NMR Studies on Solid Cyclohexaamylose Inclusion Compounds⋆

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Abstract. Orthorhombic inclusion compounds of cyclohexaamylose with methanol, *n*-propanol, acetic acid and water as guest molecules were studied using ^{13}C and ^{2}H NMR techniques. ^{13}C chemical shifts were correlated with structural data, whereas ^{2}H NMR lineshapes were used to derive information on guest molecule motions.

Key words: cyclohexaamylose, solid state ^{13}C and ^{2}H NMR, guest molecule motion.

1. Introduction

Cycloamyloses are amongst the most versatile complexing agents known [1], forming both solution and solid state complexes. In the solid, water, short chain alcohols and acids, and iodine form orthorhombic cage complexes with cyclohexaamylose (α-cyclodextrin) where the cylindrical opening in each host molecule is blocked by neighbouring molecules [2]. On the other hand for the potassium acetate, methyl orange, tri-iodide and long chain molecule complexes, the cycloamylose rings pack coaxially with the anions or long chain molecules arranged in the channel.

Complex formation in solution is amenable to study by many different techniques, such as visible and UV spectroscopy, circular dichroism, ^{1}H and ^{13}C NMR spectroscopy [1]. In the solid, few techniques other than diffraction methods have been used [1,2]. ^{13}C NMR has proved to be useful in characterizing solid clathrates such as the quinols [3,4] and Dianin's compound clathrates [5]. In addition to showing the presence of guest molecule carbons, information on the host lattice can often be obtained as well [6]. Here are reported ^{13}C NMR results obtained for several of the orthorhombic cyclohexaamylose complexes as well as some correlations of chemical shift data with structural features. Related work has recently appeared elsewhere [7]. ^{2}H NMR has proved to be useful in the study of clathrates and inclusion compounds [8, 9] and some results are presented for deuterated guests in cyclohexaamylose cavities.

2. Experimental

The cyclohexaamylose complexes were prepared using standard techniques [1,2] and cyclohexaamylose was supplied by Sigma. All of the inclusion complexes studied have water of hydration external to the host molecule cavity which may be lost on standing, so only freshly prepared complexes were studied.

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^{13}C NMR spectra were obtained at a frequency of 45.28 MHz on a Bruker CXP-180 spectrometer. Further details have been given elsewhere [5]. ^{2}H NMR lineshapes were obtained at 27.63 MHz by using the phase alternated quadrupole echo technique [10].

3. Results and Discussion

The orthorhombic cyclohexaamylose complexes have one host molecule as the asymmetric unit [12–14]. Therefore, whereas in solution the ^{13}C NMR spectrum is a simple 6 line spectrum [11], the solid state spectrum may have 36 lines because of chemical shift inequivalence induced by conformational and other crystal field effects.

Spectra of the α-cyclodextrin complexes with 1-propanol, methanol and water are shown in Figure 1. In each case the signals for C_1, C_4 and C_6 can be assigned, as these are reasonably well separated from those for C_2, C_3 and C_5. The C_1 and C_4 lines are partially resolved, although not more than three or four of the maximum of six lines expected on the basis of crystallographic inequivalence can be observed. Since the glucose units are connected by 1–4 linkages one might expect similar splitting patterns for the C_1 and C_4 carbons, but evidently this is not the case.

Structural inequivalence of the glucose units of the orthorhombic cyclohexaamylose inclusion compounds lies in the deviation of the cyclohexaamylose molecule from cylindrical
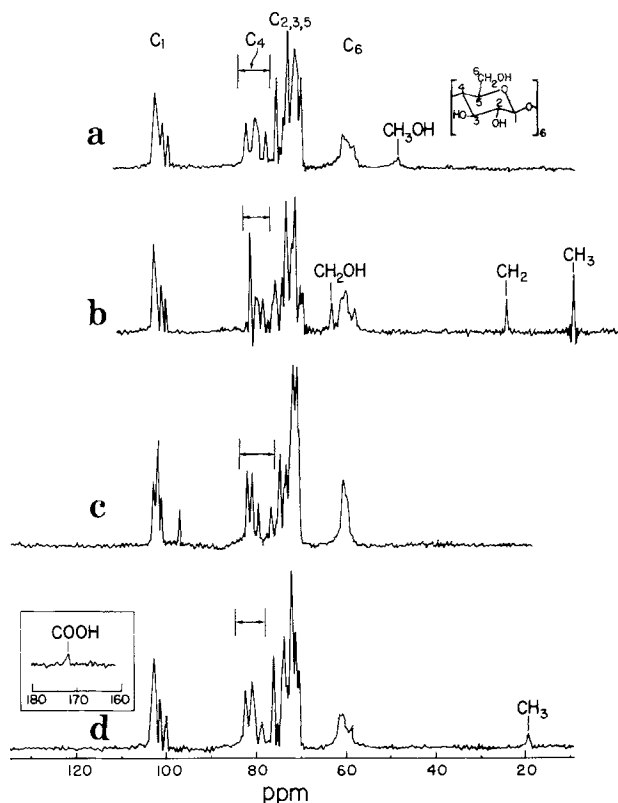

Fig. 1. ^{13}C NMR spectrum of the orthorhombic cyclohexaamylose inclusion compound with (a) methanol, (b) n-propanol, (c) water, (d) acetic acid.

symmetry. Variation in the way different glucose units are linked together can be denoted by specifying the torsion angles ψ and ϕ [12–15], where ψ is the angle $C_1(n)$–$O_4(n + 1)$---$O_4(n + 2)$ and ϕ is the angle $O_4(n)$---$C_1(n)$–$O_4(n + 1)$–$C_4(n + 1)$.

