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IUPAC Tentative Rules for the Nomenclature of Organic Chemistry. Section E. Fundamental Stereochemistry[1]

Introduction

This Section of the IUPAC Rules for Nomenclature of Organic Chemistry differs from previous Sections in that it is here necessary to legislate for words that describe concepts as well as for names of compounds.

At the present time, concepts in stereochemistry (that is, chemistry in three-dimensional space) are in the process of rapid expansion, not merely in organic chemistry, but also in biochemistry, inorganic chemistry, and macromolecular chemistry. The aspects of interest for one area of chemistry often differ from those for another, even in respect to the same phenomenon. This rapid evolution and the variety of interests have led to development of specialized vocabularies and definitions that sometimes differ from one group of specialists to another, sometimes even within one area of chemistry.

The Commission on the Nomenclature of Organic Chemistry does not, however, consider it practical to cover all aspects of stereochemistry in this Section E. Instead, it has two objects in view: to prescribe, for basic concepts, terms that may provide a common language in all areas of stereochemistry; and to define the ways in which these terms may, so far as necessary, be incorporated into the names of individual compounds. The Commission recognizes that specialized nomenclatures are required for local fields; in some cases, such as carbohydrates, amino acids, peptides and proteins, and steroids, international rules already exist; for other fields, study is in progress by specialists in Commissions or Subcommittees; and further problems doubtless await identification. The Commission believes that consultations will be needed in many cases between different groups within IUPAC and IUB if the needs of the specialists are to be met without confusion and contradiction between the various groups.

The Rules in this Section deal only with Fundamental Stereochemistry, that is, the main principles. Many of these Rules do little more than codify existing practice, often of long standing; however, others extend old principles to wider fields, and yet others deal with nomenclature that is still subject to controversy.

Rule E-0

The stereochemistry of a compound is denoted by an affix or affixes to the name that does not prescribe the stereochemistry; such affixes, being additional, do not change the name or the numbering of the compound. Thus, enantiomers, diastereoisomers, and *cis–trans* isomers receive names that are distinguished only by means of different stereochemical affixes. The only exceptions are those trivial names that have stereochemical implications (for example, fumaric acid, cholesterol).

Note: In some cases (see Rules E-2.23 and E-3.1) stereochemical relations may be used to decide between alternative numberings that are otherwise permissible.

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(1) These Rules are reproduced by the kind permission of IUPAC. These Rules may be called the IUPAC 1968 Tentative Rules, Section E, Fundamental Stereochemistry. They are issued by the Commission[2] on the Nomenclature of Organic Chemistry of the International Union of Pure and Applied Chemistry. Section A, Hydrocarbons, and Section B, Fundamental Heterocyclic Systems, were published in 1957 (2nd edition, 1966); Section C, Characteristic Groups Containing Carbon, Hydrogen, Oxygen, Nitrogen, Halogen, Sulfur, Selenium, and/or Tellurium, was published in 1965. Section D, which is in preparation and is expected to be published soon, will deal with organometallic compounds in general, chains and rings containing heterogeneous atoms, and organic derivatives of phosphorus, arsenic, antimony, bismuth, silicon, and boron. Comments on Section E should be addressed to the Secretary of the Commission.[2] Reprints of these Rules are available from Chemical Abstracts Service, Columbus, Ohio 43210.

(2) Titular members: P. E. Verkade (Chairman), S. P. Klesney (Secretary, 3609 Boston, Midland, Mich. 48640 U. S. A.), L. C. Cross, G. M. Dyson, K. L. Loening, N. Lozac'h, H. S. Nutting, J. Rigaudy, S. Veibel. Associate members: R. S. Cahn, H. Grünewald. Observers: K. Bláha, K. Hirayama, K. A. Jensen, W. Klyne.

E-1. Types of Isomerism

E-1.1.—The following nonstereochemical terms are relevant to the stereochemical nomenclature given in the Rules that follow.

(a) The term structure may be used in connection with any aspect of the organization of matter.

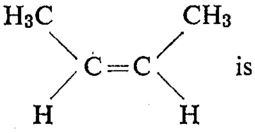
Hence: structural (adjectival)

(b) Compounds that have identical molecular formulas but differ in the nature or sequence of bonding of their atoms or in arrangement of their atoms in space are termed isomers.

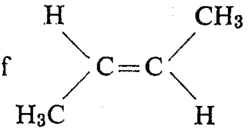
Hence: isomeric (adjectival)
isomerism (phenomenological)

Examples:

$H_3C—O—CH_3$ is an isomer of $H_3C—CH_2—OH$



is an isomer of



(In this and other Rules a broken line denotes a bond projecting behind the plane of the paper, and a thickened line denotes a bond projecting in front of the plane of the paper. In such cases a line of normal thickness denotes a bond lying in the plane of the paper.)

(c) The constitution of a compound of given molecular formula defines the nature and sequence of bonding of the atoms. Isomers differing in constitution are termed constitutional isomers.

Hence: constitutionally isomeric (adjectival)
constitutional isomerism (phenomenological)

Example:

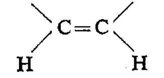
$H_3C—O—CH_3$ is a constitutional isomer of $H_3C—CH_2—OH$

Note: Use of the term "structural" with the above connotation is abandoned as insufficiently specific.

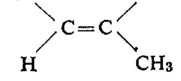
E-1.2.—Isomers are termed stereoisomers when they differ only in the arrangement of their atoms in space.

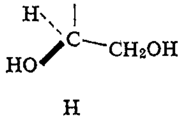
Hence: stereoisomeric (adjectival)
stereoisomerism (phenomenological)

Examples:

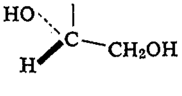


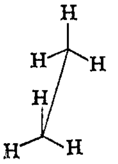
is a stereoisomer of



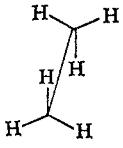


is a stereoisomer of





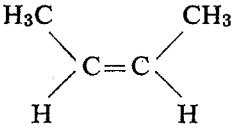
is a stereoisomer of



E-1.3.—Stereoisomers are termed *cis–trans* isomers when they differ only in the positions of atoms relative to a specified plane in cases where these atoms are, or are considered as if they were, parts of a rigid structure.

Hence: *cis–trans* isomeric (adjectival)
cis–trans isomerism (phenomenological)

Examples:



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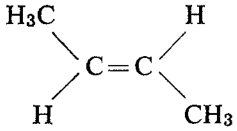
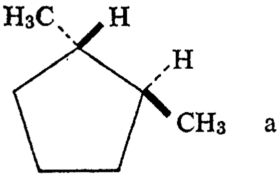
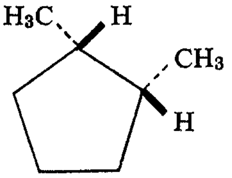




and



E-1.4.—Various views are current regarding the precise definition of the term "configuration." (a) Classical interpretation: The configuration of a molecule of defined constitution is the arrangement of its atoms in space without regard to arrangements that differ only as after rotation about one or more single bonds. (b) This definition is now usually limited so that no regard is paid also to rotation about π bonds or bonds of partial order between one and two. (c) A third view limits the definition further so that no regard is paid to rotation about bonds of any order, including double bonds.

Molecules differing in configuration are termed configurational isomers.

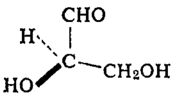
Hence: configurational isomerism

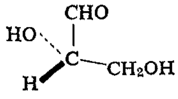
Notes: (1) Contrast conformation (Rule E-1.5). (2) The phrase "differ only as after rotation" is intended to make the definition independent of any difficulty of rotation, in particular independent of steric hindrance to rotation. (3) For a brief discussion of views (a)–(c), see Appendix 1. It is hoped that a definite concensus of opinion will be established before these Rules are made "Definitive".

Examples:

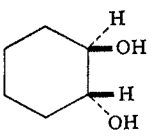
The following pairs of compounds differ in configuration:

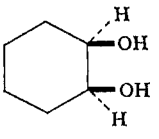
(i)



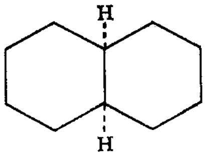


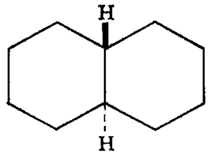
(ii)



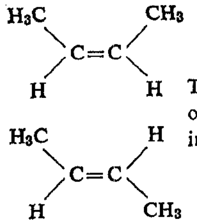


(iii)





(iv)



These isomers (iv) are configurational in view (a) or (b) but are conformational (see Rule E-1.5) in view (c)

E-1.5.—Various views are current regarding the precise definition of the term "conformation." (a) Classical interpretation: The conformations of a molecule of defined configuration are the various arrangements of its atoms in space that differ only as after rotation about single bonds. (b) This is usually now extended to include rotation about π bonds or bonds of partial order between one and two. (c) A third view extends the definition further to include also rotation about bonds of any order, including double bonds.

Molecules differing in conformation are termed conformational isomers.

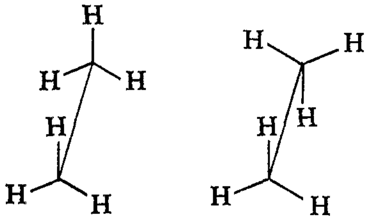
Hence: conformational isomerism

Notes: All the Notes to Rule E-1.4 apply also to E-1.5.

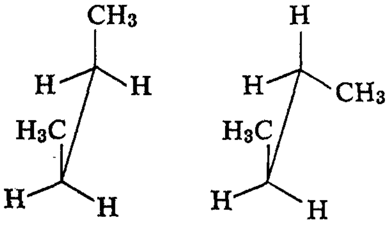
Examples:

Each of the following pairs of formulas represents a compound in the same configuration but in different conformations.

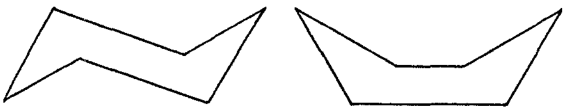
(a, b, c)



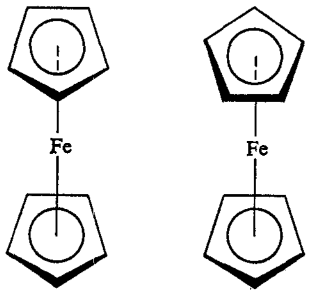
(a, b, c)



(a, b, c)



(b, c)



(c) See Example (iv) to Rule E-1.4.

E-1.6.—The terms relative stereochemistry and relative configuration are used with reference to the positions of various atoms in a compound relative to one another, especially, but not only, when the actual positions in space (absolute configuration) are unknown.

E-1.7.—The terms absolute stereochemistry and absolute configuration are used with reference to the known actual positions of the atoms of a molecule in space.[3]

E-2. *cis–trans* Isomerism[4]

Preamble.—The prefixes *cis* and *trans* have long been used for describing the relative positions of atoms or groups attached to nonterminal doubly bonded atoms of a chain or attached to a ring that is considered as planar. This practice has been codified for hydrocarbons by IUPAC (see footnote 4 below). There has, however, not been agreement on how to assign *cis* or *trans* at terminal double bonds of chains or at double bonds joining a chain to a ring. An obvious solution was to use *cis* and *trans* where doubly bonded atoms formed the backbone and were nonterminal and to enlist the sequence-rule preferences to decide other cases; however, since the two methods, when generally applied, do not always produce analogous results, it would then be necessary to use different symbols for the two procedures. A study of this combination showed that both types of symbol would often be required in one name and, moreover, it seemed wrong in principle to use two symbolisms for essentially the same phenomenon. Thus it seemed to the Commission wise to use only the sequence-rule system, since this alone was applicable to all cases. The same decision was taken independently by Chemical Abstracts Service[5] who introduced *Z* and *E* to correspond more conveniently to *seqcis* and *seqtrans* of the sequence rule.

It is recommended in the Rules below that these designations *Z* and *E* based on the sequence rule shall be used in names of compounds, but *Z* and *E* do not always correspond to the classical *cis* and *trans* which show the steric relations of like or similar groups that are often the main point of interest. So the use of *Z* and *E* in names is not intended to hamper the use of *cis* and *trans* in discussions of steric relations of a generic type or of groups of particular interest in a specified case (see Rule E-2.1 and its Examples and Notes, also Rule E-5.11).

It is also not necessary to replace *cis* and *trans* for describing the stereochemistry of substituted monocycles (see Subsection E-3). For cyclic compounds the main problems are usually different from those around double bonds; for instance, steric relations of substituents on rings can often be described either in terms of chirality (see Subsection E-5) or in terms of *cis–trans* relationships, and, further, there is usually no single

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(3) Determination of absolute configuration became possible through work by J. M. Bijvoet, A. F. Peerdeman, and A. J. van Bommel, *Nature*, **168**, 271 (1951); *cf.* J. M. Bijvoet, *Proc. Kon. Ned. Akad. Wetensch.*, **52**, 313 (1949).

