

Integrated discussion on stereogenicity and chirality for restructuring stereochemistry

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To discuss the difference between stereogenicity and chirality, we propose the concept of *RS*-stereoisomeric groups. Beginning with this concept, we have further proposed the concepts of holantimers, stereoisograms, and *RS*-stereogenicity. Thereby, we have clarified that the concept of *RS*-stereogenicity, but not conventional stereogenicity, is closely related to chirality. Thus, five *RS*-stereogenicity types are defined and examined to discuss the difference between stereogenicity and chirality. Combinatorial enumerations have also been studied by considering the *RS*-stereogenicity.

KEY WORDS: stereochemistry, stereogenicity, chirality, diastereomer

AMS subject classification: 05C25

1. Introduction

The concept of stereogenicity has been frequently confused with the concept of chirality. For example, the CIP (Cahn–Ingold–Prelog) system of stereochemical nomenclature (the *RS*-nomenclature) has originally proposed to specify the chirality of molecules, but later revised to specify the stereogenicity [1,2]. Although there appeared a convincing discussion so as to differentiate the stereogenicity from the chirality [3], the difference has not been fully demonstrated even in standard textbooks on stereochemistry [4,5].

Chirality and prochirality have been discussed both theoretically [6] and intuitively [7] so that various concepts obtained by these discussions have been applied to isomer enumerations and classification of symmetries [8]. Recently, we have discussed chirality and stereogenicity in terms of observance/violation of chirality fittingness [9] and in terms of stereoisomeric groups [10]. Although these approaches have revealed several points concerned with the difference between stereogenicity and chirality, a more detailed investigation was felt desirable with respect to a common and integrated standpoint that would enable us to discuss both stereogenicity and chirality.

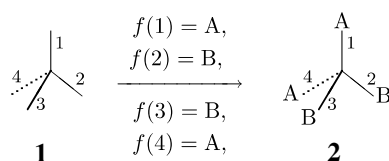


Figure 1. Numbered tetrahedral skeleton and a function generating a molecule of A^2B^2 .

In this article, we propose the concept of *RS*-stereoisomeric groups, which is a subconcept of the stereoisomeric groups proposed in the previous report [10]. The concept of *RS*-stereoisomeric groups generates the concepts of holantimers and stereoisograms. Thereby, the concept of *RS*-stereogenicity is extracted and distinguished from conventional stereogenicity, where it is shown to play an important role to discuss its relevance to chirality.

2. *RS*-Stereoisomeric groups

2.1. Definitions

The four positions of a tetrahedral skeleton of T_d -symmetry are numbered sequentially, as shown in figure 1(left). Throughout the present article, the numbering shown as **1** is selected as a reference, although any numbering can be selected as a reference. The symmetry of the reference skeleton is first taken into consideration.

The symmetry of the four positions is ascribed to the coset representation $T_d(/C_{3v})$ (figure 2) [6, 8].

$$\begin{aligned} \mathbf{G}_Y &= \mathbf{G}_C + \sigma_{d(1)} \mathbf{G}_C \\ &= T_d(/C_{3v}) = \{I, C_{2(1)}, \dots; \sigma_{d(1)}, S_{4(3)}, \dots\}, \end{aligned} \quad (1)$$

where each permutation of \mathbf{G}_Y ($= T_d(/C_{3v})$) is equalized to the corresponding symmetry operation for the sake of simplicity (i.e., $\sigma_{d(1)} = \overline{(1)(2\ 3)(4)}$, etc.) and the core portion of the twelve proper rotations is placed to be $\mathbf{G}_C = \{I, C_{2(1)}, \dots, C_{3(2)}^2\}$. On the other hand, the four positions can be permuted by the permutations belonging to the symmetric group of degree four ($S^{[4]}$).

$$\begin{aligned} \mathbf{G}_X &= S^{[4]} = \mathbf{G}_C + \tilde{\sigma}_{d(1)} \mathbf{G}_C \\ &= \{I, C_{2(1)}, \dots; \tilde{\sigma}_{d(1)}, \tilde{S}_{4(3)}, \dots\}, \end{aligned} \quad (2)$$

where each symbol with a wide tilde (e.g., $\tilde{\sigma}_{d(1)}$ or $\tilde{S}_{4(3)}$) represents the same permutation as the corresponding symbol without a wide tilde (e.g., $\sigma_{d(1)}$ and $S_{4(3)}$) but is not accompanied by the inversion of the ligand chirality.

		$\mathbf{G}_X = \tilde{\mathbf{T}}_d = \mathbf{S}^{[4]}$			
		$\mathbf{G}_C = \tilde{\mathbf{T}} = \mathbf{S}_{10}^{[4]}$		$(1)(2\ 3)(4)\mathbf{S}_{10}^{[4]}$	
{	$\mathbf{G}_C = \mathbf{T}$	$I \sim$	$(1)(2)(3)(4)$	$(1)(2\ 3)(4) \sim$	$\tilde{\sigma}_{d(1)}$
	$C_{2(1)} \sim$	$(1\ 2)(3\ 4)$	$(1\ 2\ 4\ 3) \sim$	$\tilde{S}_{4(3)}$	
	$C_{2(2)} \sim$	$(1\ 3)(2\ 4)$	$(1\ 3\ 4\ 2) \sim$	$\tilde{S}_{4(3)}^3$	
	$C_{2(3)} \sim$	$(1\ 4)(2\ 3)$	$(1\ 4)(2)(3) \sim$	$\tilde{\sigma}_{d(6)}$	
	$C_{3(1)} \sim$	$(1)(2\ 4\ 3)$	$(1)(2)(3\ 4) \sim$	$\tilde{\sigma}_{d(2)}$	
	$C_{3(3)} \sim$	$(1\ 2\ 3)(4)$	$(1\ 2)(3)(4) \sim$	$\tilde{\sigma}_{d(4)}$	
	$C_{3(2)} \sim$	$(1\ 3\ 4)(2)$	$(1\ 3\ 2\ 4) \sim$	$\tilde{S}_{4(1)}$	
	$C_{3(4)} \sim$	$(1\ 4\ 2)(3)$	$(1\ 4\ 2\ 3) \sim$	$\tilde{S}_{4(1)}^3$	
	$C_{3(1)}^2 \sim$	$(1)(2\ 3\ 4)$	$(1)(2\ 4)(3) \sim$	$\tilde{\sigma}_{d(3)}$	
	$C_{3(4)}^2 \sim$	$(1\ 2\ 4)(3)$	$(1\ 2\ 3\ 4) \sim$	$\tilde{S}_{4(2)}^3$	
	$C_{3(3)}^2 \sim$	$(1\ 3\ 2)(4)$	$(1\ 3)(2)(4) \sim$	$\tilde{\sigma}_{d(5)}$	
	$C_{3(2)}^2 \sim$	$(1\ 4\ 3)(2)$	$(1\ 4\ 3\ 2) \sim$	$\tilde{S}_{4(2)}$	
	{	$\mathbf{T}\sigma_{d(1)}$	$\sigma_{d(1)} \sim$	$\overline{(1)(2\ 3)(4)}$	$\overline{(1)(2)(3)(4)} \sim$
$S_{4(3)} \sim$		$\overline{(1\ 2\ 4\ 3)}$	$\overline{(1\ 2)(3\ 4)} \sim$	$\tilde{C}_{2(1)}$	
$S_{4(3)}^3 \sim$		$\overline{(1\ 3\ 4\ 2)}$	$\overline{(1\ 3)(2\ 4)} \sim$	$\tilde{C}_{2(2)}$	
$\sigma_{d(6)} \sim$		$\overline{(1\ 4)(2)(3)}$	$\overline{(1\ 4)(2\ 3)} \sim$	$\tilde{C}_{2(3)}$	
$\sigma_{d(2)} \sim$		$\overline{(1)(2)(3\ 4)}$	$\overline{(1)(2\ 4\ 3)} \sim$	$\tilde{C}_{3(1)}$	
$\sigma_{d(4)} \sim$		$\overline{(1\ 2)(3)(4)}$	$\overline{(1\ 2\ 3)(4)} \sim$	$\tilde{C}_{3(3)}$	
$S_{4(1)} \sim$		$\overline{(1\ 3\ 2\ 4)}$	$\overline{(1\ 3\ 4)(2)} \sim$	$\tilde{C}_{3(2)}$	
$S_{4(1)}^3 \sim$		$\overline{(1\ 4\ 2\ 3)}$	$\overline{(1\ 4\ 2)(3)} \sim$	$\tilde{C}_{3(4)}$	
$\sigma_{d(3)} \sim$		$\overline{(1)(2\ 4)(3)}$	$\overline{(1)(2\ 3\ 4)} \sim$	$\tilde{C}_{3(1)}^2$	
$S_{4(2)}^3 \sim$		$\overline{(1\ 2\ 3\ 4)}$	$\overline{(1\ 2\ 4)(3)} \sim$	$\tilde{C}_{3(4)}^2$	
$\sigma_{d(5)} \sim$		$\overline{(1\ 3)(2)(4)}$	$\overline{(1\ 3\ 2)(4)} \sim$	$\tilde{C}_{3(3)}^2$	
$S_{4(2)} \sim$		$\overline{(1\ 4\ 3\ 2)}$	$\overline{(1\ 4\ 3)(2)} \sim$	$\tilde{C}_{3(2)}^2$	
		$\mathbf{G}_Y = \mathbf{T}_d(/C_{3v})$			

Figure 2. $\mathbf{T}_d(/C_{3v})$ and $\mathbf{S}^{[4]}$.

