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Preliminary communication

The large dipole moment of cyclomaltohexaose and its role in determining the guest orientation in inclusion complexes

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Cyclomalto-oligosaccharides (cyclodextrins, CDs) are cyclic oligosaccharides composed of at least six (1→4)-linked α-D-glucopyranosyl residues, which can form inclusion complexes with various types of compounds without any covalent bonds being formed[1–6]. Van der Waals forces, hydrogen bonding, and hydrophobic interaction have been proposed as driving forces for the formation of the inclusion complexes[1,2]. The van der Waals interaction includes both dipole–dipole interaction and London dispersion force, and the energetics[7,8] and thermodynamics[9–11] of the formation of CD complexes have been discussed. For dipole–dipole interactions to contribute to the formation of the inclusion complexes, the CD molecule must have a sizable permanent or induced dipole moment along the axis of its cavity, but no specific value has been reported. We now report the confirmation by MO calculation that cyclomaltohexaose (α-cyclodextrin, α-CD) has a large dipole moment and that, for some CD–guest systems, the host–guest dipole–dipole interaction determines the orientation of the guests in the complexes.

The calculations were based on *p*-nitrophenol (PNP), benzoic acid (BA), and *p*-hydroxybenzoic acid (PHBA) as the guests, but details are given only for the α-CD–PNP system. The dipole moments of α-CD and PNP were calculated separately by the CNDO/2 MO method[12], using the geometrical values reported for the α-CD–PNP inclusion-complex determined by X-ray diffraction[13]. In the crystal, the *p*-nitrophenyl group of PNP is located in the cavity of α-CD, and the phenolic hydroxyl group protrudes from the side of the secondary hydroxyl groups of α-CD (Fig. 1). The geometry in the crystalline state is the same as that in solution[14,15].

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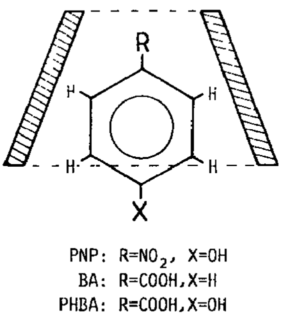

Fig. 1. Representation of the inclusion complex between α-CD and some benzene derivatives.

The results of the calculations are shown in Fig. 2. The α-CD molecule has a remarkably large dipole moment of 13.5 D (12.4 D[16] according to the molecular-mechanics MM2 calculation[17]), which is directed from the side of the secondary hydroxyl groups (wider rim) towards the side of the primary hydroxyl groups (narrower rim). Since the cavity of α-CD in the crystalline α-CD–PNP complex deviates slightly from six-fold symmetry, the dipole moment vector also deviates slightly from the six-fold symmetry pseudo-axis of the cavity. The dipole moment vector and the assumed cavity axis of six-fold symmetry of α-CD make an angle of 153°. The dipole moment of PNP is 5.0 D and is directed away from the nitro group towards the phenolic hydroxyl group. Thus, in the α-CD–PNP inclusion-complex in both the crystalline state and aqueous solution, the vectors for the dipole moments of the α-CD and PNP molecules are nearly antiparallel.

According to the geometry of the α-CD–BA complex in solution[11] and the α-CD–PHBA complex in the crystalline state[13], the dipole moments of these guests are also nearly antiparallel to that of α-CD (Fig. 2).

These results imply that the dipole–dipole interaction of the host α-CD and

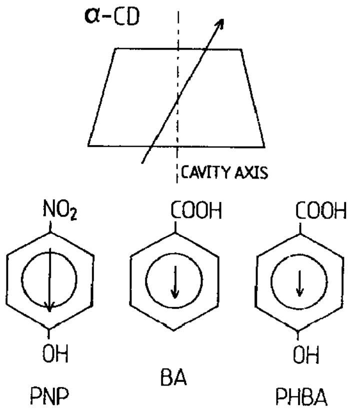

Fig. 2. The dipole moments of α-CD and some guests. The arrows represent the dipole moment vectors. The magnitudes are 13.5, 5.0, 1.5, and 1.1 D for α-CD, PNP, BA, and PHBA, respectively.

the guest PNP plays an essential role in stabilising the inclusion complex and determining the host–guest orientation.

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