(4) These Rules supersede the Tentative Rules for olefinic hydrocarbons published in the Comptes rendus of the 16th IUPAC Conference, New York, N. Y., 1951, pp 102–103.

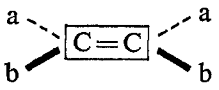
(5) J. E. Blackwood, C. L. Gladys, K. L. Loening, A. E. Petrarca, and J. E. Rush, *J. Amer. Chem. Soc.*, **90**, 509 (1968); J. E. Blackwood, C. L. Gladys, A. E. Petrarca, W. H. Powell, and J. E. Rush, *J. Chem. Doc.*, **8**, 30 (1968).

relevant plane of reference in a hydrogenated polycycle. These matters are discussed in the Preambles to Subsections E-3 and E-4.

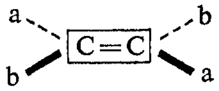
E-2.1. Definition of *cis–trans*.—Atoms or groups are termed *cis* or *trans* to one another when they lie respectively on the same or on opposite sides of a reference plane identifiable as common among stereoisomers. The compounds in which such relations occur are termed *cis–trans* isomers. For compounds containing only doubly bonded atoms the reference plane contains the doubly bonded atoms and is perpendicular to the plane containing these atoms and those directly attached to them. For cyclic compounds the reference plane is that in which the ring skeleton lies or to which it approximates. When qualifying another word or a locant, *cis* or *trans* is followed by a hyphen. When added to a structural formula, *cis* may be abbreviated to *c*, and *trans* to *t* (see also Rule E-3.3).

Examples:

[Rectangles here denote the reference planes and are considered to lie in the plane of the paper.]

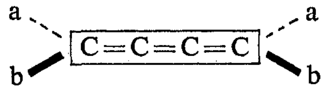


cis



trans

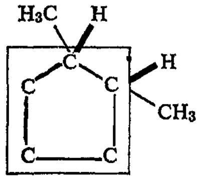
trans



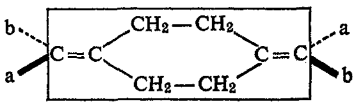
cis

The groups or atoms a,a are the pair selected for designation but are not necessarily identical; b,b are also not necessarily identical but must be different from a,a.

cis or *trans* according as a or b is taken as basis of comparison

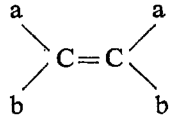


cis



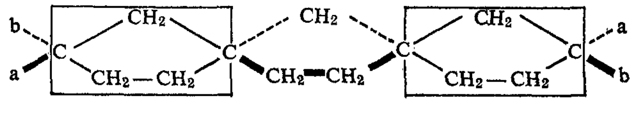
trans

Notes: The formulas above are drawn with the reference plane in the plane of the paper, but for doubly bonded compounds it is customary to draw the formulas so that this plane is perpendicular to that of the paper; atoms attached directly to the doubly bonded atoms then lie in the plane of the paper and the formulas appear as, for instance

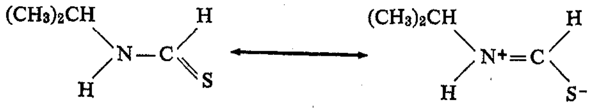


cis

Cyclic structures, however, are customarily drawn with the ring atoms in the plane of the paper, as above. However, care is needed for complex cases, such as



The central five-membered ring lies (approximately) in a plane perpendicular to the plane of the paper. The two a groups are *trans* to one another; so are the b groups; the outer cyclopentane rings are *cis* to one another with respect to the plane of the central ring. *cis* or *trans* (or *Z* or *E*; see Rule E-2.21) may also be used in cases involving a partial bond order when a limiting structure is of sufficient importance to impose rigidity around the bond of partial order. An example is

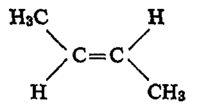


trans (or *E*)

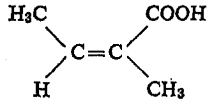
E-2.2. *cis–trans* **Isomerism around Double Bonds**

E-2.21.—In names of compounds steric relations around one or more double bonds are designated by affixes *Z* and/or *E*, assigned as follows. The sequence-rule-preferred[6] atom or group attached to one of a doubly bonded pair of atoms is compared with the sequence-rule-preferred atom or group attached to the other of that doubly bonded pair of atoms; if the selected pair are on the same side of the reference plane (see Rule 2.1) an italic capital letter *Z* prefix is used; if the selected pair are on opposite sides an italic capital letter *E* prefix is used.[7] These prefixes, placed in parentheses and followed by a hyphen, normally precede the whole name; if the molecule contains several double bonds, then each prefix is immediately preceded by the lower or less primed locant of the relevant double bond.

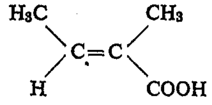
Examples:



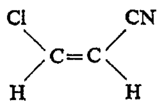
(*E*)-2-Butene



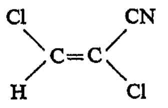
(*Z*)-2-Methyl-2-butenoic acid[8]
or (*Z*)-2-Methylisocrotonic acid
(see Exceptions below)



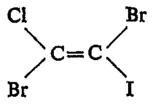
(*E*)-2-Methyl-2-butenoic acid[9]
or (*E*)-2-Methylcrotonic acid
(see Exceptions below)



(*Z*)-3-Chloroacrylonitrile



(*E*)-2,3-Dichloroacrylonitrile



(*Z*)-1,2-Dibromo-1-chloro-2-iodoethylene
(By the sequence rule, Br is preferred to Cl, but I to Br)

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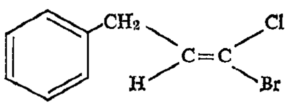
(6) For sequence-rule preferences see Appendix 2.

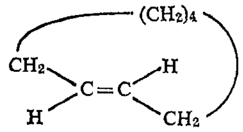
(7) These prefixes may be rationalized as from the German *zusammen* (together) and *entgegen* (opposite).

(8) The name angelic acid is abandoned because it has been associated with the designation *trans* with reference to the methyl groups.

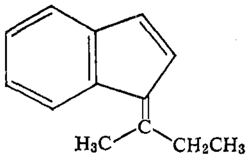
(9) The name tiglic acid is abandoned because it has been associated with the designation *cis* with reference to the methyl groups.



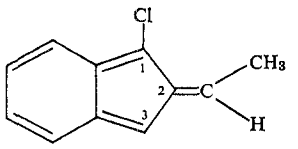
(*E*)-(3-Bromo-3-chloroallyl)benzene



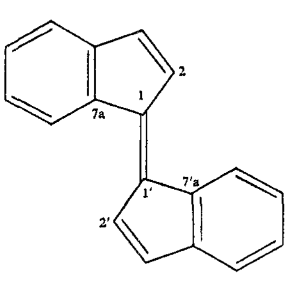
(*E*)-Cyclooctene



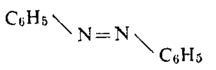
(*E*)-1-*sec*-Butylideneindene



(*Z*)-1-Chloro-2-ethylidene-2*H*-indene

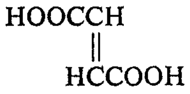


(*E*)-1,1'-Biindenylidene



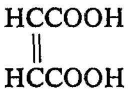
(*E*)-Azobenzene

Exceptions to Rule E-2.21.—The following are examples of accepted trivial names in which the stereochemistry is prescribed by the name and is not cited by a prefix.



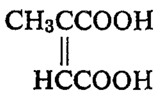
$$\begin{array}{l}\mathrm{HOOCCH}\\ \quad\|\\ \quad\mathrm{HCCOOH}\end{array}$$

Fumaric acid



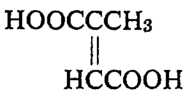
$$\begin{array}{l}\mathrm{HCCOOH}\\ \|\\ \mathrm{HCCOOH}\end{array}$$

Maleic acid



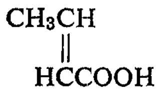
$$\begin{array}{l}\mathrm{CH_3CCOOH}\\ \quad\|\\ \quad\mathrm{HCCOOH}\end{array}$$

Citraconic acid[10]



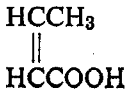
$$\begin{array}{l}\mathrm{HOOCCCH_3}\\ \quad\|\\ \quad\mathrm{HCCOOH}\end{array}$$

Mesaconic acid[10]



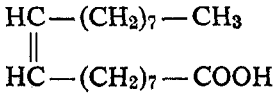
$$\begin{array}{l}\mathrm{CH_3CH}\\ \quad\|\\ \quad\mathrm{HCCOOH}\end{array}$$

Crotonic acid



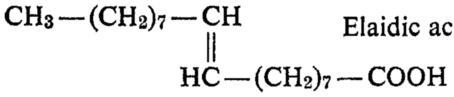
$$\begin{array}{l}\mathrm{HCCH_3}\\ \|\\ \mathrm{HCCOOH}\end{array}$$

Isocrotonic acid



$$\begin{array}{l}\mathrm{HC-(CH_2)_7-CH_3}\\ \|\\ \mathrm{HC-(CH_2)_7-COOH}\end{array}$$

Oleic acid



$$\begin{array}{l}\mathrm{CH_3-(CH_2)_7-CH}\\ \qquad\qquad\qquad\;\|\\ \qquad\qquad\qquad\mathrm{HC-(CH_2)_7-COOH}\end{array}$$

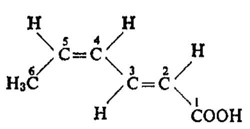
Elaidic acid

E-2.22 (Alternative to Part of E-2.21).—(a) When more than one series of locants starting from unity is required to designate the double bonds in a molecule, or when the name consists of two words, the *Z* and *E* prefixes together with their appropriate locants may be placed before that part of the name where ambiguity is most effectively removed.

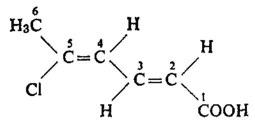
(b) [Alternative to (a)] When several *Z* or *E* prefixes are required they are arranged in order as follows: of the four atoms or groups attached to each doubly bonded pair of atoms, that one preferred by the sequence rule is selected; the single atoms or groups thus selected are then arranged in their sequence rule order (determined in respect of their position in the whole molecule), and the prefixes *Z* and/or *E* for the respective double bonds are placed in that order, but *without* their locants.

Note: In method (a) the final choice is left to an author or editor because of the variety of cases met and because the problems are not always the same in different languages. The presence of the locants usually eases translation from the name to a formula, but this method (a) may involve the logical difficulty explained for the third example below. Method (b) always gives a single unambiguous order and is not subject to the logical difficulty just mentioned, but translation from the name to the formula is harder than for method (a). Method (a) may be more suitable for cursive text, and method (b) for compendia. If method (b) is used it should be used whenever more than one double bond is involved, but method (a) is to be used only under the special conditions detailed in the rule.

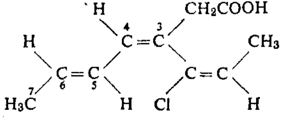
Examples:



(a) (2*E*,4*Z*)-2,4-Hexadienoic acid
(b) (*E*,*Z*)-2,4-Hexadienoic acid



(a) (2*E*,4*Z*)-5-Chloro-2,4-hexadienoic acid
(b) (*Z*,*E*)-5-Chloro-2,4-hexadienoic acid



(a) 3-[(*E*)-1-Chloropropenyl]-(3*Z*,5*E*)-3,5-heptadienoic acid
(b) (*E*,*Z*,*E*)-3-(1-Chloropropenyl)-3,5-heptadienoic acid

[The last example shows the disadvantages of both methods. In method (a) there is a fault of logic, namely, the 3*Z*,5*E* are not the property of the unsubstituted heptadienoic acid chain, but the 3*Z* arises only because of the side chain that is cited before the 3*Z*,5*E*. In method (b) it is some trouble to assign the *E*,*Z*,*E* to the correct double bonds.]

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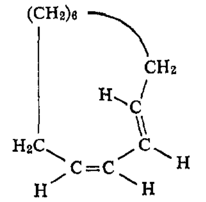
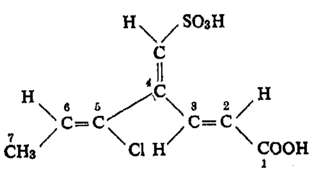
[10] Systematic names are recommended for derivatives of these compounds formed by substitution on carbon.



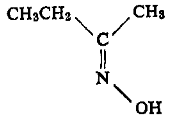
(a) (1*Z*,3*E*)-1,3-Cyclododecadiene
(b) (*Z*,*E*)-1,3-Cyclododecadiene

[The lower locant is assigned to the *Z* double bond.]

