that those residues which tend to form more stable helical sequences also tend to nucleate the formation of these regions better.

## IV. Conclusions

Water-soluble random copolymers containing L-phenylalanine and $N^5$-(3-hydroxypropyl)-L-glutamine were synthesized and characterized. From an analysis of the thermally induced helix-coil transitions of these copolymers, the Zimm-Bragg parameters $\sigma$ and $s$ for poly(L-phenylalanine) were deduced. The values for $s$ show that L-phenylalanine is a moderately strong helix former, stronger than L-alanine, but weaker than L-leucine. These results are in good agreement with the earlier qualitative results of other workers. The greater stability of the $\alpha$-helical form of poly(L-phenylalanine) compared to poly(L-alanine) and of poly(L-leucine) compared to both poly(L-phenylalanine) and poly(L-alanine) has been attributed to hydrophobic interactions.

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# Ring Closure in Chain Molecules with $C_n$, $I$, or $S_{2n}$ Symmetry[1]

**Nobuhiro Gō[2] and Harold A. Scheraga***

*Department of Chemistry, Cornell University, Ithaca, New York 14850.*

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ABSTRACT: Mathematical methods are developed for the exact generation of conformations of cyclic chain molecules with $C_n$, $I$, or $S_{2n}$ symmetry, when bond lengths and bond angles are maintained fixed. The methods are illustrated for the case of cyclohexane. An explicit expression is given for the dihedral angles of the flexible boat form of cyclohexane. Application of these methods to conformational energy calculations of cyclic oligopeptides is discussed.

There is considerable interest in the conformations of cyclic oligopeptides, which may or may not have symmetry. In order to study their conformations, it is necessary to generate ring structures of such molecules. The problem of the exact ring closure of a chain molecule with fixed bond lengths and bond angles has already been solved without assuming any symmetry,[3-5] and differs from that in which symmetry is assumed. This paper is concerned with solving the mathematical problem of finding a set of dihedral angles in a cyclic chain molecule whose conformation has $C_n$, $I$, or $S_{2n}$ symmetry. Although the methods have been developed with applications to cyclic oligopeptides in mind, they are applicable to any cyclic chain molecule with symmetry. Therefore, the methods are illustrated for the simple case of cyclohexane. The origin of the rigidity and flexibility of the chair and boat forms, respectively, of cyclohexane is discussed from both the point of view of the theory developed earlier[3] and that presented here.

## I. Nature of Symmetry in Cycle Structures

In general, a chain molecule can be regarded as a series of *units* linked by single bonds about which rotation can take place (see Figure 1). The $i$th bond (with dihedral angle for rotation around it being denoted as $\omega_i$) between atom $B_{i-1}$ in the $(i - 1)$th unit and atom $A_i$ in the $i$th unit links these two units. The $i$th *structure*, consisting of the $i$th unit and atoms $B_{i-1}$ and $A_{i-1}$, is a rigid one; *i.e.*, the relative positions of the atoms in the structure do not change even when $\omega_i$ and $\omega_{i+1}$ do. Each unit may consist either of a single atom or of two or more atoms. In the case of a polyethylene-type molecule, atoms $A_i$ and $B_i$ are a single identical atom. When atoms $B_{i-1}$, $A_i$, $B_i$, $A_{i+1}$ lie in a single plane, the structure is said to have a *planar backbone* (as in the polypeptide chain); this definition of a planar backbone includes the trivial case in which atoms $A_i$ and $B_i$ are a single identical atom. It also includes an important special case where the $i$th structure has a plane of symmetry in which atoms $B_{i-1}$, $A_i$, $B_i$, $A_{i+1}$ (and any other atoms that define the backbone of the chain) lie.

For symmetry to exist in a molecule, there must, first of all, be symmetry in the covalent structure. In a molecule with $C_n$ symmetry, rotation about the symmetry axis by $2\pi/n$ leads to the same structure, and the following relation holds among its dihedral angles

$$\omega_{i+km} = \omega_i \quad (i = 1, 2, \ldots, m;\ k = 1, 2, \ldots, n - 1) \qquad (1)$$

where $n$ is the number characterizing the symmetry, and $m$ is the number of dihedral angles in a *symmetry unit* [a succession of units (in the sense defined above) whose conformation (or its mirror image) repeats in a manner specified by the symmetry]. In the case of $I$ symmetry, inversion through a point leads to the same structure, and the following relation holds

$$\omega_{i+m} = -\omega_i \quad (i = 1, 2, \ldots, m) \qquad (2)$$

In the case of $S_{2n}$ symmetry, rotation about the symmetry axis by $\pi \pm \pi/n$, and then inversion through a point on the symmetry axis, leads to the same structure, and the following relation holds

$$\omega_{i+2km} = \omega_i \quad (i = 1, 2, \ldots, m;\ k = 1, 2, \ldots, n - 1) \qquad (3)$$

$$\omega_{i+(2k+1)m} = -\omega_i$$

$$(i = 1, 2, \ldots, m;\ k = 0, 1, 2, \ldots, n - 1)$$

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(2) On leave of absence from the Department of Physics, Faculty of Science, University of Tokyo, Tokyo, Japan, Summer, 1971, and from the Department of Physics, Faculty of Science, Kyushu University, Fukuoka, Japan, Summer 1972.

(3) N. Gō and H. A. Scheraga, *Macromolecules*, 3, 178 (1970); this paper will be referred to hereinafter as A, with equation numbers cited as (A-*x*).

(4) The solution is a trivial one when bond lengths and bond angles are allowed to vary. The necessity (or the advantage) of treating bond lengths and bond angles as fixed was discussed earlier[5] and reviewed briefly in paper A.

(5) N. Gō and H. A. Scheraga, *J. Chem. Phys.*, 51, 4751 (1969).

The case of $n = 1$, *i.e.*, $S_2$ symmetry, is identical with that of $I$ symmetry.

Equations 2 and 3 will be derived rigorously in section III, but they are presented here for the purpose of specifying the kinds of symmetry to be treated in this paper.

## II. Cyclic Chain Molecules with $C_n$ Symmetry

If $F_i$ is an $i$th *unit*, consisting of rigidly arranged atoms such as $A_i$ and $B_i$ as defined in Figure 1, a molecule whose chemical structure is

$$\overline{\llcorner\,(\mathrm{F}_1\mathrm{F}_2\cdots\mathrm{F}_m)_n\,\lrcorner}$$

can assume conformations with $C_n$ symmetry. In order to develop practical methods to obtain sets of dihedral angles which generate conformations with $C_n$ symmetry, we proceed as follows.

Consider a right-handed local cartesian coordinate system for each *structure*. The $i$th coordinate system is defined in such a way that the origin is at atom $B_{i-1}$ and the $x$ axis is along the vector pointing from atom $B_{i-1}$ to atom $A_i$. The $y$ axis is defined by selecting a suitable atom in the $i$th structure. To remain general in this section, we need not specify how the $y$ axis is defined. (For a structure with a planar backbone, it is natural to define the $y$ axis in such a way that the $x,y$ plane coincides with the plane of the backbone, and this is actually done in section III.) If a given point in space is expressed by position vectors $\mathbf{r}_i$ and $\mathbf{r}_{i-1}$ with respect to the $i$th and $(i-1)$th coordinate system, respectively, the relation between them is

$$\mathbf{r}_{i-1} = \mathbf{T}_{i-1}\mathbf{R}_i\mathbf{r}_i + \mathbf{p}_{i-1} \tag{4}$$

where $\mathbf{T}_{i-1}$ is a $3 \times 3$ orthogonal matrix for rotation to bring the $i$th coordinate system into the same orientation as that of the $(i-1)$th coordinate system when $\omega_i = 0$, $\mathbf{p}_{i-1}$ is the position vector of atom $B_{i-1}$ with respect to the $(i-1)$th coordinate system, and $\mathbf{R}_i$ is a matrix for rotation about the $x$ axis by $\omega_i$ and is given by

$$\mathbf{R}_i \equiv \mathbf{R}(\omega_i) = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos\omega_i & -\sin\omega_i \\ 0 & \sin\omega_i & \cos\omega_i \end{bmatrix} \tag{5}$$

In this section the $mn$th local coordinate system will sometimes also be called the 0th one because of the cyclic nature of the molecule. The $m$th coordinate system may be transformed to the 0th system by repetitive use of eq 4 to give

$$\mathbf{r}_0 = \mathbf{U}\mathbf{r}_m + \mathbf{p} \tag{6}$$

where

$$\mathbf{U} = \mathbf{T}_0\mathbf{R}_1\mathbf{T}_1\mathbf{R}_2\cdots\mathbf{T}_{m-1}\mathbf{R}_m \tag{7}$$

$$\mathbf{p} = \mathbf{p}_0 + \mathbf{T}_0\mathbf{R}_1\mathbf{p}_1 + \mathbf{T}_0\mathbf{R}_1\mathbf{T}_1\mathbf{R}_2\mathbf{p}_2 + \ldots + \mathbf{T}_0\mathbf{R}_1\mathbf{T}_1\mathbf{R}_2\cdots\mathbf{T}_{m-2}\mathbf{R}_{m-1}\mathbf{p}_{m-1} \tag{8}$$

The matrix U brings the $m$th coordinate system into the same orientation as that of the 0th one, and the vector **p** is the position vector of the origin of the $m$th coordinate system with respect to the 0th one.

