The Structure of the Cyclodextrin Complex. XXI. Crystal Structures of Heptakis(2,6-di-*O*-methyl)-β-cyclodextrin Complexes with *p*-Iodophenol and *p*-Nitrophenol

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Crystal structures of heptakis(2,6-di-*O*-methyl)-β-cyclodextrin complexes with *p*-iodophenol and *p*-nitrophenol were determined by the X-ray analysis. These two crystals were isomorphous with the space group $P2_12_12_1$ and cell dimensions: a=14.796(3), b=18.853(5), and c=28.989(6) Å for the *p*-iodophenol complex, and a=14.779(2), b=18.965(3), and c=28.741(4) Å for the *p*-nitrophenol complex. The structures were solved by the heavy atom method combined with the phase refinement by the tangent formula and refined by the block-diagonal least-squares method to the R-values of 0.12 (*p*-iodophenol complex) and 0.10 (*p*-nitrophenol complex). The host molecule has a round shape, which is maintained by the intramolecular hydrogen bonds between the O(3)H hydroxyl group and O(2)CH_3 methoxyl group of the adjacent residue. The guest molecules in the both complexes are not included within the host cavity but located in the intermolecular space between host molecules. The host cavity includes water molecules and a methoxyl group of the adjacent host. Hydrogen bonds are formed only within the host cavity.

Cyclodextrins form a number of host-guest complexes with a variety of guest molecules.[1] In the crystalline state, guest molecules are usually included within the cavity of the host macrocycle.[2] Methylated cyclodextrins also form inclusion complexes with many guests, although the geometry of the host-guest interaction differs from that of corresponding cyclodextrin complexes because of the change in size and shape of the host cavity.[3] Therefore, it has been believed that the guest molecule should be fit into the host cavity to form the complex, even if only partially. Recently we have found that some disubstituted benzenes form 1 : 1 crystalline complexes with heptakis(2,6-di-*O*-methyl)-β-cyclodextrin (DM-β-CDx) but are not included within the host cavity. The short communication on the structure of the DM-β-CDx complexes with *p*-iodophenol (*p*-IP) and *p*-nitrophenol (*p*-NP) has been published.[4] In this paper, we destribe details of these crystal structures and discuss the host-guest interaction in comparison with cyclodextrin and other methylated cyclodextrin complexes.

Experimental

The DM-β-CDx complex with *p*-IP was crystallized at 50 °C by standing an aqueous solution of DM-β-CDx saturated with *p*-IP. Crystals of the *p*-NP complex were obtained at room temperature by the slow evaporation of an aqueous solution containing DM-β-CDx and *p*-NP in ca. 1 : 1 molar ratio. Lattice parameters of the crystals and diffraction intensity data were measured at room temperature on a Nicolet P3/F diffractometer with graphite-monochromated Cu $K\alpha$ radiation. By using θ-2θ scan mode, 4045 (*p*-IP complex) and 4670 (*p*-NP complex) independent reflections with $|F_o| \geqq 3\sigma(F)$ were obtained up to 118° in 2θ.

The structure of the *p*-IP complex was solved by the combination of the heavy atom method and the phase-refinement by the tangent-formula. On the electron-density map calculated by using the iodine phases, light atoms could

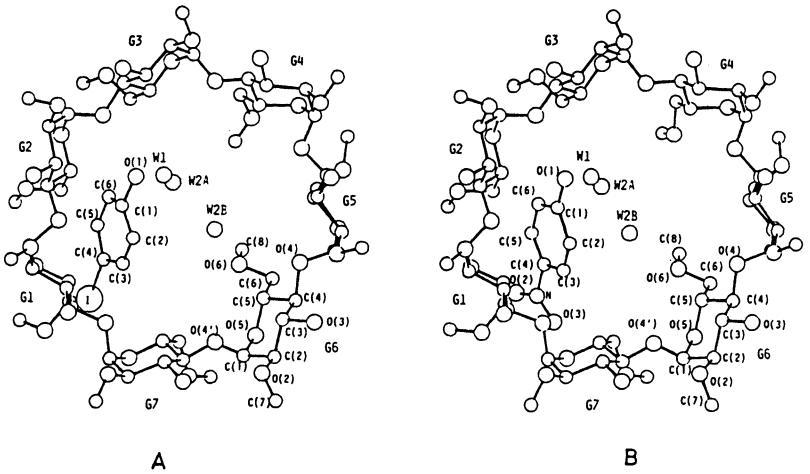

Fig. 1. Structures and numbering scheme of the DM-β-CDx complexes with *p*-IP (A) and *p*-NP (B).

