JOC Article

Stereogenicity Revisited. Proposal of Holantimers for Comprehending the Relationship between Stereogenicity and Chirality

Shinsaku Fujita

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

fujitas@chem.kit.ac.jp

Received December 30, 2003

The close relationship between stereogenicity and chirality has frequently caused serious confusion in the stereochemistry of organic molecules and inorganic complexes. To clarify the entangled relationship between them, we have proposed the concept of "holantimer". In addition, we have newly defined the concept of "stereoisogram" in order to correlate a set of stereoiomers based on holantimeric and enantiomeric relationships. These concepts have been applied to tetrahedral organic molecules as well as to square-planar inorganic complexes. The stereogenicity characterized by a stereoisogram has been called "*RS*-stereogenicity", which has been clarified to be a property that should be correlated to chirality. The stereoisograms of tetrahedral molecules have been examined and classified into five types, i.e., type I (chiral/*RS*-stereogenic), type II (chiral/*RS*-astereogenic), type III (chiral/*RS*-stereogenic), type IV (achiral/*RS*-astereogenic), and type V (achiral/*RS*-stereogenic), where *RS* descriptors are concluded to be specified in cases of types I, III, and V. On the other hand, the stereoisograms of square-planar complexes have been classified to two types, i.e., type II and type IV. As a result, the confusion on the *RS*-nomenclature has been concluded to appear within the *RS*-stereogenic relationships. Such a new viewpoint of stereogenicity and chirality as described in the present paper provides us with a methodology for restructuring stereochemistry.

1. Introduction

Organic and inorganic stereochemistry have been based on a common theoretical standpoint in which they are based on polyhedral and polygonal models. Thus, a tetrahedral model proposed by van't Hoff for organic stereochemistry[1] and octahedral and square-planar models proposed by Werner for inorganic stereochemistry[2] have been used to comprehend the stereochemistries of organic and inorganic compounds, as summarized in textbooks on organic[3] and inorganic stereochemistry.[4] Several stereochemical discussions have appeared with respect to thetrahedral, octahedral, and square-planar models.[5,6] Unfortunately, however, the common theoretical standpoint has not been fully investigated as follows despite numerous investigations on the distinct fields of stereochemistry.[3,4]

1. In organic stereochemistry, for instance, an enantiomeric pair of chiral tetrahedral molecules (**1** and **2**) have been discriminated by the *RS*-nomenclature proposed by Cahn, Ingold, and Prelog.[7] In inorganic chemistry, on the other hand, a diastereomeric pair of achiral square-planar complexes (**3** and **4**) has been characterized by another nomenclature proposed by Brown, Cook, and Sloan.[8,9] These two cases of ligancy 4 (Figure 1) have been discussed rather separately, because they belong to distinct disciplines of chemistry (organic and inorganic).

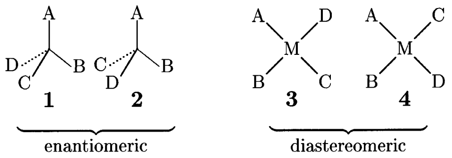


FIGURE 1. ABCD molecules of ligancy 4. The symbols A−D represent atoms or achiral ligands. The symbol M denotes a metal ion.

2. When we take chiral ligands into consideration, we encounter additional complicated cases, as shown in Figure 2. Thus, a diastereomeric pair of achiral tetrahedral molecules (**5** and **6**) in organic chemistry have been discriminated by the *RS*-nomenclature,[7] whereas an enantiomeric pair of chiral square-planar complexes (**7** and **8**) in inorganic chemistry has not been characterized

---

(1) van't Hoff, J. H. *Arch. Néerl. Sci. Exactes Nat.* **1874**, *9*, 445−454.

(2) Werner, A. *Anorg. Chem.* **1893**, *3*, 267.

(3) Eliel, E.; Wilen, S. H. *Stereochemisty of Organic Compounds*; John Wiley & Sons: New York, 1994.

(4) von Zelewsky, A. *Stereochemistry of Coordination Compounds*; John Wiley & Sons: Chichester, 1996.

(5) Mislow, K.; Siegel, J. *J. Am. Chem. Soc.* **1984**, *106*, 3319−3328.

(6) Mestroni, G.; Alessio, E.; Zassinovich, G.; Marzilli, L. G. *Comments Inorg. Chem.* **1991**, *12*, 67−91.

(7) Cahn, R. S.; Ingold, C. K.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 385.

(8) Brown, M. F.; Cook, B. R.; Sloan, T. E. *Inorg. Chem.* **1975**, *14*, 1273−1278.

(9) IUPAC *Nomenclature of Inorganic Chemistry, Recomendations 1990*; Blackwell Scientific: Oxford, 1990.

10.1021/jo030393v CCC: $27.50

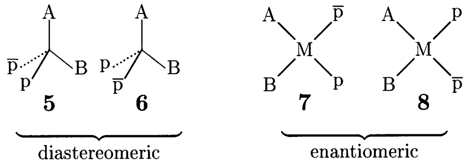


FIGURE 2. ABp$\bar{\mathrm{p}}$ molecules of ligancy 4. The symbols p and $\bar{\mathrm{p}}$ represent chiral ligands with opposite chirality.

by the *RS*-nomenclature. The additional two cases of ligancy 4 (Figure 2) have also been discussed rather separately.

