© 2001 The Chemical Society of Japan Bull. Chem. Soc. Jpn., **74**, 1015—1020 (2001) 1015

Desymmetrization of Achiral Skeletons by Mono-Substitution. Its Characterization by Subduction of Coset Representations

Shinsaku Fujita

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

(Received November 1, 2000)

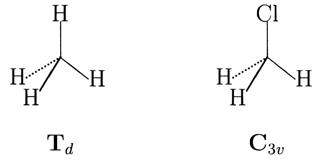
A set of equivalent positions in an achiral skeleton is regarded as an orbit as-signed to a coset representation $\mathbf{G}(/\mathbf{G}_i)$, where the subgroup $\mathbf{G}_i$ is $\mathbf{C}_{nv}$ or $\mathbf{C}_n$. Desymmetrization of the achiral skeleton by substituting a single ligand is examined by virtue of the subduction of the coset representation $\mathbf{G}(/\mathbf{G}_i) \downarrow \mathbf{G}_i$, which is determined to be $\alpha\mathbf{G}_i(/\mathbf{G}_i) + \beta\mathbf{G}_i(/\mathbf{G}_k{}^{(i)})$. The multiplicities ($\alpha$ and β) of the resulting coset representations are calculated from the data of the participating groups and the normalizer of $\mathbf{G}_i$.

From the foundation of stereochemistry by van't Hoff,[1] molecules belonging to various symmetries have been designed explicitly or implicitly by desymmetrization of achiral skeletons with appropriate substituents.[2–5] Such desymmetrization processes have been investigated by means of group-theoretical concepts such as local symmetry (or site symmetry),[6,7] which was originally used in the field of crystallography.[8] For the purpose of obtaining deeper insight into stereochemical phenomena,[9–13] we have pointed out the importance of orbits corresponding to coset representations (CRs),[9] of which subductions have been proposed and applied to the characterization of desymmetrization processes by us.[14] The subduction method has been further applied to the design of prochiral molecules[15] and that of chiral molecules.[16] The latter two reports have dealt with one extreme of high-symmetry cases, where an orbit fully accomodates substituents of the same kind or of the opposite chiralities, giving a molecule of the highest possible symmetry. However, the other extreme of lower-symmetry cases remains uninvestigated, where an orbit accomodates one substituent of a given symmetry along with the other substituents of the same kind. Hence, the first target of the present paper is to deal with such lower-symmetry cases in general. The second target is to clarify the diagrammatical or stereochemical meaning of the subductions by examining such extreme cases.

Results and Discussion

1. Terminology. Let me first comment on the terminology for characterizing stereochemical equivalence. The topicity terms (i.e. homotopic, enantiotopic and diastereotopic) have been widely used in organic stereochemistry.[17–22] Since these terms are too narrow to express the entire aspect of stereochemistry, they have been used in combination with another type of topicity terms (i.e. chirotopic and achirotopic).[7] In place of using such types of topicity terms, I adopt the sphericity terms (i.e. homospheric, enantiospheric and hemispheric)[9] as a unified terminology and use them throughout this paper in order to clarify their effectiveness for determining symmetrical properties of molcecules. Thus a set of equivalent positions or atoms in a molecule or skeleton is considered to construct an orbit, which is assigned to a coset representation $\mathbf{G}(/\mathbf{G}_i)$. Then the orbit is characterized as being *homospheric* if the global symmetry $\mathbf{G}$ and the local symmetry $\mathbf{G}_i$ are both achiral groups; *enantiopheric* if $\mathbf{G}$ is achiral and $\mathbf{G}_i$ is chiral; and *hemispheric* if both $\mathbf{G}$ and $\mathbf{G}_i$ are chiral groups. For example, the four hydrogens of a methane molecule (CH_4) are equivalent so as to construct an orbit (Fig. 1). Since the global symmetry of the methane is $\mathbf{T}_d$ and the local symmetry of each hydrogen is $\mathbf{C}_{3v}$, the orbit is assigned to a coset representation $\mathbf{T}_d(/\mathbf{C}_{3v})$.[23] Then, the orbit is determined to be homospheric, since the global symmetry $\mathbf{T}_d$ and the local symmetry $\mathbf{C}_{3v}$ are both achiral groups.

2. Problem-Setting. To illustrate the problem-setting of the present paper, let us consider a special case in which methane as a $\mathbf{T}_d$-skeleton is transformed into chloromethane by the mono-substitution of chlorine (Fig. 1). This process is regarded as the desymmetrization of the $\mathbf{T}_d$-skeleton into a $\mathbf{C}_{3v}$-molecule from one viewpoint of global symmetry. The other viewpoint is based on local symmetry, which gives a more sophisticated result. Thus, the local symmetry of each hydrogen in methane is $\mathbf{C}_{3v}$ so that the four-membered orbit containing the hydrogen is ascribed to the coset representation (CR) represented by the symbol $\mathbf{T}_d(/\mathbf{C}_{3v})$. The process from $\mathbf{T}_d$ to $\mathbf{C}_{3v}$ is translated into the subduction of the CR, represented by



H_4: $\mathbf{T}_d(/\mathbf{C}_{3v})$ Cl: $\mathbf{C}_{3v}(/\mathbf{C}_{3v})$

H_3: $\mathbf{C}_{3v}(/\mathbf{C}_{s})$

Fig. 1. Orbits and coset representations.