Although the tetrahedral skeleton is dually subject to these two groups (i.e., the point group \mathbf{T}_d and the symmetric group $\mathbf{S}^{[4]}$), the actions of the two groups are different especially when the positions are occupied by chiral ligands. We have recently revealed that the dual actions can be integrated by considering a stereoisomeric group ($\mathbf{G} = \mathbf{T}_d(/C_{3v})\text{-}\mathbf{S}^{[4]}$) shown in figure 2 [10], where the left

column contains the permutations of the coset representations $\mathbf{T}_d(/C_{3v})$ (surrounded by a vertical box), the upper row contains the permutations of the symmetric group $\mathbf{S}^{[4]}$ (surrounded by a horizontal box), and the permutations of the coset representation corresponding to the proper rotations are contained as a common part ($\mathbf{G}_C = \mathbf{T}$ or $\mathbf{S}_{10}^{[4]}$). The newly appearing part (the bottom-right section of figure 2) comprises the same permutations of the common part (the upper-right section of figure 2) that are characterized by the opposite chiralities. Each symbol of this section (e.g., \tilde{I} or $\tilde{C}_{2(1)}$) represents the same permutation as the common part (e.g., I or $C_{2(1)}$ in \mathbf{T} or $\mathbf{S}_{10}^{[4]}$) but is accompanied by the inversion of the ligand chirality. Note that each number with an overbar represents the conversion of a chiral ligand into the corresponding chiral ligand with the opposite handedness.

In this paper, the stereoisomeric group referred to as $\mathbf{G} = \mathbf{T}_d(/C_{3v})\text{-}\mathbf{S}^{[4]}$ (figure 2) is more specifically called an *RS*-stereoisomeric group, since the stereoisomeric groups defined in the previous paper [10] should be differentiated from the present *RS*-stereoisomeric groups. The prefix *RS* stems from the fact that the *RS*-stereoisomeric group is concerned with right- and left-handedness and is related to the *RS*-nomenclature [1,2]. Note the tetrahedral skeleton ($\mathbf{G} = \mathbf{T}_d(/C_{3v})\text{-}\mathbf{S}^{[4]}$) is a special case in which the *RS*-stereoisomeric group is identical with the stereoisomeric group.

Let us consider a permutation $\tilde{\sigma}_{d(1)} = (1)(2\ 3)(4)$ by stating from $\sigma_{d(1)} = \overline{(1)(2\ 3)(4)}$. Then, the *RS*-stereoisomeric group (\mathbf{G}) is represented as follows:

$$\mathbf{G} = \mathbf{G}_Y + \tilde{\sigma}_{d(1)}\mathbf{G}_Y. \quad (3)$$

The *RS*-stereoisomeric group \mathbf{G} of this case contains normal subgroups represented by \mathbf{G}_Y (equation 1) and \mathbf{G}_X (equation 2). Moreover, the \mathbf{G} contains another normal subgroup represented by

$$\begin{aligned} \mathbf{G}_Z &= \mathbf{G}_C + \tilde{I}\mathbf{G}_C \\ &= \{I, C_{2(1)}, \dots; \tilde{I}, \tilde{C}_{2(1)}, \dots\}, \end{aligned} \quad (4)$$

where we place $\tilde{I} = \overline{(1)(2)(3)(4)}$. In the present article, the group \mathbf{G}_X is called an *RS-permutation group*. The *RS* is attached to differentiate it from usual permutation groups. The group \mathbf{G}_Y is simply called a *point group*, although it is a permutation group (more precisely speaking, a coset representation) to specify discrete objects with handedness of ligands. Note that the term “point groups” is also used to refer to those for continuous objects. The group \mathbf{G}_Z is called an *inversion group*.

In the light of the discussions above, an *RS*-stereoisomeric group can be defined generally by starting a coset representation (\mathbf{G}_Y) of a point group, where \mathbf{G}_Y comprises a maximum chiral part \mathbf{G}_C and the permutations of the remaining improper rotations. When the coset representation is of degree n , a representative of the improper rotations corresponds to a permutation of degree n (σ). Then we

consider a permutation of degree n ($\tilde{\sigma}$) that is the same permutation as σ but is not accompanied by the inversion of the ligand chirality. Thereby, we have an *RS*-stereoisomeric group by the following equation:

$$\mathbf{G} = \mathbf{G}_Y + \tilde{\sigma}\mathbf{G}_Y. \quad (5)$$

The \mathbf{G} contains the following normal subgroups:

$$\mathbf{G}_Y = \mathbf{G}_C + \sigma\mathbf{G}_C, \quad (6)$$

$$\mathbf{G}_X = \mathbf{G}_C + \tilde{\sigma}\mathbf{G}_C, \quad (7)$$

$$\mathbf{G}_Z = \mathbf{G}_C + \tilde{I}\mathbf{G}_C. \quad (8)$$

Of course, \mathbf{G}_C is a normal subgroup of \mathbf{G} . The following relationship is easily obtained:

$$\mathbf{G} = \mathbf{G}_X + \sigma\mathbf{G}_X. \quad (9)$$

Four ligands selected from a set of achiral ligands $\{A, B, C, D\}$ and chiral ligands $\{p, \bar{p}, q, \bar{q}, r, \bar{r}, s, \bar{s}\}$ are placed on the positions of the tetrahedral skeleton to give a molecule. If the permutations belonging to \mathbf{G}_C are operated on the molecule, there appear homomers of the original (reference) molecule. If each permutation belonging to $\sigma\mathbf{G}_C$ (equation 6) is operated on the reference molecule, there appears the enantiomer of the reference molecule. If each permutation belonging to $\tilde{\sigma}\mathbf{G}_C$ (equation 7) is operated on the reference molecule, there appears the *RS*-diastereomers of the reference molecule. Each permutation belonging to $\tilde{I}\mathbf{G}_C$ (equation 8) generates another diastereomer of the reference molecule, which is here called a *holantimer*. By the comparison between the permutations of \mathbf{G}_C (e.g., those in figure 2) and those of $\tilde{I}\mathbf{G}_C$ (e.g., those in figure 2), we can restate that two molecules (derivatives) based on the same skeleton are defined as being *holantimeric*, if all of the ligands in the one molecule have the opposite chiralities of the corresponding ligands in the other molecule. They are called *holantimers* with each other.

2.2. Subgroups and derivatives of tetrahedral skeletons

2.2.1. Proper and improper permutations

The point subgroup \mathbf{G}_Y shown in equation 6 is concerned with chirality/achirality, where the operations contained in the coset \mathbf{G}_C have been called *proper rotations*, while the ones contained in the coset $\sigma\mathbf{G}_C$ have been called *improper rotations*. For example, the operations contained in the coset \mathbf{T} ($\subset \mathbf{T}_d$) are proper rotations, while the operations contained in the coset $\sigma_{d(1)}\mathbf{T}$ are improper rotations (figure 2). Thus, enantiomeric relationships depend on whether improper rotations are relevant or not.

On the other hand, the *RS*-permutation subgroup \mathbf{G}_X shown in equation 7 is concerned with stereogenicity/astereogenicity (more precisely *RS*-stereogenicity/*RS*-astereogenicity). Parallel to the chirality case, the permutations contained in the coset \mathbf{G}_C are here called *proper permutations* and the ones in the coset $\tilde{\sigma}\mathbf{G}_C$ are called *improper permutations*. For example, the operations contained in the coset $\tilde{\mathbf{T}} (=S_{10}^{[4]})$ are proper permutations, while the operations contained in the coset $\tilde{\sigma}_{d(1)}\tilde{\mathbf{T}} (= (1)(2\ 3)(4)S_{10}^{[4]})$ are improper permutations (figure 2). By this definition, diastereomeric relationships (more precisely *RS*-diastereomeric relationships) depend on whether improper permutations are relevant or not.

Further, the inversion subgroup \mathbf{G}_Z shown in equation 8 is concerned with the inversion of ligands where the operations contained in the coset \mathbf{G}_C are here called *proper coincidence* and the ones in the coset $\tilde{I}\mathbf{G}_C$ are called *improper coincidence* (or inversion). For example, the operations contained in the coset $\mathbf{T} (=S_{10}^{[4]})$ are proper coincidences, while the operations contained in the coset $\tilde{I}\tilde{\mathbf{T}} (= (1)(2)(3)(4)S_{10}^{[4]})$ are improper coincidences (figure 2). By this definition, holantimeric relationships depend on whether improper coincidences are relevant or not.

