The Structure of the Cyclodextrin Complex. XVI. Crystal Structure of Heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrin–*p*-Iodophenol (1 : 1) Complex Tetrahydrate

Kazuaki HARATA,* Kaneto UEKAMA,† Masaki OTAGIRI,† and Fumitoshi HIRAYAMA†

Research Institute for Polymers and Textiles, 1-1-4, Yatabe-Higashi, Tsukuba, Ibaraki 305
†Faculty of Pharmaceutical Sciences, Kumamoto University, 5-1, Oe-honmachi, Kumamoto 862
(Received October 7, 1982)

The crystal structure of heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrin–*p*-iodophenol (1 : 1) tetrahydrate, $C_{63}H_{112}O_{35}\cdot C_6H_5OI\cdot 4H_2O$, was determined by the X-ray method. The crystal is orthorhombic with the space group $P2_12_12_1$, $Z=4$, $a=14.997(2)$, $b=21.368(2)$, and $c=28.205(3)$ Å. The structure was solved by the heavy atom method combined with the rigid-body least-squares technique and refined by the block-diagonal least-squares method to the final *R*-value of 0.094 for 3268 reflections ($\sin\theta/\lambda<0.49$). Heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrin is in the shape of a truncated elliptical cone. The macrocyclic ring is remarkably distorted from a regular heptagonal structure. The iodophenyl group of the guest is inserted into the host cavity. The phenolic hydroxyl group protrudes from the cavity, forming hydrogen bonds with two water molecules. The iodine atom is located at the center of the macrocyclic ring, while the benzene ring occupies its position at the base side of the cone. The crystal is built up of columns which are formed by the stack of host molecules in a head-to-tail mode along the two-fold screw axis which is parallel to the crystallographic b axis. Four water molecules fill intermolecular spaces in the crystal.

Recently, extensive attention has focused on the chemical modification of cyclodextrins.[1,2] Many substituted cyclodextrins have been studied to improve complexing and catalytic abilities of these macrocyclic oligosaccharides. Methylated cyclodextrins are quite interesting compounds to investigate the effect of substituents on the macrocyclic conformation and host-guest interaction. Previously, we have determined crystal structures of some permethylated α-cyclodextrin complexes.[3-5] In those structures, the macrocyclic ring is distorted by the steric hindrance which is caused by the methyl groups introduced to secondary hydroxyl groups. Permethylated α-cyclodextrin forms inclusion complexes with benzene derivatives, but their host-guest geometry is quite different from the corresponding α-cyclodextrin complexes. On the other hand, Stezowski and his co-workers have reported the structure of heptakis(2,6-di-*O*-methyl)-β-cyclodextrin-adamantanol complex,[6] and shown that the host macrocyclic ring is almost round just like as β-cyclodextrin.[7-11] In this paper, we present the crystal structure of the heptakis-(2,3,6-tri-*O*-methyl)-β-cyclodextrin–*p*-iodophenol (abbreviated to methyl-β-CDx–*p*-IPH) complex. This is the first structural determination of permethylated β-cyclodextrin.

Experimental

Methyl-β-CDx was dissolved in a *p*-IPH saturated aqueous solution. The solution was allowed to stand at 40 °C, then colorless prismatic crystals were obtained. Lattice parameters and reflection intensities were measured on a Nicolet P3/F diffractometer with graphite-monochromated Cu *Kα* radiation. By using θ-2θ scan mode, 3286 independent reflections with $|F_o|\geqq 3\sigma(F)$ were obtained up to 90° in 2θ. No corrections were made for absorption and extinction effects.

Crystal Data: $C_{63}H_{112}O_{35}\cdot C_6H_5OI\cdot 4H_2O$, *F.W.*=1721.6, orthorhombic, space group $P2_12_12_1$, $Z=4$, $a=14.977(2)$, $b=21.368(2)$, $c=28.205(3)$ Å, $V=9026(2)$ Å^3, $D_x=1.267$, $D_m=1.25$ g cm^{-3}.

