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Note

Carbon-13 n.m.r. spectroscopy of *O*-(2-hydroxyethyl) derivatives of D-glucose

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Hydroxyalkyl derivatization of polysaccharides is a common method of improving the water solubility of these materials. The resulting polysaccharide ethers are copolymers of many monomers. Most analytical methods for the determination of the monomer composition of these complex polymers involve their hydrolytic (or methanolytic) degradation. The 2-hydroxyethyl ethers of cellulose[1–3] and starch[4] and the 2-hydroxypropyl ethers of cellulose[5,6] and guar[7] have been treated in this way. In our laboratory and elsewhere[5,6], carbon-13 n.m.r. spectroscopy has then been the method of choice for the analysis of the mixtures obtained by the hydrolysis[8,9] or methanolysis[9,10] of cellulose ethers. The resonance assignments were made with the help of data on separated or specifically synthesized monosaccharides. In an extension of this approach, this Note reports the assignments for the *O*-(2-hydroxyethyl) derivatives of D-glucopyranose.

Although in the case of *O*-(2-hydroxyethyl)cellulose it was found advantageous to reduce the hydrolysis products to the corresponding glucitols[3], it is possible that with starch or cyclodextrin derivatives of relatively low degree of substitution, reduction may be superfluous. One of the problems with hydroxyalkyl derivatives is the nonstoichiometric formation of cyclic acetals (inner glucosides) upon acid hydrolysis when a single 2-hydroxyalkyl group is attached at O-2 of D-glucose. This has been observed with *O*-(2-hydroxypropyl)cellulose[5], and can be expected with *O*-(2-hydroxyethyl) derivatives of glucans[11] and probably of other polysaccharides as well. The cyclic acetals of 2-*O*-(2-hydroxyethyl)-D-glucose are included in this study.

RESULTS AND DISCUSSION

Table I summarizes the ^{13}C chemical shift data for the 2-hydroxyethyl derivatives of D-glucose investigated in this work. Three independent and complementary criteria were used to obtain the assignments. (*a*) General expectations regarding

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TABLE I

CARBON-13 CHEMICAL SHIFTS OF *O*-(2-HYDROXYETHYL)-D-GLUCOSES AND RELATED DERIVATIVES IN Me$_2$SO-d_6

Compound	*Chemical shifts (p.p.m. from TSP[a])*							
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-2'*	*C-1'*
D-*Glucopyranose*								
α	93.83	73.99	74.70	72.21	73.58	62.84		
β	98.50	76.45	78.38	71.91	78.35	62.84		
*2-O-(2-Hydroxyethyl)-*D*-glucopyranose*								
α	91.40	82.33	73.47	71.97	73.33	62.58	62.11	73.10
β	97.88	85.08	77.42	71.70	78.18	62.58	62.11	74.96
*3-O-(2-Hydroxyethyl)-*D*-glucopyranose*								
α	93.73	73.53	84.18	71.48	73.48	62.58	62.46	75.11
β	98.32	76.04	87.48	71.33	78.03	62.58	62.41	75.22
*6-O-(2-Hydroxyethyl)-*D*-glucopyranose*								
α	93.80	73.88	74.71	72.22	72.58	72.42	61.84	74.19
β	98.48	76.39	78.30	71.98	76.83	72.44	61.84	74.24
*1,2-O-Ethylene-*D*-glucopyranose*								
α	95.75	76.26	71.42	68.33	76.41	64.26	59.43[b]	67.30[b]
β	99.68	81.24	74.83	72.01	80.13	62.40	66.92[c]	67.20[c]
*1,2-O-Ethylene-*D*-glucofuranose*								
α	99.30	77.78	75.17	82.63	70.70	65.36	60.42[d]	64.75[d]

[a] TSP = sodium 2,2,3,3-tetradeuterio-4,4-dimethyl-4-silapentanoate. [b–d] Assignments are interchangeable.

substituent effects on ^{13}C chemical shifts of monosaccharides[12,13] were substantially augmented by the results from our previous work on *O*-methyl[9], *O*-ethyl[10], and *O*-(carboxymethyl)[8] derivatives of D-glucose. (*b*) Methine and methylene carbons were differentiated by attached-proton-test experiments[14,15], which invert the phases of resonances of carbons bearing an even number of protons with respect to those bearing an odd number. (*c*) In many cases, unequivocal assignments were obtained from the isotopic multiplets in the spectra of materials having partially deuterated hydroxyls[16]. These multiplets are due to upfield deuterium isotope effects on ^{13}C chemical shifts: 0.09–0.12 p.p.m. for directly bonded hydroxyls (the β effect) and 0.07 p.p.m. or less for hydroxyls on vicinal carbons (the γ effect).

