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THE ^{13}C-N.M.R. SPECTRA OF METHYL (METHYL *O*-METHYL-α-D-GLUCOPYRANOSID)URONATES

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ABSTRACT

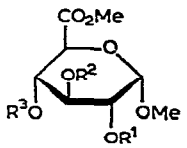
^{13}C-N.m.r. spectra of all of the methyl ethers of methyl (methyl α-D-glucopyranosid)uronate have been interpreted. The data can be used as an aid in the analysis of ^{13}C-n.m.r. spectra of α-D-glucopyranosyluronic acid-containing polysaccharides.

INTRODUCTION

Correct assignment of the lines in ^{13}C-n.m.r. spectra of polysaccharides is difficult, even when the structure of the polymer has been established by independent chemical methods. Comparison with the spectra of properly chosen model compounds is used frequently to solve this problem. Monosaccharides and methyl glycosides are readily available model compounds, but their spectra differ significantly from those of the corresponding glycosyl units in polysaccharides, owing to the effects of glycosidic bonding. Many authors have noted that the spectra of glycosyl units in oligo- or poly-saccharides are similar to those of the corresponding, monomeric, *O*-methylated methyl glycosides[1]. Therefore, methylated sugars are considered to be the most suitable models for the interpretation of the spectra of polysaccharides. In this connection, the measurement and interpretation of ^{13}C-n.m.r. spectra of *O*-methyl derivatives of methyl (methyl α-D-glucopyranosid)uronate is an important prerequisite for the application of ^{13}C-n.m.r. spectroscopy in structural studies of polyuronides containing α-D-glucuronic acid residues. Such data can also be applied for identification of methyl ethers of D-glucuronic acid by means of ^{13}C-n.m.r. spectroscopy.

RESULTS AND DISCUSSION

The ^{13}C-n.m.r. spectral characteristics of compounds **1–11** are recorded in Table I. The regularities in the effect of substitution, epimerization, and/or anomeriza-



1 $R^1 = R^2 = R^3 = H$
2 $R^1 = Me; R^2 = R^3 = H$
3 $R^1 = R^3 = H; R^2 = Me$
4 $R^1 = R^2 = H; R^3 = Me$
5 $R^1 = R^2 = Me; R^3 = H$
6 $R^1 = R^3 = Me; R^2 = H$
7 $R^1 = H; = R^2 = R^3 = Me$
8 $R^1 = R^2 = R^3 = Me$
9 $R^1 = R^2 = Me; R^3 = Ac$
10 $R^1 = R^3 = Me; R^2 = Ac$
11 $R^2 = R^3 = Me; R^1 = Ac$

tion on chemical shifts are commonly used[1] for ^{13}C-n.m.r. signal assignments. It has been established that *O*-methylation results in a downfield shift (7–11 p.p.m.) of the α-carbon signal (α-effect); the similar β-effect depends on the configuration of the β-carbon and equals[2–4] 1–2 and 4–5 p.p.m. upfield for a β-carbon with an equatorial and axial substituent, respectively. Chemical shifts of the γ-carbons are insignificantly affected by *O*-methylation. However, numerous deviations from these generalizations have been noted, especially for compounds with flexible conformations[5] or for polymethylated carbohydrates[6]. Therefore, selective ^{13}C–^1H decoupling has been applied when unequivocal assignment was impossible. The p.m.r. spectra of **2** and **9–11** have been measured and interpreted for this purpose. The ^{13}C-n.m.r. spectra of these compounds were subsequently measured with selective irradiation of H^i, where H^i is the proton at carbon i. Unequivocal assignment of the lines in the spectra of **2** and **9–11** was effected in this way, and the data obtained were used as a basis for further assignments. The interpretation of the spectrum of **1** accords with that presented by other authors[7]. Signals in the spectra of **5–7** have been assigned by a comparison with the spectra of **9–11**, and by application of the following regularities concerning the effects of acetylation of hydroxyl groups in carbohydrates upon the shifts of the signals for α-, β-, and γ-carbons: (*1*) shifts of the signals for α-carbons are only slightly affected by acetylation in conformationaly flexible systems (0–2 p.p.m. downfield); (*2*) β-effects caused by acetylation are more constant than those resulting from methylation (~2 p.p.m. upfield, independently of the configuration); and (*3*) γ-effects are insignificant (< 0.5 p.p.m.).

Finally, assignments of the signals in the spectra of **2–4** and **8** have been made by assuming that the γ-effects caused by methylation are small. The assignment of the resonance line at 70.55 p.p.m. to C-5 in the spectrum of **2** was confirmed by selective double-resonance ^{13}C–{H-5}. In the p.m.r. spectrum, the doublet for H-5 appears at 4.13 p.p.m. ($J_{4,5}$ 8.7 Hz).

The α-, β-, and γ-effects resulting from methylation of hydroxyl groups in **2–8** are given in Table II. These data show that the α-effect is constant and independent of the site of methylation (9.0–10.3 p.p.m. downfield).

