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Note

Fourier-transform ^{13}C nuclear magnetic resonance spectra of D-glucose 3- and 6-sulfates

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Substituent effects of the methyl group in some methylated inositols[1] and hexopyranosides[2] have been reported by Dorman *et al.* There are similar reports on substituent effects of the methyl group in methyl glycosides[3,4], and the ^{13}C chemical shifts of some sugar acetates[5] and oligosaccharides[5,6] have been discussed from this viewpoint. Concerning substituent effects of the *O*-sulfate group in carbohydrate sulfates, however, only limited data[7] have been reported, dealing with heparin and its degradation products. In view of this paucity of data, the Fourier-transform ^{13}C n.m.r. spectra of two simple carbohydrate sulfates, D-glucose 3- and 6-sulfates, were examined and compared with the spectrum of the parent sugar, D-glucose. Study of substituent effects of the sulfate group on ^{13}C chemical shifts can be expected to be useful for placement of sulfate groups in carbohydrate sulfates of biochemical and pharmacological interest.

Table I gives ^{13}C shift-data for sulfuric esters of *n*-propanol, cyclopentanol, and cyclohexanol. These esters may be regarded as model compounds for aliphatic primary and secondary sulfates, whose ^{13}C chemical shifts are arbitrarily assignable simply by comparing their spectra with those of the parent alcohols. As seen from Table I, there are marked downfield shifts (8–11 p.p.m.) of α-carbon atoms and moderate upfield shifts (2–3 p.p.m.) of β-carbon atoms, whereas no appreciable shifts are observed for γ- and δ-carbon atoms. The shift-directions of α- and β-carbon

TABLE I

^{13}C CHEMICAL SHIFTS[a] AND SUBSTITUENT SHIFTS (*Δ*) OF SULFURIC ESTERS OF SIMPLE ALCOHOLS

	n-Propyl			*Cyclopentyl*			*Cyclohexyl*		
	Alcohol	*Sulfate*	*Δ*	*Alcohol*	*Sulfate*	*Δ*	*Alcohol*	*Sulfate*	*Δ*
α-Carbon	128.8	120.4	−8.4	118.9	107.9	−11.0	122.4	111.7	−10.7
β-Carbon	166.7	169.5	+2.8	156.9	158.9	+2.0	156.5	159.5	+3.0
γ-Carbon	182.5	182.0	−0.5	168.6	168.6	0.0	167.4	168.3	+0.9
δ-Carbon	—	—	—	—	—	—	166.0	166.9	+0.9

[a]Chemical shifts are expressed in p.p.m. upfield from CS_2.

signals upon *O*-sulfation were the same as those produced by methylation, and the shift-values are also of approximately the same magnitude.

These criteria allowed straightforward assignment of ^{13}C signals of D-glucose 3- and 6-sulfates (see Fig. 1). The Fourier-transform spectrum of D-glucose was practically the same as its continuous-wave spectrum (which has been completely assigned[2,4,8]), except for a newly observable narrow separation of the C-3β and C-5β signals. Comparison of the spectrum of the 3-sulfate with that of D-glucose, reveals that the signals of C-1β, C-1α, and the C-6 pair of D-glucose correspond directly with the signals *a*, *b*, and *j*, respectively, of the 3-sulfate. The most noteworthy change is the appearance of a new pair of signals, *c* and *d*, between the signals of C-1α and the adjacent signal (C-3β or C-5β) of D-glucose. The signals *c* and *d* were unambiguously assigned to C-3 of the anomeric 3-sulfates having downfield shifts of 9.5 and 8.5 p.p.m. The signal at lower field (*c*) was firmly assigned to the β-anomer and that at higher field (*d*) to the α-anomer, as the anomeric ratio was equal to that in the C-1 pair of signals (*a* = C-1β and *b* = C-1α). The peak *i* could be assigned to the overlapping C-4 signals, displaying an upfield shift of 2.2 p.p.m; this shift value is reasonable for the β-carbon atoms β-disposed to the sulfate group. Of four signals left unassigned, the signal *h* of the 3-sulfate (absent in the spectrum of D-glucose) is evidently, from its low intensity, a signal of the α-anomer. The signal *f*, which from its high intensity can be assigned to the β-anomer, has the same shift as C-3α of D-glucose, but is not C-3α, as the C-3α signal of the 3-sulfate is the signal *d*. On the

