Anisochrony in Rotatable Ligands and Symmetry Non-Equivalence Characterized by Subduction of Coset Representations

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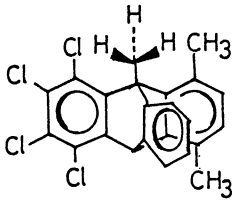
A general method of characterizing symmetry equivalence and non-equivalence in a molecule is developed on the basis of the one-one correspondence between an orbit and a coset representation. This method provides us with a theoretical foundation to understand anisochrony in rotatable ligands. A given molecule is regarded as a combination of a three-dimensional skeleton and ligands. The ligand is referred to as a segment or a fragment according to its environment. Thus, the fragment is defined as a ligand-in-isolation; and the segment denotes a ligand built into a molecule. The symmetry of the ligand as a fragment is restricted to the local symmetry. This restriction is examined by using methyl and methylene ligands as examples. A methyl fragment has a homospheric $\mathbf{C}_{3v}(/\mathbf{C}_s)$ orbit that consists of three hydrogen atoms. On the other hand, a methylene fragment has an enantiospheric $\mathbf{C}_s(/\mathbf{C}_1)$ orbit that contains two hydrogen atoms. Such an orbit is incorporated into various molecules to afford restricted orbits, which are characterized by subduction of coset representations. The restricted orbits are discussed in terms of global and local orbits. This discussion provides a general approach to rationalize various types of anisochronies.

Relationship between global and local symmetries in a molecule has been investigated in order to clarify stereochemical behaviors of the molecule.[1] In particular, chemical shift equivalence (isochrony) and non-equivalence (anisochrony) of nuclei have been discussed in the light of such stereochemical relationships.[2,3]

Anisochrony of methyl protons has been observed in several molecules at low temperatures. Nakamura et al.[4] reported that the bridgehead methyl segment of 1,2,3,4-tetrachloro-5,8,9-trimethyltriptycene (**1**) exhibited three chemical shifts at −90 °C. Anderson and Rawson[5] observed split methyl signals (2:1) in the NMR spectrum of **2** at −141 °C.



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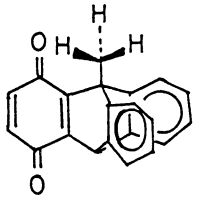

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On the other hand, anisochrony of geminal groups in an appropriate intramolecular environment was observed independent of temperature.[6] One of such anisochronies was observed in molecules having the general formula ($XYC(CU_2R)_2$). According to Jenning's review,[7] this type of anisochronies can be rationalized by combining the prochirality concept of Hanson[8] with the topic relationships of Mislow and Raban.[2] Eliel reviewed nuclear magnetic resonances with reference to prochiralities.[9] However, since the conventional prochirality concept is not based on a mathematical formulation, rather tedious procedures are required for judging such anisochronies.

Flanzen and Binsch[10] pointed out two general possibilities for realizing another type of anisochrony of geminal groups: Class A is characterized by the general formula $RU_2C\text{-}CX_3^*$, with X* being a chiral substituent; Class B conforms to the general formula $(RU_2C)_3C\text{-}CXYZ$. Reisse et al.[11] added another class $(RU_2C)_3C\text{-}CX_3^*$ to this classification. These phenomena were also analyzed in terms of topic relationships.[1,2] Reisse et al.[11] concluded that anisochronies of diastereotopic and constitutional heterotopic groups stemmed from a single source: symmetry non-equivalence of nuclei. However, such symmetry non-equivalence has been investigated by applying Newmann's projections or other diagrams to every molecule; and there has appeared no comprehensive understanding on this issue.

We recently discussed several applications of coset representations (CRs) and of their subductions.[12-14] These applications are based on the one-one correspondence between a CR and a set (an orbit) of equivalent atoms (or objects). We have clarified that such topic relationships should be used subsidiarily to sphericities (chirality fittingnesses) of such CRs, since diastereotopic and heterotopic relations cannot provide equivalence classes from a mathematical point of view.[14] In other words, the terms "diastereotopic" and "heterotopic" indicate that two objects are different; but are incapable of clarifying how different they are. On the other hand, the chirality fittingness characterizes an orbit as being *homospheric, enantiospheric,* or *hemispheric.* This classification clarifies how different (or how equivalent) such two objects are. In the present paper, we deal with another application of such CRs, which aims at providing a general approach to symmetry (non-)equivalence as well as at rationalizing various types of anisochronies.

1. Orbits of Ligands

An orbit is an equivalence class whose members can be any kind of objects. For discussing stereochemical relationships, such objects may be atoms, bonds, or faces. Moreover, a ligand, which is a set of one or more atoms, can also be such an object. Thereby, a set of equivalent ligands is regarded as an orbit.[15]

The term "ligand" has been used in various meanings, which depend upon how to manipulate the three-dimensional (3D) structure of the ligand. This fact has attracted little attention of organic chemists, inasmuch as such different usages have provided no confusion in most cases. For the purpose of discussing stereochemical relationships in detail, however, we should use this term in a stricter fashion. There are at least three ways to treat the 3D structure of a ligand according to the fact that the ligand has three kinds of attributes: (1) chirality/achirality, (2) a point group, and (3) an internal 3D structure, in ascending order of concreteness. In order to make our discussion clearcut, we here introduce a new term "proligand"; this takes account of the chirality/achirality. The term "ligand" is used for discussing (2) and (3).

A Set of Equivalent Proligands as an Orbit. The molecule **1** (or **2**) is regarded as a combination of a triptycene skeleton and a methyl ligand.[16] These examples contain only one methyl ligand to be examined. However, we should discuss a more general case in which two or more equivalent ligands are taken into consideration.

Before we manipulate such ligands directly, we begin with equivalence and non-equivalence of proligands. A *proligand* is defined as a point ligand that is structureless but has chirality; such a proligand is either chiral or achiral. The term proligand has been introduced in order to explicate a logical standpoint that primarily takes neither the point group nor the internal structure of ligand into consideration. In the present discussion, the proligand concept is coupled with the concept of local symmetry. Although several predecessors of the present cencept (proligand) have been reported for discussing stereochemistry,[8,17] they pay little attention on such implications that are revealed by the proligand term. For simplicity's sake, we here deal with achiral proligands, which apparently behave like atoms. A more general approach will be discussed elsewhere.[18]

We then define a *promolecule* as a three-dimensional (3D) object that consists of a skeleton and proligands. We differentiate such promolecules from molecules, since this differentiation simplifies discussions on stereochemical relationships.

A set of equivalent proligands is regarded as an *orbit*, which is characterized by a coset representation (CR). For illustrating this relationship, we depict several promolecules derived from adamantane skeletons (Fig. 1). Each A is an achiral proligand; the remaining part of each promolecule is regarded as a skeleton without losing generality.[19] Table 1 indicates properties of each orbit concerning the proligands (A's), where other orbits are not taken into account.

Let **G** be the symmetry of a promolecule, which is referred to as a *global symmetry*. Then, a CR for an orbit is represented by $\mathbf{G}(/\mathbf{G}_i)$, where $\mathbf{G}_i$ is an appropriate subgroup of **G**. This CR indicates that $\mathbf{G}_i$ is the *local symmetry* for each member of the orbits.[14] The number of the members is equal to the length of the orbit, which is calculated to be $|\mathbf{G}|/|\mathbf{G}_i|$, where $|\mathbf{G}|$ and $|\mathbf{G}_i|$ denote the orders of **G** and $\mathbf{G}_i$, respectively. For example, the orbit of four equivalent A's of **3** is assigned to the CR, $\mathbf{T}_d(/\mathbf{C}_{3v})$.[20] This assignment is accomplished by using a table of marks for $\mathbf{T}_d$ point group.[13,14] In terms of the CR ($\mathbf{T}_d(/\mathbf{C}_{3v})$), the local symmetry of each A in this molecule is concluded to be $\mathbf{C}_{3v}$, which appears in the parentheses of the symbol of the CR. The achiral proligand (A) is presumed implicitly to have $\mathbf{C}_{\infty v}$ symmetry in isolation; but is restricted to the $\mathbf{C}_{3v}$ local symmetry in this promolecule. The local symmetries in the other promolecules are listed in Table 1, in which they are placed by

