Non-linear Least Squares Program for the Analysis of ^{13}C Spin–Lattice Relaxation Data based on a Symmetric Top Model. Description of the Method and Application

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A non-linear least squares program has been developed to analyse data for the dipole–dipole relaxation time of carbon (T_1^{DD}) based on the symmetric top model of molecular rotational diffusion. The program employs four parameters in the simulation, *i.e.* two rotational diffusion constants and two angles related to the axis of molecular motion. The internal rotation of methyl groups is also incorporated. The application of the program to methylbenzofurans indicated the reliability and wide applicability of the method. The factors affecting the methyl rotation barrier are also examined with the aid of MNDO MO calculations, and a novel inter-relation is found with the bond length of $C-CH_3$.

Recently n.m.r. ^{13}C T_1 data have attracted much attention in the discussion of molecular motion in solution.[1] This relies partly on methodological developments in Fourier transform n.m.r. spectroscopy which makes T_1 data readily available, and partly on the theoretical treatment of magnetic resonance phenomena [2,3] and molecular motions.[4–6] Hitherto various models have been examined to extend the most simple isotropic model of molecular motion in which only one rotational diffusion constant or correlation time is assumed. These models stem from the expression for T_1^{DD} derived by Woessnor [4] who took account of anisotropic molecular motions using three rotational diffusion constants, D_1—D_3. Among these studies, one which assumes symmetry in the molecular motion, *i.e.* a symmetric top model in which D_2 and D_3 coincide, may be most widely applicable to organic compounds as Lambert *et al.* noted.[1] According to Lambert *et al.*, the expression for T_1^{DD} is greatly simplified while retaining the essential relaxation features of anisotropic motion,† and internal motions are easily incorporated.

In the present study a computer program has been written which simulates T_1^{DD} data using the symmetric top model. The application of the program to the data for methylbenzofurans examined by Platzer [13] led to promising results. Rotation of methyl groups is discussed in relation to the molecular as well as the electronic structures.

Methods

The significance of T_1^{DD} in the symmetric top model has been reviewed by Lambert *et al.*[1]

Rigid Part of Molecules.—$R_{j.\text{calc.}}$, *i.e.* $1/T_1^{DD}$ calculated for carbon C_j relaxing with a dipole–dipole interaction with protons H ($i = 1 - M$), is expressed by equation (1) where D_1

$$R_{j.\text{calc.}} = \sum_{i=1}^{M} \gamma_C^2 \gamma_H^2 \hbar^2 \frac{1}{r_{C_jH_i}{}^6} \left(\frac{A_{ji}}{6D_2} + \frac{B_{ji}}{D_1 + 5D_2} + \frac{C_{ji}}{4D_1 + 2D_2} \right) \qquad (1)$$

and D_2 are the rotational diffusion constants, and A—C are geometric factors related to the angle Δ_{ji} between the direction of the $C_j \cdots H_i$ pair and the axis of symmetry of the top molecule, *i.e.* equations (2). In equation (1) cross relaxation

$$\begin{aligned} A_{ji} &= (3\cos^2\Delta_{ji} - 1)^2/4 \\ B_{ji} &= 3\sin^2(2\Delta_{ji})/4 \\ C_{ji} &= 3\sin^4(\Delta_{ji})/4 \end{aligned} \qquad (2)$$

between protons is omitted as is usually the case. The problem is then to fit the data of $R_{j,\text{obs.}}$ by adjusting the parameters. This may be accomplished by minimizing the function F by a non-linear least-squares procedure [equation (3) where N

$$F = \sum_{j=1}^{N} (R_{j.\text{obs.}} - R_{j.\text{calc.}})^2 \qquad (3)$$

indicates the number of carbons whose T_1^{DD} values are available]. Of course, N should equal or exceed the number of parameters to be determined. Unless N is larger than the number of parameters after allowing for geometrically equivalent data, the resulting errors in the parameters will become serious.

Among the various kinds of non-linear least-squares analysis we had adopted here a version of the DFP (Davidon–Fletcher–Powell) method,[14,15] which is a variable method. It is widely

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† Applications of the full anisotropic model ($D_1 \neq D_2 \neq D_3$) have been attempted by several investigators.[7–12] To our knowledge, however, only Somorjai and Deslauries [12] made their simulation without making any serious assumptions and used six parameters, *i.e.* three each for the rotational diffusion constants and the Euler angles. In other studies axes of the rotational motion were usually fixed and set equal to those of the moment of inertia, yielding a three-parameter simulation for the D values. The rotational diffusion constants thus derived were often not easy to interpret, and also internal motions or break down of the diffusion process were possibly responsible.[7,9,10] Stilbs and Moseley [10a] developed a program to include error analysis and warned that a poor fit in the simulation does not always imply the presence of, *e.g.* internal motions. They also pointed out a serious problem: that no conclusion about the rotational behaviour of cholesterol is possible because of the large errors estimated in the D values.