The signs and absolute values of the β-effects depend on the position of the

TABLE I

^{13}C-N.M.R. SPECTRAL DATA FOR SOLUTIONS OF **1–11** IN $CDCl_3$

Compound	*Position of Me group*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*MeO-1*	*MeO-2*	*MeO-3*	*MeO-4*	*MeO-6*	*CH_3CO*	*CH_3CO*
1	0	100.5	71.6[a]	73.6	71.7[a]	70.8	170.7	55.9				52.75		
2	2	97.9	80.6	72.4	71.95	70.55	170.8	55.8	58.7			52.7		
3	3	99.6	71.5[a]	82.75	71.5	71.2[a]	170.8	56.0		60.8		52.6		
4	4	99.9	72.2	73.95	81.2	70.25	170.2	55.85			60.5	52.6		
5	2,3	98.2	81.0	82.0	71.8	70.85	170.8	55.85	59.0	61.1		52.6		
6	2,4	97.6	81.2	72.8	81.2	69.9	170.2	55.8	58.65		60.5	52.5		
7	3,4	99.9	72.0	83.7	81.2	70.6	170.1	55.85		60.9	60.2	52.6		
8	2,3,4	98.35	81.5	83.1	81.5	70.2	170.3	55.7	59.2	60.95	60.5	52.6		
9	2,3(4-Ac)	98.1	80.9	80.2	71.45	68.7	169.9	56.0	59.4	60.95		52.8	20.8	168.8
10	2,4(3-Ac)	97.9	79.2	72.9	79.5	69.75	170.0	55.7	58.8		59.7	52.6	21.1	169.9
11	3,4(2-Ac)	97.7	73.0	81.2[a]	81.0[a]	70.1	170.3	55.7		60.9	60.6	52.6	20.9	169.9

[a]Alternative assignment is possible.

TABLE II

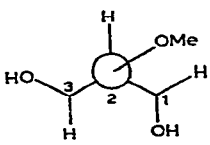
INFLUENCE OF METHYLATION ON α-, β-, AND γ-EFFECTS IN **1–8**

	Methylation on C-2			*Methylation on C-3*			*Methylation on C-4*		
	α-Effect	*β-Effect*	*γ-Effect*	*α-Effect*	*β-Effect*	*γ-Effect*	*α-Effect*	*β-Effect*	*γ-Effect*
Transition	**1 → 2**			**1 → 3**			**1 → 4**		
	9.0	−2.15(1)	0.25(4)	9.15	−0.1 (2)	−0.45(1)	9.5	0.35(3)	0.6(2)
		−1.2 (3)			−0.2 (4)	0.4 (5)		−0.55(5)	−0.5(6)
Transition	**3 → 5**			**2 → 5**			**2 → 6**		
	9.5	−1.4 (1)	0.3 (4)	9.6	0.4 (2)	0.3 (1)	9.25	0.4 (3)	0.6(2)
		−0.75(3)			−0.15(4)	0.3 (5)		−0.65(5)	−0.6(6)
Transition	**4 → 6**			**4 → 7**			**3 → 7**		
	9.0	−2.3 (1)	0 (4)	9.75	−0.2 (2)	0 (1)	9.7	0.95(3)	0.5(2)
		−1.15(3)			0 (4)	0.35(5)		−0.6 (5)	−0.7(6)
Transition	**7 → 8**			**6 → 8**			**5 → 8**		
	9.5	−1.55(1)	0.3 (4)	10.3	0.3 (2)	0.75(1)	9.7	1.1 (3)	0.5(2)
		−0.6 (3)			0.3 (4)	0.3 (5)		−0.65(5)	−0.5(6)

methoxyl group, and differ for each of the β-carbons in every pair. β-Effects caused by etherification of HO-2 are always negative, and the absolute values of the β-effects are always higher for C-1 than for C-3. The β-effects decrease when the hydroxyl group at C-3 is etherified. The β-effects associated with substitution at C-3 are small (< 0.5 p.p.m.) and irregular. Methylation of HO-4 causes positive β-effects on C-3 (0.35–1.1 p.p.m.) and negative ones on C-5 (0.55–0.65 p.p.m.).

The absolute values of γ-effects are less than 0.75 p.p.m. The γ-effects are positive for C-4 (when HO-2 is methylated), irregular for C-1 and C-5 (substitution at C-3), positive for C-2, and negative for C-6 (etherification of HO-4).

The dependence of the β-effects upon the position of methoxyl groups, especially the downfield β-effects, was unexpected, but may be explained as follows. It may be assumed that the overall β-effect caused by methylation consists of a small positive component (~1 p.p.m.) caused by the inductive effect of MeO groups, and a negative component caused by γ-gauche interaction of the β-carbon Me protons with protons at neighbouring positions. The more preponderant the rotamers around the C^i–O bond in which such an interaction occurs, the higher is the negative component. Variations of the chemical shifts caused by methylation of HO-2 and HO-4 show that the preponderant rotamers around C-2–O and C-4–O linkages in all of the compounds studied are those in which the methyl groups are turned towards C-1 (**12**) and C-5 (**13**), respectively.



