1.6 Glossary of stereochemical terms[14]

A values: The free energy difference ($-\Delta G°$) between equatorial and axial conformations of a substituted cyclohexane, positive if equatorial is preferred. For a compilation of values, see ref. [64], and references cited therein.

$A^{1,2}$, $A^{1,3}$ strain: see *allylic strain*.

Absolute asymmetric synthesis: A synthesis in which *achiral* reactants are converted to *nonracemic, chiral* products, and where the *enantioselectivity* is induced only by an external force such as circularly polarized light in a photochemical reaction [65].

Absolute configuration: The arrangement in space of the ligands of a *stereogenic unit*, which may be specified by a stereochemical descriptor such as *R* or *S, D* or *L, P* or *M*. See also *chirality sense, chirality element, stereogenic element*

Achiral: See *chiral*.

Achirotopic: See *chirotopic*.

Allylic strain: The destabilization of a molecule, or an individual conformation, by *van der Waals* repulsion between substituents on a double bond and those in an allylic position [66]. Two types have been identified (see bold bond in figure): $A^{1,2}$ strain occurs between substituents on an allylic carbon and the adjacent sp^2 carbon. $A^{1,3}$ strain occurs between substituents on an allylic carbon and the distal sp^2 carbon. The latter effect can be quite strong [67]. Originally [66], the terms were defined in the context of cyclohexane derivatives, but more recently the effects have been recognized as important factors in conformational dynamics of acyclic systems [67].
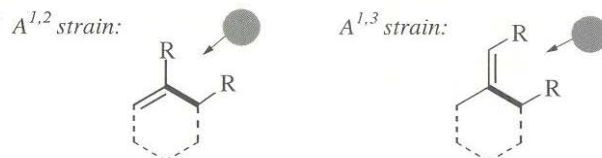
Alternating symmetry axis (S_n): An axis about which a rotation by an angle of $360/n$, followed by a reflection across a plane perpendicular to the axis results in an entity that is indistinguishable from (superimposable on) the original. Also called a rotation-reflection axis. See also *symmetry axis*.

Alpha (α), beta (β): Stereodescriptors used commonly in carbohydrate [68] and steroid [69] nomenclature to describe *relative configuration*. In steroids, "any [substituent] that lies on the same side of the ring plane as the C_3-hydroxyl group of cholesterol [see illustration] is described as β-oriented, and the carbon to which the group is joined has the β-configuration. The opposite orientations and configurations are designated α" [69]. The α, β nomenclature is often extended to other ring systems, but a reference stereocenter must be

---

14 Note that other terms defined in this glossary are italicized.

specified, either explicitly or by convention (see for example ref. [70]). Often, reference is made to a 2-dimensional drawing in which a reference plane is specified. If the reference plane is horizontal, β is above and α is below the plane, as illustrated below. If the plane is vertical, β is toward the viewer.

In carbohydrates, the β-anomer has the C_1-hydroxyl or alkoxyl group on the opposite side of a *Fischer projection* as the substituent (∗) that defines D or L (see *Fischer-Rosanoff convention*); this need not be the position at which the ring is closed. The α-anomer has the two on the same side [68].
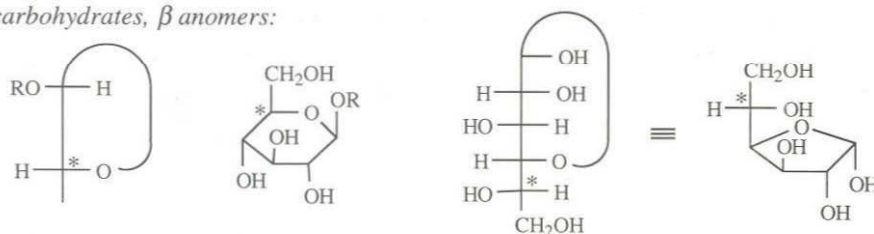
steroids

specified plane within other molecules
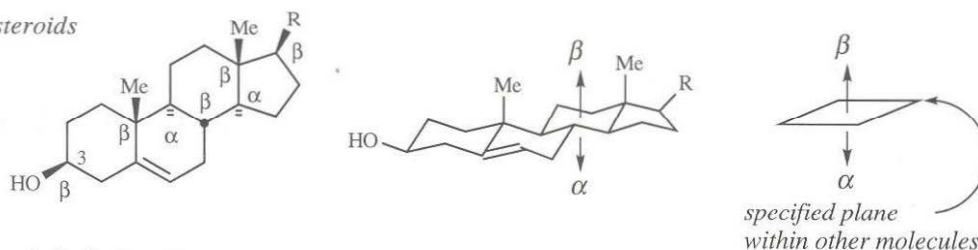
carbohydrates, α anomers:
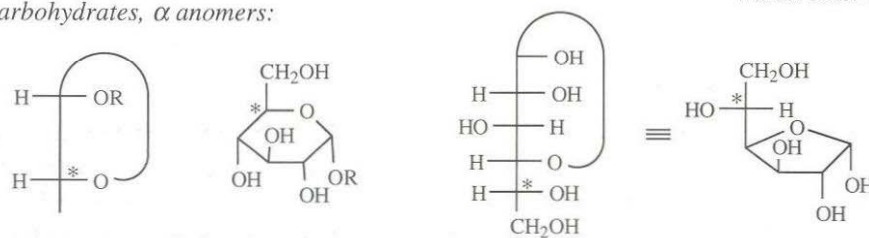
*carbohydrates, β anomers:*

Angle strain: Destabilization of a molecule due to a variation of bond angles from "optimal" values (109° 28' for a tetrahedral atom). Also called *Baeyer strain*.

Anomeric effect: Originally, the unexpected stability of a C-1 alkoxy group of a glycopyranoside occupying the *axial* position. This effect is now more generally considered to be a conformational preference of an X–C–Y–C moiety for a *synclinal (gauche) conformation* (where X and Y are hetero atoms, and at least one is a nitrogen, oxygen, or fluorine). See illustration, below [71,72].

synclinal (gauche)   *antiperiplanar*
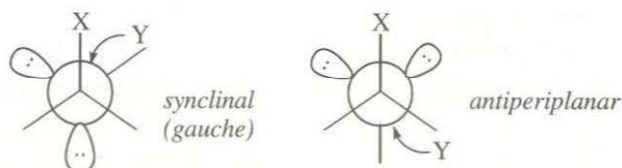
Antarafacial, suprafacial: In a reaction where a molecule undergoes two changes in bonding (either making or breaking), the relative spatial arrangement is suprafacial if the changes occur on the same face of the molecular fragment and antarafacial if on opposite faces [73].

Anti: See *torsion angle; syn, anti.* Also used to describe *antarafacial* addition or elimination reactions [74]. Formerly used to describe the configuration of azomethines such as oximes and hydrazones (See *E, Z*).

Anticlinal: See *torsion angle.*

Antiperiplanar: See *torsion angle.*

Aracemic: Synonym for *nonracemic* [75]. See also *scalemic.*

Asymmetric: Lacking all symmetry elements, *i.e.,* belonging to symmetry point group C_1.

Asymmetric carbon atom: van't Hoff's definition for a carbon atom having four different ligands (*i.e.* Cabcd). See also *stereogenic center, stereogenic element.*

Asymmetric center: See *stereogenic center.*

Asymmetric destruction: See *kinetic resolution.*

Asymmetric induction: The preferential formation of one *enantiomer* or *diastereomer* over another, due to the influence of a *stereogenic element* in the substrate, reagent, catalyst, or environment (such as solvent). Also, the preferential formation of one configuration of a stereogenic element under similar circumstances. When two reactants of a reaction are stereogenic, the stereogenic elements of each reactant may operate either in concert (matched pair) or in opposition (mismatched pair). This phenomenon is known [58,59] as double asymmetric induction, or double diastereoselection. See Section 1.5.

Asymmetric synthesis: A reaction or reaction sequence that *selectively* creates one configuration of one or more new *stereogenic elements* by the action of a chiral reagent or auxiliary, acting on *heterotopic* faces, atoms, or groups of a substrate. The stereoselectivity is primarily influenced by the chiral catalyst, reagent, or auxiliary, despite any stereogenic elements that may be present in the substrate. See Section 1.2.

Asymmetric transformation: The conversion of a mixture (usually 1:1) of stereoisomers into a single stereoisomer or a mixture in which one isomer predominates. An *"asymmetric transformation of the first kind"* involves such a conversion without separation of the stereoisomers. An *"asymmetric transformation of the second kind"* also involves separation, such as an equilibration accompanied by selective crystallization of one stereoisomer [76]. The terms "first- and second-order asymmetric transformations" to describe these processes are inappropriate. See also *stereoconvergent.*

Atropisomers: Stereoisomers arising from *restricted rotation* around a single bond (*i.e., conformers*), with a high enough rotational barrier that the isomers can be isolated (16 - 20 kcal/mole at room temperature), such as *ortho-*

disubstituted biaryls [77]. The chirality sense of a conformation may be described using the *P, M* system.

Axial, equatorial: Bonds or ligands of a cyclohexane (or saturated 6-membered heterocycle) chair conformation. The axial bonds are parallel to the C_3 (S_6) axis of cyclohexane (or the corresponding position of a heterocycle), and each equatorial bond is parallel to two of the ring bonds. In a cyclohexene, the corresponding allylic bonds or ligands are called pseudoaxial (ax') and pseudoequatorial (eq'). In a trigonal bipyramidal structure, the three ligands in a plane with the central atom are also known as equatorial.
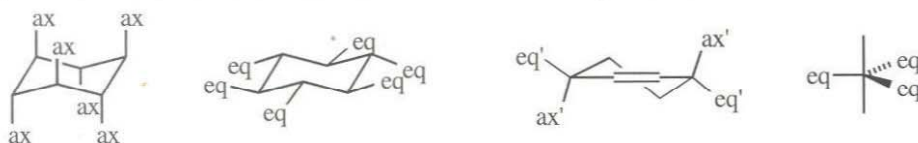
Axis of chirality: See *chirality element, stereogenic axis, stereogenic element.*

Baeyer strain: See *angle strain.*

Bisecting and eclipsing conformations: In a structure with the grouping $R_3C–C=X$, the conformation in which a torsion angle R-C-C=X is *antiperiplanar*, and the torsion angles to the other two R groups is equal or nearly so is the *bisecting* conformation. The conformation in which a torsion angle R-C-C=X is *synperiplanar* is called *eclipsing.*
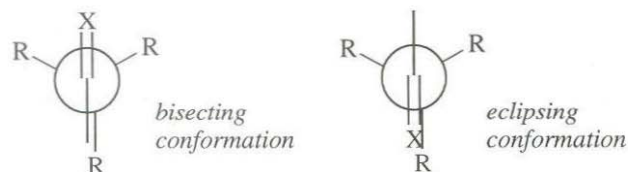

Boat: See *chair, boat, twist;* and *half-chair, half-boat.*

Bond opposition strain: See *eclipsing strain.*

Bowsprit, Flagpole: In the cyclohexane boat conformation the ligands on the two carbons that are out of the plane of the other four. Endocyclic ligands are *flagpole,* exocyclic ligands are *bowsprit.*

Bürgi-Dunitz trajectory: The angle of approach of a nucleophile toward a carbonyl carbon, 107° (probably more accurately 105±5°) [78-80]. See Section 4.1.

The Bürgi-Dunitz trajectory
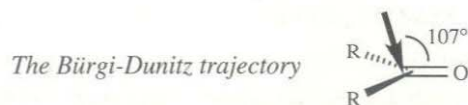
Cahn-Ingold-Prelog method: See *CIP method.*

CDA, chiral derivatizing agent: A reagent of known enantiomeric purity that is used for derivatization and analysis of enantiomer mixtures by spectroscopic or chromatographic means. See Section 2.3.1.

