

Combinatorial Enumeration of *RS*-Stereoisomers Itemized by Chirality, *RS*-Stereogenicity, and Sclerality

Shinsaku Fujita

Shonan Institute of Chemoinformatics and Mathematical Chemistry,
Kaneko 479-7 Ooimachi, Ashigara-Kami-Gun, Kanagawa-Ken,
258-0019 Japan

E-mail: fujitas@chem.kit.ac.jp

(Received May 29, 2007)

Abstract

Promolecules are derived from a given skeleton by putting proligands (ligands with chirality/achirality only) on its substitution positions. They are regarded as *RS*-stereoisomers, which are characterized by the concepts of chirality, *RS*-stereogenicity, and sclerality. They are categorized into five types by means of *RS*-stereoisomeric groups: Type I (chiral/*RS*-stereogenic/ascleral), Type II (chiral/*RS*-astereogenic/scleral), Type III (chiral/*RS*-stereogenic/scleral), Type IV (achiral/*RS*-astereogenic/ascleral), and Type V (achiral/*RS*-stereogenic/scleral). They are counted under the action of the maximum point subgroup, the maximum *RS*-permutation subgroup, and the maximum ligand-inversion subgroup, which are subgroups of an *RS*-stereoisomeric group. After respective cycle indices with chirality fittingness are derived for Type I to Type V, the itemized numbers of promolecules are obtained as generating functions. The general method is applied to the enumerations of allene derivatives and of methane derivatives. The results are verified in comparison with manual enumerations reported previously.

1 Introduction

Chirality and stereogenicity have provided organic chemists with serious confusion, as found in the history of the CIP (Cahn, Ingold and Prelog) system. In fact, the earlier version of the CIP

system [1] was claimed to specify chirality, but the basis of the revised version [2] was changed from chirality into stereogenicity. According to this revision, the IUPAC Recommendations 1996 [3] describes that an “chirality center” is the traditional example of the “stereogenic unit”. This implies that “stereogenicity” includes “chirality” as a subsidiary concept within the conventional terminology.

The term “chirality” corresponds to the relational term “enantiomerism” in a one-to-one fashion, because two chiral compounds with mirror-image configurations are called “enantiomers”. Because the term “diastereomerism” is defined as “stereoisomerism” other than “enantiomerism” [3], we are forced to adopt the dichotomy between “enantiomerism” and “diastereomerism”. As a result, we have to claim that the term “stereogenic” corresponds to “stereoisomerism” so that the term “stereogenic unit” consist of “chirality center” (corresponding “enantiomerism”) and remaining units corresponding to “diastereomerism”. To avoid the confusion, however, we should demonstrate that “stereogenicity” and “chirality” are entirely distinct concepts, although they are closely related.

We have analyzed the difference between “chirality” and “stereogenicity” by referring to the difference between point groups and permutation groups [4–7]. As a result of this analysis, we have pointed out that a source of the confusion is the conventional terminology on “diastereomers” and “stereogenic units”, both of which suffer from diverse connotation just as the term “nonnatives” coming from the dichotomy between natives and nonnatives indefinitely refers to all people other than natives.

As a project of avoiding the confusion, we have developed the concept of *RS-stereoisomers* by using newly-defined *stereoisograms* [8–10]. Thereby, the *RS*-stereoisomeric relationship have been divided into three relationships, i.e., *enantiomeric*, *RS-diastereomeric*, and *holantimeric*. Moreover, the three relationships have been clarified to correspond to three attributes, i.e., *chirality*, *RS-stereogenicity*, and *sclerality*. By combining the three attributes, compounds as *RS*-stereoisomers have been categorized into five types, i.e.,

- Type I (chiral/*RS*-stereogenic/ascleral),
- Type II (chiral/*RS*-astereogenic/scleral),
- Type III (chiral/*RS*-stereogenic/scleral),
- Type IV (achiral/*RS*-astereogenic/ascleral), and
- Type V (achiral/*RS*-stereogenic/scleral).

The concept of *stereoisograms* has been discussed on a more mathematical basis [11, 12], where an *RS*-stereoisomeric group has been defined to control stereoisograms of a given skeleton so that its subgroups are categorized into five types in agreement of the existence of Types I to V. Pseudoasymmetry [9] and prochirality [13] have been discussed by using stereoisograms.

As another project, on the other hand, we have developed *the proligand method* for counting stereoisomers [14–16] by integrating the concepts of proligands and promolecules [17–19] with the concept of sphericities [20]. The merit of Fujita’s proligand method in comparison with Pólya’s theorem has been briefly discussed in an article of ours [21].

As a continuation of the two projects, the next problem to be solved is to obtain the numbers of *RS*-stereoisomers of Types I to V on the basis of a given skeleton, where we rely on Fujita’s proligand method. For this purpose, we will discuss the importance of three subgroups of the *RS*-stereoisomeric group, i.e., the maximum point subgroup, the maximum *RS*-permutation subgroup, and the maximum ligand-inversion subgroup. Under the action of the three subgroups, we will enumerate compounds as *RS*-stereoisomers with itemization in regard to Types I to V.

2 RS-Stereoisomers

2.1 RS-Stereoisomeric Groups

According to the concepts of proligands and promolecules [17–19], let us consider a promolecule in which a set of proligands occupies a set of substitution positions of a given skeleton. By following the treatment described in a previous article [12], suppose that the set of substitution positions is governed by a coset representation $\mathbf{G}_{C\sigma}$ of a point group symmetry:

$$\mathbf{G}_{C\sigma} = \mathbf{G}_C + \sigma\mathbf{G}_C, \quad (1)$$

by an *RS*-permutation group:

$$\mathbf{G}_{C\tilde{\sigma}} = \mathbf{G}_C + \tilde{\sigma}\mathbf{G}_C \quad (2)$$

as well as by a ligand-inversion group:

$$\mathbf{G}_{C\hat{I}} = \mathbf{G}_C + \hat{I}\mathbf{G}_C. \quad (3)$$

Totally, the set of substitution positions of the skeleton belongs to the following *RS*-stereoisomeric group:

$$\mathbf{G} = \mathbf{G}_C + \sigma\mathbf{G}_C + \tilde{\sigma}\mathbf{G}_C + \hat{I}\mathbf{G}_C. \quad (4)$$

where the group \mathbf{G}_C corresponds to the maximum chiral subgroup of the point group, the element σ corresponds to a rotoreflection of the point group, the element $\tilde{\sigma}$ corresponds to a permutation σ but does not provide the reflection of ligands, the element \hat{I} represents an operation which provides the reflection of ligands but does not the reflection of the skeleton. The point group $\mathbf{G}_{C\sigma}$ (eq. 1) is specifically called *the maximum point subgroup* of the *RS*-stereoisomeric group \mathbf{G} (eq. 4). Because $\mathbf{G}_{C\sigma}$ contains subgroups other than the subgroups of \mathbf{G}_C , these subgroup are called *point groups* or more strictly *achiral point groups*, which characterize point-group symmetries of derivatives, as discussed in general [20]. The *RS*-permutation group $\mathbf{G}_{C\tilde{\sigma}}$ (eq. 2) is specifically called *the maximum RS-permutation subgroup* of the *RS*-stereoisomeric group \mathbf{G} (eq. 4), where subgroups of $\mathbf{G}_{C\tilde{\sigma}}$ other than the subgroups of \mathbf{G}_C are called *RS-permutation groups* collectively. The ligand-inversion group $\mathbf{G}_{C\hat{I}}$ (eq. 3) is specifically called *the maximum ligand-inversion subgroup* of the *RS*-stereoisomeric group \mathbf{G} (eq. 4), where subgroups of $\mathbf{G}_{C\hat{I}}$ other than the subgroups of \mathbf{G}_C are called *ligand-inversion groups* collectively.

By following the treatment described in Ref. [12], let us examine an allene skeleton shown in Fig. 1. According to the discussion for deriving eq. 1, the four positions of the allene skeleton of the \mathbf{D}_{2d} -point-group symmetry are governed by the coset representation $(\mathbf{C}_s \setminus) \mathbf{D}_{2d}$, which is shown in eq. 5. This is the concrete form of the maximum point group $\mathbf{G}_{C\sigma}$ for characterizing allene derivatives. Each operation contained in the coset $\sigma_{d(1)} \mathbf{D}_2$ is characterized by an overbar, which indicates the alternation of the chirality of a ligand accommodated in each position.

$$\begin{aligned} \mathbf{D}_{2d} &= \mathbf{D}_2 + \sigma_{d(1)} \mathbf{D}_2 \\ &= \{I, C_{2(3)}, C_{2(1)}, C_{2(2)}; \sigma_{d(1)}, \sigma_{d(2)}, S_4^3, S_4\} \\ &\sim \{(1)(2)(3)(4), (1\bar{3})(2\bar{4}), (1\bar{2})(3\bar{4}), (1\bar{4})(2\bar{3}); \\ &\quad \overline{(1)(2\bar{4})(3)}, \overline{(1\bar{3})(2\bar{4})}, \overline{(1\bar{4}\bar{3}\bar{2})}, \overline{(1\bar{2}\bar{3}\bar{4})}\} \end{aligned} \quad (5)$$

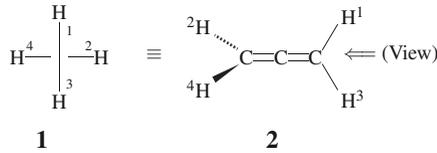


Figure 1: Convention for drawing allene derivatives

Let the symbol $\mathbf{D}_{2\tilde{\sigma}}$ denote the concrete form of the maximum *RS*-permutation subgroup (eq. 2) in order to treat allene derivatives. The maximum *RS*-permutation subgroup is given by eq. 6, in which the chirality of a ligand accommodated in each position does not altered during each operation of the coset $\tilde{\sigma}_{d(1)}\mathbf{D}_2$.

$$\begin{aligned} \mathbf{D}_{2\tilde{\sigma}} &= \mathbf{D}_2 + \tilde{\sigma}_{d(1)}\mathbf{D}_2 \\ &= \{I, C_{2(3)}, C_{2(1)}, C_{2(2)}; \tilde{\sigma}_{d(1)}, \tilde{\sigma}_{d(2)}, \tilde{S}_4^3, \tilde{S}_4\} \\ &\sim \{(1)(2)(3)(4), (1\ 3)(2\ 4), (1\ 2)(3\ 4), (1\ 4)(2\ 3); \\ &\quad (1)(2\ 4)(3), (1\ 3)(2)(4), (1\ 4\ 3\ 2), (1\ 2\ 3\ 4)\}, \end{aligned} \quad (6)$$

where the tilde over each operation means no alternation of ligand chirality. It should be noted that \mathbf{D}_{2d} and $\mathbf{D}_{2\tilde{\sigma}}$ correspond to the same permutation group if the alternation of ligand chirality is not taken into consideration.

Let the symbol $\mathbf{D}_{2\hat{I}}$ denote the concrete form of the maximum ligand-inversion group (eq. 3) in order to treat allene derivatives. The maximum ligand-inversion group is given by eq. 7, in which the chirality of a ligand accommodated in each position is altered during each operation of the coset $\hat{I}\mathbf{D}_2$.

$$\begin{aligned} \mathbf{D}_{2\hat{I}} &= \mathbf{D}_2 + \hat{I}\mathbf{D}_2 \\ &= \{I, C_{2(3)}, C_{2(1)}, C_{2(2)}; \hat{I}, \hat{C}_{(3)}, \hat{C}_{(1)}, \hat{C}_{(2)}\} \\ &\sim \{(1)(2)(3)(4), (1\ 3)(2\ 4), (1\ 2)(3\ 4), (1\ 4)(2\ 3); \\ &\quad \overline{(1)(2)(3)(4)}, \overline{(1\ 3)(2\ 4)}, \overline{(1\ 2)(3\ 4)}, \overline{(1\ 4)(2\ 3)}\} \end{aligned} \quad (7)$$

where a circumflex (hat) over each operation means the alternation of ligand chirality. It should be noted that the maximum chiral subgroup \mathbf{D}_2 and the coset $\hat{I}\mathbf{D}_2$ in eq. 7 correspond to the same permutation group if the alternation of ligand chirality is not taken into consideration.