Table 1. Coset Representations for Orbits of Proligands

Promolecule	Member(s) of an orbit	Local symmetry	Coset representation	Chirality fittingness (Sphericity)
3	A_4	$\mathbf{C}_{3v}$	$\mathbf{T}_d(/\mathbf{C}_{3v})$	Homospheric
4	A_4	$\mathbf{C}_s$	$\mathbf{D}_{2d}(/\mathbf{C}_s)$	Homospheric
5	A	$\mathbf{C}_{3v}$	$\mathbf{C}_{3v}(/\mathbf{C}_{3v})$	Homospheric
6	A_3	$\mathbf{C}_s$	$\mathbf{C}_{3v}(/\mathbf{C}_s)$	Homospheric
7	A_6	$\mathbf{C}_1$	$\mathbf{C}_{3v}(/\mathbf{C}_1)$	Enantiospheic
8	A_4	$\mathbf{C}_1$	$\mathbf{D}_2(/\mathbf{C}_1)$	Hemispheric
9	A_2	$\mathbf{C}_s$	$\mathbf{C}_{2v}(/\mathbf{C}_s)$	Homospheric
10	A_4	$\mathbf{C}_1$	$\mathbf{S}_4(/\mathbf{C}_1)$	Enantiospheric
11	A	$\mathbf{C}_3$	$\mathbf{C}_3(/\mathbf{C}_3)$	Hemispheric
12	A_3	$\mathbf{C}_1$	$\mathbf{C}_3(/\mathbf{C}_1)$	Hemispheric
13	A	$\mathbf{C}_s$	$\mathbf{C}_s(/\mathbf{C}_s)$	Homospheric
14	A_2	$\mathbf{C}_1$	$\mathbf{C}_s(/\mathbf{C}_1)$	Enantiospheric
15	A_2	$\mathbf{C}_1$	$\mathbf{C}_2(/\mathbf{C}_1)$	Hemispheric

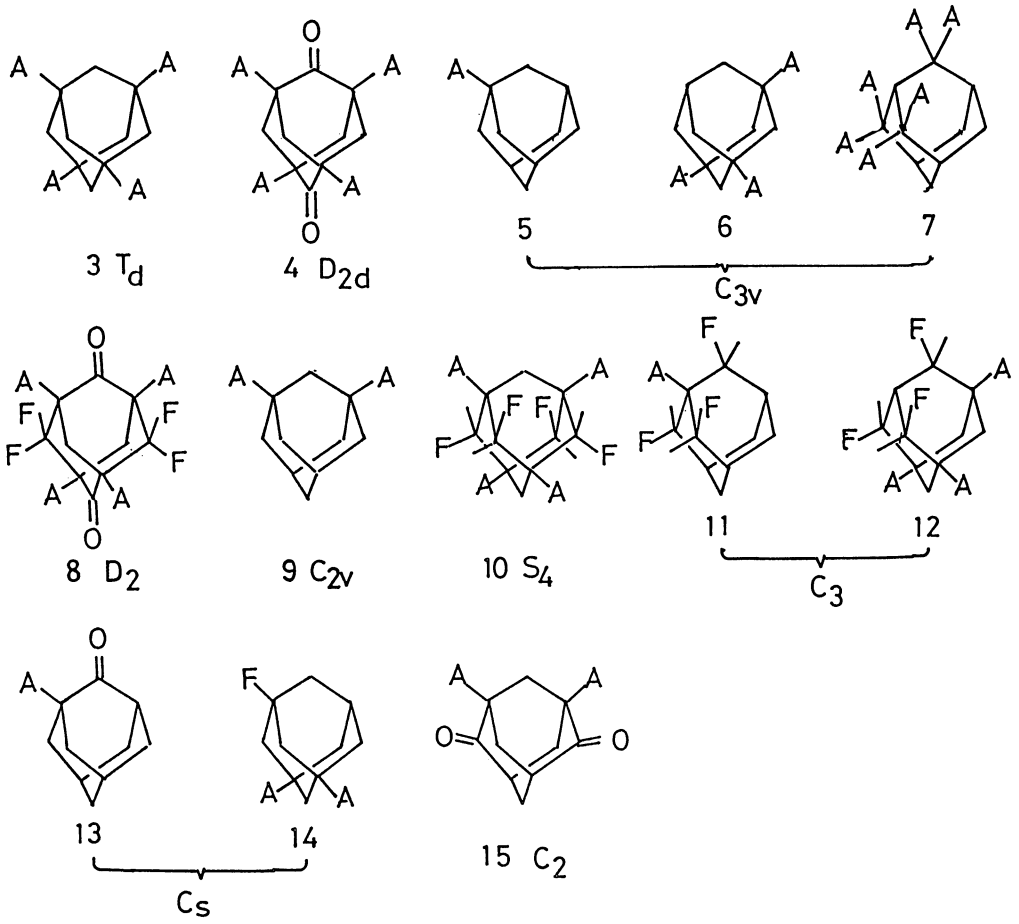


Fig. 1. Promolecules based on adamantane skeletons.
Capital A's in each promolecule denote achiral proligands. The remaining part of the promolecule is regarded as a skeleton. A capital F denotes a fluorine atom, which is here considered to be a component of a skeleton.

the sides of the corresponding CRs.

A proligand in a promolecule is called a *segment* and a proligand in isolation is referred to as a *fragment*. The segment may be different from the corresponding fragment in their symmetries. The promolecules (**5** to **7**) belong to the same C_{3v} symmetry; however, they have different types of orbits concerning A's (Table 1). Thus, one A of **5** constructs a $C_{3v}(/C_{3v})$ orbit; three A's of **6** belong to a $C_{3v}(/C_s)$ orbit; and six A's of **7** build a $C_{3v}(/C_1)$ orbit. The respective local symmetries are C_{3v}, C_s and C_1, as found in the parentheses of the symbols.

A Set of Equivalent Ligands as an Orbit. We now discuss symmetry changes that take place when proligands are replaced by achiral ligands having a 3D structure. The treatment described in this section is concerned with the symmetries of the ligands to such a limited extent that only their point groups are taken into consideration; but without considering their internal structures. Suppose that the achiral proligand (A) in the promolecule (**5**) of C_{3v} symmetry is replaced by a methyl ligand. The resulting molecule (**22**) retains the global C_{3v} symmetry, because the C_{3v} symmetry of the methyl fragment is equal to the local C_{3v} symmetry due to the $C_{3v}(/C_{3v})$ CR (Table 1). Thereby, the methyl segment has the same C_{3v} symmetry as the fragment. Thus, this operation gives rise to no restriction of the fragment symmetry. We also use the terms *segment* and *fragment* for discussing properties of ligands.[21]

In the case of the promolecule (**6**), the replacement of each A by a methyl ligand produces a molecule (**23**) that has a global C_{3v} symmetry equal to that of **6**. However, this conservation of the global symmetry is different from that of **22** described above, because the C_{3v} point group (for the methyl as a fragment) involves the C_s point group (for the local symmetry) as a subgroup. In contrast with the global symmetry, each of the resulting methyl segments has a C_s local symmetry, to which the original C_{3v} symmetry of the methyl ligand (as a fragment) is restricted.

These facts can be generalized as follows: If the symmetry of a fragment is equal to or involves the local symmetry of a promolecule, the resulting molecule has the same symmetry (point group) as does the promolecule; and the segment derived from the frag-

ment is restricted so as to have the symmetry equal to the local symmetry.

Chirality Fittingness of an Orbit. In order to discuss the chirality/achirality of a molecule (or a promolecule), we have introduced the concept "chirality fittingness" (sphericity) in a previous paper.[14] Thus, any $\mathbf{G}(/\mathbf{G}_i)$ orbit is classified into one of the three categories according to $\mathbf{G}$ vs. $\mathbf{G}_i$.

Global symmetry	Local symmetry	Chirality fittingness	Number of orbits	
$\mathbf{G}$	$\mathbf{G}_i$	(Sphericity)	$\downarrow\mathbf{G}$	$\downarrow\mathbf{G}^{max}$
Achiral	Achiral	Homospheric	1	1
Achiral	Chiral	Enantiospheric	1	2
Chiral	Chiral	Hemispheric	1	1

Table 1 collects coset representations and chirality fittingness. For illustrating the chirality fittingness, let us examine homospheric and enantiospheric orbits. For example, the two proligands (A_2) in the promolecule (**9**) (or equivalently the two hydrogen atoms in difluoromethane (CH_2F_2) construct a $\mathbf{C}_{2v}(/\mathbf{C}_s)$ orbit, which is homospheric because both of the $\mathbf{C}_{2v}$ and $\mathbf{C}_s$ point groups are achiral. The two members (A_2) of the orbit are interchangeable by the proper rotations (I and C_2) and the improper rotations ($\sigma_{v(1)}$ and $\sigma_{v(2)}$) contained in the $\mathbf{C}_{2v}$ group. In other words, the homospheric orbit remains unchanged even if we restrict the $\mathbf{C}_{2v}$ into $\mathbf{C}_2=\{I, C_2\}$. As a result, the number of orbits is 1 under the action of $\mathbf{C}_{2v}$ (no restriction) and is unchanged to be 1 under the action of $\mathbf{C}_2$ (restriction denoted by $\downarrow\mathbf{C}_2$). Let $\mathbf{G}^{max}$ be such a subgroup of $\mathbf{G}$ that is composed of all of the proper rotations of $\mathbf{G}$. Then, this case can be generalized as follows. The restriction to the $\mathbf{G}^{max}$ (denoted by $\downarrow\mathbf{G}^{max}$) produces no division of a homospheric $\mathbf{G}(/\mathbf{G}_i)$ orbit.

