*Carbohydrate Research,* 135 (1985) C12–C16
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

**Preliminary communication**

# C.p.–m.a.s. $^{13}$C-n.m.r. study of the molecular dynamics of some solid-state inclusion-complexes of cyclomaltohexaose and cyclomaltoheptaose

YOSHIO INOUE*, FU-HUA KUAN, YÛJI TAKAHASHI, and RIICHIRÔ CHÛJÔ
*Department of Polymer Chemistry, Tokyo Institute of Technology, O-okayama 2-chome, Meguro-ku, Tokyo 152 (Japan)*

(Received September 25th, 1984; accepted for publication, October 31st, 1984)

In previous papers[1,2], we have analysed the chemical shifts and line-shapes of cross-polarisation (c.p.)–magic-angle sample-spinning (m.a.s.) $^{13}$C-n.m.r. spectra of guest *p*-nitrophenol (PNP), *p*-hydroxybenzoic acid, benzoic acid, and *m*-nitrophenol included in the host cyclomaltohexaose (cyclohexa-amylose, $\alpha$-CD) and cyclomaltoheptaose (cyclohepta-amylose, $\beta$-CD) in the solid state. In these papers, we demonstrated that this is a sensitive method for obtaining microscopic information about chemical and physical properties of the guests included in the CD cavities. The c.p.–m.a.s. $^{13}$C resonances of the protonated carbons of the guests broaden and disappear from the spectra following complexation with $\alpha$-CD, whereas all the carbons of PNP included in $\beta$-CD show sharp resonances. Although we have explained these phenomena in terms of the molecular motion of the guests in the CD cavity, there were some ambiguities. We now report a reinvestigation involving new data on the inclusion complex of hexakis(2,3,6-tri-*O*-methyl)cyclomaltohexaose ($\alpha$-TMCD) with PNP. The molecular structure of the crystalline $\alpha$-CD– and $\alpha$-TMCD–PNP inclusion complexes have been characterised by X-ray diffraction[3,4].

$\alpha$-TMCD was synthesised from $\alpha$-CD[5], and recrystallised several times from hot water. The crystal of $\alpha$-TMCD–PNP (1:1) complex was prepared by the reported method[4]. C.p.–m.a.s. $^{13}$C-n.m.r. spectra were recorded with a JEOL JNM FX-200 spectrometer operated at 50 MHz. The instrumental conditions were m.a.s. rate, ~3.5 kHz; c.p. contact time, 2 ms; proton-decoupling field strength ($\omega_1$), 50–55 kHz. The details of the preparation of other materials and of the n.m.r. operations have been reported[2].

Figs. 1–4 show c.p.–m.a.s. $^{13}$C spectra of crystalline PNP[1,2], and PNP complexed with $\alpha$-CD[1,2], $\beta$-CD[2], and $\alpha$-TMCD. There are several striking changes in the PNP resonances upon complexation. The most outstanding difference between the spectra of PNP in the free state and in the $\alpha$-CD complex is, as pointed out previously[1,2], the virtual disappearance of the C-2 and C-3 resonances upon complexation, whereas all of the PNP resonances appeared clearly in the spectra of the $\beta$-CD–PNP and $\alpha$-TMCD–PNP complexes. However, in the spectrum of the $\alpha$-TMCD complex, the PNP C-2 and C-3 resonances have decreased intensities with severe line-broadening, as compared with the C-1 and C-4 resonances in the same spectrum.

---

*To whom inquiries should be addressed.

