

## Non-Selective, Proton Spin-Lattice Relaxation Rates measured at 400 MHz: a Quantitative Determination of the Geometry of Diamagnetic Molecules in Solution

By LAURANCE D. HALL\* and KIM F. WONG

(*Department of Chemistry, University of British Columbia, Vancouver, B.C., Canada V6T 1W5*)

WILLIAM E. HULL

(*Bruker Analytische Messtechnik, GMBH, F512 Rheinsteten 1/Karlsruhe, W. Germany*)

and JOHN D. STEVENS

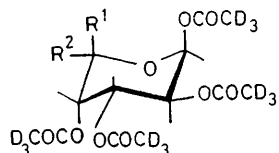
(*Department of Organic Chemistry, University of New South Wales, P.O. Box 1, Kensington, N.S.W., Australia 2033*)

**Summary** Initial slope, non-selective, spin-lattice relaxation rates have been determined at 400 MHz for 1,2,3,4-tetra-*O*-acetyl- $\beta$ -D-arabinopyranose (**1**) and for its 5,5-dideuterio derivative (**2**) and its two isomeric 5-deuterio derivatives (**3**) and (**4**); simple comparisons of these data give the specific interproton relaxation contributions arising *via* the dipole-dipole mechanism, from which the magnitudes of interproton distances can be calculated,

the values of which are in very close agreement with values obtained by neutron diffraction.

PREVIOUS reports<sup>1-4</sup> have alluded to the possibility of using proton spin-lattice relaxation rates ( $R_1$ -values) to measure the geometry of molecules in solution, and we now report the quantitative determination of the conformation of 1,2,3,4-tetra-*O*-trideuterioacetyl- $\beta$ -D-arabinopyranose (**1**)

(m.p. 99–100 °C)<sup>5</sup> using non-selective relaxation rates, with specific deuteration to identify<sup>3,6</sup> the magnitude of specific interproton relaxation contributions ( $\rho_{i,j}$ -values); the calculated interproton distances are in close agreement with those obtained for (1) in the solid state, using neutron diffraction.<sup>7†</sup>



$$(1) R^1 = H-5ax, R^2 = H-5eq$$

$$(2) R^1 = D-5ax, R^2 = D-5eq$$

$$(3) R^1 = H-5ax, R^2 = D-5eq$$

$$(4) R^1 = D-5ax, R^2 = H-5eq$$

The non-selective  $R_1$ -values for all protons of (1) of the 5,5-dideuterio derivative (2) (m.p. 101–102 °C), and of the isomeric 5-deuterio derivatives (3) and (4) (m.p. 99–100 °C) were determined with the conventional two-pulse sequence<sup>8</sup> and correct<sup>9</sup> application of the initial slope approximation,<sup>10</sup> see Table 1. Following a previously reported procedure<sup>2</sup>

TABLE 1. Non-selective spin-lattice relaxation rates<sup>a</sup> ( $10^{-3} s^{-1}$ ,  $\pm 5\%$ ) for compounds (1)–(4), measured at 400 MHz in degassed deuteriobenzene solutions

Compound	H-1	H-2	H-3	H-4	H-5ax	H-5eq
(1)	201	210	283	402	1119	973
(2)	174	187	191	170	—	—
(3)	181 <sup>b</sup>	203 <sup>b</sup>	264	288 <sup>b</sup>	310	—
(4)			211			

<sup>a</sup> Initial slope values determined between 0.001 and  $\tau$  s of the magnetisation recovery curve (semi-log plot), with  $\tau$  taken to: (1) 0.60, (2) 3.00, and (3) and (4), 1.40 s. The errors are taken as twice the largest standard error (2.5%) in the least-squares fit of the experimental curve. <sup>b</sup> Only average  $R_1$ -values for these resonances of the two isotopomers could be evaluated because not all the individual transitions were separately resolved

comparison of the initial slope, non-selective  $R_1$ -value for the H-1 resonances of compounds (3) and (4) [ $R_1^{H-1}$  (ns)  $181 \times 10^{-3} s^{-1}$ ] with the single-selective values [ $R_1^{H-1}$  (H-1)  $120 \times 10^{-3} s^{-1}$ ] giving a ratio of 1.51, served to

TABLE 2. Interproton distances (Å) for 1,2,3,4-tetra-*O*-acetyl- $\beta$ -D-arabinopyranose calculated from the specific, interproton dipole-dipole relaxation contributions and assuming that  $r_{5ax,5eq} = 1.80$  Å

Protons (i,j)	2,5ax	2,5eq	3,5ax	3,5eq	4,5ax	4,5eq	1,5eq	1,2	2,3	3,4	5ax, 5eq
$r_{i,j}$ from $R_1$ -values <sup>a</sup>	3.65 ( $\pm 0.38$ ) <sup>d</sup>		2.68 ( $\pm 0.07$ )	3.33 ( $\pm 0.32$ )	2.48 ( $\pm 0.04$ ) <sup>d</sup>	3.9 ( $\pm 1.6$ ) <sup>e</sup>	2.43 ( $\pm 0.07$ ) <sup>e</sup>	3.19 ( $\pm 0.41$ ) <sup>e</sup>	2.43 ( $\pm 0.04$ ) <sup>e</sup>	—	—
$r_{i,j}$ from neutron diffraction <sup>b</sup>	3.97	3.99	2.64	3.81	2.38	2.53	4.06	2.49	3.08	2.45	1.80
% Difference <sup>c</sup>	-8	-9	+2	-13	+4	-2	-4	-2	+4	-1	—

<sup>a</sup> Error calculations based on a 5% error in the measured  $R_1$ -values. <sup>b</sup>  $\pm 0.01$  Å. <sup>c</sup> Expressed as a 1% difference from the neutron diffraction value. <sup>d</sup> Only the average value could be determined for these protons because their resonances were not separately resolved for the isotopomers (3) and (4). <sup>e</sup> Calculations based on the assumption that  $\rho_{1,5ax} = \rho_{2,4} = \rho_{3,5eq}$ .

