Pseudo-Point Groups for Symmetry Characterization and Combinatorial Enumeration of Nonrigid Compounds

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The concept of equi-axial transformations is proposed to characterize conformational changes of flexible compounds such as the inversion of ammonia and the ring-flipping of 1,3,5-trioxane. In order to discuss the symmetries of the equi-axial transformations, pseudo-point groups are introduced after the definition of a pseudo-dihedral rotation. Pseudo-point groups are classified into anisoenergetic and isoenergetic groups. In the light of this classification, orbits generated by a pseudo-point group are characterized by the concept of chronality, which is defined by examining coset representations. Thus, the terms *homochronal, enantiochronal, and hemichronal* are coined for the characterization of orbits. The enumeration methods of the USCI (unit-subduced-cycle-index) approach are applied to the ammonia and 1,3,5-trioxane cases by using the pseude-point group $\hat{\boldsymbol{D}}_{3h}$.

The Pólya–Redfield theorem[1,2] and the Read–Redfield theorem[2,3] have long been standard methods for combinatorial enumeration. Their applications to chemistry have been summarized in books[4,5] and a review.[6] An alternative method based on double-cosets has been used for the same purpose.[7] Since all of the methods give isomer numbers concerned only with molecular formulas, methods for more detailed enumeration have later been developed. The latter have, thus, provided us with itemized enumeration regarding both molecular formulas and symmetries, where they are based on utilizing mark tables,[8] on combining double cosets and framework groups[9] and on combining mark tables and double cosets.[10]

We have recently presented the USCI (unit-subduced-cycle-index) approach,[11,12] which enables us to carry out itemized enumeration of compounds with respect both to molecular formulas and to symmetries. The USCI approach provides us with four versatile methods: (1) a generating-function method based on subduced cycle indices,[11] (2) a generating-function method based on partial cycle indices,[13,14] (3) a method based on the elementary superposition theorem,[14] and (4) a method based on the partial superposition theorem.[14] Comparisons among the four methods have been reported for the enumeration of digraphs.[15] Mathematical foundations of the USCI approach have been discussed by comparing cosets with double cosets.[16]

The methods of the USCI approach have been applied to isomer enumerations of rigid skeletons[17—19] and of skeletons with rotatable substitution positions.[20,21] We have also reported another approach for treating skeletons with rotatable substitution positions; the approach is based on the concepts of proligands and promolecules, where chiral and achiral ligands are taken into consideration.[22—24] In all of the cases, the symmetry of a skeleton is represented by a point group, either directly or after some conceptual transformation.

On the other hand, there still remain such nonrigid compounds that require groups other than point groups, e.g., ammonia, 1,3,5-trioxane, and cyclohexane. Although enumeration of cyclohexane derivatives has been reported by Leonard et al.,[25,26] their ring-flip-rotation operator (R_6) is effective only for cyclohexane derivatives. An alternative method reported by Flurry[27,28] is based on an isodynamic operator which has been presented by Altmann.[29] The isomer numbers derived by the previous methods are concerned only with molecular formulas, since they are based on the Pólya–Redfield theorem.

The purpose of the present paper is to give a foundation to the itemized enumeration of such nonrigid compounds as ammonia, 1,3,5-trioxane and cyclohexane. We propose the concepts of *equi-axial transformation* and of *pseudo-point groups* for describing such processes as the inversion of ammonia. For obtaining itemized results with respect to both molecular formulae and symmetries, we have to clarify a group-subgroup relationship and to prepare a mark table and a USCI table for a pseudo-point group to be considered.

Results and Discussions

1 Theoretical Foundations. 1.1 Equi-Axial Transformations and Pseudo-Point Groups. Let us consider the inversion of ammonia as shown in Fig. 1 (**1a**⇄**1b**). This inversion has several symmetrical features. (1) The C_3-axis of the molecule can be considered to be fixed during the process of the inversion. (2) The symmetry of the starting molecule (**1a**) is the same as that of the product molecule (**1b**). (3) The position of the nitrogen atom is invariant during the inversion. Since the first feature can be referred to as being *equi-axial*, such a transformation is called *an equi-axial transformation.*

We here consider a pair of molecules (**1a** and **1b**) whose substitution positions are numbered from 1 to 3. It should be noted that we distinctly use the terms *compound* and *molecule*; thus, ammonia as a compound is considered to consist of a pair of molecules. The pair coincides with itself on the action of the twelve symmetry operations of group $\boldsymbol{C}_{3v}$, i.e.,

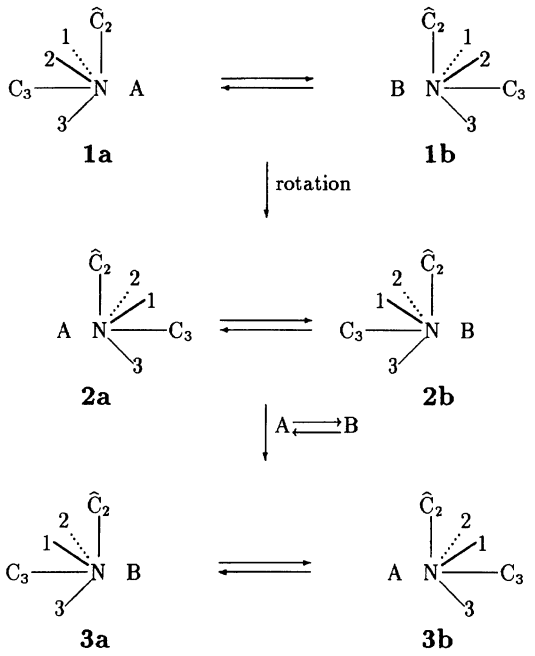


Fig. 1. The definition of the operation $\hat{C}_2'$ for the ammonia skeleton.

$$\boldsymbol{C}_{3v} = \left\{I, C_3, C_3^2, \sigma_{v(1)}, \sigma_{v(2)}, \sigma_{v(3)}\right\}, \tag{1}$$

where each symmetry operation is considered to act on each fixed molecule (A or B) of the pair. However, additional operations should be introduced to treat the inversion. Since the inversion process possesses the symmetrical features described above, we can introduce a pseudo-dihedral rotation ($\hat{C}_2'$-operation) which is a combination of rotation and exchange (A⇄B), as shown in Fig. 1. We coin the symbol $\hat{C}_2'$ for emphasizing its apparent similarity to the C_2'-operation of the group $\boldsymbol{D}_{3h}$. Thus, the pseudo-dihedral rotation comes from the apparent consideration of a $\hat{C}_2$ axis (called a *pseudo-dihedral axis*) perpendicular to the major C_3 axis.