Because water acts as a rather inefficient guest molecule, the cyclodextrin hexahydrate forms the most asymmetric complex with a partially collapsed ring structure. ψ and ϕ show a large variation for this complex, ψ having values between 131.2 and 178.6° and ϕ between 147 and 171°. The fact that the C_1 and C_4 carbon signal splittings are also the largest for the three materials studied here suggests that a connection might exist between the C_1 and C_4 chemical shifts and the torsional angles. On the assumption that cross-polarization times are similar for all carbons involved, a reasonable assignment can be made for both C_1 and C_4 carbons taking into account both line positions and intensities (Table I).

Table I.   Chemical shift of cyclodextrin C_1 and C_4 carbons and torsion angle ψ

Guest								
n-Propanol			Methanol			Water		
$\sigma(C_1)$ (ppm)	$\sigma(C_4)$ (ppm)	ψ (deg)	$\sigma(C_1)$ (ppm)	$\sigma(C_4)$ (ppm)	ψ (deg)	$\sigma(C_1)$ (ppm)	$\sigma(C_4)$ (ppm)	ψ (deg)
100.4	78.55	149.5	99.5	78.4	148	97.4	77.0	131.7
101.35	79.65	167.1	100.65		167.1	101.35	79.7	162.6
	80.1	169.1		79.9	167.6		81.1	169.9
102.95		171.4	102.4		168.1	102.2		172.9
	81.4	179.6		82.55	177.9		82.3	175.8
		183.5			183.8	102.9		178.6

A reasonable correlation exists between C_4 chemical shifts and ψ, as illustrated in Figure 2. The degree to which the correlation is valid is somewhat hampered by the lack of data for small angles ψ, the data for larger ψ perhaps giving a better indication of the scatter one might expect because of effects other than the torsional angle. Similarly, ψ correlates reasonably well with C_1 chemical shifts (see Figure 2) whereas correlations of ϕ with shift data are not so apparent.

The establishment of correlations of chemical shift data with structural parameters such as torsional angle may have implications for assigning peaks in other glucose polymers, e.g. cellulose [18]. For this material, multiple splitting of the C_1 carbon was observed.

The C_2, C_3 and C_5 lines, of which there are 18, overlap, and generally are not readily assigned. Another feature of the cyclohexaamylose spectrum which is potentially useful is the C_6 carbon line. In the case of the water (Figure 1c) and iodine (not shown) complexes, the C_6 signal is relatively sharp and occurs at 61.0 ± 0.5 ppm. On the other hand, in the case of the methanol, propanol and acetic acid complexes, a secondary peak occurs at 58.5 ± 0.5 ppm. For the methanol and propanol complexes electron density associated with the C_6 carbon was shown to be disordered over two sites, with significant population of both sites, so that appearance of a split C_6 ^{13}C line may be taken as a sign of disorder.

All of the spectra (Figure 1a–d) for complexes of essentially the same structure are slightly different, and must reflect minor differences in detailed structure. However the spectra are similar enough so that at least it should be possible to identify other orthorhombic complexes of unknown structure from their ^{13}C NMR spectra.
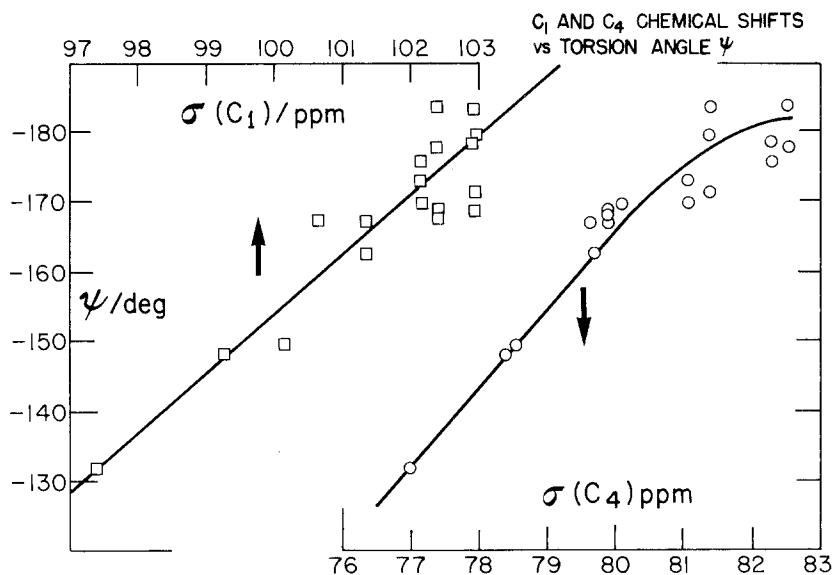
Fig. 2.   Carbon 1 and Carbon 4 chemical shifts of cyclohexaamylose inclusion compounds plotted as a function of torsion angle ψ.

