

Constrained Thermal Motion Refinement for a Rigid Molecule with Librating Side Groups

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Fourth-order thermal motion equations applicable to a rigid molecule with librating side groups are derived for a molecule located on an arbitrary site. It is assumed that the displacements of the rigid body and librating side groups can be characterized by Gaussian distributions. The equations are used to analyse methyl-group librational motion in the molecule naphthyridinomycin. The results correlate well qualitatively with semi-empirical quantum mechanical energy calculations. Calculation of the trace of the libration-translation coupling tensor **S** is possible. Allowance for more than one internal mode contributing to an atom is discussed.

Introduction

Recently a thermal motion analysis was developed for a rigid molecule with librating side groups (Prince & Finger, 1973). The treatment utilized the cumulant expansion technique of Johnson (1969). The resulting equations for thermal motion were derived, however, only for a molecule situated on a centre of symmetry. In this article, the thermal motion analysis of a rigid molecule with librating side groups is extended to a molecule located on an arbitrary site. Results of the analysis are applied to the thermal librational motion of the methyl groups present in the molecule naphthyridinomycin (Sygusch, Brisse & Hanessian, 1974).

Mathematical analysis

The instantaneous displacement of an atom from its equilibrium position due to rigid-body rotation has been derived to fourth order by Prince & Finger (1973) and is

$$\mathbf{u} = \left(1 - \frac{\lambda^2}{6}\right) (\boldsymbol{\lambda} \times \mathbf{r}) + \left(\frac{1}{2} - \frac{\lambda^2}{24}\right) [\boldsymbol{\lambda} \times (\boldsymbol{\lambda} \times \mathbf{r})] \quad (1)$$

where **u** represents the displacement vector, **λ** represents an axial vector with magnitude *λ* about which instantaneous rotation of the rigid body occurs, **r** represents an atomic position vector.

It should be noted that the position vector is defined from the centre of mass of the rigid body about which instantaneous rotation of the rigid body is presumed to occur. The expression of the *i*th component of **u** can be simplified by the use of appropriate symmetric tensors. Expanding to fourth order *u_i* has the form (Prince & Finger, 1973):

$$u_i = \sum_{j=1}^3 \{ \mathbf{A}(\mathbf{r})_{ij} \lambda_j + \sum_{k=1}^3 \mathbf{B}(\mathbf{r})_{ijk} \lambda_j \lambda_k + \sum_{l=1}^3 [\mathbf{C}(\mathbf{r})_{ijkl} \lambda_j \lambda_k \lambda_l + \sum_{m=1}^3 \mathbf{D}(\mathbf{r})_{ijklm} \lambda_j \lambda_k \lambda_l \lambda_m] \} \quad (2)$$

where **A**, **B**, **C** and **D** represent the symmetric tensors whose coefficients are defined by the correspondence to the appropriate terms in (1). These coefficients are linear functions of **r** and are listed in Table 1.

If **r_a** and **r_b** designate two rigid-atom position vectors which define an axis of libration **r' = r_b - r_a** then under rigid-body rotation this axis will have displacement **u'** according to (1). It should be noted that this displacement **u'** and a subsequent displacement **u''** are independent of any coordinate origin chosen since the axis of rotation is based upon a positional difference vector. Prince & Finger have derived the instantaneous displacement **v** due to librational motion for any atom **r** about this axis while the rigid body as a whole is undergoing rotational motion, then

$$\mathbf{v} = (1 - \theta^2/6) [\boldsymbol{\theta} \times (\mathbf{r}' + \mathbf{u}')] + (\frac{1}{2} - \theta^2/24) \{ \boldsymbol{\theta} \times [\boldsymbol{\theta} \times (\mathbf{r}' + \mathbf{u}')] \} \quad (3)$$

where **r''** represents the positional difference vector **r - r_b**, **r** being an atom which librates about axis **r'**, **θ** is the axial vector of magnitude *θ* defined as *θ*(**r' + u'**)/|**r' + u'**|, **u''** is the instantaneous rigid-body rotational displacement of positional difference vector **r''**.

