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Note

Use of methanolysis in the characterization of *O*-(2-hydroxypropyl)cellulose by ^{13}C-n.m.r. spectroscopy

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^{13}C-N.m.r. spectra of *O*-(2-hydroxypropyl)cellulose (HOPrcel) (**1**) and its hydrolyzates readily provide information[1] about the degree of substitution (d.s.) at individual oxygen atoms, and also the total molar substitution (m.s.). With the intact polymer, data are best obtained[1] at high field (*e.g.*, 100 MHz for ^{13}C), whereas, as expected, a hydrolyzate affords a spectrum far superior in signal dispersion, even at a relatively low field (*e.g.*, 22.6 MHz for ^{13}C), as has been observed[2] with other cellulose derivatives. Nevertheless, quantitative acid hydrolysis of the polymer, without concomitant decomposition, is difficult to attain.

We have found that, for effecting depolymerization of HOPrcel, acid-catalyzed methanolysis is an excellent alternative to hydrolysis. In contrast to a phase separation observed with aqueous acid, the polymer remains in solution in methanolic hydrogen chloride under reflux, and, in 18 h at relatively low acidity (10% HCl), undergoes virtually complete degradation to monomeric products. Evidence for this statement comes from the ^{13}C-n.m.r. spectrum illustrated in Fig. 1a, which shows that there is only a trace signal (at δ 103.2) attributable to C-1 of the residues in the polymer, or in oligomers from it. Methanolysis proved to be especially effective for the depolymerization of **2**, a more highly substituted form of HOPrcel which, although remarkably resistant to hydrolysis, readily underwent methanolysis, as may be seen in Fig. 1b. Another substantial advantage of the reaction is that it leads to a diminution in the proportion of bicyclic acetals[1,3] and of incompletely hydrolyzed fragments present, relative to an acid hydrolyzate[1], and, hence, to a less complex spectrum.

For analysis of the spectra in Fig. 1, ^{13}C-chemical shifts were calculated (see Table I) for 2,6-di- and 2,3,6-tri-*O*-substituted derivatives (**3** and **4**) of methyl α- and β-D-glucopyranoside, expected[1] to be the principal methanolysis products, by use of the substituent effects employed[1] for *O*-(2-hydroxypropyl)-α,β-D-glucose. Signals at δ 104.9 and 98.7 in Fig. 1 are the resonances of C-1 of **4** and **3**, respectively, showing that the α:β ratio was ~10:3. Minor signals in this region, at δ

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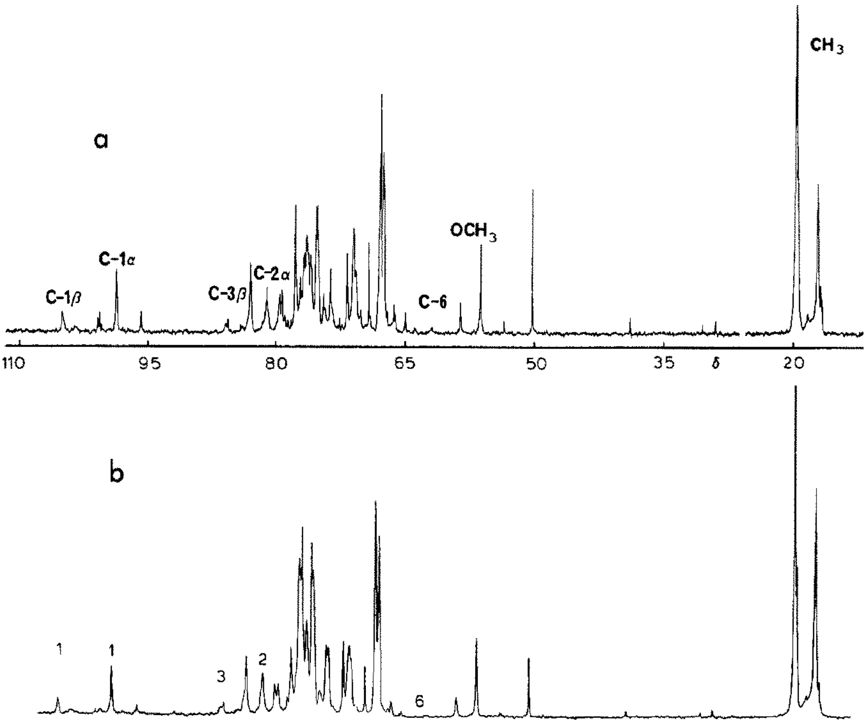

Fig. 1. ^{13}C-N.m.r. spectrum (100.6 MHz) of methanolyzate of *O*-(2-hydroxypropyl)cellulose (a) **1**, and (b) **2** (solvent, D_2O; temp. 25°). (The signal at δ 50.4 is due to MeOD.)

100.8, 100.6, and 95.7, are attributable to bicyclic acetals, the structures of which are described elsewhere[4]. A pair of signals at δ 85.7 and 85.6, corresponding to the calculated value for 3-*O*-(β) substitution (see Table I), have an overall intensity 3/5ths of that of the C-1(β), thereby giving a d.s. value of 0.6 for C-3 of **1**. As the C-2(α) signal, at δ 81.0, is of almost the same intensity as the C-1(α) resonance, O-2 must be close to being fully substituted by one or more 2-hydroxypropyl substituents.