Center of chirality: See *stereogenic center.*

Center of symmetry, center of inversion (i): A point in an object that is the origin of a set of Cartesian axes, such that when all coordinates describing the object (x, y, z) are converted to $(-x, -y, -z)$, an identical entity is obtained. Equivalent to a two-fold *alternating axis* (S_2).
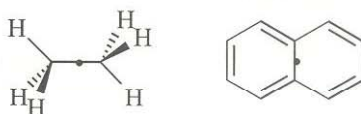
Centers of inversion (•)

Chair, boat, twist-boat: The cyclohexane *conformation* (point group D_{3d}) in which carbons 1, 2, 4, and 5 are coplanar and atoms 3 and 6 are on opposite sides of the plane is the *chair.* When atoms 3 and 6 are on the same side of the '1-2-4-5' plane, and also lie in a mirror plane, the conformation (point group C_{2v}) is called a *boat.* If atoms 3 and 6 are moved to either side of the boat's '3-6' mirror plane, the conformation (point group D_2) is the *twist-boat.* The chair and twist-boat conformations are at energy minima ($\Delta G = 5.6 - 8.5$ kcal/mole for cyclohexane [81]) while the boat is at a higher energy saddle-point. The *twist-boat* is sometimes called the *skew* conformation (however, see *torsion angle*). These terms are also applied to similar conformations of substituted cyclohexanes and to heterocyclic analogs. See also *axial, equatorial.*

chair   *boat*   *twist-boat*
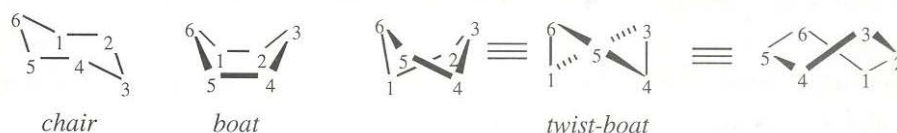
Chair-chair inversion: See *ring reversal*

Chiral: A geometric figure, or group of points is chiral if it is nonsuperimposable on its mirror image [82]. A *chiral* object lacks all of the second order (improper) symmetry elements, σ (*mirror plane*), i (*center of symmetry*), and S (*rotation-reflection axis*). In chemistry, the term is (properly) only applied to entire molecules, not to parts of molecules. A chiral compound may be either *racemic* or *nonracemic.* An object that has any of the second order symmetry elements (*i.e.,* that is superimposable on its mirror image) is *achiral.* It is inappropriate to use the adjective *chiral* to modify an abstract noun: one cannot have a chiral opinion and one cannot execute a chiral resolution or synthesis.

Chiral auxiliary: A chiral molecule that is covalently attached to a substrate so as to render enantiotopic faces or groups in the substrate diastereotopic. After the

diastereoselective reaction, the auxiliary should be removable and recoverable intact. See Section 1.2.

Chirality: The property that is responsible for the nonsuperimposablility of an object, or a group of points, with its mirror image.

Chirality axis: See *chirality element.*

Chirality center: See *chirality element.*

Chirality element, element of chirality: A *stereogenic axis, center,* or *plane* that is *reflection variant*. See also *stereogenic element.*

Chirality plane: See *chirality element.*

Chirality sense: The property that distinguishes enantiomorphs such as a right or left threaded screw. For molecules, the chirality sense may be described by *R, S;* or *P, M.* See also *absolute configuration.*

Chirality transfer: Asymmetric induction in which one stereogenic element is sacrificed as another is created.

Chiroptic: Referring to the optical properties of chiral substanccs, such as optical rotation, circular dichroism, and optical rotatory dispersion.

Chirotopic: The property of "any atom, and, by extension, any point or segment of the molecular model, whether occupied by an atomic nucleus or not, that resides in a chiral environment" [83]. *Achirotopic* is the property of any atom or point that does not reside in a chiral environment (see also [84]). "Chirotopic atoms located in chiral molecules are enantiotopic by external comparison between enantiomers. Chirotopic atoms located in achiral molecules are enantiotopic by internal and therefore also by external comparison.... All enantiotopic atoms are chirotopic" [83].

CIP (Cahn, Ingold, Prelog) method, CIP system: The CIP sequencing rules establish the conventional ordering of ligands for the unambiguous description of absolute configuration by descriptors such as *R, S; P, M; E, Z.*

There are several steps in the method, which is abbreviated as follows (for the definitive rules, see ref. [85,86]:

Ligancy complementation: All atoms other than hydrogen are complemented to quadriligancy by providing one or two duplicate representations of any ligands which are doubly or triply bonded, respectively, and then adding the necessary number of phantom atoms of atomic number zero [85]. For example, the representation of a carbonyl is expanded as follows:
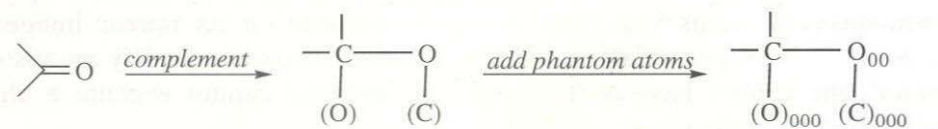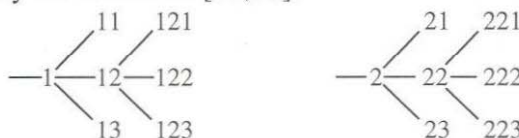

where 0 denotes a phantom atom.

Sequence rules:

0.   Nearer end of axis or side of plane precedes further.

1.   Higher atomic number precedes lower.

2.   Higher atomic mass precedes lower.

3.   Cis (Z) precedes trans (E). Some special cases require the following qualification [86]: when two ligands (indistinguishable by rules 1 and 2) differ by one having the ligand of higher rank in a cis position (Z) to the core of the stereogenic unit, and the other in a trans position (E), the former takes precedence.

4.   Like pair precedes unlike pair. (For a listing of like and unlike pairs, see *l,u* in this glossary).

5.   *R* precedes *S;* and *M* precedes *P*

To implement the sequence rules, it is useful to construct a digraph of the ligands to be compared, as shown below. The ligands of the proximal atoms (1 and 2) are placed in the digraph such that 11 has precedence over 12, 12 over 13, 21 over 22, etc. Another layer of ligands, labeled 111, 112, ... 233, could be constructed if necessary (only one such set is shown below). In implementing the sequence rules, 1 is first compared with 2. If there is no difference, 11 is compared with 21, then 12 with 22, etc., until a decision is reached. If comparison of ligands in the next sphere is necessary, the branches of highest priority are followed [85,86].

$$
\begin{array}{ccc}
 & 11 \quad 121 & \\
-1\!\!&\!\!\!-12\!-\!122 & \\
 & 13 \quad 123 &
\end{array}
\qquad
\begin{array}{ccc}
 & 21 \quad 221 & \\
-2\!\!&\!\!\!-22\!-\!222 & \\
 & 23 \quad 223 &
\end{array}
$$

For the vast majority of cases, *CIP* rank can be determined using only ligancy complementation and sequence rule 1. The rules result in the following (descending) sequence of CIP rank for several common functional groups [87]: $COOCH_3$, COOH, COPh, CHO, $CH(OH)_2$, *o*-tolyl, *m*-tolyl, *p*-tolyl, Ph, C≡CH, *t*-Bu, cyclohexyl, vinyl, isopropyl, benzyl, allyl, *n*-pentyl, ethyl, methyl, D, H.

For the assignment of CIP descriptors, see *R, S; P, M;* and *E, Z.*

cis, trans: A stereochemical prefix to describe the relationship between two ligands on a double bond or a ring: cis if on the same side, trans if on opposite sides. For alkenes, the cis-trans nomenclature can be ambiguous and the *E, Z* descriptor is preferred. In a ring, the reference conformation (real or hypothetical) is planar, and approximates a circle or an oval, not a kidney. See *cis-trans isomers.*

cis   *(circle/oval)*   *(kidney)*   *trans*
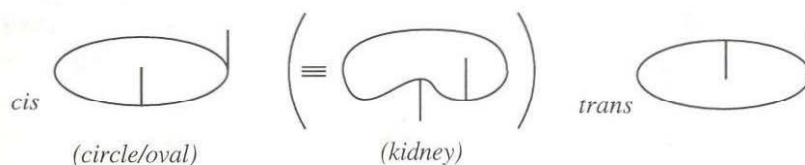
cisoid conformation (usage discouraged): See *s-cis, s-trans.*

cis-trans isomers: Stereoisomeric alkenes or cycloalkanes (or heterocyclic analogs), that differ in the position of ligands relative to a reference plane: cis if on the same side, *trans* if on opposite sides.

trans   *cis*   *cis*   *cis*   *trans*
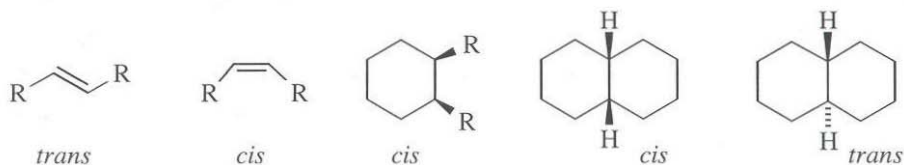
Clinal: See *torsion angle.*

Configuration: The arrangement of atoms in space that distinguishes *stereoisomers*, excluding *conformational isomers. Atropisomers* are a special case of conformational isomers that, because they are isolable at room temperature, may have an absolute configuration descriptor assigned to the *stereogenic axis.* See also *absolute configuration, chirality sense, relative configuration.*

Conformation: In a molecule of a given *constitution* and *configuration,* the spatial array of atoms affording distinction between *stereoisomers* that can be interconverted by rotation around single bonds. The *chirality sense* of conformations may be specified using the *P, M* nomenclature.

Conformational analysis: The analysis of the chemical and physical properties of different conformations of a molecule.

Conformational isomers (conformers): Stereoisomers at potential energy minima (local or global) having identical *constitution* and *configuration,* which differ only in *torsion angles.*

Constitution: The description of the number and kind of atoms in a molecule and their bonding (including bond multiplicities, but not *relative* or *absolute configuration,* or *conformation*).

Constitutional isomers: Isomers that differ in connectivity, such as CH_3CH_2OH and CH_3OCH_3.

Cram's rule (cyclic model): A model for predicting the major stereoisomer resulting from nucleophilic addition to an aldehyde or a ketone having an adjacent stereocenter that is capable of chelation (especially 5-membered ring chelation). After chelate formation, the nucleophile adds from the side opposite the larger of the remaining substituents on the α-stereocenter [48]. See Section 4.2.
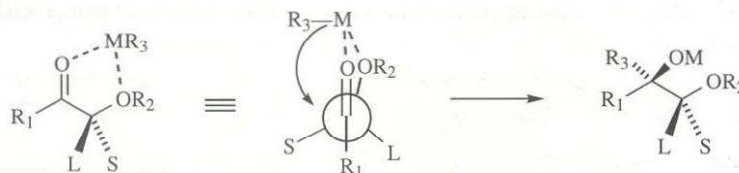
Cram's rule (open chain model): A model to predict the major stereoisomer resulting from nucleophilic addition to a ketone or aldehyde having an adjacent *stereocenter.* The rule originally formulated by Cram in 1952 [47] has evolved into the current Felkin-Anh formulation [79,88,89], illustrated below. In the transition structure, the largest substituent of the stereocenter, or the substituent having the lowest-lying σ^* orbital (L) is perpendicular to the carbonyl, and the nucleophile attacks from the opposite side, on a trajectory that places it approximately 107° away from the carbonyl (the *Bürgi-Dunitz trajectory*). The favored transition structure (a), has this trajectory nearly eclipsing the site of the smaller of the two remaining substituents. See Section 4.1.

favored TS
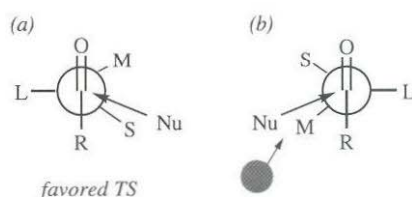
CSA (Chiral solvating agent): A diamagnetic additive of known enantiomeric purity used to induce anisochrony in *enantiomers* of a *racemate* for NMR analysis. See Section 2.3.4.