Table 1. Atomic Coordinates ($\times 10^4$) and B_{eq} Values (Å^2) of the DM-β-CDx Complex with p-IP

	x	y	z	B_{eq}		x	y	z	B_{eq}
C(1,G1)	4631(16)	3475(13)	4276(7)	6.8	O(6,G4)	−323(25)	6682(25)	5938(14)	26.6
C(2,G1)	5382(16)	3808(12)	3991(7)	5.7	C(1,G5)	1320(17)	9159(11)	4299(9)	8.0
C(3,G1)	5040(14)	4471(15)	3751(7)	6.6	C(2,G5)	2046(21)	9548(13)	4593(9)	8.8
C(4,G1)	4185(16)	4295(12)	3457(8)	6.6	C(3,G5)	2289(18)	9076(13)	5022(8)	7.3
C(5,G1)	3503(15)	4005(13)	3781(7)	6.2	C(4,G5)	1434(16)	8941(12)	5273(7)	6.2
C(6,G1)	2658(18)	3709(12)	3474(10)	8.2	C(5,G5)	763(17)	8472(14)	4964(8)	7.1
C(7,G1)	6990(15)	3863(15)	4152(10)	8.4	C(6,G5)	−214(35)	8382(18)	5155(20)	20.9
C(8,G1)	2623(66)	2592(30)	3177(16)	40.2	C(7,G5)	3253(24)	10419(13)	4424(12)	11.9
O(2,G1)	6120(12)	4012(9)	4298(5)	7.7	C(8,G5)	−1303(29)	8678(29)	5729(19)	22.1
O(3,G1)	5737(9)	5754(8)	3461(5)	6.4	O(2,G5)	2781(14)	9704(9)	4311(6)	9.2
O(4,G1)	3869(10)	4976(7)	3279(4)	5.9	O(3,G5)	2863(13)	9547(10)	5305(6)	9.0
O(5,G1)	3852(12)	3366(8)	3987(5)	6.9	O(4,G5)	1690(11)	8474(8)	5656(6)	7.1
O(6,G1)	2890(18)	3298(12)	3083(6)	12.9	O(5,G5)	569(11)	8971(10)	4573(7)	9.1
C(1,G2)	3840(15)	3969(9)	6036(7)	5.2	O(6,G5)	−545(18)	8891(19)	5415(10)	19.2
C(2,G2)	4793(15)	3868(10)	5887(6)	4.9	C(1,G6)	2089(17)	7460(12)	2866(7)	6.4
C(3,G2)	4951(13)	4100(10)	5376(7)	4.6	C(2,G6)	2398(20)	8237(13)	2873(7)	7.7
C(4,G2)	4238(14)	3715(11)	5083(7)	5.2	C(3,G6)	2561(18)	8469(11)	3376(8)	7.4
C(5,G2)	3303(12)	3890(12)	5247(6)	5.0	C(4,G6)	1593(20)	8422(11)	3621(8)	7.8
C(6,G2)	2569(16)	3449(13)	4964(9)	7.1	C(5,G6)	1268(19)	7570(12)	3614(8)	7.2
C(7,G2)	6189(20)	3865(16)	6312(9)	9.8	C(6,G6)	319(14)	7468(15)	3838(9)	7.5
C(8,G2)	2128(21)	2318(17)	4744(10)	11.8	C(7,G6)	3550(42)	8641(21)	2355(12)	22.1
O(2,G2)	5376(11)	4228(8)	6195(4)	6.3	C(8,G6)	−427(23)	6507(21)	4184(14)	14.9
O(3,G2)	5850(9)	3920(7)	5254(4)	4.9	O(2,G6)	3200(16)	8256(12)	2682(6)	12.1
O(4,G2)	4362(9)	4013(7)	4629(5)	5.3	O(3,G6)	2701(13)	9230(8)	3378(6)	8.7
O(5,G2)	3237(11)	3643(7)	5732(5)	6.6	O(4,G6)	1754(10)	8548(7)	4129(5)	5.6
O(6,G2)	2791(12)	2742(9)	4963(6)	8.2	O(5,G6)	1244(11)	7441(7)	3110(5)	6.5
C(1,G3)	2348(16)	6236(11)	6840(8)	6.5	O(6,G6)	376(14)	6721(10)	4015(7)	10.2
C(2,G3)	3306(17)	6013(10)	6984(7)	5.8	C(1,G7)	3560(19)	4981(13)	2799(6)	7.2
C(3,G3)	3791(12)	5659(11)	6598(7)	5.4	C(2,G7)	4143(17)	5624(13)	2587(6)	6.4
C(4,G3)	3205(14)	4975(12)	6456(7)	5.5	C(3,G7)	3922(18)	6323(13)	2785(7)	6.9
C(5,G3)	2263(15)	5254(11)	6337(7)	5.3	C(4,G7)	2831(16)	6372(11)	2805(7)	5.6
C(6,G3)	1623(18)	4621(11)	6191(8)	6.9	C(5,G7)	2396(14)	5780(11)	3014(6)	5.0
C(7,G3)	4435(21)	6642(14)	7471(9)	9.6	C(6,G7)	1367(17)	5770(15)	2986(8)	7.8
C(8,G3)	1278(18)	3431(14)	6362(8)	8.1	C(7,G7)	5680(28)	5440(28)	2253(10)	18.3
O(2,G3)	3764(12)	6651(8)	7090(4)	6.9	C(8,G7)	112(19)	6064(12)	2497(9)	11.3
O(3,G3)	4696(11)	5419(9)	6709(6)	7.7	O(2,G7)	5064(11)	5457(11)	2625(5)	8.4
O(4,G3)	3651(9)	4695(7)	6039(5)	5.5	O(3,G7)	4311(13)	6876(10)	2550(5)	9.2
O(5,G3)	1890(10)	5584(8)	6725(4)	5.5	O(4,G7)	2677(10)	7018(8)	3046(4)	6.3
O(6,G3)	1717(11)	4093(9)	6489(5)	7.1	O(5,G7)	2637(10)	5129(8)	2786(5)	6.2
C(1,G4)	1222(18)	8585(12)	6091(8)	7.1	O(6,G7)	1096(13)	5933(10)	2532(6)	8.9
C(2,G4)	2039(18)	8615(13)	6454(9)	8.1	C(1,IP)	283(19)	4129(21)	4672(16)	16.5
C(3,G4)	2506(16)	7912(11)	6498(8)	6.7	C(2,IP)	−336(23)	3581(17)	4810(11)	12.8
C(4,G4)	1880(15)	7300(10)	6556(8)	5.8	C(3,IP)	−686(21)	3253(16)	4418(10)	10.0
C(5,G4)	1126(22)	7291(14)	6177(9)	9.4	C(4,IP)	−406(18)	3501(15)	3950(10)	8.9
C(6,G4)	471(24)	6648(18)	6193(12)	12.9	C(5,IP)	−20(26)	4068(18)	3906(12)	13.0
C(7,G4)	2941(23)	9654(16)	6661(10)	10.9	C(6,IP)	516(26)	4391(24)	4248(19)	19.5
C(8,G4)	69(36)	6462(23)	5656(16)	22.2	O(1,IP)	576(22)	4505(18)	5095(10)	22.2
O(2,G4)	2611(14)	9171(10)	6316(6)	9.0	I(1,IP)	−1050(2)	2978(1)	3417(1)	11.3
O(3,G4)	3123(11)	7968(9)	6876(5)	7.5	O(W1)	3306(27)	5966(29)	5258(10)	28.8
O(4,G4)	2358(11)	6722(7)	6514(5)	6.4	O(W2A)	1447(21)	5580(21)	5038(14)	13.3
O(5,G4)	707(11)	8039(10)	6197(5)	7.9	O(W2B)	1679(31)	6119(38)	4539(24)	16.9