On the other hand, the two proligands (A_2) in the promolecule (**14**) (or equivalently the two hydrogen atoms in chlorofluoromethane (CH_2ClF)) belong to a $\mathbf{C}_s(/\mathbf{C}_1)$ orbit. This orbit is enantiospheric, because the $\mathbf{C}_s$ is achiral and the $\mathbf{C}_1$ is chiral. The two members (A_2) of the orbit are interchangeable by the improper rotation (σ) but not interchangeable by the proper rotation (I) contained in the $\mathbf{C}_s$ group. As a result, the number of orbits is 1 under the action of $\mathbf{C}_s$ (no restriction) but the orbit is divided into two orbits under the action of $\mathbf{C}_1$ (restriction denoted by $\downarrow\mathbf{C}_1$). This case can be generalized as follows. The restriction to the $\mathbf{G}^{max}$ (denoted by $\downarrow\mathbf{G}^{max}$) divides an enantiospheric $\mathbf{G}(/\mathbf{G}_i)$ orbit into two parts.

Enantiospheric Orbit under a Chiral Environment. Several symmetrical properties of a segment can be discussed in terms of coset representations and chirality fittingnesses (sphericities) collected in Table 1; thus, these determine behaviors of the segment (A) under chiral environments (such as actions of chiral shift reagents and of chiral solvents). The following general theorem is important throughout the present discussions:

Theorem 1 (Fujita[14]). An enantiospheric orbit is capable of separating into two hemispheric orbits of the same length under a chiral environment, whether the change is reversible or irreversible.

This general theorem stems from the difference in the behavior of the enantiospheric orbit toward $\mathbf{G}$ and $\mathbf{G}^{max}$. The theorem can be applied to the orbits of proligands and of ligands. For example, since the six A's (or achiral ligands) of **7** belong to an enantiospheric orbit governed by $\mathbf{C}_{3v}(/\mathbf{C}_1)$, Theorem 1 predicts that they are divided into two sets of three equivalent (hemispheric) segments if **7** is placed under an external chiral environment (e.g, by the action of a chiral shift reagent). If the resulting anisochrony is large enough to determine, there emerge two sets of signals of equal intensities for A's. Similar predictions are obtained with respect to **10** and **14**, since they have an enantiospheric orbit (Table 1). To the best of our knowledge, no example has been reported for such splittings that concern four or more ligands, although several anisochronies concerning two ligands have been observed by the actions of chiral solvents.[22]

Each of the other promolecules (or the corresponding molecules) collected in Table 1 has a homospheric (or hemispheric) orbit only; such an anisochronous effect is predicted not to be observed.

2. Local Orbits and Global Orbits

In the preceding section, we have discussed an orbit of ligands, where we took no account of the internal structure of each ligand. The latter issue is a matter we aim at in this section. Figure 2 illustrates the fundamental principle of formulating a ligand that has an internal 3D structure. Suppose that a ligand-in-isolation (fragment) belongs to **F**-point group. It consists of several atoms, which construct its own orbits. The orbits in the fragment are referred to as *infraorbits*. Each of the infraorbits are govorned by a coset representation ($\mathbf{F}(/\mathbf{F}_p)$), where $\mathbf{F}_p$ is an appropriate subgroup of $\mathbf{F}$. Each $\mathbf{F}(/\mathbf{F}_p)$ infraorbit has the length of $|\mathbf{F}|/|\mathbf{F}_p|$, where $|\mathbf{F}|$ and $|\mathbf{F}_p|$ are the orders of $\mathbf{F}$ and $\mathbf{F}_p$ respectively.

Let us next incorporate this fragment into a molecule. Just as the fragment symmetry ($\mathbf{F}$) of the ligand is restricted into a local symmetry ($\mathbf{F}_q$) when incorporated as a segment, so the infraorbits ($\mathbf{F}(/\mathbf{F}_p)$'s) are restricted to the same local symmetry. The resulting orbits are called *local orbits*. The generation of the local orbits is controlled by the subduction, $\mathbf{F}(/\mathbf{F}_p)\downarrow\mathbf{F}_q$.[12] If we now inspect the whole molecule, we find that an appropriate set of such local orbits, each of which belongs to a segment, constructs an orbit of the molecule. We call the latter orbit a *global orbit*.

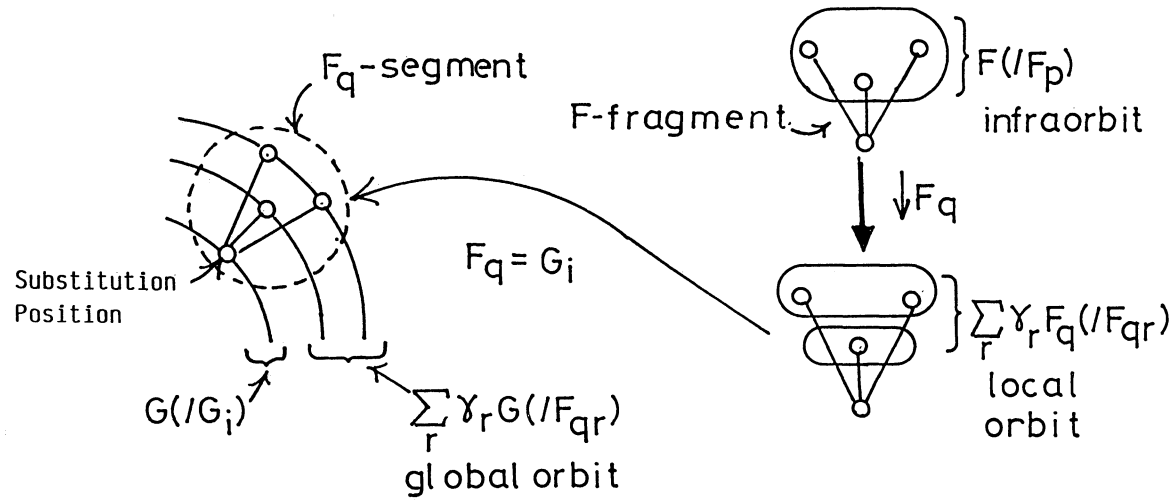


Fig. 2. Infraorbits, local orbits, and global orbits.

Since global orbits and local orbits characterize the same objects from different points of view, there is a close relationship between them.

This relationship is described by means of the following theorems, which can be proved by a slight modification of a mathematical treatment reported elsewhere.[15]

Theorem 2. Suppose that a promolecule has a $\mathbf{G}(/\mathbf{G}_i)$ orbit with $|\mathbf{G}|/|\mathbf{G}_i|$ achiral proligands; and that each of the achiral proligands in the orbit is replaced by an achiral ligand having an $\mathbf{F}(/\mathbf{F}_p)$ infraorbit ($\mathbf{F} \not\geqslant \mathbf{G}_i$). Then, the resulting molecule belongs to $\mathbf{G}$ symmetry. The $|\mathbf{F}|/|\mathbf{F}_p|$-membered infraorbit is divided according to $\mathbf{F}(/\mathbf{F}_p)\downarrow\mathbf{F}_q$, where $\mathbf{G}_i=\mathbf{F}_q$.

The resulting local and global orbits are represented by

Theorem 3. a) If the infraorbit ($\mathbf{F}(/\mathbf{F}_p)$) is restricted in the light of Theorem 2, the restriction is represented by

$$\mathbf{F}(/\mathbf{F}_p)\downarrow\mathbf{F}_q = \sum_{r=1}^{c_q} \gamma_r \mathbf{F}_q(/\mathbf{F}_{qr}), \tag{1}$$

wherein each $\mathbf{F}_{qr}$ is a subgroup of $\mathbf{F}_q$; c_q is the number of representative subgroups; and γ_r is the multiplicity of the $\mathbf{F}_{qr}$ subgroup. The resulting orbits ($\mathbf{F}_q(/\mathbf{F}_{qr})$'s) in the right-hand side are local orbits. Each $\mathbf{F}_q(/\mathbf{F}_{qr})$ orbit has the length of $|\mathbf{F}_q|/|\mathbf{F}_{qr}|$.

b) The corresponding global orbits are represented by

$$\sum_{r=1}^{c_q} \gamma_r \mathbf{G}(/\mathbf{F}_{qr}), \tag{2}$$

wherein c_q is the number of representatives of conjugate subgroups appearing in $\mathbf{F}_q$. Each $\mathbf{G}(/\mathbf{F}_{qr})$ orbit has the length of $|\mathbf{G}|/|\mathbf{F}_{qr}|$. Note that

$$\frac{|\mathbf{G}|}{|\mathbf{G}_i|} \times \left(\sum_{r=1}^{c_q} \frac{\gamma_r |\mathbf{F}_q|}{|\mathbf{F}_{qr}|} \right) = \sum_{r=1}^{c_q} \frac{\gamma_r |\mathbf{G}|}{|\mathbf{F}_{qr}|}, \tag{3}$$

since $\mathbf{G}_i$ is identical with $\mathbf{F}_q$.

