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A GENERAL SURVEY OF PROTON SPIN–LATTICE RELAXATION-RATES FOR PENTOPYRANOSE ACETATES

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ABSTRACT

A survey has been made of the spin–lattice relaxation-rates at 100 MHz of the ring protons of all eight of the D-pentopyranose tetra-acetates and of methyl α-D-xylopyranoside triacetate. Qualitative intercomparisons clearly demonstrate the diagnostic utility of these R_1-values for configurational assignments.

INTRODUCTION

The availability of Fourier-transform n.m.r. spectrometers in recent years has made it feasible to determine spin–lattice (longitudinal) relaxation-rates (R_1-values) of protons in reasonably complex organic molecules. Previous communications from the U.B.C. laboratory have presented values for 2-deoxy-2-halogeno-D-glucopyranose derivatives[1,2], for anomeric protons of some hexoses and pentoses in aqueous solution[3,4] and in the presence of gadolinium ions[5], for anomeric protons of some oligosaccharides and polysaccharides[6], for all of the ring protons of 1,6-anhydro-β-D-hexopyranose triacetates[7], and for various furanose derivatives[8]. Summaries of some of these studies have been presented[9,10].

It is apparent that more widespread application of proton R_1-values (or of their reciprocals, the spin–lattice relaxation-times, T_1-values) in structural and other studies requires the determination of reference data for a wide variety and a large number of compounds. We have chosen the pentopyranose acetates for this study because they are readily available, have been the subject of a number of n.m.r. studies, give reasonably well-dispersed spectra at 100 MHz (albeit not in a common solvent), and present us with some molecules that are essentially conformationally homogeneous and others that exist in solution as a mixture of at least two conformers. Emphasis has been deliberately restricted here to *qualitative* discussions of these data in order to stress the diagnostic utility of R_1-values for making simple, rapid configurational assignments. Readers who are interested in the detailed quantitation of

proton relaxation-rates or who are concerned with the apparently cavalier neglect of the many potential problems associated with relaxation studies of scalar-coupled spin systems are referred elsewhere[11-14].

EXPERIMENTAL

α-D-Xylopyranose tetra-acetate (**1**) and β-D-xylopyranose tetra-acetate (**2**) were prepared by the procedures of Hudson and Johnson[15].

α-D-Arabinopyranose tetra-acetate (**3**) was prepared by the procedure of Kuszmann and Vargha[16]. A mixture of D-arabinose (5 g), anhydrous sodium acetate (2 g), and acetic anhydride (40 mL) was stirred at room temperature (~28°) for 4 days. A small amount of solid remained in the mixture, which was then stirred at 50° for 3 h. Water (6 mL) was added, and the solution was cooled to room temperature, diluted with water (400 mL), and extracted with chloroform (4 × 25 mL). The combined extracts were washed with saturated, aqueous sodium hydrogencarbonate, filtered, and evaporated. The liquid product crystallized on standing and was then thinned with 10 mL of 95% ethanol followed by 7.5 mL of water. After much crystallization had taken place at room temperature, the mixture was kept at 2° overnight. The crystals were collected, washed with cold 50% ethanol, and dried to give crude **3** (6.045 g, 57%). This product was recrystallized by dissolving 1 part in 1 part of 95% ethanol, adding 1.5 parts of water, and warming the mixture to 50°. The clear solution was seeded and kept at 50°. After much crystallization had taken place, 0.5 part of water was added and the mixture allowed to cool slowly to room temperature overnight. The crystals were collected and washed with 20% aqueous alcohol, to give **3**, m.p. 96–97°; lit.[17], for the L enantiomorph, m.p. 97°. The product was shown to be free of the β isomer by g.l.c. using poly(ethyleneglycol adipate) as the stationary phase.

The procedure of Hudson and Dale[17] was used to prepare β-D-arabinopyranose tetra-acetate (**4**), m.p. 98–99°, $[\alpha]_D^{22}$ −146° (*c* 1, chloroform), $[\alpha]_D^{22}$ −157° (*c* 0.94, acetone); lit. m.p. 98–100°, $[\alpha]_D^{20}$ −147.8° (chloroform)[16]; m.p. 85°, $[\alpha]_D^{22}$ −155.6° (acetone)[18].

β-D-Ribopyranose tetra-acetate (**6**) was prepared[19] by treating crystalline D-ribose with acetic anhydride and pyridine at room temperature. Crystallization of the product from 95% ethanol gave **6**, m.p. 112–113°.