CSP (Chiral stationary phase): A *nonracemic* chiral stationary phase for the chromatographic separation of *enantiomers.* See Section 2.4.

CSR (Chiral shift reagent): A paramagnetic lanthanide complex of known enantiomeric purity used to induce anisochrony in *enantiomers* of a *racemate* for NMR analysis. See Section 2.3.3.

D, L: See *Fischer-Rosanoff convention*

d, l, dl: Obsolete alternatives for (+)- and (−)- used to designate the sign of rotation of *enantiomers* at 589 nm (the sodium D line), and (±)- for a *racemate.* Sometimes used as arbitrary descriptors for a single enantiomorph.

Diastereoisomers: See *diastereomers.*

Diastereomer excess (percent diastereomer excess, % de): In a reaction in which two (and only two) diastereomeric products are possible, the percent diastereomeric excess, % de is given by:

$$\% \text{ de} = \frac{|D_1 - D_2|}{D_1 + D_2} \cdot 100 = |\%D_1 - \%D_2| \ .$$

where D_1 and D_2 are the mole fractions of the two diastereomeric products. If a reaction can produce more than two diastereomers, the ratio should itself be reported, or the selectivity reported as *% ds, i.e.,* with the product ratio(s) normalized to 100%. See *diastereoselectivity.*

*Diastereomers (diastereoisomers):* Stereoisomers that are not enantiomers (including alkene *E, Z* isomers).

Diastereoselectivity (percent diastereoselectivity, % ds): In a reaction in which more than one diastereomer may be formed (with mole fractions D_1, D_2, ... D_n produced) the diastereoselectivity is the mole fraction formed of the major product (or the desired product), expressed as a percent:

$$\% \ ds = \frac{D^*}{D_1 + D_2 \ldots + D_n} \cdot 100 \ ,$$

where D^* is the mole fraction of the desired isomer [90]. See Section 1.4. See also *enantioselectivity*.

Diastereotopic: The relationship of two ligands of an atom that are constitutionally equivalent, but in positions that are not symmetry related. Replacement of either ligand yields a pair of diastereomers. Also, faces of a trigonal atom that are not symmetry related, such that addition to either face gives a pair of diastereomers. Reflection variant faces may be specified as *Re* or *Si,* and ligands, L, may be specified as L_{Re} or L_{Si}, by noting on which face of a triangle the ligand in question sits (see *heterotopic*). Note that addition of a ligand to the *Re* face of a trigonal atom affords a tetrahedral array with the new ligand in the L_{Re} position. Reflection invariant descriptors are *re, si,* as illustrated below [91,92]. See also *Re, Si, homotopic,* and *enantiotopic*.
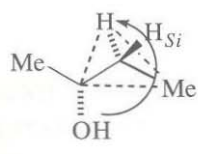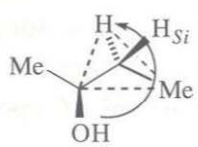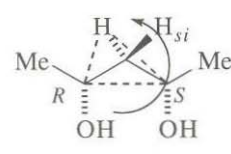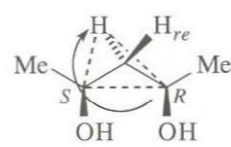
DIASTEREOTOPIC LIGANDS
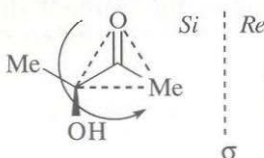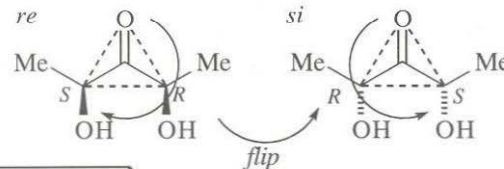

DIASTEREOTOPIC FACES

Dihedral angle: The angle between two defined planes. The term is most commonly applied to vicinal bonds on a *Newman projection*. See also *torsion angle*.

Dissymetric: Obsolete synonym for *chiral*. Not equivalent to *asymmetric*, since chiral substances may have symmetry. See also *asymmetric*.

*Double asymmetric induction:* See *asymmetric induction.*

Dunitz angle: See *Bürgi-Dunitz trajectory.*

E, Z: Descriptors for the arrangement of ligands around double bonds. On either end of the double bond, the group of highest *CIP* rank is identified. If the two higher-ranking groups are on the same side of the double bond, the descriptor of the stereoisomer is *Z* (zusammen = together); if on opposite sides, *E* (entgegen = apart). See also *cis, trans* isomers. For enolates, some authors modify this rule such that the OM ligand (anionic oxygen with its metal) takes the highest priority. See *E(O), Z(O).*
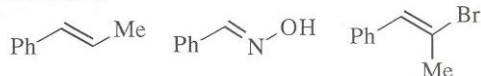
E isomers:　　　　　　　　　　　　　　　　　Z isomers:
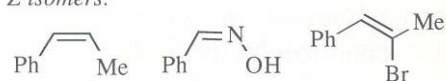
E(O), Z(O): Descriptors for the arrangement of ligands around enolate double bonds. The standard *E/Z* stereochemical descriptor is modified such that the OM group is given priority over the carbonyl substituent, independent of the metal and the other substituent [93]. The priority descriptors for the α-carbon are maintained, as illustrated by the following examples:

Z(O)-enolates:
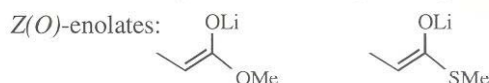
Eclipsed, Eclipsing: Two ligands on adjacent atoms are *eclipsed* if their torsion angle is near 0° (*i.e., synperiplanar*). See also *bisecting conformation, eclipsing strain, torsion angle.*

Eclipsing conformation: See *bisecting conformation.*

Eclipsing strain: See *torsional strain.*

Element of chirality: See *chirality element*

Enantioconvergent: See *stereoconvergent*

Enantiomer: A *stereoisomer* that is not superimposable on its mirror image. See also *enantiomorphous.*

Enantiomer excess, ee (percent enantiomer excess, % ee): For a mixture of a pure *enantiomer* and its *racemate*, the percent excess of the pure enantiomer over the racemate. % ee is given by:

$$\% \text{ ee} = \frac{|E_1 - E_2|}{E_1 + E_2} \cdot 100 = |\%E_1 - \%E_2| \ ,$$

where E_1 and E_2 are the mole fractions of the two enantiomers. See *enantiomer purity.*

Enantiomer purity: A description of the enantiomer composition of a sample, historically expressed as *% ee*. Because this term implies that the impurity is the racemate (not the minor enantiomer), many authors prefer to use *enantiomer ratio, er*, normalized to 100%.

Enantiomer ratio, er: The ratio of two _enantiomers_. When used as an expression of enantiomer purity, this ratio is often normalized to 100% (_i.e.,_ 99:1, 80:20).

Enantiomerically enriched (enantioenriched): A sample that has one _enantiomer_ in excess.

Enantiomerically pure, enantiopure: A sample which contains (within the limits of detection) only one enantiomer. Note that this is not synonymous with _homochiral_ [94].

Enantiomorphous: Not superimposable on its mirror image.

Enantioselectivity (percent enantioselectivity, % es): In a reaction or reaction sequence in which one enantiomer (E_1) is produced in excess, the enantioselectivity is the mole fraction formed of the major enantiomer, expressed as a percent:

$$\% \ es = \frac{E_1}{E_1 + E_2} \cdot 100 \ .$$

See also _diastereoselectivity._

Enantiotopic: The relationship of two ligands of an atom that are related by a _mirror plane, center of symmetry,_ or _alternating axis,_ but not by a simple (proper) _symmetry axis._ Replacement of either ligand yields a pair of _enantiomers._ Also, faces of a trigonal atom that are not symmetry related, such that addition to either face gives a pair of enantiomers. Note that addition of a ligand to the _Re_ face affords a tetrahedral array with the new ligand in the L_{Re} position. The faces may be specified as _Re_ or _Si,_ and reflection variant ligands are best specified as L_{Re} or L_{Si}, as illustrated below [91,92]. See also _Re, Si, homotopic, heterotopic,_ and _diastereotopic._

ENANTIOTOPIC LIGANDS (H)   ENANTIOTOPIC FACES
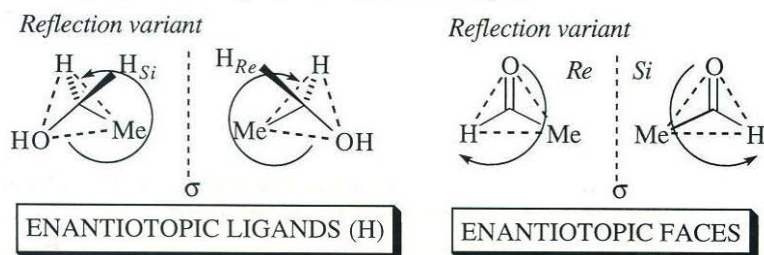
endo, exo: The stereochemical prefix that describes the relative configuration of a substituent on a bridge (not a bridgehead) of a bicyclic system. If the substituent is oriented toward the larger of the other bridges, it is _endo;_ if it is oriented toward the smaller bridge, it is _exo._
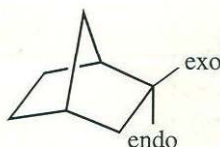
ent: A prefix to the name of a chiral molecule to indicate its _enantiomer._

Envelope: The conformation of a five-membered ring in which four atoms are coplanar, and the fifth (the flap) is out of the plane.

Epimerization: The interconversion of *epimers*.

*Epimers: Diastereomers* that differ in *configuration* at one of two or more *stereogenic units*.

Equatorial: See *axial, equatorial.*

erythro, threo: Terms used to describe relative configuration at adjacent stereocenters. Originally, the term was derived from carbohydrate nomenclature (*cf.* crythrose, threose). In this sense, if the molecule is drawn in a *Fischer projection,* the *erythro* isomer has identical or similar substituents on the same side of the vertical chain and the *threo* isomer has them on opposite sides. In the early 1980s, proposals appeared to redefine these terms based on *zig-zag projections* [95] and *CIP priority* [96], but the latter usages are now discouraged [97]. See *l, u; pref, parf; syn, anti.*

exo: See *endo, exo.*

Felkin-Anh model: See *Cram's rule (open chain model).*

Fischer Projection (or Fischer-Tollens projection): A planar projection formula in which the vertical bonds lie behind the plane of the paper and the horizontal bonds lie above the plane. Used commonly in carbohydrate structures, where each carbon in turn is placed in the proper orientation for planar projection.