When the molecule has $C_n$ symmetry, the 0th and $m$th local coordinate systems are symmetry related; *i.e.*, the 0th coordinate system can be made to overlap the $m$th one by a rotation of $2\pi/n$ around the symmetry axis. In order to achieve this overlap, **U** and **p** must be related in a specific manner which we now demonstrate. Consider two more coordinate systems (the 0′th and $m'$th) having the same orientations as the 0th and $m$th ones, respectively, but having both their origins at the same point on the symmetry axis. If $\mathbf{r}_{0'}$ and $\mathbf{r}_{m'}$ are the position vectors of a given point in space with respect to the 0′th and $m'$th coordinate systems, then

$$\mathbf{r}_{0'} = \mathbf{r}_0 + \mathbf{q} \tag{9}$$

$$\mathbf{r}_{m'} = \mathbf{r}_m + \mathbf{q} \tag{10}$$

and

$$\mathbf{r}_{0'} = \mathbf{U}[\mathbf{u}, \pm(2\pi/n)]\mathbf{r}_{m'} \tag{11}$$

where **q** is the position vector of the origin of the 0th (or $m$th, respectively) coordinate system with respect to the 0′th (or $m'$th, respectively) one, and **u** is a unit vector (with direction cosines $u_x$, $u_y$, $u_z$ in the 0th coordinate system) lying along the symmetry axis. The matrix $\mathbf{U}(\mathbf{u},\phi)$ in eq 11, where $\phi = \pm 2\pi/n$, is given by[6] equation 12

$$\mathbf{U}(\mathbf{u},\phi) = \begin{bmatrix} u_x^2(1-\cos\phi)+\cos\phi & u_xu_y(1-\cos\phi)-u_z\sin\phi & u_xu_z(1-\cos\phi)+u_y\sin\phi \\ u_yu_x(1-\cos\phi)+u_z\sin\phi & u_y^2(1-\cos\phi)+\cos\phi & u_yu_z(1-\cos\phi)-u_x\sin\phi \\ u_zu_x(1-\cos\phi)-u_y\sin\phi & u_zu_y(1-\cos\phi)+u_x\sin\phi & u_z^2(1-\cos\phi)+\cos\phi \end{bmatrix} \tag{12}$$

and expresses a rotation by an angle $\phi$ about the unit vector **u**; *i.e.*, eq 11 indicates that the $m'$th coordinate system can be obtained by rotating the 0′th coordinate system about an axis (the symmetry axis of the molecule in this case) going through the common origin. From eq 9 to 11, we obtain

$$\mathbf{r}_0 = \mathbf{U}[\mathbf{u}, \pm(2\pi/n)]\mathbf{r}_m + \{\mathbf{U}[\mathbf{u}, (2\pi/n)] - \mathbf{I}\}\mathbf{q} \tag{13}$$

where **I** is the unit matrix. By comparing eq 6 and 13, we see that

$$\mathbf{U} = \mathbf{U}[\mathbf{u}, \pm(2\pi/n)] \tag{14}$$

and

$$\mathbf{p} = \{\mathbf{U}[\mathbf{u}, \pm(2\pi/n)] - \mathbf{I}\}\mathbf{q} \tag{15}$$

This means that U and **p**, given for the general case by eq 7 and 8, must have the forms given by the right-hand sides of eq 14 and 15, respectively, in a molecule with $C_n$ symmetry, with certain vectors **u** and **q** whose meaning is described above. The necessary conditions that **U** and **p** must satisfy *in order to generate a conformation with* $C_n$ symmetry can be derived by eliminating the vector **u** from eq 14 and **q** from eq 15. Taking the trace of both sides of eq 14, and using eq 12, we have

$$\mathrm{Tr}\mathbf{U} \equiv \sum_{i=1}^{3} u_{ii} = 1 + 2\cos(2\pi/n) \tag{16}$$

Also, from eq 15, we have

$$\mathbf{u}\cdot\mathbf{p} = 0 \tag{17}$$

which means that the vector **p** must be perpendicular to the symmetry axis.

It is shown below that these equations also represent sufficiency conditions; *i.e.*, if **U** and **p**, given by eq 7 and 8, respectively, satisfy eq 16 and 17, then it is possible to find vectors **u** and **q** and to determine them uniquely so

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[6] H. Jeffreys and B. Jeffreys, "Methods of Mathematical Physics," Cambridge University Press, Cambridge, 1956, 3rd ed, p 122.

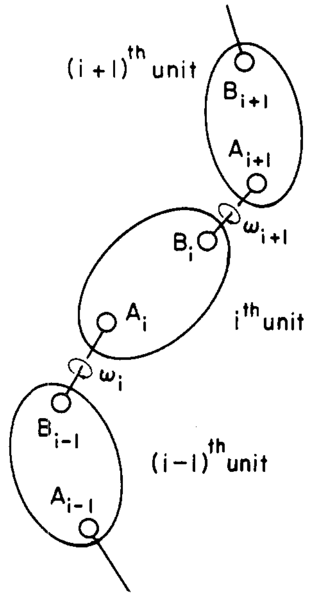

**Figure** 1. Definition of *units*.

that U and p have the forms given by the right-hand sides of eq 14 and 15, respectively. The sufficiency conditions are demonstrated as follows. When the matrix U of eq 7 satisfies eq 16, the vector u can be determined automatically from the elements of U because U has the form of eq 12 with $\phi = \pm 2\pi/n$. Then, by equating eq 7 and 12 (which are functions of the $\omega$'s), we obtain $u_x$, $u_y$, $u_z$. When the vector **p** of eq 8 satisfies eq 17, with the vector **u** determined above, we can choose a vector **q** so that eq 15 is satisfied. In fact, **q** may be taken as $[a\mathbf{u} - (1/2)\mathbf{p} + (1/2)(\mathbf{p} \times \mathbf{u}) \cot \pi/n]$, where $a$ is an arbitrary number. (Actually, **q** is never used; it is given here simply to show that it can be chosen.) Therefore, eq 16 and 17 are the sought conditions that U and p must satisfy in order that they define a $C_n$ symmetry operation.[7]

The conditions stated in eq 16 and 17, that U and p must satisfy, can also be regarded as the ones which determine the dihedral angles $\omega_1, \ldots, \omega_m$ in a symmetry unit, because U and p are generated from these dihedral angles by eq 7 and 8, respectively. Thus, eq 16 and 17 reduce the number of independent variables from $m$ to $(m - 2)$. Once the dihedral angles of a symmetry unit are determined, those of the remainder of the molecule are given by eq 1. Our next problem is to express two dependent dihedral angles in terms of $(m - 2)$ independent dihedral angles in a symmetry unit by solving eq 16 and 17. It is convenient to consider the case of molecules with $C_2$ symmetry[8] separately from those with $C_n$ $(n \geq 3)$ symmetry. In the case of $C_2$ symmetry, the first equation in footnote 7, which is equivalent to eq 16 and 17, can be solved analytically to give explicit formulas for two dependent dihedral angles in terms of $(m - 2)$ independent ones. In the case of $C_n$ $(n \geq 3)$ symmetry, eq 16 and 17 can be reduced to a single algebraic equation in a single unknown, which can be solved easily by numerical methods. The case of $C_2$ symmetry will be treated first.