The occupancy factor of W2A and W2B is 0.6 and 0.4, respectively.

not be located because of the low resolution. Then, phases of 803 reflections with $|E| \geqq 1.4$ were refined by the tangent-formula. Most of light atoms were found on the E-map. The structure was refined by the block-diagonal least-squares method to the R-value of 0.12. A set of the coordinates of DM-β-CDx of the p-IP complex was used to determine the isomorphous structure of the p-NP complex, which was refined to the R-value of 0.10. The quantity minimized was $\sum w(|F_o|-|F_c|)^2$ with $w=1.0$ for all the reflections used. Final atomic coordinates are given in Tables 1 and 2. Tables of observed and calculated structure factors and anisotropic temperature factors are deposited to the Chemical Society of Japan (Document No. 8798). The computations were carried out on a FACOM M380 computer at the Research Information Processing System (RIPS) Center, Agency of Industrial Science and Technology, Tsukuba.

Crystal Data: (1) p-Iodophenol complex, $C_{56}H_{98}O_{35} \cdot C_6H_5OI \cdot 2H_2O$, F.W.=1587.4, orthorhombic, space group $P2_12_12_1$, $Z=4$, $a=14.796(3)$, $b=18.853(5)$, $c=28.989(6)$ Å, $V=8086(3)$ Å^3, $D_X=1.304$ g·cm^{-3}, (2) p-nitrophenol complex,

Table 2. Atomic Coordinates ($\times 10^4$) and B_{eq} Values (Å^2) of the DM-β-CDx Complex with *p*-NP

	x	y	z	B_{eq}		x	y	z	B_{eq}
C(1,G1)	4601(10)	3525(7)	4280(5)	6.6	C(1,G5)	1314(11)	9197(7)	4300(5)	7.4
C(2,G1)	5364(9)	3854(8)	3995(5)	6.4	C(2,G5)	2013(12)	9561(7)	4608(5)	8.0
C(3,G1)	5036(9)	4521(5)	3763(4)	5.8	C(3,G5)	2243(10)	9133(8)	5028(5)	6.8
C(4,G1)	4191(9)	4352(7)	3474(4)	6.0	C(4,G5)	1381(10)	8937(8)	5280(5)	7.1
C(5,G1)	3471(10)	4007(8)	3802(5)	7.3	C(5,G5)	705(11)	8467(9)	4955(5)	7.7
C(6,G1)	2629(11)	3756(11)	3492(6)	10.8	C(6,G5)	−239(20)	8364(12)	5144(8)	18.4
C(7,G1)	6965(10)	3879(10)	4129(5)	8.2	C(7,G5)	3203(15)	10380(9)	4465(7)	11.8
C(8,G1)	2722(44)	2595(18)	3116(12)	47.1	C(8,G5)	−1341(18)	8618(19)	5725(10)	20.0
O(2,G1)	6105(6)	3994(5)	4311(3)	7.3	O(2,G5)	2764(8)	9727(6)	4329(4)	9.2
O(3,G1)	5744(6)	4772(5)	3464(3)	6.7	O(3,G5)	2811(7)	9527(5)	5340(4)	8.4
O(4,G1)	3888(6)	5018(5)	3297(3)	6.3	O(4,G5)	1636(7)	8442(5)	5656(3)	7.0
O(5,G1)	3831(7)	3392(5)	3984(3)	7.8	O(5,G5)	547(7)	9010(6)	4568(3)	8.2
O(6,G1)	2871(11)	3334(10)	3096(4)	16.6	O(6,G5)	−594(10)	8855(11)	5420(6)	16.7
C(1,G2)	3810(11)	3940(6)	6061(4)	6.3	C(1,G6)	2023(11)	7514(7)	2841(5)	6.9
C(2,G2)	4814(9)	3836(7)	5923(5)	6.2	C(2,G6)	2353(12)	8282(9)	2874(5)	8.2
C(3,G2)	4937(9)	4094(7)	5408(4)	5.6	C(3,G6)	2524(13)	8516(8)	3394(5)	8.2
C(4,G2)	4254(9)	3689(7)	5114(4)	5.6	C(4,G6)	1549(12)	8433(8)	3625(5)	8.1