$$\mathbf{T}_d(/\mathbf{C}_{3v}) \downarrow \mathbf{C}_{3v} = \mathbf{C}_{3v}(/\mathbf{C}_{3v}) + \mathbf{C}_{3v}(/\mathbf{C}_{3s}), \tag{1}$$

Where the local symmetry of the original skeleton (methane) is equal to the global symmetry of the target molecule (chloromethane). The resulting CR $\mathbf{C}_{3v}(/\mathbf{C}_{3v})$ on the right-hand side of Eq. 1 corresponds to the one-membered orbit of chlorine, while the remaining CR $\mathbf{C}_{3v}(/\mathbf{C}_{s})$ corresponds to the three-membered orbit of the unchanged hydrogens.

Such modes of subduction as found in Eq. 1 have been calculated mathematically to provide subduction tables, as collected in Appendix C of our book.[11] The present article provides another quantitative but diagrammatical approach to treat subduction modes. The CR $\mathbf{T}_d(/\mathbf{C}_{3v})$ is derived from the coset decomposition:

$$\mathbf{T}_d = \mathbf{C}_{3v}I + \mathbf{C}_{3v}C_{2(1)} + \mathbf{C}_{3v}C_{2(2)} + \mathbf{C}_{3v}C_{2(3)}, \tag{2}$$

where the symbol I represents an identity element. In other words, the CR $\mathbf{T}_d(/\mathbf{C}_{3v})$ governs the set of cosets $\mathbf{T}_d/\mathrm{C}_3$ represented by

$$\mathbf{T}_d/\mathrm{C}_3 = \{\mathbf{C}_{3v}I, \mathbf{C}_{3v}C_{2(1)}, \mathbf{C}_{3v}C_{2(2)}, \mathbf{C}_{3v}C_{2(3)}\}. \tag{3}$$

The four cosets appearing in Eq. 2 or in Eq. 3 are schematically assigned to the four positions of a methane skeleton, as shown in the left diagram of Fig. 2.

The substitution of a chlorine atom corresponds to the fixation of the $\mathbf{C}_{3v}$ shown in the left diagram of Fig. 2. This fixation corresponds to the selection of a coset $\mathbf{C}_{3v}$ $(= \mathbf{C}_{3v}I)$ *as* a representative (Fig. 2, left), which can be correlated to the CR $\mathbf{C}_{3v}(/\mathbf{C}_{3v})$ in Eq. 1. On the other hand, the remaining set of cosets $\mathbf{C}_{3v}C_{2(i)}$ $(i = 1, 2, 3)$ in Fig. 2 can be correlated to the CR $\mathbf{C}_{3v}(/\mathbf{C}_{s})$ in Eq. 1. The stereochemical meaning of the latter set is made clear by the coalescence of the three participant cosets to give a double coset decomposition:[24]

$$\mathbf{T}_d = \mathbf{C}_{3v}I\mathbf{C}_{3v} + \mathbf{C}_{3v}C_{2(1)}\mathbf{C}_{3v}, \tag{4}$$

which is related to Eq. 2. Note that $\mathbf{C}_{3v}I\mathbf{C}_{3v}$ is equal to $\mathbf{C}_{3v}$ and we have $\mathbf{C}_{3v}C_{2(1)}\mathbf{C}_{3v} = \mathbf{C}_{3v}C_{2(1)} + \mathbf{C}_{3v}C_{2(2)} + \mathbf{C}_{3v}C_{2(3)}$, as shown schematically on the right of Fig. 2 (enclosed with a frame). The local symmetry $\mathbf{C}_s$ of $\mathbf{C}_{3v}(/\mathbf{C}_s)$ (Eq. 1) can be explained by means of the double coset decomposition. Thus the representative $C_{2(1)}$ of the double coset $\mathbf{C}_{3v}C_{2(1)}\mathbf{C}_{3v}$ gives $\mathbf{C}_{3v(2)} = C_{2(1)}{}^{-1}\mathbf{C}_{3v(1)}C_{2(1)}$, from which we derive $\mathbf{C}_{3v(2)} \cap \mathbf{C}_{3v} = \mathbf{C}_{s(2)}$ for the CR $\mathbf{C}_{3v}(/\mathbf{C}_s)$.

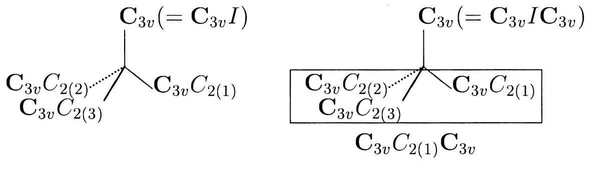


Fig. 2. Cosets, double cosets, and stereochemical equivalence.

