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The Structure of the Cyclodextrin Complex. XX. Crystal Structure of Uncomplexed Hydrated γ-Cyclodextrin

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Crystal structure of uncomplexed γ-cyclodextrin, $C_{48}H_{80}O_{40}\cdot 14.1H_2O$, was determined by the X-ray method. The crystal is monoclinic and the space group is $P2_1$ with cell dimensions; $a=16.847(2)$, $b=11.098(2)$, $c=20.271(2)$ Å, and $\beta=104.97(1)°$. The structure was solved by the inspection of a Patterson map and the R-map method combined with the rigid-body least-squares technique and refined by the block-diagonal least-squares method to the R-value of 0.061 for 5099 reflections ($\sin\theta/\lambda \geqq 0.57$). γ-Cyclodextrin is in a round shape and somewhat distorted from the regular octagonal symmetry. Intramolecular hydrogen bonds are formed between adjacent glucose residues and maintain the round structure of γ-cyclodextrin. γ-Cyclodextrin molecules are arranged in a cage-type packing, and 7.1 water molecules, occupying 14 sites, are located within the host cavity.

Cyclodextrins are cyclic oligosaccharides consisting of six or more D-glucose residues, which are connected to form a macrocycle by the α-1,4-linkage. Because of the cylindrically-shaped intramolecular cavity, cyclodextrins form inclusion complexes with a wide variety of molecules and ions,[1)] which can be fitted into the cavity, even if only partially. X-Ray studies of a number of crystalline complexes of α-cyclodextrin and β-cyclodextrin have revealed the geometrical feature of the host-guest interaction as well as the conformation of the macrocyclic ring,[2)] and chemical and physical properties of the inclusion complexes have been interpreted on that basis. On the other hand, only a few crystal structures have been reported for γ-cyclodextrin[3)] and its complexes.[4,5)] Maclennan and Stezowski have reported the crystal structure of uncomplexed γ-cyclodextrin at 120 K,[3)] and suggested that one glucose residue is statistically disordered. The low accuracy of their structure analysis, however, has prevented them from discussing the detailed bonding geometry and the conformation of the macrocycle in comparison with other cyclodextrins. We have been investigating the crystal structure of uncomplexed γ-cyclodextrin at room temperature, and have elucidated the structure with the accuracy comparable to that of other cyclodextrins. The preliminary report of this study[6)] has shown the round structure of γ-cyclodextrin having no disordered glucose residue. We here report details of the crystal structure of γ-cyclodextrin in comparison with the structure of α-cyclodextrin and β-cyclodextrin.

Experimental

Materials and Measurements. γ-Cyclodextrin was purchased from Nihon Shokuhin Kako Co., Ltd., and recrystallized three times from water. Crystals were obtained at room temperature by the slow evaporation of an aqueous solution containing γ-cyclodextrin and D-xylose in ca. 1 : 1 molar ratio. Lattice parameters and diffraction intensities were measured at 22 °C on a Nicolet P3/F diffractometer with graphite-monochromated Cu $K\alpha$ radiation. The crystal was sealed in a thin glass capillary with a drop of mother solution. By using θ—2θ scan mode, 5099 independent reflections with $|F_o| \geqq 3\sigma(F)$ were obtained up to 118° in 2θ. No corrections were made for absorption or extinction effects.

Crystal Data: $C_{48}H_{80}O_{40}\cdot 14.1H_2O$, F.W.=1551.2, monoclinic, space group $P2_1$, $Z=2$, $a=16.847$ (2), $b=11.098$ (2), $c=20.271$ (2) Å, $\beta=104.97$ (1)°, $V=3661.4$ Å^3, $D_x=1.415$ g·cm^{-3}.