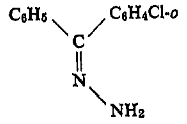


(a) 5-Chloro-4-(*E*-sulfomethylene)-(2*E*,5*Z*)-2,5-heptadienoic acid
(b) (*Z*,*E*,*E*)-5-Chloro-4-(sulfomethylene)-2,5-heptadienoic acid

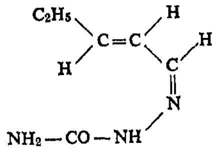
[In application of the sequence rule, the relation of the SO_3H to CCl (rather than to C-3), and of the CH_3 to Cl, are decisive.]



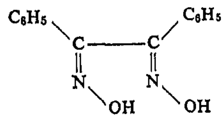
(a) Butanone (*E*)-oxime[11]
(b) (*E*)-Butanone oxime



(a) 2-Chlorobenzophenone (*Z*)-hydrazone
(b) (*Z*)-2-Chlorobenzophenone hydrazone



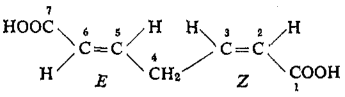
(a) (*E*)-2-Pentenal (*Z*)-semicarbazone
(b) (*Z*,*E*)-2-Pentenal semicarbazone



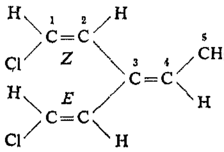
(a) Benzil (*Z*,*E*)-dioxime
(b) (*Z*,*E*)-Benzil dioxime

E-2.23.—When Rule C-13.1 or E-2.22(b) permits alternatives, preference for lower locants and for inclusion in the principal chain is allotted as follows, in the order stated, so far as necessary: *Z* over *E* groups; *cis* over *trans* cyclic groups; *R* over *S* groups (also *r* over *s*, etc., as in the sequence rule); if the nature of these groups is not decisive, then the lower locant for such a preferred group at the first point of difference.

Examples:

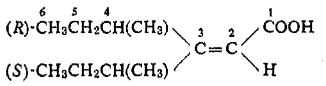


(a) (2*Z*,5*E*)-2,5-Heptadienedioic acid
(b) (*E*,*Z*)-2,5-Heptadienedioic acid
[The lower numbers are assigned to the *Z* double bond.]



(a) 1-Chloro-3-[2-chloro-(*E*)-vinyl]-(1*Z*,3*Z*)-1,3-pentadiene
(b) (*E*,*Z*,*Z*)-1-Chloro-3-(2-chlorovinyl)-1,3-pentadiene

[According to Rule C-13.1 the principal chain must include the C=C—CH_3 group because this gives lower numbers to the double bonds (*1,3 rather than 1,4*); *then the* Cl-*containing Z* group is chosen for the remainder of the principal chain in accord with Rule E-2.23.]



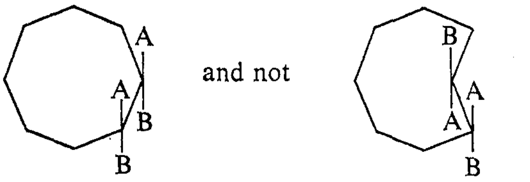
(a, b) (*Z*)-(4*R*)-3-[(*S*)-*sec*-Butyl]-4-methyl-2-hexenoic acid

[The principal chain is chosen to include the (*R*)-group, and the prefix *Z* refers to the (*R*)-group.]

E-3. Relative Stereochemistry of Substituents in Monocyclic Compounds[12]

Preamble.—*cis* and *trans* prefixes are commonly used to designate the positions of substituents on rings relative to one another; when the ring is, or is considered to be, rigidly planar or approximately so and is placed horizontally, these prefixes define which groups are above and which below the (approximate) plane of the ring. This differentiation is often important, so this classical terminology is retained in Subsection E-3; since the difficulties inherent in end groups do not arise for cyclic compounds, it is unnecessary to resort to the less immediately informative *E/Z* symbolism.

When the *cis–trans* designation of substituents is applied, rings are considered in their most extended form; reentrant angles are not permitted; for example

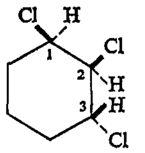


cis apparently *trans*

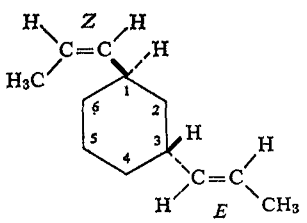
The absolute stereochemistry of optically active or racemic derivatives of monocyclic compounds is described by the sequence-rule procedure (see Rule E-5.9 and Appendix 2). The relative stereochemistry may be described by a modification of sequence-rule symbolism as set out in Rule E-5.10. If either of these procedures is adopted, it is then superfluous to use also *cis* or *trans* in the names of individual compounds.

E-3.1.—When alternative numberings of the ring are permissible according to the Rules of Section C, that numbering is chosen which gives a *cis* attachment at the first point of difference; if that is not decisive, the criteria of Rule E-2.23 are applied. *cis* and *trans* may be abbreviated to *c* and *t*, respectively, in names of compounds when more than one such designation is required.

Examples:



1,*c*-2,*t*-3-Trichlorocyclohexane



1-(*Z*)-Propenyl-*trans*-3-(*E*)-propenylcyclohexane

E-3.2.—When one substituent and one hydrogen atom are attached at each of two positions of a monocycle, the steric relations of the two substituents are expressed as *cis* or *trans*, followed by a hyphen and placed before the name of the compound.

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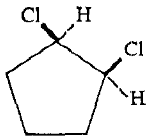
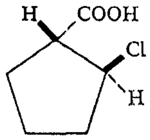
(11) The terms *syn*, *anti*, and *amphi* are abandoned for such compounds.

(12) Formulas in Examples to this Rule denote relative (not absolute) configurations.

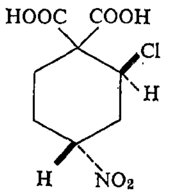
Examples:



cis-1,2-Dichlorocyclopentane



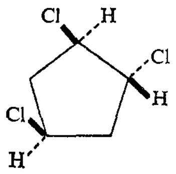
trans-2-Chloro-1-cyclopentanecarboxylic acid



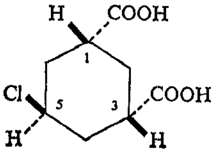
trans-2-Chloro-4-nitro-1,1-cyclohexanedicarboxylic acid

E-3.3.—When one substituent and one hydrogen atom are attached at each of more than two positions of a monocycle, the steric relations of the substituents are expressed by adding *r* (for *reference* substituent), followed by a hyphen, before the locant of the lowest numbered of these substituents and *c* or *t* (as appropriate), followed by a hyphen, before the locants of the other substituents to express their relation to the reference substituent.

Examples:



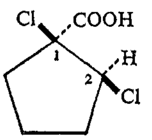
r-1,*t*-2,*c*-4-Trichlorocyclopentane (not *r*-1, *t*-2, *t*-4 which would follow from the alternative direction of numbering; see Rule E-3.1)



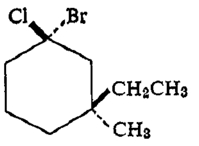
t-5-Chloro-*r*-1,*c*-3-cyclohexanedicarboxylic acid

E-3.4.—When two different substituents are attached at the same position of a monocycle, then the lowest numbered substituent named as suffix is selected for designation as reference group in accordance with Rule E-3.2 or E-3.3; or, if none of the substituents is named as suffix, then of the lowest numbered pair that one preferred by the sequence rule is selected as reference group; and the relation of the sequence-rule preferred group at each other position, relative to the reference group, is cited as *c* or *t* (as appropriate).

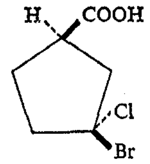
Examples:



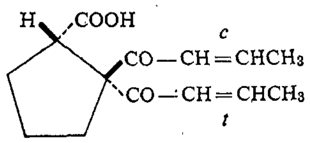
1,*t*-2-Dichloro-*r*-1-cyclopentanecarboxylic acid



r-1-Bromo-1-chloro-*t*-3-ethyl-3-methylcyclohexane (alphabetical order of prefixes)



c-3-Bromo-3-chloro-*r*-1-cyclopentanecarboxylic acid



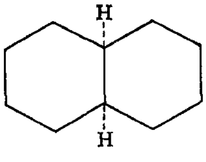
2-Crotonoyl-*t*-2-isocrotonoyl-*r*-1-cyclopentanecarboxylic acid

E-4. Fused Rings

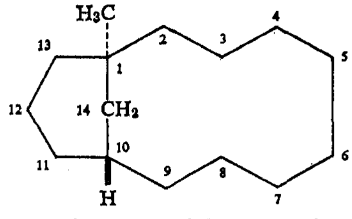
Preamble.—In simple cases the relative stereochemistry of substituted fused-ring systems can be designated by the methods used for monocycles. For the absolute stereochemistry of optically active and racemic compounds the sequence-rule procedure can be used in all cases (see Rule E-5.9 and Appendix 2), and for related relative stereochemistry the procedure of Rule E-5.10 can be applied. Sequence-rule methods are, however, not descriptive of geometrical shape for other than quite simple cases. There is as yet no generally acceptable system for designating in an immediately interpretable manner the stereochemistry of polycyclic bridged ring compounds (for instance, the *endo–exo* nomenclature, which should solve one set of problems, has been used in different ways). These and related problems (*e.g.*, cyclophanes, catenanes) will be considered in a later document.

E-4.1.—Steric relations at saturated bridgeheads common to two rings are denoted by *cis* or *trans*, followed by a hyphen and placed before the name of the ring system, according to the relative positions of the exocyclic atoms or groups attached to the bridgeheads. Such rings are said to be *cis* fused or *trans* fused.

Examples:



cis-Decalin



1-Methyl-*trans*-bicyclo[8.3.1]tetradecane

E-4.2.—Steric relations at more than one pair of saturated bridgeheads in a polycyclic compound are denoted by *cis* or *trans*, each followed by a hyphen and, when necessary, the corresponding locant of the lower numbered bridgehead and a second hyphen, all placed before the name of the ring system. Steric relations between the nearest atoms[13] of *cis*- or *trans*-bridgehead

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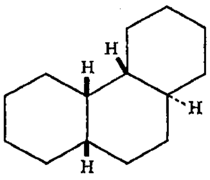
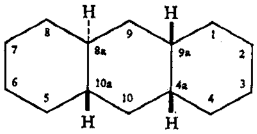
[13] The term "nearest atoms" denotes those linked together through the smallest number of atoms, irrespective of actual separation in space. For instance, in the second Example to this Rule, the atom 4a is "nearer" to 10a than to 8a.

pairs may be described by affixes *cisoid* or *transoid*, followed by a hyphen and, when necessary, the corresponding locants and a second hyphen, the whole placed between the designations of the *cis*- or *trans*-ring junctions concerned. When a choice remains among nearest atoms, the pair containing the lower numbered atom is selected. *cis* and *trans* are not abbreviated in such cases. In complex cases, however, designation may be more simply effected by the sequence-rule procedure (see Appendix 2).

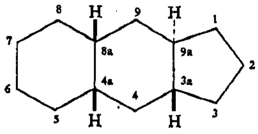
Examples:



cis-cisoid-trans-Perhydrophenanthrene



cis-cisoid-4a,10a-*trans*-Perhydroanthracene or *rel*-(4a*R*,8a*S*,9a*S*,10a*S*)-Perhydroanthracene[14]



trans-3a-*cisoid*-3a,4a-*cis*-4a-Perhydrobenz[*f*]indene or *rel*-(3a*R*,4a*S*,8a*R*,9a*R*)-Perhydrobenz[*f*]indene

E-5. Chirality

E-5.1.—The property of nonidentity of an object with its mirror image is termed chirality. An object, such as a molecule in a given configuration or conformation, is termed chiral when it is not identical with its mirror image; it is termed achiral when it is identical with its mirror image.

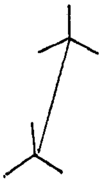
Notes: (1) Chirality is equivalent to handedness, the term being derived from the Greek Χειρ = hand.

(2) All chiral molecules are molecules of optically active compounds, and molecules of all optically active compounds are chiral. There is a 1:1 correspondence between chirality and optical activity.

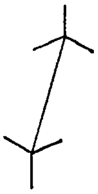
(3) In organic chemistry the discussion of chirality usually concerns the individual molecule or, more strictly, a model of the individual molecule. The chirality of an assembly of molecules may differ from that of the component molecules, as in a chiral quartz crystal or in an achiral crystal containing equal numbers of dextrorotatory and levorotatory tartaric acid molecules.