α-D-Ribopyranose tetra-acetate (**5**) was prepared[20] by treating **6** with a mixture of acetic anhydride–acetic acid (1 : 1) and zinc chloride. An ethanol solution of the equilibrated acetates gave **6** on seeding, and a second crop of **6** was obtained by concentrating the filtrate. The new filtrate gave crystalline **5** upon refrigeration. Recrystallization of crude **5** from 95% ethanol gave prisms, m.p. 80–82°, $[\alpha]_D^{22}$ +67° (*c* 1.77, chloroform); lit.[21] m.p. 75–78°, $[\alpha]_D$ +54° (chloroform).

α-D-Lyxopyranose tetra-acetate (**7**) was prepared by acetylation of D-lyxose with acetic anhydride–acetic acid (1 : 1) and zinc chloride. An ethanol solution of the products gave **7** on seeding, and recrystallization from ethanol gave prisms, m.p. 97–98°; lit.[22] m.p. 96° (low-melting modification).

TABLE I

PROTON SPIN-LATTICE RELAXATION-RATES (R_1-VALUES × 10^3, s^{-1}) FOR 0.1M SOLUTIONS OF PENTOPYRANOSE TETRA-ACETATES

Compound	*Solvent*	*Major conformer*	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-5'*[a]
1 α-D-Xylopyranose tetra-acetate	C_6D_6	$^4C_1$	167	286	154	263	833	833
2 β-D-Xylopyranose tetra-acetate	C_6D_6	$^4C_1$	244	192[b]		263	909	1110
2 β-D-Xylopyranose tetra-acetate	$(CD_3)_2CO:C_6D_6$ (1:4)	$^4C_1$	217	172	204	270	769	909
3 α-D-Arabinopyranose tetra-acetate	$CDCl_3:C_6D_6$ (1:1)	$^1C_4$	294	161	400	400	1000	1430
4 β-D-Arabinopyranose tetra-acetate	C_6D_6	$^1C_4$	200	278	294	357	1000	1110
5 α-D-Ribopyranose tetra-acetate	C_6D_6	$^4C_1$	213	370	313	370	714	714
6 β-D-Ribopyranose tetra-acetate	$(CD_3)_2CO$	$^1C_4 \rightleftharpoons {}^4C_1$	110	196	233	233	667	625
7 α-D-Lyxopyranose tetra-acetate	C_6D_6	$^4C_1$	161	270	286	244	1110	1000
8 β-D-Lyxopyranose tetra-acetate	C_6D_6	$^1C_4 \rightleftharpoons {}^4C_1$	303	303	303	238	909	909
9 Methyl α-D-xylopyranoside triacetate	C_6D_6	$^4C_1$	222	270	128	222	714	714

[a]The hydrogen on C-5 giving the higher-field signal is designated H-5'. [b]Signals for H-2 and H-3 could not be differentiated.

β-D-Lyxopyranose tetra-acetate (**8**) was prepared from β-D-lyxopyranose (2 g, Pfanstiehl Laboratories), which was added to a stirred mixture of pyridine (15 mL) and acetic anhydride (15 mL) cooled in an ice–water bath. The mixture was stirred for 6 h at 0° and then kept at 20° overnight. After the usual work-up, an ethanol solution of the crude acetates was seeded with **7** and the mixture was kept at 0° for 40 h, to give **7** (0.70 g). The residue left on evaporation of the solvent was chromatographed on 140 g of silicic acid (Mallinkrodt CC4, 100–200 mesh) with ethyl acetate–benzene (1:9). G.l.c. [poly(ethyleneglycol adipate) stationary phase] was used to monitor the elution (**8** is well separated from **7** and from the two furanose tetra-acetates on this stationary phase), and appropriate fractions were combined and evaporated to give **8** as a colourless liquid, $[\alpha]_D^{22}$ −80° (*c* 1, chloroform); lit.[22] $[\alpha]_D^{20}$ −83.4° (chloroform).

Solutions (0.1M) of the acetates in the solvents listed in Table I were degassed in n.m.r. tubes by using the freeze–pump–thaw procedure, and the tubes were sealed under vacuum. Relaxation rates were measured with a Varian XL-100 (15) spectrometer fitted with a Varian Fourier-transform system and a Varian 620L (16K) computer, using the data-acquisition and -processing methods described previously[4].

RESULTS AND DISCUSSION

The R_1-values obtained in this study are given in Table I. Although the same solvent has not been used for each compound, it is apparent that the R_1-values for the anomeric hydrogens (H-1) of the tetra-acetates **1**, **4**, **6**, and **7** are significantly lower than those for **2**, **3**, and **8**. In the former group, H-1 is equatorial in the chair conformation which preponderates in solution[18]; in the latter group, H-1 is axial in the preponderant chair conformation.

