The Structure of the Cyclodextrin Complex. XV. Crystal Structure of Hexakis-(2,3,6-tri-*O*-methyl)-α-cyclodextrin–*p*-Nitrophenol (1 : 1) Complex Monohydrate

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The crystal structure of the hexakis(2,3,6-tri-*O*-methyl)-α-cyclodextrin (abbreviated to methyl-α-CDx) complex with *p*-nitrophenol, $C_{54}H_{96}O_{30}\cdot C_6H_5NO_2\cdot H_2O$, was investigated by the X-ray method. The crystal is monoclinic, the space group being $P2_1$ with $Z=2$; the cell dimensions are $a=11.307(1)$, $b=14.578(1)$, $c=22.118(2)$ Å, and $\beta=93.62(1)°$. The structure was determined by means of the Patterson map and the trial-and-error method combined with the rigid-body least-squares technique, and refined by the block-diagonal least-squares method to the final *R*-value of 0.048 for 4976 reflections ($\sin\theta/\lambda<0.54$). The methyl-α-CDx molecule has the shape of a truncated hexagonal cone, into which the *p*-nitrophenol molecule is inserted. The phenolic hydroxyl group is located at the center of the methyl-α-CDx cavity, while the nitro group protrudes outside from the base-side of the host cone and is in contact with the adjacent methyl-α-CDx molecule. The water molecule, which is also located within the cavity, links the methyl-α-CDx and *p*-nitrophenol molecules by hydrogen bonds. Methyl-α-CDx molecules are stacked along the crystallographic a axis in a heat-to-tail mode to form a channel-type structure.

Crystal structures of cyclodextrins and their inclusion complexes have been intensively investigated, as the crystal structure analysis is a most powerful tool to visualize how a guest molecule is included within the cavity of macrocyclic oligosaccharides. We have shown the structures of α-cyclodextrin complexes with mono- and disubstituted benzenes, and demonstrated that the guest molecules are bound inside the α-cyclodextrin ring or situated within a column which is formed by the stack of α-cyclodextrin rings. In the complexes with monosubstituted benzenes,[1,2] the phenyl group is located inside the host cavity, but the substituent group protrudes from the secondary hydroxyl side of the α-cyclodextrin ring. When disubstituted benzenes are included,[3-5] the bulkier substituent is inserted into the α-cyclodextrin ring, while the smaller substituent is located outside the cavity. Such characteristics found in the inclusion geometry have been interpreted mainly in terms of the stereospecific relationship between α-cyclodextrin and guest molecules.

Permethylated α-cyclodextrin, hexakis(2,3,6-tri-*O*-methyl)-α-cyclodextrin (abbreviated to methyl-α-CDx), also forms inclusion complexes. It is quite interesting to compare structures of these complexes with those of α-cyclodextrin complexes in respect to the macrocyclic conformation and geometry of inclusion. Previously, we have shown that *p*-iodoaniline[6] and benzaldehyde[7] are included in the methyl-α-CDx cavity in a manner which is quite different from that found in the corresponding α-cyclodextrin complexes. This paper will describe the crystal structure of the methyl-α-CDx complex with *p*-nitrophenol, and will discuss its comparison with other methyl-α-CDx complexes and the α-cyclodextrin–*p*-nitrophenol complex.[4]

Experimental

An aqueous solution, which contains methyl-α-CDx and *p*-nitrophenol in a 1 : 1 molar ratio, was allowed to stand at 40 °C. The methyl-α-CDx–*p*-nitrophenol (1 : 1) complex monohydrate was crystallized in a prismatic form. Lattice parameters and reflection intensities were measured on a Nicolet P3/F diffractometer with graphite-monochromated Cu *Kα* radiation. By using the θ-2θ scan mode, 4976 independent reflections with $|F_o|\geq 3\sigma(F)$ were obtained up to 118° in 2θ. No corrections were made for absorption and extinction effects.

Crystal Data: $C_{54}H_{96}O_{30}\cdot C_6H_5NO_3\cdot H_2O$; *F. W.*=1382.5; monoclinic; space group $P2_1$; $Z=2$; $a=11.307(1)$, $b=14.578(1)$, $c=22.118(2)$ Å, $\beta=93.62(1)°$; $V=3638.6$ Å^3; $D_x=1.262$, $D_m=1.25$ g cm^{-3}.