(4) The chirality of a molecule can be discussed only if the configuration or conformation of the molecule is specifically defined or is considered as defined by common usage. In such discussions structures are treated as if they were (at least temporarily) rigid. For instance, ethane is configurationally achiral although many of its conformations, such as (A), are chiral; in fact, a configuration of a mobile molecule is chiral only if all its possible conformations are chiral; and conformations of ethane such as (B) and (C) are achiral.

(A)

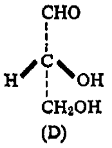


(B)

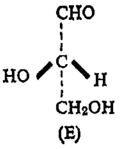


(C)

Examples:

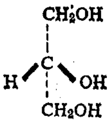


(D)



(E)

(D) and (E) are mirror images and are not identical, not being superposable. They represent chiral molecules. They represent (D) dextrorotatory and (E) levorotatory glyceraldehyde.



(F)

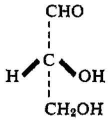
(F) is identical with its mirror image. It represents an achiral molecule, namely, a molecule of 1,2,3-propanetriol (glycerol).

E-5.2.—The term asymmetry denotes absence of any symmetry. An object, such as a molecule in a given configuration or conformation, is termed asymmetric if it has no element of symmetry.

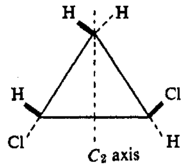
Notes: (1) All asymmetric molecules are chiral, and all compounds composed of them are therefore optically active; however, not all chiral molecules are asymmetric since some molecules having axes of rotation are chiral.

(2) Notes (3) and (4) to Rule E-5.1 apply also in discussions of asymmetry.

Examples:



has no element of symmetry and represents a molecule of an optically active compound.



has a C_2 axis of rotation; it is chiral although not asymmetric, and is therefore a molecule of an optically active compound.

E-5.3.—(a) An asymmetric atom is one that is tetrahedrally bonded to four different atoms or groups, none of the groups being the mirror image of any of the others.

(b) An asymmetric atom may be said to be at a chiral center since it lies at the center of a chiral tetrahedral structure. In a general sense, the term "chiral center" is not restricted to tetrahedral structures; the structure may, for instance, be based on an octahedron or tetragonal pyramid.

(c) When the atom by which a group is attached to the remainder of a molecule lies at a chiral center, the group may be termed a chiral group.

Notes: (1) The term "asymmetric", as applied to a carbon atom in rule E-5.3 (a), was chosen by van't Hoff because there is no plane of symmetry through a tetrahedron whose corners are occupied by four atoms or groups that differ in scalar properties. For dif-

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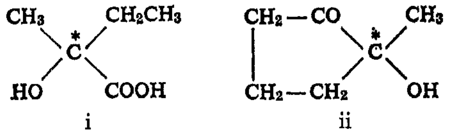
[14] For the designation *rel*, see Rule E-5.10.

ferences of vector sense between the attached groups, see Rule E-5.8.

(2) In Subsection E-5 the word "group" is used to denote the series of atoms attached to one bond. For instance, in i the groups attached to C* are -CH_3, -OH, -CH_2CH_3, and -COOH; in ii they are -CH_3, -OH,-$COCH_2CH_2CH_2$, and -$CH_2CH_2CH_2CO$.

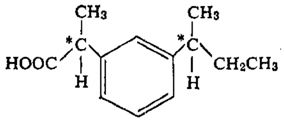

i ii

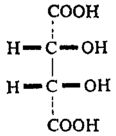
(3) For the chiral axis and chiral plane (which are less common than the chiral center), see Appendix 2.

(4) There may be more than one chiral center in a molecule and these centers may be identical, or structurally different, or structurally identical but of opposite chirality; however, the presence of an equal number of structurally identical chiral groups of opposite chirality, and no other chiral group, leads to an achiral molecule. These statements apply also to chiral axes and chiral planes. Identification of the sites and natures of the various factors involved is essential if the overall chirality of a molecule is to be understood.

(5) Although the term "chiral group" is convenient for use in discussions it should be remembered that chirality attaches to molecules and not to groups or atoms. For instance, although the *sec*-butyl group may be termed chiral in dextrorotatory 2-*sec*-butylnaphthalene, it is not chiral in the achiral compound $(CH_3CH_2)(CH_3)CH\text{-}CH_3$.

Examples:


In this chiral compound there are two asymmetric carbon atoms, marked C*, each lying at a chiral centre. These atoms form part of different chiral groups, namely, —$CH(CH_3)COOH$ and —$CH(CH_3)CH_2CH_3$.


In this molecule (*meso*-tartaric acid) the two central carbon atoms are asymmetric atoms and each is part of a chiral group —CH(OH)COOH. These groups, however, although structurally identical, are of opposite chirality, so that the molecule is achiral.

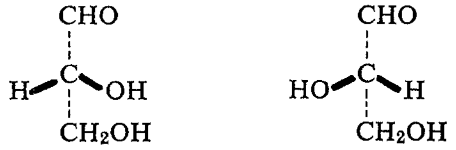
E-5.4.—Molecules that are mirror images of one another are termed enantiomers and may be said to be enantiomeric. Chiral groups that are mirror images of one another are termed enantiomeric groups.

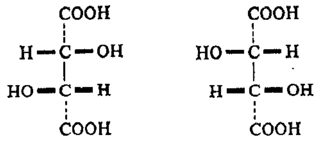
Hence: enantiomerism (phenomenological)

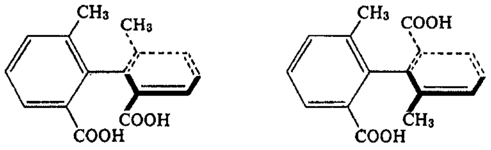
Note: Although the adjective enantiomeric may be applied to groups, enantiomerism strictly applies only to molecules [see Note (5) to Rule E-5.3].

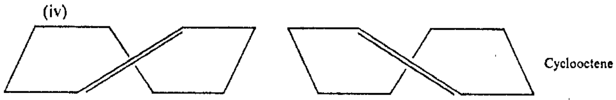
Examples:

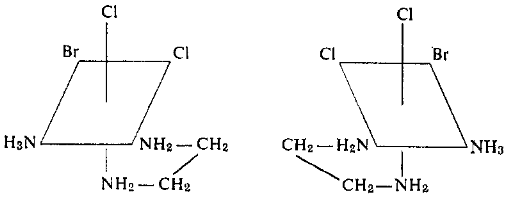
The following pairs of molecules are enantiomeric.

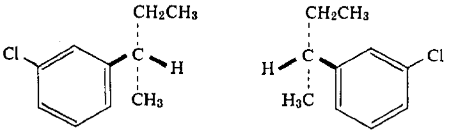
(i)


(ii)


(iii)


(iv)


(v)


(vi)

The *sec*-butyl groups in (vi) are enantiomeric.

E-5.5.—When equal amounts of enantiomeric molecules are present together, the product is termed racemic, independently of whether it is crystalline, liquid, or gaseous. A homogeneous solid phase composed of equimolar amounts of enantiomeric molecules is termed a racemic compound. A mixture of equimolar amounts of enantiomeric molecules present as separate solid phases is termed a racemic mixture. Any homogeneous solid containing equimolar amounts of enantiomeric molecules is termed a racemate.

Examples:

The mixture of two kinds of crystal (mirror-image forms) that separate below 28° from an aqueous solution containing equal amounts of dextrorotatory and levorotatory sodium ammonium tartrate is a racemic mixture.

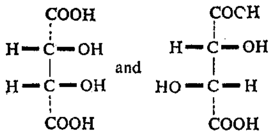
The symmetrical crystals that separate from such a solution above 28°, each containing equal amounts of the two salts, provide a racemic compound.

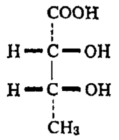
E-5.6.—Stereoisomers that are not enantiomeric are termed diastereoisomers.

Hence: diastereoisomeric (adjectival)
diastereoisomerism (phenomenological)

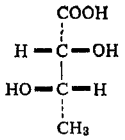
Note: Diastereoisomers may be chiral or achiral.

Examples:


are diastereoisomers; the former is achiral, and the latter is chiral.



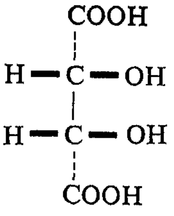
and



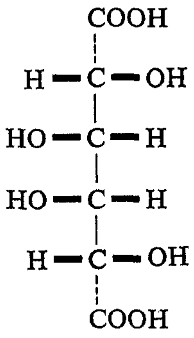
are diastereoisomers; both are chiral.

E-5.7.—A compound whose individual molecules contain equal numbers of enantiomeric groups, identically linked, but no other chiral group, is termed a *meso* compound.

Example:



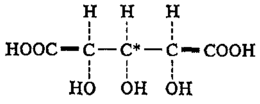
meso-Tartaric acid



Galactaric acid

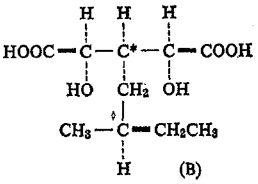
E-5.8.—An atom is termed pseudoasymmetric when bonded tetrahedrally to one pair of enantiomeric groups (+)-a and (−)-a and also to two atoms or groups b and c that are different from group a, different from each other, and not enantiomeric with each other.

Examples:



(A)

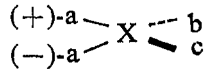
C* are pseudoasymmetric



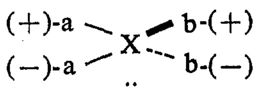
(B)

Notes: (1) The orientation, in space, of the atoms around a pseudoasymmetric atom is not reversed on reflection; for a chiral atom (see Note to Rule E-5.3) this orientation is always reversed.

(2) Molecules containing pseudoasymmetric atoms may be achiral or chiral. If ligands b and c are both achiral, the molecule is achiral as in the first example to this Rule. If either or both of the nonenantiomeric ligands b and c are chiral, the molecule is chiral, as in the second example to this Rule, that is the molecule is not identical with its mirror image. A molecule (i) is also chiral if b and c are enantiomeric, that is, if the molecule



i



ii

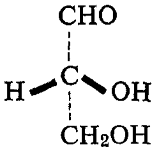
can be symbolized as ii, but then, by definition, it does not contain a pseudoasymmetric atom.

(3) Compounds differing at a pseudoasymmetric atom belong to the larger class of diastereoisomers.

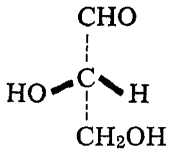
(4) In example (A), interchange of H and OH on C* gives a different achiral compound, which is an achiral diastereoisomer of (A) (see Rule E-5.6). In example (B), diastereoisomers are produced by inversion at C* or ${}^{\Diamond}$C, giving in all four diastereoisomers, all chiral because of the $-CH(CH_3)CH_2CH_3$ group.

E-5.9.—Names of chiral compounds whose absolute configuration is known are differentiated by preffixes *R*, *S*, etc., assigned by the sequence-rule procedure (see Appendix 2), preceded when necessary by the appropriate locants.

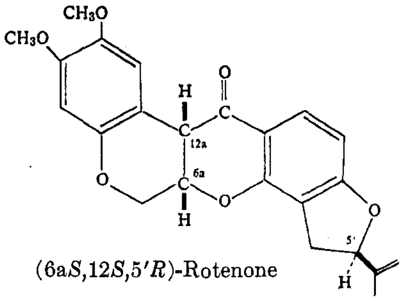
Examples:



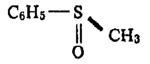
(*R*)-Glyceraldehyde



(*S*)-Glyceraldehyde



(6a*S*,12*S*,5′*R*)-Rotenone



Methyl phenyl (*R*)-sulfoxide

E-5.10.—(a) Names of compounds containing chiral centers, of which the relative but not the absolute configuration is known, are differentiated by prefixes *R**, *S** (spoken R star, S star), preceded when necessary by the appropriate locants, these prefixes being assigned by the sequence-rule procedure (see Appendix 2) on the arbitrary assumption that the prefix first cited is *R*.

(b) In complex cases the stars may be omitted and, instead, the whole name is prefixed by *rel* (for *relative*).

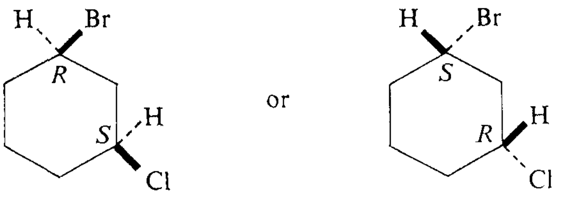
(c) When only relative configuration is known, enantiomers are distinguished by a prefix (+) or (−), referring to the direction of rotation of plane-polarized light passing through them (wavelength, temperature, solvent, and/or concentration should also be specified, particularly when known to affect the sign).