It should be noted that Theorems 2 and 3 concern the highest attainable symmetry. These theorems determine symmetry equivalence and non-equivalence in a general fashion. Theorems 2 and 3 are true for any cases; but we hereafter bear special cases in mind: each ligand has an additional $\mathbf{F}(/\mathbf{F})$ orbit at which the ligand is linked to a member of the $\mathbf{G}(/\mathbf{G}_i)$ orbit, so that a free bond rotation at the linking position is allowed.

Comparison between Eqs. 1 and 2 indicates no increase in the number of orbits. In addition, Eqs. 1 and 2 afford a splitting ratio:

$$\begin{aligned}
&\frac{|\mathbf{F}_q|}{\underbrace{|\mathbf{F}_{q1}|}_{\gamma_1}} : \cdots : \frac{|\mathbf{F}_q|}{\underbrace{|\mathbf{F}_{q2}|}_{\gamma_2}} : \cdots : \cdots : \frac{|\mathbf{F}_q|}{\underbrace{|\mathbf{F}_{qc_q}|}_{\gamma_{c_q}}} : \cdots \\
&= \frac{|\mathbf{G}|}{\underbrace{|\mathbf{F}_{q1}|}_{\gamma_1}} : \cdots : \frac{|\mathbf{G}|}{\underbrace{|\mathbf{F}_{q2}|}_{\gamma_2}} : \cdots : \cdots : \frac{|\mathbf{G}|}{\underbrace{|\mathbf{F}_{qc_q}|}_{\gamma_{c_q}}} : \cdots \\
&= \frac{1}{\underbrace{|\mathbf{F}_{q1}|}_{\gamma_1}} : \cdots : \frac{1}{\underbrace{|\mathbf{F}_{q2}|}_{\gamma_2}} : \cdots : \cdots : \frac{1}{\underbrace{|\mathbf{F}_{qc_q}|}_{\gamma_{c_q}}} : \cdots
\end{aligned}$$

These facts mean that non-equivalence can be discussed in terms not only of global orbits but also of local orbits. When two atoms belong to the same global (or local) orbit, they are symmetrically equivalent; otherwise, they are symmetrically non-equivalent. Moreover, such expressions as Eq. 1 can be preestimated in the form of tables of subduction (see below), which simplify our discussions on symmetry equivalence to a great extent. The present methodology, obviously, does not require terms concerning topic

relationships, such as enantiotopic and diastereotopic. In the subsequent sections, we will apply these theorems to several cases and reveal merits of the present approach.

3. Methyl Segments in Various Molecules

Global and Local Orbits for Methyl Segments. Figure 3 illustrates the same concepts as shown in Fig. 2 more concretely by using a D_{2d} skeleton and methyl ligands. In this case, we start from the skeleton (**16**) of D_{2d} symmetry. For simplicity's sake, we use a schematic top view (right) in place of a usual structural diagram (left). Each position of **16** (belonging to $D_{2d}(/C_s)$) is replaced by an achiral proligand (A) to produce the promolecule (**4**). Then the replacement of A's of **4** by methyl ligands produces the molecule (**17**), which has D_{2d} symmetry in a conformation of the highest attainable symmetry. In this conformation, the twelve hydrogen atoms in **17** are split into two orbits (H_4^a and H_8^b), which are governed by $D_{2d}(/C_s)$ and $D_{2d}(/C_1)$, respectively. These orbits are global orbits concerning these twelve hydrogens.

Let us now focus our attention on one of the four methyl ligands in **17**. Each of these methyl ligands is decided to be a C_s segment on the basis of the local symmetry determined by the $D_{2d}(/C_s)$ CR concerning the A_4 of **4**. This C_s segment contains atoms (H^a and H_2^b), which are subject to $C_s(/C_s)$ and $C_s(/C_1)$ if the labeling with a and b is taken into account. These orbits are local orbits concerning the methyl segment.

It should be noted that an object can exhibit simultaneous memberships of several distinct orbits that are presumed from different points of view. Thus, H^a is

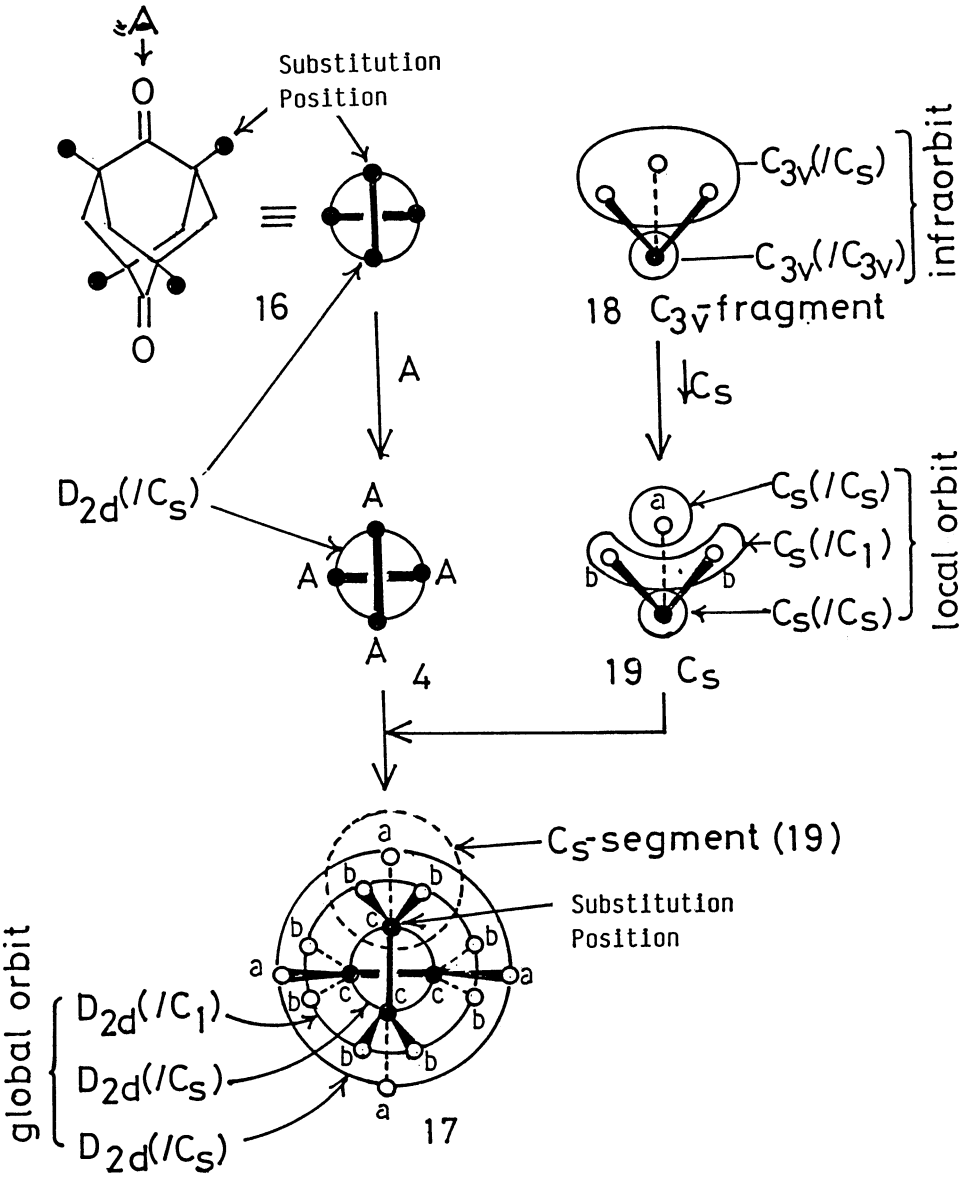


Fig. 3. Infraorbits, local orbits, and global orbits in **17**.

a member of the 4-membered global orbit denoted by $\mathbf{D}_{2d}(/\mathbf{C}_s)$, and, at the same time, belongs to the one-membered local orbit governed by $\mathbf{C}_s(/\mathbf{C}_s)$. Similarly, H^b belongs to the 8-membered $\mathbf{D}_{2d}(/\mathbf{C}_1)$ global orbit and to the 2-membered $\mathbf{C}_s(/\mathbf{C}_1)$ local orbit. The global orbit and the local orbit are linked with each other through the CR $\mathbf{D}_{2d}(/\mathbf{C}_s)$ of the substitution positions.

