

Promolecules with a Subsymmetry of $D_{\infty h}$: Combinatorial Enumeration and Stereochemical Properties

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Promolecules having a $D_{\infty h}$ skeleton are enumerated by means of a method using unit-subduced cycle indices, which is modified so as to be based on factor groups. Molecules derived from the promolecules are also enumerated by combining the method with a previous method reported for enumerating rotatable molecules. The stereochemical properties of the promolecules are related to those of the corresponding molecules in terms of infraorbits and local orbits. In particular, the prochirality of a promolecule and of a molecule is ascribed to an appropriate enantiospheric orbit. This determination is mathematically founded so that it requires no tentative consideration of a fixed conformer of the highest attainable symmetry.

INTRODUCTION

Organic chemistry was originally based on two-dimensional (2D) structural formulas. Hence, in order to construct stereochemistry, organic chemists have considered 3D objects mainly by starting from such 2D formulas. Although this treatment has been one of the most versatile methodologies, it has, in turn, provided them with several difficulties.

One such difficulty is the problem concerning prochirality. Thus, the term "prochirality" is polysemous according to the IUPAC rule:¹

E-4.12(a) An achiral object having at least one pair of features that can be distinguished only by reference to a chiral object or to a chiral reference frame is said to be prochiral, and the property of having such a pair of features is termed prochirality.

E-4.12(b) In a molecule an achiral center or atom is said to be prochiral if it would be held to be chiral when two attached atoms or groups, that taken in isolation are indistinguishable, are considered to differ.

The word "polysemous" is used in place of "ambiguous", because these rules provide strict but distinct results in characterizing stereochemical equivalence and nonequivalence. The rule a indicates that it regards an object as being 3D from the beginning. As a result, the "prochirality" term of rule a is faithful to the meaning of the prefix *pro* (before).

On the other hand, rule b, which is the successor of Hanson's definition,^{2,3} implies the first consideration of a 2D object and the subsequent modification converting this into the corresponding 3D object. This definition is incompatible with the prochirality of rule a in several cases. In order to get rid of this incompatibility, the definition of rule b describes the limitation within "an achiral center or atom". This limitation disregards or distorts the original meaning of the prefix.

The two distinct definitions of prochirality have provided serious confusion in discussions on stereochemical problems. For example, ethanol (**1a**) is "prochiral" in terms of rule a, and its methylene carbon atom is prochiral in the sense of rule b. On the other hand, the methylene carbon atom of **2** is prochiral in the light of rule b, while **2** is chiral and by no means prochiral if we consider rule a (see Figure 1).

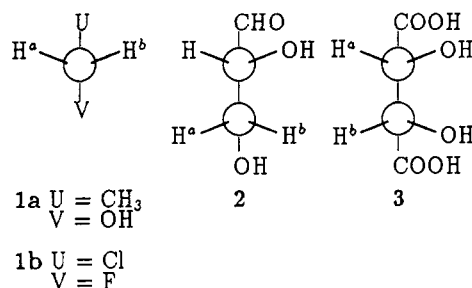


Figure 1. Molecules exemplifying the IUPAC rule.

Although **1a** and **2** (strictly their methylene carbons) are both prochiral under rule b, they are thoroughly different in the stereochemical sense. **1a** can be converted into a chiral compound only if an appropriate attack of a chiral reagent takes place. On the other hand, **2** requires no chiral reagents to afford one of two diastereomers. These different behaviors under chiral and achiral environments should be precisely characterized for comprehending stereochemistry. Thus, for the purpose of performing asymmetric syntheses, it is a critical factor to know whether a chiral reagent is necessary or not. In this meaning, the conventional usage of prochirality in the sense of rule b would provide us with undesired confusion.

Moreover, *meso*-tartaric acid **3** is a trouble-making example for the prochirality of rule b. This compound is achiral and prochiral in the light of rule a, since substitution of one of the two enantiotopic hydrogens on C-2 or C-3 (H^a or H^b) by an appropriate atom breaks the degeneracy and produces a chiral molecule. However, the compound (**3**) is not prochiral in the light of the IUPAC rule b and Hanson's definition, because the molecule (**3**) has no prochiral centers; both C-2 and C-3 are chiral centers with inverse configurations.

1 and **3** thus afford different results under rule b. This differentiation is by no means rational in stereochemical sense. Thus, Mislow and Siegel⁴ has pointed out that the phenomenon concerning **3** is precisely what happens when a similar replacement of H^a or H^b takes place on the prochiral center of chlorofluoromethane (**1b**).

The above discussions indicate that the prochirality of rule b should be replaced by the term of stereogenicity and that the prochirality of rule a should be maintained. In agreement of this conclusion, Mislow and Siegel⁴ have discussed the prochirality concept, where they proposed the concept of chirotopicity. They have also proposed (pro) P -chirality, which has been modified by Halevi.⁵

molecule	rule a	rule b
1a,b	prochiral	prochiral
2		prochiral
3	prochiral	

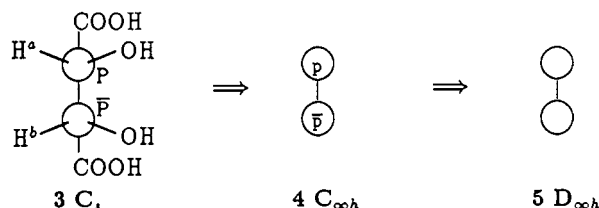


Figure 2. Molecule, promolecule, and skeleton.

In a previous paper,⁶ we have discussed the chirality fittingness (sphericity) of an orbit, where prochirality was ascribed to the *enantiosphericity* of an orbit. We have afforded theoretical foundation of the renewed prochirality and proposed the concept of chirogenic site, where we have mainly discussed rigid molecules.⁷

For characterizing the prochirality of a nonrigid molecule, we have introduced a useful method based on the concepts of *proligand* and *promolecule*.⁸ This method has allowed us to deal with promolecules having a tetrahedral skeleton or an allene skeleton. Since this method uses finite group theory, some modification is necessary in order that the method is applied to stereochemical problems on such compounds as *meso*-tartaric acid. This issue is the main subject of the present paper, where we present two methods that are capable of treating infinite groups.

MANUAL ENUMERATION OF PROMOLECULES

According to the previous definition,⁸ a proligand is regarded as a hypothetical ligand that is structureless but has chirality (or achirality); thereby, a promolecule is considered to be a three-dimensional (3D) object that consists of a rigid skeleton and such proligands. The previous treatment is concerned with cases in which the skeleton has a central atom and belongs to a point group of finite order. On the other hand, the present one deals with other cases in which such a skeleton has a central bond and belongs to a point group of infinite order.

Let us consider *meso*-tartaric acid (3). This compound has conformers due to internal rotation around the central bond (Figure 2); the highest attainable symmetry of 3 is C_s or C_i . When we replace the two $\text{CH}(\text{OH})\text{COOH}$ ligands (P and \bar{P}) by proligands (p and \bar{p}) that are antipodal to each other, we obtain the corresponding promolecule (4) of $C_{\infty h}$ symmetry. The promolecule 4 is in turn considered to be constructed from $D_{\infty h}$ -skeleton 5 and the proligands. Since these 3D objects belong to groups of infinite order, the previous treatment for finite cases⁸ should be extended to hold for the present case.

Since the two joint (terminal) positions of the $D_{\infty h}$ -skeleton (5) is fixed (or stabilized) on the action of $C_{\infty v}$, they are formally determined to belong to an orbit governed by $D_{\infty h}/C_{\infty v}$, where $|D_{\infty h}/C_{\infty v}|$ is equal to 2. The symbol $D_{\infty h}/C_{\infty v}$ denotes the coset representation (CR) derived from a coset decomposition, $D_{\infty h} = C_{\infty v} + C_{\infty v}C_2$. The CR contains (1)(2) for each element of the coset $C_{\infty v}$, and (1 2) for each element of the coset $C_{\infty h}C_2$. The integers correspond to the two joint positions. The $C_{\infty v}$ in the parentheses of the CR represent the local symmetry of each of the joint positions.

Let us consider the subduction of the CR by the subgroup $C_{\infty v}$, which corresponds to the derivation of a $C_{\infty v}$ molecule from the $D_{\infty h}$ skeleton. Let the symbol $D_{\infty h}/C_{\infty v} \downarrow C_{\infty v}$ denote this subduction, which is the restriction of the CR into (1)(2) for each element of $C_{\infty v}$. As a result, the two joint positions become nonequivalent to each other. Hence, we have

$$D_{\infty h}/C_{\infty v} \downarrow C_{\infty v} = 2C_{\infty v}/C_{\infty v}$$

where the local symmetry, $C_{\infty v}$, remains invariant.

