(12) Zhu, S.; Zhang, J. Exhaustive Generation of Structural Isomers for a Given Empirical Formula—A New Algorithm. *J. Chem. Inf. Comput. Sci.* **1982**, *22*, 34-38.
(13) Masinter, L. M.; Sridharan, N. S.; Lederberg, J.; Smith, D. H. Applications of Artificial Intelligence for Chemical Inference. 12. Exhaustive Generation of Cyclic and Acyclic Isomers. *J. Am. Chem. Soc.* **1974**, *96*, 7702-7714.
(14) Carhart, R. E.; Smith, D. H.; Brown, H.; Djerassi, C. Application of Artificial Intelligence for Chemical Inference. 17. An Approach to Computer-Assisted Elucidation of Molecular Structure. *J. Am. Chem. Soc.* **1975**, *97*, 5755-5762.
(15) Carhart, R. E.; Smith, D. H.; Gray, N. A.; Nourse, J. G.; Djerassi, C. GENOA: A Computer Program for Structure Elucidation Utilizing Overlapping and Alternative Substructures. *J. Org. Chem.* **1981**, *46*, 1708-1718.
(16) Zupan, J.; Novič, M.; Bohanec, S.; Razinger, M.; Lah, L.; Tušar, M.; Košir, I. Expert System for Solving Problems in Carbon-13 Nuclear Magnetic Resonance Spectroscopy. *Anal. Chim. Acta* **1987**, *200*, 333-345.
(17) Carhart, R. E.; Smith, D. H.; Brown, H.; Sridharan, N. S. Applications of Artificial Intelligence for Chemical Inference. 16. Computer Generation of Vertex-Graphs and Ring Systems. *J. Chem. Inf. Comput. Sci.* **1975**, *15*, 124-131.
(18) Nakayama, T.; Fujiwara, Y. Structure Generation on the Basis of BCT Representation of Chemical Structures. *J. Chem. Inf. Comput. Sci.* **1981**, *21*, 218-223.
(19) Zupan, J. *Algorithms for Chemists*; John Wiley & Sons: Chichester, 1989.
(20) Zupan, J.; Bohanec, S. Creation and Use of Chemical Data Bases with Substructure Search Capability. *Vestn. Slov. Kem. Drus.* **1987**, *34* (1), 71-81.
(21) Kalinowski, H. O.; Berger, S.; Braun, S. *Carbon-13 NMR Spectroscopy*; John Wiley & Sons: Chichester, 1988.
(22) Lah, L.; Tušar, M.; Zupan, J. Simulation of ^{13}C NMR spectra. *Tetrahedron Comput. Methodol.* **1989**, *2* (2), 5-15.
(23) Lederberg, J.; Sutherland, G. L.; Buchanan, B. G.; Feigenbaum, E. A.; Robertson, A. V.; Duffield, A. M.; Djerassi, C. Application of Artificial Intelligence for Chemical Inference. 1. The Number of Possible Organic Compounds. Acyclic Structures Containing C, H, O, and N. *J. Am. Chem. Soc.* **1969**, *91*, 2973-2976.
(24) Kerber, A.; Lane, R.; Moser, D. Ein *Strukturgenerator für molekulare* Graphen. *Anal. Chim. Acta* **1990**, *235*, 221-228.

Subductive and Inductive Derivation for Designing Molecules of High Symmetry

SHINSAKU FUJITA

Ashigara Research Laboratories, Fuji Photo Film Company, Ltd., Minami-Ashigara, Kanagawa, 250-01 Japan

Received May 14, 1991

Two types of derivations of molecules, subductive and inductive, are presented to design molecules of high symmetry. A subductive derivation consists of substituting a parent molecule with another set of atoms; on the other hand, an inductive derivation is composed of substituting a parent skeleton with a set of ligands that have three-dimensional structure. These derivations are discussed on the basis of subduction and induction of coset representations.

Since van't Hoff founded organic stereochemistry,[1] three-dimensional molecular models have been employed to comprehend stereochemical phenomena. Although the physicochemical explanation of chemical bonding has been changing, the importance of such models remains invariant. Thus, many organic molecules of high symmetry, achiral and chiral, have been designed and synthesized on the basis of molecular models.[2] Farina and Morandi[3] have proposed a principle for designing such molecules, in which a parent molecule of higher symmetry is desymmetrized with appropriate substituents. However, no theoretical rationalization has been reported for the desymmetrization process. We have presented the concept of promolecule for characterizing stereochemical relationships in nonrigid molecules.[4] This concept is also effective for rigid molecules; we can, however, discuss their symmetrical properties without employing the concept. The latter treatment is capable of rationalizing the Farina–Morandi proposal comprehensively; this issue is the object of the present paper. Thus, we propose here subductive and inductive derivations, which are the general methodologies for designing molecules of high symmetry.

SUBDUCTIVE DERIVATION OF MOLECULES

We first explain a minimum set of notations concerning subduction of coset representations.[5] A molecule is considered to be a derivative of a parent molecule, where the hydrogens of the parent are replaced by another set of atoms. Let **G** be the point group that represents the symmetry of the parent molecule. A set of equivalent atoms (or substituents) in the parent molecule

$$\Delta = \{\delta_1, \delta_2, ..., \delta_r\}$$

constitutes an orbit that is assigned to a coset representation (CR) $\mathbf{G}(/\mathbf{G}_i)$, where $\mathbf{G}_i$ is a subgroup of **G**. The notation $\mathbf{G}(/\mathbf{G}_i)$ comes from a coset decomposition represented by

$$\mathbf{G} = \mathbf{G}_i g_1 + \mathbf{G}_i g_2 + ... + \mathbf{G}_i g_r \quad (1)$$

where each g_k represents a representative of the coset $\mathbf{G}_i g_k$. Let us consider the set of the cosets

$$\mathbf{G}/\mathbf{G}_i = \{\mathbf{G}_i g_1, \mathbf{G}_i g_2, ..., \mathbf{G}_i g_r\} \quad (2)$$

When we apply a symmetry operation ($g \in \mathbf{G}$) to each of the cosets, we have a permutation

$$\pi_g = \begin{pmatrix} \mathbf{G}_i g_1 & \mathbf{G}_i g_2 & \cdots & \mathbf{G}_i g_r \\ \mathbf{G}_i g_1 g & \mathbf{G}_i g_2 g & \cdots & \mathbf{G}_i g_r g \end{pmatrix} \quad (3)$$

Suppose that g runs over all of the symmetry operations of **G**. The resulting set of permutations constructs the CR of **G**, i.e.

$$\mathbf{G}(/\mathbf{G}_i) = \{\pi_g | \forall\ g \in \mathbf{G}\} \quad (4)$$

The assignment of Δ to $\mathbf{G}(/\mathbf{G}_i)$ is based on the correspondence between Δ and $\mathbf{G}/\mathbf{G}_i$: $\delta_k \leftrightarrow \mathbf{G}_i g_k$ ($k = 1, 2, ..., r$).