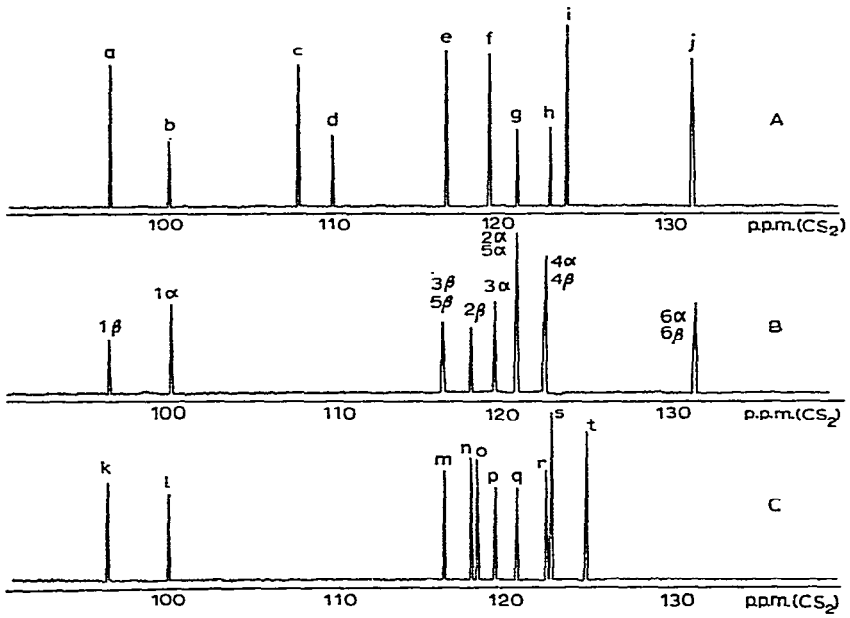

Fig. 1. Proton-decoupled, natural-abundance ^{13}C n.m.r. spectra of freshly dissolved D-glucose 3-sulfate (A), D-glucose (B), and D-glucose 6-sulfate (C) in D_2O.

other hand, signals *e* and *g* for the 3-sulfate were not new but exhibited nearly the same chemical shifts as the signal of C-3β or C-5β and the overlapped signal of C-2α+C-5α, respectively, in the spectrum of D-glucose. As the substituent effect of the sulfate group on the β-carbon atom (C-2) is greater than on the γ-carbon atom (C-5), and as the shift-direction of the β-carbon is toward high field (on the basis of the results presented in Table I), the signals *f* and *h* were assigned to C-2β and C-2α, respectively. Accordingly, signals *e* and *g* were considered to be the C-5 pair and, from their intensities, were assigned to C-5β and C-5α, respectively.

In the spectrum of the 6-sulfate, the C-1, C-2, C-3, and C-4 pairs were found without appreciable shifts from those of D-glucose in the signals *k* (C-1β), *l* (C-1α), *m* (C-3β), *n* or *o* (C-2β), *p* (C-3α), *q* (C-2α), and *s* (an overlapped signal of the C-4 pair). Prominent downfield shifts of the α-carbon atoms (the C-6 pair) are evident, their resonances appearing as the overlapping signal *t* displaying substituent shifts of −6.5 (α-anomer) and −6.6 p.p.m. (β-anomer). The β-carbon atoms (the C-5 pair) gave rise to the signals *n* or *o* (C-5β), and *r* (C-5α), which were shifted by 1.6-2.0 and 1.7 p.p.m., respectively, toward high field from the corresponding C-5 carbon atoms in D-glucose. The assignment of the closely neighboring signals *n* and *o* was uncertain, although it seemed more probable that C-2β should correspond to *n* (substituent shift, 0.0 p.p.m.) rather than to *o* (substituent shift, +0.3 p.p.m.). Tentative assignments and substituent shifts of carbon atoms in D-glucose 3- and 6-sulfates are shown in Table II.

TABLE II

TENTATIVE ASSIGNMENTS[a] AND SUBSTITUENT SHIFTS (Δ) FOR D-GLUCOSE 3- AND 6-SULFATES

	D-Glucose		*D-Glucose 3-sulfate*				*D-Glucose 6-sulfate*			
	α-Anomer	*β-Anomer*	*α-Anomer*	*Δ*	*β-Anomer*	*Δ*	*α-Anomer*	*Δ*	*β-Anomer*	*Δ*
C-1	99.6	96.1	99.9	0.0	96.3	+0.2	99.7	−0.2	95.9	−0.2
C-2	120.6	117.8	121.7	+1.1	119.0	+1.2	120.5	−0.1	117.8	0.0
C-3	119.2	116.1 or 116.2	109.7	−9.5	107.6	−8.5 or −8.6	119.2	0.0	116.3	+0.2 or +0.1
C-4	122.3	122.3	124.5	+2.2	124.5	+2.2	122.6	+0.3	122.6	+0.3
C-5	120.6	116.2 or 116.1	120.7	+0.1	116.5	+0.3 or +0.4	122.3	+1.7	118.1	+1.9 or +2.0
C-6	131.2	131.3	131.3	+0.1	131.3	0.0	124.7	−6.5	124.7	−6.6

[a]Chemical shifts are expressed in p.p.m. upfield from CS_2.

EXPERIMENTAL

Materials. — The sodium salt of D-glucose 3-sulfate was synthesized according to the literature[9]. The sodium salt of D-glucose 6-sulfate was prepared by the phenyl-sulfuryl chloride method[10] previously described. The sulfuric esters of *n*-propanol, cyclopentanol, and cyclohexanol were prepared by the pyridine–sulfur trioxide method, and their sodium salts were recrystallized several times from ethanol.

^{13}C n.m.r. spectra. — Natural abundance ^{13}C n.m.r. spectra were observed at 25.1 MHz with a JEOL JNM-PFT-100 spectrometer with D_2O internal lock. All of the spectra were proton-decoupled by noise-modulation and obtained by accumulating 32 times (*n*-propanol, cyclopentanol, and cyclohexanol) and 2000 times (other examples). The neat samples (*n*-propanol, cyclopentanol, and cyclohexanol) and 40% D_2O solutions (other samples) were measured at room temperature, and chemical shifts are expressed in p.p.m. upfield from a CS_2 standard. The substituent shifts of the sulfuric esters of *n*-propanol, cyclopentanol, and cyclohexanol were calculated without minor corrections for solvent effects.

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