Determination and Refinement of the Structure

The structure was solved by the heavy atom method. The electron-density map, which was calculated with iodine phases, revealed the outline of methyl-β-CDx. Owing to the low resolution of the map, however, it was quite difficult to estimate coordinates of light atoms. A trial structure of methyl-β-CDx was set up so as to fit the electron-density map, then the orientational and rotational parameters of each 2,3,6-tri-*O*-methylglucose residue were corrected by the rigid-body least-squares technique. After the refinement of the methyl-β-CDx structure by the block-diagonal least-squares method, the light atoms of *p*-IPH and water molecules were found on a difference-Fourier map. Successive refinements of the structure by the block-diagonal least-squares method achieved the *R*-value of 0.094. 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."[12] The atomic parameters are given in Table 1. Tables of observed and calculated structure factors, anisotropic temperature factors, and bond distances, angles, and conformation angles of methyl-β-CDx are kept at The Chemical Society of Japan (Document No. 8324). The computation was carried out on a FACOM M-200 computer at the RIPS Center, Tsukuba.

Description and Discussion of the Structure

Outline of the Structure. The structure and numbering scheme of the complex are shown in Figs. 1 and 2. Methyl-β-CDx is in the shape of an elliptically-distorted and truncated cone. The guest *p*-IPH molecule is inserted into the methyl-β-CDx ring. The iodine atom is located at the center of the host cavity, while

Table 1. Atomic coordinates ($\times 10^4$) and B_{eq} values (B/Å^2)[a)]