2.2.2. Stereogenic and astereogenic subgroups

As discussed in the preceding paragraphs, the subgroup \mathbf{G}_Y (e.g., \mathbf{T}_d in equation 6) is concerned with chirality and specifies enantiomeric relationships. On the other hand, the subgroup \mathbf{G}_X (e.g., $S^{[4]}$ in equation 6) is concerned with *RS*-stereogenicity and specifies *RS*-diastereomeric relationships.

The two subgroups \mathbf{G}_Y and \mathbf{G}_X are isomorphic to each other in the light of their constructions (cf. figure 2). For example, let us consider \mathbf{T}_d (equalized to $\mathbf{T}_d(/C_{3v})$) as the subgroup \mathbf{G}_Y . The \mathbf{T}_d has a non-redundant set of subgroups:

$$\text{SSG}_{\mathbf{T}_d} = \{\mathbf{T}_d, \mathbf{T}, \mathbf{D}_{2d}, \mathbf{C}_{3v}, \mathbf{C}_{2v}, \mathbf{D}, \mathbf{S}_4, \mathbf{C}_3, \mathbf{C}_s, \mathbf{C}_2, \mathbf{C}_1\}, \quad (10)$$

where an appropriate representative is selected from each set of conjugate subgroups [11].

Among these subgroups, \mathbf{T} , \mathbf{D} , \mathbf{C}_3 , \mathbf{C}_2 , and \mathbf{C}_1 are chiral subgroups, because they involve proper rotations only. On the other hand, the remaining subgroups, i.e., \mathbf{T}_d , \mathbf{D}_{2d} , \mathbf{C}_{3v} , \mathbf{C}_{2v} , \mathbf{S}_4 , and \mathbf{C}_s , are achiral subgroups, because they involve proper and improper rotations.

According to the isomorphism, the symmetric group $S^{[4]}$ as an *RS*-permutation (\mathbf{G}_X) has the non-redundant set of subgroups corresponding to the $\text{SSG}_{\mathbf{T}_d}$ (equation 10), as listed in table 1. To emphasize the correspondence between the point group \mathbf{T}_d and the symmetric group $S^{[4]}$ ($=\tilde{\mathbf{T}}_d$), each subgroup of $S^{[4]}$ is represented by the symbol for the isomorphic subgroup of \mathbf{T}_d , which is differentiated with a tilde. Note that table 1 becomes identical with the table for the point group \mathbf{T}_d [11] by removing each tilde.

Table 1
RS-permutation subgroups of $\tilde{\mathbf{T}}_d$

Subgroups of $\tilde{\mathbf{T}}_d$	Permutations	The present notation	Subgroups of $\mathbf{S}^{[4]}$
$\tilde{\mathbf{T}}_d$	$\{I, C_{2(1)}, \dots; \tilde{\sigma}_{d(1)}, \tilde{S}_{4(3)}, \dots\}$	\mathbf{G}_Y	$\mathbf{S}^{[4]} (= \mathbf{S}_{11}^{[4]})$
$\tilde{\mathbf{T}}$	$\{I, C_{2(1)}, \dots\}$	\mathbf{G}_C	$\mathbf{S}_{10}^{[4]}$
$\tilde{\mathbf{D}}_{2d}$	$\{I, C_{2(1)}, C_{2(2)}, C_{2(3)}; \tilde{\sigma}_{d(1)}, \tilde{S}_{4(3)}, \tilde{S}_{4(3)}^3, \tilde{\sigma}_{d(6)}\}$		$\mathbf{S}_9^{[4]}$
$\tilde{\mathbf{C}}_{3v}$	$\{I, C_{3(1)}, C_{3(1)}^2; \tilde{\sigma}_{d(1)}, \tilde{\sigma}_{d(2)}, \tilde{\sigma}_{d(3)}\}$		$\mathbf{S}_8^{[4]}$
$\tilde{\mathbf{C}}_{2v}$	$\{I, C_{2(3)}; \tilde{\sigma}_{d(1)}, \tilde{\sigma}_{d(6)}\}$		$\mathbf{S}_7^{[4]}$
$\tilde{\mathbf{D}}$	$\{I, C_{2(1)}, C_{2(2)}, C_{2(3)}\}$		$\mathbf{S}_6^{[4]}$
$\tilde{\mathbf{S}}_4$	$\{I, C_{2(1)}; \tilde{S}_{4(1)}, \tilde{S}_{4(1)}^3\}$		$\mathbf{S}_5^{[4]}$
$\tilde{\mathbf{C}}_3$	$\{I, C_{3(1)}, C_{3(1)}^2\}$		$\mathbf{S}_4^{[4]}$
$\tilde{\mathbf{C}}_s$	$\{I, \tilde{\sigma}_{d(1)}\}$		$\mathbf{S}_3^{[4]}$
$\tilde{\mathbf{C}}_2$	$\{I, C_{2(1)}\}$		$\mathbf{S}_2^{[4]}$
$\tilde{\mathbf{C}}_1$	$\{I\}$		$\mathbf{S}_1^{[4]}$

Since \mathbf{T} is the common part (\mathbf{G}_C) of \mathbf{T}_d and $\tilde{\mathbf{T}}_d (= \mathbf{S}^{[4]})$, it contains common subgroups as follows: $\mathbf{T} = \tilde{\mathbf{T}}$, $\mathbf{D} = \tilde{\mathbf{D}}$, $\mathbf{C}_3 = \tilde{\mathbf{C}}_3$, $\mathbf{C}_2 = \tilde{\mathbf{C}}_2$, and $\mathbf{C}_1 = \tilde{\mathbf{C}}_1$.

Parallel to the classification of chiral/achiral subgroups, the subgroups listed in table 1 can be classified into stereogenic/astereogenic subgroups (precisely speaking *RS*-stereogenic/*RS*-astereogenic subgroups). Thus, the subgroups $\tilde{\mathbf{T}} (= \mathbf{T})$, $\tilde{\mathbf{D}} (= \mathbf{D})$, $\tilde{\mathbf{C}}_3 (= \mathbf{C}_3)$, $\tilde{\mathbf{C}}_2 (= \mathbf{C}_2)$, and $\tilde{\mathbf{C}}_1 (= \mathbf{C}_1)$ are *RS*-stereogenic subgroups, because they involve proper permutations only. On the other hand, the remaining subgroups, i.e., $\tilde{\mathbf{T}}_d$, $\tilde{\mathbf{D}}_{2d}$, $\tilde{\mathbf{C}}_{3v}$, $\tilde{\mathbf{C}}_{2v}$, $\tilde{\mathbf{S}}_4$, and $\tilde{\mathbf{C}}_s$, are astereogenic subgroups, because they involve proper and improper permutations. Obviously, we can state the following proposition: *If a molecule belongs to an RS-stereogenic (sub)group, it is concluded to be specified by the RS-nomenclature. Otherwise, it is not to be specified by the RS-nomenclature.*

2.2.3. Derivation by Placing Ligands

A molecule based on the tetrahedral skeleton can be generated by placing an appropriate set of ligands on the positions of the tetrahedral skeleton. The generation process is formulated to be a function in which each $f(i)$ ($i = 1, 2, 3, 4$) is equal to a ligand, as shown in figure 1 (right). For example, let us consider a function that each of the positions 1 and 4 is occupied by an achiral ligand A (i.e., $f(1) = A$ and $f(4) = A$) and each of the positions 2 and 3 by an achiral ligand B (i.e., $f(2) = B$ and $f(3) = B$). Then, we can obtain the molecule **2** with the formula A^2B^2 .

When the permutations belonging to the *RS*-stereoisomeric group $\mathbf{G} (= \mathbf{T}_d / \mathbf{C}_{3v}) - \mathbf{S}^{[4]}$ shown in figure 2) act on the molecule, they produce stereoisomers shown in figure 3. From another point of view, this derivation can be interpreted as an operation in which the same function is applied to all of the numbered

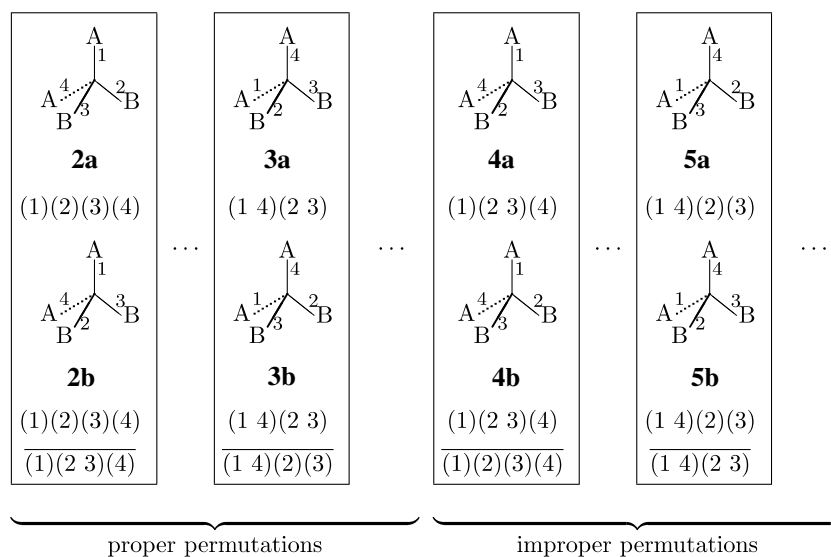


Figure 3. Isomer equivalence of A^2B^2 under the RS -stereoisomeric group $(T_d/C_{3v})\text{-S}^{[4]}$.