For the case of $n = 2$, we shall start with the equation in footnote 7 rather than with eq 16 and 17, and solve for the dependent variables $\omega_{m-1}$ and $\omega_m$ in terms of the independent variables $\omega_1, \ldots, \omega_{m-2}$. In order to emphasize that $\omega_{m-1}$ and $\omega_m$ are unknowns, we shall designate them as $\xi$ and $\eta$, respectively, and denote $\mathbf{R}_{m-1}$ and $\mathbf{R}_m$ as **X** and **Y**, respectively. Also we shall express **U** and **p** of eq 7 and 8 as follows

$$\mathbf{U} = \mathbf{AXBY} \tag{18}$$

$$\mathbf{p} = \mathbf{a} + \mathbf{AXb} \tag{19}$$

where

$$\mathbf{A} = \mathbf{T}_0\mathbf{R}_1\mathbf{T}_1\mathbf{R}_2 \cdots \mathbf{T}_{m-3}\mathbf{R}_{m-2}\mathbf{T}_{m-2} \tag{20}$$

$$\mathbf{B} = \mathbf{T}_{m-1} \tag{21}$$

$$\mathbf{a} = \mathbf{p}_0 + \mathbf{T}_0\mathbf{R}_1\mathbf{p}_1 + \ldots + \mathbf{T}_0\mathbf{R}_1\mathbf{T}_1\mathbf{R}_2 \cdots \mathbf{T}_{m-3}\mathbf{R}_{m-2}\mathbf{p}_{m-2} \tag{22}$$

$$\mathbf{b} = \mathbf{p}_{m-1} \tag{23}$$

Then the first equation in footnote 7 takes the form

$$\mathbf{a} + \mathbf{AXb} + \mathbf{AXBYa} + \mathbf{AXBYAXb} = 0 \tag{24}$$

where **B** and **b** are constants and **A** and **a** are given quantities (*i.e.*, completely determined by a given set of independent variables $\omega_1, \ldots, \omega_{m-2}$). Our problem is to solve eq 24 for the unknown $\xi$ and $\eta$ for given **A**, **B**, **a**, and **b**.

Equation 24 can be transformed to

$$\mathbf{Y}(\mathbf{a} + \mathbf{AXb}) = -\mathbf{B}^{-1}\mathbf{X}^{-1}\mathbf{c} - \mathbf{d} \tag{25}$$

with

$$\mathbf{c} = \mathbf{A}^{-1}\mathbf{a} \tag{26}$$

and

$$\mathbf{d} = \mathbf{B}^{-1}\mathbf{b} \tag{27}$$

From the $x$ component of eq 25, we have

$$\alpha \cos \xi + \beta \sin \xi + \gamma = 0 \tag{28}$$

with

$$\begin{aligned} \alpha &= a_{12}b_2 + a_{13}b_3 + b_{21}c_2 + b_{31}c_3 \\ \beta &= -a_{12}b_3 + a_{13}b_2 + b_{21}c_3 - b_{31}c_2 \\ \gamma &= a_1 + d_1 + a_{11}b_1 + b_{11}c_1 \end{aligned} \tag{29}$$

where $a_i$, $b_i$, $c_i$, and $d_i$ are the $i$th components of vectors **a**, **b**, **c**, and **d**, respectively, and $a_{ij}$ and $b_{ij}$ are the $i,j$ elements of matrices **A** and **B** (and, therefore, the $j,i$ elements of matrices $\mathbf{A}^{-1}$ and $\mathbf{B}^{-1}$ because both are orthogonal matrices), respectively. Equation 28 contains only one unknown, *viz.*, $\xi$. The necessary and sufficient condition for the existence of solution(s) of eq 28 is given by

$$\alpha^2 + \beta^2 - \gamma^2 \geq 0 \tag{30}$$

When this is satisfied, eq 28 has the solution

$$\begin{aligned} \cos \xi &= \frac{-\alpha\gamma \pm \beta(\alpha^2 + \beta^2 - \gamma^2)^{1/2}}{\alpha^2 + \beta^2} \\ \sin \xi &= \frac{-\beta\gamma \mp \alpha(\alpha^2 + \beta^2 - \gamma^2)^{1/2}}{\alpha^2 + \beta^2} \end{aligned} \tag{31}$$

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(7) It should be noted here that, for $n = 2$, a single vector equation

$$(\mathbf{I} + \mathbf{U})\mathbf{p} = 0$$

is equivalent to eq 16 and 17. This equation can be derived from eq 16 and 17 by substituting $\phi = \pi$ (the result of eq 16 for $n = 2$) in eq 12, and then computing $(\mathbf{I} + \mathbf{U})\mathbf{p}$ and substituting eq 17 into the result. On the other hand, if this equation holds, then

$$\det(\mathbf{I} + \mathbf{U}) = 0$$

since **p** is a nonvanishing vector. The solution of this equation is $\phi = \pi$ (eq 16) which [when substituted in $(\mathbf{I} + \mathbf{U})\mathbf{p}$] gives zero if $\mathbf{u} \cdot \mathbf{p} = 0$ (eq 17).

(8) An example of such a molecule, with a twofold symmetry axis, is gramicidin S (with $\phi = \pi$); G. M. Schmidt, D. C. Hodgkin, B. M. Oughton, *Biochem. J.*, 65, 744 (1957).

from which $\xi$ can be obtained. The $\pm$ and $\mp$ signs in eq 31 are interdependent in the sense that, if the upper (or lower, respectively) sign is taken in one equation, the upper (or lower, respectively) sign must be taken in the other equation. Therefore, there are two solutions of eq 31 except when the equality sign holds in eq 30; in this case, there is only one solution. Once $\xi$ is known, $\eta$ can be obtained by using the $y$ and $z$ components of eq 25. The result is

$$\cos\eta = \frac{e_2f_2 + e_3f_3}{e_2^2 + e_3^2} \qquad \sin\eta = \frac{e_2f_3 - e_3f_2}{e_2^2 + e_3^2} \tag{32}$$

where $e_i$ and $f_i$ are the $i$th components of vectors **e** and **f**, respectively, defined by

$$\mathbf{e} = \mathbf{a} + \mathbf{AXb} \qquad \mathbf{f} = -\mathbf{B}^{-1}\mathbf{X}^{-1}\mathbf{c} - \mathbf{d} \tag{33}$$

Equation 32 yields one solution $\eta$ for each value of $\xi$.

Thus, to obtain $\omega_{m-1}$ and $\omega_m$ in terms of the $(m - 2)$ independent values of $\omega_1, \ldots, \omega_{m-2}$ for the case of $C_2$ symmetry, eq 31 and 32 must be solved for $\xi$ and $\eta$, respectively.

We now consider molecules with $C_n$ ($n \geq 3$) symmetry, and make use of eq 16 and 17. By performing the indicated subtraction of the $i,j$ elements of the matrix **U** in eq 12, we obtain

$$\begin{bmatrix} u_{23} - u_{32} \\ u_{31} - u_{13} \\ u_{12} - u_{21} \end{bmatrix} = -2\sin\phi\ \mathbf{u} \tag{34}$$

From eq 34, it can be seen that eq 17 is equivalent[9] to

$$p_1(u_{23} - u_{32}) + p_2(u_{31} - u_{13}) + p_3(u_{12} - u_{21}) = 0 \tag{35}$$

