Two Types of Inclusion realised in the Complexation between *p*-Dimethylaminobenzoic Acid and 2,6-Dimethyl-β-cyclodextrin

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U.v. absorption, induced circular dichroism, and n.m.r. spectroscopic studies indicate that 2,6-dimethyl-β-cyclodextrin and *p*-dimethylaminobenzoic acid form an axial inclusion complex in water, but that they form an equatorial or lid-type supramolecular complex in chloroform.

The accuracy of induced circular dichroism (i.c.d.) in determining the orientation[1] and chirality[2] of aromatic molecules accommodated in cyclodextrins (CDs) has been confirmed by many reports in the literature. Axial-,[1] equatorial-,[1b] and lid-type[3] inclusions are known as types of 1 : 1 host–guest complexes, and the type of inclusion has been determined solely by the kind of aromatic guest molecules and CDs. For example, pyrene[1d] and *p*-disubstituted benzenes[1a] form only axial inclusion complexes with β-CD with 1 : 1 stoicheiometry. This behaviour is thought to hold for many solvents as *N*,*N*-dimethylformamide, dimethyl sulphoxide,[4a] and ethylene glycol[4b] have been used in addition to water. We report here a new phenomenon observed in the complexation between *p*-dimethylaminobenzoic acid (DMBA) and 2,6-dimethyl-β-CD (DM-β-CD),[5] in which an axial inclusion complex is formed in water and an equatorial or a lid-type

