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STEREOGENICITY
BASED ON ORBITS GOVERNED BY COSET REPRESENTATIONS

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The chirality fittingness of orbits (homospheric, enantiospheric, and hemispheric) provides a new scheme of determining topicities (homotopic, enantiotopic, diastereotopic, and heterotopic). Thereby, transpositions of ligands on a skeleton are classified into four categories: homotopic, enantiotopic, diastereotopic, and heterotopic transpositions. The homotopic transpositions are concluded to be non-stereogenic. On the other hand, the other transpositions are proved to be stereogenic.

1 Introduction

Since the terminology in stereochemistry has been to a great extent empirically developed, it has not escaped some ambiguity. Thus, there have appeared many reviews for clarifying or getting rid of such ambiguity.[1]–[7] The term *stereogenic* was originally proposed by McCasland[8] in order to avoid confusions provided by so-called "asymmetric" and "pseudoasymmetric" carbon atoms. The term stereogenic has been utilized as a key concept in the revised CIP-system for describing chirality and related matters.[9] Later, Mislow and Siegel[10] have extended the definition of a stereogenic atom so as to manipulate a stereogenic element (unit); this is defined as an element (uint) bearing several groups of such nature that an interchange of two groups produces a stereoisomer. They also discussed the conceptual distinction between the stereogenicity and chirotopicity. The term stereogenic has been adopted by several authors[11] in place of the terms "asymmetric" and "chiral".

Recently, we discussed a molecular model as a combination of sets of equivalent atoms, faces or segments. Thus, each of the sets is called an orbit, which was clarified to be subject to a coset representation (CR).[12]–[17] This correspondence between the orbit and the CR afforded a foundation to the SCR notation (the notation based on subduced coset representations) for designating symmetrical properties of a molecule[18] as well as to chirality fittingness for specifying prochirality and local chirality.[19] In a continuation of this work, we here discuss the stereogenicity in terms of the chirality fittingness of an orbit.

2 Topicity Based On Chirality Fittingness of an Orbit

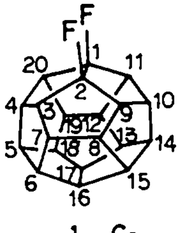
Terms concerning *topicity* were proposed by Mislow and Raban[20] and have been widely adopted in chemical and biochemical fields. These terms were classified by means of a flow chart based on pairwise relations.[21] We recently discussed a membership criterion for redefining the topicity.[19] In order to discuss the stereogenicity, we shall formulate the topicity in a stricter fashion.

Chirality fittingness of an orbit. In the previous papers,[18, 19] we consider a molecule of G symmetry to have an $\mathbf{G}(/\mathbf{G}_i)$ orbit that consists of a set of atoms, faces, or segments. The $\mathbf{G}(/\mathbf{G}_i)$ orbit is governed by the CR $\mathbf{G}(/\mathbf{G}_i)$ that is derived from a coset decomposition of $\mathbf{G}$ by $\mathbf{G}_i$. We have discussed three cases for such $\mathbf{G}(/\mathbf{G}_i)$ orbits: homospheric, enantiospheric and hemispheric. These three attributes of the orbits are called chirality fittingness.[19] Thus, when both $\mathbf{G}$ and $\mathbf{G}_i$ are achiral point groups, the $\mathbf{G}(/\mathbf{G}_i)$ orbit is defined as *homospheric*. If $\mathbf{G}$ is an achiral point group but $\mathbf{G}_i$ is a chiral point group, the $\mathbf{G}(/\mathbf{G}_i)$ orbit is defined as *enantiospheric*. When both $\mathbf{G}$ and $\mathbf{G}_i$ are chiral point groups, the $\mathbf{G}(/\mathbf{G}_i)$ orbit is defined as *hemispheric*.

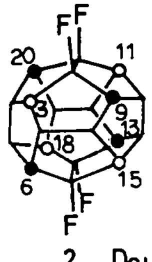
$$\begin{array}{l}\text{chirality fittingness}\\ \text{(sphericity)}\end{array} \left\{ \begin{array}{l}\text{homospheric}\\ \text{enantiospheric}\\ \text{hemispheric}\end{array}\right.$$

In the present paper, we regard a molecule as a three-dimensional object that consists of a skeleton and ligands,[22] where the substitution positions of the skeleton are replaced by the ligands. A set of equivalent positions in the skeleton is regarded as an orbit governed by a CR ($\mathbf{G}(/\mathbf{G}_i)$), where ligands on the orbit are subject to a whole symmetry ($\mathbf{G}$) and a local symmetry ($\mathbf{G}_i$) through the CR. It is dependent upon a problem at issue what part of the molecule is selected as a skeleton and what parts are regarded as ligands.