By using the operation $\hat{C}_2'$, we obtain the set $\hat{\boldsymbol{D}}_{3h}$, where the $\hat{C}_2'$-operation is numbered to be $\hat{C}_{2(1)}'$ for distinguishing from other generated operations of the same kind.

$$\hat{\boldsymbol{D}}_{3h} = \boldsymbol{C}_{3v} + \hat{C}_{2(1)}'\boldsymbol{C}_{3v}, \tag{2}$$

$$= \{I, C_3, C_3^2, \sigma_{v(1)}, \sigma_{v(2)}, \sigma_{v(3)}, \hat{C}_{2(1)}', \hat{C}_{2(2)}', \hat{C}_{2(3)}', \hat{\sigma}_h, \hat{S}_3, \hat{S}_3^5\}, \tag{3}$$

where each operation with a hat symbol is defined by the following equations:

$$\hat{C}_{2(2)}' = \hat{C}_{2(1)}'C_3,\ \hat{C}_{2(3)}' = \hat{C}_{2(1)}'C_3^2,$$
$$\hat{\sigma}_h = \hat{C}_{2(1)}'\sigma_{v(1)},\ \hat{S}_3 = \hat{C}_{2(1)}'\sigma_{v(2)},\ \hat{S}_3^5 = \hat{C}_{2(1)}'\sigma_{v(3)}.$$

The set $\hat{\boldsymbol{D}}_{3h}$ is a group which is isomorphic to the point group $\boldsymbol{D}_{3h}$. Such a group as $\hat{\boldsymbol{D}}_{3h}$ is called a *pseudo-point group*, since the intersection between the axis of an equi-axial transformation and the newly-defined pseudo-dihedral axis is presumed to be a fixed point. The introduction of the pseudo-dihedral rotation $\hat{C}_2'$ produces a set of operations which are called *pseudo-rotations*, e.g., $\hat{C}_{2(1)}'\boldsymbol{C}_{3v}$ in the example described above.

The subgroups of $\hat{\boldsymbol{D}}_{3h}$ are obtained as follows, where an appropriate representative of each set of conjugate subgroups is listed.

$$\boldsymbol{C}_1 = \{I\}, \tag{4a}$$
$$\hat{\boldsymbol{C}}_2 = \left\{I, \hat{C}_{2(1)}'\right\}, \tag{4b}$$
$$\boldsymbol{C}_s = \{I, \sigma_{v(1)}\}, \tag{4c}$$
$$\hat{\boldsymbol{C}}_s = \{I, \hat{\sigma}_h\}, \tag{4d}$$
$$\boldsymbol{C}_3 = \left\{I, C_3, C_3^2\right\}, \tag{4e}$$
$$\hat{\boldsymbol{C}}_{2v} = \left\{I, \hat{C}_2', \sigma_{v(1)}, \hat{\sigma}_h\right\}, \tag{4f}$$
$$\boldsymbol{C}_{3v} = \left\{I, C_3, C_3^2, \sigma_{v(1)}, \sigma_{v(2)}, \sigma_{v(3)}\right\}, \tag{4g}$$
$$\hat{\boldsymbol{C}}_{3h} = \left\{I, C_3, C_3^2, \hat{\sigma}_h, \hat{S}_3, \hat{S}_3^5\right\}, \tag{4h}$$
$$\hat{\boldsymbol{D}}_3 = \left\{I, C_3, C_3^2, \hat{C}_{2(1)}', \hat{C}_{2(2)}', \hat{C}_{2(3)}'\right\}, \tag{4i}$$

$$\hat{\boldsymbol{D}}_{3h} = \left\{I, C_3, C_3^2, \sigma_{v(1)}, \sigma_{v(2)}, \sigma_{v(3)}, \hat{C}_{2(1)}', \hat{C}_{2(2)}', \hat{C}_{2(3)}', \hat{\sigma}_h, \hat{S}_3, \hat{S}_3^5\right\}. \tag{4j}$$

These are the members of a non-redundant set of subgroups (SSG)[12] for the pseudo-point group $\hat{\boldsymbol{D}}_{3h}$.

$$SSG_{\hat{\boldsymbol{D}}_{3h}} = \left\{\boldsymbol{C}_1, \hat{\boldsymbol{C}}_2, \boldsymbol{C}_s, \hat{\boldsymbol{C}}_s, \boldsymbol{C}_3, \hat{\boldsymbol{C}}_{2v}, \boldsymbol{C}_{3v}, \hat{\boldsymbol{C}}_{3h}, \hat{\boldsymbol{D}}_3, \hat{\boldsymbol{D}}_{3h}\right\}. \tag{5}$$

The operation $\hat{C}_2'$ is useful to describe the ring-flipping of 1,3,5-trioxane, as shown in Fig. 2. Since the fixed conformer **4a** or **4b** belongs to $\boldsymbol{C}_{3v}$, the same pseudo-point group $\hat{\boldsymbol{D}}_{3h}$ can be used to characterize the symmetry of the conformational change of 1,3,5-trioxane. Thus, the six positions, axial and equatorial, are interchanged with each other on the action of the group $\hat{\boldsymbol{D}}_{3h}$.

Pseudo-rotation operations are classified into proper rotations and improper rotations, just as rotations (usual symmetry operations) are classified into either. Figure 3 illustrates the operation $\hat{C}_{2(2)}'$ as an example of a proper pseudo-rotation, where the symbol Q represents a chiral proligand.[22] On the other hand, the operation $\hat{\sigma}_h$ depicted in Fig. 4 is an improper pseudo-rotation, where the symbol $\overline{\text{Q}}$ represents a chiral proligand which is an antipode of the proligand Q.