Table I. Several Subductions Concerning the $D_{\infty h}/C_{\infty v}$

subduced representation	coset representation(s) generated	chirality fittingness
$D_{\infty h}/C_{\infty v} \downarrow D_{\infty h}$	$D_{\infty h}/C_{\infty v}$	homospheric
$D_{\infty h}/C_{\infty v} \downarrow C_{\infty v}$	$2C_{\infty v}/C_{\infty v}$	homospheric
$D_{\infty h}/C_{\infty v} \downarrow C_{\infty h}$	$C_{\infty h}/C_{\infty}$	enantiospheric
$D_{\infty h}/C_{\infty v} \downarrow D_{\infty}$	D_{∞}/C_{∞}	hemispheric
$D_{\infty h}/C_{\infty v} \downarrow C_{\infty}$	$2C_{\infty}/C_{\infty}$	hemispheric

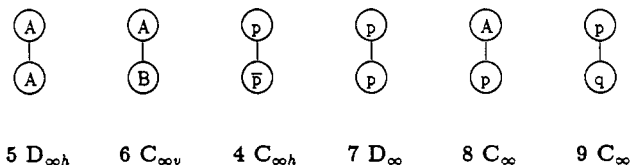


Figure 3. Promolecules based on the $D_{\infty h}$ skeleton.

Since the above derivation is rather intuitive, a more general treatment should be described for further discussions. We here use the following theorem without proof.⁹ When promolecules are derived from the skeleton, it is sufficient to take account of groups having C_{∞} as a subgroup.

Theorem 1: Let G be a finite or infinite group and G_i be a normal subgroup of G . Suppose that G_j is a subgroup of G and $|G|/|G_i|$ is a positive integer. Then we have

$$G/(G_i) \downarrow G_j = \frac{|G||G_j \cap G_i|}{|G_i||G_j|} G_j/(G_j \cap G_i) \quad (1)$$

When G_j is a subgroup of G_i , we have $G_i \cap G_j = G_j$. It follows that

$$G/(G_i) \downarrow G_j = |G|/|G_i| G_j/(G_j) (G_j \leq G_i) \quad (2)$$

In the light of Theorem 1, we have the subductions collected in Table I, where chirality fittingness is formally defined in the same line as reported.⁶ Let us consider achiral proligands (A and B), chiral proligands (p and q) and their antipodes. When the skeleton (5) is restricted to C_{∞} , the two joint positions become nonequivalent to be subject to distinct C_{∞}/C_{∞} orbits, as derived by Theorem 1 (Table I). Since the C_{∞}/C_{∞} is hemispheric, the chirality fittingness allows two promolecules, $A-p$ and $p-q$, to belong to C_{∞} symmetry. These molecules are chiral and, respectively, have $A-\bar{p}$ and $\bar{p}-q$ as antipodes.

In a similar way, we can manually enumerate six types of promolecules, which are depicted in Figure 3. Figure 3 involves three achiral promolecules, $A-A$, $A-B$, and $p-\bar{p}$.

COMBINATORIAL ENUMERATION OF PROMOLECULES

Since the manual enumeration in the preceding section is rather qualitative, a stricter and quantitative treatment is desirable to comprehend the combinatorial enumeration of such promolecules.

Combinatorial and computational enumerations of stereoisomers have long attracted the attention of organic and theoretical chemists.¹⁰⁻¹² Pólya's theorem¹³⁻¹⁸ and other methods¹⁹⁻²² have been used to solve such enumeration problems. Enumeration of nonrigid stereoisomers has also reported.^{13,23} These enumerations have dealt with itemization concerning molecular formulas only. More elaborate enumerations itemized with respect to molecular formulas as well as to symmetries have recently appeared by using various methods.²⁴⁻²⁹

We have developed alternative enumeration methods based on unit-subduced cycle indices (USCIs).^{30,31} These methods require tables of marks (or their inverses) and tables of

USCIs.³² These tables can be obtained in the cases of finite groups; they are, however, unavailable for infinite groups. Since the present case involves the $D_{\infty h}$ group of infinite order, we should modify the USCI approach so as to be capable of treating infinite groups.

Factor Groups and Coset Representations. In order to get rid of difficulties due to infinite order, we consider factor groups suitable for solving enumeration problems. The following theorem reveals the close relationship between a coset representation and a factor group.

Theorem 2: Let H be a normal subgroup of a finite or infinite G . Suppose that the symbol $G/(H)$ represents a coset representation associated with the coset decomposition of G by H , where $|G|/|H|$ is a positive integer. If g and g' are both involved in the same coset, the permutation of $G/(H)$ corresponding to g is identical with that corresponding to g' .

Proof. Let us consider the decomposition

$$G = Hg_1 + Hg_2 + \dots + Hg_r + \dots + Hg_r \quad (3)$$

where $r = |G|/|H|$. Suppose that g and g' are involved in the coset Hg_k , where $k = 1, 2, \dots, r$. Then, we can select $Eh \in H$ and $Eh' \in H$ that satisfy $g = hg_k$ and $g' = h'g_k$.

As a result, we have the following equations for any coset Hg_k :

$$Hg_j g = Hg_j hg_k = g_j H h g_k = g_j H g_k$$

$$Hg_j g' = Hg_j h' g_k = g_j H h' g_k = g_j H g_k$$

Hence, we obtain $Hg_j g = Hg_j g'$, where $j = 1, 2, \dots, r$. It follows that

$$\begin{pmatrix} Hg_1 & Hg_2 & \dots & Hg_r \\ Hg_{1g} & Hg_{2g} & \dots & Hg_{rg} \end{pmatrix} = \begin{pmatrix} Hg_1 & Hg_2 & \dots & Hg_r \\ Hg_{1g'} & Hg_{2g'} & \dots & Hg_{rg'} \end{pmatrix} \quad (4)$$

Hence, the theorem has been proved.

Theorem 2 indicates that the coset representation $G/(H)$ that contains an infinite number of permutations can be discussed by examining the regular representation (RR) of the factor group G/H of finite order. Note that the RR is represented by the symbol $K/(K_1)$, where $K = G/H$ and $K_1 = H/H$. The symbol G/H is used for designating a set of cosets

$$G/H = \{Hg_1, Hg_2, \dots, Hg_r\} \quad (5)$$

on which a coset representation $G/(H)$ acts. If the G/H constructs a factor group, we use the symbol G/H specifically to show this situation.

Consider the factor group of G modulo H , which is finite and denoted by

$$K = G/H = \{Hg_1, Hg_2, \dots, Hg_r\} \quad (6)$$

Then, it has a nonredundant set of subgroups (SSG)

$$\text{SSG} = \{K_1, K_2, \dots, K_s\} \quad (7)$$

where K_1 is an identity group and K_s is equal to K . Any K_i can be constructed by selecting an appropriate subset of K , i.e.

$$K_i = \{Hg_1, Hg_2, \dots, Hg_r\} \quad (8)$$

where $Hg_1 = Hg_1 = H$. Thereby, the following theorem can be easily proved.

Table II. Mark Table for $D_{\infty h}/C_{\infty h}(=K)^a$

	K_1	K_2
$K/(K_1)$	2	0
$K/(K_2)$	1	1

^a The subgroups are represented by $K_1 = C_{\infty}/C_{\infty h}$ and $K_2 = K = D_{\infty h}/C_{\infty h}$.

Theorem 3: Let us construct G_i by collecting all the elements involved in all of the cosets of K_i , i.e.

$$G_i = Hg_1 + Hg_2 + \dots + Hg_r \quad (\text{for } i = 1, 2, \dots, s) \quad (9)$$

(1) Then, the G_i is a subgroup of G .

(2) H is a normal subgroup of G_i .

(3) $K_i (\leq K)$ is a factor group represented by

$$K_i = G_i/H \quad (\text{for } i = 1, 2, \dots, s) \quad (10)$$

Equation 10 allows us to select the set of subgroups of G corresponding to the SSG (eq 7) as follows

$$\text{FF} = \{G_1, G_2, \dots, G_s\} \quad (11)$$

where $G_1 = H$ and $G_s = G$. We call this set of subgroups a factor family of G modulo H .

