Preliminary communication

Concerning the tumbling motion of disaccharides in aqueous solution

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Information concerning the overall tumbling-motion of oligosaccharide molecules in solution, and also the relative, spatial rigidity of the individual sugar-rings, is clearly fundamental to any complete description of the solution geometry of these important derivatives. In principle, both of these classes of information should be available from the spin–lattice relaxation-rates of the individual, ring-carbon atoms, and we now add direct experimental evidence to prove that this is so in practice, at least for disaccharides and for their methyl glycosides; however, the method has an important limitation which is also documented here.

If the carbon atoms of a molecule that is tumbling isotropically in solution are relaxed exclusively *via* the dipole–dipole mechanism (which can be trivially determined by measurement of $^{13}C-^{1}H$ nuclear Overhauser enhancement-factors[1]), carbon atoms that bear the same number (N_H) of directly bonded, hydrogen substituents, each of equal C–H bond-length (r_{C-H}) will have identical R_1-values. This relationship[2] is embodied in the simplified formulation of the dipole–dipole mechanism given in equation *I*,

$$R_1 = N_H \cdot \hbar^2 \cdot \gamma_C^2 \cdot \gamma_H^2 \cdot r_{C-H}^{-6} \cdot \tau_c \qquad (I)$$

where τ_c is the motional correlation time of the C–H vector of the carbon nucleus under study.

This model appears to fit the data given in Table I for α,β-D-glucose (1) and for α,β-D-galactose (2). Thus, the near identity of the R_1-values of the carbon atoms of each sugar, including the C-4 resonance of D-galactose (*vide infra*), implies that all four systems tumble isotropically or almost so, and, for each sugar, the α and β anomers tumble at *approximately* the same rate. This appears to provide further experimental support[3] for the assumptions previously made[4] during studies of the proton relaxation-rates of free sugars; and, despite the data presented here for disaccharides, we believe this to be a reasonable conclusion for monosaccharides, as it is for their methyl glycosides[3].

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TABLE I

CARBON-13 SPIN–LATTICE RELAXATION-RATES (msec^{-1})^a AND ^{13}C–^{1}H NUCLEAR OVERHAUSER ENHANCEMENT-FACTORS^b (IN PARENTHESES, %) FOR SUGARS IN AQUEOUS SOLUTION (1 MOLAR)^c

Resonance — Compound^d	C1'	C2'	C3'	C4'	C5'	C6'	C1 a	C1 β	C2 a	C2 β	C3 a	C3 β	C4 a	C4 β	C5 a	C5 β	C6 a	C6 β	OCH$_3$
D-Glucose (1)							970 (99)	830 (99)	910 (97)	870 (99)	980 (99)	920 (102)	940 (98)	940 (98)	910 (97)	940 (100)	1640 (98)	1720 (98)	
D-Galactose (2)							810 (98)	870 (98)	830 (98)	860 (97)	910 (99)	900 (100)	920 (99)	1010 (100)	890 (99)	920 (97)	1600 (98)	1370 (100)	
Methyl β-lactoside (3)	4010 (100)	4030 (102)	4040 (100)	4900 (100)	4250 (98)	5670 (98)	3970 (100)		4130 (98)		4000 (100)		4180 (100)		3960 (98)		7600 (97)		1150 (100)
D-Lactose (4)	4120 (99)	4050 (97)	3920 (102)	4730 (100)	3970 (97)	5010 (100)	5180 (98)	3510 (102)	3920 (99)	4010 (100)	3620 (100)	3860 (97)	3720 (101)	4010 (100)	3650 (102)	3850 (97)	7810 (100)	7810 (100)	
Methyl β-cellobioside (5)	4430 (100)	4730 (100)	4270 (103)	4110 (100)	4390 (102)	8210 (100)	4250 (102)		4230 (99)		4210 (100)		4680 (100)		4300 (100)		9190 (100)		1290 (97)

^{a}Measured with a Varian CFT-20 (16K) spectrometer at 35°, using the spin inversion-recovery method^{10}; 12–15 data points were determined for each resonance, and the R_1-values were calculated from semilogarithmic plots of peak heights, using a weighted, least-squares-fit, computer program [estimated errors are ±50 msec^{-1} for 1 and 2, and ±200 msec^{-1} for 3, 4, and 5. ^{b}Measured by using the gated decoupling technique^9, and based on integrated areas. ^{c}In 99.7% D$_2$O. ^{d}Assignments were based on the literature, 1 (ref. 11), 2 (ref. 11), 3 (ref. 12), 4 (ref. 12), and 5 (ref. 12).