α-D-Xylopyranose tetra-acetate (**1**). This compound is essentially conformationally homogeneous in solution, the $^4C_1$ conformation being the major contributor[18]. As mentioned above, R_1 for H-1 is relatively low, in keeping with the fact that there is only one reasonably near neighbour, H-2. Comparing the values for H-2, H-3, and H-4, we see that the H-3 value is low compared to those for H-2 and H-4, consistent with the fact that H-3 is *trans*-diaxial to H-2 and H-4, and opposed to the axial H on C-5. The R_1-values for H-2 and H-4 are much higher, because each has a *gauche* vicinal neighbour as well as being mutually *syn*-diaxial. The two geminal hydrogens have the same, high relaxation-rates, reflecting their being geminal and one being gauche to H-4 and the other being axially opposed to H-3.

A comparison of the R_1-values of **1** with those of methyl α-D-xylopyranoside triacetate (**9**) shows that, although the values for H-2, H-3, H-4, H-5, and H-5′ in **9** average ~15% less than those of **1**, the R_1-value of H-1 in **9** is significantly higher than that of H-1 in **1**. This difference is consistent with the known tendency of an axial MeO-1 to assume an antiperiplanar orientation with respect to C-2, thereby placing the methoxyl hydrogen atoms in the neighbourhood of H-1; it is also consistent with the known detection of interglycosidic relaxation contributions[6,23].

β-D-*Arabinopyranose tetra-acetate* (**4**). This isomer is also essentially conformationally homogeneous in solution, existing as the $^1C_4$ conformer. As for **1**, R_1 for H-1 is relatively low, the result of H-1 having only one *gauche* neighbour. H-2 and H-3 have similar R_1-values, each having a *gauche* neighbour and being mutually trans-diaxial. H-3 additionally experiences an opposing axial H on C-5 and this should increase its R_1-value compared with that of H-2. For H-4, R_1 is higher than those for H-2 and H-3, as this hydrogen has three *gauche* neighbours. The geminal hydrogens on C-5 are both *gauche* to H-4, and H-5*a* is also axially opposed to H-3. It is interesting that the R_1-values for these two hydrogens are very similar, axial H-3 apparently having little effect upon axial H-5. This apparent lack of effect has been studied further by using suitably deuterated arabinose derivatives[14].

Of the remaining isomers, four exist in solution as mixtures of conformers in which one conformer preponderates to the extent of at least 75%. These are *β*-D-xylopyranose tetra-acetate (**2**) (major conformer, $^4C_1$), α-D-arabinopyranose tetra-acetate (**3**) ($^1C_4$), α-D-ribopyranose tetra-acetate (**5**) ($^4C_1$), and α-D-lyxopyranose tetra-acetate (**7**) ($^4C_1$).

α-D-*Ribopyranose tetra-acetate*. The R_1-values for the ring hydrogen atoms in this compound are consistent with their relative positions in a molecule in the $^4C_1$ conformation. The equatorial H-1, with only one *gauche* neighbour, has a lower R_1-value than the other hydrogens. Both H-2 and H-4 have two *gauche* neighbours and are *syn*-diaxial. Their R_1-values are the same, and are higher than the value for H-3, which has two *gauche* neighbours only. H-5 in this compound is the axial hydrogen on C-5 in the $^4C_1$ conformation (*i.e.*, H-5_S), and we would expect its R_1-value to be slightly lower than that for H-5′ (*i.e.*, H-5_R), as it has neither *gauche* nor opposed axial neighbours.

α-D-*Arabinopyranose tetra-acetate*. In this isomer, H-1 is axially oriented and is opposed by axial hydrogens on C-3 and C-5. Its R_1-value reflects its proximity to H-5′ (H-5_R). Axial H-2 has only *trans*-diaxial neighbouring hydrogens and its R_1-value is consequently low. H-3 and H-4 have three *gauche* neighbours and one *gauche* and two axially opposed hydrogens, respectively, and consequently their R_1-values are high. The environment of H-4 is similar to that of H-4 in **4**, and their relaxation rates are very similar. Of the two geminal hydrogens on C-5, the axially oriented one, H-5′ in the $^1C_4$ conformation (H-5_R) has two axially opposed hydrogens, one of which, H-1, is particularly close, in addition to *gauche*-oriented H-4 and geminal H-5. We would expect R_1 for this hydrogen to be significantly higher than that of H-5 (H-5_S), and this is observed.