C(5,G2)	3289(9)	3836(7)	5262(4)	5.7	C(5,G6)	1251(11)	7647(7)	3604(5)	6.6
C(6,G2)	2562(11)	3431(8)	4988(5)	7.5	C(5,G6)	319(11)	7529(7)	3797(5)	7.2
C(7,G2)	6209(12)	3835(13)	6367(6)	11.4	C(7,G6)	3413(23)	8605(14)	2281(8)	19.9
C(8,G2)	2140(15)	2318(10)	4730(6)	11.9	C(8,G6)	−468(15)	6580(13)	4145(9)	14.9
O(2,G2)	5386(7)	4208(5)	6233(3)	7.5	O(2,G6)	3237(10)	8285(7)	2679(3)	10.9
O(3,G2)	5847(6)	3902(5)	5272(3)	6.4	O(3,G6)	2719(9)	9252(5)	3380(4)	9.7
O(4,G2)	4368(6)	3992(4)	4650(3)	5.8	O(4,G6)	1733(7)	8567(4)	4116(3)	6.3
O(5,G2)	3222(7)	3603(4)	5747(3)	6.7	O(5,G6)	1191(7)	7483(5)	3102(3)	7.0
O(6,G2)	2819(8)	2729(5)	4967(4)	8.3	O(6,G6)	298(8)	6809(7)	3965(5)	10.5
C(1,G3)	2351(10)	6169(8)	6888(5)	7.4	C(1,G7)	3643(10)	5067(8)	2809(4)	6.7
C(2,G3)	3323(10)	5966(7)	7011(4)	6.3	C(2,G7)	4157(10)	5644(9)	2593(5)	7.3
C(3,G3)	3779(10)	5623(7)	6611(4)	6.1	C(3,G7)	3882(11)	6362(8)	2816(5)	7.3
C(4,G3)	3227(10)	4965(7)	6471(4)	5.7	C(4,G7)	2843(9)	6441(7)	2794(5)	6.0
C(5,G3)	2261(9)	5207(7)	6347(4)	5.9	C(5,G7)	2371(9)	5790(7)	3021(5)	6.2
C(6,G3)	1611(12)	4599(8)	6211(4)	7.9	C(6,G7)	1379(11)	5756(10)	2998(5)	9.2
C(7,G3)	4454(12)	6602(10)	7490(5)	9.2	C(7,G7)	5613(14)	5367(19)	2248(6)	18.0
C(8,G3)	1266(14)	3390(8)	6378(6)	10.0	C(8,G7)	107(12)	6071(14)	2512(8)	13.8
O(2,G3)	3771(7)	6632(5)	7123(3)	7.3	O(2,G7)	5102(7)	5515(6)	2646(3)	7.9
O(3,G3)	4682(7)	5396(5)	6741(3)	7.5	O(3,G7)	4318(8)	6927(6)	2570(4)	8.8
O(4,G3)	3658(6)	4678(4)	6069(3)	5.9	O(4,G7)	2667(6)	7067(5)	3047(3)	6.3
O(5,G3)	1854(6)	5538(5)	6752(3)	6.3	O(5,G7)	2674(7)	5169(5)	2798(3)	6.6
O(6,G3)	1697(8)	4052(5)	6527(3)	8.5	O(6,G7)	1114(8)	5958(7)	2554(4)	10.5
C(1,G4)	1194(11)	8520(8)	6100(5)	7.4	C(1,NP)	165(12)	4081(10)	4725(7)	10.8
C(2,G4)	1954(11)	8596(8)	6476(6)	8.1	C(2,NP)	−398(14)	3467(11)	4738(7)	11.4
C(3,G4)	2448(11)	7876(7)	6496(5)	7.4	C(3,NP)	−787(13)	3210(9)	4331(6)	9.5
C(4,G4)	1821(11)	7273(7)	6560(5)	6.7	C(4,NP)	−526(14)	3585(10)	3925(6)	10.7
C(5,G4)	1107(12)	7264(8)	6171(6)	8.4	C(5,NP)	−17(16)	4180(12)	3876(10)	15.4
C(6,G4)	398(14)	6701(10)	6235(7)	11.0	C(6,NP)	399(16)	4453(11)	4263(9)	14.5
C(7,G4)	2906(15)	9593(10)	6691(7)	11.7	O(1,NP)	554(13)	4356(9)	5113(5)	17.1
C(8,G4)	−498(20)	6170(20)	5660(15)	31.4	N(1,NP)	−966(13)	3306(9)	3493(6)	13.1
O(2,G4)	2548(8)	9121(5)	6329(4)	9.2	O(2,NP)	−987(14)	3687(9)	3149(5)	16.6
O(3,G4)	3032(8)	7946(5)	6908(4)	8.3	O(3,NP)	−1364(18)	2714(7)	3501(5)	19.8
O(4,G4)	2343(7)	6663(5)	6528(3)	6.7	O(W1)	3337(19)	5867(19)	5256(8)	33.7
O(5,G4)	634(7)	7939(6)	6191(3)	8.0	O(W2A)	1428(18)	5476(11)	5080(9)	14.5
O(6,G4)	−19(15)	6562(9)	5786(7)	20.9	O(W2B)	1683(22)	6107(22)	4434(17)	18.6