	x	y	z	B_{eq}/Å^2		x	y	z	B_{eq}/Å^2
C(1,G1)	8899(17)	4615(12)	4775(8)	5.84	O(6,G4)	10281(14)	5645(11)	1976(6)	9.04
C(2,G1)	8119(17)	4161(12)	4943(8)	5.55	C(1,G5)	7212(19)	4057(11)	625(8)	5.45
C(3,G1)	7613(16)	3906(12)	4514(8)	5.24	C(2,G5)	7756(17)	3732(11)	268(8)	5.00
C(4,G1)	7212(15)	4522(12)	4272(7)	4.56	C(3,G5)	8762(17)	3697(13)	444(7)	5.83
C(5,G1)	7934(18)	4974(12)	4115(8)	5.90	C(4,G5)	9061(13)	4348(10)	595(6)	3.78
C(6,G1)	7690(18)	5541(12)	3869(8)	5.92	C(5,G5)	8430(15)	4663(12)	942(8)	5.47
C(7,G1)	8855(21)	3761(14)	5646(8)	7.38	C(6,G5)	8659(19)	5332(10)	1078(8)	5.91
C(8,G1)	6912(19)	2920(14)	4443(9)	7.06	C(7,G5)	6690(20)	3090(17)	-87(10)	8.70
C(9,G1)	6519(23)	6344(14)	3931(9)	8.77	C(8,G5)	9573(24)	2843(17)	128(12)	11.08
O(2,G1)	8507(11)	3628(7)	5167(5)	5.35	C(9,G5)	9031(22)	6281(13)	718(9)	7.52
O(3,G1)	6942(11)	3539(8)	4667(5)	6.02	O(2,G5)	7469(12)	3123(8)	188(6)	6.43
O(4,G1)	6733(10)	4270(7)	3880(5)	4.80	O(3,G5)	9297(13)	3482(8)	79(6)	6.76
O(5,G1)	8451(11)	5145(7)	4528(5)	4.87	O(4,G5)	9930(11)	4242(8)	814(5)	5.99
O(6,G1)	6940(14)	5768(8)	4140(6)	7.74	O(5,G5)	7549(10)	4669(7)	734(5)	4.69
C(1,G2)	12086(17)	4121(14)	4125(8)	6.90	O(6,G5)	8838(13)	5635(8)	642(6)	7.13
C(2,G2)	11783(20)	3718(13)	4404(8)	6.71	C(1,G6)	5213(18)	3453(16)	2091(10)	8.71
C(3,G2)	10736(18)	3716(11)	4449(8)	5.53	C(2,G6)	5528(17)	2881(12)	1855(7)	5.45
C(4,G2)	10403(14)	4357(11)	4513(7)	4.54	C(3,G6)	6382(21)	3035(11)	1580(9)	6.82
C(5,G2)	10768(16)	4810(11)	4138(7)	4.88	C(4,G6)	6234(15)	3583(11)	1231(8)	4.88
C(6,G2)	10564(21)	5490(12)	4273(11)	9.01	C(5,G6)	5907(17)	4165(11)	1492(7)	5.40
C(7,G2)	12917(23)	2868(21)	4440(13)	11.85	C(6,G6)	5609(20)	4784(14)	1190(8)	7.55
C(8,G2)	10119(21)	2780(13)	4813(10)	7.52	C(7,G6)	5244(33)	1843(16)	2187(12)	13.21
C(9,G2)	10437(39)	6560(22)	3894(18)	19.03	C(8,G6)	7477(26)	2263(17)	1268(13)	11.36
O(2,G2)	12053(14)	3078(10)	4310(6)	8.45	C(9,G6)	4269(25)	4444(26)	783(12)	15.16
O(3,G2)	10553(12)	3340(8)	4879(5)	5.98	O(2,G6)	5719(17)	2440(10)	2207(6)	9.90
O(4,G2)	9474(9)	4299(7)	4462(4)	4.50	O(3,G6)	6538(16)	2476(9)	1302(6)	8.65
O(5,G2)	11723(11)	4763(8)	4121(5)	5.50	O(4,G6)	7098(11)	3713(8)	1062(5)	5.50
O(6,G2)	10712(23)	5818(12)	3840(10)	14.97	O(5,G6)	5052(11)	4000(8)	1749(5)	6.01
C(1,G3)	12643(19)	3946(13)	2152(9)	6.50	O(6,G6)	5168(14)	4542(12)	747(6)	9.66
C(2,G3)	12596(17)	3274(12)	2430(8)	5.81	C(1,G7)	5919(18)	4591(12)	3750(8)	6.10
C(3,G3)	12004(19)	3344(11)	2876(7)	5.54	C(2,G7)	5187(19)	4146(12)	3672(9)	6.56
C(4,G3)	12350(17)	3894(11)	3190(8)	5.28	C(3,G7)	5389(16)	3681(12)	3247(7)	5.08
C(5,G3)	12235(17)	4492(12)	2877(7)	5.91	C(4,G7)	5541(18)	4143(12)	2810(7)	6.03
C(6,G3)	12505(16)	5130(13)	3096(9)	6.20	C(5,G7)	6353(17)	4568(11)	2924(7)	5.03
C(7,G3)	12770(42)	2276(23)	2157(13)	17.71	C(6,G7)	6639(21)	5040(20)	2540(10)	10.90
C(8,G3)	11354(24)	2444(19)	3275(11)	10.88	C(7,G7)	4749(21)	4064(17)	4505(9)	8.80
C(9,G3)	13676(23)	5610(15)	3552(11)	9.80	C(8,G7)	4600(19)	2683(13)	3322(9)	6.91
O(2,G3)	12260(16)	2820(9)	2124(6)	8.28	C(9,G7)	6312(36)	5880(15)	2037(15)	15.38
O(3,G3)	12159(14)	2788(9)	3121(6)	7.85	O(2,G7)	5051(12)	3732(9)	4084(5)	6.60
O(4,G3)	11704(11)	3924(8)	3581(5)	5.40	O(3,G7)	4591(11)	3328(8)	3150(5)	5.65
O(5,G3)	12850(10)	4437(8)	2480(4)	5.43	O(4,G7)	5898(11)	3705(8)	2443(5)	5.71
O(6,G3)	13361(14)	5046(9)	3310(6)	7.89	O(5,G7)	6013(14)	4961(8)	3321(6)	7.60
C(1,G4)	10625(18)	4634(12)	705(8)	6.24	O(6,G7)	5938(14)	5349(11)	2342(8)	10.51
C(2,G4)	11527(15)	4288(13)	644(7)	5.42	C(1,IP)	8133(24)	2476(16)	3314(11)	9.48
C(3,G4)	11687(17)	3911(13)	1108(8)	5.79	C(2,IP)	8922(22)	2743(15)	3480(10)	8.72
C(4,G4)	11738(15)	4449(12)	1525(7)	4.57	C(3,IP)	9296(27)	3342(17)	3301(12)	11.37
C(5,G4)	10937(18)	4822(11)	1543(7)	5.23	C(4,IP)	8787(23)	3593(15)	2905(10)	8.94
C(6,G4)	11119(20)	5364(13)	1866(8)	6.99	C(5,IP)	8053(24)	3288(15)	2690(12)	10.27
C(7,G4)	11394(37)	4061(21)	-194(9)	15.42	C(6,IP)	7735(23)	2761(15)	2916(11)	9.03
C(8,G4)	12679(23)	3065(17)	900(10)	9.36	O(IP)	7909(19)	1914(11)	3483(8)	11.76
C(9,G4)	10376(29)	6176(13)	2320(12)	11.56	I(IP)	9246(2)	4467(1)	2639(1)	11.29
O(2,G4)	11427(13)	3834(9)	293(6)	7.72	O(W1)	4033(17)	5378(11)	2170(8)	12.20
O(3,G4)	12600(12)	3688(8)	1062(6)	6.74	O(W2)	3689(21)	6343(13)	1613(8)	13.39
O(4,G4)	11730(10)	4057(8)	1948(5)	5.28	O(W3)	3456(20)	6150(14)	654(7)	13.54
O(5,G4)	10765(11)	5113(7)	1079(5)	5.45	O(W4)	1647(21)	6303(15)	749(9)	14.92