3. Although the *RS*-nomenclature of stereochemistry has been originally proposed to characterize the chirality in organic stereochemistry,[7] the achiral case of **5** and **6** has indicated that the *RS*-nomenclature does not designate the chirality of molecules. Later, the *RS*-nomenclature has been clarified to designate the stereogenicity,[5] so that the *RS*-nomenclature has been revised to characterize the stereogenicity in organic stereochemistry.[10] Difficulties and confusion caused by infelicitous stereochemical nomenclature such as the conceptual change of the RS-nomenclature have been discussed in detail.[11,12] However, the relationship between the chirality and the stereogenicity has not been so clarified that there exist rather vague descriptions with respect to how the chirality or the stereogenicity is related to the *RS*-nomenclature.

4. Since enantiomeric relationships have been defined rigorously by geometrical consideration, the enantiomeric pair of **1** and **2** in Figure 1 can be recognized to be parallel with that of **7** and **8** in Figure 2. On the other hand, diastereomeric relationships have been defined subsidiarily as "other stereochemical relationships than enantiomeric relationships", as discussed in a textbook[3] and in a recent review.[12] As a result, it requires some troublesome efforts to recognize whether the diastereomeric relationship between **3** and **4** in Figure 1 is different or not from the diastereomeric one between **5** and **6** in Figure 2.

5. The diastereomeric relationships described above seem to be related to the permutability of ligands.[13] Thus, the permutation between the C and the D in **3** produces the corresponding diastereomer **4**, while the permutation between the p and the $\bar{\mathrm{p}}$ in **5** also produces the corresponding diastereomer **6**. However, the enantiomeric relationship between **1** and **2** (Figure 1) or between **7** and **8** (Figure 2) can be ascribed to the same permutabilities.

To answer such problems as enumerated above, the common theoretical standpoint should be investigated more intimately. We have studied the tetrahedral model[14] and the square-planar model,[15] where the chirality and the prochirality of derivatives based on the models have been theoretically characterized in combination with their stereogenicity and prostereogenicity. Although we have reported a more intuitive discussion[16] along with comprehensive group-theoretical discussions[17,18] with respect to the chirality/prochirality, we have reported only a rather mathematical approach to the stereogenicity/prostereogenicity.[19] Hence, another intuitive discussion on the stereogenicity/prostereogenicity is desirable to obtain the entire prospect to stereochemistry. In addition, this disussion should be applied to both organic stereochemistry and inorganic one. To pursue these purposes, we will propose the concepts of *holantimers* and *stereoisograms*, which are capable of dealing with both chirality and stereogenicity.

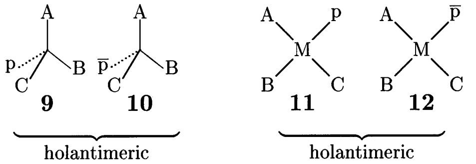


FIGURE 3. Holantimeric molecules with ABCp and ABC$\bar{\mathrm{p}}$. The symbols A−C represent atoms or achiral ligands, and the symbols p and $\bar{\mathrm{p}}$ represent chiral ligands with opposite chirality.

2. Definitions

2.1. Holantimers. Two molecules are defined as being enantiomeric if the one molecule is the nonsuperimposable mirror image of the other. When a molecule is regarded as a skeleton with ligands, its mirror image comprises the corresponding mirror skeleton and the corresponding ligands of opposite chirality.

On the other hand, two molecules based on the same skeleton are defined as being *holantimeric* if the chirality of each ligand in the one molecule is changed into the opposite one to give the other molecule based on that same skeleton.[20] They are called *holantimers* with each other. For example, the pair of **9** and **10** in Figure 3 is in a holantimeric relationship on the basis of a tetrahedral skeleton. Note that the achiral ligands (A−C) in **9** are converted into themselves in **10** and that the chiral ligand (p) in **9** is converted into $\bar{\mathrm{p}}$ of opposite chirality in **10**.

Although we have proposed the concepts of promolecules nd proligands,[21,22] we here use the terms "molecules" and "ligands" for the sake of simplicity, as long as they cause no confusion. It should be noted that a

---

[10] Prelog, V.; Helmchen, G. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 567−583.

[11] Eliel, E. L. *Chirality* **1997**, *9*, 428−430.

[12] Mislow, K. *Chirality* **2002**, *14*, 126−134.

[13] Prelog, V. *Science* **1976**, *193*, 17−24.

[14] Fujita, S. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 1585−1603.

[15] Fujita, S. *Helv. Chim. Acta* **2002**, *85*, 2440−2457.

[16] Fujita, S. *J. Org. Chem.* **2002**, *67*, 6055−6063.

[17] Fujita, S. *J. Am. Chem. Soc.* **1990**, *112*, 3390−3397.

[18] Fujita, S. *Symmetry and Combinatorial Enumeration in Chemistry*; Springer-Verlag: Berlin-Heidelberg, 1991.

[19] Fujita, S. J. *Math. Chem.* **2003**, *33*, 113−143.

[20] The terms "holantimer" and "holantimeric" are coined by Greek words "holo" and "anti", where the "holo" or "hol" represents "whole" and "entire" and the "anti" represents "opposite to". It should be noted that each ligand may be achiral, where the resulting ligand is superimposable to the original one.

[21] Fujita, S. *Tetrahedron* **1991**, *47*, 31−46.

