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Pseudochirality[1,2]

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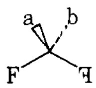
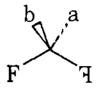
Abstract: An algebraic description of pseudochirality (pseudoasymmetry) is presented which is analogous to that given of regular chirality by Wheland. It is found that a chemical structure is pseudochiral if it lacks certain kinds of symmetry based on combinations of chirality reversal operations and point group operations. Pseudochirality groups are defined which include these operations. The derivation of these groups for chemical structures with one or more sets of chiral ligands is described, and a tabulation of general classes of pseudochirality groups based on the usual classes of point groups is given.

The concept of pseudoasymmetry is reasonably well known as a special case of stereoisomerism.[4] It is well known that carbon atoms with four different substituents are chiral, and that the enantiomeric forms can be interconverted by reflection in any mirror plane. However, if two of the substituents are themselves enantiomeric chiral ligands, two isomeric forms result which are meso and cannot be interconverted by reflection in a mirror plane. Such a pair of stereoisomers have been termed a *pseudoasymmetric pair.*[5] A symbolic example of such a pair is **1a** and **1b,** a real example is *meso*-pentaric acid. These are diastereomers and differ in physical properties such as melting point. In all chemical structures in this paper, chiral ligands are designated by open circles or by letters which are themselves chiral in two dimensions. The enantiomeric ligands are then designated by filled circles or reversed letters. This notation has been used extensively by Prelog.[6-9]

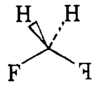


1a



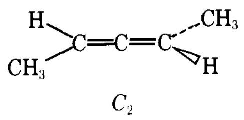
1b

An important distinction must be made between pseudoasymmetric structures (**1a** and **1b**) typically termed "meso" and structures such as **2** which exist in only *one* achiral meso form. Such a structure will be designated meso from now on, while the pseudoasymmetric structures will be termed pseudoasymmetric or pseudochiral. This is a departure from standard terminology which designates all such structures as meso. The intrinsic difference between the pseudochiral and meso situations will be established later in this paper.

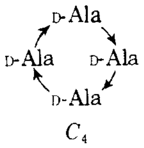


2

The purpose here is to give an algebraic description of this phenomenon analogous to that for regular chirality. A rigid structure is chiral if it lacks an alternating axis of symmetry.[10] It may, however, have pure rotation symmetry, such as 1,2-dimethylallene (C_2 symmetry) or cyclotetra-D-alanine (in a C_4 conformation).



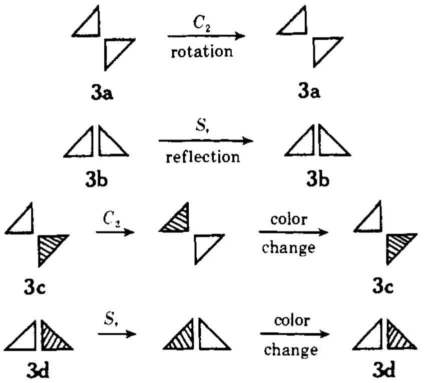
C_2



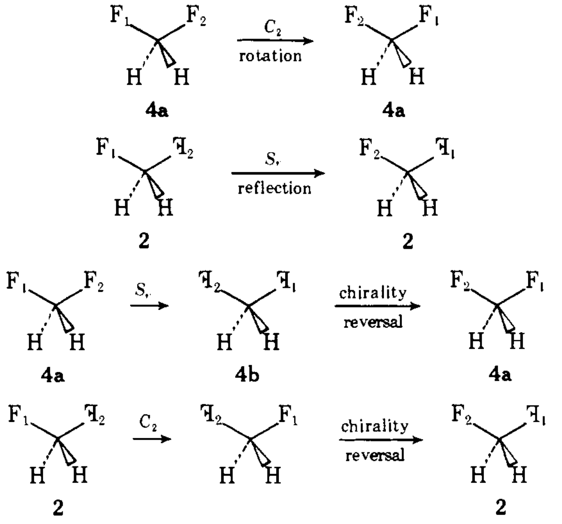
C_4

Symmetry Operations

To get at the desired algebraic description, an apparent digression must be made. Consider the configurations of triangles **3a–d** and the effect of various symmetry operations on them. Configuration **3a** is invariant to a C_2 rotation as shown. Configuration **3b** is invariant to reflection in a vertical plane. These are the two types of symmetry operations traditionally encountered. Two more will now be defined. Configuration **3c** is not invariant to a C_2 rotation since the triangles are colored differently. However, this configuration is invariant to the sequence of operations shown. First, a C_2 rotation is done followed by a color change operation which colors the white triangle black and the black triangle white. This combined operation will be designated $\underline{C}_2$. Similarly, the sequence of reflection and color change leaves configuration **3d** unchanged. This operation will be designated $\underline{S}_v$. Thus a total of *four* symmetry operations are defined. This situation (of four types of symmetry operations) has been well studied and is termed *dichromatic antisymmetry.*[11]



Now a similar sequence will be done on the structures **2**, **4a**, and **4b.** Structure **4a** is invariant to a C_2 rotation, and structure **2** is invariant to a S_v reflection (aside from ligand numbering). However, structure **4a** is also invariant to the sequence of operations shown. First, **4a** is reflected in the plane S_v which reverses the configuration of the chiral ligands. The operator, *chirality reversal*, is performed which reverses the chirality of all ligands. This changes the ligands back to their original configuration. This sequence of operations will be symbolized S_{vp}. Similarly, the sequence of rotation and chirality reversal leaves **2** unchanged. This combination will be symbolized C_{2p}. These two combination operations will be termed *pseudochirality operations.*



Some further clarification of the effect of these pseudochirality operations may be helpful. A C_{np} *operation* in its simplest form reverses the chirality of all chiral ligands in a structure, while it is simply a C_n rotation for the rest of the structure. Therefore a structure with a C_{np} *element* of symmetry is invariant to the C_n rotation except that all (+)-chiral ligands are taken to (−)-chiral ligands of the same constitution. A C_{np} axis (for a set of chiral ligands) cannot pass through any of the ligands in the set, and any structure with a C_{np} element of symmetry has an equal number of (+)- and (−)-chiral ligands. An S_{np} rotation–reflection *operation* leaves all (+)-chiral ligands as (+)-chiral ligands, while it is simply an S_n rotation–reflection for the rest of the structure. A structure with an S_{np} *element* of symmetry is invariant to the S_n operation except that all (+)-chiral ligands are taken into (+)-chiral ligands of the same constitution. An S_{np} axis can pass through chiral ligands, and there are no restrictions on the relative number of (+)- and (−)-ligands.

