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Unique and Unambiguous Specification of Stereoisomerism about a Double Bond in Nomenclature and Other Notation Systems

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In a previous communication, rules for unambiguous specification of stereoisomerism about a double bond using the descriptors E and Z were reported. These rules have been complemented to permit the derivation of a unique set of configurational descriptors for a compound. Use of these descriptor sets with chemical nomenclature and other forms of constitutional description of a compound is discussed.

In a previous paper (1) a set of rules was described which permits unambiguous specification of stereoisomerism about a double bond employing the configurational descriptiors E and Z. The purpose of this paper is to report the extension of these rules to permit the derivation of a unique set of configurational descriptors for each compound which contains one or more stereogenic (2) double bonds. The descriptor E or Z is assigned to each such double bond using Rules I and II (1). Three additional rules, III–V, provide for the derivation of the unique descriptor set for each compound.

RULES FOR SPECIFYING CONFIGURATIONS ABOUT DOUBLE BONDS

E and Z are defined as follows:

I. For each double bond to be described configurationally, the priority of the two groups attached to each of the doubly bound atoms is determined according to the sequence rules of Cahn, Ingold, and Prelog (3).

II. That configuration in which the two groups of higher priority are on the *same* side of the reference plane, Q (Figure 1), is assigned the stereochemical descriptor Z; the configuration in which these groups are on *opposite* sides is assigned the descriptor E.
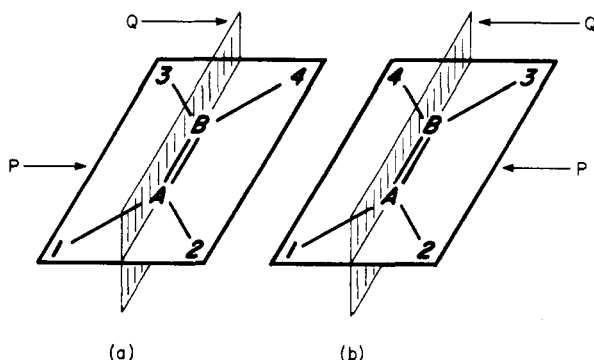

Figure 1. Geometory of a pair of doubly-bound atoms, A and B, and their nearest neighbors

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The application of these rules is illustrated below for the two stereoisomers of 1-bromo-2-chloro-1-iodoethylene. The groups of higher priority are marked in heavy type.
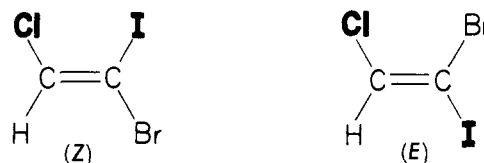
The rules stated for the assignment of the configurational descriptors E and Z are based entirely on the structure of the molecule. To distinguish uniquely between compounds which are constitutionally identical but which differ in configuration at one or more double bonds, it is necessary to identify the double bond with which each descriptor is associated. This is accomplished by application of Rules III–V (below), which result from a logical extension Rules I and II.

III. After assignment of the configurational descriptor, E or Z, to each stereogenic double bond, determine which of the four groups attached to each doubly-bound atom-pair is the *most* preferred according to the sequence rules of Cahn, Ingold and Prelog (3).

IV. The stereogenic double bonds are then ranked in decreasing order of the most perferred group attached to each doubly-bound atom-pair. If the double bonds cannot be ordered completely on the basis of a comparison of the most preferred groups, any ties are resolved by comparison of the second most preferred groups, followed, if necessary, by a comparison of the third most preferred groups, and the fourth most preferred groups in turn.

V. The configurational descriptors (E and Z) are arranged in decreasing order according to the rank of each respective double bond. When the configuration of one or more stereogenic double bonds is unknown, a question mark (?) is used as the descriptor for that double bond and is placed in order with the other descriptors. This set of descriptors, together with some representation of constitution, provides unique and unambiguous specification of stereoisomerism about the double bonds in a compound.