Let us work out 1,2-difluorododecahedrane (**1**).[23] The skeleton of this molecule is a dodecahedrane that has 20 substitution positions to be considered. The ligands are determined to be two fluorine atoms and 18 hydrogen atoms. This molecule belongs to $\mathbf{C}_{2v}$ symmetry, where the dodecahedrane skeleton and the ligands are now restricted to the $\mathbf{C}_{2v}$ symmetry.[24] By the action of the $\mathbf{C}_{2v}$ point group, these positions are divided into 7 orbits (Δ_1 to Δ_7).[25] For instance, the Δ_1 orbit ($\{1,2\}$) is subject to the CR ($\mathbf{C}_{2v}(/\mathbf{C}_s)$) and therefore determined to be homospheric.[26] The Δ_2 orbit consists of $\{3,11,9,20\}$ and is governed by CR ($\mathbf{C}_{2v}(/\mathbf{C}_1)$); hence, this orbit is enantiospheric. Table 1 summarizes such orbits appearing in **1** as well as their governing CRs and chirality fittingness.



1 C_{2v}



2 D_{2h}

Table 1: Orbits and coset representations in **1**

Orbit	Positions	Members (Ligands)	coset representation	Chirality fittingness (Sphericity)
Δ_1	$\{1,2\}$	F_2	$\mathbf{C}_{2v}(/\mathbf{C}_s)$	homospheric
Δ_2	$\{3,11;\ 9,20\}$	H_4	$\mathbf{C}_{2v}(/\mathbf{C}_1)$	enantiospheric
Δ_3	$\{4,10\}$	H_2	$\mathbf{C}_{2v}(/\mathbf{C}_s)$	homospheric
Δ_4	$\{7,12;\ 8,19\}$	H_4	$\mathbf{C}_{2v}(/\mathbf{C}_1)$	enantiospheric
Δ_5	$\{5,14\}$	H_2	$\mathbf{C}_{2v}(/\mathbf{C}_s)$	homospheric
Δ_6	$\{6,13;\ 15,18\}$	H_4	$\mathbf{C}_{2v}(/\mathbf{C}_1)$	enantiospheric
Δ_7	$\{16,17\}$	H_2	$\mathbf{C}_{2v}(/\mathbf{C}_s)$	homospheric

If we consider proper rotations only among the symmetry operations of an achiral point group $\mathbf{G}$, we have a chiral point group $\hat{\mathbf{G}}$, where $|\ \mathbf{G}\ | = 2\ |\ \hat{\mathbf{G}}\ |$. According to this restriction,[27] a homospheric orbit

($\mathbf{G}(/\mathbf{G}_i)$) is converted into a hemispheric orbit $\hat{\mathbf{G}}(/\hat{\mathbf{G}}_i)$, where the length of the former orbit is equal to that of the latter. This fact indicates that the homospheric orbit is superposed to itself by proper rotations as well as by improper rotations. On the other hand, the restriction divides an enantiospheric orbit into two hemisheric orbits $\hat{\mathbf{G}}(/\mathbf{G}_i)$, each length of which is one half of that of the original orbit. This fact means that the enantiospheric orbit can be divided into two halves,[28] which cannot be superposed to each other by proper rotations only, but can be interchanged with each other by improper rotations. For instance, the Δ_2 orbit of **1** can be divided into two halves, *i.e.* {3,11} and {9,20}, if we only take proper rotations into consideration. Such subdivisions are represented by a semicolon in each couple of braces, as shown in Table 1.

Definition of topicity. These discussions indicate that each position is characterized as a member of a homo-, enantio-, or hemi-spheric orbit. For some purposes, we further examine the membership of each position in either (left-handed or right-handed) half of an enantiospheric orbit. As a result, the present approach conceptually needs not introduce such terms as concerning "topicity", which refer to a relation between two positions. In other words, we can discuss such relations by characterizing the two positions as members of the same orbit or of different orbits. We can, for example, recognize the relationship among positions {3, 11, 9, and 20} without the topicity terms; thus, by indicating that they have the same membership in an enantiospheric orbit (Δ_2). However, the terms concerning topicity have long been used in organic chemistry and are so familar to organic chemists that we cannot now discontinue their usage. Hence, it is impartial as well as convenient to use the terms after the redefinition from the present point of view.

The term *homotopic* is defined as being the same membership of two positions (atoms, faces, or ligands) (1) in a homospheric orbit, (2) in either half of an enantiospheric orbit, or (3) in a hemispheric orbit.[29] For instance, the 5- and 14-positions of **1** are related to each other in a homotopic fashion by the first criterion, since they belong to the homospheric orbit (Δ_5) governed by $\mathbf{C}_{2v}(/\mathbf{C}_s)$. The 3- and 11-positions of **1** are homotopic by the second criterion, since they construct one half of the Δ_2 orbit that is enantiospheric because of the corresponding CR ($\mathbf{C}_{2v}(/\mathbf{C}_1)$).