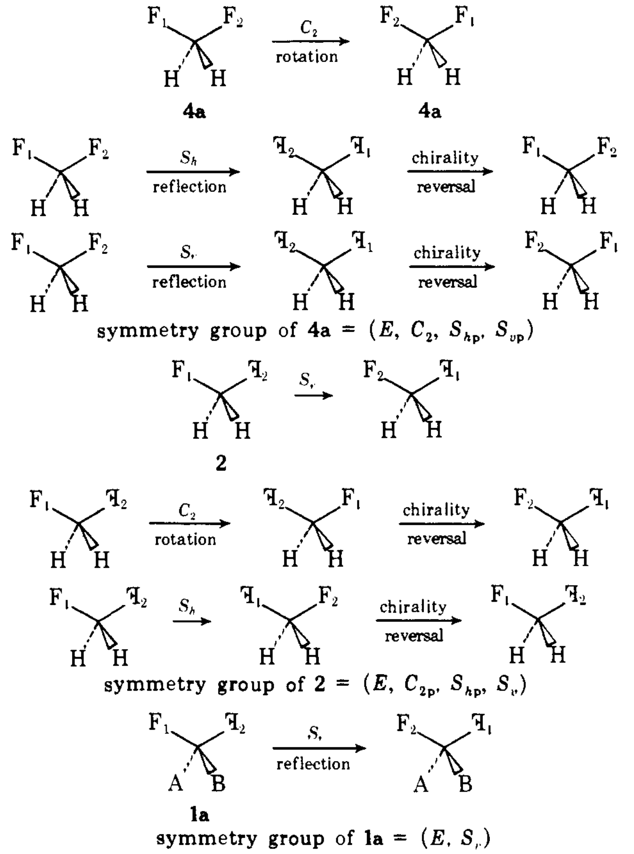
Comparison of the color change and chirality change operations shows one significant difference. Reflection does not change color, while it does change chirality. This means that the reflection operation in the color change case corresponds to the reflection plus chirality change operations in the chirality change case.

Group Theoretic Properties

It is well known that all the symmetry operations of a structure form a group, hence the group properties of these pseudochirality operators will be investigated.

In Scheme I are shown three structures and the symmetry operations to which they are invariant. It is a simple matter to verify that these operations form the groups indicated (hereafter termed pseudochirality groups). For structures **4a** and **2**, the group is isomorphic to the symmetry point group C_{2v}. In fact, these structures would have C_{2v}

Scheme I



symmetry if the ligands were not chiral. Structure **1a** would have C_s symmetry without chiral ligands. The problem now is to determine how these groups can be derived and what relation they have to the problem at hand.

The mathematical problem here can be concisely stated. The group that includes *all* of the symmetry and pseudochirality operators is the direct product $C \times S$. S is the symmetry point group, and C is the chirality change group. In the present example, C is isomorphic to the cyclic group of order two C_2. In the general case, C will be the direct product of cyclic groups of order 2. The direct product $C \times S$ has the property shown diagrammatically in eq 1. The arrows refer to homomorphisms between the groups. The homomorphism i_s is not unique. Composing the homomorphisms shown in eq 1 gives the following results. Injecting C into $C \times S$ (i_c) followed by the projection p_c gives the same result as the identity mapping of C onto itself, 1_c. Similarly, i_s followed by p_s gives 1_s. The significance of all this to the problem at hand can now be stated. The possible pseudochirality groups correspond to the possible injections i_s. The desired group is the image in $C \times S$ of i_s. The image of i_s in $C \times S$ cannot contain the operation which simply reverses the chiral ligands without rotation or reflection. Such an operation clearly cannot be a symmetry operation for a structure. Stated differently, C and S are disjoint except for the identity. This is a property of direct products. Now the composition of i_s with p_c gives a projection of S onto C. It has already been noted that C is isomorphic to C_2, hence each pseudochirality group determines a homomorphism of S onto C_2. This property suggests an easy way of deriving these groups, using chemically familiar group theoretic methods. Each homomorphism of a group onto C_2 determines a one-dimensional irreducible representation of the group. Thus the desired pseudochirality groups correspond to the one-dimensional, real irreducible representations of the symmetry point group.

$$\begin{tikzcd} C \arrow[loop left, "1_c"] \arrow[r, shift left, "i_c"] & C \times S \arrow[l, shift left, "p_c"] \arrow[r, shift left, "p_s"] & S \arrow[l, shift left, "i_s"] \arrow[loop right, "1_s"] \end{tikzcd} \qquad (1)$$

The derivation of the pseudochirality groups obtainable from C_{2h} is sketched in Scheme II along with examples. The desired groups are obtained by "imposing" the one-dimensional irreducible representation on the point group. For example, consider the B_g representation. Imposition maps E and i to +1 and C_2 and S_h to −1. This corresponds to the pseudochirality group (E, C_{2p}, i, S_{hp}). This group is given the unique designation $C_{2h}{:}B_g$. The structure with this symmetry is meso **5** (one isomeric form). Similarly the B_u representation yields a pseudochirality group and a meso structure **6**. Now imposition of the A_g representation maps all the group elements to +1. However, it must be remembered that chiral ligands are present. This group includes no pseudochirality operators and describes the symmetry of a pseudochiral structure with C_{2h} point group symmetry. The two pseudoenantiomeric forms (**7a, 7b**) of such a structure are shown. The reason for using the term *pseudochiral* rather than pseudoasymmetric is now apparent. This example satisfies the requirement for being "pseudoasymmetric" yet has nontrivial rotation symmetry, hence the term pseudochirality is preferred. This parallels the reason for using the term chirality rather than asymmetry to describe traditional enantiomerism.[10,12]

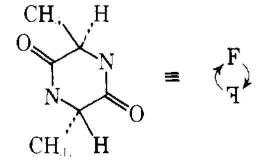
The final representation is A_u, and imposition yields the group (E, C_2, i_p, S_{hp}). This group includes no alternating axis of symmetry, hence any structure with this symmetry must be chiral and exist in two enantiomeric forms, as does the example (**8a, 8b**).

