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NMR SPECTRA AND CONFORMATION OF GLUCOSE AND SOME RELATED CARBOHYDRATES IN DIMETHYLSULPHOXIDE SOLUTION

B.Casu and M.Reggiani
Istituto Scientifico di Chimica e Biochimica G.Ronzoni, Milano
G.G.Gallo and A.Vigevani
Laboratori Ricerche Lepetit S.p.A., Milano

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In a recent paper(1) we reported NMR data of some pyranoid sugars in dimethylsulphoxide (DMSO) solution and we showed how the configuration of the reducing group of solid sugars can be readily determined from the proton resonance of the O_1H hydroxyl. In DMSO solution, where these sugars do not give mutarotation within a reasonable time, the resonances of the O_1H proton of the α-anomers fall, in fact, within the range 3.70 - 3.96 τ and those of the β-anomers in the range 3.40-3.58 τ, being the O_1H/C_1H coupling constants 4.0-4.5 cps and 6.0-7.0 cps respectively.

In the same paper a tentative assignment of the NMR signals of the non-reducing hydroxyl protons as well as of the C_1H proton was given for α-glucose. Spectra taken at 100 Mc/sec and spectra of deuterated products have more recently shown that some of the assignments reported for α-glucose are incorrect. The signal at τ 5.06, formerly believed to be a triplet and attributed to the primary O_6H, is actually due to the C_1H proton. In fact, the only resonance displayed by deu

TABLE I - Chemical shifts, τ (ppm) and coupling constants (cps, given in parentheses) of glucose and some related sugars in DMSO.

Sugars	O_1H doublet		C_1H pair of doublets		O_2H, O_3H, O_4H doublets	O_6H triplet
	equat.	axial	equat.	axial		
α-D-Glucose*		3.85(4.5)	5.08(4.5; 3.0)		5.28(5.0) 5.40(4.5) 5.60(6.5)	5.70(5.0)
β-D-Glucose*	3.50(6.5)			5.70(6.5; 6.5)	5.25(3.5) three OHs	5.58(5.5)
α-D-Galactose		3.95(4.5)	5.05(4.5; <3.0)		5.57(5.5) 5.75(4.5) two OHs	5.52(5.5)
α-D-Xylose*		3.90(4.5)	5.15(4.5; 3.5)		5.24(4.0) 5.36(3.5) 5.60(6.5)	
			doublet			
Methyl-α-D-glucoside			5.48(3.0)		5.22(5.0) 5.32(3.5) 5.40(6.5)	5.62(5.5)
Methyl-β-D-glucoside				5.95(7.0)	Unresolved peaks at 4.90 - 5.25	5.55(6.0)

The spectra were taken on a Varian A-60 Spectrometer at 60 Mc/sec, with TMS as internal reference. The spectra of the compounds labelled with an asterisk were also taken at 100 Mc/sec on a Varian HA-100 Spectrometer, by courtesy of Dr.A.Melera of Varian A.G., Zurich, to whom we are indebted.

terated α-glucose in DMSO is a doublet at approximately the same frequency of the original triplet-shaped signal. This signal of α-glucose very likely consists of a pair of doublets, whose inner components are very closed up and unresolved. A complete reassignment of the spectrum of α-glucose is given in Table I together with the assignments for β-glucose, α-galactose, α-xylose, methyl-α-glucoside and methyl-β-glucoside. Figs. 1 and 2 show the spectra at 100 Mc/sec of α- and β-glucose in DMSO.

Since chemical reactions on carbohydrates are now extensively performed in DMSO, it was of interest to investigate whether the conformation of the pyranose ring of sugars in this solvent could be determined from NMR spectra. Hydroxyl resonances do not appear to be useful in this respect. Their chemical shifts do not seem to depend only on the axial or equatorial orientation of the O-H bonds with respect to the ring. The degree of accessibility of the DMSO molecules to the different hydroxyl groups to give the strongest hydrogen bonds certainly affects the O-H resonances. Furthermore, the coupling constants of the O-H doublets could define only the dihedral angles between the O-H bonds and the adjacent C-H bonds, provided a relationship of the Karplus type(2) is applicable to $\underset{H}{C}-\underset{H}{O}$ systems. On the other hand, the conformation of the pyranose ring can be determined by calculating the C_1H/C_2H dihedral angle from the splitting of the C_1H signal, as it was made in D_2O solution(3,4,5). Due to the removal of the O-H absorptions and to the reduced multiplicity of the C_1H signal, more accurate measurements of the above splitting can be made on deuterated materials.

Deuteration has been performed either by adding a few drops of D_2O to the usual 0.5 ml NMR sample or by exchanging twice the solid sugar with D_2O and pumping off the aqueous

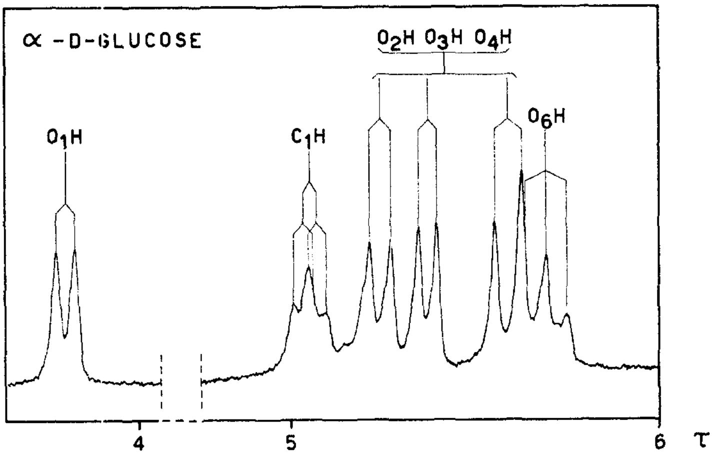

Fig. 1. 100 Mc/sec NMR spectrum of α-D-glucose in DMSO.

