

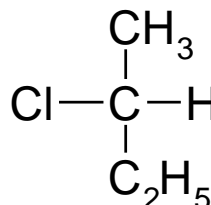
## Ch 5 Tetrahedral Stereochemistry

### Enantiomers

- Two non-superimposable mirror image molecules
- They are stereoisomers with the same atoms and bonds, but different spatial geometries.
- The two molecules of the pair have mirror image chiral centers.

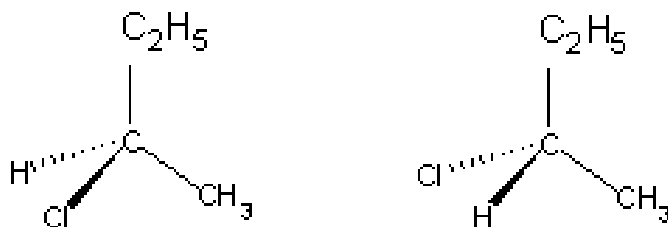
### Chiral Center

- A carbon (or other) atom with four *different* substituents:
- Often the chiral carbon is designated w/ an asterisk: \*C



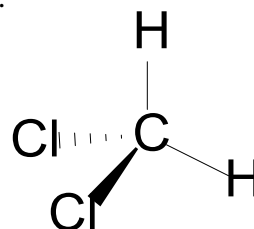
### Chiral Molecule

- A molecule with a chiral center that is not superimposable on its mirror image and does not possess a plane of symmetry.
- The molecules below are enantiomeric. As shown, they are non-superimposable.
- They are also mirror images, and this can be seen if either molecule is rotated 180°.



### Plane of Symmetry

- A plane that splits a molecule into two mirror image halves.
- The molecule at right has at least one symmetry plane. For instance, the plane that is directly between the Cl's, and includes both H's, makes a pair of mirror images.
- As a result, the molecule is achiral, which means it is the same as its mirror image.

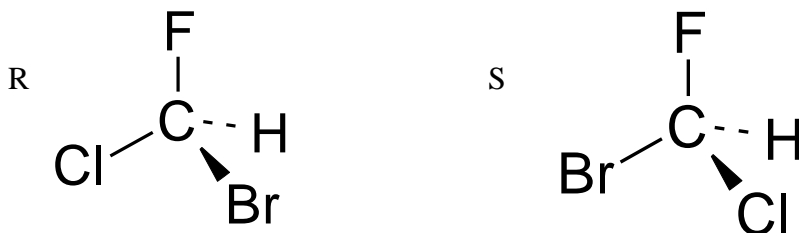


### Optical Activity of Organic Molecules

- This was first observed by Jean Baptist Biot in 1815.
- Optical activity is the rotation of a polarized plane of light by a chiral molecule.
- A levorotary (l or -) compound rotates the plane to the left.
- A dextrorotary (d or +) compound rotates the plane to the right.
- Enantiomers each have same absolute value of rotation angle, but in opposite directions.

### Configuration (R and S)

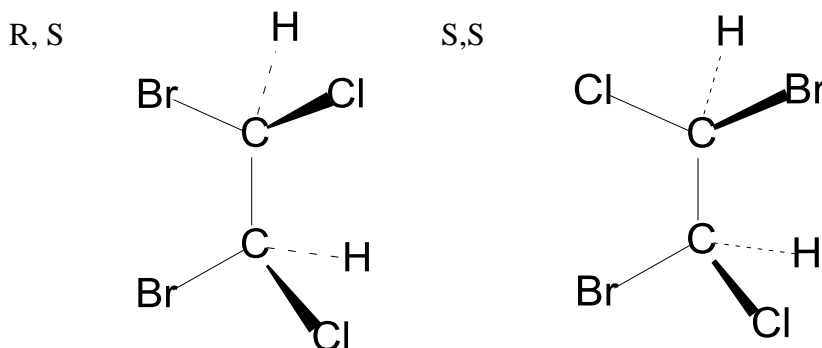
- Use system to rank 1 (highest), 2, 3, 4 (lowest). Basic rules are:
  - o Higher atomic number ( $Z$ ) gets higher priority.  
For instance  $\text{Br} > \text{Cl} > \text{O}$ , and Br is 1.
  - o If both atoms are the same, look at the atomic number of following atoms.  
For instance  $\text{BrO}^- > \text{H}_3\text{CO}^- > \text{HO}^-$ , and  $\text{BrO}^-$  is 1.
- If  $^1\text{H}$  is present, it will be 4 (lowest).
- Point 4 away and look at 1, 2, and 3.
- "R" if 1, 2, 3 is clockwise.
- "S" if counterclockwise
- R and S are not related to (+) and (-) light rotation.
- Absolute configuration (R and S) can be found by X-ray spectroscopy.



