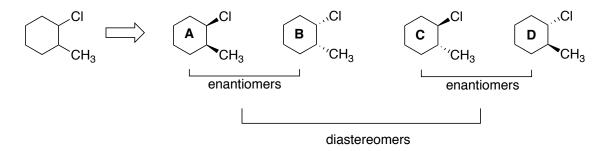
## **CHAPTER 5: STEREOCHEMISTRY (cont.)**

Assign (R) or (S) configurations to the chiral carbons in the following molecules:

$$H_3COH$$
 $H_3COH$ 
 $H_3C$ 

## **Molecules With Multiple Chiral Atoms.**

1-chloro-2-methylcyclohexane has four possible stereoisomers ( $2^2 = 4$ ); they are:



A and B are enantiomers and C and D are enantiomers, but "diastereomer" describes the relationship of A or B with C or D.

Using IUPAC rules,  $\bf A$  is now named (1R,2S)-1-chloro-2-methylcyclohexane. You try naming  $\bf B$  through  $\bf D$ .

A: \_(1R,2S)\_\_\_\_-1-chloro-2-methylcyclohexane

B: \_\_\_\_\_-1-chloro-2-methylcyclohexane

C: \_\_\_\_\_-1-chloro-2-methylcyclohexane

D: \_\_\_\_\_-1-chloro-2-methylcyclohexane

We predict four stereoisomers for the example below. Draw them, assign (R) and (S) to the chiral atoms, then determine which are enantiomers and which are diastereomers.

The (-) / levorotatory isomer of epinephrine, below, has profound effects on the cardiovascular system. Draw (+)-epinephrine (remember, enantiomers have exactly the opposite stereochemistry).

(-)-Epinephrine

What can you say with certainty about the optical rotation of (+)-epinephrine?

What can you say with certainty about the biological properties of (+)-epinephrine?

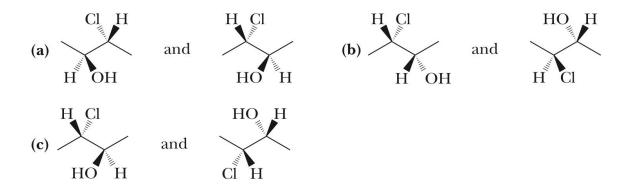
**Meso Compounds.** Some molecules that have chiral carbons do not obey the "2" rule. For example, consider the following four structures of 1,2-dimethylcyclohexane

Although **C** and **D** are enantiomers, **A** and **B** are the same; hence, although *trans*-1,2-dimethylcyclohexane is chiral, *cis*-1,2-dimethylcyclohexane is not - and it carries a unique name: *meso*. A molecule that is *meso* has more than one chiral carbon, but *is not chiral*. So ultimately, 1,2-dimethylcyclohexane only has three different stereoisomers; **A** is meso, and is a diastereomer of **C** and **D**, while **C** and **D** are enantiomers of each other.

Can you identify which of the following are meso compounds? Look for symmetry.

Are the molecules within each set, below, identical, enantiomers or diastereomers?

If you find these difficult by simply looking at the molecules and comparing their shape, start by assigning (R) and (S) to the chiral atoms - this may simplify the task.



**Fischer Projections.** Molecules depicted this way are all drawn with the assumption that the horizontal bonds are coming toward you and the vertical bonds are going away from you - like this:

**Fischer Projection** 

If that representation is still a little foreign, you can convert this to a molecular representation you might recognize by pretending that you're looking at the underside of a dog. The horizontal bonds are the four legs, and are coming toward you, and the vertical bonds are the head and tail, going away from you. Simply pick up the dog and put it on its feet. No joke - it works!

To assign chirality to atoms in molecules that are drawn in a Fischer projection, you can either simply imagine the horizontal/vertical bonds forward/back (the easier way to do it) or stand the dog up on its feet. Which ever method works for you - give it a try. Assign (R) or (S) to the chiral carbons in the following molecule:

$$\begin{array}{c} \text{CO}_2\text{H} \\ \text{H}_3\text{C} & \text{H} \\ \text{H} & \text{OH} \\ \text{NH}_2 \end{array}$$

**Prochirality.** Some molecules that are NOT chiral can have *prochiral* atoms if adding a fourth atom can create asymmetry. *Re* and *Se* are used to describe the face of a planar molecule such as this ketone to indicate the rotation from highest to lowest priority (left). From the perspective of viewing the alkene (right) in the plane of the paper, each of the two prochiral carbons can be labeled *Re* or *Se* - give it a try:

$$\begin{array}{c} Re \, \text{face (clockwise)} \\ \downarrow \\ \downarrow \\ H_3C \\ \hline \\ CH_2CH_3 \\ \hline \\ Si \, \text{face (counterclockwise)} \end{array} \qquad \begin{array}{c} H\\ \downarrow \\ H_3C \\ \hline \\ CH_2CH_3 \\ \hline \\ H_3C \\ \hline \\ CH_2CH_3 \\ \hline \\ H_3C \\ \hline \\ CH_2CH_3 \\ \hline \\ (R) \text{-2-Butanol} \\ \hline \\ (R) \text{-2-Butanol} \\ \hline \end{array}$$

Prochirality can also describe hydrogen atoms attached to achiral carbons. In the following example, if the pro-R hydrogen was replaced with a higher priority atom, the resulting absolute configuration would be (R). You try:

pro-S  
pro-R 
$$\rightarrow$$
 H H  
H Br  
+H<sub>3</sub>N H

Question 5.61 from text: One of the steps in fatty-acid biosynthesis is the dehydration of (R)-3-hydroxybutyryl ACP to give *trans*-crotnyl ACP. Does the reaction remove the pro-R or pro-S hydrogen from C2?

(R)-3-Hydroxybutyryl ACP

trans-Crotonyl ACP

Question 5.70 from the text: (S)-1-Chloro-2-methylpentane undergoes light-induced reaction with  $Cl_2$  to yield a mixture of products, among which are 1,4-dichloro-2-methylbutane and 1,2-dichloro-2-methylbutane.

(a) Write the reaction, showing the correct stereochemistry of the reactant

(b) One of the products is optically active, but the other is optically inactive. Which is which?

Question 5.76 from the text: Ketones reaction with sodium acetylide to give alcohols. For example, the reaction of sodium acetylide with 2-butanone yields 3-methyl-1-pentyn-3-ol.

$$H_3C$$
 $C$ 
 $CH_2CH_3$ 
 $CH_3CH_3$ 
 $CH_3CH_3$ 
 $CH_3CH_3$ 
 $CH_3CH_3$ 
 $CH_3CH_3$ 
 $CH_3CH_3$ 
 $CH_3CH_3$ 

- (a) Is the product chiral?
- (b) Assuming that the reaction takes place with equal likelihood from the *Re* and *Si* faces of the carbonyl group, is the product optically active? Explain.