According to the relative intensities (1:1.65) of the CH_3 signals at δ 17.4 and 19.9, representing inner- and end-unit methyl carbon atoms, respectively, the ratio (I:E)[1] of inner substituent groups to terminal *plus* individual substituents is the same as found by measurements on the corresponding signals for both **1** and its acid hydrolyzate. As a signal attributable to unsubstituted C-6 is barely apparent at δ 62.4, the d.s. value for O-6 of **1** must be $\geqslant$0.95. Overall, the results obtained were the same as those given[1] by the spectrum of the hydrolyzate of **1**, *i.e.*, d.s. and m.s. values of 2.5 and 4.0, respectively.

On the basis of Fig. 1b, d.s. values for O-2, -3, and -6 of **2** are close to 1.0. For example, the intensities of the C-1(β) and C-3(β) signals, at δ 104.9 and 85.5, respectively (see Table I), are approximately equal. Consequently, at this high

TABLE I

SUBSTITUENT EFFECTS, AND CALCULATED ^{13}C-CHEMICAL SHIFTS (δ) FOR METHYL *O*-(2-HYDROXYPROPYL)-α,β-D-GLUCOPYRANOSIDES

	2-Hydroxypropyl ether of methyl D-*glucopyranoside (δ)*[a]		*Effect (in p.p.m.) of substitution of methyl* D-*glucopyranoside at oxygen atom number*						*Cumulative substituent effect, in p.p.m (Calc. ^{13}C chemical shift, δ) for methyl* O-*(2-hydroxypropyl)-* D-*glucopyranoside*			
			2		*3*		*6*		*2,6-*		*2,3,6-*	
Atom	α	β	α	β	α	β	α	β	α	β	α	β
C-1	100.6	104.5	−2.1	0	+0.1	0	+0.1	+0.1	−2.0	+0.1	−1.9	+0.1
									(98.8)	(104.6)	(98.7)	(104.6)
C-2	72.8	74.7	+8.5	+8.8	−0.2	−0.3	0	0	+8.5	+8.8	+8.3	+8.5
									(81.3)	(83.5)	(81.1)	(83.2)
C-3	74.7	77.4	−0.6	−0.6	+9.5	+9.0	0	−0.2	−0.6	−0.8	+8.9	+8.2
									(74.1)	(76.6)	(83.6)	(85.6)
C-4	71.1	71.2	−0.1	0	−0.3	−0.2	+0.3	+0.4	+0.2	+0.4	−0.1	+0.2
									(71.3)	(71.6)	(71.0)	(71.4)
C-5	73.1	77.4	−0.2	+0.1	+0.1	+0.1	−1.1	−1.0	−1.3	−0.9	−1.2	−0.8
									(71.8)	(76.5)	(71.9)	(76.6)
C-6	62.2	62.4	0	0	−0.1	0	+9.3	+9.2	+9.3	+9.2	+9.2	+9.2
									(71.5)	(71.6)	(71.4)	(71.6)
OMe	56.5	58.7	0	0	0	0	0	0	0	0	0	0
									(56.5)	(58.7)	(56.5)	(58.7)

[a] Based on assignments given in ref. 5.

level of derivatization, even the relatively unreactive 3-hydroxyl group of D-glucosyl residues in cellulose is substituted by at least one substituent group. From these observations, and the fact that the relative intensities of the two CH_3 signals give an I:E ratio of 1.15:1.0, the overall d.s. and m.s. values for HOPrcel **2** are 3.0 and 6.5, respectively. Analysis of **2** by a different method[6] has given an m.s. value of 7–8.

In addition to its use for the depolymerization of **1** and **2** (as well as samples of HOPrcel of lower m.s.), methanolysis has also been found to be highly effective with 2-hydroxypropyl and 2-hydroxyethyl derivatives of starch at low d.s. levels ($\leq$0.5). For analysis of the ^{13}C spectra of the methanolyzates of the latter polymers, the data of Table I, and related chemical-shift data in ref. 2, are deemed to be appropriate.

EXPERIMENTAL

^{13}C-N.m.r. spectra. — The spectra were recorded at 27° with a Bruker WH-400 spectrometer operated at 100.6 MHz. Pulse widths were 4.0 μs and repetition

times 1.0 s, and signal intensities were obtained from the computer print-out, as well as from measurements of the areas of scale-expanded signals. Chemical shifts (δ) are reported with reference to tetramethylsilane, taking δ 50.4 as the chemical shift of MeOD, introduced as an internal reference into the D_2O solvent.

Methanolysis of O-*(2-hydroxypropyl)cellulose.* — The viscous solution of **1** (or **2**) (3.0 g) in methanol (50 mL) containing 10% of HCl was boiled under reflux for 18 h, the water-cooled condenser being capped with "parafilm". The methanolyzate was then made neutral with finely powdered barium carbonate, the suspension was filtered through Celite, and the filtrate was evaporated. Ethanol was added to the residue, the suspended matter was centrifuged off, and the solution was evaporated; yield, 2.5 g. The 100-MHz, ^{13}C-n.m.r. spectrum of the residue in D_2O is shown in Fig. 1a (or 1b).

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