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REGULAR ARTICLE

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Graphs to chemical structures 3. General theorems with the use of different sets of sphericity indices for combinatorial enumeration of nonrigid stereoisomers

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Abstract The extended sphericity indices of k-cycles, which were defined in Part 2 of this series (S. Fujita, *Theor Chem Acc*, Online: http://www.springerlink. com/index/10.1007/ s00214-004-0606-z) according to the enantiospheric, homospheric, or hemispheric nature of each k-cycle, are further extended to prove more general theorems for enumerating nonrigid stereoisomers with rotatable ligands. One of the extended points is the use of different sets of sphericity indices to treat one or more orbits contained in skeletons and ligands. Another is to take account of chirality in proligands and sub-proligands, the latter of which are introduced to consider further inner structures of ligands. Two theorems for enumerating nonrigid stereoisomers are proved by adopting two schemes of their derivation, i.e., the scheme "positions of a skeleton ⇐ proligands ⇐ ligands (positions of a ligand ⇐ sub-proligands)" and the scheme "(positions of a skeleton ⇐ proligands ⇐ ligands (positions of a ligand)) ⇐ sub-proligands". The theorems are applied to the stereoisomerism of trihydroxyglutaric acids. Thereby, it is demonstrated where Pólya's theorem and other previous methods are deficient, when applied to the enumeration of stereoisomers.

Keywords Cycle index · Chirality fittingness · Extended sphericity index · Isomer enumeration · Nonrigid stereoisomer

1 Introduction

The enumeration of the stereoisomers of trihydroxyglutaric acid (HOOC–CHOH–CHOH–CHOH–COOH) has been a representative problem which has required the detailed consideration of geniuses in the history of stereochemistry [1–3]. This problem was solved intuitively so that there existed two achiral molecules (**1** and **2**) and a pair of enantiomers (**3** and $\overline{\mathbf{3}}$) (Fig. 1). The achiral molecules (**1** and **2**) were recognized as "pseudoasymmetry", which required an exceptional treatment, as described in [4]. However, the problem has repelled systematic mathematical approaches although there appeared several pioneering studies. For example, Ugi et al. [5] applied their procedure based on the concept of chemical identity group to solve this problem. Although their procedure was straightforward, such a chemical identity group was not so easy in general to obtain as a concrete form, where, for example, the chemical identity group for trihydroxyglutaric acids was a permutation group of degree 8 and of order 18. Moreover, their approach was inadequate to treat comprehensively stereoisomers other than trihydroxyglutaric acids, because it did not take explicit account of inner structures of ligands, e.g., chirality/achirality of ligands.

Another promising mathematical approach to solve the problem is Fujita's USCI (unit-subduced-cycle-index) approach [6], in which different figure-inventories are used in the enumeration of isomers derived from nonrigid parent molecules. Although the USCI approach is versatile to give symmetry-itemized enumeration, necessary mark tables and USCI tables are not so easy to obtain. If the problems at issue do not require symmetry-itemization, methods simpler than the USCI approach would be desirable.

To solve such problems that require no symmetry-itemization, Pólya's theorem and Pólya's corona [7,8] have been used as a further promising mathematical approach. However, it was pointed out in a previous book [9] that they are insufficient to deal with chemical structures (or stereoisomers) in which both achiral and chiral ligands are taken into consideration.

As a more succinct method, Fujita [10,11] has developed the proligand method that is based on the concepts of proligand and promolecule, where sphericity indices (SIs) are used to solve such problems that take account of both achiral and chiral (pro)ligands. Although this method can solve enumeration problems, several essential improvements are necessary to properly solve problems like as the isomer enumeration of trihydroxyglutaric acids.

In this paper, Fujita's proligand method [10,11] will be extended to enable using different sets of sphericity indices

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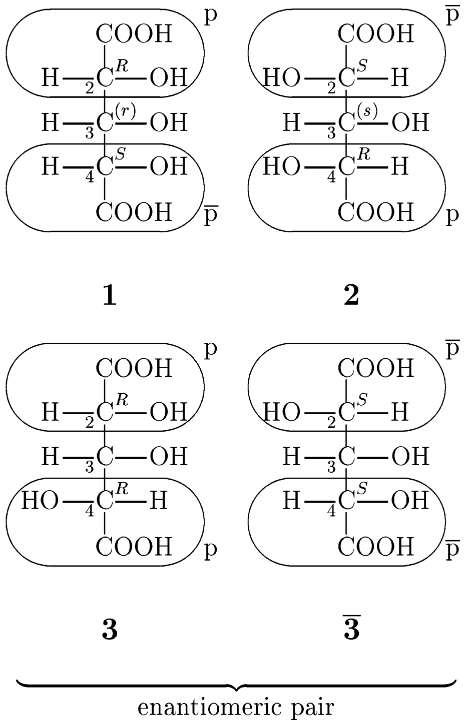


Fig. 1 Two achiral 2,3,4-trihydroxyglutaric acids (**1** and **2**) and a pair of enantiomers (**3** and $\overline{\mathbf{3}}$)

(SIs), so that two equivalence classes of positions are discriminated to accommodate different sets of ligands. In addition, further inner structures of the ligands will be considered in terms of sub-proligands so as to give several theorems for solving more complicated problems. After these extensions, the extended Fujita's proligand method will be applied to solve the enumeration problem of trihydroxyglutaric acids.

2 Enumeration of nonrigid isomers via promolecules

2.1 Enumeration of promolecules

Let $\widehat{\mathbf{G}}$ be a sum of coset representations (CRs) of a point group $\mathbf{G}$, which governs a set $\mathcal{O}$ of $\hat{n}$ positions of a skeleton. Suppose that a permutation G ($\in \widehat{\mathbf{G}}$) is represented by the following equation:

$$G = \begin{cases} g & \text{(for a proper permutation)} \\ \overline{g} & \text{(for an improper permutation)} \end{cases}$$

where

$$g = \left(\begin{matrix} \cdots \\ \cdots \end{matrix} \underbrace{\begin{vmatrix} x_1^{(\alpha)} & x_2^{(\alpha)} & \cdots & x_i^{(\alpha)} & \cdots & x_r^{(\alpha)} \\ x_{1'}^{(\alpha)} & x_{2'}^{(\alpha)} & \cdots & x_{i'}^{(\alpha)} & \cdots & x_{r'}^{(\alpha)} \end{vmatrix}}_{g^{(\alpha)}} \begin{matrix} \cdots \\ \cdots \end{matrix} \right) \tag{1}$$

$$\overline{g} = \left(\begin{matrix} \cdots \\ \cdots \end{matrix} \underbrace{\begin{vmatrix} x_1^{(\alpha)} & x_2^{(\alpha)} & \cdots & x_i^{(\alpha)} & \cdots & x_r^{(\alpha)} \\ \overline{x}_{1'}^{(\alpha)} & \overline{x}_{2'}^{(\alpha)} & \cdots & \overline{x}_{i'}^{(\alpha)} & \cdots & \overline{x}_{r'}^{(\alpha)} \end{vmatrix}}_{\overline{g}^{(\alpha)}} \begin{matrix} \cdots \\ \cdots \end{matrix} \right) \tag{2}$$

The permutation g is called "a proper permutation" because it corresponds to a proper rotation of the point group $\mathbf{G}$, while the permutation $\overline{g}^{(\alpha)}$ is called "an improper permutation" because it corresponds to an improper rotation of the point group $\mathbf{G}$. The $\hat{n}$ positions of $\mathcal{O}$ are occupied by a set of proligands. The overbar represents the inversion of the chirality of each proligand.

A CR selected from $\widehat{\mathbf{G}}$ is represented by the symbol $\widehat{\mathbf{G}}^{(\alpha)}$, which governs an orbit $\mathcal{O}_\alpha$ ($\subset \mathcal{O}$). For the sake of simplicity, the representation $\widehat{\mathbf{G}}^{(\alpha)}$ is regarded as a permutation group which governs $r^{(\alpha)}$ positions contained in the orbit:

$$\mathcal{O}_\alpha = \{x_1^{(\alpha)}, x_2^{(\alpha)}, \ldots, x_i^{(\alpha)}, \ldots, x_r^{(\alpha)}\}.$$

Thus, we place $\bigcup_\alpha \mathcal{O}_\alpha = \mathcal{O}$. Let us select a permutation $G^{(\alpha)}$ from a group $\widehat{\mathbf{G}}^{(\alpha)}$ as follows:

$$G^{(\alpha)} = \begin{cases} g^{(\alpha)} & \text{(for a proper permutation)} \\ \overline{g}^{(\alpha)} & \text{(for an improper permutation)} \end{cases}$$

where

$$g^{(\alpha)} = \begin{pmatrix} x_1^{(\alpha)} & x_2^{(\alpha)} & \cdots & x_i^{(\alpha)} & \cdots & g_r^{(\alpha)} \\ x_{1'}^{(\alpha)} & x_{2'}^{(\alpha)} & \cdots & x_{i'}^{(\alpha)} & \cdots & x_{r'}^{(\alpha)} \end{pmatrix} \tag{3}$$

$$\overline{g}^{(\alpha)} = \begin{pmatrix} x_1^{(\alpha)} & x_2^{(\alpha)} & \cdots & x_i^{(\alpha)} & \cdots & x_r^{(\alpha)} \\ \overline{x}_{1'}^{(\alpha)} & \overline{x}_{2'}^{(\alpha)} & \cdots & \overline{x}_{i'}^{(\alpha)} & \cdots & \overline{x}_{r'}^{(\alpha)} \end{pmatrix}, \tag{4}$$

where $r^{(\alpha)}$ is abbreviated to r. The permutation $g^{(\alpha)}$ is a proper permutation that corresponds to a proper rotation of the point group $\mathbf{G}$, while the permutation $\overline{g}^{(\alpha)}$ is an improper permutation that corresponds to an improper rotation of the point group $\mathbf{G}$. Note that α runs so that $G^{(\alpha)}$ covers G ($\in \widehat{\mathbf{G}}$). The r positions of $\mathcal{O}_\alpha$ are occupied by a set of proligands. The overbar represents the inversion of the chirality of each proligand if the proligand is chiral.

Suppose that the cycle structure of $G^{(\alpha)}$ ($\in \widehat{\mathbf{G}}^{(\alpha)}$) is represented by

$$[1^{\mu_1(G)} 2^{\mu_2(G)} \cdots r^{\mu_r(G)}]^{(\alpha)},$$

where $\sum_{k=1}^{r} k\mu_k(G) = r$. Note that $G^{(\alpha)}$ is simply represented by G and the superscript (α) of $r^{(\alpha)}$ is omitted for the sake of simplicity. Each of the k-cycles corresponds to a sphericity index (SI) $\$_k$ (or an extended sphericity index (eSI) $\psi_{(\$)k}$), which is represented by a_k, c_k, or b_k (or $\psi_{(a)k}$, $\psi_{(c)k}$, or $\psi_{(b)k}$) according to the following sphericity of the k-cycle:

Homospheric k-cycle: The sphericity index (SI) $\$_k$ is a_k if G (and also $G^{(\alpha)}$) corresponds to an improper element and k is odd [10]. When we take account of extended sphericity indices (eSIs) [11], we use the eSI $\psi_{(a)k}$ in place of the usual SI a_k.

Enantiospheric k-cycle: The SI $\$_k$ is c_k if G (and also $G^{(\alpha)}$) corresponds to an improper element and k is even [10]. When we take account of eSIs [11], we use the eSI $\psi_{(c)k}$ in place of the usual SI c_k.

Hemispheric k-cycle: The SI $\$_k$ is b_k if G (and also $G^{(\alpha)}$) corresponds to a proper element [10]. When we take account of eSIs [11], we use the eSI $\psi_{(b)k}$ in place of the usual SI b_k.

Hence, the element G corresponds to a product of sphericity indices (PSI):

$$[\$_1^{\mu_1(G)}\$_2^{\mu_2(G)}\cdots\$_r^{\mu_r(G)}]^{(\alpha)},$$

or a product of extended sphericity indices (PeSIs):

$$[\psi_{(\$)1}^{\mu_1(G)}\psi_{(\$)2}^{\mu_2(G)}\cdots\psi_{(\$)r}^{\mu_r(G)}]^{(\alpha)}.$$

Following Fujita's proligand method [11], a cycle index with chirality fittingness (CI-CF) for the present case is defined as follows:

$$\text{CI-CF}(\widehat{\mathbf{G}};\$_k) = \frac{1}{|\widehat{\mathbf{G}}|}\sum_{G\in\widehat{\mathbf{G}}}\prod_{\alpha}[\$_1^{\mu_1(G)}\$_2^{\mu_2(G)}\cdots\$_r^{\mu_r(G)}]^{(\alpha)}, \tag{5}$$

where α runs so that $G^{(\alpha)}$ covers G and where the symbol $\$_k$ (for $k = 1, 2, \ldots, r$) represents the SI a_k, c_k, or b_k.

Because an achiral promolecule or a pair of enantiomeric promolecules is enumerated as one promolecule (one stereoisomer) under the action of $\widehat{\mathbf{G}}$, the consideration of Eq. 5 gives Theorem 1. Theorem 1 for enumerating stereoisomers has essentially the same meaning as described for the enumeration of stereoisomers (Theorem 1 of [10]) and stereoisomers having rotatable ligands (Theorem 1 of [11]). However, the present theorem takes account of the orbits ($\mathcal{O}_\alpha$) contained in the skeleton.

Theorem 1 (Enumeration of Promolecules) *Let $\widehat{\mathbf{G}}$ be a sum of CRs of a point group, which governs a set $\mathcal{O}$ of $\hat{n}$ positions of a given skeleton. Suppose that the cycle structure of each CR ($\widehat{\mathbf{G}}^{(\alpha)}$) is represented by*

$$(1^{\mu_1(G)}2^{\mu_2(G)}\cdots s^{\mu_r(G)})^{(\alpha)},$$

where $\sum_{k=1}^{r} k\mu_k(H) = r$. Each position of $\mathcal{O}_\alpha$ governed by $\widehat{\mathbf{G}}^{(\alpha)}$ is occupied by an achiral or chiral proligand selected from a set of proligands,

$$\mathbf{X}^{(\alpha)} = \{\mathrm{X}_1, \mathrm{X}_2, \ldots, \mathrm{X}_n;\ \mathrm{p}_1, \mathrm{p}_2, \ldots, \mathrm{p}_{n'}; \overline{\mathrm{p}}_1, \overline{\mathrm{p}}_2, \ldots, \overline{\mathrm{p}}_{n'}\}, \tag{6}$$

where n and n' are non-negative integers and where each X_j represents an achiral proligand and each pair of p_j and $\overline{\mathrm{p}}_j$ represents an enantiomeric pair of chiral proligands. Although each proligand contained in $\mathbf{X}^{(\alpha)}$ depends on the orbit $\mathcal{O}_\alpha$, note that the dependence is omitted for the sake of simplicity. Consider isomers having θ_1 of X_1, θ_2 of X_2, …, θ_n of X_n; θ'_1 of p_1, θ'_2 of p_2, …, $\theta'_{n'}$ of $\mathrm{p}_{n'}$; and θ''_1 of $\overline{\mathrm{p}}_1$, θ''_2 of $\overline{\mathrm{p}}_2$, … $\theta''_{n'}$ of $\overline{\mathrm{p}}_{n'}$, where the partition $[\theta^{(\alpha)}]$ satisfies the following equation:

$$\begin{aligned}[\theta^{(\alpha)}]:\ &\theta_1+\theta_2+\cdots+\theta_n\\ &+\theta'_1+\theta'_2+\cdots+\theta'_{n'}\\ &+\theta''_1+\theta''_2+\cdots+\theta''_{n'} = r.\end{aligned} \tag{7}$$

Since the partition $[\theta^{(\alpha)}]$ depends on the orbit $\mathcal{O}_\alpha$, we place $[\theta] = [\ldots, \theta^{(\alpha)}, \ldots]$ for the sake of simplicity. Let the symbol M_θ denote the number of such isomers (promolecules) as having $[\theta]$ under the action of $\widehat{\mathbf{G}}$ (via $\widehat{\mathbf{G}}^{(\alpha)}$), where achiral isomers and enantiomeric pairs are enumerated combinatorially. A generating function for calculating M_θ is represented by

$$\begin{aligned}&\sum_{[\theta]} M_\theta \prod_{\alpha}[\mathrm{X}_1^{\theta_1}\cdots\mathrm{X}_n^{\theta_n}\mathrm{p}_1^{\theta'_1}\cdots\mathrm{p}_{n'}^{\theta'_{n'}}\overline{\mathrm{p}}_1^{\theta''_1}\cdots\overline{\mathrm{p}}_{n'}^{\theta''_{n'}}]^{(\alpha)}\\ &= \text{CI-CF}(\widehat{\mathbf{G}};\$_k),\end{aligned} \tag{8}$$

where the summation is concerned with all of the partitions ($[\theta]$) shown in Eq. 7 and the right-hand side is given by Eq. 5. The SIs $\$_k$ in the CI-CF are ligand inventories replaced by

$$a_k = \mathrm{X}_1^k + \mathrm{X}_2^k + \cdots + \mathrm{X}_m^k, \tag{9}$$

$$\begin{aligned}c_k = {}&\mathrm{X}_1^k + \mathrm{X}_2^k + \cdots + \mathrm{X}_m^k\\ &+2\mathrm{p}_1^{k/2}\overline{\mathrm{p}}_1^{k/2} + 2\mathrm{p}_2^{k/2}\overline{\mathrm{p}}_2^{k/2} + \cdots + 2\mathrm{p}_n^{k/2}\overline{\mathrm{p}}_{m'}^{k/2},\end{aligned} \tag{10}$$

$$\begin{aligned}b_k = {}&\mathrm{X}_1^k + \mathrm{X}_2^k + \cdots + \mathrm{X}_m^k\\ &+\mathrm{p}_1^k + \mathrm{p}_2^k + \cdots + \mathrm{p}_{m'}^k + \overline{\mathrm{p}}_1^k + \overline{\mathrm{p}}_2^k + \cdots + \overline{\mathrm{p}}_{m'}^k.\end{aligned} \tag{11}$$

where the dependence on the orbit ($\mathcal{O}_\alpha$) is omitted for the sake of simplicity.