Fischer projection   hash/wedge view   ball and stick stereo view
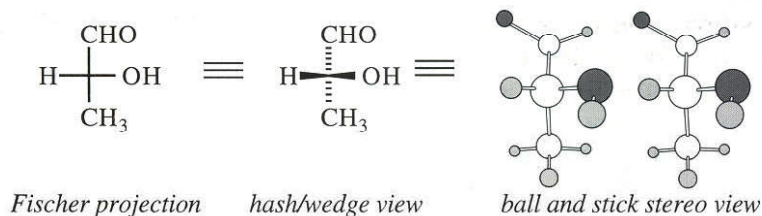
Fischer-Rosanoff convention: A method for the specification of absolute configuration, still in common use for amino acids and sugars. When drawn in a *Fischer projection* with C_1 at the top, if the functional group of the specified stereocenter is on the right, the absolute configuration is D, if on the left, it is L. For amino acids, the reference stereocenter is C_2; for sugars it is the highest numbered stereocenter [98].

D-glucose   L-glucose   D-serine   L-serine

* Reference stereocenter
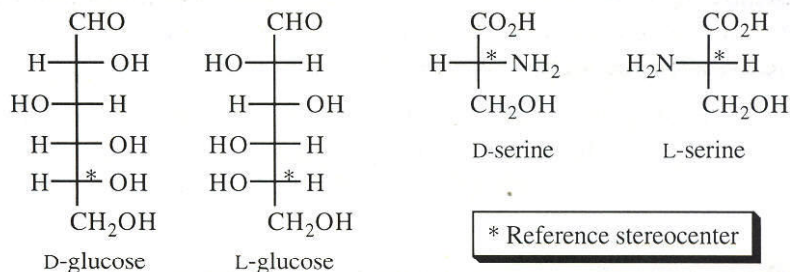
Flagpole: See *bowsprit, flagpole*

Free rotation, restricted rotation: In the context of an experimental observation, *free rotation* is sufficiently fast (*i.e.,* the rotational barrier is sufficiently low) that different *conformations* are not observable. Conversely, *restricted rotation* is sufficiently slow (the barrier is sufficiently high) that conformational isomers can be observed.

*Gauche:* Synonomous with a *synclinal* alignment of groups attached to adjacent atoms (*i.e.,* a torsion angle of near +60° or –60°). See *torsion angle.*

Geometric isomers: Synonym for *cis-trans* double bond isomers.

Half-boat: See *half-chair, half-boat.*

Half-chair, half-boat: Terms used most commonly to describe conformations of cyclohexenes in which four contiguous carbon atoms atoms lie in a plane. If the other two atoms lie on opposite sides of the plane, the conformation is a half-chair; if they are on the same side, it is a half-boat, as shown below. Also used for 5-membered rings, where three adjacent atoms define the plane.
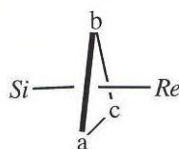
cyclohexene
half-chair
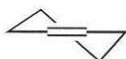
cyclopentane
half-chair

Helicity: The chirality sense of a helix. May be specified by *P, M.*

Heterochiral: See *homochiral.*

Heterotopic: Either *diastereotopic* or *enantiotopic.* Refers to either the *Re* or *Si* half space of a two-dimensional chiral triangle, as shown below [91,92]. See also *Re, Si, enantiotopic, diastereotopic.*

Si ——|—— Re

CIP rank a>b>c

Homochiral: A descriptor for objects and molecules having the same *chirality sense* [99]. Thus, "two equal and similar right hands are homochirally similar. Equal and similar right and left hands are heterochirally similar..." [82]. A set of right shoes, or an assembly of molecules (such as a mixture of amino acids) that have the same *relative configuration* or *chirality sense* are homochiral [99,100]. This term should not be used to describe enantiomerically pure compounds, since the term homochiral describes a relationship, not a property [94].

Homofacial, heterofacial: The *relative configuration* of stereocenters (in different molecules) having three identical ligands and one different is homofacial if the fourth ligand is on the same *heterotopic* face in both, and heterofacial if on opposite faces, as shown below. [91,92,101]. See also *relative configuration.*
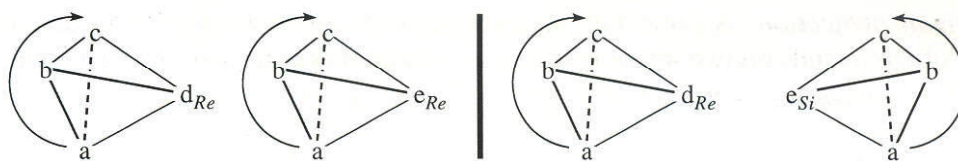
homofacial: *d* and *e* both reside on the *Re* face of the *abc* triangle

heterofacial: *d* is on the *Re* side of the *abc* triangle, whereas *e* is on the *Si* face.

Homotopic: Ligands that are related by an *n*-fold rotation axis. Similarly, faces of a trigonal atom that are related by an *n*-fold rotation axis. Replacement of any of the ligands or addition to either of the faces gives an identical compound. See also *heterotopic, enantiotopic,* and *diastereotopic.*

Inversion: See *Walden inversion, pyramidal inversion,* and *ring inversion.*

Isomers: Compounds that have the same molecular formula but which have different *constitutions* (*constitutional isomers*), *configurations* (*enantiomers, diastereomers*), or *conformations* (*conformational isomers*), and therefore have different chemical and/or physical properties.

Kinetic resolution: The separation (or partial separation) of *enantiomers* due to a difference in the rate of reaction of the two enantiomers in a *racemic mixture* with an *nonracemic chiral* reagent.

l, u: Descriptors for the specification of *relative configuration.* A pair of stereogenic units has the relative configuration *l* (for *like*) if the descriptor pairs are *RR, SS, RRe, SSi, ReRe, SiSi, MM, PP, RM, SP, ReM,* or *SiP*. The pair is specified as *u* (*unlike*) if they have descriptor pairs *RS, RSi, ReS, ReSi, MP, RP, SM, ReP,* and *SiM* [86]. Reflection invariant descriptors (*r, s, re, si, p,* and *m*) may be substituted in place of the reflection variant descriptors above. Note the use of lower case *l* and *u* letters, implying a *reflection invariant* relationship.

lk, ul: An extension of the *l, u* nomenclature to describe topicity. If a reagent of configuration *R* (or the *Re* face of a trigonal atom) preferentially approaches the *Re* face of a trigonal atom, the topicity is *lk* (*like*); it is *ul* (*unlike*) if it approaches the *Si* face. Similarly, the approach of an achiral reagent to diastereotopic faces of a trigonal atom is *lk* if the *Re* face is preferred in the *R* enantiomer, and vice versa; the topicity is *ul* if the *Si* face is preferred in the *R* enantiomer, and vice versa. In short, if the first letters of the two *stereochemical descriptors* are the same, the topicity is *lk*. If they are different, it is *ul* [102]. See the more complete listing of like and unlike pairs under *l, u*. Note the use of lower case *l* and *u* letters, implying a *reflection invariant* relationship. *Lk* and *Ul* would be used if the topicity were *reflection variant,* which would occur if one of the components was reflection invariant.

M, P: See *P, M*.

meso: A stereoisomer that has two or more *stereogenic units*, but which is *achiral* because of a *symmetry plane*. The plane reflects *enantiomorphic* groups.

Newman projection: A projection formula that represents the spatial arrangement of the ligands on two adjacent atoms as viewed down the bond joining them.

2-butanol:

| zig-zag projection | Newman projection of one conformer | ball and stick stereo view |
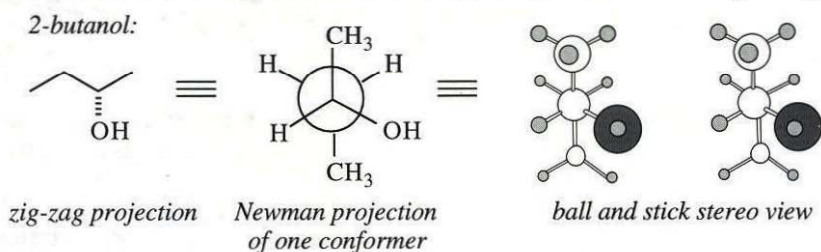
Nonbonded interactions: Attractive or repulsive "through space" forces between atoms or groups in a molecule (intermolecular or intramolecular) that are not directly bonded to each other.

Nonracemic: Not *racemic.*

*Optical activity:* The property of a substance to rotate plane polarized light. See Section 2.2

Optical purity (op, % op): The ratio of the observed *specific rotation* of a substance to the maximum possible rotation of the substance, expressed as a percent:

$$\% \text{ op} = \frac{[\alpha]}{[\alpha]_{max}} \cdot 100 \ .$$

Usually (but not always) it is equal to *enantiomer excess,* or *% ee.* This term is less frequently used now, as enantiomer ratios are often determined by non-polarimetric methods. See Section 2.2.

Optical yield: For a chemical reaction, the *enantiomer excess* of the products relative to that of the starting material, expressed as a percent. In asymmetric synthesis, the denominator may be the ee of the chiral reagent or catalyst.

P, M: Descriptors of chirality sense of a helix. Once the axis of the helix is identified, one chooses the ligands of the highest *CIP rank.* If the smallest angle between the ligands (*i.e.,* ≤ 180°) in a projection is clockwise going from front to rear, the chirality sense is *P* (plus), if counterclockwise, it is *M* (minus) [85,103]. Additionally, *P, M* may be used to describe the chirality sense of a helix of any sequence of atoms as long as they are explicitly identified. Note that it does not matter which end of the helix is viewed.
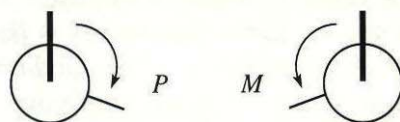
These descriptors can be used to specify enantiomeric *conformers,* such as gauche butane, and the *absolute configuration* of *stereogenic axes* and *planes.* Prelog and Helmchen have recommended the use of *P,M* instead of *R,S* for specifying the absolute configuration of planes and axes of chirality [86]. See also ref. [101], Ch. 14.

P-butane

M-2-hydroxyparacyclophane

M-2,3-pentadiene

P-binaphthol
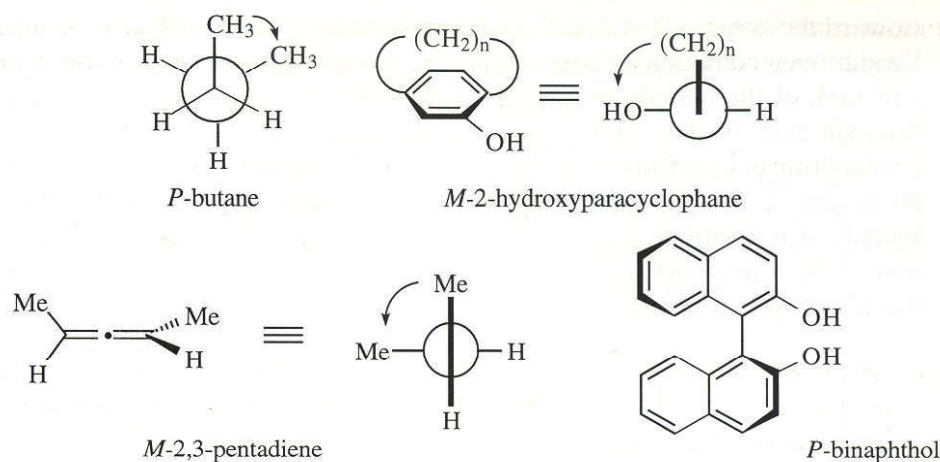
Pitzer strain: See *torsional strain.*

*Planar chirality:* See *stereogenic element.*

Point group (symmetry point group): The symmetry classification of a molecule based on its symmetry elements (axes, planes, etc.).