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.

the benzene ring occupies its position at the O(2), O(3) side. The phenolic hydroxyl group protrudes from the O(2), O(3) side and forms hydrogen bonds with two water molecules. Methyl-β-CDx molecules are stacked along the two-fold screw axis parallel to the b axis to form a head-to-tail channel-type structure.

Conformation of Methyl-β-CDx. Average bond distances and angles over seven 2,3,6-tri-*O*-methyl-glucose residues are shown in Fig. 3. Geometrical data for the methyl-β-CDx ring are given in Tables 2—4. No significant differences in the bond distances and angles are found between methyl-β-CDx and β-cyclodextrin.[8-11] The C(6)–O(6) bonds in the G2 and G4 residues are in a *gauche-trans* conformation, while the other C(6)–O(6) bonds have a *gauche-gauche* conformation. Six of seven C(9)–O(6) bonds are *trans* to the corresponding C(5)–C(6) bonds. The C(9)–O(6) bond in the G6 residue shows a somewhat different orientation; the conformation angle of C(5)–C(6)–O(6)–C(9) is 89°. All the C(7)–O(2) bonds are oriented outside the methyl-β-CDx ring, and give average conformation angles of 96° for C(7)–O(2)–C(2)–C(1) and −147° for C(7)–O(2)–C(2)–C(3). On the other hand, the C(8)–O(3) bonds are extended along the molecular axis of methyl-β-CDx, which is defined as the axis perpendicular to the least-squares plane of seven O(4) atoms. The average conformation angles of C(8)–O(3)–C(3)–C(2) and C(8)–O(3)–C(3)–C(4) are −117° and 127°, respectively. These conformations of the C(7)–O(2) and C(8)–O(3) bonds are quite similar to those of methyl-α-CDx,[3-5] and the orientation of these bonds is scarcely affected by the ring size of macrocycles.

TABLE 2. GEOMETRICAL DATA FOR METHYL-β-CDx

The estimated standard deviations are in the ranges 0.04—0.05 Å for O···O distances and 0.05—0.07 Å for C···O distances.

I. Radius of the O(4) hexagon

Residue	Radius l/Å	Residue	Radius l/Å
G1	4.92	G5	5.27
G2	5.35	G6	5.18
G3	4.99	G7	4.63
G4	4.57	Average	4.99

II. O(4)···O(4) distances between adjacent residues

Distance	l/Å	Distance	l/Å
O(4,G1)···O(4,G2)	4.42	O(4,G4)···O(4,G5)	4.20
O(4,G1)···O(4,G7)	4.41	O(4,G5)···O(4,G6)	4.45
O(4,G2)···O(4,G3)	4.24	O(4,G6)···O(4,G7)	4.29
O(4,G3)···O(4,G4)	4.32	Average	4.33

III. O(2)···O (3) distances between adjacent residues

Distance	l/Å	Distance	l/Å
O(2,G1)···O(3,G2)	3.23	O(2,G5)···O(3,G6)	3.71
O(2,G2)···O(3,G3)	3.41	O(2,G6)···O(3,G7)	3.68
O(2,G3)···O(3,G4)	3.56	O(2,G7)···O(3,G1)	3.30
O(2,G4)···O(3,G5)	3.33	Average	3.46