The existence of three types of homotopicities comes from the actions of $\mathbf{G}$ and $\hat{\mathbf{G}}$ described above. If we restrict the symmetry of a $\mathbf{G}$ molecule to the $\hat{\mathbf{G}}$ symmetry, each orbit of the first type creates a single hemispheric orbit. For example, the $\mathbf{C}_{2v}(/\mathbf{C}_s)$ orbit (Δ_5) is restricted to a hemispheric orbit ($\mathbf{C}_2(/\mathbf{C}_1)$) under a $\mathbf{C}_2$ environment. Each half of an orbit of the second type also creates a single hemispheric orbit under the action of $\hat{\mathbf{G}}$. Remember that, under the restriction to $\mathbf{C}_2$ symmetry, each half of the $\mathbf{C}_{2v}(/\mathbf{C}_1)$ orbit (Δ_2) is converted into a hemispheric orbit governed by $\mathbf{C}_2(/\mathbf{C}_1)$, *i.e.* {3,11} or {9,20}. The third type of homotopicity is an obvious case. This common nature with respect to $\hat{\mathbf{G}}$ affords a basis to give such a common name as homotopic to these cases. It should be noted that the case (1) is different from the other two cases in the sense that two positions of the former relation (1) are superimposable by a proper rotation as well as an improper rotation; on the other hand two positions of the latter relation ((2) or (3)) are superimposable by a proper rotation but not any improper rotations.[30]

When one position is a member of one half of an enantiospheric orbit and the other position is a member of the other half, the relationship between the two positions is defined as *enantiotopic*. For instance, the relationships between the 3- and 9-positions of **1** as well as between the 3- and 20-positions are enantiotopic respectively.[31] We can also use this term to designate such two halves of an enantiospheric orbit. Thereby, a set of {3,11} is enantiotopic to another set of {9,20} in the Δ_2 orbit of the molecule (**1**).

The term *diastereotopic* is used to characterize a relation between two positions, where the one belongs to an appropriate orbit subject to a CR and the other position is a member of another orbit subject to the same CR. For example, the relationship between the 3- and 6-positions of **1** is diastereotopic, since the 3-position belongs to a $\mathbf{C}_{2v}(/\mathbf{C}_1)$ orbit (Δ_2) and the 6-position is a member of another $\mathbf{C}_{2v}(/\mathbf{C}_1)$ orbit (Δ_6). By extension, the Δ_2 orbit is diastereotopic to the Δ_6 orbit, because both of the orbits are governed by the same CR ($\mathbf{C}_{2v}(/\mathbf{C}_1)$).

In some cases, two orbits of a molecule in a diastereotopic relation can be meaningly related to each other, if the symmetry of the molecule is hypothetically converted into a higher one. In connection with **1**, for instance, consider 1,2,16,17-tetrafluorododecahedrane (**2**) of D_{2h} symmetry, in which 8 marked positions construct an orbit subject to CR $D_{2h}(/C_1)$. Since this orbit is enantiospheric, the 8 positions are divided into two halves (o and •), which are enantiotopic to each other. A hypothetical defluorination of **2** into **1** results in separation into two enantiospheric orbits (Δ_2 and Δ_6 in **1**). This example gives a sound foundation to the differentiation of a diastreotopic relation from a heterotopic relation described below.[32]

The term *heterotopic* is used to refer to the case that respective orbits involving two positions to be examined are different in their orbits and in their CRs. For example, the relationship between the 9- and 14-positions of **1** is heterotopic, since the former belongs to the $C_{2v}(/C_1)$ orbit (Δ_2) and the latter to the $C_{2v}(/C_s)$ orbit (Δ_5).

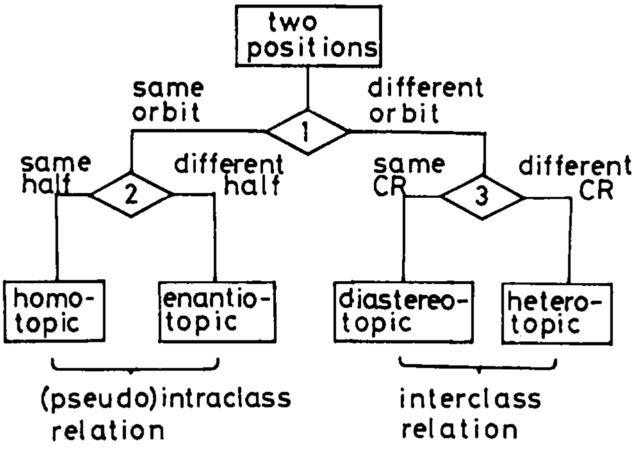


Figure 1: Flow chart for redefining topicity.

The questions for the respective decisions are as follows: (1) Do the two positions (or ligands) belong to the same orbit? (2) Do the two positions satisfy one of the three criteria for homotopicity? (The above figure depicts only the case of an enantiospheric orbit.) (3) Do the two positions belong to orbits governed by the same CR?