[22] A proligand has been defined as a structureless object that has chirality or achirality.[18] Thereby, a promolecule has been defined as a skeleton whose substitution positions are occupied by a set of proligands. Without the concepts of proligands and promolecues, the symmetry of a molecule is sometimes restricted by the substitution of ligands. For example, pentaerythritol (C(CH$_2$OH)$_4$) belongs to the D_{2d} point group in its highest attainable symmetry, because the C_s symmetry of the ligand CH$_2$OH eventually restricts the T_d of the tetrahedral skeleton into the D_{2d} of the molecule, while tetramethylmethane (C(CH$_3$)$_4$) belongs to T_d in its highet attainable symmetry. On the other hand, the ligand CH$_2$OH in pentaerithritol or CH$_3$ in tetramethylmethane is replaced by a proligand A, the rees not undergo such an eventual restriction as described above.

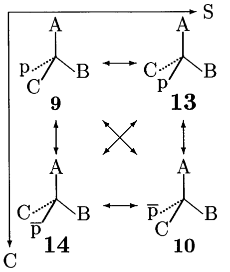


FIGURE 4. Stereoisogram for tetrahedral molecules with ABCp and ABC$\bar{p}$.

molecule can be occasionally superimposed onto the corresponding holantimer in a similar way to cases in which a molecule can be superimposed onto the corresponding enantiomer if it is achiral.

The pair of **11** and **12** in Figure 3 exhibits a holantimeric relationship on the basis of a square-planar skeleton.

2.2. Stereoisograms. To discuss the relationship between chirality and stereogenicity, we define a *stereoisogram* on the basis of enantiomers and holantimers, as exemplified in Figure 4.[23] First, the pair of holantimers (**9** and **10**) shown in Figure 3 are located on the diagonal places of Figure 4. Then, below the formula (**9**), its enantiomer (**14**) is drawn in the first column, while the enantiomer (**13**) of **10** is drawn upward in the second column. Obviously, the pair of **13** and **14** is also in a holantimeric relationship. The relationship between the two molecules in each column (the pair of **9**/**14**; or the pair of **10**/**13**) is enantiomeric. Thereby, the vertical axis is related to chirality, as designated by the symbol C. Each of the vertical pairs is linked with a vertical double-headed arrow, when it represents an enantiomeric pair. If it contains homomers (the same molecules), the homomers of the pair are linked with a vertical equality symbol.

On the other hand, the relationship between the two compounds in each row (the pair of **9**/**13** or the pair of **10**/**14**) is diastereomeric. As a result, the horizontal axis is found to be related to stereogenicity, as designated by the symbol S. Each of the horizontal pairs is linked with a horizontal double-headed arrow, when it represents a diastereomeric pair. If it contains homomers, the homomers of the pair are linked with a horizontal equality symbol.

Strictly speaking, the horizontal diastereomeric relationship appearing in each stereoisogram is concerned with the *RS*-nomenclature. Since there exist other types of diastereomeric relationships, the present stereogenicity should be called “*RS*-stereogenicity”. This point will be discussed later in the present article.

A similar stereoisogram for square-planar molecules can be drawn by starting from the pair of holantimers (**11** and **12**), as shown in Figure 5. Since the two molecules of each horizontal pair (the pair of **11** and **15** or the pair of **16** and **12**) are homomeric, they are linked with an equality symbol.

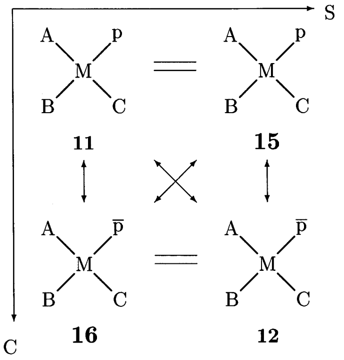


FIGURE 5. Stereoisogram for square-planar complexes with ABCp and ABC$\bar{p}$.

3. Tetrahedral Molecules

3.1. *RS*-Stereogenicty Types. Tetrahedral molecules with various substitution patterns have been enumerated with respect to their molecular formulas and to their point-group symmetries.[21] They have been classified in terms of permutation-group symmetries in addition to the point-group symmetries.[14] By means of the present approach based on the concepts of holantimers and stereoisograms, all the enumerated tetrahedral molecules are examined so as to reveal that their stereoisograms can be classified into five types (types I−V) shown in Figure 6. The types are called “*RS*-stereogenicity types”, since each of them is relevant to whether it can be specified by the *RS*-nomenclature or not. Thus, a pair (or set) of *RS*-stereogenic molecules should be differentiated in terms of the *RS*-nomenclature.

Types I −III (Figure 6) are concerned with chiral molecules, where each stereoisogram contains vertical double-headed arrows for representing enantiomeric pairs.