IV. C(8)···O(2) distances

Distance	l/Å	Distance	l/Å
C(8,G1)···O(2.G1)	3.49	C(8,G1)···O(2,G7)	3.44
C(8,G2)···O(2,G2)	3.29	C(8,G2)···O(2,G1)	3.18
C(8,G3)···O(2,G3)	3.61	C(8,G3)···O(2,G2)	3.39
C(8,G4)···O(2,G4)	3.01	C(8,G4)···O(2,G3)	3.55
C(8,G5)···O(2,G5)	3.21	C(8,G5)···O(2,G4)	3.51
C(8,G6)···O(2,G6)	3.75	C(8,G6)···O(2,G5)	3.56
C(8,G7)···O(2,G7)	3.18	C(8,G7)···O(2,G6)	3.60
Average	3.36	Average	3.46

TABLE 3. TORSION-ANGLE INDICES AND TILT-ANGLES

I. Torsion-angle index[a)]

Residue	Index ϕ/°	Residue	Index ϕ/°
G1	126	G5	122
G2	126	G6	115
G3	100	G7	130
G4	143	Average	123

a) The torsion-angle index is defined as follows: $\phi = |\phi(C(1)-C(2))| + |\phi(C(2)-C(3))| + |\phi(C(5)-O(5))| + |\phi(O(5)-C(1))| - |\phi(C(3)-C(4))| - |\phi(C(4)-C(5))|$, where $\phi(C(1)-C(2))$ is the conformation angle of O(5)-C(1)-C(2)-C(3).

II. Tilt-angle[b)]

Residue	Angle ϕ/°	Residue	Angle ϕ/°
G1	30.4	G5	34.9
G2	16.7	G6	−16.3
G3	−12.7	G7	42.6
G4	43.0	Average	19.8

b) The tilt-angle is defined as the angle made by the plane through seven O(4) atoms and the plane through C(1), C(4), O(4), and O(4′).

Seven glycosidic oxygen atoms (O(4)) form an elliptically distorted heptagon. The radius of the heptagon, which is measured from the center of gravity of seven O(4) atoms to each O(4) atom, is in the range 4.57—5.35 Å (Table 2). The O(4,G2) atom is at the longest distance from the center of gravity, the O(4,G4) atom being nearest to the center. Although the average value of 4.99 Å is in good agreement with the value (5.02 Å) found in the β-cyclodextrin complex with 1,4-diazabicyclo[2.2.2]octane,[11] the distortion of the O(4) heptagon is more remarkable in methyl-β-CDx. In spite of such distortion, the O(4)···O(4) distances between adjacent residues (4.20—4.45 Å) and the torsion-angle indices (100—143°) are similar to those of β-cyclodextrin. This indicates that, unlike methyl-α-CDx, the conformation of the pyranose ring of methyl-β-CDx is less affected by permethylation. The least-

TABLE 4. LEAST-SQUARES PLANES AND DEVIATIONS 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 seven O(4) atoms

$-0.048X+0.998Y-0.052Z=7.561$

O(4,G1)	0.482	O(4,G5)	0.645
O(4,G2)	0.259	O(4,G6)	−0.316
O(4,G3)	−0.570	O(4,G7)	−0.451
O(4,G4)	−0.048		

II. The benzene plane

$0.575X-0.537Y-0.618Z=-1.578$

C(1,IP)	−0.037	C(5,IP)	0.051
C(2,IP)	0.047	C(6,IP)	−0.013
C(3,IP)	−0.006	O(IP)	0.121
C(4,IP)	−0.042	I(IP)	−0.186

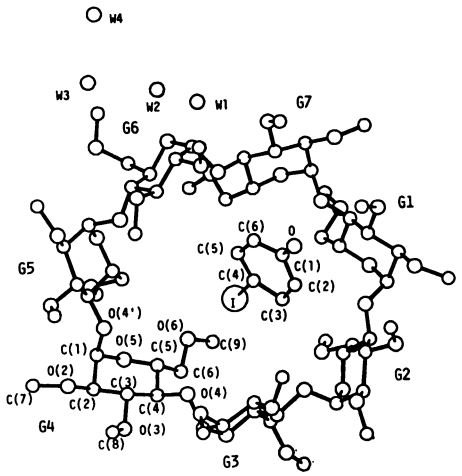

Fig. 1. A numbering scheme of the methyl-β-CDx–p-IPH complex.