Pref, parf: Descriptors of relative configuration based on *CIP priority.* The relationship between two chirality centers is pref (priority reflective) if the order of decreasing priority of the three remaining groups at one chirality center is a reflection of the order of decreasing priority of the groups at the other center. When the orders of decreasing priority are not reflective of each other, the relative configuration is parf (priority antireflective). If the chirality centers are not adjacent, the intervening bonds are neglected and the two centers are treated as if they were directly linked. If the two centers are part of a ring, they are treated as if connected by a bond that replaces the shorter path [104].

Priority reflective (pref)

Priority antireflective (parf)
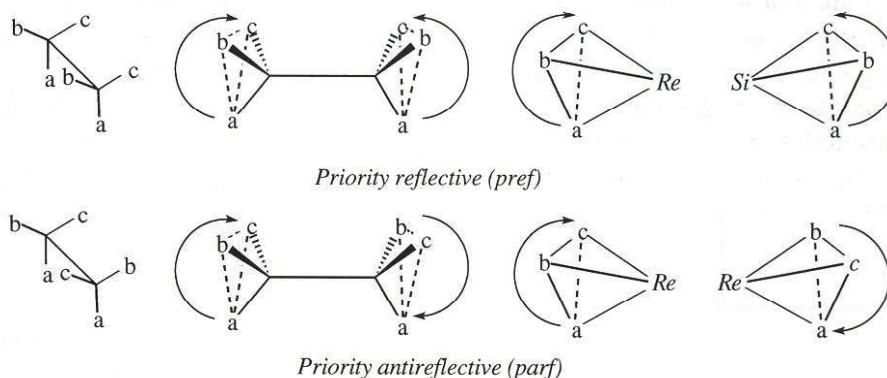
Prochiral: Tetrahedral atoms having *heterotopic* ligands, or heterotopic faces of trigonal atoms, may be described as being prochiral. Note that it is inappropriate to describe an entire molecule as being prochiral [105]. Heterotopic faces are described using *Re, Si* if *reflection variant*, and *re, si* if reflection invariant [91]. If the *CIP priority* of the three ligands is clockwise, the face

(toward the observer) is *Re;* if counterclockwise, it is *Si* [105]. For heterotopic ligands, two conventions have been used to describe prochirality. Both use the CIP rank of the ligands to specify the "prochirality sense" of each ligand. The broader rule is that of Prelog and Helmchen [91,92]. In this method, a tetrahedron is constructed of the four ligands around the prochiral center. If the ligand 'L' is sitting on the *Re* face of the triangle formed by the other three ligands, it is specified L_{Re} (or L_{re} if *reflection invariant*); similarly, the ligand would be specified L_{Si} or L_{si} if on the *Si* face. See also *enantiotopic, diastereotopic, heterotopic,* and *relative configuration.*

CIP rank a>b>c
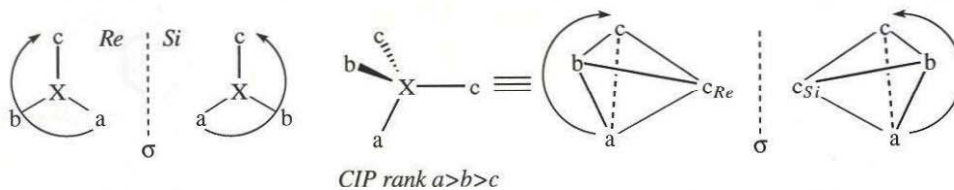
PROCHIRAL FACES   PROCHIRAL ATOMS (X), and LIGAND LABELS

Another convention, used in biochemistry to specify the hydrogen atoms of a prochiral methylene, replaces a hydrogen with a deuterium. If such replacement results in the *R* configuration, the ligand position is *pro-R*. If the *S* configuration is obtained, it is *pro-S* [105]. If *reflection invariant*, the descriptors are *pro-r* and *pro-s*.
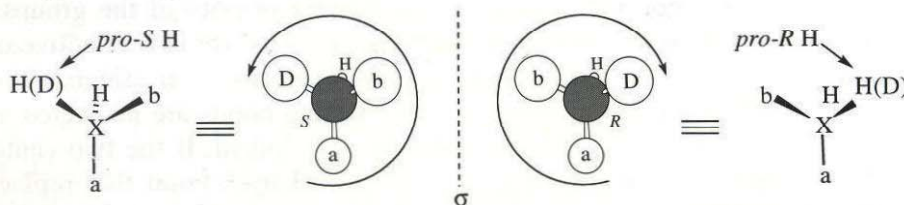
Pseudoasymmetric atom: A *stereogenic* atom of a stereoisomer that has two *enantiomorphic* ligands (reflection invariant), and two other different ligands. Exchange of any two ligands generates a *diastereomeric* compound. The *CIP* descriptors for pseudoasymmetric atoms are *r, s*. Use of this term is discouraged in favor of *stereogenic center.*

C_3 is reflection invariant C_3 is reflection invariant
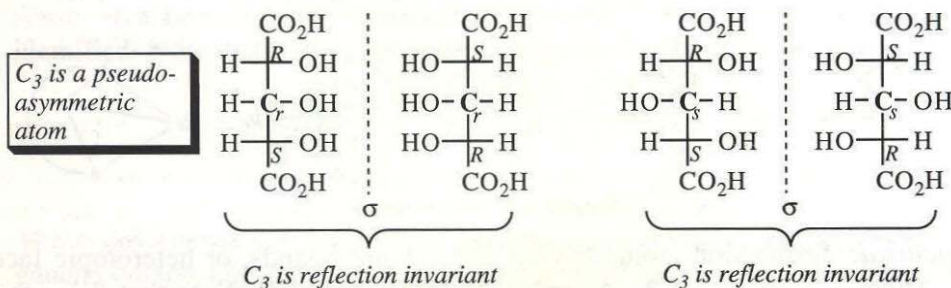
Pseudoaxial, pseudoequatorial: See *axial, equatorial.*

Pseudorotation: Term used by some authors to describe the out of plane motion of the ring atoms in cyclopentane during fast conformational interchange of the many envelope and twist conformers. Usage is discouraged.

Pyramidal inversion: The change of bond directions in a trivalent central atom having a pyramidal (tripodal) arrangement with the central atom at the apex of the pyramid. The inversion appears to move the central atom to a similar position on the other side of the pyramid. If the central atom is *stereogenic*, pyramidal inversion reverses its *absolute configuration*.

r, s: See *pseudoasymmetric atom.*

R, S: *CIP* descriptors for the specification and description of absolute configuration, as follows:

Stereogenic center: After the CIP rank of ligands is determined (see *CIP method*), the tetrahedron is arranged so that the ligand of lowest priority is to the rear. If the order of the other three ligands (highest to lowest) is clockwise, the *absolute configuration* is R (latin *rectus*, right); if counterclockwise, it is S (latin *sinister*, left).

CIP rank a>b>c>d
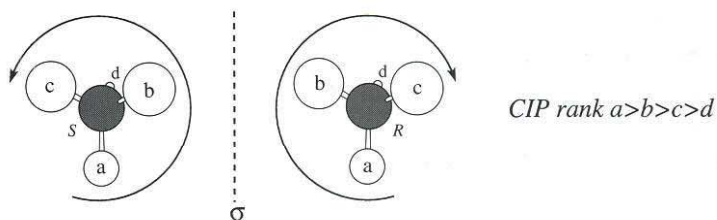
Stereogenic axis: The descriptors may be modified to R_a, S_a when applied to a stereogenic axis [85], although it is usually more convenient to use the P, M system to specify the configuration of stereogenic axes and planes [86].

Stereogenic plane: The descriptors may be modified to R_p, S_p when applied to a stereogenic plane [85], although it is usually more convenient to use the P, M system to specify the configuration of stereogenic axes and planes [86].

The symbols R^* and S^* may be used to describe *relative configuration*. Thus, R^*,R^* describes a racemate of l configuration and R^*,S^* describes a racemate of u configuration. See *l,u.*

rac: A prefix to the name of a chiral molecule to indicate that it is the *racemate.*

Racemate (racemic mixture): An equimolar mixture of two *enantiomers,* whose physical state is unspecified [26]. Some authors restrict the term 'racemate' to a crystalline compound whose unit cell contains equal numbers of enantiomeric molecules and 'racemic mixture' to a mechanical mixture of two crystals that form a eutectic of two enantiomers. The latter is now referred to as a conglomerate [26].

Racemization: The conversion of a nonracemic substance into its racemate.

Re, Si (re, si): Stereochemical descriptors for *heterotopic* faces. If the *CIP priority* of the three ligands is clockwise, the face (toward the observer) is *Re* (latin *rectus,* right); if counterclockwise, it is *Si* (latin *sinister,* left) [105].
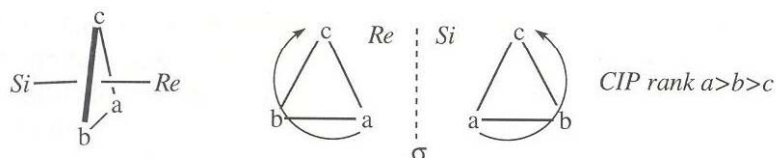
The descriptors may be used to describe the faces of trigonal atoms,
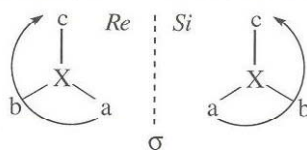
or the ligand position of a tetrahedral stereogenic unit,

Lower case descriptors *(re, si)* are used for the rare cases that are *reflection invariant* [91]:

For examples of reflection invariant stereogenic centers and faces, see *dia-stereotopic,* and *pseudoasymmetric atom.*
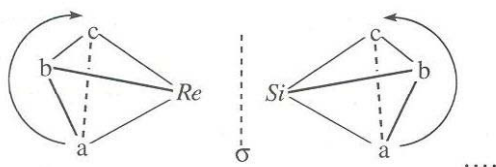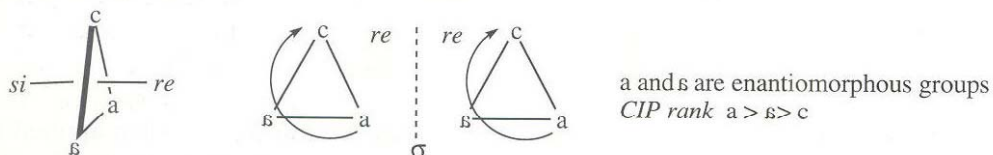
Reflection variant, reflection invariant: The terms used to describe an object and its relationship with its mirror image. If the two are identical, the object is reflection invariant. If the object is *enantiomorphous* to its mirror image, it is reflection variant.

Relative configuration: The *configuration* of any *stereogenic* element with respect to another. Relative configuration is *reflection invariant.* The relative configuration of pairs of *stereogenic* units in the same molecule may be described as *R*, R** or *l* if they have the same *CIP* descriptor, and *R*, S** or *u* if they are different. (See *l, u* for a complete list of like and unlike descriptors.) The term can also be used in an intermolecular sense as follows: if the two molecules contain stereogenic units abcd and abce, and if e and d both sit on the same *heterotopic face,* the two stereogenic units have the same relative configuration. If not, they have the opposite relative configuration. The term

may be applied to starting material and products of a reaction sequence. See also *homofacial, heterofacial.*

Same relative configuration   Opposite relative configuration
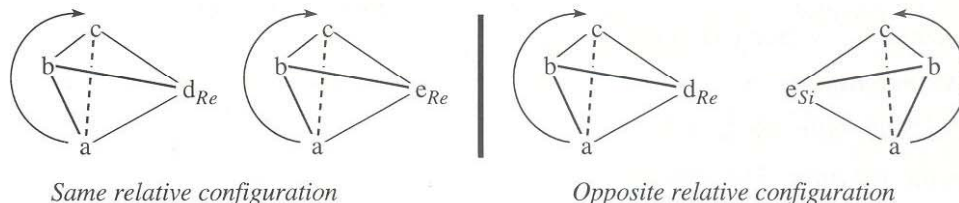
Resolution: The separation of a *racemic mixture* into (at least one of) its component enantiomers. See also *kinetic resolution.*

Restricted rotation: See *free rotation.*

Retention of configuration: The product of a chemical reaction has retained its configuration if the product has the same *relative configuration* as the starting material. See also *Walden inversion, relative configuration.*

Ring inversion (ring reversal): The interconversion of cyclohexane *conformations* having similar shapes (chair - chair), accompanied by interchange of the *equatorial* and *axial* substituents. Similarly, the interchange of any such similarly shaped conformations in a cyclic molecule.

