The Structure of the Cyclodextrin Complex. VI. The Crystal Structure of α-Cyclodextrin-m-Nitrophenol (1: 2) Complex

Kazuaki HARATA, Hisashi UEDAIRA, and Jiro TANAKA*
Research Institute for Polymers and Textiles, Sawatari-4, Kanagawa-ku, Yokohama 221
**Department of Chemistry, Faculty of Science, Nagoya University, Chikusa-ku, Nagoya 464*

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α-Cyclodextrin (α-CDx) forms a 1: 2 crystalline complex with *m*-nitrophenol (*m*-NP). The crystal structure was determined by the X-ray method. The crystal is orthorhombic, and the space group is $P2_12_12$ with $Z=2$. The cell dimensions are $a=22.231(7)$, $b=16.865(6)$, and $c=8.152(1)$ Å. The structure was solved on the basis of the nearly isomorphous structure of the α-CDx–sodium benzenesulfonate complex by using 2246 reflections, and refined by the block-diagonal least-squares method to the final *R*-value of 0.10. The framework of the crystal is built up of a stack of α-CDx molecules with a head-to-tail arrangement along the two-fold axis, showing a channel-type structure. Two *m*-NP molecules are statistically disordered on the two-fold axis. One is located in the channel, while the other is sandwiched between the α-CDx molecules. In the channel, the nitro group of *m*-NP is inserted into the α-CDx ring from the secondary hydroxyl side, and the phenolic hydroxyl group is hydrogen-bonded to the primary hydroxyl group of the next α-CDx molecule. The enthalpy change was calculated for the complex formation in an aqueous solution. The calculated results are in qualitatively agreement with the observed values. The catalytic ability of α-CDx in the hydrolysis of substituted phenyl acetates was discussed on the basis of the structural data.

α-Cyclodextrin (α-CDx), which is a doughnut-shaped oligosaccharide consisting of α-1,4-linked six D-glucose residues, forms a number of inclusion complexes with a variety of guest molecules in aqueous solutions and in the crystalline state.[1,2] In solution, α-CDx catalyzes several chemical reactions,[3] so it has been referred to as enzyme model. The stereospecific catalysis has been observed in the hydrolysis of substituted phenyl acetates;[4] *m*-nitrophenyl acetate decomposes about fifty times faster than *p*-nitrophenyl acetate. In the previous paper,[5] it was shown that the low catalytic ability of α-CDx in the hydrolysis of *para*-substituted phenyl acetates can be ascribed to the structure of the α-CDx–ester inclusion complex. The X-ray analysis of the α-CDx–*m*-nitrophenol (1: 2) complex was carried out to investigate the geometry of inclusion in relation to the stereospecificity of the α-CDx-catalyzed reactions as well as the α-CDx–substrate interaction. The energy of the complex is calculated by using the structural data to investigate the intermolecular force for complex formation.

TABLE 1. CRYSTAL DATA

$C_{36}H_{60}O_{30}\cdot 2C_6H_5NO_3\cdot 6H_2O$		
Formula weight		1359.2
Crystal system		Orthorhombic
Space group		$P2_12_12$
	Z	2
Cell dimensions	a	22.231(7) Å
	b	16.865(6)
	c	8.152(1)
Cell volume	V	3056.5 Å^3
Density	D_m	1.47 g·cm^{-3}
	D_x	1.48

Experimental

A yellowish and needle-like crystal of the α-CDx–*m*-NP (1:2) complex was obtained by allowing an aqueous solution containing α-CDx and *m*-NP with a 1: 1 molar ratio to stand. The determination of lattice parameters and the intensity measurement were carried out on a Rigaku automatic four-circle diffractometer with graphite-monochromated Cu $K\alpha$ radiation. The crystal was enclosed in a quartz capillary with a small amount of water, since the crystal breaks up in the air. 2246 independent reflections with $|F_o|\geqq 3\sigma(F)$ were collected up to 120° in 2θ by using the 2θ-ω scan technique. No correction was made for absorption and extinction. The crystal data are given in Table 1.

Determination and Refinement of the Structure

The crystal of the α-CDx–*m*-NP complex is nearly isomorphous with the crystals which have the channel-type structure. A set of coordinates of α-CDx found in the α-CDx–sodium benzenesulfonate complex[6] was used to calculate the initial phases, which were refined by the block-diagonal least-squares method. The *m*-NP and water molecules were found on an electron-density map. The primary hydroxyl groups of α-CDx were found to be statistically disordered. Each occupancy factor of 0.5 was estimated from the electron-density map, but the values were not refined. The determination of the atomic parameters of the *m*-NP molecule (*m*-NP-2) located on the c axis failed, owing to the disordered structure. The position and orientation of *m*-NP-2 were then determined by the rigid-body least-squares method; the structure of *m*-NP-2 was built up by using the bond distances and angles of *p*-NP in the α-CDx–*p*-NP complex.[5] The atomic parameters of the other molecules were refined by the block-diagonal least-squares method. The quantity minimized was $\Sigma w(|F_o|-|F_c|)^2$, with $w=1.0$ for all reflections. The final *R*-value was 0.10. The atomic scattering factors were taken from "International Tables for X-Ray Crystallography."[7] The atomic parameters are listed in Table 2. The observed and calculated structure factors are given in Table 3.**

** Tables 3 and 4 are kept as a Document at the office of The Chemical Society of Japan (Document No. 7815).

TABLE 2. FINAL ATOMIC PARAMETERS ($\times 10^4$)

The anisotropic thermal factors are of the form: $\exp[-(B_{11}h^2+B_{22}k^2+B_{33}l^2+B_{12}hk+B_{23}kl+B_{31}lh)]$.