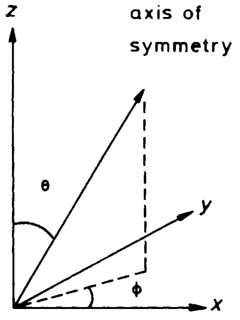

Figure 1. Definition of the axis of symmetry of molecular motion by polar co-ordinates

accepted as one of the most sophisticated search techniques, and appears to be independent of the number of variables involved.[16] This DFP method was partly improved by Fletcher.[17,*] This subroutine minimizes functions with or without the use of derivatives. We believe that taking into account the characteristics of the minimized function as much as possible is the best way to achieve successful minimization, and hence the derivatives were also added to the program in an analytical form.

Δ_{jt} in equation (2) is defined by equation (4) where *a*—*c* are

$$\cos\Delta_{jt} = a \cdot l_{jt} + b \cdot m_{jt} + c \cdot n_{jt} \qquad (4)$$

directional cosines of the axis of symmetry of the molecule, and *l*—*n* are those of the $C_j \cdots H_t$ pair. The latter are easily deduced if the co-ordinates of C and H atoms are given [equations (5)]. Directional cosines of the axis of symmetry are

$$\begin{aligned} l_{jt} &= (x_j - x_t)/r_{C_jH_t} \\ m_{jt} &= (y_j - y_t)/r_{C_jH_t} \\ n_{jt} &= (z_j - z_t)/r_{C_jH_t} \end{aligned} \qquad (5)$$

related to the polar angles θ and φ (Figure 1) [equations (6)].

$$\begin{aligned} a &= \sin\theta\cos\varphi \\ b &= \sin\theta\sin\varphi \\ c &= \cos\theta \end{aligned} \qquad (6)$$

Consequently there are four adjustable parameters in equation (1) in the general case, *i.e.* D_1 (or $\sigma = D_1/D_2$), D_2, θ, and φ. When the values of one or a few of these parameters are known, *e.g.* from symmetry requirements, derivatives with respect to these parameters can be set to zero and the simulation made with the reduced number of parameters. At the input step of the program it was specified which parameters were varied and which held constant. Errors were also estimated in the 95% confidence range, assuming the parameters were independent.

$$\frac{1}{T_1^{DD}(CH)_3} = n\gamma_C^2\gamma_H^2\hbar^2\left[\frac{1}{2}\left(\frac{A_1}{6D_2} + \frac{A_2}{6D_2 + aD_t} + \frac{A_3}{6D_2 + amD_t} + \frac{B_1}{D_1 + 5D_2} + \frac{B_2}{D_1 + 5D_2 + aD_t} + \frac{B_3}{D_1 + 5D_2 + amD_t} + \frac{C_1}{4D_1 + 2D_2} + \frac{C_2}{4D_1 + 2D_2 + aD_t} + \frac{C_3}{4D_1 + 2D_2 + amD_t}\right)\right] \qquad (7)$$

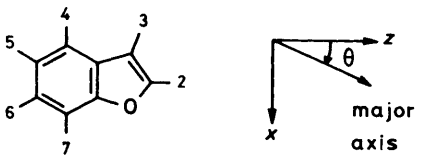

Figure 2. Benzofuran framework and definition of the major axis for molecular motion

Methyl Groups.—The T_1^{DD} value of carbon in a methyl group which is rotating internally around an axis inclined at an angle α to the axis of symmetry of the whole molecule is expressed by equation (7)[1] where $n = 3$, D_t is the internal methyl diffusion rate, *A*—*C* are given by equations (8), and *a* and *m* are factors which depend on the model of methyl rotation, *i.e.* $a = 1$ and $m = 4$ for the stochastic model and $a = r/2$ and $m = 1$ for the *r*-fold jump model. In equations (8), Δ is an angle between the C–H bond and the C–CH$_3$