The local orbit concerning a methyl segment can be interpreted otherwise. This treatment is a direct application of Theorem 3. Let us begin with a methyl ligand in isolation (fragment). The methyl fragment (**18**) has an infraorbit of three hydrogen atoms that is subject to the CR, $\mathbf{C}_{3v}(/\mathbf{C}_s)$. Since this infraorbit is homospheric, it coincides with itself by the rotations and rotoreflections of the $\mathbf{C}_{3v}$ point group. When the methyl ligand is incorporated into **4** in place of A, its infraorbit is restricted to the $\mathbf{C}_s$ local symmetry. This restriction producing **19** is represented by the symbol, $\mathbf{C}_{3v}(/\mathbf{C}_s)\downarrow\mathbf{C}_s$, which is referred to as a *subduced representation* (SR) of the CR. Such a subduced representation is intransitive and can be further reduced into a set of CRs for $\mathbf{C}_s$ point group. For the purpose of such reduction, it is important to prepare a table of subduction of CRs.[12] Table 2 lists the subduction of CRs for $\mathbf{C}_{3v}$ point group. From this table, we obtain an expression:

$$\mathbf{C}_{3v}(/\mathbf{C}_s)\downarrow\mathbf{C}_s=\mathbf{C}_s(/\mathbf{C}_1)+\mathbf{C}_s(/\mathbf{C}_s), \quad (4)$$

which is an explicit form of Eq. 1 denoting this case. Equation 4 indicates that there emerge two orbits; the one (H_2^b) is a two-membered orbit subject to $\mathbf{C}_s(/\mathbf{C}_1)$ and the other (H^a) is a one-membered orbit subject to $\mathbf{C}_s(/\mathbf{C}_s)$. This splitting corresponds to the local orbits depicted in Fig. 3. Theorem 3 indicates that the sum $(\mathbf{C}_s(/\mathbf{C}_1)+\mathbf{C}_s(/\mathbf{C}_s))$ in the right-hand side of Eq. 4 corresponds to the sum $(\mathbf{D}_{2d}(/\mathbf{C}_1)+\mathbf{D}_{2d}(/\mathbf{C}_s))$. This fact agrees with the global orbits described above.

In general, local orbits are deduced from subduction of an infraorbit. Furthermore, global orbits are deduced form the local orbits in terms of Theorem 3. Table 3 lists local and global orbits that are created by the subduction of $\mathbf{C}_{3v}(/\mathbf{C}_s)$ infraorbit of a methyl ligand incorporated in **3** to **15**. These data are easily obtained from Table 2 by restricting $\mathbf{C}_{3v}(/\mathbf{C}_s)$ into the respective local symmetries that are listed in Table 1 and in the CR-for-ligand column of Table 3.

Anisochrony in Methyl Ligands. Symmetry equivalence is ascribed to the membership of the same orbit (local and global); and symmetry non-equivalence stems from the membership of distinct orbits. Then, we ascribe anisochrony to such symmetry non-equivalence. This criterion is mathematically stricter than that of Reisse et al.,[11] in which anisochrony is ascribed to diastereotopism by external or internal comparison.

According to the local-orbit column of Table 3, we can predict isochronies for the methyl segments of **21**, **22**, and **28**, since there appears no splitting of the 3-membered infraorbits. However, the former two (**21** and **22**) are different from **28** in their behaviors. In the cases of **21** (from **3**) and **22** (from **5**), the local symmetry of $\mathbf{C}_{3v}$ provides no restriction to the methyl group. On the other hand, the $\mathbf{C}_3(/\mathbf{C}_3)$ CR restricts the proligand (A) of the promolecule (**11**) so as to

Table 2. Subduction of Coset Representations for $\mathbf{C}_{3v}$ Group

Coset representation	Subduction			
	$\downarrow\mathbf{C}_1$	$\downarrow\mathbf{C}_s$	$\downarrow\mathbf{C}_3$	$\downarrow\mathbf{C}_{3v}$
$\mathbf{C}_{3v}(/\mathbf{C}_1)$	$6\mathbf{C}_1(/\mathbf{C}_1)$	$3\mathbf{C}_s(/\mathbf{C}_1)$	$2\mathbf{C}_3(/\mathbf{C}_1)$	$\mathbf{C}_{3v}(/\mathbf{C}_1)$
$\mathbf{C}_{3v}(/\mathbf{C}_s)$	$3\mathbf{C}_1(/\mathbf{C}_1)$	$\mathbf{C}_s(/\mathbf{C}_1)+\mathbf{C}_s(/\mathbf{C}_s)$	$\mathbf{C}_3(/\mathbf{C}_1)$	$\mathbf{C}_{3v}(/\mathbf{C}_s)$
$\mathbf{C}_{3v}(/\mathbf{C}_3)$	$2\mathbf{C}_1(/\mathbf{C}_1)$	$\mathbf{C}_s(/\mathbf{C}_1)$	$2\mathbf{C}_3(/\mathbf{C}_3)$	$\mathbf{C}_{3v}(/\mathbf{C}_3)$
$\mathbf{C}_{3v}(/\mathbf{C}_{3v})$	$\mathbf{C}_1(/\mathbf{C}_1)$	$\mathbf{C}_s(/\mathbf{C}_s)$	$\mathbf{C}_3(/\mathbf{C}_3)$	$\mathbf{C}_{3v}(/\mathbf{C}_{3v})$

Table 3. Local Orbits and Global Orbits in **3**—**15** Substituted by Methyl Ligands

Molecule	Structure	CR for ligands	Local orbits	Global orbits
21	**3** (A=CH_3)	$\mathbf{T}_d(/\mathbf{C}_{3v})$	$\mathbf{C}_{3v}(/\mathbf{C}_s)$	$\mathbf{T}_d(/\mathbf{C}_s)$
17	**4** (A=CH_3)	$\mathbf{D}_{2d}(/\mathbf{C}_s)$	$\mathbf{C}_s(/\mathbf{C}_1)+\mathbf{C}_s(/\mathbf{C}_s)$	$\mathbf{D}_{2d}(/\mathbf{C}_1)+\mathbf{D}_{2d}(/\mathbf{C}_s)$
22	**5** (A=CH_3)	$\mathbf{C}_{3v}(/\mathbf{C}_{3v})$	$\mathbf{C}_{3v}(/\mathbf{C}_s)$	$\mathbf{C}_{3v}(/\mathbf{C}_s)$
23	**6** (A=CH_3)	$\mathbf{C}_{3v}(/\mathbf{C}_s)$	$\mathbf{C}_s(/\mathbf{C}_1)+\mathbf{C}_s(/\mathbf{C}_s)$	$\mathbf{C}_{3v}(/\mathbf{C}_1)+\mathbf{C}_{3v}(/\mathbf{C}_s)$
24	**7** (A=CH_3)	$\mathbf{C}_{3v}(/\mathbf{C}_1)$	$3\mathbf{C}_1(/\mathbf{C}_1)$	$3\mathbf{C}_{3v}(/\mathbf{C}_1)$
25	**8** (A=CH_3)	$\mathbf{D}_2(/\mathbf{C}_1)$	$3\mathbf{C}_1(/\mathbf{C}_1)$	$3\mathbf{D}_2(/\mathbf{C}_1)$
26	**9** (A=CH_3)	$\mathbf{C}_{2v}(/\mathbf{C}_s)$	$\mathbf{C}_s(/\mathbf{C}_1)+\mathbf{C}_s(/\mathbf{C}_s)$	$\mathbf{C}_{2v}(/\mathbf{C}_1)+\mathbf{C}_{2v}(/\mathbf{C}_s)$
27	**10** (A=CH_3)	$\mathbf{S}_4(/\mathbf{C}_1)$	$3\mathbf{C}_1(/\mathbf{C}_1)$	$3\mathbf{S}_4(/\mathbf{C}_1)$
28	**11** (A=CH_3)	$\mathbf{C}_3(/\mathbf{C}_3)$	$\mathbf{C}_3(/\mathbf{C}_1)$	$\mathbf{C}_3(/\mathbf{C}_1)$
29	**12** (A=CH_3)	$\mathbf{C}_3(/\mathbf{C}_1)$	$3\mathbf{C}_1(/\mathbf{C}_1)$	$3\mathbf{C}_3(/\mathbf{C}_1)$
30	**13** (A=CH_3)	$\mathbf{C}_s(/\mathbf{C}_s)$	$\mathbf{C}_s(/\mathbf{C}_1)+\mathbf{C}_s(/\mathbf{C}_s)$	$\mathbf{C}_s(/\mathbf{C}_1)+\mathbf{C}_s(/\mathbf{C}_s)$
31	**14** (A=CH_3)	$\mathbf{C}_s(/\mathbf{C}_1)$	$3\mathbf{C}_1(/\mathbf{C}_1)$	$3\mathbf{C}_s(/\mathbf{C}_1)$
32	**15** (A=CH_3)	$\mathbf{C}_2(/\mathbf{C}_1)$	$3\mathbf{C}_1(/\mathbf{C}_1)$	$3\mathbf{C}_2(/\mathbf{C}_1)$

belong to C_3 local symmetry. When a methyl ligand is incorporated in **11** to afford **28**, this restriction to the local symmetry results in a subduction: $C_{3v}(/C_s)\downarrow C_3=C_3(/C_1)$. Although this equation indicates no discrimination between three methyl protons of **28**, the methyl ligand is restricted to the C_3 symmetry.

