EXPERIMENTAL TESTS OF CHIRALITY ALGEBRA

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Abstract

Most chiral molecules can be dissected into a collection of ligands attached to an underlying skeleton. Application of permutation group theory and group representation theory to such a model can lead to chirality functions which can be used to approximate pseudoscalar measurements such as optical rotation or circular dichroism. Such chirality functions have been tested experimentally for the following skeletons: (1) The polarized triangle of phosphines and phosphine oxides; (2) the tetrahedron of methane derivatives; (3) the disphenoid of allene and 2, 2′-spirobiindane derivatives; (4) the polarized rectangle of [2, 2]-metacyclophanes; (5) the polarized pentagon of heterodisubstituted ferrocenes. The success of this method is fair to good for the polarized triangle, tetrahedron, and disphenoid skeletons but deteriorates rapidly for the polarized rectangle and polarized pentagon skeletons, in accord with the greater group-theoretical complexity of the latter skeletons.

1.   Introduction

The symmetry operations in a molecular point group can be classified according to the minimum number of changed coordinates (table 1). A chiral molecule contains no symmetry operations having odd minimum numbers of changed coordinates such

Table 1

Types of symmetry operations in molecular point groups

Symmetry operation	Minimum number of changed coordinates
E (identity)	0
σ (reflection plane)	1
C_n (proper rotation axis)	2
S_n (improper rotation axis or "rotation-reflection")	3
$i\,(=S_2)$ (inversion center)	

as reflections and improper rotations. Mirror images (enantiomers) of chiral molecules are not superimposable. Chirality may thus be regarded as the differentiation of a molecule from its mirror image.

The experimental observation of molecular chirality arises from pseudoscalar measurements, which have the following properties:

(1)   They depend upon the molecule but not its orientation in space.

(2)   They have identical absolute values but opposite signs for mirror images, i.e. the two enantiomers of a chiral molecule.

Chemically significant pseudoscalar measurements include the rotation of plane polarized light (optical rotation) and circular dichroism.

This paper summarizes some experimental tests of algebraic approaches for modelling molecular chirality and associated phenomena. Such algebraic methods can provide the following information:

(1)   Systematics of molecular skeletons and ligand partitions leading to chiral systems.

(2)   The determination of mathematical functions (chirality functions) by which the magnitude and sign of a pseudoscalar property (the dependent variable) can be calculated for a given skeleton using parameters which depend only upon the ligands located at specific sites on the skeleton (the independent variables).

The experimental tests of chirality algebra involve evaluation of mathematically derived chirality functions as approximations to actual experimental pseudoscalar measurements.

Although rudimentary ideas relating to chirality functions can be traced as far back as 1890 [1,2], the modern study of chirality algebra had its genesis in the stereochemical analogy model by Ruch and Ugi [3,4]. Increasingly sophisticated mathematical methods, based largely on the induction of representations of finite groups, were then developed for the determination of chirality functions [5–7]. Overviews of various aspects of chirality algebra were subsequently presented by Ruch [8], and then in much greater mathematical detail by Mead [9]. The present author has recently reviewed chirality algebra [10], as well as the more specific area of chirality polynomials [11]. The reader is referred to these articles and references cited therein for further details.

2.   Framework groups

Consider a molecule of the type ML_n, in which M is a metal or other central atom and the n ligands L may or may not be equivalent but cannot be chiral. Removal of the n ligands L from ML_n leads to the skeleton. The symmetry of the skeleton is regarded as that of the framework group [12] based on the location of the n ligands L. In this connection, framework groups provide a method for specifying the symmetry of bodies containing a finite number of particles. Such framework

groups are described by the Schoenflies symbol [13] of the underlying point group, followed by an indication of the location of each of the particles in terms of subspaces relating to the symmetry elements of the underlying point group. Such subspaces can be classified by their dimensionalities, as follows:

0-dimensional (O): a central point (e.g. a center of inversion (i) or intersection of a rotation axis with another rotation axis or a perpendicular plane of symmetry);

1-dimensional (C_n): a rotation axis;

2-dimensional $(\sigma_n, \sigma_v, \sigma_d)$: a reflection plane;

3-dimensional (X): the remaining part of full three-dimensional space external to any of the symmetry operations.

These dimensionalities have an "inverse" or "codimensional" relationship to the minimum number of changed coordinates in the corresponding symmetry operations as presented in table 1. The location of any given particle in the framework group is specified in terms of the subspace of the lowest possible dimensionality. The preference order is thus $O > C_n > \sigma > X$.