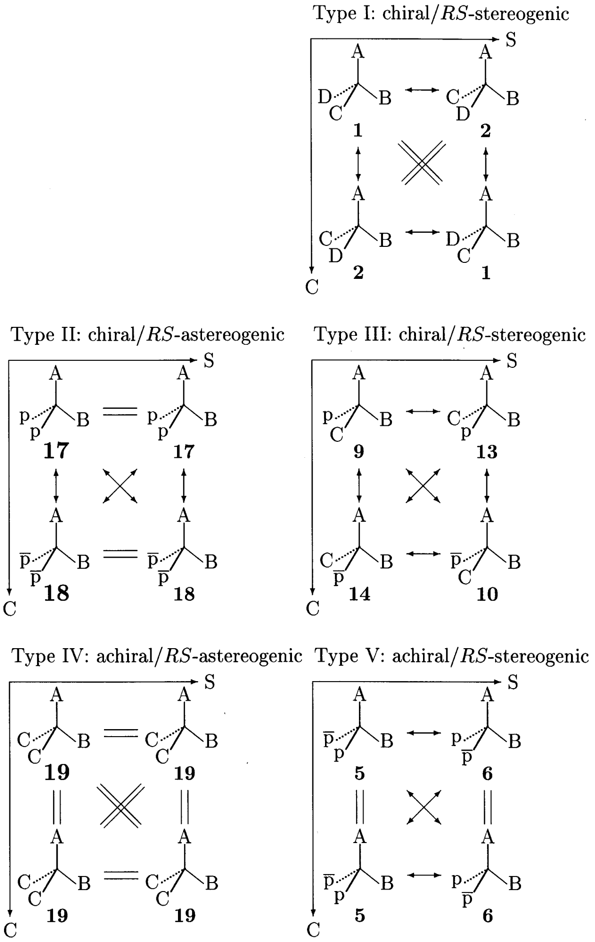
1. Type I: This type is characterized by the fact that each pair of chiral holantimers contains homomers, as shown by a diagonal equality symbol. Each column contains a pair of enantiomers (**1** and **2**). Each row also contains a pair of enantiomers (**1** and **2**).[24]
2. Type II: This type is characterized by the fact that each pair of chiral diastereomers contains homomers, as shown by a horizontal equality symbol. This means that Type II is *RS*-astereogenic.[25] Each column contains a pair of enantiomers (**17** and **18**). As a result, the holantimeric relationship of type II is superposable upon the enantiomeric relationship.
3. Type III: This type has been already explained in Figure 4 and is characterized by the fact that all of the relevant stereoisomers are different from each other. Thus, the enantiomers of each pair are different from each other, as shown by a vertical double-headed arrow.

---

(23) The term “stereoisogram” is coined by combining the words “stereoisomer” and “isogram” of Greek origin in order to designate a quartet of stereoisomers for clarifying the relationship between chirality and stereogenicity.

(24) Strictly speaking, the pair of enantiomers (**1** and **2**) in each row can be regarded as being diastereomeric from the viewpoint of *RS*-stereogenicity. In other words, the enantiomeric relationship and the diastereomeric one occasionally overlap each other in type I.

(25) The term “astereogenic” is used in place of the term “nonstereogenic”, though the latter has been used rather commonly. The usage of the former term is to emphasize that the present approach based on group theory[19] has rigorously defined “stereogenic groups” and “astereogenic groups”, which have not been involved in the conventional usage of the term “nonstereogenic”. The terms “*RS*-stereogenic” and “*RS*-astereogenic” are coined here to differentiate them from the terms “stereogenic/astereogenic”.



Type I: chiral/*RS*-stereogenic

Type II: chiral/*RS*-astereogenic

Type III: chiral/*RS*-stereogenic

Type IV: achiral/*RS*-astereogenic

Type V: achiral/*RS*-stereogenic

FIGURE 6. Stereoisograms of five types for tetrahedral molecules.

The holantimers of each pair are different to each other, as shown by a diagonal double-headed arrow. Each horizontal double-headed arrow represents two different diastereomers, which indicate *RS*-stereogenicity.

Types IV and V (Figure 6) are concerned with achiral molecules, where each stereoisogram contains vertical equality symbols for representing their achirality.

1. Type IV: This type is characterized by the fact that all of the relevant stereoisomers are the same so that all the relationships in this stereoisogram are represented by equality symbols. It follows that this type coresponds to an achiral and *RS*-astereogenic case.

2. Type V: This type is characterized by the fact that the achiral holantimers of each pair are different, as shown by a diagonal double-headed arrow. Each horizontal double-headed arrow represents two different diastereomers, which indicate *RS*-stereogenicity. It should be emphasized that there exist only the five types described above, if the local stereogenicity at the reference atom is equal to the global stereogenicity of the molecule. This point will be discussed in detail in the Scope and Limitations.

3.2. *RS*-Nomenclature Revisited. Among the five *RS*-stereogenicity types listed in Figure 6, types I, III, and V should be mentioned to clarify the methodology supporting the *RS*-nomenclature.

1. Type I can be specified by the *RS*-nomenclature. If the priority of ligands are presumed to be $A > B > C > D$, the chiral molecule (**1**) is specified to be *R*, while the chiral molecule (**2**) is specified to be *S*. The stereoisogram of type I (Figure 6) indicates that the *RS* corresponds to the diastereomeric relationship (S-axis) superposed onto the enantiomeric one (C-axis).[24] It should be emphasized that this conclusion is to discuss type I in the conceptually same line as types III and V. Thus, the permutation between C and D in **1** of type I (to produce **2** on the S-axis) is the same as the permutation between C and p in **9** of type III (to produce **13** on the S-axis) or the permutation between p and $\bar{p}$ in **5** of type V (to produce **6** on the S-axis).