- Switching the positions of any two substituents will switch the configuration.  
Exchanging Br and Cl in the R configuration, above, will switch the configuration to S.

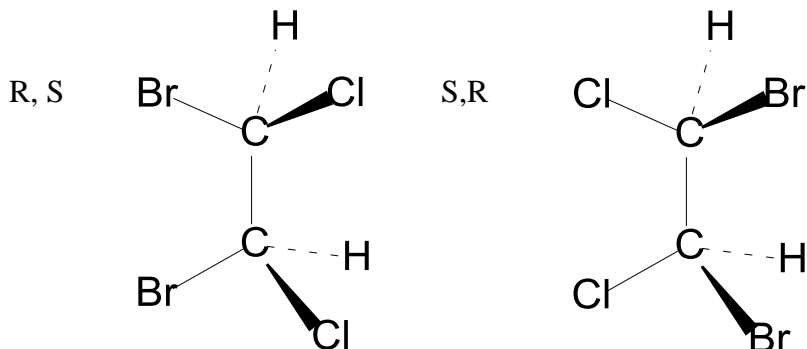
### Diastereomers

- Diastereomers are stereoisomers that are not mirror images and not superimposable.
- The R,S and S,S stereoisomers below are neither superimposable, nor mirror images.
- Also, cis and trans isomers are always diastereomers of each other because they are never superimposable.



## Meso Compounds

- R,S and S,R are the same molecule if all four substituents are same for both chiral centers.
- Rotate the drawing of one molecule  $180^\circ$  vertically to superimpose it on the other drawing.
- The two drawings are of only one molecule that is meso, not two different molecules.
- A meso compound is achiral and does not rotate light.



## Properties of Enantiomers

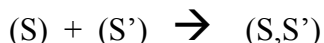
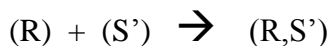
- Enantiomers have identical MP's, density, solubility, but opposite light rotations.
- Enantiomeric solids have mirror image crystal structures, as Louis Pasteur observed with sodium ammonium tartrate in 1848 (See Fig 5.6).
- Two molecules that are diastereomers, however, generally have different properties altogether.

## Racemic Mixture

- A racemic mixture contains equal amounts of both enantiomers.
- It does not rotate light because the two enantiomers cancel each other completely.
- It is denoted by either ( $\pm$ ) or the prefix *d,l*- in front of the name.

## Resolution

- Resolution is the separation of the two enantiomers in a racemic mixture.
- Resolution can be achieved by chemical reaction with only one enantiomer of another chiral molecule. If the reaction adds a 2<sup>nd</sup> chiral center with only one configuration, then the products would be two diastereomers. For instance, if racemic (R) and (S) react with a different (S') molecule to add its chiral center, the products would be (R,S') and (S,S').
- The two diastereomeric products can be separated based on a physical property difference, such as MP or BP. Then, the reaction can be reversed to separately isolate the two original enantiomers.
- Racemic Enantiomers (R and S) become Diastereomers when molecule S' is added.



## Review of Isomerism

- Constitutional isomers have the same number of each atom, but they have different bonding, such as with n-butane and 2-methylpropane. Both are C<sub>4</sub>H<sub>10</sub>, but one is a straight chain, and the other is branched.
- Stereoisomers have same bonding, as well as the same number of each atom. But, they have different geometries, that is, different spatial arrangements. Stereoisomerism includes both enantiomers and diastereomers.
- Diastereomers can be either cis/trans (about a double bond or ring) or configurational (same chiral centers, but different configurations).