Determination and Refinement of the Structure

A Patterson map showed that the *pseudo* hexagonal axis of the methyl-α-CDx molecule makes an angle of *ca.* 10° with the crystallographic a axis. The rotational parameters around this molecular axis and translational parameters along the a and c axes were determined by the trial-and-error method. After the correction of positional and orientational parameters of each 2,3,6-tri-*O*-methylglucose residue by the rigid-body least-squares technique, the atomic parameters of methyl-α-CDx were refined by the block-diagonal least-squares method. Then, a Fourier map was calculated, and *p*-nitrophenol and water molecules were found on the map. Hydrogen atoms were found on a difference-Fourier

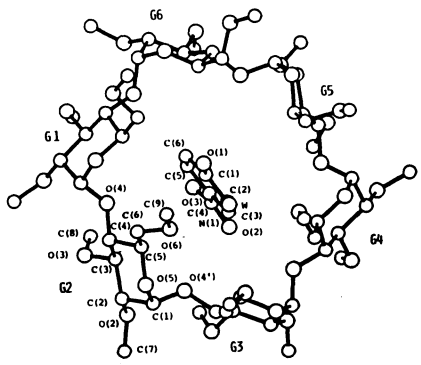

Fig. 1. The numbering scheme of the methyl-α-CDx–*p*-nitrophenol complex monohydrate. The water molecule is denoted by W.

Table 1. Atomic coordinates ($\times 10^4$) and $B_{eq}^{a)}$ values of non-hydrogen atoms