Scheme II

C_{2h} character table

C_{2h}	E	C_2	i	S_h
B_g	1	−1	1	−1
B_u	1	−1	−1	1
A_g	1	1	1	1
A_u	1	1	−1	−1

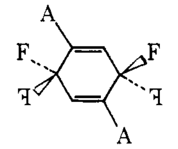
B_g 1 −1 1 −1 ⟶ E C_{2p} i S_{hp} $C_{2h}{:}B_g$



meso

5

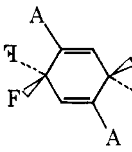
B_u 1 −1 −1 +1 ⟶ E C_{2p} i_p S_h $C_{2h}{:}B_u$



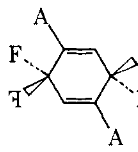
meso

6

A_g 1 1 1 1 ⟶ E C_2 i S_h $C_{2h}{:}A_g$



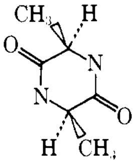
7a



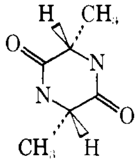
7b

pseudochiral

A_u 1 1 −1 −1 ⟶ E C_2 i_p S_{hp} $C_{2h}{:}A_u$



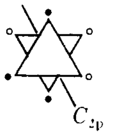
8a



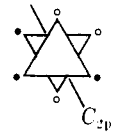
8b

chiral A

At this point, the possible types of isomerism can be described. The type of isomerism exhibited by a chemical structure is determined by the kinds of symmetry the structure has. This information is contained in Table I along with examples. Structures **9** and **10** can be thought of as octahedrally coordinated metals with two tridentate ligands, themselves containing chiral ligands. In all cases, the isomeric forms are interconverted by operations which are not included among the symmetry operations. This gets complicated in the latter case (chiral C), and the interconversions of the four isomers (**10a–d**) are indicated.



9a



9b

The desired definition of pseudochirality can now be given. *A structure is pseudochiral if it lacks C_{np} and S_{np} axes of symmetry* (for a single set of chiral ligands, vide infra). This definition resembles Wheland's familiar definition of chirality (lack of an S_n axis). A structure which satisfies both these criteria will be both chiral and pseudochiral and exist in four isomeric forms. An example is provided by structures **10a–d** (Scheme III).

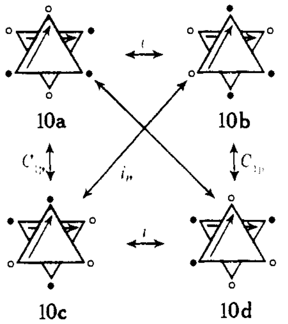
A generalization is possible by allowing more than one set of chiral ligands. Such sets can be constitutionally different or be situated in sites that are never interchanged. As

Table I. Types of Isomerism

Name	C_n	C_{np}	S_n	S_{np}	No. of isomers[a]	Kind of isomers	Examples
Meso	Yes	Yes	Yes	Yes	1	Meso	**2, 5, 6**
Pseudochiral	Yes	No	Yes	No	2	Pseudoenantiomers	**1, 7**
Chiral *A*	Yes	No	No	Yes	2	Enantiomers	**4, 8**
Chiral *B*	Yes	Yes	No	No	2	Enantiomers	**9**
Chiral *C*	Yes	No	No	No	4	Pseudoenantiomers and enantiomers	**10**

[a] This is the number of isomers which have the same pseudochirality symmetry group.

Scheme III



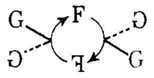
might be expected, the number of possibilities increases significantly. However, the method of determining the pseudochirality groups and types of isomerism is easily derived from the simple case. In the case of *n* sets of chiral ligands, the group *C* in (1) is the direct product of *n* cyclic groups of order two. The desired pseudochirality groups are therefore in correspondence with all the possible sums of *n* one-dimensional irreducible representations of the symmetry point group. The possible double pseudochirality groups for C_{2h} are derived in Scheme IV in an abbreviated form, except for the first one. The two representations A_g (for the set of F ligands) and B_g (for the G set) are imposed on C_{2h}. The resulting group, C_{2h}:$A_g + B_g$, is shown and an example given. The operator C_{2pF} is a C_2 rotation followed by a chirality reversal operation on the F ligands only. Only one isomeric form of each structure is shown.

Using these methods, the possible single and double pseudochirality groups have been derived and are listed in Table II. Only one representative group from each class of sym-

Scheme IV. Derivation of Double Pseudochirality Groups from C_{2h}

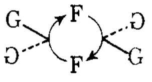
C_{2h}	E	C_2	i	S_h	C_{2h}:A_g + B_g
A_g	1	1	1	1	set G
B_g	1	−1	1	−1	set F
	E	C_{2pF}	i	S_{hpF}	

