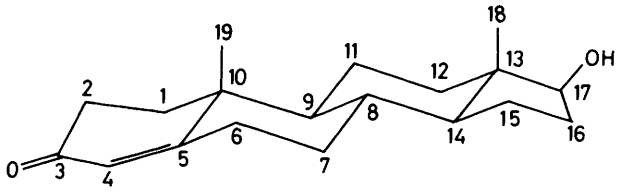
NMR Relaxation Studies on Testosterone in Solution: Magnetic Field Dependence of ^{13}C T_1 and Anisotropies in the Chemical Shift

Hideaki Fujiwara,* Yong-Zhong Da, Douwan Zheng, and Yoshio Sasaki
Faculty of Pharmaceutical Sciences, Osaka University, 1–6 Yamadaoka, Suita, Osaka 565, Japan
Yoshio Takai and Masami Sawada
The Institute of Scientific and Industrial Research, Osaka University, 8–1 Mihogaoka, Ibaraki 567, Japan

The magnetic field dependence of NMR ^{13}C relaxation times have been measured for testosterone in $CDCl_3$. The data were analysed by a computer-assisted method based on the molecular reorientational motion. For the quaternary carbons, contributions from other than the dipole–dipole relaxation mechanisms are separated into the two terms of chemical-shift anisotropy (T_1^{CA}) and spin–rotation interaction (T_1^{SR}). Anisotropies in the chemical shift are derived from T_1^{CA} thus separated. These anisotropies are comparable to the existing data, supporting this method of treatment. The barrier to internal rotation is determined for the two methyl groups; it is higher for the 19-methyl by *ca.* 2 kJ mol^{-1} than for the 18-methyl.

Recently the NMR spectra of steroids have become tractable: several techniques have been exploited to determine relaxation times[1] and NOE factors, and two-dimensional NMR experiments have been performed in order to assign spectra and to derive solution structures.[2] The ^{13}C spectrum of a representative steroid testosterone [17β-hydroxyandrost-4-en-3-one, (1)], has been assigned unequivocally by several investigators.[3] In our previous study of testosterone by NMR spectroscopy[4] the temperature dependence of ^{13}C T_1 was measured in [$^2H_6$]DMSO and treated by a computer-assisted method of analysis. As a result of this study, the dynamic properties such as the rate constants, as well as the activation energies, were derived for the molecular reorientational motion and hence a mechanism was inferred for the relaxation of quaternary carbons.



(1) Testosterone

The relaxation mechanism can also be studied by analysis of the magnetic field dependence of relaxation times. Since high-field NMR spectrometers have become available recently, such a study is expected to afford a successful separation of the components of the dipole–dipole interaction (T_1^{DD}), the chemical shift anisotropy (T_1^{CA}), and the spin–rotation interaction (T_1^{SR}). The value of T_1^{CA} affords the anisotropy in the chemical shift.[5] This anisotropy, which depends on the electronic structure of molecule, has recently attracted attention in organic structural chemistry in relation to solid-state NMR spectroscopy. In the present study, T_1^{CA} and T_1^{SR} are separately determined and $\Delta\sigma$ is estimated for the quaternary carbons. The resulting $\Delta\sigma$ values are comparable to the existing data.

Experimental

Testosterone obtained from Tokyo Kasei Co. and $CDCl_3$ from Merck were used without further purification. The sample solution of 0.56 mol dm^{-3} was sealed under Ar gas after being degassed by the freeze–pump–thaw method. Pyrex tubes with φ = 10 and 5 mm were used for the measurements under 25 and 125 MHz, respectively. The ^{13}C relaxation time T_1 was measured with JEOL PS–100 (25 MHz) and GX–500 (125 MHz) spectrometers at room temperature. The inversion–recovery method was adopted for the T_1 measurement. The relaxation times of the proton-bearing carbons and the quaternary carbons were measured separately by adopting different waiting times which were all longer than $5T_1$. The 90° pulses were 14 μs at 25 MHz and 12 μs at 125 MHz. The number of FID accumulations were 128 at 25 MHz and 64 at 125 MHz. The measurement of ^{13}C T_1 was repeated more than five times and the raw data were averaged to obtain the experimental values and their standard deviations. The NOE factors were measured with waiting times longer than $10T_1$, using 64K data points for the spectral width of 20 kHz at 125 MHz. The computer program T1ANSOC[6] was used for the analysis of T_1 data. Calculations were performed on NEAC S–1 000 and SX–2 computers at the Computation Centre, Osaka University.