The *i*th component of the librational displacement vector **v** can be expanded in a manner analogous to (2). Prince & Finger, however, were able to simplify the equation through the definition of two additional vectors **R** ≡ **r' × r''** and **R'** ≡ **r' × R**. The component *v_i* can be written as

$$v_i \simeq \theta R_i / r' + \theta^2 R'_i / 2r'^2 - \theta^3 R_i / 6r' - \theta^4 R'_i / 24r'^2 + \sum_{j=1}^3 \{ \mathbf{A}(\mathbf{R})_{ij} \lambda_j \theta / r' - \mathbf{A}(\mathbf{R})_{ij} \lambda_j \theta^3 / 6r' + \mathbf{A}(\mathbf{R}')_{ij} \lambda_j \theta^2 / 2r'^2 + \sum_{k=1}^3 [\mathbf{B}(\mathbf{R})_{ijk} \lambda_j \lambda_k \theta / r' + \mathbf{B}(\mathbf{R}')_{ijk} \lambda_j \lambda_k \theta^2 / 2r'^2 + \sum_{l=1}^3 \mathbf{C}(\mathbf{R})_{ijkl} \lambda_j \lambda_k \lambda_l \theta / r'] \} \quad (4)$$

The total displacement of the atom from its equilibrium position due to both rotational and translational motion is then **w = u + v + t**, where **t** represents the instan-

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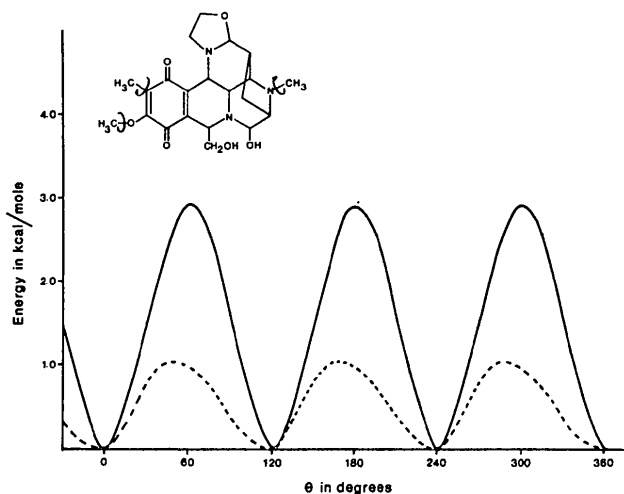


Fig. 1. Variation of potential energy as a function of torsional angle $\theta(A-B)$. Positive sense is defined as clockwise rotation when viewing from A to B . The zero position of each methyl group was defined as the crystallographically obtained position. The broken line summarizes potential energy calculations about C-C and O-C bonds. The full line represents potential energy calculations about the N-C bond.

and

$$Q_5'(i, j, k, l) = (\frac{1}{2}r'^2) [A(R')_{ik}\delta_{lj} + A(R')_{jk}\delta_{li}] \quad (13)$$

then the second cumulant ${}^2\kappa_{ij}$ and its derivatives are

$$\begin{aligned} {}^2\kappa_{ij} = & \sum_{k,l} L_{kl} [Q_2'(i, j, k, l) + \sum_{m,n} L_{mn} Q_1'(i, j, k, l, m, n) \\ & + A(\mathbf{r})_{ik}A(\mathbf{r})_{jl} + \theta Q_4'(i, j, k, l)] \\ & + \sum_m \{ S_{mi} [A(\mathbf{r})_{jm} + \theta Q_5'(i, j, m, j)] / (1 + \delta_{ij}) \\ & + S_{mj} [A(\mathbf{r})_{im} + \theta Q_5'(i, j, m, i)] / (1 + \delta_{ij}) \} \\ & + (\theta R_i R_j / r'^2) (1 - \theta) + (\theta^2 R_i' R_j' / 2r'^4) + T_{ij}; \quad (14) \end{aligned}$$