The substitution of a chlorine atom for a methane skeleton can be alternatively explained in terms of stabilizers. The stabilizer of the coset $\mathbf{C}_{3v}C2_{(i)}$ within $\mathbf{T}_d$ is $C_{2(i)}{}^{-1}\mathbf{C}_{3v}C_{2(i)}$, since we have $\mathbf{C}_{3v}C_{2(i)}\cdot C_{2(i)}{}^{-1}\mathbf{C}_{3v}C_{2(i)} = \mathbf{C}_{3v}C_{2(i)}$. By using the transversal $\{I, C_{2(1)}, C_{2(2)}, C_{2(3)}\}$, the stabilizers can be produced as follows: $\mathbf{C}_{3v(2)} = C_{2(1)}{}^{-1}\mathbf{C}_{3v(1)}C_{2(1)}$, $\mathbf{C}_{3v(3)} = C_{2(2)}{}^{-1}\mathbf{C}_{3v(1)}C_{2(2)}$, and $\mathbf{C}_{3v(4)} = C_{2(3)}{}^{-1}\mathbf{C}_{3v(1)}C_{2(3)}$, where we place $\mathbf{C}_{3v(1)} = \mathbf{C}_{3v}$. These stabilizers can be correlated to the four positions of a methane skeleton, as found in Fig. 3 (left). The conjugacy among $\mathbf{C}_{3v(2)}$, $\mathbf{C}_{3v(3)}$, and $\mathbf{C}_{3v(4)}$ by virtue of a three-fold rotation is examined so that we have $C_{3(1)}{}^{-1}\mathbf{C}_{3v(2)}C_{3(1)} = C_{3(1)}{}^{-1}C_{2(1)}{}^{-1}\mathbf{C}_{3v(1)}C_{2(1)}C_{3(1)} = C_{2(2)}{}^{-1}\mathbf{C}_{3v(1)}C_{2(2)} = \mathbf{C}_{3v(2)}$, and so on. This conjugacy means that the number of the stabilizers is three if we consider the C_3-axis due to $\mathbf{C}_{3v}$. Note that the local symmetry $\mathbf{C}_{3v}$ $(= \{I, C_{3(1)}, C^{2}{}_{3(1)}, \text{and mirrors}\})$ is based on the C_3-axis. The conjugacy among $\mathbf{C}_{3v(2)}$, $\mathbf{C}_{3v(3)}$, and $\mathbf{C}_{3v(4)}$ is not retained during the desymmetrization from $\mathbf{T}_d$ to $\mathbf{C}_{3v}$. This fact is related to the CR $\mathbf{C}_{3v}(/\mathbf{C}_s)$ in a resulting molecule of $\mathbf{C}_{3v}$-symmetry (Fig. 3, right). The local symmetry $\mathbf{C}_s$ of $\mathbf{C}_{3v}(/\mathbf{C}_s)$ appearing in Eq. 1 is derived from the relationships $\mathbf{C}_{3v(2)} \cap \mathbf{C}_{3v} = \mathbf{C}_{s(2)}$, $\mathbf{C}_{3v(3)} \cap \mathbf{C}_{3v} = \mathbf{C}_{s(3)}$, and $\mathbf{C}_{3v(4)} \cap \mathbf{C}_{3v} = \mathbf{C}_{s(4)}$; the resulting reflection groups of order 2 are conjugate to each other in $\mathbf{C}_{3v}$ as well as in $\mathbf{T}_d$.

3. General Treatment. The above discussions can be extended to a general case. The positions of an achiral akeleton of $\mathbf{G}$-symmetry are governed by a CR $\mathbf{G}(/\mathbf{G}_i)$ that is homospheric or enantiospheric. Suppose that $\mathbf{G}_i$ is a rotation-based group represented by the symbol $\mathbf{C}_{nv}$ or $\mathbf{C}_n$ n is a positive integer)[25] and that one of the positions is substituted by a substituent of $\mathbf{G}_i$- or higher symmetry.[26] According to this substitution, we have a subduction.

$$\mathbf{G}(/\mathbf{G}_i) \downarrow \mathbf{G}_i = \alpha\mathbf{G}_i(/\mathbf{G}_i) + \beta\mathbf{G}_i(\mathbf{G}_k{}^{(i)}) \tag{5}$$

as an extension of Eq. 1, where $\mathbf{G}_{\mathrm{k}}{}^{(i)}$ is a subgroup of $\mathbf{G}_i$. When $\mathbf{G}_i$ is achiral (i.e., $\mathbf{G}(/\mathbf{G}_i)$ is homospheric), the CR $\mathbf{G}_i(/\mathbf{G}_i)$ corresponding to a one-membered orbit is obviously homospheric while the CR $\mathbf{G}_i(/\mathbf{G}_k{}^{(i)})$ is either homospheric or enantiospheric. When $\mathbf{G}_i$ is chiral (i.e., $\mathbf{G}(/\mathbf{G}_i)$ is enantiospheric), the CRs $\mathbf{G}_i(/\mathbf{G}_i)$ and $\mathbf{G}_i(/\mathbf{G}_k{}^{(i)})$ are both hemispheric. Since the degree of the CR $\mathbf{G}(/\mathbf{G}_i)$ is equal to $|\mathbf{G}|/|\mathbf{G}_i|$ and so on, Eq. 5 gives the relatiohship:

$$\frac{|\mathbf{G}|}{|\mathbf{G}_i|} = \alpha\frac{|\mathbf{G}_i|}{|\mathbf{G}_i|} + \beta\frac{|\mathbf{G}_i|}{|\mathbf{G}_k^{(i)}|}, \tag{6}$$

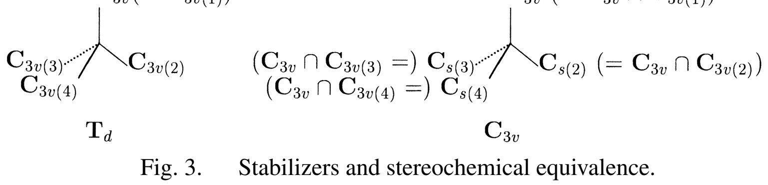


Fig. 3. Stabilizers and stereochemical equivalence.

where the symbols $|\mathbf{G}|$ etc. represent the orders of the group $\mathbf{G}$ etc.