We have already presented a theorem in which a permutation representation for a finite group is reduced into several coset representations.³⁰ The counterpart of Theorem 2 of ref 30 can be proved to hold for the present case as follows.

Theorem 4: Suppose that the factor group K (eq 6) is associated the SSR (eq 7). Then, we obtain a complete set of coset representations (SCR)

$$\text{SCR} = \{K/(K_1), K/(K_2), \dots, K/(K_s)\} \quad (12)$$

which is uniquely determined except the mode of numbering. By using these coset representations, any permutation representation P_K for K can be represented by

$$P_K = \sum_{i=1}^s \hat{\alpha}_i K/(K_i) \quad (13)$$

Each multiplicity $\hat{\alpha}_i$ is a nonnegative integer and is calculated by

$$\hat{\mu}_j = \sum_{i=1}^s \hat{\alpha}_i m_{ij} \quad (j = 1, 2, \dots, s) \quad (14)$$

where $\hat{\mu}_j$ is the mark (the number of fixed points) of K_j in P_K . The symbol m_{ij} denotes the mark of G_j in $K/(K_i)$.

In the light of Theorem 4, we are able to consider an orbit corresponding each $K/(K_i)$ CR.

Example 1. First, let us examine a factor group, $D_{\infty h}/C_{\infty h}(=K)$. The corresponding SSG is determined to be

$$\text{SSG} = \{K_1, K_2\} \quad (15)$$

where $K_1 = C_{\infty h}/C_{\infty h}$ and $K_2 = K = D_{\infty h}/C_{\infty h}$. Since K is isomorphic to C_2 , we obtain a mark table for the K group (Table II). The corresponding factor family is represented by

$$\text{FF} = \{C_{\infty h}, D_{\infty h}\} \quad (16)$$

Example 2. Next, let us examine a factor group, $D_{\infty h}/C_{\infty}(=K)$. We have the corresponding SSG represented by

$$\text{SSG} = \{K_1, K_2, K_3, K_4, K_5\} \quad (17)$$

where $K_1 = C_{\infty}/C_{\infty}$, $K_2 = D_{\infty}/C_{\infty}$, $K_3 = C_{\infty v}/C_{\infty}$, $K_4 = C_{\infty h}/C_{\infty}$, and $K_5 = K = D_{\infty h}/C_{\infty}$. Since K is isomorphic to

Table III. Mark Table for $D_{\infty h}/C_{\infty}(=K)^a$

	K_1	K_2	K_3	K_4	K_5
$K/(K_1)$	4	0	0	0	0
$K/(K_2)$	2	2	0	0	0
$K/(K_3)$	2	0	2	0	0
$K/(K_4)$	2	0	0	2	0
$K/(K_5)$	1	1	1	1	1

^a The subgroups are represented by $K_1 = C_{\infty}/C_{\infty}$, $K_2 = D_{\infty}/C_{\infty}$, $K_3 = C_{\infty v}/C_{\infty}$, $K_4 = C_{\infty h}/C_{\infty}$, and $K_5 = K = D_{\infty h}/C_{\infty}$.

C_{2v} , we obtain a mark table for the K group (Table III). The corresponding factor family is represented by

$$FF = \{C_{\infty}, D_{\infty}, C_{\infty v}, C_{\infty h}, D_{\infty h}\} \quad (18)$$

Coset Representations and Orbits. Such a coset representation can be assigned to an orbit by evaluating $\hat{\mu}_j$ values, which are then introduced into eq 14 to calculate the multiplicities $\hat{\alpha}_i$. The following example illustrates the procedure of the assignment.

Example 3. Let us examine the skeleton (5) of $D_{\infty h}$ symmetry. We consider the K group defined by

$$K = D_{\infty h}/C_{\infty} = \{C_{\infty}, C_{\infty}C_2, C_{\infty}\sigma_v, C_{\infty}\sigma_h\} \quad (19)$$

which acts on the two joint (terminal) positions of 5. Our problem is to obtain the coset representation that governs the positions. A set of subgroups involved in the SSG of K is obtained as follows:

$$K_1 = C_{\infty}/C_{\infty} = \{C_{\infty}\}$$

$$K_2 = D_{\infty}/C_{\infty} = \{C_{\infty}, C_{\infty}C_2\}$$

$$K_3 = C_{\infty v}/C_{\infty} = \{C_{\infty}, C_{\infty}\sigma_v\}$$

$$K_4 = C_{\infty h}/C_{\infty} = \{C_{\infty}, C_{\infty}\sigma_h\}$$

$$K_5 = K = D_{\infty h}/C_{\infty} = \{C_{\infty}, C_{\infty}C_2, C_{\infty}\sigma_v, C_{\infty}\sigma_h\}$$

The $\hat{\mu}_j$ value is the number of fixed points (positions) on the action of the symmetry operations contained in K_j ($j = 1, 2, \dots, 5$). For example, the two points are fixed by each operation contained in K_3 (i.e., I , the infinite number of C_{∞} , or the infinite number of σ_v); hence, $\hat{\mu}_3 = 2$. Similarly, we obtain the other $\hat{\mu}_j$ values, which are collected to form a row vector (a fixed-point vector), (2 0 2 0 0). This vector is identical with the $K/(K_3)$ row of Table III. Therefore, the two positions of 5 are subject to the $K/(K_3)$ CR.

Chirality Fittingness for Factor Groups. The factor group $K(=G/H)$ is closely associated with the coset representation G/H in terms of Theorem 4. This means that the chirality fittingness concerning the G/H CR is effective in the discussion on the factor group $K(=G/H)$.

If the G/H orbit is homospheric, it accommodates achiral ligands only. This property remains unchanged in the case of the factor group $K(=G/H)$. Because H is an achiral subgroup in this case, any G_i for K_i is concluded to be an achiral subgroup of G . In other words, the corresponding FF represented by eq 11 contains achiral subgroups of G only. Thereby, $K_i(=G_i/H)$ is associated with a homospheric G_i/H orbit. It follows that the factor group of this type can be used only if we take no account of chiral ligands.

If the G/H orbit is enantiospheric or hemispheric, it accommodates achiral and chiral ligands. The corresponding factor group $K(=G/H)$ is suitable for the cases in which we take into consideration achiral ligands as well as chiral

ligands. We summarize the above discussion in the form of a theorem.

Theorem 5: The chirality fittingness concerning the factor group $K(=G/H)$ is capable of being determined if we select the H from chiral subgroups of G .

Note that the propositions in the previous papers³¹ can be regarded as special cases in which the H group is an identity group C_1 .

In the previous paper,³¹ the chirality fittingness of the $G/(G_i)$ orbit is defined as being

homospheric if both G and G_i are achiral groups

enantiospheric if G is achiral and G_i is chiral

hemispheric if both G and G_i are chiral groups

Since we have $K = G/H$ and $K_i = G_i/H$, the coset representation $K/(K_i)$ corresponds to $G/(G_i)$ in one-to-one fashion. Thereby, we have the following definition.

Definition 1: The chirality fittingness of the $K/(K_i)$ orbit is defined as being identical with that of the corresponding $G/(G_i)$ orbit.

The definition affords the following theorem.

Theorem 6: Let us consider the factor group $K(=G/H)$, in which H is a chiral subgroup of G .

(1) if the $K/(K_i)$ orbit is homospheric, it accommodates $|K|/|K_i|$ achiral ligands (or proligands) of the same kind.

(2) If the $K/(K_i)$ orbit is enantiospheric, it accommodates a set of $|K|/|K_i|$ achiral ligands of the same kind or a set of $|K|/2|K_i|$ chiral ligands of the same kind and the same number of their antipodes.

(3) If the $K/(K_i)$ orbit is hemispheric, it accommodates a set of $|K|/|K_i|$ achiral ligands of the same kind or a set of $|K|/|K_i|$ chiral ligands of the same kind.

Subduction of Coset Representations for Factor Groups. Since the factor group defined above ($K = G/H$) is a finite group, we can consider its subduction in the same line as finite groups described in the previous paper.³⁰ Thus, Corollary 2.1 of ref 30 holds for the present case.