$$\frac{\partial^2 \kappa_{ij}}{\partial T_{mn}} = \delta_{mi} \delta_{nj}, \quad (15)$$

$$\begin{aligned} \frac{\partial^2 \kappa_{ij}}{\partial L_{kl}} = & \{ \sum_{m,u} L_{mn} [Q_1'(i, j, k, l, m, n) + Q_1'(i, j, l, k, m, n) \\ & + Q_1'(i, j, m, n, k, l) + Q_1'(i, j, m, n, l, k)] \\ & + 2Q_2'(i, j, k, l) + A(\mathbf{r})_{ik}A(\mathbf{r})_{jl} + A(\mathbf{r})_{il}A(\mathbf{r})_{jk} \\ & + \theta [Q_4'(i, j, k, l) + Q_4'(i, j, l, k)] \} / (1 + \delta_{kl}), \quad (16) \end{aligned}$$

$$\frac{\partial^2 \kappa_{ij}}{\partial S_{kl}} = Q_3'(i, j, k, l) + \theta Q_5'(i, j, k, l) \quad (17)$$

and

$$\begin{aligned} \frac{\partial^2 \kappa_{ij}}{\partial \theta} = & \sum_{k,l} L_{kl} Q_4'(i, j, k, l) + \sum_m [S_{mj} Q_5'(i, j, m, i) / (1 + \delta_{ij}) \\ & + S_{mi} Q_5'(i, j, m, j) / (1 + \delta_{ij}) \\ & + (1/r'^2) \{ R_i R_j + 2\theta [(R_i' R_j' / 2r'^2) - R_i R_j] \}]. \quad (18) \end{aligned}$$

The necessary subsums for the third cumulant ${}^3\kappa_{ijk}$ and its derivatives are defined as

$$Q_1''(i, j, k, l, m, n, p) = 2[A(\mathbf{r})_{il}A(\mathbf{r})_{jn}B(\mathbf{r})_{kmp} + A(\mathbf{r})_{jl}A(\mathbf{r})_{kn}B(\mathbf{r})_{lmp} + A(\mathbf{r})_{kl}A(\mathbf{r})_{in}B(\mathbf{r})_{jmp}], \quad (19)$$

$$\begin{aligned} Q_2''(i, j, k, l, m) = & 2 \sum_n \{ S_{ni} [A(\mathbf{r})_{jl}B(\mathbf{r})_{kmn} + A(\mathbf{r})_{kl}B(\mathbf{r})_{jmn}] \\ & + S_{nj} [A(\mathbf{r})_{il}B(\mathbf{r})_{kmn} + A(\mathbf{r})_{kl}B(\mathbf{r})_{imn}] \\ & + S_{nk} [A(\mathbf{r})_{il}B(\mathbf{r})_{jmn} + A(\mathbf{r})_{jl}B(\mathbf{r})_{lmn}] \}, \quad (20) \end{aligned}$$

$$\begin{aligned} Q_3''(i, j, k, l, m) = & 2 \sum_{n,p} L_{np} \{ \delta_{mi} [A(\mathbf{r})_{jn}B(\mathbf{r})_{kpl} + A(\mathbf{r})_{kn}B(\mathbf{r})_{jpl}] \\ & + \delta_{mj} [A(\mathbf{r})_{in}B(\mathbf{r})_{kpl} + A(\mathbf{r})_{kn}B(\mathbf{r})_{lpl}] \\ & + \delta_{mk} [A(\mathbf{r})_{in}B(\mathbf{r})_{jpl} + A(\mathbf{r})_{jn}B(\mathbf{r})_{lpl}] \}, \quad (21) \end{aligned}$$