At first sight, the data for methyl β-lactoside (3), in which all of the carbon atoms that bear an axially oriented proton have closely similar R_1-values, also appear to accord with the isotropic-tumbling model. Furthermore, the fact that the carbon atoms of both rings have similar R_1-values implies that the two rings tumble at the same effective rate, from which it may be inferred that the molecule as a whole tumbles rigidly. *Although both of the latter deductions are probably correct*, the enhanced R_1-value of C-4' (which uniquely bears an equatorially oriented proton) provides clear evidence that the tumbling has some anisotropic character, with the principal axis of rotation being directed parallel to the C-4' to H-4' vector. By analogy with a similar type of motion for substituted benzene derivatives[5], we have fitted the data for 3 to the "tumbling, rigid ellipsoid" model of Woessner[6], in which it is assumed that the motional correlation times about any two axes $(\tau_\perp)$ are identical, but differ from that about the principal axis $(\tau_\parallel)$. Assuming that, for 3, the latter axis is perpendicular to the C—H_a vectors, that it lies in the general direction joining C-4', C-1', C-4, and C-1, and that all C—H bond-lengths are 110 pm, the Woessner model[6] gives $\tau_\perp = 2.5 \times 10^{-10}$ sec.rad^{-1} and $\tau_\parallel = 1.6 \times 10^{-10}$ sec.rad^{-1}, which suggest a small, but significant, anisotropic character for the molecular tumbling.

Interpretation of the data for lactose (4) presents a new problem, because each of the carbon resonances of the nonreducing ring is degenerate (corresponding to the α and β anomers at the reducing carbon atom), and, hence, those R_1-values cannot be treated directly. This leaves only the data for the ring-carbon atoms of the reducing ring of the α and β anomers, but, again, the enhanced R_1-value of the sole carbon atom (C-1α) bearing an equatorially oriented proton indicates that the motion of the reducing ring of the α anomer is anisotropic, and, by inference, that the molecule as a whole tumbles aniso- tropically. The near identity of the R_1-values of the remaining carbon atoms, all of which bear an axially oriented proton, suggests that the α and β anomers tumble at closely similar rates.

Interpretation of the R_1-values of the primary carbon atoms (C-6 and C-6') of these derivatives is additionally complicated[7] by the possibility of rotation about the C-5—C-6 bond, which can cause departures from the "N_H-rates" implicit in equation *1*. The data for the disaccharides reported here imply that there is little such rotation for C-6, but that C-6' apparently can have a greater degree of rotational freedom (see 3 and 5).

The foregoing observations have a number of important implications for the confidence that can be placed in ^{13}C R_1-values as a measure for isotropic tumbling in solution. First, these R_1-values only *reflect* anisotropic tumbling if at least one C—H vector subtends a substantially different angle to the principal axis of rotation. For example, the R_1-values of methyl β-cellobioside (5), which, by analogy with 3, must be tumbling anisotropically, are all closely similar, simply because all of the C—H bonds are axially disposed (for this reason, it may be that *all oligomers of β-D-glucopyranose may appear to be tumbling isotropically*). Second, even when the condition is fulfilled, ^{13}C R_1-values do not necessarily enable a precise definition to be made of the principal axis about which the tumbling occurs; indeed, as may be seen from Fig. 1, the calculated values "θ", based
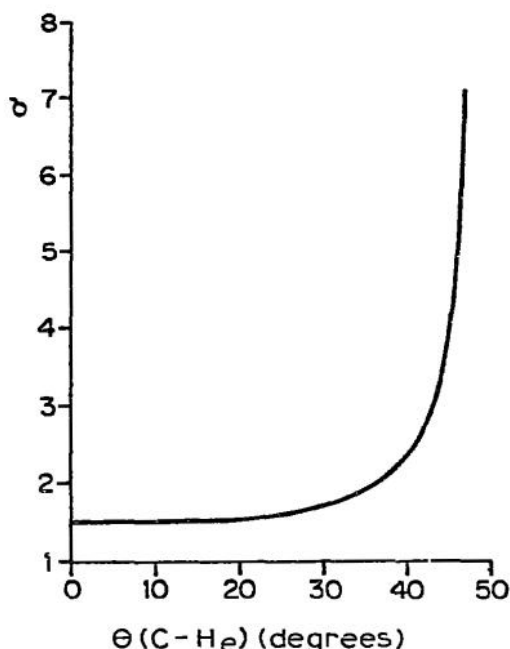
Fig. 1. Plot of σ ($\tau_{\perp}/\tau_{\parallel}$) *versus* $\theta(C-H_e)$, the angle subtended between the equatorially oriented C-4'-H-4' bond and the principal axis of rotation for methyl β-lactoside (3), based on the Woessner equation[6] with the assumption that $r_{C-H} \approx 110$ pm, that the sum of $\theta(C-H_e)$ and $\theta(C-H_a)$ is 109°28', and that $\tau_i = (6D_i)^{-1}$, where D_i is the rotational diffusion constant about the ith axis. [Note that σ is essentially indeterminate for $\theta > 45°$.

on the experimental data of 3, are essentially independent of θ for $0° \leqslant \theta \leqslant 30°$ Finally, and, perhaps, most important of all, the present study provides further[°] unequivocal evidence that the two-fold differential[9] between the R_1-values of H-1' and H-1 of disaccharides arises principally from inter-ring relaxation contributions, with anisotropic tumbling making only a minor contribution.

The conclusions given are also consistent with the data we have measured for maltose, gentiobiose, melibiose, and α,α-trehalose.

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