	x	y	z	B_{eq}/Å^2		x	y	z	B_{eq}/Å^2
C(1,G1)	852(5)	2584(4)	4825(2)	5.03	C(7,G4)	1965(7)	2064(6)	-937(3)	7.78
C(2,G1)	1594(5)	1816(4)	5116(2)	5.12	C(8,G4)	4214(6)	3908(6)	192(4)	8.87
C(3,G1)	1780(5)	1074(4)	4648(2)	4.49	C(9,G4)	-2822(6)	4342(7)	1203(4)	8.50
C(4,G1)	610(5)	747(4)	4359(2)	4.45	O(2,G4)	2394(3)	2467(3)	-376(2)	5.48
C(5,G1)	-167(5)	1556(4)	4132(2)	4.63	O(3,G4)	3030(3)	4228(3)	88(2)	5.67
C(6,G1)	-1436(5)	1313(5)	3925(3)	5.63	O(4,G4)	1853(3)	4701(3)	1159(2)	4.26
C(7,G1)	2672(8)	2685(6)	5881(4)	8.78	O(5,G4)	-269(3)	3188(3)	337(2)	4.19
C(8,G1)	3588(6)	223(6)	4763(4)	7.47	O(6,G4)	-1707(3)	3920(3)	1225(2)	5.57
C(9,G1)	-3155(6)	544(7)	4165(3)	8.42	C(1,G5)	508(5)	-586(4)	1394(2)	4.78
O(2,G1)	2722(4)	2117(3)	5351(2)	6.20	C(2,G5)	1493(5)	-474(4)	970(3)	5.25
O(3,G1)	2392(4)	316(3)	4923(2)	5.73	C(3,G5)	1820(5)	532(4)	880(2)	4.66
O(4,G1)	879(3)	184(2)	3847(2)	4.24	C(4,G5)	700(5)	1071(4)	686(2)	4.42
O(5,G1)	-258(3)	2116(3)	4616(2)	4.81	C(5,G5)	-231(5)	925(4)	1145(2)	4.50
O(6,G1)	-1965(4)	768(4)	4365(2)	6.42	C(6,G5)	-1396(5)	1406(4)	1027(3)	5.87
C(1,G2)	1925(6)	5586(4)	3604(3)	5.25	C(7,G5)	2940(11)	-1646(8)	802(6)	14.42
C(2,G2)	2870(5)	5258(4)	4083(3)	5.58	C(8,G5)	3731(6)	1005(6)	621(4)	8.01
C(3,G2)	2751(5)	4230(4)	4173(3)	5.05	C(9,G5)	-3061(6)	1460(8)	347(4)	10.10
C(4,G2)	1508(5)	3976(4)	4332(2)	4.53	O(2,G5)	2516(4)	-947(3)	1192(2)	6.99
C(5,G2)	610(5)	4354(4)	3837(2)	4.80	O(3,G5)	2646(3)	586(3)	419(2)	5.50
C(6,G2)	-660(5)	4219(5)	3971(3)	5.76	O(4,G5)	1030(3)	2017(3)	651(2)	4.18
C(7,G2)	4400(8)	6366(6)	3995(4)	9.17	O(5,G5)	-479(3)	-52(3)	1172(2)	4.82
C(8,G2)	4384(6)	3267(6)	4495(4)	7.60	O(6,G5)	-183(4)	1216(4)	442(2)	6.87
C(9,G2)	-2598(6)	4168(8)	3561(4)	9.78	C(1,G6)	307(5)	-673(4)	3774(2)	4.73
O(2,G2)	4027(4)	5441(3)	3938(2)	6.63	C(2,G6)	1174(5)	-1363(4)	3528(2)	4.59
O(3,G2)	3574(3)	3949(3)	4655(2)	5.98	C(3,G6)	1539(5)	-1070(4)	2910(3)	4.61
O(4,G2)	1448(3)	2996(2)	4353(2)	4.43	C(4,G6)	451(5)	-854(4)	2475(2)	4.46
O(5,G2)	785(3)	5336(3)	3785(2)	4.95	C(5,G6)	-466(5)	-283(4)	2782(2)	4.54
O(6,G2)	-1382(4)	4299(4)	3445(2)	7.28	C(6,G6)	-1673(5)	-225(5)	2434(3)	5.82
C(1,G3)	1888(5)	5661(4)	1206(2)	4.54	C(7,G6)	2047(7)	-1903(5)	4469(3)	6.93
C(2,G3)	3069(5)	5924(4)	1526(3)	5.13	C(8,G6)	3443(6)	-1583(5)	2629(3)	6.82
C(3,G3)	3168(5)	5529(4)	2162(3)	4.80	C(9,G6)	-3206(8)	-1052(9)	1920(7)	14.25
C(4,G3)	2103(5)	5785(4)	2515(2)	4.80	O(2,G6)	2233(3)	-1485(3)	3899(2)	5.35
C(5,G3)	929(5)	5640(4)	2145(2)	4.79	O(3,G6)	2204(3)	-1776(3)	2650(2)	5.01
C(6,G3)	-90(5)	6251(7)	2462(3)	8.37	O(4,G6)	902(3)	-335(3)	1984(1)	4.16
C(7,G3)	4944(6)	6244(6)	1133(4)	9.44	O(5,G6)	-706(3)	-634(3)	3370(2)	4.51
C(8,G3)	5048(6)	5174(7)	2634(4)	9.05	O(6,G6)	-2098(4)	-1101(4)	2293(3)	8.21
C(9,G3)	-2005(8)	6461(8)	2503(4)	11.92	C(1,NP)	1854(6)	2147(5)	2601(3)	6.44
O(2,G3)	4014(4)	5620(4)	1187(2)	6.60	C(2,NP)	2312(7)	2789(5)	2224(3)	7.40
O(3,G3)	4205(4)	5873(3)	2483(2)	6.51	C(3,NP)	3537(7)	2794(6)	2142(4)	8.93
O(4,G3)	2161(3)	5205(3)	3041(2)	4.54	C(4,NP)	4241(7)	2144(6)	2424(4)	9.66
O(5,G3)	965(3)	6019(3)	1543(2)	4.62	C(5,NP)	3814(8)	1494(6)	2808(4)	9.99
O(6,G3)	-1099(4)	5958(4)	2175(2)	8.26	C(6,NP)	2598(7)	1502(5)	2893(4)	7.95
C(1,G4)	553(4)	2538(4)	157(2)	4.27	N(1,NP)	5529(8)	2116(8)	2318(6)	14.47
C(2,G4)	1544(5)	3057(4)	-128(2)	4.82	O(1,NP)	687(4)	2105(4)	2699(2)	7.74
C(3,G4)	2175(4)	3667(4)	347(2)	4.44	O(2,NP)	5887(7)	2701(8)	2007(6)	23.70
C(4,G4)	1274(4)	4314(4)	624(2)	4.20	O(3,NP)	6126(7)	1580(8)	2592(6)	22.04
C(5,G4)	171(4)	3785(4)	808(2)	4.43	O(W)	-634(4)	3481(4)	2360(2)	7.81
C(6,G4)	-848(5)	4431(4)	922(2)	4.76					

a) $B_{eq}=8\pi^2(u_1^2+u_2^2+u_3^2)/3$, where u_i is the root-mean-square deviation in the i-th principal axis of the thermal ellipsoid.

map in the course of further refinement. The block-diagonal least-squares refinement including 100 hydrogen atoms achieved the R-value of 0.048. The quantity minimized was $\sum w(|F_o|-|F_c|)^2$ with $w=1.0$ for all the reflections. The atomic scattering factors were taken from the "International Tables for X-Ray Crystallography."[8] Final atomic coordinates and B_{eq} values of non-hydrogen atoms are listed in Table 1. Tables of observed and calculated structure factors, anisotropic temperature factors of non-hydrogen atoms, atomic parameters of hydrogen atoms, and bond distances, bond angles, and conformation angles of methyl-α-CDx are kept at The Chemical Society of Japan (Document No. 8258). The calculations were carried out on a FACOM M-200 computer at the RIPS Center, Tsukuba.