pseudochiral, 2 isomers



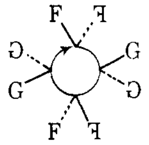
11

C_{2h}:A_g + A_u, E C_2 i_{pF} S_{hpF}
chiral, 4 isomers



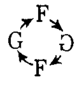
12

C_{2h}:A_g + B_u, E C_{2pF} i_{pF} S_h
pseudochiral, 2 isomers



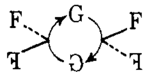
13

C_{2h}:B_g + A_u, E C_{2pG} i_{pF} S_{hpFG}
chiral, 2 isomers



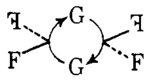
14

C_{2h}:B_g + B_u, E C_{2pFG} i_{pF} S_{hpG}
chiral, 2 isomers



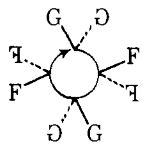
15

C_{2h}:A_u + B_u, E C_{2pF} i_{pFG} S_{hpG}
chiral, 2 isomers



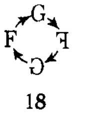
16

C_{2h}:$2A_g$, E C_2 i S_h
pseudochiral, 4 isomers



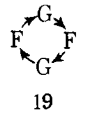
17

C_{2h}:$2B_g$, E C_{2pFG} i S_{hpFG}
pseudochiral, 2 isomers



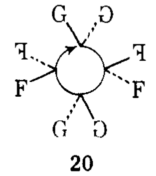
18

C_{2h}:$2A_u$, E C_2 i_{pFG} S_{hpFG}
chiral, 4 isomers



19

C_{2h}:$2B_u$, E C_{2pFG} i_{pFG} S_h
pseudochiral, 2 isomers



20

Table II. Possible Pseudochirality Groups[21]

Supergroup	Derived group name	Type	Isomers
C_1	(1) $C_1:A$	c	4[a]
	(2) $C_1:2A$	c	8
C_s	(1) Single		
	$C_s:A'$	p	2[b]
	$C_s:A''$	c	2
	(2) Double		
	$C_s:2A'$	p	4
	$C_s:2A''$	c	4
	$C_s:A' + A''$	c	4
C_i	(1) Single		
	$C_i:A_g$	p	2
	$C_i:A_u$	c	2
	(2) Double		
	$C_i:2A_g$	p	4
	$C_i:2A_u$	c	4
	$C_i:A_g + A_u$	c	4
C_2	(1) Single		
	$C_2:A$	c	4
	$C_2:B$	c	2[c]
	(2) Double		
	$C_2:2A$	c	8
	$C_2:2B$	c	4
	$C_2:A + B$	c	4
D_4	(1) Single		
	$D_4:A_1$	c	4
	$D_4:A_2$	c	2
	$D_4:B_1$	c	2
	$D_4:B_2$	c	2
	(2) Double		
	$D_4:2A_1$	c	8
	$D_4:2A_2$	c	4
	$D_4:2B_1$	c	4
	$D_4:2B_2$	c	4
	$D_4:A_1 + A_2$	c	4
	$D_4:A_1 + B_1$	c	4
	$D_4:A_1 + B_2$	c	4
	$D_4:A_2 + B_1$	c	4
	$D_4:A_2 + B_2$	c	2
	$D_4:B_1 + B_2$	c	2
C_{2v}	(1) Single		
	$C_{2v}:A_1$	p	2
	$C_{2v}:A_2$	c	2
	$C_{2v}:B_1$	m	1[d]
	$C_{2v}:B_2$	m	1[e]
	(2) Double		
	$C_{2v}:2A_1$	p	4
	$C_{2v}:2A_2$	c	4
	$C_{2v}:2B_1$	p	2
	$C_{2v}:2B_2$	p	2
	$C_{2v}:A_1 + A_2$	c	4
	$C_{2v}:A_1 + B_1$	p	2
	$C_{2v}:A_1 + B_2$	p	2
	$C_{2v}:A_2 + B_1$	c	2
	$C_{2v}:A_2 + B_2$	c	2
	$C_{2v}:B_1 + B_2$	c	2[22]
C_{3v}	(1) Single		
	$C_{3v}:A_1$	p	2
	$C_{3v}:A_2$	c	2
	(2) Double		
	$C_{3v}:2A_1$	p	4
	$C_{3v}:2A_2$	c	4
	$C_{3v}:A_1 + A_2$	c	4
C_{2h}	(1) Single		
	$C_{2h}:A_g$	p	2[f]
	$C_{2h}:B_g$	m	1[g]
	$C_{2h}:A_u$	c	2[h]
	$C_{2h}:B_u$	m	1[i]
	(2) Double		
	$C_{2h}:2A_g$	p	4[j]
	$C_{2h}:2B_g$	p	2[k]
	$C_{2h}:2A_u$	c	4[l]
	$C_{2h}:2B_u$	p	2[m]
	$C_{2h}:A_u + B_u$	c	2[n]
	$C_{2h}:A_g + B_g$	p	2[o]
	$C_{2h}:A_g + A_u$	c	4[p]
	$C_{2h}:A_g + B_u$	p	2[q]
	$C_{2h}:B_g + A_u$	c	2[r]
	$C_{2h}:B_g + B_u$	c	2[s]
C_{3h}	(1) Single		
	$C_{3h}:A'$	p	2
	$C_{3h}:A''$	c	2
	(2) Double		
	$C_{3h}:2A'$	p	4
	$C_{3h}:2A''$	c	4
	$C_{3h}:A' + A''$	c	4
D_{3h}	(1) Single		
	$D_{3h}:A_1'$	p	2
	$D_{3h}:A_2'$	p	2
	$D_{3h}:A_1''$	c	2
	$D_{3h}:A_2''$	m	1
	(2) Double		
	$D_{3h}:2A_1'$	p	4
	$D_{3h}:2A_2'$	p	2
	$D_{3h}:2A_1''$	c	4
	$D_{3h}:2A_2''$	p	2
	$D_{3h}:A_1' + A_2'$	p	2
	$D_{3h}:A_1' + A_1''$	c	4
	$D_{3h}:A_1' + A_2''$	p	2
	$D_{3h}:A_2' + A_1''$	c	2
	$D_{3h}:A_2' + A_2''$	c	2
	$D_{3h}:A_1'' + A_2''$	c	2
D_{4h}	(1) Single		
	$D_{4h}:A_{1g}$	p	2
	$D_{4h}:A_{2g}$	m	1
	$D_{4h}:B_{1g}$	m	1
	$D_{4h}:B_{2g}$	m	1
	$D_{4h}:A_{1u}$	c	2
	$D_{4h}:A_{2u}$	m	1
	$D_{4h}:B_{1u}$	m	1
	$D_{4h}:B_{2u}$	m	1
	(2) Double		
	$D_{4h}:2A_{1g}$	p	4
	$D_{4h}:2A_{2g}$	p	2
	$D_{4h}:2B_{1g}$	p	2
	$D_{4h}:2B_{2g}$	p	2
	$D_{4h}:2A_{1u}$	c	4
	$D_{4h}:2A_{2u}$	p	2
	$D_{4h}:2B_{1u}$	p	2
	$D_{4h}:2B_{2u}$	p	2
	$D_{4h}:A_{1g} + A_{2g}$	p	2
	$D_{4h}:A_{1g} + B_{1g}$	p	2
	$D_{4h}:A_{1g} + B_{2g}$	p	2
	$D_{4h}:A_{1g} + A_{1u}$	c	4
	$D_{4h}:A_{1g} + A_{2u}$	p	2
	$D_{4h}:A_{1g} + B_{1u}$	p	2
	$D_{4h}:A_{1g} + B_{2u}$	p	2
	$D_{4h}:A_{2g} + B_{1g}$	m	1
	$D_{4h}:A_{2g} + B_{2g}$	m	1
	$D_{4h}:A_{2g} + A_{1u}$	c	2
	$D_{4h}:A_{2g} + A_{2u}$	c	2
	$D_{4h}:A_{2g} + B_{1u}$	m	1
	$D_{4h}:A_{2g} + B_{2u}$	m	1
	$D_{4h}:B_{1g} + B_{2g}$	m	1
	$D_{4h}:B_{1g} + A_{1u}$	c	2
	$D_{4h}:B_{1g} + A_{2u}$	m	1
	$D_{4h}:B_{1g} + B_{1u}$	c	2
	$D_{4h}:B_{2g} + A_{1u}$	c	2
	$D_{4h}:B_{1g} + B_{2u}$	m	1
	$D_{4h}:B_{2g} + A_{2u}$	m	1
	$D_{4h}:B_{2g} + B_{1u}$	m	1
	$D_{4h}:B_{2g} + B_{2u}$	c	2
	$D_{4h}:A_{1u} + A_{2u}$	c	2
	$D_{4h}:A_{1u} + B_{1u}$	c	2
	$D_{4h}:A_{1u} + B_{2u}$	c	2
	$D_{4h}:A_{2u} + B_{1u}$	m	1
	$D_{4h}:A_{2u} + B_{2u}$	m	1
	$D_{4h}:B_{1u} + B_{2u}$	m	1