1.2 Anisoenergetic and Isoenergetic Groups. In this subsection, the preceding discussion is extended to a general case. Let $\boldsymbol{G}$ be a group. Suppose that an operation $\hat{g}(\notin \boldsymbol{G})$ satisfies $\hat{g}\boldsymbol{G}=\boldsymbol{G}\hat{g}$ and $\hat{g}\hat{g}=I$ (identity). Then, the following set $\hat{\boldsymbol{G}}$:

$$\hat{\boldsymbol{G}} = \boldsymbol{G} + \hat{g}\boldsymbol{G} \tag{6}$$

can be easily proved to be a group. When $\boldsymbol{G}$ is a point group, the resulting group $\hat{\boldsymbol{G}}$ is called a *pseudo-point*

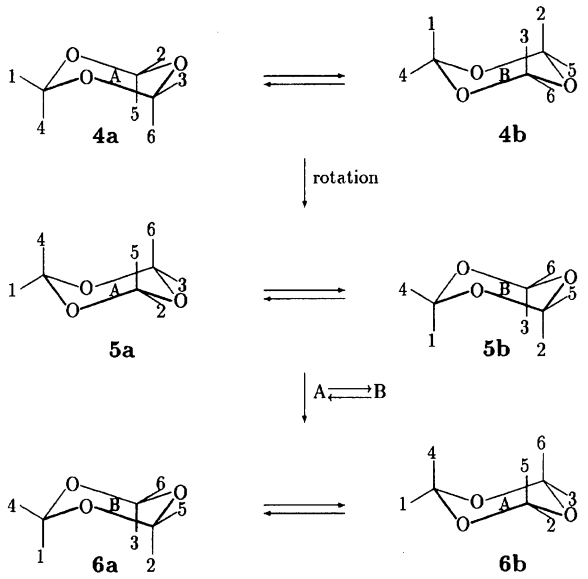


Fig. 2. The definition of the operation $\hat{C}_2'$ for the 1,3,5-trioxane skeleton.

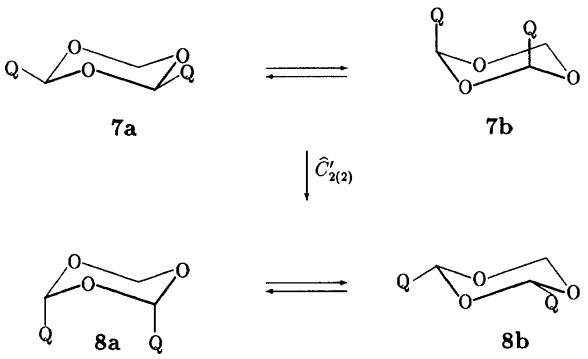


Fig. 3. The operation $\hat{C}'_{2(2)}$ for a 1,3,5-trioxane derivative.

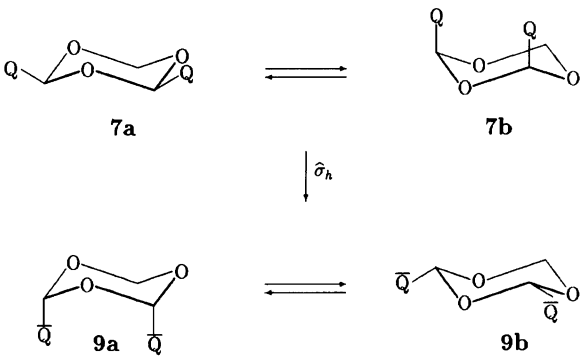


Fig. 4. The operation $\hat{\sigma}_h$ for a 1,3,5-trioxane derivative.

group. The generator $\hat{g}$ is called a pseudo-rotation operator in the present context; as a result, each operator contained in the coset $\hat{g}\boldsymbol{G}$ is also called a pseudo-rotation. The group $\hat{\boldsymbol{D}}_{3h}$ described in the preceding subsection is an example of this type of group, wherein $\hat{g}=\hat{C}_2'$ and $\boldsymbol{G}=\boldsymbol{C}_{3v}$.

When the resulting group $\hat{\boldsymbol{G}}$ acts on a pair of molecules, the starting molecule is energetically equivalent to the product one. More clearly speaking, the two molecules are homomeric or enantiomeric to each other. Accordingly, the group $\hat{\boldsymbol{G}}$ is called an *isoenergetic group*. On the other hand, the group $\boldsymbol{G}$ acts on a pair of molecules so that the starting molecule is energetically different from the product molecule. In other words, the two molecules are diastereomeric to each other. Hence, we call the group $\boldsymbol{G}$ an *anisoenergetic group*.

In the light of the criterion of determining anisoenergetic and isoenergetic groups, the subgroups of $\hat{\boldsymbol{D}}_{3h}$ are classified into anisoenergetic groups ($\boldsymbol{C}_1$, $\boldsymbol{C}_s$, $\boldsymbol{C}_3$, and $\boldsymbol{C}_{3v}$) and isoenergetic groups ($\hat{\boldsymbol{C}}_2$, $\hat{\boldsymbol{C}}_s$, $\hat{\boldsymbol{C}}_{2v}$, $\hat{\boldsymbol{C}}_{3h}$, $\hat{\boldsymbol{D}}_3$, and $\hat{\boldsymbol{D}}_{3h}$).

It should be noted that a pair of molecules can belong to an anisoenergetic group $\boldsymbol{G}$ even in a flexible state. This point will be discussed in detail by using illustrative examples.

1.3 Orbits for Pseudo-Point Groups. We have previously reported that the substitution positions of a molecule can be classified into orbits, each of which is governed by a coset representation.[11,12,30] Without any group-theoretical modification, we are here able to extend this formulation to treat the group $\hat{\boldsymbol{G}}$ defined in the preceding subsection. Thus, the substitution positions of an equilibrated pair are classified to orbits, each of which is governed by $\hat{\boldsymbol{G}}(/\boldsymbol{G}_i)$ where $\boldsymbol{G}_i$ is an anisoenergetic or isoenergetic subgroup of $\hat{\boldsymbol{G}}$.