Hence, we may regard eq 16 and 35 as the ones for obtaining the dependent variables $\omega_{m-1}$ and $\omega_m$ in terms of the independent variables $\omega_1, \ldots, \omega_{m-2}$. Keeping the expressions for **U** and **p** from eq 18 and 19, we introduce an additional matrix **C** defined by

$$\mathbf{C} = \mathbf{AXB} \tag{36}$$

so that **U** is now given by **CY**. The matrix **C** and the vector **p** are functions of the independent variables and of one unknown, $\xi \equiv \omega_{m-1}$. Equations 16 and 35 can now be written as

$$\alpha' \cos\eta + \beta' \sin\eta + \gamma' = 0 \tag{37}$$

and

$$\alpha'' \cos\eta + \beta'' \sin\eta + \gamma'' = 0 \tag{38}$$

with

$$\alpha' = c_{22} + c_{33} \qquad \beta' = c_{23} - c_{32} \qquad \gamma' = c_{11} - 1 - 2\cos(2\pi/n) \tag{39}$$

and

$$\alpha'' = p_1(c_{23} - c_{32}) - p_2c_{13} + p_3c_{12} \qquad \beta'' = -p_1(c_{22} + c_{33}) + p_2c_{12} + p_3c_{13} \qquad \gamma'' = p_2c_{31} - p_3c_{21} \tag{40}$$

where $c_{ij}$ is the $i,j$ element of matrix **C**. Solving eq 37 and 38 simultaneously, we have

$$\cos\eta = (\beta'\gamma'' - \gamma'\beta'')/(\alpha'\beta'' - \beta'\alpha'') \qquad \sin\eta = (\gamma'\alpha'' - \alpha'\gamma'')/(\alpha'\beta'' - \beta'\alpha'') \tag{41}$$

By squaring and adding each of eq 41, we eliminate $\eta$ and obtain

$$(\beta'\gamma'' - \gamma'\beta'')^2 + (\gamma'\alpha'' - \alpha'\gamma'')^2 - (\alpha'\beta'' - \beta'\alpha'')^2 = 0 \tag{42}$$

This can be regarded as an algebraic equation in a single unknown $\xi$, which can be solved numerically by Newton's method, for example. Once $\xi$ is determined, then $\eta$ is computed from eq 41, thereby providing a solution to the problem for $C_n$ ($n \geq 3$) symmetry.

In our earlier treatment[3] of ring closure in a chain molecule, in which no symmetry was assumed, we concluded that only $(m - 6)$ of the $m$ dihedral angles are independent, the remaining 6 dependent variables being determined by the condition of ring closure. In the present treatment of molecules with $C_n$ symmetry, we concluded that $(m - 2)$ dihedral angles in a *symmetry unit* are independent, and only 2 are dependent. These two conclusions constitute an apparent paradox when applied to molecules having the structure

$$(\mathrm{F_1F_2F_3})_2$$

Since such a molecule has six variable dihedral angles in the ring, there are no degrees of freedom and hence there are no or a finite number of conformations possible according to our earlier treatment.[3] According to the treatment in this paper, this molecule can assume conformations with $C_2$ symmetry which have one degree of freedom because there are three variable dihedral angles in the symmetry unit. The resolution of this apparent paradox will be given in section IV.

## III. Cyclic Chain Molecules with $I$ or $S_{2n}$ Symmetry

We turn now to cyclic chain molecules whose chemical structure is

$$(\mathrm{F_1F_2\cdots F_m\,F_1{}^*F_2{}^*\cdots F_m{}^*})_n$$

where $\mathrm{F}_i{}^*$ is a unit which is enantiomorphic to $\mathrm{F}_i$; *i.e.*, $\mathrm{F}_i$ and $\mathrm{F}_i{}^*$ are mirror images of each other (*e.g.*, D- and L-amino acid residues). Such molecules can assume conformations with $S_{2n}$ symmetry (as already indicated in section I, the case of $n = 1$, *i.e.*, $S_2$ symmetry, is conventionally designated as $I$ symmetry).

An interesting special case arises for molecules in which $\mathrm{F}_i = \mathrm{F}_i{}^*$, *i.e.*, those (like glycine) in which the structure consisting of the unit $\mathrm{F}_i$ and atoms $\mathrm{B}_{i-1}$ and $\mathrm{A}_{i+1}$ has a planar backbone which is also a plane of symmetry. In such a case, the chemical structure of the molecule is

$$(\mathrm{F_1F_2\cdots F_m})_{2n}$$

and it can assume conformations with $S_{2n}$ as well as $C_{2n}$ symmetry, as discussed in section II. While we will not

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[9] For $n = 2$, eq 35 is not independent of eq 16 because $\sin\phi$ on the right-hand side of eq 34 vanishes for $\phi = \pi$. This is one of the reasons why the case of $n = 2$ was treated separately from the others; in addition, it is possible to obtain an analytical solution for $n = 2$, while only numerical solutions can be obtained for $n \geq 3$.

assume that $F_i = F_i^*$ in the general treatment in this section, this special case is sometimes treated separately.

As before, we consider a local cartesian coordinate system for each structure. However, whereas we made use of only a right-handed coordinate system in section II, here we use a right-handed system for structures including $F_i$ (*i.e.*, the structures consisting of unit $F_i$ and atoms $B_{i-1}$ and $A_{i+1}$) and both a right- and left-handed system for structures including $F_i^*$. The left-handed coordinate system for structures including $F_i^*$ is obtained by assigning to each atom the same numerical values for the cartesian coordinates that it has in the right-handed coordinate system for structures including $F_i$. The right-handed coordinate system for structures including $F_i^*$ is obtained by keeping the origin and the $x$ and $y$ axes the same as in the left-handed system but inverting the direction of the $z$ axis. If a given point in space is expressed by position vectors $\mathbf{r}_i$ and $\mathbf{r}_i^*$ with respect to the right- and left-handed coordinate system, respectively, associated with $F_i^*$, they are related to each other by

$$\mathbf{r}_i = \mathbf{I}'\mathbf{r}_i^* \tag{43}$$

.where

$$\mathbf{I}' = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & -1 \end{bmatrix} \tag{44}$$

The transformation of coordinates between the right-handed coordinate systems corresponding to $F_{i-1}$ and $F_i$, and between the left-handed coordinate systems corresponding to $F_{i-1}^*$ and $F_i^*$, is given by eq 4, as before. In particular, for the latter, eq 4 becomes

$$\mathbf{r}_{i-1}^* = \mathbf{T}_{i-1}\mathbf{R}(\omega_i)\mathbf{r}_i^* + \mathbf{p}_{i-1} \tag{45}$$

From eq 43 and 45, and the relation $\mathbf{R}(\omega_i) = \mathbf{I}'\mathbf{R}(-\omega_i)\mathbf{I}'$, we have[10]

$$\mathbf{r}_{i-1} = \mathbf{I}'\mathbf{T}_{i-1}\mathbf{I}'\mathbf{R}(-\omega_i)\mathbf{r}_i + \mathbf{I}'\mathbf{p}_{i-1} \tag{46}$$

Equation 46 implies two theorems: (1) if two structures are linked together by a single bond to give a conformation with a dihedral angle $\omega$, the mirror image of this conformation has a dihedral angle $(-\omega)$; (2) if a cyclic chain molecule

$$\overline{(F_1F_2\cdots F_mF_1^*F_2^*\cdots F_m^*)_n}$$

has a conformation with $S_{2n}$ symmetry (or $I$ symmetry in the case of $n = 1$), and the values of any $m$ consecutive dihedral angles along the chain are $\omega_1, \omega_2, \ldots, \omega_m$, then the values of the next $m$ consecutive dihedral angles along the chain are $-\omega_1, -\omega_2, \ldots, -\omega_m$. Equations 2 and 3 in section I follow from theorem 2.

We assign serial numbers to each unit of the molecule in such a way that the $(i + 2km)$th and $[i + (2k + 1)m]$th units are $F_i$ and $F_i^*$, respectively, where $i = 1, 2, \ldots, m$, and $k = 0, 1, \ldots, n - 1$. In this section, the $(2mn)$th local coordinate system will sometimes also be called the 0th one because of the cyclic nature of the molecule. The 0th and first units are taken as $F_m^*$ and $F_1$, respectively. The relation between $\mathbf{r}_0$ and $\mathbf{r}_1$ is given by an equation of the type of eq 4, and that between $\mathbf{r}_0^*$ and $\mathbf{r}_0$ is given by eq 43. From eq 4 and 43 and the relation $\mathbf{I}' = (\mathbf{I}')^{-1}$, we have

$$\mathbf{r}_0^* = \mathbf{I}'\mathbf{T}_0\mathbf{R}_1\mathbf{r}_1 + \mathbf{I}'\mathbf{p}_0 \tag{47}$$

From eq 47, and from repetitive use of eq 4, we obtain

$$\mathbf{r}_0^* = \mathbf{I}'\mathbf{U}\mathbf{r}_m + \mathbf{I}'\mathbf{p} \tag{48}$$

which is an analog of eq 6. In eq 48, $\mathbf{U}$ and $\mathbf{p}$ are given by eq 7 and 8, respectively. The matrix $\mathbf{I}'\mathbf{U}$ brings the right-handed $m$th coordinate system into the same orientation as that of the left-handed 0th one ($\mathbf{U}$ being used for the rotation, and $\mathbf{I}'$ for the reflection through a plane). The vector $\mathbf{I}'\mathbf{p}$ is the position vector of the origin of the $m$th coordinate system with respect to the left-handed 0th one.