Description and Discussion of the Structure

Outline of the Structure. The numbering scheme of the complex is shown in Fig. 1. A space-filling representation of the inclusion feature is given in Fig. 2. The hydroxyl group of *p*-nitrophenol is inserted into the methyl-α-CDx ring, while the nitro group protrudes outside from the O(2), O(3) methoxyl side of the methyl-α-CDx ring. The water molecule is located at the O(6) side of the cavity, forming hydrogen bonds with two O(6) atoms of methyl-α-CDx and the phenolic hydroxyl group. Methyl-α-CDx molecules are stacked along the crystallographic a axis to form a head-to-tail channel-type structure as shown in Fig. 3.

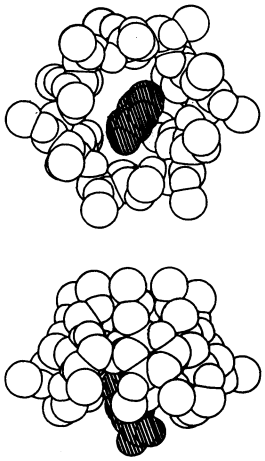

Fig. 2. A space-filling representation of the inclusion feature.

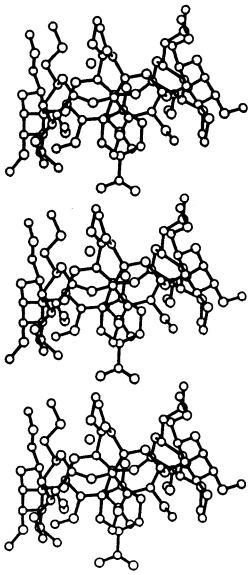

Fig. 3. The stacking feature of the methyl-α-CDx complex.

Conformation of Methyl-α-CDx. Average bond distances and angles over six 2,3,6-tri-*O*-methylglucose residues are shown in Fig. 4. Geometrical data for the macrocyclic ring are given in Tables 2 and 3. Except for the orientation of C(6)–O(6) bonds, the six 2,3,6-tri-*O*-methylglucose residues are in the same conformation. The C(6)–O(6) bonds in the G2, G3, and G4 residues take *gauche-trans* conformations about the C(5)–C(6) bonds, while the others have *gauche-gauche* conformations. Each O(6)–C(9) bond is *trans* to the corresponding C(5)–C(6) bond. The six O(2)–C(7) bonds are oriented outside the methyl-α-CDx ring, the six O(3)–C(8) bonds turning inside the ring. The conformations of the pyranose rings in cyclodextrins have been discussed in terms of the torsion-angle index and distance between glycosidic oxygen atoms.[4] The values of the torsion-angle index, which are in the range 120.4—144.4°, are similar to those found in the α-cyclodextrin–*p*-nitrophenol complex. The O(4)···O(4) distances between adjacent residues range from 4.16 to 4.53 Å. The average value of 4.31 Å is somewhat larger than the corresponding value (4.24 Å) found in the α-cyclodextrin complex. French and Murphy[9] have shown that there is a linear correlation between the O(4)···O(4) distance and the torsion-angle index in mono- and oligosaccharides. The same relationship has been also found in α-cyclodextrin complexes.[4] But, as shown in Fig. 5, no such correlation appears in the methyl-α-CDx complexes. This suggests that the methyl groups affect the conformation of the pyranose ring so as to break the linear correlation between the O(4)···O(4) distance and the torsion-angle index.

The six glycosidic oxygen atoms form an elliptically-distorted hexagon. The longest diagonal is found parallel to the guest plane. These O(4) atoms are roughly coplanar with a maximum deviation of 0.202 Å from their least-squares plane. This indicates that the planarity of the O(4) hexagon is not significantly affected by the methylation, since the corresponding maximum deviation in the α-cyclodextrin–*p*-nitrophenol complex is 0.163 Å. The O(2)···O(3) distances between the adjacent residues are in the range 3.26—3.48 Å, which are markedly larger than those found in the α-cyclodextrin–*p*-nitrophenol complex (2.65—3.07 Å). These large