skeletons generated by the action of the RS -stereoisomeric group $(G = T_d/C_{3v})\text{-S}^{[4]}$. By the inspection of these stereoisomers, the following results are obtained:

1. Among the homomers that are generated by the operations of the common part $(G_C = T \text{ or } S_{10}^{[4]})$, the molecules **2a** and **3a** are identical with the reference molecule **2a**. In other words, the corresponding operations $I (= (1)(2)(3)(4))$ and $C_{2(3)} (= (1\ 4)(2\ 3))$ fix the reference molecule **2a** invariant. The remaining operations of G_C convert **2a** into its homomers, although these are not depicted in figure 3.
2. The operations $\tilde{\sigma}_{d(1)} (= (1)(2\ 3)(4))$ and $\tilde{\sigma}_{d(6)} (= (1\ 4)(2)(3))$ contained in the upper-right part $(\tilde{\sigma}_{d(1)}G_C = (1)(2\ 3)(4)S_{10}^{[4]})$ fix the reference molecule **2a** invariant so as to give **4a** and **5a**. The remaining operations of $\tilde{\sigma}_{d(1)}G_C$ convert **2a** into its homomers (not depicted).
3. The operations $\sigma_{d(1)} (= \overline{(1)(2\ 3)(4)})$ and $\sigma_{d(6)} (= \overline{(1\ 4)(2)(3)})$ contained in the bottom-left part $(\sigma_{d(1)}G_C = T\sigma_{d(1)})$ fix the reference molecule **2a** invariant, giving **2b** and **3b**. The remaining operations of $\sigma_{d(1)}G_C$ convert **2a** into its homomers (not depicted).
4. The operations $\tilde{I} (= \overline{(1)(2)(3)(4)})$ and $\tilde{C}_{2(3)} (= \overline{(1\ 4)(2\ 3)})$ contained in the remaining part fix the reference molecule **2a** invariant so as to give **4b** and **5b**. The remaining operations of $\tilde{I}G_C$ convert **2a** into its homomers (not depicted).

Hence, the reference molecule **2a** is fixed invariant by the operations contained in the group:

$$\mathbf{G}' = \{I, C_{2(3)}; \sigma_{d(1)}, \sigma_{d(6)}; \tilde{\sigma}_{d(1)}, \tilde{\sigma}_{d(6)}; \tilde{I}, \tilde{C}_{2(3)}\}, \quad (11)$$

which is a subgroup of \mathbf{G} ($= \mathbf{T}_d(/C_{3v})\text{-S}^{[4]}$) shown in figure 2).

From the viewpoint of chirality, the molecule **2a** is concluded to belong to the group \mathbf{C}_{2v} ($= \{I, C_{2(3)}; \sigma_{d(1)}, \sigma_{d(6)}\}$), which is a subgroup of \mathbf{G}' (equation 11). Note that the group \mathbf{C}_{2v} is a subgroup of the point group \mathbf{T}_d ($= \mathbf{G}_Y$), which is equalized to the permutation representation $\mathbf{T}_d(/C_{3v})$ in this paper (figure 2). Since the group \mathbf{C}_{2v} is an achiral subgroup, the molecule **2a** is concluded to be achiral.

From the viewpoint of stereogenicity (precisely *RS*-stereogenicity), on the other hand, the molecule **2a** is concluded to belong to $\tilde{\mathbf{C}}_{2v}$ ($= \{I, C_{2(3)}; \tilde{\sigma}_{d(1)}, \tilde{\sigma}_{d(6)}\} = \mathbf{S}_7^{[4]}$), which is another subgroup of \mathbf{G}' (equation 11). Since the group $\tilde{\mathbf{C}}_{2v}$ is an *RS*-astereogenic subgroup of the *RS*-permutation group $\tilde{\mathbf{T}}_d$ ($= \mathbf{G}_X$), the molecule **2a** is concluded to be *RS*-astereogenic. This means that the molecule **2a** is not characterized by the *RS*-nomenclature.

2.3. Stereoisograms

By combining the chirality/achirality and the *RS*-stereogenicity/*RS*-astereogenicity, there emerge five types of stereoisomers to discuss stereochemistry and stereoisomerism.

2.3.1. Stereoisograms of Type I

Let us place four ligands selected from a set of achiral ligands {A, B, C, D} on the positions of the tetrahedral skeleton belonging to the *RS*-stereoisomeric group \mathbf{G} ($= \mathbf{T}_d(/C_{3v})\text{-S}^{[4]}$). Then we have a molecule that belongs to a subgroup of \mathbf{G} . For example, let us consider a function to give the molecule **6a** shown in figure 4, where position 1 is occupied by an achiral ligand A (i.e., $f(1) = A$), position 2 by an achiral ligand B (i.e., $f(2) = B$), position 3 by an achiral ligand C (i.e., $f(3) = C$), and position 4 by an achiral ligand D (i.e., $f(4) = D$). The same function is applied to all of the numbered skeletons generated by the action of the *RS*-stereoisomeric group ($\mathbf{G} = \mathbf{T}_d(/C_{3v})\text{-S}^{[4]}$). Thereby, the molecules can be generated, as shown in figure 4. The operations of the common part ($\mathbf{G}_C = \mathbf{T}$ or $\mathbf{S}_{10}^{[4]}$) generate the homomers of the reference molecule (**6a**), e.g., **7a** and **8a**. The operations of the upper-right part ($\tilde{\sigma}_{d(1)}\mathbf{G}_C = (1)(2\ 3)(4)\mathbf{S}_{10}^{[4]}$) generate the diastereomers of **6a**, e.g., **9a**, **10a**, and **11a**. The operations of the bottom-left part ($\sigma_{d(1)}\mathbf{G}_C = \mathbf{T}\sigma_{d(1)}$) generate the enantiomers of **6a**, e.g., **6b**, **7b**, and **8b**. The operations of the remaining part generate another set of diastereomers of **6a**, e.g., **9b**, **10b**, and **11b**, which represent the holantimer of **6a** according to the definition described above.

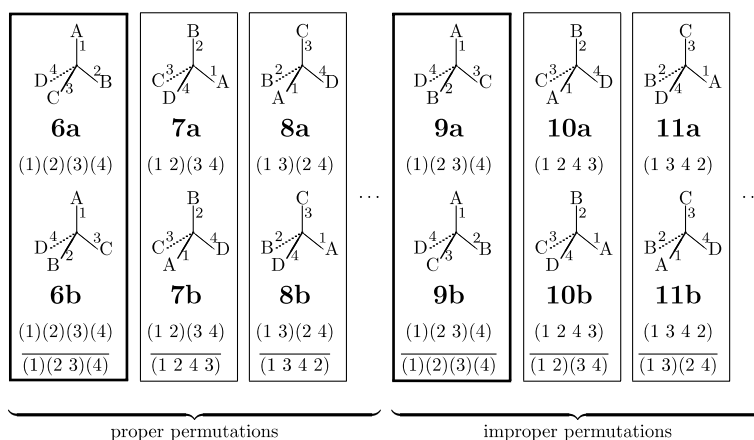


Figure 4. Isomer equivalence of ABCD under the RS -stereoisomeric group ($T_d/(C_{3v})\cdot S^{[4]}$).

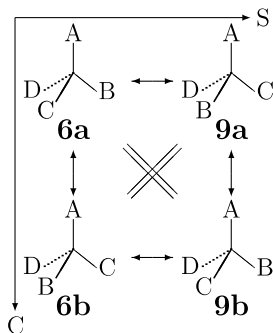


Figure 5. Stereoisogram (Type I) for tetrahedral molecules with ABCD.

The reference molecule (**6a**) and its homomers (**7a**, **8a**, etc.) are identical with the holantimer (**9b**) and its homomers (**10b**, **11b**, etc.). The enantiomer (**6b**) and its homomers (**7b**, **8b**, etc.) are identical with the RS -diastereomer (**9a**) and its homomers (**10a**, **11a**, etc.).

Among the permutations of figure 4, only I and \tilde{I} fix the reference molecule (cf. **6a** and **9b**), where we place $I = (1)(2)(3)(4)$ and $\tilde{I} = \overline{(1)(2)(3)(4)}$. It follows that the molecule **6a** belongs to the group $\{I, \tilde{I}\}$, which is a subgroup of G_Z ($\subset G$).