$$\begin{aligned} Q_4''(i, j, k, l, m) = & 2\delta_{mi} \sum_n [B(\mathbf{r})_{jln}S_{nk} + B(\mathbf{r})_{kln}S_{nj}] \\ & + \delta_{mj} \sum_n [B(\mathbf{r})_{ilin}S_{nk} + B(\mathbf{r})_{kln}S_{ni}] \\ & + \delta_{mk} \sum_n [B(\mathbf{r})_{ilin}S_{nj} + B(\mathbf{r})_{jln}S_{ni}], \quad (22) \end{aligned}$$

$$\begin{aligned} Q_5''(i, j, k, l, m) = & (1/r'^2) \{ R_i [A(\mathbf{r})_{jl}A(\mathbf{r})_{km} + A(\mathbf{r})_{kl}A(\mathbf{r})_{jm}] \\ & + R_j [A(\mathbf{r})_{il}A(\mathbf{r})_{km} + A(\mathbf{r})_{kl}A(\mathbf{r})_{im}] \\ & + R_k [A(\mathbf{r})_{il}A(\mathbf{r})_{jm} + A(\mathbf{r})_{jl}A(\mathbf{r})_{im}] \}, \quad (23) \end{aligned}$$

$$\begin{aligned} Q_6''(i, j, k, l, m) = & (1/r'^2) \{ \delta_{mi} [A(\mathbf{r})_{jl}R_k + A(\mathbf{r})_{kl}R_j] \\ & + \delta_{mj} [A(\mathbf{r})_{il}R_k + A(\mathbf{r})_{kl}R_i] \\ & + \delta_{mk} [A(\mathbf{r})_{il}R_j + A(\mathbf{r})_{jl}R_i] \}, \quad (24) \end{aligned}$$

$$Q_7''(i, j, k) = (1/r'^4) [R_i' R_j R_k + R_i R_j' R_k + R_i R_j R_k']. \quad (25)$$

The third cumulant ${}^3\kappa_{ijk}$ and its derivatives then become

$$\begin{aligned} {}^3\kappa_{ijk} = & \sum_{l,m} L_{lm} [Q_2''(i, j, k, l, m) + \sum_{n,p} L_{np} Q_1''(i, j, k, l, m, n, p) \\ & + \theta Q_5''(i, j, k, l, m)] + B(\mathbf{r})_{ilm} (S_{lj} S_{mk} + S_{mj} S_{lk}) \\ & + B(\mathbf{r})_{jlm} (S_{li} S_{mk} + S_{mi} S_{lk}) + B(\mathbf{r})_{klm} (S_{li} S_{mj} + S_{mi} S_{lj}) \\ & + \theta \sum_l [S_{li} Q_6''(i, j, k, l, i) / (1 + \delta_{ij} + \delta_{ik}) \\ & + S_{lj} Q_6''(i, j, k, l, j) / (1 + \delta_{jl} + \delta_{jk}) \\ & + S_{lk} Q_6''(i, j, k, l, k) / (1 + \delta_{kl} + \delta_{kj})] + \theta^2 Q_7''(i, j, k); \quad (26) \end{aligned}$$

$$\begin{aligned} \frac{\partial^3 \kappa_{ijk}}{\partial L_{lm}} = & \{ \sum_{n,p} L_{np} [Q_1''(i, j, k, l, m, n, p) + Q_1''(i, j, k, m, l, n, p) \\ & + Q_1''(i, j, k, n, p, l, m) + Q_1''(i, j, k, n, p, m, l)] \\ & + Q_2''(i, j, k, l, m) + Q_2''(i, j, k, m, l) \\ & + \theta [Q_5''(i, j, k, l, m) + Q_5''(i, j, k, m, l)] \} / (1 + \delta_{lm}), \quad (27) \end{aligned}$$