Theorem 7: Let K be the factor group of G modulo H , which is associated with the SSR represented by eq 7. The subduction of $K/(K_i)$ by K_j is represented by

$$K/(K_i) \downarrow K_j = \sum_{k=1}^{v_j} \hat{\beta}_k^{(ij)} K_j/(K_k^{(ij)}) \quad (20)$$

for $i = 1, 2, \dots, s$ and $j = 1, 2, \dots, s$ where $K_k^{(ij)}$ is selected from the SSR of K_j

$$SSR_{K_j} = \{K_1^{(j)}, K_1^{(j)}, \dots, K_{v_j}^{(j)}\} \quad (21)$$

Each multiplicity $\hat{\beta}_k^{(ij)}$ is a nonnegative integer calculated by

$$\hat{\nu}_l^{(i)} = \sum_{k=1}^{v_j} \hat{\beta}_k^{(ij)} m_{kl}^{(ij)} \quad (22)$$

for $l = 1, 2, \dots, v_j$, where $\hat{\nu}_l^{(i)}$ is the mark of $K_l^{(i)}$ in $K/(K_i) \downarrow K_j$.

Since the $K_j(=G_j/H)$ is a factor group, its subgroup $K_k^{(j)}(=G_k^{(j)}/H)$ is also a factor group in the light of Theorem

3. A suborbit governed by $K_j/(K_k^{(j)})$ has the length represented by

$$d_{jk} = |K_j|/|K_k^{(j)}| \quad (23)$$

In agreement with Definition 1, we can use the chirality fittingness of $K_j/(K_k^{(j)})$. Thereby, we are able to define unit-subduced cycle indices (USCIs) and unit-subduced cycle indices with chirality fittingness (USCI-CFs) for such a factor group as K

Definition 2: (USCIs and USCI-CFs for Factor Groups)

(1) A unit-subduced cycle index (USCI) for the factor group K is defined by

$$Z(K/(K_i) \downarrow K_j; s_{d_{jk}}) = \prod_{k=1}^{v_j} s_{d_{jk}} \hat{\beta}_k^{(j,k)} \quad (24)$$

for $i = 1, 2, \dots, s$ and $j = 1, 2, \dots, s$.

(2) A unit-subduced cycle index with chirality fittingness (USCI-CF) for the factor group K is defined by

$$ZC(K/(K_i) \downarrow K_j; \$_{d_{jk}}) = \prod_{k=1}^{v_j} \$_{d_{jk}} \hat{\beta}_k^{(j,k)} \quad (25)$$

for $i = 1, 2, \dots, s$ and $j = 1, 2, \dots, s$, where $\$ = a$ for a homospheric orbit, $\$ = b$ for a hemispheric orbit, and $\$ = c$ for an enantiospheric orbit in the light of Definition 1.

Example 4. Since $K(=D_{\infty h}/C_{\infty})$ is isomorphic to C_{2v} , we can obtain the table of USCI-CFs for the K group (Table IV).³² Note that the $K/(K_3)$ row stems from the following subductions:

$$K/(K_3) \downarrow K_1 = 2K_1/(K_1) \quad \text{two hemispheric orbits} \quad (26a)$$

$$K/(K_3) \downarrow K_2 = K_2/(K_1) \quad \text{a hemispheric orbit} \quad (26b)$$

$$K/(K_3) \downarrow K_3 = 2K_3/(K_3) \quad \text{two homospheric orbits} \quad (26c)$$

$$K/(K_3) \downarrow K_4 = K_4/(K_1) \quad \text{an enantiospheric orbit} \quad (26d)$$

$$K/(K_3) \downarrow K_5 = K_5/(K_3) \quad \text{a homospheric orbit} \quad (26e)$$

Combinatorial Enumeration. In the light of the USCIs or the USCI-CFs defined for the present case, the procedure described in the previous paper^{30,31} can be applied to enumeration problems based on factor groups. In the same line as Definition 3 of ref 30 and Definition 3 of ref 31, we present the definition of subduced cycle indices (SCIs) for factor groups.

Definition 3: (SCIs and SCI-CFs for Factor Groups)

(1) A subduced cycle index (SCI) is represented by

$$ZI(K_i; s_{d_{jk}}^{(i\alpha)}) = \prod_{i=1}^s \prod_{\alpha=1}^{\alpha_i} Z(K/(K_i) \downarrow K_j; s_{d_{jk}}^{(i\alpha)}) \quad (27)$$

for $j = 1, 2, \dots, s$, where the superscript $(i\alpha)$ represents the assignment of each orbit.

(2) A subduced cycle index with chirality fittingness (SCI-CF) is represented by

$$ZIC(K_i; \$_{d_{jk}}^{(i\alpha)}) = \prod_{i=1}^s \prod_{\alpha=1}^{\alpha_i} ZC(K/(K_i) \downarrow K_j; \$_{d_{jk}}^{(i\alpha)}) \quad (28)$$

for $j = 1, 2, \dots, s$, where the superscript $(i\alpha)$ represents the assignment of each orbit.

In ref 30, we have proved propositions (Lemma 1 and Theorem 4) for combinatorial enumeration. By using the SCIs defined in Definition 3, the counterparts of the pro-

positions can be proved to hold for the present enumeration in which the groups at issue are factor groups. In a similar way, these SCI-CFs are capable of enumerating promolecules with achiral and chiral proligands, since the counterparts of Lemma 2 and Theorem 3 in ref 31 can be proved to be true for this enumeration.

The following example illustrates the present procedure.

Example 5. We here enumerate promolecules based on the skeleton (**5**), where substituents on the two joint positions of **5** are selected from achiral proligands (A and B), chiral proligands (p and q) and their antipodes (\bar{p} and \bar{q}). The two joint positions construct an orbit governed by the $K/(K_3)$ CR, as shown in example 3. Hence, we adopt the USCI-CFs in the $K/(K_3)$ row of Table IV. In the present case, there is only one orbit; and hence, each of the USCI-CFs constructs the subduced cycle index for each subgroup of K .

$$K_1 = C_{\infty}/C_{\infty}: b_1^2 = (A + B + p + \bar{p} + q + \bar{q})^2 \quad (29a)$$

$$K_2 = D_{\infty}/C_{\infty}: b_2 = A^2 + B^2 + p^2 + \bar{p}^2 + q^2 + \bar{q}^2 \quad (29b)$$

$$K_3 = C_{\infty v}/C_{\infty}: a_1^2 = (A + B)^2 \quad (29c)$$

$$K_4 = C_{\infty h}/C_{\infty}: c_2 = A^2 + B^2 + 2(p\bar{p} + q\bar{q}) \quad (29d)$$

$$K_5 = D_{\infty h}/C_{\infty}: a_2 = A^2 + B^2 \quad (29e)$$

In these equations, we use ligand inventories represented by

$$a_d = A^d + B^d \quad (30a)$$

$$b_d = A^d + B^d + p^d + \bar{p}^d + q^d + \bar{q}^d \quad (30b)$$

$$c_d = A^d + B^d + 2[(p\bar{p})^{d/2} + (q\bar{q})^{d/2}] \quad (30c)$$

Equations 29a–29e are expanded and the coefficients of resulting terms are collected to form a matrix, which is multiplied by the inverse matrix of Table III. Then we obtain

$$\begin{matrix} & K_1 & K_2 & K_3 & K_4 & K_5 \\ \begin{matrix} A^2 \\ AB \\ p\bar{p} \\ p^2 + \bar{p}^2 \\ Ap + A\bar{p} \\ pq + p\bar{q} \end{matrix} & \begin{pmatrix} 1 & 1 & 1 & 1 & 1 \\ 2 & 0 & 2 & 0 & 0 \\ 2 & 0 & 0 & 2 & 0 \\ 2 & 2 & 0 & 0 & 0 \\ 4 & 0 & 0 & 0 & 0 \\ 4 & 0 & 0 & 0 & 0 \end{pmatrix} \end{matrix} \times$$

$$\begin{pmatrix} 1/4 & 0 & 0 & 0 & 0 \\ -1/4 & 1/2 & 0 & 0 & 0 \\ -1/4 & 0 & 1/2 & 0 & 0 \\ -1/4 & 0 & 0 & 1/2 & 0 \\ 1/2 & -1/2 & -1/2 & -1/2 & 1 \end{pmatrix} =$$

$$\begin{matrix} & K_1 & K_2 & K_3 & K_4 & K_5 \\ \begin{matrix} A^2 \\ AB \\ p\bar{p} \\ p^2 + \bar{p}^2 \\ Ap + A\bar{p} \\ pq + p\bar{q} \end{matrix} & \begin{pmatrix} 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 \end{pmatrix} \end{matrix} \quad (31)$$

wherein the second matrix is the inverse. For simplicity's sake, we adopt an appropriate term representative for pro-