For the assignment of an orbit to the corresponding coset representation, we have used a mark table, which has been prepared for each point group.[12] This holds true for cases concerned with pseudo-point groups. The mark table for $\hat{\boldsymbol{D}}_{3h}$ can easily be obtained as shown in Table 1, since $\hat{\boldsymbol{D}}_{3h}$ is isomorphic to $\boldsymbol{D}_{3h}$.[31,32]

Let us consider the three substitution positions of the ammonia pair (**1a**⇄**1b**). They generate an orbit having a fixed-point vector (FPV),[11] i.e.,

$$FPV = (3,1,1,3,0,1,0,0,0,0),$$

each value of which is obtained by counting fixed positions on the action of the corresponding subgroup. Since the FPV is equal to the $\hat{\boldsymbol{D}}_{3h}(/\hat{\boldsymbol{C}}_{2v})$-row of Ta-

Table 1. Mark Table for the Group $\hat{\boldsymbol{D}}_{3h}$

	$\boldsymbol{C}_1$	$\hat{\boldsymbol{C}}_2$	$\boldsymbol{C}_s$	$\hat{\boldsymbol{C}}_s$	$\boldsymbol{C}_3$	$\hat{\boldsymbol{C}}_{2v}$	$\boldsymbol{C}_{3v}$	$\hat{\boldsymbol{C}}_{3h}$	$\hat{\boldsymbol{D}}_3$	$\hat{\boldsymbol{D}}_{3h}$
$\hat{\boldsymbol{D}}_{3h}(/\boldsymbol{C}_1)$	12	0	0	0	0	0	0	0	0	0
$\hat{\boldsymbol{D}}_{3h}(/\hat{\boldsymbol{C}}_2)$	6	2	0	0	0	0	0	0	0	0
$\hat{\boldsymbol{D}}_{3h}(/\boldsymbol{C}_s)$	6	0	2	0	0	0	0	0	0	0
$\hat{\boldsymbol{D}}_{3h}(/\hat{\boldsymbol{C}}_s)$	6	0	0	6	0	0	0	0	0	0
$\hat{\boldsymbol{D}}_{3h}(/\boldsymbol{C}_3)$	4	0	0	0	4	0	0	0	0	0
$\hat{\boldsymbol{D}}_{3h}(/\hat{\boldsymbol{C}}_{2v})$	3	1	1	3	0	1	0	0	0	0
$\hat{\boldsymbol{D}}_{3h}(/\boldsymbol{C}_{3v})$	2	0	2	0	2	0	2	0	0	0
$\hat{\boldsymbol{D}}_{3h}(/\hat{\boldsymbol{C}}_{3h})$	2	0	0	2	2	0	0	2	0	0
$\hat{\boldsymbol{D}}_{3h}(/\hat{\boldsymbol{D}}_3)$	2	2	0	0	2	0	0	0	1	0
$\hat{\boldsymbol{D}}_{3h}(/\hat{\boldsymbol{D}}_{3h})$	1	1	1	1	1	1	1	1	1	1

ble 1, the orbit is determined to be governed by the coset representation $\hat{D}_{3h}(/\hat{C}_{2v})$. On the other hand, the FPV for the six substitution positions of the 1,3,5-trioxane pair (**4a**$\rightleftarrows$**4b**) is calculated to be

$$FPV = (6,0,2,0,0,0,0,0,0,0),$$

which is compared with the corresponding row of Table 1, showing that the orbit is governed by $\hat{D}_{3h}(/C_s)$.

1.4 Chronality. We have previously proposed the concept of chirality fittingness (sphericity),[30] where we use chiral and achiral groups for classifying orbits into homospheric, enantiospheric, or hemispheric ones.[12] Equation 6 that determines anisoenergetic and isoenergetic groups has the same mathematical form as the counterpart determining chiral and achiral groups. Hence, a concept parallel with the sphericity is expected to exist in the present case.

As a mathematical analogy to the sphericity concept, we here propose the concept of *chronality* which defines terms for characterizing orbits (homochronal, enantiochronal and hemichronal). Let $\hat{G}$ be an isoenergetic pseudo-point group and $\hat{H}$ an isoenergetic subgroup of $\hat{G}$. Suppose that G is an anisoenergetic subgroup of $\hat{G}$ and that H is an anisoenergetic subgroup of G.

1. An orbit governed by $\hat{G}(/\hat{H})$ is defined as being *homochronal.*
2. An orbit governed by $\hat{G}(/H)$ is defined as being *enantiochronal.*
3. An orbit governed by $G(/H)$ is defined as being *hemichronal.*

The terms with the suffix *chronal* are coined because inversions and conformational changes are time-dependent phenomena. We use the term *chronality* to refer to the three categories.

Suppose that the groups ($\hat{G}$, G, $\hat{H}$, H) satisfy Eq. 6 as well as the following equation,

$$\hat{H} = H + \hat{g}H. \tag{7}$$

Then, the group G is a maximum anisoenergetic subgroup of $\hat{G}$; and H is a maximum anisoenergetic subgroup of $\hat{H}$. We obtain $|\hat{G}|=2|G|$ and $|\hat{H}|=2|H|$.

Let us consider a homochronal orbit governed by $\hat{G}(/\hat{H})$. When the global symmetry $\hat{G}$ is restricted into G, the process is represented by the following subduction.

$$\hat{G}(/\hat{H}) \downarrow G = G(/H). \tag{8}$$

This equation is mathematically equivalent to the equation proved for characterizing homospheric orbits (Eq. 11.6 in Ref. 12), though their chemical meanings are different from each other. The subduction (Eq. 8) means that, when the symmetry of the equilibrated pair represented by $\hat{G}$ is restricted to G, no splitting of the orbit occurs.

The three substitution positions of the ammonia pair (**1a**$\rightleftarrows$**1b**) belong to an orbit governed by $\hat{D}_{3h}(/\hat{C}_{2v})$, as shown in the preceding subsection. This orbit is restricted in the light of the following subduction.

$$\hat{D}_{3h}(/\hat{C}_{2v}) \downarrow C_{3v} = C_{3v}(/C_s). \tag{9}$$

Thus, the three positions are equivalent in an equilibrated pair as well as in a frozen pair.

Let us next consider an enantiochronal orbit governed by $\hat{G}(/H)$, where the global symmetry $\hat{G}$ is restricted into G. This process is represented by either of the following subductions.

$$\hat{G}(/H) \downarrow G = 2G(/H) \tag{10}$$

$$\hat{G}(/H) \downarrow G = G(/H) + G(/H'). \tag{11}$$

In the latter equation, the group H' is conjugate to H within $\hat{G}$ but no longer conjugate after the restriction to G. These equations are mathematically equivalent to the equations proved for characterizing enantiospheric orbits (Eqs. 10.6 and 10.7 in Ref. 12). Hence, Eqs. 10 and 11 mean that the splitting of the orbit occurs under the subduction.