For example, an allene derivative (**1**) of D_{2d} symmetry (O = H) is considered to be generated from a parent molecule by substituting hydrogens for the eight terminal positions (Figure 1). The right-hand figure is a sideview of the allene molecule. Atoms in the molecule are divided into orbits (Δ_1 to Δ_4) governed by coset representations [$D_{2d}(/C_1)$, $D_{2d}(/C_2)$, $D_{2d}(/C_{2v})$, and $D_{2d}(/D_{2d})$].[5,6]

Let us next consider the desymmetrization of **G** into its subgroup $\mathbf{G}_j$. This process restricts the CR $\mathbf{G}(/\mathbf{G}_i)$ within the

0095-2338/91/1631-0540$02.50/0 © 1991 American Chemical Society

Table I. Subduction of Coset Representations for D_{2d} Point Group

coset representation	subduction							
	$\downarrow C_1$	$\downarrow C_2$	$\downarrow C_2'$	$\downarrow C_s$	$\downarrow S_4$	$\downarrow C_{2v}$	$\downarrow D_2$	$\downarrow D_{2d}$
$D_{2d}(/C_1)$	$8C_1(/C_1)$	$4C_2(/C_1)$	$4C_2'(/C_1)$	$4C_s(/C_1)$	$2S_4(/C_1)$	$2C_{2v}(/C_1)$	$2D_2(/C_1)$	$D_{2d}(/C_1)$
$D_{2d}(/C_2)$[a]	$4C_1(/C_1)$	$4C_2(/C_2)$	$2C_2'(/C_1)$	$2C_s(/C_1)$	$2S_4(/C_2)$	$2C_{2v}(/C_2)$	$2D_2(/C_2)$	$D_{2d}(/C_2)$
$D_{2d}(/C_2')$	$4C_1(/C_1)$	$2C_2(/C_1)$	$C_2'(/C_1) + 2C_2'(/C_2)$	$2C_s(/C_1)$	$S_4(/C_1)$	$C_{2v}(/C_1)$	$D_2(/C_2') + D_2(/C_2'')$	$D_{2d}(/C_2')$
$D_{2d}(/C_s)$	$4C_1(/C_1)$	$2C_2(/C_1)$	$2C_2'(/C_1)$	$C_s(/C_1) + 2C_s(/C_s)$	$S_4(/C_1)$	$C_{2v}(/C_s) + C_{2v}(/C_s')$	$D_2(/C_1)$	$D_{2d}(/C_s)$
$D_{2d}(/S_4)$[a]	$2C_1(/C_1)$	$2C_2(/C_2)$	$C_2'(/C_1)$	$C_s(/C_1)$	$2S_4(/S_4)$	$C_{2v}(/C_2)$	$D_2(/C_2)$	$D_{2d}(/S_4)$
$D_{2d}(/C_{2v})$	$2C_1(/C_1)$	$2C_2(/C_2)$	$C_2'(/C_1)$	$2C_s(/C_s)$	$S_4(/C_2)$	$2C_{2v}(/C_{2v})$	$D_2(/C_2)$	$D_{2d}(/C_{2v})$
$D_{2d}(/D_2)$[a]	$2C_1(/C_1)$	$2C_2(/C_2)$	$2C_2'(/C_2)$	$C_s(/C_1)$	$S_4(/C_2)$	$C_{2v}(/C_2)$	$2D_2(/D_2)$	$D_{2d}(/D_2)$
$D_{2d}(/D_{2d})$	$C_1(/C_1)$	$C_2(/C_2)$	$C_2'(/C_2)$	$C_s(/C_s)$	$S_4(/S_4)$	$C_{2v}(/C_{2v})$	$D_2(/D_2)$	$D_{2d}(/D_{2d})$

[a] Forbidden CR. See ref 10.

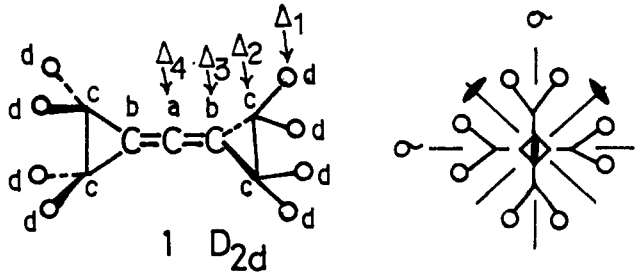

Figure 1. D_{2d} molecule with its orbits (Δ_i) and its symmetry elements.

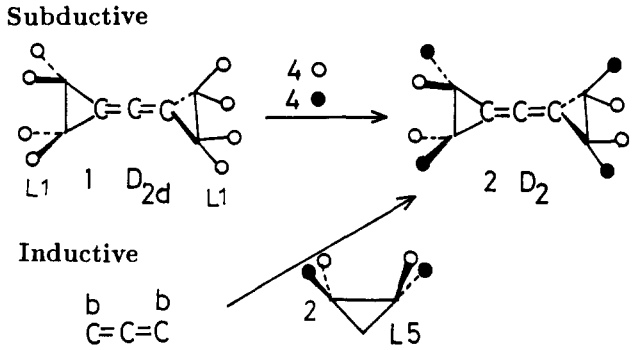

Figure 2. Subductive and inductive derivation of a D_2 molecule. L1 and L5 ligands will be illustrated in Figure 5.

subgroup $\mathbf{G}_j$; it corresponds to a subduced representation represented by

$$\mathbf{G}(/\mathbf{G}_i) \downarrow \mathbf{G}_j = \{\pi_g | \forall\ g \in \mathbf{G}_j\} \tag{5}$$

This representation is a permutation representation of the subgroup $\mathbf{G}_j$ and is factorized into a set of coset representations of $\mathbf{G}_j$. For example, Table I collects the subduction of all CRs for the D_{2d} group.

Figure 2 illustrates a subductive derivation of a molecule along with an inductive one. Substitution of H_mX_n (○ = H, ● = X) for the hydrogens of **1** creates derivatives that have subsymmetries of the D_{2d} group. For example, a D_2 molecule (**2**) is obtained by an appropriate substitution of H_4X_4 (Figure 2). We refer to this type of derivation as a *subductive derivation*. Figure 3 depicts several derivatives designed by subductive derivation.