Framework groups can be classified into the following four types [14]:

(1) *Linear*: all sites are located in a straight line (a one-dimensional subspace of three-dimensional space).

(2) *Planar*: non-linear framework groups in which all sites are located in a (flat) plane (a two-dimensional subspace of three-dimensional space).

(3) *Achiral*: non-planar framework groups in which the point group contains at least one improper rotation S_n $(n \geq 1)$, where $S_1 = \sigma$ and $S_2 = i$.

(4) *Chiral*: non-planar framework groups in which the point group contains no improper rotations.

Chiral framework groups are of no interest in chirality algebra since they are always chiral even if all ligands are the same. Linear framework groups are also of no interest in chirality algebra since they are never chiral even if all ligands are different. Planar framework groups can be made chiral by a process called polarization [14], which destroys the symmetry of the plane containing all of the sites. A chemical example of polarization is the polyhapto [15] complexation of a planar aromatic hydrocarbon (e.g. benzene) with a transition metal to destroy the σ_h ring plane as a symmetry element.

Framework groups may also be classified by the parities of their permutations or the locations of their reflection planes. Thus, the parity of a site permutation or symmetry element is odd or even, depending on whether the total number of cycles of even length is odd or even, respectively. A framework group is called an ordinary framework group when its symmetry elements are of odd parity if and only if they
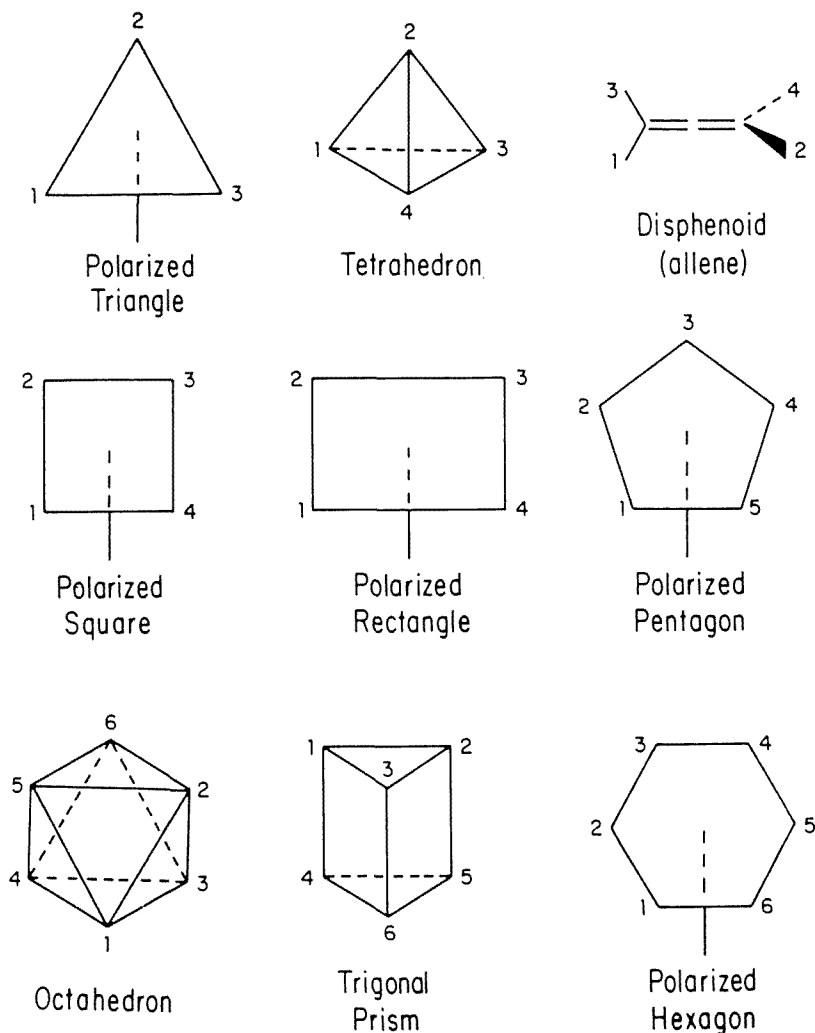
Fig. 1. Chemically significant transitive skeletons having six or fewer sites.