By combining eqs. 5, 6, and 7, the concrete form of the *RS*-stereoisomeric group \mathbf{G} for this case is calculated as follows:

$$\begin{aligned} \mathbf{D}_{2d\tilde{\sigma}\hat{I}} &= \mathbf{D}_2 + \sigma_{d(1)}\mathbf{D}_2 + \tilde{\sigma}_{d(1)}\mathbf{D}_2 + \hat{I}\mathbf{D}_2 \\ &= \{I, C_{2(3)}, C_{2(1)}, C_{2(2)}; \sigma_{d(1)}, \sigma_{d(2)}, S_4^3, S_4; \tilde{\sigma}_{d(1)}, \tilde{\sigma}_{d(2)}, \tilde{S}_4^3, \tilde{S}_4; \hat{I}, \hat{C}_{(3)}, \hat{C}_{(1)}, \hat{C}_{(2)}\} \\ &\sim \{(1)(2)(3)(4), (1\ 3)(2\ 4), (1\ 2)(3\ 4), (1\ 4)(2\ 3); \\ &\quad \overline{(1)(2)(3)(4)}, \overline{(1\ 3)(2)(4)}, \overline{(1\ 4\ 3\ 2)}, \overline{(1\ 2\ 3\ 4)}; \\ &\quad (1)(2\ 4)(3), (1\ 3)(2)(4), (1\ 4\ 3\ 2), (1\ 2\ 3\ 4), \\ &\quad \overline{(1)(2)(3)(4)}, \overline{(1\ 3)(2\ 4)}, \overline{(1\ 2)(3\ 4)}, \overline{(1\ 4)(2\ 3)}\}. \end{aligned} \quad (8)$$

2.2 Five *RS*-Stereoisomeric Types

In Ref. [12], we have proven the existence of five *RS*-stereoisomeric types by means of the existence of five types of subgroups contained in each *RS*-stereoisomeric group (\mathbf{G}). The essence of the proof is summarized in Table 1, where Types I to V are characterized by subgroups of \mathbf{G} or the corresponding factor groups. Each group listed in the column “maximum subgroup” shows that a compound of each type (Type I–V) belongs to one of the subgroups of the maximum subgroup, where the subgroup contains operations other than the operations of \mathbf{G}_C . This situation is more clearly demonstrated by referring to the groups of the column “factor group”.

Table 1: Five *RS*-Stereoisomeric Types

type	characteristics	maximum subgroup	factor group
Type I	chiral/ <i>RS</i> -stereogenic/ascleral	$\mathbf{G}_{C\hat{I}}^a$	$\{\mathbf{G}_C, \hat{\mathbf{I}}\mathbf{G}_C\}$
Type II	chiral/ <i>RS</i> -astereogenic/scleral	$\mathbf{G}_{C\tilde{\sigma}}^a$	$\{\mathbf{G}_C, \tilde{\sigma}\mathbf{G}_C\}$
Type III	chiral/ <i>RS</i> -stereogenic/scleral	\mathbf{G}_C	$\{\mathbf{G}_C\}$
Type IV	achiral/ <i>RS</i> -astereogenic/ascleral	\mathbf{G}^b	$\{\mathbf{G}_C, \hat{\mathbf{I}}\mathbf{G}_C, \tilde{\sigma}\mathbf{G}_C, \sigma\mathbf{G}_C\}$
Type V	achiral/ <i>RS</i> -stereogenic/scleral	\mathbf{G}_{σ}^a	$\{\mathbf{G}_C, \sigma\mathbf{G}_C\}$

^a Each promolecule belongs to a subgroup of the maximum subgroup, where the subgroup contains elements other than those of \mathbf{G}_C .

^b Each promolecule belongs to a subgroup of the maximum subgroup, where the subgroup contains elements of the four cosets due to \mathbf{G}_C .

To exemplify the categorization into Types I to V, Fig. 2 illustrates representative allene derivatives along with the corresponding subgroups of the *RS*-stereoisomeric group $\mathbf{D}_{2d\hat{\sigma}\hat{I}}$ (eq. 8), where the symbols A, B, X, and Y denote achiral proligands, while the pair of p and \bar{p} represents a pair of enantiomeric proligands.

The first compound (**3**) of Type I belongs to $\mathbf{C}_{\hat{I}} = \{I, \hat{I}\}$, which is a subgroup of the maximum ligand-inversion subgroup $\mathbf{D}_{2\hat{I}}$ (eq. 7), other than the subgroups of the maximum chiral subgroup \mathbf{D}_2 . From the viewpoint of the conventional stereochemistry which puts emphasis on point-group symmetries (e.g., \mathbf{D}_{2d} for the allene skeleton in this case), the compound (**3**) belongs to \mathbf{C}_1 . That is to say, it is chiral, more specifically speaking, being asymmetric. Thus, we become able to perceive the ligand-inversion symmetry $\mathbf{C}_{\hat{I}}$ of **3**, only if we use the *RS*-stereoisomeric group $\mathbf{D}_{2d\hat{\sigma}\hat{I}}$ (eq. 8) and its maximum ligand-inversion subgroup $\mathbf{D}_{2\hat{I}}$ (eq. 7).

The second compound (**4**) of Type II belongs to $\mathbf{C}_{\tilde{\sigma}} = \{I, \tilde{\sigma}_{d(1)}\}$, which is a subgroup of the maximum *RS*-permutation subgroup $\mathbf{D}_{2\tilde{\sigma}}$ (eq. 6), other than the subgroups of the maximum chiral subgroup \mathbf{D}_2 . If we take account of the usual point group (\mathbf{D}_{2d}), the compound (**4**) is concluded to belong to \mathbf{C}_1 . Thus, we are unable to perceive the *RS*-permutational symmetry $\mathbf{C}_{\tilde{\sigma}}$ of **4**, until we adopt the *RS*-stereoisomeric group $\mathbf{D}_{2d\hat{\sigma}\hat{I}}$ (eq. 8) and its maximum *RS*-permutation subgroup $\mathbf{D}_{2\tilde{\sigma}}$ (eq. 6).

The compound of Type III (**5**) belongs to $\mathbf{C}_1 = \{I\}$, which is a subgroup of the maximum chiral subgroup \mathbf{D}_2 . Even if we take account of the usual point group (\mathbf{D}_{2d}), the compound (**5**) belongs to \mathbf{C}_1 .

The compound of Type IV (**6**) belongs to $\mathbf{C}_{\tilde{\sigma}\hat{I}} = \{I, \sigma_{d(1)}, \tilde{\sigma}_{d(1)}, \hat{I}\}$, which is a subgroup of the *RS*-stereoisomeric group $\mathbf{D}_{2d\hat{\sigma}\hat{I}}$ (eq. 8), other than the subgroups of the maximum chiral

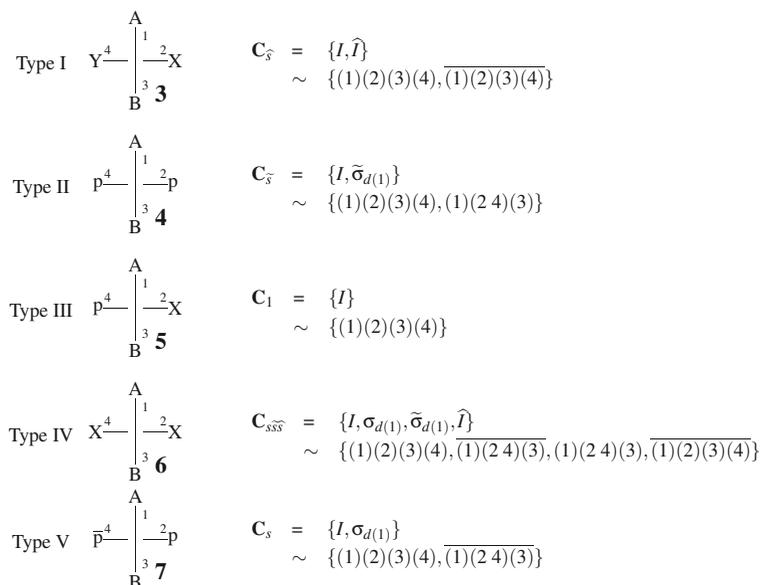


Figure 2: Examples of allene derivatives of Types I–V. The symbols A, B, X, and Y denote achiral proligands, while the pair of p and \bar{p} represents a pair of enantiomeric proligands.

subgroup \mathbf{D}_2 . It should be noted that the compound (**6**) belongs to \mathbf{C}_s if we take account of the usual point group (\mathbf{D}_{2d}).

The compound of Type V (**7**) belongs to $\mathbf{C}_s = \{I, \sigma_{d(1)}\}$ which is a subgroup of the maximum point subgroup \mathbf{D}_{2d} , other than the subgroups of the maximum chiral subgroup \mathbf{D}_2 . It should be noted that the compound (**7**) belongs to \mathbf{C}_s , even if we take account of the usual point group (\mathbf{D}_{2d}).

It is worthwhile to mention the merit of the present treatment in comparison with the conventional stereochemistry based on point-group symmetries only. So long as we rely on the conventional stereochemistry, we are unable to recognize the distinction between **3** (Type I), **4** (Type II), and **5** (Type III), because they all belong to the point group \mathbf{C}_1 . On the same line, we cannot distinguish between **6** (Type IV) and **7** (Type V) by the conventional stereochemistry, because both belong to the point group \mathbf{C}_s . This type of incapability reveals an implicit way of the conventional stereochemistry. If we exclude chiral proligands and take account of achiral proligands only, the cases of **4** (Type II), **5** (Type III), and **7** (Type V) are excluded so that the cases of **3** (Type I) and **6** (Type IV) remain to be perceived. In other words, only the remaining cases of **3** (Type I) and **6** (Type IV) are main subjects of the conventional stereochemistry. As a result, the consideration of chiral proligands is one of rather optional treatments, so that such cases as **7** (Type V) are *exceptionally* treated as pseudoasymmetric cases. Moreover, such cases as **4** (Type II) and **5** (Type III) are discussed case by case under ad hoc criteria which are devised to harmonize them with the case of **3** (Type I).

3 Formalization for Enumeration

3.1 Enumeration Under the Maximum Point Subgroup

Enumerations under point groups have been discussed under the names of Fujita's USCI (unit-subduced-cycle-index) approach [22–24] and Fujita's proligand method [14–16]. The methodology of Fujita's proligand method, in particular, should be mentioned briefly in order to work on the present enumeration under *RS*-stereoisomeric groups.

Let us consider a skeleton having n substitution positions, which are governed by *RS*-stereoisomeric group \mathbf{G} . We first examine the maximum point subgroup $\mathbf{G}_{C\sigma}$. Suppose that the action of an element of P of $\mathbf{G}_{C\sigma}$ on the skeleton is represented as a product of d -cycles ($d = 1, 2, \dots, n$), where the number of the d -cycles is equal to $v_d(P)$. According to Fujita's proligand method, the number of promolecules as enantiomers (i.e., achiral promolecules and enantiomeric pairs of chiral ones) can be counted by using the following cycle index with chirality fittingness (CI-CF):

$$\begin{aligned} \text{CI-CF}(\mathbf{G}_{C\sigma}; \$_d, b_d) \\ = \frac{1}{|\mathbf{G}_{C\sigma}|} \left\{ \sum_{P \in \mathbf{G}_C} b_1^{v_1(P)} b_2^{v_2(P)} \dots b_n^{v_n(P)} + \sum_{P \in \sigma \mathbf{G}_C} \$_1^{v_1(P)} \$_2^{v_2(P)} \dots \$_n^{v_n(P)} \right\}, \end{aligned} \quad (9)$$

where the symbol b_d denotes a sphericity index (SI) for a hemispheric d -cycle contained in \mathbf{G}_C and the symbol $\$_d$ denotes an SI (a_d) for a homospheric d -cycle (d : odd) contained in $\sigma \mathbf{G}_C$ or an SI (c_d) for an enantiospheric d -cycle (d : even) contained in $\sigma \mathbf{G}_C$. This CI-CF has been first noted in our previous article [14] in terms of Fujita's proligand method. The concept of sphericity has been originally developed by using orbits in Fujita's USCI (unit-subduced-cycle-index) approach, i.e., homospheric, enantiospheric, and hemispheric orbits [25, 20]. The same CI-CF as eq. 9 has been alternatively obtained by means of Fujita's USCI approach [20].