The subductive derivation is controlled by subduction of a coset representation (CR); the name "subductive" stems from this fact. The CR for the 8 positions of **1** is $D_{2d}(/C_1)$, which is a regular representation (RR).[7] Hence, we can discuss the subductive derivation from **1** to **2** (Figure 2) by means of subduction of the RR. The first row of Table I is concerned with the RR. For example, the D_2 derivative (**2**) is produced according to a subduction of the RR:

$$D_{2d}(/C_1) \downarrow D_2 = 2D_2(/C_1) \tag{6}$$

which is found in the intersection of the $D_{2d}(/C_1)$ row and the

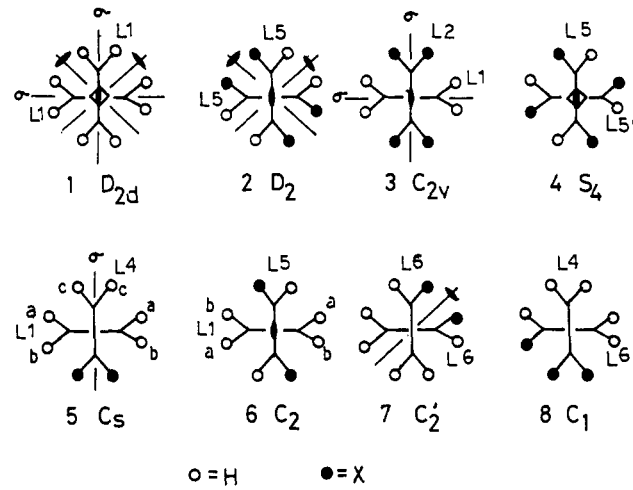

Figure 3. Molecules derived from **1**. L1 to L6 ligands will be illustrated in Figure 5.

D_2 column of Table I. The right-hand side of eq 6 is also an RR. Equation 6 means that the $D_{2d}(/C_1)$ orbit (Δ_1) is restricted to D_2 group producing two $D_2(/C_1)$ orbits. This can be verified by comparing **1** with **2** (Figure 3), where four X's (●) occupy one of the $D_2(/C_1)$ orbits and four H's (○) occupy the other $D_2(/C_1)$ orbit.

The C_s derivative (**5**) is an example in which two or more distinct orbits can take atoms of the same kind. Table I gives the following equation

$$D_{2d}(/C_1) \downarrow C_s = 4C_s(/C_1) \tag{7}$$

The resulting four orbits are occupied by H_2^a, H_2^b, H_2^c, and X_2. Note that H_2^a, H_2^b, and H_2^c are nonequivalent as labeled with *a*, *b*, and *c* (Figure 3).

The molecules (**2**–**4**) illustrate distinct modes of occupation by H_4X_4 from the viewpoint of subductive derivation. The occupation in **2** is represented by eq 6; **3** and **4** are designated by $D_{2d}(/C_1) \downarrow C_{2v} = 2C_{2v}(/C_1)$ and $D_{2d}(/C_1) \downarrow S_4 = 2S_4(/C_1)$. The other molecules (**5**–**8**) are also described by the subductions collected in the $D_{2d}(/C_1)$ row of Table I.

Figure 4 depicts several derivatives that are designed by subductive derivation based on a parent molecule (**9**). The structure (**9**) of T_d symmetry contains 24 hydrogen atoms, which construct an orbit subject to the RR, $T_d(/C_1)$. According to the subduction of the RR,[9] we can construct derivatives of the respective subgroups of T_d, e.g., **10**–**19**. For example, the compound **11** of D_{2d} symmetry is in accord with the subduction

$$T_d(/C_1) \downarrow D_{2d} = 3D_{2d}(/C_1) \tag{8}$$

The resulting three orbits are occupied by eight hydrogen atoms (○), eight X atoms (●), and another set of eight hydrogen atoms (○).

It is worth mentioning that the molecule **20** is another D_{2d} derivative which is isomeric to **11**. It shows another mode of

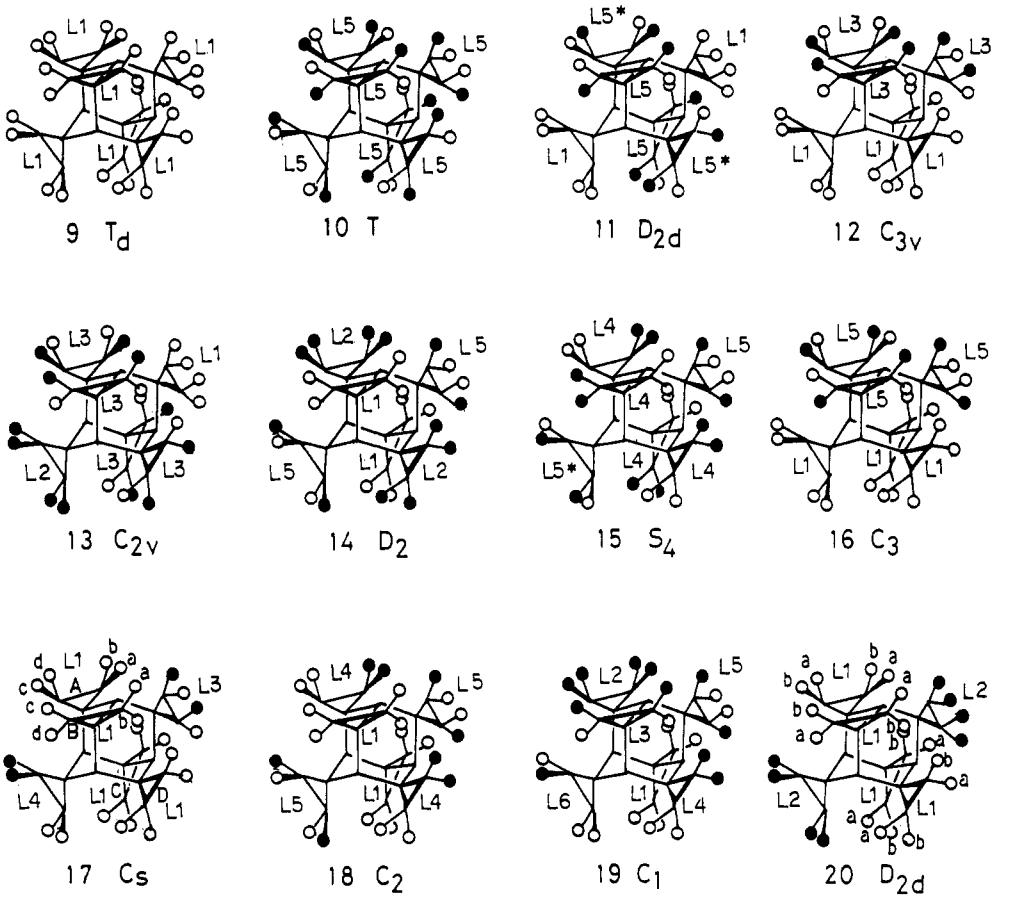

Figure 4. Molecules derived from **9**.

packing with eight O's (marked by *a*), eight ●'s and eight O's (marked by *b*). The mode of packing also agrees with eq 8. The nonequivalence of the two sets of O's becomes clearer by comparing the packing in **20** with the one appearing in the isomer **11**.

A parent molecule that has an orbit corresponding to a regular representation is called a regular body.[10] The subductive derivation based on the regular body is a versatile methodology to realize all the subsymmetries of the parent symmetry. Once we have a subduction table such as Table I, we can design a derivative of prescribed symmetry by the substitution which the table teaches.