When the molecule has $I$ or $S_{2n}$ symmetry, the 0th and $m$th local coordinate systems are symmetry related. For $I$ symmetry, the 0th coordinate system can be made to overlap the $m$th one by an inversion through an inversion center; for $S_{2n}$ $(n \geq 2)$ symmetry, this overlap is achieved by a rotation of $\pi \pm \pi/n$ around the symmetry axis, followed by an inversion through an inversion center located on the symmetry axis. To find the conditions that $\mathbf{U}$ and $\mathbf{p}$ must satisfy in order that they generate conformations with these symmetries, we again consider, as we did in section II, two more coordinate systems (the 0′th and $m$′th) having the same orientation as the 0th and $m$th ones, respectively, and having both their origins at the inversion center. Then eq 9 and 10 again hold. However, instead of eq 11, we have

$$\mathbf{r}_{0'} = -\mathbf{U}[\mathbf{u}, \pi \pm (\pi/n)]\mathbf{r}_{m'} \tag{49}$$

the negative sign appearing because of the inversion. From eq 9, 10, and 49, we obtain an equation corresponding to eq 13. By comparing it with eq 48, we obtain

$$\mathbf{I}'\mathbf{U} = -\mathbf{U}[\mathbf{u}, \pi \pm (\pi/n)] \tag{50}$$

$$\mathbf{I}'\mathbf{p} = -\{\mathbf{U}[\mathbf{u}, \pi \pm (\pi/n)] + \mathbf{I}\}\mathbf{q} \tag{51}$$

Whereas the matrix $\{\mathbf{U}[\mathbf{u}, \pm(2\pi/n)] - \mathbf{I}\}$ of eq 15 is singular (as implied by eq 17), the matrix $\{\mathbf{U}[\mathbf{u}, \pi \pm (\pi/n)] + \mathbf{I}\}$ is not. Therefore, eq 49 can always be solved for $\mathbf{q}$ for any given vector $\mathbf{p}$. Hence, eq 51 does not constitute a constraint to be imposed on the dihedral angles $\omega_1, \omega_2, \ldots, \omega_m$, and is not used to determine the dependent dihedral angles. Also, there are no conditions for the vector $\mathbf{u}$ in eq 50. For $n = 1$, eq 50 reduces to

$$\mathbf{U} = -\mathbf{I}' \tag{52}$$

and, for $n \geq 2$, it follows from eq 50 that

$$\mathrm{Tr}(\mathbf{I}'\mathbf{U}) = 2\cos(\pi/n) - 1 \tag{53}$$

When eq 52 and 53 are satisfied, the molecule has $I$ or $S_{2n}$

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(10) This equation can be simplified for the special case in which each structure has a planar backbone, including the case in which $F_i = F_i^*$, where it is convenient to define the $y$ axis of the $i$th local coordinate system in such a way that atoms $B_i$ and $A_{i-1}$, as well as atoms $B_{i-1}$ and $A_i$ lie in the $x,y$ plane. Since $\mathbf{p}_{i-1}$ also lies in the $x,y$ plane, its $z$ component is zero (hence, $\mathbf{I}'\mathbf{p}_{i-1} = \mathbf{p}_{i-1}$), and the matrix $\mathbf{T}_{i-1}$ has the following form

$$\mathbf{T}_{i-1} = \begin{bmatrix} \cos\theta_{i-1} & -\sin\theta_{i-1} & 0 \\ \sin\theta_{i-1} & \cos\theta_{i-1} & 0 \\ 0 & 0 & 1 \end{bmatrix}$$

where $\theta_{i-1}$ is the angle of rotation around the $z$ axis [the same for the $i$th and $(i-1)$th systems when $\omega_i = 0$] to bring the $i$th coordinate system into the same orientation as that of the $(i-1)$th system when $\omega_i = 0$. If $\mathbf{T}_{i-1}$ is given by this expression, then $\mathbf{I}'\mathbf{T}_{i-1}\mathbf{I}' = \mathbf{T}_{i-1}$. Thus, for the special case of a planar backbone, eq 46 becomes

$$\mathbf{r}_{i-1} = \mathbf{T}_{i-1}\mathbf{R}(-\omega_i)\mathbf{r}_i + \mathbf{p}_{i-1}$$

symmetry, respectively, and the solutions of these equations yield the dihedral angles.

Consider first the case of $I$ symmetry ($n = 1$). Since we need three parameters to specify a $3 \times 3$ orthogonal matrix, eq 52 reduces the number of independent variables from $m$ to $m - 3$. We take $\omega_1, \ldots, \omega_{m-3}$ as the independent variables , and $\omega_{m-2}$, $\omega_{m-1}$, and $\omega_m$ as the dependent variables (*i.e.*, as unknowns to be determined for a given set of $\omega_1, \ldots, \omega_{m-3}$). In order to emphasize that $\omega_{m-2}$, $\omega_{m-1}$, and $\omega_m$ are unknowns, we shall designate them as $\xi$, $\eta$, and $\zeta$, respectively, and use **X**, **Y**, and **Z** for the matrices $\mathbf{R}_{m-2}$, $\mathbf{R}_{m-1}$, and $\mathbf{R}_m$. Also we shall express U of eq 7 as follows.

$$\mathbf{U} = \mathbf{AXBYCZ} \tag{54}$$

where

$$\mathbf{A} = \mathbf{T}_0\mathbf{R}_1\mathbf{T}_1\mathbf{R}_2\cdots\mathbf{T}_{m-4}\mathbf{R}_{m-3}\mathbf{T}_{m-3} \tag{55}$$

$$\mathbf{B} = \mathbf{T}_{m-2} \tag{56}$$

$$\mathbf{C} = \mathbf{T}_{m-1} \tag{57}$$

It should be noted that **A**, **B**, and **C** of eq 54–57 differ from those of eq 20, 21, and 36. Then, eq 52 can be written as

$$\mathbf{XBYCZ} = -\mathbf{A}^{-1}\mathbf{I}' \tag{58}$$

Equating the 1,1 elements of both sides of this equation, we have

$$\alpha \cos \eta + \beta \sin \eta + \gamma = 0 \tag{59}$$

with

$$\begin{aligned} \alpha &= b_{12}c_{21} + b_{13}c_{31} \\ \beta &= b_{13}c_{21} - b_{12}c_{31} \\ \gamma &= a_{11} + b_{11}c_{11} \end{aligned} \tag{60}$$

where $a_{ij}$, $b_{ij}$, and $c_{ij}$ are the $i,j$ elements of matrices **A**, **B**, and **C**, respectively. The necessary and sufficient condition for the existence of solution(s) of eq 59 is given by

$$\alpha^2 + \beta^2 - \gamma^2 \geq 0 \tag{61}$$

When this is satisfied, eq 59 has the solution

$$\begin{aligned} \cos \eta &= \frac{-\alpha\gamma \pm \beta(\alpha^2 + \beta^2 - \gamma^2)^{1/2}}{\alpha^2 + \beta^2} \\ \sin \eta &= \frac{-\beta\gamma \mp \alpha(\alpha^2 + \beta^2 - \gamma^2)^{1/2}}{\alpha^2 + \beta^2} \end{aligned} \tag{62}$$

The ± and ∓ signs are to be understood in the same way as in eq 31. Once $\eta$ is determined, $\xi$ and $\zeta$ can be computed by using the 2,1 and 3,1 elements, and the 1,2 and 1,3 elements of both sides of eq 58, respectively. The result is

$$\begin{aligned} \cos \xi &= \frac{-a_{12}d_{21} - a_{13}d_{31}}{{d_{21}}^2 + {d_{31}}^2} \\ \sin \xi &= \frac{a_{12}d_{31} - a_{13}d_{21}}{{d_{21}}^2 + {d_{31}}^2} \end{aligned} \tag{63}$$

$$\begin{aligned} \cos \zeta &= \frac{-a_{21}d_{12} + a_{31}d_{13}}{{d_{12}}^2 + {d_{13}}^2} \\ \sin \zeta &= \frac{-a_{21}d_{13} - a_{31}d_{12}}{{d_{12}}^2 + {d_{13}}^2} \end{aligned} \tag{64}$$

where $d_{ij}$ is the $i,j$ element of a matrix defined by

$$\mathbf{D} = \mathbf{BYC} \tag{65}$$

Thus, $\omega_{m-2}$, $\omega_{m-1}$, and $\omega_m$ are determinable for the case of $n = 1$.