Intraclass and interclass relations. Figure 1 depicts the present scheme for redefining the topicity in the form of a flow chart. The decisions at the points 1 and 2 are strictly based on a membership criterion:[19] whether two positions have the same membership or not. However, the decision at the point 3 is slightly different. This difference of decisions can be explained by intoducing the concepts, (pseudo-)intraclass and interclass relations. We use the *intraclass* relation to refer to a relation that is concerned with two objects involved in the same equivalence class (orbit). The *interclass* relation is defined as a relation between two distinct equivalence classes. The *pseudo-intraclass* relation is refered to the case that is an intraclass relation from one point of view and can be regarded as an interclass relation from another point of view. Thereby, a homotopic relation is an intraclass relation, an enantiotopic one is a pseudo-intraclass relation, and the other relations are interclass relations.[33] An enantiotopic relation is concerned with two objects of an enantiospheric orbit, but at the same time indicates that the two objects are involved in the respective halves of the orbit.

This classification emphasizes our standpoint that places stress on equivalence classes (orbits) governed by coset representations. It should be noted that an intraclass and a pseudo-intraclass relation are self-contained. In other words, they can be regarded as equivalence relations from a mathematical point of view. On the other hand, an interclass relation denotes a relation without relationship. This means that such interclass relations cannot be regarded as equivalence relations. Previous confusions in stereochemistry to a large extent stem from convensions that these two (or three) types of relations have not been differentiated. Equivalence relations and the resulting equivalence classes are primary; hence the concept of chirality fittingness (sphericity) should be primarily taken into consideration. We should subsidiarily use the topicity terms, as defined by the sphericity terms.

3 Stereogenicity

We define a *stereogenic transposition on a skeleton* as an operation that interchanges two ligands so as to produce stereoisomers.[34] If such a transposition produces no stereoisomers, this operation is defined as *non-stereogenic*. A skeleton is referred to as being stereogenic if it involves at least one stereogenic transposition.[35] In other words, a stereogenic skeleton can underego non-stereogenic transpositions along with stereogenic ones. The present discussion focuses on (non-)stereogenic transformations, but not on stereogenic skeletons. For simplicity of discussion, we take no account of transpositions within a ligand. In addition, we tentatively suppose that a skeleton is rigid (or invariant) with respect to bond rotations.[36] In this section, we introduce several new concepts to clarify the stereogenicity.

Substitution equivalent. Consider 1,2-difluoro-3-hydroxydodecahedrane (**3**) as an example (Figure 2). We interchange the hydroxyl group at the 3-position and the hydrogen atom at the 6-postition. This transposition produces an isomer (**4**); hence, this is a stereogenic transposition.

In order to make clear the nature of this transformation, we introduce another formulation. Thus, the molecule (**3**) is regarded as a derivative produced by a substitution of a hydroxyl group at the 3-position of compound **1**, while **4** is derived by the OH-subsitution of **1** at the 6-position. This means that the transposition concerning **3** and **4** is equivalent to a set of the distinct substitution processes of the common intermediate (**1**), which we call a *a common skeleton*. We call the latter set of processes a *substitution equivalent* of the former transposition.

The symmetry of such common skeletons should be the same as or higher than those of original molecules. Among possible skeletons, we select a common skeleton of the highest symmetry. In this example, we replace the 3-OH of **3** (or the 6-OH of **4**) by a hydrogen atom. Then we regard the resulting 1,2-difluorododecahedrane (**1**) having 18 positions as a common skeleton of $\mathbf{C}_{2v}$ symmetry.[37]

An alternative selection is possible to yield a skeleton of lower symmetry. If we thus replace the 6-hydrogen of **3** by a hydroxyl group, we have another skeleton of $\mathbf{C}_1$ symmetry. This operation has the same effect as supposing that we distinguish the 3- and 6-positions from the other 16 positions of the common skeleton(**1**). We do not adopt this selection.

Taking account of such a substitution equivalent provides us with a convenient method of determining whether a transposition is stereogenic or not. The substitution equivalent is closely related to systematic enumerations by unit subduced cycle indices, where a derivative is produced by placing a set of ligands on the positions of a skeleton.[12]–[17] A pair of distinct replacements in the enumeration corresponds to a pair of molecules participating a transposition. Hence, we can determine stereogenicity by examining whether the pair of replacements in a substitution equivalent generate two distinct molecules or not.

Stereogenic transpositions. In accord with the topicities described in the preceding section, there are four types of transpositions; homotopic, enantiotopic, diasteretopic, and heterotopic transpositions. As shown below, these topicities are concerned with common skeletons, not with molecules to be examined.

The example illustrated in Figure 2 is a *diastereotopic transposition*. The 3- and 6-positions of the common skeleton (**1**) of $\mathbf{C}_{2v}$ symmetry belong to the respective $\mathbf{C}_{2v}(/\mathbf{C}_1)$ orbits (Δ_2 and Δ_6); that is, they are diastereotopic to each other. Hence, this transposition is a diastereotopic transposition. In general, a substitution equivalent for a diastereotopic transposition produces two distinct stereoisomers; hence this transposition is stereogenic.