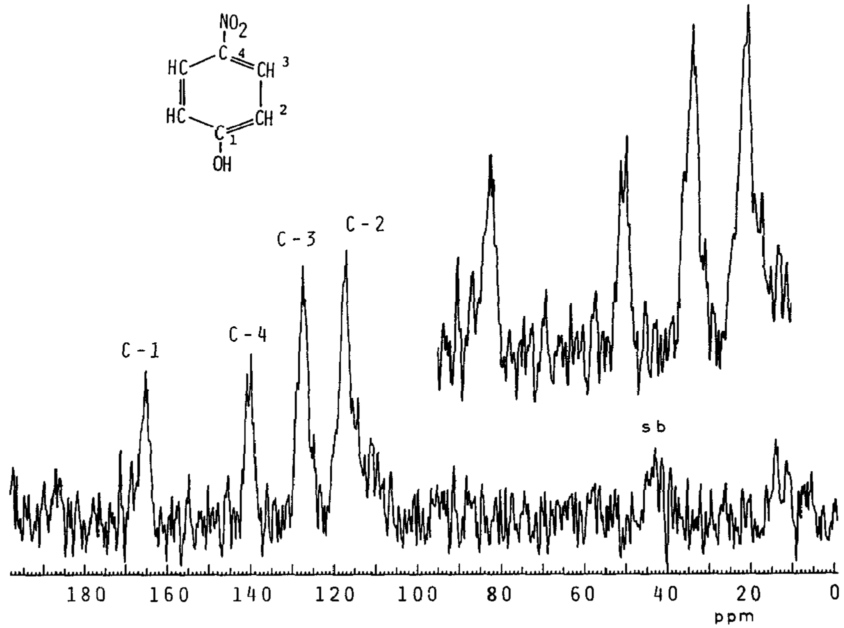

Fig. 1. C.p.–m.a.s. $^{13}$C-n.m.r. spectrum of PNP (6000 scans; contact time, 2 ms; repetition time, 10 s). The insert shows the expanded spectra. Obvious side-bands are indicated by "s.b.".

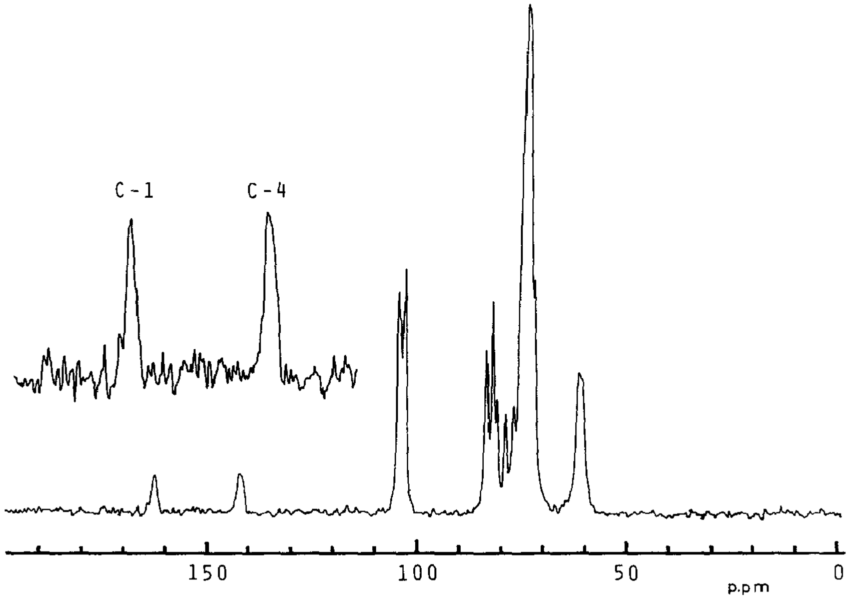

Fig. 2. C.p.–m.a.s. $^{13}$C-n.m.r. spectrum of the α-CD–PNP inclusion-complex (700 scans; contact time, 2 ms; repetition time, 5.0 s). The signals at higher field are the resonances of α-CD. The insert shows an expansion of the PNP region.