(d) When a substituent of known absolute chirality is introduced into a compound of which only the relative configuration is known, then starred symbols *R**, *S** are used and not the prefix *rel.*

Note: This Rule does not form part of the procedure formulated in the sequence-rule papers by Cahn, Ingold, and Prelog (see Appendix 2).

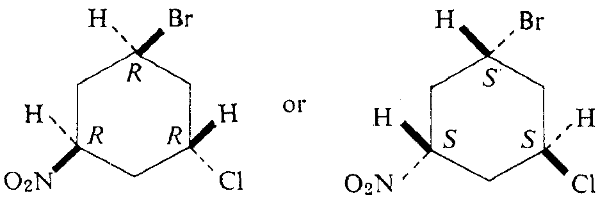
Examples:

(a)



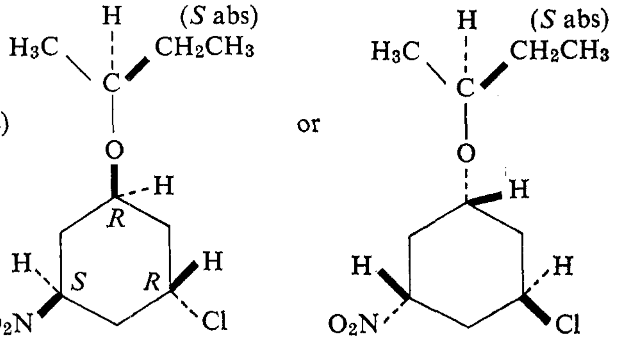
(1*R**,3*S**)-1-Bromo-3-chlorocyclohexane

(b)



rel-(1*R*,3*R*,5*R*)-1-Bromo-3-chloro-5-nitrocyclohexane

(c)



(1*R**,3*R**,5*S**)-[(1*S*)-*sec*-Butoxy]-3-chloro-5-nitrocyclohexane

E-5.11.—When it is desired to express relative or absolute configuration with respect to a class of compounds, specialized local systems may be used. The sequence rule may, however, be used additionally for positions not amenable to treatment by the local system.

Examples:

gluco, *arabino*, etc., combined when necessary with D or L, for carbohydrates and their derivatives [see IUPAC/IUB Tentative Rules for Carbohydrate Nomenclature, in press; see also *J. Org. Chem.*, **28**, 281 (1963)].

D, L for amino acids and peptides [see Comptes rendus of the 16th IUPAC Conference, New York, N. Y., 1951, pp 107–108; also published in *Chem. Eng. News*, **30**, 4522 (1952)].

D, L, and a series of other prefixes and trivial names for cyclitols and their derivatives [see IUPAC/IUB Tentative Rules for the Nomenclature of Cyclitols, 1967, IUPAC Information Bulletin, No. 32 (Aug 1968), pp 51–80; also published in *J. Biol. Chem.*, **243**, 5809 (1968)].

α, β, and a series of trivial names for steroids and related compounds [see IUPAC/IUB Revised Tentative Rules for the Nomenclature of Steroids, 1967, IUPAC Information Bulletin, No. 33 (Dec 1968), pp 23–67; also published in *J. Org. Chem.*, **34**, 1517 (1969)].

The α, β system for steroids can be extended to other classes of compounds such as terpenes and alkaloids when their absolute configurations are known; it can also be combined with stars or the use of the prefix *rel* when only the relative configurations are known.

In spite of the Rules of Subsection E-2, *cis* and *trans* are used when the arrangement of the atoms constituting an unsaturated backbone is the most important factor, as, for instance, in polymer chemistry and for carotenoids. When a series of double bonds of the same stereochemistry occurs in a backbone, the prefix all-*cis* or all-*trans* may be used.

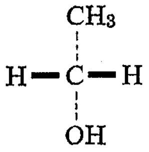
E-5.12.—(a) An achiral object having at least one pair of features that can be distinguished only by reference to a chiral object or to a chiral reference frame is said to be prochiral, and the property of having such a pair of features is termed prochirality. A consequence is that, if one of the paired features of a prochiral object is considered to differ from the other, the resultant object is chiral.

(b) In a molecule an achiral center or atom is said to be prochiral if it would be held to be chiral when two attached atoms or groups, that taken in isolation are indistinguishable, are considered to differ.

Notes: (1) For a tetrahedrally bonded atom this requires a structure Xaabc (where none of the groups a, b, or c is the enantiomer of another).

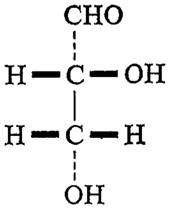
(2) For a fuller exploration of this concept, which is of particular importance to biochemists and spectroscopists, and for its extension to axes, planes, and unsaturated compounds, see K. R. Hanson, *J. Amer. Chem. Soc.*, **88**, 2731 (1966).

Examples:



$$H-\overset{CH_3}{\underset{OH}{C}}-H$$

(A)



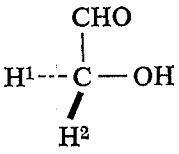
$$\begin{array}{c} CHO \\ | \\ H-C-OH \\ | \\ H-C-H \\ | \\ OH \end{array}$$

(B)

In both examples (A) and (B) the methylene carbon atom is prochiral; in both cases it would be held to be at a chiral center if one of the methylene hydrogen atoms were considered to differ from the other. An actual replacement of one of these protium atoms by, say, deuterium would produce an actual chiral center at the methylene carbon atom; as a result compound (A) would become chiral, and compound (B) would be converted into one of two diastereoisomers.

E-5.13.—Of the identical pair of atoms or groups in a prochiral compound, that one which leads to an (*R*) compound when considered to be preferred to the other by the sequence rule (without change in priority with respect to other ligands) is termed *pro-R*, and the other is termed *pro-S*.

Example:



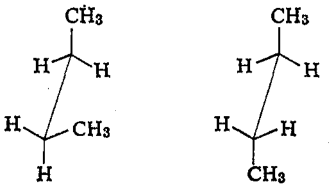
$$\begin{array}{c} CHO \\ | \\ H^1\cdots C-OH \\ / \\ H^2 \end{array}$$

H^1 is *pro-R*. H^2 is *pro-S*.

E-6. Conformations

E-6.1.—A molecule in a conformation into which its atoms return spontaneously after small displacements is termed a conformer.

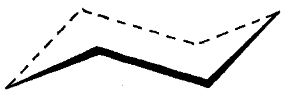
Examples:



are different conformers.

E-6.2.—(a) When, in a six-membered saturated ring compound, atoms in relative positions 1, 2, 4, and 5 lie in one plane, the molecule is described as in the chair or boat conformation according as the other two atoms lie, respectively, on opposite sides or on the same side of that plane.

Examples:



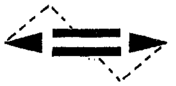
Chair

Boat

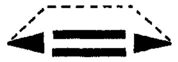
Note: These and similar representations are idealized, minor divergences being neglected.

(b) A molecule of a monounsaturated six-membered ring compound is described as being in the half-chair or half-boat conformation according as the atoms not directly bound to the doubly bonded atoms lie, respectively, on opposite sides or on the same side of the plane containing the other four (adjacent) atoms.

Examples:



Half-chair



Half-boat

(c) A median conformation through which one boat form passes during conversion into the other boat form is termed a twist conformation. Similar twist conformations are involved in conversion of a chair into a boat form or *vice versa*.

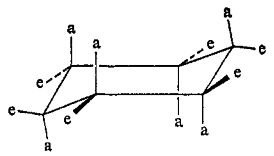
Examples:

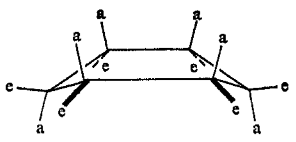
Boat Twist Boat

E-6.3.—(a) Bonds to a tetrahedral atom in a six-membered ring are termed equatorial or axial according as they or their projections make a small or a large angle, respectively, with the plane containing a majority of the ring atoms.[15] Atoms or groups attached to such bonds are also said to be equatorial or axial, respectively.

Notes: (1) See, however, pseudoequatorial and pseudoaxial [Rule 6.3(b)]. (2) The terms equatorial and axial may be abbreviated to e and a when attached to formulas; these abbreviations may also be used in names of compounds and are there placed in parentheses after the appropriate locants, for example, 1(e)-bromo-4(a)-chlorocyclohexane.

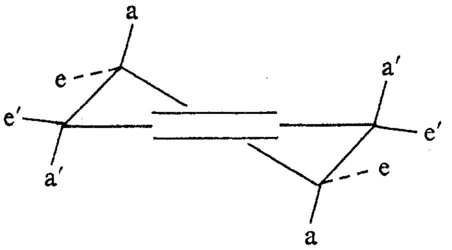
Examples:





(b) Bonds from atoms directly attached to the doubly bonded atoms in a monounsaturated six-membered ring are termed pseudoequatorial or pseudoaxial according as the angles that they make with the plane containing the majority of the ring atoms approximate those made by, respectively, equatorial or axial bonds from a saturated six-membered ring. Pseudoequatorial and pseudoaxial may be abbreviated to e′ and a′, respectively, when attached to formulas; these abbreviations may also be used in names, then being placed in parentheses after the appropriate locants.

Example:



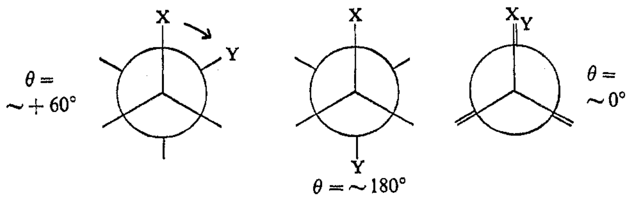
E-6.4.—Torsion angle: In an assembly of attached atoms X–A–B–Y, where neither X nor Y is collinear with A and B, the smaller angle subtended by the bonds X–A and Y–B in a plane projection obtained by viewing the assembly along the axis A–B is termed the torsion angle (denoted by the Greek lower case letter theta θ or omega ω). The torsion angle is considered positive or negative according as the bond to the front atom X or Y requires rotation to the right or left, respectively, in order that its direction may coincide with that of the bond to the rear selected atom Y or X. The multiplicity of the bonding of the various atoms is irrelevant. A torsion angle also exists if the axis for rotation is formed by a collinear set of more than two atoms directly attached to each other.

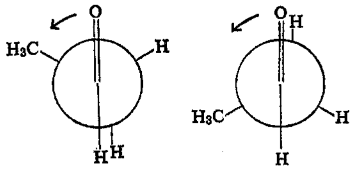
Notes: (1) It is immaterial whether the projection be viewed from the front or the rear.

(2) For the use of torsion angles in describing molecules see Rule E-6.6

Examples:

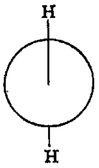
(For construction of Newman projections, as here, see Rule E-7.2.)





Newman projections of propionaldehyde

$\theta = \sim -60°$ $\theta = \sim -120°$



Newman projection of hydrogen peroxide

$\theta = \sim 180°$

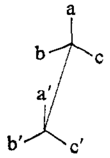
E-6.5.—If two atoms or groups attached at opposite ends of a bond appear one directly behind the other when the molecule is viewed along this bond, these atoms or groups are described as eclipsed, and that portion of the molecule is described as being in the eclipsed conformation. If not eclipsed, the atoms or

---

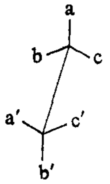
[15] The terms axial, equatorial, pseudoaxial and pseudoequatorial [see Rule E-6.3(b)] may be used also in connection with other than six-membered rings if, but only if, their interpretation is then still beyond dispute.

groups and the conformation may be described as staggered.

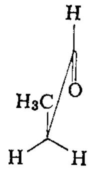
Examples:



Eclipsed conformation.
The pairs a/a', b/b', and c/c' are eclipsed.



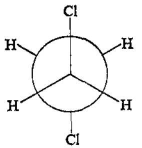
Staggered conformation.
All the attached groups are staggered.



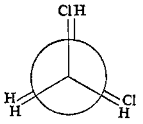
Projection of CH_3CH_2CHO.
The CH_3 and the H of the CHO are eclipsed.
The O and the H's of CH_2 in CH_2CH_3 are staggered.

E-6.6.—Conformations are described as synperiplanar (*sp*), synclinal (*sc*), anticlinal (*ac*), or antiperiplanar (*ap*) according as the torsion angle is within ±30° of 0°, ±60°, ±120°, or ±180°, respectively; the letters in parentheses are the corresponding abbreviations. Atoms or groups are selected from each set to define the torsion angle according to the following criteria: (1) if all the atoms or groups of a set are different, that one of each set that is preferred by the sequence rule; (2) if one of a set is unique, that one; or (3) if all of a set are identical, that one which provides the smallest torsion angle.