correspond to an improper rotation axis S_n $(n \geq 1)$ including $S_1 = \sigma$ and $S_2 = i$. If this is not the case, the framework group is called extraordinary. The reflection planes in framework groups can be classified into two types: separating planes and non-separating planes. A separating plane in a non-planar achiral framework group having n sites contains exactly $n - 2$ of these sites. Conversely, a reflection plane containing less than $n - 2$ sites in a skeleton having n sites is a non-separating plane. Chiral molecules with underlying achiral framework groups in which all reflection planes are separating planes can be classified into left-handed and right-handed

enantiomers, with enantiomers of the same handedness being called "homochiral" [16,17]. Such achiral skeletons have been called "category a" or shoe-like by Ruch [16,17], since left and right shoes can readily be distinguished regardless of their size, shape, or color. However, chiral molecules with underlying achiral framework groups having one or more non-separating planes have been called "category b" or potato-like by Ruch [16,17], since even though chiral, which member of an enantiomeric pair is "left-handed" and which is "right-handed" cannot be distinguished, as is the case for potatoes. In general, C_4, C_5, C_6, S_3, and S_6 rotation axes lead to framework groups which are extraordinary and potato-like.

The symmetry of a framework group or the corresponding skeleton may be related to its transitivity. Thus, a framework group having all sites equivalent is called a transitive framework group; otherwise, the framework group is called intransitive. A set of equivalent sites is called an orbit; the number of sites in an orbit is called the length of the orbit. A transitive framework group or skeleton thus has only one orbit consisting of all its sites. Transitive skeletons play a fundamental role in chirality algebra. Non-trivial chemically significant transitive skeletons having six or fewer sites are depicted in fig. 1.

3.   Group representation theory

The areas of group representation theory relevant to chirality algebra consider the effect of the skeletal distribution of ligands on the actual molecular symmetry. The ligand partition can be depicted by a symbol of the type $(a_1^{b_1} a_2^{b_2} \ldots a_k^{b_k}$, $a_m > a_{m+1}$, in which b_k refers to the number of sets of a_k identical ligands. Thus, the symbol (n) refers to an ML_n molecule in which all n ligands are equivalent. In addition, the ligand partition of an ML_n molecule can also be depicted by a collection of boxes called a Young diagram, particularly as relating to representations and conjugacy classes of the corresponding symmetric group P_n [18]. Such Young diagrams have the following properties:

(1)   The rows of boxes represent identical ligands.

(2)   The top row is always the longest row and the lengths of the rows decrease monotonically from top to bottom.

(3)   The left column is always the longest column and the lengths of the columns decrease monotonically from left to right.

Such Young diagrams can be characterized by the following three parameters.

(1) *Order* (*o*): This represents the maximum number of identical ligands in the ligand partition and is simply the length of the top row. The order also corresponds to the number of columns in the Young diagram.
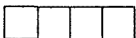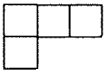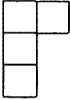
(2) *Index* (i): This represents the number of different ligands in the ligand partition and is simply the length of the left column. The index also corresponds to the number of rows in the Young diagram.

(3) *Degree* (g): This provides a basis for ordering Young diagrams and represents the minimum degree of the chirality polynomial for the corresponding ligand partition, which does not vanish identically. The degree of a Young diagram can be calculated by the following equation, in which c_k represents the length of column k:

$$g = \frac{1}{2} \sum_{k=1}^{k=\text{order}} c_k (c_k - 1). \tag{1}$$

In general, Young diagrams having high degrees depict relatively unsymmetrical ligand partitions, whereas Young diagrams having low degrees depict relatively symmetrical ligand partitions. The Young diagrams for the possible ligand partitions in an ML_4 species are depicted in table 2, together with their order, indices, and degrees.

Table 2

Young diagrams and ligand partitions for four ligand sites

Ligand partition	Young diagram	Complex type	Chirality order (o)	Chirality index (i)	Chirality polynomial degree (g)
(4)		MA_4	4	1	0
(31)		MA_3B	3	2	1
(2^2)		MA_2B_2	2	2	2
(21^2)		MA_2BC	2	3	3
(1^4)		$MABCD$	1	4	6

An important objective in chirality algebra is the determination of chiral ligand partitions, namely a ligand partition of lowest degree g (minimum asymmetry) necessary to destroy all improper rotations S_n ($n \geq 1$ including $S_1 = \sigma$ and $S_2 = i$) in an achiral skeleton to give a chiral system. The following group-theoretical algorithm [9–11,14] can be used to determine the chiral ligand partitions for a skeleton with n sites having point group G:

(1) The characters for G subduced by each irreducible representation Γ_r of the symmetric group P_n are determined from the character tables of P_n by copying down the characters of each irreducible representation Γ_r for the operations of P_n also in G.