INDUCTIVE DERIVATION OF MOLECULES

Figure 2 also illustrates another concept "inductive derivation". This concept verifies a chemists' convention in which an appropriate set of atoms (and bonds) is regarded as a functional group or a ligand. The following discussion will reveal implications involved in the convention.

Morphic Relationships between Ligands. A molecule can be alternatively considered to be a combination of a skeleton and ligands. Thus, the allene derivative (**1**) is regarded as an allene skeleton ($^{(b)}C{=}C{=}C^{(b)}$) joined to two cyclopropane rings (Figure 1) at the joint positions ($C^{(b)}$). In this case, the two cyclopropane rings are selected as ligands.[11]

When incorporated in a molecule, a ligand is governed by the global symmetry of the molecule. Hence, it should be differentiated from a ligand in isolation. We define the ligand-in-molecule as a *segment*. When the ligand is considered to be isolated from such a molecular environment, it is called a *fragment*.

Figure 5 depicts several ligands (groups) derived from a cyclopropane ring, where symmetries as fragments are shown. These fragments have their internal orbits (Table II), which are called *infraorbits*. The 3D structures of ligands are thus

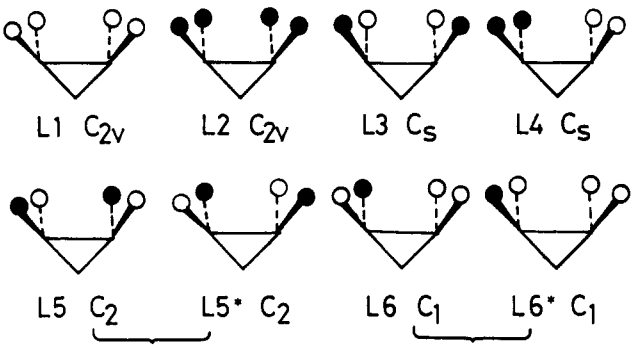

Figure 5. Cyclopropane rings as fragments.

Table II. Infraorbits in the Fragments (L1–L6)

ligand (fragment)	infraorbits	members	coset representation
L1	Δ	H_4	$C_{2v}(/C_1)$
L2	Δ	X_4	$C_{2v}(/C_1)$
L3	Δ_1	H_2	$C_s(/C_1)$
	Δ_2	X_2	$C_s(/C_1)$
L4	Δ_1	H_2	$C_s(/C_1)$
	Δ_2	X_2	$C_s(/C_1)$
L5 (L5*)	Δ_1	H_2	$C_2(/C_1)$
	Δ_2	X_2	$C_2(/C_1)$
L6 (L6*)	Δ_1	X	$C_1(/C_1)$
	Δ_2	H	$C_1(/C_1)$
	Δ_3	H	$C_1(/C_1)$
	Δ_4	H	$C_1(/C_1)$

formulated as a set of infraorbits. For simplicity of discussion, we focus our attention mainly on the four terminal positions of the cyclopropane ring.

We start with the ligand (L1) and regard the other ligands as derivatives of L1. The derivation of these ligands is strictly controlled by subduction of CRs for C_{2v} symmetry.[12] For

Table III. Ligands as Fragments

ligand	symmetry	possible morphicity
atom	$C_{\infty v}$	homomorphic, heteromorphic
proligand (point ligand)	$C_{\infty v}$,C_{∞}	homomorphic, enantiomorphic, heteromorphic
group (ligand)	C_{nv},C_n	homomorphic, enantiomorphic, diastereomorphic, heteromorphic

example, L3 and L4 are derived in terms of the following equations:

$$C_{2v}(/C_1) \downarrow C_s = 2C_s(/C_1) \quad (9)$$

$$C_{2v}(/C_1) \downarrow C'_s = 2C'_s(/C_1) \quad (10)$$

Interrelation between the two ligands is characterized by morphic terms. Morphic relationships defined by Hirschmann and Hanson[13,14] are as follows: Pairs of ligands can be described as "homomorphic" if they can be superposed in isolation (like the two methylene hydrogens of ethanol) and as "heteromorphic" if they cannot; among the latter, the subclass that can be superposed in isolation by a reflection is defined as "enantiomorphic". In the present sense, this definition is obviously concerned with fragments rather than with segments. However, this definition is insufficient to develop a consistent terminology, because enantiomorphic ligands can be regarded as being equivalent in some sense. Moreover, since the relationships between ligands-in-isolation are essentially equivalent to those between compounds, these morphic terms should correspond to meric terms (homomeric, enantiomeric, etc.) for compounds. Therefore, we now discontinue Hirschmann–Hanson's "heteromorphic" term and use the term in a different sense.

The relationship between two fragments (ligands in isolation) having the same compositions is defined as *homomorphic* if they can coincide with each other by direct isometry operations;[15] and as *enantiomorphic* if they can be superposed only by opposite isometry operations. For example, L5 and L5* are enantiomorphic to each other. Two fragments are described as *diastereomorphic* if they have the same compositions and the same connectivities, but are not superimposable, e.g., L3 and L5. Two fragments are *heteromorphic* if they have different connectivities, like L3 and L4.

Table III lists possible morphicities of ligands. An atom is regarded as a fragment having $C_{\infty v}$ symmetry.[16] Hence, there emerge two relationships: homomorphic and heteromorphic.[17] The other morphic relationships are cenceptually impossible. On the other hand, a group has C_{nv} or C_n symmetry as a fragment. Since it has a 3D structure in the form of infraorbits, there can emerge all of the four morphicities. We can consider an intermediate concept *proligand* between such an atom and such a group.[4] A proligand is defined as a point ligand that is structureless but has a chirality. Since this has $C_{\infty v}$ or C_{∞} symmetry, there are three possibilities: homo-, enantio-, and heteromorphic.

Inductive Derivations. Figure 2 shows that the D_2 molecule (**2**) is alternatively generated by a combination of C=C=C and two substituted cyclopropanes (L5). This type of derivation is called an *inductive derivation*. The purpose of this section is to clarify the behavior of infraorbits in ligands during the derivation.

When such a cyclopropane ligand is incorporated into a molecule, the resulting cyclopropane segment is governed by the global symmetry of the molecule. At the same time, it is controlled by the local symmetry of the position to which the segment attaches. The symmetry of each segment can be proven to be determined by the coset representation of a joint position in a general fashion.[10]

Since the joints (the $C^{(b)}$ positions) belong to the $D_{2d}(/C_{2v})$ orbit, the cyclopropane ring of **1** (L1) as a segment is subject to the corresponding local symmetry (C_{2v}). Hence, the segment is regarded as a C_{2v} segment, which contains four hydrogens [$C_{2v}(/C_1)$], two carbons [$C_{2v}(/C_s)$], and one carbon [$C_{2v}(/C_{2v})$]. If the ligand is considered to be isolated, the resulting fragment is regarded as belonging to the same C_{2v} symmetry. In this case, there is no perturbation of symmetry during the process of changing the fragment (Table II) to the segment. If we pay attention to the $C_{2v}(/C_1)$ orbit only, this process is represented by the following induction

$$C_{2v}(/C_1) \uparrow D_{2d}(/C_{2v}) = D_{2d}(/C_1) \quad (11)$$

Note that the top symbol (C_{2v}) is equal to that of the second parentheses in the left-hand side. This is the condition for such an induction that is effective (see the next section). In order to memorize this equation, we can formally consider that

$$\left(\frac{\not{C}_{2v}}{C_1}\right) \uparrow \left(\frac{D_{2d}}{\not{C}_{2v}}\right) = \left(\frac{D_{2d}}{C_1}\right) \quad (12)$$

Equation 11 indicates that the $C_{2v}(/C_1)$ orbit in the cyclopropane ring is induced into a $D_{2d}(/C_1)$ orbit in **1**. The former is called a *local orbit* and the latter is referred to as a *global orbit*. In this case, the local orbit (in the segment) is identical with the corresponding infraorbit (in the fragment).