The occupancy factor of W2A and W2B is 0.6 and 0.4, respectively.

$C_{56}H_{98}O_{35}\cdot C_6H_6O_3N\cdot 2H_2O$, F.W.=1506.5, orthorhombic, space group $P2_12_12_1$, Z=4, a=14.779(2), b=18.965(3), c=28.741(4) Å, V=8056(2) Å^3, D_X=1.242 g·cm^{-3}.

Description of the Structure and Discussion

As shown in Figs. 1 and 2, DM-β-CDx molecule has a round and rather symmetrical structure. The radius of the heptagon composed of seven glycosidic oxygen atoms is 4.84—5.21 Å in the *p*-IP complex and 4.92—5.16 Å in the *p*-NP complex. The average values of 5.05 and 5.07 Å is in good agreement with the radius of parent β-CDx.[5,6] The side lengths of the heptagon are in the range 4.25—4.49 Å (*p*-IP complex) and 4.33—4.44 Å (*p*-NP complex). Each 2,6-di-*O*-methylglucose residue inclines with the O(6) side turning to the inside of the macrocycle. The tilt-angles are in the range 5.6—24.4° in the *p*-IP complex and 2.2—24.7° in

the *p*-NP complex. Among the seven residues, the G6 residue is most tilted in both complexes. The distances between O(2) and O(3) of the adjacent residue, 2.72—3.10 Å in the *p*-IP complex and 2.79—3.05 Å in the *p*-NP complex, indicate that the O(3)H hydroxyl group is hydrogen-bonded to the O(2) atom of the adjacent residue. All methyl groups point away from the center of the host macrocycle, thus the host cavity of DM-β-CDx is deeper than the cavity of parent β-CDx. The comparison of the O(4)···O(4′) distance (the side length of the O(4) heptagon) with the torsion-angle index gives no obvious correlation between them, although in parent β-CDx the strong correlation has been observed between the O(4)···O(4′) distance and the torsion-angle index. The methyl group may affect the conformation of the pyranose ring to break such linear correlation.