The six substitution positions of the 1,3,5-trioxane pair (**4a**$\rightleftarrows$**4b**) generate an orbit governed by $\hat{D}_{3h}(/C_s)$. This orbit is restricted in the light of the following subduction.

$$\hat{D}_{3h}(/C_s) \downarrow C_{3v} = 2C_{3v}(/C_s). \tag{12}$$

This equation means that the six positions equivalent in the equilibrated pair are fixed to split into two halves (axial and equatorial positions) under freezing.

Equations 10 and 11 can be summarized as a theorem. This theorem is the counterpart of Theorem 10.1 of Ref. 12 that deals with the concept of enantiosphericity.

Theorem 1. *An enantiochronal orbit is capable of separating into two hemichronal orbits of the same length under a frozen environment.*

The phenomenon based on Theorem 1 is referred to by the term *pro-anisoenergeticity.* Thus, a pro-anisoenergetic compound is defined as an isoenergetic pair that has at least one enantiochronal orbit. The following terms are coined by analogy with prochirality.[12]

- isoenergetic
  - pro-anisoenergetic-I ··· enantiochronal
  - pro-anisoenergetic-II ··· enantiochronal + homochronal
  - para-isoenergetic ··· homochronal
- anisoenergetic ··· hemichronal

Ammonia itself is a para-isoenergetic compound, since it has homochronal orbits, i.e., $\hat{D}_{3h}(/\hat{C}_{2v})$ for the three hydrogen atoms and $\hat{D}_{3h}(/\hat{D}_{3h})$ for the nitrogen atom. On the other hand, 1,3,5-trioxane is a pro-anisoenergetic compound of type II, since it has an enantiochronal orbit ($\hat{D}_{3h}(/C_s)$) for the six hydrogen atoms and two homochronal orbits (both $\hat{D}_{3h}(/\hat{C}_{2v})$) for the three carbons and for the three oxygen atoms.

2 Enumeration based on Pseudo-Point Groups.

2.1 Ammonia Derivatives. Since the group

$\hat{D}_{3h}$ and the point group D_{3h} are isomorphic to each other,[31,32] they have mark tables and subduction tables with the same mathematical meaning. Moreover, they are common in the fact that their symmetrical properties are characterized by the concept of sphericity. However, the former group $\hat{D}_{3h}$ has an additional chemical meaning that stems from the chronality concept proposed in the present paper. In order to exemplify the dual character of $\hat{D}_{3h}$, the subduction of the $\hat{D}_{3h}(/\hat{C}_{2v})$-orbit is concretely written as follows.

$$\hat{D}_{3h}(/\hat{C}_{2v}) \downarrow C_1 = 3C_1(/C_1) \qquad b_1^3 \qquad (13a)$$

$$\hat{D}_{3h}(/\hat{C}_{2v}) \downarrow \hat{C}_2 = \hat{C}_2(/C_1) + \hat{C}_2(/\hat{C}_2) \qquad b_1 b_2 \qquad (13b)$$

$$\hat{D}_{3h}(/\hat{C}_{2v}) \downarrow C_s = C_s(/C_1) + C_s(/C_s) \qquad a_1 c_2 \qquad (13c)$$

$$\hat{D}_{3h}(/\hat{C}_{2v}) \downarrow \hat{C}_s = 3\hat{C}_s(/\hat{C}_s) \qquad a_1^3 \qquad (13d)$$

$$\hat{D}_{3h}(/\hat{C}_{2v}) \downarrow C_3 = C_3(/C_1) \qquad b_3 \qquad (13e)$$

$$\hat{D}_{3h}(/\hat{C}_{2v}) \downarrow \hat{C}_{2v} = \hat{C}_{2v}(/\hat{C}_s) + \hat{C}_{2v}(/\hat{C}_{2v}) \qquad a_1 a_2 \qquad (13f)$$

$$\hat{D}_{3h}(/\hat{C}_{2v}) \downarrow C_{3v} = C_{3v}(/C_s) \qquad a_3 \qquad (13g)$$

$$\hat{D}_{3h}(/\hat{C}_{2v}) \downarrow \hat{C}_{3h} = \hat{C}_{3h}(/\hat{C}_s) \qquad a_3 \qquad (13h)$$

$$\hat{D}_{3h}(/\hat{C}_{2v}) \downarrow \hat{D}_3 = \hat{D}_3(/\hat{C}_2) \qquad b_3 \qquad (13i)$$

$$\hat{D}_{3h}(/\hat{C}_{2v}) \downarrow \hat{D}_{3h} = \hat{D}_{3h}(/\hat{C}_{2v}) \qquad a_3 \qquad (13j)$$

The monomial shown in the end of each equation is the corresponding unit subduced cycle index with chirality fittingness (USCI-CF).[33]

These results are applied to the enumeration of ammonia derivatives, since the three positions of an ammonia skeleton are governed by the coset representation $\hat{D}_{3h}(/\hat{C}_{2v})$. Let us place three proligands on the substitution of the ammonia pair (**1a**⇄**1b**), where the proligands are selected from a set of three achiral proligands (X, Y, and Z), three chiral proligands (P, Q, and R), and their antipodes ($\overline{\text{P}}$, $\overline{\text{Q}}$, and $\overline{\text{R}}$). We obtain the following inventories for this enumeration:

$$a_k = x^k + y^k + z^k, \qquad (14a)$$

$$b_k = x^k + y^k + z^k + p^k + \bar{p}^k + q^k + \bar{q}^k + r^k + \bar{r}^k, \qquad (14b)$$

$$c_k = x^k + y^k + z^k + 2(p\bar{p} + q\bar{q} + r\bar{r}), \qquad (14c)$$

where each small letter in the right-hand sides corresponds to the replacement of a proligand of its capital letter. They are substituted for the dummy variable of subduced cycle indices (SCI-CFs), which are equal to the unit subduced cycle indices (USCI-CFs) because only one orbit is involved in this case.