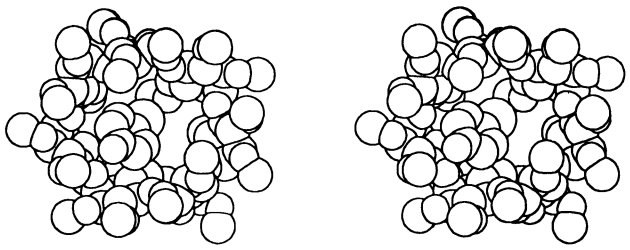

Fig. 2. A stereo-drawing of the structure of the methyl-β-CDx–p-IPH complex. Circles are drawn with three-fourths of van der Waals radii.

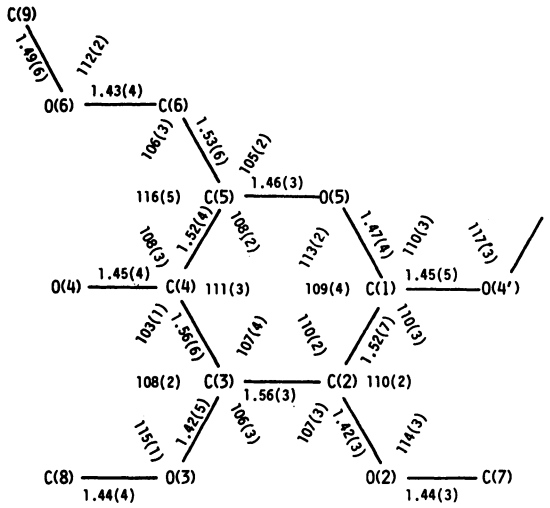

Fig. 3. Average bond distances and angles over seven 2,3,6-tri-*O*-methylglucose residues. Standard deviations in parentheses were estimated according to the equation: $\sigma=[\sum_{i=1}^{7}(x_i-\bar{x})^2/6]^{1/2}$, where x_i refers to the bond distance or angle of the i-th residue and $\bar{x}$ is the average value.

squares plane through seven O(4) atoms and deviation of atoms from the plane are given in Table 4. The maximum deviation of 0.65 Å is remarkably larger than that of β-cyclodextrin.

Compared with β-cyclodextrin, another remarkable difference is found in the tilt-angles of the 2,3,6-tri-*O*-methylglucose residues. The tilt-angles are in the range from −16.3° to 43.0°. The average value of 19.8° is similar to those (16.7—18.8°) found in the methyl-α-CDx complexes,[3-5] but the maximum value of 43.0° is larger than that of 28.1° in methyl-α-CDx.[5] The residues, G1, G2, G4, G5, and G7, incline with their O(6) side nearer to the molecular axis of methyl-β-CDx, while the G3 and G6 residues incline so that their O(2), O(3) sides are nearer to each other. The G6 residue is tilted in a direction opposite to that of the G7 residue. Therefore, the plane through C(1), C(4), O(4), and O(4') of the G6 residue makes a quite large angle, 54.5°, with the corresponding plane of the G7 residue. A similar relationship is found between the G3 and G4 residues, giving an angle of 46.4°. Such a conformational feature of methyl-β-CDx is not observed in β-cyclodextrin. In spite of the inclusion of a variety of guest molecules, the β-cyclodextrin ring is almost round, and the tilt-angle is restricted to a relatively narrow region (from −5° to 23°).[10,11] The C(8)H_3 methyl group is situated between the two O(2) atoms. The average C(8)···O(2) distances are 3.36 and 3.46 Å, which are somewhat larger than the values of 3.20 and 3.35 Å in the methyl-α-CDx–*p*-iodoaniline complex.[3] The O(2)···O(3) distances between adjacent residues are in the range 3.23—3.71 Å, and the average value of 3.46 Å is also larger than the corresponding value (3.28 Å) of the methyl-α-CDx–*p*-iodoaniline complex. These differences in the O(2)···O(3) and C(8)···O(2) distances and the tilt-angles suggest that the 2,3,6-tri-*O*-methylglucose residue of methyl-β-CDx has more flexibility around the glycosidic linkage than that of methyl-α-CDx. The large tilt-angles of the 2,3,6-tri-*O*-methylglucose residues may be ascribed to the inability of methyl-β-CDx for forming intramolecular O(2)···O(3) hydrogen bonds and the steric hindrance between the C(8)H_3 methyl group and O(2) atoms. In unsubstituted cyclodextrins, the adjacent glucose residues are mostly linked by O(2)–H···O(3) or O(3)–H···O(2) hydrogen bonds, and the macrocyclic conformation is held by such intramolecular hydrogen bonds. In the permethylated cyclodextrins, however, the methyl groups require to enlarge the O(2)···O(3) distance to avoid unfavorable interatomic repulsion between the O(2) atoms and C(8)H_3 methyl groups.