Except for methyl groups, the macrocyclic conformation of DM-β-CDx does not significantly differ from the conformation of parent β-CDx, as shown in

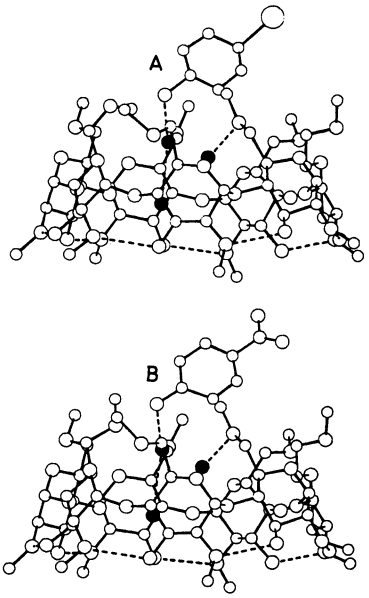

Fig. 2. Side-view of the DM-β-CDx complexes with *p*-IP (A) and *p*-NP (B). Water molecules are shown by full circles. Dashed lines indicate possible hydrogen-bonding contacts.

Table 3. Geometrical Data for Describing the Macrocyclic Conformation of DM-β-CDx

I. Distance from the center of gravity of seven O(4) atoms to each O(4) atom[a)]

Residue	Distance (*l*/Å)		Residue	Distance (*l*/Å)	
	p-IP	*p*-NP		*p*-IP	*p*-NP
G1	5.20	5.13	G5	5.11	5.08
G2	4.92	4.84	G6	4.98	4.92
G3	4.98	5.13	G7	5.13	5.14
G4	5.21	5.16	Average	5.05	5.07

a) Estimated standard deviations are 0.03 (*p*-IP complex) and 0.03 Å (*p*-NP complex).

II. Distance between O(4) and O(4′) of the adjacent residue[a)]

	Distance (*l*/Å)	
	p-IP	*p*-NP
O(4,G1)···O(4,G2)	4.38	4.41
O(4,G2)···O(4,G3)	4.41	4.41
O(4,G3)···O(4,G4)	4.49	4.44
O(4,G4)···O(4,G5)	4.25	4.33
O(4,G5)···O(4,G6)	4.43	4.44
O(4,G6)···O(4,G7)	4.48	4.41
O(4,G7)···O(4,G1)	4.29	4.34
Average	4.39	4.40

a) Estimated standaed deviations are 0.03 (*p*-IP complex) and 0.02 Å (*p*-NP complex).

III. Distance between O(2) and O(3′) of the adjacent residue[a)]

	Distance (*l*/Å)	
	p-IP	*p*-NP
O(2,G1)...O(3,G2)	2.81	2.79
O(2,G2)...O(3,G3)	2.88	2.88
O(2,G3)...O(3,G4)	2.73	2.79
O(2,G4)...O(3,G5)	3.04	2.97
O(2,G5)...O(3,G6)	2.85	2.87
O(2,G6)...O(3,G7)	3.10	3.05
O(2,G7)...O(3,G1)	2.94	2.90
Average	2.91	2.89

a) Estimated standard deviations are 0.03 (*p*-IP complex) and 0.02 Å (*p*-NP complex).

IV. Torsion-angle index[a)] and tilt-angle[b)] of each residue

Residue	Torsion-angle index (ϕ/°)		Tilt-angle (ϕ/°)	
	p-IP	*p*-NP	*p*-IP	*p*-NP
G1	112	124	5.8	5.5
G2	106	107	15.5	17.0
G3	138	122	16.1	14.2
G4	121	117	17.8	18.1
G5	107	112	5.6	2.2
G6	138	123	24.4	24.7
G7	106	113	19.7	17.6
Average	118	117	15.0	14.2

a) The torsion-angle index is defined as: $\phi=|\phi(C(1)\text{-}C(2))|+|\phi(C(2)\text{-}C(3))|+|\phi(C(5)\text{-}O(5))|+|\phi(O(5)\text{-}C(1))|-|\phi(C(3)\text{-}C(4))|-|\phi(C(4)\text{-}C(5))|$, where $\phi(C(1)\text{-}C(2))$ indicates the conformation angle of O(5)-C(1)-C(2)-C(3). b) The tilt-angle is defined as an angle made between the plane through seven O(4) atoms and the plane through C(1), C(4), O(4), and O(4′) of each residue.