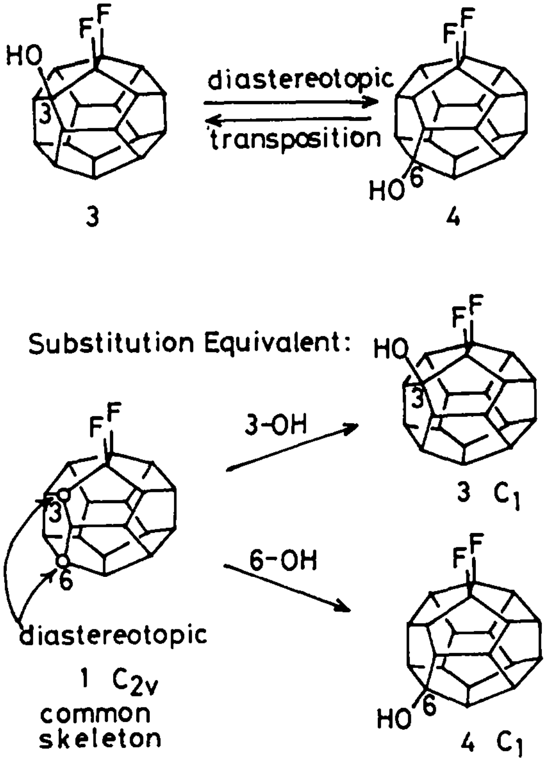


Figure 2: Substitution equivalent for a stereogenic transposition

The term diastereotopic is concerned with the common skeleton (**1**), not with the molecules (**3** and **4**). The 3-position of **1** is a member of a $C_{2v}(/C_1)$ orbit, i.e. $\Delta_2 = \{3,11;9,20\}$; the 6-position of **1** belongs to another $C_{2v}(/C_1)$ orbit, i.e. $\Delta_6 = \{6,13;15,16\}$.

A *heterotopic transposition* is illustrated by a conversion between **3** and **5** (Fig. 3). The former molecule (**3**) belongs to C_1 symmetry and the latter (**5**) has C_s symmetry. We can also select **1** as a common skeleton in this case, where we pay our attention to the 3- and 4-positions. The 3- and 4-positions of the common skeleton (**1**) are conclused to heterotopic, since the 3-position belongs to the $C_{2v}(/C_1)$ orbit (Δ_2), while the 4-position is involved in the $C_{2v}(/C_s)$ orbit (Δ_3). Obviously, a heterotopic transposition is in general stereogenic to produce an isoskeletal isomer.

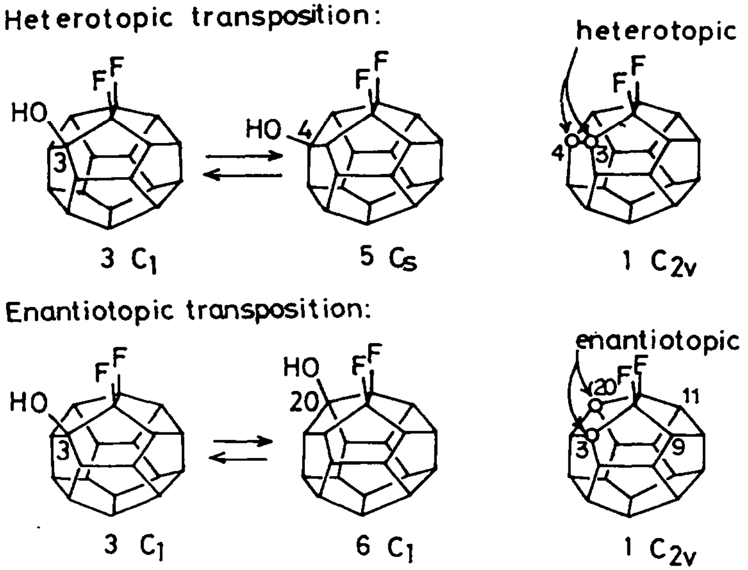


Figure 3: Heterotopic and enantiotopic transpositions as stereogenic ones

The rightmost figures depict a common skeleton appeared in substitution equivalents. The terms, heterotopic and enantiotopic, come from the common skeleton.

The interconversion between **3** and **6** (the enantiomer of **3**) is an *enantiotopic transposition*, since the positions 3 and 20 of the common skeleton (**1**) are enantiotopic to each other. In other words, these positions belong to the same $C_{2v}(/C_1)$ (Δ_2), but serapately occupy the respective halves of this orbit. Thereby, this process is stereogenic to produce a pair of enantiomers.