Determination and Refinement of the Structure. The orientation of the pseudo octagonal axis of γ-cyclodextrin was deduced from a Patterson map. The rotation around the molecular axis and the position in the unit cell were determined by the R-map method by using the model structure with the regular octagonal symmetry. After the correction of the positional and orientational parameters of each glucose residue, the structure was refined by the usual least-squares method. Water molecules were found on a difference-Fourier map. The final block-diagonal least-squares refinement of the structure, including 87 hydrogen atoms, achieved the R-value of 0.061. The quantity minimized was $\sum w(|F_o|-|F_c|)^2$, with $w=1.0$ for all the reflections. Atomic coordinates and B_{eq} values of non-hydrogen atoms are given in Table 1. Tables of observed and calculated structure factors, anisotropic temperature factors of non-hydrogen atoms, and atomic parameters of hydrogen atoms, are deposited to the Chemical Society of Japan (Document No. 8749). The computation was carried out on a FACOM M380 computer at the Center of Research Information Processing System (RIPS), Agency of Industrial Science and Technology, Tsukuba.

Description of the Structure

γ-Cyclodextrin is in the shape of a nearly regular octagon as shown in Fig. 1. Each glucose unit has the $^4C_1$ chair conformation and is connected to the next residue by the α-1,4-linkage. Average bond distances and angles are shown in Fig. 2. These values are in good agreement with the corresponding values of α-cyclodextrin[7)] and β-cyclodextrin.[8)] The C(6)–O(6) bonds show two types of orientations; gauche-gauche (to the C(5)–O(5) bond and to the C(4)–C(5) bond, respectively) in the G2, G3, G4, and G7 residues and gauche-trans in the G1, G5, and G8 residues. The C(6)–O(6) bond in the G6 residue is disordered and the occupancy factor of the O(6,G6) atom is 0.76 for the

Table 1. Atomic Coordinates (×10^4) and B_{eq} Values[a] of Non-Hydrogen Atoms[b]