Table 5. Intermolecular distances between methyl-β-CDx and *p*-IPH less than 4.0 Å[a]

Distance	*l*/Å	Distance	*l*/Å
O(IP)–C(8,G1)	3.76	C(3,IP)–C(3,G2)	3.97
I(IP)–O(6,G4)	3.50	C(3,IP)–O(4,G3)	3.90
C(1,IP)–C(8,G1)	3.79	C(5,IP)–C(5,G7)	3.80
C(2,IP)–C(8,G3)	3.74	C(6,IP)–O(4,G7)	3.66
C(3,IP)–C(8,G3)	3.63	C(6,IP)–O(2,G6)	3.69
C(3,IP)–O(4,G2)	3.87		

a) Estimated standard deviations are in the range 0.04—0.08 Å.

Host–Guest Interaction. Intermolecular distances between *p*-IPH and methyl-β-CDx are given in Table 5. The iodophenyl group is inserted into the methyl-β-CDx cavity, while the phenolic hydroxyl group protrudes from the O(2), O(3) side of the cavity. The *p*-IPH molecule is included not parallel to the molecular axis of methyl-β-CDx but tilting with the benzene ring nearer to the G1 residue; the benzene plane makes an angle of 57.5° with the O(4) plane. The iodine atom is located at the center of the methyl-β-CDx ring. The O(6) atom of the G4 residue is at the nearest distance (3.50 Å) from the iodine atom, but there are no other contacts less than 4.0 Å between the iodine atom and methyl-β-CDx. The benzene ring is located at the O(2), O(3) side of the cavity. The shortest intermolecular distance between the benzene ring and methyl-β-CDx is 3.63 Å, which is found between C(3,IP) and C(8,G3). Therefore, the *p*-IPH molecule seems to be in weak van der Waals contact with methyl-β-CDx.

The inclusion geometry of the present complex is quite different from that found in the β-cyclodextrin–*p*-IPH complex,[7] in which three *p*-IPH molecules are located in the cylindrical cavity formed by two β-cyclodextrin molecules in a head-to-head dimer-type arrangement. The iodine atom is located at a similar position which is found in the methyl-β-CDx complex, but the benzene ring is located at the O(6) side. On the other hand, in the methyl-β-CDx complex, the large tilt of 2,3,6-tri-*O*-methylglucose residues makes the O(6) side narrower. As a result, the benzene ring is more suitably accommodated to the wider O(2), O(3) side of the cavity. A similar situation has been observed in the methyl-α-CDx–*p*-iodoaniline complex, although the *p*-iodoaniline molecule is included parallel to the molecular axis of methyl-α-CDx. These indicate that the methylation affects not only the macrocyclic

TABLE 6. INTERMOLECULAR DISTANCES LESS THAN 3.5 Å

Distance		l/Å	Distance		l/Å
C(9,G1)–O(3,G5)	(b)	3.48	O(3,G4)–C(9,G6)	(a)	3.08
O(3,G1)–C(9,G5)	(b)	3.33	O(5,G4)–O(W4)	(a)	3.01
O(3,G1)–O(6,G5)	(b)	3.47	O(6,G7)–O(W1)		2.89
O(6,G1)–C(2,G5)	(b)	3.39	O(IP)–O(W4)	(c)	2.62
O(3,G2)–O(W3)	(b)	2.86	O(IP)–O(W2)	(c)	2.70
O(5,G3)–O(W1)	(a)	2.82	O(W1)–O(W2)		2.64
O(6,G3)–C(2,G7)	(a)	3.49	O(W2)–O(W3)		2.76
O(6,G3)–O(W1)	(a)	3.44	O(W3)–O(W4)		2.74

None	x,	y,	z
a	$1+x$,	y,	z
b	$3/2-x$,	$1-y$,	$1/2+z$
c	$1-x$,	$-1/2+y$,	$1/2-z$

conformation of the host molecule but also the geormety of the host-guest interaction.