† Neutron diffraction measurements were made on 1,2,3,4-tetra-*O*-acetyl- $\beta$ -D-arabinopyranose.

§ Evidence that molecules (1)–(4) tumble isotropically in deuteriobenzene comes from the carbon-13  $R_1$ -values of the pyranose ring carbons of (1) which, at 1.0 M solution in deuteriobenzene at 35 °C are ( $10^{-3} s^{-1}$ ,  $\pm 6\%$ ): C-1, 1320; C-2, 1240; C-3, 1260; C-4, 1320; and C-5, 2630; all these carbons have 100% <sup>13</sup>C-(<sup>1</sup>H)nuclear Overhauser enhancement. Furthermore, the C-H bond lengths of these carbons are all  $1.10 \pm 0.01$  Å (see ref. 6).

confirm<sup>2</sup> that H-1 and, by inference, the other protons all relax exclusively *via* the dipole-dipole mechanism.<sup>11</sup> If the explicit formalism for this mechanism is known then the magnitude of a specific interproton relaxation contribution  $\rho_{R,H-j}$  between a receptor proton R and a donor proton H-j can be calculated from the non-selective relaxation rates of R in the normal (protio) molecule  $\{R_1^R(ns,H-j)\}$  as can that  $\{R_1^R(ns,D-j)\}$  of the compound in which the proton H-j has been replaced by a deuterium D-j; this relationship is summarized in equation (1), assuming the molecule is tumbling in the extreme narrowing region.

$$\rho_{R,H-j} = 0.6959[R_1^R(ns, H-j) - R_1^R(ns,D-j)] \quad (1)$$

When this relationship was used, comparison of the  $R_1$ -values of (1) with those of (2), (3), and (4) gave directly many of the interproton  $\rho$ -values pertinent to this study; other  $\rho$ -values were then estimated by indirect comparisons. From these  $\rho$ -values, the ratios of various interproton distances were calculated using the inverse sixth-power dependence implicit in the dipole-dipole relaxation mechanism.<sup>§</sup> The results of these calculations are summarized in Table 2, along with the interproton distances in Å obtained from a separate neutron diffraction study,<sup>7</sup> the calculated ratios of distances having been normalized on the assumption that  $r_{5ax,5eq} = 1.80$  Å which is the value obtained from the neutron diffraction study. That the agreement between the two sets of distances is so close suggests that (1) in deuteriobenzene favours the same <sup>1</sup>C<sub>4</sub>-chair conformation as it does in the solid state.

A further advantage of making these measurements at 400 MHz was that the deuterium-induced changes in the chemical shifts of many of the protons could be accurately measured. Besides making feasible the above conformational assignment, these have some intrinsic value in their own right, and their numerical values are summarized in Table 3. In every instance the introduction of deuterium at C-5 resulted in a shift to high-field; especially interesting is the finding that the shifts are additive, those of the dideuterio derivative (2) being essentially the same as the sum of those of the monodeuterio derivatives (3) and (4). That deuteration at H-5ax induces a bigger shift in H-3ax than does its counterpart at H-5eq implies a distance dependence which accords with the relative ordering of the other induced-shifts.

TABLE 3. Deuterium isotope-induced chemical shifts of proton-i,  $\Delta\delta_i$  ( $\pm 0.15$  Hz, or  $\pm 0.0004$  p.p.m.),<sup>a</sup> for the deuterio-compounds **(2)**, **(3)**, and **(4)** relative to those of the protio compound **(1)** measured at 400 MHz and 30 °C.

Compound	Deuterium isotope shifts											
	H-1		H-2		H-3		H-4		H-5ax		H-5eq	
	Hz	p.p.m.	Hz	p.p.m.	Hz	p.p.m.	Hz	p.p.m.	Hz	p.p.m.	Hz	p.p.m.
<b>(2)</b>	2.4	0.0060	2.7	0.0067	2.1	0.0052	4.4	0.0110	—	—	—	—
<b>(3)</b>	0.8	0.0020	1.0 <sup>b</sup>	0.0025 <sup>b</sup>	0.4	0.0010	2.2	0.0055	6.3	0.0157	—	—
<b>(4)</b>	1.4	0.0035	1.5 <sup>b</sup>	0.0037 <sup>b</sup>	1.5	0.0037	1.9	0.0047	—	—	5.8	0.0145

<sup>a</sup>  $\Delta\delta_i = \delta_i$  (protio) -  $\delta_i$  (deuterio); hence all the values given here correspond to high-field shifts. <sup>b</sup> May be interchanged.

Taken in conjunction with the accompanying communication,<sup>9</sup> this study suggests that proton spin-lattice relaxation studies can yield remarkably accurate information concerning the geometry in solution of diamagnetic molecules. Since the method is best applied to molecules having essentially first-order spectra it provides a useful complement to studies of molecules partially oriented by a nematic phase liquid crystal, for which high intrinsic molecular symmetry is a general prerequisite.

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