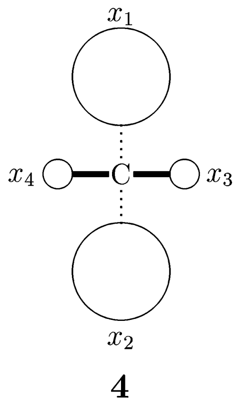
Example 1 (Enumeration of Promolecules Derived from a $\mathbf{C}_{2v}$-Skeleton. An Example of Theorem 1)

To treat trihydroxyglutaric acids, let us consider a skeleton (**4**) of $\mathbf{C}_{2v}$-symmetry, whose positions are represented by $\mathcal{O} = \{x_1, x_2, x_3, x_4\}$ as shown in Fig. 2. These positions are permuted as follows:

$$\{(1)(2)(3)(4),\ (1\ 2)(3\ 4),\ \overline{(1)(2)(3\ 4)},\ \overline{(1\ 2)(3)(4)}\},$$

where the locants of the positions only are shown for the sake of simplicity. Note that these permutations, each of which is represented as a product of cycles, correspond to the symmetry operations of the point group $\mathbf{C}_{2v}$ (= $\{I, C_2, \sigma, \sigma'\}$) and that each permutation with an overbar expresses an improper permutation ($\sim \sigma$ or σ'). This permutation representation is represented by a sum of CRs: $\widehat{\mathbf{G}} = 2\mathbf{C}_{2v}(/\mathbf{C}_s)$:

$$\begin{aligned}\widehat{\mathbf{G}}^{(1)} &= \mathbf{C}_{2v}(/\mathbf{C}_s)^{(1)} = \{(1)(2),\ (1\ 2),\ \overline{(1)(2)},\ \overline{(1\ 2)}\}\\ \widehat{\mathbf{G}}^{(2)} &= \mathbf{C}_{2v}(/\mathbf{C}_s)^{(2)} = \{(3)(4),\ (3\ 4),\ \overline{(3\ 4)},\ \overline{(3)(4)}\}\end{aligned} \tag{12}$$



4

Fig. 2 A skeleton of $\mathbf{C}_{2v}$-symmetry

Table 1 Orbits ($\mathcal{O}_\alpha$), CRs and Sphericity Indices (SIs) and Products of SIs (PSIs) for the Skeleton **4**

Symmetry operation	$\mathcal{O}_1$		$\mathcal{O}_2$		$\mathcal{O}_1 + \mathcal{O}_2$
	CR	SI	CR	SI	PSI
I	(1)(2)	b_1^2	(3)(4)	b_1^2	$(b_1^{(1)})^2(b_1^{(2)})^2$
C_2	(1 2)	b_2	(3 4)	b_2	$(b_2^{(1)})(b_2^{(2)})$
σ	(1)(2)	a_1^2	(3 4)	c_2	$(a_1^{(1)})^2(c_2^{(2)})$
σ'	(1 2)	c_2	(3)(4)	b_1^2	$(c_2^{(1)})(a_1^{(2)})^2$

Accordingly, the four positions of **4** are divided into a sum of two orbits $\mathcal{O}_1 + \mathcal{O}_2$ ($\alpha = 1, 2$), where $\mathcal{O}_1$ ($= \{x_1, x_2\}$) is governed by the CR $\widehat{\mathbf{G}}^{(1)}$ and $\mathcal{O}_2$ ($= \{x_3, x_4\}$) is governed by the CR $\widehat{\mathbf{G}}^{(2)}$.

To apply Eq. 5 to the present case of **4**, sphericity indices (SIs) are assigned to the k-cycles contained in each permutation. The results are summarized in Table 1, where the PSIs are calculated by the SIs.

From the PSIs listed in the rightmost column of Table 1, the CI-CF (Eq. 5) for the present case is calculated as follows:

$$\begin{aligned}\text{CI-CF}(\mathbf{C}_{2v}; \$_k) = \frac{1}{4}\Big\{&(b_1^{(1)})^2(b_1^{(2)})^2 + (b_2^{(1)})(b_2^{(2)}) \\ &+ (a_1^{(1)})^2(c_2^{(2)}) + (c_2^{(1)})(a_1^{(2)})^2\Big\}\end{aligned} \tag{13}$$

Suppose that the two positions of the orbit $\mathcal{O}_1$ accommodate two proligands which are selected from a set of proligands:

$$\mathbf{X}^{(1)} = \{\mathrm{X}_1, \mathrm{X}_2, \mathrm{p}_1, \mathrm{p}_2, \overline{\mathrm{p}}_1, \overline{\mathrm{p}}_2\}, \tag{14}$$

where X_1 and X_2 represent achiral proligands and a pair of p_i and $\overline{\mathrm{p}}_i$ ($i = 1, 2$) represents an enantiomeric pair of chiral ligands. And suppose that the two positions of the orbit $\mathcal{O}_2$ accommodate two proligands which are selected from a set of proligands:

$$\mathbf{X}^{(2)} = \{\hat{\mathrm{X}}_1, \hat{\mathrm{X}}_2\} \tag{15}$$

where $\hat{\mathrm{X}}_1$ and $\hat{\mathrm{X}}_2$ represent achiral proligands.

The ligand inventories (Eqs. 9–11) for the orbit $\mathcal{O}_1$ are calculated to give

$$a_k^{(1)} = \mathrm{X}_1^k + \mathrm{X}_2^k \tag{16}$$

$$c_k^{(1)} = \mathrm{X}_1^k + \mathrm{X}_2^k + 2\mathrm{p}_1^{k/2}\overline{\mathrm{p}}_1^{k/2} + 2\mathrm{p}_2^{k/2}\overline{\mathrm{p}}_2^{k/2} \tag{17}$$

$$b_k^{(1)} = \mathrm{X}_1^k + \mathrm{X}_2^k + \mathrm{p}_1^k + \mathrm{p}_2^k + \overline{\mathrm{p}}_1^k + \overline{\mathrm{p}}_2^k \tag{18}$$

On the other hand, the ligand inventories (Eqs. 9–11) for the orbit $\mathcal{O}_2$ are calculated to give

$$a_k^{(2)} = c_k^{(2)} = b_k^{(2)} = \hat{\mathrm{X}}_1^k + \hat{\mathrm{X}}_2^k \tag{19}$$

By following Theorem 1, the sets of the ligand inventories (Eqs. 16–19) are introduced into the CI–CF (Eq. 13). The expansion of the resulting equation produces the following generating function:

$$\begin{aligned}F = {}&[2\mathrm{p}_1\overline{\mathrm{p}}_1\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2 + \cdots] + [\mathrm{X}_1\mathrm{X}_2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2] \\ &+ \left[\frac{2}{2}(\mathrm{X}_1\mathrm{p}_1\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2 + \mathrm{X}_1\overline{\mathrm{p}}_1\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2) + \cdots\right] \\ &+ \left[\frac{2}{2}(\mathrm{p}_1\mathrm{p}_2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2 + \overline{\mathrm{p}}_1\overline{\mathrm{p}}_2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2) + \cdots\right] \\ &+ [\mathrm{p}_1\overline{\mathrm{p}}_1\hat{\mathrm{X}}_1^2 + \cdots] \\ &+ [\mathrm{X}_1\mathrm{X}_2\hat{\mathrm{X}}_1^2 + \cdots] \\ &+ \left[\frac{1}{2}(\mathrm{X}_1\mathrm{p}_1\hat{\mathrm{X}}_1^2 + \mathrm{X}_1\overline{\mathrm{p}}_1\hat{\mathrm{X}}_1^2) + \cdots\right] \\ &+ \left[\frac{1}{2}(\mathrm{p}_1\mathrm{p}_2\hat{\mathrm{X}}_1^2 + \overline{\mathrm{p}}_1\overline{\mathrm{p}}_2\hat{\mathrm{X}}_1^2) + \cdots\right] \\ &+ \left[\mathrm{X}_1^2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2 + \mathrm{X}_2^2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2\right] \\ &+ \left[\frac{1}{2}(\mathrm{p}_1^2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2 + \overline{\mathrm{p}}_1^2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2) + \cdots\right] \\ &+ \left[\mathrm{X}_1^2\hat{\mathrm{X}}_1^2 + \mathrm{X}_2^2\hat{\mathrm{X}}_1^2 + \cdots\right] \\ &+ \left[\frac{1}{2}(\mathrm{p}_1^2\hat{\mathrm{X}}_1^2 + \overline{\mathrm{p}}_1^2\hat{\mathrm{X}}_1^2) + \cdots\right],\end{aligned} \tag{20}$$

which is the concrete expression of Eq. 8 (Theorem 1) for the present case.

Among the terms appearing in the generating function (Eq. 20), the term $2\mathrm{p}_1\overline{\mathrm{p}}_1\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2$ corresponds to the two achiral trihydroxyglutaric acids (**1** and **2**), which are diastereomeric to each other. Note that the pair of p_1 and $\overline{\mathrm{p}}_1$ are replaced by *R*- and *S*-CH(OH)COOH, and we place $\hat{\mathrm{X}}_1$ = H and $\hat{\mathrm{X}}_2$ = OH. The coefficient 2 of the term shows the presence of the two isomers along with the absence of other isomers of this formula. On the other hand, the term $\frac{1}{2}(\mathrm{p}_1^2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2 + \overline{\mathrm{p}}_1^2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2)$ corresponds to a pair of enantiomers (**3** and $\overline{\mathbf{3}}$), where the pair is counted once by regarding the term as a unit term. □

2.2 Enumeration of achiral and chiral ligands

Each of the proligands is replaced by a ligand of a point group $\mathbf{H}$. Let $\widehat{\mathbf{H}}$ be a sum of CRs of the point group $\mathbf{H}$, which governs a set Δ of $\widehat{m}$ positions of the ligand. Suppose that a permutation H ($\in \widehat{\mathbf{H}}$) is represented by the following equation:

$$H = \begin{cases} h & \text{(for a proper permutation)} \\ \overline{h} & \text{(for an improper permutation)} \end{cases}$$

where

$$h = \left(\begin{array}{c|c|c} \cdots & \underbrace{\begin{matrix} y_1^{(\beta)} & y_2^{(\beta)} & \cdots & y_i^{(\beta)} & \cdots & y_s^{(\beta)} \\ y_{1'}^{(\beta)} & y_{2'}^{(\beta)} & \cdots & y_{i'}^{(\beta)} & \cdots & y_{s'}^{(\beta)} \end{matrix}}_{h^{(\beta)}} & \cdots \\ \cdots & & \cdots \end{array}\right) \tag{21}$$

$$\overline{h} = \left(\begin{array}{c|c|c} \cdots & \underbrace{\begin{matrix} y_1^{(\beta)} & y_2^{(\beta)} & \cdots & y_i^{(\beta)} & \cdots & y_s^{(\beta)} \\ \overline{y}_{1'}^{(\beta)} & \overline{y}_{2'}^{(\beta)} & \cdots & \overline{y}_{i'}^{(\beta)} & \cdots & \overline{y}_{s'}^{(\beta)} \end{matrix}}_{\overline{h}^{(\beta)}} & \cdots \\ \cdots & & \cdots \end{array}\right) \tag{22}$$

The permutation h is a proper permutation, while the permutation $\overline{h}$ is an improper permutation. The $\hat{m}$ positions of Δ are occupied by a set of objects (atoms, achiral ligands, or further proligands in general). The overbar represents the inversion of the chirality of each objects.

Since such objects can be regarded as a nested kind of proligands subordinate to ligands, they are here called "sub-proligands" in order to differentiate them from the proligands described above. Thereby, the substitution step "positions of a skeleton $\Leftarrow$ proligands" is contrasted with the subordinate substitution step "positions of a ligand $\Leftarrow$ sub-proligands", where the two steps in the total scheme "positions of a skeleton $\Leftarrow$ proligands $\Leftarrow$ ligands (positions of a ligand $\Leftarrow$ sub-proligands)" can be treated in a mathematically common framework.

A CR selected from $\widehat{\mathbf{H}}$ is represented by the symbol $\widehat{\mathbf{H}}^{(\beta)}$, which governs an orbit Δ_β ($\subset \Delta$). For the sake of simplicity, the representation $\widehat{\mathbf{H}}^{(\beta)}$ is regarded as a permutation group, which governs s positions contained in the orbit:

$$\Delta_\beta = \{y_1^{(\beta)}, y_2^{(\beta)}, \ldots, y_j^{(\beta)}, \ldots, y_s^{(\beta)}\}. \tag{23}$$

Thus, we place $\bigcup_\beta \Delta_\beta = \Delta$. The s positions of the ligands are occupied by a set of sub-proligands (i.e., such objects as atoms, achiral ligands, or further proligands). These positions are governed by the CR ($\widehat{\mathbf{H}}^{(\beta)}$) represented by

$$H^{(\beta)} = \begin{cases} h^{(\beta)} & \text{(for a proper permutation)} \\ \overline{h}^{(\beta)} & \text{(for an improper permutation)} \end{cases}$$

where

$$h^{(\beta)} = \begin{pmatrix} y_1^{(\beta)} & y_2^{(\beta)} & \cdots & y_j^{(\beta)} & \cdots & y_s^{(\beta)} \\ y_{1'}^{(\beta)} & y_{2'}^{(\beta)} & \cdots & y_{j'}^{(\beta)} & \cdots & y_{s'}^{(\beta)} \end{pmatrix} \tag{24}$$

$$\overline{h}^{(\beta)} = \begin{pmatrix} y_1^{(\beta)} & y_2^{(\beta)} & \cdots & y_j^{(\beta)} & \cdots & y_s^{(\beta)} \\ \overline{y}_{1'}^{(\beta)} & \overline{y}_{2'}^{(\beta)} & \cdots & \overline{y}_{j'}^{(\beta)} & \cdots & \overline{y}_{s'}^{(\beta)} \end{pmatrix} \tag{25}$$

Let the element $H^{(\beta)}$ be represented by a cycle decomposition involving the number $\nu_d(H)$ of d-cycles so as to satisfy $\sum_{d=1}^{s} d\nu_d(H) = s$. Each of the d-cycles corresponds to an SI $\$_d$, which is represented by a_d, c_d, or b_d according to the sphericity of the d-cycle. Hence, the element $H^{(\beta)}$ corresponds to a product of sphericity indices (PSI) $[\$_1^{\nu_1(H)} \$_2^{\nu_2(H)} \cdots \$_s^{\nu_s(H)}]^{(\beta)}$. Following Fujita's proligand method [11], a cycle index with chirality fittingness (CI–CF) for the present case is defined as follows:

$$\text{CI–CF}(\widehat{\mathbf{H}}; \$_d) = \frac{1}{|\widehat{\mathbf{H}}|} \sum_{H \in \widehat{\mathbf{H}}} \prod_{\beta} [\$_1^{\nu_1(H)} \$_2^{\nu_2(H)} \cdots \$_s^{\nu_s(H)}]^{(\beta)}, \tag{26}$$

where $\$_d$ is a_d, c_d, or b_d according to the sphericity of the corresponding d-cycle.

