Application of 220 MHz Nuclear Magnetic Resonance to the Solution of Stereochemical Problems: the Anomeric Configuration and Favoured Conformation of 1-Thio-α-L-arabinopyranose Tetra-acetate

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THE utility of n.m.r. spectroscopy for conformational and configurational studies of sugars and their derivatives has been well established.[1] Spectra of sugars and their derivatives are frequently very complex in the low-field region because there are several (4 or more) interacting protons, having oxygenated functions as nearest neighbours, that may have closely similar chemical environments. It is advantageous, therefore, to obtain the spectra at the highest attainable magnetic field. The field strength of the electromagnetic currently used in high-resolution n.m.r. spectrometers is 23·5 kG, corresponding to a radiofrequency of 100 MHz for protons.

In a separate report[2] on the n.m.r. spectra of acetylated 1-thioaldopyranoses, we have shown that the 100-MHz spectra of the derivatives having the β-D-*gluco*-, β-D-*galacto*-, β-D-*xylo*-, and β-D-*ribo*-configurations can be fully analyzed by comparing the differences in relative chemical shift of the ring protons when the spectra are measured in three solvents ([^{2}H]chloroform, [$^2H_6$]acetone, and [$^2H_6$]benzene). This technique failed to give an interpretable, first-order spectrum when it was applied to a 1-thio-L-arabinose tetra-acetate (I) which had been prepared from tri-*O*-acetyl-β-L-arabinopyranosyl bromide by treatment with potassium thiolacetate,[3] or with thiourea followed by deamidination and *S*-acetylation.[4] The acetate (I), $[\alpha]_D^{20}$ + 39·4° (*c* 2·2, chloroform), m.p. 39° (low-melting dimorph) and 82° (high-melting dimorph), is presumably pyranoid, but its anomeric configuration is not firmly established. The configuration at C-1 is not evident from the 100-MHz n.m.r. spectrum in [^{2}H]chloroform (see Figure 1) or either of the other two solvents. The use of a magnetic field considerably higher than 23·5 kG might, however, be expected to yield an interpretable spectrum.

With the advent of superconductive solenoids operating at liquid helium temperatures it is now possible to create magnetic fields greater than

50 kG with a field homogeneity of 1 part in 10^9, which would be suitable for high-resolution n.m.r. spectroscopy. The magnetic field strength of a currently available instrument[5] is 51·7 kG, corresponding to a radiofrequency of 220 MHz for protons. Determination of the anomeric configuration and favoured conformation of compound (I) provided us with an opportunity to demonstrate the application of 220 MHz n.m.r. spectroscopy for the characterization of sugar derivatives.

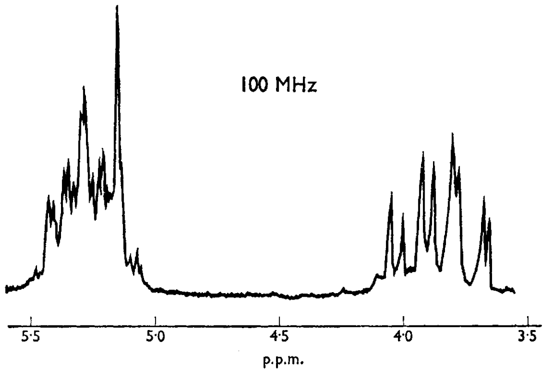

FIGURE 1. *The low-field portion of the n.m.r. spectrum of* 1-*thio*-α-L-*arabinopyranose tetra-acetate* (I) *in* [^{2}H]-*chloroform at* 100 MHz.

The complex pattern of low-field signals in the 100 MHz spectrum of (I) is clearly resolved at 220 MHz (Figure 2) into the individual signals of the four methine hydrogens, and the observed splittings establish that (I) is 1-thio-α-L-arabinopyranose tetra-acetate in the *C*1 conformation.