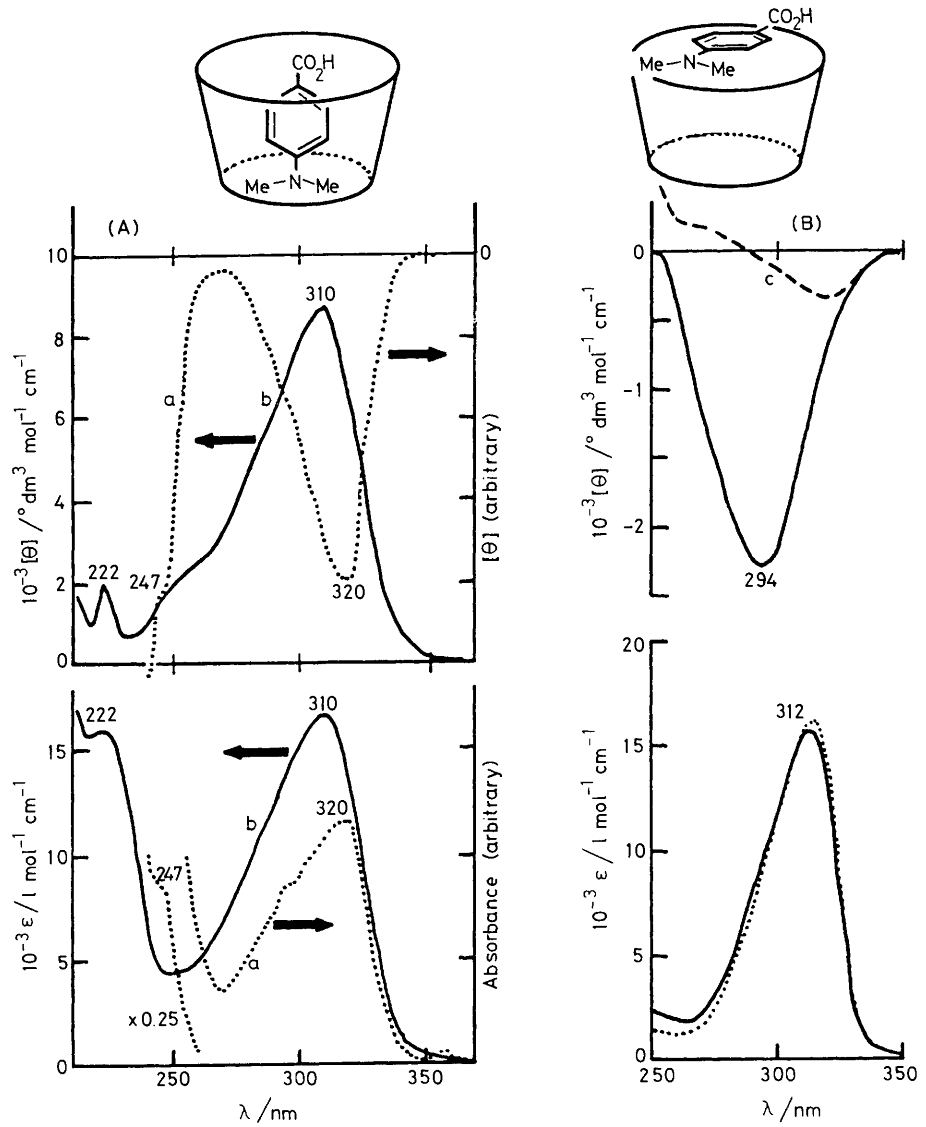

Figure 1. (A) U.v.-absorption (bottom) and i.c.d. spectra (top) of DMBA in cholesteric mesophase (curves a) or in the presence of DM-β-CD (curves b) in water. In curves b, [DMBA] = 1.1 × 10^{-4} M and [DM-β-CD] = 3.7 × 10^{-2} M, and path length = 10 mm. (B) U.v.-absorption (bottom) and i.c.d. spectra (top) of DMBA in chloroform in the absence (·····) and presence (———) of DM-β-CD. Curve c (– – – – –) represents the i.c.d. spectrum of DMBA in the presence of TM-β-CD. [DMBA] = 1.1 × 10^{-4} M and [DM-β-CD] = [TM-β-CD] = 3.7 × 10^{-2} M. Path length = 10 mm.

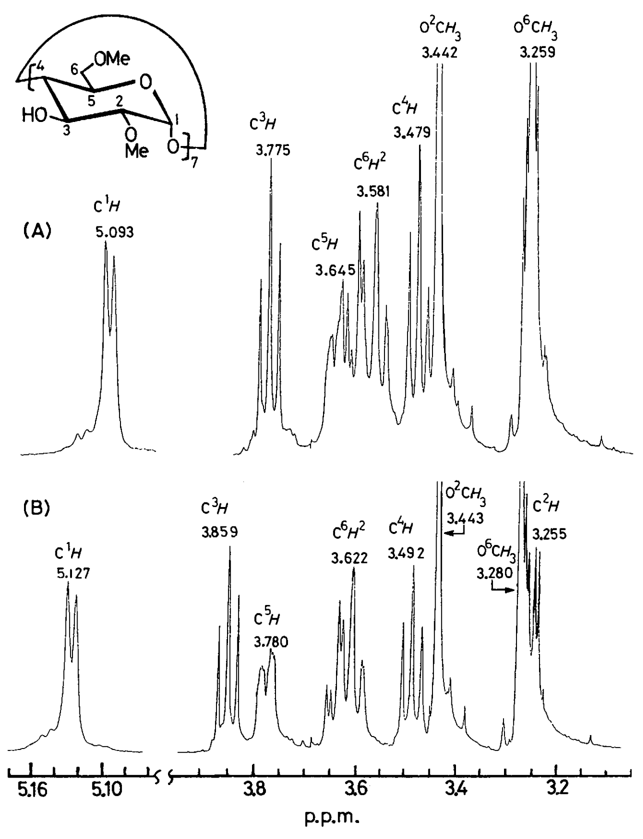

Figure 2. Partial 500 MHz ^{1}H n.m.r. spectra of 3.5 mM DM-β-CD in the (A) presence and (B) absence of 3.5 mM DMBA in deuteriated water (reference: H_2O in D_2O; 4.670 p.p.m.). The assignment is based on ref. 5.

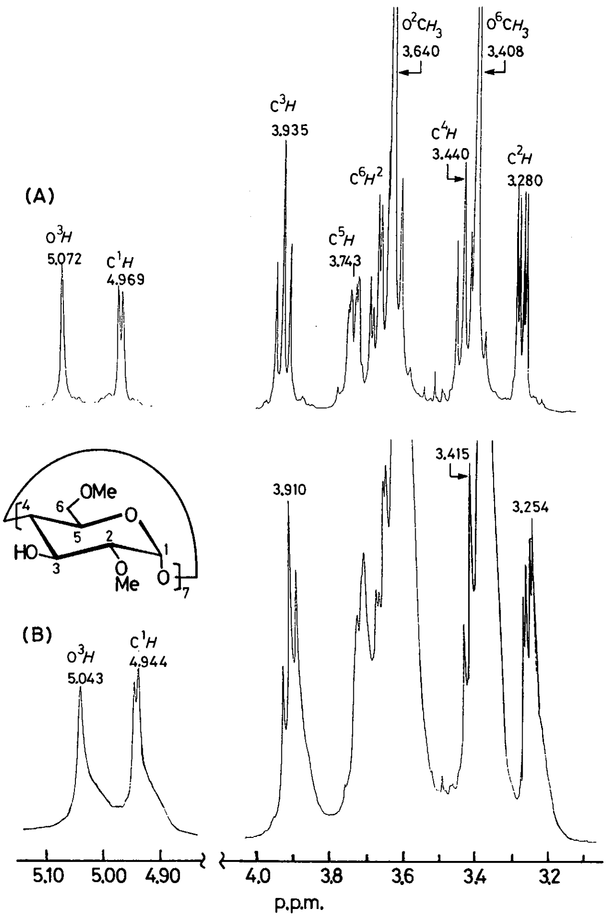

Figure 3. Partial 500 MHz ^{1}H n.m.r. spectra of 3.5 mM DM-β-CD in the (A) presence and (B) absence of 3.5 mM DMBA in deuteriated chloroform (reference: tetramethylsilane). The assignment is based on ref. 5.

supramolecular complex is formed in chloroform (*i.e.* a change of inclusion type owing to the change of solvent).