(2) The characters of the "chiral representation" Γ_* of G are determined by using $+1$ for proper rotations (E, C_n) and -1 for the improper rotations (σ, i, S_n).

(3) Standard group-theoretical methods based on orthogonality relationships [13,19] are used to determine which representations Γ_r of P_n when restricted solely to operations in G contain the chiral representation Γ_* of G. Note that representations which are irreducible in systems having full P_n symmetry are no longer necessarily irreducible when the symmetry is reduced to G.

(4) The Young diagrams corresponding to these irreducible representations of P_n indicate the chiral ligand partitions for a skeleton having point group G.

Reduction of the symmetry of a skeleton with n sites from G to a smaller (less symmetrical) point group H has the following effects:

(1)   The number of irreducible representations Γ_r of P_n containing the chiral representation Γ_* will be larger when restricted to H than when restricted to G.

(2)   If H is a normal subgroup [20] of G, every irreducible representation Γ_r of P_n which contains Γ_* when restricted to G will also contain Γ_* when restricted to H.

(3)   The degree of the lowest degree chiral ligand partition will be lower for H than for G. This relates to the obvious fact that a less symmetrical skeleton may require fewer different ligands to become chiral.

The chiral representation Γ_* of G has characters of -1 for the improper rotations and $+1$ for the proper rotations. In an ordinary framework group, the chiral representation has characters of $+1$ for the even site permutations and -1 for the odd site permutations, but such is no longer true for extraordinary framework groups. In any symmetric group, the representation (1^n) corresponding to all ligands different (i.e. n different ligand types) has characters of $+1$ for the even permutations and -1 for the odd permutations. Therefore, a framework group with n sites has (1^n) as a chiral ligand partition if and only if it is ordinary.

4.   Chirality functions and their polynomial approximations

Consider molecules of the type ML_n, in which M is a metal or other central atom and the n ligands L may or may not be equivalent. Now consider the problem of approximating a pseudoscalar measurement ψ with a function in n variables, i.e.

$$\psi \approx f(\lambda_1, \lambda_2, \ldots, \lambda_n) = f(\lambda), \text{ where } \lambda \in \Lambda^n. \tag{2}$$

In eq. (2), the n independent variables $\lambda_1, \lambda_2, \ldots, \lambda_n$ or the n coordinates of the vector λ correspond to parameters associated with the ligands at sites $1, 2, \ldots, n$, respectively, which depend only upon the ligand, the skeleton, and the pseudoscalar measurement. In principle, such ligand parameters can be obtained by fitting a series of pseudoscalar measurements of a given type on molecules having the same skeleton and a restricted set of ligands using appropriate chirality functions. The permutations of the symmetric group P_n interchange the variables $\lambda_1, \lambda_2, \ldots, \lambda_n$ with the following results if $f(\lambda_1, \lambda_2, \ldots, \lambda_n)$ is a valid chirality function:

(1)   A proper rotation of the skeletal point group leaves unchanged both the absolute value and sign of f.

(2)   An improper rotation of the skeletal point group changes the sign of f but leaves unchanged its absolute value.

(3)   Any permutation in P_n not in the skeletal point group may have any effect on the value of f.

We now consider the problem of finding the simplest type of function for a given skeleton and chiral ligand partition having the transformation properties required for a chirality function. Such a function turns out to be a polynomial $X(s_1, s_2, \ldots, s_n)$ of the same degree as that of the corresponding ligand partition. If a skeleton has several chiral ligand partitions of degrees $g_1, g_2, \ldots, g_p$, a sum of chirality polynomials of degrees $g_1, g_2, \ldots, g_p$ with a separate set of ligand parameters for each polynomial may be required to describe all chirality phenomena for the skeleton in question. Such a sum of chirality polynomials is a qualitatively complete chirality polynomial [7–11] and the individual chirality polynomials making up the sum may be regarded as components of the qualitatively complete chirality polynomial.

The chirality polynomial components $X(s_1, s_2, \ldots, s_n) = X(s)$ so defined may be regarded as functions of a vector s in an n-dimensional parameter space S^n with a smooth map $M : \Lambda^n \rightarrow S^n$ between the two ligand parameter spaces if $X(s)$ is a sufficiently close approximation to $f(\lambda)$. The lowest degree chirality polynomial $X(s)$ may be regarded as an initial term in a Taylor series approximation of a more accurate chirality function $F(s)$ of the same vector s in the same parameter space. The accuracy of the approximation of $F(s)$ by its first term $X(s)$ will naturally depend upon the skeleton and the pseudoscalar property, and cannot be predicted by theory alone. Thus, chirality polynomials are not required to work. However, they may

work, so the investigation of applications of chirality polynomials to model pseudoscalar properties is a valid pursuit.