From the viewpoint of chirality, **6a** belongs to $C_1(= \{I\})$, which is a subgroup of T (i.e., a chiral subgroup of the point group T_d). It follows that **6a** is concluded to be chiral. From the viewpoint of RS -stereogenicity, on the other hand, **6a** belongs to $C_1(= \{I\})$, which is a subgroup of \tilde{T} (i.e., a stereogenic subgroup of the RS -permutation group \tilde{T}_d). It follows that **6a** is concluded to be stereogenic.

By the inspection of figure 4, we can select the four molecules surrounded by bold-line boxes as representatives for the distinct relationships described

above, i.e., **6a** for the reference molecule, **9a** for the *RS*-diastereomeric relationship, **6b** for the enantiomeric relationship, and **9b** for the holantimeric relationship.

To discuss the relationship between chirality and stereogenicity, we define a stereoisogram on the basis of the selected four molecules, as exemplified in figure 5. First, the holantimers (**6a** and **9b**) located on the diagonal places are linked with a diagonal equality symbol, as shown in figure 5. The relationship between the two molecules in each column (the pair of **6a/6b**; or the pair of **9a/9b**) is enantiomeric. Thereby, the vertical axis (C-axis) is related to chirality, as designated by the symbol C.

On the other hand, the relationship between the two compounds in each row (the pair of **6a/9a** or the pair of **6b/9b**) is *RS*-diastereomeric. As a result, the horizontal axis (S-axis) is found to be related to stereogenicity, as designated by the symbol S.

The term “*RS*-diastereomeric” is used to specify the horizontal diastereomeric relationship appearing in each stereoisogram, because the relationship is concerned with the *RS*-nomenclature and because there exist other types of diastereomeric relationships. As a result, the present stereogenicity should be called *RS-stereogenicity*.

The stereoisogram of Type I (e.g., figure 5) corresponds to a chiral and *RS*-stereogenic case. It should be recalled that the molecule **6a** belongs to the group $\{I, \bar{I}\}$, which is a subgroup of \mathbf{G}_Z ($\subset \mathbf{G}$). The group \mathbf{G}_Z is closely related to the chiral and *RS*-stereogenic nature.

2.3.2. Stereoisograms of Type II

Let us next consider a function to give the molecule **12a** shown in figure 6, where the position 1 is occupied by an achiral ligand A (i.e., $f(1) = A$), each of the positions 2 and 3 is occupied by a chiral ligand p (i.e., $f(2) = p$ and $f(3) = p$), and position 4 is occupied by an achiral ligand B (i.e., $f(4) = B$). The same function is applied to all of the numbered skeletons generated by the action of the *RS*-stereoisomeric group ($\mathbf{T}_d(/C_{3v})\text{-S}^{[4]}$). Thereby, we obtain the molecules shown in figure 6.

The reference molecule (**12a**) and its homomers (**13a**, **14a**, etc.) are identical with the *RS*-diastereomer (**15a**) and its homomers (**16a**, **17a**, etc.). The enantiomer (**12b**) and its homomers (**13b**, **14b**, etc.) are identical with the holantimer (**15b**) and its homomers (**16b**, **17b**, etc.).

Among the permutations of figure 6, only I and $\tilde{\sigma}_{d(1)}$ fix the reference molecule (cf. **12a** and **15a**), where we place $I = (1)(2)(3)(4)$ and $\tilde{\sigma}_{d(1)} = (1)(2\ 3)(4)$. It follows that the molecule **12a** belongs to the group $\{I, \tilde{\sigma}_{d(1)}\}$, which is a subgroup of \mathbf{G}_X ($\subset \mathbf{G}$).

From the viewpoint of chirality, **12a** belongs to $\mathbf{C}_1 (= \{I\})$, which is a subgroup of \mathbf{T} (i.e., a chiral subgroup of the point group \mathbf{T}_d). It follows that **12a** is concluded to be chiral. From the viewpoint of *RS*-stereogenicity, on the

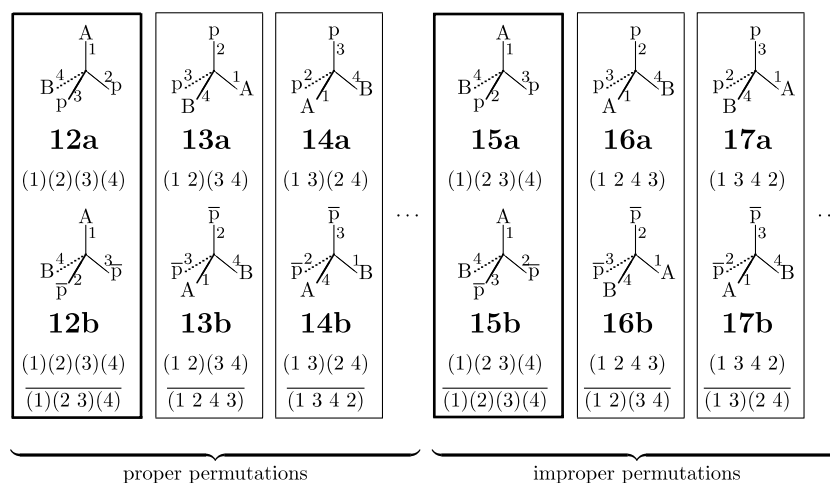


Figure 6. Isomer equivalence of ABp^2 ($AB\bar{p}^2$) under the RS -stereoisomeric group (T_d/C_{3v})- $S^{[4]}$.

other hand, **12a** belongs to $\tilde{C}_s (= \{I, \tilde{\sigma}_{d(1)}\})$, which is an RS -astereogenic subgroup of the RS -permutation group \tilde{T}_d . It follows that **12a** is concluded to be RS -astereogenic.

When we select the four molecules surrounded by bold-line boxes shown in figure 6, we can construct a stereoisogram of Type II (figure 7), where the four molecules act as representatives for the distinct relationships described above, i.e., **12a** for the reference molecule, **15a** for the RS -diastereomeric relationship, **12b** for the enantiomeric relationship, and **15b** for the holantimeric relationship.

The stereoisogram of Type II (e.g., figure 7) corresponds to a chiral and RS -astereogenic case. It should be recalled that the molecule **12a** belongs to the group $\{I, \tilde{\sigma}_{d(1)}\}$, which is a subgroup of G_X ($\subset G$). The group G_X is closely related to the chiral and RS -astereogenic nature.

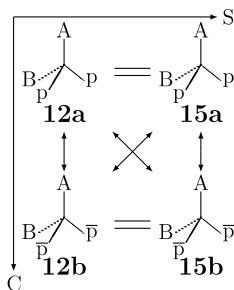


Figure 7. Stereoisogram (Type II) for tetrahedral molecules with ABp^2 ($AB\bar{p}^2$).

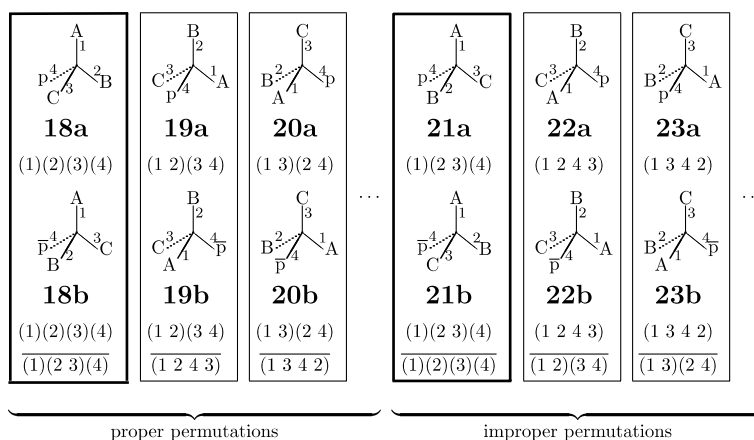


Figure 8. Isomer equivalence of $ABCp$ ($ABC\bar{p}$) under the RS -stereoisomeric group ($T_d/C_{3v}-S^{[4]}$).

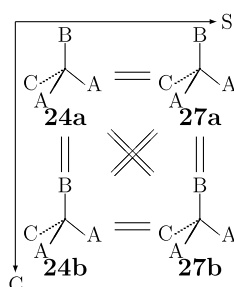
2.3.3. Stereoisograms of Type III

When we consider a function in which position 1 is occupied by an achiral ligand A (i.e., $f(1) = A$), position 2 by an achiral ligand B (i.e., $f(2) = B$), position 3 by an achiral ligand C (i.e., $f(3) = C$), and position 4 by a chiral ligand p (i.e., $f(4) = p$), we obtain the molecule **18a** shown in figure 8. The same function is applied to all of the numbered skeletons generated by the action of the RS -stereoisomeric group ($T_d/C_{3v}-S^{[4]}$). Thereby, we obtain the molecules shown in figure 8.

The reference molecule (**18a**) and its homomers (**19a**, **20a**, etc.); the RS -diastereomer (**21a**) and its homomers (**22a**, **23a**, etc.); the enantiomer (**18b**) and its homomers (**19b**, **20b**, etc.); and the holantimer (**21b**) and its homomers (**22b**, **23b**, etc.) construct distinct sets of stereoisomers. As a result, only the identity operation I among the permutations of figure 8 fixes the reference molecule (**18a**), where we place $I = (1)(2)(3)(4)$. It follows that the molecule **18a** belongs to the identity group $\{I\}$, which is a subgroup of G_C ($\subset G$).

