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CARBON-13 NUCLEAR MAGNETIC RESONANCE SPECTRA OF CYCLODEXTRINS AND ITS PERACETATES

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Carbon-13 chemical shifts for α-, β-, and γ-cyclodextrins and its peracetates, and also amylose, in several solvents, are reported with full assignment. It was found that the steric effects imposed by cyclic nature of the dextrins on the conformation of the glucopyranose residues in the dextrins are clearly reflected in their spectra.

Cyclodextrins are a series of homologous oligosaccharides produced by the action of an amylase from *Bacillus macerans* on starch. Of the members of the series, α-, β-, and γ-dextrins are respectively composed of 6, 7, and 8 D-glucopyranose residues that are linked at α, 1 - 4 in a macrocyclic form. Owing to the simple symmetry of α-, β-, and γ-dextrins belonging to points groups, C_6, C_7, and C_8, respectively,[1,2] all the constituent glucopyranose residues in the dextrins are chemically and physically indistinguishable. Therefore, unlike most of oligosaccharides, the conformational analysis of the dextrins must be fairly simple, resembling those of monosaccharides. This consideration has already been substantiated by the ^1H NMR studies of these compounds,[5-8] which conclusively demonstrated that all the glucopyranose units in the three dextrins exist in substantially undistorted C1 chair conformation in D_2O and DMSO solutions as well as in alkaline solution.

In the present study we wish to report some preliminary studies on the ^{13}C NMR of cyclodextrins and its peracetates, and also amylose ($\overline{DP}n$ = 130), in several solvents. The cyclodextrins and its peracetates used were the same as those previously described.[8,9] To facilitate signal assignments, 6-deoxy-β-dextrin and its acetate were also prepared.[10] Proton-noise-decoupled ^{13}C NMR spectra were obtained at 25°C with a JNM-PFT-100 ^{13}C Fourier transform NMR spectrometer operating at 25.15 MHz, equipped with a JEC-6 spectrum computer. In preliminary experiments, no chemical shift variation due to a change in solute concentration was observed. Therefore, the concentration of the sample solution varied with its solubility. Cyclohexane was used as an external reference for the dextrins in D_2O, DMSO, and 1N-NaOH solutions, and TMS as an internal reference for the dextrin acetates in $CDCl_3$ and C_6D_6 solutions. The chemical shifts (acculate to ± 0.1 ppm) so measured were referenced to external CS_2 by means of the equations, $\delta_{CS_2} = 165.5 + \delta_{C_6H_{12}}$ ppm and $\delta_{CS_2} = 192.8 + \delta_{TMS}$ ppm. Hence, the chemical shifts thus obtained are given in ppm upfield from the external CS_2 reference.

In the ^{13}C NMR spectrum of β-dextrin in a 1N-NaOH solution (Fig.1), six resonances are clearly resolved, as expected from the above-mentioned molecular symmetry of the dextrin. The resonances at the lowest field of 89.1 ppm and at the highest one of 131.4 ppm can immediately be assigned to the anomeric and the hydroxymethyl carbons, respectively.[11-16] Furthermore,