Table II *(Continued)*

Super-group	Derived group name	Type	Isomers
D_{2d}	(1) Single		
	$D_{2d}{:}A_1$	p	2
	$D_{2d}{:}A_2$	m	1
	$D_{2d}{:}B_1$	c	2
	$D_{2d}{:}B_2$	m	1[u]
	(2) Double		
	$D_{2d}{:}2A_1$	p	4
	$D_{2d}{:}2A_2$	p	2
	$D_{2d}{:}2B_1$	c	4
	$D_{2d}{:}2B_2$	p	2
	$D_{2d}{:}A_1 + A_2$	p	2
	$D_{2d}{:}A_1 + B_1$	c	4
	$D_{2d}{:}A_1 + B_2$	p	2
	$D_{2d}{:}A_2 + B_1$	c	2
	$D_{2d}{:}A_2 + B_2$	c	2
	$D_{2d}{:}B_1 + B_2$	c	2
D_{3d}	(1) Single		
	$D_{3d}{:}A_{1g}$	p	2
	$D_{3d}{:}A_{2g}$	m	1[v]
	$D_{3d}{:}A_{1u}$	c	2
	$D_{3d}{:}A_{2u}$	m	1
	(2) Double		
	$D_{3d}{:}2A_{1g}$	p	4
	$D_{3d}{:}2A_{2g}$	p	2
	$D_{3d}{:}2A_{1u}$	c	4
	$D_{3d}{:}2A_{2u}$	p	2
	$D_{3d}{:}A_{1g} + A_{2g}$	p	2
	$D_{3d}{:}A_{1g} + A_{1u}$	c	4
	$D_{3d}{:}A_{1g} + A_{2u}$	p	2
	$D_{3d}{:}A_{2g} + A_{1u}$	c	2
	$D_{3d}{:}A_{2g} + A_{2u}$	c	2
	$D_{3d}{:}A_{1u} + A_{2u}$	c	2
S_4	(1) Single		
	$S_4{:}A$	p	2[t]
	$S_4{:}B$	c	2
	(2) Double		
	$S_4{:}2A$	p	4
	$S_4{:}2B$	c	4
	$S_4{:}A + B$	c	4
T_d	(1) Single		
	$T_d{:}A_1$	p	2
	$T_d{:}A_2$	c	2
	(2) Double		
	$T_d{:}2A_1$	p	4
	$T_d{:}2A_2$	c	4
	$T_d{:}A_1 + A_2$	c	4
T_h	(1) Single		
	$T_h{:}A_g$	p	2
	$T_h{:}A_u$	c	2
	(2) Double		
	$T_h{:}2A_g$	p	4
	$T_h{:}2A_u$	c	4
	$T_h{:}A_g + A_u$	c	4
O_h	(1) Single		
	$O_h{:}A_{1g}$	p	2
	$O_h{:}A_{2g}$	m	1
	$O_h{:}A_{1u}$	c	2
	$O_h{:}A_{2u}$	m	1
	(2) Double		
	$O_h{:}2A_{1g}$	p	4
	$O_h{:}2A_{2g}$	p	2
	$O_h{:}2A_{1u}$	c	4
	$O_h{:}2A_{2u}$	p	2
	$O_h{:}A_{1g} + A_{2g}$	p	2
	$O_h{:}A_{1g} + A_{1u}$	c	4
	$O_h{:}A_{1g} + A_{2u}$	p	2
	$O_h{:}A_{2g} + A_{1u}$	c	2
	$O_h{:}A_{2g} + A_{2u}$	c	2
	$O_h{:}A_{1u} + A_{2u}$	c	2
I_h	(1) Single		
	$I_h{:}A_g$	p	2
	$I_h{:}A_u$	c	2
	(2) Double		
	$I_h{:}2A_g$	p	4
	$I_h{:}2A_u$	c	4
	$I_h{:}A_g + A_u$	c	4
T	(1) Single		
	$T{:}A$	c	4
	(2) Double		
	$T{:}2A$	c	8
O	(1) Single		
	$O{:}A_1$	c	4
	$O{:}A_2$	c	2
	(2) Double		
	$O{:}2A_1$	c	8
	$O{:}2A_2$	c	4
	$O{:}A_1 + A_2$	c	4
I	(1) Single		
	$I{:}A$	c	4
	(2) Double		
	$I{:}2A$	c	8
$C_{\infty v}$	(1) Single		
	$C_{\infty v}{:}\Sigma^+$ (ref 23)		
	$C_{\infty v}{:}\Sigma^-$	c	2
	(2) Double		
	$C_{\infty v}{:}2\Sigma^-$	c	4
	The other combinations are not possible		
$D_{\infty h}$	(1) Single		
	$D_{\infty h}{:}\Sigma_g{}^+$ Not possible		
	$D_{\infty h}{:}\Sigma_g{}^-$	m	1[w]
	$D_{\infty h}{:}\Sigma_u{}^+$ Not possible		
	$D_{\infty h}{:}\Sigma_u{}^-$	c	2[x]
	(2) Double		
	$D_{\infty h}{:}2\Sigma_g{}^-$	p	2
	$D_{\infty h}{:}2\Sigma_u{}^-$	c	4
	$D_{\infty h}{:}\Sigma_g + \Sigma_u{}^-$	c	2
	The other combinations are not possible		
D_∞	(1) Single		
	$D_\infty{:}\Sigma^+$	c	4
	$D_\infty{:}\Sigma^-$	c	2
	(2) Double		
	$D_\infty{:}2\Sigma^+$	c	8
	$D_\infty{:}2\Sigma^-$	c	4
	$D_\infty{:}\Sigma^+ + \Sigma^-$	c	4
C_∞	(1) Single		
	$C_\infty{:}\Sigma$	c	4
	(2) Double		
	$C_\infty{:}2\Sigma$	c	8
$C_{\infty h}$	(1) Single		
	$C_{\infty h}{:}\Sigma_g$	p	2
	$C_{\infty h}{:}\Sigma_u$	c	2
	(2) Double		
	$C_{\infty h}{:}2\Sigma_g$	p	4
	$C_{\infty h}{:}2\Sigma_u$	c	4
	$C_{\infty h}{:}\Sigma_g + \Sigma_u$	c	4
K_h	(1) Single		
	$K_h{:}S_g$ Not possible		
	$K_h{:}S_u$	c	2[y]
	(2) Double		
	$K_h{:}2S_u$	c	4
K	Yields no derived groups		