TABLE 2. GEOMETRICAL DATA FOR METHYL-α-CDx

Distance	*l*/Å	Distance	*l*/Å
I. O(4)···O(4) distance			
O(4,G1)···O(4,G2)	4.29(1)	O(4,G5)···O(4,G6)	4.53(1)
O(4,G1)···O(4,G6)	4.19(1)	O(4,G1)···O(4,G4)	8.99(1)
O(4,G2)···O(4,G3)	4.44(1)	O)4,G2)···O(4,G5)	8.46(1)
O(4,G3)···O(4,G4)	4.22(1)	O(4,G3)···O(4,G6)	8.50(1)
O(4,G4)···O(4,G5)	4.16(1)		
II. O(2)···O(3) distance			
O(2,G1)···O(3,G2)	3.26(1)	O(2,G3)···O(3,G4)	3.30(1)
O(2,G6)···O(3,G1)	3.45(1)	O(2,G4)···O(3,G5)	3.27(1)
O(2,G2)···O(3,G3)	3.30(1)	O(2,G5)···O(3,G6)	3.48(1)
III. O(2)···C(8) distance			
O(2,G1)···C(8,G1)	3.25(2)	O(2,G1)···C(8,G2)	3.21(2)
O(2,G2)···C(8,G2)	3.43(2)	O(2,G2)···C(8,G3)	3.21(2)
O(2,G3)···C(8,G3)	3.42(2)	O(2,G3)···C(8,G4)	3.33(2)
O(2,G4)···C(8,G4)	3.17(2)	O(2,G4)···C(8,G5)	3.37(2)
O(2,G5)···C(8,G5)	3.45(2)	O(2,G5)···C(8,G6)	3.41(2)
O(2,G6)···C(8,G6)	3.22(2)	O(2,G6)···C(8,G1)	3.45(2)

IV. Tilt-angle[a] and torsion-angle index[b]

Residue	Tilt-angle ϕ/°	Torsion-angle index ϕ/°
G1	25.9	140.3
G2	16.0	124.4
G3	9.3	140.1
G4	28.1	148.3
G5	14.8	120.4
G6	18.7	144.4

a) The tilt-angle is defined as the angle made by the plane through six O(4) atoms and the plane through O(4′), C(1), C(2), and O(4) of each 2,3,6-tri-*O*-methylglucose residue. b) The torsion-angle index is defined as follows: $|\phi(C(1)-C(2))|+|\phi(C(2)-C(3))|+|\phi(C(5)-O(5))|+|\phi(O(5)-C(1))|-|\phi(C(3)-C(4))|-|\phi(C(4)-C(5))|$, where $\phi(C(1)-C(2))$ is the conformation angle of O(5)–C(1)–C(2)–C(3).

Table 3. Least-squares plane and deviation (d/Å) of atoms from the plane

The plane equation is of the $AX+BY+CZ=D$ form, where X, Y, and Z are the coordinates in Å units along the a, b, and c* axes, respectively.

I. The plane through six O(4) atoms			
$0.984X-0.174Y+0.042Z=0$ 799			
O(4,G1)	−0.037	O(4,G4)	0.019
O(4,G2)	−0.140	O(4,G5)	−0.194
O(4,G3)	0.150	O(4,G6)	0.202
II. The benzene plane			
$0.110X+0.620Y+0.777Z=6.594$			
C(1,NP)	−0.002	C(6,NP)	0.004
C(2,NP)	−0.005	N(1,NP)	−0.054
C(3,NP)	0.011	O(1,NP)	−0.019
C(4,NP)	−0.010	O(2,NP)	−0.009
C(5,NP)	0.002	O(3,NP)	0.001

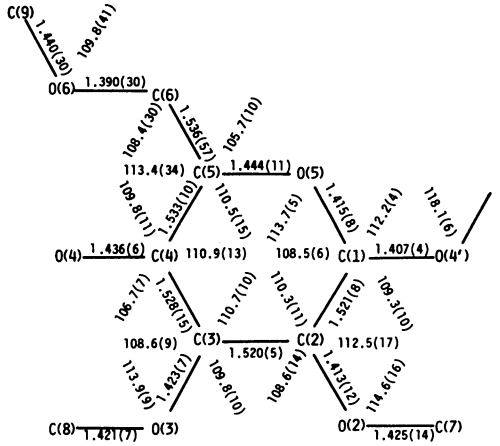

Fig. 4. Average bond distances (l/Å) and angles (ϕ/°) over six 2,3,6-tri-*O*-methylglucose residues. Standard deviations in parentheses were estimated according to the equation: $\sigma=[\sum_{i=1}^{6}(x_i-\bar{x})^2/5]^{1/2}$, where x_i refers to the bond distance or angle in the i-th residue and $\bar{x}$ is the average value.