Molecular Packing. Methyl-β-CDx molecules are stacked to form a channel-type structure in a head-to-tail mode along the two-fold screw axis which is parallel to the b axis. The methyl-β-CDx molecule is nearly parallel to the ac plane; the O(4) plane is tilted by an angle of 4.1° with respect to the ac plane. Two adjacent methyl-β-CDx molecules, which are related by the two-fold screw axis parallel to the b axis, are laterally shifted to each other. As a result, the channel runs not straight but zigzag. This packing feature differs from that of the typical channel-type structure, in which the guest molecule is enclosed within the column formed by the stack of host molecules. The zigzag packing of the methyl-β-CDx molecules enables the *p*-IPH molecule to have contacts with the water molecules, which are located outside the methyl-β-CDx ring as shown in Fig. 4. The phenolic hydroxyl group forms hydrogen bonds with two water molecules, W2 and W4. Intermolecular distances less than 3.5 Å are given in Table 6. There are no significantly short intermolecular contacts. The crystal is built up of columns of methyl-β-CDx. The water molecules are located outside the column. They fill intermolecular spaces between columns, and are linked one another by the W1···W2···W3···W4 hydrogen bonds. These water molecules are also hydrogen-bonded to the oxygen atoms of methyl-β-CDx: O(W1)··· O(5,G3), O(W1)···O(6,G7), and O(W3)···O (3,G2).

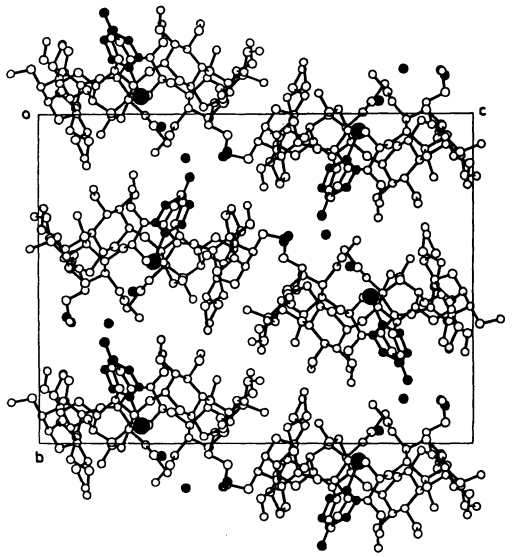

Fig. 4. The crystal structure viewed down along the a axis. Atoms in *p*-IPH and water molecules are denoted by black dots.

References

1) M. L. Bender and M. Komiyama, "Cyclodextrin Chemistry," Springer-Verlag, Berlin (1978).
2) I. Tabushi, *Acc. Chem. Res.*, **15**, 66 (1982).
3) K. Harata, K. Uekama, M. Otagiri, and F. Hirayama, *Bull. Chem. Soc., Jpn.*, **55**, 407 (1982).
4) K. Harata, K. Uekama, M. Otagiri, F. Hirayama, and Y. Sugiyama, *Bull. Chem. Soc. Jpn.*, **55**, 3386 (1982).
5) K. Harata, K. Uekama, M. Otagiri, and F. Hirayama, *Bull. Chem. Soc. Jpn.*, **55**, 3904 (1982).
6) M. Czugler, E. Eckle, and J. J. Stezowsk, *J. Chem. Soc., Chem. Commun.*, **1981**, 1291.
7) J. J. Stezowski, K. H. Jogun, E. Eckle, and K. Bartels, *Nature*, **274**, 617 (1978).
8) J. A. Hamilton, M. N. Sabesan, and L. Steinrauf, *Carbohydr. Res.*, **89**, 33 (1981).
9) R. Tokuoka, T. Fujiwara, and K. Tomita, *Acta Crystallogr., Sect. B*, **37**, 1157 (1981).
10) K. Lindner and W. Saenger, *Carbohydr. Res.*, **99**, 103 (1982).
11) K. Harata, *Bull. Chem. Soc. Jpn.*, **55**, 2315 (1982).
12) "International Tables for X-Ray Crystallography," Kynoch Press, Birmingham (1974), Vol. IV.