The other molecules collected in Table 3 exhibit a division of the infraorbit of each methyl fragment, which stems from a restriction to the corresponding local symmetry. This division causes an anisochrony of three protons of each methyl ligand. The present restriction is concerned with a conformation having the highest attainable symmetry, which is possible to exist when a sufficient energy barrier is realized under an appropriate condition (e.g., at low temperature). Otherwise, we should take account of bond rotations concerning the methyl segment. The CR ($C_{3v}(/C_s)$) in the left-hand side of Eq. 4 predicts that a free rotation equalizes three methyl protons in **17**. On the other hand, the right-hand side indicates that, if the rotation is slow on the NMR time scale, two anisochronous methyl proton signals (intensity ratio 2:1) can be observed. Note that $|C_s|/|C_1|$ is equal to 2 and $|C_s|/|C_s|$ is equal to 1. Among the molecules listed in Table 3, **23** (from **6**), **26** (from **9**), and **30** (from **13**) involve A's of the same situation as does **17** (from **4**). Thereby, the same prediction can be made for each of these molecules.

The equalization of the methyl protons under free bond rotation can be explained more logically. This process is equivalent to considering CH_3B, where the symbol B denotes an achiral proligand. This hypothetical promolecule belongs to C_{3v} symmetry. Hence, the carbon atom of the CH_3B constructs a $C_{3v}(/C_{3v})$ orbit. By using the C_{3v} local symmetry in place of C_s, we have $C_{3v}(/C_s)\downarrow C_{3v}=C_{3v}(/C_s)$ for the three protons. This equation indicates the equivalence of the methyl protons under free bond rotation.

The methyl protons of **2** are characterized in a similar way. The corresponding promolecule can be obtained by substituting an achiral proligand (A) for the methyl group of **2**. It belongs to C_s symmetry; the A constructs a one-membered orbit governed by C_s ($/C_s$). Since the local symmetry is determined to be C_s, the methyl segment in **2** is also restricted according to Eq. 4. Therefore, the same prediction as above can be obtained, although **4** has D_{2d} and **2** has C_s, as their global symmetries. Since $|C_s|/|C_1|=2$ and $|C_s|/|C_s|=1$, splitting of 2:1 intensity ratio is predicted to be observed in its low-temperature NMR spectrum. This prediction has already been verified experimentally.[5]

Each methyl segment in **24** (from **7**) is restricted to C_1 local symmetry. The subduction represented by $C_{3v}(/C_s)\downarrow C_1=3C_1(/C_1)$ (Table 2) indicates the symmetry non-equivalence of the three methyl protons in a conformation of the highest attainable symmetry. Hence, the three protons can be anisochronous if a bond rotation about a methyl segment is slow on the NMR time scale. If the rotation is fast, an average chemical shift is predicted to be observed because of the CR ($C_{3v}(/C_s)$). This example contains six methyl ligands and indicates an advantage of the present method over conventional ones which use Newmann's projections. In the cases in which so many ligands participate, it would be very tedious task to determine sterochemical non-equivalence in terms of Newmann's projections.

The same prediction is obtained with respect to **27** (from **10**) and **31** (from **14**), which are also characterized by C_1 local symmetry, although the global symmetry of the three molecules are different from each other. It should be noted that the global symmetries of these molecules are achiral (i.e., contain proper and improper rotations); but the local symmetries are chiral (i.e., contain proper rotations only).

A local symmetry of a chiral molecule is always chiral. Since the local symmetry of the ligand (A) in **8** is C_1 the corresponding subduction is represented by $C_{3v}(/C_s)\downarrow C_1=3C_1(/C_1)$. Hence, we can predict non-equivalence of three methyl protons in **25** (from **8**). We can obtain the same prediction about **29** (from **12**) and **32** (from **15**) in the same line, since they have C_1 local symmetries. Note that this type of anisochrony is observed only in a fixed conformation; the free rotation of a methyl ligand equalizes the three methyl protons. Anisochrony observed in the molecule (**1**) is rationalized in a similar way.[4]

The equalization under free bond rotation is equivalent to considering CH_3* where * denotes a chiral proligand. This hypothetical promolecule belongs to C_3 symmetry. Hence, the carbon atom constructs a $C_3(/C_3)$ orbit. By using the C_3 local symmetry in place of the C_1, we have $C_{3v}(/C_s)\downarrow C_3=C_3(/C_1)$ for the three protons. This equation means the equality of the three protons under free bond rotation.

4. CH_2X Segments in Various Molecules

Global Orbits and Local Orbits for CH_2X Segments. Suppose that A's of **3** to **15** are replaced by CH_2X ligands in place of methyl ligands described in the preceding section. The two protons of the CH_2X ligand construct an infraorbit governed by $C_s(/C_1)$. Table 4 collects the results of applying Theorems 2 and 3 to the present cases, where only orbits of the two protons are listed.

Table 5 lists the subduction of CRs for C_s point group. These data control restrictions of ligand symmetries, as collected in the local-orbit column of Table 4. The resulting global orbits are also collected in Table 4.

The case of **33** should be mentioned in contrast with **21**.[23] Although they are derived from the same promolecule (**3**), they are different in their resulting symmetries. Since the condition $\mathbf{F} \gtrdot \mathbf{G}_i$ is true for the case of the methyl ligands applied to **3**, Theorem 2

Table 4. Local Orbits and Global Orbits in **3**—**15** Substituted by CH_2X Ligands

Molecule	Structure	CR for ligands[a]	Local orbits	Global orbits
33	**3** (A=CH_2X)	$\mathbf{D}_{2d}(/\mathbf{C}_s)$*	$\mathbf{C}_s(/\mathbf{C}_1)$	$\mathbf{D}_{2d}(/\mathbf{C}_1)$
34	**4** (A=CH_2X)	$\mathbf{D}_{2d}(/\mathbf{C}_s)$	$\mathbf{C}_s(/\mathbf{C}_1)$	$\mathbf{D}_{2d}(/\mathbf{C}_1)$
35	**5** (A=CH_2X)	$\mathbf{C}_s(/\mathbf{C}_s)$*	$\mathbf{C}_s(/\mathbf{C}_1)$	$\mathbf{C}_s(/\mathbf{C}_1)$
36	**6** (A=CH_2X)	$\mathbf{C}_{3v}(/\mathbf{C}_s)$	$\mathbf{C}_s(/\mathbf{C}_1)$	$\mathbf{C}_{3v}(/\mathbf{C}_1)$
37	**7** (A=CH_2X)	$\mathbf{C}_{3v}(/\mathbf{C}_1)$	$2\mathbf{C}_1(/\mathbf{C}_1)$	$2\mathbf{C}_{3v}(/\mathbf{C}_1)$
38	**8** (A=CH_2X)	$\mathbf{D}_2(/\mathbf{C}_1)$	$2\mathbf{C}_1(/\mathbf{C}_1)$	$2\mathbf{D}_2(/\mathbf{C}_1)$
39	**9** (A=CH_2X)	$\mathbf{C}_{2v}(/\mathbf{C}_s)$	$\mathbf{C}_s(/\mathbf{C}_1)$	$\mathbf{C}_{2v}(/\mathbf{C}_1)$
40	**10** (A=CH_2X)	$\mathbf{S}_4(/\mathbf{C}_1)$	$2\mathbf{C}_1(/\mathbf{C}_1)$	$2\mathbf{S}_4(/\mathbf{C}_1)$
41	**11** (A=CH_2X)	$\mathbf{C}_1(/\mathbf{C}_1)$*	$2\mathbf{C}_1(/\mathbf{C}_1)$	$2\mathbf{C}_1(/\mathbf{C}_1)$
42	**12** (A=CH_2X)	$\mathbf{C}_3(/\mathbf{C}_1)$	$2\mathbf{C}_1(/\mathbf{C}_1)$	$2\mathbf{C}_3(/\mathbf{C}_1)$
43	**13** (A=CH_2X)	$\mathbf{C}_s(/\mathbf{C}_s)$	$\mathbf{C}_s(/\mathbf{C}_1)$	$\mathbf{C}_s(/\mathbf{C}_1)$
44	**14** (A=CH_2X)	$\mathbf{C}_s(/\mathbf{C}_1)$	$2\mathbf{C}_1(/\mathbf{C}_1)$	$2\mathbf{C}_s(/\mathbf{C}_1)$
45	**15** (A=CH_2X)	$\mathbf{C}_2(/\mathbf{C}_1)$	$2\mathbf{C}_1(/\mathbf{C}_1)$	$2\mathbf{C}_2(/\mathbf{C}_1)$

a) The structure marked by an asterisk is desymmetrized in a mismatched fashion.