2. Type III can also be specified by the *RS*-nomenclature. Thus, the chiral molecule (**9**) is specified to be *R*, while the chiral molecule (**13**) is specified to be *S*, if the priority of ligands are presumed to be $A > B > C > p$. The stereoisogram of type III (Figure 6) indicates that the *RS* corresponds to the diastereomeric relationship (S-axis), which is different from the enantiomeric relationship (C-axis related to **9** vs **14**). Strictly speaking, **9** of the formula ABCp should be compared with **13** of the same formula ABCp, but not with **14** of the different formula ABC$\bar{p}$.

3. Type V corresponds to so-called pseudoasymmetric molecules. Although the molecules (**5** and **6**) are achiral, they can also be specified by the *RS*-nomenclature. Thus, the achiral molecules (**5** and **6**) are specified to be *R* and *S*, respectively, if the priority of ligands are presumed to be $A > B > p > \bar{p}$. The stereoisogram of type V (Figure 6) indicates that the *RS* corresponds to the diastereomeric relationship (S-axis), which is represented by the horizontal double-headed arrow.

By the inspection of the stereoisograms for types I, III, and V, the *RS*-nomenclature is found to be based on the *RS*-stereogenicity, which is represented by a horizontal double-headed arrow appearing in each S-axis. It should be emphasized that RS descriptors should be specified in cases of types I, III, and V because of their *RS*-stereogenic nature.

Obviously, the comparison between the stereoisogram of type V and those of types I and III (especially their C-axes) indicates that the *RS*-nomenclature does not correspond to the chirality. Although type V is designated by a lowercase letter (*r* or *s*) in place of the corresponding uppercase one (*R* or *S*), the *RS*-nomenclature for type V conceptually has the same meaning as types I and III.

As found easily, the three items enumerated above are concerned with representative confusion on the *RS*-nomenclature. The *RS*-nomenclature for types III and V specifies conventional diastereomeric relationships though they are different in their chirality and achirality. Along the same line, even the *RS*-nomenclature for type I is concluded to specify a diastereomeric relationship that is eventually superposed onto an enantiomeric relationship. Thus, the present formulation enables us to conclude that the confusion has appeared within the *RS*-stereogenic relationships understandable by the concepts of holantimers and stereoisograms.

3.3. Classification of Tetrahedral Molecules. The *RS*-stereogenicity types of tetrahedral molecules are collected in Figure 7 in addition to their point groups. Note that an appropriate enantiomer is depicted for each enantiomeric pair of chiral molecules.

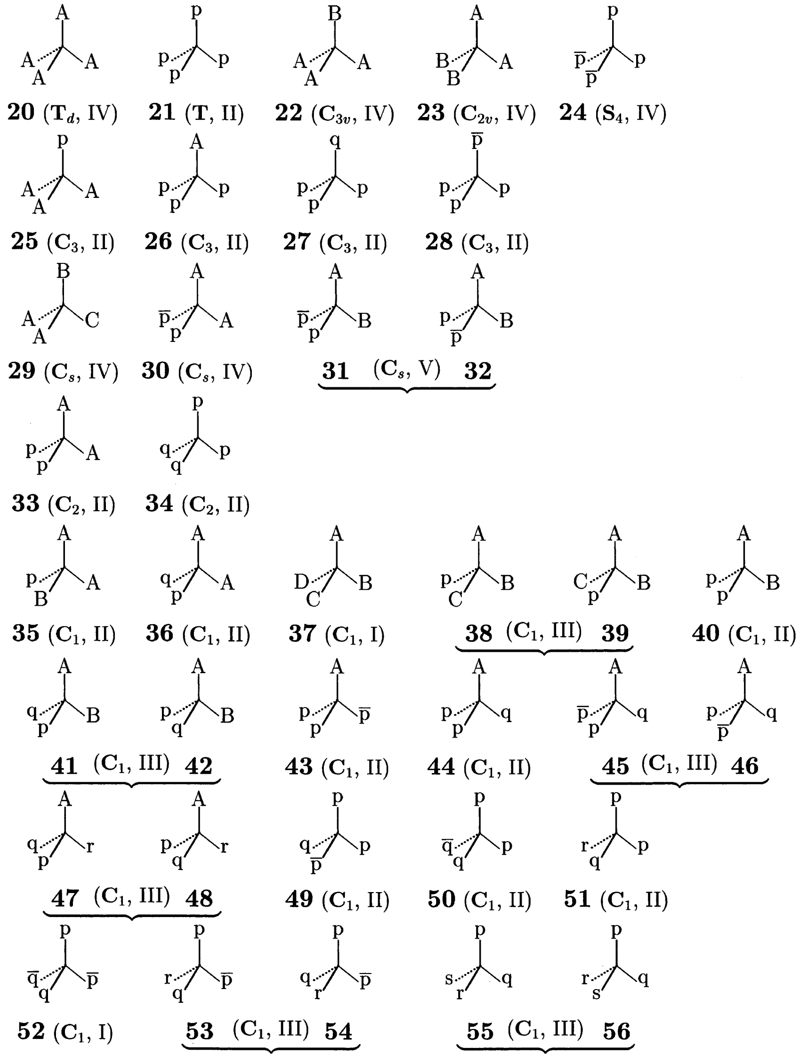


FIGURE 7. Point groups and *RS*-stereogenicity types (types I−V) for tetrahedral molecules. The symbols A−D represent atoms or achiral ligands. The symbols p, q, r, and s represents chiral ligands, while each symbol with an overbar represents the corresponding chiral ligand with the opposite chirality.