3.1. ^{13}C NMR OF GUEST MOLECULES

Table II shows the average chemical shifts for neat liquid guest materials, as well as for encaged guest molecules. In most cases the spectral lines for the encaged guest are near to those for the neat liquid. The largest change occurs for the *n*-propanol carbon bearing the hydroxyl group, and this must reflect a change in the hydrogen-bond environment on going from the neat liquid to the molecule in the cyclohexaamylose cage.

Table II. ^{13}C chemical shifts of guest molecules

Guest	Chemical shift (ppm)	
	In α-cyclodextrin	Neat liquid
Acetic acid	− 20.8, − 173.5	− 19.5, − 172.2
Methanol	− 49	− 49
Propanol	− 63.6, − 25.0, − 10.0	− 68.3, − 23.8, − 10.0

In the case of the methanol and acetic acid compounds, the guest lines are very broad and probably reflect a disordered environment for the guest molecules. In the case of the methanol compound the presence of two distinct guest sites within the host cavity has already been shown [12].

3.2. ^{2}H NMR OF GUEST MOLECULES

^{2}H NMR lineshapes of methanol-d_4 in the orthorhombic cyclohexaamylose hydrate at 310 and 193 K are shown in Figures 3a and b. It can be assumed that the OD deuteron has
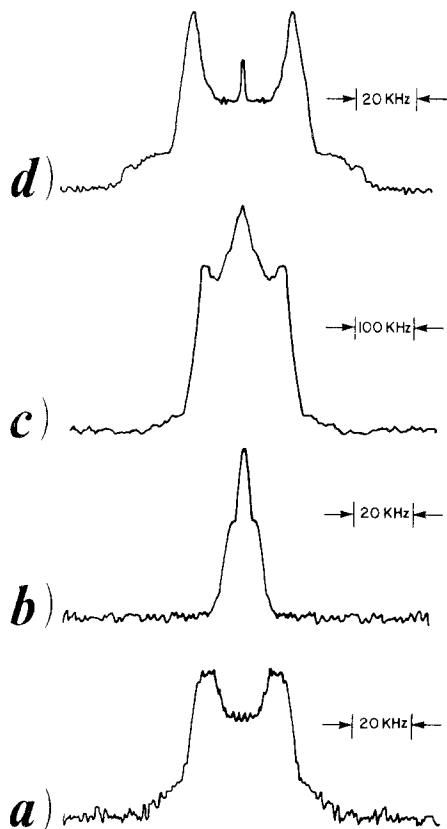
Fig. 3. ^{2}H NMR lineshapes of the cyclohexaamylose inclusion compound with (a) CD_3OH at 193 K, (b) CD_3OH at 310 K, (c) CH_3OH, D_2O at 300 K, (d) CD_3COOH at 300 K.

exchanged with OH groups of the cyclohexaamylose and H_2O protons, so that the signal observed is for the CD_3 group only. At room temperature, the lineshape resembles that expected for a large asymmetry parameter ($\eta \sim 0.9$). This is usually indicative of nonaxial motion and may well reflect motions between the two disorder sites found in the structural study [12]. An upper limit to the motionally averaged quadrupole coupling constant is ~ 12 kHz, compared to 14 kHz for the CD_3 group of CD_3OH in the β-quinol clathrate [8] at room temperature. Below 240 K, the ^{2}H lineshape broadens and becomes a broad doublet below 220 K. From the lineshape at 193 K, the mean quadrupole coupling constant is ~ 40 kHz, although there does seem to be a distribution of values. The mean value is significantly less than expected for a rotating CD_3 group, 47 kHz [16].

In order to learn about motions of water molecules external to the guest cavity, cyclohexaamylose was recrystallized from D_2O, and the inclusion compound prepared from CH_3OH and D_2O. The ^{2}H lineshape (Figure 3c) is a broad doublet, with a large central component, which probably reflects dynamic effects. The quadrupole coupling constants indicated lie in the range 180–200 kHz, and on cooling to ~ 200 K, a broad doublet results with coupling constants in the range 210–230 kHz. This is a normal range for hydrogen bonded D_2O molecules and OD groups [17]. The smaller values observed near room temperature reflect

some librational averaging, although large scale motions such as twofold flips or more general spherical reorientation of all D_2O molecules, are excluded.

In the case of the acetic acid–d_3 cyclohexaamylose hydrate, the ^2H lineshape is a superposition of two doublets of slightly different widths. The quadrupole coupling constants derived from the lineshapes are 48 and 56 kHz. A value of ~ 55 kHz is expected for an acetic acid molecule with a rotating CD_3 group [18], so that one population of guest acetic acid molecules has only CD_3 group rotation, the other CD_3, group rotation plus some additional small angle motion. There is also evidence that as the sample ages and loses water of crystallization, the ^2H doublet width decreases, so that the acetic acid molecule has greater motional freedom.

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