	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{23}	B_{31}
C(1,G1)	1445(5)	2422(7)	3587(15)	24(3)	40(5)	146(21)	-5(7)	57(20)	-22(14)
C(2,G1)	1172(5)	2880(7)	5017(16)	16(2)	47(5)	168(21)	-2(6)	-19(20)	-30(13)
C(3,G1)	492(5)	2612(7)	5228(14)	16(2)	40(5)	136(20)	3(6)	-14(17)	-19(12)
C(4,G1)	167(4)	2799(6)	3622(13)	14(2)	43(5)	121(17)	-4(5)	57(18)	-15(11)
C(5,G1)	479(5)	2331(8)	2207(14)	12(2)	73(7)	126(20)	5(7)	15(21)	2(12)
C(6,G1)	208(6)	2625(12)	521(15)	22(3)	137(13)	110(21)	21(11)	11(31)	0(13)
O(2,G1)	1514(4)	2656(5)	6449(12)	27(2)	52(4)	232(19)	8(5)	-43(17)	-69(12)
O(3,G1)	241(3)	3110(5)	6499(10)	26(2)	51(4)	125(13)	7(5)	-28(14)	-13(9)
O(4,G1)	-414(3)	2447(4)	3846(9)	16(2)	33(3)	131(13)	0(4)	12(12)	-12(8)
O(5,G1)	1098(3)	2639(5)	2158(10)	21(2)	56(4)	153(15)	1(5)	79(14)	-2(9)
O(6A,G1)	474(8)	2301(13)	-643(21)	26(4)	91(12)	160(33)	26(13)	-12(36)	8(21)
O(6B,G1)	221(9)	3309(11)	102(24)	39(6)	48(8)	220(36)	10(12)	56(33)	-27(26)
C(1,G2)	2394(5)	-447(7)	3649(18)	16(3)	49(6)	238(27)	-2(6)	63(24)	9(16)
C(2,G2)	2528(6)	82(7)	5123(18)	22(3)	29(4)	271(26)	0(6)	33(22)	-67(16)
C(3,G2)	2014(5)	694(7)	5296(15)	24(3)	39(5)	139(21)	-8(6)	25(18)	-30(14)
C(4,G2)	1952(5)	1152(7)	3659(15)	18(2)	38(5)	162(21)	4(6)	26(19)	-22(14)
C(5,G2)	1846(6)	592(7)	2257(14)	35(4)	42(5)	119(20)	39(8)	25(18)	18(16)
C(6,G2)	1824(8)	990(10)	571(18)	57(6)	74(9)	174(27)	72(12)	70(26)	84(22)
O(2,G2)	2541(5)	-431(5)	6495(12)	54(4)	43(4)	228(19)	11(6)	19(17)	-143(16)
O(3,G2)	2186(4)	1265(5)	6553(11)	35(2)	42(4)	158(16)	1(5)	1(14)	-57(11)
O(4,G2)	1417(3)	1618(4)	3878(10)	18(2)	27(3)	154(14)	-5(4)	22(11)	-6(9)
O(5,G2)	2348(4)	30(5)	2217(10)	25(2)	45(4)	209(16)	9(5)	62(16)	54(11)
O(6A,G2)	1924(11)	562(12)	-609(22)	60(8)	59(9)	135(31)	57(15)	-23(31)	-6(29)
O(6B,G2)	2222(9)	1314(12)	109(25)	38(6)	62(10)	210(38)	-7(13)	24(36)	-27(28)
C(1,G3)	923(5)	-2945(7)	3520(18)	20(3)	42(5)	217(26)	8(6)	10(22)	-6(15)
C(2,G3)	1358(6)	-2886(7)	5022(17)	30(3)	40(5)	167(22)	-9(7)	32(20)	-19(16)
C(3,G3)	1549(5)	-2001(7)	5242(13)	22(3)	41(5)	91(18)	6(6)	-2(16)	1(12)
C(4,G3)	1822(5)	-1684(6)	3651(13)	18(2)	33(4)	100(17)	-2(6)	-2(16)	-5(12)
C(5,G3)	1392(5)	-1794(7)	2177(14)	26(3)	40(5)	127(20)	-22(7)	-15(18)	7(14)
C(6,G3)	1718(7)	-1622(11)	558(16)	42(5)	107(11)	99(21)	-52(13)	-10(26)	23(17)
O(2,G3)	1024(4)	-3169(6)	6372(12)	32(2)	62(5)	212(19)	-13(6)	112(18)	-45(13)
O(3,G3)	2008(3)	-1968(5)	6469(10)	22(2)	57(4)	127(14)	-1(5)	36(14)	-15(9)
O(4,G3)	1858(3)	-852(4)	3934(10)	15(2)	34(3)	153(14)	-6(4)	-13(12)	-2(9)
O(5,G3)	1239(3)	-2652(5)	2129(10)	19(2)	45(4)	152(14)	-7(4)	-31(13)	39(9)
O(6A,G3)	1385(11)	-1815(11)	-658(23)	53(8)	142(18)	94(30)	-68(21)	4(42)	10(26)
O(6B,G1)	2131(9)	-2026(11)	84(26)	48(7)	49(8)	221(38)	-20(13)	-67(33)	107(29)
O(W1)	1409(7)	6339(7)	-689(14)	96(6)	55(5)	231(24)	33(10)	-7(20)	-70(21)
O(W2)	1674(4)	3399(6)	-602(12)	37(3)	56(5)	219(20)	-19(6)	-24(17)	27(13)
O(W3)	1778(4)	4890(7)	709(11)	34(3)	72(5)	179(16)	-8(7)	17(18)	-3(12)
C(1,N1)	316(5)	4971(7)	5231(13)	24(3)	27(4)	151(19)	3(6)	-14(18)	-4(13)
C(2,N1)	612(6)	4936(7)	3741(17)	35(4)	32(5)	227(26)	3(7)	-29(24)	40(19)
C(3,N1)	320(7)	4956(10)	2291(17)	62(6)	36(5)	209(25)	-24(13)	-34(27)	55(21)
O(1,N1)	1160(7)	4928(12)	3670(24)	21(4)	70(9)	241(36)	15(11)	-40(41)	-11(24)
O(2,N1)	1155(9)	4784(13)	6963(24)	33(5)	82(12)	211(38)	3(14)	34(38)	4(26)
O(3,N1)	303(9)	4939(19)	8086(21)	41(7)	138(17)	134(29)	59(21)	53(49)	25(24)
N(1,N1)	601(9)	4879(15)	6868(28)	20(5)	64(12)	236(46)	3(13)	13(45)	21(26)