$$C_1 \quad b_1^3 = (x + y + z + p + \bar{p} + q + \bar{q} + r + \bar{r})^3, \qquad (15a)$$

$$\hat{C}_2 \quad b_1 b_2 = (x + y + z + p + \bar{p} + q + \bar{q} + r + \bar{r}) \times (x^2 + y^2 + z^2 + p^2 + \bar{p}^2 + q^2 + \bar{q}^2 + r^2 + \bar{r}^2), \qquad (15b)$$

$$C_s \quad a_1 c_2 = (x+y+z)[x^2+y^2+z^2+2(p\bar{p}+q\bar{q}+r\bar{r})], \qquad (15c)$$

$$\hat{C}_s \quad a_1^3 = (x + y + z)^3, \qquad (15d)$$

$$C_3 \quad b_3 = x^3 + y^3 + z^3 + p^3 + \bar{p}^3 + q^3 + \bar{q}^3 + r^3 + \bar{r}^3, \qquad (15e)$$

$$\hat{C}_{2v} \quad a_1 a_2 = (x + y + z)(x^2 + y^2 + z^2), \qquad (15f)$$

$$C_{3v} \quad a_3 = x^3 + y^3 + z^3, \qquad (15g)$$

$$\hat{C}_{3h} \quad a_3 = x^3 + y^3 + z^3, \qquad (15h)$$

$$\hat{D}_3 \quad b_3 = x^3 + y^3 + z^3 + p^3 + \bar{p}^3 + q^3 + \bar{q}^3 + r^3 + \bar{r}^3, \qquad (15i)$$

$$\hat{D}_{3h} \quad a_3 = x^3 + y^3 + z^3. \qquad (15j)$$

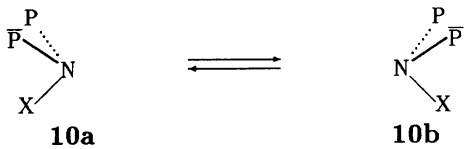
After expansion of each of these equations (Eqs. 15a—15j), we collect the coefficients of resulting monomials to construct Table 2. For simplicity's sake, we tentatively select a representative from a set of equivalent monomials; for example, the term x^3 is shown as the representative of x^3, y^3, and z^3. It should be noted that we count an enantiomeric pair once in the present enumeration. The coefficient of the term for such an enantiomeric pair should be doubled, as shown by the symbol 2*. For example, the values of the x^2p-row are doubled in this way, since x^2p is a representative of an enantiomeric pair $x^2p+x^2\bar{p}$. On the other hand, the isomer represented by the term $xp\bar{p}$ is a *meso*-compound; hence, the corresponding row of Table 2 is not doubled.[33]

Table 2 is regarded as a matrix, which is multiplied by the inverse of the mark table shown in Table 1. The resulting matrix is found in Table 3, which involves the number of isomers with a nomomial term and a given symmetry at the corresponding intersection.

The pair appearing at the intersection between the $xp\bar{p}$-row and the C_s-column is represented by the following scheme (Scheme 1).

Table 2. Coefficients Calculated by Eqs. 15a—15j

Term	C_1	$\hat{C}_2$	C_s	$\hat{C}_s$	C_3	$\hat{C}_{2v}$	C_{3v}	$\hat{C}_{3h}$	$\hat{D}_3$	$\hat{D}_{3h}$
x^3	1	1	1	1	1	1	1	1	1	1
x^2y	3	1	1	3	0	1	0	0	0	0
xyz	6	0	0	6	0	0	0	0	0	0
x^2p	2*3	2*1	0	0	0	0	0	0	0	0
xyp	2*6	0	0	0	0	0	0	0	0	0
xp^2	2*3	2*1	0	0	0	0	0	0	0	0
$xp\bar{p}$	6	0	2	0	0	0	0	0	0	0
xpq	2*6	0	0	0	0	0	0	0	0	0
p^3	2*1	2*1	0	0	2*1	0	0	0	2*1	0
$p^2\bar{p}$	2*3	2*1	0	0	0	0	0	0	0	0
p^2q	2*3	2*1	0	0	0	0	0	0	0	0
pqr	2*6	0	0	0	0	0	0	0	0	0
$pp\bar{q}$	2*6	0	0	0	0	0	0	0	0	0



10a **10b**

Scheme 1.

Table 3. Isomer Numbers Based on the Ammonia Pair

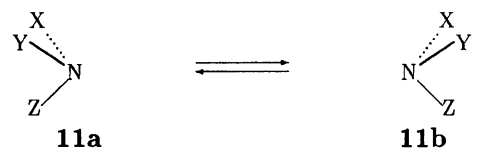
Term	C_1	$\hat{C}_2$	C_s	$\hat{C}_s$	C_3	$\hat{C}_{2v}$	C_{3v}	$\hat{C}_{3h}$	$\hat{D}_3$	$\hat{D}_{3h}$
x^3	0	0	0	0	0	0	0	0	0	1
x^2y	0	0	0	0	0	1	0	0	0	0
xyz	0	0	0	1	0	0	0	0	0	0
x^2p	0	1	0	0	0	0	0	0	0	0
xyp	1	0	0	0	0	0	0	0	0	0
xp^2	0	1	0	0	0	0	0	0	0	0
$xp\bar{p}$	0	0	1	0	0	0	0	0	0	0
xpq	1	0	0	0	0	0	0	0	0	0
p^3	0	0	0	0	0	0	0	0	1	0
$p^2\bar{p}$	0	1	0	0	0	0	0	0	0	0
p^2q	0	1	0	0	0	0	0	0	0	0
pqr	1	0	0	0	0	0	0	0	0	0
$p\bar{p}q$	1	0	0	0	0	0	0	0	0	0

The global symmetry of the pair (**10a**⇄**10b**) can be discussed in the light of the fact that the group C_s is an anisoenergetic group. The starting molecule **10a** and the product molecule **10b** belong to the point group C_s in their fixed forms; hence, they are both achiral, being *meso*-forms. They are diastereomeric to each other, though they are interchanged under equilibrated conditions. Even if we take account of an inversion between them, there appear no additional operations that superpose them. This corresponds to the fact that the group C_s is anisoenergetic.