When the $\mathbf{H}$ is an achiral point group, there exists the maximum chiral subgroup $\mathbf{H}'$, the order of which is equal to the half of the order of $\mathbf{H}$. Let $\widehat{\mathbf{H}}'$ be a sum of CRs of the maximum chiral subgroup of $\mathbf{H}'$ of $\mathbf{H}$. Then the sum ($\widehat{\mathbf{H}}'$) contains proper rotations represented by h (Eq. 21). Each CR ($\widehat{\mathbf{H}}'^{(\beta)}$) contains proper rotations represented by $h^{(\beta)}$ (Eq. 24).

Then, by following Fujita's proligand method [11], a cycle index with chirality fittingness (CI–CF) for the present case is defined as follows:

$$\text{CI–CF}(\widehat{\mathbf{H}}'; b_d) = \frac{1}{|\widehat{\mathbf{H}}'|} \sum_{H \in \widehat{\mathbf{H}}'} \prod_{\beta} [b_1^{\nu_1(H)} b_2^{\nu_2(H)} \cdots b_s^{\nu_s(H)}]^{(\beta)}, \tag{27}$$

where only one SI b_d appears because $\widehat{\mathbf{H}}'$ contains proper permutations but no improper permutations.

Because an achiral ligand or a pair of enantiomeric ligands is enumerated as one ligand under the action of $\widehat{\mathbf{H}}$ (if achiral), the consideration of Eq. 26 gives Theorem 2. Theorem 2 for enumerating ligands has essentially the same meaning as described for the enumeration of stereoisomers (Theorem 1 of [10]) and stereoisomers having rotatable ligands (Theorem 1 of [11]). However, the present theorem takes account of the orbits (Δ_β) contained in the ligand.

Theorem 2 (Enumeration of ligands under the action of a point group) *Let* $\widehat{\mathbf{H}}$ *be a sum of CRs of a point group* $\mathbf{H}$*, which is an achiral or chiral group and governs a set* Δ *of* $\hat{m}$ *positions of such a given ligand as described above. Let* $\widehat{\mathbf{H}}^{(\beta)}$ *be a CR contained in the sum* $\widehat{\mathbf{H}}$*, where the* $\widehat{\mathbf{H}}^{(\beta)}$ *governs the orbit* Δ_β *(Eq. 23) and* β *runs to cover* $\widehat{\mathbf{H}}$*. Suppose that the cycle structure of each permutation of* $\widehat{\mathbf{H}}^{(\beta)}$ *is represented by*

$(1^{\nu_1(H)} 2^{\nu_2(H)} \cdots s^{\nu_s(H)})^{(\beta)}$,

where $\sum_{d=1}^{s} d\nu_d(H) = s$*. Each position of* Δ_β *governed by* $\widehat{\mathbf{H}}^{(\beta)}$ *is occupied by an achiral or chiral sub-proligand selected from a set of sub-proligands,*

$$\mathbf{Y}^{(\beta)} = \{\mathrm{Y}_1, \mathrm{Y}_2, \ldots, \mathrm{Y}_m; \quad \mathrm{q}_1, \mathrm{q}_2, \ldots, \mathrm{q}_{m'}; \overline{\mathrm{q}}_1, \overline{\mathrm{q}}_2, \ldots, \overline{\mathrm{q}}_{m'}\}, \tag{28}$$

where m and m′ are non-negative integers and where each Y_j *represents an achiral sub-proligand and each pair of* q_j *and* $\overline{\mathrm{q}}_j$ *represents an enantiomeric pair of chiral sub-proligands. Note that, although each sub-proligand contained in* $\mathbf{Y}^{(\beta)}$ *depends on the orbit* Δ_β*, the dependence is omitted for the same of simplicity. Consider isomers having* ρ_1 *of* Y_1*,* ρ_2 *of* Y_2*, ...,* ρ_m *of* Y_m*;* ρ'_1 *of* q_1*,* ρ'_2 *of* q_2*, ...,* $\rho'_{m'}$ *of* $\mathrm{q}_{m'}$*; and* ρ''_1 *of* $\overline{\mathrm{q}}_1$*,* ρ''_2 *of* $\overline{\mathrm{q}}_2$*, ...* $\rho''_{m'}$ *of* $\overline{\mathrm{q}}_{m'}$*, where the partition* $[\rho^{(\beta)}]$ *satisfies the following equation:*

$$\begin{aligned} [\rho^{(\beta)}]: \ & \rho_1 + \rho_2 + \cdots + \rho_m \\ & + \rho'_1 + \rho'_2 + \cdots + \rho'_{m'} \\ & + \rho''_1 + \rho''_2 + \cdots + \rho''_{m'} = s. \end{aligned} \tag{29}$$

Since the partition $[\rho^{(\beta)}]$ *depends on the orbit* Δ_β*, we place* $[\rho] = [\ldots, \rho^{(\beta)}, \ldots]$ *for the sake of simplicity. Let the symbol* B_ρ *denote the number of such ligands as having* $[\rho]$ *under the action of* $\widehat{\mathbf{H}}$ *(via* $\widehat{\mathbf{H}}^{(\beta)}$*), where achiral ligands and enantiomeric pairs are enumerated combinatorially. A generating function for calculating* B_ρ *is represented by*

$$\begin{aligned} & \sum_{[\rho]} B_\rho \prod_{\beta} [\mathrm{Y}_1^{\rho_1} \cdots \mathrm{Y}_m^{\rho_m} \mathrm{q}_1^{\rho'_1} \cdots \mathrm{q}_{m'}^{\rho'_{m'}} \overline{\mathrm{q}}_1^{\rho''_1} \cdots \overline{\mathrm{q}}_{m'}^{\rho''_{m'}}]^{(\beta)} \\ & \quad = \text{CI–CF}(\widehat{\mathbf{H}}; \$_d), \end{aligned} \tag{30}$$

where the summation is concerned with all of the partitions ($[\rho]$) *shown in Eq. 29 and the right-hand side is given by Eq. 26. The SIs* $\$_d$ *in the CI–CF are ligand inventories replaced by*

$$a_d = \mathrm{Y}_1^d + \mathrm{Y}_2^d + \cdots + \mathrm{Y}_m^d, \tag{31}$$

$$\begin{aligned} c_d &= \mathrm{Y}_1^d + \mathrm{Y}_2^d + \cdots + \mathrm{Y}_m^d \\ &\quad +2\mathrm{q}_1^{d/2}\overline{\mathrm{q}}_1^{d/2} + 2\mathrm{q}_2^{d/2}\overline{\mathrm{q}}_2^{d/2} + \cdots + 2\mathrm{q}_{m'}^{d/2}\overline{\mathrm{q}}_{m'}^{d/2}, \end{aligned} \tag{32}$$

$$\begin{aligned} b_d &= \mathrm{Y}_1^d + \mathrm{Y}_2^d + \cdots + \mathrm{Y}_m^d \\ &\quad +\mathrm{q}_1^d + \mathrm{q}_2^d + \cdots + \mathrm{q}_{m'}^d + \overline{\mathrm{q}}_1^d + \overline{\mathrm{q}}_2^d + \cdots + \overline{\mathrm{q}}_{m'}^d. \end{aligned} \tag{33}$$

where the dependence on the orbit (Δ_β) *is omitted for the sake of simplicity.*

Although the proof of this theorem is omitted, it can be done in a similar manner to Theorem 1 of [10] and Theorem 1 of [11]. It should be noted that the inventories a_d (Eq. 31), c_d (Eq. 32), and b_d (Eq. 33) are used if $\mathbf{H}$ (or $\widehat{\mathbf{H}}$) is achiral, while the inventory b_d (Eq. 33) only is used if $\mathbf{H}$ (or $\widehat{\mathbf{H}}$) is chiral.

Example 2 (Enumeration of isomeric ligands derived from a methyl skeleton under the action of the point group $\mathbf{C}_{3v}$. *an example for Theorem 2)* Because the three positions of the methyl ligand ($\Delta = \{y_1, y_2, y_3\}$) are governed by the CR $\mathbf{C}_{3v}(/\mathbf{C}_s)$:

$$\begin{aligned} \mathbf{C}_{3v}(/\mathbf{C}_s) = \{&(1)(2)(3), (1\ 2\ 3), (1\ 3\ 2); \\ &\overline{(1)(2\ 3)}, \overline{(2)(1\ 3)}, \overline{(3)(1\ 2)}\}, \end{aligned} \tag{34}$$

where each overbar shows that the permutation is accompanied by the inversion of the chirality of a ligand so as to be an improper permutation. In this case, Eq. 26 is calculated as follows:

$$\begin{aligned} \text{CI–CF}(\mathbf{C}_{3v}; \$_d) &= \frac{1}{6}(b_1^3 + 3a_1c_2 + 2b_3) \\ &= \frac{1}{6}b_1^3 + \frac{1}{2}a_1c_2 + \frac{1}{3}b_3. \end{aligned} \tag{35}$$

Suppose that each position of Δ is occupied by an achiral or chiral sub-proligand selected from a set of sub-proligands (cf. Eq. 28):

$$\begin{aligned} \mathbf{Y} = \{&\mathrm{Y}_1, \mathrm{Y}_2, \mathrm{Y}_3; \\ &\mathrm{q}_1, \mathrm{q}_2, \mathrm{q}_3; \overline{\mathrm{q}}_1, \overline{\mathrm{q}}_2, \overline{\mathrm{q}}_3\}, \end{aligned} \tag{36}$$

Then, Eqs. 31, 32, and 33 are applied to the present case so as to give the following ligand inventories:

$$a_d = \mathrm{Y}_1^d + \mathrm{Y}_2^d + \mathrm{Y}_3^d, \tag{37}$$

$$\begin{aligned} c_d &= \mathrm{Y}_1^d + \mathrm{Y}_2^d + \mathrm{Y}_3^d \\ &\quad +2\mathrm{q}_1^{d/2}\overline{\mathrm{q}}_1^{d/2} + 2\mathrm{q}_2^{d/2}\overline{\mathrm{q}}_2^{d/2} + 2\mathrm{q}_3^{d/2}\overline{\mathrm{q}}_3^{d/2}, \end{aligned} \tag{38}$$

$$\begin{aligned} b_d &= \mathrm{Y}_1^d + \mathrm{Y}_2^d + \mathrm{Y}_3^d \\ &\quad +\mathrm{q}_1^d + \mathrm{q}_2^d + \mathrm{q}_3^d + \overline{\mathrm{q}}_1^d + \overline{\mathrm{q}}_2^d + \overline{\mathrm{q}}_3^d. \end{aligned} \tag{39}$$

These inventories are introduced into the CI–CF (Eq. 35), which is expanded to give the following generating function:

$$\begin{aligned} f = {} & [\mathrm{Y}_1^3 + \mathrm{Y}_2^3 + \mathrm{Y}_3^3] + \left[\mathrm{Y}_1^2\mathrm{Y}_3 + \mathrm{Y}_1^2\mathrm{Y}_2 + \cdots\right] + \mathrm{Y}_1\mathrm{Y}_2\mathrm{Y}_3 \\ & + \left[\frac{1}{2}(\mathrm{Y}_1^2\mathrm{q}_1 + \mathrm{Y}_1^2\overline{\mathrm{q}}_1) + \cdots\right] \\ & + \left[\frac{2}{2}(\mathrm{Y}_1\mathrm{Y}_2\mathrm{q}_1 + \mathrm{Y}_1\mathrm{Y}_2\overline{\mathrm{q}}_1) + \cdots\right] \\ & + \left[\frac{1}{2}(\mathrm{Y}_1\mathrm{q}_1^2 + \mathrm{Y}_1\overline{\mathrm{q}}_1^2) + \cdots\right] + \left[2\mathrm{Y}_1\mathrm{q}_1\overline{\mathrm{q}}_1 + \cdots\right] \\ & + \left[\frac{2}{2}(\mathrm{Y}_1\mathrm{q}_1\mathrm{q}_2 + \mathrm{Y}_1\overline{\mathrm{q}}_1\overline{\mathrm{q}}_2) + \cdots\right] \\ & + \left[\frac{2}{2}(\mathrm{Y}_1\mathrm{q}_1\overline{\mathrm{q}}_2 + \mathrm{Y}_1\overline{\mathrm{q}}_1\mathrm{q}_2) + \cdots\right] \\ & + \left[\frac{1}{2}(\mathrm{q}_1^3 + \overline{\mathrm{q}}_1^3) + \cdots\right] + \left[\frac{1}{2}(\mathrm{q}_1^2\overline{\mathrm{q}}_1 + \mathrm{q}_1\overline{\mathrm{q}}_1^2) + \cdots\right] \\ & + \left[\frac{1}{2}(\mathrm{q}_1^2\mathrm{q}_2 + \overline{\mathrm{q}}_1^2\overline{\mathrm{q}}_2) + \cdots\right] + \left[\frac{1}{2}(\mathrm{q}_1^2\overline{\mathrm{q}}_2 + \overline{\mathrm{q}}_1^2\mathrm{q}_2) + \cdots\right] \\ & + \left[\frac{2}{2}(\mathrm{q}_1\mathrm{q}_2\mathrm{q}_3 + \overline{\mathrm{q}}_1\overline{\mathrm{q}}_2\overline{\mathrm{q}}_3)\right] \\ & + \left[\frac{2}{2}(\mathrm{q}_1\mathrm{q}_2\overline{\mathrm{q}}_3 + \overline{\mathrm{q}}_1\overline{\mathrm{q}}_2\mathrm{q}_3) + \cdots\right] \\ & + \left[\frac{2}{2}(\mathrm{q}_1\overline{\mathrm{q}}_1\overline{\mathrm{q}}_2 + \mathrm{q}_1\overline{\mathrm{q}}_1\mathrm{q}_2) + \cdots\right] \end{aligned} \tag{40}$$

The coefficient of each term gives the B_ρ of Eq. 30 (Theorem 2). □

When the $\mathbf{H}$ is an achiral point group, investigations on the action of its maximum chiral subgroup $\mathbf{H}'$ are the next target. Because an achiral ligand or each chiral ligand of a enantiomeric pair is enumerated as one ligand under the action of $\widehat{\mathbf{H}}'$, the consideration of Eq. 27 gives Theorem 3.

Theorem 3 (Enumeration of ligands under the action of the maximum chiral subgroup) *Suppose that the conditions of Theorem 2 hold true. Let us consider the maximum chiral subgroup* $\mathbf{H}'$ *of the point group* $\mathbf{H}$, *when the* $\mathbf{H}$ *described in Theorem 2 is achiral. Let the symbol* B'_ρ *denote the number of such ligands as having* $[\rho]$ *under the action of* $\widehat{\mathbf{H}}'$ *(via* $\widehat{\mathbf{H}}'^{(\beta)}$*), where achiral ligands and chiral ligands (both enantiomeric ligands) are enumerated combinatorially. A generating function for calculating* B'_ρ *is represented by*

$$\begin{aligned} & \sum_{[\rho]} B'_\rho \prod_\beta [\mathrm{Y}_1^{\rho_1} \cdots \mathrm{Y}_m^{\rho_m} \mathrm{q}_1^{\rho'_1} \cdots \mathrm{q}_{m'}^{\rho'_{m'}} \overline{\mathrm{q}}_1^{\rho''_1} \cdots \overline{\mathrm{q}}_{m'}^{\rho''_{m'}}]^{(\beta)} \\ & \quad = \text{CI–CF}(\widehat{\mathbf{H}}'; b_d), \end{aligned} \tag{41}$$

where the summation is concerned with all of the partitions ($[\rho]$) *shown in Eq. 29 and the right-hand side is given by Eq. 27. The SI* b_d *in the CI–CF is a ligand inventory replaced by*

$$\begin{aligned} b_d &= \mathrm{Y}_1^d + \mathrm{Y}_2^d + \cdots + \mathrm{Y}_m^d \\ &\quad +\mathrm{q}_1^d + \mathrm{q}_2^d + \cdots + \mathrm{q}_{m'}^d + \overline{\mathrm{q}}_1^d + \overline{\mathrm{q}}_2^d + \cdots + \overline{\mathrm{q}}_{m'}^d. \end{aligned} \tag{42}$$

where the dependence on the orbit (Δ_β) is omitted for the sake of simplicity.