The n substitution positions of the skeleton accommodate n proligands selected from the following warehouse:

$$\mathbf{X} = \{X_1, X_2, \dots, X_n; p_1, p_2, \dots, p_n; \bar{p}_1, \bar{p}_2, \dots, \bar{p}_n\}, \quad (10)$$

where X_1, X_2 , etc. represent achiral proligands; p_1, p_2 , etc. represent chiral proligands; and \bar{p}_1, \bar{p}_2 , etc. represent chiral proligands of opposite chirality. For the sake of simplicity, the subscript n appearing in eq. 10 is tentatively selected to be equal to the number (n) of positions but it may be freely varied according to enumeration problems to be solved without losing generality. The selection of such substituents produces an isomer having θ_1 of X_1 , θ_2 of X_2 , \dots θ_n of X_n ; θ'_1 of p_1 , θ'_2 of p_2 , \dots θ'_n of p_n ; θ''_1 of \bar{p}_1 , θ''_2 of \bar{p}_2 , \dots θ''_n of \bar{p}_n , where these numbers satisfy the following partition:

$$\begin{aligned} [\theta] &= \theta_1 + \theta_2 + \dots + \theta_n \\ &\quad + \theta'_1 + \theta'_1 + \dots + \theta'_n \\ &\quad + \theta''_1 + \theta''_1 + \dots + \theta''_n = n. \end{aligned} \quad (11)$$

Then, each proligand is characterized by a molecular formula represented as follows:

$$W_\theta = X_1^{\theta_1} X_2^{\theta_2} \dots X_n^{\theta_n} p_1^{\theta'_1} p_2^{\theta'_2} \dots p_n^{\theta'_n} \bar{p}_1^{\theta''_1} \bar{p}_2^{\theta''_2} \dots \bar{p}_n^{\theta''_n}. \quad (12)$$

Let the symbol B_θ denote the number of such isomers as having the molecular formula W_θ , where each pair of enantiomers or each achiral promolecule is counted just once. By using the CI-CF (eq. 9), Theorem 1 of Ref. [14] (or equivalently Theorem 2 of Ref. [16]) gives the following generating function:

$$\sum_{[\theta]} B_\theta W_\theta = \text{CI-CF}(\mathbf{G}_{C\sigma}; \$_d, b_d), \quad (13)$$

where the summation is concerned with the partitions represented by $[\theta]$ (eq. 11) and the SIs are replaced by the following ligand inventories:

$$a_d = X_1^d + X_2^d + \cdots + X_n^d \quad (14)$$

$$c_d = X_1^d + X_2^d + \cdots + X_n^d + 2p_1^{d/2} \bar{p}_1^{d/2} + 2p_2^{d/2} \bar{p}_2^{d/2} + \cdots + 2p_n^{d/2} \bar{p}_n^{d/2} \quad (15)$$

$$b_d = X_1^d + X_2^d + \cdots + X_n^d + p_1^d + p_2^d + \cdots + p_n^d + \bar{p}_1^d + \bar{p}_2^d + \cdots + \bar{p}_n^d. \quad (16)$$

The skeleton having n substitution positions described above can be considered to be governed by the maximum chiral subgroup \mathbf{G}_C of the group $\mathbf{G}_{C\sigma}$. Thereby, the following CI-CF is obtained:

$$\text{CI-CF}(\mathbf{G}_C; b_d) = \frac{1}{|\mathbf{G}_C|} \sum_{P \in \mathbf{G}_C} b_1^{v_1(P)} b_2^{v_2(P)} \cdots b_n^{v_n(P)}. \quad (17)$$

Let the symbol β_θ denote the number of such isomers as having W_θ , where achiral isomers and two enantiomers of each pair are counted separately. By using the CI-CF (eq. 17), Theorem 3 of Ref. [16] gives the following generating function:

$$\sum_{[\theta]} \beta_\theta W_\theta = \text{CI-CF}(\mathbf{G}_C; b_d), \quad (18)$$

where each SI (b_d) is replaced by the ligand inventory represented by eq. 16 and the molecular formula (W_θ) is represented by eq. 12.

Achiral promolecules (Types IV and V) are counted by means of the following CI-CF:

$$\text{CI-CF}^{(IV/V)}(\mathbf{G}_{C\sigma}; \$_d) = 2\text{CI-CF}(\mathbf{G}_{C\sigma}; \$_d, b_d) - \text{CI-CF}(\mathbf{G}_C; b_d) \quad (19)$$

$$= \frac{1}{|\mathbf{G}_C|} \sum_{P \in \sigma\mathbf{G}_C} \$_1^{v_1(P)} \$_2^{v_2(P)} \cdots \$_n^{v_n(P)}, \quad (20)$$

where we use the relationship $|\mathbf{G}_{C\sigma}| = 2|\mathbf{G}_C|$.

Let the symbol $B_\theta^{(IV/V)}$ denote the number of such achiral isomers as having W_θ . By using the CI-CF (eq. 20), Theorem 4 (eq. 50) of Ref. [16] gives the following generating function:

$$\sum_{[\theta]} B_\theta^{(IV/V)} W_\theta = \text{CI-CF}^{(IV/V)}(\mathbf{G}_{C\sigma}; \$_d), \quad (21)$$

where each SI ($\$_d$, i.e. a_d or c_d) is replaced by the ligand inventories represented by eqs. 14 and 15 and the molecular formula (W_θ) is represented by eq. 12. Note that each achiral compound is counted just once.

Chiral isomers (Types I, II, and III) are counted by means of the following CI-CF:

$$\begin{aligned} & \text{CI-CF}^{(I/II/III)}(\mathbf{G}_{C\sigma}; \$_d, b_d) \\ &= \text{CI-CF}(\mathbf{G}_{C\sigma}; \$_d, b_d) - \text{CI-CF}^{(IV/V)}(\mathbf{G}_{C\sigma}; \$_d, b_d) \end{aligned} \quad (22)$$

$$= \frac{1}{|\mathbf{G}_{C\sigma}|} \left\{ \sum_{P \in \mathbf{G}_C} b_1^{v_1(P)} b_2^{v_2(P)} \cdots b_n^{v_n(P)} - \sum_{P \in \sigma\mathbf{G}_C} \$_1^{v_1(P)} \$_2^{v_2(P)} \cdots \$_n^{v_n(P)} \right\}, \quad (23)$$

where each pair of enantiomers is counted just once. By comparison between eq. 9 and eq. 23, we find a remarkable correspondence between them, where the second summations alter their plus-minus signs.

In order to count allene derivatives by starting from the skeleton (1), eqs. 9 and 17 are applied to the cycle structures appearing in eq. 5, so that we obtain the following CI-CFs:

$$\text{CI-CF}(\mathbf{D}_{2d}; \$d, b_d) = \frac{1}{8}(b_1^4 + 3b_2^2 + 2a_1^2c_2 + 2c_4) \quad (24)$$

$$\text{CI-CF}(\mathbf{D}_2; b_d) = \frac{1}{4}(b_1^4 + 3b_2^2). \quad (25)$$

Thereby, eqs. 20 and 23 for allene derivatives take the following concrete forms:

$$\text{CI-CF}^{(\text{IV/V})}(\mathbf{D}_{2d}; \$d) = \frac{1}{2}(a_1^2c_2 + c_4) \quad (26)$$

$$\text{CI-CF}^{(\text{II/III})}(\mathbf{D}_{2d}; \$d, b_d) = \frac{1}{8}(b_1^4 + 3b_2^2 - 2a_1^2c_2 - 2c_4). \quad (27)$$

3.2 Enumeration Under the Maximum *RS*-Permutation Subgroup

In a previous paper [11], we have reported enumerations under the *RS*-permutation groups by Fujita's USCI approach, where itemization into Types I to V was conducted manually. In the present article, we apply Fujita's proligand method to such enumeration problems, where we focus on combinatorial itemization into Types I to V. Thus, let us examine the skeleton having n substitution positions under the maximum *RS*-permutation subgroup $\mathbf{G}_{C\bar{C}}$. Suppose that an element of P (or P') of $\mathbf{G}_{C\bar{C}}$ is represented as a product of d -cycles ($d = 1, 2, \dots, n$), where the number of the d -cycles is equal to $v_d(P)$ (or $v_d(P')$). The number of promolecules as *RS*-diastereomers (i.e., *RS*-astereogenic promolecules and *RS*-diastereomeric pairs of *RS*-stereogenic ones) can be counted by using the following cycle index with chirality fittingness (CI-CF):

$$\begin{aligned} & \text{CI-CF}(\mathbf{G}_{C\bar{C}}; b_d) \\ &= \frac{1}{|\mathbf{G}_{C\bar{C}}|} \left\{ \sum_{P \in \mathbf{G}_C} b_1^{v_1(P)} b_2^{v_2(P)} \dots b_n^{v_n(P)} + \sum_{P' \in \bar{\mathbf{G}}_C} b_1^{v_1(P')} b_2^{v_2(P')} \dots b_n^{v_n(P')} \right\}, \quad (28) \end{aligned}$$

where only hemispheric cycles are taken into consideration because of no alternation of chiralities. This means that two enantiomers of each pair as well as each achiral compound are counted separately.

On the same line as the dichotomy of chirality/achirality has derived eq. 20 from eq. 9, the dichotomy of *RS*-stereogenicity/*RS*-astereogenicity converts the CI-CF (eq. 28) into the following CI-CF for counting promolecules of Type II and IV (*RS*-astereogenic promolecules):

$$\begin{aligned} & \text{CI-CF}^{(\text{II/IV})}(\mathbf{G}_{C\bar{C}}; b_d) \\ &= 2\text{CI-CF}(\mathbf{G}_{C\bar{C}}; b_d) - \text{CI-CF}(\mathbf{G}_C; b_d) \quad (29) \end{aligned}$$

$$= \frac{1}{|\mathbf{G}_C|} \sum_{P' \in \bar{\mathbf{G}}_C} b_1^{v_1(P')} b_2^{v_2(P')} \dots b_n^{v_n(P')}. \quad (30)$$

Note that eq. 30 counts two enantiomers of each pair separately, although it counts each *RS*-astereogenic promolecule just once. Thus, A^3p and $A^3\bar{p}$, for example, are not equalized under the action of $\mathbf{G}_{C\bar{C}}$.

It follows that the CI-CF for counting promolecules of Type I, III, and V (*RS*-stereogenic promolecules) is represented as follows:

$$\begin{aligned} \text{CI-CF}^{(I/III/V)}(\mathbf{G}_{C\bar{\sigma}}; b_d) &= \text{CI-CF}(\mathbf{G}_{C\bar{\sigma}}; b_d) - \text{CI-CF}^{(II/IV)}(\mathbf{G}_{C\bar{\sigma}}; b_d) \end{aligned} \quad (31)$$

$$= \frac{1}{|\mathbf{G}_{C\bar{\sigma}}|} \left\{ \sum_{P \in \mathbf{G}_C} b_1^{v_1(P)} b_2^{v_2(P)} \dots b_n^{v_n(P)} - \sum_{P' \in \bar{\sigma}\mathbf{G}_C} b_1^{v_1(P')} b_2^{v_2(P')} \dots b_n^{v_n(P')} \right\}. \quad (32)$$

As found easily, eq. 28 and eq. 32 correspond to each other, where the second summations alter their plus-minus signs.

