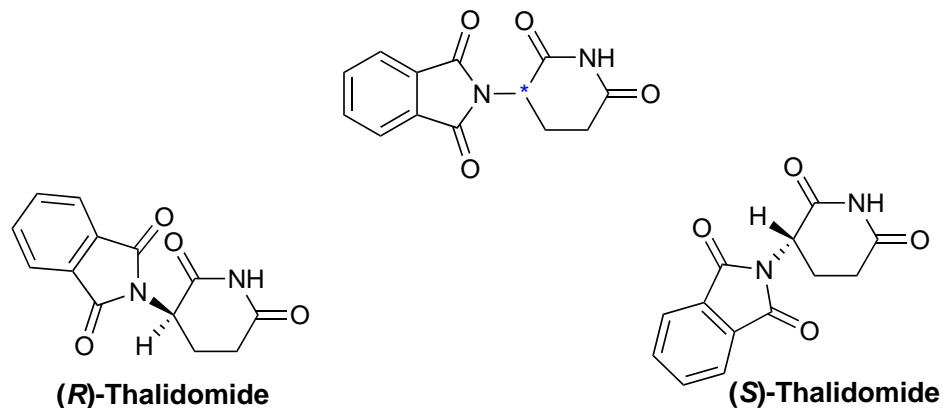
Section 4.14**XIV. Special Topic: Stereochemistry in the Real World; Thalidomide, The Consequences of Being Wrong-Handed**

Figure 8

A- R enantiomer is harmless but the S enantiomer is a potent teratogen.

- 1- See Figure 4.64 on page 187 for an example.

Section 4.15**XV. Summary**

New Concepts - chirality - handedness
 Reactions, Mechanisms, and Tools - R/S

Web pages:

<http://www.chem.arizona.edu/courses/chem242/stereochem3/>

<http://www.wp.cc.nc.us/~chemdept/Organic/stereo.html>