Although the proof of this theorem is omitted, it can be done in a similar manner to Theorem 1 of [10] and Theorem 1 of [11].

Example 3 (Enumeration of isomeric ligands derived from a methyl skeleton under the action of the point group $\mathbf{C}_3$*. an example for Theorem 3)* As a continuation of Example 2, let us consider proper permutations among $\mathbf{C}_{3v}(/\mathbf{C}_s)$, i.e.,

$$\mathbf{C}_3(/\mathbf{C}_1) = \{(1)(2)(3), (1\ 2\ 3), (1\ 3\ 2)\} \tag{43}$$

In this case, Eq. 27 is calculated as follows:

$$\begin{aligned}\text{CI–CF}(\mathbf{C}_3; b_d) &= \frac{1}{3}(b_1^3 + 2b_3)\\ &= \frac{1}{3}b_1^3 + \frac{2}{3}b_3.\end{aligned} \tag{44}$$

The same set of sub-proligands as $\mathbf{Y}$ (Eq. 36) is used again so that the ligand inventory b_d (Eq. 42) is calculated to be Eq. 39, which is introduced into the CI–CF (Eq. 44), which is expanded to give the following generating function:

$$\begin{aligned} g = {} & [\mathrm{Y}_1^3 + \mathrm{Y}_2^3 + \mathrm{Y}_3^3] + \left[\mathrm{Y}_1^2\mathrm{Y}_3 + \mathrm{Y}_1^2\mathrm{Y}_2 + \cdots\right] + 2\mathrm{Y}_1\mathrm{Y}_2\mathrm{Y}_3\\
& + \left[\frac{1}{2}(\mathrm{Y}_1^2\mathrm{q}_1 + \mathrm{Y}_1^2\overline{\mathrm{q}}_1) + \cdots\right]\\
& + \left[\frac{4}{2}(\mathrm{Y}_1\mathrm{Y}_2\mathrm{q}_1 + \mathrm{Y}_1\mathrm{Y}_2\overline{\mathrm{q}}_1) + \cdots\right]\\
& + \left[\frac{2}{2}(\mathrm{Y}_1\mathrm{q}_1^2 + \mathrm{Y}_1\overline{\mathrm{q}}_1^2) + \cdots\right] + \left[2\mathrm{Y}_1\mathrm{q}_1\overline{\mathrm{q}}_1 + \cdots\right]\\
& + \left[\frac{4}{2}(\mathrm{Y}_1\mathrm{q}_1\mathrm{q}_2 + \mathrm{Y}_1\overline{\mathrm{q}}_1\overline{\mathrm{q}}_2) + \cdots\right]\\
& + \left[\frac{4}{2}(\mathrm{Y}_1\mathrm{q}_1\overline{\mathrm{q}}_2 + \mathrm{Y}_1\overline{\mathrm{q}}_1\mathrm{q}_2) + \cdots\right]\\
& + \left[\frac{2}{2}(\mathrm{q}_1^3 + \overline{\mathrm{q}}_1^3) + \cdots\right] + \left[\frac{2}{2}(\mathrm{q}_1^2\overline{\mathrm{q}}_1 + \mathrm{q}_1\overline{\mathrm{q}}_1^2) + \cdots\right]\\
& + \left[\frac{2}{2}(\mathrm{q}_1^2\mathrm{q}_2 + \overline{\mathrm{q}}_1^2\overline{\mathrm{q}}_2) + \cdots\right] + \left[\frac{2}{2}(\mathrm{q}_1^2\overline{\mathrm{q}}_2 + \overline{\mathrm{q}}_1^2\mathrm{q}_2) + \cdots\right]\\
& + \left[\frac{4}{2}(\mathrm{q}_1\mathrm{q}_2\mathrm{q}_3 + \overline{\mathrm{q}}_1\overline{\mathrm{q}}_2\overline{\mathrm{q}}_3)\right]\\
& + \left[\frac{4}{2}(\mathrm{q}_1\mathrm{q}_2\overline{\mathrm{q}}_3 + \overline{\mathrm{q}}_1\overline{\mathrm{q}}_2\mathrm{q}_3) + \cdots\right]\\
& + \left[\frac{4}{2}(\mathrm{q}_1\overline{\mathrm{q}}_1\overline{\mathrm{q}}_2 + \mathrm{q}_1\overline{\mathrm{q}}_1\mathrm{q}_2) + \cdots\right]\end{aligned} \tag{45}$$

The coefficient of each term gives the B'_ρ of Eq. 41 (Theorem 3). □

Since Eq. 30 gives the number of achiral ligands (A) plus enantiomeric pairs (C), we can place A + C = CI–CF($\widehat{\mathbf{H}}$; $\$_d$). Since Eq. 41 gives the number of achiral ligands (A) plus chiral ligands (C) plus their enantiomeric ligands (C), we can place A + 2C = CI–CF($\widehat{\mathbf{H}}'$; b_d). Then we have C = CI–CF ($\widehat{\mathbf{H}}'$; b_d)− CI–CF($\widehat{\mathbf{H}}$; $\$_d$) and A = 2CI–CF ($\widehat{\mathbf{H}}$; $\$_d$) − CI–CF ($\widehat{\mathbf{H}}'$; b_d).

Let us examine the term appearing in Eqs. 30 and 41.

$$\mathrm{p}_\rho = \prod_\beta [\mathrm{Y}_1^{\rho_1}\cdots\mathrm{Y}_m^{\rho_m}\mathrm{q}_1^{\rho'_1}\cdots\mathrm{q}_{m'}^{\rho'_{m'}}\overline{\mathrm{q}}_1^{\rho''_1}\cdots\overline{\mathrm{q}}_{m'}^{\rho''_{m'}}]^{(\beta)} \tag{46}$$

Although this term can represent an achiral or chiral ligand, it is here presumed to represent a chiral one, i.e., $\rho'_j \neq \rho''_j$ ($\exists j$ when $j = 1, 2, \ldots, m'$). Then, the term corresponding to its enantiomeric ligand is represented by the following term.

$$\overline{\mathrm{p}}_\rho = \prod_\beta [\mathrm{Y}_1^{\rho_1}\cdots\mathrm{Y}_m^{\rho_m}\mathrm{q}_1^{\rho''_1}\cdots\mathrm{q}_{m'}^{\rho''_{m'}}\overline{\mathrm{q}}_1^{\rho'_1}\cdots\overline{\mathrm{q}}_{m'}^{\rho'_{m'}}]^{(\beta)} \tag{47}$$

Because both p and $\overline{\mathrm{p}}$ appear in the summation of Eq. 30, the C (one enantiomeric pair of ligands) of Eq. 30 corresponds to the term represented by a combination of enantiomeric molecular formulas:

$$\frac{1}{2}(\mathrm{p}_\rho + \overline{\mathrm{p}}_\rho). \tag{48}$$

On the other hand, 2C (one chiral ligand and its enantiomeric ligand) of Eq. 41 corresponds to the terms represented by enantiomeric molecular formulas:

$$\mathrm{p}_\rho + \overline{\mathrm{p}}_\rho. \tag{49}$$

Hence, the C obtained by Eq. 49 minus Eq. 48, which is equal to Eq. 48, represents the number of enantiomeric pairs. It follows that we obtain the following theorem by starting from Theorems 2 and 3.

Theorem 4 (Enumeration of achiral ligands and enumeration of chiral ligands) *Suppose that the conditions of Theorems 2 and 3 hold true. Let the symbol A_ρ denote the number of achiral isomeric ligands of such isomers as having* $[\rho]$ *(Eq. 29). Let the symbol C_ρ denote the number of enantiomeric pairs of chiral isomeric ligands having* $[\rho]$ *(Eq. 29). Generating functions for calculating A_ρ and C_ρ are represented by*

$$\begin{aligned}&\sum_{[\rho]} A_\rho \prod_\beta [\mathrm{Y}_1^{\rho_1}\cdots\mathrm{Y}_m^{\rho_m}\mathrm{q}_1^{\rho'_1}\cdots\mathrm{q}_{m'}^{\rho'_{m'}}\overline{\mathrm{q}}_1^{\rho''_1}\cdots\overline{\mathrm{q}}_{m'}^{\rho''_{m'}}]^{(\beta)}\\ &\quad = 2\text{CI–CF}(\widehat{\mathbf{H}}; \$_d) - \text{CI–CF}(\widehat{\mathbf{H}}'; b_d)\end{aligned} \tag{50}$$

$$\begin{aligned}&\sum_{[\rho]} C_\rho \prod_\beta [\mathrm{Y}_1^{\rho_1}\cdots\mathrm{Y}_m^{\rho_m}\mathrm{q}_1^{\rho'_1}\cdots\mathrm{q}_{m'}^{\rho'_{m'}}\overline{\mathrm{q}}_1^{\rho''_1}\cdots\overline{\mathrm{q}}_{m'}^{\rho''_{m'}}]^{(\beta)}\\ &\quad = \text{CI–CF}(\widehat{\mathbf{H}}'; b_d) - \text{CI–CF}(\widehat{\mathbf{H}}; \$_d)\end{aligned} \tag{51}$$

where the summation is concerned with all of the partitions ($[\rho]$) *shown in Eq. 29 and the right-hand sides are derived from Eqs. 26 and 27. The SIs $\$_d$ in the CI–CF are ligand inventories replaced by a_d (Eq. 31), c_d (Eq. 32), and b_d (Eq. 33), where the dependence on the orbit (Δ_β) is omitted for the sake of simplicity.*

It should be noted that Eq. 51 contains a pair of enantiomeric ligands in a form of Eq. 48.

Example 4 (Enumerations of achiral and chiral isomeric ligands derived from a methyl skeleton. an example for Theorem 4) As a continuation of Examples 2 and 3, Eq. 50 of Theorem 4 is applied to the enumeration of achiral ligands derived from a methyl ligand. Thus, by starting from f of Eq. 40 and g of Eq. 45, we obtain the following generating function:

$$\begin{aligned} 2f - g = {} & [\mathrm{Y}_1^3 + \mathrm{Y}_2^3 + \mathrm{Y}_3^3] + [\mathrm{Y}_1^2\mathrm{Y}_3 + \mathrm{Y}_1^2\mathrm{Y}_2 + \cdots] \\ & +[2\mathrm{Y}_1\mathrm{q}_1\overline{\mathrm{q}}_1 + \cdots] \end{aligned} \tag{52}$$

The coefficient of each term gives the A_ρ of Eq. 50 (Theorem 4).

On the other hand, Eq. 51 of Theorem 4 is applied to the enumeration of chiral ligands derived from a methyl ligand. Thus, by starting from f of Eq. 40 and g of Eq. 45, we obtain the following generating function:

$$\begin{aligned} g - f = {} & \mathrm{Y}_1\mathrm{Y}_2\mathrm{Y}_3 + \left[\frac{1}{2}(\mathrm{Y}_1^2\mathrm{q}_1 + \mathrm{Y}_1^2\overline{\mathrm{q}}_1) + \cdots\right] \\ & + \left[\frac{2}{2}(\mathrm{Y}_1\mathrm{Y}_2\mathrm{q}_1 + \mathrm{Y}_1\mathrm{Y}_2\overline{\mathrm{q}}_1) + \cdots\right] \\ & + \left[\frac{1}{2}(\mathrm{Y}_1\mathrm{q}_1^2 + \mathrm{Y}_1\overline{\mathrm{q}}_1^2) + \cdots\right] \\ & + \left[\frac{2}{2}(\mathrm{Y}_1\mathrm{q}_1\mathrm{q}_2 + \mathrm{Y}_1\overline{\mathrm{q}}_1\overline{\mathrm{q}}_2) + \cdots\right] \\ & + \left[\frac{2}{2}(\mathrm{Y}_1\mathrm{q}_1\overline{\mathrm{q}}_2 + \mathrm{Y}_1\overline{\mathrm{q}}_1\mathrm{q}_2) + \cdots\right] \\ & + \left[\frac{1}{2}(\mathrm{q}_1^3 + \overline{\mathrm{q}}_1^3) + \cdots\right] \\ & + \left[\frac{1}{2}(\mathrm{q}_1^2\overline{\mathrm{q}}_1 + \mathrm{q}_1\overline{\mathrm{q}}_1^2) + \cdots\right] \\ & + \left[\frac{1}{2}(\mathrm{q}_1^2\mathrm{q}_2 + \overline{\mathrm{q}}_1^2\overline{\mathrm{q}}_2) + \cdots\right] \\ & + \left[\frac{1}{2}(\mathrm{q}_1^2\overline{\mathrm{q}}_2 + \overline{\mathrm{q}}_1^2\mathrm{q}_2) + \cdots\right] \\ & + \left[\frac{2}{2}(\mathrm{q}_1\mathrm{q}_2\mathrm{q}_3 + \overline{\mathrm{q}}_1\overline{\mathrm{q}}_2\overline{\mathrm{q}}_3)\right] \\ & + \left[\frac{2}{2}(\mathrm{q}_1\mathrm{q}_2\overline{\mathrm{q}}_3 + \overline{\mathrm{q}}_1\overline{\mathrm{q}}_2\mathrm{q}_3) + \cdots\right] \\ & + \left[\frac{2}{2}(\mathrm{q}_1\overline{\mathrm{q}}_1\overline{\mathrm{q}}_2 + \mathrm{q}_1\overline{\mathrm{q}}_1\mathrm{q}_2) + \cdots\right] \end{aligned} \tag{53}$$

The coefficient of each term gives the C_ρ of Eq. 51 (Theorem 4). □

2.3 Enumeration of nonrigid isomers

Among the total scheme "positions of a skeleton ⇐ proligands ⇐ ligands (positions of a ligand ⇐ sub-proligands)", the two substitution steps "positions of a skeleton ⇐ proligands" and "positions of a ligand ⇐ sub-proligands" have been discussed in the preceding subsections. We are now ready to discuss the remaining step "proligands ⇐ ligands" so as to discuss enumeration of nonrigid isomers.

Let us return to CI–CF($\widehat{\mathbf{G}}$; $\$_k$) (Eq. 5), where the proligands are replaced by ligands enumerated by Theorem 4. For the sake of simplicity, the term X_ρ for achiral ligands and the term p_ρ for chiral ligands are placed as follows:

$$\prod_\beta [\mathrm{Y}_1^{\rho_1}\cdots\mathrm{Y}_m^{\rho_m}\mathrm{q}_1^{\rho'_1}\cdots\mathrm{q}_{m'}^{\rho'_{m'}}\overline{\mathrm{q}}_1^{\rho''_1}\cdots\overline{\mathrm{q}}_{m'}^{\rho''_{m'}}]^{(\beta)} = \begin{cases} \mathrm{X}_\rho & \text{for } \rho'_j = \rho''_j (j = 1, 2, \ldots, m'). \\ \mathrm{p}_\rho & \text{othewise} \end{cases} \tag{54}$$

Note that the term p_ρ of Eq. 54 covers p_ρ of Eq. 46 and $\overline{\mathrm{p}}_\rho$ of Eq. 47 when $[\rho]$ covers the partition represented by Eq. 29. According to the sphericity of each k-cycle, chirality fittingness [12] teaches that a homospheric orbit accommodates achiral ligands only (i.e., X_ρ of Eq. 54) an enantiospheric obit accommodates chiral ligands (i.e., p_ρ or $\overline{\mathrm{p}}_\rho$ of Eq. 54) in a compensated chiral packing (i.e., a pairwise packing) as well as achiral ligands, and a hemispheric orbit freely accommodates achiral and chiral ligands. The ligand inventories (Eqs. 9–11) for Theorem 1 are replaced by the following inventories:

$$\hat{a}_k = \sum_{[\rho]} A_\rho \mathrm{X}_\rho^k \tag{55}$$

$$= 2\text{CI–CF}(\widehat{\mathbf{H}}; \$_{kd}) - \text{CI–CF}(\widehat{\mathbf{H}}'; b_{kd}) \tag{56}$$

$$\hat{c}_k = \sum_{[\rho]} A_\rho \mathrm{X}_\rho^k + 2\sum_{[\rho]} C_\rho \mathrm{p}_\rho^{k/2}\overline{\mathrm{p}}_\rho^{k/2} \tag{57}$$

$$\hat{b}_k = \sum_{[\rho]} A_\rho X_\rho^k + 2\sum_{[\rho]} C_\rho \mathrm{p}_\rho^k \tag{58}$$

$$= \text{CI–CF}(\widehat{\mathbf{H}}'; b_{kd})\,, \tag{59}$$

where X_ρ and p_ρ ($\overline{\mathrm{p}}_\rho$) are represented by Eq. 54. It should be noted that the term $\mathrm{p}^{k/2}\overline{\mathrm{p}}^{k/2}$ in $\hat{c}_k$ appears twice when $[\rho]$ covers the partition represented by Eq. 29. and that the term $\overline{\mathrm{p}}^k$ automatically appears in $\hat{b}_k$ when $[\rho]$ covers the partition represented by Eq. 29. The SIs ($\hat{a}_k, \hat{c}_k, \hat{b}_k$) in the left-hand side of Eqs. 55, 57, and 58 are SIs for a skeleton, while $\$_{kd}$ (i.e., a_{kd}, c_{kd}, and b_{kd}) and b_{kd} in the right-hand side of Eqs. 56 and 59 are SIs for ligands. The two types of SIs are differentiated for the sake of rigor, although they are mathematically equivalent.