[a] 10. [b] 1. [c] 9. [d,e] 21 and 22 arbitrary. [f] 7. [g] 5. [h] 6. [i] 17. [k] 18. [l] 19. [m] 20. [n] 16. [o] 11. [p] 12. [q] 13. [r] 14. [s] 15. [t] Reference 8a, Figure 10. [u] Reference 8a, Figure 10. [v] Reference 8a, Figure 10. [w] *meso*-Tartaric acid. [x] *dl*-Tartaric acid. [y] Single asymmetric carbon. These last three examples are trivial since chiral ligands are being treated as two-values points.

Table III. Summary of Derived Groups

	Single					Double						
	M	P2	C2	C4	Tot	M	P2	P4	C2	C4	C8	Tot
C_1	0	0	0	1	1	0	0	0	0	0	1	1
C_s	0	1	1	0	2	0	0	1	0	2	0	3
C_i	0	1	1	0	2	0	0	1	0	2	0	3
C_2	0	0	1	1	2	0	0	0	0	2	1	3
C_3	0	0	0	1	1	0	0	0	0	0	1	1
D_3	0	0	1	1	2	0	0	0	0	2	1	3
D_4	0	0	3	1	4	0	0	0	3	6	1	10
C_{2v}	2	1	1	0	4	0	4	1	3	2	0	10
C_{3v}	0	1	1	0	2	0	0	1	0	2	0	3
C_{2h}	2	1	1	0	4	0	4	1	3	2	0	10
C_{3h}	0	1	1	0	2	0	0	1	0	2	0	3
D_{3h}	2	1	1	0	4	0	3	1	2	1	0	10
D_{4h}	6	1	1	0	8	12	12	1	9	2	0	36
D_{2d}	2	1	1	0	4	0	4	1	3	2	0	10
D_{3d}	2	1	1	0	4	0	4	1	3	2	0	10
S_4	0	1	1	0	2	0	0	1	0	2	0	3
T_d	0	1	1	0	2	0	0	1	0	2	0	3
T_h	0	1	1	0	2	0	0	1	0	2	0	3
O_h	2	1	1	0	4	0	4	1	3	2	0	10
I_h	0	1	1	0	2	0	0	1	0	2	0	3
T	0	0	0	1	1	0	0	0	0	0	1	1
O	0	0	1	1	2	0	0	0	0	2	1	3
I	0	0	0	1	1	0	0	0	0	0	1	1
C_∞	0	0	1	0	1	0	0	0	0	1	0	1
$D_{\infty h}$	1	0	1	0	2	0	1	0	1	1	0	3
C_∞	0	0	0	1	1	0	0	0	0	0	1	1
D_∞	0	0	1	1	2	0	0	0	0	2	1	3
$C_{\infty h}$	0	1	1	0	2	0	0	1	0	2	0	3
K_h	0	0	1	0	1	0	0	0	0	1	0	1
K	0	0	0	0	0	0	0	0	0	0	0	0
Total:	19	16	26	10	71	12	37	16	31	49	10	155

metry point groups is used. For example, C_{2v} is representative of all C_{nv}, n even. The information given for each group is its name, type (m = meso, p = pseudochiral, c = chiral), number of isomers, and the location or name of any examples. There is a simple relationship:

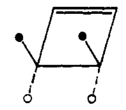
$$ne = 2^{s+1}$$

where n is the number of isomers, e is the number of types of symmetry elements the structure has, and s is the number of sets of chiral ligands. Some of the infinite groups yield no derived groups, or groups that cannot be realized in any chemical structure and are included only for completeness (see Table III for summary of derived groups). Since chiral ligands are being considered as two-valued points, the group K_h:S_u represents a single asymmetric carbon atom.