Rotamers: Stereoisomers of the same constitution and configuration, that differ only by torsion angles.

Rotation angle (α): The rotation of the plane of polarized light after passing through an *optically active* sample. If the angle of rotation is clockwise, the sample is dextrorotatory and the sign of rotation is positive (+). If the angle is counterclockwise, the sample is levorotatory, and the sign of rotation is (–). See also *optical activity, specific rotation,* and Section 2.2.

Rotation-reflection axis: See *alternating symmetry axis* .

Rotational barrier: The energy barrier between two *conformers.*

s-cis, s-trans: Conformational descriptors for the single bond linking two double bonds (darkened below). The *synperiplanar* conformation is *s*-cis, and the *antiperiplanar* conformation is *s*-trans. See *torsion angle.*

s-cis   s-trans

Sawhorse formula: A perspective drawing that indicates the spatial arrangements of the ligands on two adjacent tetrahedral atoms. The bond between the two atoms is a diagonal line, with the nearer atom at the bottom.

sawhorse projection   ball and stick view

Scalemic: Not *racemic* [106,107]. Synonomous with *aracemic, nonracemic.*

Sense of chirality: See *chirality sense.*

Sequence rules: See *CIP method.*

Si, si: See *Re, Si.*

Skew: See *chair, boat, twist-boat.*

Specific rotation: The specific rotation of a sample, [α], is defined as:

$$[\alpha]_\lambda^t = \frac{100\alpha}{l \cdot c} ,$$

where *t* is temperature, λ is wavelength of the light, α is the observed *rotation*, *l* is the sample path length (in dm), and *c* is the concentration (in g/100 mL). [α] is normally reported without units, but the concentration and the solvent are usually specified in parentheses after the value of [α]. See Section 2.2.

Staggered conformation: The *conformation* of two tetrahedral carbons is staggered if the *torsion angle* between the ligands is approximately ±60°.
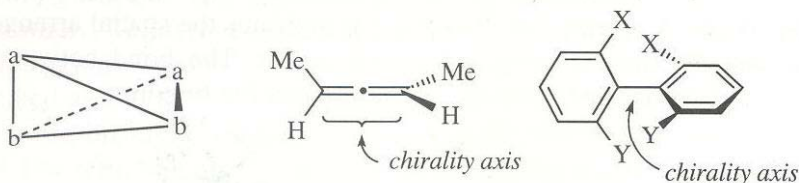
Stereocenter: See *stereogenic center.*

Stereochemical descriptor: A letter-symbol or prefix to specify configuration or conformation, such as *R, S, E, Z, P, M, cis, trans,* etc.

Stereoconvergent: A reaction or reaction sequence is stereoconvergent if stereo-isomerically different starting materials yield the same stereoisomeric product. The sequence may be more specifically labeled either *enantioconvergent* or *diastereoconvergent.*

Stereoelectronic effect: An effect on structure and reactivity due to the orientation and alignment of bonded or nonbonded electron pairs [108].

Stereogenic axis: A set of two pairs of tetrahedrally arranged bonding positions (D_2 or C_{2v} point symmetry), each occupied by two different ligands. Exchange of the ligands of either pair reverses the *absolute configuration.* Examples include unsymmetrically substituted allenes and 2,6,2',6'-tetrasubstituted biphenyls. If the axis is *reflection variant*, it may be called a *chirality axis.* The absolute configuration may be described by either *P, M* or *R, S.* (Note that for a stereogenic axis, $R \equiv M$ and $S \equiv P$). See also *stereogenic element.*

chirality axis   *chirality axis*

Stereogenic center (stereocenter): An atom in a molecule (or a focal set of atoms) with four equivalent tetrahedral bonding positions (T_d point symmetry), occupied by four different ligands. Exchange of any two ligands reverses the

absolute configuration. If the center is reflection variant, it may be called a *chirality center*. If it is reflection invariant, it is sometimes called a *pseudoasymmetric atom,* although usage of this term is discouraged. *Stereogenic center* is thus an extension of the 'asy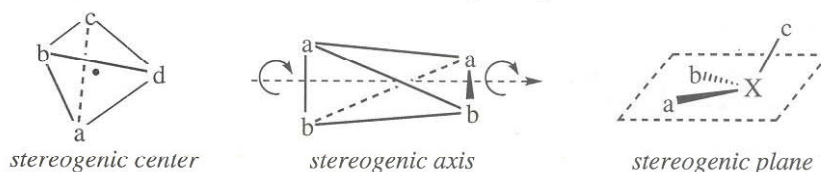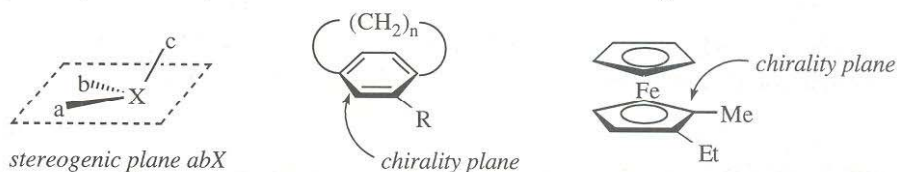mmetric carbon atom' of van't Hoff and LeBel, and now includes species such as N^+abcd and the sulfur atom of unsymmetric sulfoxides (where the fourth 'ligand' is a lone pair), as well as tetrahedral arrays of ligands with T_d symmetry. The *absolute configuration* may be described by the *CIP method.* See *R,S*.

Stereogenic element, stereogenic unit: A *center, axis,* or *plane* in a molecule in which exchange of two ligands leads to a new *stereoisomer.* If the stereogenic element is reflection variant, the elements are *chirality center, chirality axis,* and *chirality plane.* The bonding positions of stereogenic <u>centers</u> have point symmetry T_d; the bonding positions of stereogenic <u>axes</u> have point symmetry D_2 or C_{2v}; the bonding positions of stereogenic <u>planes</u> have point symmetry C_s. As a result, there must be four different ligands (abcd) on a T_d bonding center to create stereogenicity. On an axis, only the two ligands of each pair need be different (ab/ab), the two pairs may be the same. In a stereogenic plane, only one of the ligands in the plane need be different. See also *stereogenic axis, stereogenic center, stereogenic plane.*

stereogenic center   *stereogenic axis*   *stereogenic plane*

Stereogenic plane: A planar structural fragment that, because of *restricted rotation* or structural requirements, cannot lie in a symmetry plane. If the stereogenic plane is reflection variant, the element may be called a *chirality plane.* For example with a monosubstituted paracyclophane, the stereogenic plane includes the plane of the benzene ring. For a 1,2-disubstituted ferrocene, the disubstituted cyclopentadiene lies in a chirality plane. The *absolute configuration* may be specified by either *R, S* or *P, M.* See also *stereogenic element.*

stereogenic plane abX   *chirality plane*   *chirality plane*

Stereoheterotopic: Either *enantiotopic* or *diastereotopic*.

Scalemic: Not *racemic* [106,107]. Synonomous with *aracemic, nonracemic.*

Sense of chirality: See *chirality sense.*

Sequence rules: See *CIP method.*

Si, si: See *Re, Si.*

Skew: See *chair, boat, twist-boat.*

Specific rotation: The specific rotation of a sample, [α], is defined as:

$$[\alpha]_\lambda^t = \frac{100\alpha}{l\cdot c} ,$$

where *t* is temperature, λ is wavelength of the light, α is the observed *rotation*, *l* is the sample path length (in dm), and *c* is the concentration (in g/100 mL). [α] is normally reported without units, but the concentration and the solvent are usually specified in parentheses after the value of [α]. See Section 2.2.

Staggered conformation: The *conformation* of two tetrahedral carbons is staggered if the *torsion angle* between the ligands is approximately ±60°.
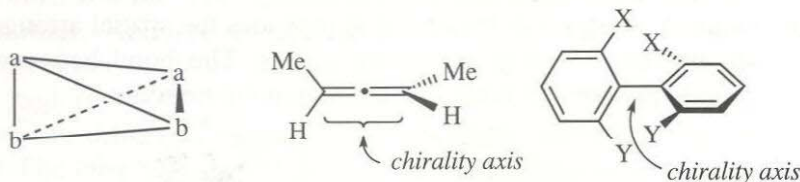
Stereocenter: See *stereogenic center.*

Stereochemical descriptor: A letter-symbol or prefix to specify configuration or conformation, such as *R, S, E, Z, P, M, cis, trans,* etc.

Stereoconvergent: A reaction or reaction sequence is stereoconvergent if stereo-isomerically different starting materials yield the same stereoisomeric product. The sequence may be more specifically labeled either *enantioconvergent* or *diastereoconvergent.*

Stereoelectronic effect: An effect on structure and reactivity due to the orientation and alignment of bonded or nonbonded electron pairs [108].

Stereogenic axis: A set of two pairs of tetrahedrally arranged bonding positions (D_2 or C_{2v} point symmetry), each occupied by two different ligands. Exchange of the ligands of either pair reverses the *absolute configuration.* Examples include unsymmetrically substituted allenes and 2,6,2',6'-tetrasubstituted biphenyls. If the axis is *reflection variant*, it may be called a *chirality axis*. The absolute configuration may be described by either *P, M* or *R, S.* (Note that for a stereogenic axis, $R \equiv M$ and $S \equiv P$). See also *stereogenic element.*

Stereogenic center (stereocenter): An atom in a molecule (or a focal set of atoms) with four equivalent tetrahedral bonding positions (T_d point symmetry), occupied by four different ligands. Exchange of any two ligands reverses the

absolute configuration. If the center is reflection variant, it may be called a *chirality center.* If it is reflection invariant, it is sometimes called a *pseudoasymmetric atom,* although usage of this term is discouraged. *Stereogenic center* is thus an extension of the 'asymmetric carbo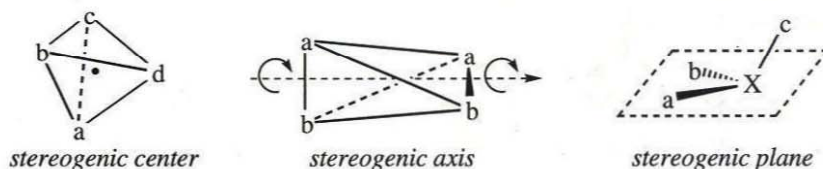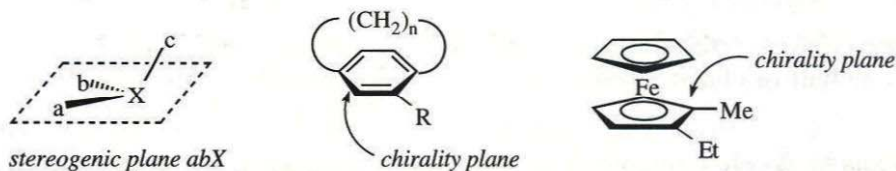n atom' of van't Hoff and LeBel, and now includes species such as N^+abcd and the sulfur atom of unsymmetric sulfoxides (where the fourth 'ligand' is a lone pair), as well as tetrahedral arrays of ligands with T_d symmetry. The *absolute configuration* may be described by the *CIP method.* See *R,S.*