In order to interpret the i.c.d. spectra, the polarization directions of the u.v.-bands of the aromatic guest molecule must be clarified. For this purpose, we utilized a cholesteric mesophase made of cholesteryl nonanoate and cholesteryl chloride in a weight ratio of 7:3.[6] The helical sense of this mesophase is left-handed, so the long-axis polarized transitions of the aromatic molecules trapped in this mesophase produce a negative i.c.d., while the short-axis polarized transitions yield a positive i.c.d. signal.[6] As shown in Figure 1(A) curves a, DMBA produces a negative i.c.d. peak with a shoulder associated with the absorption maximum at 320 nm and another shoulder at 247 nm, indicating that these bands correspond to the long-axis polarized transitions. The spectra of DMBA were then recorded in the presence of DM-β-CD in water (curves b). A positive i.c.d. peak appeared at 310 nm, corresponding to the absorption peak. If we interprete this phenomenon on the basis of the assumption applied to CD complexes[1,3] that transitions polarized parallel to the CD axis produce a positive i.c.d., whereas those with perpendicular polarization produce a negative i.c.d., the inclusion is assigned as axial, as has been reported for the complexation between several *p*-disubstituted benzenes and β-CD.[1a] The absorption spectrum of DMBA in $CHCl_3$ [Figure 1(B)] is similar in shape to that in water [Figure 1(A)], while its i.c.d. spectrum in the presence of DM-β-CD is completely different, *i.e.*, the sign of the i.c.d. signal is negative throughout the entire range of the longest wavelength absorption envelope. Since, as confirmed here, the band is polarized along the long-axis of DMBA, the negative i.c.d. suggests that the orientation of the long-axis of DMBA is rather close to the normal of the CD axis. The complex stoicheiometry in this system was found to be 1:1, from the experiment carried out under the condition that [DM-β-CD] + [DMBA] = 2.4×10^{-3} M (const) (not shown). Using a cell of 1 mm pathlength, the observed $|[\theta]|$ = *ca.* 200° $dm^3\ mol^{-1}\ cm^{-1}$ at 294 nm when [DM-β-CD] = [DMBA].

In order to further conjecture the supramolecular structure in $CHCl_3$, three additional experiments were performed. Firstly, to a solution, which gave the spectra shown in Figure 1(B), an amount of MeOH was added and the i.c.d. spectra recorded. The intensity of the trough at 294 nm did not decrease even by the addition of 10 volume percent of MeOH, if volume expansion was taken into account. Secondly, an i.c.d. spectrum of DMBA was recorded in the presence of 2,3,6-trimethyl-β-CD (TM-β-CD),[5] which contains no OH groups, instead of DM-β-CD. The spectrum is shown as curve c in Figure 1(B). The shape observed differs completely from that found in the presence of DM-β-CD. Finally, complex formation constants between DMBA and DM-β-CD (103 M^{-1}) or TM-β-CD (75 M^{-1}) were obtained in chloroform using the Benesi–Hildebrand method.[7] From these observations, it is inferred that hydrogen bonding, between a carboxyl group of DMBA and hydroxy groups of DM-β-CD, is insignificant in producing the negative i.c.d. shown in Figure 1(B), but that another factor, such as a steric factor, causes the long-axis of DMBA to lie approximately normal to the DM-β-CD axis.

In addition, in order to see the supramolecular structure formation in $CHCl_3$ by another solution-state method, n.m.r. spectroscopy was adopted. In D_2O (Figure 2), all signals of DM-β-CD are shifted to higher fields by the inclusion of the guest molecule because of the shielding effect of an aromatic ring.[8] In particular, the shifts of protons at C^1, C^2, and C^5 are marked. As seen from the structure (inset of Figure 2), these protons are, respectively, in the middle, at the secondary, and the primary side of the CD cavity. Accordingly, the large chemical shift of these protons does not contradict with the deep axial inclusion deduced from Figure 1(A) (it has been shown that protons at C^3 and C^5 of CD shift to upper fields by the axial inclusion of aromatic molecules[8]). On the contrary, all n.m.r. spectral signals were shifted to lower fields by the complexation in $CDCl_3$ (Figure 3), albeit that the shifts were generally smaller than in D_2O. This indicates that the inclusion in $CDCl_3$ is essentially different from that in D_2O. It is difficult to determine how it is different. However, if, as can be inferred from the results in Figure 1, a DMBA molecule is to lie with its long axis normal to the axis of DM-β-CD, it may exist at the (wider) secondary site, since the shift of hydroxy protons is the largest of the proton shifts in $CDCl_3$.

The most plausible supramolecular structures conceivable from the data given are depicted in Figure 1. Two types of inclusion were realized by the change of solvent between one host and one guest molecule.

Received, 24th November 1988; Com. 8/04657C

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