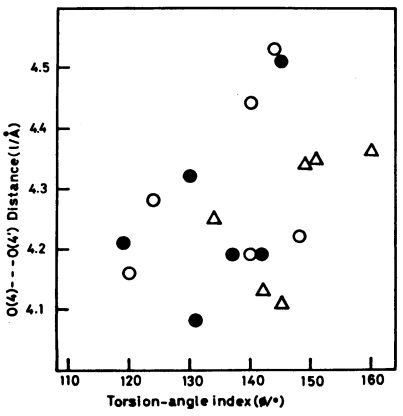

Fig. 5. Plot of the O(4)···O(4′) distance against the torsion-angle index in the methyl-α-CDx complexes with *p*-nitrophenol (○), *p*-iodoaniline (△), and benzaldehyde (●).

O(2)···O(3) distances may be ascribed to the repulsive interaction between the C(8) methyl group and two adjacent O(2) atoms. The C(8) methyl group is nearly equidistant from these two O(2) atoms; the C(8)···O(2) distances of these two kinds are in the ranges 3.17—3.45 Å and 3.21—3.45 Å, respectively. Such repulsive interaction also inclines 2,3,6-tri-*O*-methylglucose residues in such a way that the O(6) side of the cavity becomes smaller. The tilt-angles range from 9.3° to 28.1°. The average value of 18.8° is larger than the corresponding values of 16.7° in the *p*-iodoaniline complex[6] and 17.7° in the benzaldehyde complex.[7] This suggests that the methyl-α-CDx ring changes its macrocyclic conformation so as to fit itself to the shape of included group or molecule.

Methyl-α-CDx–Guest Interaction. Bond distances and angles in *p*-nitrophenol and intermolecular distances between the methyl-α-CDx and guest molecules are given in Fig. 6. The hydroxyphenyl group of the guest is inserted into the methyl-α-CDx ring. The phenolic hydroxyl group is located nearly at the center of the cavity, while the benzene ring is surrounded by O(2)-C(7)H_3 and O(3)C(8)H_3 methoxyl groups. The nitro group, which protrudes outside the ring from the O(2), O(3) side of methyl-α-CDx, is in contact with methyl groups of the next methyl-α-CDx molecule. The guest plane is nearly perpendicular to the O(4)-hexagon plane, making an angle of 89.1°. The molecular axis of *p*-nitrophenol deviates from the normal of the O(4)-hexagon plane; the nitro group approaches to the G3 and G4 residues. As a result, the C(6,NP)–H bond is oriented toward the C(3)H methine groups of the G1 and G6 residues, while the C(2,NP)H group is in contact with the C(5)H methine groups of the G3 and G4 residues. All the intermolecular hydrogen-hydrogen distances are greater than 2.35 Å, as shown in Fig. 6. This indicates that the benzene ring has weak van der Waals contacts with the atoms which constitute the interior surface of the methyl-α-CDx cavity.

The host-guest interaction in the present complex is quite different from that found in the α-cyclodextrin–*p*-nitrophenol complex,[4] in which the guest molecule is

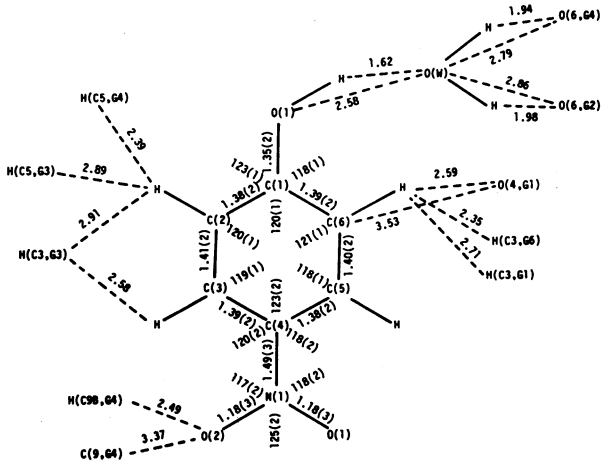

Fig. 6. Bond distances (l/Å) and angles (ϕ/°) in *p*-nitrophenol and intermolecular distances (l/Å) among methyl-α-CDx, water, and *p*-nitrophenol molecules.

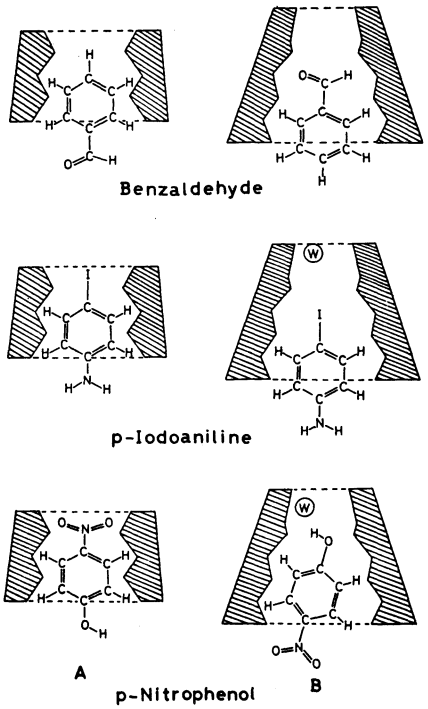

Fig. 7. Schematic drawings of the inclusion features of α-cyclodextrin (A) and methyl-α-CDx (B) complexes. Water molecules are denoted by W.