	x	y	z		x	y	z
C(1,N2)	-24	-23	6035	C(6,N2)	-524	396	6590
C(2,N2)	330	-468	7068	O(1,N2)	517	-877	9854
C(3,N2)	184	-495	8731	O(2,N2)	-176	415	3362
C(4,N2)	-311	-70	9290	O(3,N2)	606	-322	3850
C(5,N2)	-662	382	8225	N(1,N2)	142	22	4295

Description and Discussion of the Structure

The structure and numbering scheme of the complex are shown in Figs. 1 and 2. The schematic drawing of the crystal structure is given in Fig. 3. The α-CDx molecules are stacked along the two-fold axis to form an endless cylinder, showing a channel-type structure. One *m*-NP molecule (*m*-NP-2) is included in the cylinder, while the other (*m*-NP-1) is located outside the α-CDx ring.

Structure of α-CDx. Bond distances, angles, and conformation angles are given in Tables 4—6. The geometrical data for α-CDx are shown in Table 7. The bond distances and angles are in good agreement with those found in the other α-CDx complexes with the channel-type structure.6,8—10) The primary hydroxyl groups are statistically disordered, showing *gauche-trans* and *gauche-gauche* conformations. The C–O bonds of these groups are abnormally short, but a similar shortening of the disordered C–O bond has been observed in α-L-sorbose11) and the α-CDx complexes with Methyl Orange.9) The α-CDx ring is distorted from the regular hexagonal symmetry owing to the inclusion of the planar molecule. The diagonal O(4, G3)···O(4, G3*) distance is longer by 0.4 Å than the O(4, G2)···O(4, G2*) distance. The distortion of the α-CDx ring

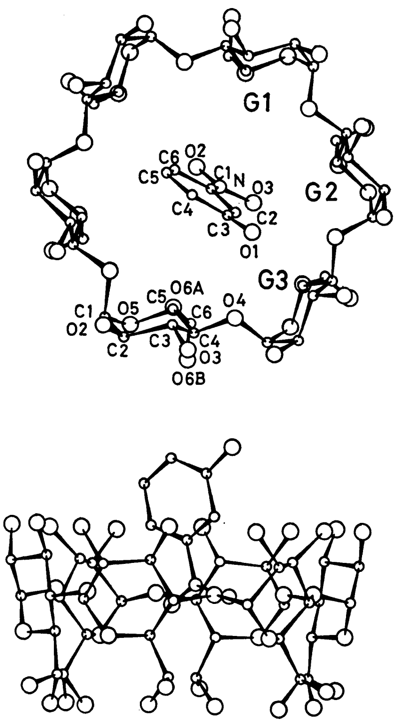

Fig. 1. The structure and numbering scheme of the α-cyclodextrin-*m*-nitorophenol complex.

Table 5. Average bond distances and angles for the glucose residue

Standard deviations given in parentheses were estimated according to $\sigma=[\sum_{i=1}^{3}(x_i-\bar{x})^2/2]^{1/2}$, where x_i is the bond distance or angle in the i-th glucose residue and $\bar{x}$ is the average value. A prime (′) indicates an atom in the adjacent glucose residue.

I. Bond distances (l/Å)			
C(1)-C(2)	1.538(23)	C(4)-C(5)	1.536(31)
C(1)-O(5)	1.429(12)	C(4)-O(4)	1.431(7)
C(1)-O(4′)	1.402(29)	C(5)-C(6)	1.548(28)
C(2)-C(3)	1.565(20)	C(6)-O(6A)	1.249(29)
C(2)-O(2)	1.422(18)	C(6)-O(6B)	1.171(57)
C(3)-C(4)	1.535(11)	C(5)-O(5)	1.474(12)
C(3)-O(3)	1.444(13)		
II. Bond angles (ϕ/°)			
C(2)-C(1)-O(5)	107.5(16)	C(3)-C(4)-O(4)	103.5(3)
C(2)-C(1)-O(4′)	109.1(12)	C(5)-C(4)-O(4)	106.9(9)
O(5)-C(1)-O(4′)	110.5(10)	C(4)-C(5)-C(6)	111.2(31)
C(1)-C(2)-C(3)	108.5(1)	C(4)-C(5)-O(5)	106.3(14)
C(1)-C(2)-O(2)	105.7(4)	C(6)-C(5)-O(5)	105.1(21)
C(3)-C(2)-O(2)	110.9(11)	C(5)-C(6)-O(6A)	112.2(35)
C(2)-C(3)-C(4)	108.8(14)	C(5)-C(6)-O(6B)	121.5(15)
C(2)-C(3)-O(3)	107.5(11)	C(4)-O(4)-C(1′)	118.7(15)
C(4)-C(3)-O(3)	107.9(9)	C(5)-O(5)-C(1)	114.0(14)
C(3)-C(4)-C(5)	110.4(17)		

is small compared with the α-CDx-*p*-NP complex; the maximum difference in the O(4)···O(4) distances is 0.9 Å in the *p*-NP complex. The O(4)···O(4) distances between the adjacent glucose residues indicate that the deformation of the pyranose ring is also small in the *m*-NP complex.

