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Crystal Structures of Hexakis(2,6-di-*O*-methyl)-α-cyclodextrin Complexes with Iodine and 1-Propanol

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Crystal structures of the title compounds were determined by the X-ray analysis. The host molecule in the both complexes has a round shape, which is maintained by intramolecular O(3)-H···O(2) hydrogen bonds, and arranged in a cage-type packing mode. The guest molecules are included within the cavity of the macrocyclic ring and situated at the wider O(2), O(3) side of the cavity.

Recent X-ray studies of methylated cyclodextrin complexes have shown that the methylation markedly affects the geometry of host-guest interaction because of the change in size and shape of the host cavity.1) Heptakis(2,6-di-*O*-methyl)-β-cyclodextrin, which has a round and rather symmetrical shape like parent β-cyclodextrin, forms a 1:1 crystalline complex with *p*-iodophenol.2) In this complex, the guest molecule is not included within the host cavity, but located in a space between host molecules. The macrocyclic ring of permethylated cyclodextrins is remarkably distorted because of the incapability of forming intramolecular hydrogen bonds and the steric hindrance involving methyl groups. Permethylated β-cyclodextrin includes *p*-iodophenol within its cavity, but the inclusion feature differs from the β-cyclodextrin–*p*-iodophenol complex.3) X-Ray analyses of permethylated α-cyclodextrin complexes1,4) have shown that the host molecule includes mono- and disubstituted benzenes with the host-guest geometry different from the corresponding α-cyclodextrin complexes. On the other hand, the macrocyclic conformation and host-guest interaction are yet unknown for hexakis(2,6-di-*O*-methyl)-α-cyclodextrin (dimethyl-α-CDx) complexes. In this paper, we briefly describe the crystal and molecular structure of the dimethyl-α-CDx complexes with iodine and 1-propanol.

Dimethyl-α-CDx was purchased from Toshin Chemical Co. Ltd., and recrystallized from hot water before use. Brown crystals of the dimethyl-α-CDx–iodine complex were obtained by standing an iodine-saturated aqueous solution of dimethyl-α-CDx at 50 °C. The dimethyl-α-CDx–1-propanol complex was crystallixed at 50 °C from a 20% 1-propanol solution by the slow evaporation. Lattice parameters and diffraction intensities were measured at room temperature on a Nicolet P3/F diffractometer with graphite-monochromated CuKα radiation. Crystal data were as follows: (1) iodine complex, $C_{36}H_{84}O_{30}\cdot I_2$, F.W.=1259.9, monoclinic, space group $P2_1$, $Z=2$, $a=14.124(2)$ $b=10.667(2)$, $c=21.443(3)$ Å, $\beta=106.29(1)°$, $V=3103.9$ Å^3, $D_x=1.348$ g·cm^{-3}, (2) 1-propanol complex, $C_{36}H_{84}O_{30}\cdot C_3H_8O$, F.W.=1057.1, monoclinic, space group $P2_1$, $Z=2$, $a=14.136(2)$, $b=10.680(1)$, $c=21.479(2)$ Å, $\beta=106.00(1)°$, $V=3117.1$ Å^3, $D_x=1.126$ g·cm^{-3}.

The first attempt to solve the structure of the iodine complex by the heavy atom method was unsuccessful because of the low resolution of the electron-density map. The structure of the 1-propanol complex was solved by the inspection of a Patterson map and the R-map method combined with the rigid-body least-squares technique, and refined by the block-diagonal least-squares method to the *R*-values of 0.058 for 4299 reflections. A set of atomic coordinates of dimethyl-α-CDx of the 1-propanol complex was used to solve the structure of the iodine complex which was refined to the *R*-value of 0.077 for 3584 reflections.5)