included upside down. As shown in Fig. 7, the nitrophenyl group is tightly bound in the α-cyclodextrin cavity, while the hydroxyl group protrudes from the O(2), O(3) hydroxyl side of the cavity, forming hydrogen bonds with adjacent α-cyclodextrin molecules. Such a change in the inclusion geometry may be ascribed to the difference in the shape and size of the host cavity. The α-cyclodextrin cavity is quite suitable to accomodate the nitrophenyl group. The methylation enlarges the O(2), O(3) side of the cavity, but the large inclination of 2,3,6-tri-*O*-methylglucose residues makes the O(6) side of the cavity so narrow that the nitrophenyl group can not be deeply inserted. In this case, the choice of the substitutent group to be included seems to depend upon the steric hindrance. A similar upside-down inclusion has also been observed in the benzaldehyde complex[7] (Fig. 7). In that case, the inclusion of the whole molecule may be more suitable to fulfill the methyl-α-CDx cavity than the inclusion of the phenyl group only. Unlike these two methyl-α-CDx complexes, the *p*-iodoaniline molecule is included in the same orientation in α-cyclodextrin and methyl-α-CDx rings, although the iodophenyl group slides to the O(2), O(3) side in the methyl-α-CDx ring. The inclusion of either the iodophenyl group or the aminophenyl group is sterically possible, but the iodophenyl group may be more suitably accomodated because of the stronger van der Waals interaction. The water molecule in the *p*-nitrophenol complex, which is located on the O(6) side of the cavity, links the *p*-nitrophenol molecule to the host methyl-α-CDx molecule through the hydrogen bonds (Fig. 6), O(1,NP)–H···O(W), O(W)–H···O-(6,G2), and O(W)–H···O(6,G4). These hydrogen

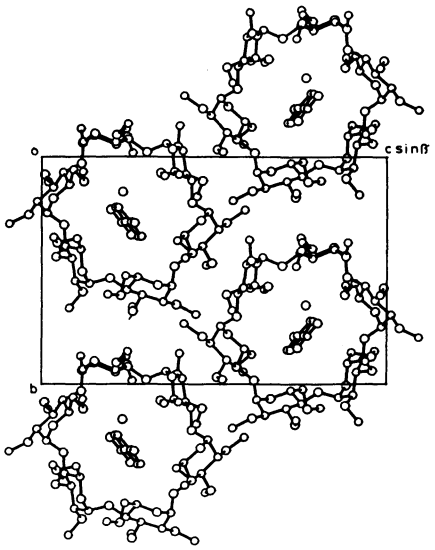

Fig. 8. The crystal structure viewed down along the a axis.

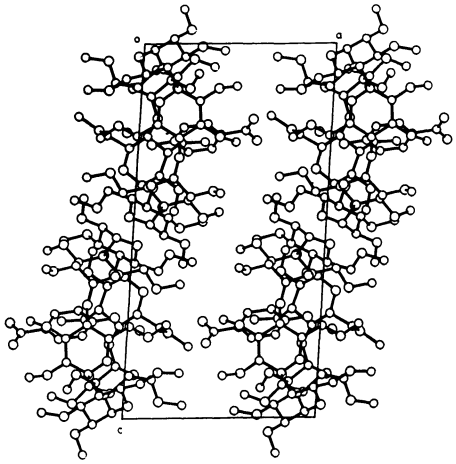

Fig. 9. The crystal structure viewed down along the b axis.

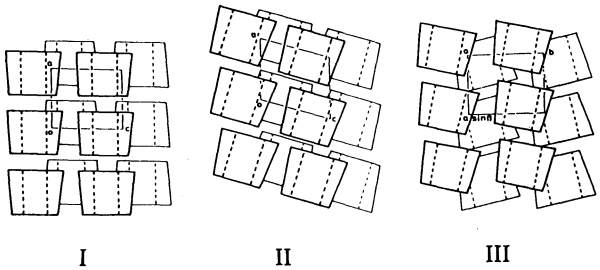

Fig. 10. Schematic drawings of the packing feature of methyl-α-CDx in the complexes with *p*-iodoaniline (I), benzaldehyde (II), and *p*-nitrophenol (III).

bonds may play an important role to fix the guest molecule inside the cavity, as the benzene ring is in loose contact with methyl-α-CDx.