Table 6. Conformation angles (ϕ/°) in α-cyclodextrin

A prime (′) indicates an atom in the adjacent glucose residue.

	G1	G2	G3	Average
C(1)-C(2)-C(3)-C(4)	−59.4	−55.5	−55.2	−56.7
C(2)-C(3)-C(4)-C(5)	59.6	56.6	55.7	57.3
C(3)-C(4)-C(5)-O(5)	−61.5	−57.5	−55.4	−58.1
C(4)-C(5)-O(5)-C(1)	67.6	62.9	62.9	64.5
C(5)-O(5)-C(1)-C(2)	−68.5	−64.2	−65.9	−66.2
O(5)-C(1)-C(2)-C(3)	61.4	59.0	58.8	59.7
O(4′)-C(1)-C(2)-O(2)	57.8	56.5	60.6	58.3
O(2)-C(2)-C(3)-O(3)	69.1	72.3	71.7	71.0
O(3)-C(3)-C(4)-O(4)	−72.7	−70.6	−73.7	−72.3
O(4)-C(4)-C(5)-C(6)	78.0	71.9	79.4	76.4
O(5)-C(5)-C(6)-O(6A)	−64.1	−40.2	−57.8	−54.0
O(5)-C(5)-C(6)-O(6B)	53.9	57.4	49.2	53.5
C(4)-C(5)-C(6)-O(6A)	−175.0	−158.4	−171.7	−168.4
C(4)-C(5)-C(6)-O(6B)	57.1	60.8	64.7	60.9
C(2)-C(1)-O(4′)-C(4′)	−130.3	−132.4	−129.3	−130.7
O(5)-C(1)-O(4′)-C(4′)	111.5	107.2	113.1	110.6
C(1)-O(4′)-C(4′)-C(3′)	127.8	129.9	129.1	128.9
C(1)-O(4′)-C(4′)-C(5′)	−114.7	−112.7	−116.4	−114.6

Table 7. Geometrical data for α-cyclodextrin

An asterisk (*) indicates an atom related by the two-fold symmetry.

I. Selected interatomic distances between glucose residues (l/Å)			
O(4, G1)-O(4, G2)	4.303		
O(4, G2)-O(4, G3)	4.279		
O(4, G3)-O(4, G1*)	4.186		
O(2, G1)-O(3, G2)	2.788		
O(3, G1)-O(2, G3*)	2.821		
O(2, G2)-O(3, G3)	2.858		
O(4, G1)-O(4, G1*)	8.444		
O(4, G2)-O(4, G2*)	8.346		
O(4, G3)-O(4, G3*)	8.745		
II. Least-squares planes and deviations of atoms (l/Å)			
i) $-0.3217X+0.9334Y-0.1590Z=3.0664$			
C(1, G1)[a]	−0.747	C(4, G1)[a]	0.751
C(2, G1)	−0.020	C(5, G1)	−0.020
C(3, G1)	0.018	O(5, G1)	0.021
ii) $0.6457X+0.7498Y-0.1445Z=3.1405$			
C(1, G2)[a]	−0.695	C(4, G2)[a]	0.693
C(2, G2)	−0.010	C(5, G2)	−0.010
C(3, G2)	0.010	O(5, G2)	0.011
iii) $0.9585X-0.2357Y-0.1603Z=3.3949$			
C(1, G3)[a]	−0.711	C(4, G3)[a]	0.679
C(2, G3)	−0.012	C(5, G3)	−0.012
C(3, G3)	0.011	O(5, G3)	0.013
iv) $0.0000X+0.0000Y+1.0000Z=3.1679$			
O(4, G1)	−0.034	O(4, G1*)	−0.034
O(4, G2)	−0.004	O(4, G2*)	−0.004
O(4, G3)	0.038	O(4, G3*)	0.038

a) The atom not included in the plane.

Structure of m-*Nitrophenol.* Both *m*-NP molecules (*m*-NP-1 and *m*-NP-2) are statistically disordered on the two-fold axis, as shown in Fig. 2. The benzene ring of

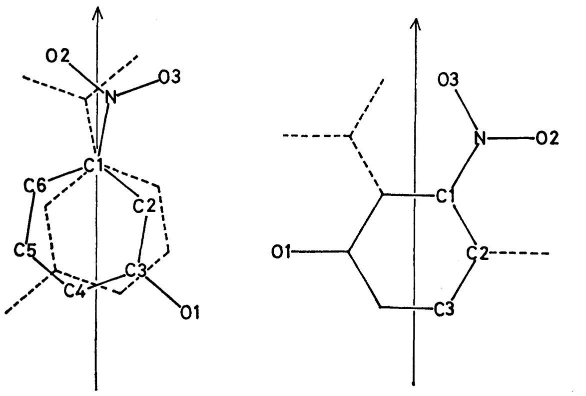

Fig. 2. Schematic drawings of the disordered structures of *m*-NP-1 (right) and *m*-NP-2 (left). The transposed structure by the two-fold axis is shown by broken lines.