Replacement of the two cyclopropane rings of **1** by an appropriate pair of ligands (in Figure 5) can create a molecule of every subgroup of D_{2d} in terms of inductive derivation. If we focus our attention on the respective cyclopropane rings, Figure 3 can also be regarded as a collection of such derivatives that are created by the inductive derivation.

The molecules (**1–8**) contain a common parent skeleton, $C^{(b)}$=C=$C^{(b)}$. Although this skeleton belongs to D_{2d} in the original molecule (**1**),[18] it is restricted within the respective symmetry during the process of providing each molecule. In particular, the behavior of joint positions [$C^{(b)}$] should be taken into account. The restriction of the joints is controlled by the subduction shown in the $D_{2d}(/C_{2v})$ row of Table I.

For constructing the molecule (**2**), the subduction represented by $D_{2d}(/C_{2v}) \downarrow D_2 = D_2(/C_2)$ characterizes such behavior of the two joint carbons ($D_{2d} \rightarrow D_2$). Since the two joint positions belong to the $D_2(/C_2)$ orbit, segments to be selected must be governed by the local symmetry (C_2). Two L5 ligands (C_2 fragments) are, therefore, selected so as to produce the molecule (**2**) of D_2 symmetry. In this case, the symmetry of the fragment is retained in the corresponding segment. If we focus our attention on the terminal positions only, the process creating **2** is now represented by the following induction

$$C_2(/C_1) \uparrow D_2(/C_2) = D_2(/C_1) \quad (13)$$

The other data listed in the CR-of-joint column of Table IV are also selected from the $D_{2d}(/C_{2v})$ row of Table I. The point group in the respective parentheses is the local symmetry of the position [$C^{(b)}$], which indicates the symmetry of the

Table IV. Symmetrical Properties of Cyclopropane Rings in **1–8**

molecule	ligand	no. of ligands	symmetry as segment	symmetry as fragment	CR of joints
1	L1	2	C_{2v}	C_{2v}	$D_{2d}(/C_{2v})$
2	L5	2	C_2	C_2	$D_2(/C_2)$
3	L1	1	C_{2v}	C_{2v}	$C_{2v}(/C_{2v})$
	L2	1	C_{2v}	C_{2v}	$C_{2v}(/C_{2v})$
4	L5,L5*	2	C_2	C_2	$S_4(/C_2)$
5	L4	1	C_s	C_s	$C_s(/C_s)$
	L1	1	C_s	C_{2v}	$C_s(/C_s)$
6	L5	1	C_2	C_2	$C_2(/C_2)$
	L1	1	C_2	C_{2v}	$C_2(/C_2)$
7	L6	2	C_1	C_1	$C_2'(/C_1)$
8	L4	1	C_1	C_s	$C_1(/C_1)$
	L6	1	C_1	C_1	$C_1(/C_1)$

Table V. Symmetrical Properties of Cyclopropane Rings in 9–20

molecule	ligand	no. of ligands	symmetry as segment	symmetry as fragment	CR of joints
9	L1	6	C_{2v}	C_{2v}	$T_d(/C_{2v})$
10	L5	6	C_2	C_2	$T(/C_2)$
11	L1	2	C_{2v}	C_{2v}	$D_{2d}(/C_{2v})$
	L5,L5*	4	C_2	C_2	$D_{2d}(/C_2')$
12	L3	3	C_s	C_s	$C_{3v}(/C_s)$
	L1	3	C_s	C_{2v}	$C_{3v}(/C_s)$
13	L1	1	C_{2v}	C_{2v}	$C_{2v}(/C_{2v})$
	L2	1	C_{2v}	C_{2v}	$C_{2v}(/C_{2v})$
	L3	4	C_1	C_s	$C_{2v}(/C_1)$
14	L5	1	C_2	C_2	$D_2(/C_2)$
	L1	2	C_2	C_{2v}	$D_2(/C_2')$
	L2	2	C_2	C_{2v}	$D_2(/C_2'')$
15	L5,L5*	2	C_2	C_2	$S_4(/C_2)$
	L4	4	C_1	C_s	$S_4(/C_1)$
16	L5	3	C_1	C_2	$C_3(/C_1)$
	L1	3	C_1	C_{2v}	$C_3(/C_1)$
17	L3	1	C_s	C_s	$C_s(/C_s)$
	L4	1	C_s	C_s	$C_s(/C_s)$
	L1	2	C_1	C_{2v}	$C_s(/C_1)$
	L1	2	C_1	C_{2v}	$C_s(/C_1)$
18	L5	1	C_2	C_2	$C_2(/C_2)$
	L5	1	C_2	C_2	$C_2(/C_2)$
	L1	2	C_1	C_{2v}	$C_2(/C_1)$
	L4	2	C_1	C_s	$C_2(/C_1)$
19	L1	1	C_1	C_{2v}	$C_1(/C_1)$
	L2	1	C_1	C_{2v}	$C_1(/C_1)$
	L3	1	C_1	C_s	$C_1(/C_1)$
	L4	1	C_1	C_s	$C_1(/C_1)$
	L5	1	C_1	C_2	$C_1(/C_1)$
	L6	1	C_1	C_1	$C_1(/C_1)$
20	L2	2	C_{2v}	C_{2v}	$D_{2d}(/C_{2v})$
	L1	4	C_2	C_{2v}	$D_{2d}(/C_2')$

corresponding cyclopropane segment. For the purpose of creating molecules (**2**, **3**, **4**, and **7**) (Table IV), the symmetries of the cyclopropane fragments are selected so as to be equal to those of the corresponding segments. Thus, there emerge no restrictions of symmetry during these procedures. On the other hand, the symmetry restriction of ligands takes place in the construction of the molecules (**5**, **6**, and **8**). The latter point will be discussed in the next section.

The molecule (**9**) of T_d symmetry is considered to be an adamantane skeleton having six cyclopropane rings (L1) of the same kind. When the six cyclopropane rings of the molecule (**9**) are replaced by appropriate ligands in Figure 5, we have the corresponding derivatives in terms of inductive derivation. If we change our viewpoint to pay attention to respective cyclopropane rings, the derivatives (**10**–**20**) shown in Figure 4 can alternatively be regarded as the results of such inductive derivations.