A number of tables of single and double antisymmetry groups exist S_w (also called magnetic symmetry groups).[11] The present derivation is necessary because of some important differences between the two problems, which change the number and kind of groups obtained. It has already been noted that the operations are labeled differently. Furthermore, double antisymmetry groups of the type C_{2h}:$A_u + B_u$ and C_{2h}:$B_u + A_u$ are considered to be different. In the present case, such a distinction leads to constitutional isomerism. Antisymmetry groups resulting from the totally symmetric representation are trivial. In the present case, they yield pseudochiral structure, the major form of isomerism here. Finally, degeneracies which occur in the antisymmetry groups are removed in the present case. For example, the groups C_{2v}:B_1 and C_{2v}:B_2 (Scheme V) are considered as a degenerate pair since the planes of symmetry differ only by labels. However, these two groups can be represented by different chemically realizable stereoisomers (**21** and **22**) and therefore must be considered different. The assignment of each example to its pseudochirality group *is* arbitrary, unless the molecular orientation is fixed.

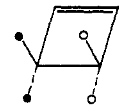
Scheme V

C_{2v}	E	C_2	$S_{(xz)}$	$S_{(yz)}$
B_1	1	−1	1	−1
B_2	1	−1	−1	1



21

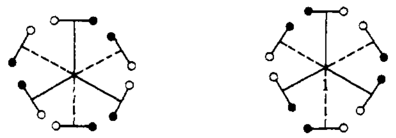
C_{2v}:B_1	E	C_{2p}	S	S_p
C_{2v}:B_2	E	C_{2p}	S_p	S



22

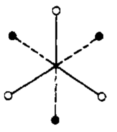
Groups with three or more sets of chiral ligands would be derived similarly. There would be about 400 such groups with three sets of chiral ligands. Such chemical structures are easily realizable, particularly as cyclic peptides. It is interesting that there can be no meso structure with three or more sets of chiral ligands. This can be easily proved by noting that meso structures occur only for D_{nh} groups with two sets of chiral ligands. A meso structure can result only if the homomorphism of the symmetry group onto the chirality change group is onto with respect to both rotation and reflection symmetry. Since D_n has only two generators, it cannot be mapped (epimorphically) onto $C_2 \times C_2 \times C_2$. Hence no meso structure is possible.

A further generalization can be made by considering nonrigid structures.[13,14] Longuet-Higgins[15] has given the nonrigid symmetry group for ethane, symbolized here as G_{36}. The possible pseudochirality groups are determined in the same manner as above, by imposition onto the one-dimensional real irreducible representations of the group. There are four of these, and examples are provided by structures **23–26**. Longuet-Higgins has given the character table and the labels for the irreducible representations.[15]



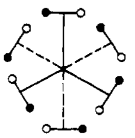
23a **23b**

G_{36}:A_1 pseudochiral



24

G_{36}:A_2 meso



25

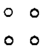
G_{36}:A_4 meso

26a **26b**

G_{36} A_3 chiral

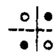
Overview and Extensions

An overview of this work is hopefully ascertainable from the following discussion. Consider the three configurations of chiral ligands, A, B, and C. In configuration C, the solid



A

B

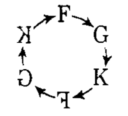


C

vertical line is above the plane, and the dotted horizontal line is below the plane. The symmetry of these structures can be specified in several ways. The first and simplest is to specify just the rotation symmetry. A has D_4 rotation symmetry, B has C_2 rotation symmetry, and C has D_2 rotation symmetry. Knowing only rotation symmetry is sufficient to describe some properties of chemical structures. For example, the number of isomers is determined using just the rotation symmetry.[16] The π-molecular orbitals of benzene can be determined from just the rotation group C_6.[17] Specifications of only rotation symmetry is, however, insufficient to determine other properties such as chirality. This leads to the next higher level of symmetry specification, namely point group symmetry. A has D_4 symmetry, B has C_{2h} symmetry, and C has D_{2d} symmetry. From these specifications it is apparent that A exists in two enantiomeric forms, and B and C are superimposible on their mirror images. The point group description is a great deal more useful than the rotation group description, and most applications of group theory to chemistry require it. The point group designation is, however, inadequate to ascertain pseudochirality.

The present work extends this sequence by one. Of the examples given, A is $D_{4h}{:}A_{1u}$, B is $D_{2h}{:}B_{2g}$, and C is $D_{2d}{:}A_1$. This indicates that B is meso and C is pseudochiral and exists in two pseudoenantiomeric forms. The information gained (pseudochirality) by specifying the pseudochiral symmetry and point group symmetry instead of just the point group symmetry is analogous to the information gained (chirality) by specifying point group symmetry instead of just rotation symmetry.

This sequence can be extended and the work generalized in any number of ways. What is needed is a designation of the group C in (1). For example, the members of this group could include operations which change ligand constitution. The structure **27** yields a representation for $C_{6h}{:}B_g + E_{1g}$.