The value of α is equal to tha mark (the number of fixed points), which is calculated to be

$$\alpha = \frac{|\mathbf{N_G}(\mathbf{G}_i)|}{|\mathbf{G}_i|}, \tag{7}$$

where the symbol $|\mathbf{N_G}(\mathbf{G}_i)|$ represents the normalizer of the subgroup $\mathbf{G}_i$ within its super-group $\mathbf{G}$.

Equation 7 can be proved as follows. We have a coset decomposition of the normalizer,

$$\mathbf{N_G}(\mathbf{G}_i) = \sum_{g \in \mathbf{X}} \mathbf{G}_i g, \tag{8}$$

where g is a representative selected from a transversal $\mathbf{X}$, the size of which is equal to the number of cosets $\mathbf{G}_i g$ appearing in Eq. 8, i.e., $|\mathbf{N_G}(\mathbf{G}_i)|/|\mathbf{G}_i|$. Since g ($\in \mathbf{X}$) is an element of the normalizer $\mathbf{N_G}(\mathbf{G}_i)$, we have $\mathbf{G} = g^{-1}\mathbf{G}_i g$. It follows that

$$\mathbf{G}_i g \mathbf{G}_i = \mathbf{G}_i g(g^{-1}\mathbf{G}_i g) = \mathbf{G}_i g. \tag{9}$$

Equation 9 means that the double coset $\mathbf{G}_i g \mathbf{G}_i$ contains only one coset $\mathbf{G}_i g$. Hence, $\mathbf{G}_i g \mathbf{G}_i$ for each $g(\in \mathbf{X})$ is correlated to the CR $\mathbf{G}_i(/\mathbf{G}_i)$. Equation 9 shows at the same time that the number (i.e. α) of the double cosets $\mathbf{G}_i g \mathbf{G}_i$ for each $g(\in \mathbf{X})$ is equal to the number of the cosets $\mathbf{G}_i g$, which has been calculated to be $|\mathbf{N_G}(\mathbf{G}_i)|/|\mathbf{G}_i|$ by means of Eq. 8.

Finally, Eqs. 6 and 7 give the value of β, being

$$\beta = \frac{(|\mathbf{G}| - |\mathbf{N_G}(\mathbf{G}_i)|)|\mathbf{G}_k^{(i)}|}{|\mathbf{G}_i|^2}. \tag{10}$$

Equation 5 is a special case for the subduction of coset representations, which has been calculated algebraically and is listed as subduction tables for representative point groups.[11] In contrast, Eqs. 7 and 10 give another way of calculating the multiplicities (α and β), which are derived from the data of the participating groups and the normalizer of $\mathbf{G}_i$. Since the special case describes modes of monosubstitution, such a restriction is rather fruitful since it gives a determinative result such as Eqs. 7 and 10.

4. Methane Derivatives. Let us examine the chloromethane case described above. Equation 1 is an example for a general expression of Eq. 5. The normalizer of $\mathbf{C}_{3v}$ in $\mathbf{T}_d$ is $\mathbf{C}_{3v}$ itself so that we obtain $\alpha = |\mathbf{C}_{3v}|/|\mathbf{C}_{3v}| = 1$ for chloromethane (Eq. 1). By virtue of Eq. 10, we obtain $\beta = [(24 - 6) \times 2]/6^2 = 1$, since we have $|\mathbf{G}| = |\mathbf{T}_d| = 24$, $|\mathbf{G}_i| = |\mathbf{C}_{3v}| = 6$, $|\mathbf{N_G}(\mathbf{G}_i)| = |\mathbf{C}_{3v}| = 6$, and $|\mathbf{G}_k^{(i)}| = |\mathbf{C}_s| = 2$. This result is in agreement with Eq. 1.

Let us consider further substitution of chloromethane with a fluorine atom (Fig. 4). Thus, the homospheric $\mathbf{C}_{3v}(/\mathbf{C}_s)$-orbit in chloromethane is to be examined. This example is a case in which a homospheric orbit is desymmetrized into a homospheric one-membered orbit and an enantiospheric orbit.