For the purpose of counting allene derivatives under the maximum *RS*-permutation group, eq. 28 is applied to the cycle structures appearing in eq. 6, so that we obtain the following CI-CF:

$$\text{CI-CF}(\mathbf{D}_{2\bar{\sigma}}; b_d) = \frac{1}{8}(b_1^4 + 3b_2^2 + 2b_1^2 b_2 + 2b_4) \quad (33)$$

Thereby, eqs. 30 and 32 for allene derivatives take the following concrete forms:

$$\text{CI-CF}^{(II/IV)}(\mathbf{D}_{2\bar{\sigma}}; b_d) = \frac{1}{2}(b_1^2 b_2 + b_4) \quad (34)$$

$$\text{CI-CF}^{(I/III/V)}(\mathbf{D}_{2\bar{\sigma}}; b_d) = \frac{1}{8}(b_1^4 + 3b_2^2 - 2b_1^2 b_2 - 2b_4). \quad (35)$$

3.3 Enumeration Under the Maximum Ligand-Inversion Subgroup

Let us examine the skeleton having n substitution positions under the maximum ligand-inversion subgroup $\mathbf{G}_{C\bar{I}}$. Suppose that an element of P (or P') of $\mathbf{G}_{C\bar{I}}$ is represented as a product of d -cycles ($d = 1, 2, \dots, n$), where the number of the d -cycles is equal to $v_d(P)$ (or $v_d(P')$). The number of promolecules as holantimers (i.e., ascleral promolecules and holantimeric pairs of scleral ones) can be counted by using the following cycle index with chirality fittingness (CI-CF):

$$\begin{aligned} \text{CI-CF}(\mathbf{G}_{C\bar{I}}; \$d, b_d) &= \frac{1}{|\mathbf{G}_{C\bar{I}}|} \left\{ \sum_{P \in \mathbf{G}_C} b_1^{v_1(P)} b_2^{v_2(P)} \dots b_n^{v_n(P)} + \sum_{P' \in \bar{I}\mathbf{G}_C} \$1^{v_1(P')} \$2^{v_2(P')} \dots \$n^{v_n(P')} \right\}. \end{aligned} \quad (36)$$

Because the maximum ligand-inversion subgroup ($\mathbf{G}_{C\bar{I}}$) does not contain such operations that cause equivalence of two enantiomers, eq. 36 counts two enantiomers of each pair separately.

On the same line as the dichotomy of chirality/achirality has derived eq. 20 from eq. 9, the dichotomy of sclerality/asclerality converts the CI-CF (eq. 36) into the following CI-CF for counting promolecules of Type I and IV (ascleral promolecules):

$$\begin{aligned} \text{CI-CF}^{(I/IV)}(\mathbf{G}_{C\bar{I}}; \$d) &= 2\text{CI-CF}(\mathbf{G}_{C\bar{I}}; \$d, b_d) - \text{CI-CF}(\mathbf{G}_C; b_d) \end{aligned} \quad (37)$$

$$= \frac{1}{|\mathbf{G}_C|} \sum_{P' \in \bar{I}\mathbf{G}_C} \$1^{v_1(P')} \$2^{v_2(P')} \dots \$n^{v_n(P')}. \quad (38)$$

This equation means that Type I (chiral/*RS*-stereogenic) and Type IV (achiral/*RS*astereogenic) are counted all together from the viewpoint of asclerality, where it counts each ascleral promolecule just once. Note that eq. 38 counts two enantiomers of each pair (Type I) or each achiral promolecule (Type IV) separately from the viewpoint of chirality/achirality.

It follows that the CI-CF for counting promolecules of Types II, III, and V (scleral promolecules) is represented as follows:

$$\begin{aligned} \text{CI-CF}^{(\text{II/III/V})}(\mathbf{G}_{\bar{C}I}; \$d, b_d) \\ = \text{CI-CF}(\mathbf{G}_{\bar{C}I}; \$d, b_d) - \text{CI-CF}^{(\text{IV})}(\mathbf{G}_{\bar{C}I}; \$d) \end{aligned} \quad (39)$$

$$= \frac{1}{|\mathbf{G}_{\bar{C}I}|} \left\{ \sum_{P \in \mathbf{G}_C} b_1^{v_1(P)} b_2^{v_2(P)} \dots b_n^{v_n(P)} - \sum_{P'' \in \mathbf{I}\mathbf{G}_C} \$1_1^{v_1(P'')} \$2_2^{v_2(P'')} \dots \$n_n^{v_n(P'')} \right\}. \quad (40)$$

Refer to the note described just after eq. 36.

In order to count allene derivatives, eq. 36 is applied to the cycle structures appearing in eq. 7, so that we obtain the following CI-CF:

$$\text{CI-CF}(\mathbf{D}_{2f}; \$d, b_d) = \frac{1}{8}(b_1^4 + 3b_2^2 + a_1^4 + 3c_2^2). \quad (41)$$

Thereby, eqs. 38 and 40 for allene derivatives take the following concrete forms:

$$\text{CI-CF}^{(\text{IV})}(\mathbf{D}_{2f}; \$d) = \frac{1}{4}(a_1^4 + 3c_2^2) \quad (42)$$

$$\text{CI-CF}^{(\text{II/III/V})}(\mathbf{D}_{2f}; \$d, b_d) = \frac{1}{8}(b_1^4 + 3b_2^2 - a_1^4 - 3c_2^2). \quad (43)$$

3.4 Itemization into Five Types

3.4.1 Evaluation of Type IV

By inspection of eqs. 20, 30, and 38, we find as the next task the evaluation of CI-CF for counting promolecules of Type IV which are involved commonly. This task cannot be solved in general so long as we have not obtained the full information on the group-subgroup relationship of each *RS*-stereoisomeric group. However, we can find such a CI-CF through trial and error, as shown below in special cases such as an allene skeleton and a tetrahedral skeleton.

Let us examine whether each products of SIs for *P* in eq. 20 (i.e., $\$1_1^{v_1(P)} \$2_2^{v_2(P)} \dots \$n_n^{v_n(P)}$) causes pseudoasymmetry or not. If the element *P* fixes a pseudoasymmetric promolecule (Type V), the product of SIs is replaced by the modified sum of products, $\sum_{\phi} \$1_{1\phi}^{v_1(P)} \$2_{2\phi}^{v_2(P)} \dots \$n_{n\phi}^{v_n(P)}$, so that the modified sum is not concerned with the pseudoasymmetric promolecule. Thereby, we obtain the following CI-CF:

$$\text{CI-CF}^{(\text{IV})}(\mathbf{G}_{C\phi}; \$d) = \frac{1}{|\mathbf{G}_C|} \sum_{P \in \sigma\mathbf{G}_C} \sum_{\phi} \$1_{1\phi}^{v_1(P)} \$2_{2\phi}^{v_2(P)} \dots \$n_{n\phi}^{v_n(P)}, \quad (44)$$

which counts promolecules of Type IV (achiral, *RS*-astereogenic, and ascleral).

For example, because one of the products of SIs ($a_1^2 c_2$) in eq. 26 is related to a pseudoasymmetric promolecule (e.g., **7**), we should select $a_1^2 a_2$ and $a_2 c_2$, which contain a duplicated component represented by a_2^2 . This means that the product $a_1^2 c_2$ is replaced by $a_1^2 a_2 + a_2 c_2 - a_2^2$ so

as to exclude contamination by pseudoasymmetry. The other product of SIs (c_4) is not related to pseudoasymmetry. Hence, eq. 44 for this case takes the following form:

$$\text{CI-CF}^{(\text{IV})}(\mathbf{D}_{2d}; \$_d) = \frac{1}{2}(a_1^2 a_2 + a_2 c_2 - a_2^2 + c_4). \quad (45)$$

3.4.2 Evaluation of Other Types

To evaluate the number of promolecules of Type V, the subtraction of eq. 44 from 20 gives the following equation:

$$\begin{aligned} & \text{CI-CF}^{(\text{V})}(\mathbf{G}_{C\sigma}; \$_d) \\ &= \text{CI-CF}^{(\text{IV/V})}(\mathbf{G}_{C\sigma}; \$_d) - \text{CI-CF}^{(\text{IV})}(\mathbf{G}_{C\sigma}; \$_d) \end{aligned} \quad (46)$$

$$= \frac{1}{|\mathbf{G}_C|} \sum_{P \in \sigma \mathbf{G}_C} \$_1^{v_1(P)} \$_2^{v_2(P)} \dots \$_n^{v_n(P)} - \frac{1}{|\mathbf{G}_C|} \sum_{P \in \sigma \mathbf{G}_C} \sum_{\phi} \$_1^{v_{1\phi}(P)} \$_2^{v_{2\phi}(P)} \dots \$_n^{v_{n\phi}(P)}. \quad (47)$$

Obviously, eq. 47 is concerned with achiral promolecules only, each of which is counted just once.

By the subtraction of eq. 45 from eq. 26, we can calculate eq. 47 for allene derivatives as follows:

$$\begin{aligned} \text{CI-CF}^{(\text{V})}(\mathbf{D}_{2d}; \$_d) &= \frac{1}{2}(a_1^2 c_2 + c_4) - \frac{1}{2}(a_1^2 a_2 + a_2 c_2 - a_2^2 + c_4) \\ &= \frac{1}{2}(a_1^2 c_2 - a_1^2 a_2) - \frac{1}{2}(a_2 c_2 - a_2^2). \end{aligned} \quad (48)$$

The last side of eq. 48 can be confirmed by considering the transitivity of the pseudoasymmetric promolecule (7). The product $a_1^2 c_2$ counts unnecessary promolecules (ABX_2 , AX_3 , and X_4) in which the pair p/\bar{p} of 7 is replaced by X_2 (two achiral proligands of the same kind). Because the unnecessary promolecules can be correlated to the product $a_1^2 a_2$, they are excluded by means of the subtraction $a_1^2 c_2 - a_1^2 a_2$. On the other hand, the product $a_1^2 c_2$ also contains unnecessary promolecules in which the AB of 7 is replaced by A_2 (two achiral proligands of the same kind). The latter promolecules can be correlated to the subtraction of the products $a_2 c_2 - a_2^2$, where the subtracting product a_2^2 corresponds to unnecessary promolecules ($\text{A}_2 \text{X}_2$) in which the AB of 7 is replaced by A_2 (two achiral proligands of the same kind) and the pair p/\bar{p} is replaced by X_2 (two achiral proligands of the same kind).

In summary, eqs. 45 and 48 have been derived by taking account of the following correspondence between the products of SIs and the types of promolecules:

$$\begin{aligned} a_1^2 c_2: & \text{ ABp}\bar{p} + \text{ABX}_2 + \text{A}_2 p\bar{p} + \text{A}_2 \text{X}_2 + \text{AX}_3 + \text{X}_4 \\ a_1^2 a_2: & \text{ ABX}_2 + \text{A}_2 \text{X}_2 + \text{AX}_3 + \text{X}_4 \\ a_2 c_2: & \text{ A}_2 p\bar{p} + \text{A}_2 \text{X}_2 \\ a_2^2: & \text{ A}_2 \text{X}_2 \end{aligned}$$

where promolecules represented by $\text{ABp}\bar{p}$ (7) have a pseudoasymmetric center (Type V). It should be noted that the transitivities of a homospheric cycle a_d and an enantiospheric cycle c_d are characterized by the ligand inventories shown in eqs. 14 and 15 or more specifically by those shown below (eqs. 64 and 65).