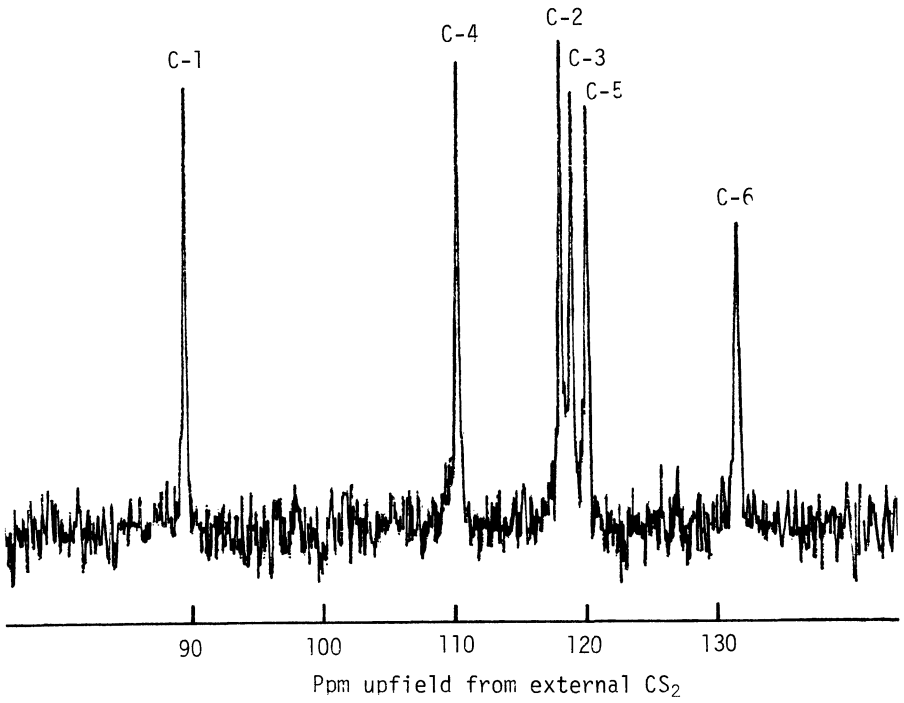

Fig.1. The proton-noise-decoupled, natural abundance ^{13}C NMR spectrum of β-cyclodextrin in a 1N-NaOH solution (150 mg/0.5 ml) at 25.15 MHz. sweep width; 4116 Hz and accumulation; 3500 times.

the general conclusion[11-16] that the chemical shifts for pyranose carbons other than the anomeric nuclei, bearing an etherified oxygen, lie in the range of 110 - 115 ppm allows the resonance at 110.1 ppm to arise from C-4. Not only the assignment of the C-5 resonance but also the confirmation of the above assignment of the C-4 and C-6 signals can be obtained from comparison of the spectra of β-dextrin and 6-deoxy-β-dextrin (Table 1). When all the C-5 hydroxymethyl groups of β-dextrin were converted to C-5-methyl groups, the C-5 resonance in β-dextrin must be shifted upfield by at least 4 ppm, the positions of the C-2 and C-3 signals being barely affected.[12] The resonance at 120.0 ppm was now found to be shifted upfield by 4.4 ppm, and hence assigned to C-5. Furthermore, upon deoxylation at C-6, it was noted that the C-6 resonance of β-dextrin undergoes a 43.5 ppm upfield shift. These shifts are in parallel with those observed for methyl α-D-glucopyranoside and methyl 6-deoxy-α-D-glucopyranoside (Table 1). On the assumption that the steric environments of C-2 and C-3 of the glucose units in the dextrins would not be so much different from those of the analogous carbons in the reducing glucose moiety of α-maltose,[3-6] the remaining two resonances at 118.0 and 118.8 ppm could be assigned to C-2 and C-3, respectively, by comparison with the signal assignments in the reducing glucose unit of α-maltose.[15-16] An additional support for this assignment is available from the bond polarization data,[13,14] from which it is inferred that the increase in the shielding of C-3 in the dextrin, consequent upon the sterically crowded environment[2,5-8] of this carbon situating at the interior side of the dextrin ring, would be accompanied by a decrease in the shielding of the appended proton (H-3). This is indeed the case, since the ^{1}H NMR studies[6-8] indicated that the H-3 signal of the dextrins appears at a lower field than that of H-2.

Table 1. Carbon-13 chemical shifts[a] for α-, β-, and γ-cyclodextrins and its related compounds.

Compound	Solvent	C-1	C-2	C-3	C-4	C-5	C-6	OCH_3
methyl α-D-glucopyranoside[b]	D_2O	92.9	120.6	118.9	122.4	120.9	131.3	137.2
methyl 6-deoxy-α-D-glucopyranoside	D_2O	92.7	120.4	119.1	116.8	124.4	175.2	136.9
α-cyclodextrin	D_2O	90.5	118.6	120.0	110.7	120.3	131.6	
	DMSO	89.7	118.3	119.5	109.5	119.5	131.5	
	1N-NaOH	89.1	118.0	118.8	110.1	120.0	131.4	
β-cyclodextrin	D_2O	90.1	118.8	119.8	110.8	120.0	131.6	
	DMSO	89.7	118.5	119.2	110.1	119.6	131.6	
	1N-NaOH	89.1	118.0	118.8	110.1	120.0	131.4	
γ-cyclodextrin	D_2O	90.3	119.1	119.7	111.5	120.2	131.7	
	DMSO	89.9	118.3	118.9	110.6	119.4	131.5	
	1N-NaOH	88.9	117.8	118.4	110.3	120.0	131.4	
amylose	DMSO	91.6	118.4	119.8	113.8	120.0	131.2	
	1N-NaOH	92.4	119.0	120.1	114.7	120.8	131.6	
6-deoxy-β-cyclodextrin	DMSO	89.4	118.5	119.1	103.4	125.1	174.3	
	1N-NaOH	89.1	117.8	118.5	103.9	124.4	174.9	