The structure and numbering scheme of both complexes are shown in Fig. 1. The dimethyl-α-CDx molecule is in the round shape and more symmetrical than permethylated α-CDx. Between the two complexes, no significant difference is found in the conformation of the host molecule. All pyranose rings are in the $^{4}C_{1}$ chair conformation. Conformational differences among 2,6-di-*O*-methylglucose residues are observed in C(6)-O(6) bonds and methoxyl groups. The C(6)-O(6) bond in the G3 and G6 residues are in a *gauche-trans* conformation, while the other residues show a *gauche-gauche* conformation. The O(6)-C(8) bond in the G6 residue turns to the inside of the macrocycle and caps the O(6) side of the host cavity. The other O(6)-C(8) and all O(2)-C(7) bonds point away from the center of the macrocyclic ring. Geometrical data describing the macrocyclic conformation are given in Table 1. Six glycosidic oxygen atoms, which are coplanar, form a nearly regular hexagon with the radius of 4.25 Å. The average glycosidic oxygen angle (118.8°) and O(4)···O(4') distance (4.25 Å) between adjacent residues are in good agreement with those of α-CDx (119° and 4.24 Å, respectively).6) All 2,6-di-*O*-methylglucose residues incline with their O(6) side turning to the inside of the dimethyl-α-CDx ring. The tilt-angle shows that the G3 and G6 residues incline much more than the other residues. The O(2)···O(3') distance between adjacent residues is in the range 2.87-3.16 Å. These distances are similar to those found in, α-CDx, but

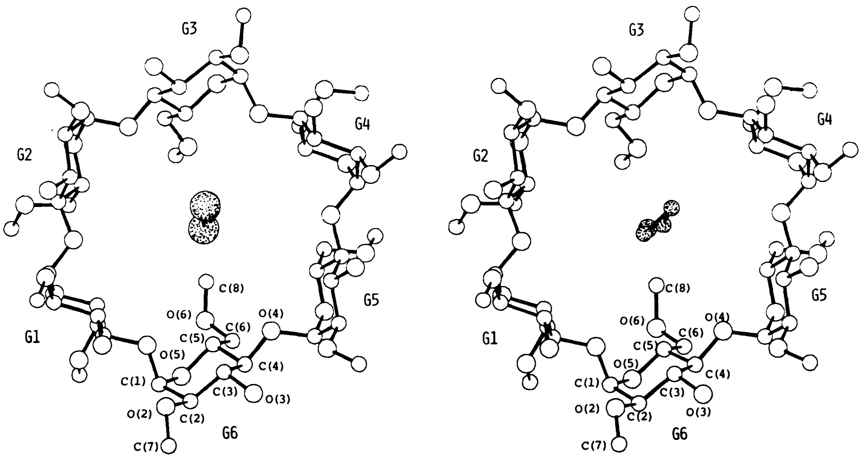

Fig. 1. Structure and numbering scheme of the dimethyl-α-CDx complexes with iodine (left) and 1-propanol (right). The guest molecules are shaded.

Table 1. Geometrical data describing the macrocyclic conformation of dimethyl-α-CDx in the 1-propanol complex 1)

	I 2)	II 3)	III 4)	IV 5)	V 6)		VI 7)	
G1	119.3	4.30	8.0	-0.021	O(4,G1)-O(4,G2)	4.26	O(2,G1)-O(3,G2)	2.92
G2	119.1	4.27	11.4	0.148	O(4,G2)-O(4,G3)	4.20	O(2,G2)-O(3,G3)	2.87
G3	118.3	4.17	21.3	-0.103	O(4,G3)-O(4,G4)	4.36	O(2,G3)-O(3,G4)	3.07
G4	120.4	4.31	11.9	-0.019	O(4,G4)-O(4,G5)	4.15	O(2,G4)-O(3,G5)	3.17
G5	118.4	4.29	14.3	0.153	O(4,G5)-O(4,G6)	4.34	O(2,G5)-O(3,G6)	2.88
G6	117.5	4.15	20.4	-0.130	O(4,G6)-O(4,G1)	4.20	O(2,G6)-O(3,G1)	2.96
Average	118.8	4.25	14.6	0.111 8)		4.25		2.98