The ligand inventories represented by Eqs. 55, 57, and 58 are introduced into Eq. 8 of Theorem 1 to generate a generating function for enumerating nonrigid isomers. Thereby, Theorem 1 is rewritten to be a slightly different format, where CI–CF($\widehat{\mathbf{G}}$; $\$_k$) (Eq. 81) is used to replace the proligands by the ligands enumerated by Theorem 4. The summation appearing in the left-hand side of Eq. 8 now contains terms corresponding to sub-proligands of $\mathbf{Y}^{(\beta)}$ (Eq. 36).

The power of each term can be determined by the partitions $[\theta]$ (Eq. 7) and $[\rho]$ (Eq. 29) so that these are rewritten into a partition represented by

$$\begin{aligned} [\Theta^{(\alpha,\beta)}]: \ & \Theta_1 + \Theta_2 + \cdots + \Theta_m + \Theta'_1 + \Theta'_2 + \cdots + \Theta'_{m'} \\ & +\Theta''_1 + \Theta''_2 + \cdots + \Theta''_{m'} = rs. \end{aligned} \tag{60}$$

Thereby, the molecular formula of the resulting nonrigid isomer is calculated to be

$$\prod_{\alpha}\prod_{\beta}[\mathrm{Y}_1^{\Theta_1}\cdots\mathrm{Y}_m^{\Theta_m}\mathrm{q}_1^{\Theta'_1}\cdots\mathrm{q}_{m'}^{\Theta'_{m'}}\overline{\mathrm{q}}_1^{\Theta''_1}\cdots\overline{\mathrm{q}}_{m'}^{\Theta''_{m'}}]^{(\alpha,\beta)} \tag{61}$$

where the symbol (α, β) shows the dependence of each term in the molecular formula. When $\mathcal{O}_\alpha$ and Δ_β run to cover $\mathcal{O}$ and Δ, we place a partition $[\Theta]$ as follows:

$$[\Theta] : \begin{bmatrix} \cdots & \cdots & \cdots \\ \cdots & [\Theta^{(\alpha,\beta)}] & \cdots \\ \cdots & \cdots & \cdots \end{bmatrix}$$

It follows that Theorem 1 is combined with Theorems 2 and 3 (via Theorem 4) so as to yield the following theorem:

Theorem 5 (Preliminary theorem for enumerating nonrigid stereoisomers) *Suppose that each of the proligands of* $\mathbf{X}^{(\alpha)}$ *(Eq. 6 in Theorem 1) is substituted by a ligand that is generated from sub-proligands selected from* $\mathbf{Y}^{(\beta)}$ *(Eq. 36 in Theorem 2). Let* M_Θ *denote the number of nonrigid isomers that have the molecular formula shown in Eq. 61. A generating function for calculating* M_Θ *is represented by*

$$\sum_{[\Theta]} M_\Theta \prod_{\alpha}\prod_{\beta}[\mathrm{Y}_1^{\Theta_1}\cdots\mathrm{Y}_m^{\Theta_m}\mathrm{q}_1^{\Theta'_1}\cdots\mathrm{q}_{m'}^{\Theta'_{m'}}\overline{\mathrm{q}}_1^{\Theta''_1}\cdots\overline{\mathrm{q}}_{m'}^{\Theta''_{m'}}]^{(\alpha,\beta)} = \text{CI–CF}(\widehat{\mathbf{G}}; \hat{\$}_k), \tag{62}$$

where the CI–CF$(\widehat{\mathbf{G}}; \hat{\$}_k)$ *on the right-hand side is represented by Eq. 5 after changing* $\$_k$ *into* $\hat{\$}_k$ *and the* $\hat{\$}_k$ *(*$\hat{a}_k$*,* $\hat{c}_k$*, or* $\hat{b}_k$*) is replaced by the ligand inventories (Eqs. 55, 57, 58).*

Among the inventories used in Theorem 5, the inventories $\hat{a}_k$ and $\hat{b}_k$ (Eqs. 55, 58) are obtained as the generating functions (Eqs. 56, 59), which are in turn calculated by Eq. 26 (Theorem 2) and Eq. 27 (Theorem 3). However, the inventory $\hat{c}_k$ (Eq. 57), which corresponds to occupation modes for enantiospheric orbits, is not expressed in the form of a generating function. Hence, the next target is to obtain the $\hat{c}_k$ as a generating function.

Compare Eq. 58 for $\hat{b}_k$ with Eq. 57 for $\hat{c}_k$. Thereby, one can find that the term p_ρ^k of Eq. 58 corresponds to the term $\mathrm{p}_\rho^{k/2}\overline{\mathrm{p}}_\rho^{k/2}$ of Eq. 57, so that a generating function for $\hat{c}_k$ can be obtained by using Eq. 27 (Theorem 3) after adequate modification. Thus, Eq. 27 is converted into the following equation:

$$\text{CI–CF}(\widehat{\mathbf{H}}'; c_{kd}) = \frac{1}{|\widehat{\mathbf{H}}'|}\sum_{H\in\widehat{\mathbf{H}}'}\prod_{\beta}[c_k^{\nu_1(H)}c_{2k}^{\nu_2(H)}\cdots c_{sk}^{\nu_s(H)}]^{(\beta)}, \tag{63}$$

where each c_{kd} is represented by Eq. 32. Thereby, the following lemma is obtained:

Lemma 1 (Enantiospheric occupation modes as generating functions) *The ligand inventory* $\hat{c}_k$ *(Eq. 57) is represented as a generating function:*

$$\hat{c}_k = \sum_{[\rho]} A_\rho \mathrm{X}_\rho^k + 2\sum_{[\rho]} C_\rho \mathrm{p}_\rho^{k/2}\overline{\mathrm{p}}_\rho^{k/2} = \text{CI–CF}(\widehat{\mathbf{H}}'; c_{kd}), \tag{64}$$

where CI–CF$(\widehat{\mathbf{H}}'; c_{kd})$ *is given by Eq. 63 and where each* c_{kd} *is represented by Eq. 32 after converting d into kd.*

Example 5 (Enantiospheric occupation modes for methyl ligands estimated as generating functions. an example for Lemma 1)

Lemma 1 is applied to the case of Example 3. Thus, Eq. 44 is converted according to Eq. 64 into the following equation:

$$\hat{c}_2 = \frac{1}{3}c_2^3 + \frac{2}{3}c_6\,, \tag{65}$$

where we place $k = 2$ and $d = 1$. The inventories in the right-hand side of Eq. 65 are replaced by the ligand inventories derived from Eq. 38 so as to give the following generating function:

$$\begin{aligned} g' = {} & [\mathrm{Y}_1^6 + \cdots] + [\mathrm{Y}_1^4\mathrm{Y}_2^2 + \cdots] + [2\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2] \\ & + [2\mathrm{Y}_1^4\mathrm{q}_1\overline{\mathrm{q}}_1 + \cdots] + [4\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{q}_1\overline{\mathrm{q}}_1 + \cdots] \\ & + [4\mathrm{Y}_1^2\mathrm{q}_1^2\overline{\mathrm{q}}_1^2 + \cdots] + [8\mathrm{Y}_1^2\mathrm{q}_1\overline{\mathrm{q}}_1\mathrm{q}_2\overline{\mathrm{q}}_2 + \cdots] \\ & + [4\mathrm{q}_1^3\overline{\mathrm{q}}_1^3 + \cdots] + [8\mathrm{q}_1^2\overline{\mathrm{q}}_1^2\mathrm{q}_2\overline{\mathrm{q}}_2 + \cdots] \\ & + [16\mathrm{q}_1\mathrm{q}_2\mathrm{q}_3\overline{\mathrm{q}}_1\overline{\mathrm{q}}_2\overline{\mathrm{q}}_3]\,. \end{aligned} \tag{66}$$

The coefficient of each term in the right-hand side of Eq. 66 represents the number of occupation modes for enantiomeric ligand pairs plus achiral ligand pairs. Each coefficient is confirmed in terms of Lemma 1 by combining $2f - g$ (Eq. 52 for A_ρ) and $g - f$ (Eq. 53 for C_ρ) given in Example 4. For example, the term $4\mathrm{Y}_1^2\mathrm{q}_1^2\overline{\mathrm{q}}_1^2$ of Eq. 66 comes from the term $2\mathrm{Y}_1\mathrm{q}_1\overline{\mathrm{q}}_1$ of Eq. 52 (which gives the value 2 because the corresponding ligands are achiral) and the term $\frac{1}{2}(\mathrm{Y}_1\mathrm{q}_1^2 + \mathrm{Y}_1\overline{\mathrm{q}}_1^2)$ of Eq. 53 (which gives the value 2 because the corresponding ligands are chiral). The coefficient 1 of the term $\mathrm{Y}_1^4\mathrm{Y}_2^2$ indicates the presence of one occupation mode for an achiral ligand pair: $\mathrm{Y}_1^2\mathrm{Y}_2/\mathrm{Y}_1^2\mathrm{Y}_2$, while the coefficient 2 of the term $\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2$ indicates the presence of two occupation modes for a pair of enantiomeric ligands R-$\mathrm{Y}_1\mathrm{Y}_2\mathrm{Y}_3$/$S$-$\mathrm{Y}_1\mathrm{Y}_2\mathrm{Y}_3$. □

Lemma 1 allows us to rewrite Theorem 5 by using the ligand inventories represented as generating functions, i.e., Eq. 56 ($\hat{a}_k$), Eq. 64 ($\hat{c}_k$), and Eq. 59 ($\hat{b}_k$). Thereby, we obtain the following theorem:

Theorem 6 (The first theorem for enumerating nonrigid stereoisomers) *Suppose that each of the proligands of* $\mathbf{X}^{(\alpha)}$ *(Eq. 6 in Theorem 1) is substituted by a ligand that is generated from sub-proligands selected from* $\mathbf{Y}^{(\beta)}$ *(Eq. 36 in Theorem 2). Let* M_Θ *denote the number of nonrigid isomers that have the molecular formula shown in Eq. 61. A generating function for calculating* M_Θ *is represented by*

$$\sum_{[\Theta]} M_\Theta \prod_{\alpha}\prod_{\beta}[\mathrm{Y}_1^{\Theta_1}\cdots\mathrm{Y}_m^{\Theta_m}\mathrm{q}_1^{\Theta'_1}\cdots\mathrm{q}_{m'}^{\Theta'_{m'}}\overline{\mathrm{q}}_1^{\Theta''_1}\cdots\overline{\mathrm{q}}_{m'}^{\Theta''_{m'}}]^{(\alpha,\beta)} = \text{CI–CF}(\widehat{\mathbf{G}}; \hat{\$}_k), \tag{67}$$

where the CI–CF($\widehat{\mathbf{G}}$; $\hat{\$}_k$) *on the right-hand side is represented by Eq. 5 after changing* $\$_k$ *into* $\hat{\$}_k$ *and where the* $\hat{\$}_k$ *(*$\hat{a}_k$*,* $\hat{c}_k$*, or* $\hat{b}_k$*) is replaced by the ligand inventories (Eqs. 56, 64, 59). The inventories* $\$_{kd}$ *(*a_{kd}*,* c_{kd}*, or* b_{kd}*) appearing in Eqs. 56, 64, and 59 are represented by Eqs. 31, 32, and 33.*

Example 6 (Enumeration of nonrigid isomers having rotatable methyl ligands (1). An Example for Theorem 6)
Let us return to the skeleton (**4**), where the orbit $\mathcal{O}_1$ (= $\{x_1, x_2\}$) accommodates methyl ligands enumerated in Examples 2, 3, 4, and 5 and the orbit $\mathcal{O}_2$ (= $\{x_3, x_4\}$) simply accommodates achiral ligands selected from $\mathbf{X}^{(2)}$ (= $\{\hat{\mathrm{X}}_1, \hat{\mathrm{X}}_2\}$). As shown in Fig. 3, the six positions due to $\mathcal{O}_1$, which are designated as ($y_1^{(1)}$,$y_2^{(1)}$,$y_3^{(1)}$) and (($y_1^{(1)}$)′,($y_2^{(1)}$)′, ($y_3^{(1)}$)′), accommodate the sub-proligands described in Examples 2, 3, 4, and 5. The two positions due to $\mathcal{O}_2$, which are designated as ($y_1^{(2)}$, ($y_1^{(2)}$)′), accommodate an achiral sub-proligand $\hat{\mathrm{Y}}_1$ or $\hat{\mathrm{Y}}_2$ in place of the achiral ligands $\hat{\mathrm{X}}_1$ or $\hat{\mathrm{X}}_2$.

By starting from Eq. 13 of Example 1, we obtain the following CI–CF:

$$\text{CI–CF}(\mathbf{C}_{2v}; \hat{\$}_k) = \frac{1}{4}\Big\{(\hat{b}_1^{(1)})^2(\hat{b}_1^{(2)})^2 + (\hat{b}_2^{(1)})(\hat{b}_2^{(2)}) + (\hat{a}_1^{(1)})^2(\hat{c}_2^{(2)}) + (\hat{c}_2^{(1)})(\hat{a}_1^{(2)})^2\Big\} \tag{68}$$

where $\$_k$ of Eq. 13 is converted into $\hat{\$}_k$.

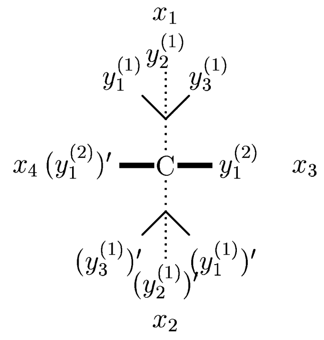
The inventories $\hat{\$}_k$ for the orbit $\mathcal{O}_1$ are calculated by employing Eq. 56 for $\hat{a}_k$, Eq. 64 for $\hat{c}_k$, and Eq. 59 for $\hat{b}_k$.

$$\hat{a}_1^{(1)} = a_1^{(1)}c_2^{(1)} = 2f - g \qquad \text{(Eq. 52)} \tag{69}$$

$$\hat{c}_2^{(1)} = \frac{1}{3}(c_2^{(1)})^3 + \frac{2}{3}c_6^{(1)} = g' \qquad \text{(Eq. 66)} \tag{70}$$

$$\hat{b}_1^{(1)} = \frac{1}{3}(b_1^{(1)})^3 + \frac{2}{3}b_3^{(1)} = g \qquad \text{(Eq. 45)} \tag{71}$$

$$\hat{b}_2^{(1)} = \frac{1}{3}(b_2^{(1)})^3 + \frac{2}{3}b_6^{(1)} \tag{72}$$



5

Fig. 3 A skeleton for generating nonrigid molecules

where the superscript (1) of each sphericity index in the right-hand side designates the dependence on the orbit $\mathcal{O}_1$. Note that we use Eq. 37 for $a_d^{(1)}$, Eq. 38 for $c_d^{(1)}$, and Eq. 39 for $b_d^{(1)}$ and expand the resulting equations to generate the corresponding inventories as generating functions. Some of them have been already calculated in Examples 4, 5, and 3. The inventory $\hat{b}_2^{(1)}$ can be obtained in a similar manner to $\hat{b}_1^{(1)}$ (Example 3).