The original T_d symmetry of the adamantane skeleton is retained in **9**, but is restricted to the respective symmetries in **10**–**20**. The six bridge carbons (joints) belonging to $T_d(/C_{2v})$ in the skeleton (or equivalently **9**) are subduced by the following equations:[9] $T_d(/C_{2v}) \downarrow T = T(/C_2)$ for **10**, $T_d(/C_{2v}) \downarrow D_{2d} = D_{2d}(/C_2') + D_{2d}(/C_{2v})$ for **11** and **20**, $T_d(/C_{2v}) \downarrow C_{3v} = C_{3v}(/C_s)$ for **12**, $T_d(/C_{2v}) \downarrow C_{2v} = C_{2v}(/C_1) + 2C_{2v}(/C_{2v})$ for **13**, $T_d(/C_{2v}) \downarrow D_2 = D_2(/C_2) + D_2(/C_2') + D_2(/C_2'')$ for **14**, $T_d(/C_{2v}) \downarrow S_4 = S_4(/C_1) + S_4(/C_2)$ for **15**, $T_d(/C_{2v}) \downarrow C_3 = C_{3v}(/C_1)$ for **16**, $T_d(/C_{2v}) \downarrow C_s = 2C_s(/C_1) + 2C_s(/C_s)$ for **17**, $T_d(/C_{2v}) \downarrow C_2 = 2C_2(/C_1) + 2C_2(/C_2)$ for **18**, and $T_d(/C_{2v}) \downarrow C_1 = 6C_1(/C_1)$ for **19**. The right-hand side of each equation indicates the CRs of joints, which are listed in Table V. All of the ligands (L1–L6) are governed by the respective CRs of joints when incorporated as segments.

For exemplifying these derivations, let us examine the molecule (**11**) of D_{2d} symmetry. The desymmetrization of T_d (**9**) to D_{2d} is accompanied by the subduction $[D_{2d}(/C_2') + D_{2d}(/C_{2v})]$ cited above. Since the $D_{2d}(/C_2')$ orbit is four-membered and enantiospheric,[6] it takes four ligands in such a manner that two C_2 ligands (L5's) and the antipodes (L5*'s) satisfy the global symmetry (D_{2d}); in other words, they satisfy the C_2' local symmetry. Note that these four ligands (two L5's and two L5*'s) construct the single orbit so as to satisfy the enantiospheric ity. Since each L5 ligand consists of two $C_2(/C_1)$ orbits (Table II), this process is associated with the following induction

$$C_2(/C_1) \uparrow D_{2d}(/C_2') = D_{2d}(/C_1) \qquad (14)$$

where the ligand agrees with the C_2' subgroup. This equation means that eight O's (or ●'s) in the L5's and L5*'s construct a $D_{2d}(/C_1)$ orbit, when incorporated in **11**.

Because the other orbit of **11** $[D_{2d}(/C_{2v})]$ is two-membered and homospheric, it accommodates two achiral (C_{2v}) ligands, which are here selected as being equal to L1. This process is associated with the following induction

$$C_{2v}(/C_1) \uparrow D_{2d}(/C_{2v}) = D_{2d}(/C_1) \qquad (15)$$

This equation indicates that eight O's provided from the L1 ligands construct a $D_{2d}(/C_1)$ orbit, when incorporated in **11**. Equations 14 and 15 afford the same kind of orbits $[D_{2d}(/C_1)]$. However, they are different, if we pay attention to the cyclopropane rings. This fact emphasizes the difference between proligands (or point ligands) and ligands having three-dimensional structure.

The derivation of **10** (T symmetry) affords a theoretical foundation to the design of a T molecule reported by Farina and Morandi.[3] The six positions in **10** have C_2 local symmetries due to the CR, $T(/C_2)$. Thereby, six of the C_2 fragments (L5's) occupy these positions to give the T molecule (**10**). This process is associated with the following induction

$$C_2(/C_1) \uparrow T(/C_2) = T(/C_1) \qquad (16)$$

RELATIONSHIP BETWEEN THE TWO DERIVATIONS

A subductive derivation creates a set of global orbits, while an inductive derivation alternatively generates the same set of global orbits via an orbit of ligands (segments). This section is devoted to examine the relationship between the two types of orbits. The two types of derivations are purely geometrical operations. However, they are closely related to experimental procedures, which can be developed by expert organic chemists. In fact, organic chemists have unconciously applied these derivations to their discussions on chemical conversions. For example, the conversion R-COOH → R-COOCH$_3$ can be interpreted nominally as a replacement of a hydrogen atom by a methyl group;[19] mechanistically as a replacement of a hydroxyl by a methoxy group; and conceptually (e.g., in a synthetic route) as a conversion from a carboxyl group to a methoxycarbonyl one. Whereas such a shift of viewpoints has scarcely influenced conclusions on reaction mechanisms etc., it has given serious effects to discussions on stereochemistry. The latter fact has attracted little attention of organic chemists. For a comprehensive understanding on stereochemistry, we should develop a conceptual framework to cover such a shift of viewpoints. This task is accomplished by clarifying the fate of ligand symmetries. In general, the symmetry of a ligand is controlled by the local symmetry of the joint position. Since the ligand has a 3D structure in the form of infraorbits (Table II), it is necessary to examine the effect of the local symmetry on the infraorbits. This task can be accomplished by comparing the subductive and inductive derivations.

Figure 6 depicts the relationship between subductive and inductive derivations by using the molecule **2** as an example. Subductive derivation creates global orbits (Δ_{11} etc.), which agree with eq 6. Figure 6 (upper) illustrates the generation of the Δ_{11} and Δ_{12} orbits. On the other hand, inductive derivation (Figure 6, below) regards each cyclopropane ring as a lump, i.e., a ligand. The two ligands of **2** are equivalent and

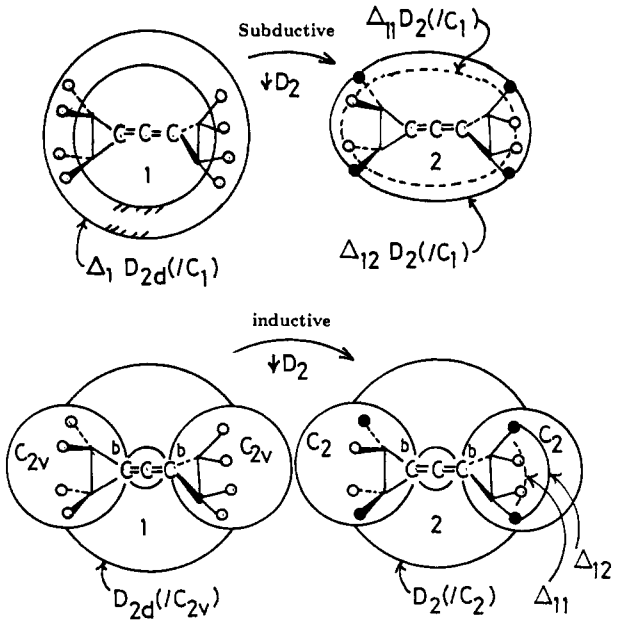

Figure 6. Orbits during subductive and inductive derivation for **2**.

construct an orbit governed by the CR, $D_2(/C_2)$. This CR is identical with the CR of the joints $[C^{(b)}]$.