Table IV. Table of USCI-CFs for $D_{\infty h}/C_{\infty}(=K)^a$

	$\downarrow K_1$	$\downarrow K_2$	$\downarrow K_3$	$\downarrow K_4$	$\downarrow K_5$
$K/(K_1)$	b_1^4	b_2^2	c_2^2	c_2^2	c_4
$K/(K_2)$	b_1^2	b_1^2	c_2	c_2	c_2
$K/(K_3)$	b_1^2	b_2	a_1^2	c_2	a_2
$K/(K_4)$	b_1^2	b_2	c_2	a_1^2	a_2
$K/(K_4)$	b_1	b_1	a_1	a_1	a_1

^a The subgroups are represented by $K_1 = C_{\infty}/C_{\infty}$, $K_2 = D_{\infty}/C_{\infty}$, $K_3 = C_{\infty v}/C_{\infty}$, $K_4 = C_{\infty h}/C_{\infty}$, and $K_5 = K = C_{\infty h}/C_{\infty}$.

molecules with formulas equivalent chemically; e.g., A^2 is used for A^2 and B^2 . The last matrix of eq 31 affords the number of promolecules with a given formula and symmetry, which appears at the corresponding intersection. For example, there is one promolecule with AB that belongs to K_3 symmetry. Note that $K_3 = C_{\infty v}/C_{\infty}$.

Equation 31 in example 5 shows that there are six types of promolecules, which have been depicted in Figure 3. This enumeration is strictly controlled by eqs 26a–26e. Thus, the two proligands of each promolecule in Figure 3 satisfy the chirality fittingness determined by Definition 1. For example, $K_4/(K_1)$ in eq 26d corresponds to $C_{\infty h}/C_{\infty}$ because of $K_4 = C_{\infty h}/C_{\infty}$ and $K_1 = C_{\infty}/C_{\infty}$. This means that the $K_4/(K_1)$ CR is enantiospheric. The latter fact is equivalent to the $\downarrow C_{\infty h}$ row of Table I that has been obtained in the light of Theorem 1.

COMBINATORIAL ENUMERATION OF MOLECULES

In the previous sections, we take account of proligands (A , B , p , q , and their antipodes) to produce a promolecule. When such proligands are replaced by appropriate ligands, the promolecule is converted into a molecule. For simplicity's sake, suppose that each of the proligands is replaced by a ligand which is derived from a methyl group by substituting appropriate atoms (U , V , W , X , Y , or Z) for the three hydrogens. This enumeration is equivalent to an enumeration problem in which the six hydrogens of ethane are replaced by the atoms. Note that free rotation is permitted around the central bond of the ethylene molecule. The total number of isomers derived from ethane has been reported, but the result is not itemized with respect to symmetries.³³

The three hydrogen atoms of the methyl group construct an orbit governed by C_{3v}/C_3 . Hence, we obtain the following SCIs, where we take no account of chirality fittingness:

$$C_1: s_1^3 = (U + V + W + X + Y + Z)^3 \quad (32a)$$

$$C_3: s_1 s_2 = (U + V + W + X + Y + Z)(U^2 + V^2 + W^2 + X^2 + Y^2 + Z^2) \quad (32b)$$

$$C_3: s_3 = U^3 + V^3 + W^3 + X^3 + Y^3 + Z^3 \quad (32c)$$

$$C_{3v}: s_3 = U^3 + V^3 + W^3 + X^3 + Y^3 + Z^3 \quad (32d)$$

These generating functions are expanded, and the coefficients of the resulting terms are collected to form a matrix. This matrix is multiplied by the inverse of a mark table for C_{3v} , i.e.

$$\begin{matrix} & C_1 & C_3 & C_3 & C_{3v} \\ U^3, \text{ etc.} & \begin{pmatrix} 1 & 1 & 1 & 1 \\ 3 & 1 & 0 & 0 \\ 6 & 0 & 0 & 0 \end{pmatrix} \times \\ U^2 V, \text{ etc.} & \\ UVW, \text{ etc.} & \end{matrix} \begin{pmatrix} 1/6 & 0 & 0 & 0 \\ -1/2 & 1 & 0 & 0 \\ -1/6 & 0 & 1/2 & 0 \\ 1/2 & -1 & -1/2 & 1 \end{pmatrix} =$$

$$\begin{matrix} & C_1 & C_3 & C_3 & C_{3v} \\ U^3, \text{ etc.} & \begin{pmatrix} 0 & 0 & 0 & 1 \\ 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 \end{pmatrix} \\ U^2 V, \text{ etc.} & \\ UVW, \text{ etc.} & \end{matrix} \quad (33)$$

wherein the second matrix is the inverse.

In Appendix 2 of ref 34, we have proved Lemma 3 for enumerating molecules having rotatable ligands. The counterpart of this lemma can be proved to be true for the present case in which the groups at issue are factor groups. Hence, we obtain the following figure inventories by using eq 33.

$$a_d = (U^3 + V^3 + \dots) + [(U^2 V)^d + (U^2 W)^d + \dots] \quad (34a)$$

$$b_d = (U^3 + V^3 + \dots) + [(U^2 V)^d + (U^2 W)^d + \dots] + 2[(UVW)^d + (UVX)^d + \dots] \quad (34b)$$

$$c_d = (U^3 + V^3 + \dots) + [(U^2 V)^d + (U^2 W)^d + \dots] + 2[(UVW)^d + (UVX)^d + \dots] \quad (34c)$$

These figure inventories are used in place of eqs 30a–30c. Thereby, the counterparts for eqs 29a–29e are obtained as follows:

$$K_1 = C_{\infty}/C_{\infty}: b_1^2 = [(U^3 + V^3 + \dots) + (U^2 V + U^2 W + \dots) + 2(UVW + \dots)]^2 \quad (35a)$$

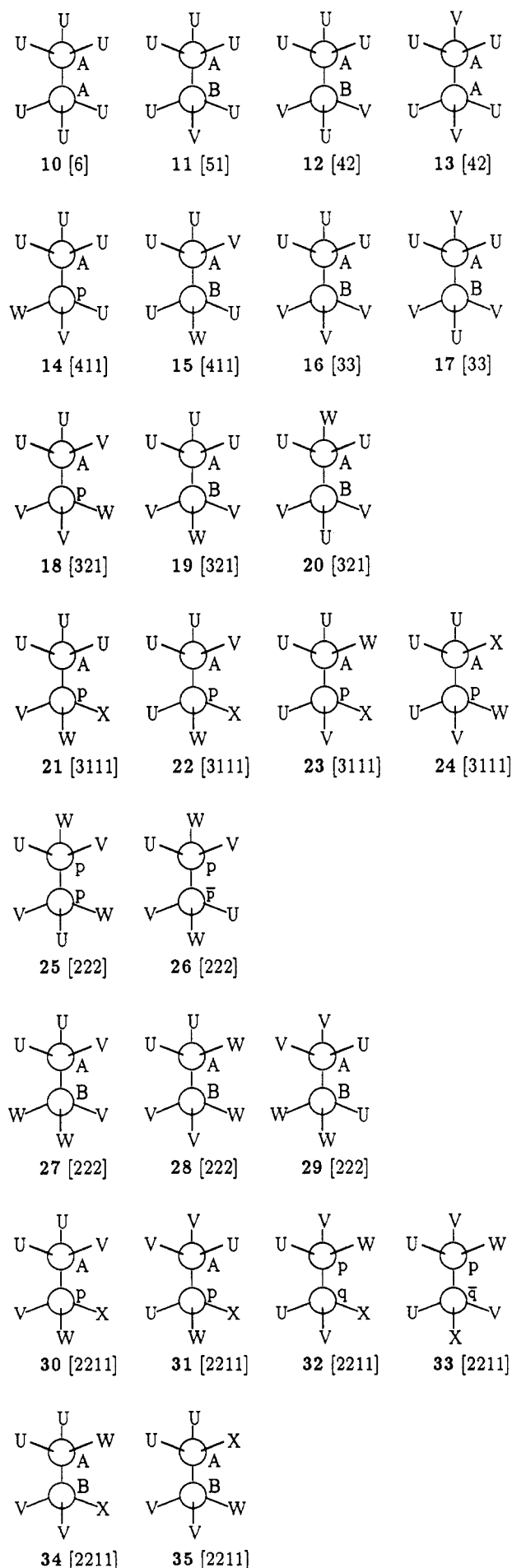
$$K_2 = D_{\infty}/C_{\infty}: b_2 = (U^6 + V^6 + \dots) + (U^4 V^2 + U^4 W^2 + \dots) + 2(U^2 V^2 W^2 + \dots) \quad (35b)$$

$$K_3 = C_{\infty v}/C_{\infty}: a_1^2 = [(U^3 + V^3 + \dots) + (U^2 V + U^2 W + \dots)]^2 \quad (35c)$$

$$K_4 = C_{\infty h}/C_{\infty}: c_2 = (U^6 + V^6 + \dots) + (U^4 V^2 + U^4 W^2 + \dots) + 2(U^2 V^2 W^2 + \dots) \quad (35d)$$

$$K_5 = D_{\infty h}/C_{\infty}: a_2 = (U^6 + V^6 + \dots) + (U^4 V^2 + U^4 W^2 + \dots) \quad (35e)$$