	OC	*x*	*y*	*z*	B_{eq}/Å^2		*OC*	*x*	*y*	*z*	B_{eq}/Å^2
C(1,G1)	1.0	−4005(4)	929(8)	2816(4)	4.76	C(2,G6)	1.0	4169(4)	1699(9)	5063(3)	4.84
C(2,G1)	1.0	−3974(4)	985(9)	3572(4)	4.65	C(3,G6)	1.0	3812(4)	2725(8)	4582(3)	4.34
C(3,G1)	1.0	−3132(4)	612(8)	4030(3)	4.15	C(4,G6)	1.0	3866(4)	2382(8)	3855(3)	4.02
C(4,G1)	1.0	−2812(4)	−505(8)	3775(4)	4.61	C(5,G6)	1.0	3418(5)	1198(8)	3645(3)	4.40
C(5,G1)	1.0	−2817(5)	−365(9)	3043(4)	5.29	C(6,G6)	1.0	3327(6)	771(9)	2924(4)	6.38
C(6,G1)	1.0	−2527(6)	−1450(12)	2736(5)	7.99	O(2,G6)	1.0	4034(3)	1930(7)	5712(2)	6.26
O(2,G1)	1.0	−4201(3)	2149(6)	3754(3)	5.46	O(3,G6)	1.0	4224(4)	3825(6)	4790(3)	5.18
O(3,G1)	1.0	−3206(3)	433(6)	4708(2)	4.85	O(4,G6)	1.0	3490(3)	3353(5)	3412(2)	3.81
O(4,G1)	1.0	−1997(3)	−682(5)	4207(3)	5.09	O(5,G6)	1.0	3850(3)	286(6)	4109(3)	5.26
O(5,G1)	1.0	−3656(3)	−151(6)	2659(3)	5.44	O(6,G6)	0.76	4056(4)	529(7)	2796(3)	5.08
O(6,G1)	1.0	−2403(6)	−1020(10)	2065(5)	13.50	O(6′,G6)	0.24	3257(15)	−182(18)	2775(10)	4.98
C(1,G2)	1.0	−3882(4)	4501(9)	1109(4)	5.02	C(1,G7)	1.0	1433(4)	−1994(9)	5445(4)	5.07
C(2,G2)	1.0	−4101(4)	4889(9)	1765(4)	4.89	C(2,G7)	1.0	1983(5)	−1231(9)	5986(4)	5.14
C(3,G2)	1.0	−3752(4)	3989(8)	2333(4)	4.18	C(3,G7)	1.0	2315(5)	−155(9)	5672(4)	4.94
C(4,G2)	1.0	−3994(4)	2717(8)	2102(3)	4.58	C(4,G7)	1.0	2760(4)	−621(8)	5149(3)	4.45
C(5,G2)	1.0	−3772(5)	2419(8)	1443(4)	4.94	C(5,G7)	1.0	2162(5)	−1408(9)	4608(4)	5.09
C(6,G2)	1.0	−4117(7)	1251(10)	1111(4)	6.86	C(6,G7)	1.0	2543(6)	−2004(10)	4103(4)	6.12
O(2,G2)	1.0	−3819(4)	6068(6)	1960(3)	6.91	O(2,G7)	1.0	1516(4)	−805(7)	6438(3)	7.22
O(3,G2)	1.0	−4046(3)	4227(6)	2920(2)	5.20	O(3,G7)	1.0	2895(3)	514(6)	6191(2)	5.26
O(4,G2)	1.0	−3562(3)	1931(5)	2644(2)	4.64	O(4,G7)	1.0	3000(3)	412(5)	4841(2)	4.52
O(5,G2)	1.0	−4093(3)	3324(6)	930(2)	5.25	O(5,G7)	1.0	1866(3)	−2396(6)	4966(3)	5.35
O(6,G2)	1.0	−5024(4)	1295(8)	942(3)	8.59	O(6,G7)	1.0	3252(4)	−2697(6)	4450(3)	6.20
C(1,G3)	1.0	−1391(4)	6298(8)	252(3)	3.98	C(1,G8)	1.0	−1809(5)	−1826(10)	4497(6)	7.27
C(2,G3)	1.0	−2014(4)	7109(8)	462(4)	4.10	C(2,G8)	1.0	−1427(5)	−1716(12)	5266(5)	7.70
C(3,G3)	1.0	−2384(4)	6496(7)	972(3)	3.77	C(3,G8)	1.0	−557(5)	−1156(11)	5374(5)	6.62
C(4,G3)	1.0	−2731(4)	5276(7)	695(3)	3.57	C(4,G8)	1.0	−58(6)	−1923(9)	5008(6)	6.31
C(5,G3)	1.0	−2067(4)	4515(8)	514(4)	4.43	C(5,G8)	1.0	−486(5)	−1927(11)	4248(6)	7.72
C(6,G3)	1.0	−2392(5)	3370(8)	151(5)	5.56	C(6,G8)	1.0	−53(7)	−2810(17)	3841(7)	13.43