Results and Discussion

The experimental T_1 values are listed in Table 1. It is seen that the magnetic field dependence is more pronounced than the temperature dependence reported in the previous study,[4] which indicates that a study of the former will be more useful. The T_1 data for proton-bearing carbons are simulated by the program T1ANSOC[6] assuming a full contribution from the dipole–dipole mechanism, since the experimental NOE factors are larger than 1.8 (including errors of the order of ±0.2 for these carbons). The calculated values of T_1 are also listed in Table 1 (as $T_1^{DD}{}_{calc}$); the molecular dynamics parameters obtained are listed in Table 2. The dynamic models adopted are the isotropic and axially symmetric top models.[6] The anisotropic model gives smaller standard deviations (sd) between the observed and calculated relaxation times for the proton-bearing carbons (Table 2) although the fully anisotropic model failed to give a satisfactory simulation because of the rather small distribution of the directional cosines for the C–H vectors in testosterone. These results are in common with those observed in [$^2H_6$]DMSO.[4]

The molecular dynamics parameters determined here for testosterone in $CDCl_3$ are seen to correspond approximately to

Table 1. ^{13}C T_1 [a] Analysis of testosterone in $CDCl_3$ at 25 and 125 MHz.

		125 MHz				25 MHz		
			$T_1^{DD}{}_{calc}$				$T_1^{DD}{}_{calc}$	
Shift (ppm)	Site	$T_{1,obs}$	Model 1 [b]	Model 2 [b]	η_{obs}	$T_{1,obs}$	Model 1	Model 2
199.91	3 [c]	8.57 ± 0.20	33.93	29.65	0.61	18.44 ± 0.24	28.81	23.37
171.53	5 [c]	6.09 ± 0.17	25.09	19.46	0.61	13.52 ± 0.17	21.30	15.81
123.80	4	1.62 ± 0.13	1.91	1.75	1.83	1.85 ± 0.10	1.62	1.96
81.44	17	1.77 ± 0.11	1.78	1.77	1.85	1.48 ± 0.09	1.51	1.37
53.96	9	1.74 ± 0.10	1.80	1.66	1.85	1.50 ± 0.11	1.53	1.38
50.52	14	1.74 ± 0.16	1.80	1.70	1.78	1.49 ± 0.04	1.53	1.34
42.84	13 [c]	10.48 ± 0.31	15.54	13.80	1.82	10.94 ± 0.16	13.19	11.14
38.70	10 [c]	12.69 ± 0.55	17.81	16.12	1.76	12.26 ± 0.29	15.11	12.45
36.48	12	0.93 ± 0.09	0.96	0.95	1.81	0.82 ± 0.04	0.82	0.88
35.74	1	1.56 ± 0.07	0.97	1.23	1.90	1.20 ± 0.05	0.82	0.95
35.74	8	1.56 ± 0.07	1.77	1.74	1.90	1.20 ± 0.05	1.51	1.35
33.91	2	0.94 ± 0.10	0.97	0.96	1.91	0.89 ± 0.01	0.82	0.82
32.81	6	0.92 ± 0.06	0.97	0.94	1.93	0.79 ± 0.02	0.82	0.84
31.59	7	0.91 ± 0.09	0.96	0.86	1.77	0.75 ± 0.04	0.81	0.75
30.34	16	0.99 ± 0.05	0.96	0.94	1.96	0.81 ± 0.06	0.82	0.87
23.37	15	0.91 ± 0.04	0.96	1.09	1.98	0.73 ± 0.05	0.81	0.79
20.70	11	0.89 ± 0.05	0.96	0.88	1.91	0.75 ± 0.03	0.81	0.75
17.42	19 [d]	1.91 ± 0.14	1.91	1.91	1.98	1.82 ± 0.07	1.82	1.82
11.09	18 [d]	3.00 ± 0.19	3.00	3.00	1.93	2.56 ± 0.10	2.56	2.56

[a] The unit of T_1 is s. [b] The molecular dynamics models are: isotropic model (model 1) and axially symmetric model (model 2). [c] Quaternary carbon. [d] Methyl carbon.

Table 2. Molecular dynamics parameters of testosterone in $CDCl_3$ measured at 25 and 125 MHz.