Molecular Packing. Projections of the crystal structure are shown in Figs. 8 and 9. The crystal is composed of endless columns formed by the stack of

Table 4. Intermolecular distances between non-hydrogen atoms less than 3.7 Å

Distance		*l*/Å	Distance		*l*/Å
C(9,G1)–O(3,G2)	(e)	3.55(2)	C(9,G3)–C(7,G4)	(c)	3.58(2)
O(2,G1)–C(7,G2)	(f)	3.65(2)	O(6,G3)–C(7,G4)	(c)	3.27(2)
O(3,G1)–C(6,G2)	(e)	3.60(1)	C(9,G4)–O(2,NP)	(b)	3.37(2)
O(5,G1)–C(7,G6)	(d)	3.22(1)	O(3,G4)–O(6,G5)	(c)	3.38(1)
C(9,G2)–C(8,G3)	(b)	3.57(2)	O(3,G4)–C(9,G5)	(c)	3.39(2)
C(4,G3)–O(3,G6)	(a)	3.57(1)	O(5,G4)–C(2,G5)	(c)	3.69(1)
C(9,G3)–O(6,G6)	(a)	3.59(2)	O(6,G6)–O(3,NP)	(b)	3.65(2)

Code	Symmetry operator	Code	Symmetry operator
a	$x, 1+y, z$	d	$-x, 1/2+y, 1-z$
b	$-1+x, y, z$	e	$-x, -1/2+y, 1-z$
c	$-x, 1/2+y, -z$	f	$1-x, -1/2+y, 1-z$

methyl-α-CDx along the a axis. The normal of the methyl-α-CDx ring plane inclines at 10.3° with respect to the column axis. A similar packing of methyl-α-CDx is also found in the complexes with *p*-iodoaniline[6] and benzaldehyde.[7] But, as shown in Fig. 10, there are significant differences in the packing mode among these complexes. In the *p*-iodoaniline complex, the methyl-α-CDx ring is almost perpendicular to the a axis, so that the straight channel runs through methyl-α-CDx rings. On the other hand, the normal of the methyl-α-CDx ring plane in the benzaldehyde complex inclines at 17.0° with the column axis. Since the adjacent methyl-α-CDx rings along the column axis are laterally shifted within their molecular plane, the channel runs not straight but zigzag along the axis. The methyl-α-CDx ring in the *p*-nitrophenol complex also inclines, but the angle of inclination is smaller than that of the benzaldehyde complex. The channel runs almost straight through the methyl-α-CDx rings, and the guest molecules are linearly arranged in the channel. The rings planes of the methyl-α-CDx molecules related by the two-fold screw axis make an angle of 20° with each other. This is the most significant difference in the molecular packing between the *p*-nitropenol complex and the complexes with *p*-iodoaniline and benzaldehyde (Fig. 10).

An Aspect of Driving Force of the Complex Formation. The binding force of cyclodextrin complexes has been discussed on structural,[10] spectroscopic,[11–15] thermodynamic,[16] and theoretical[1,17] bases, and several interactions and forces have been proposed to explain the inclusion phenomena. Saenger and his co-workers[10] have suggested in their model to explain the inclusion mechanism that the intramolecular hydrogen bonds between O(2)H and O(3)H hydroxyl groups play an important role in the complex formation. The methyl-α-CDx complexes, however, indicate that such hydrogen bonds are not necessarily required to form the inclusion complex. Since the macrocyclic conformation of methyl-α-CDx is relatively restricted by the steric hindrance involving the $C(8)H_3$ methyl groups, the participation of the conformational change may be small, although the conformation of the uncomplexed methyl-α-CDx has not yet been defined. The inclusion geometry of methyl-α-CDx complexes indicates that the selection of groups to be included is made mainly by van der Waals interaction and repulsive interaction. Therefore, van der Waals force may significantly participate in the complex formation. Since the thermodynamic data of methyl-α-CDx complexes have not been published, it is difficult to estimate the degree of contribution of hydrophobic interaction to the complex formation in aqueous solution. But, it is possible to speculate the importance of the hydrophobic interaction from the structures of methyl-α-CDx complexes. Both ends of α-cyclodextrin cavity are rimmed with hydroxyl groups which form hydrophilic environment around the cavity The methylation not only enlarges the hydrophobic cavity of the host molecule but also makes the environment around the cavity highly hydrophobic. Therefore, compared with α-cyclodextrin, the contribution of hydrophobic interaction can be expected to be enhanced.

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