Stereogenic element, stereogenic unit: A *center, axis,* or *plane* in a molecule in which exchange of two ligands leads to a new *stereoisomer.* If the stereogenic element is reflection variant, the elements are *chirality center, chirality axis,* and *chirality plane.* The bonding positions of stereogenic <u>centers</u> have point symmetry T_d; the bonding positions of stereogenic <u>axes</u> have point symmetry D_2 or C_{2v}; the bonding positions of stereogenic <u>planes</u> have point symmetry C_s. As a result, there must be four different ligands (abcd) on a T_d bonding center to create stereogenicity. On an axis, only the two ligands of each pair need be different (ab/ab), the two pairs may be the same. In a stereogenic plane, only one of the ligands in the plane need be different. See also *stereogenic axis, stereogenic center, stereogenic plane.*

stereogenic center   *stereogenic axis*   *stereogenic plane*

Stereogenic plane: A planar structural fragment that, because of *restricted rotation* or structural requirements, cannot lie in a symmetry plane. If the stereogenic plane is reflection variant, the element may be called a *chirality plane.* For example with a monosubstituted paracyclophane, the stereogenic plane includes the plane of the benzene ring. For a 1,2-disubstituted ferrocene, the disubstituted cyclopentadiene lies in a chirality plane. The *absolute configuration* may be specified by either *R, S* or *P, M.* See also *stereogenic element.*

stereogenic plane abX   *chirality plane*   *chirality plane*

Stereoheterotopic: Either *enantiotopic* or *diastereotopic.*

Stereoisomers: Isomers of the same *constitution* that differ only in the position of atoms and ligands in space (*i.e., enantiomers* and *diastereomers*).

Stereoselectivity: In a reaction, the preferential formation of one *stereoisomer* over another (or others). See also *diastereoselectivity, enantioselectivity.*

Stereospecific: A pair of reactions are stereospecific if *stereoisomeric* educts afford stereoisomeric products. A stereospecific process is necessarily 100% *stereoselective,* but the converse is not necessarily true, even if the stereoselectivity is 100%. Use of the term to describe a reaction that is merely highly stereoselective is discouraged.
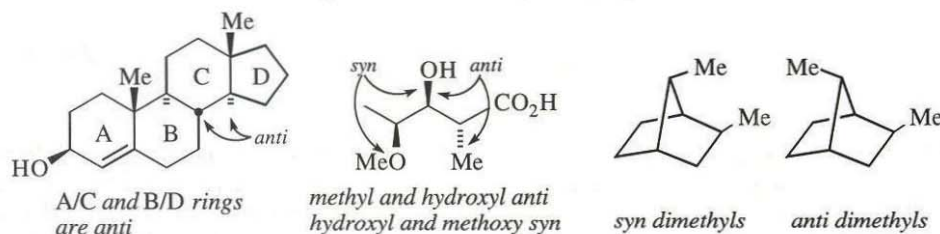
Structure: The *constitution, configuration,* and *conformation* of a molecule. Formerly, the term was used as a synonym for *constitution* alone.

Structural isomers: Obsolete term for *constitutional isomers.*

Superimposable, superposable: Two objects are superimposable if they can be brought into coincidence by translation and rotation. For chemical structures, *free rotation* around single bonds is permissible. Thus, two molecules of *R*-2-butanol are considered superimposable independent of their conformations.

Suprafacial: See *antarafacial, suprafacial.*

syn, anti: Prefixes that describe the relative configuration of two substituents with respect to a defined plane or ring (syn if on the same side, anti if opposite). Such planes may be defined arbitrarily, but some that are in common usage are illustrated below. Formerly, these terms were used to describe the configuration of oximes, hydrazones, etc. (see *E, Z*). See also *torsion angle.*

A/C *and* B/D *rings are anti*   *methyl and hydroxyl anti hydroxyl and methoxy syn*   *syn dimethyls*   *anti dimethyls*

Synclinal: See *torsion angle.*

Symmetry axis (C_n): An axis of an object, about which a rotation by an angle of 360/n gives an entity that is superimposable on the original. See also *alternating symmetry axis.*

Symmetry elements: Axes, centers, or planes of symmetry.

Symmetry plane (σ): A mirror plane which bisects an object, such that reflection of one half produces a fragment that is superimposable on the other half.

Thorpe-Ingold effect: The original phenomenon observed by Thorpe and Ingold was an accelerating effect on cyclizations [109,110]. They attributed the effect to a bond angle compression, as shown below, whereby geminal substituents enlarge bond angle α by *van der Waals* repulsion, and thereby compress bond

angle β. (It is likely that this explanation is an oversimplification. For a recent study on geminal effects on ring closure rates, see ref. [111]).
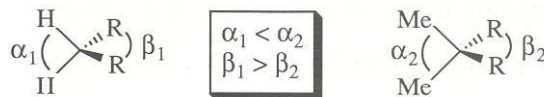
Threo: See *erythro, threo.*

Torsion angle: The angle, in a molecular fragment A–B–C–D (having ABC and BCD bond angles ≤ 180°), between the planes ABC and BCD (see the *Newman projection,* below), always defined such that the absolute value is less than 180°. If (looking from either direction) the turn from A to D or D to A is clockwise, the torsion angle is positive; if it counterclockwise, it is negative (see also *P, M*). If the torsion angle is 0° to ±90°, the angle is *syn;* if between ±90° and 180°, it is *anti.* Similarly, angles from 30 to 150° and –30 to –150° are *clinal.* Combination gives *synperiplanar* for angles between 0° and ±30°; 30° to 90° and –30° to –90° are *synclinal;* 90° to 150° and –90° to –150° are *anticlinal;* and ±150° to 180° are *antiperiplanar* [103]. Often the *synperiplanar* conformation is called eclipsed, the *antiperiplanar* conformation anti, and the *synclinal* conformation gauche or skew.
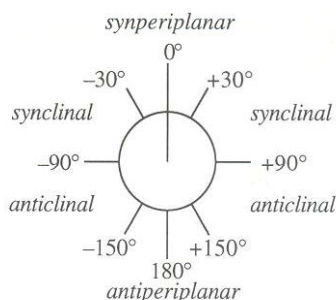
Torsional strain: Destabilization of a molecule due to a variation of a *torsional angle* from an optimal value (*e. g.,* 60° in a saturated molecule). Also called *Pitzer strain, eclipsing strain.*

Torsional isomers: See conformational isomers.

trans: See *cis, trans isomers.*

Transannular interaction: Literally: cross-ring interactions. Non-bonded interaction between ligands attached to nonadjacent atoms in a ring, for example in a cyclohexane *boat* or in medium-sized rings.

transition state, transition structure: In a chemical reaction, the transition *state* is the ensemble of molecular structures that are at the free energy saddle point between reactants and products. The transition *structure* corresponds to the single set of atomic coordinates at the saddle point of the potential energy surface (internal, or enthalpic energy at 0° K). Thus, coordinates of the transition state vary with temperature, whereas those of the transition structure do not. In a practical sense, a structure that is drawn on a piece of paper

(whether derived from a computation or not) should be referred to as a transition structure, since it is static. The transition state is an ensemble of similar structures undergoing translational, vibrational, and rotational motion.

transoid conformation (usage discouraged): See *s-cis, s-trans.*

twist-boat: See *chair, boat, twist-boat.*

u: See *l, u.*

ul: See *lk, ul.*

van der Waals interactions: Attractive or repulsive interactions resulting from close approach of two molecules [112-114]. Modern usage (especially in molecular mechanics calculations) also uses the term van der Waals interactions to describe the attractive and repulsive interactions created by intramolecular approach of molecular fragments [115]. See also *nonbonded interactions.*

Walden inversion: Conversion of Xabcd into Xabcd (for an identity reaction) or Xabce, of opposite *configuration.* Synonymous with *inversion of configuration.*

Walden inversion
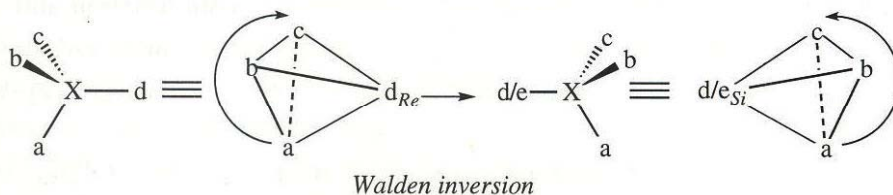
Z: See *E, Z.*

Z(O): See *E(O), Z(O).*

Zig-zag projection: A stereochemical projection in which the main chain of an acyclic compound is drawn in the plane of the paper with 180° torsion angles, with substituents above the plane drawn with bold or solid wedges, and hashed lines for substituents behind the plane.

zig-zag projection
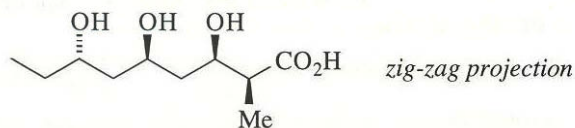
1.7 References

1. M. Gardner *The Ambidexterous Universe: Mirror Asymmetry and Time-Resolved Worlds, 2nd Ed*; Charles Scribner's Sons: New York, 1979.
2. *Chirality. From Weak Bosons to the alpha Helix*; R. Janoschek, Ed.; Springer: New York, 1991.
3. R. A. Hegstrom; D. K. Kondpudi *Scientific American* **1990**, *262*, 108-115.
4. S. C. Stinson *Chem. Eng. News* **1994**, *May 16*, 10-25.
5. *Chirality in Industry: The Commercial Manufacture and Applications of Optically Active Compounds*; A. N. Collins; G. N. Sheldrake; J. Crosby, Eds.; Wiley: New York, 1992.
6. R. A. Sheldon *Chirotechnology. Industrial Synthesis of Optically Active Compounds*; Marcel Dekker: New York, 1993.
7. J. W. Scott In *Topics in Stereochemistry*; E. L. Eliel, N. L. Allinger, Eds.; Wiley-Interscience: New York, 1991; Vol. 19, p 209-226.
8. R. Crossley *Tetrahedron* **1992**, *48*, 8155-8178.
9. S. C. Stinson *Chem. Eng. News* **1993**, *Sep 27*, 38-65.
10. E. J. Ariens, quoted in *Chem. Eng. News* **1990**, *Mar 19*, 40.
11. E. J. Ariens *Trends. Pharm. Sci.* **1986**, *7*, 200-205.
12. *Stereochemistry and Biological Activity of Drugs*; E. J. Ariens; W. Soudijin; P. B. M. W. M. Timmermans, Eds.; Blackwell: Oxford, 1983.
13. G. F. Russel; J. I. Hills *Science* **1971**, *172*, 1043-1044.
14. L. Friedman; J. G. Miller *Science* **1971**, *172*, 1044-1045.
15. J. Solms; L. Vuataz; R. H. Egli *Experientia* **1965**, *21*, 692-694.
16. C. H. Easson; E. Stedman *Biochem. J.* **1933**, *27*, 1257-1266.
17. S. Hanessian *Total Synthesis of Natural Products*; Pergamon: Oxford, 1983.
18. G. M. Coppola; H. F. Schuster *Asymmetric Synthesis. Construction of Chiral Molecules Using Amino Acids*; Wiley-Interscience: New York, 1987.
19. *Carbohydrates as Raw Materials*; W. Lichtenthaler, Ed.; VCH: New York, 1991.
20. T.-L. Ho *Enantioselective Synthesis: Natural Products from Chiral Terpenes*; Wiley: New York, 1992.
21. J. W. Scott In *Asymmetric Synthesis*; J. D. Morrison, Ed.; Academic: Orlando, 1984; Vol. 4, p 1-226.
22. G. W. J. Fleet *Chem. Br.* **1989**, *25*, 287-292.
23. T. Money *Nat. Prod. Rep.* **1985**, 253-289.
24. T. Money In *Studies in Natural Products Chemistry*; Atta-Ur-Rahman, Ed.; Elsevier: Amsterdam, 1989; Vol. 4, p 625-697.
25. S. Hanessian; J. Franco; B. Larouche *Pure Appl. Chem.* **1990**, *62*, 1887-1910.
26. J. Jacques; A. Colbert; S. H. Wilen *Enantiomers, Racemates and Resolutions*; Wiley-Interscience: New York, 1981.
27. R. E. Ireland *Organic Synthesis*; Prentice-Hall: Englewood Cliffs, NJ, 1969.
28. T.-L. Ho *Tactics of Organic Synthesis*; Wiley-Interscience: New York, 1994.
29. W. Marckwald *Chem. Ber.* **1904**, *37*, 1368-1370.
30. C.-H. Wong; G. M. Whitesides *Enzymes in Synthetic Organic Chemistry*; Pergamon: Oxford, 1994.
31. H. L. Holland *Organic Synthesis with Oxidative Enzymes*; VCH: New York, 1991.
32. A. J. Pratt *Chem. Brit.* **1989**, *25*, 282-286.
33. J. B. Cohen; T. S. Patterson *Chem. Ber.* **1904**, *37*, 1012-1014.
34. W. Marckwald *Chem. Ber.* **1904**, *37*, 349-354.
35. E. Erlenmeyer; F. Landesberger *Biochem. Z.* **1914**, *64*, 366-381.
36. F. R. Japp *Nature* **1898**, *58*, 452-460.
37. E. L. Eliel *Tetrahedron* **1974**, *30*, 1503-1513.

