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DEFINING STEREOCHEMISTRY AS A FUNCTION OF DISTANCE

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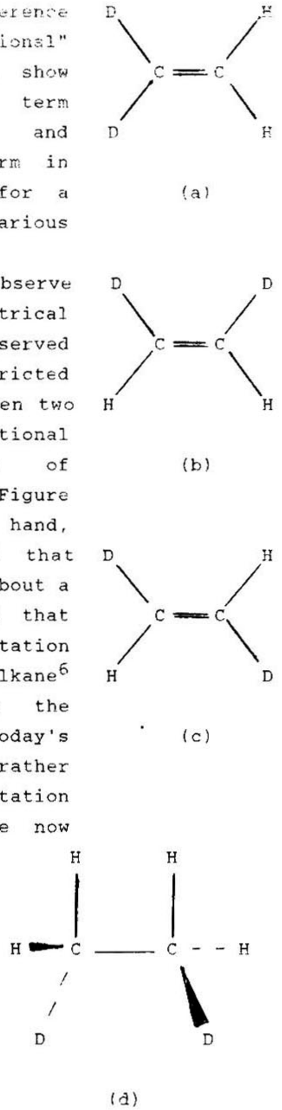
ABSTRACT: An efficient means of differentiating the various classes of stereoisomers is proposed using the properties of metric versus graph theoretical distance. Such a scheme is useful not only for the more common coordination 4 central atom with four different ligands that traditionally exists in "organic" chemistry (viz., carbon), but also for higher coordination central atoms such as are now becoming more common in "inorganic" chemistry.

As the necessary background and history of the problem, let us note that the term "isomer", derived from "iso" = equal and "-mer" = parts[1], was first applied in chemistry in the 1820s to describe the difference between silver cyanate (AgNCO) and silver fulminate (AgOCN).[2] Initially, the term was applied to many types of compounds that at the time seemed to be similar. This included: (1) differences in properties caused by different arrangements of identical molecules or ions in a crystal -- an idea now referred to as "polymorphism"; (2) molecules of identical percent composition but of different molecular weight -- "polymerism"; and (3) molecules of identical percent composition and molecular weight[3]. However, as more examples of this third class were discovered, the term came to be reserved for only this class of compounds. This, in turn, was followed by subdividing this limited class into stereo- vs. structural isomers -- where stereoisomers are those that have "the same geometrical (linear) ordering" of atoms in a molecule, and structural isomers are those that do not. The decision as to what is considered to be "the same ordering" reduces to: Does each atom in the pair have respectively the same neighbors? Note that in the silver cyanate vs. silver fulminate example mentioned above, only the carbon atom has the same set of neighboring atoms -- a concept that, for today's chemists is considered of sufficient importance to be assigned a special term of its own ("constitution")[4]; consequently, these two molecules are only structural isomers, and not stereoisomers.

The term "stereoisomerism" historically was further subdivided into two classes: "geometrical" and "optical". However, in retrospect, many modern chemistry books claim that the distinction between these two classes does not appear to be as significant as when it was first introduced. In fact, the Encyclopedia Britannica asserts that: "A simple and precise definition of optical and geometrical isomerism appear to be impossible."[5] Nevertheless, in a very general sense, we believe that there is a "built-in" heuristic such that structural isomers have a "linear" difference, geometrical isomers a "planar" difference and optical isomers a "three-dimensional" difference. Furthermore, we shall show below that by the defining of a term commonly used in graph theory, and comparing it to the corresponding term in metric geometry, we do have the basis for a line of demarcation between the various classes of stereoisomers.