Suppose that one of the three hydrogens is substituted by a fluorine atom (the right diagram of Fig. 4. This desymmetrization process corresponds to the following subduction:

$$\mathbf{C}_{3v}(/\mathbf{C}_s) \downarrow \mathbf{C}_s = \mathbf{C}_s(/\mathbf{C}_s) + \mathbf{C}_s(/\mathbf{C}_1), \tag{11}$$

which is in agreement with Eq. 5. Since the normalizer of $\mathbf{C}_s$ in $\mathbf{C}_{3v}$ is determined to be $\mathbf{C}_s$ itself, Eq. 7 gives

$$\alpha = \frac{|\mathbf{C}_s|}{|\mathbf{C}_s|} = \frac{2}{2} = 1, \tag{12}$$

which is equal to the coefficient of the CR $\mathbf{C}_s(/\mathbf{C}_s)$ on the right-hand side of Eq. 11. According to Eq. 10, we have

$$\beta = \frac{(6-2)\times 1}{2^2} = 1, \tag{13}$$

which is equal to the coefficient of the CR $\mathbf{C}_s(/\mathbf{C}_1)$ on the right-hand side of Eq. 11.

Let us next consider the conversion of dichloromethane into dichlorofluoromethane (Fig. 5), where the homospheric $\mathbf{C}_{2v}(/\mathbf{C}_s)$-orbit of two hydrogens in dichloromethane is to be examined. This example is a case in which a homospheric orbit is desymmetrized into two homospheric one-membered orbit and no other orbits.

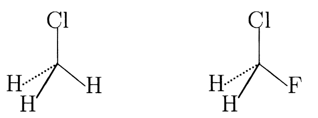
The desymmetrization process of the $\mathbf{C}_{2v}(/\mathbf{C}_s)$-orbit corresponds to the following subduction:

$$\mathbf{C}_{2v}(/\mathbf{C}_s) \downarrow \mathbf{C}_s = 2\mathbf{C}_s(/\mathbf{C}_s), \tag{14}$$

which is in agreement with Eq. 5. The normalizer of $\mathbf{C}_s$ in $\mathbf{C}_{2v}$ is determined to be $\mathbf{C}_{2v}$. Note that the $\mathbf{C}_s$ is not conjugate to the other reflective subgroup of the $\mathbf{C}_{2v}$. Hence, Eq. 7 gives

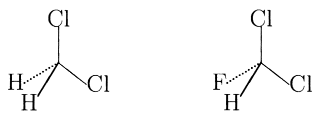
$$\alpha = \frac{|\mathbf{C}_{2v}|}{|\mathbf{C}_s|} = \frac{4}{2} = 2, \tag{15}$$

which is equal to the coefficient of the CR $\mathbf{C}_s(/\mathbf{C}_s)$ on the right-hand side of Eq. 14. On the other hand, we have



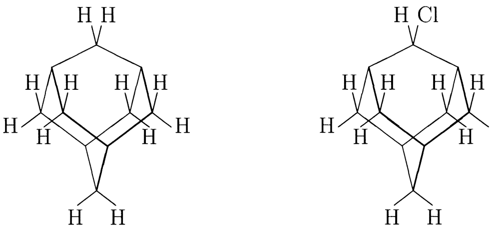
$\mathbf{C}_{3v}$		$\mathbf{C}_s$	
Cl:	$\mathbf{C}_{3v}(/\mathbf{C}_{3v})$	Cl:	$\mathbf{C}_s(/\mathbf{C}_s)$
H_3:	$\mathbf{C}_{3v}(/\mathbf{C}_s)$	F:	$\mathbf{C}_s(/\mathbf{C}_s)$
		H_2:	$\mathbf{C}_s(/\mathbf{C}_1)$

Fig. 4.　Chloromethane and Chlorofluoromethane.



$\mathbf{C}_{2v}$		$\mathbf{C}_s$	
Cl_2:	$\mathbf{C}_{2v}(/\mathbf{C}_s)$	F:	$\mathbf{C}_s(/\mathbf{C}_s)$
H_2:	$\mathbf{C}_{2v}(/\mathbf{C}_s)$	H:	$\mathbf{C}_s(/\mathbf{C}_s)$
		Cl_2:	$\mathbf{C}_s(/\mathbf{C}_1)$

Fig. 5.　Dichloromethane and Dichlorofluoromethane.



Adamantane ($\mathbf{T}_d$)		2-Chloroadamantane ($\mathbf{C}_s$)	
H_{12} (methylenes) :	$\mathbf{T}_d(/\mathbf{C}_s)$	Cl:	$\mathbf{C}_s(/\mathbf{C}_s)$
		H:	$\mathbf{C}_s(/\mathbf{C}_s)$
		$5H_2$ (remaining):	$\mathbf{C}_s(/\mathbf{C}_1)$

Fig. 6. Adamantane and 2-chloroadamantane.

$$\beta = \frac{(4-4)\times|\mathbf{G}_k^{(i)}|}{2^2} = 0 \tag{16}$$

according to Eq. 10. This value is in agreement with Eq. 14, which contains no such CRs.

5. Adamantane Derivatives. Twelve hydrogens on the methylene bridges of adamantane construct an orbit assigned to the CR $\mathbf{T}_d(/\mathbf{C}_s)$, as shown on the left of Fig. 6. The number of them is calculated to be $|\mathbf{T}_d|/|\mathbf{C}_s| = 24/2 = 12$. The CR is homospheric, since $\mathbf{T}_d$ and $\mathbf{C}_s$ are both achiral. This example is a case in which a homospheric orbit is desymmetrized into two homospheric one-membered orbit and five enantiospheric orbits.