On the other hand, the inventories $\hat{\$}_k$ for the orbit $\mathcal{O}_2$ are calculated as follows:

$$\hat{a}_1^{(2)} = a_1^{(2)} = \hat{\mathrm{Y}}_1 + \hat{\mathrm{Y}}_2 \tag{73}$$

$$\hat{c}_2^{(2)} = c_2^{(2)} = \hat{\mathrm{Y}}_1^2 + \hat{\mathrm{Y}}_2^2 \tag{74}$$

$$\hat{b}_1^{(2)} = b_1^{(2)} = \hat{\mathrm{Y}}_1 + \hat{\mathrm{Y}}_2 \tag{75}$$

$$\hat{b}_2^{(2)} = b_2^{(2)} = \hat{\mathrm{Y}}_1^2 + \hat{\mathrm{Y}}_2^2 \tag{76}$$

The inventories for $\mathcal{O}_1$ (Eqs. 69–72) and the inventories for $\mathcal{O}_2$ (Eqs. 73–76) are introduced into Eq. 68, which is expanded to give the following generating function:

$$\begin{aligned} F = \cdots & [6\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] + \cdots \\ & +[5\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1^2 + \cdots] + \cdots \\ & +[12\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{q}_1\overline{\mathrm{q}}_1\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] + \cdots \\ & +[8\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{q}_1\overline{\mathrm{q}}_1\hat{\mathrm{Y}}_1^2 + \cdots] + \cdots , \end{aligned} \tag{77}$$

where the remaining terms are omitted.

To exemplify enumeration results in which the orbit $\mathcal{O}_1$ accommodates achiral sub-proligands only (Y_1, Y_2, and Y_3), Fig. 4 shows stereoisomers corresponding to the term $6\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2$ in the right-hand side of Eq. 77, where the coefficient 6 represents two achiral isomers (**6** and **7**) and four pairs of enantiomers.

The two achiral isomers (**6** and **7**) have a so-called "pseudoasymmetric carbon", where p and $\overline{\mathrm{p}}$ represent a pair of a chiral ligand (*S*-$\mathrm{CY}_1\mathrm{Y}_2\mathrm{Y}_3$) and its enantiomeric ligand (*R*-$\mathrm{CY}_1\mathrm{Y}_2\mathrm{Y}_3$). Note that the *RS*-nomenclature is applied by using the priority $\mathrm{Y}_1 > \mathrm{Y}_2 > \mathrm{Y}_3 >$(valence bond). This is a general case for the two achiral trihydroxyglutaric acids (**1** and **2**), which are diastereomeric to each other.

The pair of **8** and $\overline{\mathbf{8}}$ corresponds to the combined term $\frac{1}{2}(\mathrm{p}^2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2 + \overline{\mathrm{p}}^2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2)$ listed in Eq. 20 of Example 2, where we place $\hat{\mathrm{X}}_1 = \hat{\mathrm{Y}}_1$ and $\hat{\mathrm{X}}_2 = \hat{\mathrm{Y}}_2$ for achiral ligands. This is a general case for a pair of enantiomeric trihydroxyglutaric acids (**3** and $\overline{\mathbf{3}}$), where the pair is counted once by regarding the term $\frac{1}{2}(\mathrm{p}^2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2 + \overline{\mathrm{p}}^2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2)$ as a unit term.

The other pairs (**9**/$\overline{\mathbf{9}}$, **10**/$\overline{\mathbf{10}}$, and **11**/$\overline{\mathbf{11}}$) listed in Fig. 4 contain four achiral ligands which are different from each other. They correspond to the term $\mathrm{X}_1\mathrm{X}_2\hat{\mathrm{X}}_1\hat{\mathrm{X}}_2$ listed in Eq. 20 of Example 2, where we place, for example, $\mathrm{X}_1 = \mathrm{A} = \mathrm{Y}_1^2\mathrm{Y}_2$, $\mathrm{X}_2 = \mathrm{B} = \mathrm{Y}_2\mathrm{Y}_3^2$, $\hat{\mathrm{X}}_1 = \hat{\mathrm{Y}}_1$, and $\hat{\mathrm{X}}_2 = \hat{\mathrm{Y}}_2$ for the achiral ligands of the pair **9**/$\overline{\mathbf{9}}$.

To exemplify enumeration results in which the orbit $\mathcal{O}_1$ accommodates achiral sub-proligands (Y_1 and Y_2) and chiral ones (q_1 and $\overline{\mathrm{q}}_1$), Figs. 5, 6 and 7 show stereoisomers

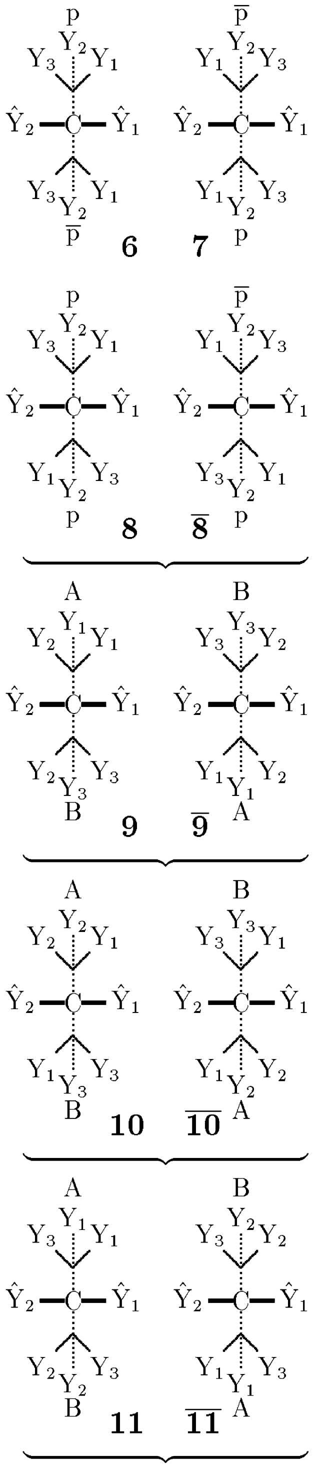


Fig. 4 Stereoisomers (achiral ones and enantiomer pairs) corresponding to the term $6Y_1^2Y_2^2Y_3^2\hat{Y}_1\hat{Y}_2$. The coefficient 6 represents two achiral isomers (**6** and **7**) and four pairs of enantiomers. The symbols A and B represent achiral ligands, while p and $\overline{p}$ represent a pair of a chiral ligand and its enantiomeric ligand

corresponding to the term $12Y_1^2Y_2^2q_1\overline{q}_1\hat{Y}_1\hat{Y}_2$ in the right-hand side of Eq. 77. The coefficient 12 indicates the presence of twelve stereoisomers (enantiomeric pairs or achiral isomers).

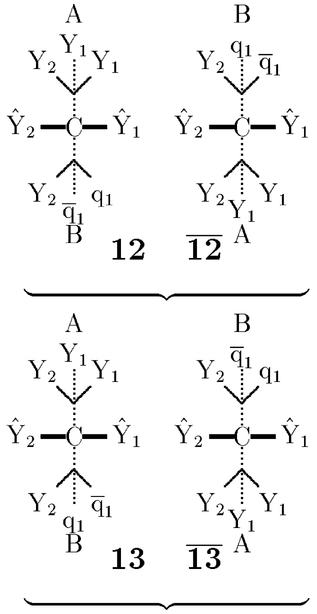


Fig. 5 Two pairs of enantiomers selected from stereoisomers corresponding to the term $12Y_1^2Y_2^2q_1\overline{q}_1\hat{Y}_1\hat{Y}_2$, where the factorization for $\mathcal{O}_1$ is $Y_1^2Y_2/Y_2q_1\overline{q}_1$. Another set of two pairs of enantiomers is represented by the factorization $Y_1Y_2^2/Y_1q_1\overline{q}_1$

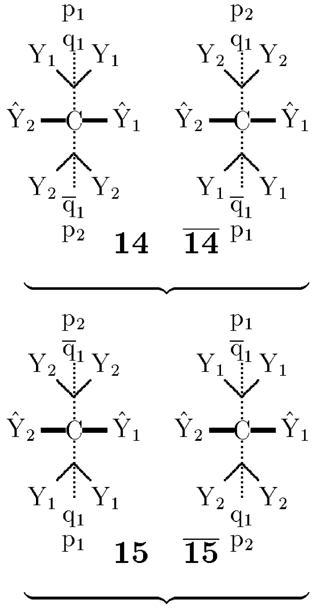


Fig. 6 Two pairs of enantiomers selected from stereoisomers corresponding to the term $12Y_1^2Y_2^2q_1\overline{q}_1\hat{Y}_1\hat{Y}_2$, where the factorization for $\mathcal{O}_1$ is $Y_1^2q/Y_2^2\overline{q}_1$ ($Y_2^2q/Y_1^2\overline{q}_1$)

Figure 5 shows two pairs of enantiomers selected from stereoisomers (**12**/$\overline{\mathbf{12}}$ and **13**/$\overline{\mathbf{13}}$) corresponding to the factorization into $Y_1^2Y_2/Y_2q_1\overline{q}_1$ for $\mathcal{O}_1$. The same situation holds true for the factorization $Y_1Y_2^2/Y_1q_1\overline{q}_1$, where another set of two pairs of enantiomers appears. Thus, Fig. 5 totally corresponds to four stereoisomers among the twelve stereoisomers under the action of the group at issue.

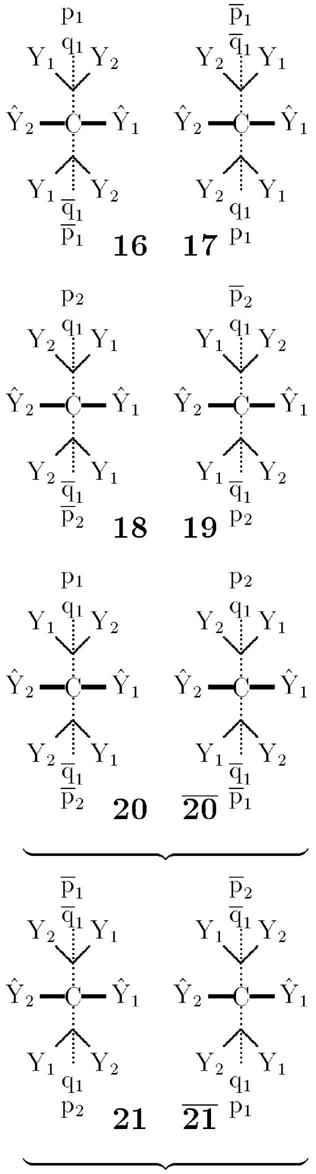


Fig. 7 Four achiral isomers and two pairs of enantiomers selected from stereoisomers corresponding to the term $12\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{q}_1\overline{\mathrm{q}}_1\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2$, where the factorization for $\mathcal{O}_1$ is $\mathrm{Y}_1\mathrm{Y}_2\mathrm{q}/\mathrm{Y}_1\mathrm{Y}_2\overline{\mathrm{q}}_1$

Figure 6 shows two pairs of enantiomers selected from stereoisomers (**14**/$\overline{\mathbf{14}}$ and **15**/$\overline{\mathbf{15}}$) corresponding to the factorization into $\mathrm{Y}_1^2\mathrm{q}/\mathrm{Y}_2^2\overline{\mathrm{q}}_1$ for $\mathcal{O}_1$. Thus, Fig. 6 totally corresponds to two stereoisomers among the twelve stereoisomers under the action of the group at issue.

Figure 7 shows four achiral isomers (**16**, **17**, **18**, and **19**) and two pairs of enantiomers (**20**/$\overline{\mathbf{20}}$ and **21**/$\overline{\mathbf{21}}$), which correspond to the factorization into $\mathrm{Y}_1^2\mathrm{q}/\mathrm{Y}_2^2\overline{\mathrm{q}}_1$ for $\mathcal{O}_1$. Thus, Fig. 7 totally corresponds to six stereoisomers among the twelve stereoisomers under the action of the group at issue.

As a result, the numbers of isomers depicted in Figs. 5, 6, and 7 are summed up to give 2 (+2) + 2 + 6 = 12, which is equal to the coefficient of the term $\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{q}_1\overline{\mathrm{q}}_1\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2$ appearing in the right-hand side of Eq. 77. □

3 Enumeration of nonrigid isomers via extended cycle indices with chirality fittingness

3.1 Extended cycle indices with chirality fittingness

The inventories used in Theorem 6 ($\hat{\$}_k$, i.e., $\hat{a}_k$ (Eq. 56), $\hat{c}_k$ (Eq. 64), and $\hat{b}_k$ (Eq. 59)) take expanded forms after introducing $\$_{kd}$ (i.e., a_{kd} (Eq. 31), c_{kd} (Eq. 32), and b_{kd} (Eq. 33)). Obviously, the same result can be obtained by the introduction of unexpanded inventories ($\hat{\$}_k$) into Eq. 67 of Theorem 6, where the intermediate cycle index is then expanded after the introduction of $\$_{kd}$. Such unexpanded forms, which are called "extended sphericity indices" (eSIs), are represented by the symbols $\psi_{(\$)k}$ (i.e., $\psi_{(a)k}$, $\psi_{(c)k}$, and $\psi_{(b)k}$) in place of $\hat{\$}_k$ (i.e., $\hat{a}_k$, $\hat{c}_k$, and $\hat{b}_k$) as follows:

$$\psi_{(a)k} = 2\text{CI–CF}(\widehat{\mathbf{H}};\$_{kd}) - \text{CI–CF}(\widehat{\mathbf{H}}';b_{kd}) \tag{78}$$

$$\psi_{(c)k} = \text{CI–CF}(\widehat{\mathbf{H}}';c_{kd}), \tag{79}$$

$$\psi_{(b)k} = \text{CI–CF}(\widehat{\mathbf{H}}';b_{kd}) \tag{80}$$

where CI–CF($\widehat{\mathbf{H}}$; $\$_{kd}$) and CI–CF($\widehat{\mathbf{H}}'$; $\$_{kd}$) in the right-hand side are used in unexpanded forms. In a similar way to the CI–CF shown in Eq. 5, an extended cycle index with chirality fittingness (eCI–CF) is defined by using eSIs (Eqs. 78–80) as follows:

$$\text{eCI–CF}(\widehat{\mathbf{G}};\psi_{(\$)k}) = \frac{1}{|\widehat{\mathbf{G}}|}\sum_{G\in\widehat{\mathbf{G}}}\prod_{\alpha}[\psi_{(\$)1}^{\mu_1(G)}\psi_{(\$)2}^{\mu_2(G)}\cdots\psi_{(\$)r}^{\mu_r(G)}]^{(\alpha)}, \tag{81}$$

where α runs so that $G^{(\alpha)}$ covers G and where the symbol $\psi_{(\$)k}$ (for $k = 1, 2, \ldots, r$) represents the eSI $\psi_{(a)k}$, $\psi_{(c)k}$, or $\psi_{(b)k}$ according to the sphericity of the k-cycle. The intermediate cycle index CI–CF′($\widehat{\mathbf{G}}[\widehat{\mathbf{H}}]$; $\$_d$) is defined as follows:

$$\text{CI–CF}'(\widehat{\mathbf{G}}[\widehat{\mathbf{H}}];\$_d) = \text{eCI–CF}(\widehat{\mathbf{G}};\psi_{(\$)k}), \tag{82}$$

where the right-hand side is obtained by introducing eSIs (Eqs. 78–80). Note that the SI $\$_d$ in the left-hand side is different from the eSI $\psi_{(\$)k}$ in the right-hand side.

3.2 Enumeration of nonrigid molecules

In the light of the discussions described above, Theorem 6 can be converted into Theorem 7. The symbol $\widehat{\mathbf{G}}$ represents a kind of wreath product, where ligands of different groups can be used as [$\widehat{\mathbf{H}}$].