1) The estimated standard deviations of I, II, V, and VI are 0.6°, 0.01 Å, 0.01 Å, and 0.01 Å, respectively. 2) The glycosidic oxygen angle. 3) The distance from the center of gravity of the six O(4) atoms to each O(4) atom. 4) The tilt-angle defined by the angle between the O(4) plane and the plane through C(1), C(4), O(4), and O(4') atoms of each residue. 5) The deviation of atoms from the O(4) plane. 6) The O(4)···O(4') distance between adjacent residues. 7) The O(2)···O(3') distance between adjacent residues. 8) The root-mean-square deviation.

shorter than the corresponding distances of permethylated α-CDx (3.2-3.5 Å).1) The O(3)H hydroxyl groups form O(3)-H···O(2) hydrogen bonds with an adjacent O(2) atom. These intramolecular hydrogen bonds impose conformational restrictions on the macrocyclic ring and maintain the round structure. When these hydrogen bonds are blocked by the permethylation, a marked distortion of the macrocyclic ring occurs with the increase of the O(2)···O(3') distance and tilt-angle.

Iodine and 1-propanol molecules are included within the host cavity as shown in Fig. 1. They are located at the center of the ring composed of six C(3)H methine groups. α-CDx also includes iodine and 1-propanol in the crystalline state,6,7) but the inclusion feature differs from the dimethyl-α-CDx complexes. The guest molecules in the α-CDx complexes are located at the center of the C(5)H methine ring. Though the methylation extends the host cavity of α-CDx, the O(6) side of the cavity becomes narrower as indicated by the tilt-angles. As the result, the guest molecules are shifted towards the O(2), O(3) side, compared with the guests in the α-CDx complexes. The 1-propanol molecule in the α-CDx complex is hydrogen-bonded to a primary hydroxyl group of α-CDx. No such host-guest hydrogen bond can be formed in the dimethyl-α-CDx complex since the hydroxyl group of 1-propanol is located at the center of the dimethyl-α-CDx cavity.

The crystal structure of the iodine complex is shown in Fig. 2. Dimethyl-α-CDx molecules are stacked along the b axis. Since the dimethyl-α-CDx ring is so tilted with respect to the b axis, which makes an angle of 56.6° with the O(4) plane, adjacent two dimethyl-α-CDx molecules are laterally shifted to each other by about half a molecule. Thus the dimethyl-α-CDx molecules do not form a continuous channel, but the host cavity is isolated like a closed cage. The both sides of the cavity are closed by a symmetry-related molecule. Although a similar cage-type packing feature is widely observed in cyclodextrin complexes with guests which are sufficiently small to be enclosed within the host cavity,$^{8)}$ this is the first observation of a typical cage-type packing in methylated cyclodextrin complexes.

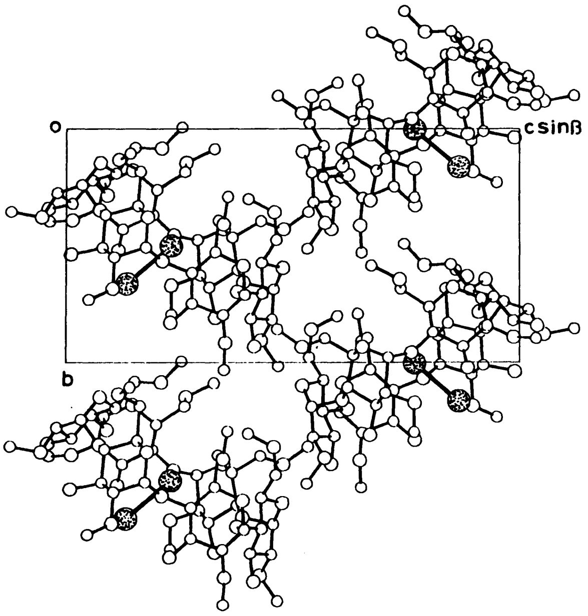

Fig. 2. The crystal structure of the iodine complex viewed along the a axis. Iodine molecules are shaded.

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