In the cases of $S_{2n}$ symmetry ($n \geq 2$), we have only one equation (*viz.*, eq 53), and the number of independent variables is therefore reduced from $m$ to $m - 1$. We take $\omega_m$ as an unknown to be determined for a given set of independent variables $\omega_1, \omega_2, \ldots, \omega_{m-1}$. The notations $\zeta$ and **Z** will be used in place of $\omega_m$ and $\mathbf{R}_m$, as before. Also, we shall express **U** of eq 7 as follows.

$$\mathbf{U} = \mathbf{EZ} \tag{66}$$

where

$$\mathbf{E} = \mathbf{T}_0\mathbf{R}_1\mathbf{T}_1\mathbf{R}_2\cdots\mathbf{T}_{m-2}\mathbf{R}_{m-1}\mathbf{T}_{m-1} \tag{67}$$

Then, eq 53 takes the following form.

$$\alpha' \cos \zeta + \beta' \sin \zeta + \gamma' = 0 \tag{68}$$

with

$$\begin{aligned} \alpha' &= e_{22} - e_{33} \\ \beta' &= e_{23} + e_{32} \\ \gamma' &= e_{11} + 1 - 2 \cos (\pi/n) \end{aligned} \tag{69}$$

This equation has solution(s), when

$$\alpha'^2 + \beta'^2 - \gamma'^2 \geq 0 \tag{70}$$

When this is satisfied, eq 68 has the solution

$$\begin{aligned} \cos \zeta &= \frac{-\alpha'\gamma' \pm \beta'(\alpha'^2 + \beta'^2 - \gamma'^2)^{1/2}}{\alpha'^2 + \beta'^2} \\ \sin \zeta &= \frac{-\beta'\gamma' \mp \alpha'(\alpha'^2 + \beta'^2 - \gamma'^2)^{1/2}}{\alpha'^2 + \beta'^2} \end{aligned} \tag{71}$$

The ± and ∓ signs are to be understood in the same way as in eq 31. Thus, $\omega_m$ is determinable for molecules with $S_{2n}$ symmetry.

## IV. Geometry of Cyclohexane

Primarily for the purpose of illustrating the methods developed in sections II and III, we apply them here to the generation of conformations of cyclohexane. Since the conformations of cyclohexane have been the subject of thorough theoretical studies,[11-13] most of the results obtained here are not new, except that an explicit expression is given for the dihedral angles in the flexible boat form of cyclohexane. While the emphasis here is on the illustration of the foregoing theory, nevertheless, a new view is provided as to the origin of the rigidity and flexibility of the chair and boat forms, respectively, of cyclohexane. This insight is essential for resolving the paradox mentioned at the end of section II.

The cyclohexane molecule consists of six identical units F = $CH_2$, with each unit having a plane of symmetry, *i.e.*, F* = F. Therefore, the molecule may have $C_1$ (no symmetry), $C_2$, $C_3$, $C_6$, $I$, and $S_6$ symmetry. Since only the positions of the backbone atoms are essential for generating ring structures, we shall consider only the positions of the

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(11) H. Sachse, *Z. Physik. Chem.*, 10, 203 (1892).

(12) P. Hazebrook and L. J. Oosterhoff, *Discuss. Faraday Soc.*, 10, 87 (1951).

(13) J. D. Dunitz, *J. Chem. Educ.*, 47, 488 (1970).

**Table I**
**Cartesian Coordinates of Carbon Atoms of Cyclohexane in the *i*th Local Coordinate System**[a]

| Carbon Atoms | Cartesian Coordinates | | |
|---|---|---|---|
| | $x$ | $y$ | $z$ |
| $i-1$ | 0 | 0 | 0 |
| $i$ | 1 | 0 | 0 |
| $i+1$ | $1 + \cos\theta$[b] | $\sin\theta$ | 0 |

[a] The bond length between carbon atoms is taken as unity. angle $\theta$ is the supplement of the C–C–C bond angle, which is close to the tetrahedral angle 109.47°. Therefore, $\cos\theta \simeq \frac{1}{3}$.

carbon atoms. The cartesian coordinates of carbon atoms $(i-1)$, $i$, and $(i+1)$ in the $i$th local coordinate system are given in Table I, from which it follows that eq 4 takes the following form.

$$\mathbf{r}_{i-1} = \mathbf{T}\mathbf{R}_i\mathbf{r}_i + \mathbf{p} \tag{72}$$

where

$$\mathbf{T} = \begin{bmatrix} \cos\theta & -\sin\theta & 0 \\ \sin\theta & \cos\theta & 0 \\ 0 & 0 & 1 \end{bmatrix} \tag{73}$$

$\mathbf{R}_i$ is given by eq 5, and

$$\mathbf{p} = \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix} \tag{74}$$

We shall consider first the case of $S_6$ symmetry. For this symmetry ($n = 3$, $m = 1$), the relation between the backbone dihedral angles is $\omega_1 = -\omega_2 = \omega_3 = -\omega_4 = \omega_5 = -\omega_6$, according to eq 3. The matrices **E** and **Z** in eq 66 are **T** of eq 73 and **R** of eq 5, respectively. Hence, the quantities of eq 69 are given by

$$\begin{aligned} \alpha' &= \cos\theta - 1 \\ \beta' &= 0 \\ \gamma' &= \cos\theta \end{aligned} \tag{75}$$

According to eq 70, eq 68 has solution(s) for the coefficients given by eq 75 when $\cos\theta \leq \frac{1}{2}$, which is satisfied because $\cos\theta \simeq \frac{1}{3}$ (see Table I). From eq 71 we have

$$\begin{aligned} \cos\omega_1 &= \cos\theta/(1 - \cos\theta) \\ \sin\omega_1 &= \mp(1 - 2\cos\theta)^{1/2}/(1 - \cos\theta) \end{aligned} \tag{76}$$

If $\cos\theta = \frac{1}{3}$, then $\cos\omega_1 = \frac{1}{2}$, $\sin\omega_1 = \mp(3)^{1/2}/2$, and $\omega_1 = \mp\pi/3$. These solutions of eq 76 correspond to the so-called chair form of cyclohexane. This conformation is rigid, because $\omega_1$ is allowed only at isolated values (*i.e.*, is not allowed to vary continuously).

Now let us consider the case of $I$ symmetry, for which there are three variable dihedral angles in a symmetry unit. If the values of three consecutive angles are $\omega_1$, $\omega_2$, and $\omega_3$, those of the next three angles are $-\omega_1$, $-\omega_2$, and $-\omega_3$, according to eq 2. The matrices in eq 54 are as follows in this case: $\mathbf{A} = \mathbf{B} = \mathbf{C} = \mathbf{T}$, $\mathbf{X} = \mathbf{R}(\omega_1)$, $\mathbf{Y} = \mathbf{R}(\omega_2)$, and $\mathbf{Z} = \mathbf{R}(\omega_3)$. Then the quantities of eq 60 are given by

$$\begin{aligned} \alpha &= -\sin^2\theta \\ \beta &= 0 \\ \gamma &= \cos\theta\,(1 + \cos\theta) \end{aligned} \tag{77}$$

Equation 59 has solution(s) for the coefficients given by eq 77, when $\cos\theta \leq \frac{1}{2}$ (according to eq 61). This is again satisfied because $\cos\theta \simeq \frac{1}{3}$. From eq 62 we have

$$\begin{aligned} \cos\omega_2 &= \cos\theta/(1 - \cos\theta) \\ \sin\omega_2 &= \mp(1 - 2\cos\theta)^{1/2}/(1 - \cos\theta) \end{aligned} \tag{78}$$

The values of $\omega_1$ and $\omega_3$ are determined from eq 63 and 64 to be $\omega_1 = \omega_3 = -\omega_2$. Thus, this conformation with $I$ symmetry is again the same rigid chair form.

