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Preliminary communication

Molecular motion of *p*-substituted phenols in solid-state cyclomaltohexaose inclusion-complexes

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The cycloamyloses (cyclodextrins) are cyclic, (1→4)-linked α-D-glucosaccharides containing at least six units, which have the shape of a hollow, truncated cone with primary and secondary hydroxyl-groups crowning opposite ends of its torus, can form inclusion complexes with a variety of guest molecules in the solid state as well as in solution, and can catalyse the reaction of included compounds[1,2].

In solution, according to the results of ^{13}C-n.m.r. relaxation studies, the dynamic coupling between mononuclear aromatic compounds and cyclomaltohexaose (cyclohexaamylose, α-cyclodextrin, α-CD) in inclusion complexes is weak and the aromatic ring in the α-CD cavity is able to rotate rapidly[3,4].

We now report on the motional freedom of *p*-nitrophenol (PNP) and *p*-hydroxybenzoic acid (PHBA) in α-CD inclusion-complexes in the solid state by using high-resolution ^{13}C-n.m.r. spectroscopy and a cross polarisation/magic-angle spinning (CP/MAS) technique. The inclusion complexes have been characterised by ^{1}H- and ^{13}C-n.m.r. spectroscopy of solutions[5-9] and by the X-ray method in the solid state[10]. In solution as well as in the solid state, α-CD forms 1:1 inclusion-complexes with PNP and PHBA, in which the nitrophenyl or carboxyphenyl group is located in the cavity, and the phenolic hydroxyl group protrudes from the secondary-hydroxyl side of the cavity[5-10]. ^{13}C-CP/MAS n.m.r. spectra have been measured for α-CD inclusion-complexes with some guest compounds[11,12].

The yellow, crystalline, α-CD–PNP inclusion-complex was prepared by cooling an aqueous solution containing α-CD and PNP (1:1 molar ratio[10]), and the colorless, crystalline, α-CD–PHBA complex was prepared by the same procedure. ^{13}C-CP/MAS n.m.r. spectra were recorded with a JEOL JNM FX-200 spectrometer and a CP/MAS accessory, operated at 50 MHz. Cross polarisation was carried out with r.f. field-strengths of ~15 gauss (^{1}H) and ~60 gauss (^{13}C), and a contact time of 2 ms. The spinning rate of the sample at the magic angle was 3.5 kHz. Chemical shifts were measured with respect to the high-field resonance of adamantane, which was taken as 29.7 p.p.m. downfield from the resonance of Me_4Si.

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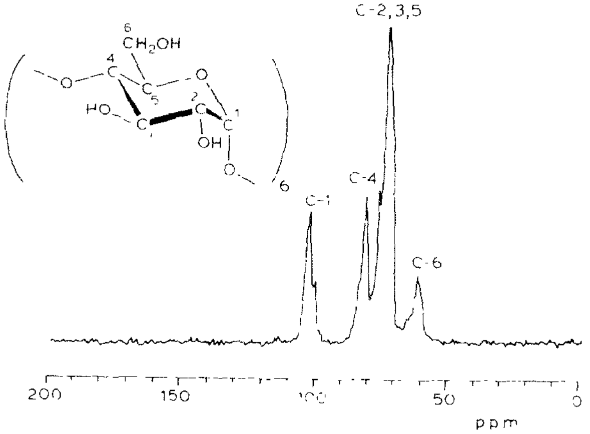

Fig. 1. ^{13}C-CP/MAS n.m.r. spectra (50 MHz) of α-CD in the solid state (400 scans with a repetition time of 5.0 s).

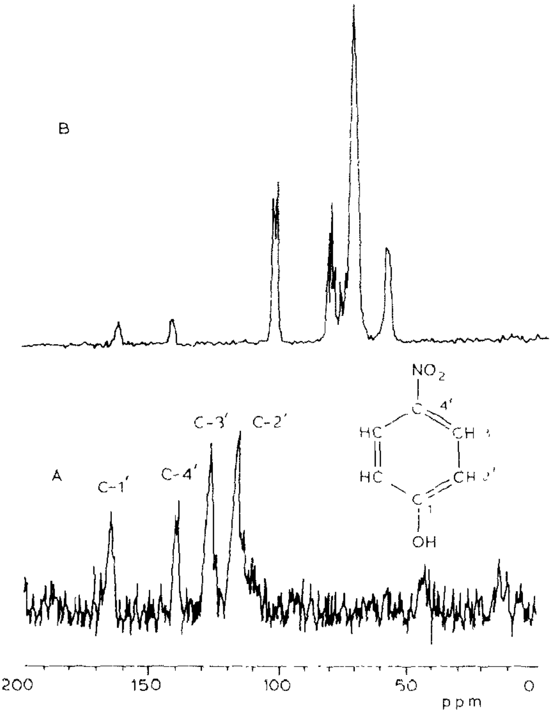

Fig. 2. ^{13}C-CP/MAS n.m.r. spectra (50 MHz) of (A) PNP (6000 scans; repetition time, 10 s) and (B) α-CD–PNP inclusion-complex in the solid state (700 scans; repetition time, 5.0 s).