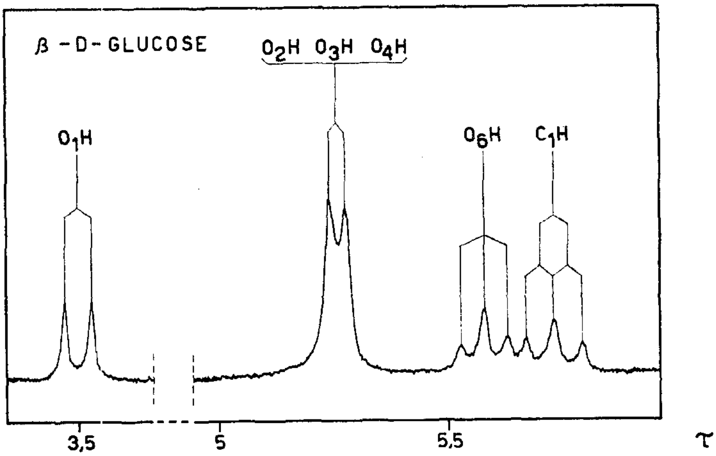

Fig. 2. 100 Mc/sec NMR spectrum of β-D-glucose in DMSO.

solvent before adding DMSO. When using the first procedure, the hydroxyl resonances may not completely disappear. Their intensity is, however, sufficiently reduced to permit identification of the C_1H doublet. Only the signal of the original anomer is generally shown by this technique, since mutarotation does not occur within the time of measurement, but the C_1H signals may shift slightly downfield when more than 10% D_2O is added to DMSO. By the second procedure the reducing sugars mutarotate during the deuteration and consequently the signals of both anomers are shown undisplaced.

The chemical shifts and the coupling constants of the C_1H resonances of deuterated sugars in DMSO solution are given in Table II and compared with values in D_2O solution. C_1H protons absorb in DMSO at fields slightly higher (about 0.3 ppm) than in D_2O. β-anomers absorb at fields higher than α-anomers, as already observed in D_2O(8). As far as the splitting of the C_1H signals is concerned, the C_1H/C_2H coupling constants show values well comparable with those in D_2O solution. The C_1H/C_2H dihedral angles of the investigated products in DMSO solution should be therefore the same or nearly the same as those calculated using a modified Karplus equation(3,4,5) from data in D_2O. The values of coupling constants obtained in DMSO are those expected for pyranose rings substantially in the chair "C 1" conformation.

In DMSO solution we have investigated also some α-1,4-linked polyglucoses, in particular cyclodextrins and amylose, for which a non-chair conformation of the pyranose units has been proposed(9,10). The use of DMSO appeared helpful in the case of β-cyclodextrin and amylose, because they are sparingly soluble in D_2O. The chemical shift of the C_1H is 4.88 τ for amylose, 5.19 τ for α-cyclodextrin and 5.15 τ for β-cy-

TABLE II - Chemical shifts, τ values (ppm) and coupling constants, $J_{H_1H_2}$ (cps) of the C_1H resonances of some deuterated sugars in DMSO and in D_2O.

Sugars	Equatorial				Axial			
	DMSO		D_2O		DMSO		D_2O	
	τ	J	τ	J	τ	J	τ	J
α-D-Glucose	5.06	3.0	4.78 4.78 4.80 4.84	2.4^{a} 3.0^{b} 3.2^{c} 3.0^{d}				
β-D-Glucose					5.68	6.5	5.36 5.37 5.42 5.42	7.5^{a} 7.4^{b} 6.8^{c} 7.4^{d}
α-D-Galactose	5.05	<3.0	4.77 4.74	2.7^{b} 1.8^{d}				
α-D-Xylose	5.14	3.5	4.82 4.83	2.2^{a} 2.6^{d}				
Methyl-α-D-glucoside	5.45	3.0	5.21 5.25	3.0^{b} 3.3^{c}				
Methyl-β-D-glucoside					5.95	7.0	5.54 5.62 5.65	7.7^{e} 7.4^{b} 7.4^{c}

a) data from reference 3; b) data from reference 6; c) data from reference 5; d) data from reference 7; e) data from reference 4.

clodextrin. These values fall within the "equatorial range". The splitting of the above peaks cannot be precisely measured because of the poor resolution. However, the peak shape suggests coupling constants of about 3 cps and therefore C_1H/C_2H dihedral angles of about 60° are derived. These data are consistent with a chair "C 1" conformation of the glucose units.

A further account of NMR conformational investigations on dextrins and amylose, including studies of hydroxyl resonances, will be given elsewhere.

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