To evaluate the number of promolecules of Type II, the subtraction of eq. 44 from 30 gives the following equation:

$$\begin{aligned} & \text{CI-CF}^{(\text{II})}(\mathbf{G}_{C\bar{\sigma}}; \$d, b_d) \\ &= \text{CI-CF}^{(\text{II/IV})}(\mathbf{G}_{C\bar{\sigma}}; b_d) - \text{CI-CF}^{(\text{IV})}(\mathbf{G}_{C\sigma}; \$d) \quad (49) \\ &= \frac{1}{|\mathbf{G}_C|} \sum_{P' \in \bar{\sigma}\mathbf{G}_C} b_1^{v_1(P')} b_2^{v_2(P')} \dots b_n^{v_n(P')} - \frac{1}{|\mathbf{G}_C|} \sum_{P \in \sigma\mathbf{G}_C} \sum_{\phi} \$1^{v_{1\phi}(P)} \$2^{v_{2\phi}(P)} \dots \$n^{v_{n\phi}(P)}, \quad (50) \end{aligned}$$

where two enantiomers of each pair are counted separately.

By the subtraction of eq. 45 from eq. 34, eq. 50 for allene derivatives is calculated as follows:

$$\text{CI-CF}^{(\text{II})}(\mathbf{D}_{2\bar{\sigma}}; \$d, b_d) = \frac{1}{2}(b_1^2 b_2 + b_4) - \frac{1}{2}(a_1^2 a_2 + a_2 c_2 - a_2^2 + c_4). \quad (51)$$

To evaluate the number of promolecules of Type I, the subtraction of eq. 44 from 38 gives the following CI-CF:

$$\begin{aligned} & \text{CI-CF}^{(\text{I})}(\mathbf{G}_{C\bar{I}}; \$d) \\ &= \text{CI-CF}^{(\text{I/IV})}(\mathbf{G}_{C\bar{I}}; \$d) - \text{CI-CF}^{(\text{IV})}(\mathbf{G}_{C\sigma}; \$d) \quad (52) \\ &= \frac{1}{|\mathbf{G}_C|} \sum_{P'' \in \bar{I}\mathbf{G}_C} \$1^{v_1(P'')} \$2^{v_2(P'')} \dots \$n^{v_n(P'')} - \frac{1}{|\mathbf{G}_C|} \sum_{P \in \sigma\mathbf{G}_C} \sum_{\phi} \$1^{v_{1\phi}(P)} \$2^{v_{2\phi}(P)} \dots \$n^{v_{n\phi}(P)}, \quad (53) \end{aligned}$$

where two enantiomers of each pair are counted separately.

By the subtraction of eq. 45 from eq. 42, eq. 53 for allene derivatives is calculated as follows:

$$\text{CI-CF}^{(\text{I})}(\mathbf{D}_{2\bar{I}}; \$d) = \frac{1}{4}(a_1^4 + 3c_2^2) - \frac{1}{2}(a_1^2 a_2 + a_2 c_2 - a_2^2 + c_4). \quad (54)$$

Finally, in order to evaluate the number of promolecules of Type III, the subtraction of eqs. 53 (Type I), 50 (Type II), and 20 (Type IV/V) from eq. 17 gives the following CI-CF:

$$\begin{aligned} & \text{CI-CF}^{(\text{III})}(\mathbf{G}_C; \$d, b_d) \\ &= \text{CI-CF}(\mathbf{G}_C; b_d) - \text{CI-CF}^{(\text{I})}(\mathbf{G}_{C\bar{I}}; \$d) - \text{CI-CF}^{(\text{II})}(\mathbf{G}_{C\bar{\sigma}}; \$d, b_d) \\ &\quad - \text{CI-CF}^{(\text{IV/V})}(\mathbf{G}_{C\sigma}; \$d) \quad (55) \\ &= \frac{1}{|\mathbf{G}_C|} \sum_{P \in \mathbf{G}_C} b_1^{v_1(P)} b_2^{v_2(P)} \dots b_n^{v_n(P)} - \frac{1}{|\mathbf{G}_C|} \sum_{P'' \in \bar{I}\mathbf{G}_C} \$1^{v_1(P'')} \$2^{v_2(P'')} \dots \$n^{v_n(P'')} \\ &\quad - \frac{1}{|\mathbf{G}_C|} \sum_{P' \in \bar{\sigma}\mathbf{G}_C} b_1^{v_1(P')} b_2^{v_2(P')} \dots b_n^{v_n(P')} - \frac{1}{|\mathbf{G}_C|} \sum_{P \in \sigma\mathbf{G}_C} \$1^{v_1(P)} \$2^{v_2(P)} \dots \$n^{v_n(P)} \\ &\quad + \frac{2}{|\mathbf{G}_C|} \sum_{P \in \sigma\mathbf{G}_C} \sum_{\phi} \$1^{v_{1\phi}(P)} \$2^{v_{2\phi}(P)} \dots \$n^{v_{n\phi}(P)}. \quad (56) \end{aligned}$$

In order to count allene derivative, the subtraction of eqs. 54, 51, and 26 from eq.25 is carried out according to eq. 56 so as to give the following CI-CF:

$$\begin{aligned} \text{CI-CF}^{(\text{III})}(\mathbf{D}_2; b_d, \$d) &= \frac{1}{4}(b_1^4 + 3b_2^2) - \frac{1}{4}(a_1^4 + 3c_2^2) - \frac{1}{2}(b_1^2 b_2 + b_4) \\ &\quad - \frac{1}{2}(a_1^2 c_2 + c_4) + (a_1^2 a_2 + a_2 c_2 - a_2^2 + c_4). \quad (57) \end{aligned}$$

Because we have obtained CI-CFs for Types I–V respectively, we are able to obtain the number of promolecules of Type T (T = I–V) on the same line as eq. 21 etc. The results are summarized as a theorem:

Theorem 1 Let the symbol $B_{\theta}^{(T)}$ denote the number of promolecules of Type T (T = I–V) having W_{θ} . The number $B_{\theta}^{(T)}$ is obtained as the coefficient of the term W_{θ} representing a molecular formula (eq. 12), which appears in the following generating function:

$$\sum_{[\theta]} B_{\theta}^{(T)} W_{\theta} = \text{CI-CF}^{(T)}(\mathbf{G}'; \$_d, (b_d)), \quad (58)$$

where each SI ($\$_d$, i.e. a_d or c_d ; or b_d if necessary) is replaced by the ligand inventories represented by eqs. 14–16. The CI-CFs in the right-hand side of eq. 58 are represented respectively by eqs. 53 (Type I), 50 (Type II), 56 (Type III), 44 (Type IV), and 47 (Type V), where \mathbf{G}' is selected as found in each CI-CF.

3.4.3 Total Features of Enumeration

As commented below each equation for counting chiral promolecules, eqs. 53 (Type I), 50 (Type II), and 56 (Type III) count two enantiomers of a pair separately. On the other hand, eqs. 44 (Type IV) and 47 (Type V) are concerned with achiral promolecules (Table 1) so that they count an achiral promolecule just once. It follows that eq. 9 can be derived from eqs. 53 (Type I), 50 (Type II), 56 (Type III), 44 (Type IV), and 47 (Type V) as follows:

$$\begin{aligned} & \text{CI-CF}(\mathbf{G}_{C\sigma}; \$_d, b_d) \\ &= \frac{1}{2} \text{CI-CF}^{(I)}(\mathbf{G}_{C\bar{I}}; \$_d) + \frac{1}{2} \text{CI-CF}^{(II)}(\mathbf{G}_{C\bar{\sigma}}; \$_d, b_d) + \frac{1}{2} \text{CI-CF}^{(III)}(\mathbf{G}_C; \$_d, b_d) \\ & \quad + \text{CI-CF}^{(IV)}(\mathbf{G}_{C\sigma}; \$_d) + \text{CI-CF}^{(V)}(\mathbf{G}_{C\sigma}; \$_d), \end{aligned} \quad (59)$$

because eq. 9 counts each pair of enantiomers (and also each achiral promolecule) just once. Note that $2|\mathbf{G}_C| = |\mathbf{G}_{C\sigma}|$. In addition, eq. 17 can be derived by summing up eqs. 53 (Type I), 50 (Type II), 56 (Type III), 44 (Type IV), and 47 (Type V) as follows:

$$\begin{aligned} & \text{CI-CF}(\mathbf{G}_C; b_d) \\ &= \text{CI-CF}^{(I)}(\mathbf{G}_{C\bar{I}}; \$_d) + \text{CI-CF}^{(II)}(\mathbf{G}_{C\bar{\sigma}}; \$_d, b_d) + \text{CI-CF}^{(III)}(\mathbf{G}_C; \$_d, b_d) \\ & \quad + \text{CI-CF}^{(IV)}(\mathbf{G}_{C\sigma}; \$_d) + \text{CI-CF}^{(V)}(\mathbf{G}_{C\sigma}; \$_d), \end{aligned} \quad (60)$$

because eq. 17 counts two enantiomers of each pair separately as well as each achiral promolecule just once.

In accord with eqs. 59 and 60, the CI-CFs for allene derivatives (i.e., eqs. 54 (Type I), 51 (Type II), 57 (Type III), 45 (Type IV), and 48 (Type V)) give eqs. 24 and 25.

Because eqs. 53 (Type I), 56 (Type III), and 47 (Type V) are concerned with *RS*-stereogenicity (Table 1), they count two *RS*-diastereomers of an *RS*-diastereomeric pair separately. On the other hand, eqs. 50 (Type II) and 44 (Type IV) are concerned with *RS*-astereogenic promolecules so that they count an *RS*-astereogenic promolecule just once. It follows that eq. 28 can be derived from eqs. 53 (Type I), 50 (Type II), 56 (Type III), 44 (Type IV), and 47 (Type V) as follows:

$$\text{CI-CF}(\mathbf{G}_{C\bar{\sigma}}; b_d)$$

$$\begin{aligned}
 &= \frac{1}{2}\text{CI-CF}^{(\text{I})}(\mathbf{G}_{C\bar{I}}; \$_d) + \text{CI-CF}^{(\text{II})}(\mathbf{G}_{C\bar{\sigma}}; \$_d, b_d) + \frac{1}{2}\text{CI-CF}^{(\text{III})}(\mathbf{G}_C; \$_d, b_d) \\
 &\quad + \text{CI-CF}^{(\text{IV})}(\mathbf{G}_{C\sigma}; \$_d) + \frac{1}{2}\text{CI-CF}^{(\text{V})}(\mathbf{G}_{C\sigma}; \$_d), \tag{61}
 \end{aligned}$$

because eq. 28 counts each pair of *RS*-diastereomers (and also each *RS*-astereogenic promolecule) just once. Note that $2|\mathbf{G}_C| = |\mathbf{G}_{C\bar{\sigma}}|$.

In accord with eq. 61, the CI-CFs for allene derivatives (i.e., eqs. 54 (Type I), 51 (Type II), 57 (Type III), 45 (Type IV), and 48 (Type V)) give eq. 33.

Because eqs. 50 (Type II), 56 (Type III), and 47 (Type V) are concerned with sclerality (Table 1), they count two holantimers of a holantimeric pair separately. On the other hand, eqs. 53 (Type I) and 44 (Type IV) are concerned with ascleral promolecules so that they count an ascleral promolecule just once. It follows that eq. 36 can be derived from eqs. 53 (Type I), 50 (Type II), 56 (Type III), 44 (Type IV), and 47 (Type V) as follows:

$$\begin{aligned}
 &\text{CI-CF}(\mathbf{G}_{C\bar{I}}; \$_d, b_d) \\
 &= \text{CI-CF}^{(\text{I})}(\mathbf{G}_{C\bar{I}}; \$_d) + \frac{1}{2}\text{CI-CF}^{(\text{II})}(\mathbf{G}_{C\bar{\sigma}}; \$_d, b_d) + \frac{1}{2}\text{CI-CF}^{(\text{III})}(\mathbf{G}_C; \$_d, b_d) \\
 &\quad + \text{CI-CF}^{(\text{IV})}(\mathbf{G}_{C\sigma}; \$_d) + \frac{1}{2}\text{CI-CF}^{(\text{V})}(\mathbf{G}_{C\sigma}; \$_d), \tag{62}
 \end{aligned}$$

because eq. 36 counts each pair of *RS*-holantimers (and also each ascleral promolecule) just once. Note that $2|\mathbf{G}_C| = |\mathbf{G}_{C\bar{I}}|$.