Before doing this, however, we observe that originally, the term "geometrical isomerism" was applied to the observed difference that results from restricted rotation about a double bond between two carbon atoms. For example, the rotational barrier between the two forms of dideuterioethylene (parts b and c of Figure 1) is 65 kcal/mole. On the other hand, although it was originally believed that there was free unrestricted rotation about a single bond, it was soon discovered that about 3 kcal/mole was expended for rotation about a comparable single bond in an alkane[6] (part d of Figure 1). Because the difference is considered, by today's standards, to be only quantitative, rather than qualitative, isomers formed by rotation about both single and double bonds are now referred to as "conformational isomers". Note that many earlier texts, such as Cram & Hammond[7] in the 1950s and Morrison & Boyd[8] in the 1960s, consider "conformational isomers" to be strictly rotation about a single bond vs. "geometrical isomerism" about a double bond, while later authors, such as Streitwieser &



(a)

(b)

(c)

(d)

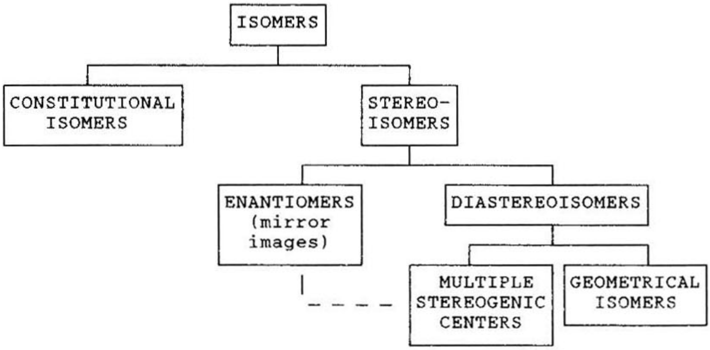
FIGURE 1

Heathcock[9] in the early 1980s, discontinue the use of the term "geometrical isomerism" and consider rotation around either a single or double bond as "conformational isomerism".

Meanwhile, we note that one of the most salient uses of graph theory in chemistry is to represent the "constitution" of a molecule by either a simple or a multiple graph -- with the vertices corresponding to the atoms and the edges to the chemical bonds that we postulate to describe the way these atoms are held together in forming a chemical compound. Note that the idea behind the word "constitution" is that of a "local" (in contradistinction to "global") topology with our focus on how the individual atoms are connected to one another. This is equivalent to saying that, within limits, we may ignore the embedding of the molecule in a three dimensional space as well as other aspects of topology that are inherent in the molecule[10].

In a recent summarization of this division of isomers in *Chemical & Engineering News*[11], the term "constitutional isomer" is used in place of "structural isomer". The class of stereoisomers is then further subdivided into "Enantiomers (mirror images)" and "Diastereomers (not mirror images)". (Table 1), with a note that the Diastereomer can be further subdivided into Geometric isomers and diastereomers with multiple stereogenic centers. (No mention is made of the fact that enantiomers can also have stereogenic centers.)

TABLE 1



A different, we believe better, way to distinguish stereoisomers is provided by consideration of "distance" between ligands. Here the word "distance" will be considered from two different perspectives, which will be referred to as "graph theoretical distance" (abbreviated GTD) vs. "metric distance" (abbreviated MD), which may be defined as follows:

> GRAPH THEORETICAL DISTANCE between two atoms is the length of the shortest path between these two atoms. Note that such a measure considers that each pair of adjacent atoms are a unit "distance" apart. Consequently, measurement is made by counting the minimum number of edges traversed; i.e., an integer.
>
> METRIC DISTANCE between two atoms is the physical (real number, rather than integer) length of the shortest path in the three dimensional embedding space that the lowest energy conformer of the molecule lies in. Note this "distance" has both a numerical (not usually integer) value and a unit of length, such as picometers, or Angstroms, etc.