By substituting one of the twelve hydrogens with a chlorine atom, the adamantane skeleton is desymmetrized into 2-chloroadamantane of $\mathbf{C}_s$-symmetry, as shown on the right of Fig. 6. In agreement with Eq. 5, the desymmetrization process is characterized by the following subduction:

$$\mathbf{T}_d(/\mathbf{C}_s) \downarrow \mathbf{C}_s = 2\mathbf{C}_s(/\mathbf{C}_s) + 5\mathbf{C}_s(/\mathbf{C}_1). \tag{17}$$

The coefficient 2 on the CR $\mathbf{C}_s(/\mathbf{C}_s)$ corresponds to the chlorine and the hydrogen on the same carbon. On the other hand, the remaining ten hydrogens are divided into five orbits corresponding to the CR $\mathbf{C}_s(/\mathbf{C}_1)$.

Since the normalizer of $\mathbf{C}_s$ in $\mathbf{T}_d$ is determined to be $\mathbf{C}_{2v}$, Eq. 7 gives

$$\alpha = \frac{|\mathbf{C}_{2v}|}{|\mathbf{C}_s|} = \frac{4}{2} = 2, \tag{18}$$

which is equal to the coefficient of the CR $\mathbf{C}_s(/\mathbf{C}_s)$ on the right-hand side of Eq. 17. On the other hand, we have

$$\beta = \frac{(24-4)\times 1}{2^2} = 5, \tag{19}$$

by virture of Eq. 10. This value is equal to the coefficient of the CR $\mathbf{C}_s(/\mathbf{C}_1)$ appearing on the right-hand side of Eq. 17.

6. Hetera-adamantane Derivatives. Adamantane has six methylenes, which construct an orbit assigned to the CR $\mathbf{T}_d(/\mathbf{C}_{2v})$, where the number of the methylenes is calculated to be $|\mathbf{T}_d|/|\mathbf{C}_{2v}| = 24/4 = 6$ (the left diagram of Fig. 7). The CR is homospheric, since $\mathbf{T}_d$ and $\mathbf{C}_{2v}$ are both achiral.

Adamantane ($\mathbf{T}_d$)		Oxa-adamantane ($\mathbf{C}_{2v}$)	
C_6 (methylenes) :	$\mathbf{T}_d(/\mathbf{C}_{2v})$	O:	$\mathbf{C}_{2v}(/\mathbf{C}_{2v})$
		C (opposite):	$\mathbf{C}_{2v}(/\mathbf{C}_{2v})$
		C_4 (remaining):	$\mathbf{C}_{2v}(/\mathbf{C}_1)$

Fig. 7. Adamantane and an oxa derivative.

Suppose that one of the six methylenes is replaced by an oxygen atom (the right diagram of Fig. 7).[27] This desymmetrization process is characterized by the following subduction:

$$\mathbf{T}_d(/\mathbf{C}_{2v}) \downarrow \mathbf{C}_{2v} = 2\mathbf{C}_{2v}(/\mathbf{C}_{2v}) + \mathbf{C}_{2v}(\mathbf{C}_1), \tag{20}$$

which is in agreement with Eq. 5. The coefficient 2 on the CR $\mathbf{C}_{2v}(/\mathbf{C}_{2v})$ corresponds to the oxygen and the opposite methylene, each of which is assigned to a one-membered $\mathbf{C}_{2v}(/\mathbf{C}_{2v})$-orbit. Note that the five methylenes have remained unsubstituted, the one methylene described above is discriminated from the others. Thus the set of the other four methylenes corresponds to the CR $\mathbf{C}_{2v}(/\mathbf{C}_1)$.

Since the normalizer of $\mathbf{C}_{2v}$ in $\mathbf{T}_d$ is determined to be $\mathbf{D}_{2d}$, Eq. 7 gives

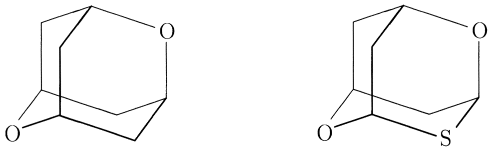
$$\alpha = \frac{|\mathbf{D}_{2d}|}{|\mathbf{C}_{2v}|} = \frac{8}{4} = 2, \tag{21}$$

which is equal to the coefficient of the CR $\mathbf{C}_{2v}(/\mathbf{C}_{2v})$ appearing on the right-hand side of Eq. 20. According to Eq. 10, on the other hand, we have

$$\beta = \frac{(24-8)\times 1}{4^2} = 1, \tag{22}$$

which is equal to the coefficient of the CR $\mathbf{C}_{2v}(/\mathbf{C}_1)$ appearing on the right-hand side of Eq. 20.

2,6-Dioxaadamantane belongs to the global symmetry $\mathbf{D}_{2d}$, where we examine four carbons on the methylene bridges.



Dioxa-adamantane ($\mathbf{D}_{2d}$)		Dioxathia-adamantane ($\mathbf{C}_2$)	
C_4 (methylenes) :	$\mathbf{D}_{2d}(/\mathbf{C}'_2)$	S:	$\mathbf{C}_2(/\mathbf{C}_2)$
		C (opposite):	$\mathbf{C}_2(/\mathbf{C}_2)$
		C_2 (remaining):	$\mathbf{C}_2(/\mathbf{C}_1)$

Fig. 8. Dioxa-adamantane and an dioxathia derivative.