a) In ppm upfield from the external CS_2 reference. b) Data taken from Ref.13.

Table 2. Carbon-13 chemical shifts[a] for peracetylated α-, β-, and γ-cyclodextrins and its related compound.

Compound	Solvent	Carbonyl carbons	C-1	C-2	C-3	C-4	C-5	C-6	Methyl carbons
α-cyclodextrin peracetate	$CDCl_3$	22.2,[b] 23.6	96.3	121.9	121.9	115.6	123.3	129.6	172.0[c]
	C_6D_6	22.4, 23.6	96.3	121.3	121.7	115.5	122.7	129.2	172.2[c]
β-cyclodextrin peracetate	$CDCl_3$	22.1, 22.4, 23.4	96.0	121.9	122.4	116.0	123.1	130.2	172.0[c]
	C_6D_6	22.4,[b] 23.5	95.3	122.1	122.1	115.1	122.1	129.4	172.1[c]
γ-cyclodextrin peracetate	$CDCl_3$	22.2, 22.5, 23.5	96.5	121.9	122.5	116.9	123.1	130.2	172.1[c]
	C_6D_6	22.2, 22.4, 23.3	96.1	121.6	121.6	116.3	122.4	129.6	172.1,[b] 172.2
6-deoxy-β-cyclodextrin peracetate	$CDCl_3$	22.1, 23.4	96.2	121.6	122.4	110.3	125.6	176.2	172.0[b]

a) In ppm upfield from the external CS_2 reference. b) Of double intensity. c) Of triple intensity.

The ^{13}C chemical shifts thus determined for the three dextrins and the related compounds in D_2O, DMSO, and 1N-NaOH solutions are presented in Table 1, in which no systematic variation in the chemical shifts due to the difference in the ring size of the three dextrins was observed. The most remarkable feature of the spectra of the dextrins is the positions of the C-1 and C-4 resonances which are shifted downfield by about 2 - 3 and 3 - 5 ppm, respectively, comparing with the corresponding chemical shifts of their linear chain analogs such as α-maltose[15,16] and amylose. This fact may be understood as a consequence of the conformational restraints imposed on the dextrins by their looped arrangement, which may lead to significant alterations in bond angles and dimensions about the glycosidic C-1-O and C-4-O bonds. In addition, small solvent-induced shifts were observed for the C-2, C-3, and C-6 resonances of the three dextrins. The magnitudes of downfield shift are in the order, 1N-NaOH > DMSO > D_2O, indicating variation in the mode of solvation. In this connection, it is interesting to note that all the carbon resonances of amylose are shifted downfield in DMSO compared with in a 1N-NaOH solution. The uniform downfield shift seems to correspond to the conformational change of amylose from

expanded random-coil conformation[17] in an alkaline solution to a fairly compact one[17] in DMSO.

As for the dextrin acetates, the chemical shifts measured for the peracetates of the three dextrins in $CDCl_3$ and C_6D_6 solutions are shown in Table 2. It is noteworthy that the resonances due to C-1 and C-4 which bear no acetyl group undergo large upfield shifts (5 - 7 ppm) compared with the free sugars, while those due to C-2, C-3, and C-5 show constant, but not large upfield shifts (2 - 4 ppm). The greater increase in shielding of C-1 and C-4 may be attributed to the steric effects or the close proximity of the acetyl groups surrounding the both sides[2] of the cavity of the dextrins, which will outweigh the smaller deshielding effect of the acetyl groups to give a net upfield shift.

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