The case of $C_6$ symmetry will be considered next. In this case the matrix **U** of eq 7 is given by $\mathbf{TR}(\omega_1)$. When this is introduced into eq 16, we obtain

$$\cos\omega_1 = (2 - \cos\theta)/(1 + \cos\theta) \tag{79}$$

However, no angle $\omega$ satisfies eq 79, because $\cos\omega \simeq \frac{5}{4}$ for $\cos\theta \simeq \frac{1}{3}$. This proves the nonexistence of a conformation of cyclohexane with $C_6$ symmetry.

The case of $C_3$ symmetry will be considered next. The dihedral angles along the chain obey the following relationship according to eq 1: $\omega_1 = \omega_3 = \omega_5$, $\omega_2 = \omega_4 = \omega_6$. The values of $\omega_1$ and $\omega_2$ are determined as follows. The matrix **U** of eq 7 is given by **AXBY**, where $\mathbf{A} = \mathbf{B} = \mathbf{T}$ and $\mathbf{X} = \mathbf{R}(\omega_1)$, $\mathbf{Y} = \mathbf{R}(\omega_2)$. According to eq 5 and 72, the vector **p** of eq 8 is given by

$$\mathbf{p} = \begin{bmatrix} 1 + \cos\theta \\ \sin\theta \\ 0 \end{bmatrix} \tag{80}$$

Then the quantities of eq 39 and 40 are given by

$$\begin{aligned} \alpha' &= -\sin^2\theta + (1 + \cos^2\theta)\cos\omega_1 \\ \beta' &= -2\cos\theta\sin\omega_1 \\ \gamma' &= \cos^2\theta - \sin^2\theta\cos\omega_1 \end{aligned} \tag{81}$$

$$\begin{aligned} \alpha'' &= -2\cos\theta\,(1 + \cos\theta)\sin\omega_1 - \sin^2\theta\sin\omega_1 \\ \beta'' &= (1 + \cos\theta)\{\sin^2\theta - (1 + \cos^2\theta)\cos\omega_1\} - \\ &\qquad \sin^2\theta\cos\theta\,(1 + \cos\omega_1) \\ \gamma'' &= \sin^2\theta\sin\omega_1 \end{aligned} \tag{82}$$

If the left-hand side of eq 42 is written as $f(\omega_1)$, the graph of $f(\omega_1)$ is given in Figure 2 for $\cos\theta = \frac{1}{3}$ and $\sin\theta = 2(2)^{1/2}/3$. The graphical solutions of eq 42 are $\omega_1 = \pm\pi/3$. By substituting this value into eq 39, 40, and 41, we obtain $\omega_2 = \mp\pi/3$. Again we have the rigid chair form. In summary, by looking for conformations of cyclohexane with $S_6$, $I$, or $C_3$ symmetry, we obtained one rigid conformation which is usually called the chair form. In fact, the symmetry of the chair form is $D_{3d}$, and the point groups $S_6$, $I$, and $C_3$ are subgroups of the group $D_{3d}$.

Now let us consider the case of $C_2$ symmetry. According to eq 1, the dihedral angles along the chain have the following relationships: $\omega_1 = \omega_4$, $\omega_2 = \omega_5$, and $\omega_3 = \omega_6$. Hence we will compute $\omega_1$, $\omega_2$, and $\omega_3$. The matrices and vectors in eq 18 and 19 are as follows: $\mathbf{A} = \mathbf{TR}(\omega_1)\mathbf{T}$, $\mathbf{B} = \mathbf{T}$, $\mathbf{X} = \mathbf{R}(\omega_2)$, $\mathbf{Y} = \mathbf{R}(\omega_3)$, and

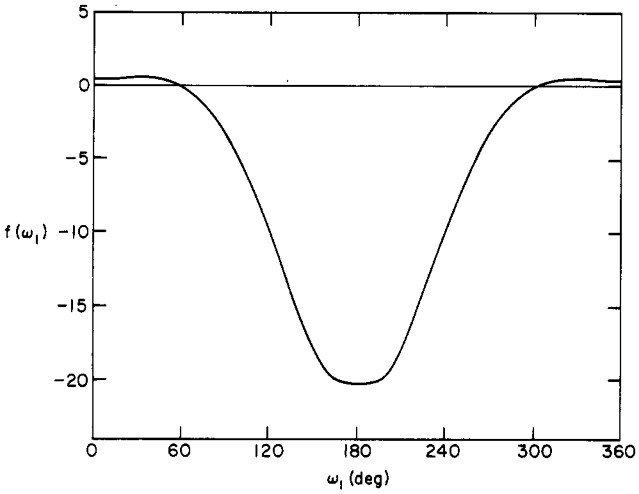

**Figure 2.** Graph of the left-hand side of eq 42 for the conformation of cyclohexane with $C_3$ symmetry.

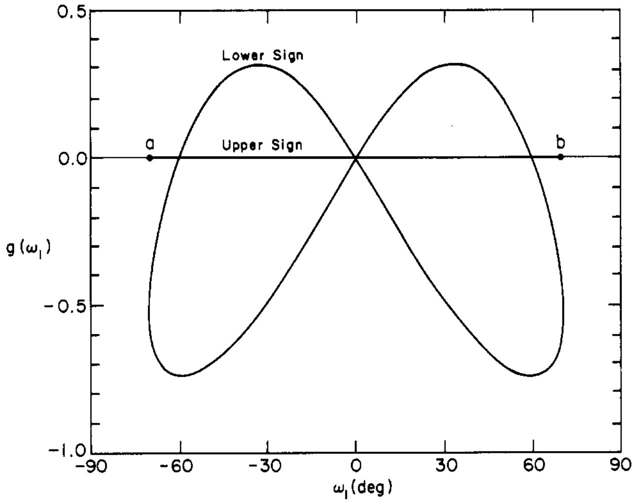

**Figure 3.** Graph of the left-hand side of eq A-20 for cyclohexane. The upper and lower signs refer to those in eq 94. The value of $g(\omega_1)$ at $\omega_1 = 0°$ and the line segment between points *a* and *b* correspond to the flexible boat forms. The two points at $\omega_1 = \pm 60°$ correspond to the rigid chair form.

$$\mathbf{a} = \begin{bmatrix} 1 + \cos\theta \\ \sin\theta \\ 0 \end{bmatrix} \qquad \mathbf{b} = \begin{bmatrix} 1 \\ 0 \\ 0 \end{bmatrix} \tag{83}$$

At this point we define several new quantities.

$$x = -\cos\theta\,(1 + \cos\theta) + \sin^2\theta\cos\omega_1$$
$$y = \sin\theta\,(1 + \cos\theta) + \cos\theta\sin\theta\cos\omega_1 \tag{84}$$
$$z = -\sin\theta\sin\omega_1$$

$$w = \{(1 + \cos\theta)(1 + \cos\theta + \cos^2\theta) - \sin^2\theta\,(1 + \cos\theta)\cos\omega_1\}/\sin\theta \tag{85}$$

$$q_z = \pm(y^2 + z^2 - w^2)^{1/2} \tag{86}$$

The quantity $q_z$ of eq 86 is real, when the following inequality is satisfied.

$$\frac{1 + 2\cos\theta}{2(1 - \cos\theta)} + \frac{\sqrt{3}}{2}\frac{1}{\sin\theta} \geq \cos\omega_1 \geq \frac{1 + 2\cos\theta}{2(1 - \cos\theta)} - \frac{\sqrt{3}}{2}\frac{1}{\sin\theta} \tag{87}$$

The first inequality is always satisfied because $\cos\theta \simeq 1/3$. Using the quantities defined above, the vectors in eq 26 and 27 are given by

$$\mathbf{c} = \begin{bmatrix} -x \\ -y \\ -z \end{bmatrix} \qquad \mathbf{d} = \begin{bmatrix} \cos\theta \\ -\sin\theta \\ 0 \end{bmatrix} \tag{88}$$

and the quantities in eq 29 are given by

$$\alpha = -y\sin\theta$$
$$\beta = -z\sin\theta \tag{89}$$
$$\gamma = w\sin\theta$$