38. E. L. Eliel In *Asymmetric Synthesis*; J. D. Morrison, Ed.; Academic: Orlando, 1983; Vol. 2, p 125-155.

39. P. D. Richie *Asymmetric Synthesis and Asymmetric Induction*; Oxford: London, 1933.

40. G. Kortum *Sammlung Chimie U. Chemische Technology*; F. Enke: Stuttgart, 1933.

41. J. D. Morrison; H. S. Mosher *Asymmetric Organic Reactions*; Prentice-Hall: Englewood Cliffs, NJ, 1971.

42. *Asymmetric Synthesis*; J. D. Morrison, Ed.; Academic: Orlando, 1983-85.

43. *Comprehensive Organic Synthesis. Selectivity, Strategy, and Efficiency in Modern Organic Chemistry*; B. M. Trost; I. Fleming, Eds.; Pergamon: Oxford, 1991.

44. *Stereoselective Synthesis*; G. Helmchen; R. W. Hoffmann; J. Mulzer; E. Schaumann, Eds.; Georg Thieme: Stuttgart, 1995; Vol. E21.

45. N. A. Porter; B. Giese; D. P. Curran *Acc. Chem. Res.* **1992**, *24*, 296-304.

46. G. S. Miracle; S. M. Cannizzaro; N. A. Porter *Chemtracts-Org. Chem.* **1993**, *6*, 147-171.

47. D. J. Cram; F. A. A. Elhafez *J. Am. Chem. Soc.* **1952**, *74*, 5828-5835.

48. D. J. Cram; K. R. Kopecky *J. Am. Chem. Soc.* **1959**, *81*, 2748-2755.

49. X. Chen; E. R. Hortelano; E. L. Eliel; S. V. Frye *J. Am. Chem. Soc.* **1992**, *114*, 1778-1784.

50. S. V. Frye; E. L. Eliel *Tetrahedron Lett.* **1985**, *26*, 3907-3910.

51. B. Weber; D. Seebach *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 84-86.

52. D. Seebach; A. K. Beck; B. Schmidt; Y. M. Wang *Tetrahedron* **1994**, *50*, 4363-4384.

53. H. Brunner *Acc. Chem. Res.* **1979**, *12*, 250-257.

54. *Catalytic Asymmetric Synthesis*; I. Ojima, Ed.; VCH: New York, 1993.

55. R. Noyori *Asymmetric Catalysis in Organic Synthesis*; Wiley-Interscience: New York, 1994.

56. D. Seebach; D. A. Plattner; A. K. Beck; Y. M. Wang; D. Hunziker; W. Petter *Helv. Chim. Acta* **1992**, *75*, 2171-2209.

57. C. Zioudrou; P. Chrysochou *Tetrahedron* **1977**, *33*, 2103-2108.

58. S. Masamune; W. Choy; J. S. Petersen; L. R. Sita *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 1-76.

59. K. B. Sharpless *Chemica Scripta* **1985**, *25*, 71-77.

60. T. Kogure; E. L. Eliel *J. Org. Chem.* **1984**, *49*, 576-578.

61. S. Masamune; S. A. Ali; D. L. Snitman; D. S. Garvey *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 557-558.

62. C. T. Buse; C. H. Heathcock *J. Am. Chem. Soc.* **1977**, *99*, 8109-8110.

63. T. Katsuki; A. W. M. Lee; P. Ma; V. S. Martin; S. Masamune; K. B. Sharpless; D. Tuddenham; F. J. Walker *J. Org. Chem.* **1982**, *47*, 1373-1378.

64. J. March In *Advanced Organic Chemistry, 4th ed.*; Wiley-Interscience: New York, 1992, p 145.

65. G. Bredig *Angew. Chem.* **1923**, *36*, 456-458.

66. F. Johnson *Chem. Rev.* **1968**, *68*, 375-413.

67. R. W. Hoffmann *Chem. Rev.* **1989**, *89*, 1841-1860.

68. W. Pigman; D. Horton In *The Carbohydrates. Chemistry and Biochemistry, 2nd ed.*; Academic: New York, 1972, p 1-67.

69. L. F. Fieser; M. Fieser *Natural Products Related to Phenanthrene, 3rd ed*; Reinhold: New York, 1949.

70. D. H. R. Barton *Experientia* **1950**, *6*, 316-320.

71. *The Anomeric Effect and Associated Stereoelectronic Effects. ACS Symposium Series 539*; G. R. J. Thatcher, Ed.; American Chemical Society: Washington, 1993.

72. A. J. Kirby *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*; Springer: Berlin, 1983.

73. P. Muller, ed. *Pure Appl. Chem.* **1994**, *66*, 1077-1184.

74. V. Gold *Pure Appl. Chem.* **1983**, *55*, 1281-1371.

75. E. L. Eliel; S. H. Wilen *Chem. Eng. News* **1991**, *July 22*, 2.

76. M. M. Harris In *Progress in Stereochemistry*; W. Klyne, P. B. D. de la Mare, Eds.; Butterworths: London, 1958, p 157-195.

77. R. Kuhn In *Stereochemie. Eine Zusammenfassung der Ergebnisse, Grundlagen und Probleme*; K. Freudenberg, Ed.; Franz Deuticke: Leipzig, 1933, p 801-824.

78. H. B. Bürgi; J. D. Dunitz; E. Schefter *J. Am. Chem. Soc.* **1973**, *95*, 5065-5067.

79. N. T. Anh; O. Eisenstein *Nouv. J. Chimie* **1977**, *1*, 61-70.

80. H. B. Bürgi; D. Dunitz; J. M. Lehn; G. Wipff *Tetrahedron* **1974**, *30*, 1563-1572.

81. H. M. Pickett; H. L. Strauss *J. Am. Chem. Soc.* **1970**, *92*, 7281-7290.

82. L. Kelvin In *Baltimore Lectures*; C. J. Clay and Sons: London, 1904, p 436 and 619.

83. K. Mislow; J. Siegel *J. Am. Chem. Soc.* **1984**, *106*, 3319-3328.

84. R. Dagani *Chem. Eng. News* **1984**, *June 11*, 21-23.

85. R. S. Cahn; C. K. Ingold; V. Prelog *Angew. Chem. Int. Ed. Engl.* **1966**, *5*, 385-415, 511.

86. V. Prelog; G. Helmchen *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 567-583.

87. L. C. Cross; W. Klyne, collators *Pure Appl. Chem.* **1976**, *45*, 11-30.

88. M. Chérest; H. Felkin; N. Prudent *Tetrahedron Lett.* **1968**, 2199-2204.

89. N. T. Anh *Topics in Current Chemistry* **1980**, *88*, 145-162.

90. D. Seebach; R. Naef *Helv. Chim. Acta* **1981**, *64*, 2704-2708.

91. V. Prelog; G. Helmchen *Helv. Chim. Acta* **1972**, *55*, 2581-2598.

92. C. E. Wintner *J. Chem. Educ.* **1983**, *60*, 550-553.

93. S. Masamune; T. Kaiho; D. S. Garvey *J. Am. Chem. Soc.* **1982**, *104*, 5521-5523.

94. E. L. Eliel; S. H. Wilen *Chem. Eng. News* **1990**, *Sep 19*, 2.

95. C. H. Heathcock; C. T. Buse; W. A. Kleschick; M. C. Pirrung; J. E. Sohn; J. Lampe *J. Org. Chem.* **1980**, *45*, 1066-1081.

96. R. Noyori; I. Nishida; J. Sakata *J. Am. Chem. Soc.* **1981**, *103*, 2106-2108.

97. C. H. Heathcock In *Asymmetric Synthesis*; J. D. Morrison, Ed.; Academic: Orlando, 1984; Vol. 3, p 111-212.

98. M. A. Rosanoff *J. Am. Chem. Soc.* **1906**, *28*, 114-121.

99. E. Ruch *Theor. Chim. Acta (Berl.)* **1968**, *11*, 183-192.

100. E. Ruch *Acc. Chem. Res.* **1972**, *5*, 49-56.

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

102. D. Seebach; V. Prelog *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 654-660.

103. W. Klyne; V. Prelog *Experientia* **1960**, *16*, 521-523.

104. F. A. Carey; M. E. Kuehne *J. Org. Chem.* **1982**, *47*, 3811-3815.

105. K. R. Hanson *J. Am. Chem. Soc.* **1966**, *88*, 2731-2742.

106. C. H. Heathcock; B. L. Finkelstein; E. T. Jarvi; P. A. Radel; C. R. Hadley *J. Org. Chem.* **1988**, *53*, 1922-1942.

107. C. H. Heathcock *Chem. Eng. News* **1991**, *Feb 4*, 3.

108. P. Deslongchamps *Stereoelectronic Effects in Organic Chemistry*; Pergamon: Oxford, 1983.

109. R. M. Beesley; C. K. Ingold; J. F. Thorpe *J. Chem. Soc.* **1915**, *107*, 1080-1106.

110. C. K. Ingold *J. Chem. Soc.* **1921**, *119*, 305-329.

111. M. E. Jung; B. T. Vu *Tetrahedron Lett.* **1996**, *37*, 451-454.

112. G. C. Maitland; M. Rigby; E. B. Smith; W. A. Wakeham *Intermolecular Forces. Their Origin and Determination*; Clarendon: Oxford, 1981.

113. T. Kihara *Intermolecular Forces*; Wiley: New York, 1976.

114. H. Margenau; N. R. Kestner *Theory of Intermolecular Forces*; Pergamon: Oxford, 1969.

115. U. Burkert; N. L. Allinger *Molecular Mechanics. ACS Monograph 177*; American Chemical Society: Washington, DC, 1982.