The Δ_{11} (O) and Δ_{12} (●) of **2** are global orbits that are distinctly subject to the $D_2(/C_1)$ CRs. If we lump the appropriate four atoms together so as to belong to a cyclopropane ring, we obtain a ligand (L5). This ligand (C_2 segment) has C_2 symmetry in isolation as well as in the molecule (**2**). If we bear this C_2 segment in mind, we find that the two O's construct a $C_2(/C_1)$ orbit; and the two ●'s construct another $C_2(/C_1)$ orbit. The same conclusion holds for the other cyclopropane ligand of **2**. They are called *local orbits* in the sense that they are concerned with the respective cyclopropane segments. As a result, the two $C_2(/C_1)$ local orbits concerning O, each of which belongs to the respective cyclopropane ring, are correlated to the $D_2(/C_1)$ global orbit (Δ_{11}). Those concerning ● correspond to the other $D_2(/C_1)$ global orbit (Δ_{12}). Note that the CR $[D_2(/C_2)]$ of the joints mediates between the global and local orbits. The common symbol (C_2) in the $D_2(/C_2)$ and the $C_2(/C_1)$ orbits is formally reduced so as to generate the symbol $[D_2(/C_1)]$ of the global orbit. This fact agrees with the induction represented by eq 13.

These discussions can be generalized to a theorem:

(*a*) *If* $\mathbf{G}_j \leq \mathbf{G}_i \leq \mathbf{G}$, the coset representation $\mathbf{G}(/\mathbf{G}_i)$ governs a $\mathbf{G}_i$ segment that has a set of suborbits represented by $\sum_j \beta_j \mathbf{G}_i(/\mathbf{G}_j)$, where the summation is over a given set of subgroups satisfying the above relation; and each β_j is a nonnegative integer.

(*b*) The resulting global orbits are represented by $\sum_j \beta_j \mathbf{G}(/\mathbf{G}_j)$, which are derived from the local orbits $\sum_j \beta_j \mathbf{G}_i(/\mathbf{G}_j)$.

The latter proposition is formally represented by the induction

$$\sum_j \beta_j \mathbf{G}_i(/\mathbf{G}_j) \uparrow \mathbf{G}(/\mathbf{G}_i) = \sum_j \beta_j \mathbf{G}(/\mathbf{G}_j) \qquad (17)$$

The mathematical proof has been reported elsewhere.[10] In most cases, such a $\mathbf{G}_i$ segment has a joint position $[\mathbf{G}_i(/\mathbf{G}_i)]$ through which the segment linked to an appropriate member of the $\mathbf{G}(/\mathbf{G}_i)$ orbit.

In the preceding paragraphs, we have examined the relationship between global and local orbits just for the case where the symmetry of a segment is equal to that of the corresponding fragment. However, we should examine a more general case in which the symmetry of a segment is inferior to that of a fragment. Tables IV and V contain many cases in which the symmetry of a segment is different from that of a fragment.

For example, let us consider the cyclopropane ring of **5** (Table IV). The ligand (L1) belongs to C_{2v} symmetry as a fragment. On the other hand, it is restricted to C_s if it is built into the molecule as a segment. In other words, the ligand (L1) is a C_{2v} fragment, but a C_s segment in the molecule **5**. Note that the C_s symmetry is the local symmetry determined by the CR $[C_s(/C_s)]$ of the joint (Table IV). This restriction influences the corresponding infraorbits of the fragment. This effect is represented by the following subduction:

$$C_{2v}(/C_1) \downarrow C_s = 2C_s(/C_1) \text{ for four hydrogen atoms} \qquad (18)$$

where we take into account the terminal hydrogen atoms only, for simplicity of discussion. Equation 18 indicates that the four hydrogens are divided into two $C_s(/C_1)$ orbits. If they are hypothetically distinguished by labeling with *a* and *b*, this labeling indicates such nonequivalence explicitly. The resulting molecule **5** has C_s symmetry in which a pair of hydrogens (denoted by H^a) and another pair (H^b) construct distinct $C_s(/C_1)$ orbits. These pairs are nonequivalent over all symmetry operations of C_s, as verified easily by inspection. It should be noted that this process is essentially equivalent to that for generating L3 (or L4) from L1, except that the latter process gives rise to the actual replacement of atoms. The process of generating **5** corresponds to the induction

$$C_s(/C_1) \uparrow C_s(/C_s) = C_s(/C_1) \qquad (19)$$

The ligand L1 behaves differently in the molecule **6**. It is incorporated as a C_2 segment. We recognize this process as follows. First, the ligand as a C_{2v} fragment is restricted into C_2 symmetry, where its infraorbit is subduced in terms of

$$C_{2v}(/C_1) \downarrow C_2 = 2C_2(/C_1) \text{ for four hydrogen atoms} \qquad (20)$$

Then, this ligand is incorporated into the molecule **6** of C_2 symmetry as a C_2 segment in agreement with the CR $[C_2(/C_2)]$ of the corresponding joint. These facts are verified by comparing a pair of hydrogens (H^a) with the other (H^b) in **6**. As a result, the molecule **6** contains two $C_2(/C_1)$ global orbits (H_2^a and H_2^b) derived from the L1 ligand. The process of generating **6** corresponds to the induction

$$C_2(/C_1) \uparrow C_2(/C_2) = C_2(/C_1) \qquad (21)$$

Let us consider more complicated cases. We have discussed the inductive derivation of **11** by means of eqs 14 and 15. These equations are also effective to design compound **20**, which has the same D_{2d} symmetry and is isomeric to **11**. The C_{2v} symmetry of the ligand (L1) is restricted to C_2 according to $C_{2v}(/C_1) \downarrow C_2 = 2C_2(/C_1)$ and then incorporated into **20** in agreement with eq 14. This treatment clarifies nonequivalency between eight O's (marked by *a*) and eight O's (marked by *b*), where the labeling with *a* and *b* corresponds to the occupation in **11**. The occupation concerning L2 is governed by the induction represented by eq 15.