$$\begin{aligned} A_1 &= 1/8(1 - 3\cos^2\alpha)^2(3\cos^2\Delta - 1)^2 \\ A_2 &= 9/16\sin^2 2\alpha\sin^2 2\Delta \\ A_3 &= 9/16\sin^4\alpha\sin^4\Delta \\ B_1 &= 3/8\sin^2 2\alpha(3\cos^2\Delta - 1)^2 \\ B_2 &= 3/4(\cos^2 2\alpha + \cos^2\alpha)\sin^2 2\Delta \\ B_3 &= 3/4(\sin^2\alpha + 1/4\sin^2 2\alpha)\sin^4\Delta \\ C_1 &= 3/8\sin^4\alpha(3\cos^2\Delta - 1)^2 \\ C_2 &= 3/4(\sin^2\alpha + 1/4\sin^2 2\alpha)\sin^2 2\Delta \\ C_3 &= 3/16[(1 + \cos^2\alpha)^2 + 4\cos^2\alpha]\sin^4\Delta \end{aligned} \qquad (8)$$

internal rotation axis of a methyl group. In principle D_t may be determined by solving equation (7) for an experimental value of $T_1^{DD}(CH_3)$ provided D_1 and D_2 are available from the T_1^{DD} data of the rigid part of molecule. Equation (7) is, however, too complex to be solved for D_t, *i.e.* a polynomial of the sixth power with respect to D_t needs to be solved. Accordingly, we adopted a simulation method as described above to accomplish this process. Thus, an initial value of D_t is adjusted to make the *F* value in equation (9) as small as possible. In equation (9) $R^{CH_3}{}_{calc.}$ means $1/T_1^{DD}(CH_3)$ in

$$F = (R^{CH_3}{}_{obs.} - R^{CH_3}{}_{calc.})^2 \qquad (9)$$

equation (7). In this case, of course, the residual *F* value should become as small as zero.

Results and Discussion

Platzer[13] has made an extensive study of the ^{13}C relaxation times of several methylbenzofurans (Figure 2), the data of which have been used here to examine the molecular motion and internal rotation of methyl groups. Although Platzer discussed the results on the basis of a trial and error method and by adopting a colinear model in the interpretation of the T_1^{DD} values of the methyl groups, data processing as described above is more reliable and widely applicable. The application of the program is summarized in the Table, together with

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[*] A subroutine program DAFLEP had been introduced, registered at the Computation Center, Osaka University, by Professor T. Kotani (College of General Education).

Analysis of T_1^{DD} data in monomethylbenzofurans by the computer program based on the symmetric top model

Benzofuran	$10^{10}D_2$/s	D_1/D_2	θ (°)	S.d./s [b]	D_i/D_2 [c]	V_0/kJ mol^{-1}
2-Methyl [a]	1.80 ± 0.03	2.99 ± 0.15	−0.3 ± 1.3	0.31	24.9	7.4
	1.7	3.0	0		30	7.3
3-Methyl	2.42 ± 0.05	1.83 ± 0.12	−24.1 ± 5.7	0.36	15.3	7.9
4-Methyl	2.71 ± 0.06	1.28 ± 0.09	2.1 ± 0.2	0.29	26.5	6.3
5-Methyl [a]	1.66 ± 0.04	2.25 ± 0.17	9.0 ± 6.8	0.35	92.0	4.4
	1.7	2.2	10		∞	
6-Methyl [a]	1.84 ± 0.04	3.29 ± 0.15	−20.7 ± 2.2	0.35	47.5	5.8
	1.8	3.0	−19		∞	
7-Methyl	2.65 ± 0.02	1.32 ± 0.02	−36.9 ± 2.5	0.07	29.5	6.0

[a] Platzer's results are cited in the lower line. [b] Standard deviation in the T_1^{DD} data calculated as: s.d. = $[\sum_{i=1}^{N}(T_1{}^{DD}{}_{i,\text{obs.}} - T_1{}^{DD}{}_{i,\text{calc.}})^2]^{\frac{1}{2}}/(N-P)^{\frac{1}{2}}$, where N = number of T_1 data and P = number of unknown parameters. [c] Six-fold jump model is adopted for the methyl rotation.