Then $\omega_2$ is given by the following equations, when $\omega_1$ satisfies eq 87.

$$\cos\omega_2 = \frac{yw + zq_z}{y^2 + z^2}$$
$$\sin\omega_2 = \frac{zw - yq_z}{y^2 + z^2} \tag{90}$$

The vectors in eq 33 are given by

$$\mathbf{e} = \begin{bmatrix} 1 - x \\ y \\ -z \end{bmatrix} \qquad \mathbf{f} = \begin{bmatrix} 1 - x \\ w \\ q_z \end{bmatrix} \tag{91}$$

Then $\omega_3$ is given by

$$\cos\omega_3 = \frac{yw - zq_z}{y^2 + z^2}$$
$$\sin\omega_3 = \frac{zw + yq_z}{y^2 + z^2} \tag{92}$$

when $\omega_1$ satisfies eq 87. In contrast to the situation found in the cases of conformations with $S_6$, *I*, or $C_3$ symmetry, the conformations with $C_2$ symmetry have one degree of freedom; *i.e.*, $\omega_1$ is a variable in the range satisfying eq 87. The conformation with $C_2$ symmetry obtained above is the well-known so-called flexible boat form. Equations 90 and 92 with eq 84, 85, and 86 provide an explicit expression for the dihedral angles in the flexible boat form of cyclohexane.

The rigidity of the chair form, and the flexibility of the boat form are a straightforward result of the theory developed in sections II and III. However, the origin of the rigidity and the flexibility can best be understood by looking for all possible conformations of cyclohexane without assuming any *a priori* symmetry. This can be done by using the method developed in paper A.[3] Because the theory developed there is quite general, any conformations of cyclohexane with or without any symmetry should be obtained therefrom. However, it is interesting to see how the continuous solution of the so-called flexible boat form of cyclohexane is obtained, because the theory developed previously in A,[3] at first sight, predicts only rigid conformations for cyclohexane (the paradox stated at the end of section II).

If no symmetry is assumed then the quantities in eq A-16, A-17, and A-18 are defined as follows: all $\mathbf{T}_i$'s are $\mathbf{T}$ of eq 73, all $\mathbf{R}_i$'s are $\mathbf{R}(\omega_i)$ of eq 5, and all $\mathbf{q}_i$'s are $\mathbf{p}$ of eq 80. The vector $\mathbf{s}$ in eq A-16 is the zero vector, and $\mathbf{u} = \mathbf{e}_1$ and $\mathbf{v} = \mathbf{e}_2$ in eq A-17 and A-18, respectively, where $\mathbf{e}_1$ and $\mathbf{e}_2$ are column vectors, whose transposed (row) vectors are $\mathbf{e}_1{}^* = (1,0,0)$ and $\mathbf{e}_2{}^* = (0,1,0)$, respectively. The cartesian coordinates of the vector $\mathbf{r}$ of eq A-21 are $x$, $y$, and $z$ of eq 84. Equation A-26 has solution(s), when eq A-27 and A-28 are satisfied. Equation A-27 is always satisfied in this case. Equation A-28 is the same as eq 87. When eq 87 is satisfied, $\omega_2$ is given by eq 90 (from eq A-29). When $x$ and $w$ of eq 84 and 85 are substituted into eq A-33, we have

$$\cos \omega_4 = \cos \omega_1 \tag{93}$$

Equation A-35 is then

$$\sin \omega_4 = \pm \sin \omega_1 \tag{94}$$

When eq 93 and 94 are substituted into eq A-36, we obtain

$$\begin{aligned} \cos \omega_3 &= \frac{yw \mp zq_z}{y^2 + z^2} \\ \sin \omega_3 &= \frac{\pm zw + yq_z}{y^2 + z^2} \end{aligned} \tag{95}$$

The three ± (and ∓) signs in eq 94 and 95 are interdependent in a sense that, if the upper (respectively, lower) sign is taken in one equation, the upper (respectively, lower) sign must be taken in the other two equations. But they are independent of the ± sign in eq 86. When the upper sign is taken in eq 94 and 95, eq 95 becomes identical with eq 92. When $\omega_2$, $\omega_3$, and $\omega_4$ given by eq 90, 95, 93, and 94 are substituted into the left-hand side of eq A-20 [which we will write as $g(\omega_1)$], the graph of this quantity (for $\cos \theta = \frac{1}{3}$ and $\sin \theta = 2(2)^{1/2}/3$) shown in Figure 3 is obtained. When the upper sign is taken in eq 94 and 95 (or equivalently when $\omega_1 = \omega_4$), $g(\omega_1)$ always vanishes, *i.e.*, all $\omega_1$'s which satisfy the inequality of eq 87 are a solution of eq A-20. This continuous range of solutions is given by the horizontal line segment which exists only between points $a$ and $b$. This solution is identical with the flexible boat form of $C_2$ symmetry. When the lower sign is taken in eq 94 and 95 (or equivalently when $\omega_1 = -\omega_4$), there are three solutions, $\omega_1 = 0°, \pm 60°$. When $\omega_1 = 0°$, $\omega_4$ also vanishes, and there is no other solution than the one already obtained for the case of $\omega_1 = \omega_4$. When $\omega_1 = \pm 60°$, it is found from eq 90 (for $\omega_2$), 95 (for $\omega_3$), 93 and 94 (for $\omega_4$), A-17 (for $\omega_5$), and A-18 (for $\omega_6$) that $-\omega_2 = \omega_3 = -\omega_4 = \omega_5 = -\omega_6 = \pm 60°$. This is the chair form with $D_{3d}$ symmetry.

By looking for all possible conformations of cyclohexane without assuming any *a priori* symmetry, we have found no other conformation than those already found by assuming one of the possible symmetries. It is interesting that, when the upper sign is taken in eq 94, eq A-20 (which is usually an algebraic equation for $\omega_1$) becomes an identity. This is what appeared to be a paradox in section II. In the case of conformations with $C_2$ symmetry, the conclusion of paper A about the number of independent variables (*i.e.*, that there is no degree of freedom in cyclohexane) must be modified, because eq A-20 is satisfied for a continuous range of $\omega_1$ satisfying eq 87, or equivalently eq A-20 is an identity for this range.

## IV. Summary and Discussion

Mathematical methods have been developed to find a set of dihedral angles in a conformation of a cyclic chain molecule having $C_n$, $I$, or $S_{2n}$ symmetry, which are characterized by eq 1–3, respectively. The condition of ring closure decreases the number of independent variables from $m$ (*i.e.*, the number of variable dihedral angles in a symmetry unit) to $m - 2$, $m - 3$, and $m - 1$ in the case of $C_n$, $I$, and $S_{2n}$ symmetry, respectively. Methods for solving the appropriate algebraic equations for 2, 3, and 1 dependent angle(s) in terms of $m - 2$, $m - 3$, and $m - 1$ independent angles (in the case of $C_n$, $I$, and $S_{2n}$ symmetry, respectively) have been presented.

This conclusion appears to contradict the one found earlier in paper A,[3] in which the problem of ring closure was treated without assuming any *a priori* symmetry. The earlier[3] conclusion was that, where there are $m$ angles in the cyclic chain, the number of independent variables is $m - 6$. At first glance, this conclusion implies that there are no independent variables in cyclohexane, meaning that any *existing* conformation of cyclohexane, should be rigid. However, the result obtained in this paper says that there is one degree of freedom in the conformation of cyclohexane with $C_2$ symmetry. This apparent paradox is resolved by observing that an algebraic equation which occurred in paper A[3] turns out to be an identity for conformations with $C_2$ symmetry.

The methods developed here have been applied in a theoretical conformational energy study[14] of *cyclo*(hexaglycyl). This molecule may conceivably have conformations with $C_6$, $S_6$, $I$, $C_3$, or $C_2$ symmetry. However, in fact, conformations with all of these symmetries except $C_6$ are found[14] to be possible. The method developed here is also being applied[15] to a theoretical study of the conformations of gramicidin S, which is known to have $C_2$ symmetry.[8]

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(14) N. Gō and H. A. Scheraga, *Macromolecules*, submitted for publication.

(15) M. Dygert, N. Gō, and H. A. Scheraga, in preparation.