TABLE 8. BOND DISTANCES AND ANGLES IN *m*-NITROPHENOL WITH ESTIMATED STANDARD DEVIATIONS

An asterisk (*) indicates an atom related by the two-fold symmetry.

I. Bond distances (l/Å)	
C(1, N1)-C(2, N1)	1.382(17)
C(1, N1)-C(1*, N1)	1.410(16)
C(2, N1)-C(3, N1)	1.349(20)
C(3, N1)-C(3*, N1)	1.431(21)
C(2*, N1)-O(1, N1)	1.218(23)
C(1, N1)-N(1, N1)	1.485(25)
N(1, N1)-O(2, N1)	1.246(30)
N(1, N1)-O(3, N1)	1.198(33)
II. Bond angles (ϕ/°)	
C(1, N1)-C(2, N1)-C(3,N1)	122.7(13)
C(2, N1)-C(3, N1)-C(3*, N1)	118.8(13)
C(2, N1)-C(1, N1)-C(1*, N1)	118.5(11)
C(1*, N1)-C(2*, N1)-O(1, N1)	121.2(14)
C(3*, N1)-C(2*, N1)-O(1, N1)	116.1(15)
C(2, N1)-C(1, N1)-N(1, N1)	125.6(13)
C(1*, N1)-C(1, N1)-N(1, N1)	115.6(12)
C(1, N1)-N(1, N1)-O(2, N1)	119.4(19)
C(1, N1)-N(1, N1)-O(3, N1)	120.1(21)
O(2, N1)-N(1, N1)-O(3, N1)	120.4(24)

m-NP-1 shows the two-fold symmetry. The bond distances and angles (Table 8) are normal. The nitrophenyl group of *m*-NP-2 is not parallel to the two-fold axis, but makes an angle of 14.2°. The *m*-NP-2 molecule seems to be loosely bound, since the average thermal factor of the molecule is relatively large (22.7 Å^2).

Geometry of Inclusion. Intermolecular distances between α-CDx and *m*-NP-2 are given in Table 9. In the channel, the *m*-NP-2 molecules are located at a position similar to that of the *N,N*-dimethylaminophenyl group found in the Methyl Orange complexes.[9] The nitro group is inserted into the α-CDx cavity from the secondary hydroxyl side. The phenolic hydroxyl group is hydrogen-bonded to O(6A, G3) of the next α-CDx molecule. The benzene ring is surrounded by O(3)···O(6) hydrogen bonds. Thus, the adjacent α-CDx molecules are connected not only by the O(3)···O(6) hydrogen bonds, but also by the guest molecule. The nitro group is in close contact with the glycosidic oxygen atom.

TABLE 9. SELECTED INTERMOLECULAR DISTANCES

I. O(3)···O(6) distances along the channel (l/Å)		
O(3, G1)-O(6A, G1)	(a)	2.749
O(3, G2)-O(6A, G2)	(a)	2.664
O(3, G3)-O(6A, G3)	(a)	2.733
O(3, G1)-O(6B, G1)	(a)	2.957
O(3, G2)-O(6B, G2)	(a)	2.901
O(3, G3)-O(6B, G3)	(a)	2.961
II. Intermolecular distances involving *m*-nitrophenol (l/Å)		
C(1, N1)-O(3, G1)		3.310
C(3, N1)-O(6B,G1)		3.309
N(1, N1)-O(3, G1)		3.103
O(1, N1)-O(W3)		2.779
O(1, N1)-C(2, G2)	(g)	3.090
O(1, N1)-O(2, G2)	(g)	2.953
O(3, N2)-O(4, G3)		2.922
O(3, N2)-C(5, G3)		3.328
O(1, N2)-C(5, G3)	(c)	3.124
O(1, N2)-C(6, G3)	(c)	3.007
O(1, N2)-O(6A, G3)	(c)	2.529
C(5, N2)-O(6A, G3)	(e)	3.042
III. Intermolecular distances involving water (l/Å)		
O(W1)-O(W3)		2.818
O(W2)-O(W3)		2.741
O(W2)-O(5, G1)		2.889
O(W2)-O(2, G1)	(a)	2.735
O(W1)-O(5, G3)	(b)	2.884
O(W1)-O(2, G3)	(d)	2.676
O(W2)-O(6B, G3)	(f)	2.783
O(W3)-O(2, G2)	(g)	2.790

Code	Symmetry operator		
None	x,	y,	z
a	x,	y,	$1+z$
b	x,	$-1+y$,	z
c	x,	y,	$-1+z$
d	x,	$-1+y$,	$1+z$
e	$-x$,	$-y$,	$-1+z$
f	$1/2-x$,	$-1/2+y$,	$-z$
g	$1/2-x$,	$-1/2+y$,	$1-z$

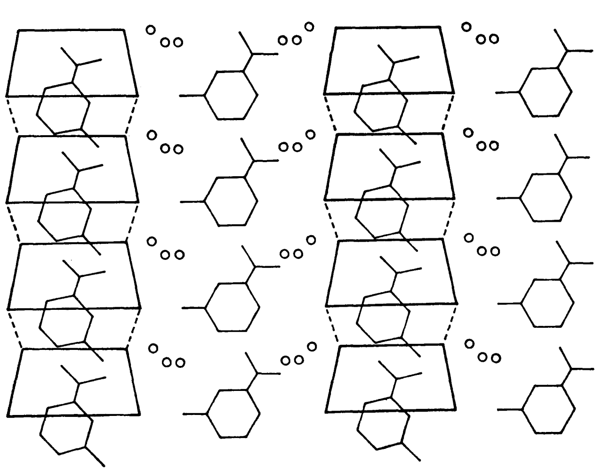

Fig. 3. A schematic drawing of the crystal structure. Circles indicate water molecules. Broken lines denote hydrogen bonds linking α-cyclodextrin molecules along the channel.