The CI-CFs for allene derivatives (i.e., eqs. 54 (Type I), 51 (Type II), 57 (Type III), 45 (Type IV), and 48 (Type V)) give eq. 41 in accord with eq. 62.

It is worthwhile to point out a similarity among eq. 59 for the maximum point subgroup ($\mathbf{G}_{C\sigma}$), eq. 61 for the maximum *RS*-permutation subgroup ($\mathbf{G}_{C\bar{\sigma}}$), and eq. 62 for the maximum ligand-inversion subgroup ($\mathbf{G}_{C\bar{I}}$). That is to say, the maximum chiral subgroup \mathbf{G}_C is commonly contained as a normal subgroup of index 2 in each of the maximum subgroups, i.e., $\mathbf{G}_{C\sigma}$ (cf. eq. 1), $\mathbf{G}_{C\bar{\sigma}}$ (cf. eq. 2), and $\mathbf{G}_{C\bar{I}}$ (cf. eq. 3). Hence, eq. 17 can be commonly used to examine the the maximum subgroups so that eq. 60 is considered to correspond triply to $\mathbf{G}_{C\sigma}$ (chirality/achirality), $\mathbf{G}_{C\bar{\sigma}}$ (*RS*-stereogenicity/*RS*-astereogenicity), and $\mathbf{G}_{C\bar{I}}$ (sclerality/asclerality).

4 Enumeration Results

4.1 Allene Derivatives

To exemplify the usefulness of the present approach, let us count allene derivatives by using eq. 54 (Type I), eq. 51 (Type II), eq. 57 (Type III), eq. 45 (Type IV), and eq. 48 (Type V). According to eq. 10, we take account of the following warehouse for allene derivatives:

$$\mathbf{X} = \{A, B, X, Y; p, q, r, s; \bar{p}, \bar{q}, \bar{r}, \bar{s}\}, \tag{63}$$

where the letters A, B, X, and Y represent achiral proligands and the pairs of p/\bar{p} , q/\bar{q} , r/\bar{r} , and s/\bar{s} represent pairs of enantiomeric proligands. Thereby, eqs. 14–16 for counting allene derivatives are obtained as follows:

$$a_d = A^d + B^d + X^d + Y^d \tag{64}$$

$$c_d = A^d + B^d + X^d + Y^d + 2p^{d/2}\bar{p}^{d/2} + 2q^{d/2}\bar{q}^{d/2} + 2r^{d/2}\bar{r}^{d/2} + 2s^{d/2}\bar{s}^{d/2} \tag{65}$$

$$b_d = A^d + B^d + X^d + Y^d + p^d + q^d + r^d + s^d + \bar{p}^d + \bar{q}^d + \bar{r}^d + \bar{s}^d. \tag{66}$$

The ligand inventories (eqs. 64–66) are introduced into the CI-CF for Type I (eq. 54) and the resulting equation is expanded so as to give the corresponding generating function for counting Type-I promolecules:

$$f^{(I)} = 2[A^2B^2 + \dots] + 2[A^2BX + \dots] + 6ABXY \\ + 2[A^2p\bar{p} + \dots] + 2[p^2\bar{p}^2 + \dots] + 6[p\bar{p}q\bar{q} + \dots], \quad (67)$$

where each pair of brackets shows terms having the same kind of partition. Note that two enantiomers of a pair are counted separately. For example, the coefficient 6 of the term 6ABXY shows the existence of three pairs of enantiomers (i.e., six allene derivatives).

By introducing the ligand inventories (eqs. 64–66) into the CI-CF for Type II (eq. 51), we obtain the corresponding generating function for counting Type-II promolecules:

$$f^{(II)} = [(A^3p + A^3\bar{p}) + \dots] + [(A^2Bp + A^2B\bar{p}) + \dots] \\ + [(A^2p^2 + A^2\bar{p}^2) + \dots] + [(A^2pq + A^2p\bar{q}) + \dots] \\ + [(ABp^2 + AB\bar{p}^2) + \dots] \\ + [(Ap^2\bar{p} + A\bar{p}^2p) + \dots] + [(Ap^3 + A\bar{p}^3) + \dots] + [(Ap^2q + A\bar{p}^2\bar{q}) + \dots] \\ + [(p^4 + \bar{p}^4) + \dots] + [(p^3\bar{p} + \bar{p}^3p) + \dots] \\ + [(p^3q + \bar{p}^3\bar{q}) + \dots] + [(p^2p\bar{q} + \bar{p}^2p\bar{q}) + \dots] \\ + [(p^2q^2 + \bar{p}^2\bar{q}^2) + \dots] + [(p^2q\bar{q} + \bar{p}^2q\bar{q}) + \dots] \\ + [(p^2qr + \bar{p}^2q\bar{r}) + \dots], \quad (68)$$

where each pair of brackets shows terms having the same kind of partition. Note again that two enantiomers of a pair are counted separately. Thus, a pair of such terms as $(A^3p + A^3\bar{p})$ shows the existence of two enantiomers of a pair, and so on.

The introduction of the ligand inventories (eqs. 64–66) into the CI-CF for Type III (eq. 57) gives the corresponding generating function for counting Type-III promolecules:

$$f^{(III)} = 2[(A^2Bp + A^2B\bar{p}) + \dots] + 2[(A^2p^2 + A^2\bar{p}^2) + \dots] \\ + 2[(A^2pq + A^2p\bar{q}) + \dots] + 2[(ABp^2 + AB\bar{p}^2) + \dots] \\ + 2[(Ap^2\bar{p} + A\bar{p}^2p) + \dots] + 2[(Ap^2q + A\bar{p}^2\bar{q}) + \dots] \\ + 2[(p^2p\bar{q} + \bar{p}^2p\bar{q}) + \dots] \\ + 2[(p^2q^2 + \bar{p}^2\bar{q}^2) + \dots] + 2[(p^2q\bar{q} + \bar{p}^2q\bar{q}) + \dots] \\ + 2[(p^2qr + \bar{p}^2q\bar{r}) + \dots] \\ + 6[(ABXp + ABX\bar{p}) + \dots] + 6[(ABpq + ABp\bar{q}) + \dots] \\ + 6[(Ap\bar{p}q + A\bar{p}p\bar{q}) + \dots] + 6[(Apqr + A\bar{p}q\bar{r}) + \dots] \\ + 6[(p\bar{p}qr + p\bar{p}q\bar{q}) + \dots] + 6[(pqrs + \bar{p}q\bar{r}s) + \dots] \\ + 4[ABp\bar{p} + \dots], \quad (69)$$

where each pair of brackets shows terms having the same kind of partition. Note that two enantiomers of a pair are counted separately. The term $2(A^2Bp + A^2B\bar{p})$ in the right-hand side of eq. 69 shows the existence of two pairs of enantiomers (i.e., four allene derivatives). On the same line, the term $6(ABXp + ABX\bar{p})$ indicates six pairs of enantiomers (i.e., twelve allene derivatives). On the other hand, the term $4ABp\bar{p}$ should be regarded as being equal to the term $2(ABp\bar{p} + AB\bar{p}p)$, which shows the existence of two pairs of enantiomers (i.e., four allene derivatives).

The ligand inventories (eqs. 64–66) are introduced into the CI-CF for Type IV (eq. 45) and the resulting equation is expanded to give the corresponding generating function for counting Type-IV promolecules:

$$f^{(IV)} = [A^4 + \dots] + [A^3B + \dots] + [A^2B^2 + \dots] + [A^2BX + \dots] + [A^2p\bar{p} + \dots] + [p^2\bar{p}^2 + \dots]. \quad (70)$$

Finally, the enumeration of Type-IV promolecules is accomplished by introducing the ligand inventories (eqs. 64–66) into the CI-CF for Type V (eq. 48). Thereby, we obtain the following generating function:

$$f^{(V)} = 2[ABp\bar{p} + \dots]. \quad (71)$$

Because of such promolecules of Type V are achiral, the coefficient 2 of the term $2ABp\bar{p}$ in eq. 71 indicates that there exists two *RS*-diastereomers corresponding to the formula $ABp\bar{p}$.

The above-mentioned results (eqs. 67–71) itemized with respect to *RS*-stereoisomeric types (Types I–V) are in agreement with the manual itemization by using stereoisograms [10]. For the full list, see Figs. 8–10 of Ref. [10]. To show the effect of itemization into Types I–V, however, it is worthwhile to examine several values among the above results.

As already mentioned, the term $4ABp\bar{p}$ appearing in eq. 69 should be interpreted as $2(ABp\bar{p} + AB\bar{p}p)$, because the promolecules of Type III is chiral and the enantiomers have the same molecular formula. This value is in agreement with the fact that there exist two pairs of enantiomers (**8/8** and **9/9**), which are depicted in Fig. 3. We find that these four promolecules are characterized by a single stereoisogram of Type III [10]. Strictly speaking, however, the present enumeration is incapable of correlating these promolecules, because the result simply reveals that the four promolecules have the same formula $ABp\bar{p}$.

On the other hand, the value 2 of the term $2ABp\bar{p}$ appearing in eq. 71 shows that there exist two achiral promolecules (**7** and **10**), because Type-V promolecules are achiral. They are also depicted in in Fig. 3. The two promolecules (**7** and **10**) are characterized by a single stereoisogram of Type V [10]. It should be again noted that the present enumeration simply reveals that the four promolecules have the same formula $ABp\bar{p}$ but does not correlate these promolecules.

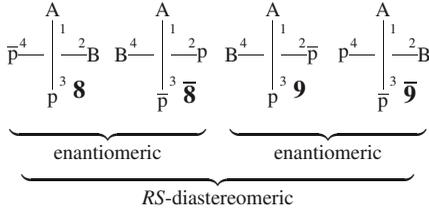
4.2 Methane Derivatives

4.2.1 Basic Formulas for Enumeration

The *RS*-stereoisomeric group ($\mathbf{T}_{d\bar{\sigma}\bar{I}}$) for treating methane derivatives has been discussed on the basis of a tetrahedral skeleton belonging to the point group \mathbf{T}_d [8, 11, 26]. In order to apply the present method of combinatorial enumeration to the tetrahedral skeleton, we take account of three maximum subgroups (eqs. 1–3), i.e., the maximum point subgroup (\mathbf{T}_d), the maximum *RS*-permutation subgroup ($\mathbf{T}_{\bar{\sigma}}$), and the maximum ligand-inversion subgroup ($\mathbf{T}_{\bar{I}}$):

$$\begin{aligned} \mathbf{T}_d &= \{I, C_{2(1)}, C_{2(2)}, C_{2(3)}, C_{3(1)}, C_{3(3)}, C_{3(2)}, C_{3(4)}, C_{3(1)}^2, C_{3(4)}^2, C_{3(3)}^2, C_{3(2)}^2; \\ &\quad \sigma_{d(1)}, S_{4(3)}, S_{4(3)}^3, \sigma_{d(6)}, \sigma_{d(2)}, \sigma_{d(4)}, S_{4(1)}, S_{4(1)}^3, \sigma_{d(3)}, S_{4(2)}^3, \sigma_{d(5)}, S_{4(2)}\} \quad (72) \\ &= \{(1)(2)(3)(4), (1\ 2)(3\ 4), (1\ 3)(2\ 4), (1\ 4)(2\ 3), (1)(2\ 4\ 3), (1\ 2\ 3)(4), \\ &\quad (1\ 3\ 4)(2), (1\ 4\ 2)(3), (1)(2\ 3\ 4), (1\ 2\ 4)(3), (1\ 3\ 2)(4), (1\ 4\ 3)(2); \\ &\quad (1)(2\ 3)(4), (1\ 2\ 4\ 3), (1\ 3\ 4\ 2), (1\ 4)(2)(3), (1)(2)(3\ 4), (1\ 2)(3)(4), \\ &\quad (1\ 3\ 2\ 4), (1\ 4\ 2\ 3), (1)(2\ 4)(3), (1\ 2\ 3\ 4), (1\ 3)(2)(4), (1\ 4\ 3\ 2)\} \quad (73) \end{aligned}$$

Allene Derivatives of Type III with the formula ABp \bar{p}



Allene Derivatives of Type V with the formula ABp \bar{p}

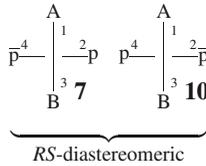


Figure 3: Allene derivatives of Types III and V

$$\begin{aligned}
 \mathbf{T}_{\tilde{\sigma}} &= \{I, C_{2(1)}, C_{2(2)}, C_{2(3)}, C_{3(1)}, C_{3(3)}, C_{3(4)}, C_{3(2)}, C_{3(4)}, C_{3(1)}^2, C_{3(4)}^2, C_{3(3)}^2, C_{3(2)}^2; \\
 &\quad \tilde{\sigma}_{d(1)}, \tilde{S}_{4(3)}, \tilde{S}_{4(3)}^3, \tilde{\sigma}_{d(6)}, \tilde{\sigma}_{d(2)}, \tilde{\sigma}_{d(4)}, \tilde{S}_{4(1)}, \tilde{S}_{4(1)}^3, \tilde{\sigma}_{d(3)}, \tilde{S}_{4(2)}^3, \tilde{\sigma}_{d(5)}, \tilde{S}_{4(2)}\} \quad (74) \\
 &= \{(1)(2)(3)(4), (12)(34), (13)(24), (14)(23), (1)(243), (123)(4), \\
 &\quad (134)(2), (142)(3), (1)(234), (124)(3), (132)(4), (143)(2); \\
 &\quad (1)(23)(4), (1243), (1342), (14)(2)(3), (1)(2)(34), (12)(3)(4), \\
 &\quad (1324), (1423), (1)(24)(3), (1234), (13)(2)(4), (1432)\} \quad (75)
 \end{aligned}$$

$$\begin{aligned}
 \mathbf{T}_{\hat{I}} &= \{I, C_{2(1)}, C_{2(2)}, C_{2(3)}, C_{3(1)}, C_{3(3)}, C_{3(2)}, C_{3(4)}, C_{3(1)}^2, C_{3(4)}^2, C_{3(3)}^2, C_{3(2)}^2; \\
 &\quad \hat{I}, \hat{C}_{2(1)}, \hat{C}_{2(2)}, \hat{C}_{2(3)}, \hat{C}_{3(1)}, \hat{C}_{3(3)}, \hat{C}_{3(2)}, \hat{C}_{3(4)}, \hat{C}_{3(1)}^2, \hat{C}_{3(4)}^2, \hat{C}_{3(3)}^2, \hat{C}_{3(2)}^2\} \quad (76) \\
 &= \{(1)(2)(3)(4), (12)(34), (13)(24), (14)(23), (1)(243), (123)(4), \\
 &\quad (134)(2), (142)(3), (1)(234), (124)(3), (132)(4), (143)(2); \\
 &\quad \overline{(1)(2)(3)(4)}, \overline{(12)(34)}, \overline{(13)(24)}, \overline{(14)(23)}, \overline{(1)(243)}, \overline{(123)(4)}, \\
 &\quad \overline{(134)(2)}, \overline{(142)(3)}, \overline{(1)(234)}, \overline{(124)(3)}, \overline{(132)(4)}, \overline{(143)(2)}\} \quad (77)
 \end{aligned}$$

As for the maximum point subgroup \mathbf{T}_d , the cycle structures appearing in eq. 73 are used by following eqs. 9 and 17. Thereby, we obtain the following CI-CFs:

$$\text{CI-CF}(\mathbf{T}_d; \$d, b_d) = \frac{1}{24}(b_1^4 + 3b_2^2 + 8b_1b_3 + 6a_1^2c_2 + 6c_4) \quad (78)$$

$$\text{CI-CF}(\mathbf{T}; b_d) = \frac{1}{12}(b_1^4 + 3b_2^2 + 8b_1b_3), \quad (79)$$

because $|\mathbf{T}_d| = 24$ and $|\mathbf{T}| = 12$. It follows that eqs. 20 and 23 for methane derivatives take the following concrete forms:

$$\text{CI-CF}^{(\text{IV/V})}(\mathbf{T}_d; \$_d) = \frac{1}{2}(a_1^2 c_2 + c_4) \quad (80)$$

$$\text{CI-CF}^{(\text{II/III})}(\mathbf{T}_d; \$_d, b_d) = \frac{1}{24}(b_1^4 + 3b_2^2 + 8b_1 b_3 - 6a_1^2 c_2 - 6c_4). \quad (81)$$

The action of the maximum *RS*-permutation subgroup ($\mathbf{T}_{\bar{\sigma}}$) can be characterized by the cycle structures appearing in eq. 75. Hence, eq. 28 for this case is calculated to give the following CI-CF:

$$\text{CI-CF}(\mathbf{T}_{\bar{\sigma}}; b_d) = \frac{1}{24}(b_1^4 + 3b_2^2 + 8b_1 b_3 + 6b_1^2 b_2 + 6b_4). \quad (82)$$

Thereby, eqs. 30 and 32 for methane derivatives take the following concrete forms:

$$\text{CI-CF}^{(\text{II/IV})}(\mathbf{T}_{\bar{\sigma}}; b_d) = \frac{1}{2}(b_1^2 b_2 + b_4) \quad (83)$$

$$\text{CI-CF}^{(\text{III/V})}(\mathbf{T}_{\bar{\sigma}}; b_d) = \frac{1}{24}(b_1^4 + 3b_2^2 + 8b_1 b_3 - 6b_1^2 b_2 - 6b_4). \quad (84)$$

The ligand-inversion subgroup $\mathbf{T}_{\bar{i}}$ acts on the tetrahedral skeleton, where the cycle structures appearing in eq. 77 represent the modes of the action. Hence, by using eq. 36, we obtain the following CI-CF:

$$\text{CI-CF}(\mathbf{T}_{\bar{i}}; b_d, \$_d) = \frac{1}{24}(b_1^4 + 3b_2^2 + 8b_1 b_3 + a_1^4 + 3c_2^2 + 8a_1 a_3). \quad (85)$$

Thereby, eqs. 38 and 40 for methane derivatives take the following concrete forms:

$$\text{CI-CF}^{(\text{IV})}(\mathbf{T}_{\bar{i}}; \$_d) = \frac{1}{12}(a_1^4 + 3c_2^2 + 8a_1 a_3) \quad (86)$$

$$\text{CI-CF}^{(\text{II/III/V})}(\mathbf{T}_{\bar{i}}; b_d) = \frac{1}{24}(b_1^4 + 3b_2^2 + 8b_1 b_3 - a_1^4 - 3c_2^2 - 8a_1 a_3). \quad (87)$$

4.2.2 Itemization and Enumeration Results

The discussion described for deriving eq. 45 is also effective in the case of methane derivatives. Hence, eq. 44 for this case takes the following form:

$$\text{CI-CF}^{(\text{IV})}(\mathbf{T}_d; \$_d) = \frac{1}{2}(a_1^2 a_2 + a_2 c_2 - a_2^2 + c_4). \quad (88)$$

The ligand inventories (eqs. 64–66) are introduced into the CI-CF for Type IV (eq. 88) and the resulting equation is expanded to give the corresponding generating function for counting Type-IV methane derivatives:

$$g^{(\text{IV})} = [A^4 + \dots] + [A^3 B + \dots] + [A^2 B^2 + \dots] \\ + [A^2 B X + \dots] + [A^2 p \bar{p} + \dots] + [p^2 \bar{p}^2 + \dots]. \quad (89)$$

By the subtraction of eq. 88 from eq. 80, eq. 47 for methane derivatives of Type V is calculated as follows:

$$\text{CI-CF}^{(\text{V})}(\mathbf{T}_d; \$_d) = \frac{1}{2}(a_1^2 c_2 + c_4) - \frac{1}{2}(a_1^2 a_2 + a_2 c_2 - a_2^2 + c_4) \\ = \frac{1}{2}(a_1^2 c_2 - a_1^2 a_2) - \frac{1}{2}(a_2 c_2 - a_2^2). \quad (90)$$

The enumeration of Type-V promolecules is accomplished by introducing the ligand inventories (eqs. 64–66) into the CI-CF for Type V (eq. 90). Thereby, we obtain the following generating function:

$$g^{(V)} = 2[ABp\bar{p} + \dots], \quad (91)$$

which corresponds to pseudoasymmetric cases.

The subtraction of eq. 88 from eq. 83 gives the following CI-CF:

$$\text{CI-CF}^{(II)}(\mathbf{T}_{\bar{G}}; \$d, b_d) = \frac{1}{2}(b_1^2 b_2 + b_4) - \frac{1}{2}(a_1^2 a_2 + a_2 c_2 - a_2^2 + c_4), \quad (92)$$

which is the concrete form of eq. 50 for methane derivatives of Type II.

By introducing the ligand inventories (eqs. 64–66) in to the CI-CF for Type II (eq. 92), we obtain the corresponding generating function for counting Type-II methane derivatives:

$$\begin{aligned} g^{(II)} = & [(A^3 p + A^3 \bar{p}) + \dots] + [(A^2 B p + A^2 B \bar{p}) + \dots] \\ & + [(A^2 p^2 + A^2 \bar{p}^2) + \dots] + [(A^2 p q + A^2 p \bar{q}) + \dots] \\ & + [(AB p^2 + AB \bar{p}^2) + \dots] \\ & + [(A p^2 \bar{p} + A \bar{p}^2 p) + \dots] + [(A p^3 + A \bar{p}^3) + \dots] + [(A p^2 q + A \bar{p}^2 \bar{q}) + \dots] \\ & + [(p^4 + \bar{p}^4) + \dots] + [(p^3 \bar{p} + \bar{p}^3 p) + \dots] \\ & + [(p^3 q + \bar{p}^3 \bar{q}) + \dots] + [(p^2 \bar{p} q + \bar{p}^2 p \bar{q}) + \dots] \\ & + [(p^2 q^2 + \bar{p}^2 \bar{q}^2) + \dots] + [(p^2 q \bar{q} + \bar{p}^2 q \bar{q}) + \dots] \\ & + [(p^2 q r + \bar{p}^2 \bar{q} \bar{r}) + \dots], \end{aligned} \quad (93)$$

where each pair of brackets shows terms having the same kind of partition. Note again that two enantiomers of a pair are counted separately.

By the subtraction of eq. 88 from eq. 86, eq. 53 for methane derivatives of Type I is calculated as follows:

$$\text{CI-CF}^{(I)}(\mathbf{T}_{\bar{I}}; \$d) = \frac{1}{12}(a_1^4 + 3c_2^2 + 8a_1 a_3) - \frac{1}{2}(a_1^2 a_2 + a_2 c_2 - a_2^2 + c_4). \quad (94)$$

The ligand inventories (eqs. 64–66) are introduced into the CI-CF for Type I (eq. 94) and the resulting equation is expanded so as to give the corresponding generating function for counting Type-I methane derivatives:

$$g^{(I)} = 2ABXY + 2[p\bar{p}q\bar{q} + \dots], \quad (95)$$

where each pair of brackets shows terms having the same kind of partition. Note that two enantiomers of a pair are counted separately.

By subtracting eqs. 94, 92, and 80 from eq. 79, we obtain eq. 56 for methane derivatives of Type III as follows:

$$\begin{aligned} \text{CI-CF}^{(III)}(\mathbf{T}; \$d, b_d) = & \frac{1}{12}(b_1^4 + 3b_2^2 + 8b_1 b_3) - \frac{1}{12}(a_1^4 + 3c_2^2 + 8a_1 a_3) - \frac{1}{2}(b_1^2 b_2 + b_4) \\ & - \frac{1}{2}(a_1^2 c_2 + c_4) + (a_1^2 a_2 + a_2 c_2 - a_2^2 + c_4). \end{aligned} \quad (96)$$

The introduction of the ligand inventories (eqs. 64–66) into the CI-CF for Type III (eq. 96) gives the corresponding generating function for counting Type-III methane derivatives:

$$\begin{aligned} g^{(III)} = & +2[(ABXp + ABX\bar{p}) + \dots] + 2[(ABpq + ABp\bar{q}) + \dots] \\ & + 2[(A\bar{p}\bar{p}q + A\bar{p}p\bar{q}) + \dots] + 2[(Apqr + A\bar{p}q\bar{r}) + \dots] \\ & + 2[(p\bar{p}qr + p\bar{p}q\bar{r}) + \dots] + 2[(pqrs + p\bar{q}r\bar{s}) + \dots], \end{aligned} \quad (97)$$

where each pair of brackets shows terms having the same kind of partition. Note that two enantiomers of a pair are counted separately.

The above-mentioned results (eqs. 89, 91, 93, 95, and 97) itemized with respect to *RS*-stereoisomeric types (Types I–V) are in agreement with the manual itemization by using stereoisograms [11]. For the full list, see Fig. 10 of [10] and Fig. 15 of [11]. To show the effect of itemization into Types I–V, it is worthwhile to compare methane derivatives with allene derivatives of the same type.

4.3 Comparison Between Allenes and Methanes

Let us compare the coefficient of the term *ABXY* in eq. 67 with that of eq. 95, where both of the equations are concerned with Type I. The value 6 of eq. 67 indicates that there exist three pairs of enantiomers (**11/11̄**, **3/3̄**, and **12/12̄**), which are depicted in Fig. 4. Each pair corresponds to a single stereoisogram of Type I. Because any Type I promolecule is ascleral (Table 1), the chirality and the *RS*-stereogenicity are superposed upon each other. It follows that the corresponding relationships, i.e., the enantiomeric relationship and the *RS*-diastereomeric relationship are superposed upon each other, as shown by underbraces below each pair (**11/11̄**, **3/3̄**, or **12/12̄**).

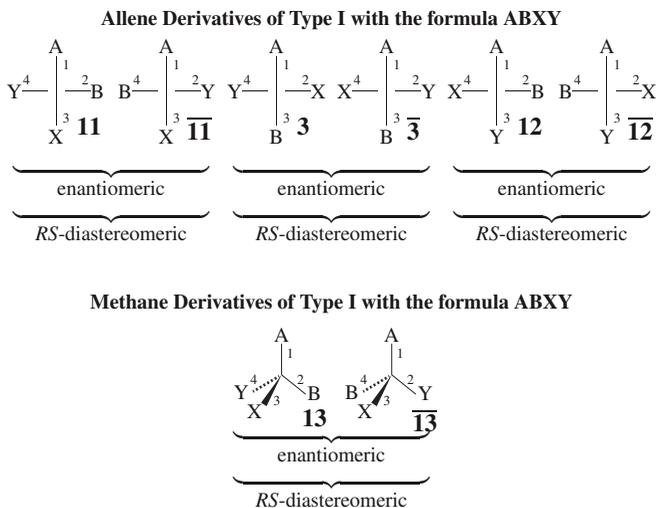
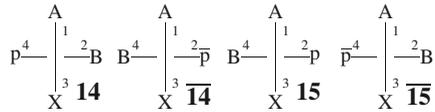


Figure 4: Allene and methane derivatives of Type I

The value 2 of the term *2ABXY* in eq. 95 indicates that there exists one pair of enantiomers (**13/13̄**), which are also depicted in Fig. 4. The pair corresponds to a single stereoisogram of Type I, where the chirality and the *RS*-stereogenicity are superposed upon each other so that the enantiomeric relationship and the *RS*-diastereomeric relationship are superposed upon each other.

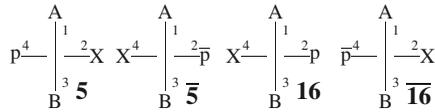
As found easily, if the allene nucleus *C=C=C* of each pair (**11/11̄**, **3/3̄**, or **12/12̄**) is hypothetically reduced into a one-carbon nucleus, there emerges the pair of enantiomers (**13/13̄**). This

Allene Derivatives of Type III with the formula ABXp



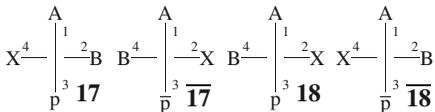
enantiomeric enantiomeric

RS-diastereomeric



enantiomeric enantiomeric

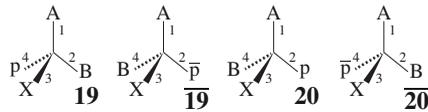
RS-diastereomeric



enantiomeric enantiomeric

RS-diastereomeric

Methane Derivatives of Type III with the formula ABXp



enantiomeric enantiomeric

RS-diastereomeric

Figure 5: Allene and methane derivatives of Type III

hypothetical process rationalizes the difference between the value 6 of the term 6ABXY in eq. 67 and the corresponding value 2 in eq. 95.

Let us next compare the coefficient of the term (ABXp + ABXp̄) in eq. 69 with that of eq. 97. The coefficient 6 of the term 6(ABXp + ABXp̄) in eq. 69 indicates that there exist six pairs of enantiomers (**14/14̄**, **15/15̄**, **5/5̄**, **16/16̄**, **17/17̄**, and **18/18̄**), which are depicted in Fig. 5. Among them, the set of **14/14̄** and **15/15̄**, the set of **5/5̄** and **16/16̄**, and the set of **17/17̄** and **18/18̄** are respectively linked with a large horizontal brace, which shows that each of the sets appears in a single stereoisogram. Although holantimeric relationships are not denoted, they

are contained in respective stereoisograms, along with the enantiomeric relationships and the *RS*-diastereomeric ones which are denoted in Fig. 5.

On the other hand, the value 2 of the term $2(\overline{ABXp} + \overline{ABX\bar{p}})$ in eq. 97 indicates that there exist two pairs of enantiomers ($\overline{19/19}$ and $\overline{20/20}$), which are also depicted in Fig. 5. These two pairs appear in a single stereoisogram.

Let us apply the above-mentioned hypothetical procedure to this case, where the allene nucleus $C=C=C$ of each set (e.g., $\overline{14/14}$ and $\overline{15/15}$) is reduced into a one-carbon nucleus. Thereby, we obtain the two pairs of enantiomers ($\overline{19/19}$ and $\overline{20/20}$). On the same line, each of the remaining sets (i.e., the set of $\overline{5/5}$ and $\overline{16/16}$ as well as the set of $\overline{17/17}$ and $\overline{18/18}$) produces also the two pairs of enantiomers ($\overline{19/19}$ and $\overline{20/20}$). This hypothetical process rationalizes the difference between the value 6 of the term $6(\overline{ABXp} + \overline{ABX\bar{p}})$ in eq. 69 and the corresponding value 2 in eq. 97.

Finally, let us compare between Fig. 4 (Type I) and Fig. 5 (Type III). By replacing the chiral proligand (*p*) by an achiral one (*Y*), the set of $\overline{14/14}$ and $\overline{15/15}$ shown in Fig. 5 is converted into the pair of enantiomers ($\overline{11/11}$) shown in Fig. 4. The same replacement applied to the set of $\overline{5/5}$ and $\overline{16/16}$ as well as to the set of $\overline{17/17}$ and $\overline{18/18}$ turns out to generate the pair of $\overline{3/3}$ as well as the pair of $\overline{12/12}$. Moreover, the same replacement applied to the two pairs of Type-III enantiomers ($\overline{19/19}$ and $\overline{20/20}$) produces one pair of Type-I enantiomers ($\overline{13/13}$). Thus, the conversions of Type III into Type I described here demonstrate clearly the superposition of an *RS*-diastereomeric relationship onto an enantiomeric relationship, which is concealed so long as we rely on the conventional stereochemistry.

5 Conclusion

Molecules or promolecules are categorized into five types by means of chirality, *RS*-stereogenicity, and sclerality, i.e., Type I (chiral/*RS*-stereogenic/ascleral), Type II (chiral/*RS*-astereogenic/scleral), Type III (chiral/*RS*-stereogenic/scleral), Type IV (achiral/*RS*-astereogenic/ascleral), and Type V (achiral/*RS*-stereogenic/scleral). Molecules or promolecules based on a given skeleton are counted under the action of the maximum point subgroup, the maximum *RS*-permutation subgroup, and the maximum ligand-inversion subgroup, which are subgroups of *RS*-stereoisomeric group, so that their numbers itemized with respect to Type I to Type V are obtained. Thereby, allene derivatives and methane derivatives are counted respectively in an itemized fashion and the results are verified in comparison with manual enumerations reported previously.

References

- [1] R. S. Cahn, C. K. Ingold, and V. Prelog, *Angew. Chem. Int. Ed. Eng.*, **5**, 385 (1966).
- [2] V. Prelog and G. Helmchen, *Angew. Chem. Int. Ed. Eng.*, **21**, 567–583 (1982).
- [3] IUPAC Recommendations 1996. Basic Terminology of Stereochemistry., *Pure Appl. Chem.*, **68**, 2193–2222 (1996).
- [4] S. Fujita, *Bull. Chem. Soc. Jpn.*, **74**, 1585–1603 (2001).
- [5] S. Fujita, *Bull. Chem. Soc. Jpn.*, **75**, 1949–1962 (2002).

- [6] S. Fujita, *Helv. Chim. Acta*, **85**, 2440–2457 (2002).
- [7] S. Fujita, *J. Math. Chem.*, **33**, 113–143 (2003).
- [8] S. Fujita, *J. Org. Chem.*, **69**, 3158–3165 (2004).
- [9] S. Fujita, *Tetrahedron*, **60**, 11629–11638 (2004).
- [10] S. Fujita, *Memoirs of the Faculty of Engineering and Design, Kyoto Institute of Technology*, **53**, 19–38 (2005).
- [11] S. Fujita, *J. Math. Chem.*, **35**, 265–287 (2004).
- [12] S. Fujita, *MATCH Commun. Math. Comput. Chem.*, **54**, 39–52 (2005).
- [13] S. Fujita, *Tetrahedron*, **62**, 691–705 (2006).
- [14] S. Fujita, *Theor. Chem. Acc.*, **113**, 73–79 (2005).
- [15] S. Fujita, *Theor. Chem. Acc.*, **113**, 80–86 (2005).
- [16] S. Fujita, *Theor. Chem. Acc.*, **115**, 37–53 (2006).
- [17] S. Fujita, *Tetrahedron*, **47**, 31–46 (1991).
- [18] S. Fujita, *J. Chem. Inf. Comput. Sci.*, **32**, 354–363 (1992).
- [19] S. Fujita, *Polyhedron*, **12**, 95–110 (1993).
- [20] S. Fujita, “Symmetry and Combinatorial Enumeration in Chemistry,” Springer-Verlag, Berlin-Heidelberg (1991).
- [21] S. Fujita, *Croat. Chem. Acta*, **79**, 411–427 (2006).
- [22] S. Fujita, *Theor. Chim. Acta*, **76**, 247–268 (1989).
- [23] S. Fujita, *J. Math. Chem.*, **5**, 121–156 (1990).
- [24] S. Fujita, “Diagrammatical Approach to Molecular Symmetry and Enumeration of Stereoisomers,” University of Kragujevac, Faculty of Science, Kragujevac (2007).
- [25] S. Fujita, *J. Am. Chem. Soc.*, **112**, 3390–3397 (1990).
- [26] S. Fujita, *MATCH Commun. Math. Comput. Chem.*, **52**, 3–18 (2004).