Rules III–V are, of course, required only when there are two or more stereogenic double bonds in the molecule not

all of which have the same descriptor (E, Z, ?). Application of Rules I-V to chemical nomenclature is illustrated by the following examples:
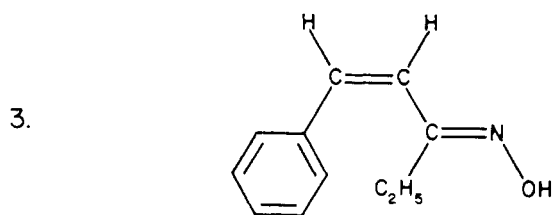
I.
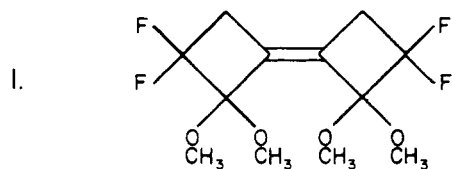
(Z)-3,3,3′,3′-Tetrafluoro[bicyclobutylidene]-2,2′-dione bis(dimethyl acetal)
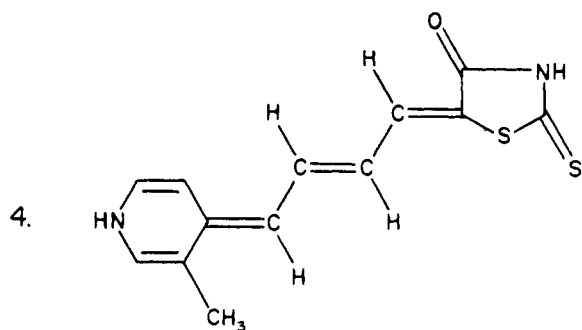
The inverted CA Index name is:

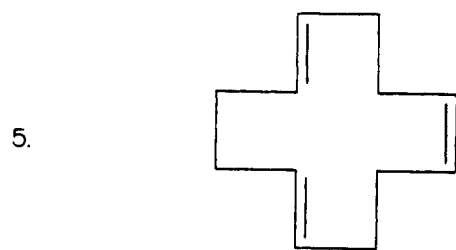[Bicyclobutylidene]-2,2′-dione, 3,3,3′,3′-tetrafluoro-, bis(dimethyl acetal), (Z)-

2.
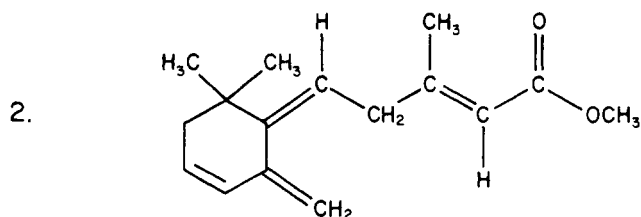
(E,Z)-Methyl 5-(6,6-dimethyl-2-methylene-3-cyclohexen-1-yl-idene)-3-methyl-2-pentenoate
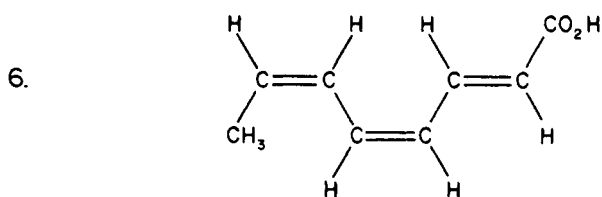
3.

