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Preliminary communication

A quantitative measurement of the aglycon-sugar, proton-relaxation contributions of glycosides, including disaccharides

JOFFRE M BERRY, LAURANCE D HALL, DOUGLAS W WELDER, and KIM F WONG

The Department of Chemistry, The University of British Columbia, Vancouver, British Columbia V6T 1W5 (Canada)

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A recent report[1] drew attention to the substantial difference (approximately two-fold) that exists between the spin–lattice relaxation-rates (R_1-values) of the anomeric protons of reducing (H-1) and nonreducing (H-1′) disaccharides in aqueous solution. It was suggested that this differential reflects the additional, relaxation contributions that H-1′ receives from the protons on the ring of the reducing moiety; this speculation received additional support from a study of ^{13}C relaxation-rates, and we now provide unequivocal, confirmatory evidence.

According to the formalism of the dipole–dipole relaxation-mechanism, which is given in abbreviated form in equation *1*, the relaxation contributions made by a deuterium nucleus should be ~6% of that of a proton nucleus located at the same position. Thus,

$$(R_1)_{D\rightarrow R} \propto I(I+1)\cdot(\gamma_D{}^2\cdot\gamma_D{}^2)\cdot\tau_c(D\rightarrow R)/(r_{D\rightarrow R})^6 \qquad (1)$$

comparison of the proton R_1-values of a normal sugar with those of its specifically deuterated analogs should provide a direct method[2,3] for identifying and measuring specific, inter-proton, relaxation contributions. We now illustrate how this approach may be used to evaluate the relaxation contributions that the protons on a sugar ring receive from the protons of an aglycon.

It can trivially be shown[2] that the *non-selective* (ns) R_1-value of the anomeric proton of a methyl glycoside, R_1 (ns, OCH_3), and that of its trideuteriomethyl analog, R_1 (ns, OCD_3), are related by the expression *2*,

$$\{R_1(\text{ns}, OCH_3) - R_1(\text{ns}, OCD_3)\} = 3\{0.937\cdot\rho_{H\text{-}1,OCH_3}\}/2, \qquad (2)$$

where $\rho_{H\text{-}1,OCH_3}$ is the relaxation contribution that the H-1 resonance receives from the methoxyl group, and is the value to be determined. A closely similar expression may be derived for data from a *single-selective*, relaxation experiment in which only the H-1 resonance is subjected to the 180°-pulse[4,5]; now, expression *3* applies.

TABLE I

SPIN–LATTICE RELAXATION-RATES[a] ($msec^{-1}$ ±5%) FOR THE ANOMERIC PROTONS OF METHYL D-GLUCOSIDES[b]

Compound	R_1 *(ns)*	$R_1(\widetilde{H\text{-}1})$	R_1 *(ns)*/$R_1(\widetilde{H\text{-}1})$
Methyl β-D-glucopyranoside (1)	640	430	1.49
Trideuteriomethyl β-D-glucopyranoside (2)	420	280	1.50
Methyl α-D-glucopyranoside (3)	330	220	1.50
Trideuteriomethyl α-D-glucopyranoside (4)	210	140	1.50

[a]Measured by using the three-pulse, inversion-recovery sequence[8] with a Varian XL-100 (15) spectrometer fitted with a Varian 620 L (16K) computer and a Linc Tape unit (model C0600); the R_1-values were calculated from the semi-log plots using a least-squares fit computer program. [b]0.1 Molar solutions in D_2O (99.7%) at 35°

$$\{R_1(\widetilde{H\text{-}1}, OCH_3) - R_1(\widetilde{H\text{-}1}, OCD_3)\} = \{0.937 \cdot \rho_{H\text{-}1,OCH_3}\} \quad (3)$$

The experimental data for the methyl D-glycopyranosides (1–4) are summarized in Table I, and the calculated values for $\rho_{H\text{-}1,OCH_3}$ are given in Table II. That the ratio $R_1(ns)/R_1(\widetilde{H\text{-}1})$ is 1.5 for every compound confirms[4] that the H-1 resonances all relax *via* the dipole–dipole mechanism, and that the non-selective R_1-values have been determined with the correct, initial-slope approximation[6]. It is noteworthy that the relaxation contribution received from the methoxyl protons by H-1 of the β anomer (1) is nearly twice that received by H-1 of the α anomer (3). This parallels the $^1H-\{^1H\}$ n.O.e. data reported by Lemieux[7], and indicates that the distribution of rotamers about the C-1–O-1 bond of a glycoside can be very dependent on the anomeric configuration.

The effectiveness of this approach in the disaccharide area is illustrated by the data for compound 5 and its 6,6-dideuterio analog (6); the R_1-values of the anomeric protons of these substances are summarized in Table III. It can be calculated that the anomeric proton of 5 receives 26% (480 $msec^{-1}$) of its relaxation from the protons attached to C-6.

Being mindful of the highly specific, antigenic properties of many cell-surface oligosaccharides, and of the importance of aminocyclitol antibiotics, we suggest that conformational studies of such compounds by use of the methods outlined here should be of great interest.

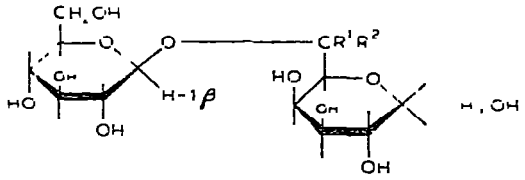
TABLE II

CALCULATED VALUES FOR THE RELAXATION CONTRIBUTIONS ($msec^{-1}$) THAT H-1 RECEIVES FROM THE METHOXYL GROUP ($\rho_{H\text{-}1,OCH_3}$)

Compound	*From* R_1 *(ns)*	*From* $R_1(\widetilde{H\text{-}1})$	*Average value*	$\frac{(\rho_{H\text{-}1,\beta OCH_3})_{av}}{(\rho_{H\text{-}1,\alpha OCH_3})_{av}}$
1	157	160	159	1.9
3	85	85	85	

TABLE III

NON-SELECTIVE SPIN–LATTICE RELAXATION-RATES ($msec^{-1}$ ±5%) FOR THE ANOMERIC PROTONS OF DISACCHARIDES[a]



5 $R^1 = R^2 = H$
6 $R^1 = R^2 = D$

Compound	*H-1 (reducing residue)*			*H 1' (nonreducing group)*	
	H-1α	*H-1β*	*Ratio H-1β/H-1α*	*H-1'β*	*Ratio H-1'β/H-1β*
5	450	1060	2 36	1820	1 72
6	450	950	2 11	1150	1.21

[a] 0 1 Molar solutions in D_2O (100.0%) at 35°

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