Model	Parameters	at 125 MHz	at 25 MHz
Isotropic	$D/10^9$ s^{-1}	7.77 ± 0.95	8.59 ± 0.76
	sd/s [a]	0.206	0.161
Axially symmetric	$D_2/10^9$ s^{-1}	1.88 ± 0.15	1.79 ± 0.14
	D_1/D_2	19.3 ± 3.2	15.3 ± 2.7
	θ	41 ± 9°	25 ± 14°
	φ	−39 ± 6°	−49 ± 21°
	sd/s	0.152	0.135

[a] sd is the standard deviation between the observed and the recalculated relaxation times for the proton-bearing carbons.

Table 3. Molecular dynamics parameters [a] for the internal rotation of methyl groups in testosterone.

		Model 1 [b]		Model 2 [b]		
Methyl group	$T_{1,obs}$	D_i	V_0	D_i	V_0	Conditions
19-Methyl	1.82	7.75	11.9	8.29	11.7	in $CDCl_3$ (25 MHz)
	1.91	7.23	12.0	7.33	12.0	in $CDCl_3$ (125 MHz)
	1.51	0.95	11.8	0.95	11.8	in [$^2H_6$]DMSO (40 °C) [c]
	2.45	1.26	12.2	1.25	12.2	in [$^2H_6$]DMSO (70 °C) [c]
	3.67	1.64	12.6	1.66	12.6	in [$^2H_6$]DMSO (100 °C) [c]
18-Methyl	2.56	15.63	10.1	15.5	10.1	in $CDCl_3$ (25 MHz)
	3.00	18.40	9.7	17.20	9.9	in $CDCl_3$ (125 MHz)
	2.19	2.54	9.2	3.45	8.4	in [$^2H_6$]DMSO (40 °C) [c]
	3.93	3.50	9.3	4.68	8.5	in [$^2H_6$]DMSO (70 °C) [c]
	5.74	4.29	9.6	5.02	9.1	in [$^2H_6$]DMSO (100 °C) [c]

[a] The units of T_1, D_i, and V_0 are s, 10^{11} s^{-1}, and kJ mol^{-1}, respectively. [b] The dynamics models for the molecular reorientational motion are isotropic (model 1) and axially symmetric (model 2) ones. [c] The data in [$^2H_6$]DMSO are cited [4] for comparison and were measured at 25 MHz.

those determined in [$^2H_6$]DMSO at 70 °C. These parameters were found to be dependent on the solvent viscosity, in [$^2H_6$]DMSO.* However the value of ln D obtained in $CDCl_3$ is lower than that expected from the viscosity dependence in [$^2H_6$]DMSO. Further examination was not attempted, but two factors can be cited to explain the above discrepancy. Firstly, the viscosity of a solution is different to that of the pure solvent, and secondly solute–solvent interactions can affect the dynamic properties of solutes in solvents. The values of θ and φ, which indicate the tilted angles between the major axis of the reorientational motion and that of the moment of inertia (see Figure 1 in ref. 6), are non-zero and do not change significantly between the two solvents. Also the ratio of the two rate constants D_1 and D_2, which indicates the anisotropy in the molecular motion, does not show any clear difference between these two solvents.

Internal Rotation of Methyl Groups.—This effect can be taken into account by the program T1ANSOC when the rotation occurs around an axis tilted by a definite angle from the major axis of molecular reorientational motion. In this case, the ^{13}C T_1 of a methyl carbon is reproduced by an appropriate value of the rate constant D_i for the internal motion. Therefore, ^{13}C T_1 for methyl groups thus calculated coincides with the observed values, as shown in Table 1. The resulting D_i values are listed in Table 3. The barrier to internal rotation V_0 is easily derived for the methyl group from equation (1) where D_{i0} is the rate

$$D_i = D_{i0}\exp(-V_0/RT) \quad (1)$$

constant pertinent to the zero barrier and is equal to 0.86×10^{13} s^{-1} at 30 °C, adopting $(kT/I)^{\frac{1}{2}}$ as its measure.[4]

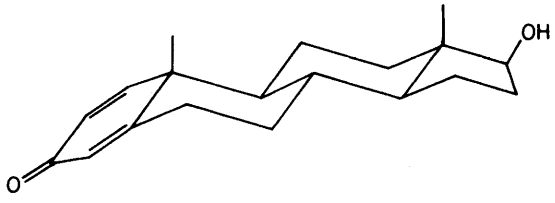
* Here, the temperature-dependent viscosity is predicted by the relation, $\log \eta = -0.998\,82 + 14.149/T + 111{,}256/T^2$, derived from the data between 25 and 55 °C.[7]

Table 4. ^{13}C T_1 [a] analysis of testosterone in $CDCl_3$ at 125 MHz.