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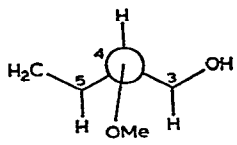

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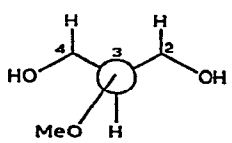
This conclusion is in good agreement with the higher absolute values of the β-effects at C-1 *vs.* C-3 when HO-2 is methylated, and with the opposite signs of the β-effects at C-3 and C-5 when HO-4 undergoes methylation. The small β-effects at C-2 and C-4 can be attributed to the preponderance of those rotamers around the C-3–O linkage in which the Me group occupies the position furthest away from H-2 and H-4 (*i.e.*, **14** and **15**).



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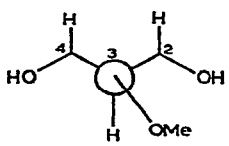

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The above considerations should be valid for methyl ethers of D-glucose[7,8]. However, relevant experimental data are scarce, and hence do not allow confirmation.

The chemical shifts of MeO groups at C-1–C-4 are constant, and independent of the number and the position of other MeO groups in the molecule. This circumstance can be used to identify methyl ethers **1–8** by ^{13}C-n.m.r. spectroscopy. The

TABLE III

^{13}C-N.M.R. SPECTRAL DATA FOR SOLUTIONS OF **2–4** IN D_2O

Compound	*Position of Me group*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*MeO-1*	*MeO-2*	*MeO-3*	*MeO-4*	*MeO-6*
2	2	97 8	80.5	72.4	72.0	71.5	172.3	56.0	58 6			52.7
3	3	100 4	71.4	83.0	71.4	71.0	172.3	56.3		60 8		52.6
4	4	100.3	71.4	72.8	81.8	69.8	172.3	56.2			60 5	52 6

substantial differences in chemical shifts of C-1–C-4 also allow identification of isomers **2–4** and **5–7** by means of the ^{13}C-n.m.r. spectra.

Solvent effects on chemical shifts should be important for further application of the above data to the interpretation of ^{13}C-n.m.r. spectra of natural polyuronides. Therefore, spectra of compounds **2–4** in D_2O have also been measured (Table III). Comparison of the data in Tables I and III shows the highest solvent effect for C-6 (up to 2 p.p.m.), while that for the ring carbons is somewhat less important.

EXPERIMENTAL

The synthesis of **1–8** has been described elsewhere[9]. Compounds **9–11** were obtained by treatment of **5–8** with acetic anhydride–pyridine (1 : 1) for 10 h at 20°, and purified by preparative t.l.c. on silica gel. The ^{13}C-n.m.r. spectra were measured at ambient temperature with a WP-60 Bruker instrument in the deuterio-lock mode (internal Me_4Si and Me_2SO for solutions in $CDCl_3$ and D_2O, respectively). The shift of Me_2SO *vs.* Me_4Si (39.5 p.p.m.[3]) was confirmed separately. Proton-decoupled FT-spectra were measured using a repetition time of 1.1 sec., pulse width of 3 sec (30°), 3750-Hz sweep-width, and 4K real data points. Selective decoupling ($^{13}C^i$–H^i experiments were made after the determination of proton chemical shifts by p.m.r. spectroscopy. The p.m.r. data (δ) for **9–11** are as follows.

9: 4.92 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1); 3.37 (dd, 1 H, $J_{2,3}$ 9.0 Hz, H-2); 3.63 (t, 1 H, $J_{3,4}$ 8.8 Hz, H-3); 5.01 (dd, 1 H, $J_{4,5}$ 9.8 Hz, H-4); 4.17 (d, 1 H, H-5); 3.45, 3.52, 3.73 (3 s, 3 H, 6 H, 3 H, 4 OMe); and 2.07 (s, 3 H, Ac).

10: 4.87 (d, 1 H, $J_{1,2}$ 3.4 Hz, H-1); 3.30 (dd, 1 H, $J_{2,3}$ 9.3 Hz, H-2); 5.35 (dd, 1 H, $J_{3,4}$ 9.5 Hz, H-3); 3.48 (t, 1 H, $J_{4,5}$ 9.8 Hz, H-4); 4.13 (d, 1 H, H-5); 3.37, 3.40, 3.43, 3.79 (4 s, 12 H, 4 OMe); and 2.10 (s, 3 H, Ac).

11: 4.87 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1); 4.73 (dd, 1 H, $J_{2,3}$ 9.6 Hz, H-2); 3.55* (H-3 and H-4, $J_{3,4}$ 9.0 Hz**); 4.03 (d, 1 H, $J_{4,5}$ 9.6 Hz, H-5); 3.39, 3.50, 3.55, 3.80 (4 s, 12 H, 4 OMe); and 2.12 (s, 3 H, Ac).

*Chemical shift determined by addition of several portions of $Eu(dpm)_3$, followed by extrapolation of δ H-3/$c_{Eu(dpm)_3}$ and δ H-4/$c_{Eu(dpm)_3}$ plots to zero $Eu(dpm)_3$ concentration.

Determined from the spectrum of **2 by addition of $Eu(dpm)_3$.

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