Let us first examine Figure 7 to comprehend the *RS*-stereogenicity described above:

1. Among the tetrahedral molecules collected in Figure 7, the C_1-molecule (**52**) belongs to type I in addition to **37** (= **1**) described in Figure 6.

2. As for tetrahedral molecules of type III, we can find six diastereomeric pairs, i.e., **38** (= **9**) and **39** (= **13**); **41** and **42**; **45** and **46**; **47** and **48**; **53** and **54**; and **55** and **56**. Each of the pairs is designated by an underbrace, since it is characterized by a single stereoisogram. Among the six cases, the first one has been discussed in Figures 4 and 6.

3. As type V, the diastereomeric pair of **31** (= **5**) and **32** (= **6**) is found to be only one example. This case has been already discussed in Figures 2 and 6.

Let us next examine Figure 7 to find *RS*-astereogenic molecules:

1. Chiral molecules belonging to T, C_3, and C_2 are classified as type II. Among C_1-molecules collected in Figure 7, molecules containing A^2 or p^2 are classified to type II.

2. Achiral molecules belonging to T_d, C_{3v}, C_{2v}, and S_4 are classified to type IV. Among C_s-molecules collected in Figure 7, molecules containing A^2 are classified to type IV.

3.4. Scope and Limitations. This section is devoted to the application of the present approach to various stereochemical problems that have been discussed otherwise by several authors.[5,11,12]

3.4.1. *RS*-Stereogenicity and Diastereomers. Let us now consider the isomers of 2,3,4-trihydroxyglutaric acid (Figure 8), where the carbon atom at the 3-position is taken account of. The enantiomeric pair of **57** and **58** can be ascribed to the promolecule of the ABp^2 (and $AB\bar{p}^2$), when we place p = *R*-CH(OH)COOH, $\bar{p}$ = *S*-CH(OH)COOH, A = OH, and B = H, as surrounded by ovals. According to the criterion described in Figure 6, the pair belongs to type II, which is chiral and astereogenic. The astereogenic nature is concerned with the reference atom (i.e., the carbon atom at the 3-position).

On the other hand, the diastereomeric pair of **59** and **60** can be ascribed to the promolecules of the $ABp\bar{p}$, which belong to type V according to the criterion described in Figure 6. Hence, **59** (or **60**) is achiral and stereogenic with respect to the 3-carbon atom. Note that the achirality and the stereogenicity are regarded as local properties around

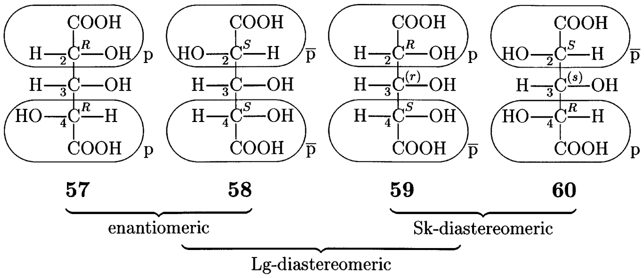


FIGURE 8. Enantiomers of chiral 2,3,4-trihydroxyglutaric acid and diastereomeric achiral 2,3,4-trihydroxyglutaric acids.

the 3-carbon atom. Since the symmetry around the 3-carbon atom is identical with the whole molecular symmetry of **59** (or **60**) in this case, the achirality is concluded to be concerned with the whole molecule.

In terms of the conventional stereochemistry, the enantiomeric pair (**57** and **58**) and the diastereomeric pair (**59** and **60**) are diastereomeric to each other, since stereoisomeric relationships other than enantiomeric ones have been defined to be diastereomeric. It should be noted here that the relationship between the enantiomeric pair and the diastereomeric pair is not specified by means of the criterion based on Figure 6. This means that there are at least two kinds of diastereomeric relationships: the one can be specified by type III or V (Figure 6) as exemplified by the pair **59** and **60** and the other cannot be specified by the criterion of Figure 6, as exemplified by the relationship between the first pair (**57** and **58**) and the second pair (**59** and **60**) listed in Figure 8. The former one is referred to as a "skeleton-based diastereomeric relationship" or an "Sk-diastereomeric" relationship. The latter one is called a "ligand-based diastereomeric" or simply an "Lg-diastereomeric" relationship, which can be recognized as being stereoisomeric by equalizing p and $\bar{p}$.

3.4.2. Local and Global Stereogenicities. As discussed in the preceding paragraphs (cf. Figure 8), Sk-diastereomeric relationships and Lg-diastereomeric ones are concerned with cases in which the two holantimers of each pair are both achiral or both chiral (cf. Figure 6). These cases are related to cases in which the local stereogenicity around the reference atom is identical with the global stereogenicity. When the local stereogenicity is different from the global one, each pair of holantimers can contains a chiral molecule and an achiral one.

Chiral and Achiral 2,3,4-Trihydroxyglutaric Acids. Let us consider the 2-carbon in each isomer of the chiral 2,3,4-trihydroxyglutaric acids, as shown in the left stereoisogram of Figure 9, where the segment surrounded by an oval is considered to be a chiral ligand p or $\bar{p}$. The shift of the reference atom to be considered results in another viewpoint that characterizes the chiral molecule **57**, which is regarded as a molecule of ABCp (A = OH, B = COOH, C = H, p shown by the oval). As a result, the holantimer of the chiral molecule **57** is an achiral molecule **59**. It should be noted that the shift of the reference atom means that the resulting *RS*-nomenclature is concerned with the local stereogenicity at the 2-carbon atom.