An individual polynomial component $X(s_1, s_2, \ldots, s_n)$ of a qualitatively complete chirality function is homogeneous and depends only on the s-differences $s_i - s_k$ ($i, k = 1, 2, \ldots, n$) in all important cases. It has the general form:

$$X(s_1, s_2, \ldots, s_n) = \sum_{k=1}^{k \leq |G|} a_k \, p_k(s_1 . s_2, \ldots, s_n), \tag{3}$$

where $|G|$ is the number of operations in the skeletal point group G and the p_k's are homogeneous polynomials which are also functions of s-differences and are defined by the required transformation properties. For a shoe-like skeleton, the chirality polynomial is a simple product of g s-differences, i.e.

$$X(s_1, s_2, \ldots, s_n) = \prod (s_i - s_k), \tag{4}$$

where the indices i and k for each factor correspond to a pair of sites outside a given reflection plane. The degree g of the lowest degree chirality polynomial for a shoe-like skeleton thus corresponds to the number of reflection planes, all of which are necessarily separating planes in the shoe-like skeleton. The chirality polynomials for potato-like skeletons do not have the simple form of eq. (4), since they contain sums as well as products of differences of ligand parameters. Also, the degrees of the lowest degree chirality polynomials for potato-like skeletons are less than the total number of reflection planes. Determination of the chirality polynomials for potato-like skeletons requires a group-theory derived algorithm based on projection operators, which is described in detail elsewhere [7,9–11,14]. The chirality polynomial for an intransitive framework group is the product of the chirality polynomials for its individual orbits.

5.   Experimental tests of chirality algebra

The following two general approaches can be used for experimental tests of chirality algebra:

(1) *First approximation (chirality polynomials)*: Pseudoscalar measurements of a given type (e.g. optical rotation at a specific wavelength or circular dichroism) on molecules having a given skeleton and a limited set of different ligands are used to determine parameters for each ligand in the set to use in chirality polynomials obtained by the standard group-theory derived algorithm discussed elsewhere [7,9–11,14]. The self-consistency of the ligand parameters found by this method is a measure of the success of this approximation.

(2) *Second approximation*: Pseudoscalar measurements of a given type are made for a specially designed set of chiral molecules having a given skeleton and

with distributions of ligands chosen from a set not much larger than the number of sites so that the sums of any functions $f(\lambda_1, \ldots, \lambda_n)$ meeting the necessary minimal criteria for valid chirality functions is required mathematically to be identical to zero. The deviation from zero of the sum of experimentally determined pseudoscalar properties for this set of chiral molecules is then a measure of the errors arising from this approach.

The first approximation requires a much larger set of data than the second approximation for a given skeleton in order to check the accuracy of the approximation through determination of a sufficiently large set of self-consistent ligand parameters. However, the first approximation leads to chirality polynomials and sets of ligand parameters which can be used to calculate the same pseudoscalar property for unknown molecules having the same skeleton and ligands chosen from the set for which ligand parameters have been obtained. The second approximation, unlike the first approximation, does not assume a polynomial form for the chirality function and therefore may work in some cases where the first approximation fails.

The methods of chirality algebra have been tested for the following skeletons:

(1)   *Polarized triangle*

The simplest non-trivial skeleton which has been tested experimentally is the C_{3v} polarized triangle. The lowest degree chirality polynomial for this skeleton has the form

$$X(C_{3v}) = (s_3 - s_2)(s_3 - s_1)(s_2 - s_1), \tag{5}$$

corresponding to the (1^3) chiral ligand partition. Note the degree 3 chirality polynomial, with each factor corresponding to one of the separating planes of the shoe-like polarized triangle in accord with the general eq. (4).

Richter [21] has studied the molar rotations of optically active phosphines and phosphine oxides, which have the polarized triangle skeleton. Distribution of four different ligands (a, b, c, d) among the three skeletal sites can lead to a quadruple of the following type ($X = O$ or lone pair):

The sum of the molar rotations of the four members of such a quadruple is predicted to be identically zero for any chirality function, either polynomial or otherwise, with the transformation properties required by chirality algebra. Of the 7 quadruples of type **1** above obtained by Richter [21] for the 7 optically active phosphines and

the 16 optically active phosphine oxides, 5 had zero sums of molar rotations within a 90% confidence limit, whereas the sums of the molar rotations of the 2 remaining quadruples deviated significantly from zero. A satisfactory set of ligand parameters for the degree 3 chirality polynomial $X(1^3)$ in eq. (5) could not be obtained from the available data.