The pattern of substitution for the pair (**10a**⇄**10b**) is in rigorous accordance with the subduction represented by Eq. 13c; thereby, it can be discussed by means of the chronality concept. Thus, the substituents P and $\overline{\mathrm{P}}$ in the pair belong to a two-membered $C_s(/C_1)$-orbit which is hemichronal and enantiospheric. The hemichronal nature reveals that the P$\overline{\mathrm{P}}$ pair in **10a** is diastereomeric to the counterpart in **10b**, though they are interchanged under equilibrated conditions. The enantiospheric nature corresponds to the fact that P and $\overline{\mathrm{P}}$ are both chiral and enantiomeric in isolation, becoming enantiotopic when incorporated.[34] The substituent X in the pair (**10a**⇄**10b**) constructs a one-membered $C_s(/C_s)$-orbit. The hemichronality of the $C_s(/C_s)$-orbit indicates that the X in **10a** is diastereomeric to the X in **10b**. At the same time, the homospheric nature of the orbit determines the X to be achiral.

On the other hand, the pair appearing at the intersection between the *xyz*-row and the $\hat{C}_s$-column in Table 3 is represented by the following scheme (Scheme 2).

The global symmetry of the pair (**11a**⇄**11b**) can be discussed in the light of the fact that the group $\hat{C}_s$ is an isoenergetic group. The starting molecule **11a** and the product molecule **11b** belong to the point group C_1 in their fixed forms; hence, they are both chiral under frozen condition, being enantiomeric to each other. When we take into consideration an inversion between them, an additional operation superposing them is so generated that it constructs the group $\hat{C}_s=\{I, \hat{\sigma}_h\}$.



11a **11b**

Scheme 2.

The pattern of substitution for the pair (**11a**⇄**11b**) is in accordance with the subduction represented by Eq. 13b. Each substituent (X, Y, or Z) in the pair belongs to a one-membered $\hat{C}_s(/\hat{C}_s)$-orbit which is enantiochronal and homospheric. The enantiochronality of the orbit indicates that the X in **11a** is enantiomeric to the X in **11b**. At the same time, the homospheric nature of the orbit determines the X to be achiral.

2.2 1,3,5-Trioxane Derivatives. The next problem is the enumeration of 1,3,5-trioxane derivatives with achiral subsituents H and X. Since the six-positions of the 1,3,5-trioxane pair (**1a**⇄**1b**) generate an orbit governed by $\hat{D}_{3h}(/C_s)$, we take account of the following subductions.

$$\hat{D}_{3h}(/C_s) \downarrow C_1 = 6C_1(/C_1) \qquad s_1^6 \qquad (16a)$$

$$\hat{D}_{3h}(/C_s) \downarrow \hat{C}_2 = 3\hat{C}_2(/C_1) \qquad s_2^3 \qquad (16b)$$

$$\hat{D}_{3h}(/C_s) \downarrow C_s = 2C_s(/C_1) + 2C_s(/C_s) \qquad s_1^2s_2^2 \qquad (16c)$$

$$\hat{D}_{3h}(/C_s) \downarrow \hat{C}_s = 3\hat{C}_s(/\hat{C}_1) \qquad s_2^3 \qquad (16d)$$

$$\hat{D}_{3h}(/C_s) \downarrow C_3 = 2C_3(/C_1) \qquad s_3^2 \qquad (16e)$$

$$\hat{D}_{3h}(/C_s) \downarrow \hat{C}_{2v} = \hat{C}_{2v}(/C_1) + \hat{C}_{2v}(/C_s) \qquad s_2s_4 \qquad (16f)$$

$$\hat{D}_{3h}(/C_s) \downarrow C_{3v} = 2C_{3v}(/C_s) \qquad s_3^2 \qquad (16g)$$

$$\hat{D}_{3h}(/C_s) \downarrow \hat{C}_{3h} = \hat{C}_{3h}(/C_1) \qquad s_6 \qquad (16h)$$

$$\hat{D}_{3h}(/C_s) \downarrow \hat{D}_3 = \hat{D}_3(/C_1) \qquad s_6 \qquad (16i)$$

$$\hat{D}_{3h}(/C_s) \downarrow \hat{D}_{3h} = \hat{D}_{3h}(/C_s) \qquad s_6 \qquad (16j)$$

The monomial shown in the end of each equation is the corresponding unit subduced cycle index (USCI).[11] We use the following inventory for the enumeration:

$$s_k = 1 + x^k, \qquad (17)$$

where x corresponds to the replacement of X. It is substituted for the dummy variables of subduced cycle indices (SCIs), which are again equal to the unit subduced cycle indices (USCI) because only one orbit is involved in this case.

$$C_1 \quad s_1^3 = (1+x)^6, \qquad (18a)$$

$$\hat{C}_2 \quad s_2^3 = (1+x^2)^3, \qquad (18b)$$

$$C_s \quad s_1^2s_2^2 = (1+x)^2(1+x^2)^2, \qquad (18c)$$

$$\hat{C}_s \quad s_2^3 = (1+x^2)^3, \qquad (18d)$$

$$C_3 \quad s_3^2 = (1+x^3)^2, \qquad (18e)$$

$$\hat{C}_{2v} \quad s_2s_4 = (1+x^2)(1+x^4), \qquad (18f)$$

$$C_{3v} \quad s_3^2 = (1+x^3)^2, \tag{18g}$$

$$\hat{C}_{3h} \quad s_6 = 1+x^6, \tag{18h}$$

$$\hat{D}_3 \quad s_6 = 1+x^6, \tag{18i}$$

$$\hat{D}_{3h} \quad s_6 = 1+x^6. \tag{18j}$$

Equation 18a—18j are expanded to give Table 4, which is regarded as a matrix. Then it is multiplied by the inverse of the mark table shown in Table 1. The resulting matrix is found Table 5, which involves the number of isomers with a monomial term and a given symmetry at the corresponding intersection.

Figure 5 illustrates three 1,3,5-trioxane derivatives of C_s-symmetry. The starting molecule and the product molecule of each pair belong to the point group C_s in their fixed forms. When we take account of a flipping between them, there appear no additional operations that superpose them.

Since the group C_s is an anisoenergetic group, the starting molecule and the product one in each pair of Fig. 5 are diastereomeric to each other. In other words, they are energetically different, though they are interchanged under equilibrated conditions. The conformational change represented by the pair (**12a**⇄**12b**) has been recognized as an axial-equatorial conversion. The introduction of the anisoenergeticity provides us with a systematic tool for characterizing the symmetrical properties of such conversions.