Non-stereogenic transpositions. Figure 4 depicts homotopic transpositions, all of which are non-stereogenic. Homotopic transpositions are subdivided into three categories in accordance with three types of homotopicities.

The molecule (**3**) is converted into **3a** by interchanging 3-OH and 11-H. The latter molecule (**3**) is superimposable to the former by a proper rotation (a C_2 operation). We use the term *homomeric* to denote this type of relation beween two molecules. In the light of this definition, we describe that this transposition is non-stereogenic, since it generates a homomer of the starting molecule. If we consider **1** as a common skeleton in the corresponding substitution equivalent, the 3- and 11-positions belong to one half of a enantiospheric orbit (Δ_2 in Table 1) and are homotopic in the light of the first criterion of the above definition. Hence, this transposition is a homotopic transposition.

The second type of homotopic transposition is exemplified by the conversion between **7** and its homomer (**7a**). In the corresponding common skeleton (**1**), the 5- and 14-positions are the members of a

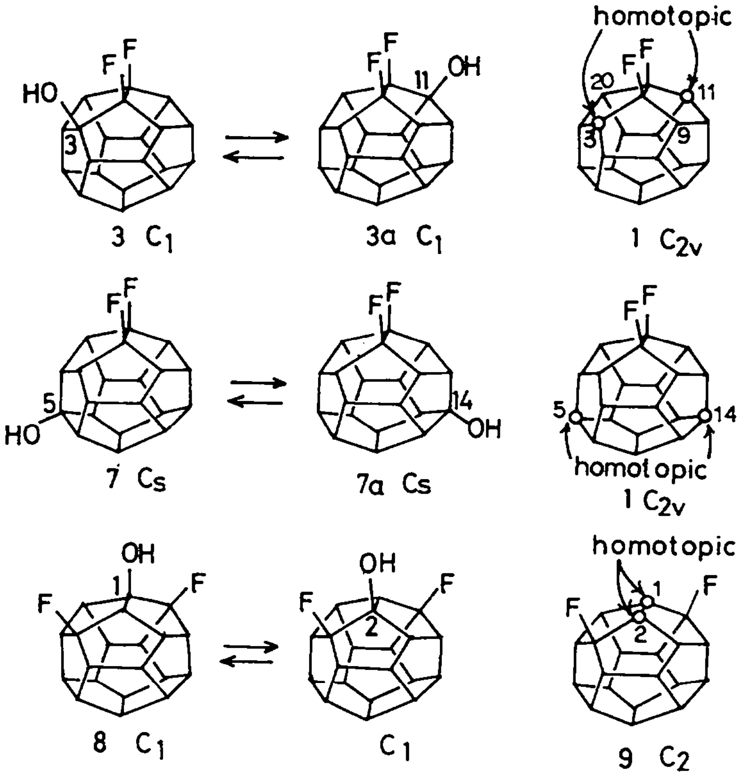


Figure 4: Homotopic transpositions as non-stereogenic ones

Note that $\Delta_2 = \{3,11;9,20\}$ is an enantiospheric orbit governed by $C_{2v}(/C_1)$ and $\Delta_5 = \{5,14\}$ is a homospheric orbit governed by $C_{2v}(/C_s)$ in the common skeleton (**1**). In the common skeleton (**9**), $\Delta_1 = \{1,2\}$ is a hemispheric orbit governed by $C_2(/C_1)$.

homospheric orbit (Δ_5 governed by $C_{2v}(/C_s)$), which are homotopic to each other by means of the second criterion of the definition. Hence, this process is homotopic transposition and non-stereogenic.

The interconversion between **8** and its homomer (**8a**) is one of the third-type homotopic transpositions, becuase the corresponding common skeleton is a C_2 molecule (**9**), in which the 1- and 2-positions construct hemispheric orbit governed by the CR $C_2(/C_1)$.

The occupation of one ligand on a homospheric orbit (or of one half of an enantiospheric orbit, or of a hemispheric orbit) in the common skeleton of a substitution equivalent can easily proved to produce a molecule that is homomeric to a molecule produced by another occupation of the ligand on the same orbit. In general, any homotopic transpositions produce homomers and hence the homotopic transposition is non-stereogenic. Because the present discussion is concerned with all possible cases, we end up with a simple theorem: *a homotopic transposition is non-stereogenic; the other types of transpositions are all stereogenic.*

$$\begin{array}{ll} \text{homotopic transposition} & \cdots\ \text{non-stereogenic} \\ \left.\begin{array}{l} \text{enantiotopic transposition} \\ \text{diastereotopic transposition} \\ \text{heterotopic transposition} \end{array}\right\} & \cdots\ \text{stereogenic} \end{array}$$

So-called "pseudoasymmetric carbon atoms". The test using the topicity of a common skeleton in a substitution equivalent is a convenient method of checking stereogenicity. Two chiral stereoisomers of 2,3,4-trihydroxyglutaric acid, **10** and **11**, have been already discussed.[10] From the present point of view, the two isomers are represented by **12** and **13**, in which Q and $\overline{Q}$ denote a pair of antipodal ligands (CH(OH)COOH). For a transposition on the central carbon of **12**, we consider a common skeleton (**14**) of C_2 symmetry (Figure 5), in which the resulting two positions construct a hemispheric orbit governed by $C_2(/C_1)$. This fact indicates that this transposition is a homotopic transposition, which is concluded to be non-stereogenic. Similarly, a transposition on **13** is also homotopic and hence non-stereogenic.