(2)   *Tetrahedron*

The lowest degree chirality polynomial for the T_d (regular tetrahedron) has the form:

$$X(T_d) = (s_4 - s_3)(s_4 - s_2)(s_4 - s_1)(s_3 - s_2)(s_3 - s_1)(s_2 - s_1), \qquad (6)$$

corresponding to the (1^4) chiral ligand partition. Note the degree 6 chirality polynomial with each factor corresponding to one of the separating planes of the shoe-like tetrahedron in accord with the general eq. (4). In the case of methane derivatives based on the tetrehedron skeleton, distribution of five different ligands (a, b, c, d, e) among the 4 skeletal sites can lead to a quintuple of the following type:

IIa   **IIb**   **IIc**   **IId**   **IIe**
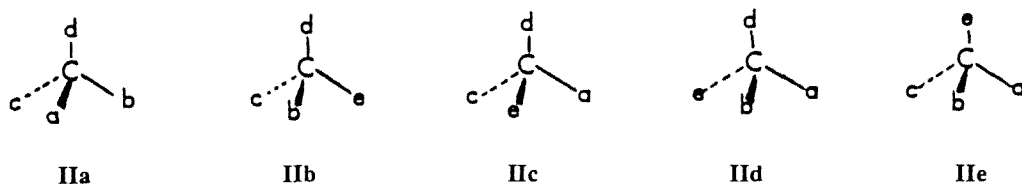
The sum of the values for a given pseudoscalar property of the five members of such a quintuple is predicted to be identically zero for any chirality function meeting the minimum criteria required by chirality algebra. Studies on the optical rotations of 13 such quintuples obtained from 54 methane derivatives of known absolute configurations [22] indicate approximate zero sums of the five molar rotations of each quintuple in most cases. Significant deviations arise only in the cases of hydrogen bonding ligand pairs (e.g. NH_2/CH_2OH, $NHCHO/CH_2OH$, NH_2/CO_2H), bulky ligands (e.g. $CH_2OSi(CH_3)_3$), and derivatives containing the ligand $N=CHC_6H_5$ having significant absorption in the Na_D visible region where the optical activity measurements were performed. Meaningful ligand parameters for the degree 6 chirality polynomial $X(1^4)$ in eq. (6) were obtained for the ligands H, CH_3, C_2H_5, CH_2OH, $NH_3^+Cl^-$, $NH_2CH_3^+Cl^-$, $N(CH_3)_2$, $NH(CH_3)_2^+Cl^-$, and $NHCH_3$.

(3)   *Disphenoid*

The four-site D_{2d} disphenoid skeleton is found in both allene and 2, 2'-spiro-biindane derivatives. This skeleton has two chiral ligand partitions, namely the degree 2 (2^2) partition as well as the degree 6 (1^4) partition corresponding to the

single chiral ligand partition of the tetrahedron discussed above. The lowest degree qualitatively complete chirality polynomial for the disphenoid skeleton thus has two components leading to the equation

$$X(D_{2d}) = X(2^2) + X(1^4), \tag{7}$$

in which $X(2^2)$ is the degree 2 polynomial

$$X(2^2) = (t_4 - t_2)(t_3 - t_1) \tag{8}$$

and $X(1^4)$ is the degree 6 polynomial of eq. (6). However, the $X(1^4)$ component vanishes identically for chiral disphenoids having (21^2) and (2^2) ligand partitions so that in these cases, only the degree 2 component $X(2^2)$ in eq. (8) needs to be considered.

Ruch, Runge, and Kresze [23] have calculated a set of self-consistent ligand parameters for H, C_6H_5, CO_2H, CH_3, and C_2H_5 in allenes from optical rotation data on phenylallene carboxylic acid derivatives. Such derivatives having two identical ligands, namely derivatives with the (21^2) ligand partition, were used so that the degree 6 $X(1^4)$ component (eq. (6)) vanishes identically and thus could be neglected. However, the same set of ligand parameters could also be used to estimate the optical rotation in allenes having four different substituents (i.e. those with the (1^4) ligand partition) indicating that $X(1^4)$ in eq. (7) is negligible relative to $X(2^2)$ for this system. Difficulties in obtaining extensive series of chiral allene derivatives of high optical purity limited the scope of this study.
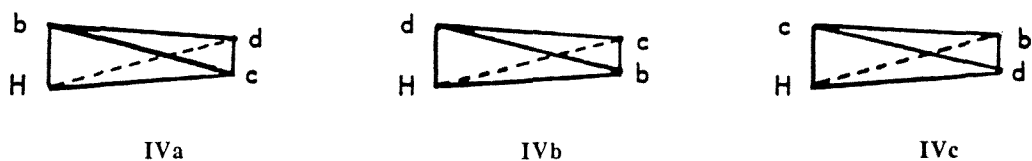
Neudeck, Richter, and Schlögl [24] have made an extensive study of the molar rotations of approximately 100 derivatives of the 2, 2′-spirobiindane skeleton
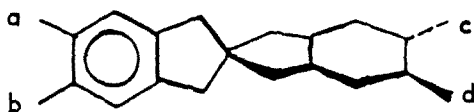
III