Theorem 7 (The second theorem for enumerating nonrigid stereoisomers) *Suppose that each of the proligands of* $\mathbf{X}^{(\alpha)}$ *(Eq. 6 in Theorem 1) is substituted by a ligand that is generated from sub-proligands selected from* $\mathbf{Y}^{(\beta)}$ *(Eq. 36 in Theorem 2). Let* M_Θ *denote the number of nonrigid isomers that have the molecular formula shown in Eq. 61. A generating function for calculating* M_Θ *is represented by*

$$\sum_{[\Theta]} M_\Theta \prod_{\alpha}\prod_{\beta}[\mathrm{Y}_1^{\Theta_1}\cdots\mathrm{Y}_m^{\Theta_m}\mathrm{q}_1^{\Theta'_1}\cdots\mathrm{q}_{m'}^{\Theta'_{m'}}\overline{\mathrm{q}}_1^{\Theta''_1}\cdots\overline{\mathrm{q}}_{m'}^{\Theta''_{m'}}]^{(\alpha,\beta)}$$

$$= \text{CI–CF}'(\widehat{\mathbf{G}}[\widehat{\mathbf{H}}];\$_d), \tag{83}$$

where the CI–CF$'(\widehat{\mathbf{G}}[\widehat{\mathbf{H}}]; \$_d)$ *on the right-hand side is represented by Eq. 82. The inventories* $\$_d$ *(*a_d*,* c_d*, or* b_d*) appearing in the right-hand side of Eq. 83 (i.e., in Eqs. 78–80) are represented by Eqs. 31, 32, and 33.*

It should be noted that Theorem 6 stems from the scheme "positions of a skeleton ⇐ proligands ⇐ ligands (positions of a ligand ⇐ sub-proligands)", while Theorem 7 stems from the scheme "(positions of a skeleton ⇐ proligands ⇐ ligands (positions of a ligand)) ⇐ sub-proligands".

Example 7 (Enumeration of nonrigid isomers having rotatable methyl ligands (2). An example for Theorem 7) The same problem as described in Example 6 is solved by virtue of Theorem 7. In place of Eq. 68 of Example 6, we obtain the following eCI–CF by applying Eq. 81 to the present case.

$$\begin{aligned}&\text{eCI–CF}(\mathbf{C}_{2v}; \psi_{(\$)k})\\&\quad= \frac{1}{4}\Big\{(\psi^{(1)}_{(b)1})^2(\psi^{(2)}_{(b)1})^2 + (\psi^{(1)}_{(b)2})(\psi^{(2)}_{(b)2})\\&\qquad+ (\psi^{(1)}_{(a)1})^2(\psi^{(2)}_{(c)2}) + (\psi^{(1)}_{(c)2})(\psi^{(2)}_{(a)1})^2\Big\}. \qquad (84)\end{aligned}$$

First, we consider the eSIs for methyl ligands ($\mathbf{C}_{3v}$ and related symmetries), which are accommodated in the orbit $\mathcal{O}_1$. In place of Eqs. 69–72 (expanded forms), the following eSIs (unexpanded forms) are calculated by applying Eqs. 78, 79, and 80 to the present case:

$$\psi^{(1)}_{(a)1} = a^{(1)}_1 c^{(1)}_2 \qquad (85)$$

$$\psi^{(1)}_{(c)2} = \frac{1}{3}(c^{(1)}_2)^3 + \frac{2}{3}c^{(1)}_6 \qquad (86)$$

$$\psi^{(1)}_{(b)1} = \frac{1}{3}(b^{(1)}_1)^3 + \frac{2}{3}b^{(1)}_3 \qquad (87)$$

$$\psi^{(1)}_{(b)2} = \frac{1}{3}(b^{(1)}_2)^3 + \frac{2}{3}b^{(1)}_6 \qquad (88)$$

where the superscript (1) of each sphericity index in the right-hand side designates the dependence on the orbit $\mathcal{O}_1$. It should be noted that Eqs. 85–88 have already appeared in the derivation process of Eqs. 69–72 in Example 6 as expanded forms.

Second, we consider the eSIs for achiral ligands ($\mathbf{C}_{\infty v}$ and related symmetries), which are accommodated in the orbit $\mathcal{O}_2$. The eSIs for the orbit $\mathcal{O}_2$ are calculated as follows:

$$\psi^{(2)}_{(a)1} = a^{(2)}_1 \qquad (89)$$

$$\psi^{(2)}_{(c)2} = c^{(2)}_2 \qquad (90)$$

$$\psi^{(2)}_{(b)1} = b^{(2)}_1 \qquad (91)$$

$$\psi^{(2)}_{(b)2} = b^{(2)}_2 \qquad (92)$$

It follows that Theorem 7 (Eq. 82) gives the intermediate cycle index as follows:

$$\begin{aligned}&\text{CI–CF}'(\mathbf{C}_{2v}[\mathbf{C}_{3v}, \mathbf{C}_{\infty v}]; \$_d)\\&\quad= \frac{1}{36}(b^{(1)}_1)^6(b^{(2)}_1)^2 + \frac{1}{9}(b^{(1)}_1)^3(b^{(1)}_3)(b^{(2)}_1)^2\\&\qquad+\frac{1}{9}(b^{(1)}_3)^2(b^{(2)}_1)^2 + \frac{1}{12}(b^{(1)}_2)^3(b^{(2)}_2)\\&\qquad+\frac{1}{6}(b^{(1)}_6)(b^{(2)}_2) + \frac{1}{4}(a^{(1)}_1)^2(c^{(1)}_2)^2(c^{(2)}_2)\\&\qquad+\frac{1}{12}(c^{(1)}_2)^3(a^{(2)}_1)^2 + \frac{1}{6}(c^{(1)}_6)(a^{(2)}_1)^2 \qquad (93)\end{aligned}$$

We use Eq. 37 for $a^{(1)}_d$, Eq. 38 for $c^{(1)}_d$, and Eq. 39 for $b^{(1)}_d$ for $\mathcal{O}_1$, while we apply Eqs. 73–76 to Eqs. 89–92 for $\mathcal{O}_2$. They are introduced into Eq. 93, which is expanded to give the same generating function F as Eq. 77 of Example 6. □

3.3 Special cases without chiral sub-proligands

Theorem 7 takes account of both achiral sub-proligands and chiral ones, as found in $\mathbf{Y}^{(\beta)}$ (Eq. 28 of Theorem 2). When we take account of achiral sub-proligands only, i.e.,

$$\mathbf{Y}'^{(\beta)} = \{\mathrm{Y}_1, \mathrm{Y}_2, \ldots, \mathrm{Y}_m\}, \qquad (94)$$

Theorem 7 can be reduced into a simpler format. Under this condition, the SIs listed in Eqs. 31, 32, and 33 are degenerate to give the same equation. Thereby, we obtain the following corollary:

Corollary 1 (Simplified cases in the enumeration of nonrigid stereoisomers. Corollary for Theorem 7) *Suppose that each of the proligands of* $\mathbf{X}^{(\alpha)}$ *(Eq. 6 in Theorem 1) is substituted by a ligand that is generated from* achiral *sub-proligands selected from* $\mathbf{Y}'^{(\beta)}$ *(Eq. 94). Let* M_Θ *denote the number of nonrigid isomers that have the molecular formula shown in Eq. 61, where the terms of chiral sub-proligands are omitted. A generating function for calculating* M_Θ *is represented by*

$$\begin{aligned}&\sum_{[\Theta]} M_\Theta \times \prod_{\alpha}\prod_{\beta}[\mathrm{Y}_1^{\Theta_1}\cdots\mathrm{Y}_m^{\Theta_m}]^{(\alpha,\beta)}\\&\quad= \text{CI–CF}'(\widehat{\mathbf{G}}[\widehat{\mathbf{H}}]; \$_d), \qquad (95)\end{aligned}$$

where the CI–CF$'(\widehat{\mathbf{G}}[\widehat{\mathbf{H}}]; \$_d)$ *on the right-hand side is represented by Eq. 82. The inventories* $\$_d$ *(*a_d*,* c_d*, or* b_d*) appearing in the right-hand side of Eq. 95 are represented by*

$$a_d = c_d = b_d = \mathrm{Y}_1^d + \mathrm{Y}_2^d + \cdots + \mathrm{Y}_m^d \qquad (96)$$

for each $\mathcal{O}_\alpha$*.*

The degenerate SI (Eq. 96) influences the eSIs (Eqs. 78–80), which can be rewritten in case of Theorem 1 as follows:

$$\psi_{(a)k} = 2\text{CI–CF}(\widehat{\mathbf{H}}; \$_{kd}) - \text{CI–CF}(\widehat{\mathbf{H}}'; b_{kd}) \qquad (97)$$

$$\psi_{(c)k} = \text{CI–CF}(\widehat{\mathbf{H}}'; b_{kd}), \qquad (98)$$

$$\psi_{(b)k} = \text{CI–CF}(\widehat{\mathbf{H}}'; b_{kd}). \qquad (99)$$

Obviously, this modification has been used in theorems described in Part 2 of the present series [11]. It should be noted that the replacement of Eq. 79 by Eq. 98 is permitted only if the three SIs (Eqs. 31–33) coalesce into a single one (Eq. 96) because of considering achiral sub-proligands only.

Example 8 (Enumeration of nonrigid stereoisomers aimed at examining isomeric trihydroxyglutaric acids. An example for Corollary 1)

The same problem as described in Examples 6 and 7 is solved by virtue of Theorem 1 under the condition in which only achiral sub-proligands are considered. We here use the same eCI–CF($\mathbf{C}_{2v}[\mathbf{C}_{3v}, \mathbf{C}_{\infty v}]$; $\psi_{(\$)k}$) (Eq. 84), the same unexpanded eSIs (Eqs. 85–92), and the same intermediate cycle index CI–CF′($\mathbf{C}_{2v}$; $\$_d$) (Eq. 93) as obtained in Example 7.

In Example 7, we have used Eq. 37 for $a_d^{(1)}$, Eq. 38 for $c_d^{(1)}$, and Eq. 39 for $b_d^{(1)}$ for the orbit $\mathcal{O}_1$ as well as Eqs. 73–76 for the orbit $\mathcal{O}_2$, because we take account of chiral and achiral sub-proligands. In contrast, we use here the following inventories:

$$a_d^{(1)} = c_d^{(1)} = b_d^{(1)} = \mathrm{Y}_1^d + \mathrm{Y}_2^d + \mathrm{Y}_3^d \tag{100}$$

for the orbit $\mathcal{O}_1$ and

$$a_d^{(2)} = c_d^{(2)} = b_d^{(2)} = \hat{\mathrm{Y}}_1^d + \hat{\mathrm{Y}}_2^d \tag{101}$$

for the orbit $\mathcal{O}_2$ according to Eq. 96, because the present case takes account of achiral sub-proligands only. The inventories (Eqs. 100, 101) are introduced into the intermediate CI (Eq. 93 of Example 7) and the resulting equation is expanded to give the following generating function,

$$\begin{aligned} F' = {} & [\mathrm{Y}_1^6\hat{\mathrm{Y}}_1^2 + \cdots] + [\mathrm{Y}_1^5\mathrm{Y}_2\hat{\mathrm{Y}}_1^2 + \cdots] + [2\mathrm{Y}_1^4\mathrm{Y}_2^2\hat{\mathrm{Y}}_1^2 + \cdots] \\ & + [2\mathrm{Y}_1^4\mathrm{Y}_2\mathrm{Y}_3\hat{\mathrm{Y}}_1^2 + \cdots] + [2\mathrm{Y}_1^3\mathrm{Y}_2^3\hat{\mathrm{Y}}_1^2 + \cdots] \\ & + [3\mathrm{Y}_1^3\mathrm{Y}_2^2\mathrm{Y}_3\hat{\mathrm{Y}}_1^2 + \cdots] + [5\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1^2] \\ & + [\mathrm{Y}_1^6\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] + [\mathrm{Y}_1^5\mathrm{Y}_2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] \\ & + [2\mathrm{Y}_1^4\mathrm{Y}_2^2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] + [3\mathrm{Y}_1^4\mathrm{Y}_2\mathrm{Y}_3\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] \\ & + [2\mathrm{Y}_1^3\mathrm{Y}_2^3\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] + [4\mathrm{Y}_1^3\mathrm{Y}_2^2\mathrm{Y}_3\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] \\ & + [6\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2]. \end{aligned} \tag{102}$$

The generating function F' (Eq. 102) contains terms for achiral sub-proligands (Y_1, Y_2, and Y_3) only. This should be compared with the generating function F (Eq. 77 of Examples 6, 7) which contains terms for both chiral and achiral sub-proligands.

For example, the stereoisomers corresponding to the term $6\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2$ have been already depicted in Fig. 4. Among the six stereoisomers (Fig. 4), the two achiral isomers (**6** and **7**) correspond to the achiral trihydroxyglutaric acids (**1** and **2**), when we place Y_1 = OH, Y_2 = COOH, Y_3 = H, $\hat{\mathrm{Y}}_1$ = OH, and $\hat{\mathrm{Y}}_2$ =H. On the other hand, the pair of **8**/$\overline{\mathbf{8}}$ corresponds to the pair of **3** and $\overline{\mathbf{3}}$. □

3.4 Other previous methods as special cases of Theorem 7

3.4.1 On Pólya's corona

Pólya's corona was introduced in his famous article [7,8] to solve enumeration problems of nonrigid molecules due to rotations around bonds. As proved in Part 2 of this series [11], Pólya's corona is concerned only with the enumeration of graphs but not with the enumeration of chemical structures. This point is further confirmed by considering Pólya's corona as a special case of Theorem 7. Thus, eSIs (Eqs. 78–80) are reduced into a dummy variable ψ_k without chirality fittingness:

$$\psi_k = \mathrm{CI}(\widehat{\mathbf{H}}; s_{kd}), \tag{103}$$

where SIs (Eqs. 31–33) are reduced into a dummy variable s_k without chirality fittingness. The eCI–CF of Eq. 81 is reduced into a format without chirality fittingness and the dependence on α:

$$\mathrm{eCI}(\widehat{\mathbf{G}}; \psi_k) = \frac{1}{|\widehat{\mathbf{G}}|} \sum_{G \in \widehat{\mathbf{G}}} \psi_1^{\mu_1(G)} \psi_2^{\mu_2(G)} \cdots \psi_{(r)}^{\mu_r(G)}. \tag{104}$$

The intermediate cycle index CI–CF′($\widehat{\mathbf{G}}[\widehat{\mathbf{H}}]$; $\$_d$) is also reduced into the following format:

$$\mathrm{CI}'(\widehat{\mathbf{G}}[\widehat{\mathbf{H}}]; s_d) = \mathrm{eCI}(\widehat{\mathbf{G}}; \psi_k). \tag{105}$$

This means that only achiral ligands (or proligands or sub-proligands) are taken into consideration in Pólya's Corona. The following example clarifies this situation.

Example 9 (Enumeration of nonrigid isomers as graphs. An example for Pólya's corona as a special case of Theorem 6)

The same problem as described in Example 7 is solved by virtue of Pólya's Corona as a special case of Theorem 6.