From the viewpoint of chirality, **18a** belongs to $C_1(= \{I\})$, which is a subgroup of $T(= G_C)$ (i.e., a chiral subgroup of the point group $T_d(= G_Y)$). It follows that **18a** is concluded to be chiral. From the viewpoint of RS -stereogenicity, on the other hand, **18a** belongs to $\tilde{C}_1(= \{I\})$, which is a subgroup of $\tilde{T}(= G_C)$ (i.e., an RS -stereogenic subgroup of the RS -permutation group $\tilde{T}_d(= G_X)$). It follows that **18a** is concluded to be RS -stereogenic.

By selecting the four molecules surrounded by bold-line boxes shown in figure 8, we can construct a stereoisogram of Type III (figure 9). The four molecules are selected as representatives for the distinct relationships described above, i.e., **18a** for the reference molecule, **21a** for the RS -diastereomeric relationship, **18b** for the enantiomeric relationship, and **21b** for the holantimeric relationship.

Figure 11. Stereoisogram (Type IV) for tetrahedral molecules with A²BC.

The reference molecule (**24a**) and its homomers (**25a**, **26a**, etc.); the *RS*-diastereomer (**27a**) and its homomers (**28a**, **29a**, etc.); the enantiomer (**24b**) and its homomers (**25b**, **26b**, etc.); and the holantimer (**27b**) and its homomers (**28b**, **29b**, etc.) construct distinct sets of stereoisomers. All of them are homomeric to each other. Among the permutations of figure 10, four permutations, i.e., I ($=(1)(2)(3)(4)$), $\sigma_{d(1)}$ ($=(1)(2\ 3)(4)$), $\tilde{\sigma}_{d(1)}$ ($=(1)(2\ 3)(4)$), and \tilde{I} ($=(1)(2)(3)(4)$), fix the reference molecule (**24a**). It follows that the molecule **24a** belongs to the group $\{I, \sigma_{d(1)}, \tilde{\sigma}_{d(1)}, \tilde{I}\}$, which is a subgroup of \mathbf{G} .

From the viewpoint of chirality, **24a** belongs to \mathbf{C}_s ($=\{I, \sigma_{d(1)}\}$), which is an achiral subgroup of the point group \mathbf{T}_d ($=\mathbf{G}_Y$). It follows that **24a** is concluded to be achiral. From the viewpoint of *RS*-stereogenicity, on the other hand, **24a** belongs to $\tilde{\mathbf{C}}_s$ ($=\{I, \tilde{\sigma}_{d(1)}\}$), which is an *RS*-astereogenic subgroup of the *RS*-permutation group $\tilde{\mathbf{T}}_d(\mathbf{G}_X)$. It follows that **24a** is concluded to be *RS*-astereogenic.

By selecting the four molecules surrounded by bold-line boxes shown in figure 10, we can construct a stereoisogram of Type IV (figure 11). The four molecules are selected as representatives for the distinct relationships described above, i.e., **24a** for the reference molecule, **27a** for the *RS*-diastereomeric relationship, **24b** for the enantiomeric relationship, and **27b** for the holantimeric relationship. However, all of them are homomeric to each other.

The stereoisogram of Type IV (e.g., figure 11) corresponds to an achiral and *RS*-astereogenic case. It should be recalled that the molecule **24a** belongs to the group $\{I, \sigma_{d(1)}, \tilde{\sigma}_{d(1)}, \tilde{I}\}$, which is a subgroup of \mathbf{G} . The group \mathbf{G} is closely related to the achiral and *RS*-astereogenic nature.

2.3.5. Stereoisograms of Type V

Let us consider a function in which position 1 is occupied by an achiral ligand A (i.e., $f(1) = A$), position 2 by a chiral ligand p (i.e., $f(2) = p$), position 3 by a ligand \bar{p} of the opposite chirality (i.e., $f(3) = \bar{p}$), and position 4 by an achiral ligand B (i.e., $f(4) = B$). Thereby, we obtain the molecule **30a** shown in figure 12. The same function is applied to all of the numbered

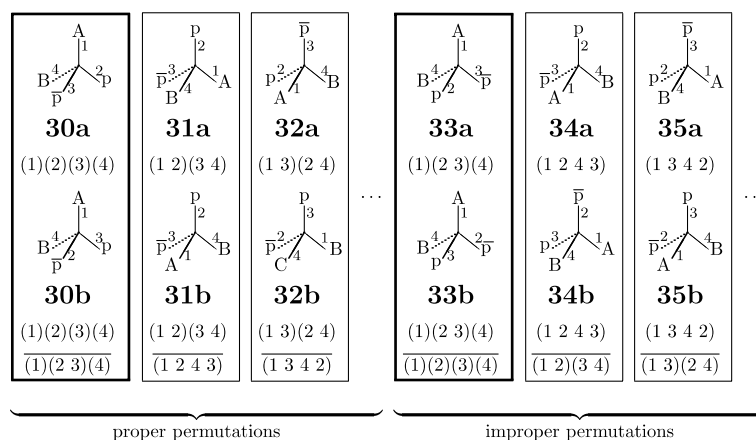


Figure 12. Isomer equivalence of $AB\bar{p}\bar{p}$ under the RS -stereoisomeric group ($T_d/(C_{3v})\text{-}S^{[4]}$).

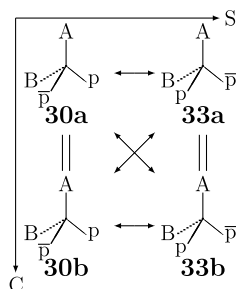


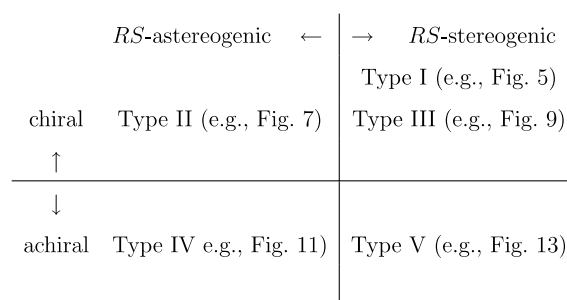
Figure 13. Stereoisogram (Type V) for tetrahedral molecules with $AB\bar{p}\bar{p}$.

skeletons generated by the action of the RS -stereoisomeric group ($T_d/(C_{3v})\text{-}S^{[4]}$). Thus we obtain the molecules shown in figure 12.

The reference molecule (**30a**) and its homomers (**31a**, **32a**, etc.) are identical with the enantiomer (**30b**) and its homomers (**31b**, **32b**, etc.). This fact means that **30a** is achiral. The RS -diastereomer (**27a**) and its homomers (**34a**, **35a**, etc.) are identical with the holantimer (**33b**) and its homomers (**34b**, **35b**, etc.). Among the permutations of figure 12, two permutations, i.e., $I (= (1)(2)(3)(4))$ and $\sigma_{d(1)} (= (1)(2\ 3)(4))$, fix the reference molecule (**30a**). It follows that the molecule **30a** belongs to the group $\{I, \sigma_{d(1)}\} (= C_s)$, which is a subgroup of $G_Y (\subset G)$.

From the viewpoint of chirality, **30a** is concluded to be achiral, since it belongs to C_s , which is an achiral subgroup of the point group $T_d (= G_Y)$. From the viewpoint of RS -stereogenicity, on the other hand, **30a** belongs to $\tilde{C}_1 (= \{I\})$, which is a subgroup of $\tilde{T} (= G_C)$ (i.e., an RS -stereogenic subgroup of the RS -permutation group $\tilde{T}_d (= G_X)$). It follows that **30a** is concluded to be RS -stereogenic.

By selecting the four molecules surrounded by bold-line boxes shown in figure 12, we can construct a stereoisogram of Type V (figure 13). The four

Figure 14. RS -stereogenicity types.

molecules are selected as representatives for the distinct relationships described above, i.e., **30a** for the reference molecule, **33a** for the RS -diastereomeric relationship, **30b** for the enantiomeric relationship, and **33b** for the holantimeric relationship. However, the enantiomers are identical with the reference molecule, which is achiral.

The stereoisogram of Type V (e.g., figure 13) corresponds to an achiral and RS -stereogenic case. It should be recalled that the molecule **30a** belongs to the group $\{I, \sigma_{d(1)}\}$, which is a subgroup of $\mathbf{G}_Y (\subset \mathbf{G})$. The group \mathbf{G}_Y is closely related to the achiral and RS -stereogenic nature. This case has long been referred to as pseudo-asymmetry.

2.3.6. RS -Stereogenicity types

As discussed in the preceding paragraphs (cf. figures 5, 7, 9, 11, and 13), there are five types that specify stereogenicity/astereogenicity along with chirality/achirality. These types are here called RS -stereogenicity types, as listed in figure 14. It should be emphasized that these five types are effective to classify molecules based on other skeletons because of the definition of RS -stereoisomeric groups.