Let us next discuss the two diastereomers (**16** and **17**) of 2,3,4-trihydroxyglutaric acid, in which the central carbon atom has been dubbed "pseudoasymmetric" (Figure 6). These molecules are formulated by means of the present procedure to be **18** and **19**, each of which can be considered to belong to C_s symmetry. For the purpose of discussing a transposition on the central carbon of **18** or **19**, we consider a common skeleton (**20**) of C_s symmetry. Note that the hypothetical removal of H and OH keeps the C_s symmetry invariant. The resulting two positions belong seperately to $C_s(/C_s)$ orbits; that is, they are diastereotopic. Hence, this transposition is concluded to be a diastreotopic one, which is stereogenic to result in the interconversion between the diastreomers (**18** and **19**).

So-called "chirotopicity *vs.* stereogenicity". We have already discussed that the concept "chirotopicity" proposed by Mislow *et al.* [10] can be replaced by the chirality fittingness (sphericity) of an orbit.[19] We proposed the term *homospheric* in place of "achirotopic" and the terms *enantiospheric* and *hemispheric* in place of "chirotopic". It should be emphasized that these two systems of terminology are conceptually distinct. That is to say, the present terms concerning the sphericity (chirality fittingness) are the attributes of an orbit, whereas the terms regarding the chirotopicity are the attributes of an indivisual ligand.[38] In other words, the sphericity is concerned with a molecule as a whole in the form of such orbits; on the other hand, the chirotopicity focuses on a part of the molecule. Although it was emphasized that chirotopicity and stereogenicity are independent attributes,[10, 4] the standpoint based on the chirotopicity is still insufficient to differentiate the attributes.

From the present point of view, the so-called chirotopicity is described by the sphericity of an orbit appearing in *the skeleton of a molecule at issue.* For example, the 3-OH ligand of **3** is a member of a $C_1(/C_1)$ orbit, since this molecule belongs to C_1 symmetry (asymmetric). The symbol $C_1(/C_1)$ indicates that this orbit is hemispheric. In the chirotopicity convention, C_1 in the parentheses indicates that this ligand is chirotopic.

On the other hand, stereogenicity is concerned with an orbit appearing in *a common skeleton* that is considered in a substitution equivalent. For example, the 3- and 11-positions construct one half of the

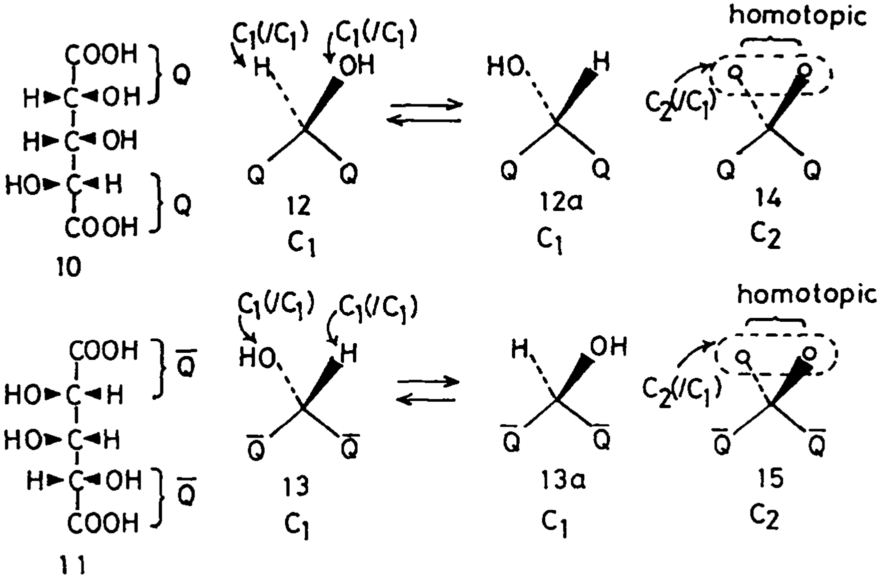


Figure 5: Chiral 2,3,4-trihydroxyglutaric acids

The rightmost figures (**14** and **15**) depict common skeletons, where each of the $C_2(/C_1)$ orbits is hemispheric.