Moreover, the chronality concept derived from (an)isoenergeticity gives more detailed information, Equation 16c indicates that every 1,3,5-trioxane derivative of C_s-symmetry has two two-membered $C_s(/C_1)$-orbit and two one-membered $C_s(/C_s)$-orbits. This prediction holds true for each pair shown in Fig. 5. For example, two H^bs and two H^cs, respectively, construct such two-membered orbits. These two orbits are differentiated by the fact that they take *cis*- or *trans*-situation with respect to the X substituent. The situation is not changed under equilibrated conditions. The X (and H^a) generates a one-membered orbit.

The two H^bs are equatorial in the starting molecule (**12a**), while they are axial in the product molecule (**12b**). They are interchangeable and discussed by means of a single $C_s(/C_1)$-orbit in the present paper. The energetical difference under frozen conditions stems from the fact that the $C_s(/C_1)$-orbit is hemichronal.

Figure 6 illustrates three pairs corresponding to the x^2 row of Table 5, where the pair (**13a**⇄**13b**) shown in Fig. 5 is duplicated for the consistency of discussion.

The $\hat{C}_2$-symmetry of pair (**15a**⇄**15b**) should be emphasized, since the pair has the corresponding antipodal pair that involves the antipode of **15a** and that of **15b**. Note that **15a** and **15b** are homomeric, while the antipode of **15a** is homomeric to that of **15b**. The antipodal pairs are chiral and not racemized whether ring flipping occurs or not. This is because $\hat{C}_2$ is a chiral

Table 4. Coefficients Calculated by Eqs. 18a—18j

Term	C_1	$\hat{C}_2$	C_s	$\hat{C}_s$	C_3	$\hat{C}_{2v}$	C_{3v}	$\hat{C}_{3h}$	$\hat{D}_3$	$\hat{D}_{3h}$
$1,x^6$	1	1	1	1	1	1	1	1	1	1
x,x^5	6	0	2	0	0	0	0	0	0	0
x^2,x^4	15	3	3	3	0	1	0	0	0	0
x^3	20	0	4	0	2	0	2	0	0	0

Table 5. Isomer Numbers Based on the 1,3,5-Trioxane Pair

Term	C_1	$\hat{C}_2$	C_s	$\hat{C}_s$	C_3	$\hat{C}_{2v}$	C_{3v}	$\hat{C}_{3h}$	$\hat{D}_3$	$\hat{D}_{3h}$
$1,x^6$	0	0	0	0	0	0	0	0	0	1
x,x^5	0	0	1	0	0	0	0	0	0	0
x^2,x^4	0	1	1	0	0	1	0	0	0	0
x^3	1	0	1	0	0	0	1	0	0	0

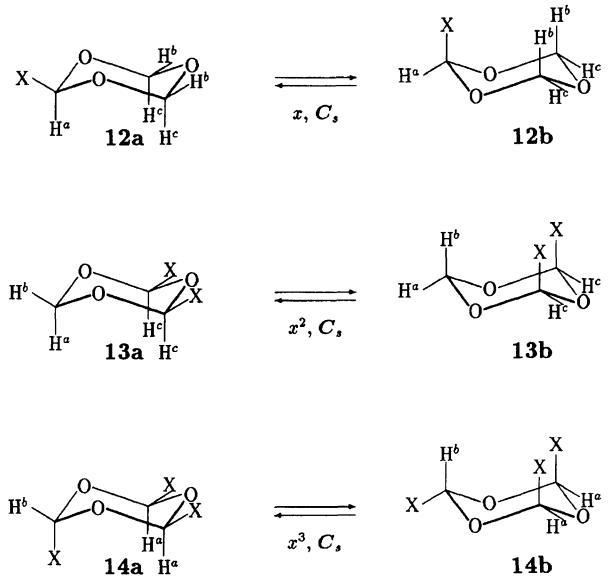


Fig. 5. 1,3,5-Trioxane derivative of C_s.

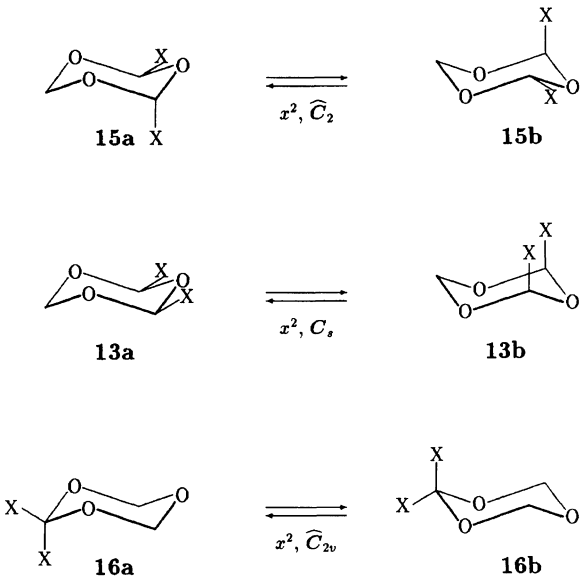


Fig. 6. Disubstitued 1,3,5-trioxane derivatives.

and isoenergetic group.

The two X-atoms of the pair (**15a**⇄**15b**) belong to a two-membered orbit governed by $\hat{C}_2(/C_1)$. This orbit is enantiochronal so that each X is fixed to either an axial or an equatorial position under frozen conditions.

The pair (**16a**⇄**16b**) is an example of $\hat{C}_{2v}$ which is an achiral and isoenergetic group. The two X-atoms of the pair belong to a two-membered orbit governed by $\hat{C}_{2v}(/C_s)$. This orbit is enantiochronal, so that each X is fixed to either an axial or an equatorial position under frozen conditions.

Conclusion

Equi-axial transformations and pseudo-point groups are formulated for the characterization of the symmetries of flexible compounds. The theoretical framework concerning chirality fittingness (sphericity) proposed previously by us[30] can be applied to the present cases after changing its chemical meaning. Thus, pseudo-point groups are classified into anisoenergetic and isoenergetic groups as well as into chiral and achiral groups. In the light of the former classification, orbits generated by a pseudo-point group are characterized by the concept of chronality which is the counterpart of the sphericity concept. The concept of pro-anisoenergeticity is introduced as an analogy to the prochirality concept and applied to the classification of nonrigid compounds. The subduction of coset representations and the enumeration methods of the USCI (unit-subduced-cycle-index) approach are applied to the pseudo-point groups. These applications are exemplified by the combinatorial enumerations based on ammonia and 1,3,5-trioxane skeletons.

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