2.4. Classification of tetrahedral molecules

Tetrahedral molecules have been combinatorial enumerated and listed as a table [8,12]. They can be classified into the five RS -stereogenicity types defined in the present article (figure 14). Thus, the RS -stereogenicity types of tetrahedral molecules are collected in figure 15 in addition to their point groups and their RS -permutation groups (table 1). Note that an appropriate enantiomer is depicted for each enantiomeric pair of chiral molecules (Types I, II, and III).

Types I, III, and V are concerned with RS -stereogenic molecules (figure 15). Each of these molecules belongs to an RS -stereogenic group, which is a subgroup of $\tilde{\mathbf{T}} (= \mathbf{G}_C \subset \mathbf{G}_X)$. In other words, it is characterized by horizontal double-headed arrows appearing in its stereoisogram (e.g., figures 5, 9, or 13).

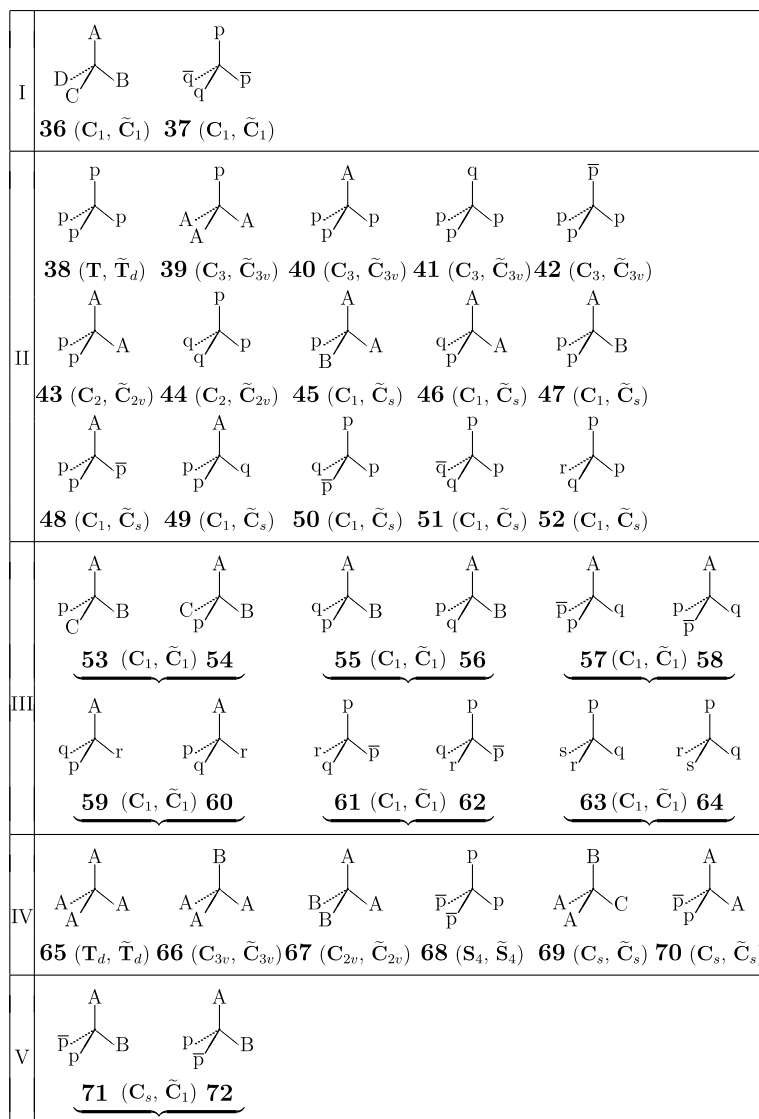


Figure 15. *RS*-stereogenicity types (Types I to V) for tetrahedral molecules. The symbols A, B, C, and D represent atoms or achiral ligands. The symbols p, q, r, and s represent chiral ligands, while each symbol with an overbar represent the corresponding chiral ligand with the opposite chirality.

Thereby, it is specified in terms of the *RS*-nomenclature whether it is chiral or achiral.

Two *RS*-stereogenic molecules linked with a horizontal brace for Type III are chiral *RS*-diastereomers, which are equalized in the corresponding *RS*-permutation group (i.e., they are contained in one stereoisogram). Note that each of the two *RS*-stereogenic molecules accompanies the corresponding

enantiomer. Two *RS*-stereogenic molecules linked with a horizontal brace for Type V are achiral *RS*-diastereomers, which are equalized in the corresponding *RS*-permutation group (i.e., they are contained in one stereoisogram).

On the other hand, Type I does not contain such a pair as linked with a horizontal brace so that it represents cases in which the enantiomeric relationship is superposed onto the diastereomeric relationship.

By the formulation described above, the conventional confusion on chirality and stereogenicity is clarified to stem from the mixing of Type I, Type III, and Type V:

1. No differentiation between Type I (chiral) and Type III (chiral) has caused a mixation of an enantiomeric relationship with a diastereomeric relationship. The diastereomeric relationship for Type I (S-axis in a stereoisogram, e.g., figure 5) is superposed onto the enantiomeric relationship (C-axis), whereas the diastereomeric relationship for Type III (S-axis in a stereoisogram, e.g., figure 9) is not superposed onto the enantiomeric relationship (C-axis). The latter indicates that the *RS*-nomenclature specifies the diastereomeric relationship concerned with the S-axis.
2. An unconvincing differentiation between Type I (chiral) and Type V (achiral) has caused another mixation of an enantiomeric relationship with a diastereomeric relationship. They should be differentiated in terms of their S-axes (stereogenic/astereogenic) but by no means in terms of their C-axes (chiral/achiral). Obviously, the *RS*-nomenclature specifies a diastereomeric relationship for Type V, since this type does not accompany an enantiomeric relationship. Hence, it is natural to say that the *RS*-nomenclature for Type I is concerned with the diastereomeric relationship and only indirectly with the enantiomeric relationship.

3. Combinatorial enumerations on *RS*-permutation groups

3.1. Racemic pairs on the action of *RS*-permutation groups

In order to accomplish combinatorial enumerations, we could use the *RS*-stereoisomeric group \mathbf{G} if the subgroup lattice of \mathbf{G} was available. However, the construction of the subgroup lattice of \mathbf{G} is usually difficult. Hence, an alternative method based on an appropriate subgroup of \mathbf{G} is to be developed.

Fortunately, a chiral molecule can be paired with its enantiomeric molecule. For example, figure 4 shows that **6a** and **6b** construct a pair of enantiomers, as surrounded by a bold-line box. Any combination of a molecule (any homomer) and an enantiomer (any homomer) can be used as a reference racemic pair. We call such a pair a *racemic pair*. The racemic pair is permuted pairwise on the action of the *RS*-permutation group $\tilde{\mathbf{T}}_d (= \mathbf{G}_X)$, as shown in figure 4. The same

situation holds true for the pair of **12a** and **12b** shown in figure 6 and for the pair of **18a** and **18b** shown in figure 8.

As for an achiral molecule, the reference molecule is identical with its mirror image. Hence, they are treated as a virtual racemic pair containing the two homomers. For example, the pair of **24a** and **24b** in figure 10 and the pair of **30a** and **30b** in figure 12 represent this situation.

By this formulation, we can accomplish enumerations of racemic pairs on the basis of the *RS*-permutation group \mathbf{G}_X in place of the direct enumerations based on the *RS*-stereoisomeric group \mathbf{G} . The former enumerations based on \mathbf{G}_X are capable of revealing most features of the latter enumerations based on the *RS*-stereoisomeric group \mathbf{G} .

In each enumeration based on \mathbf{G}_X , a molecule and its *RS*-diastereomer of Type I, III, or V are counted to be one stereoisomer, where they belong to an *RS*-stereogenic group that is a subgroup of \mathbf{G}_X . On the other hand, a molecule of type II or IV is counted to be one stereoisomer on the action of \mathbf{G}_X , where it belongs to an *RS*-astereogenic group that is a subgroup of \mathbf{G}_X .