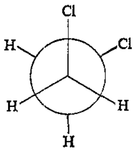
Examples:



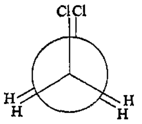
antiperiplanar



anticlinal

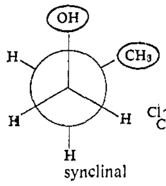


synclinal

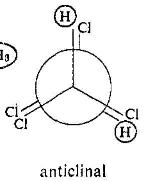


synperiplanar

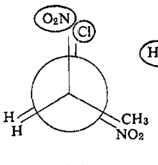
In the above conformations, all CH_2Cl-CH_2Cl, the two Cl atoms decide the torsion angle.



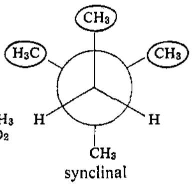
synclinal



anticlinal

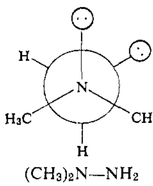


synperiplanar

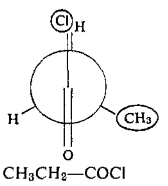


synclinal

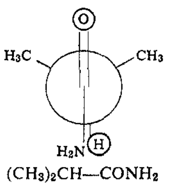
Criterion for:	synclinal	anticlinal	synperiplanar	synclinal
rear atom	2	2	1	3
front atom	2	2	1	2



$(CH_3)_2N$—NH_2
synclinal[16]



CH_3CH_2—$COCl$
anticlinal



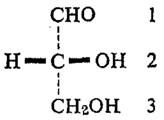
$(CH_3)_2CH$—$CONH_2$
antiperiplanar

Criterion for:	synclinal	anticlinal	antiperiplanar
rear atom	2	2	2
front atom	2	1	1

E-7. Stereoformulas

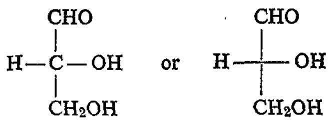
E-7.1.—In a Fischer projection the atoms or groups attached to a tetrahedral center are projected on to the plane of the paper from such an orientation that atoms or groups appearing above or below the central atom lie behind the plane of the paper and those appearing to left and right of the central atom lie in front of the plane of the paper, and that the principal chain appears vertical with the lowest numbered chain member at the top.

Examples:



$$\begin{array}{cl} \text{CHO} & 1 \\ | & \\ \text{H}-\text{C}-\text{OH} & 2 \\ | & \\ \text{CH}_2\text{OH} & 3 \end{array}$$

Orientation



$$\begin{array}{c} \text{CHO} \\ | \\ \text{H}-\text{C}-\text{OH} \\ | \\ \text{CH}_2\text{OH} \end{array} \quad \text{or} \quad \begin{array}{c} \text{CHO} \\ | \\ \text{H}-\!\!+\!\!-\text{OH} \\ | \\ \text{CH}_2\text{OH} \end{array}$$

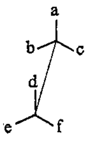
Fischer projection

Notes: (1) The first of the two types of Fischer projection should be used whenever convenient.

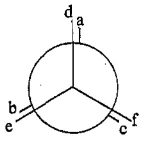
(2) If a Fischer projection formula is rotated through 180° in the plane of the paper, the upward and downward bonds from the central atom still project behind the plane of the paper, and the sideways bonds project in front of that plane. If, however, the formula is rotated through 90° in the plane of the paper, the upward and downward bonds now project in front of the plane of the paper and the sideways bonds project behind that plane.

E-7.2.—To prepare a Newman projection a molecule is viewed along the bond between two atoms; a circle is used to represent these atoms, with lines from outside the circle toward its center to represent bonds to other atoms; the lines that represent bonds to the nearer and the further atom end at, respectively, the center and the circumference of the circle. When two such bonds would be coincident in the projection, they are drawn at a small angle to each other.[17]

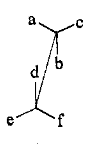
Examples:



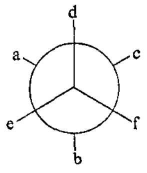
Perspective



Newman projection



Perspective



Newman projection

E-7.3. General Note.—Formulas that display stereochemistry should be prepared with extra care so as to be unambiguous and, whenever possible, self-explanatory. It is inadvisable to try to lay down rules that will cover every case, but the following points should be borne in mind.

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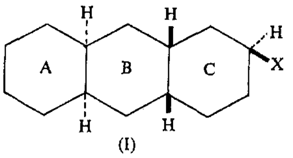
(16) The lone pair of electrons (represented by two dots) on the nitrogen atoms are the unique substituents that decide the description of the conformation (these are the "phantom atoms" of the sequence-rule symbolism).

(17) *Cf.* M. S. Newman, *Rec. Chem. Progr.*, **13**, 111 (1952); *J. Chem. Educ.*, **33**, 344 (1955); "Steric Effects in Organic Chemistry," John Wiley & Sons Inc., New York, N. Y., 1956, p 5-6.

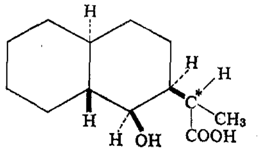
A thickened line (▬) denotes a bond projecting from the plane of the paper toward an observer, a broken line (- - -) denotes a bond projecting away from an observer, and, when this convention is used, a full line of normal thickness (——) denotes a bond lying in the plane of the paper. A wavy line (∿∿∿) may be used to denote a bond whose direction cannot be specified or, if it is explained in the text, a bond whose direction it is not desired to specify in the formula. Dotted lines (· · · · · ·) should preferably not be used to denote stereochemistry, and never when they are used in the same paper to denote mesomerism, intermediate states, etc. Wedges should not be used as complement to broken lines (but see below). Single large dots have sometimes been used to denote atoms or groups attached at bridgehead positions and lying above the plane of the paper, with open circles to denote them lying below the plane of the paper, but this practice is strongly deprecated.

Hydrogen or other atoms or groups attached at sterically designated positions should never be omitted.

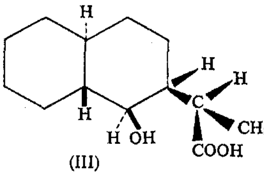
In chemical formulas, rings are usually drawn with lines of normal thickness, that is, as if they lay wholly in the plane of the paper even though this may be known not to be the case. In a formula such as (I) it is then clear that the H atoms attached at the A/B ring junction lie further from the observer than these bridgehead atoms, that the H atoms attached at the B/C ring junction lie nearer to the observer than those bridgehead atoms, and that X lies nearer to the observer than the neighboring atom of ring C.



(I)



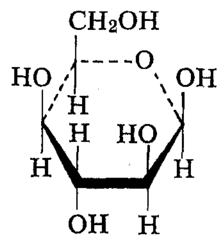
(II)



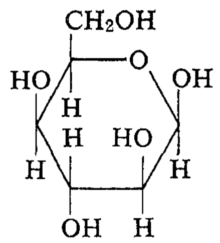
(III)

However, ambiguity can then sometimes arise, particularly when it is necessary to show stereochemistry within a group such as X attached to the rings that are drawn planar. For instance, in formula (II), the atoms O and C*, lying above the plane of the paper, are attached to ring B by thick bonds, but then, when showing the stereochemistry at C*, one finds that the bond *from* C* *to* ring B projects away from the observer and so should be a broken line. Such difficulties can be overcome by using wedges in place of lines, the broader end of the wedge being considered nearer to the observer, as in (III).

In some fields, notably for carbohydrates, rings are conveniently drawn as if they lay perpendicular to the plane of the paper, as represented in (IV); however, conventional formulas such as (V), with the lower bonds considered as the nearer to the observer, are so well established that it is rarely necessary to elaborate this to form (IV).

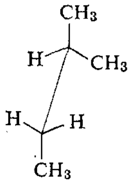


(IV)

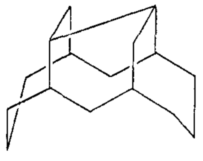


(V)

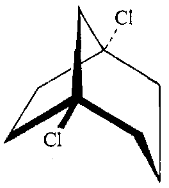
By a similar convention, in drawings such as (VI) and (VII), the lower sets of bonds are considered to be nearer than the upper to the observer. In (VII), note the gaps in the rear lines to indicate that the bonds crossing them pass in front (and thus obscure sections of the rear bonds). In some cases, when atoms have to be shown as lying in several planes, the various conventions may be combined, as in (VIII). In all cases the overriding aim should be clarity.



(VI)



(VII)



(VIII)

Appendix 1. Configuration and Conformation

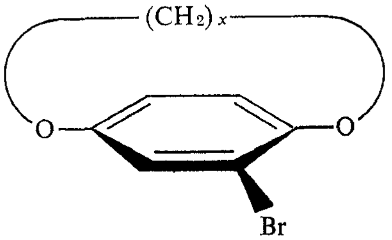
See Rules E-1.4 and E-1.5.

Various definitions have been propounded to differentiate configurations from conformations.

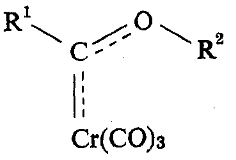
The original usage was to consider as conformations those arrangements of the atoms of a molecule in space that can be interconverted by rotation(s) around a single bond, and as configurations those other arrangements whose interconversion by rotation requires bonds to be broken and then re-formed differently. Interconversion of different configurations will then be associated with substantial energies of activation, and the various species will be separable, but interconversion of different conformations will normally be associated with less activation energy, and the various species, if separable, will normally be more readily interconvertible. These differences in activation energy and stability are often large.

Nevertheless, rigid differentiation on such grounds meets formidable difficulties. Differentiation by energy criteria would require an arbitrary cut in a continuous series of values. Differentiation by stability of isolated species requires arbitrary assumptions about conditions and half-lives. Differentiation on the basis of rotation around single bonds meets difficulties connected both with the concept of rotation and with the selection of single bonds as requisites, and these need more detailed discussion here.

Enantiomeric biaryls are nowadays usually considered to differ in conformation, any difficulty in rotation about the 1,1′ bond due to steric hindrance between the neighboring groups being considered to be overcome by bond bending and/or bond stretching, even though the movements required must closely approach bond breaking if these substituents are very large. Similar doubts about the possibility of rotation occur with a molecule such as (A), where rotation of the benzene ring around the oxygen-to-ring single bonds affords easy interconversion if x is large but appears to be physically impossible if x is small; and no critical size of x can be reasonably established. For reasons such as this, Rules E-1.4 and E-1.5 are so worded as to be independent of whether rotation appears physically feasible or not (see Note 2 to those Rules).



(A)



(B)

The second difficulty arises in the many cases where rotation is around a bond of fractional order between one and two, as in the helicenes, crowded aromatic molecules, metallocenes, amides, thioamides, and carbene-metal coordination compounds (such as B). The term conformation is customarily used in these cases and that appears a reasonable extension of the original conception, though it will be wise to specify the usage if the reader might be in doubt.

When interpreted in these ways, Rules E-1.4 and E-1.5 reflect the most frequent usage of the present day and provide clear distinctions in most situations. Nevertheless, difficulties remain and a number of other usages have been introduced.

It appears to some workers that, once it is admitted that change of conformation may involve rotation about bonds of fractional order between one and two, it is then illogical to exclude rotation about classical double bonds because interconversion of open-chain *cis–trans* isomers depends on no fundamentally new principle and is often relatively easy, as for certain alkene derivatives such as stilbenes and for azo compounds, by irradiation. This extension is indeed not excluded by Rules E-1.4 and E-1.5, but if it is applied that fact should be explicitly stated.

A further interpretation is to regard a stereoisomer possessing some degree of stability (that is, one associated with an energy hollow, however shallow) as a configurational isomer, the other arrangements in space being termed conformational isomers; the term conformer (Rule E-6.1) is then superfluous. This definition, however, requires a knowledge of stability (energy relations) that is not always available.

In another view a configurational isomer is any stereoisomer that can be isolated or (for some workers) whose existence can be established (for example, by physical methods); all other arrangements then represent conformational isomers; but it is then impossible to differentiate configuration from conformation without involving experimental efficiency or conditions of observation.

Yet another definition is to regard a conformation as a precise description of a configuration in terms of bond distances, bond angles, and dihedral angles.

In none of the above views except the last is attention paid to extension or contraction of the bond to an atom that is attached to only one other atom, such as —H or =O. Yet such changes in interatomic distance due to nonbonded interactions may be important, for instance in hydrogen bonding, in differences due to crystal form, in association in solution, and in transition states. This area may repay further consideration.