$$\frac{\partial^3 \kappa_{ijk}}{\partial S_{lm}} = Q_3''(i, j, k, l, m) + Q_4''(i, j, k, l, m) + \theta Q_6''(i, j, k, l, m) \quad (28)$$

and

$$\begin{aligned} \frac{\partial^3 \kappa_{ijk}}{\partial \theta} = & \sum_{ml} L_{lm} Q_5''(i, j, k, l, m) + 2\theta Q_7''(i, j, k) \\ & + \sum_l [S_{li} Q_6''(i, j, k, l, i) / (1 + \delta_{ij} + \delta_{ik}) \\ & + S_{lj} Q_6''(i, j, k, l, j) / (1 + \delta_{jl} + \delta_{jk}) \\ & + S_{lk} Q_6''(i, j, k, l, k) / (1 + \delta_{kl} + \delta_{kj})]. \quad (29) \end{aligned}$$

Discussion

These equations are the generalized form of the equations developed by Prince & Finger. They have been incorporated into a least-squares refinement program which has been used to analyse methyl-group librational motion in the molecular crystal of naphthyridinomycin (see inset in Fig. 1). The details of the X-ray structure solution have been presented elsewhere (Sygusch, Brisse & Hanessian, 1974; Sygusch, 1974). The conventional crystallographic residual $R(|F|)$ for the constrained thermal-motion refinement was 0.043. Thermal librational amplitudes for the three methyl groups obtained in naphthyridinomycin and in durene (Prince, Schroeder & Rush, 1973) are given in Table 2. From Table 2, it is apparent that the thermal amplitudes of the C-C and O-C methyl groups are statistically identical in naphthyridinomycin and are very similar to the C-C methyl-group librational amplitudes determined by Prince, Schroeder & Rush (1973) in durene. The amplitude for librational motion about the N-C bond was found to be significantly smaller than the amplitudes about the other two bonds. To examine this difference, PCILO conformational energy calculations (Diner, Malrieu & Claverie, 1969) were undertaken on naphthyridinomycin. A 1.08 Å standard bond length was assumed for all methyl groups. Then for each methyl group, the conformational energy was evaluated as a function of the torsional angle about bonds N-C, C-C and O-C. The results are presented in Fig. 1. The variations in energy about bonds C-C and O-C were indistinguishable to within 0.1 kcal mol⁻¹ and thus were presented as a single curve. The rate of change of potential energy about the zero position is significantly greater for the N-C methyl group than for the other two; thus a smaller amplitude of libration is predicted for the N-C methyl group. This correlates well qualitatively with the experimental θ

Table 2. Methyl-group libration

Mean square amplitude θ units are in radians².

Rotation axis	Naphthyridinomycin	Durene
N-C	0.003 (18)	
C-C	0.076 (28)	0.142 (5)*
O-C	0.106 (39)	

* Average of two chemically identical methyl groups.

values suggesting that the smaller amplitude about the N-C bond is indeed real.

It has been pointed out by Schomaker & Trueblood (1968) that the trace of **S** cannot be determined since only the differences $S_{ii} - S_{jj}$ enter into their calculations. The inclusion of third and fourth-order terms removes this indeterminacy in the trace of **S** and allows determination individually of the diagonal elements of **S**. In practice, however, we find that the diagonal elements are poorly determined (*i.e.* they have a large standard deviation) and are highly correlated (0.999). This is true since the indeterminacy is only removed at third order in the equations and thus differences in the derivatives for the S_{ii} cannot enter strongly into the sums for the normal equation matrix. Imposition of the constraint that the trace of **S** be zero yielded low standard deviations and no significant correlations among the remaining diagonal elements of **S**.

It is possible that more than one internal mode may contribute to the displacement of an atom from its equilibrium position. If the coupling between the various modes contributing to the displacement of an atom is neglected, the instantaneous displacement can be represented as the sum of the individual modes in addition to the overall molecular displacement. The neglect of coupling can be minimized if the internal mode displacements are chosen to be orthogonal.

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