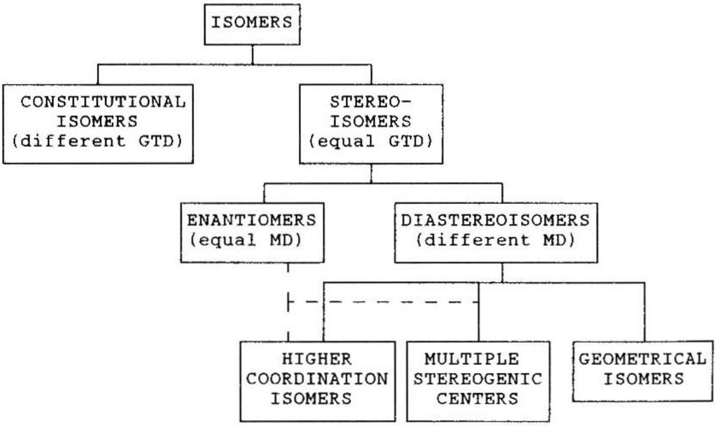
At this point, note that between corresponding atoms in every pair of geometrical isomers as well as every pair of optical isomers, we have the same GTD -- which is independent of which conformer of the molecule is being considered. We hereby propose using this property to define "stereoisomers":

> Isomers in which the GTDs between sets of
> corresponding atoms is pairwise the same.

Consideration of distance in the three different dideuterioethenes illustrates the differences between non-stereo and stereo-isomers and between the different geometrical isomers:

In Figure 1a, the GTD between the two deuterium atoms = 2, while in the two 1,2-dideuterioethenes (Figures 1b and 1c), GTD = 3. Consequently, GTD alone is sufficient to distinguish between stereo and non-stereo-isomers, but not between geometrical isomers (or optical isomers). Let us now consider the metric distance between the deuterium atoms in Figures 1b and 1c. Using the measured bond lengths of C-H (or C-D) = 107 pm, and C=C = 133 pm[12], and H-C-H bond angles of 118° (and H-C=C bond angles of 121°), we can easily (by trigonometry) compute the metric distance between the D atoms; namely, 243 pm for cis (Figure 1b) and 304 pm for trans (Figure 1c). In other words, we note that geometrical isomers have equal GTDs and unequal MDs. The above subdivision of isomers is summarized in pictorial form by the formation of a graph corresponding to the tree used in Table 1 (Table 2).

TABLE 2


ISOMERS
CONSTITUTIONAL ISOMERS (different GTD)
STEREO-ISOMERS (equal GTD)
ENANTIOMERS (equal MD)
DIASTEREOISOMERS (different MD)
HIGHER COORDINATION ISOMERS
MULTIPLE STEREOGENIC CENTERS
GEOMETRICAL ISOMERS

Two items to note at this point about Table 2 are:

(1) This table contains a block not included in Table 1, which we have labelled "Higher Coordination Isomers". This will be discussed in detail below.

and

(2) A second additional block, that we might logically have expected, for topological isomers,[13] has not been included. The reason for this omission is the non-relevance of distance in topological isomers. When no path exists between two atoms, such as in different chains of a catenane, we say the GTD = infinity; however, the MD for the corresponding atoms is a variable, but finite, quantity.

As we next examine the phonomenon associated with sp^3 hybridized orbitals and "optical" isomerism, we note that when a central atom has four different ligands, it produces two isomers which differ in how they are oriented in three-dimensional space (Figure 2). Note that both the GTDs and MDs between any two identical atoms of these two isomers are respectively equal. In a similar manner, consider the presence of more than one atom in a molecule having four different constituent groups attached to it, as shown in Figure 3. Note that because three points (atoms) determine a plane and because we allow free rotation about the single bonds, we may bring four of these atoms into the reference plane. This has been selected as the conformer having the two carbon and two hydrogen atoms coplanar. Note that the GTDs between any two equivalent atoms in all four cases are equal. Additionally, observe that the metric distances between the chlorine atoms in (a) and (d) and in (b) and (c) are equal; but NOT between (a) and (b). The unequal pairs of isomers are called "diastereoisomers". Note that diastereoisomers may be grouped together with geometric isomers. In fact, modern texts consider geometrical isomers as a special case of diastereoisomers.