(E,Z)-1-Phenyl-1-penten-3-one oxime

4.
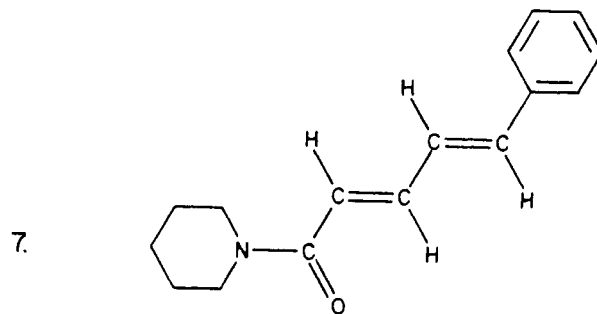
(Z,E,E)-5-{4-[3-Methyl-4(1H)-pyridylidene]-2-butenylidene}-rhodanine

5.

(E,E,Z)-1,5,9-Cyclododecatriene

6.

(E,Z,Z)-2,4,6-Octatrienoic acid

7.

(E,E)-1-(5-Phenyl-2,4-pentadienoyl)piperidine

8.
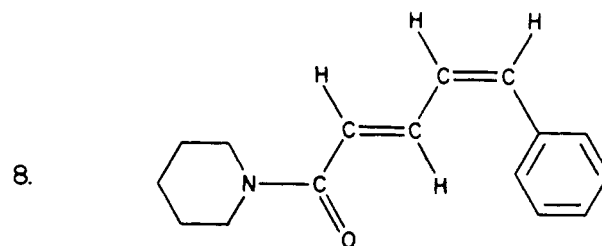
(E,Z)-1-(5-Phenyl-2,4-pentadienoyl)piperidine

9.
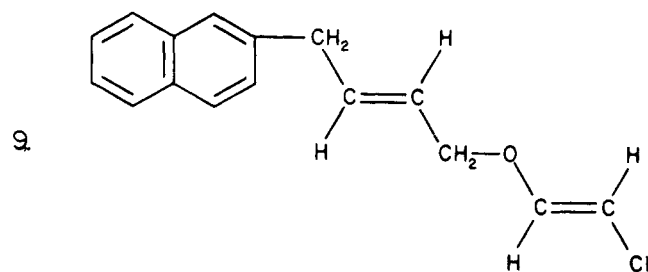
(E,E)-2-{4-[(2-Chlorovinyl)oxy]-2-butenyl}naphthalene

10.
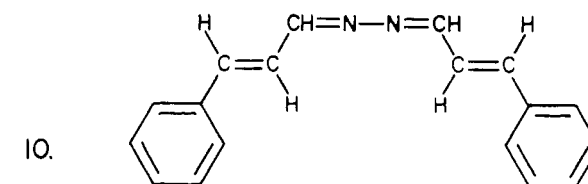
($?$,$?$,E,E)-Cinnamaldehyde azine

## APPLICATION OF THE RULES TO SPECIAL STRUCTURAL SITUATIONS

In addition to the double bond systems already discussed, two special constitutional situations exist which

give rise to geometrical isomerism. These are exemplified by the *cumulenes* which have odd numbers of double bonds, and by the *1,n-dialkylidenecycloalkanes* in which the cycloalkanes are symmetrically substituted and have $2n - 2$ members where $n = 3,4,5 \ldots$. The conditions for the existence of stereoisomerism in these systems are the same as for simple double bond systems (i.e., systems of isolated or conjugated double bonds).

To describe the configuration of a system consisting of an odd number of cumulated double bonds $[X(=X=X)_n=X$, where $n = 1,2,3 \ldots]$ or of an alternating sequence of double bonds and symmetrically substituted, even-membered rings in which the sum of the number of rings and double bonds is odd, Rules I-V are applied using the four atoms attached to the first and last atoms of the double bond system for the necessary priority determinations (the first and last atoms are equivalent to the doubly-bound atom-pair in simple double bond systems). The following examples illustrate the application of Rules I-V to describe the configuration of these special structural types.
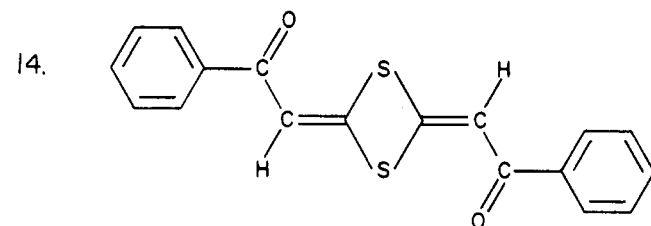
II.
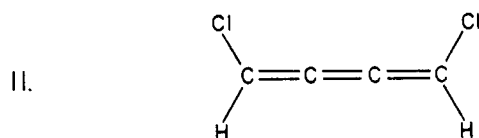
(Z)-1,4-Dichlorobutatriene