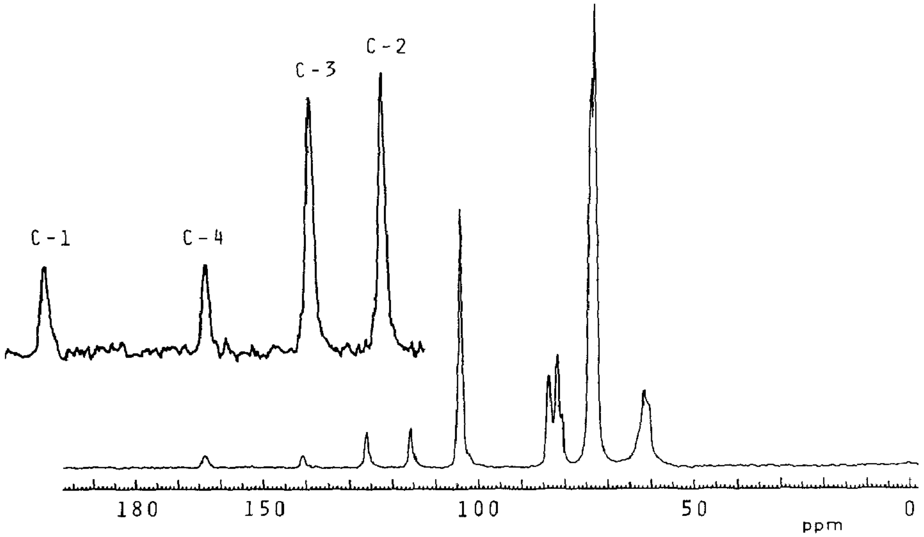

Fig. 3. C.p.–m.a.s. $^{13}$C-n.m.r. spectrum of the β-CD–PNP inclusion-complex (620 scans; contact time, 2 ms; repetition time, 5.0 s). The signals at higher field are the resonances of β-CD. The insert shows an expansion of the PNP region.

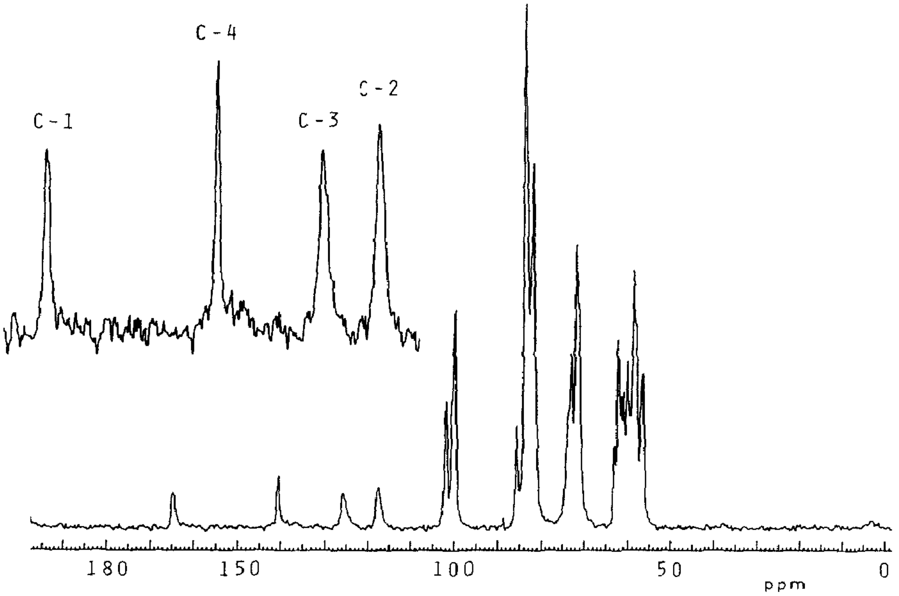

Fig. 4. C.p.–m.a.s. $^{13}$C-n.m.r. spectrum of the α-TMCD–PNP inclusion-complex (500 scans; contact time, 2 ms; repetition time, 5.0 s). The signals at higher field are the resonances of α-TMCD. The insert shows an expansion of the PNP region.

