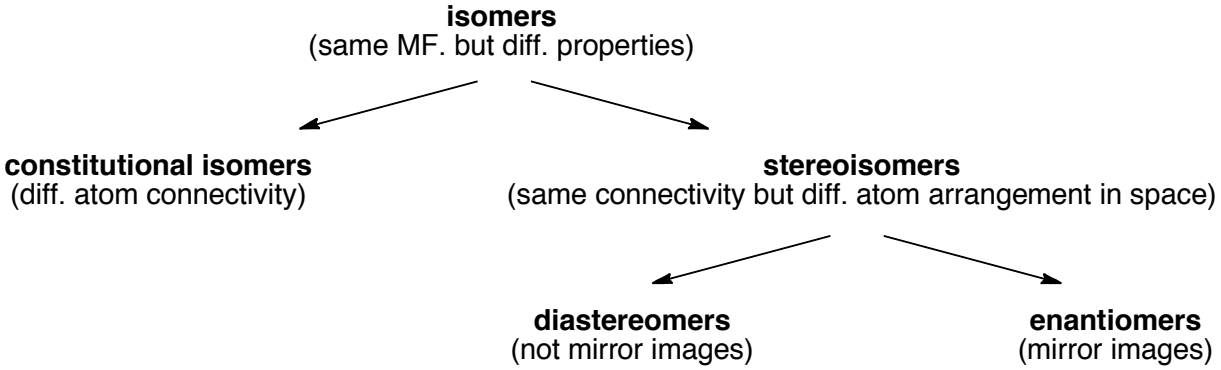
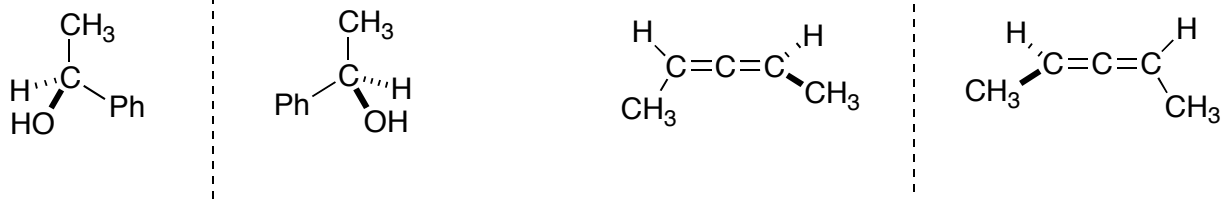
Chemistry 0310 - Organic Chemistry 1

Chapter 5. Stereochemistry

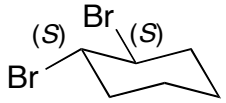
The stereochemistry of an organic molecule is a consequence of its three-dimensional structure. Compounds with different connectivity *or* stereochemistry are isomers and have different properties in a biological environment.

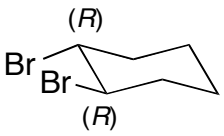


Chiral compounds are not superimposable on their mirror images, whereas **achiral** molecules have identical mirror images. The presence of an internal plane of symmetry (mirror plane), a point of inversion, or an S_4-axis (rotation reflection axis, improper rotation axis) is characteristic for achiral objects. **Chirality** is therefore a property of structures that contain elements of asymmetry, such as an **asymmetric carbon** atom or center of asymmetry (a C with four unequal substituents), an axis of asymmetry (as in an allene), or a plane of asymmetry.



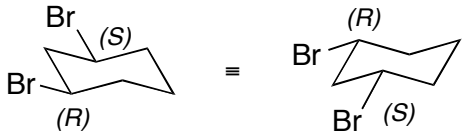
A name such as *trans*-1,2-dibromocyclohexane specifies the **relative configuration** but not the **absolute configuration** of a molecule. The former is indicated by *cis/trans* relationships and the latter by the R,S-nomenclature according to the CIP (Cahn-Ingold-Prelog) system.

trans-1,2-dibromocyclohexane can be 

or 

In the CIP system, the substituents on an asymmetric carbon atom are assigned decreasing priorities based upon decreasing molecular weight. If the priority in the first shell of substituents is ambiguous, further sets of atoms are compared. With the atom with the lowest priority pointing away from the viewer, a circular path is traced from the atom of the highest priority to the atoms of the next lower priorities. If the circular path is clockwise, the enantiomer is assigned the (*R*)-stereochemistry, if it is counterclockwise, we assign the (*S*)-stereochemistry.

If a molecule is achiral, but nonetheless contains asymmetric carbons, it is called a ***meso*** compound.

meso-1,3-dibromocyclohexane: 

A 1 : 1 mixture of enantiomers is called a **racemic mixture**. Mixtures that are enriched in one enantiomer over another are called **scalemic** or **enantiomerically enriched**. Enantiomers rotate the plane of polarized light in equal amounts but in opposite directions. The **specific rotation** is the degree that the plane of polarization of the light is rotated after passing through a solution of an enantiomer.

$$[\alpha]_D^{25} = specific\ rotation = \frac{\alpha}{c \bullet l}$$

D: sodium-D-line (589 nm); α: observed rotation angle; c: concentration in g/mL; l: length of cell in dm.

There is no intuitive correlation between the configuration of enantiomers and the sign (+, or -) or the value of their specific rotation, but *ab initio* calculations of Rosenfeld's equation can be used to compute the optical rotation values. The rotation of an enantiomerically enriched mixture can be used to assess its degree of **optical purity** (ratio of enantiomers) if the $[\alpha]_D$ of a pure enantiomer is known. For two enantiomers A and A':

$$\%\ \text{optical purity} = \%\ \text{enantiomeric excess (ee)} = \frac{[A]-[A']}{[A]+[A']} \times 100 = \frac{[\alpha]_D^{obs}}{[\alpha]_D^{pure enant.}} \times 100$$

The ratio of enantiomers [*A*]/[*A'*] can be calculated accordingly:

$$\frac{[A]}{[A']} = \frac{100 + \%ee}{100 - \%ee}$$

The process of separating enantiomers is called **resolution**. Generally, chemical resolution is performed by the reversible conversion of a racemic mixture to diastereomers, which can be separated according to their different physical properties.
The chlorination of (*S*)-2-bromobutane provides single enantiomers, a racemic mixture, or diastereomers, depending on what carbon atoms are chlorinated. Diastereomers are formed via diastereomeric transition states and are generally obtained in unequal ratios.

Fischer projection formulas are two-dimensional representations of configurations that are still widely used in biochemistry.

Fischer projection formulas of D-(2*S*,3*S*) and *meso*-tartaric acid: