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Chirality and Stereogenicity for Allene Derivatives. Observance and Violation of Chirality Fittingness

Shinsaku Fujita

Department of Chemistry and Materials Technology, Kyoto Institute of Technology,
Matsugasaki, Sakyoku, Kyoto 606-8585

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Allene derivatives have been combinatorially enumerated under a point group $\mathbf{D}_{2d}$ as well as under a permutation group $\mathbf{S}_9^{[4]}$, which is a subgroup of the symmetric group of degree 4 and is isomorphic to the point group $\mathbf{D}_{2d}$. These enumerations have been compared in terms of the observance and the vilolation of chirality fittingness, where two types of Young's tableaus (point-group symmetry and permutation-group symmetry) have been used to clarify the relationship between stereochemistry and permutability of allene derivatives. The concept of chirality/achirality for stereochemistry has been compared with the concept of stereogenicity/astereogenicity for permutability. Enantiomers, which have been characterized by equivalency under point-group symmetry, have been classified into two classes according to whether or not they have been assigned to orbits (equivalence classes) under permutation-group symmetry. On the other hand, diastereomers have been related to equivalence classes (orbits) under permutation-group symmetry only. The terms *enantiostereogenic* and *diastereogenic* have been coined to discuss the behavior under permutaiton-group symmetry. The CIP (Cahn–Ingold–Prelog) system is examined in terms of stereogenicity/astereogenicity. A new combination of chirality and stereogenicity described in the present paper provides us with a tool for restructuring stereochemistry.

The sequence rule proposed by Cahn, Ingold and Prelog (the CIP system)[1] has been widely used in organic stereochemistry. The CIP system originally aimed at specifying the absolute configuration of enantiomers, as shown in the title "Specification of Molecular Chirality".[1] The terms "chiral, prochiral, pseudoasymmetric, and propseudoasymmetric centers" have been used to characterize modes of arrangements based on a tetrahedral model.[2,3] According to the convincing argument by Mislow and Siegel,[4] the terms "stereogenic" and "prostereogenic" proposed earlier by McCasland[5] have been adopted in the revised CIP system in the form of the descriptors of stereogenic units etc.[6–9] As a result, the revised CIP system has been conceptually changed into a method for "specifying molecular stereogenicity", apart from its original purpose that was "to specify molecular chirality".

Although the change from "chirality" into "stereogenicity" in the revision has been conceptually enormous, the significance of the change has been left vague because of the pragmatic success of the CIP system. In fact, the nature of stereogenicity has seldom been investigated, whereas that of chirality has been discussed on the basis of the point-group theory. Moreover, the relationship between "chirality" and "stereogenicity", has attracted little attention because of the lack of a common standpoint for integrating them.

To clarify the nature of chirality, we have already proposed the concept of sphericity that controls chirality fittingness for ligand substitution,[10] where we have emphasized the importance of a coset representation (CR) $\mathbf{G}(/\mathbf{G}_i)$ and of its subduction.[11] After the proposal of additional concepts "proligands and promolecules",[12,13] we have then applied these concepts to the redefinition of prochirality,[10] topicity,[14,15] and anisochrony.[16]

Although the sphericity concept has originally aimed at investigating the nature of chirality, it has been also applied to redefine the stereogenicity concept.[15] As an extension, we have recently used the sphericity concept to clarify the meaning of the CIP system, where we have shown that the CIP system has not specified the stereochemisty (the chiral rearrangement) of a tetrahedral model but has rather determined its permutational nature.[17] Our previous investigation, however, has been restricted within a tetrahedral skeleton,[17] where central stereogenicity (or conventionally central chirality) has been taken into consideration. It follows that a further investigation about axial stereogenicity (or conventionally axial chirality) is desirable in order to show the generality of our approach.

As compounds of such axial stereogenicity, allene derivatives (or elongated tetrahedral ones) have provided more complicated situations than tetrahedral compounds. For example, (S_a)- (**1**) and (R_a)-1,3-dichloroallene (**2**) depicted in Fig. 1 are enantiomeric to each other, though they are designated to have (S_a)- and (R_a)-configurations in terms of the CIP system. Note that the right diagram (**6**) of Fig. 2 is used in place of the left formula (**5**) for the sake of simplicity. On the other hand, the CIP system differentiates between **3** and **4** to have (S_a)- and (R_a)-configurations by the equivalent procedures, where p and $\bar{\mathrm{p}}$ represent a pair of enantiomeric ligands. Since the relationship between **3** and **4** is regarded as being diastereomeric from a stereochemical point of view (but not from the viewpoint of the CIP system), they may be designated by the corresponding lowercase letters ((s_a) and (r_a)). However, the "enantiomeric" relationship between **1** and **2** (enclosed with a solid line) cannot be differentiated from the diastereomeric one between **3** and **4** (enclosed with a solid line) within the scope of the CIP system, because the two relationships are specified by the same procedure, which is based on the permutability of ligands. Moreover, the CIP system gives no infomation on the enantiomeric relationship between **3** and $\overline{\mathbf{3}}$ (enclosed with a dashed line) nor between **4** and $\overline{\mathbf{4}}$ (enclosed with a dashed line).

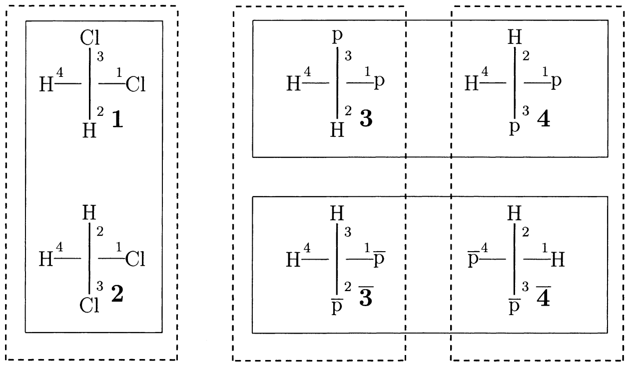
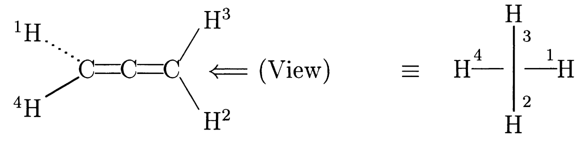


Fig. 1. Enantiomeric and diastereomeric relationships for allene derivatives.



5 **6**

Fig. 2. Convention for drawing allene derivatives.

As clarified in the preceding paragraphs, it is natural to question whether the relationship determined between **1** and **2** by virtue of the CIP system is enantiomeric (enclosed with a dotted line) or diastereomeric (enclosed with a solid line). To answer this question, the present paper will deal with an allene skeleton (or elongated tetrahedral one) in detail as a representative of axial stereogenicity. In the section of Exhaustive Enumerations, two types of Young's tableaus (i.e. those of permutation and those of symmetry) will be used to explain stereochemistry as well as stereoisomerism. The two types of Young's tableaus will be discussed in terms of observance and violation of chirality fittingness. Thereby, combinatorial enumerations under point-group symmetry and under permutation-group symmetry will be applied to isomer enumerations of allene derivatives. By using the results of the combinatorial enumerations, in the section of Discussion I will deal with the application of the sphericity to stereoisomerism and with the comparison between chirality/achirality and stereogenicity/astereogenicity.

Exhaustive Enumerations

1. Desymmetrization of an Allene Skeleton. An allene skeleton belongs to a $\mathbf{D}_{2d}$-point group, where the four vertices are numbered from 1 to 4, as shown in Fig. 2. The four positions construct an orbit (equivalence class) governed by a coset representation (CR) $\mathbf{D}_{2d}(/\mathbf{C}_s)$.[14]

A derivative of allene is considered to be generated by putting a set of ligands on the four positions of an allene skeleton (**5**). During this derivation, the $\mathbf{D}_{2d}$-symmetry of the allene skeleton is reduced into its subsymmetry ($\mathbf{G}_i$). The derivation process is represented by a subduction of the CR $\mathbf{D}_{2d}(/\mathbf{C}_s)$ into $\mathbf{G}_i$, which is denoted by $\mathbf{D}_{2d}(/\mathbf{C}_s) \downarrow \mathbf{G}_i$.[10,14] Such a subduction produces a sum of CRs for each subgroup, which can be precalculated algebraically by using mark tables and inverse mark tables for $\mathbf{D}_{2d}$ and the subgroup.[14] The results are collected in the subduction column of Table 1.

The sum of CRs for each subgroup represents the mode of equivalency of four ligands in a derivative belonging to the subgroup. The mode can be expressed by a Young's tableau of symmetry (or more precisely a Young's tableau of point-group symmetry), where one row corresponds to each of the CRs, as shown in Table 1.

Each of the CRs corresponds to an orbit of ligands, which is characterized by its sphericity,[10,14] as collected in Table 1. For example, the subgroup $\mathbf{C}_s$ produced by the subduction $\mathbf{D}_{2d}(/\mathbf{C}_s) \downarrow \mathbf{C}_s$ involves one $\mathbf{C}_s(/\mathbf{C}_1)$ and two $\mathbf{C}_s(/\mathbf{C}_s)$. The former CR $\mathbf{C}_s(/\mathbf{C}_1)$ represents a two-membered orbit, which is enantiospheric because the global symmetry $\mathbf{C}_s$ is an achiral group and the local symmetry $\mathbf{C}_1$ is a chiral group (Table 2). On the other hand, the latter CR $\mathbf{C}_s(/\mathbf{C}_s)$ represents a one-membered orbit, which is homospheric because of the achirality of $\mathbf{C}_s$ for both the global symmetry and the local one (Table 2).

According to Table 2, the enantiosphericity of the $\mathbf{C}_s(/\mathbf{C}_1)$-orbit is concisely represented by a dummy variable c_2, where the subscript 2 designates the size of the orbit ($|\mathbf{C}_s|/|\mathbf{C}_1| = 2/1 = 2$). On the other hand, the homosphericity of the $\mathbf{C}_s(/\mathbf{C}_s)$-orbit is represented by a dummy variable a_1, where the subscript 1 is equal to the size of the orbit ($|\mathbf{C}_s|/|\mathbf{C}_s| = 2/2 = 1$). Thereby, the division brought out by the subduction $\mathbf{D}_{2d}(/\mathbf{C}_s) \downarrow \mathbf{C}_s$ is assigned to a monomial $a_1^2 c_2$, which is called a unit subduced cycle index with chirality fittingness (USCI-CF). The USCI-CFs for the subgroups of $\mathbf{D}_{2d}$ are listed also in Table 1, where a $\mathbf{G}(/\mathbf{G}_i)$-orbit is assigned to $a_{|\mathbf{G}|/|\mathbf{G}_i|}$ for a homospheric orbit, $b_{|\mathbf{G}|/|\mathbf{G}_i|}$ for a hemispheric orbit, and $c_{|\mathbf{G}|/|\mathbf{G}_i|}$ for an enantiospheric orbit according to Table 2. When such sphericity is ignored, a unit subduced cycle index (USCI) without chirality fittingness can be obtained, as listed also in Table 1, where a dummy variable $s_{|\mathbf{G}|/|\mathbf{G}_i|}$ is substituted for $a_{|\mathbf{G}|/|\mathbf{G}_i|}$, $b_{|\mathbf{G}|/|\mathbf{G}_i|}$, and $c_{|\mathbf{G}|/|\mathbf{G}_i|}$.

2. Chirality Fittingness by Sphericity. An orbit accommodates an appropriate set of ligands according to the sphericity of the orbit. This feature is called *chirality fittingness*, as summarized in Table 2.[10,14] Strictly speaking, we should use the term "proligand"[12,13] in place of the term "ligand" when we discuss chirality fittingness generally. However, we here use the term "ligand", since this is more familiar to organic chemists than the term "proligand" and such usage causes no confusion within the scope of this article.

Let us first examine an allene derivative **7** belonging to $\mathbf{C}_s$-symmetry, where one enantiospheric $\mathbf{C}_s(/\mathbf{C}_1)$-orbit and two homospheric $\mathbf{C}_s(/\mathbf{C}_s)$-orbits are involved (Fig. 3). According to chirality fittingness (Table 2), the orbits of **7** can accommodate A^2BC as a ligand set, where the symbols A, B, and C represent achiral ligands. This mode of accommodation is represented

Table 1. Subduction of a $\mathbf{D}_{2d}(/\mathbf{C}_s)$-Orbit

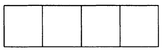
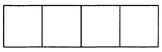
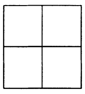
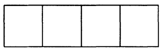
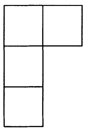
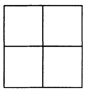
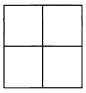
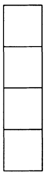
Subgroup of $\mathbf{D}_{2d}$	Tableau of Symmetry	Cycle structure	Subduction of $\mathbf{D}_{2d}(/\mathbf{C}_s)$	Sphericity	USCI with CF
$\mathbf{D}_{2d}$		4^1	$\mathbf{D}_{2d}(/\mathbf{C}_s)$	homospheric	a_4
$\mathbf{D}$		4^1	$\mathbf{D}_2(/\mathbf{C}_1)$	hemispheric	b_4
$\mathbf{C}_{2v}$		2^2	$\mathbf{C}_{2v}(/\mathbf{C}_s)$	homospheric	a_2^2
			$\mathbf{C}_{2v}(/\mathbf{C}'_s)$	homospheric	
$\mathbf{S}_4$		4^1	$\mathbf{S}_4(/\mathbf{C}_1)$	enantiospheric	c_4
$\mathbf{C}_s$		$2^1 1^2$	$\mathbf{C}_s(/\mathbf{C}_1)$	enantiospheric	$a_1^2 c_2$
			$\mathbf{C}_s(/\mathbf{C}_s)$	homospheric	
			$\mathbf{C}_s(/\mathbf{C}_s)$	homospheric	
$\mathbf{C}'_2$		2^2	$\mathbf{C}'_2(/\mathbf{C}_1)$	hemispheric	b_2^2
			$\mathbf{C}'_2(/\mathbf{C}_1)$	hemispheric	
$\mathbf{C}_2$		2^2	$\mathbf{C}_2(/\mathbf{C}_1)$	hemispheric	b_2^2
			$\mathbf{C}_2(/\mathbf{C}_1)$	hemispheric	
$\mathbf{C}_1$		1^4	$\mathbf{C}_1(/\mathbf{C}_1)$	hemispheric	b_1^4
			$\mathbf{C}_1(/\mathbf{C}_1)$	hemispheric	
			$\mathbf{C}_1(/\mathbf{C}_1)$	hemispheric	
			$\mathbf{C}_1(/\mathbf{C}_1)$	hemispheric	

Table 2. Sphericities of Orbits[10]

$\mathbf{G}$	$\mathbf{G}_i$	Sphericity of $\mathbf{G}(/\mathbf{G}_i)$	Chirality fittingness (objects allowed)	USCI-CF	USCI
achiral	achiral	homospheric	achiral	$a_{\lvert\mathbf{G}\rvert/\lvert\mathbf{G}_i\rvert}$	$s_{\lvert\mathbf{G}\rvert/\lvert\mathbf{G}_i\rvert}$
achiral	chiral	enantiospheric	achiral,[a)] chiral[b)]	$c_{\lvert\mathbf{G}\rvert/\lvert\mathbf{G}_i\rvert}$	$s_{\lvert\mathbf{G}\rvert/\lvert\mathbf{G}_i\rvert}$
chiral	chiral	hemispheric	achiral,[c)] chiral	$b_{\lvert\mathbf{G}\rvert/\lvert\mathbf{G}_i\rvert}$	$s_{\lvert\mathbf{G}\rvert/\lvert\mathbf{G}_i\rvert}$

a) An achiral object is restricted to be chiral. The half and the other half of the orbit are superimposable by a rotoreflection operator of **G**.

b) The orbit accommodates the half number ($|\mathbf{G}|/2|\mathbf{G}_i|$) of chiral objects and the half number of chiral objects of opposite chirality so as to accomplish compensated chiral packing.

c) An achiral object is restricted to be chiral.

by a Young's tableau of symmetry (S) shown in Fig. 3(a). The ligand set A^2BC generates another derivative **8** belonging to $\mathbf{C}_1$-symmetry, where four hemispheric $\mathbf{C}_1(/\mathbf{C}_1)$-orbits are involved (Fig. 3). This mode of accommodation is represented by a Young's tableau of symmetry (S) shown in Fig. 3(c).

If such chirality fittingness is ignored, a permutation group isomorphic to the point group $\mathbf{D}_{2d}$ should be considered. The permutation group is decided to be a subgroup ($\mathbf{S}_9^{[4]}$) of the symmetric group of order 4 ($\mathbf{S}^{[4]}$). As a result, the point group $\mathbf{C}_s(\subset \mathbf{D}_{2d})$ corresponds to $\mathbf{S}_3^{[4]}$ ($\subset \mathbf{S}_9^{[4]}$). Thereby, the modes of accommodation are represented by Young's tableaus of permutation (P), as shown in Figs. 3(b) and (d). It follows that the two types of Young's tableaus take the same modes of packing, as long as we consider achiral ligands only.

It should be noted here that if the symmetric group of order 4 ($\mathbf{S}^{[4]}$) were selected in place of the permutation group $\mathbf{S}_9^{[4]}$, other Young's tableaus of permutation shown in Fig. 3(b′) and (d′) should be selected. Obviously, these selections are concerned with isomerization processes. In other words, the group $\mathbf{S}^{[4]}$ deals with constitutional isomerism as well as stereoisomerism. Because the present article centers its discussion on stereoisomerism, the permutation group $\mathbf{S}_9^{[4]}$ is selected.

Let us next examine an allene derivative **9** of formula $A_2p\bar{p}$, which belongs to $\mathbf{C}_s$-symmetry. The enantiospheric $\mathbf{C}_s(/\mathbf{C}_1)$-orbit accommodates chiral ligands p and $\bar{p}$ that are enantiomeric in isolation. This mode of subsitutution is a compensated

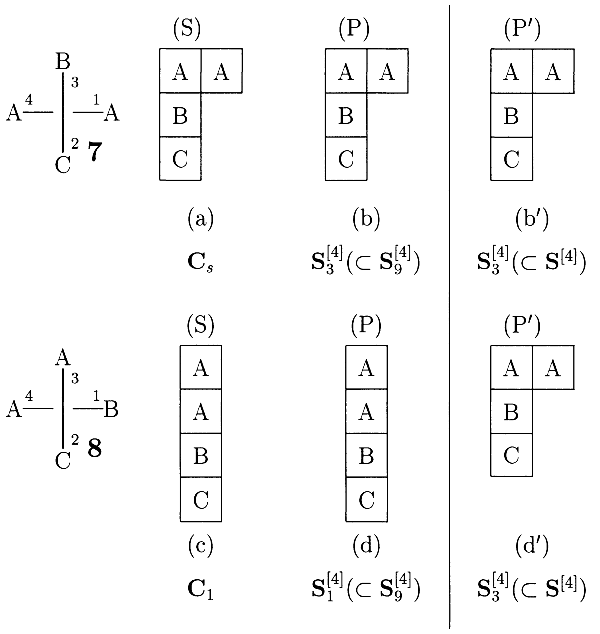


Fig. 3. Ligand packing for A^2BC-promolecules under point-group symmetries (S) and under permutation-group symmetries (P and P′).

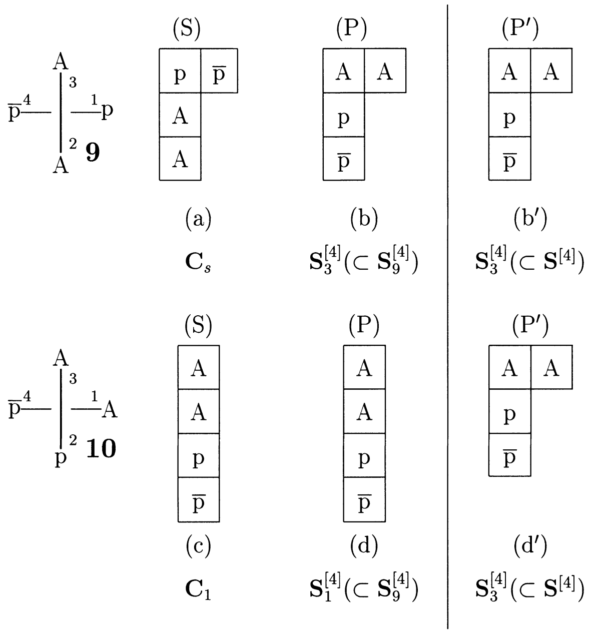


Fig. 4. Ligand packing for $A^2p\bar{p}$-promolecules under point-group symmetries (S) and under permutation-group symmetries (P and P′).

chiral packing according to Table 2. The ligands p and $\bar{p}$ are equivalent and in consequence are accommodated in a row of a Young's tableau of Fig. 4(a). The two achiral ligands (A) are nonequivalent, because they are separately involved in one-membered $\mathbf{C}_s(/\mathbf{C}_s)$-orbits, as depicted in the Young tableau (Fig. 4(a)).

Under the permutation group $\mathbf{S}_3^{[4]}$ ($\subset \mathbf{S}_9^{[4]}$), the mode of accommodation is represented by a Young's tableau of permutation (P), as shown in Fig. 4(b). Thus, the two As are equivalent as a result of disregarding chirality fittingness. It follows that the two types of Young's tableaus take different modes of packing if chiral ligands are considered along with achiral ones.

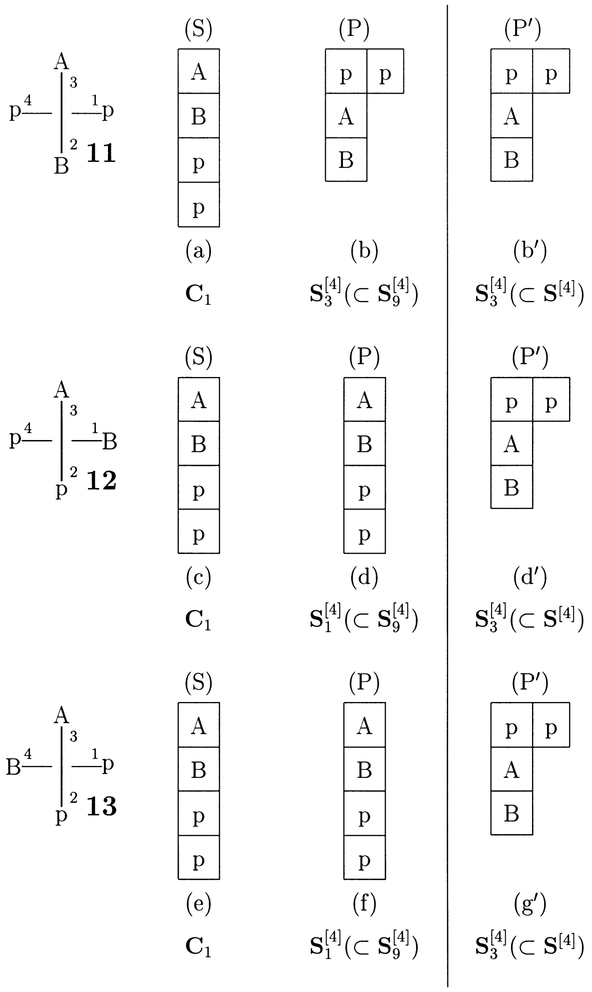


Fig. 5. Ligand packing for ABp^2-promolecules under point-group symmetries (S) and under permutation-group symmetries (P and P′).

Here, we should emphasize the difference between the Young's tableau of symmetry (Fig. 4(a)) and the Young's tableau of permutation (Fig. 4(b)): the former shows the observance of chirality fittingness, while the latter shows the violation of chirality fittingness. Since each $\mathbf{C}_s(/\mathbf{C}_s)$-orbit is homospheric, it is incapable of accomodating any chiral ligand. As a result, such a packing as Fig. 4(b) is forbidden in the light of chirality fittingness listed in Table 2. This point will be discussed later in detail.

The ligand set $A^2p\bar{p}$ generates another derivative **10** belonging to $\mathbf{C}_1$-symmetry, where four hemispheric $\mathbf{C}_1(/\mathbf{C}_1)$-orbits are involved (Fig. 4). In this case, two types of Young's tableaus apparently take similar modes of packing, as found in Figs. 4(c) and (d).

The third example is an allene derivative **11** of formula ABp_2, which belongs to $\mathbf{C}_1$-symmetry. Each of the hemispheric $\mathbf{C}_1(/\mathbf{C}_1)$-orbits accommodates a ligand according to a

Young's tableau (S) of Fig. 5(a). The two chiral ligands (p) are nonequivalent so that they are involved in distinct one-membered $\mathbf{C}_1(/\mathbf{C}_1)$-orbits.

Under the permutation group $\mathbf{S}_3^{[4]}$ ($\subset \mathbf{S}_9^{[4]}$), the mode of accommodation is represented by a Young's tableau of permutation (P), as shown in Fig. 5(b). Thus, the two chiral ligands (p) become equivalent by disregarding chirality fittingness. It should be emphasized that the Young's tableau (P) of Fig. 5(b) does not agree with the stereochemical nonequivalency between the two chiral ligands (p).

The ligands set ABp^2 generates derivatives **12** and **13** belonging to $\mathbf{C}_1$-symmetry, where four hemispheric $\mathbf{C}_1(/\mathbf{C}_1)$-orbits are involved (Fig. 5). On the other hand, these derivatives belong to $\mathbf{S}_1^{[4]}$ within the permutation group $\mathbf{S}_9^{[4]}$. Hence, two types of Young's tableaus apparently take similar modes of packing, as found in Figs. 5(d) and (f).

3. Combinatorial Enumeration. 3.1 Allene Derivatives under Point-Group Symmetry. For a mathematical formulation of ligands, we consider a set of achiral ligands:

$$L_a = \{\mathrm{A, B, C, D}\} \tag{1}$$

and a set of chiral ligands:

$$L_c = \{\mathrm{p}, \bar{\mathrm{p}}, \mathrm{q}, \bar{\mathrm{q}}, \mathrm{r}, \bar{\mathrm{r}}, \mathrm{s}, \bar{\mathrm{s}},\}, \tag{2}$$

where the symbols with and without an overline represent a pair of enantiomeric ligands. Then, suppose that four ligands selected as a set from these sets are placed on the four positions of an allene skeleton belonging to the point group $\mathbf{D}_{2d}$.

For combinatorial enumeration by considering achiral and chiral ligands, unit subduced cycle indices with chirality fittingness (USCI-CFs)[18,19] listed in the rightmost column of Table 1 are used. The previous enumeration[13] has adopted the SCI method[20] (the generating-function method based on subduced cycle indices (SCIs)) among the four methods of the USCI approach. In the present enumeration, we will use the PCI method[21] (the generating-function method based on partial cycle indices (PCIs)) after the extension taking account of chirality fittingness. By using the data listed in Table 1 and the inverse mark table for $\mathbf{D}_{2d}$ listed in Appendix B.1 of Ref. 14, one can obtain the following partial cycle indices with chirality fittingness (PCI-CFs):

$$\begin{aligned}\mathrm{PCI-CF}(\mathbf{C}_1,\$_d) = {} & \frac{1}{8}b_1^4 - \frac{1}{8}b_2^2 - \frac{1}{4}b_2^2 - \frac{1}{4}a_1^2c_2 \\ & + \frac{1}{4}a_2^2 + \frac{1}{4}b_4\end{aligned} \tag{3}$$

$$\mathrm{PCI-CF}(\mathbf{C}_2,\$_d) = \frac{1}{4}b_2^2 - \frac{1}{4}c_4 - \frac{1}{4}a_2^2 - \frac{1}{4}b_4 + \frac{1}{2}a_4 \tag{4}$$

$$\mathrm{PCI-CF}(\mathbf{C}_2{}',\$_d) = \frac{1}{2}b_2^2 - \frac{1}{2}b_4 \tag{5}$$

$$\mathrm{PCI-CF}(\mathbf{C}_s,\$_d) = \frac{1}{2}a_1^2c_2 - \frac{1}{2}a_2^2 \tag{6}$$

$$\mathrm{PCI-CF}(\mathbf{S}_4,\$_d) = \frac{1}{2}c_4 - \frac{1}{2}a_4 \tag{7}$$

$$\mathrm{PCI-CF}(\mathbf{C}_{2v},\$_d) = \frac{1}{2}a_2^2 - \frac{1}{2}a_4 \tag{8}$$

$$\mathrm{PCI-CF}(\mathbf{D}_2,\$_d) = \frac{1}{2}b_4 - \frac{1}{2}a_4 \tag{9}$$

$$\mathrm{PCI-CF}(\mathbf{D}_{2d},\$_d) = a_4 \tag{10}$$

where the symbol $\$_d$ represents a set of a_d, b_d, and c_d. For example, PCI-CF($\mathbf{C}_1$, $\$_d$) (Eq. 3) is obtained when the row vector (taken from the inverse mark table),

$$(\frac{1}{8},-\frac{1}{8},-\frac{1}{4},-\frac{1}{4},0,\frac{1}{4},\frac{1}{4},0),$$

is multiplied by the hypothetical column vector (taken from Table 1),

$$(b_1^4,\ b_2^2,\ b_2^2,\ a_1^2c_2,\ c_4,\ a_2^2,\ b_4,\ a_4).$$

According to the three kinds of dummy variables (a_d corresponds to a homospheric orbit, b_d to a hemispheric orbit, and each c_d to an enantiospheric orbit), we use three kinds of ligand inventories as follows:

$$a_d = A^d + B^d + C^d + D^d \tag{11}$$

$$\begin{aligned}b_d = {} & A^d + B^d + C^d + D^d + p^d + \bar{p}^d + q^d + \bar{q}^d \\ & + r^d + \bar{r}^d + s^d + \bar{s}^d\end{aligned} \tag{12}$$

$$\begin{aligned}c_d = {} & A^d + B^d + C^d + D^d + 2p^{d/2}\bar{p}^{d/2} + 2q^{d/2}\bar{q}^{d/2} \\ & + 2r^{d/2}\bar{r}^{d/2} + 2s^{d/2}\bar{s}^{d/2}.\end{aligned} \tag{13}$$

The dummy variable a_d corresponds to a homospheric orbit, which accommodates achiral ligands only (Table 2). This mode of accommodation is represented by Eq. 11. Since a hemispheric orbit equally accommodates achiral and chiral ligands (Table 2), the corresponding dummy variable b_d exhibits the mode of accommodation represented by Eq. 12. Equation 13 shows a compensated chiral packing of the corresponding enantiospheric orbit (Table 2). After these inventories are introduced to the PCI-CFs (3 to 10), the resulting equations are expanded to give generating functions for respective subgroups. The following results are selected examples of such generating functions:

$$\begin{aligned}f_{\mathbf{C}_2} = {} & [\frac{1}{2}(A^2p^2 + A^2\bar{p}^2) + \frac{1}{2}(A^2q^2 + A^2\bar{q}^2) + \cdots] + \\ & + [\frac{1}{2}(p^2q^2 + \bar{p}^2\bar{q}^2) + \frac{1}{2}(p^2r^2 + \bar{p}^2\bar{r}^2) + \cdots]\end{aligned} \tag{14}$$

$$\begin{aligned}f_{\mathbf{C}_s} = {} & (A^3B + A^3C + \cdots) + (A^2BC + A^2BD + \cdots) + \\ & + (A^2p\bar{p} + A^2q\bar{q} + \cdots) + (2ABp\bar{p} + 2ABq\bar{q} + \cdots)\end{aligned} \tag{15}$$

A pair of enantiomers is counted in as a coefficient of a term such as $(1/2)(A^2p^2 + A^2\bar{p}^2)$. On the same line, the term *ABCD* is used to designate a pair of enantiomers in place of (1/2)-[*ABCD*(right) + *ABCD*(left)]. A so-called meso-compound is counted in the form of a term such as $A^2p\bar{p}$.

The coefficients of Eqs. 14 and 15 are collected in the $\mathbf{C}_2$-

Table 3. Number of (Pro)molecules Derived from an Allene Skeleton (Part I)

Proligand partition		Number of (pro)molecules							
	S	$\mathbf{C}_1$	$\mathbf{C}_2$	$\mathbf{C}'_2$	$\mathbf{C}_s$	$\mathbf{S}_4$	$\mathbf{C}_{2v}$	$\mathbf{D}_2$	$\mathbf{D}_{2d}$
	P	$\mathbf{S}_1^{[4]}$	$\mathbf{S}_2^{[4]}$	$\mathbf{S}_{2'}^{[4]}$	$\mathbf{S}_3^{[4]}$	$\mathbf{S}_5^{[4]}$	$\mathbf{S}_7^{[4]}$	$\mathbf{S}_6^{[4]}$	$\mathbf{S}_9^{[4]}$
A^4	S	0	0	0	0	0	0	0	1
	(P)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)
A^3B	S	0	0	0	1	0	0	0	0
	(P)	(0)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
A^3p	S	1	0	0	0	0	0	0	0
	(P)	(0)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
A^2B^2	S	0	0	1	0	0	1	0	0
	(P)	(0)	(0)	(1)	(0)	(0)	(1)	(0)	(0)
A^2BC	S	1	0	0	1	0	0	0	0
	(P)	(1)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
A^2Bp	S	3	0	0	0	0	0	0	0
	(P)	(1)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
A^2p^2	S	0	1	2	0	0	0	0	0
	(P)	(0)	(0)	(1)	(0)	(0)	(1)	(0)	(0)
$A^2p\bar{p}$	S	1	0	0	1	0	0	0	0
	(P)	(1)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
A^2pq	S	3	0	0	0	0	0	0	0
	(P)	(1)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
ABCD	S	3	0	0	0	0	0	0	0
	(P)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
ABCp	S	6	0	0	0	0	0	0	0
	(P)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
ABp^2	S	3	0	0	0	0	0	0	0
	(P)	(1)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
$ABp\bar{p}$	S	2	0	0	2*	0	0	0	0
	(P)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
ABpq	S	6	0	0	0	0	0	0	0
	(P)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

*The value listed in our book (Table 21.3)[14] should be corrected.

and $\mathbf{C}_s$-columns of Tables 3 and 4 (the “S”-row of each ligand partition). In Eqs. 14 and 15, terms in each pair of brackets represent derivatives of the same type. Hence, an appropriate term is selected as a representative from each pair of brackets to make Tables 3 and 4 (e.g. A^2p^2 and p^2q^2 for Eq. 14; and A^3B, A^2BC, $A^2p\bar{p}$, and $ABp\bar{p}$ for Eq. 15). Results for other subgroups are obtained similarly and are collected also in Tables 3 and 4. The present results based on the PCI method are identical with those based on the SCI method reported previously.[13]

3.2 Allene Derivatives under Permutation-Group Symmetry. Let us next consider the violation of chirality fittingness when a set of four ligands selected from L_a (Eq. 1) and L_b (Eq. 2) is placed on the four positions of an allene skeleton. This treatment takes no account of such specific modes as a compensating chiral packing. By placing $s_d = a_d = b_d = c_d$ in PCI-CFs (Eqs. 3 to 10), we obtain the corresponding PCIs without chirality fittingness:

$$\mathrm{PCI}(\mathbf{S}_1^{[4]},\$_d) = \frac{1}{8}s_1^4 - \frac{1}{8}s_2^2 - \frac{1}{4}s_1^2 s_2 + \frac{1}{4}s_4 \tag{16}$$

$$\mathrm{PCI}(\mathbf{S}_2^{[4]},\$_d) = 0 \tag{17}$$

$$\mathrm{PCI}(\mathbf{S}_{2'}^{[4]},\$_d) = \frac{1}{2}s_2^2 - \frac{1}{2}s_4 \tag{18}$$

$$\mathrm{PCI}(\mathbf{S}_3^{[4]},\$_d) = \frac{1}{2}s_1^2 s_2 - \frac{1}{2}s_2^2 \tag{19}$$

$$\mathrm{PCI}(\mathbf{S}_5^{[4]},\$_d) = 0 \tag{20}$$

$$\mathrm{PCI}(\mathbf{S}_7^{[4]},\$_d) = \frac{1}{2}s_2^2 - \frac{1}{2}s_4 \tag{21}$$

$$\mathrm{PCI}(\mathbf{S}_6^{[4]},\$_d) = 0 \tag{22}$$

$$\mathrm{PCI}(\mathbf{S}_9^{[4]},\$_d) = s_4, \tag{23}$$

As a result, we find several PCIs of zero value: PCI($\mathbf{S}_2^{[4]}$, s_d), PCI($\mathbf{S}_5^{[4]}$, s_d), and PCI($\mathbf{S}_6^{[4]}$, s_d). This means that there exist no molecules of these permutation symmetries.

According to the violation of chirality fittingness, we use the following ligand inventory for the enumeration of permutation isomers.

$$\begin{aligned} s_d = {} & A^d + B^d + C^d + D^d + p^d + \bar{p}^d + q^d + \bar{q}^d \\ & + r^d + \bar{r}^d + s^d + \bar{s}^d. \end{aligned} \tag{24}$$

The inventory (Eq. 24) is introduced into the PCI (Eqs. 16 to 23) and the resulting equations are expanded to give generating functions for respective subgroups. The coefficients of the generating functions are listed also in Tables 3 and 4 (the “P”-

Table 4. Number of (Pro)molecules Derived from an Allene Skeleton (Part II)

Proligand partition		Number of (pro)molecules							
	S	$\mathbf{C}_1$	$\mathbf{C}_2$	$\mathbf{C}'_2$	$\mathbf{C}_s$	$\mathbf{S}_4$	$\mathbf{C}_{2v}$	$\mathbf{D}_2$	$\mathbf{D}_{2d}$
	P	$\mathbf{S}_1^{[4]}$	$\mathbf{S}_2^{[4]}$	$\mathbf{S}_{2'}^{[4]}$	$\mathbf{S}_3^{[4]}$	$\mathbf{S}_5^{[4]}$	$\mathbf{S}_7^{[4]}$	$\mathbf{S}_6^{[4]}$	$\mathbf{S}_9^{[4]}$
Ap^3	S	1	0	0	0	0	0	0	0
	(P)	(0)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
$Ap^2\bar{p}$	S	3	0	0	0	0	0	0	0
	(P)	(1)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
Ap^2q	S	3	0	0	0	0	0	0	0
	(P)	(1)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
$Ap\bar{p}r$	S	6	0	0	0	0	0	0	0
	(P)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Apqr	S	6	0	0	0	0	0	0	0
	(P)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
p^4	S	0	0	0	0	0	0	1	0
	(P)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(1)
$p^3\bar{p}$	S	1	0	0	0	0	0	0	0
	(P)	(0)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
p^3q	S	1	0	0	0	0	0	0	0
	(P)	(0)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
$p^2\bar{p}^2$	S	0	0	1	0	1	0	0	0
	(P)	(0)	(0)	(1)	(0)	(0)	(1)	(0)	(0)
$p^2\bar{p}q$	S	3	0	0	0	0	0	0	0
	(P)	(1)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
p^2q^2	S	0	1	2	0	0	0	0	0
	(P)	(0)	(0)	(1)	(0)	(0)	(1)	(0)	(0)
$p^2q\bar{q}$	S	3	0	0	0	0	0	0	0
	(P)	(1)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
p^2qr	S	3	0	0	0	0	0	0	0
	(P)	(1)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
$p\bar{p}q\bar{q}$	S	3	0	0	0	0	0	0	0
	(P)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
$p\bar{p}qr$	S	6	0	0	0	0	0	0	0
	(P)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
pqrs	S	6	0	0	0	0	0	0	0
	(P)	(3)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

row of each ligand partition).

Discussion

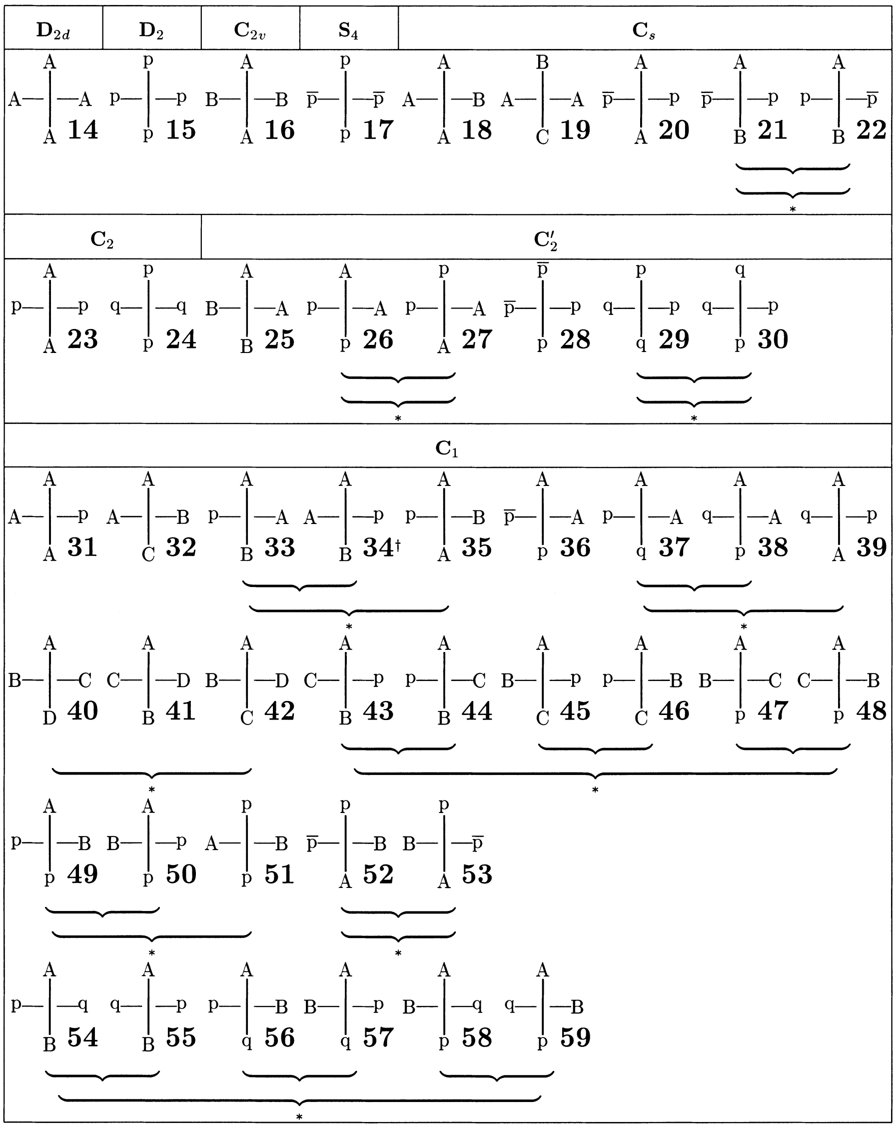
1. Allene Derivatives Enumerated. The data listed in Tables 3 and 4 are itemized from three points of view: partitions, point-group symmetries, and permutation-group symmetries. Thus, the row (S) of each partition gives the numbers of enantiomer pairs for respective point groups. The row (P) of each partition gives the numbers of diastereomer sets for respective point groups.

According to the data in Tables 3 and 4, we can depict all of the allene derivatives, which are classified by their point-group symmetries, as shown in Figs. 6 and 7. To construct these figures, we adopt a criterion in which an arbitrary enantiomer is depicted as a representative, if a derivative is chiral. Each derivative listed in Figs. 6 and 7 is counted as one isomer under point-group symmetries (the rows (S) of Tables 3 and 4). Figures 6 and 7 also include the information on the enumerations under permutation-group symmetries (rows (P) in Tables 3 and 4). Two or more derivatives that are diastereomeric are tied with an underbrace having no asterisk. They are counted as one isomer under permutation-group symmetries. On the other hand, two or more derivatives corresponding to the same ligand set are tied with an underbrace marked with an asterisk, where these derivatives are constitutionally isomeric or diastereomeric from a stereochemical point of view.

Each independent formula (without an underbrace) corresponds to an achiral derivative or to a representative for a pair of enantiomers, where it has no diastereomers. However, consitutional isomers are not always linked with an underbrace, if they are placed separately because of their point groups (e.g., **16** and **25** for the partition A^2B^2; **23**, **26**, and **27** for the partition A^2p^2).

In order to show the methodology adopted here, it is worthy to mention the results of the partition ABCq listed in Table 3 as one of the most extreme cases, where the row (S) represents six $\mathbf{C}_1$-isomers, while the row (P) indicates three $\mathbf{S}_1^{[4]}$-isomers. The six $\mathbf{C}_1$-isomers are found to be **43** to **48**, as depicted in Fig. 6. They are classified into three pair of diastereomers, i.e. {**43**, **44**}, {**45**, **46**}, and {**47**, **48**}, which correspond to the three $\mathbf{S}_1^{[4]}$-isomers. Obviously, the three $\mathbf{S}_1^{[4]}$-isomers (pairs) are constitutionally isomeric. Note that these six derivatives accompany the respecitive enantiomeric isomers ($ABC\bar{p}$).

The partition $ABp\bar{p}$ is also illustrative as a special case, in



† The formula (**66**) listed in our book (Fig. 21.5)[14] should be corrected.

Fig. 6. Derivatives of allene (Part I).

which a pair of enantiomeric ligands (p and $\bar{\mathrm{p}}$) are involved. Table 3 shows that the partition $\mathrm{ABp\bar{p}}$(S) corresponds to two $\mathbf{C}_s$-isomers and two $\mathbf{C}_1$-isomers. As shown in Fig. 6, the two $\mathbf{C}_s$-isomers (**21** and **22**) are diastereomeric, and distinctly the two $\mathbf{C}_1$-isomers (**52** and **53**) are diastereomeric.

The row (P) of the partition $\mathrm{ABp\bar{p}}$ indicates the presence of three $\mathrm{S}_1^{[4]}$-isomers, which can be determined to be the following three pairs: {**21** and **22**}, {**52** and **53**}, and {$\overline{\mathbf{52}}$, $\overline{\mathbf{53}}$}. It should be noted that the third pair ({$\overline{\mathbf{52}}$, $\overline{\mathbf{53}}$}) is hidden as the enantiomeric pair of the second one ({**52** and **53**}), according to the criterion adopted in listing these derivatives.

The following sections will extend such discussions as described above by comparing the two types of combinatorial enumerations.

2. Chirality Relevant to Enantioisomerism. The sphericity concept (Table 2) has been mainly used to characterize stereochemistry, i.e. relationships in a molecule.[14] We have recently reported that the sphericity concept is also applicable to the characterization of stereoisomerism (especially, enantioisomerism) based on a tetrahedral model, i.e. relationship among tetrahedral molecules.[17] Its application to stereoisomerism among allene derivatives provides us with a deeper and more general insight into phenomena concerned with stereoisomerism.

2.1 Chiral Molecules and Enantiosphericity for Stereoisomerism. Let us consider a molecule having a ligand set ABp^2 (**51**). When the point group $\mathbf{D}_{2d}$ acts on **51a** (the top row of Fig. 8), its four proper rotations generate four homomers of formula ABp^2 (**51a**, **51b**, **51c**, and **51d**) and its four improper rotations generate four enantiomers of formula $\mathrm{AB\bar{p}}^2$ ($\overline{\mathbf{51}}$**a**, $\overline{\mathbf{51}}$**b**, $\overline{\mathbf{51}}$**c**, and $\overline{\mathbf{51}}$**d**). Since such an operation as $\sigma_{d(1)}$ shown in Fig. 8 is an improper rotation, the corresponding permutation is accompanied by the configuration inversion of each ligand. To show this effect explicitly, the permutaion is overlined, e.g. $\overline{(1)(2\ 3)(4)}$ and the numbering of ligands in each formula is also overlined, e.g. $\bar{1}$. If such a ligand is achiral and structure-

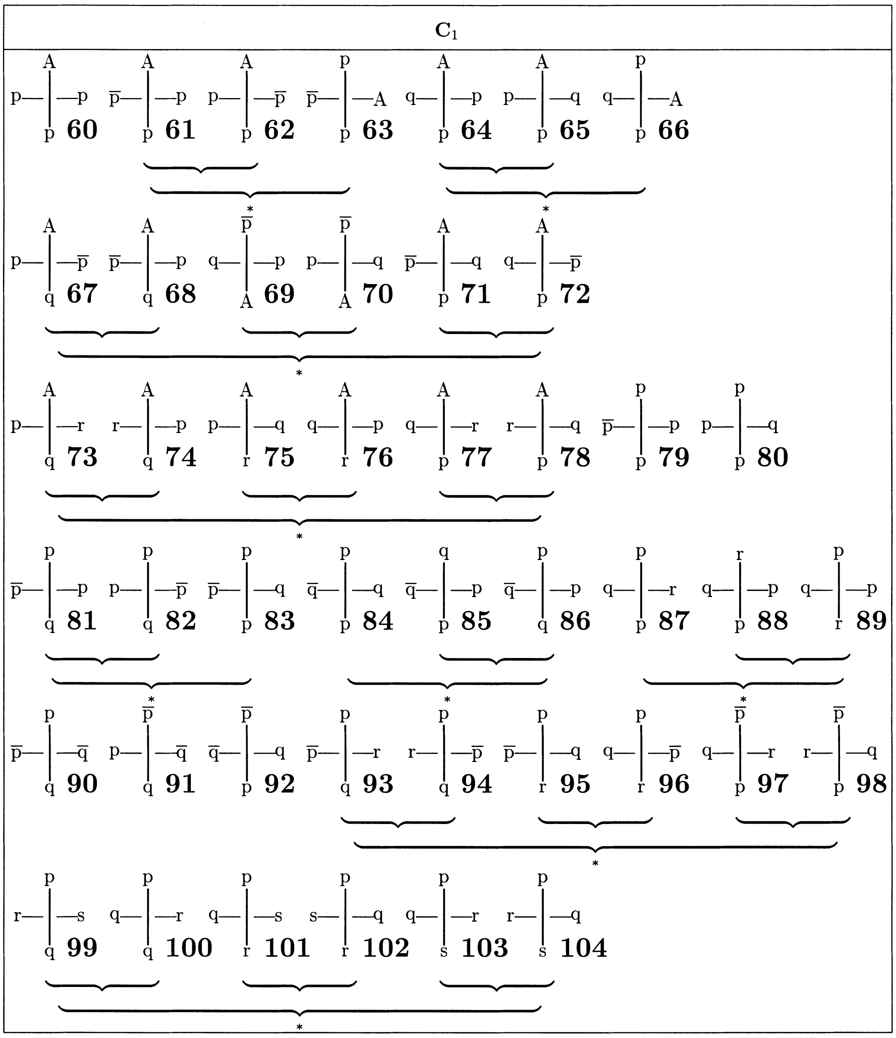


Fig. 7. Derivatives of allene (Part II).

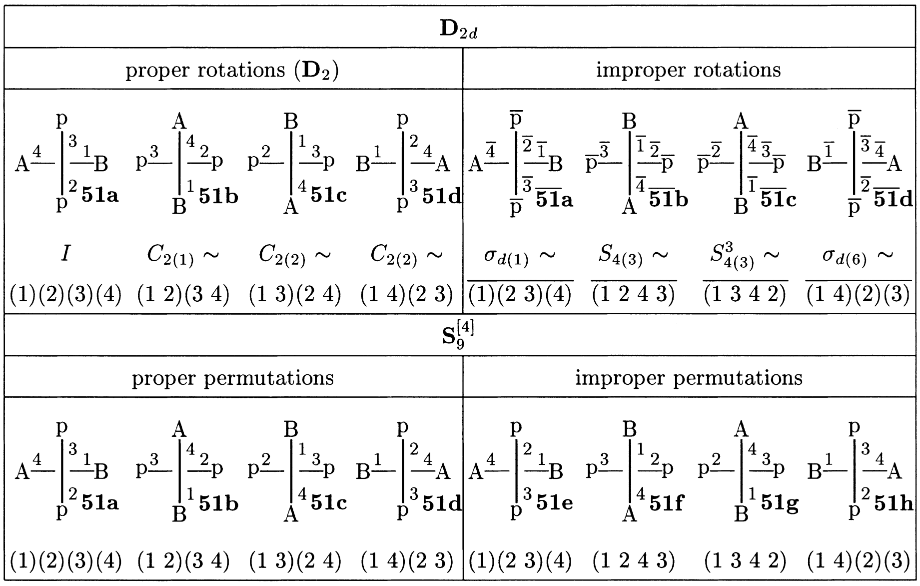


Fig. 8. Isomer equivalence for ABp^2 of $\mathbf{C}_1$-symmetry under $\mathbf{D}_{2d}$ and $\mathbf{S}_9^{[4]}$.

less, the effect of such improper rotation is hidden, so that an achiral ligand (e.g., A) is regarded as being equal to its enanti-

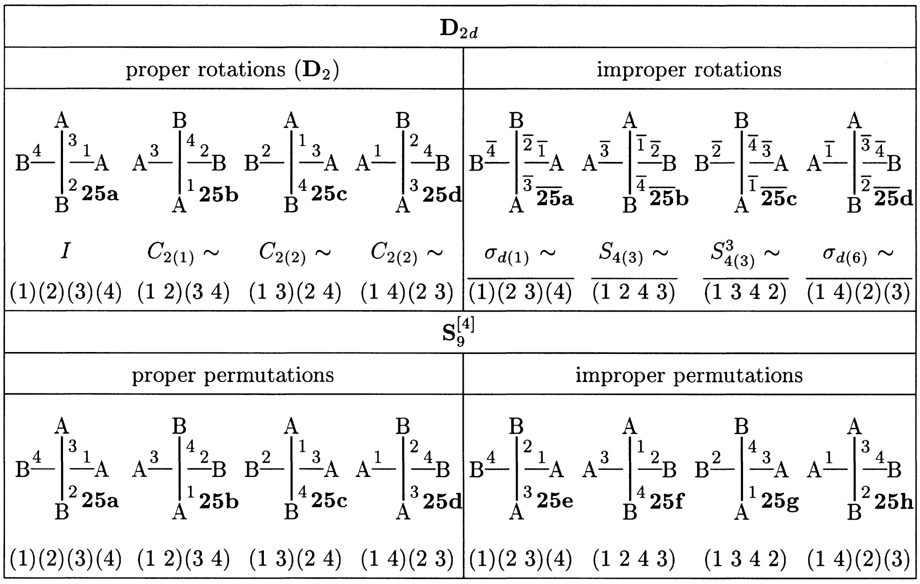


Fig. 9. Isomer equivalence for A^2B^2 of $\mathbf{C}'_2$-symmetry under $\mathbf{D}_{2d}$ and $\mathbf{S}^{[4]}_9$.

omeric ligand (e.g., $\bar{A}$). It follows that the set of the homomers (**51a** to **51d**) and the enantiomers ($\overline{\mathbf{51a}}$ to $\overline{\mathbf{51d}}$) constructs an eight-membered orbit of stereoisomers under the action of $\mathbf{D}_{2d}$, where the symmetry of the molecule (**51**) is regarded to be $\mathbf{C}_1$. Thereby, the orbit is assigned to a coset representation $\mathbf{D}_{2d}(/\mathbf{C}_1)$, the size of which is calculated to be $|\mathbf{D}_{2d}|/|\mathbf{C}_1| = 8$.

The accomodation mode of the $\mathbf{D}_{2d}(/\mathbf{C}_1)$-orbit with ABp^2-homomers and the $AB\bar{p}^2$-homomers is a compensated chiral packing for stereoisomers, which is mathematically parallel to a compensated chiral packing for ligands or proligands (Table 2). Because the $\mathbf{D}_{2d}(/\mathbf{C}_1)$-orbit is enantiospheric (Table 2), one half of the orbit is capable of accomodating the four homomers (**51a** to **51d**) and the other half is capable of accomodating the same number of the corresponding enantiomers ($\overline{\mathbf{51a}}$ to $\overline{\mathbf{51d}}$). The local symmetry $\mathbf{C}_1$ corresponds to the point-group symmetry of the molecule. Hence, the isomer symmetry $\mathbf{C}_1$ is regarded as a local symmetry in stereoisomerism, which is now formulated by virtue of such a set of eight stereomers generated on the action of $\mathbf{D}_{2d}$.

It should be noted that each homomer (**51a** to **51d**) is equivalent to each enantiomer ($\overline{\mathbf{51a}}$ to $\overline{\mathbf{51d}}$) under the action of $\mathbf{D}_{2d}$. Hence, the formula **51** in Fig. 6 is selected arbitrarily as a representative of the set of the homomers and its enantiomers.

The top row of Fig. 9 shows the action of the point group $\mathbf{D}_{2d}$ on a chiral molecule having a ligand set A^2B^2 (**25**). The four proper rotations generate four homomers (**25a**, **25b**, **25c**, and **25d**) while the four improper rotations generate four enantiomers ($\overline{\mathbf{25a}}$, $\overline{\mathbf{25b}}$, $\overline{\mathbf{25c}}$, and $\overline{\mathbf{25d}}$). The set of the homomers (**25a** to **25d**) and the enantiomers ($\overline{\mathbf{25a}}$ to $\overline{\mathbf{25d}}$) can be divided into four pairs, i.e., {**25a**, **25c**}, {**25b**, **25d**}, {$\overline{\mathbf{25a}}$, $\overline{\mathbf{25c}}$}, and {$\overline{\mathbf{25b}}$, $\overline{\mathbf{25d}}$}, where each pair contains identical molecules. These pairs construct a four-membered orbit of stereoisomers under the action of $\mathbf{D}_{2d}$. Since the symmetry of the molecule (**25**) is determined to be $\mathbf{C}'_2$, the orbit is assigned to a coset representation $\mathbf{D}_{2d}(/\mathbf{C}'_2)$, the size of which is calculated to be $|\mathbf{D}_{2d}|/|\mathbf{C}'_2| = 8/2 = 4$.

The accomodation mode of the $\mathbf{D}_{2d}(/\mathbf{C}'_2)$-orbit is a compensated chiral packing for stereoisomers. According to the enantiosphericity of the $\mathbf{D}_{2d}(/\mathbf{C}'_2)$-orbit (Table 2), one half of the orbit is capable of accomodating the two homomer pairs ({**25a**, **25c**} and {**25b**, **25d**}) and the other half is capable of accomodating the same number of the corresponding enantiomeric pairs ({$\overline{\mathbf{25a}}$, $\overline{\mathbf{25c}}$} and {$\overline{\mathbf{25b}}$, $\overline{\mathbf{25d}}$}). The $\mathbf{C}'_2$-symmetry, which is regarded as a local symmetry in stereoisomerism, corresponds to the point-group symmetry of the molecule.

In general, the homomers of a chiral molecule derived from an achiral skeleton, as well as its enantiomers construct an orbit of stereoisomers, which is governed by a coset representation (CR) based on the point group of the skeleton. The local symmetry of the CR determines the symmetry of the chiral molecule. The chiral local symmetry indicates that the orbit of stereoisomers is enantiospheric.

2.2 Achiral Molecules and Homosphericity for Stereoisomerism. Let us consider a molecule having a ligand set $A^2p\bar{p}$ (**20**). When the point group $\mathbf{D}_{2d}$ acts on **20a** (Fig. 10), its four proper rotations generate four homomers (**20a**, **20b**, **20c**, and **20d**) and its four improper rotations also generate four homomers ($\overline{\mathbf{20a}}$, $\overline{\mathbf{20b}}$, $\overline{\mathbf{20c}}$, and $\overline{\mathbf{20d}}$). Note that there appear pairs of identical derivatives, i.e., **20a** and $\overline{\mathbf{20d}}$; **20b** and $\overline{\mathbf{20b}}$; **20c** and $\overline{\mathbf{20c}}$; and **20d** and $\overline{\mathbf{20a}}$. Mathematically speaking, the action of $\mathbf{C}_s(=\{I, \sigma_{d(6)}\})$ fixes **20** to produce **20a** and $\overline{\mathbf{20d}}$. It follows that the set of the homomers (**20a** to **20d**) constructs a four-membered orbit of stereoisomers. The orbit is assigned to a coset representation $\mathbf{D}_{2d}(/\mathbf{C}_s)$, the local symmmetry of which shows that the molecule having a ligand set $A^2p\bar{p}$ (**20**) belongs to $\mathbf{C}_s$-symmetry.

When the point group $\mathbf{D}_{2d}$ acts on **21a** (Fig. 11), its four proper rotations generate a set of four homomers (**21a**, **21b**, **21c**, and **21d**) and its four improper rotations generate another set of four homomers ($\overline{\mathbf{21a}}$, $\overline{\mathbf{21b}}$, $\overline{\mathbf{21c}}$, and $\overline{\mathbf{21d}}$). They are divided into four sets of the same formula (**21a** and $\overline{\mathbf{21d}}$; **21b** and $\overline{\mathbf{21b}}$; **21c** and $\overline{\mathbf{21c}}$; and **21d** and $\overline{\mathbf{21a}}$), which construct a four-membered orbit under the point group $\mathbf{D}_{2d}$. The action of $\mathbf{C}_s(=\{I, \sigma_{d(6)}\})$ fixes **21** to produce **21a** and $\overline{\mathbf{21d}}$. Hence, the point

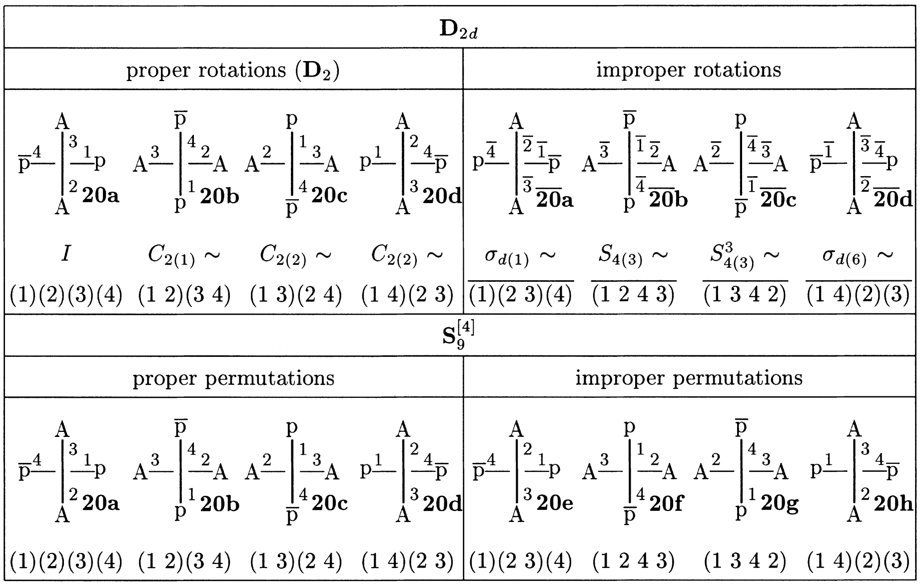


Fig. 10. Isomer equivalence for $A^2p\bar{p}$ of $\mathbf{C}_s$-symmetry under $\mathbf{D}_{2d}$ and $\mathbf{S}_9^{[4]}$.

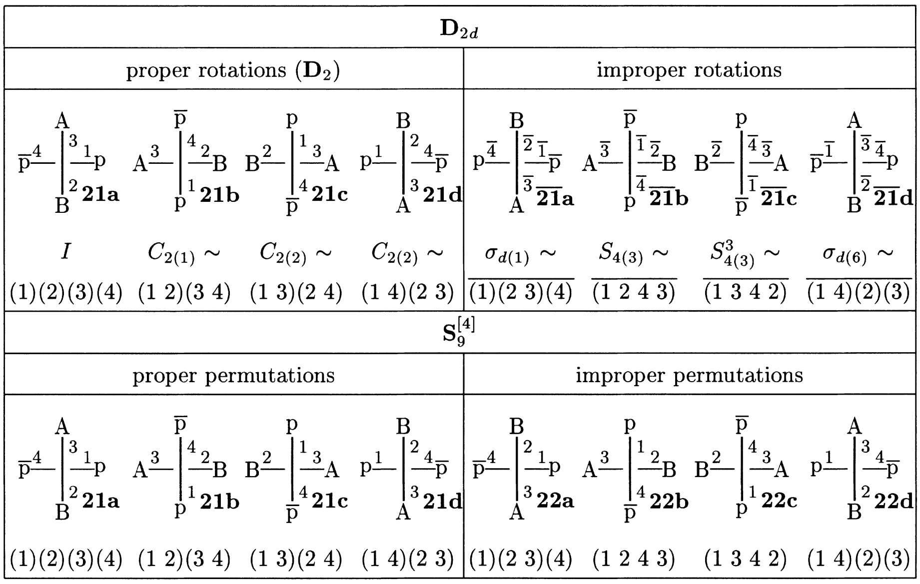


Fig. 11. Isomer equivalence for $ABp\bar{p}$ of $\mathbf{C}_s$-symmetry under $\mathbf{D}_{2d}$ and $\mathbf{S}_9^{[4]}$.

group $\mathbf{C}_s$ is regarded as the local symmetry of the stereoisomerism so that the four-membered orbit containing the homomer pair (**21a** and **21d**) is assigned to a coset representation $\mathbf{D}_{2d}(/\mathbf{C}_s)$.

In general, the homomers of such an achiral molecule construct an orbit of stereoisomers, which is governed by a coset representation (CR) based on the point group of the skeleton. Since the local symmetry of the CR is determined to be an achiral subgroup (i.e. the symmetry of the achiral molecule), the orbit of stereoisomers is homospheric.

3. Stereogenicity Relevant to Diastereoisomerism. To comprehend Young's tableaus of permutation, we here examine permutablity of ligands without taking account of chirality fittingness. The action of the permutation group $\mathbf{S}_9^{[4]}$ on derivatives of an allene skeleton generates equivalence classes (orbits) of permutation symmetry. When such orbits are combined with stereochemical equivalency, we can define the concept of stereogenicity in a stricter fashion. Stereogenic molecules are further classified into enantiostereogenic (or shortly, enantiogenic) and diastereogenic ones.

3.1 Astereogenic Molecules. A molecule is defined as being *astereogenic*, if it is converted into homomeric derivatives under such a permutation symmetry as $\mathbf{S}_9^{[4]}$. The bottom row of Fig. 8 shows the result of the permutation symmetry ($\mathbf{S}_9^{[4]}$), where chirality fittingness is disregarded. For the sake of simplicity, the permutations of $\mathbf{S}_6^{[4]}$ (isomorphic to $\mathbf{D}_2$) are called *proper permutations*, and the remaining ones ($\in \mathbf{S}_9^{[4]} - \mathbf{S}_6^{[4]}$) are called *improper permutations*. When the permutation group $\mathbf{S}_9^{[4]}$ (isomorphic to $\mathbf{D}_{2d}$) acts on **51a**, the proper permutations generate four homomers (**51a**, **51b**, **51c**, and **51d**) and the improper permutations also generate four homomers (**51a**, **51b**, **51c**, and **51d**), as shown in the bottom row of Fig. 8. Hence, the derivative **51** is decided to be an astereogenic molecule. The eight homomers are divided into four sets of homomers (**51a** and **51e**; **51b** and **51g**; **51c** and **51f**; and **51d** and **51h**), which construct a four-membered orbit under the action of $\mathbf{S}_9^{[4]}$. The permutation symmetry of the molecule (**51**) is determined to be $\mathbf{S}_3^{[4]}$ (= {(1)(2)(3)(4), (1)(2 3)(4)}; isomorphic to $\mathbf{C}_s$), since the permutations of the $\mathbf{S}_3^{[4]}$ fix **51** to give the homomer pair (**51a** and **51e**). Hence, the four-membered orbit is assigned to a coset representation $\mathbf{S}_9^{[4]}(/\mathbf{S}_3^{[4]})$, the size of which is calculated to be $|\mathbf{S}_9^{[4]}|/|\mathbf{S}_3^{[4]}| = 8/2 = 4$.

It should be noted that **51** (ABp^2) is converted into its enantiomer $\overline{\mathbf{51}}$ ($AB\bar{p}^2$) on the action of $\mathbf{D}_{2d}$ (the top row of Fig. 8), whereas they are not interconvertible within the permutation group $\mathbf{S}_9^{[4]}$ (the bottom row of Fig. 8). In other words, the permutation group fails to determine the enantiomeric relationship between **51** (ABp^2) and $\overline{\mathbf{51}}$ ($AB\bar{p}^2$). The relationship between **51** (ABp^2) and $\overline{\mathbf{51}}$ ($AB\bar{p}^2$) is here called *ligand-based enantiomeric*.[17] The derivative **20** is also astereogenic, as shown in the bottom row of Fig. 10. When the permutation group $\mathbf{S}_9^{[4]}$ (isomorphic to $\mathbf{D}_{2d}$) acts on **20a**, the resulting derivatives are all homomeric to the original derivative **20a**.

3.2 Stereogenic Molecules. A molecule is defined as being *stereogenic*, if it is converted into homomeric derivatives and other stereoisomeric derivatives under a permutation group such as $\mathbf{S}_9^{[4]}$. The resulting stereoisomeric derivatives may be enantiomers or diastereomers from a stereochemical point of view. Strictly speaking, the term "stereogenic" is concerned only with diastereomers and by no means with enantiomers from a permutational point of view, even if a diastereomeric relationship and an enantiomeric relationship occasionally overlap. However, it is convenient to classify stereogenic molecules by considering whether diastereomeric and enantiomeric relationships overlap or not. Thus, if a molecule is converted into its enantiomer under a permutation-group symmetry, it is defined as being *enantiostereogenic* (or shortly, enantiogenic); otherwise, it is defined as being *diastereogenic*.

Enantiostereogenic Molecules— The bottom row of Fig. 9 shows the action of the group $\mathbf{S}_9^{[4]}$ on a chiral molecule having a ligand set A^2B^2 (**25**). The four proper permutations generate four homomers (**25a**, **25b**, **25c**, and **25d**) while the four improper permutations generate four enantiomers (**25e**, **25f**, **25g**, and **25h**). Hence, the set of the homomers (**25a** to **25d**) and the enantiomers (**25e** to **25h**) constructs an eight-membered orbit of stereoisomers under the action of $\mathbf{S}_9^{[4]}$. The derivative **25** is enantiostereogenic, where the enantiomers (**25a** and **25e**) are interconvertible within $\mathbf{D}_{2d}$ and within $\mathbf{S}_9^{[4]}$. The relationship between **25a** and **25e** is here called *skeleton-based enantiomeric*.[17] Since the symmetry of the molecule (**25**) is determined to be $\mathbf{S}_2^{[4]}$, the orbit is assigned to a coset representation $\mathbf{S}_9^{[4]}(/\mathbf{S}_2^{[4]})$, the size of which is calculated to be $|\mathbf{S}_9^{[4]}|/|\mathbf{S}_2^{[4]}| = 8/2 = 4$.

The permutability due to $\mathbf{S}_9^{[4]}$ in this case is akin to the action of $\mathbf{D}_{2d}$ depicted in the top row of Fig. 9 because all the participating ligands are achiral. However, it should be noted that the set of **25e** etc. for $\mathbf{S}_9^{[4]}$ is conceptually different from the set of $\overline{\mathbf{25a}}$ for $\mathbf{D}_{2d}$, if the achiral ligands have hidden internal structure.

From the derivatives listed in Figs. 6 and 7, we can select the following derivatives as being enantiostereogenic: **25**, **28**, **32**, **36**, **40**, **41**, and **42** (Fig. 6); and **90**, **91**, and **92** (Fig. 7). Note that they are not tied with an underbrace and that the remaining derivatives without an underbrace listed in Figs. 6 and 7 are astereogenic.

We should here mention skeleton-based enantiomers (chiral/enantiostereogenic) by comparing with ligand-based enantiomers (chiral/astereogenic or chiral/diastereogenic).[17] For example, the two skeleton-based enantiomers for **25** (A^2B^2) are convertible within $\mathbf{D}_{2d}$ as well as within $\mathbf{S}_9^{[4]}$, as shown in Fig. 9. On the other hand, **51a** (ABp^2) and $\overline{\mathbf{51a}}$ ($AB\bar{p}^2$) shown in the top row of Fig. 8 are ligand-based enantiomers, as mentioned above. They are convertible within the point group $\mathbf{D}_{2d}$ but inconvertible within the permutation group $\mathbf{S}_9^{[4]}$.

Diastereogeric Molecules— The bottom row of Fig. 11 shows another action of the permutation symmetry ($\mathbf{S}_9^{[4]}$), where chirality fittingness is disregarded. When the permutation group $\mathbf{S}_9^{[4]}$ (isomorphic to $\mathbf{D}_{2d}$) acts on **21a**, the proper permutations (i.e., the operations of $\mathbf{S}_6^{[4]}$ isomorphic to $\mathbf{D}_2$) generate four homomers (**21a**, **21b**, **21c**, and **21d**) and the improper permutations generate four diastereomers (**22a**, **22b**, **22c**, and **22d**), as shown in the bottom row of Fig. 11. This means that **21** and **22** are equivalent to each other under the permutation group $\mathbf{S}_9^{[4]}$. The parallel discussion can show that **22** can be converted into **21** on the action of the permutation group $\mathbf{S}_9^{[4]}$. Such derivatives as **21** and **22** are here called *skeleton-based diastereomeric molecules*.

Each pair of derivatives tied with an underbrace (with no asterisk) in Figs. 6 and 7 is permutable on the action of the permutation group $\mathbf{S}_9^{[4]}$. As a result, the pair is a pair of diastereogenic molecules. For example, we can select the following diastereogenic derivatives from the derivatives listed in Fig. 6: **21** and **22**; **26** and **27**; **29** and **30**; **33** and **34**; **37** and **38**; **43** and **44**; **45** and **46**; **47** and **48**; **49** and **50**; **52** and **53**; **54** and **55**; **56** and **57**; and **58** and **59**.

Chirality vs Stereogenicity

1. Stereoisomerism vs Permutability. In this paper, stereoisomerism is correlated to point-group symmetry, while permutability is correlated to permutation-group symmetry. Note that the present usage of the term "stereoisomerism" is narrower than the conventional one. Thereby, the stereoisomerism is concerned with enantiomeric relationships, where the concept of chirality/achirality is one main item to be considered. On the other hand, the permutability is concerned with diastereomeric relationships, where the concept of stereogenic/astereogenic is one main item to be taken into account. Such separate consideration provides us with a deeper insight into stereochemical phenomena, even if enantiomeric relationships and diastereomeric ones overlap occasionally. In this context, we should examine the enumeration results collected in Tables 3 and 4. This discussion provides us with the answer to the question given in Introduction, i.e., whether the relationship determined between **1** and **2** by virtue of the CIP system is enantiomeric or diastereomeric.

To examine the relationship between **1** and **2**, we refer to the results for the partition A^2B^2 listed in Table 3. The A^2B^2-row (S) predicts one $\mathbf{C}'_2$-isomer and one $\mathbf{C}_{2v}$-isomer, while the

A^2B^2-row (P) indicates one $\mathbf{S}_{2'}^{[4]}$-isomer and one $\mathbf{S}_{7}^{[4]}$-isomer. The $\mathbf{C}'_2$-isomer (**25**) is in turn assigned to $\mathbf{S}_{2'}^{[4]}$ so that it is determined to be stereogenic (enantiostereogenic), as shown in Fig. 9. On the other hand, the $\mathbf{C}_{2v}$-isomer is decided to be **16** that corresponds to the $\mathbf{S}_{7}^{[4]}$-isomer. Hence, it is achiral and astereogenic.

From the present point of view, the relationship determined between **1** and **2** (corresponding to the partition A^2B^2) by virtue of the CIP system is concluded to be diastereomeric, where the distereomeric relationship (counted as one $\mathbf{S}_{2'}^{[4]}$-isomer) and the enantiomeric one (counted as one $\mathbf{C}'_2$-isomer) occasionally overlap. The overlapped case is called "enantiostereogenic", as described above.

To examine the relationship between **3** and **4**, we refer to the results for the partition A^2p^2 listed in Table 3. The A^2p^2-row (S) predicts two $\mathbf{C}'_2$-isomer and one $\mathbf{C}_2$-isomer, while the A^2p^2-row (P) indicates one $\mathbf{S}_{2'}^{[4]}$-isomer and one $\mathbf{S}_{7}^{[4]}$-isomer. The $\mathbf{C}'_2$-isomers (**26** and **27**; also **3** and **4**) is in turn assigned to $\mathbf{S}_{2'}^{[4]}$ so that each of them is determined to be stereogenic (diastereogenic), as shown in Fig. 9. On the other hand, the $\mathbf{C}_2$-isomer is decided to be **23** that corresponds to the $\mathbf{S}_{7}^{[4]}$-isomer, which is chiral but astereogenic.

The ABp^2-row (S) of Table 3 predicts three $\mathbf{C}_1$-isomers, while the ABp^2-row (P) indicates one $\mathbf{S}_{1}^{[4]}$-isomer and one $\mathbf{S}_{3}^{[4]}$-isomer. This apparent difference can be explained by the diastereomeric relationship between **49** and **50** depicted in Fig. 6. Under permutation-group symmetry, **49** and **50** are equivalent so that they are counted once as one $\mathbf{S}_{1}^{[4]}$-isomer, which is characterized as being stereogenic (diastereogenic). On the other hand, **51** is recognized to be astereogenic so as to be counted as one $\mathbf{S}_{3}^{[4]}$-isomer. The diasteromeric pair of **49** and **50** is constitutionally isomeric to the self-diastereomer **51**.

The $A^2p\bar{p}$-row (S) of Table 3 predicts one $\mathbf{C}_1$-isomer and one $\mathbf{C}_s$-isomer, while the $A^2p\bar{p}$-row (P) indicates one $\mathbf{S}_{1}^{[4]}$-isomer and one $\mathbf{S}_{3}^{[4]}$-isomer. The $\mathbf{C}_1/\mathbf{S}_{1}^{[4]}$-isomer (**35**) is stereogenic (enantiostereogenic). The $\mathbf{C}_s/\mathbf{S}_{3}^{[4]}$-isomer (**20**) is astereogenic, as shown in Fig. 10.

The $ABp\bar{p}$-row (S) of Table 3 predicts two $\mathbf{C}_1$-isomers and two $\mathbf{C}_s$-isomers, while the $ABp\bar{p}$-row (P) indicates three $\mathbf{S}_{1}^{[4]}$-isomers. The two $\mathbf{C}_s$-isomers (**21** and **22**) are equivalent under permutation symmetry so as to degenerate into one $\mathbf{S}_{1}^{[4]}$-isomer (a diastereogenic isomer), as shown in the bottom row of Fig. 11. The two $\mathbf{C}_1$-isomers (**52** and **53** in Fig. 6) are equivalent under permutation symmetry so that they are regarded as a single $\mathbf{S}_{1}^{[4]}$-isomer. Their enantiomers ($\overline{\mathbf{52}}$ and $\overline{\mathbf{53}}$) are regarded as another $\mathbf{S}_{1}^{[4]}$-isomer because of their equivalency under permutation symmetry. The existence of three $\mathbf{S}_{1}^{[4]}$-isomers in total is consistent with the enumeration result listed in the $ABp\bar{p}$-row (P) of Table 3. It should be noted that $\overline{\mathbf{52}}$ and $\overline{\mathbf{53}}$ are not depicted in Fig. 6 because of a convention in which an arbitrary enantiomer is depicted as a representative for each pair of such enantiomers.

2. Stereogenicity and the CIP System. From the viewpoint of the present permutation-group symmetry, the CIP system for axial chirality (strictly speaking, axial stereogenicity) is regarded to be based on the numbering of a molecule of $\mathbf{S}_{1}^{[4]}$-symmetry (isomorphic to $\mathbf{C}_1$) or $\mathbf{S}_{2'}^{[4]}$-symmetry (isomorphic to $\mathbf{C}'_2$).

From the data listed in Tables 3 and 4 and in Figs. 6 and 7, the CIP system is concluded to deal with stereogenic derivatives (enantiostereogenic and diastereogenic ones). Each enantiostereogenic derivative corresponds to a pair of enantiomers, while a pair of diastereogenic derivatives corresponds to a pair of diastereomers.

In the case of enantiostereogenic derivatives, "chirality" and "stereogenicity" are apparently parallel to each other. For example, a derivative **25** is determined to be stereogenic, or more precisely to be enantiostereogenic, so that it is capable of possessing the corresponding enantiomer. Hence, it may be permitted to say that the CIP system describes "chirality" in such a special case. As long as chirality fittingness is ignored in the permutation group, however, the CIP system based on the permutablity of ligands does not by any means describe "chirality". Instead, it deals with "stereogenicity" (enantiostereogenicity and diastereogenicity), which has been characterized clearly in the present paper.

A diastereomeric pair of **21** and **22**, both of which are achiral, reinforces the conclusion that the CIP system does not describe "chirality". By the present examination of the permutation group $\mathbf{S}_{9}^{[4]}$, each derivative (**21** or **22**) of the pair is determined to be stereogenic, or more precisely to be diastereogenic, so that it is capable of possessing the corresponding diastereomer.

It should be noted that the terms "enantiostereogenic" and "diastereogenic" are concerned with the attributes of derivatives and that the term "enantiomeric" and "diastereomeric" are concerned with the relationships between derivatives.

Conclusion

Chirality for allene derivatives is formulated as the observance of chirality fittingness under a point-group symmetry $\mathbf{D}_{2d}$. On the other hand, stereogenicity for allene derivatives is formulated as the violation of chirality fittingness, where a permutation symmetry $\mathbf{S}_{9}^{[4]}$, which is isomorphic to a point group $\mathbf{D}_{2d}$, gives equivalence classes (orbits) of the allene derivatives. Two types of Young's tableaus (point-group symmetry and permutation-group symmetry) are applied to the discussion on the stereochemistry and permutability of allene derivatives. Thereby, the concept of chirality/achirality has been compared with the concept of stereogenicity/astereogenicity. The CIP (Cahn–Ingold–Prelog) system is examined in terms of stereogenicity/astereogenicity. A new combination of chirality and stereogenicity described in he present paper provides us with a tool for restructuring stereochemistry.

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