O(2,G3)	1.0	−1635(3)	8238(5)	728(3)	5.26	O(2,G8)	1.0	−1908(3)	−964(9)	5577(3)	9.11
O(3,G3)	1.0	−3010(3)	7253(5)	1117(3)	4.78	O(3,G8)	1.0	−164(4)	−1198(11)	6090(3)	10.43
O(4,G3)	1.0	−3005(3)	4675(5)	1222(2)	3.98	O(4,G8)	1.0	732(3)	−1320(6)	5108(3)	5.38
O(5,G3)	1.0	−1741(3)	5197(5)	25(2)	4.38	O(5,G8)	1.0	−1296(4)	−2511(7)	4188(4)	8.50
O(6,G3)	1.0	−3016(4)	3558(6)	−463(3)	6.29	O(6,G8)	1.0	−431(6)	−2689(15)	3137(6)	20.71
C(1,G4)	1.0	1833(4)	6627(8)	1274(4)	4.35	O(W1)	1.0	−3888(5)	218(9)	−543(4)	9.93
C(2,G4)	1.0	1332(5)	7684(8)	1427(5)	5.87	O(W2)	1.0	−2323(5)	366(8)	310(4)	9.62
C(3,G4)	1.0	466(5)	7252(8)	1447(4)	5.08	O(W3)	1.0	−4656(4)	3222(7)	−3409(5)	11.00
C(4,G4)	1.0	66(4)	6638(7)	777(4)	3.94	O(W4)	1.0	−5744(4)	3068(8)	−41(4)	8.71
C(5,G4)	1.0	607(4)	5565(7)	671(4)	4.07	O(W5)	1.0	−5182(6)	2891(10)	−2156(5)	12.81
C(6,G4)	1.0	284(4)	4929(11)	5(5)	7.66	O(W6)	1.0	−1727(10)	5900(15)	2630(6)	21.08
O(2,G4)	1.0	1761(4)	8213(7)	2047(4)	8.72	O(W7)	0.82	−4539(5)	2559(9)	−722(4)	7.77
O(3,G4)	1.0	−20(4)	8334(7)	1495(4)	7.51	O(W8)	0.18	−4553(24)	3781(40)	−697(19)	8.17
O(4,G4)	1.0	−705(3)	6153(5)	841(2)	4.26	O(W9)	0.82	3618(5)	560(8)	1360(3)	6.79
O(5,G4)	1.0	1401(3)	6084(5)	657(2)	4.37	O(W10)	0.18	2831(24)	−38(31)	1421(14)	7.05
O(6,G4)	1.0	136(4)	5748(11)	−553(3)	11.18	O(W11)	0.56	1310(7)	694(12)	1713(7)	8.55
C(1,G5)	1.0	3950(4)	3833(7)	2984(4)	4.00	O(W12)	0.44	1185(17)	114(28)	2744(13)	16.98
C(2,G5)	1.0	3984(4)	5229(8)	3076(4)	4.81	O(W13)	0.44	1039(18)	1597(46)	1799(22)	30.04
C(3,G5)	1.0	3143(4)	5751(7)	2768(4)	4.25	O(W14)	0.27	343(33)	3507(65)	2116(28)	24.94
C(4,G5)	1.0	2823(4)	5359(7)	2039(3)	3.73	O(W15)	0.25	1388(17)	3251(81)	3109(13)	23.19
C(5,G5)	1.0	2793(4)	3958(7)	2013(3)	3.88	O(W16)	0.56	−247(19)	−552(27)	2583(11)	21.71
C(6,G5)	1.0	2526(5)	3467(8)	1287(4)	4.97	O(W17)	0.56	−138(26)	1106(28)	3354(16)	28.37
O(2,G5)	1.0	4275(3)	5541(6)	3783(3)	6.21	O(W18)	0.56	1072(11)	4854(33)	2986(9)	22.01
O(3,G5)	1.0	3197(3)	7042(6)	2815(3)	5.90	O(W19)	0.29	−835(37)	1996(57)	1285(18)	31.78
O(4,G5)	1.0	1990(3)	5809(5)	1813(2)	4.05	O(W20)	0.71	−1512(17)	890(30)	1832(14)	27.20
O(5,G5)	1.0	3616(3)	3522(5)	2295(2)	4.28	O(W21)	0.38	−466(19)	4367(44)	2154(15)	20.95
O(6,G5)	1.0	2370(4)	2210(6)	1281(3)	6.15	O(W22)	0.44	1058(22)	1536(55)	2937(18)	28.36
C(1,G6)	1.0	3834(4)	479(9)	4800(3)	4.87	O(W23)	0.62	−1376(13)	3060(30)	2386(11)	23.34