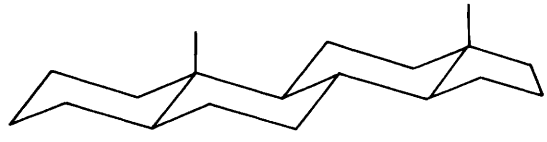
Shift (ppm)	Site	$T_{1.obs}$	$T_1^{DD}{}_{calc}$ [b] Model 1	Model 2	T_1^{others}	T_1^{CA}	T_1^{SR}	Δσ (ppm)	N_α [c]	η_{calc} [c]	η_{obs} [c]
199.91	3	8.57	33.9	29.7	11.5	14.7	52.1	196.2	3	0.57	0.61
171.53	5	6.09	25.1	19.5	8.04	10.2	38.0	235.6	3	0.62	0.61
42.84	13	10.5	15.5	13.8	32.2	74.3	56.8	87.3	7	1.51	1.82
38.70	10	12.7	17.8	16.1	44.1	208.0	56.1	52.2	6	1.57	1.76

[a] The unit of T_1 is s. [b] The values of $T_1^{DD}{}_{calc}$ of model 2 (axially symmetric model) are cited for the calculation of η_{calc} since this model is more elaborate, whereas those of model 1 (isotropic model) are cited for the calculation of Δσ as in this case T_1^{CA} is expressed by an isotropic model using a single τ_c value. [c] N_α indicates the total number of α-protons, and η is the NOE factor.

The values of V_0 thus derived are included in Table 3, as are the previous results observed for the same parameters in [$^2H_6$]DMSO. It is seen that the V_0 values observed in the present case in $CDCl_3$ do not depend on the NMR frequency of measurement and that they are consistent with those observed in [$^2H_6$]DMSO in the previous report. These facts support the experimental methods and interpretation of the ^{13}C T_1 data in these studies. Our results indicate that the 18-methyl group rotates faster than the 19-methyl group, in testosterone. This trend is in common with that in 1-dehydrotestosterone (**2**), for which ^1H relaxation times (T_1) are 1.1 s (18-methyl) and 0.6 s (19-methyl)[2b] whereas opposite results are reported in 5α-androstane (**3**), for which V_0 amounts to 12.6 kJ mol^{-1} (18-methyl) and 9.6 kJ mol^{-1} (19-methyl).[8] Furthermore, the rate constant D_i is larger for 19-methyl than that for 18-methyl in several derivatives of 5α-androstane.[8] These results indicate that unsaturation in the A-ring tends to hinder the internal rotation of the 19-methyl. This tendency may be explained by the interaction of methyl groups with the steroid axial hydrogens: asymmetric placement of hydrogens will enhance a rotational barrier, thereby slowing down the rate of internal rotation.[8]



(**2**) 1-Dehydrotestosterone



(**3**) 5α-Androstane

Relaxation Times of the Quaternary Carbons.—In this case the contribution of other than the dipole–dipole relaxation, T_1^{others}, can be derived after estimating the part of T_1^{DD} from the molecular dynamics parameters listed in Table 2 and then subtracting this part from the experimental relaxation data as shown in equation (2). T_1^{others} can then be separated into the

$$1/T_1^{others} = 1/T_{1.obs} - 1/T_1^{DD}{}_{calc} \quad (2)$$

two parts of T_1^{SR} (spin–rotation interaction term) and T_1^{CA} (chemical-shift anisotropy term) from the analysis of the magnetic field dependence, by means of the 'iteration method' already reported[9] and of the 'τ_c correction method' (see the Appendix). The results are summarized in Table 4. The value of $T_1^{DD}{}_{calc}$ parallels the number of α-protons, and the contribution of T_1^{DD} becomes distinct for the sp^3 carbons of C(10) and C(13). From the analysis of the temperature dependence in [$^2H_6$]DMSO in the previous report,[4] it is suggested that the quaternary sp^2 carbons relax through both the chemical-shift anisotropy and the spin–rotation interaction, whereas the quaternary sp^3 carbons relax mainly through the spin–rotation interaction and the dipole–dipole interactions with the protons in the vicinity. This tendency is proved quantitatively in the present study (see Table 4). The NOE factors are calculated from the results of T_1 data simulation to be $1.988 \times T_{1.obs}/T_1^{DD}{}_{calc}$. These values agree closely with the experimental ones (Table 4), hence supporting this method of analysis.