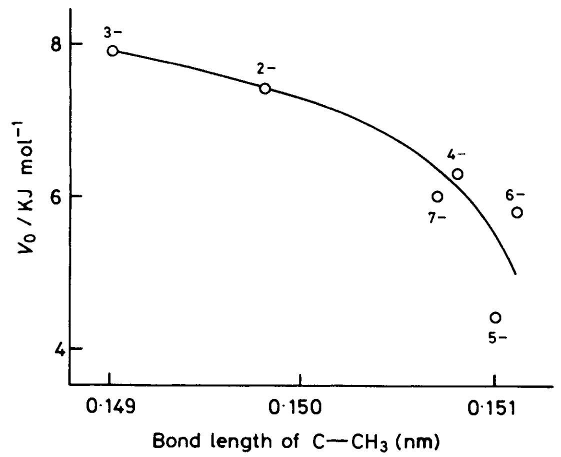

Figure 3. Correlation between V_0 and the bond length of C–CH_3 in monomethylbenzofurans. The number indicates the site of the methyl substituent

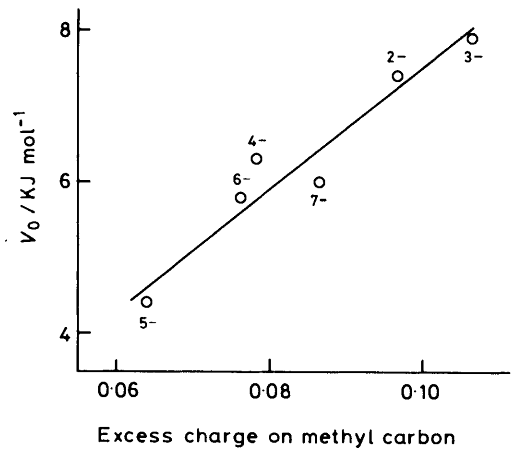

Figure 4. Correlation between V_0 and the excess charge on the methyl carbon. The number indicates the site of the methyl substituent

Platzer's calculation. In this case, φ (Figure 1) is zero from the planarity of the molecule, and D_2, $\sigma(=D_1/D_2)$, and θ are adjusted for the simulation. Final values of these parameters are tested to show if they are independent of the initial values.

σ and θ change drastically depending on the site of methyl substitution (Table). This fact and the fairly small standard deviations in the Table clearly support the validity of the model assumed. In another sense the results imply that the program is applicable to signal assignment based on differences in T_1^{DD} values: assignments can be made by simulating the T_1^{DD} data with definite assignments and by calculating the T_1^{DD} values of carbons of unknown assignments utilizing predetermined parameters such as D_2 and σ.

The methyl rotation barrier V_0 is obtained from D_i from the relation $V_0 = -RT\ln(D_i/D_{i0})$, and it is also cited in the Table. In this relation D_{i0} is the diffusion constant for a zero barrier and is 0.86×10^{13} s^{-1} (at 30 °C) by adopting $(kT/I)^{\frac{1}{2}}$ as its measure.[1]

To examine the dependence of V_0 on the site of methyl substitution, MNDO MO calculations [18] were made and ground-state structures were deduced by geometrical optimization. The optimized molecular structures were then used in the above simulation of T_1^{DD} data for the rigid part of the molecule. In Figure 3 V_0 values are plotted against the bond lengths between the methyl carbon and the attached carbon. As might be expected, V_0 decreases with increasing bond length, reflecting the weakness of the methyl group in binding to the framework of the molecule. V_0 also increases with increasing the excess charge on the methyl carbon (Figure 4). This is phenomenologically similar to the case of the potential energy barrier of the amino-group in anilines.[19] Hence, it reflects the increased bond order of the C–CH_3 linkage induced by hyperconjugation which acts so as to draw positive charges into the methyl group.* These features have stimulated a more extended study of the inter-relation between V_0 and the bond length for various kinds of compounds. Although a precise estimate of the bond length is necessary for such an investigation, it has recently become available for relatively simple molecules from n.m.r. spectroscopy using liquid crystal media.[20] Inter-relations of this sort are of value not only for the estimation of the bond length from $T_1^{DD}(CH_3)$ but also for a discussion of steric hindrance in methyl groups.

Lambert and Nienhuis [21] suggested, from a discussion of V_0 in terms of substituent constants and of ^{13}C shifts, that V_0 in toluenes is governed by electronic interactions between bonds and hence by the electron density at carbons *ortho* to the methyl group. However, a similar discussion may not be

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* More rigorously, V_0 should be related to the excess charge on the methyl hydrogens. However, this excess charge shows only a small dependence on the site of attachment, *i.e.* one order smaller than that for the methyl carbon, so that no definite relation was observable for this charge.

applicable in the present case, because the structural environment changes considerably around the methyl group depending on the site of attachment. In fact, no definite relation was observable between V_0 and excess charges on the *ortho*-carbons (or oxygen), whichever excess charges on the *ortho*-atoms were considered. V_0 was also independent of excess charges at the carbon attached to the methyl group.

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