The spinning side-bands, which appeared clearly in the spectra of the free state PNP (shown by "s.b." in Fig. 1), were reduced in their intensities and could not be detected in the spectra of the inclusion complexes (Figs. 2–4), although the spinning side-bands were not removed artificially. The non-equivalence of two PNP C-2 carbons, leading to line-broadening and splitting of their resonances, also disappeared upon complexation with β-CD and α-TMCD.

For free PNP, the resonance of the carbon bonded to nitrogen (C-4) was split into an asymmetric doublet because of the $^{14}N-^{13}C$ dipolar coupling, which cannot be completely suppressed by m.a.s.[6,7]. The splitting of this doublet (~60 Hz) is comparable with that found for the nitro carbons of crystalline 4-nitrotoluene[6] and 2,6-dimethyl-3-nitroaniline[7]. This result shows that the free PNP molecule in the crystalline state is almost static. In contrast, the $^{14}N-^{13}C$ splitting of the PNP C-4 resonance could not be observed in the spectra of complexes with α-CD, β-CD, and α-TMCD.

All these observations indicate that the PNP molecule included in the CD cavity is undergoing molecular motion. Since typical values[8] for the chemical shift anisotropy for aromatic carbons are in the range of 150–200 p.p.m., the disappearance of the spinning side-bands suggests that the life-time of molecular motion of PNP in the CD cavity is shorter than $\sim 1.5 \times 10^{-4}$ s.

Rothwell and Waugh[9] have developed the theory for $T_2$ (the inverse of the line-width) for a $^{13}C$ spin dipolar coupled to a proton spin under conditions of random rotational motion and proton spin r.f. decoupling. According to the theory, the plot of line-width *vs.* the correlation time for molecular motion, $\tau_c$ (which corresponds to the inverse of rate of molecular motion), shows a maximum when the $\tau_c$ value is equal to the modulation period of the proton decoupling ($1/\omega_1$), and where the line is the broadest. In the "short correlation" limit ($\omega_1 \tau_1 \ll 1$), the line-width is reduced by the rapid motional averaging; in the "long correlation" limit ($\omega_1 \tau_1 \gg 1$), the line-width is also reduced by the efficient $^{13}C-^{1}H$ dipolar decoupling. As is evident from the theory, the influence of the decoupling field is more significant for the resonance of carbon having directly bonded proton(s) and undergoing restricted motion.

Thus, the selective disappearance of the resonances of protonated carbons, C-2 and C-3, of PNP upon complexation with α-CD would arise from the restricted motion of the PNP molecule with a rate close to, or identical with, the nutation rate of the proton-decoupling field as suggested previously[1,2]. In this case, the correlation time for motion is $\sim 3 \times 10^{-5}$ s. The $^{13}C$ line-broadening due to the dipolar coupling with $^{14}N$ is not effectively suppressed by the rotational motion about the C–N bond[10]. Since the C-4 resonance in the spectrum of the α-CD complex is clearly broader than that in the spectra of other complexes, the motion of the PNP molecule in the α-CD cavity is the rotation about the axis which spans C-1, C-4, and N. This supposition is supported by the X-ray crystallographic study[3], which showed that the C-1–C-4 axis of included PNP nearly coincides with the axis of the α-CD cavity. Such rotational motion could not affect the line-widths of C-1 and C-4 resonances.