## 1-Butene Hydration (with H<sub>2</sub>O and an acid catalyst)

- Covered in Section 8.12 of McMurry. See Figure 8.11
- Adds an H to C #1 and an OH to C #2 to create racemic 2-butanol.
- The intermediate 2° carbocation is sp<sup>2</sup> and planar. This means it is flat and has two sides (top and bottom).
- The H<sub>2</sub>O molecule can add equally as well to either side, so that the product is a racemic mixture of equal proportions of S and R.
- H<sup>+</sup> is then removed to create the alcohol.
- Generally, if a new chiral center is formed from **achiral** (optically inactive) reactants, then the product will be a **racemic** mixture (also optically inactive).
- Enzyme-catalyzed biological reactions are often exceptions to that rule, and often result in only one enantiomer of a chiral molecule.

## Chiral Alkene Hydration

- Covered in Section 8.13 of McMurry. See Figure 8.12.
- R-4-methyl-1-hexene (is chiral at C #4, and is also optically active) can be hydrated to create 4-methyl-2-hexanol, which has a 2<sup>nd</sup> chiral center at C #2.
- The 2<sup>nd</sup> chiral center can be either R or S, however not in equal amounts because the two sides of the intermediate 2° carbocation do not react equally.
- So, the product mixture is two diastereomers (2R,4R and 2S,4R), but they are not formed in equal amounts.
- Generally, if a new chiral center is formed from **chiral** (optically active) reactants, then the product will be an unequal mixture of **diastereomers** (also optically active).

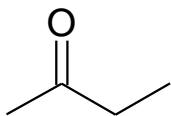
## Chirality of N, P and S

- N normally has three bonds and one lone pair. If the three substituents are all different, then the lone pair can function as the fourth substituent, so that all four are different.
- So, N with three different substituents and a lone pair is chiral.
- However, the  $sp^3$  N can briefly rehybridize to  $sp^2$  so that the lone pair becomes a p orbital. The three  $sp^2$  orbitals are then all in one plane, and the two lobes of the p orbital are on both sides of the plane. When the N returns to  $sp^3$ , the lone pair may reform on the opposite side of its original location.
- Essentially, this allows N to very quickly invert between R and S configurations.
- For this reason, chiral N's are self-racemizing, and optical activity is not observed.
- Trivalent phosphorus compounds (phosphines) with three different substituents are also chiral in the same manner as N. P's inversions, however, are much slower than N's. So, chiral phosphines can be isolated.
- Sulfur can be trivalent if it has a positive charge, as in sulfonium cations ( $R_3S^+$ ). As with P, the S inversion is slow enough that chiral sulfoniums can be isolated.

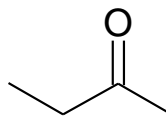
## Prochirality

- A prochiral center is a C that can become a chiral center in one reaction.
- If 2-butanone ( $CH_3COCH_2CH_3$ ), which is a ketone, is hydrogenated with  $H_2$  and a catalyst, it becomes 2-butanol ( $CH_3CHOHCH_2CH_3$ ), which is an alcohol.
- C #2 in the alcohol product is a chiral center. So, C #2 in the ketone reactant is prochiral.
- The carbonyl carbon (C #2 in the reactant) is  $sp^2$ , which is flat and planar, so it has two sides (faces): top and bottom.
- The substituents' priorities for the two faces can be ranked, just as with a chiral center. The difference is that clockwise is called Re (not R), and CCW is called Si (not S).

Re (goes CW)

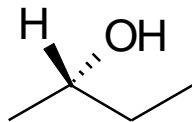


Si (goes CCW)



- Picture an  $H_2$  molecule adding to the top of the two faces, so that the H atom which attaches to the C is up (wedged), and the other H adds to make an OH that is down (dashed).

Re becomes S



Si becomes R