V. Deviation of each O(4) atoms from the least-squares plane through seven O(4) atoms

Residue	Deviation (*d*/Å)		Residue	Deviation (*d*/Å)	
	p-IP	*p*-NP		*p*-IP	*p*-NP
G1	−0.01	−0.01	G5	0.17	0.13
G2	0.13	0.11	G6	0.01	0.03
G3	−0.04	−0.02	G7	−0.11	−0.10
G4	−0.16	−0.14	r.m.s. deviation	0.11	0.09

Table 4. Comparison of Geometrical parameters among β-Cyclodextrin and Methylated β-Cyclodextrins

Average values are given with standard deviations.

	β-CDx[a)]	DM-β-CDx	TM-β-CDx[b)]
Radius of the O(4) heptagon (l/Å)	5.0(0.2)	5.1(0.1)	5.0(0.3)
O(4)...O(4′) distance (l/Å)	4.3(0.1)	4.4(0.1)	4.3(0.1)
O(2)...O(3′) distance (l/Å)	2.9(0.1)	2.9(0.1)	3.5(0.2)
Glycosidic O(4) angle (ϕ/°)	118(1)	117(2)	117(3)
Planarity of the O(4) heptagon (d/Å)[c)]	0.18	0.09	0.44
Torsion-angle index (ϕ/°)	120(7)	117(6)	123(13)
Tilt-angle (ϕ/°)	12(10)	14(8)	20(25)

a) See Ref. 5. b) Heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrin (Ref. 7). c) The root-mean-square deviation of the seven O(4) atoms.

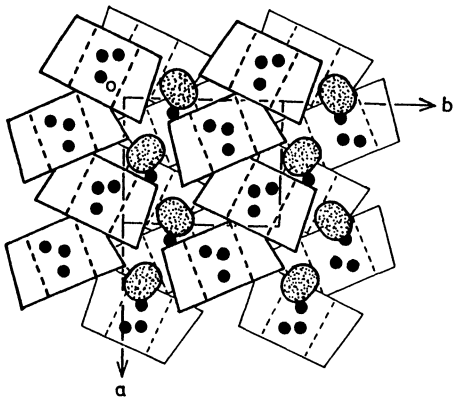

Fig. 3. A schematic drawing of the crystal structure. Water molecules are shown by full circles. Shaded ellipses indicate guest molecules.

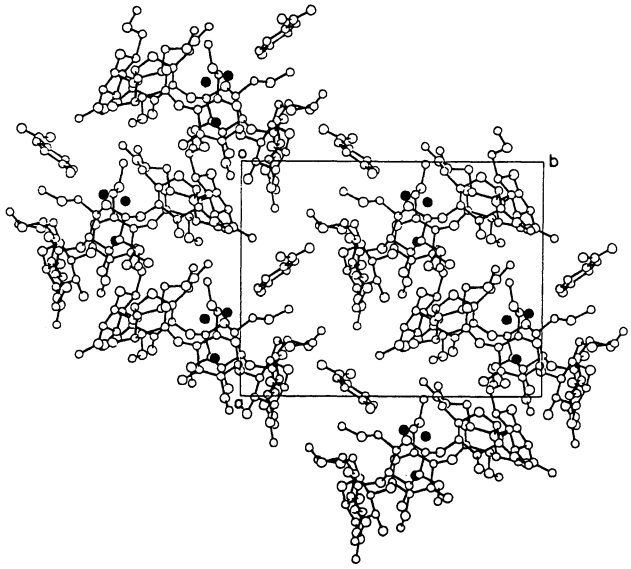

Fig. 4. The crystal structure of the DM-β-CDx complex with *p*-NP viewed along the c axis. Water molecules are shown by full circles. Symmetry-related molecules by the two-fold screw axis along the c axis are not shown because of the clarity of representation.

Table 4. By the methylation of O(3)H hydroxyl groups, the distance between O(2) and O(3) of the adjacent residue is increased from 2.9 Å to 3.5 Å. Moreover, each residue much more inclines with the tilt-angle in the range from −16.3° to 43.0°.[7] This indicates that the round shape of the macrocycle is maintained by the intramolecular O(2)···O(3′) hydrogen bonds in β-CDx and DM-β-CDx. The methylation of the O(2)H hydroxyl group does not affect the formation of intramolecular hydrogen bonds because the O(2)C(7)H_3 methoxyl group points away from the adjacent O(3)H hydroxyl group. The further methylation at the O(3) position blocks the formation of O(2)···O(3′) hydrogen bonds, and as the result, the macrocycle can no more retain the round structure.