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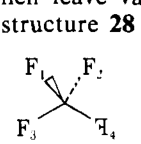
The development here is somewhat similar to the treatment of polychromatic symmetry.[11,18]

The group C could also include operations which reverse the chirality of ligands *individually*, rather than all at once. If one also includes all permutations of constitutionally identical ligands (not just those which represent the point group), one obtains the hyperoctahedral groups used by Mead[19] to obtain chirality functions for molecules with chiral ligands. Pseudochirality groups are subgroups of these hyperoctahedral groups. One could classify stereoisomers more generally by finding other subgroups of the hyperoctahedral group which leave various stereoisomers invariant. For example, structure **28** is left invariant by the



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permutation $(\bar{1})(\bar{2})(34)$ which is the operation of reflection in the vertical plane followed by reversal of the chirality ligands 1 and 2. This structure (**28**) is also invariant to the C_3 rotation (123)(4). All products of these two permutations, $(123)(4)(\bar{1})(\bar{2})(34) = (\bar{1}\bar{2}34)$, etc., generate a group of order 24 which is isomorphic to T_d and is a subgroup of the hyperoctahedral group. Other generalizations are possible by modifying the combination of the groups. The diagram shown in (1) is for the direct product, which is a rather trivial *extension* of C by S.[20a] More generalized extensions are represented by the diagrams 2 and 3. Some nonrigid symmetry groups can be expressed as semidirect products.[20b]

semidirect product

$$\begin{tikzcd} C \arrow[r] & C\times_s S \arrow[r, shift left] & S \arrow[l, shift left] \end{tikzcd} \qquad (2)$$

general extension

$$\begin{tikzcd} C \arrow[r] & C\mathrm{ext}S \arrow[r] & S \end{tikzcd} \qquad (3)$$

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References and Notes

(1) Supported by the National Science Foundation.
(2) Taken in part from J. G. Nourse, Ph.D. Thesis, California Institute of Technology, 1974.
(3) National Institute of Health Predoctoral Trainee, 1970–1973. Current address: Department of Chemistry, Princeton University, Princeton, N.J. 08540.
(4) K. Mislow, "Introduction to Stereochemistry", W. A. Benjamin, New York, N.Y., 1966, p 91.
(5) V. Prelog, *Chem. Br.*, 382 (1968).
(6) V. Prelog, Pacific Coast Lecture, California Institute of Technology, Oct 13, 1970. The present investigation was prompted by this lecture. The content of this talk, considerably expanded and detailed, has been published more recently.[8]
(7) V. Prelog and H. Gerlach, *Helv. Chim. Acta*, 2288 (1964).
(8) (a) V. Prelog and G. Helmchen, *Helv. Chim. Acta*, **55**, 2581 (1972); (b) G. Helmchen and V. Prelog, *ibid.*, **55**, 2599, 2612 (1972).
(9) These ligands are assumed to be freely rotating (except in cyclic structures) and, for the purposes here, can be considered as two-valued points. In cyclic structures (such as cyclic peptides), ring direction is defined by arrows as in **5** and **10**. This again is Prelog's[7] notation for structures of this kind.
(10) G. W. Wheland, "Advanced Organic Chemistry", 2nd ed, Wiley, New York, N.Y., 1949, Chapter 5.
(11) (a) A. V. Shubnikov, N. V. Belov, et al., "Colored Symmetry", Macmillan, New York, N.Y., 1964; (b) V. L. Indenborm, *Sov. Phys.-Crystallogr.* (*Engl. Transl.*), **4**, 578 (1959); (c) E. I. Galyarskil and A. M. Zamorzaev, *ibid.*, **8**, 68 (1963); (d) A. M. Zamorzaev, *ibid.*, **12**, 717 (1965); (e) A. V. Shubnikov and V. A. Koptsik, "Symmetry in Science and Art", Plenum Publishing Co., New York, N.Y., 1974.
(12) One of the referees has objected to the use of the word *pseudochirality* in preference to *pseudoasymmetry*. It is not the purpose of this paper to suggest standard chemical nomenclature, nevertheless, the term *pseudochirality* is used deliberately for the mathematical and semantic reasons given in the text. Structures for which the distinction between the descriptions *pseudochiral* and *pseudoasymmetric* is meaningful (namely those with nontrivial rotation symmetry) will be relatively rare but have been suggested in the existing literature (see footnotes to Table II).
(13) J. E. Leonard, Ph.D. Thesis, submitted May 24, 1971, California Institute of Technology. This reference includes an interesting discussion of nonrigid symmetry groups and meso structures. Of particular interest is the derivation of a group for *meso*-biphenyls which have no achiral conformations easily accessible.[14]
(14) K. Mislow and R. Bolstad, *J. Am. Chem. Soc.*, **77**, 6712 (1955).
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(17) F. A. Cotton, "Chemical Applications of Group Theory", Wiley-Interscience, New York, N.Y., 1963, p 125.
(18) V. L. Indenbom, N. V. Belov, and N. N. Neronova, *Sov. Phys.-Crystallogr.* (*Engl. Transl.*), **5**, 477 (1960).
(19) (a) A. Mead, E. Ruch, and A. Schönhofer, *Theor. Chim. Acta*, **29**, 269 (1973); (b) A. Mead, *Top. Curr. Chem.*, **49**, 1 (1974).
(20) (a) M. Hall, "The Theory of Groups", Macmillan, New York, N.Y., 1959, Chapter 15; (b) C. M. Woodman, *Mol. Phys.*, **19**, 753 (1970).
(21) Explanation of symbols and headings is as follows: the supergroup is the point group from which the pseudochirality group is derived; *single* pseudochirality groups are those for one set of chiral ligands; and *double* pseudochirality groups are for two sets of chiral ligands. This corresponds to earlier terminology for antisymmetry groups and has nothing to do with double-point groups. The derived group designation G: R encompasses the supergroup G, and the representation(s) R imposed as discussed in the text. The *type* refers to the isomer type for which c is chiral, p is pseudochiral, and m is meso. Superscripted letters on the number of isomers refer to footnotes giving the location of examples for some of the groups.
(22) H. Hirschmann and Kenneth R. Hanson, *J. Org. Chem.*, **36**, 3293 (1971). Their structures **3a** and **3b** are $C_{2v}{:}B_1 + B_2$ chiral; **22** is $C_{2h}{:}B_g$ meso; **28** is $D_2{:}B_1$ chiral.
(23) This group is not physically realizable because there cannot be $\infty\sigma$ planes in a structure containing discrete chiral units. This is another difference from dichromatic antisymmetry in which infinite symmetry planes are possible.