An example of the deuterium effects is given in Fig. 1, which shows the isotopic multiplets in the ^{13}C-n.m.r. spectrum of 1,2-*O*-ethylene-α-D-glucofuranose. Large spacings due to the β effect are seen on the resonances of carbons 3, 5, and 6. In addition, the resonances of C-5 and C-6 exhibit the smaller spacings of the γ effect. The resonance of C-4 is a triplet with small spacings due to the γ effects of the hydroxyls on carbons 3 and 5, whereas the signal for C-2 is only a

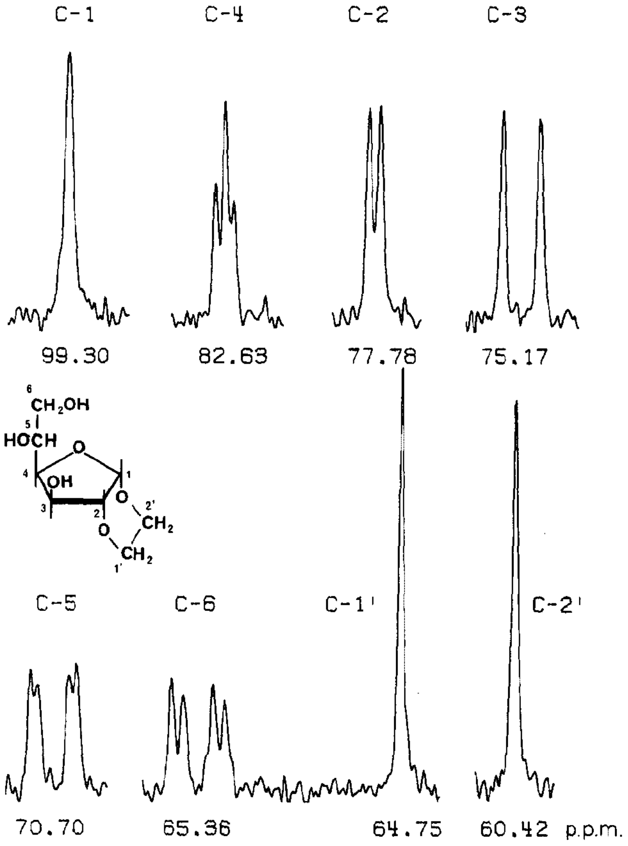

Fig. 1. Isotopic multiplets in the ^{13}C-n.m.r. spectrum of 1,2-*O*-ethylene-α-D-glucofuranose in an Me_2SO-d_6 solution to which a calculated amount of D_2O was added to give an OH/OD ratio of ~1. The listed chemical shift values are of the protio form.

doublet since it has only one hydroxyl-bearing neighbor (C-3). Similarly, the closely spaced resonances of C-2 and C-5 of 1,2-*O*-ethylene-α-D-glucopyranose were readily differentiated since the former appeared as a doublet due to one hydroxylated neighbor (C-3), whereas the latter was a triplet due to two hydroxylated neighbors (C-4 and C-6). However, ambiguity remained regarding the carbons of the ethylene moiety of the cyclic acetals. The assignments for the 3- and 6-*O*-(2-hydroxyethyl) derivatives are in general agreement with those previously made for aqueous solutions by Parfondry and Perlin[17].

The effects of *O*-(2-hydroxyethyl) substitution on ^{13}C chemical shifts are summarized in Table II. They are similar in magnitude to the effects of carboxymethyl[8] or ethyl[10] substitutions. Previous work with methyl[9], ethyl[10], and carboxymethyl[8] derivatives has shown that substituent effects on the ^{13}C chemical shifts of D-glucopyranose are additive to within very narrow limits. Thus, the data in Table

TABLE II

EFFECTS OF *O*-(2-HYDROXYETHYL) SUBSTITUTION ON THE CARBON-13 CHEMICAL SHIFTS OF D-GLUCOSE

Position substituted[a]	*Chemical shift difference (p.p.m.)*					
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*
2 α	−2.43	8.44	−1.23	−0.24	−0.25	−0.26
2 β	−0.63	8.63	−0.96	−0.21	−0.17	−0.26
3 α	−0.10	−0.36	9.48	−0.73	−0.10	−0.26
3 β	−0.18	−0.41	9.10	−0.58	−0.32	−0.26
6 α	−0.03	−0.01	−0.01	0.01	−1.00	9.58
6 β	−0.02	−0.06	−0.08	0.07	−1.52	9.60

[a] 2 α indicates substitution on O-2 of the α anomer, etc.

II could serve for the calculation of the chemical shifts of multiply-substituted *O*-(2-hydroxyethyl) derivatives of D-glucose that may be among the hydrolysis products of the hydroxyethyl ethers of starch and cyclodextrins, as well as that of cellulose.

EXPERIMENTAL

The *O*-(2-hydroxyethyl) derivatives, including the bicyclic compounds but excluding 2-*O*-(2-hydroxyethyl)-D-glucopyranose, were obtained from V-LABS, Covington, Louisiana. They were syrupy anomeric mixtures, except for 1,2-*O*-ethylene-α-D-glucofuranose, which was crystalline. An aqueous solution of the furanose was treated with sulfuric acid, the acid neutralized with barium carbonate, the solution filtered, and the filtrate evaporated on a rotary evaporator. The result, as inferred from the ^{13}C-n.m.r. spectrum, was an anomeric mixture of 2-*O*-(2-hydroxyethyl)-D-glucopyranoses containing very small amounts of the cyclic acetals. ^{13}C-N.m.r. spectra were recorded at 90.56 MHz as previously described[8,9].

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