They construct an orbit assigned to the CR $\mathbf{D}_{2d}(/\mathbf{C}'_2)$, as shown on the left of Fig. 8. The CR is enantiospheric, since the global symmetry $\mathbf{D}_{2d}$ is achiral and the local symmetry $\mathbf{C}'_2$ is chiral. The number of the methylenes is calculated to be $|\mathbf{D}_{2d}|/|\mathbf{C}'_2| = 8/2 = 4$. This example is a case in which an enantiospheric orbit is desymmetrized into hemispheric orbits.

Suppose that one of the four methylenes is substituted by a sulfur atom. The enantiosphericity of the $\mathbf{D}_{2d}(/\mathbf{C}'_2)$-orbit causes a chiral synthesis (so-called asymmetric synthesis) to give a chiral molecule shown on the right of Fig. 8, where an arbitrary enantiomer is shown as a representative. In agreement with Eq. 5, this desymmetrization process is characterized by the following subduction:

$$\mathbf{D}_{2d}(/\mathbf{C}'_2) \downarrow \mathbf{C}'_2 = 2\mathbf{C}'_2(/\mathbf{C}'_2) + \mathbf{C}'_2(/\mathbf{C}_1). \qquad (23)$$

The coefficient 2 on the CR $\mathbf{C}'_2(/\mathbf{C}'_2)$ corresponds to the sulfur and the opposite methylene, each of which is assigned to a one-membered $\mathbf{C}'_2(/\mathbf{C}'_2)$-orbit. On the other hand, the set of the remaining two methylenes corresponds to the CR $\mathbf{C}'_2(/\mathbf{C}_1)$. Note that the symbols on the right-hand side of Eq. 23 contain primes in order to avoid confusion, though the discrimination due to conjugacy loses meaning during the desymmetrization. For the sake of simplicity, such prime symbols have been omitted on the right of Fig. 8.

According to Eq. 7, we have

$$\alpha = \frac{|\mathbf{D}_2|}{|\mathbf{C}'_2|} = \frac{4}{2} = 2, \qquad (24)$$

since the normalizer of $\mathbf{C}'_2$ in $\mathbf{D}_{2d}$ is determined to be $\mathbf{D}_2$. The resulting value 2 is equal to the coefficient of the CR $\mathbf{C}'_2(/\mathbf{C}'_2)$ on the right-hand side of Eq. 23. According to Eq. 10, on the other hand, we have

$$\beta = \frac{(8-4)\times 1}{2^2} = 1, \qquad (25)$$

which is equal to the coefficient of the CR $\mathbf{C}'_2(/\mathbf{C}_1)$ on the right-hand side of Eq. 23.

Fixed Axes and Planes

The subduction of a homospheric or enantiospheric orbit represented by $\mathbf{G}(/\mathbf{G}_i) \downarrow \mathbf{G}_i$ corresponds to the fixation of the axis of $\mathbf{G}_i$, if $\mathbf{G}_i$ is regarded to be $\mathbf{C}_{nv}$ or $\mathbf{C}_n$ and we have $n \geqq 2$. For example, the case of methane (Fig. 1) is the fixation of the C_3 axis through one of the four hydrogens. This process causes the fixation of one hydrogen, since the C_3 axis contains the fixed hydrogen only.[28] On the other hand, the case of heteraadamantane (Fig. 7) causes the fixation of two methylenes, since the C_2 axis contains the two methylenes, as shown in Eq. 20. Such stereochemical examination of the case of $n \geqq 2$ shows that the C_n axis for $\mathbf{C}_{nv}$ or $\mathbf{C}_n$ contains one or two positions. As a result, α in Eq. 5 is concluded to be equal to one or two if n is equal to 2 or greater than 2.

The discussion described in the preceding paragraph in combination with Eq. 7 shows the existence of two cases (if $n \geqq 2$), i.e., one case where the normalizer of $\mathbf{C}_{nv}$ (or $\mathbf{C}_n$ is $\mathbf{C}_{nv}$ (or $\mathbf{C}_n$) itself where no dihedral two-fold axes are present and the other case where the normalizer of $\mathbf{C}_{nv}$ (or $\mathbf{C}_n$) is $\mathbf{D}_{nd}$ (or $\mathbf{D}_n$) where dihedral two-fold axes are present, perpendicular to the C_n axis. Hence we have $\alpha = |\mathbf{C}_{nv}|/|\mathbf{C}_{nv}| = 1$ (or $\alpha = |\mathbf{C}_n|/|\mathbf{C}_n| = 1$) or $\alpha = |\mathbf{D}_{nd}|/|\mathbf{C}_{nv}| = 2$ (or $\alpha = |\mathbf{D}_n|/|\mathbf{C}_n| = 2$) if we presume $n \geqq 2$.