Examination of compound **17** reveals another restriction of the ligand (L1). The C_{2v} symmetry of the ligand (L1) is restricted to C_1 according to $C_{2v}(/C_1) \downarrow C_1 = 4C_1(/C_1)$ before being incorporated into **17**. This splitting is illustrated by labeling with *a* to *d*. Then, each of the four $C_1(/C_1)$ orbits is induced according to the equation

$$C_1(/C_1) \uparrow C_s(/C_1) = C_s(/C_1) \qquad (22)$$

Note that the $C_s(/C_1)$ symbol in the left-hand side represents the CR of the corresponding joint (Table V), and the same symbol in the right-hand side designates the CR of the resulting global orbit. Thereby, each pair labeled with the same letter appearing in the L1(A) and L1(B) constructs the respective $C_s(/C_1)$ orbit (global orbit) of **17**. This induction ensures the equivalence between L1(A) and L1(B), which is

enantiotopic after being built in **17**.

It is worthwhile to mention morphic and topic relationships. The two ligands [L1(A) and L1(B)] in **17** are homomorphic and enantiotopic; L1(A) and L1(C) in **17** are homomorphic but diastereotopic.

CONCLUSION

The design of highly symmetric molecules is discussed in terms of subductive and inductive derivations. In a subductive derivation, global orbits are generated by desymmetrization of parent orbits, which is described by the subduction of coset representations. In an inductive derivation, infraorbits in a ligand (as a fragment) are restricted to local orbits (of the corresponding segment) and then incorporated into a molecule to afford global orbits. This process is described in terms of the induction of coset representations. The relationship between the two derivations is discussed.

REFERENCES AND NOTES

(1) van't Hoff, J. H. *Arch. Néerl. Sci. Exactes Nat.* **1874**, *9*, 445.
(2) (a) Prelog, V. *Science* **1976**, *193*, 17. (b) Nakazaki, M. *Top. Stereochem.* **1984**, *15*, 199. (c) Nakazaki, M.; Naemura, K. *Yuki Gosei Kagaku Kyokaishi* **1977**, *35*, 883. (d) Eaton, P. E. *Tetrahedron* **1979**, *35*, 2189. (e) Naemura, K. *Yuki Gosei Kagaku Kyokaishi* **1987**, *45*, 48. (f) Paquette, L. A. *Chem. Rev.* **1989**, *89*, 1051. (g) Prelog, V.; Thix, J. *Helv. Chim. Acta* **1982**, *65*, 2622.
(3) Farina, M.; Morandi, C. *Tetrahedron* **1974**, *30*, 1819.
(4) Fujita, S. *Tetrahedron* **1991**, *47*, 31.
(5) Fujita, S. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 315.
(6) Fujita, S. *J. Am. Chem. Soc.* **1990**, *112*, 3390.
(7) The regular representation (RR) is a kind of coset representation that stems from a coset decomposition of G by an identity group (C_1).
(8) For this type of D_2 molecules, see Skell, P. S.; Wescott, L. D.; Golstein, J. J. P.; Engel, R. R. *J. Am. Chem. Soc.* **1965**, *87*, 2829.
(9) For the subduction table of T_d group, see ref 6.
(10) Fujita, S. *Theor. Chim. Acta* **1990**, *78*, 45.
(11) Such a segment (ligand) has both chemical and mathematical meanings. The concept of "block" described in ref. 10 has a mathematical meaning only where it is concerned with a set of equivalent objects. The segment can be now restated as being a set of blocks so as to have a chemical meaning in addition.
(12) (a) Fujita, S. *Theor. Chim. Acta* **1989**, *76*, 247. (b) Fujita, S. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 3771. (c) Fujita, S. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 203. (d) Fujita, S. *Tetrahedron* **1990**, *46*, 365. (e) Fujita, S. *J. Math. Chem.* **1990**, *5*, 99. (f) Fujita, S. *J. Math. Chem.* **1990**, *5*, 121. (g) Fujita, S. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 1876. (h) Fujita, S. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 2033.
(13) Hirschmann, H.; Hanson, K. R. *Tetrahedron* **1974**, *30*, 3649.
(14) Hirschmann, H.; Hanson, K. R. *Top. Stereochem.* **1983**, *14*, 183.
(15) Yale, P. B. *Geometry and Symmetry*; Dover: New York, 1988.
(16) Strictly speaking, an atom in isolation has a spherical symmetry. However, it can be treated as a $C_{\infty v}$ object for simplicity of discussion.
(17) It may be subtle which term (diastereomorphic or heteromorphic) should be adopted in this case. We use the term "diastereomorphic" for denoting ligands having a 3D structure.
(18) Strictly speaking, the skeleton in isolation belongs to $D_{\infty d}$; and the two $C^{(b)}$ joints construct a $D_{\infty d}(/C_{\infty v})$ orbit. However, we can start from such an appropriate symmetry as this $[D_{2d}(/C_{2v})]$ for simplifying our discussion.
(19) The name "methyl acetate" stems from the viewpoint that regards the methyl group as a substituent.

Application of Standard Robotic Methods to Water Analysis

J. R. LEE and T. L. ISENHOUR*

Department of Chemistry, Kansas State University, Manhattan, Kansas 66506

J. C. MARSHALL

Department of Chemistry, Saint Olaf College, Northfield, Minnesota 55507

Received May 15, 1991

The use of standard methods in water and wastewater analysis[1,2] does not ensure the complete standardization of analytical procedures because of variability in implementation. Mechanical systems are reproducible; thus, a robotic system can be used to guarantee an almost perfectly reproducible execution of an analytical procedure. The purpose of this research is to establish the Standard Robotic Method (SRM) paradigm. This paper describes in detail how to convert a standard analytical method for water hardness and calcium to an SRM.[2,3]

INTRODUCTION

To date, the majority of robot applications involve programming the robot to perform a specific, invariant task.[4] Once the instructions for a given task have been developed and stored, the almost perfect reproducibility of the robot allows the task to be repeated without variation any number of times. Significantly, such a procedure could be activated at any time and by anyone with the same results.

There are standard methods of analysis in many fields. These methods specify, in detail, exactly how an analysis is to be performed. It is not uncommon for such methods to specify the exact details of sample preparation, reagent preparation and purity, specific laboratory apparatus, how the measurements should be made, and how the data should be analyzed. Such standard methods, once stored as instructions in a robot's environment, are reproducible by anyone using the system. The robotic environment containing instructions for standard method(s) of analysis could be moved to or reproduced in any other laboratory. The exportability of reproducible methods for chemical analysis by robotics, in the form of a Standard Robotic Method (SRM), is the subject of this paper.

This paper will describe a system that can transform a classical standard method of analysis into an SRM. A frame-structured production system is used to build the SRM.[5,6] The general procedure can be described in three steps:

(1) Obtain the standard method for the problem.
(2) Convert the method to an SRM by parsing and mapping.
(3) Test, optimize, and save the procedure.

The conversion of a standard analytical method for the determination of hardness and calcium in water to an SRM will be used to demonstrate the system.

THEORY

For the purposes of this paper, a standard method or procedure is one that has been subjected to a thorough evaluation, has demonstrated its applicability for a specific purpose on the basis of extensive use, and has been successful, collaboratively tested, and then approved by some recognized agency

0095-2338/91/1631-0546$02.50/0 © 1991 American Chemical Society