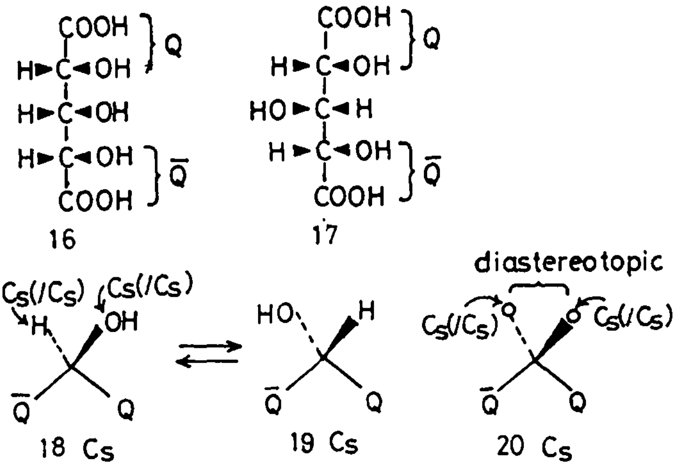


Figure 6: Meso 2,3,4-trihydroxyglutaric acids

The rightmost figure (**20**) depicts a common skeleton, where each of the $C_s(/C_s)$ orbits is homospheric.

$C_{2v}(/C_1)$ orbit (Δ_2) (*i.e.* they are homotopic) in the common skeleton **1** for the transposition between 3-OH and 11-H of **3**. Then, we have concluded that this homotopic transposition is non-stereogenic. It should again be emphasized that this homotopic relation stems from the sphericity of the common skeleton (**1**) and is not concerned with the molecule to be examined (**3**).

4 Conclusion

A new scheme of determining topicities is proposed in the light of chirality fittingness of orbits (homospheric, enantiospheric, and hemispheric). Thus, these concepts create the new definitions of the terms, homotopic, enantiotopic, diastereotopic and heterotopic. A new method of checking stereogenicity is presented by using a substitution equivalent, the orbits of which are examined in terms of chirality fittingness.

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[22] We use the term "ligand" to comprise both atoms and groups.

[23] IUPAC name: 1,2-difluoro-undecacyclo[9.9.0.0^{2,9}.0.^{3,7}.0^{4,20}. 0^{5,18}.0^{6,16}.0^{8,15}.0^{10,14}. 0^{12,19}.0^{13,17}]icosane. CAS name: 1,2-difluoro-hexadecahydro-5,2,1,6,3,4-[2,3]- butanediyl[1,4]diylidenedipentaleno[2,1,6-*cde*:2',1',6'- *gha*]pentalene

[24] This subduction corresponds to an equation: $\mathbf{I}_h(/\mathbf{C}_{3v}) \downarrow \mathbf{C}_{2v} = 3\mathbf{C}_{2v}(/\mathbf{C}_1) + 4\mathbf{C}_{2v}(/\mathbf{C}_s)$.

[25] The numbering of the 20 vertices is based on the IUPAC nomenclature. See A. Moyano, F. Serratosa, P. Camps, J. M. Drudis, *J. Chem. Educ.*, **59**, 126 (1982).

[26] This assignment needs a table of marks for the $\mathbf{C}_{2v}$ group. For the procedure of such assignment, see Ref. [12].

[27] In the real 3-dimensional world, any improper rotation is a rather hypothetical operation. However, if we neglect improper rotations, we cannot characterize the relationship between the two halves of an enantiospheric orbit.

[28] These two halves can be classified as left-handed and right-handed by means of an appropriate criterion; this criterion is an issue to be examined elsewhere.

[29] Previously, we overlooked this case in the definition of homotopicity. See Ref. [19].

[30] In order to explicate this difference, we propose the term *holotopic* to denote the case (1). We introduce the term *hemitopic* to denote the cases (2) and (3), if necessary. Thus, the present term homotopic involves holotopic and hemitopic.

[31] Although these two relationships are enantiotopic, they are different from each other.

[32] However, the distinction between diastereotopic and heterotopic depends upon a skeleton selected.

[33] As shown in the text, some diastereotopic relations can be regarded as pseudo-intraclass relations.

[34] The term "stereoisomer" is here used to denote *isoskeletal isomers*, which are defined as two molecules having an identical skeleton and an identical set of ligands but different modes of substitution. The latter term is similar to, but conceptually distinct from "permutational isomers", which was introduced by Ugi *et al.*[39] This point will be discussed elsewhere.

[35] This definition stems from Mislow's one on a stereogenic unit. See Ref. [10].

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[37] In contrast, the molecule (1) has been originally supposed to be a derivative of dodecahedrane having 20 positions, where the dodecahedrane is regarded as a skeleton.

[38] We use the term "topic" in order to denote a *relation*, but not to designate an *attribute*. The terms homotopic *etc.* agree with this criterion, since they are concerned with relations. On the other hand, the terms achirotopic and chirotopic do not satisfy this criterion, because they are used to designate attributes. The conventional usage of the topic are concluded to mix up these two distinct categories.

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