In constant, the case of $n = 1$ (i.e. $\mathbf{G}_i = \mathbf{C}_s$) means the fixation of a mirror plane. As a result, there may appear cases in which more than 2 positions are fixed (i.e. α may be more than 2 in Eq. 5), though such a mirror plane caused the fixation of two positions in the example of adamantane into 2-chloroadamantane (Fig. 6). For example, the mono-substitution of perhydrofullerene is represented by the following subduction:[29]

$$\mathbf{I}_h(/\mathbf{C}_s) \downarrow \mathbf{C}_s = 4\mathbf{C}_s(/\mathbf{C}_s) + 28\mathbf{C}_s(/\mathbf{C}_1) \qquad (26)$$

The local symmetry $\mathbf{G}_k{}^{(i)}$ of the second CR $\mathbf{G}_i(/\mathbf{G}_k{}^{(i)})$ in Eq. 5 can be shown to be $\mathbf{C}_s$ or $\mathbf{C}_1$. Suppose that $\mathbf{G}_i$ is $\mathbf{C}_{nv}$ or $\mathbf{C}_n$. Because of $\mathbf{G}_k{}^{(i)} = g^{-1}\mathbf{G}_i g \cap \mathbf{G}_i$ (Theorem 2 of Ref. 24), a stereochemical examination shows that the conjugate groups, $g^{-1}\mathbf{G}_i g$ and $\mathbf{G}_i$, have no C_n axis in common ($n \geqq 2$). This means that $g^{-1}\mathbf{G}_i g \cap \mathbf{G}_i$ is $\mathbf{G}_s$ or C_1. If $\mathbf{G}_i$ is $\mathbf{C}_s$ ($n = 1$), $g^{-1}\mathbf{G}_i g \cap \mathbf{G}_i$ is obviously determined to be $\mathbf{C}_1$.

Conclusion

Desymmetrization of achiral skeletons by mono-substitution is examined by virtue of the subduction of a coset representation, $\mathbf{G}(/\mathbf{G}_i) \downarrow \mathbf{G}_i$. The resulting molecule contains one or more one-membered homospheric or hemispheric $\mathbf{G}_i(/\mathbf{G}_i)$-orbits and one or more $\mathbf{G}_i(/\mathbf{G}_k{}^{(i)})$-orbit, we where the $\mathbf{G}_k{}^{(i)}$ is a subgroup of $\mathbf{G}_i$. The multiplicities of these coset representations are calculated from the data of the participating groups and the normalizer of $\mathbf{G}_i$.

References

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

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

3 M. Farina and C. Morandi, *Tetrahedron*, **30**, 1819 (1974).

4 V. Prelog, *Science*, 193, 17 (1976).

5 M. Nakazaki and K. Naemura, *J. Org. Chem.*, **46**, 106 (1981).

6 R. L. Flurry, *J. Am. Chem. Soc.*, **103**, 2901 (1981).

7 K. Mislow and J. Siegel, *J. Am. Chem. Soc.*, **106**, 3319 (1984).

8 T. Hahn and A. Vos, in "International Tables for Crystallography. Brief Teaching Edition of Volume A. Space-Group Symmetry," ed by T. Hahn, D. Reidel, Dordrecht (1988) pp. 9–36.

9 S. Fujita, *J. Am. Chem. Soc.*, **112**, 3390 (1990).

10 S. Fujita, *Tetrahedron*, **56**, 735 (2000).

11 S. Fujita, "Symmetry and Combinatorial Enumeration in Chemistry," Springer-Verlag, Berlin-Heidelberg (1991).

12 S. Fujita, *Tetrahedron*, **46**, 5943 (1990).

13 S. Fujita, *Bull. Chem. Soc. Jpn.*, **64**, 439 (1991).

14 S. Fujita, *Theor. Chim. Acta*, **76**, 247 (1989).

15 S. Fujita, Bull. *Chem. Soc. Jpn.*, **73**, 2009 (2000).

16 S. Fujita, Bull. *Chem. Soc. Jpn.*, **73**, 1979 (2000).

17 K. Mislow and M. Raban, *Top. Stereochem.*, **1**, 1 (1967).

18 H. Hirschmann and K. R. Hanson, *Eur. J. Biochem.*, **22**, 301 (1971).

19 E. L. Eliel, *J. Chem. Educ.*, **57**, 52 (1980).

20 E. L. Eliel, *Top. Curr. Chem.*, **105**, 1 (1982).

21 H. G. Floss, M.-D. Tsai, and R. W. Woodard, *Top. Stereochem.*, **15**, 253 (1984).

22 J. Jonas, *Coll. Czech. Chem. Commun.*, **53**, 2676 (1988).

23 A strict assignment based on mark tables has been discussed in Chapter 6 of Ref. 11.

24 S. Fujita, *J. Graph Theory*, **18**, 349 (1994).

25 This assumption does not restrict the scope of the discussion described here, because local symmetries other than $\mathbf{C}_{nv}$ or $\mathbf{C}_{n}$ are forbidden by stereochemical examination. See Section 7.2 of Ref. 11.

26 Even if a substituent of $\mathbf{G}_i$- or higher symmetry is used, the substituent on the position governed by $\mathbf{G}(/\mathbf{G}_i)$ is restricted to the local symmetry $\mathbf{G}_i$.

27 The present article deals with stereochemical relationship between adamantane (Fig. 7, left) and 2-oxaadamantane (Fig. 7, right) and dose not discuss whether the direct derivation from the former to the latter is possible chemically or not. If chemically possible examples are desired, such derivation from adamantane-2,6-dione to its monothione can be selected.

28 The central carbon of methane is not considered in this discussion.

29 S. Fujita, *Bull. Chem. Soc. Jpn.*, **64**, 3215 (1991).