From the separated values of the T_1^{CA} anisotropy in the chemical shift, Δσ can be derived for the quaternary carbons [equation (A3)]; the results are included in Table 4. Positive values are tentatively assigned for Δσ in Table 4 although only absolute values are available from the relaxation time. The Δσ value of C=O is *ca.* 200 ppm, approximately equal to the value of acetone (193 ppm).[5] This value is seen to be decreased when an electronegative atom is attached to the C=O group. That is, Δσ = 136.2 ppm for the N–C=O carbon in strychnine in the previous report[9] and Δσ = 171.2 ppm for the F–C=O carbon.[5]

In conclusion, the magnetic field dependence of ^{13}C T_1 values for testosterone can be analysed successfully to give the chemical shift anisotropies of quaternary carbons, through the separation of the experimental relaxation time into its components. Thus, this method of analysis is shown to be important and useful in the study of the dynamics and structures of molecules in solution.

Appendix

The 'τ_c Correction Method' for the Separation of T_1^{other} *into the Two Terms of* T_1^{CA} *and* T_1^{SR}.—In the previous report,[9] the authors have proposed the 'iteration method' which is summarized in equations (A1) and (A2). Here, the isotropic

$$\frac{1}{[T_1^{CA(125)}]_0} = \frac{1/T_1^{others(125)} - 1/T_1^{others(25)}}{1 - \{\tau_c^{(25)}/25\tau_c^{(125)}\}} \quad (A1)$$

$$\frac{1}{[T_1^{CA(125)}]_n} = \frac{1}{[T_1^{CA(125)}]_0} - \frac{1}{[T_1^{SR(125)}]_{n-1}} \cdot \frac{1 - \{\tau_c^{(125)}/\tau_c^{(25)}\}}{1 - \{\tau_c^{(25)}/25\tau_c^{(125)}\}} \quad (A2)$$

model has been assumed for the simple expressions of T_1^{CA} and

T_1^{SR} [equations (A3) and (A4)].[5,10] Also τ_c, which is equal to

$$1/T_1^{CA} = (2/15)(2\pi\nu_0\Delta\sigma)^2\tau_c \quad (A3)$$

$$1/T_1^{SR} = (\pi I^2/3h^2)\{(C_\parallel^2 + 2C_\perp^2)/3\}(1/\tau_c) \quad (A4)$$

$1/6D$, is allowed to differ at the two NMR frequencies of 25 and 125 MHz, since it is experimentally difficult to maintain a constant sample temperature when the NMR frequency is changed by using different spectrometers. The numerals in parentheses indicate the frequencies at which the spectra were measured. $[\ ]_0$ indicates a first estimate and $[\ ]_n$ means the nth one. Equation (A2) is iterated to obtain a self-consistent value of $T_1^{CA(125)}$. Then $T_1^{SR(125)}$ is obtained according to equation (A5). In fact, equation (A2) was repeated about five times only

$$1/T_1^{others} = 1/T_1^{CA} + 1/T_1^{SR} \quad (A5)$$

to reach the final values in Table 4.

In the present study, an alternative method is proposed which may be called the 'τ_c correction method'. This does not need repeated calculations, in contrast with the 'iteration method'.

Equations (A6) and (A7) hold for the T_1^{others} obtained at the

$$1/T_1^{others(125)1} = 1/T_1^{CA(125)1} + 1/T_1^{SR(125)1} \quad (A6)$$

$$1/T_1^{others(25)2} = 1/T_1^{CA(25)2} + 1/T_1^{SR(25)2} \quad (A7)$$

two NMR frequencies. Here, (125)1 indicates the value at 125 MHz corresponding to a correlation time $\tau_c^{(1)}$, and (25)2 means the value at 25 MHz corresponding to the time $\tau_c^{(2)}$. Equation (A7) is corrected below for the difference in the NMR frequency and τ_c. From the expressions for T_1^{CA} and T_1^{SR} [equations (A3) and (A4)], equations (A8)–(A11) are obtained.