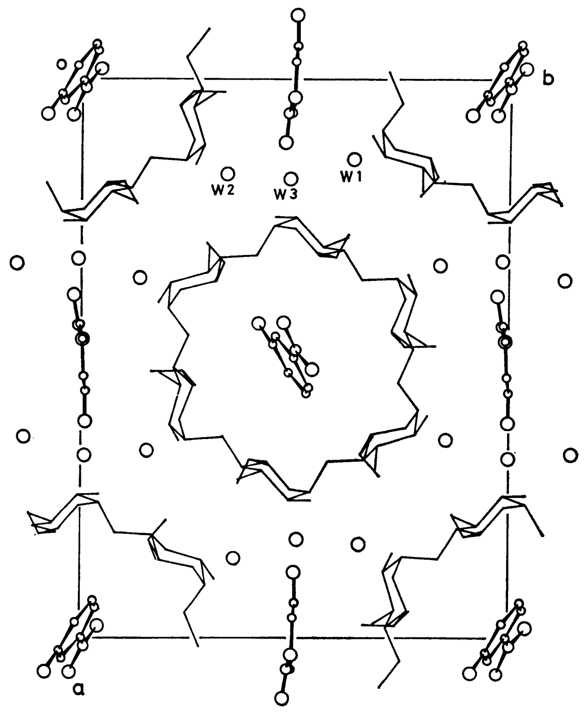

Fig. 4. The crystal structure projected to the ab plane. Circles indicate atoms in water and *m*-nitrophenol molecules.

The shortest distance is 2.922 Å, which is slightly shorter than the normal van der Waals contact of 3.04 Å.[12)]

Crystal Structure. The crystal structures are shown in Figs. 4 and 5. The framework of the crystal is built up of a stack of α-CDx molecules with the head-to-tail arrangement along the two-fold axis. The *m*-NP-1 molecule is located nearly parallel to the ac plane in the space between the α-CDx molecules. The phenolic hydroxyl group forms two hydrogen bonds with O(W3) and O(2, G2) (Table 9). The benzene ring is sandwiched by the two α-CDx molecules. Water molecules are distributed in the space outside the channel, and they are linked each other by hydrogen bonds. W1 and W2 are also found in the other channel-type crystals,[6,8–10)] but W3 is replaced by the sodium or potassium ion. W1 and W2 form O(2)···water···O(5) hydrogen bonds connecting the adjacent two α-CDx molecules along the channel. The space where *m*-NP-1 is located is filled with water molecules in the other channel-type crystals.

The channel-type structure with the head-to-tail arrangement of α-CDx molecules has been observed in the complexes with ionic guests. In these complexes, the primary hydroxyl groups of α-CDx form hydrogen bonds with the ionized group of the guest molecule. In the *m*-NP complex, however, the guest molecule has no ionized group. The phenolic hydroxyl group is hydrogen-bonded to the primary hydroxyl group of α-CDx. Therefore, the ionic guest is not necessarily required to form the channel-type structure, but the hydrogen bond with the primary hydroxyl group seems to be important.

Calculation of the Heat of the Complex Formation in Aqueous Solution

Method of Calculation. In the crystalline state, the uncomplexed α-CDx molecule contains two water molecules in its cavity.[13)] If we assume the same structure in aqueous solution, the two water molecules will be released by the complex formation. The heat of the complex formation of α-CDx with *m*-NP and *p*-NP in aqueous solution was calculated for the following equilibrium at 25 °C:

$$\alpha\text{-CDx}\cdot 2\mathrm{H_2O} + \text{guest} \rightleftarrows \alpha\text{-CDx–guest} + 2\mathrm{H_2O}. \qquad (1)$$

The enthalpy change is expressed as

$$\Delta H = H(\alpha\text{-CDx–guest}) + H(2\mathrm{H_2O}) - H(\alpha\text{-CDx–}2\mathrm{H_2O}) - H(\text{guest}), \qquad (2)$$

$$= \Delta H^{\mathrm{s}} + \Delta H^{\mathrm{c}} + \Delta H^{\mathrm{i}}, \qquad (3)$$

where ΔH^{s}, ΔH^{c}, and ΔH^{i} are the enthalpy changes for the solvation, the conformation, and the interaction of α-CDx with the included molecules, respectively. The interaction energy and conformational energy were calculated on the basis of the non-bonded interatomic interaction.[6)] The procedure of evaluating the solvation energy is generally the same as used in the earlier work,[6)] but the following modifications were made: (1) the cavity term was calculated according to Pierotti[14)] and (2) the dipole-dipole interaction was taken into account in the calculation of the electrostatic term (see Appendix).