Owing to the circumstances outlined above, the Rules E-1.4 and E-1.5 have been deliberately made imprecise, so as to permit some alternative interpretations, but they are not compatible with all the definitions mentioned above. The time does not seem ripe to legislate for other than the commoner usages or to choose finally between these. It is, however, encouraging that no definition in this field has (yet) involved atomic vibrations for which, in all cases, only time-average positions are considered.

Finally it should be noted that an important school of thought uses conformation with the connotation of "a particular geometry of the molecule, *i.e.*, a description of atoms in space in terms of bond distances, bond angles, and dihedral angles," a definition much wider than any discussed above.

Appendix 2. Outline of the Sequence-Rule Procedure

The sequence-rule procedure is a method of specifying the absolute molecular chirality (handedness) of a compound, that is, a method of specifying which of two enantiomeric forms each chiral element of a molecule exists. For each chiral element in the molecule it provides a symbol, usually *R* or *S*, which is independent of nomenclature and numbering. These symbols define the chirality of the specific compound considered; they may not be the same for a compound and some of its derivatives; and they are not necessarily constant for chemically similar situations within a chemical or a biogenetic class. The procedure is applied directly to a three-dimensional model of the structure, and not to any two-dimensional projection thereof.

The method has been developed to cover all compounds with ligancy up to 4 and with ligancy 6,[18] and for all configurations and conformations of such compounds. The following is an outline confined to the most common situations; it is essential to study the original papers, especially the 1966 paper,[19] before using the sequence rule for other than fairly simple cases.

General Basis.—The sequence rule itself is a method of arranging atoms or groups (including chains and rings) in an order of precedence, often referred to as an order of preference; for discussion this order can conveniently be generalized as a > b > c > d, where > denotes "is preferred to."

The first step, however, in considering a model is to identify the nature and position of each chiral element that it contains. There are three types of chiral element, namely, the chiral center, the chiral axis, and the chiral plane. The chiral center, which is very

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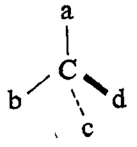
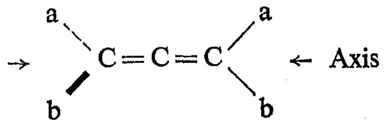
(18) Ligancy refers to the number of bonds from an atom, independently of the nature of the bonds.

(19) R. S. Cahn, C. Ingold, and V. Prelog, *Angew. Chem., Int. Ed. Engl.*, **5**, 385 (1966); errata, *ibid.*, **5**, 511 (1966); *Angew. Chem.*, **78**, 413 (1966). Earlier papers: R. S. Cahn and C. K. Ingold, *J. Chem. Soc.* (London), 612, (1951); R. S. Cahn, C. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956). For a partial, simplified account see R. S. Cahn, *J. Chem. Educ.*, **41**, 116 (1964); *errata, ibid.*, **41**, 503 (1964).

much the most commonly met, is exemplified by an asymmetric carbon atom with the tetrahedral arrangement of ligands, as in (1). A chiral axis is present in, for instance, the chiral allenes such as (2) or the chiral

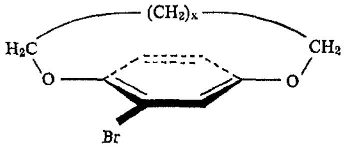


(1)

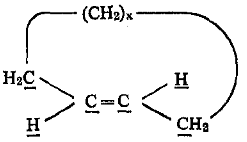


(2)

biaryl derivatives. A chiral plane is exemplified by the plane containing the benzene ring and the bromine and oxygen atoms in the chiral compound (3), or by the underlined atoms in the cycloalkene (4). Clearly,



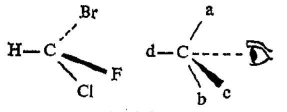
(3)



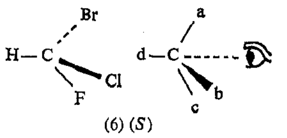
(4)

more than one type of chiral element may be present in one compound; for instance, group "a" in (2) might be a *sec*-butyl group which contains a chiral center.

The Chiral Center.—Let us consider first the simplest case, namely, a chiral center (such as carbon) with four ligands, a, b, c, d which are all different atoms, tetrahedrally arranged, as in CHFClBr. The four ligands are arranged in order of preference by means of the sequence rule; this contains five subrules, which are applied in succession so far as necessary to obtain a decision. The first subrule is all that is required in a great majority of actual cases; it states that ligands are arranged in order of decreasing atomic number, in the above case (a) Br > (b) Cl > (c) F > (d) H. There would be two (enantiomeric) forms of the compound and we can write these as (5) and (6). In the sequence-rule procedure the model is viewed from the side remote from the least-preferred ligand (d), as illustrated. Then, tracing a path from a to b to c in (5) gives a clockwise course, which is symbolized by (*R*) (Latin *rectus*, right; for right hand); in (6) it gives an anticlockwise course, symbolized as (*S*) (Latin *sinister*, left). Thus (5) would be named (*R*)-bromochlorofluoromethane, and (6) would be named (*S*)-bromochlorofluoromethane. Here already it may be noted that converting one enantiomer into another changes each *R* to *S*, and each *S* to *R*, always. It will be seen also that the chirality prefix is the same whether the alphabetical order is used, as above, for naming the substituents or whether this is done by the order of complexity (giving fluorochlorobromomethane).



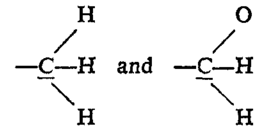
(5) (*R*)



(6) (*S*)

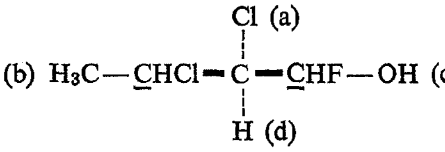
Next, suppose we have $H_3C{-}CHClF$. We deal first with the atoms directly attached to the chiral center; so the four ligands to be considered are Cl > F > C (of CH_3) > H. Here the H's of the CH_3 are not concerned, because we do not need them in order to assign our symbol.

However, atoms directly attached to a center are often identical, as, for example, the underlined C's in $H_3\underline{C}{-}CHCl{-}\underline{C}H_2OH$. For such a compound we at once establish a preference (a) Cl > (b, c) $\underline{C},\underline{C}$ > (d) H. Then to decide between the two $\underline{C}$'s we work outward, to the atoms to which they in turn are directly attached and we then find



which we can conveniently write as C(H,H,H) and C(O,H,H). We have to compare H,H,H with O,H,H, and since oxygen has a higher atomic number than hydrogen we have O > H and thence the complete order Cl > C (of CH_2OH) > C (of CH_3) > H, so that the chirality symbol can then be determined from the three-dimensional model.

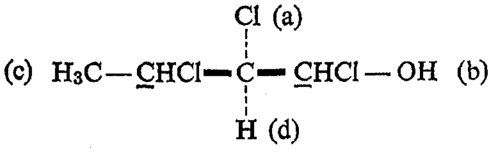
We must next meet the first complication. Suppose that we have a molecule (7)



$$\text{(b) } H_3C{-}\underline{C}HCl{-}\overset{\text{Cl (a)}}{\underset{\text{H (d)}}{C}}{-}\underline{C}HF{-}OH \text{ (c)}$$

(7) (*S*)

To decide between the two $\underline{C}$'s we first arrange the atoms attached to them in *their* order of preference, which gives $\underline{C}$(Cl,C,H) on the left and $\underline{C}$(F,O,H) on the right. Then we compare the preferred atom of one set (namely, Cl) with the preferred atom (F) of the other set, and as Cl > F we arrive at the preferences a > b > c > d shown in (7) and chirality (*S*). If, however, we had a compound (8)

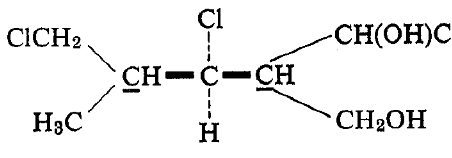


$$\text{(c) } H_3C{-}\underline{C}HCl{-}\overset{\text{Cl (a)}}{\underset{\text{H (d)}}{C}}{-}\underline{C}HCl{-}OH \text{ (b)}$$

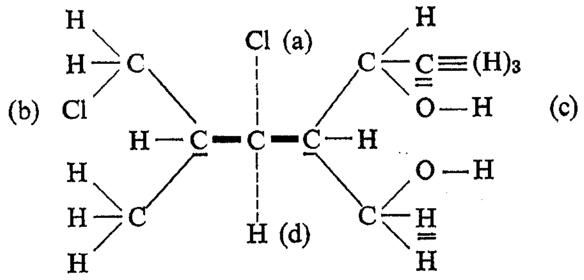
(8) (*R*)

we should have met $\underline{C}$(Cl,C,H) and $\underline{C}$(Cl,O,H) and, since the atoms of first preference are identical (Cl), we should have had to make the comparisons with the atoms of second preference, namely, O > C, which leads to the different chirality (*R*) as shown in (8).

Branched ligands are treated similarly. Setting them out in full gives a picture that at first sight looks complex but the treatment is in fact simple. For instance, in compound (9) a first quick glance again shows (a) Cl> (b, c) $\underline{C}$, $\underline{C}$ > (d) H. When we expand the two $\underline{C}$'s we find they are both $\underline{C}$(C,C,H), so we continue exploration. Considering first the left-hand ligand we arrange the branches and their sets of atoms in order thus: C(Cl,H,H) > C(H,H,H). On the right-hand side we have C(O,$\underline{\underline{C}}$,H) > C(O,$\underline{\underline{H}}$,H) (because $\underline{\underline{C}}$ > $\underline{\underline{H}}$). We compare first the preferred of these branches from each side and we find C(Cl,H,H) > C(O,C,H) because Cl > O, and that gives the left-hand branch preference over the right-hand branch. That is all we need to do to establish chirality (*S*) for this



(9)

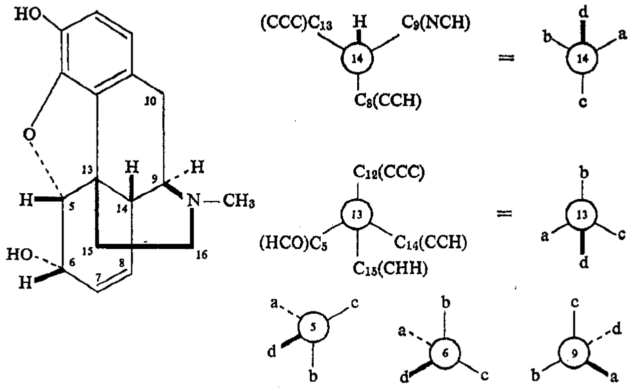


(9) (*S*)

highly branched compound (9). Note that it is immaterial here that, for the lower branches, the right-hand C(O,H,H) would have been preferred to the left-hand C(H,H,H); we did not need to reach that point in our comparisons and so we are not concerned with it; but we should have reached it if the two top (preferred) branches had both been the same CH_2Cl.

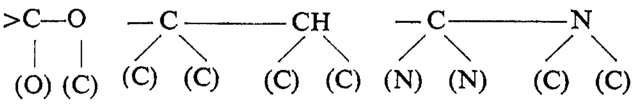
Rings, when met during outward exploration, are treated in the same way as branched chains.

With these simple procedures alone, quite complex structures can be handled; for instance, the analysis alongside formula (10) for natural morphine explains why the specification is as shown. The reason for considering C-12 as C(C,C,C) is set out in the next paragraphs.



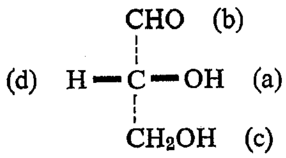
(10) (5*R*, 6*S*, 9*R*, 13*S*, 14*R*)-Morphine

Now, using the sequence rule depends on exploring along bonds. To avoid theoretical arguments about the nature of bonds, simple classical forms are used. Double and triple bonds are split into two and three bonds, respectively. A >C=O group is treated as i (below) where the (O) and the (C) are duplicate representations of the atoms at the other end of the double bond. —C≡CH is treated as ii and —C≡N is treated as iii.



i ii iii

Thus in D-glyceraldehyde (11) the CHO group is treated as C(O,(O),H) and is thus preferred to the C(O,H,H) of the CH_2OH group, so that the chirality symbol is (*R*).

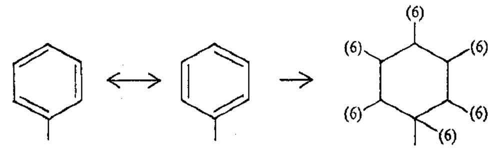


D-Glyceraldehyde (11) (*R*)

Only the doubly bonded atoms themselves are duplicated, and not the atoms or groups attached to them; the duplicated atoms may thus be considered as carrying three phantom atoms (see below) of atomic number zero. This may be important in deciding preferences in certain complicated cases.

