

Some Useful Stereochemical Definitions

For an/the authoritative treatise on the subject of stereochemistry see:

Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*, Wiley, New York, 1994

Stereochemistry is the sub-discipline of chemistry that deals with properties of molecules in the third dimension. Accordingly, molecules do not “have stereochemistry.” Nearly all have stereochemical features and many have relative and/or absolute configuration, but they do not “have stereochemistry.” Please avoid phrases like “the stereochemistry of the molecule was established by ...”

Relationships Between Two Molecules

Isomers: Two distinct molecules having the same molecular formula.

Constitutional Isomers:

Constitution refers to the nature and/or sequence of the bonding between the atoms. *Constitutional isomers* differ in this connectivity. Interconversion of any two constitutional isomers requires rearranging of (interchanging) two or more of the bonds.

Configurational Isomers:

Configuration in molecules refers to a particular spatial arrangement of atoms without regard to arrangements that differ only by torsion about single bonds. *Configurational isomers* share the same constitution, but they differ in the configuration about one or more stereogenic centers (which most often are coincident with atomic nuclei) in the molecule. Interconversion of configurational isomers usually requires interchange of two bonds [examples of exceptions are the (high-barrier) rotation about the double bond of an *E*- and *Z*-olefin pair or about the Ar-Ar bond of a chiral biaryl having large substituents on the carbons *ortho* to the biaryl bond].

Enantiomer:

A configurational isomer that has a non-superimposable mirror image. A chiral molecule (or object) has one and only one enantiomer (or, said another way, every chiral compound exists as a single pair of enantiomers)

Diastereomers:

Configurational isomers of one another that are not enantiomers. Molecules with more than one stereogenic center, exist as diastereomers. If two diastereomers differ in the configuration at one (and only one) stereogenic center, they are epimers.

Conformational Isomers:

Conformation denotes the different spatial arrangements of atoms in a molecule obtained upon torsion about one or more single bonds. *Conformational isomers* have the same molecular formula, constitution, and configuration (if applicable) but different geometries. Interconversion of conformational isomers does not require bond-cleavage and therefore usually occurs with considerably lower energy barriers than the interconversion of constitutional or configurational isomers. Isolable conformational isomers (at which point they are usually then referred to as configurational isomers) usually have a barrier to interconversion of >25 kcal/mole.

Stereoisomers:

Two molecules that differ only in the spatial arrangement of their atoms. Thus, technically, configurational *and* conformational isomers together represent the collection of stereoisomers of a given molecule. Practical usage of the term stereoisomers is typically limited to just the configurational isomers.

Properties of Sites within a Single Molecule

Stereogenic Center:

A point about which interchange of any two groups produces a stereoisomer. These are sometimes called stereocenters. (In the case of tetravalent carbon centers, these are first introduced to most students of organic chemistry, inappropriately, as "chiral centers" or "asymmetric centers.")

Chirotopic Point (a term that is relatively rarely used or encountered)

Any point that resides within a chiral environment (*e.g.*, within a chiral molecule). Points that remain invariant under a rotation-reflection operation of an achiral molecule are achirotopic, (but there are chirotopic points in achiral molecules – *e.g.*, consider the chlorine nuclei in MeCHCl_2).

Topicity [usually of atoms, groups, or faces (*e.g.*, of π -bonds)]:

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|-----------------------|---|
| <u>Homotopic</u> | <ul style="list-style-type: none">• sites with identical molecular environments in every aspect• interchangeable by rotation about a C_n-axis ($n > 1$)• substitution with test groups does not result in formation of an isomer |
| <u>Heterotopic</u> | <ul style="list-style-type: none">• sites with non-identical molecular environments |
| <i>enantiotopic</i> | <ul style="list-style-type: none">• interchangeable by S_n (rotation-reflection) operations only• substitution with test groups results in enantiomers |
| <i>diastereotopic</i> | <ul style="list-style-type: none">• not interchangeable by any symmetry operation• substitution with test groups yields diastereomers |

Properties of Single Molecules

Achiral:

A molecule (or object) is achiral if it is superimposable on its mirror image. A molecule that has reflection symmetry [*i.e.*, a plane of symmetry (C_s) or rotation-reflection symmetry (S_n)] will be achiral. Molecules containing a center of symmetry (often called an inversion center) belong to the $S_{(2, 6, 10, \text{etc.})}$ point-group and are, therefore, achiral.

Chiral:

A molecule (or object) is chiral if it is not superimposable on its mirror image. A molecule that lacks reflection symmetry will be chiral. In particular, note that the term chiral often is—but should never be—equated with collections of chiral molecules that are "optically pure," "optically active," "enantiomerically enriched," or "non-racemic." Importantly [and emphatically], *collections* of molecules (*i.e.*, samples) can be neither chiral nor achiral. Likewise, operations, processes, and activities (like reactions, syntheses, and separations) cannot be chiral or achiral.

Properties of Groups (or Samples) of Chiral Molecules

Racemic:

A group of molecules is racemic if it comprises an equal number of two enantiomers.

Scalemic:

A group of molecules is scalemic if it comprises an unequal mixture of enantiomeric (*i.e.*, chiral) molecules. A property of such a sample is that it will rotate plane polarized light and, therefore, may (properly) be referred to as optically active.

Homo- vs. heterochiral:

Although the term homochiral is sometimes used to describe highly enantiomerically enriched, non-racemic mixtures, it is *incorrect* to do so. Homochiral refers to two (or more) moieties having the same sense of handedness. For example, a homochiral 2:1 ligand:metal complex is one in which both chiral ligands are of the same antipodal nature; the analogous heterochiral complex comprises one ligand of each enantiomer (and, as a result, is a meso (achiral) compound).