Parameters. The van der Waals volumes of the

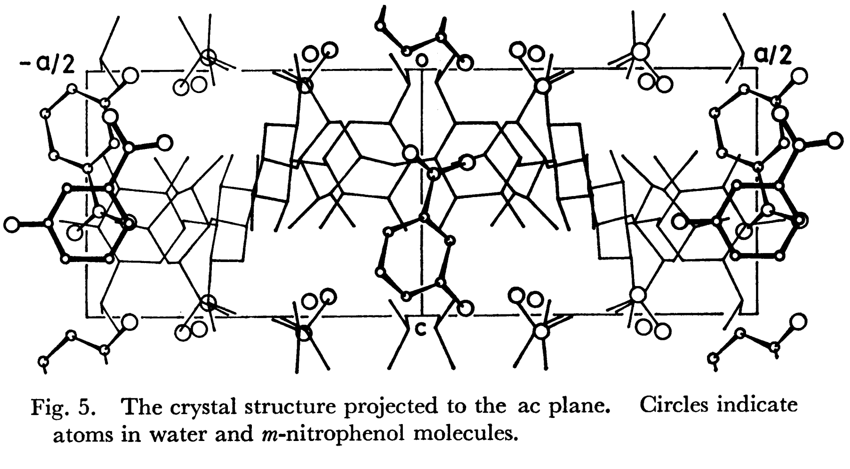

Fig. 5. The crystal structure projected to the ac plane. Circles indicate atoms in water and *m*-nitrophenol molecules.

Table 10. Van der Waals volumes

H_2O	20.58 Å^3
m-NP	113.1
p-NP	113.1
α-CDx-2H_2O	1120.0
α-CDx-*m*-NP	1232.3
α-CDx-*p*-NP	1186.5

complexes were estimated from the X-ray data, and those of the other molecules were calculated by using the van der Waals volumes of atoms and groups.[12] The group dipole moments were taken from the literature[15] and the average polarizabilities were estimated from the atomic polarizabilities.[16] The coefficients of the Lennard-Jones potential function were calculated according to Goebel *et al.*[17,18] The atomic charges of the glucose residue were taken from Rao,[19] and those of *m*-NP and *p*-NP were calculated by the CNDO/2 MO method.[20]

Table 11. Atomic charges

I. *m*-Nitrophenol			
C(1)	0.06	O(1)H	−0.12
C(2)	−0.04	O(2)	−0.33
C(3)	0.19	O(3)	−0.34
C(4)	−0.02	H(C2)	0.04
C(5)	0.02	H(C4)	0.02
C(6)	0.00	H(C5)	0.02
N	0.47	H(C6)	0.03
II. *p*-Nitrophenol			
C(1)	0.01	O(1)H	−0.09
C(2)	0.05	O(2)	−0.34
C(3)	−0.06	O(3)	−0.34
C(4)	0.21	H(C2)	0.03
C(5)	−0.05	H(C3)	0.02
C(6)	0.04	H(C5)	0.02
N	0.47	H(C6)	0.03

Results of the Calculation and Discussion

The calculated enthalpy changes are given in Table 12. These values are in qualitatively agreement with the observed ones.[21] The enthalpy change of the *p*-NP complex is three times greater than that of the *m*-NP complex. In both complexes, the effect of the solvation energy is small and negative for the complex formation. The hydrogen-bond energy was not included in the calculation, but a part of it was taken into account in terms of the electrostatic energy and the van der Waals energy. The contribution of the hydrogen-bond energy to the complex formation has been considered to be small in aqueous solution.[3]

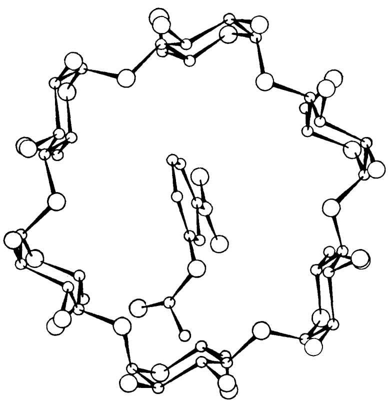

Fig. 6. An expected structure of the α-cyclodextrin-*m*-nitrophenyl acetate complex.

In the crystalline complexes, a remarkable change of the α-CDx conformation is observed between the complexed state and the uncomplexed state.[22] The calculated conformational energy of the *m*-NP complex is lower than that of the uncomplexed state, suggesting that the α-CDx conformation is stabilized by the complex formation. On the other hand, the *p*-NP complex gives a higher conformational energy than the uncomplexed α-CDx. This high energy may be due to the deformation of the α-CDx ring caused by the deep penetration of the bulky and planar molecule. Thus, the inclusion of *p*-NP makes the α-CDx conformation unstable, but the strong interaction of *p*-NP with α-CDx gives the large interaction energy. In the case of the *m*-NP complex, only the partial penetration of the guest molecule is possible because of the steric hindrance. The relatively weak interaction between α-CDx and *m*-NP gives a small deformation of the α-CDx ring. The calculated results indicate the importance of the interaction energy, and suggest that the conformational energy and the solvation energy are not the major components of the binding force in the *m*-NP and *p*-NP complexes. This has also been pointed out by Bergeron *et al.* on the basis of the spectroscopic investigations of α-CDx complexes with substituted *p*-nitrophenols.[23]

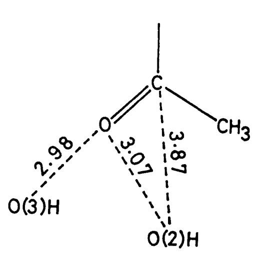

Fig. 7. A schematic drawing of the contact between the acetyl group of *m*-nitrophenyl acetate and the secondary hydroxyl groups of α-cyclodextrin.

Table 12. Calculated enthalpy change for the complex formation

	ΔH^s mol^{-1} kcal	ΔH^c mol^{-1} kcal	ΔH^i mol^{-1} kcal	ΔH mol^{-1} kcal	ΔH(obsd)$^{a)}$ mol^{-1} kcal
α-CDx-*m*-NP	1.64	−0.69	−4.61	−3.66	−7.8
α-CDx-*p*-NP	1.42	0.92	−13.68	−11.34	−7.3

a) See Ref. 22.