Table 5. Subduction of Coset Representations $\mathbf{C}_s$ Group

Coset representation	Subduction	
	$\downarrow\mathbf{C}_1$	$\downarrow\mathbf{C}_s$
$\mathbf{C}_s(/\mathbf{C}_1)$	$2\mathbf{C}_1(/\mathbf{C}_1)$	$\mathbf{C}_s(/\mathbf{C}_1)$
$\mathbf{C}_s(/\mathbf{C}_s)$	$\mathbf{C}_1(/\mathbf{C}_1)$	$\mathbf{C}_s(/\mathbf{C}_s)$

indicates that the symmetry ($\mathbf{T}_d$) of **3** retains in **21**. On the other hand, the condition is not satisfied in the substitution of CH_2X ($\mathbf{C}_s$ symmetry), since $\mathbf{F}=\mathbf{C}_s$ and $\mathbf{G}_i=\mathbf{C}_{3v}$. Hence, the symmetry of **3** is restricted into $\mathbf{D}_{2d}$ so as to satisfy the conditions $\mathbf{F} \geqslant \mathbf{G}_i$ (i.e., $\mathbf{F}=\mathbf{G}_i=\mathbf{C}_s$).[24] This restriction produces **33** of $\mathbf{D}_{2d}$ symmetry, for which Theorem 2 holds. The cases of **35** and **41** (marked with an asterisk in Table 4) are explained in a similar way.

Anisochrony in CH_2X Ligands. Two methylene protons in a CH_2X ligand (fragment) construct a $\mathbf{C}_s(/\mathbf{C}_1)$ orbit. Since this infraorbit is enantiospheric, the two protons are equivalent in isolation; they coincide with each other by improper rotations only, not by proper rotations. Under *any* chiral environment, they are split to construct two hemispheric orbits in terms of Theorem 1. The chiral environment required in Theorem 1 may come from a local symmetry. From the data of Table 4 (the CR-for-ligand column), we can select **37**, **38**, **40**, **41**, **42**, **44**, and **45** as examples of such chiral local symmetries. Note that **37**, **40**, and **44** are achiral; on the other hand, **38**, **41**, **42**, and **45** are chiral. The restriction of such a CH_2X ligand is expressed by the subduction,

$$\mathbf{C}_s(/\mathbf{C}_1)\downarrow\mathbf{C}_1=2\mathbf{C}_1(/\mathbf{C}_1), \quad (5)$$

which is selected from Table 5. The two members of the $\mathbf{C}_s(/\mathbf{C}_1)$ orbit are presumed to coincide with each other only by a reflection concerning a mirror plane, if they are isolated hypothetically. However, since they are restricted to the $\mathbf{C}_1$ local symmetry in terms of Eq. 5, they are not superposed even if a free rotation is permitted. Thus, these molecules are predicted to show anisochronies of the geminal protons.

Anisochrony of $XYC(CU_2R)_2$ is obviously ascribed to the same effect as operating in **44**; $RU_2C\text{-}CX_3^*$ is explained in the same line as **41**; and anisochrony of $(RU_2C)_3C\text{-}CXYZ$ is equivalent to that of **42**. Other cases can be rationalized by the same rule. Some of these examples have once been discussed in terms of "intrinsic assymetry".[9] However, Reisse et al.[11] have concluded that continued use of the term is no longer justified. The present analysis strengthens their conclusion; but has an advantage over their method. While the Reisse method requires internal and external comparison for determining diastereotopism, the present method does not require such operations that are based on stereoisomerism; in other words, stereochemical non-equivalence (diastereotopism) is ascribed to membership of distinct orbits.

To the best of our knowledge, such anisochrony has never been reported that concerns four or more CH_2X ligands, probably because there have existed no methods effective to design complicated cases. The present method is capable of predicting anisochronies of such complicated compounds. Experimental verification will be challenging and is open to further investigation.

5. Criteria for Judging Symmetry Equivalence and Non-Equivalence

Our principal idea is here restated as follows: When a fragment is incorporated in a molecule, the CR of its infraorbit is restricted to the corresponding local symmetry; the restriction is represented by a subduction of the CR to the local symmetry. This idea has been exemplified by the discussions in the preceding sections. Thereby, it is generalized in the form of the following criteria.

a) Suppose that, in Theorem 3, the $\mathbf{F}(/\mathbf{F}_p)$ infraorbit is homospheric (for example, in a methyl ligand). The local symmetry $\mathbf{F}_q$ may be achiral or chiral.

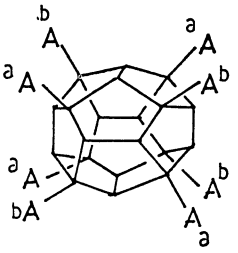
- If $\mathbf{F}(/\mathbf{F}_p)\downarrow\mathbf{F}_q$ produces a subdivision of the $\mathbf{F}(/\mathbf{F}_p)$ in terms of Eq. 1, the nuclei in the $\mathbf{F}(/\mathbf{F}_p)$ infraorbit are capable of exhibiting anisochrony due to $\mathbf{F}(/\mathbf{F}_p)\downarrow\mathbf{F}_q$. This anisochrony is observed at such a low temparature as affording slow bond rotations on the NMR time scale; otherwise, it exhibits an average chemical shift.
- If $\mathbf{F}(/\mathbf{F}_p)\downarrow\mathbf{F}_q$ provides no subdivision, there emerges no anisochronies.

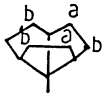
b) Suppose that, in Theorem 3, an $\mathbf{F}(/\mathbf{F}_p)$ infraorbit is enantiospheric (for example, in a CH_2X ligand) and that the local symmetry $\mathbf{F}_q$ is achiral. The conclusion for the case a) holds for this case.

c) Suppose that, in Theorem 3, an $\mathbf{F}(/\mathbf{F}_p)$ infraorbit is enantiospheric (for example, in a CH_2X ligand) and

that the local symmetry $\mathbf{F}_q$ is chiral. Equation 1 provides the splitting of the enantiospheric orbit so as to yield two hemispheric orbits. Since this splitting is inherent, split signals can be observed with no respect to the NMR time scale.

These criteria indicate guidelines for determining anisochronies of nuclei; more detailed discussions should be based on concrete forms of SRs. In order to show the scope of these criteria, we examine more complicated molecules (**47**—**49**). The corresponding promolecule (**46**) has a $\mathbf{T}_h(/\mathbf{C}_3)$ orbit that consists of A_8. Since this orbit is enantiospheric, these eight A's are capable of splitting into two 4-membered hemispheric orbits (A_4^a and A_4^b) under an external chiral condition (Theorem 1).



46 A=proligand
47 A=CH_3
48 A= 
49 A=CH_2OH $\mathbf{D}_{2h}$

The local symmetry of the proligands (A's) is $\mathbf{C}_3$ (chiral) in **46**. The $\mathbf{C}_3$ point group is a subgroup of the $\mathbf{C}_{3v}$ group of a methyl fragment. Hence, when each A is replaced by a methyl ligand, the resulting molecule (**47**) retains $\mathbf{T}_h$ symmetry. The incorporated methyl segment is restricted to the local symmetry in terms of

$$\mathbf{C}_{3v}(/\mathbf{C}_s)\downarrow\mathbf{C}_3=\mathbf{C}_3(/\mathbf{C}_1). \tag{6}$$

This equation indicates that, under any condition, there occurs no splitting of three protons in each methyl segment. In contrast with this, the methyl symmetry is lowered from $\mathbf{C}_{3v}$ to $\mathbf{C}_3$. This effect results in splitting of 8 methyl segments into two sets of equivalent methyl segments (A_4^a and A_4^b in **47**; A=CH_3) under an external chiral condition (e,g., by the action of a chiral shift reagent).

When a ligand has an enantiospheric $\mathbf{C}_{3v}(/\mathbf{C}_1)$ infraorbit as shown in **48**, the criterion c) is satisfied. Thus, we obtain

$$\mathbf{C}_{3v}(/\mathbf{C}_1)\downarrow\mathbf{C}_3=2\mathbf{C}_3(/\mathbf{C}_1). \tag{7}$$

This equation is selected from the $\mathbf{C}_{3v}(/\mathbf{C}_1)$ row of Table 2. Equation 7 means that we can observe two ^{13}C signals for methylene carbons (C_3^a and C_3^b) independent of temperature, if this splitting provides chemical shifts different enough to determine. Experimental verification regarding such a general type of anisochronies predicted here is open to further investigation.