Figure 3 shows the packing feature in the crystal. The DM-β-CDx molecules are stacked along the a axis. Since the DM-β-CDx molecule inclines by an angle of 25° against the a axis, the stacked molecules do not form a column structure but show a zigzag pattern. The O(2), O(3) side of the DM-β-CDx cavity is blocked by the O(6) side of the adjacent DM-β-CDx molecule which is related by the two-fold screw axis along the a axis. The O(6) side of the cavity is open to the intermolecular space, where the guest molecule is located. It is noteworthy that the guest *p*-IP and *p*-NP mole-

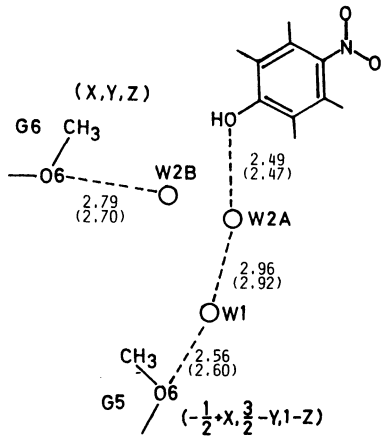

Fig. 5. A possible hydrogen bond scheme in the DM-β-CDx complex with *p*-NP. Corresponding hydrogen bond distances of the *p*-IP complex are given in parentheses.

cules are not included within the DM-β-CDx cavity but located in the crevice running zigzag along the a axis. Such geometrical relationship between host and guest is not observed in other cyclodextrin or methylated cyclodextrin complexes, except for the α-CDx-*m*-nitrophenol (1:2) complex, in which one guest is included within the host cavity and the other being located in the intermolecular space.[8] It is not easy to explain fully why the guest molecule is excluded from the host cavity, since the inclusion of the guest molecule by DM-β-CDx has been observed in the crystalline complex with 2-adamantanol.[9] One possible reason is that the intermolecular space has highly hydrophobic property because of many methyl groups. The guest molecule could be located in the intermolecular space rather than in the host cavity when the size and shape of the intermolecular space are more suitable for the guest molecule. On the other hand, in the crystal of native cyclodextrins, the intermolecular space is usually filled with water molecules which form a hydrogen bond network with many hydroxyl groups of the host molecule.

The DM-β-CDx cavity includes water molecules and one methoxyl group, O(6,G5)C(8,G5)H_3, which is inserted from the O(2), O(3) side. A possible hydrogen-bond scheme inside the host cavity is shown in Fig. 5. The W2 water molecule is disordered and occupies two sites, W2A and W2B. W2B is hydrogen-bonded to O(6,G6), while W2A forms hydrogen bonds with the hydroxyl group of the guest and W1 water molecule which is also hydrogen-bonded to O(6,G5) of the adjacent DM-β-CDx molecule related by the two-fold screw axis. Although the host cavity is extended and deepened by the methylation, the effective space of the cavity to include the guest molecule is reduced by the insertion of one methoxyl group of adjacent DM-β-CDx. Such close contact between host molecules may play an important role to exclude the guest molecule from the host cavity. It has been considered that the guest molecule should be included within the host cavity in the crystalline state. The present study, however, shows that the guest molecule is not necessarily included by the host molecule even if the complex has a 1:1 host-guest stoichiometry.

References

1) J. Szejtli, "Cyclodextrins and their Inclusion Complexes," Academiai Kiado, Budapest (1982).

2) W. Saenger, "Inclusion Compounds," ed by J. L. Atwood, J. E. D. Davies, and D. D. MacNicol, Academic press, London (1984), Vol. 2, pp. 231—259.

3) K. Harata, K. Uekama, M. Otagiri, and F. Hirayama, *J. Inclusion Phenom.*, **1**, 279 (1984).

4) K. Harata, *Chem. Lett.*, **1984**, 1644.

5) K. Lindner and W. Saenger, *Carbohydr. Res.*, **99**, 103 (1982).

6) K. Harata, *Bull. Chem. Soc. Jpn.*, **55**, 2315 (1982).

7) K. Harata, K. Uekama, M. Otagiri, and F. Hirayama, *Bull. Chem. Soc. Jpn.*, **56**, 1732 (1983).

8) K. Harata, H. Uedaira, and J. Tanaka, *Bull. Chem. Soc. Jpn.*, **51**, 1267 (1978).

9) M. Czugler, E. Eckle, and J. J. Stezowski, *J. Chem. Soc., Chem. Commun.*, **1981**, 1291.