After expanding each of these generating functions, we collect the coefficient of the term $U^u V^v W^w X^x Y^y Z^z$ to form a fixed-point matrix, which is found as the first matrix in eq 36. For simplicity's sake, we use the partition $[uvwxyz]$ corresponding to the $U^u V^v W^w X^x Y^y Z^z$ term, where we omit each zero term and presume $u \geq v \geq w \geq x \geq y \geq z$ without losing generality. For example, we use the partition $[3111]$ in place of $U^3 V W X$, $U^3 V W Y$, etc. The fixed-point matrix is multiplied by the inverse of the mark table for the K group. The resulting

Figure 4. Molecules based on the D_{3h} skeleton.

matrix affords the number of molecules with a given partition and symmetry K_i at the corresponding intersection.

$$\begin{array}{c}
 \begin{array}{c}
 K_1 \quad K_2 \quad K_3 \quad K_4 \quad K_5 \\
 \begin{array}{c}
 [6] \\
 [51] \\
 [42] \\
 [411] \\
 [33] \\
 [321] \\
 [3111] \\
 [222] \\
 [2211] \\
 [21111] \\
 [111111]
 \end{array}
 \end{array}
 \begin{pmatrix}
 1 & 1 & 1 & 1 & 1 \\
 2 & 0 & 2 & 0 & 0 \\
 3 & 1 & 3 & 1 & 1 \\
 6 & 0 & 2 & 0 & 0 \\
 4 & 0 & 4 & 0 & 0 \\
 8 & 0 & 4 & 0 & 0 \\
 16 & 0 & 0 & 0 & 0 \\
 10 & 2 & 6 & 2 & 0 \\
 20 & 0 & 4 & 0 & 0 \\
 40 & 0 & 0 & 0 & 0 \\
 80 & 0 & 0 & 0 & 0
 \end{pmatrix}
 \begin{pmatrix}
 1/4 & 0 & 0 & 0 & 0 \\
 -1/4 & 1/2 & 0 & 0 & 0 \\
 -1/4 & 0 & 1/2 & 0 & 0 \\
 -1/4 & 0 & 0 & 1/2 & 0 \\
 1/2 & -1/2 & -1/2 & -1/2 & 1
 \end{pmatrix}
 =
 \begin{array}{c}
 \begin{array}{c}
 K_1 \quad K_2 \quad K_3 \quad K_4 \quad K_5 \\
 \begin{array}{c}
 [6] \\
 [51] \\
 [42] \\
 [411] \\
 [33] \\
 [321] \\
 [3111] \\
 [222] \\
 [2211] \\
 [21111] \\
 [111111]
 \end{array}
 \end{array}
 \begin{pmatrix}
 0 & 0 & 0 & 0 & 1 \\
 0 & 0 & 1 & 0 & 0 \\
 0 & 0 & 1 & 0 & 1 \\
 1 & 0 & 1 & 0 & 0 \\
 0 & 0 & 2 & 0 & 0 \\
 1 & 0 & 2 & 0 & 0 \\
 4 & 0 & 0 & 0 & 0 \\
 0 & 1 & 3 & 1 & 0 \\
 4 & 0 & 2 & 0 & 0 \\
 10 & 0 & 0 & 0 & 0 \\
 20 & 0 & 0 & 0 & 0
 \end{pmatrix}
 \end{array}
 \quad (36)$$

For illustrating this enumeration, Figure 4 depicts molecules enumerated by eq 36 except those of [21111] and [111111]. Note that an arbitrary enantiomer is depicted for each racemic pair of enantiomers.

DISCUSSION

Promolecules and Molecules. Let us first compare eq 31 with eq 36. For example, there exists one promolecule of K_5 symmetry, which belongs to the $A-A$ type, as found in eq 31. The promolecule is related to the molecules that appear at the intersections between the K_5 column and the first row (the [6] partition) and between the same column and the third row (the [42] partition) in the last matrix of eq 36. This fact can be verified with the corresponding structures 10 and 13 depicted in Figure 4.

For the systematic verification of such correlation, ligands in the molecules (10–35) are classified into achiral ones (U^3 in 10, U^2V in 11, etc.) and chiral ones (UVW in 14, UVX in 23, etc.). This classification is designated by the symbols beside the two small circles in each molecule depicted in Figure 4. Thus, we use the symbol A or B for designating an achiral proligand and p , \bar{p} , q , or \bar{q} for denoting a chiral proligand. Thereby, the molecules in Figure 4 are classified into either of the six promolecules depicted in Figure 3. The results are collected in Table V.

Prochirality as Promolecules. Table VI collects the chirality fittingness of each orbit involved in the promolecules

Table V. Promolecules and Molecules

promolecule	symmetry	partition	formula	molecule
$A-A$	K_5	[6]	U^6	10
		[42]	U^4V^2	13
$A-B$	K_3	[51]	U^5V	11
		[42]	U^4V^2	12
		[411]	U^4VW	15
		[33]	U^3V^3	16, 17
		[321]	U^3V^2W	19, 20
		[222]	$U^2V^2W^2$	27, 28, 29
		[2211]	U^2V^2WX	34, 35
		[222]	$U^2V^2W^2$	26
$p-\bar{p}$	K_4	[222]	$U^2V^2W^2$	25
$p-p$	K_2	[222]	$U^2V^2W^2$	25
$A-p$	K_1	[411]	U^4VW	14
		[321]	U^3V^2W	18
		[3111]	U^3VWX	21, 22, 23, 24
		[2211]	U^2V^2WX	30, 31
$p-q$	K_1	[2211]	U^2V^2WX	32, 33

Table VI. Orbits in Promolecules

promolecule	orbit(s) (infinite point group)	orbit(s) (finite factor group)	chirality fittingness
$A-A$	$D_{\infty h}/C_{\infty v}$	$K_5/(K_3)$	homospheric
$A-B$	$2C_{\infty v}/C_{\infty v}$	$2K_3/(K_3)$	homospheric
$p-\bar{p}$	$C_{\infty h}/C_{\infty}$	$K_4/(K_1)$	enantiospheric
$p-p$	D_{∞}/C_{∞}	$K_2/(K_1)$	hemispheric
$A-q$	$2C_{\infty}/C_{\infty}$	$2K_1/(K_1)$	hemispheric
$p-q$	$2C_{\infty}/C_{\infty}$	$2K_1/(K_1)$	hemispheric

enumerated by eq 31. This conclusion is obtained by means of the coset representation that governs an orbit derived from the corresponding infinite point group. The same conclusion is alternatively obtained through the counterpart using a factor group. For example, the $A-A$ promolecule has a $D_{\infty h}/C_{\infty v}$ orbit, which is homospheric. This is alternatively concluded by means of the corresponding $K_5/(K_3)$ CR, which is homospheric because of $K_5 = D_{\infty h}/C_{\infty}$ and $K_3 = C_{\infty v}/C_{\infty}$ in the light of Definition 1.

Since the $p-\bar{p}$ promolecule has one enantiospheric orbit, it is concluded to be prochiral. The promolecule generally represents a meso-type compound. Although the corresponding molecule 26 has several conformers, the prochirality of 26 is determined by means of $p-\bar{p}$ without examining the conformers. Thus, meso-tartaric acid represented by the general formula 26 is concluded to be prochiral in the level of a promolecule.