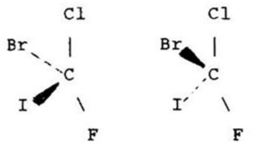
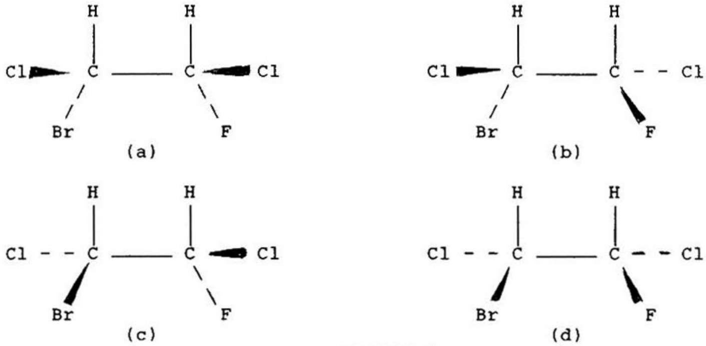


FIGURE 2



(a) (b) (c) (d)

FIGURE 3

At this point, however, it should be noted that the logical extension to higher coordination than 4 produces some important differences: In Figure 4, we examine a hexa-coordinated atom, such as sulfur, with six different ligands. The GTD between any two ligands of the sulfur atom is 2, but even in the case that we have equal (unit) bond lengths between sulfur atom and each of its ligands, there are two distinctive distances corresponding to co-axial (2 units long) and non-co-axial ($\sqrt{2}$ = 1.4142... units long); e.g., a-S-c vs. a-S-b. In other words, for a single hexa-valent atom, we have the opportunity for both mirror image properties (optical isomers) and diastereoisomers. This idea carries on the same possibilities for even higher coordination.[14] For example, for an atom with octa-coordination, we find there is the always the same GTD between ligands of the central atom, namely 2; but now, even in the simplest case, there are three distinct MDs = $\sqrt{2}$, $\sqrt{3}$, and 2 units long, etc.

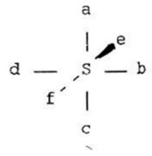


FIGURE 4

In conclusion, we see that the more traditional method of sub-dividing the class of isomers (illustrated by Table 1) would be greatly improved by consideration of the two different types of distance measure (Table 2), and that this distance-based system allows for much cleared lines of demarcation between the classes, as well as inclusion of a major catagory of compounds that was overlooked by the traditional method.

REFERENCES

[1] **Webster's New Collegiate Dictionary** (G & C Merriam Co., Springfield, Mass., 1981) p. 608.

[2] A. Streitwieser and C.H. Heathcock, **Introduction to Organic Chemistry**, 2nd Ed., (Macmillan, New York, 1981) p.29.

[3] Encyclopedia Britannica, Inc., Chicago, 1971, 12, p.686.

[4] W. Schubert and I. Ugi, J.Am.Chem.Soc. 100 (1978) 37-41.

[5] Ibid #3, 21, p.223.

[6] Ibid #2, p.280.

[7] D.J. Cram and G.S. Hammond, **Organic Chemistry**, (McGraw-Hill, New York, 1959) p.119.

[8] R.T. Morrison and R.M. Boyd, **Organic Chemistry**, 2-nd Ed. (Allyn & Bacon, Inc., Boston, 1966)p.216.

[9] Ibid #2, p.281.

[10] S. B. Elk, J.Chem.Inf.Comput.Sci. 34 (1994) 325-330.

[11] S. Borman, (News Focus) "A Primer on Isomerism", Chemical & Engineering News, July 9, 1990, p. 10-11.

[12] R. Chang, **Chemistry**, 4-th Ed., (McGraw-Hill, Inc., New York, 1991) p. 372.

[13] G. Schill, **Catenanes, Rotaxanes and Knots**, (Academic Press, New York, 1971).

[14] S. B. Elk, J.Chem.Inf.Comput.Sci., 32 (1992) 14-22.