3.2. Enumeration of tetrahedral molecules

Let us enumerate racemic pairs based on the *RS*-permutation group $\tilde{\mathbf{T}}_d (= \mathbf{G}_X)$ as an example. This enumeration is mathematically equivalent to the enumeration of the violation case of chirality-fittingness that has been reported in a previous article [9]. Thus, we here use the partial-cycle-index (PCI) method of enumeration which we have proposed previously [8]. Thereby, we obtain the PCIs as follows:

$$\text{PCI}(\tilde{\mathbf{C}}_1, s_d) = \frac{1}{24}s_1^4 + \frac{1}{8}s_2^2 - \frac{1}{4}s_1^2s_2 + \frac{1}{3}s_1s_3 + \frac{1}{4}s_4, \quad (12)$$

$$\text{PCI}(\tilde{\mathbf{C}}_2, s_d) = 0, \quad (13)$$

$$\text{PCI}(\tilde{\mathbf{C}}_3, s_d) = \frac{1}{2}s_1^2s_2 - \frac{1}{2}s_2^2 - s_1s_3 + s_4, \quad (14)$$

$$\text{PCI}(\tilde{\mathbf{C}}_4, s_d) = 0, \quad (15)$$

$$\text{PCI}(\tilde{\mathbf{S}}_4, s_d) = 0, \quad (16)$$

$$\text{PCI}(\tilde{\mathbf{D}}_2, s_d) = 0, \quad (17)$$

$$\text{PCI}(\tilde{\mathbf{C}}_{2v}, s_d) = \frac{1}{2}s_2^2 - \frac{1}{2}s_4, \quad (18)$$

$$\text{PCI}(\tilde{\mathbf{C}}_{3v}, s_d) = s_1s_3 - s_4, \quad (19)$$

$$\text{PCI}(\tilde{\mathbf{D}}_{2d}, s_d) = 0, \quad (20)$$

$$\text{PCI}(\tilde{\mathbf{T}}, s_d) = 0, \quad (21)$$

$$\text{PCI}(\tilde{\mathbf{T}}_d, s_d) = s_4. \quad (22)$$

Among these PCIs, we find several PCIs of zero value: $\text{PCI}(\tilde{\mathbf{C}}_2, s_d)$, $\text{PCI}(\tilde{\mathbf{C}}_3, s_d)$, $\text{PCI}(\tilde{\mathbf{S}}_4, s_d)$, $\text{PCI}(\tilde{\mathbf{D}}_2, s_d)$, $\text{PCI}(\tilde{\mathbf{D}}_{2d}, s_d)$, and $\text{PCI}(\tilde{\mathbf{T}}, s_d)$, which show that there exist no racemic pairs of these permutation symmetries.

Since four ligands selected from a set of achiral ligands {A, B, C, D} and chiral ligands $p, \bar{p}, q, \bar{q}, r, \bar{r}, s, \bar{s}$ are placed on the positions of the tetrahedral skeleton to give a molecule, we use the following ligand inventory for the enumeration of racemic pairs:

$$s_d = A^d + B^d + C^d + D^d + p^d + \bar{p}^d + q^d + \bar{q}^d + r^d + \bar{r}^d + s^d + \bar{s}^d. \quad (23)$$

The inventory represented by equation 23 is introduced to the PCIs (eqs. 12 to 22); then the resulting equations are expanded to give the generating functions for the respective subgroups. For example, we obtain

$$\begin{aligned} f_{\tilde{C}_s} = & (A^2BC + A^2BD + \dots) + (A^2Bp + A^2B\bar{p} + \dots) + (A^2p\bar{p} + A^2q\bar{q} + \dots) \\ & + (A^2pq + A^2\bar{p}\bar{q} + \dots) + (A^2p^2 + A^2\bar{p}^2 + \dots) + (Ap^2\bar{p} + A\bar{p}^2p + \dots) \\ & + (Ap^2q + A\bar{p}^2\bar{q} + \dots) + (p^2\bar{p}q + p\bar{p}^2\bar{q} + \dots) + (p^2qr + \bar{p}^2\bar{q}\bar{r} + \dots), \end{aligned} \quad (24)$$

$$\begin{aligned} f_{\tilde{C}_{2v}} = & (A^2B^2 + A^2C^2 + \dots) + (A^2p^2 + A^2\bar{p}^2 + \dots) \\ & + (p^2\bar{p}^2 + q\bar{q}^2 + \dots) + (p^2q^2 + \bar{p}^2\bar{q}^2 + \dots) \end{aligned} \quad (25)$$

In the present enumeration of racemic pairs, such a term as $(A^2Bp + A^2B\bar{p})$ represents one racemic pair. We select either of them, e.g., A^2Bp , as a representative for the sake of simplicity. These data (equations 24 and 25) are collected in the \tilde{C}_s - and the \tilde{C}_{2v} -column. The data for the remaining subgroups are also collected in table 2.

Table 2 also involves *RS*-stereogenicity types described above (Types I to V) in addition to point-group symmetries, which have been enumerated in previous articles [9, 12]. Note that Types I, II, and III are concerned with chiral molecules, while Types IV and V are concerned with achiral molecules.

These molecules have been depicted in figure 15. Each pair of two molecules (precisely *RS*-diastereomeric racemic pairs) linked with a horizontal brace (Types III and V) is required to represent the one that should be counted as one racemic pair, as exemplified by figure 8 for Type III and figure 12 for Type IV. This requirement is confirmed by the data listed in the \tilde{C}_1 -column of table 2. The presence of such *RS*-diastereomers (precisely *RS*-diastereomeric racemic pairs) are ascribed to the fact that the \tilde{C}_1 is *RS*-stereogenic.

4. Conclusion

We have proposed the concept of *RS*-stereoisomeric groups in order to discuss the difference between stereogenicity and chirality, where each *RS*-stereoisomeric group comprises a coset representation of a point group as well

Table 2
Number of racemic pairs derived from a tetrahedral skeleton.

Proligand partition	<i>RS</i> -Stereo-genicity type	Number of promolecules											Point group
		\tilde{C}_1 $S_1^{[4]}$	\tilde{C}_2 $S_2^{[4]}$	\tilde{C}_s $S_3^{[4]}$	\tilde{C}_3 $S_4^{[4]}$	\tilde{S}_4 $S_5^{[4]}$	\tilde{D}_2 $S_6^{[4]}$	\tilde{C}_{2v} $S_7^{[4]}$	\tilde{C}_{3v} $S_8^{[4]}$	\tilde{D}_{2d} $S_9^{[4]}$	\tilde{T} $S_{10}^{[4]}$	\tilde{T}_d $S^{[4]}$	
ABCD	I	1	0	0	0	0	0	0	0	0	0	0	C_1
p \bar{p} q \bar{q}	I	1	0	0	0	0	0	0	0	0	0	0	C_1
p ⁴	II	0	0	0	0	0	0	0	0	0	0	1	T_d
A ³ p	II	0	0	0	0	0	0	0	1	0	0	0	C_{3v}
Ap ³	II	0	0	0	0	0	0	0	1	0	0	0	C_{3v}
p ³ q	II	0	0	0	0	0	0	0	1	0	0	0	C_{3v}
p ³ \bar{p}	II	0	0	0	0	0	0	0	1	0	0	0	C_{3v}
A ² p ²	II	0	0	0	0	0	0	1	0	0	0	0	C_2
p ² q ²	II	0	0	0	0	0	0	1	0	0	0	0	C_2
A ² Bp	II	0	0	1	0	0	0	0	0	0	0	0	C_1
A ² pq	II	0	0	1	0	0	0	0	0	0	0	0	C_1
ABp ²	II	0	0	1	0	0	0	0	0	0	0	0	C_1
Ap ² \bar{p}	II	0	0	1	0	0	0	0	0	0	0	0	C_1
Ap ² q	II	0	0	1	0	0	0	0	0	0	0	0	C_1
p ² \bar{p} q	II	0	0	1	0	0	0	0	0	0	0	0	C_1
p ² q \bar{q}	II	0	0	1	0	0	0	0	0	0	0	0	C_1
p ² qr	II	0	0	1	0	0	0	0	0	0	0	0	C_1
ABCp	III	1	0	0	0	0	0	0	0	0	0	0	C_1
ABpq	III	1	0	0	0	0	0	0	0	0	0	0	C_1
Ap \bar{p} q	III	1	0	0	0	0	0	0	0	0	0	0	C_1
Apqr	III	1	0	0	0	0	0	0	0	0	0	0	C_1
p \bar{p} qr	III	1	0	0	0	0	0	0	0	0	0	0	C_1
pqrs	III	1	0	0	0	0	0	0	0	0	0	0	C_1
A ⁴	IV	0	0	0	0	0	0	0	0	0	0	1	T_d
A ³ B	IV	0	0	0	0	0	0	0	1	0	0	0	C_{3v}
A ² B ²	IV	0	0	0	0	0	0	1	0	0	0	0	C_{2v}
p ² \bar{p} ²	IV	0	0	0	0	0	0	1	0	0	0	0	S_4
A ² BC	IV	0	0	1	0	0	0	0	0	0	0	0	C_s
A ² p \bar{p}	IV	0	0	1	0	0	0	0	0	0	0	0	C_s
ABp \bar{p}	V	1	0	0	0	0	0	0	0	0	0	0	C_s

as an *RS*-permutation group that is isomorphic to the point group. By starting from the concept, we have further proposed the concepts of holantimers and stereoisograms. Thereby, we have proposed the concept of *RS*-stereogenicity, which is a more specific concept than the conventional stereogenicity. We have clarified that *RS*-stereogenicity is closely related to chirality. Five *RS*-stereogenicity types are defined and examined in detail to discuss the difference between

stereogenicity and chirality. Combinatorial enumerations on the action of an *RS*-permutation group have been also studied by considering *RS*-stereogenicity.

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