We have called a ligand-in-isolation a *fragment*; and a ligand-in-molecule is referred to as a *segment* in order to characterize the process of such incorporation of ligands more strictly.^{4,6} In the present paper, we also use the terms for designating the state of proligands. As fragments, achiral proligands can be considered to belong to $C_{\infty v}$, and chiral proligands are regarded as belonging to C_{∞} . These symmetries are compatible with the local symmetries found in Table VI and are concluded to be maintained as segments.

Prochirality as Molecules. If a promolecule is achiral, then the corresponding molecule is achiral; and the converse is true. If a promolecule is prochiral, then the corresponding molecule is prochiral; however, the converse is not always true. Hence, the question cannot be answered in the level of promolecules: Are the remaining two achiral promolecules ($A-A$ and $A-B$) prochiral or not? In this section, we will solve this question.

For discussing the prochirality of molecules having rotatable ligands, the following methodologies have been proposed.

1. Methods postulating a fixed conformer:

- (a) Direct method based on IUPAC rule E-4.12(a)¹

(b) Method based on chirotopic and achirotopic segments⁴

(c) Method based on an enantiospheric orbit⁶

(d) Method based on the induction of local orbits to global orbits^{35,36}

2. Method based on the concept of promolecule⁸

The methods 1a–1d postulate a fixed conformer of the highest attainable symmetry; hence, they are direct applications of the corresponding methods for determining the prochirality of rigid molecules. For example, the prochirality of molecule 13 is determined by method 1c as follows. If we regard the depicted structure (13) as a fixed conformer of C_{2h} symmetry, we find that the two V 's belong to C_{2h}/C_s and the four U 's belong to C_{2h}/C_1 . The C_{2h}/C_1 orbit is enantiospheric so that 13 is prochiral.

The same conclusion is obtained by means of method 1d. Thus, we find that the two local orbits (C_s/C_s and C_s/C_1) in each ligand are induced into C_{2h}/C_s for V^2 and C_{2h}/C_1 for U^4 , the latter of which is a basis for determining the prochirality of 13. We can select an eclipsed conformer of C_{2v} symmetry for this examination; the conclusion is true for such selection. Note that the principal axes of these conformers are perpendicular to the respective central bonds.

Strictly speaking, a conclusion by each of the methods 1a–1d is concerned with a fixed conformer, not with a molecule having rotatable ligands. In the same line, the concept of promolecule for method 2⁸ has originally been described in such a manner that a promolecule is related to a fixed conformer of the highest attainable symmetry.

By the original version of method 2, the prochirality of 13 can be concluded as follows. The corresponding promolecule ($A-A$) has a $D_{\infty h}/C_{\infty v}$ orbit. Since the local symmetry is modified in the light of $C_{\infty v} \cap C_s$, the $D_{\infty h}$ symmetry of the promolecule is restricted so as to satisfy the modified local symmetry (C_s). Hence, the symmetry of 13 as a fixed conformer is determined to be C_{2h} (or C_{2v}); the joint positions construct an orbit governed by C_{2h}/C_s . As a result, the infraorbitals (in the fragment) produce two local orbits (in the segment),^{35,36} C_s/C_s for V and C_s/C_1 for U^2 , where no restrictions emerge. Then these local orbits construct the corresponding global orbits (in the molecule),^{35,36} i.e., C_{2h}/C_s and C_{2h}/C_1 . The C_{2h}/C_1 orbit causes prochirality. This result is identical to the above one derived by method 1d. Note that we have applied the following criterion to the above case: when a proligand is substituted by a ligand, the local symmetry of the proligand as a segment controls the symmetry of the ligand as segment. So long as we use method 2 in the original version, it is essentially equivalent to method 1d.

In order to take account of free rotation more strictly, we should use method 2 after substantial extension, where we intend to relate a promolecule to a molecule having rotatable ligands, not to a fixed conformer. For this purpose, we presume another criterion:

When a proligand is substituted by a ligand, the local chirality/achirality of the proligand as a segment (not the local symmetry itself) controls the symmetry of the ligand as segment.

Thereby, the determination by method 2 requires no tentative consideration of such a fixed conformer.

Let us examine molecule 13, which is considered to be derived from an $A-A$ promolecule. Molecule 13 is characterized to have a [42] partition and K_5 symmetry. This molecule contains two U^2V ligands of C_s symmetry in isolation, each of which consists of two infraorbitals,³⁵ C_s/C_s for V and C_s/C_1 for U^2 .

When the ligands are introduced in the molecule, they are restricted by the local achirality of the joint positions in the $A-A$ promolecule; the local achirality is associated with the $C_{\infty v}$ group that is involved in the $D_{\infty h}/C_{\infty v}$ CR. Since C_s and $C_{\infty v}$ are both achiral, there emerges no restrictions in agreement with the criterion. As a result, the infraorbitals (in the ligand as a fragment) produce two local orbits (in the ligand as a segment),^{35,36} i.e., $C_s/(C_s)$ for V and $C_s/(C_1)$ for U^2 . They are, however, considered not to be induced into global orbits in order to assure free rotation of the ligands. The resulting molecule (13) can be represented by the symbol $D_{\infty h}/C_{\infty v}$ [$2[C_s/(C_1), C_s/(C_s)]$]. In the same line as the SCR (set-of-coset-representation) notation reported for rigid molecules,^{37,32} 13 is designated by the symbol $D_{\infty h}/C_{\infty v}$ [$2C_s/[C_1(U_2), /C_s(V)]$], which is called an EWP (extended wreath product) notation.³⁸ This notation contains the CR symbols for the promolecule as well as the CR symbols for the ligands incorporated, where each of the ligand symmetries is restricted so as to match the local chirality/achirality of the promolecule. Note that the usage of the original symbol for the promolecule $D_{\infty h}/C_{\infty v}$ is to indicate the internal rotation of the molecule. The power of the mathematical term U^2 is here replaced by the subscript in accordance with the chemical convention.

In the light of this model, the resulting local orbit ($C_s/(C_1)$ for U^2) is enantiospheric; this fact indicates that 13 is prochiral. In general, if there emerges at least one enantiospheric (or hemispheric) local orbit, the resulting achiral molecule is concluded to be prochiral.

Let us next examine molecule 11, which is derived from the achiral $A-B$ promolecule. The promolecule has two $C_{\infty v}/(C_{\infty v})$ orbits. For converting the promolecule into the molecule 11, we substitute a U^2V ligand and a U^3 ligand for A and B , where their symmetries are C_s and C_{3v} as fragments.

Since C_s and C_{3v} are achiral and compatible with the local achirality ($C_{\infty v}$) at A and B , the C_s fragment produces two local orbits in the corresponding segment, i.e., $C_s/(C_s)$ (for V) and $C_s/(C_1)$ (for U^2); and the C_{3v} fragment creates one local orbit $C_{3v}/(C_s)$ (for U^3).

The resulting molecule (11) can be represented by the symbol $C_{\infty v}/C_{\infty v}$ [$C_s/(C_1), C_s/(C_s)]-C_{\infty v}/C_{\infty v}$ [$C_{3v}/(C_s)$]. Thereby, the EWP notation for 11 is $C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(U_2), /C_s(V)]-C_{\infty v}/C_{\infty v}$ [$C_{3v}/[C_s(U_3)]$]. The local orbit ($C_s/(C_1)$ for U^2) is enantiospheric; this fact provides us with the conclusion that 11 is prochiral.

The molecule (26) of type $p-\bar{p}$ has been concluded to be prochiral in the level of a promolecule. The corresponding achiral $p-\bar{p}$ promolecule has a $C_{\infty h}/C_{\infty}$ orbit for p and \bar{p} . In place of the p and \bar{p} proligands, the molecule contains two antipodal UVW ligands of C_1 symmetry, each of which consists of three infraorbitals: $C_1/(C_1)$'s for U , V , and W .

When introduced in the molecule, they are restricted by the local chirality concerning p and \bar{p} , i.e., C_{∞} . Since the local C_{∞} group is chiral and compatible with the C_1 symmetry of the ligands, the infraorbitals can construct the corresponding local orbits without any restriction. As a result, molecule 26 can be represented by the symbol $C_{\infty h}/C_{\infty}$ [$2[C_1/(C_1), C_1/(C_1), C_1/(C_1)]$]. The EWP notation of 26 is represented to be $C_{\infty h}/C_{\infty}$ [$2C_1/[C_1(U), /C_1(V), /C_1(W)]$]. The prochirality of 26 is, thus, determined by the symbol $C_{\infty h}/C_{\infty}$ in the EWP notation.