which, like allene, has the four sites and D_{2d} symmetry of the disphenoid so that the same chirality functions can be used. However, extensive series of chiral 2, 2′-spirobiindanes of known optical purity are more readily available than such series of the chiral allenes discussed above. Molar rotation data on 5, 5′-disubstituted 2, 2′-spirobiindanes (III) having the (21^2) ligand partition were used to calculate self-consistent ligand parameters for the H, CH_3, C_2H_5, CH_2OH, CHO, CH_3CO, CO_2H, CH_2CH_3, CN, and OCH_3 ligands in the degree 2 $X(2^2)$ component (eq. (8)); for such derivatives, the degree 6 $X(1^4)$ component (eq. (6)) vanishes identically and thus can be neglected. The magnitude of the degree 6 $X(1^4)$ component (eq. (6)), which

does not vanish identically for 5, 5', 6-trisubstitued 2, 2'-spirobiindanes having the (1^4) ligand partition, can be estimated from the sums of the molar rotations of isomer triples schematically represented as

IVa	IVb	IVc

For a given isomer triple (IV), the degree 2 $X(2^2)$ component (eq. (8)) vanishes identically so that the deviation of this sum from zero represents exclusively the degree 6 $X(1^4)$ component (eq. (6)). Analysis of optical rotation data on such an isomer triple (IV), where $b = CH_3$, $c = C_2H_5$, and $d = CO_2CH_3$, suggests that the degree 6 $X(1^4)$ chirality polynomial is responsible for about 25% of the molar rotation, i.e. relatively small but far from negligible.

(4)   *Polarized rectangle*

The four-site C_{2v} polarized rectangle skeleton is theoretically significant since it is the simplest potato-like skeleton having more than one chiral ligand partition. The C_{2h} [2, 2]-metacyclophane skeleton (V) is permutationally equivalent to the C_{2v}

V
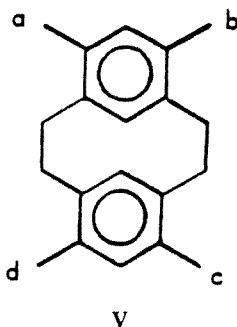
polarized rectangle so that the same chirality functions can be used. Thus, the lowest degree qualitatively complete chirality polynomial for the C_{2v} polarized rectangle, which is also applicable to the C_{2h} [2, 2]-metacyclophane skeleton, has the form

$$X(C_{2v}) = X(31) + X(21^2), \tag{9}$$

in which

$$X(31) = s_1 - s_2 - s_3 + s_4 \tag{10}$$

and

$$X(21^2) = (t_4 - t_1)(t_3 - t_2)(t_4 - t_3 - t_2 + t_1), \tag{11}$$

where sites 1, 2, 3, 4 are labelled a, b, c, d, respectively, in structure **V**. For 4-monosubstituted derivatives ($a \neq H$) and 4, 14-homodisubstituted derivatives ($a = d \neq H$), the degree 3 component $X(21^2)$ (eq. (11)) of the qualitatively complete chirality polynomial (eq. (9)) vanishes identically, so that the resulting qualitatively complete chirality polynomial is simply the linear "quadrant rule" of eq. (10).