When the same ligand as for **48** is incorporated in **3** ($\mathbf{T}_d$ symmetry), the resulting molecule exhibits a different nature. Since the local symmetry is $\mathbf{C}_{3v}$ (Table 1), the ligand suffers no restriction, i.e., $\mathbf{C}_{3v}(/\mathbf{C}_1)\downarrow\mathbf{C}_{3v}=\mathbf{C}_{3v}(/\mathbf{C}_1)$. Hence, there emerges no anisochrony. If this ligand is applied to any one of the promolecules listed in Fig. 1, its respective behavior can be explained by the $\mathbf{C}_{3v}(/\mathbf{C}_1)$ row of Table 2.

The criterion c) determines the fate of enantiospheric infraorbits incorporated into a chiral local symmetry in any case. When the achiral proligand (A) is substituted by CH_2X, the resulting molecule (**49**) no longer retains $\mathbf{T}_h$ symmetry; but is restricted to $\mathbf{D}_{2h}$ symmetry. Since the $\mathbf{C}_s$ symmetry of CH_2X is incompatible with the local symmetry ($\mathbf{C}_3$) of **46**, this desymmetrization occurs so that the local symmetry is created by $\mathbf{C}_3\cap\mathbf{C}_s=\mathbf{C}_1$. According to this restriction, the original $\mathbf{T}_h(/\mathbf{C}_3)$ orbit is converted into $\mathbf{D}_{2h}(/\mathbf{C}_1)$ orbit.[25] Note that the length of the $\mathbf{T}_h(/\mathbf{C}_3)$ orbit ($|\mathbf{T}_h|/|\mathbf{C}_3|=24/3=8$) is equal to that of the $\mathbf{D}_{2h}(/\mathbf{C}_1)$ orbit ($|\mathbf{D}_{2h}|/|\mathbf{C}_1|=8/1=8$). As a result, the resulting molecule (**49**) of the $\mathbf{D}_{2h}$ global symmetry exibits a $\mathbf{C}_1$ local symmetry at the $\mathbf{D}_{2h}(/\mathbf{C}_1)$ orbit. Thereby, the CH_2X ligand is controlled by

$$\mathbf{C}_s(/\mathbf{C}_1)\downarrow\mathbf{C}_1=2\mathbf{C}_1(/\mathbf{C}_1), \tag{8}$$

which is selected from the $\mathbf{C}_s(/\mathbf{C}_1)$ row of Table 5. This equation satisfies the criterion c); hence, the two protons of the CH_2X in **49** show anisochrony independent of NMR time scale. The corresponding global orbits are concluded to be $2\mathbf{D}_{2h}(/\mathbf{C}_1)$ in terms of Theorem 3. It is important to recognize that such an enantiosphericity of an infraorbit is by no means referred to as "prochirality". The prochirality should concern the enantiosphericity of a global orbit or of its equivalents.

6. Conclusion

A ligand is chracterized as a fragment when isolated and as a segment when incorporated in a molecule. The symmetry of the ligand-in-isolation (fragment) is restricted into the symmetry of the ligand-in-molecule (segment) in accord with the local symmetry of the molecule. As a result, any orbit in the ligand (an infraorbit) is restricted into local orbits. The relationship between such local orbits and global orbits is discussed in terms of subduction of coset representations. This discussion provides a general approach to rationalize various types of anisochronism.

References

1) K. Mislow and J. Siegel, *J. Am. Chem. Soc.*, **106**, 3319 (1984).

2) K. Mislow and M. Raban, *Top. Stereochem.*, **1**, 1 (1967).

3) Convensional usages of the terms "isochrony" and "anisochrony" have been criticized by Fulea.[26] However, his criticism proves to be simply based on the difference between his definition and the convensional one. According to his

definition, the terms are used to refer to a relationship between *states* of two nuclei; hence, any nuclei can be isochronous under one condition and anisochronous under another condition. On the other hand, the terms are conventionally used to refer to a relationship between *properties* (attributes) of two nuclei, though this standpoint has never been mentioned explicitly. Our usage in the present paper restates such an convensional usage more explicitly: Isochronous (chemical-shift equivalent) nuclei are defined as the ones that exhibit equal chemical shifts independent of any environments; anisochronous (chemical-shift non-equivalent) nuclei are defined as the ones that exhibit different chemical shifts but are capable of showing equal chemical shifts under an appropriate condition.

4) M. Nakamura, M. Ōki, H. Nakanishi, and O. Yamamoto, *Bull. Chem. Soc. Jpn.*, **47**, 2415 (1974).

5) J. E. Anderson and D. I. Rawson, *J. Chem. Soc., Chem. Commun.*, **1973**, 830.

6) a) R. M. Silverstein, G. C. Bassler, and T. C. Morrill, "Spectrometric Identification of Organic Compounds," 4th ed, John-Wiley & Sons, New York (1981), p. 201; b) A. Raman, "Nuclear Magnetic Resonance," Springer-Verlag, New York-Berlin-Heidelbelg (1986); c) T. H. Siddall and W. E. Stewart, *Prog. Nucl. Magn. Reson. Spectros.*, **5**, 33 (1969).

7) W. B. Jenning, *Chem. Rev.*, **75**, 307 (1975).

8) K. R. Hanson, *J. Am. Chem. Soc.*, **88**, 2731 (1966).

9) E. L. Eliel, *Top. Curr. Chem.*, **105**, 1 (1982).

10) G. R. Franzen and G. Binsch, *J. Am. Chem. Soc.*, **95**, 175 (1973).

11) J. Reisse, R. Ottinger, P. Bickart, and K. Mislow, *J. Am. Chem. Soc.*, **100**, 911 (1978).

12) a) S. Fujita, *Theor. Chim. Acta*, **76**, 247 (1989); b) S. Fujita, *Bull. Chem. Soc. Jpn.*, **62**, 3771 (1989); c) S. Fujita, *Bull. Chem. Soc. Jpn.*, **63**, 203 (1990); d) S. Fujita, *Tetrahedron*, **46**, 365 (1990); e) S. Fujita, *J. Math. Chem.*, **5**, 99 (1990); f) S. Fujita, *Bull. Chem. Soc. Jpn.*, **63**, 1876 (1990); g) S. Fujita, *Bull. Chem. Soc. Jpn.*, **63**, 2033 (1990).

13) S. Fujita, *Bull. Chem. Soc. Jpn.*, **63**, 315 (1990).

14) S. Fujita, *J. Am. Chem. Soc.*, **112**, 3390 (1990).

15) S. Fujita, *Theor. Chim. Acta*, **77**, 307 (1990).

16) We here use the term "ligand" in place of "group", since the latter chemical term may be confused with the mathematical "group" of group theory.

17) V. Prelog, *Science*, **193**, 17 (1976).

18) S. Fujita, *Tetrahedron*, **47**, 31 (1991).

19) The selection of a skeleton depends upon the purpose of our discussion. For example, adamantane ($C_{10}H_{16}$) itself can be selected to generate a skeleton, $C_{10}\pi_{16}$, where π denotes a substitution position. Thereby, the promolecule (**10**) is produced as a result of an $H_8F_4A_4$ substitution; on the other hand, the promolecule (**14**) comes from an $H_{13}FA_2$ substitution. In these processes, the original symmetry ($\mathbf{T}_d$) of the skeleton is restricted to $\mathbf{S}_4$ for **10** and to $\mathbf{C}_s$ for **14**. When we further replace the A's by ligands, we can start from such proligands as having $\mathbf{S}_4$ and $\mathbf{C}_s$ symmetries. If we do not introduce the concept of promolecule, we should go back to the original $\mathbf{T}_d$ symmetry in every examination. This is the reason for introducting the concept of promolecule in additon to the concept of skeleton.

20) For a concrete form of the CR, see Ref. 12.

21) The term "(imprimitive) block" used Ref. 14 denotes a geometical object that meets mathematical requirements only; hence, such a block is not always equivalent to a ligand. On the other hand, the term "segment" used in this paper designates a ligand-in-molecule, which has a chemical meaning as well as a mathematical one. In other words, a segment is a set of blocks selected so as to possess a chemical meaning.

22) W. H. Pirkle, S. D. Beare, and R. L. Muntz, *J. Am. Chem. Soc.*, **91**, 4575 (1969).

23) The molecules with an asterisk are called mismatched molecules, since the condition $\mathbf{F} \geqslant \mathbf{G}_i$ is not true for these cases. On the other hand, molecules satisfying this condition are called matched molecules. More detailed discussions is reported in Ref. 18.

24) This desymmetrization can be discussed in terms of a subduction table of $\mathbf{T}_d$.[14] It corresponds to the subduction: $\mathbf{T}_d(/\mathbf{C}_{3v})\downarrow\mathbf{D}_{2d}=\mathbf{D}_{2d}(/\mathbf{C}_s)$.

25) This desymmetrization can be expressed by $\mathbf{T}_h(/\mathbf{C}_3)\downarrow\mathbf{D}_{2h}=\mathbf{D}_{2h}(/\mathbf{C}_1)$. A subduction table for $\mathbf{T}_h$ will be reported elsewhere.

26) A. O. Fulea, *Rev. Roum. Chim.* **33**, 39 (1988).