β-D-*Xylopyranose tetra-acetate*. The relative R_1-values for the ring hydrogen atoms in this isomer are consistent with the axial orientation of all hydrogens except H-5. H-2 has the lowest R_1-value, consistent with its having only one axially opposed hydrogen as well as two *trans*-axial neighbours. H-3, with two axially opposed hydrogens as well as two *trans*-axial neighbours, has a slightly lower R_1-value than H-1, which also has two axially opposed hydrogens, one of which is the much closer

H-5′. The axial hydrogen on C-5, being axially opposed by both H-1 and H-3, has an R_1-value slightly higher than that of H-5, which has only one *gauche* neighbour.

α-D-Lyxopyranose tetra-acetate. The equatorial H-1 in this isomer has a low R_1-value, similar to that of **1**. Both H-2 and H-3 have at least two neighbouring hydrogens suitably located for effective relaxation. H-4, with only one *gauche* neighbour and two diaxial, vicinal hydrogens, has an R_1-value slightly lower than that of H-2 and H-3.

The remaining two members of the series, β-D-ribopyranose tetra-acetate (**6**) and β-D-lyxopyranose tetra-acetate (**8**), exist in solution as ~1:1 mixtures of the two chair forms. In **6**, R_1 for H-1 is uncommonly low and a comparison of the R_1-values for H-3 and H-4 with those of hydrogens *gauche* to two neighbouring hydrogens in other molecules, *e.g.*, H-2 in **5**, indicates that these values are also lower than might be expected. The geminal hydrogen atoms in this isomer also have relaxation rates lower than those in any of the other compounds studied. We note that deuterated acetone was the solvent used for **6** and that an earlier paper in this series[7] has shown that R_1-values for protons are dependent on the solvent used, principally because the overall tumbling rate of solute molecules is very dependent on the microviscosity of the solvent.

In **8**, the high R_1-value for H-1 is similar to those found for **2** and **3**, both of which are largely in the conformation in which H-1 is axial, as is H-1 in **8** in the $^4C_1$ conformation. The relative values of R_1 for H-2 and H-3 and for H-4 also require a significant contribution from the $^4C_1$ conformation, in which H-4 experiences only one *gauche* interaction. On the other hand, as H-2 and H-3 have the same R_1-value, H-3 does not experience the one *gauche* (H-2) and two opposed axial hydrogens (H-1 and H-5*a*) in all molecules. Clearly, the relative R_1-values for this compound require the occurrence of at least two ring conformations.

We have not attempted, at this stage, to relate quantitatively the R_1-values

TABLE II

INTER-HYDROGEN DISTANCES, *d* (IN Å), AND VALUE OF $1/d^6 \times 10^5$ FOR TETRAHYDROPYRAN (*d* VALUES ESTIMATED BY USING A BARTON MODEL)

		d	$1/d^6 \times 10^5$			d	$1/d^6 \times 10^5$
H-1*e*	H-1*a*	1.83	2663	H-1*a*	H-2*e*	2.59	331
	H-2*e*	2.56	355		H-2*a*	3.16	100
	H-2*a*	2.58	339		H-3*e*	3.88	29
	H-3*e*	4.44	13		H-3*a*	2.66	282
	H-3*a*	3.90	28		H-4*e*	4.22	18
	H-4*e*	5.04	6		H-4*a*	4.05	23
	H-4*a*	4.22	18		H-5*e*	3.75	36
	H-5*e*	4.30	16		H-5*a*	2.47	440
	H-5*a*	3.75	36				
H-2*e*	H-3*e*	2.59	331	H-2*a*	H-3*e*	2.57	347
	H-3*a*	2.59	331		H-3*a*	3.15	102
	H-4*e*	4.44	13		H-4*a*	2.61	316
	H-4*a*	3.84	31				

obtained with hydrogen–hydrogen distances. The treatment above has relied upon simple qualitative arguments based upon relative hydrogen–hydrogen distances within a tetrahydropyran model. Rather than use computer simulations, these distances (d, in Å) were obtained from a "Barton type" model of tetrahydropyran using regular C-C bonds (154 mm) and C-O bonds of 144 mm. Table II gives the various distances together with values of $(1/d^6) \times 10^5$, which give the relative contributions to relaxation by dipole–dipole interactions. These values show that there are four main groups of such interactions: (*a*) geminal [value of $(1/d^6) \times 10^5$, 2700], (*b*) H-1*a* and H-5*a* (440), (*c*) *gauche* and opposed axial (~340), and (*d*) vicinal *trans*-diaxial (100).

It is instructive to view these inter-proton distances graphically[24], since this shows, with particular clarity, the steepness of the inverse, sixth-power dependence implicit in the dipole–dipole relaxation mechanism.

The reflection of this dependence in the rather simplistic configurational comparisons described here augurs well for future applications of proton R_1-values in structural studies of carbohydrates.

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