According to Eq. 104, the eCI–CF($\mathbf{C}_{2v}[\mathbf{C}_{3v}, \mathbf{C}_{\infty v}]$; $\psi_{(\$)k}$) shown in Eq. 84 is converted into the following reduced form:

$$\begin{aligned} \mathrm{eCI}(\mathbf{C}_{2v}; \psi_k) = {} & \frac{1}{4} \Big\{ (\psi_1^{(1)})^2(\psi_1^{(2)})^2 + (\psi_2^{(1)})(\psi_2^{(2)}) \\ & + (\psi_1^{(1)})^2(\psi_2^{(2)}) + (\psi_2^{(1)})(\psi_1^{(2)})^2 \Big\}. \end{aligned} \tag{106}$$

In place of Eqs. 85–88, the ψ_k (Eq. 103) for the orbit $\mathcal{O}_1$ is calculated as follows:

$$\psi_k^{(1)} = \frac{1}{6}(s_k^{(1)})^3 + \frac{1}{3}s_{3k}^{(1)} + \frac{1}{2}(s_k^{(1)})(s_{2k}^{(1)}). \tag{107}$$

In place of Eqs. 85–88, the ψ_k (Eq. 103) for the orbit $\mathcal{O}_2$ is calculated as follows:

$$\psi_k^{(2)} = s_k^{(2)} \tag{108}$$

Introduction of Eqs. refe107 and 108 into Eq. 106 gives the intermediate cycle index as follows:

$$\begin{aligned} & \mathrm{CI}'(\mathbf{C}_{2v}[\mathbf{C}_{3v}, \mathbf{C}_{\infty v}]; \$_d) \\ & = \frac{1}{144}(s_1^{(1)})^6(s_1^{(2)})^2 + \frac{1}{36}(s_1^{(1)})^3(s_3^{(1)})(s_1^{(2)})^2 \\ & \quad + \frac{1}{24}(s_1^{(1)})^4(s_2^{(1)})(s_1^{(2)})^2 + \frac{1}{36}(s_3^{(1)})^2(s_1^{(2)})^2 \\ & \quad + \frac{1}{12}(s_1^{(1)})(s_2^{(1)})(s_3^{(1)})(s_1^{(2)})^2 + \frac{1}{16}(s_1^{(1)})^2(s_2^{(1)})^2(s_1^{(2)})^2 \\ & \quad + \frac{1}{24}(s_2^{(1)})^3(s_2^{(2)}) + \frac{1}{12}(s_6^{(1)})(s_2^{(2)}) \\ & \quad + \frac{1}{8}(s_2^{(1)})(s_4^{(1)})(s_2^{(2)}) + \frac{1}{144}(s_1^{(1)})^6(s_2^{(2)}) \end{aligned}$$

$$+\frac{1}{36}(s_1^{(1)})^3(s_3^{(1)})(s_2^{(2)}) + \frac{1}{24}(s_1^{(1)})^4(s_2^{(1)})(s_2^{(2)})$$
$$+\frac{1}{36}(s_3^{(1)})^2(s_2^{(2)}) + \frac{1}{12}(s_1^{(1)})(s_2^{(1)})(s_3^{(1)})(s_2^{(2)})$$
$$+\frac{1}{16}(s_1^{(1)})^2(s_2^{(1)})^2(s_2^{(2)}) + \frac{1}{24}(s_2^{(1)})^3(s_1^{(2)})^2$$
$$+\frac{1}{12}(s_6^{(1)})(s_1^{(2)})^2 + \frac{1}{8}(s_2^{(1)})(s_4^{(1)})(s_1^{(2)})^2. \tag{109}$$

Since this example does not take account of inner structures of objects, we use the following inventory:

$$s_d^{(1)} = \mathrm{Y}_1^d + \mathrm{Y}_2^d + \mathrm{Y}_3^d. \tag{110}$$

for the orbit $\mathcal{O}_1$ and the other inventory:

$$s_d^{(2)} = \hat{\mathrm{Y}}_1^d + \hat{\mathrm{Y}}_2^d. \tag{111}$$

for the orbit $\mathcal{O}_2$. The inventories (Eqs. 110 and 111) are introduced into Eq. 109 and the resulting equation is expanded to give the following generating function:

$$\begin{aligned}F'' = {} & [\mathrm{Y}_1^6\hat{\mathrm{Y}}_1^2 + \cdots] + [\mathrm{Y}_1^5\mathrm{Y}_2\hat{\mathrm{Y}}_1^2 + \cdots] + [2\mathrm{Y}_1^4\mathrm{Y}_2^2\hat{\mathrm{Y}}_1^2 + \cdots]\\ & +[2\mathrm{Y}_1^4\mathrm{Y}_2\mathrm{Y}_3\hat{\mathrm{Y}}_1^2 + \cdots] + [2\mathrm{Y}_1^3\mathrm{Y}_2^3\hat{\mathrm{Y}}_1^2 + \cdots]\\ & +[3\mathrm{Y}_1^3\mathrm{Y}_2^2\mathrm{Y}_3\hat{\mathrm{Y}}_1^2 + \cdots] + [4\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1^2]\\ & +[\mathrm{Y}_1^6\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] + [\mathrm{Y}_1^5\mathrm{Y}_2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots]\\ & +[2\mathrm{Y}_1^4\mathrm{Y}_2^2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] + [2\mathrm{Y}_1^4\mathrm{Y}_2\mathrm{Y}_3\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots]\\ & +[2\mathrm{Y}_1^3\mathrm{Y}_2^3\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] + [3\mathrm{Y}_1^3\mathrm{Y}_2^2\mathrm{Y}_3\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots]\\ & +[4\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2].\end{aligned} \tag{112}$$

It is worthwhile to compare between the generating functions F' (Eq. 102) and F'' (Eq. 112), where different coefficients appear at the following terms in the generating functions.

5 : 4 for the term $\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1^2$
3 : 2 for the term $\mathrm{Y}_1^4\mathrm{Y}_2\mathrm{Y}_3\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2$
4 : 3 for the term $\mathrm{Y}_1^3\mathrm{Y}_2^2\mathrm{Y}_3\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2$
6 : 4 for the term $\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2$. (113)

Among them, stereoisomers for the term $\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1\ \hat{\mathrm{Y}}_2$ have been depicted in Fig. 4. The value 6 in F' (Eq. 102) corresponds to two achiral isomers (**6** and **6**) and four pairs of enantiomers (**8**/$\overline{\mathbf{8}}$, **9**/$\overline{\mathbf{9}}$, **10**/$\overline{\mathbf{10}}$, and **11**/$\overline{\mathbf{11}}$). On the other hand, two achiral isomers (**6** and **6**) and one pair of enantiomers (**8**/$\overline{\mathbf{8}}$) coalesce into one graph and the remaining three pairs of enantiomers (**9**/$\overline{\mathbf{9}}$, **10**/$\overline{\mathbf{10}}$, and **11**/$\overline{\mathbf{11}}$) represent three graphs in F'' (Eq. 112). Thus, the value 4 in F'' (Eq. 112) corresponds to four graphs. □

Example 9 exemplifies the limitations of Pólya's theorem and Pólya's corona, which still remain in the same situation as the 1870s of "proto"-stereochemistry when the two achiral isomers (**6** and **7**) and one pair of enantiomers (**8**/$\overline{\mathbf{8}}$) were not discriminated in a rational way. See the stereoisomers of trihydroxyglutaric acid discussed in Fig. 1.

3.4.2 On chemical identity groups by Ugi el al.

The concept of chemical identity groups proposed by Ugi et al. [5] can be regarded as further simplified cases from the present point of view. Thus, the dummy variable (Eq. 103), which has been obtained by starting from the eSIs (Eqs. 78–80), is further reduced into a dummy variable ϕ_k,

$$\phi_k = \mathrm{CI}(\widehat{\mathbf{H}}'; s_{kd}), \tag{114}$$

where the achiral group **H** is replaced by the maximum chiral subgroup **H**′. The eCI (Eq. 104), which has been derived from the eCI–CF of Eq. 81, is further reduced into a format:

$$\mathrm{eCI}(\widehat{\mathbf{G}}'; \phi_k) = \frac{1}{|\widehat{\mathbf{G}}'|}\sum_{G\in\widehat{\mathbf{G}}'} \phi_1^{\mu_1(G)}\phi_2^{\mu_2(G)}\cdots\phi_{(r)}^{\mu_r(G)}, \tag{115}$$

where the $\widehat{\mathbf{G}}$ of Eq. 104 is replaced by its maximum chiral subgroup $\widehat{\mathbf{G}}'$. The intermediate cycle index (Eq. 105), which is obtained from CI–CF′($\widehat{\mathbf{G}}[\widehat{\mathbf{H}}]$; $\$_d$) (Eq. 82), is further reduced into the following format:

$$\mathrm{CI}'(\widehat{\mathbf{G}}'[\widehat{\mathbf{H}}']; s_d) = \mathrm{eCI}(\widehat{\mathbf{G}}'; \phi_k). \tag{116}$$

The enumeration based on Eq. 116 is equivalent to the enumeration based on the concept of chemical identity groups proposed by Ugi et al. [5], as exemplified by the following example.

Example 10 (Enumeration of nonrigid isomers under the action of chiral point groups) The same problem as described in Examples 7 and 9 is solved by virtue of the further simplified method described above. Because the point group $\mathbf{C}_2$ is considered in place of $\mathbf{C}_{2v}$, we take account of the permutation group:
{(1)(2)(3)(4), (1 2)(3 4)},
which governs $\mathcal{O}_1 = \{x_1, x_2\}$ and $\mathcal{O}_2 = \{x_3, x_4\}$. Hence, Eq. 115 for the present treatment is calculated to be:

$$\mathrm{eCI}'(\mathbf{C}_2; \phi_k) = \frac{1}{2}\left\{(\phi_1^{(1)})^2(\phi_1^{(2)})^2 + (\phi_2^{(1)})(\phi_2^{(2)})\right\}. \tag{117}$$

To enumerate methyl ligands, we use $\mathbf{C}_3$ in place of $\mathbf{C}_{3v}$. According to Eq. 114, we obtain the following equation for $\mathcal{O}_1$:

$$\phi_k^{(1)} = \frac{1}{3}(s_k^{(1)})^3 + \frac{2}{3}s_{3k}^{(1)}, \tag{118}$$

in place of Eq. 107. In place of Eqs. 108, the ϕ_k (Eq. 114) for the orbit $\mathcal{O}_2$ is calculated as follows:

$$\phi_k^{(2)} = s_k^{(2)}. \tag{119}$$

The introduction of Eqs. 118 and 119 into Eq. 117 gives the intermediate cycle index as follows:

$$\begin{aligned}&\mathrm{CI}'(\mathbf{C}_2[\mathbf{C}_3, \mathbf{C}_\infty]; s_d)\\ &\quad = \frac{1}{18}(s_1^{(1)})^6(s_1^{(2)})^2 + \frac{2}{9}(s_1^{(1)})^3(s_3^{(1)})(s_1^{(2)})^2\\ &\qquad +\frac{2}{9}(s_3^{(1)})^2(s_1^{(2)})^2 + \frac{1}{6}(s_2^{(1)})^3(s_2^{(2)})\\ &\qquad +\frac{1}{3}(s_6^{(1)})(s_2^{(2)}).\end{aligned} \tag{120}$$

Because this example does not take account of inner structures of objects, we can use the following inventory:

$$s_d^{(1)} = \mathrm{Y}_1^d + \mathrm{Y}_2^d + \mathrm{Y}_3^d \tag{121}$$

for the orbit $\mathcal{O}_1$ and the other inventory:

$$s_d^{(2)} = \hat{\mathrm{Y}}_1^d + \hat{\mathrm{Y}}_2^d \tag{122}$$

for the orbit $\mathcal{O}_2$. The inventories (Eqs. 121 and 122) are introduced into Eq. 120 and the resulting equation is expanded to give the following generating function:

$$\begin{aligned} F''' = {} & [\mathrm{Y}_1^6\hat{\mathrm{Y}}_1^2 + \cdots] + [\mathrm{Y}_1^5\mathrm{Y}_2\hat{\mathrm{Y}}_1^2 + \cdots] + [2\mathrm{Y}_1^4\mathrm{Y}_2^2\hat{\mathrm{Y}}_1^2 + \cdots] \\ & + [3\mathrm{Y}_1^4\mathrm{Y}_2\mathrm{Y}_3\hat{\mathrm{Y}}_1^2 + \cdots] + [2\mathrm{Y}_1^3\mathrm{Y}_2^3\hat{\mathrm{Y}}_1^2 + \cdots] \\ & + [4\mathrm{Y}_1^3\mathrm{Y}_2^2\mathrm{Y}_3\hat{\mathrm{Y}}_1^2 + \cdots] + [6\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1^2] \\ & + [\mathrm{Y}_1^6\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] + [2\mathrm{Y}_1^5\mathrm{Y}_2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] \\ & + [3\mathrm{Y}_1^4\mathrm{Y}_2^2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] + [6\mathrm{Y}_1^4\mathrm{Y}_2\mathrm{Y}_3\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] \\ & + [4\mathrm{Y}_1^3\mathrm{Y}_2^3\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] + [8\mathrm{Y}_1^3\mathrm{Y}_2^2\mathrm{Y}_3\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2 + \cdots] \\ & + [10\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2]. \end{aligned} \tag{123}$$

The coefficient 10 of the term $\mathrm{Y}_1^2\mathrm{Y}_2^2\mathrm{Y}_3^2\hat{\mathrm{Y}}_1\hat{\mathrm{Y}}_2$ appearing in F''' (Eq. 123) shows the presence of ten isomers, which have been already depicted in Fig. 4. It should be noted that each of the ten stereoisomers depicted in Fig. 4 is counted as one isomer in terms of the generating function F''' (Eq. 123). This result should be compared with F' (Eq. 102) and F'' (Eq. 112). □

It should be pointed out that an essentially equivalent equation to Eq. 120 can be alternatively obtained by using the chemical identity group $\mathrm{S}_{17\mathrm{a}}$ of order 18 and degree 8, which was reported by Ugi et al. [5, page 146]. They enumerated isomers of trihydroxyglutaric acid on the basis of the concrete form of $\mathrm{S}_{17\mathrm{a}}$ for a propane skeleton with eight positions. The procedure described in Example 10 is simpler and more straightforward than the procedure of Ugi et al. [5] because the former can omit the involvement of the concrete form of the chemical identity group $\mathrm{S}_{17\mathrm{a}}$. In order to examine stereoisomeric equivalences, Ugi et al. [5] took account of a further permutation group of order 144 (called "the group of constitution preserving ligand permutations"), which contains the group $\mathrm{S}_{17\mathrm{a}}$ as its subgroup. The action of the permutation group of order 144, however, can be replaced by the generating-function method described in Example 10. For the order 144, see Eq. 109 of Example 9, which indicates that "the group of constitution preserving ligand permutations" is equivalent to the group of graph enumeration. It should be emphasized that Examples 9 and 10 are special cases of Theorem 7.

3.4.3 Superiority of the proligand method

As exemplified by Example 10, the use of "chemical identity groups" is equivalent to the use of chiral point groups. As exemplified by Examples 9 and 10, the use of "the groups of constitution preserving ligand permutations" is equivalent to the use of graphs. It follows that the combined use of the two types of groups [5] did not take account of reflection operations which should play an important role as key operations to judge stereochemical relationships such as enantiomeric ones. The judgement by reflection operations was not explicitly formulated in the combined use of the two types of groups [5], although enantiomeric relationships should be judged in terms of reflection operations. Strictly speaking, the combined use of the two types of groups determines stereoisomeric relationships only, where an additional manual judgement by reflection operations is necessary to decide whether the stereoisomeric relationships are enantiomeric ones or diastereomeric ones. In fact, the permutability of ligands was used to judge the stereoisomeric relationships in the approach by Ugi et al. [5], where the ligands are regarded as structureless objects.

On the other hand, the proligand approach described in the present paper provides us with Theorems 6 and 7, in which reflection operations are taken into explicit consideration. In order to demonstrate the merit of proligand approach, it is worthwhile to compare the CI′ (Eq. 120) of Example 10 with the intermediate cycle index CI–CF′ (Eq. 93) of Example 7. Obviously, the terms (s_d) of Eq. 120 appear as hemispheric terms (b_d) in Eq. 93, while the remaining terms of Eq. 93 are concerned with homospheric or enantiospheric orbits (a_d or c_d). This fact reveals the feature of the concept of chemical identity groups by Ugi et al. [5], so that the chemical identity groups lack the sphericity concept of the present approach. This means that the concept of chemical identity groups treats chirality phenomena in terms of permutability of ligands. Such a treatment may cause confusion with respect to the relationship between chirality and stereogenicity, as recently demonstrated by Fujita [13–15].

4 Conclusions

The proligand approach for enumerating nonrigid stereoisomers, which was reported in Part 2 of this series [11], is extended to be capable of treating general cases. One of the extended points is the use of different sets of sphericity indices to treat one or more orbits contained in skeletons and proligands. Another one of the extended points is to take account of chirality in proligands and sub-proligands. Thereby, several theorems for enumerating nonrigid stereoisomers are proved generally and applied to the stereoisomerism of trihydroxyglutaric acid. Among them, Theorem 6 stems from the scheme "positions of a skeleton ⇐ proligands ⇐ ligands (positions of a ligand ⇐ sub-proligands)", while Theorem 7 stems from the scheme "(positions of a skeleton ⇐ proligands ⇐ ligands (positions of a ligand)) ⇐ sub-proligands". The theorems reveal in what Pólya's theorem and other previous methods are deficient.

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