The X-ray studies also showed that the guest molecule is more loosely packed in the α-TMCD cavity than in the α-CD cavity[3,4]. This fact explains the appearance of the C-2 and C-3 resonances in the spectrum of the α-TMCD complex, in that the molecular motion of a PNP molecule in the α-TMCD cavity is expected to be faster than that in the α-CD cavity. The mean line-width of C-2 and C-3 resonances is ~80 Hz, which corresponds, according to the theory of Rothwell and Waugh[9], to a correlation time of $\sim 9 \times 10^{-7}$ s (shorter correlation-time side). Since the line-width of the C-4 resonance in the spectrum of the α-TMCD complex is sharper compared with those of the C-1 resonance in the same spectrum and the C-4 resonance in the α-CD complex, the molecular motion of PNP in the α-TMCD cavity cannot be the rotation about the C-1—C-4—N axis. This expectation is supported also by the X-ray crystallographic structure[4], *i.e.*, in the α-TMCD cavity, the PNP C-1—C-4—N axis is not parallel to the axis of the α-TMCD cavity. The motion of PNP other than the rotation about the C-1—C-4 axis may also reduce the line-width of the C-1 resonance as well as those of the C-2, C-3, and C-4 resonances.

The mean line-width of the C-2 and C-3 resonances of PNP in the β-CD complex is ~ 50 Hz, which corresponds to the correlation time of $\sim 7 \times 10^{-7}$ s (short correlation-time side) or $\sim 8 \times 10^{-4}$ s (long correlation-time side). At present, there is no clear evidence to decide which correlation time is realistic. In a previous paper[2], we deduced that the molecular motion of PNP is more extensively restricted in the β-CD cavity than in that of α-CD. This deduction was based on the results derived for the inclusion complexes in solution by observation of carbon-13 relaxation time[11]. As pointed out previously[2], not all of the results for solutions necessarily correspond with those for the solids. In the latter state, stronger intermolecular interactions, which are brought about by fixation of the molecular geometry and packing, must be considered. The direct measurements of relaxation parameters and the observations of variable temperature c.p.—m.a.s. $^{13}$C-n.m.r. spectra[12] may be useful for detailed characterisation of molecular motion in the solid state.

Thus, c.p.—m.a.s. $^{13}$C-n.m.r. spectra clearly indicate that the guest PNP included in the CD cavity undergoes molecular motion even in the solid state, and that the rate of motion depends on the inclusion state.

## ACKNOWLEDGMENTS

The authors thank Mr. T. Okuda for preparations of the crystals of PNP, and the PNP—α- and —β-CD inclusion complexes, and Dr. T. Fujito and Mr. K. Deguchi of JEOL Ltd., Tokyo, for recording the c.p.—m.a.s. $^{13}$C-n.m.r. spectra.

## REFERENCES

1 Y. Inoue, T. Okuda, and R. Chûjô, *Carbohydr. Res.*, 116 (1983) C5–C8.
2 Y. Inoue, T. Okuda, F.-H. Kuan, and R. Chûjô, *Carbohydr. Res.*, 129 (1984) 9–20.
3 K. Harata, *Bull. Chem. Soc. Jpn.*, 50 (1977) 1416–1424.
4 K. Harata, K. Uekama, M. Otagiri, and F. Hirayama, *Bull. Chem. Soc. Jpn.*, 55 (1982) 3904–3910.
5 B. Casu, M. Reggiani, G. G. Gallo, and A. Vigevani, *Tetrahedron*, 24 (1968) 803–821.
6 J. G. Hexem, M. H. Frey, and S. J. Opella, *J. Chem. Phys.*, 77 (1982) 3847–3856.
7 A. Naito, S. Ganapathy, and C. A. McDowell, *J. Magn. Reson.*, 48 (1982) 367–381.
8 M. Mehring, *High Resolution NMR Spectroscopy in Solids*, Springer-Verlag, New York, 1976.
9 W. P. Rothwell and J. S. Waugh, *J. Chem. Phys.*, 74 (1981) 2721–2732.
10 M. Okazaki and C. A. McDowell, *Chem. Phys. Lett.*, 102 (1983) 20–24.
11 Y. Inoue and Y. Miyata, *Bull. Chem. Soc. Jpn.*, 54 (1981) 809–816.
12 J. R. Lyerla, C. S. Yannoni, and C. A. Fyfe, *Acc. Chem. Res.*, 15 (1982) 208–216.