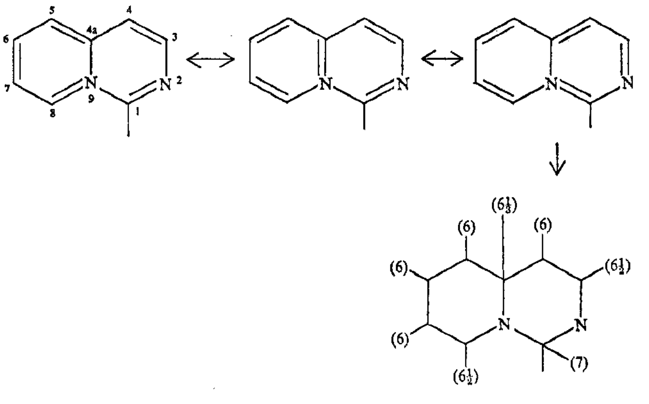
Aromatic rings are treated as Kekulé structures. For aromatic hydrocarbon rings it is immaterial which Kekulé structure is used because "splitting" the double bonds gives the same result in all cases; for instance, for phenyl the result can be represented as (12a) where "(6)" denotes the atomic number of the duplicate representations of carbon.

(12)



(12a)

(13)



For aromatic hetero rings, each duplicate is given an atomic number that is the mean of what it would have if the double bond were located at each of the possible positions. A complex case is illustrated in (13). Here C-1 is doubly bonded to one or other of the nitrogen atoms (atomic number 7) and never to carbon, so its added duplicate has atomic number 7; C-3 is doubly bonded either to C-4 (atomic number 6) or to N-2 (atomic number 7), so its added duplicate has atomic number $6^1/_2$; so has that of C-8; but C-4a may be doubly bonded to C-4, C-5, or N-9, so its added duplicate has atomic number 6.33.

One last point about the chiral center may be added here. Except for hydrogen, ligancy, if not already four, is made up to four by adding "phantom atoms" which have atomic number zero and are thus always last in order of preference. This has various uses but perhaps the most interesting is where nitrogen occurs in a rigid skeleton, as, for example, in α-isosparteine (14). Here the phantom atom can be placed where the nitrogen lone pair of electrons is; then N-1 appears as shown alongside the formula; and the chirality (*R*) is the

TABLE I

SOME COMMON GROUPS IN ORDER OF SEQUENCE-RULE PREFERENCE[a]

A. Alphabetical Order (Higher Number Denotes Greater Preference)

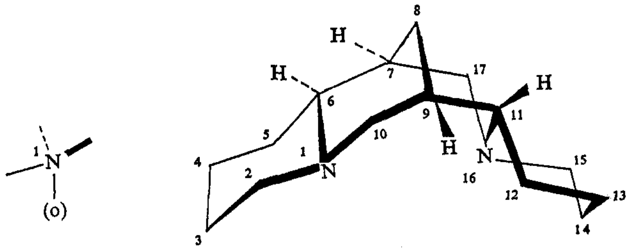
64	Acetoxy	38	Carboxyl	9	Isobutyl	55	Nitroso
36	Acetyl	74	Chloro	8	Isopentyl	6	*n*-Pentyl
48	Acetylamino	17	Cyclohexyl	20	Isopropenyl	61	Phenoxy
21	Acetylenyl	52	Diethylamino	14	Isopropyl	22	Phenyl
10	Allyl	51	Dimethylamino	69	Mercapto	47	Phenylamino
43	Amino	34	2,4-Dinitrophenyl	58	Methoxy	54	Phenylazo
44	Ammonio $^{+}H_3N-$	28	3,5-Dinitrophenyl	39	Methoxycarbonyl	18	Propenyl
37	Benzoyl	59	Ethoxy	2	Methyl	4	*n*-Propyl
49	Benzoylamino	40	Ethoxycarbonyl	45	Methylamino	29	1-Propynyl
65	Benzoyloxy	3	Ethyl	71	Methylsulfinyl	12	2-Propynyl
50	Benzyloxycarbonylamino	46	Ethylamino	66	Methylsulfinyloxy	73	Sulfo
13	Benzyl	68	Fluoro	72	Methylsulfonyl	25	*m*-Tolyl
60	Benzyloxy	35	Formyl	67	Methylsulfonyloxy	30	*o*-Tolyl
41	Benzyloxycarbonyl	63	Formyloxy	70	Methylthio	23	*p*-Tolyl
75	Bromo	62	Glycosyloxy	11	Neopentyl	53	Trimethylammonio
42	*tert*-Butoxycarbonyl	7	*n*-Hexyl	56	Nitro	32	Trityl
5	*n*-Butyl	1	Hydrogen	27	*m*-Nitrophenyl	15	Vinyl
16	*sec*-Butyl	57	Hydroxy	33	*o*-Nitrophenyl	31	2,6-Xylyl
19	*tert*-Butyl	76	Iodo	24	*p*-Nitrophenyl	26	3,5-Xylyl

B. Increasing Order of Sequence Rule Preference

1	Hydrogen	20	Isopropenyl	39	Methoxycarbonyl[b]	58	Methoxy
2	Methyl	21	Acetylenyl	40	Ethoxycarbonyl[b]	59	Ethoxy
3	Ethyl	22	Phenyl	41	Benzyloxycarbonyl[b]	60	Benzyloxy
4	*n*-Propyl	23	*p*-Tolyl	42	*tert*-Butoxycarbonyl[b]	61	Phenoxy
5	*n*-Butyl	24	*p*-Nitrophenyl	43	Amino	62	Glycosyloxy
6	*n*-Pentyl	25	*m*-Tolyl	44	Ammonio $^{+}H_3N-$	63	Formyloxy
7	*n*-Hexyl	26	3,5-Xylyl	45	Methylamino	64	Acetoxy
8	Isopentyl	27	*m*-Nitrophenyl	46	Ethylamino	65	Benzoyloxy
9	Isobutyl	28	3,5-Dinitrophenyl	47	Phenylamino	66	Methylsulfinyloxy
10	Allyl	29	1-Propynyl	48	Acetylamino	67	Methylsulfonyloxy
11	Neopentyl	30	*o*-Tolyl	49	Benzoylamino	68	Fluoro
12	2-Propynyl	31	2,6-Xylyl	50	Benzyloxycarbonylamino	69	Mercapto HS−
13	Benzyl	32	Trityl	51	Dimethylamino	70	Methylthio CH_3S-
14	Isopropyl	33	*o*-Nitrophenyl	52	Diethylamino	71	Methylsulfinyl
15	Vinyl	34	2,4-Dinitrophenyl	53	Trimethylammonio	72	Methylsulfonyl
16	*sec*-Butyl	35	Formyl	54	Phenylazo	73	Sulfo HO_3S-
17	Cyclohexyl	36	Acetyl	55	Nitroso	74	Chloro
18	1-Propenyl	37	Benzoyl	56	Nitro	75	Bromo
19	*tert*-Butyl	38	Carboxyl	57	Hydroxy	76	Iodo

[a] ANY alteration to structure, or substitution, etc., may alter the order of preference. [b] These groups are ROC(=O)−.

consequence. The same applies to N-16. Phantom atoms are similarly used when assigning chirality symbols to chiral sulfoxides (see example to Rule E-5.9).



(14) (1*R*, 6*R*, 7*S*, 9*S*, 11*R*, 16*R*)-Sparteine

Symbolism.—In names of compounds, the *R* and *S* symbols, together with their locants, are placed in parentheses, normally in front of the name, as shown for morphine (10) and sparteine (14), but this may be varied in indexes or in languages other than English. Positions within names are required, however, when more than a single series of numerals is used, as for esters and amines. When relative stereochemistry is more important than absolute stereochemistry, as for steroids or carbohydrates, a local system of stereochemical designation may be more useful and sequence-rule symbols need then be used only for any situations where the local system is insufficient.

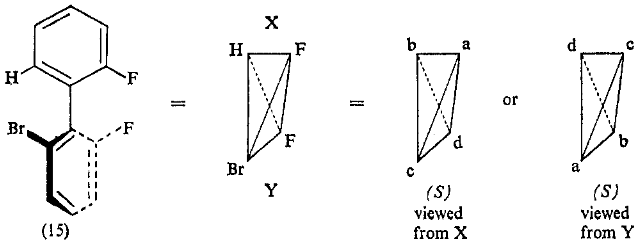
Racemates containing a single center are labeled (*RS*). If there is more than one center the first is labeled (*RS*) and the others are (*RS*) or (*SR*) according to whether they are *R* or *S* when the first is *R*. For instance, the 2,4-pentanediols $CH_3-CH(OH)-CH_2-CH(OH)-CH_3$ are differentiated as

one chiral form (2*R*,4*R*)–
other chiral form (2*S*,4*S*)–
meso compound (2*R*,4*S*)–
racemic compound (2*RS*,4*RS*)–

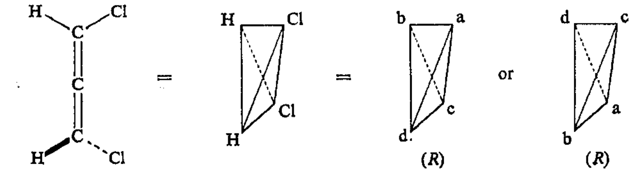
Finally the principles by which some of the least rare of other situations are treated will be very briefly summarized.

Pseudoasymmetric Atoms.—A subrule decrees that *R* groups have preference over *S* groups and this permits pseudoasymmetric atoms, as in abC(c-*R*)(c-*S*) to be treated in the same way as chiral centers, but as such a molecule is achiral (not optically active) it is given the lower case symbol *r* or *s*.

Chiral Axis.—The structure is regarded as an elongated tetrahedron and viewed along the axis—it is immaterial from which end it is viewed; the nearer pair of ligands receives the first two positions in the order of preference, as shown in (15) and (16).



(15)

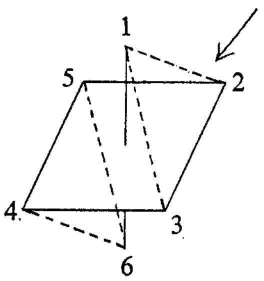


(16)

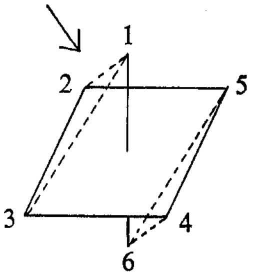
Chiral Plane.—The sequence-rule-preferred atom directly attached to the plane is chosen as "pilot atom." In compound (3) (page 2864) this is the C of the left-hand CH_2 group. Now this is attached to the left-hand oxygen atom in the plane. The sequence-rule-preferred path from this oxygen atom is then explored in the plane until a rotation is traced which is clockwise (*R*) or anticlockwise (*S*) when viewed from the pilot atom. In (3) this path is O → C → C(Br) and it is clockwise (*R*).

Other Subrules.—Other subrules cater for new chirality created by isotopic labeling (higher mass number preferred to lower) and for steric differences in the ligands. Isotopic labeling rarely changes symbols allotted to other centers.

Octahedral Structures.—Extensions of the sequence rule enable ligands arranged octahedrally to be placed in an order of preference, including polydentate ligands, so that a chiral structure can then always be represented as one of the enantiomeric forms (17) and (18). The face 1–2–3 is observed from the side remote from the face 4–5–6 (as marked by arrows), and the path 1 → 2 → 3 is observed; in (17) this path is clockwise (*R*), and in (18) it is anticlockwise (*S*).

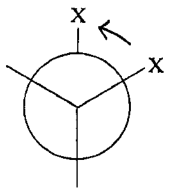


(*R*) (17)

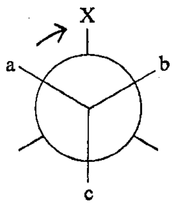


(18) (*S*)

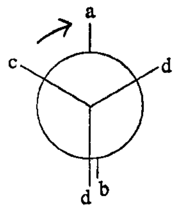
Conformations.—The torsion angle between selected bonds from two singly bonded atoms is considered. The selected bond from each of these two atoms is that to a unique ligand, or otherwise to the ligand preferred by the sequence rule. The smaller rotation needed to make the front ligand eclipsed with the rear one is noted (this is the rotatory characteristic of a helix); if this rotation is right-handed it leads to a symbol *P* (plus); if left-handed to *M* (minus). Examples are



(*M*)



(*P*)



(*P*)

Details and Complications.—For details and complicating factors the original papers should be consulted. They include treatment of compounds with high symmetry or containing repeating units (*e.g.*, cyclitols), also π bonding (metallocenes, etc.), mesomeric compounds and mesomeric radicals, and helical and other secondary structures.