Keller, Krieger, Langer, Lehner, and Derflinger have made detailed studies of the molar rotations [25] and circular dichroism [26] of 30 monosubstituted and disubstituted [2, 2]-metacyclophane derivatives. The double values predicted by eq. (10) for the molar rotations and circular dichroisms of the 4, 14-homodisubstituted derivatives relative to the corresponding monosubstituted derivatives are found for only a few of these cases, indicating the insufficiency of this simple linear approximation. This observation, as well as the observation of major discrepancies in the calculated ligand parameter for bromine from optical rotation measurements on the five 4, 12-heterodisubstituted derivatives $a = c = H$, $d = Br$, and $b = CO_2H$, CO_2^-, CO_2CH_3, $CONH_2$, CN (structure **V**), suggest major difficulties in applying the methods of chirality algebra to the [2, 2]-metacyclophane derivatives having the polarized rectangle skeleton.
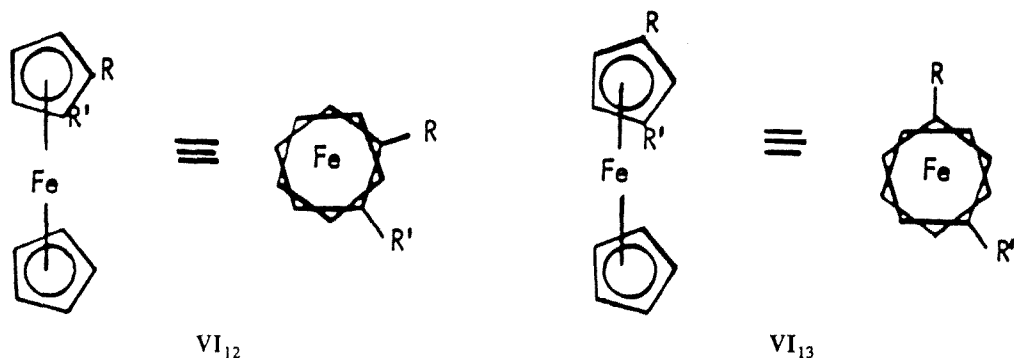
(5)   *Polarized pentagon*

Another potato-like skeleton which has been studied experimentally is the C_{5v} polarized pentagon. The lowest degree chirality polynomials for this skeleton have the forms [14]

$$X(C_{5v}) = (s_5 - s_1)^3 + (s_1 - s_2)^3 + (s_2 - s_3)^3$$
$$+ (s_3 - s_4)^3 + (s_4 - s_5)^3, \tag{12}$$

$$X(C_{5v})' = (s_{5'} - s_{2'})^3 + (s_{1'} - s_{3'})^3 + (s_{2'} - s_{4'})^3$$
$$+ (s_{3'} - s_{5'})^3 + (s_{4'} - s_{1'})^3, \tag{12'}$$

corresponding to the 1, 2-heterodisubstituted and 1, 3-heterodisubstituted isomers, respectively, of the (31^2) chiral ligand partition. Note that the degrees of these polynomials are only 3, even though a polarized pentagon has 5 symmetry planes (σ_v). This is a good example of how the degree of the lowest degree chirality polynomial for a potato-like skeleton is less than the number of symmetry planes.

The polarized pentagon skeleton can be used to study chiral heterodisubstituted ferrocenes of the following types:

In cases where three of the five skeletal sites are hydrogen atoms assigned to the ligand parameter of zero as a reference point, the degree 3 chirality polynomial for the polarized pentagon in eq. (12) reduces to

$$X(31^2) = s_a s_b^2 - s_a^2 s_b, \tag{13}$$

in which $a = 1$ and $b = 2$ for the 1, 2-heterodisubstituted derivative VI_{12} and $a = 1$ and $b = 3$ for the 1, 3-heterodisubstituted derivative VI_{13}. However, attempted application of eq. (13) to 17 heterodisubstituted ferrocene derivatives by Rapić, Schlögl, and Steinitz [27] failed to give sets of ligand parameters that could reproduce the observed molar rotations in eq. (13) without major discrepancies. This difficulty was suggested to arise from the proximity of the 589 nm wavelength of the light used for the optical rotation measurements to the positions of the longest wavelength maxima in the 540–440 nm range in the electronic spectra, so that the optical rotation measurements no longer fall in the transparent region required for the semi-empirical equations of chirality algebra to be valid.

6. Summary

The success of functions derived from chirality algebra in approximating experimental pseudoscalar measurements depends upon the complexity of the skeleton, particularly the numbers of sites and chiral ligand partitions. Thus, chirality functions provide fair to good approximations of optical rotation data for chiral derivatives of simple shoe-like skeletons, such as the polarized triangle of phosphines and phosphine oxides, the tetrahedron of methane derivatives, and the disphenoids of allene and 2, 2′-spirobiindane derivatives. However, approximations provided by chirality algebra deteriorate rapidly in chiral derivatives of more complicated skeletons or even relatively simple potato-like skeletons such as the polarized rectangle of [2, 2]-metacyclophanes or the polarized pentagon of heterodisubstituted ferrocenes.

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