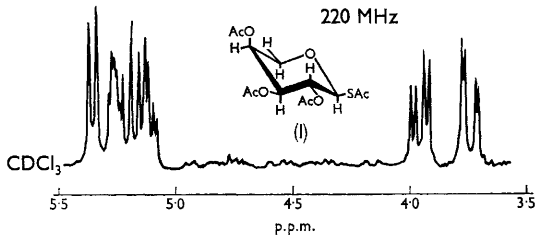

FIGURE 2. *The low-field portion of the n.m.r. spectrum of* 1-*thio*-α-L-*arabinopyranose tetra-acetate* (I) *in* [^{2}H]*chloroform at* 220 MHz.

The low-field doublet at 5·35 p.p.m. is assigned to H-1. It is coupled to H-2, whose resonance is observed at 5·19 p.p.m. as a triplet. The high degree of tilt in the resonance at 5·11 p.p.m. indicates that this proton is spin-coupled, with a large coupling constant, to another proton whose chemical shift is only slightly different; this perturbed pair of doublets can thus be assigned to H-3. Since the H-2 signal is almost a 1 : 2 : 1 triplet, H-1, H-2, and H-3 must be spin-coupled to another with approximately the same coupling constant, about 7·5 Hz. This value indicates that the three protons are axial, and therefore establishes the α-L-configuration and *C*1 conformation for (I). The smaller splittings in the signal at 5·11 p.p.m. indicate that H-3 is also coupled to H-4 where the orientation of the latter is equatorial. The signal for H-4 occurs at 5·26 p.p.m. as a multiplet; the other splittings in this signal are due to coupling with the methylene protons at C-5. The two pairs of doublets at 3·74 and 3·96 p.p.m. are assigned† to H-5 and H-5′, and the coupling constants $J_{4,5} = 2·3$ and $J_{4,5'} = 4·7$ Hz were derived by treating H-5, H-5′, and H-4 as an ABX system; first-order analysis gave essentially the same values (Table). The fact that these couplings are significantly different indicates that they are dependent, to a certain extent, on configuration (at C-4) as well as on conformation. In comparison with the hexose homomorph (1-thio-β-D-galactopyranose penta-acetate), which shows[2] diaxial couplings of the order of 10 Hz, the diaxial couplings of (I) (about 7·5 Hz) are somewhat smaller, suggesting that in (I) there may be an appreciable contribution from the less favoured, alternative (1*C*) chair conformation.

TABLE

Chemical shifts and coupling constants for 1-*thio*-α-L-*arabinopyranose tetra-acetate* (*I*) *in* [^{2}H]*chloroform*

	Chemical shifts in p.p.m.		
Proton	First-order values	Calculated values	Coupling constants in Hz
H-1	5·35	5·35	$J_{1,2} = 7·0$
H-2	5·19	5·19	$J_{2,3} = 8·0$
H-3	5·11	5·11	$J_{3,4} = 3·3$
H-4	5·26	5·26	$J_{4,5} = 2·3$
H-5	3·74	3·75	$J_{4,5} = 4·7$
H-5′	3·96	3·95	$J_{5,5'} = 12·5$

The first-order analysis of the four methine

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† In a normal six-membered ring the signals for axial hydrogen atoms resonate at higher field than their geminal, equatorial neighbours. This probably holds true in the case of (I), but since H-4 bisects the angle of the C-5 methylene group, the coupling data do not provide independent confirmation of the assignments, and so the C-5 proton resonances have not been specifically differentiated. Examples are known where axial hydrogen atoms resonate at lower field than their geminal, equatorial neighbours: C. V. Holland, D. Horton, and J. S. Jewell, *J. Org. Chem.*, 1967, **32**, 1818.

signals, whose range of chemical shifts is a mere 0·25 p.p.m. and which exhibit large vicinal couplings, clearly demonstrates that 220 MHz spectra will be of great value for establishing structure, configuration, and conformation in sugars and their derivatives.

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