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Short Communications

Comment on the Recent Controversy over the Theory of Chirality Functions

C. Alden Mead

Chemistry Department, University of Minnesota, Minneapolis, Minnesota 55455, U.S.A.

Derflinger, *et al.*, have criticized the concept of qualitative completeness on the grounds that a chirality function may be qualitatively complete and still vanish identically for certain nonracemic, non-isomeric mixtures. It is pointed out that the functions considered by them are ones in which the full chirality function splits into parts which can be thought of as contributions from "effective fragments" of the molecule, and that their mixtures are indeed racemic in these fragments. The function can be augmented in a very simple way so as not to vanish for such mixtures, and the idea of qualitative completeness is in no way disturbed by this process.

Key words: Theory of chirality functions – Qualitative completeness – Nonracemic mixtures ~

1. Introduction

Recently, a controversy of sorts has erupted in the pages of this journal. In two consecutive articles [1–2], Derflinger *et al.* have made a number of criticisms of the theory of chirality functions as formulated by Ruch and Schönhofer [3–4], and in particular to the concept of "qualitative completeness" introduced by these authors. Their two articles were followed by a reply by Ruch [5], and a comment on the situation by the editor [6]. There is, however, one point raised in Ref. [2] which we believe is worthy of a further comment.

A qualitatively complete chirality function is one which does not vanish identically (i.e., independently of the values of parameters characterizing the ligands) for any non-racemic mixture of isomers. In Ref. [2], it is shown by means of examples that a function may be qualitatively complete, and still vanish identically for certain non-racemic mixtures of non-isomers. For the case of the methane derivatives, this had

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already been remarked on by Richter, Richter, and Ruch [7], and by Haase and Ruch [8], so it is not really new. Nevertheless, it does raise a question which is not fully dealt with in Refs. [5, 7–8]. The question is: how can one formulate an approximation Ansatz for chirality functions in such a way that the resulting function is guaranteed not to vanish identically for *any* non-racemic mixture, whether of isomers or not? The answer to this question may be needed in some practical applications, since a function which may vanish identically for non-racemic mixtures will necessarily be incapable of describing completely the experimental data. Since the answer turns out also to be exceedingly simple, requiring no elaborate mathematics, the author felt that it would be worthwhile to write a short paper on the subject.

2. Problem and Solution

It will be sufficient for our purposes to confine ourselves to the allene skeleton, as shown in Fig. 1. It will be evident that similar considerations will apply in other cases.

The qualitatively complete chirality function obtained for this skeleton by means of the second approximation procedure of Ruch and Schönhofer [3] has the form

$$\chi = \phi(\mathrm{A}, \mathrm{C}) - \phi(\mathrm{B}, \mathrm{C}) - \phi(\mathrm{A}, \mathrm{D}) + \phi(\mathrm{B}, \mathrm{D}) + \theta(\mathrm{A}, \mathrm{B}, \mathrm{C}) + \theta(\mathrm{D}, \mathrm{B}, \mathrm{A}) + \theta(\mathrm{A}, \mathrm{C}, \mathrm{D}) + \theta(\mathrm{B}, \mathrm{D}, \mathrm{C}), \tag{1}$$

where ϕ is symmetric in its two arguments, and θ totally antisymmetric in its three arguments. The two components of the function (1) have been chosen to be sums of terms depending on as few ligands as possible while still satisfying the requirements of chirality and of qualitative completeness. Qualitative completeness does not require that one choose functions depending on as few ligands as possible; it is done solely in the interest of simplicity.

Each term in the function (1) depends on properties of only some of the ligands making up the molecule; in other words, each term can be thought of as the contribution of a fragment of the molecule. Thus, the first ϕ-term in (1) can be visualized as being the contribution of the fragment shown in Fig. 2, while the first θ-term can be thought of as the contribution of the fragment shown in Fig. 3(a). One sees from the form of the θ-terms, however, that the fragment contributes as if it had the

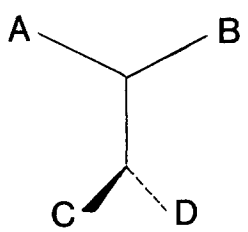

Fig. 1.

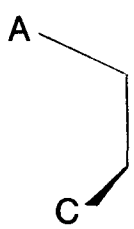

Fig. 2.

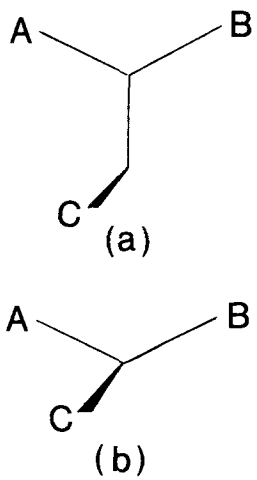

Fig. 3.

form shown in Fig. 3(b), i.e., as if all its sites were equivalent. We call the fragment shown in Fig. 3(b) the "effective fragment" corresponding to the actual fragment shown in Fig. 3(a).

It is easy to see that qualitatively complete chirality functions obtained in this way will always be representable as sums of contributions from effective fragments which may or may not be identical with actual fragments. The same is true of the polynomial functions obtained by the first procedure of Ruch and Schönhofer.

It is now clear how one can construct non-racemic mixtures for which such a chirality function vanishes identically. One merely has to see that the mixture is *racemic in the effective fragments*. Since the same effective fragment may appear in two molecules which are not isomers of one another, it is obvious that one will in general be able to construct mixtures which are racemic in the effective fragments, but not in the molecules themselves, and one easily verifies that the examples of Derflinger *et al.* are of this type. Thus, in the nonracemic mixture illustrated in Fig. 3 of Ref. [2], one finds the fragment of our Fig. 2 on the left in row one (with a coefficient of 2), and on the left in row three. Its mirror image is on the right in row one (with coefficient 2) and in the middle of row three. The effective fragment of our Fig. 3(b) is on the left in row one (with coefficient 2); in the middle of row two; and in the middle of row three. Its mirror image is on the right in row one with coefficient 2; on the left in row two; and on the left in row three.

It is also clear how to construct a function that will not vanish for non-racemic mixtures: one simply needs to make sure that there are contributions from the molecule as a whole, which are not capable of being split up into additive contributions from effective fragments. This can be done, e.g., by multiplying a function such as (1) by an arbitrary totally symmetric function of all the ligands. The idea of qualitative completeness is not disturbed at all by this procedure, nor is the resulting function necessarily particularly complicated. Whether one wishes to augment the function in this way will, of course, depend on the nature of the application being considered. Derflinger and Keller [2] state that, while it is possible to

extend the concept of qualitative completeness to deal with cases of this kind, it leads to functions which "are more complicated in their structure [than functions such as (1)], and thus make practical applications difficult." We would have to disagree, as we have just seen that no revision of the idea of qualitative completeness is necessary, nor are the resulting functions unduly complicated.

Professor Ruch has informed the author that he and his group have in preparation a more extensive work dealing with these and related matters.

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