The S-axis of this stereoisogram (the left of Figure 9) corresponds to the *RS*-nomenclature around the 2-carbon atom. Thus, if we presume that the permutability specifies the *R* or *S*, the *RS*-nomenclature for the 2-carbon atom is concluded to be based on the pair of the chiral molecule (**57**) and the achiral one (**59**). In other words, it by no means specifies the enantiomeric relationship between **57** and **58**, which is represented by the C-axis of the stereoisogram in the left of Figure 9.

It should be noted, however, that the sequence priority of $\bar{p}$ in **58** (OH > COOH > $\bar{p}$ > H) is the same as the sequence priority of p in **59** (OH > COOH > p > H). This is the reason that *R* or *S* determined for the pair of **57** and **59** can be used effectively to determine the pair of **57** and **58**.

Let us next consider the 4-carbon as a reference atom in each isomer, as shown in the right stereoisogram of Figure 9, where the segment surrounded by an oval is considered to be a chiral ligand p or $\bar{p}$. Note that the symbols p and $\bar{p}$ represent different meanings from the left stereoisogram. As a result, the chiral molecule **57**, which is regarded as a molecule of ABCp (A = OH, B = COOH, C = H, p shown by the oval), gives the corresponding an achiral holantimer **60**.

The S-axis of this stereoisogram (the right of Figure 9) corresponds to the *RS*-nomenclature around the 4-carbon atom. The permutability at the 4-carbon atom specifies the *RS*-nomenclature with respect to the pair of the chiral molecule (**57**) and the achiral one (**60**). Again, it by no means specifies the enantiomeric relationship between **57** and **58**, which is represented by the C-axis of the stereoisogram in the right of Figure 9.

Chiral and Achiral Tartaric Acids. The concept of global/local stereogenicities can be applied to the stereochemistry of tartaric acids (Figure 10), where chiral tartaric acids are represented by p−p and $\bar{p}$−$\bar{p}$; and achiral tartaric acid is represented by p−$\bar{p}$. This viewpoint implies that the two positions of a stick-like skeleton are occupied with two ligands. Although the central reference atom does not exist in the skeleton, any molecules based on the skeleton are concluded to be astereogenic.

This conclusion can be confirmed by using the concept of holantimers and stereoisograms, as shown in Figure 11. Since the holantimer of p−p is represented by $\bar{p}$−$\bar{p}$, the corresponding stereoisogram is obtained, as shown in the left of Figure 11. This is one of the chiral/*RS*-astereogenic cases. The stereoisogram for p−$\bar{p}$ shown in the right of Figure 11 indicates that this is one of achiral/*RS*-astereogenic cases. It should be noted that these conclusions are not concerned with the local stereogenicity relevant to p or $\bar{p}$ itself. All molecules based on the stick-like skeleton can ben classified into type IV (e.g., A−B, A−A, and p−$\bar{p}$; achiral) and type II (e.g., A−p (A−$\bar{p}$), p−p ($\bar{p}$−$\bar{p}$), and p−q ($\bar{p}$−$\bar{q}$); chiral). They are all *RS*-astereogenic whether they are chiral or achiral (Figure 11).

The conventional way for determining *R* or *S* in each isomer of tartaric acid is accompanied with the shift of a reference atom. For example, let us select the 2-carbon atom of a chiral tartaric acid as a reference atom, as found in **61** (Figure 12). When the segment encircled by an oval is regarded as p, the molecule **61** corresponds to ABCp (A = OH, B = COOH, C = H, p shown by the oval). As a result, the holantimer of the chiral molecule **61** is an achiral molecule **63**, which corresponds to ABC$\bar{p}$ (Figure 12).

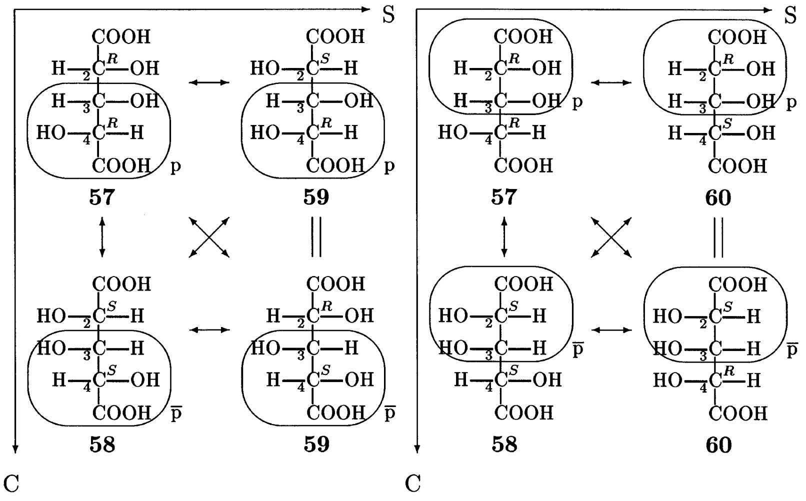


FIGURE 9. Stereoisograms of another type for chiral and achiral 2,3,4-trihydroxyglutaric acids.