Note that the EWP notation does not distinguish enantiomorphic p and \bar{p} . If this distinguishment should be emphasized, we can use the symbol, $C_{\infty h}/C_{\infty}$ [$C_1/[C_1(U), /C_1(V), /C_1(W)], C_1/[C_1(U), /C_1(W), /C_1(V)]$]. However,

Table VII. Prochirality as Molecules

molecule	chirality	EWP notation
10	achiral	$D_{\infty h}/C_{\infty v}$ [$2C_{3v}/[C_s(U_3)]$]
11	prochiral	$C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(U_2), /C_s(V)]-C_{\infty v}/C_{\infty v}$ [$C_{3v}/[C_s(U_3)]$]
12	prochiral	$C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(V_2), /C_s(U)]-C_{\infty v}/C_{\infty v}$ [$C_{3v}/[C_s(U_3)]$]
13	prochiral	$D_{\infty h}/C_{\infty v}$ [$2C_s/[C_1(U_2), /C_s(V)]$]
15	prochiral	$C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(U_2), /C_s(V)]-C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(U_2), /C_s(W)]$]
16	achiral	$C_{\infty v}/C_{\infty v}$ [$C_{3v}/[C_s(U_3)]-C_{\infty v}/C_{\infty v}$ [$C_{3v}/[C_s(V_3)]$]
17	prochiral	$C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(U_2), /C_s(V)]-C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(V_2), /C_s(U)]$]
19	prochiral	$C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(U_2), /C_s(W)]-C_{\infty v}/C_{\infty v}$ [$C_{3v}/[C_s(U_3)]$]
20	prochiral	$C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(U_2), /C_s(W)]-C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(V_2), /C_s(U)]$]
26	prochiral	$C_{\infty h}/C_{\infty}$ [$2C_1/[C_1(U), /C_1(V), /C_1(W)]$]
27	prochiral	$C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(U_2), /C_s(V)]-C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(W_2), /C_s(V)]$]
28	prochiral	$C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(U_2), /C_s(W)]-C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(V_2), /C_s(W)]$]
29	prochiral	$C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(V_2), /C_s(U)]-C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(W_2), /C_s(U)]$]
34	prochiral	$C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(U_2), /C_s(W)]-C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(V_2), /C_s(X)]$]
35	prochiral	$C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(U_2), /C_s(X)]-C_{\infty v}/C_{\infty v}$ [$C_s/[C_1(V_2), /C_s(W)]$]

the problem concerning the unique sequence of the local orbits is open to further investigation.

Table VII collects the results concerning the achiral molecules depicted in Figure 4. Among the achiral molecules depicted in Figure 4, only two molecules (10 and 16) are paraachiral (not prochiral).⁶ Once we obtain such EWP notations as shown in Table VII, we can determine prochirality by examining whether or not the notation contains an enantiospheric CR of any type. It should be emphasized that the enantiospheric CR detected is to be attacked by a chiral reagent for synthesizing a chiral molecule.

Comments on Chiral Molecules. Let us examine the chiral molecule (21), which is ascribed to the chiral promolecule ($A-p$). The chiral $A-p$ promolecule has two C_{∞}/C_{∞} orbits, where the local C_{∞} is a chiral group. This molecule contains a U^3 ligand (fragment) of C_{3v} symmetry having an infraorbit ($C_{3v}/(C_s)$) along with a VWX ligand (fragment) of C_1 symmetry having three infraorbitals ($C_1/(C_1)$).

In agreement of the local chirality (C_{∞}), the C_{3v} group is restricted into the corresponding maximal chiral one, C_3 . As a result, the former infraorbit produces a local orbit, $C_3/(C_1)$ for V^3 , where C_{3v} is restricted into C_3 to give $C_{3v}/(C_s) \downarrow C_3 = C_3/(C_1)$. The other C_1 ligand is compatible with the local chirality. Each of the corresponding infraorbitals produces a local orbit $C_1/(C_1)$ where there emerges no restriction. Hence, molecule 21 can be represented by the symbol, C_{∞}/C_{∞} [$C_1-[C_1(V), /C_1(W), /C_1(X)]-C_{\infty}/C_{\infty}$ [$C_3/[C_1(U_3)]$]. Note that the three U 's are subject to a $C_3/(C_1)$ orbit. This notation indicates that they are equivalent through internal rotation.

Let us consider the U^2 moiety in the U^2V ligand of 18, which corresponds to the molecule (2). As pointed out above, this would be concluded to be prochiral in light of the IUPAC rule b. The conclusion is contradicted through a discussion based on the present method. From the present point of view, the moiety is restricted according to the local chirality due to C_{∞} . Since the maximal chiral subgroup of C_s is C_1 , the above criterion indicates that the CR for the U^2 moiety is incorporated into 18 so as to satisfy $C_s/(C_1) \downarrow C_1 = 2C_1(C_1)$. This means that the two U 's in a molecule belong to distinct orbits; hence,

Table VIII. Chiral Molecules

molecule	chirality	EWP notation
14	chiral	$C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(V),/C_1(W)]]-C_{\infty}/C_{\infty}[C_3[C_1(U_3)]]$
18	chiral	$C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(V),/C_1(W)]]-C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(U),/C_1(V)]]$
21	chiral	$C_{\infty}/C_{\infty}[C_1[C_1(V),/C_1(W),/C_1(X)]]-C_{\infty}/C_{\infty}[C_3[C_1(U_3)]]$
22	chiral	$C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(U),/C_1(V)]]-C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(W),/C_1(X)]]$
23	chiral	$C_{\infty}/C_{\infty}[C_1[C_1[C_1(U),/C_1(U),/C_1(W)]]-C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(V),/C_1(X)]]$
24	chiral	$C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(U),/C_1(X)]]-C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(V),/C_1(W)]]$
25	chiral	$D_{\infty}/C_{\infty}[2C_1[C_1(U),/C_1(V),/C_1(W)]]$
30	chiral	$C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(U),/C_1(V)]]-C_{\infty}/C_{\infty}[C_1[C_1(V),/C_1(W),/C_1(X)]]$
31	chiral	$C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(V),/C_1(V)]]-C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(W),/C_1(X)]]$
32	chiral	$C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(V),/C_1(W)]]-C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(V),/C_1(X)]]$
33	chiral	$C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(V),/C_1(W)]]-C_{\infty}/C_{\infty}[C_1[C_1(U),/C_1(X),/C_1(V)]]$

they are stereochemically nonequivalent to each other. In other words, they are diastereotopic.

Among the chiral molecule depicted in Figure 4, **32** (corresponding to $p-q$) and **33** (corresponding to $p-\bar{q}$) construct a three-erythro pair; this fact is determined in the level of promolecule. In general, such diastereomeric relationship as the three-erythro one can be determined in the level of promolecule. Moreover, an enantiomeric relationship is also determined in the level of promolecule. Note that the enantiomers of **32** and **33** can be represented by $\bar{p}-\bar{q}$ and $\bar{p}-q$ as promolecules.

The relationship between **25** (corresponding to $p-p$) and **26** (corresponding to $p-\bar{p}$) represents a general case for exemplifying *racemic*- and *meso*-tartaric acid. This relationship can also be determined in the level of promolecule. The EWP notation of **25** (Table VIII) and that of **26** (Table VII) have the same ligand part but different promolecule parts.

It is worthwhile mentioning that a method of pruning trees^{39,23} is useful to obtain promolecules from molecules, where they are regarded as 3D objects rather than as graphs. Thereby, any organic compound having a straight or branched chain is reduced to a promolecule based on a tetrahedral skeleton⁸ or to the present promolecule having a $D_{\infty h}$ skeleton. For example, ethanol (**3**) can be discussed on the basis of such a promolecule having a tetrahedral skeleton; on the other hand, fluoroethane (**11**; $U = H$, $V = F$) can be examined in light of a promolecule based on a $D_{\infty h}$ skeleton.

CONCLUSION

For enumerating promolecules of a subsymmetry of $D_{\infty h}$, we have developed a method based on factor groups. This method has expanded the USCI (unit-subduced cycle index) approach to be applicable to infinite groups. Molecules based on the promolecules have also been enumerated. Their stereochemical properties, especially their prochirality, are discussed in the light of the chirality fittingness derived from coset representations.

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