$$T_1^{SR(25)2} = \{\tau_c^{(25)2}/\tau_c^{(25)1}\}T_1^{SR(25)1} \quad (A8)$$

$$T_1^{CA(25)2} = \{\tau_c^{(25)1}/\tau_c^{(25)2}\}T_1^{CA(25)1} \quad (A9)$$

$$T_1^{SR(25)1} = T_1^{SR(125)1} \quad (A10)$$

$$T_1^{CA(25)1} = 25T_1^{CA(125)1} \quad (A11)$$

Therefore, equation (A7) is transformed into equation (A12),

$$\frac{1}{T_1^{others(25)2}} = \frac{\tau_c^{(25)2}}{\tau_c^{(125)1}} \cdot \frac{1}{25\ T_1^{CA(125)1}} + \frac{\tau_c^{(125)1}}{\tau_c^{(25)2}} \cdot \frac{1}{T_1^{SR(125)1}} \quad (A12)$$

in which $\tau_c^{(25)1}$ is replaced by $\tau_c^{(125)1}$ since τ_c itself does not depend on the NMR frequency if other conditions are the same. Elimination of the term $T_1^{SR(125)1}$ from equation (A12) using equation (A6) followed by rearrangement gives equation (A13).

$$1/T_1^{CA(125)1} = \{1/T_1^{others(125)1} - (\tau_c^{(25)2}/\tau_c^{(125)1})(1/T_1^{others(25)2})\}/\{1 - (1/25)(\tau_c^{(25)2}/\tau_c^{(125)1})^2\} \quad (A13)$$

Therefore, T_1^{CA} at 125 MHz can be calculated from the data of T_1^{others} and τ_c obtained at 125 MHz and at 25 MHz. T_1^{SR} can then be calculated from equation (A5).

The 'iteration method' is more appropriate when the values of τ_c at the two NMR frequencies are not very different, or when T_1^{SR} is long and the spin–rotation mechanism does not contribute significantly. In this case, the correction term (*i.e.* the 2nd term) on the right-hand side of equation (A2) is small and $[T_1^{CA(125)}]_n$ will converge rather easily. When this is not the case, the 'τ_c correction method' will be efficient. However, in the latter method, T_1^{CA} and T_1^{SR} are assumed only as possible mechanisms for T_1^{others} and the τ_c and ν_0 dependences of T_1^{CA} and T_1^{SR} are utilized rigorously to eliminate the term of T_1^{SR}. Therefore, the latter method is expected to become more sensitive to the approximation (isotropic model) pertinent to equation (A4) of T_1^{SR}. In the present study the two methods gave consistent results, and no further comparisons were made.

References

1 (*a*) D. M. Quinn, *Biochem.*, 1982, **21**, 3548; (*b*) A. Doelle and T. Bluhm, *Prog. Nucl. Magn. Reson. Spectrosc.*, 1989, **21**, 175.

2 (*a*) W. R. Croasmun and R. M. K. Carlson in 'Two-Dimensional NMR Spectroscopy,' eds. W. R. Croasmun and R. M. K. Carlson; 'Methods in Stereochemical Analysis,' ed. A. P. Marchand, VCH Publishers, New York, 1987, vol. 9, ch. 7; (*b*) L. D. Hall and J. K. M. Sanders, *J. Am. Chem. Soc.*, 1980, **102**, 5703.

3 (*a*) J. R. Hanson and M. Siverns, *J. Chem. Soc., Perkin Trans. 1*, 1975, 1956; (*b*) H. J. Reich, M. Jautelat, M. T. Messe, F. J. Weigert, and J. D. Roberts, *J. Am. Chem. Soc.*, 1969, **91**, 7445; (*c*) S. Q. Rizvi and J. R. Williams, *J. Org. Chem.*, 1981, **46**, 1127.

4 H. Fujiwara, Y.-Z. Da, D. Zheng, Y. Takai, M. Sawada, and Y. Sasaki, *J. Chem. Soc., Perkin Trans. 2*, 1990, 97.

5 B. R. Appleman and B. P. Dailey, in 'Advances in Magnetic Resonance,' ed. J. S. Waugh, Academic Press, New York, 1974, vol. 7, p. 231.

6 H. Fujiwara, T. Takagi, M. Sugiura, and Y. Sasaki, *J. Chem. Soc., Perkin Trans. 2*, 1983, 903.

7 R. G. Sears, W. Siegfried, and D. E. Sands, *J. Chem. Eng. Data*, 1964, **9**, 261.

8 G. C. Levy, A. Kumar, and D. Wang, *J. Am. Chem. Soc.*, 1983, **105**, 7536.

9 H. Fujiwara, Y.-Z. Da, T. Takagi, and Y. Sasaki, *Chem. Pharm. Bull.*, 1989, **37**, 2887.

10 T. C. Farrar and E. D. Becker, 'Pulse and Fourier Transform NMR,' Academic Press, New York, 1971.

Paper 9/03748I
Received 4*th September* 1989
Accepted 10*th November* 1989