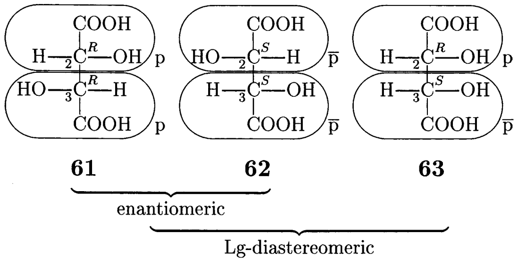


FIGURE 10. Enantiomeric tartaric acids and achiral tartaric acid.

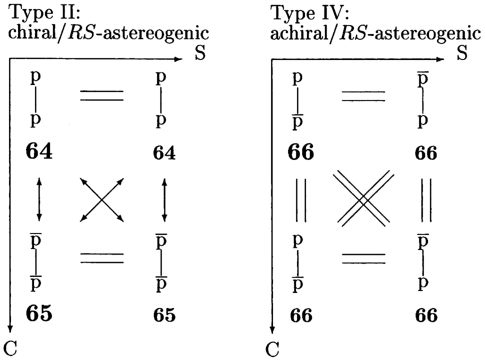


FIGURE 11. Stereoisograms of molecules of two-ligancy.

The *RS*-nomenclature around the 2-carbon atom corresponds to the S-axis of this stereoisogram (Figure 12), where it is based on the pair of the chiral molecule (**61**) and the achiral one (**63**). Again, it by no means specifies the enantiomeric relationship between **61** and **62**, which is represented by the C-axis of the stereoisogram in Figure 12.

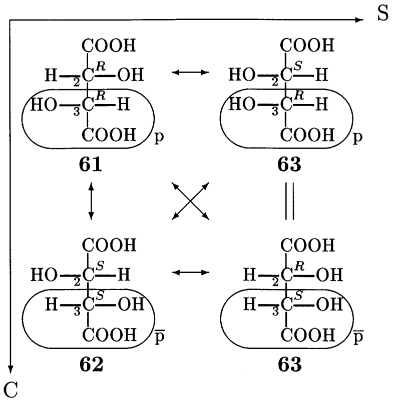


FIGURE 12. Stereoisograms of another type for chiral and achiral tartaric acids.

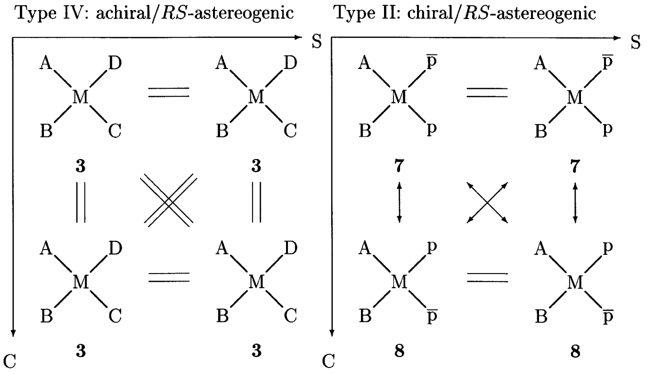


FIGURE 13. Stereoisograms of two types for square-planar complexes.

4. Square-Planar Complexes

Stereoisograms can be also drawn for square-planar complexes. For example, the complex **7** gives the corresponding holantimer **8** to generate the stereoisogram shown in the right of Figure 13. The *RS*-astereogenic character of each complex is designated by a horizontal equality symbol appearing in the S-axis. In the case of the complex **3**, all the participating molecules are identical with each other so as to show the *RS*-astereogenic character of the complex.

As found easily, any square-planar complex is concluded to be *RS*-astereogenic. Hence, they are not specified by the *RS*-nomenclature. Since any achiral square-planar complex is identical with its enantiomer as exemplified in the left of Figure 13, there are only two types of stereoisograms for square-planar complexes, i.e., achiral/*RS*-astereogenic ones (the left of Figure 13) and chiral/*RS*-astereogenic ones (the right of Figure 13).

It should be emphasized here that the concept of *RS*-stereogenicity is not equal to the concept of stereogenicity. The *RS*-stereogenicity has been defined above by using stereoisograms. The stereogenicity involves the *RS*-stereogenicity and other kinds of stereogenicity. For example, an *RS*-astereogenic complex **3** (Figure 13) is stereogenic, since it can produce **4** and other isomers by permutations (e.g., Figure 1). Another *RS*-astereogenic complex **7** (Figure 13) is stereogenic, since it can produce **8** and other isomers by permutations (e.g., Figure 2). To characterize such stereogenicity, point groups and permutation groups should be integrated. This point has been discussed elsewhere.[15]

5. Conclusions

The concept of holantimer has been proposed to discuss the relationship between stereogenicity and chirality. By means of this concept, a stereoisogram correlating stereoiomers has been defined and applied to tetrahedral organic molecules as well as to square-planar inorganic complexes. The stereogenicity characterized by a stereoisogram has been called "*RS*-stereogenicity", which is a property that should be correlated to chirality. The stereoisograms of tetrahedral molecules have been examined so that they can be classified into five types, i.e., type I (chiral/*RS*-stereogenic), type II (chiral/*RS*-astereogenic), type III (chiral/*RS*-stereogenic), type IV (achiral/*RS*-astereogenic), and type V (achiral/*RS*-stereogenic). On the other hand, the stereoisograms of square-planar complexes have been classified to two types, i.e., type II and type IV. RS descriptors are concluded to be specified in cases of types I, III, and V.

JO030393V