Figs. 1–3 show ^{13}C-CP/MAS n.m.r. spectra of α-CD, PNP, PHBA, amd their inclusion complexes. In the spectra of α-CD and the phenols, all resonances appear in the region expected from the corresponding spectra observed in solution[4,8], and are assigned as shown. The most outstanding difference between the spectra of free and complexed α-CD and phenol compounds is the broadening and virtual disappearance of the peaks for C-2′ and C-3′ (117 and 128 p.p.m. for PNP, and 117 and 134 p.p.m. for PHBA) (Figs. 2 and 3). These peaks are due to the protonated carbons. It is inconceivable that poor adjustment of experimental conditions caused the disappearance of these peaks, since those due to the quaternary carbons of the phenols and all the carbons of α-CD appear with high signal-to-noise ratios. The same reason suggests that the line broadening is not mainly due to the chemical-shift dispersion.

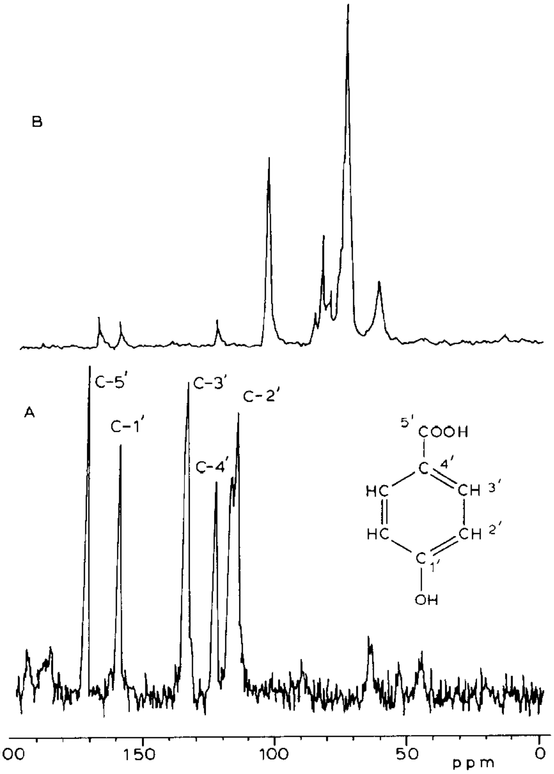

Fig. 3. ^{13}C-CP/MAS n.m.r. spectra (50 MHz) of (A) PHBA (200 scans; repetition time, 20 s) and (B) α-CD–PHBA inclusion-complex in the solid state (700 scans; repetition time, 5.0 s).

Two mechanisms are possible for the disappearance of the resonances[13]. Firstly, C-2′ and C-3′ of the respective compounds, which are magnetically equivalent (within the resolution of ~2 p.p.m.) in the free state, become significantly non-equivalent in the α-CD cavity, and the aromatic ring undergoes 180° flips about its two-fold axis (through C-1′,4′) with a rate close to the chemical-shift differences between the C-2′ and C-3′ resonances, which means that the rate is intermediate on the n.m.r. time-scale and hence the peaks coalesce. This magnitude may be [14–16] of the order $\sim 10^2$ s^{-1}. If the rate of flip is high compared to the chemical-shift difference, two signals (C-2′ and C-3′) would be observable, as in solution spectra[6,8,15]. For very slow flips or a rigid state, up to four lines might be discerned for these carbons. The resonances due to the quaternary carbons of each guest compound can hardly be affected by the 180°-flip motion, because they are situated on the axes of rotation.

Secondly, the aromatic ring flips librationally around its two-fold axis with a rate close to the nutation frequency of the proton decoupling field, so that the decoupling process becomes inefficient and the ^{13}C resonance broadens. This broadening is particularly likely for carbons having directly bonded protons[13,17] and where the rate of motion may be of the order $\sim 10^5$ s^{-1}.

These two mechanisms for line broadening assume rotational motion of the aromatic ring. The difference between the solid-state n.m.r. line-shapes, which indicates the presence of flip motion, and X-ray data, which indicate an apparent immobility, can be reconciled with a model where the aromatic ring undergoes librational flip motion with a very small amplitude[18]. The rotation of the aromatic ring with a large angle may be restricted in the α-CD cavity because of severe steric hindrance[10]. Thus, the second mechanism is the more likely.

It is concluded that the *p*-substituted phenols in the α-CD inclusion-complexes have freedom of flip motion about their two-fold axes even in the solid state. This is consistent with the fact that mononuclear aromatic compounds included in the α-CD cavity are able to rotate rapidly in solution. The differences in the time scale and mode of motion between the solid state and solutions may be due to perturbation from the rigid crystalline field in the former state.

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