12.
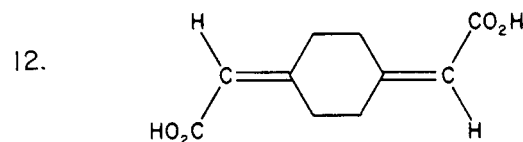
(E)-$\Delta^{1,\alpha:4,\alpha'}$-Cyclohexanediacetic acid

13.
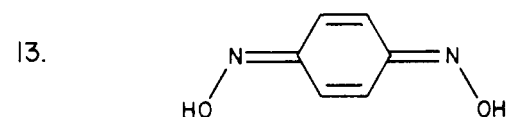
(Z)-p-Benzoquinone dioxime

14.

(E)-2,2''-(1,3-Dithietan-2,4-diylidene)diacetophenone

Work is presently under way to extend the applicability of the E and Z descriptors to more general systems which involve alternating sequences of double bonds and rings and to certain types of single bond torsional isomerism [4].

Although the use of E and Z has been illustrated with chemical nomenclature (as it will be used in *Chemical Abstracts* Indexes beginning with Volume 66), the descrip-

tors can be used with any representation of the constitution of a compound, including linear notations, atom-bond connection tables and structural diagrams. For example, E and Z are used as integral parts of the atom-bond connection table record for each compound in the CAS Chemical Compound Registry System [5]. The descriptor sets used in the CAS Registry are the same as those derived for use in *CA* Indexes (see examples 1 through 14); derivations for both purposes are done in a single operation.

The advantage of the method reported herein for delineating stereoisomerism about double bonds is that it provides for unambiguous communication of stereochemical information without the need for a special knowledge of nomenclature or other notation systems. Furthermore, the few required rules are based upon the sequence rules of Cahn, Ingold, and Prelog which are already employed by many chemists for chirality specification. Finally, the method increases the possibility for automatic interconversion between chemical nomenclature and other representations of structure [6], particularly atom-bond connection tables [5, 7].

CONCLUSION

In this and the preceding paper we have described procedures for unique identification of double bond stereoisomers. We have shown how these procedures can be used with chemical nomenclature as well as with other constitutional descriptions of a compound. Use of these procedures by the practicing chemist, as well as by information services such as CAS, will result in improved communication and more exact retrieval of information on compounds which exhibit stereoisomerism about double bonds.

ACKNOWLEDGMENT

LITERATURE CITED

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(2) A stereogenic double bond is one in which the groups attached to the doubly-bound atoms are of such nature that an interchange of the groups attached to one of the doubly-bound atoms will produce a stereoisomer. See McCasland, G.E., "A New General Method for the Naming of Stereoisomers," p. 2, Chemical Abstracts Service, Columbus, Ohio, 1953.

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(4) Mislow, K., "Introduction to Stereochemistry," p. 75, W. A. Benjamin, Inc., New York, 1965.

(5) Morgan, H. L., J. Chem. Doc. 5, 107 (1965); Leiter, D. P., H. L. Morgan, and R. E. Stobaugh, *ibid.*, 5, 238 (1965).

(6) Vander Stouw, G. G., I. Naznitsky, and J. E. Rush, *ibid.*, 7, 165 (1967).

(7) Petrarca, A. E., M. F. Lynch, and J. E. Rush, *ibid.*, 7, 154 (1967).