Catalytic Property of α-Cyclodextrin

In the α-CDx catalyzed hydrolysis of substituted phenyl acetates, the reaction mechanism has been interpreted in terms of the nucleophilic attack of the secondary hydroxyl group of α-CDx on the carbonyl carbon atom of the ester.[4)] The low reactivity of α-CDx in the hydrolysis of *para*-substituted phenyl esters has been discussed on the basis of the geometry of the α-CDx–*p*-NP complex.[5)] The nitrophenyl group is so rigidly fixed in the α-CDx ring that the carbonyl carbon atom of the ester could hardly have close contacts with the secondary hydroxyl groups without the large deformation of the α-CDx ring.

In the α-CDx–*m*-NP complex, the guest molecule was found to be partially inserted into the α-CDx ring from the secondary hydroxyl side. The phenolic hydroxyl group is separated by more than 4.7 Å from the secondary hydroxyl groups. When *m*-nitrophenyl acetate forms a complex in the same manner, the acetyl group may have close contacts with the secondary hydroxyl groups. The expected structure of the *m*-nitrophenyl acetate complex is shown in Fig. 6, where the conformation of the acetyl group was assumed to be the same as that found in *p*-nitrophenyl acetate.[24)] The distances between the carbonyl oxygen atom and the vicinal secondary hydroxyl groups are 2.98 and 3.07 Å (Fig. 7), suggesting that the structure of the complex is stabilized by hydrogen bonds. The carbonyl carbon atom is located at the distance of 3.87 Å from the secondary hydroxyl group. Unlike *p*-NP, *m*-NP is loosely bound to the α-CDx cavity. The carbonyl carbon atom can easily approach closer to the secondary hydroxyl group by the small displacement of the guest molecule and the deformation of the α-CDx ring. The hydrolysis of the ester bond is interpreted in terms of the tetrahedral intermediate.[25,26)] When the carbonyl carbon atom is attacked by the O(2) hydroxyl group (Fig. 7), which is possibly ionized in a relatively high pH condition,[4)] the hydrogen bond involving the O(3) hydroxyl group may stabilize the tetrahedral intermediate and lower the activation energy. Acetyl α-CDx, which is formed by the release of *m*-NP, may be decomposed by water. Although simplified, this proposed reaction mechanism is similar to that of the chymotrypsin-catalysis,[27)] indicating that α-CDx is a good enzyme model.

Appendix

The pair potential of the dipole-dipole interaction between μ_1 of the solvent molecule and μ_{2i} of the i-th group of the solute molecule is given by $-2\mu_1^2\mu_{2i}^2/(3kTr^6)$,[28)] where k is the Boltzmann constant. The distance between these dipoles is

$$r = (R^2+l^2-2Rl\cos\theta)^{1/2}, \qquad \text{(A1)}$$

where l and R are the distances from the center of the solute molecule to the i-th group of the solute molecule and to the solvent molecule respectively, and where θ is the angle made by the corresponding two vectors. Then, by averaging over l and θ, we obtain

$$U_{\mathrm{e}i}(R) = \frac{-\mu_1^2\mu_{2i}^2}{kT\varepsilon(R_2-l_{2i}^{\circ})^3}\int_0^{R_2-l_{2i}^{\circ}}\int_0^{\pi}\frac{l^2\sin\theta\mathrm{d}\theta\mathrm{d}l}{r^6}, \qquad \text{(A2)}$$

where l_{2i}° is the radius of the i-th group. The effective dielectric constant was assumed to be

$$\varepsilon = 1 + (\varepsilon_0-1)(1-\exp[(R_1+R_2-R)/2R_1]), \qquad \text{(A3)}$$

where R_1 and R_2 are the van der Waals radii of the solvent and solute molecules respectively, and where ε_0 is the dielectric constant of the solvent. Thus, the electrostatic energy is

$$H_{\mathrm{e}}^{\mathrm{s}} = \frac{-D}{2R_2^3}\sum_i\frac{\mu_{2i}^2}{\left(1-\frac{D\alpha_{2i}}{R_2^3}\right)} + 4\pi\rho\int_{R_0}^{\infty}\sum_i U_{\mathrm{e}i}(R)R^2\mathrm{d}R, \qquad \text{(A4}$$

with $D=2(\varepsilon_0-1)/(2\varepsilon_0+1)$ and $R_0=R_1+R_2$, where ρ is the number density of the solvent.

The van der Waals interaction energy is given by[29)]

$$H_{\mathrm{v}}^{\mathrm{s}} = 4\pi\rho\left[1-\frac{3(n^2-1)}{4(n^2+2)}\right]\int_{R_0}^{\infty}\sum_i U_{\mathrm{v}i}(R)R^2\mathrm{d}R. \qquad \text{(A5)}$$

The pair potential of the i-th atom in the solute molecule and the solvent molecule is

$$U_{\mathrm{v}i}(R) = \frac{3}{2(R_2-l_{2i}^{\circ})^3}\int_0^{R_2-l_{2i}^{\circ}}\int_0^{\pi}\left(\frac{a_i}{r^{12}}-\frac{c_i}{r^6}\right)l^2\sin\theta\mathrm{d}\theta\mathrm{d}l, \text{(A6)}$$

where a_i and c_i are the coefficients of the potential function, and where l_{2i}° is the radius of the i-th atom.

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