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.
b) *OC* indicates the occupancy factor.

former and 0.24 for the latter. Some geometrical parameters describing the macrocyclic conformation are summarized in Table 2. Eight glycosidic oxygen atoms (O(4)) form a nearly regular octagon with the radius of 5.81—5.94 Å and the side length of 4.43—4.59 Å. These O(4) atoms are coplanar within the maximum deviation of 0.192 Å. The torsion-angle index of 97.0—120.4° is somewhat larger than those of other two cyclodextrins. Since the O(4)···O(4′) distance is in rather narrow region, the correlation

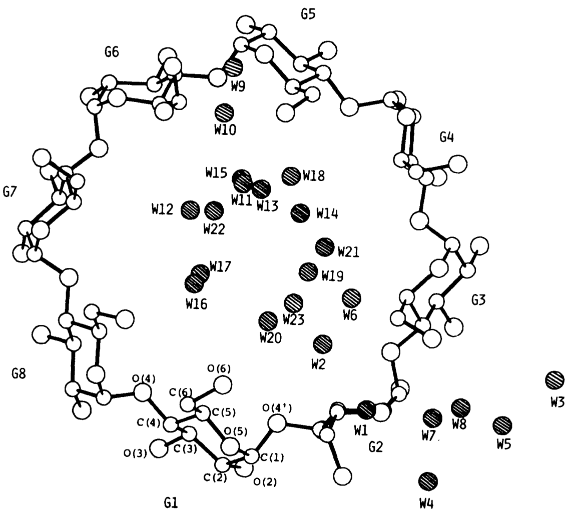

Fig. 1. The Structure and numbering scheme of γ-cyclodextrin hydrate. Water molecules are shaded.

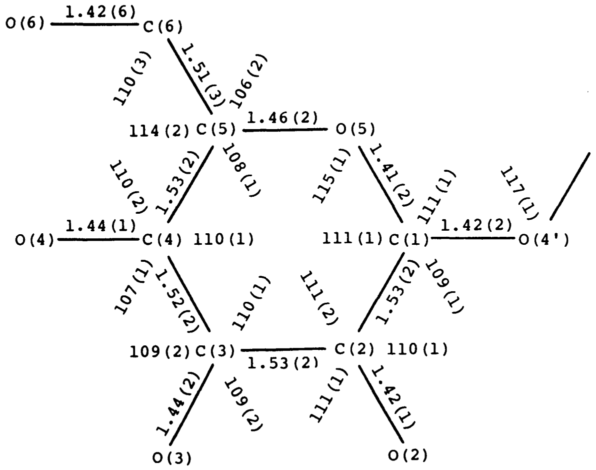

Fig. 2. Average bond distances and angles for the eight glucose residues. Standard deviations in parentheses were estimated according to the equation: $\sigma=[\sum_{i=1}^{8}(x_i-\bar{x})^2/7]^{1/2}$ where x_i refers to the bond distance or angle of the i-th residue and $\bar{x}$ is the average value.

between the O(4)··· O(4′) distance and the torsion-angle index is less obvious than the correlation found in α-cyclodextrin,[9] β-cyclodextrin,[10] or in mono- and disaccharides.[11] The tilt-angle is distributed in the range form −2.5° to 23.8°. The G2 and G4 residues are almost normal to the plane through the eight O(4) atoms, while the other residues incline with their O(6) side turning to the inside of the macrocycle. The average value of 13.9° is similar to that of β-cyclodextrin (12.5°), but smaller than that of α-cyclodextrin (19.2°). The O(2)··· O(3′) distances of 2.76—2.91 Å between adjacent residues indicate that adjacent two residues are linked by the O(2)··· O(3′) hydrogen bond. Although no hydrogen bond is observed between O(2,G7)H and O(3,G8)H hydroxyl groups, four O(2)-H··· O(3) and three O(3)-H··· O(2) hydrogen

Table 2. Geometrical Parameters Describing the Macrocyclic Conformation of γ-Cyclodextrin

I. Distance from the Center of Gravity of Eight O(4) Atoms to Each O(4) Atom[a)]

Residue	Distance (l/Å)	Residue	Distance (l/Å)
G1	5.84	G5	5.88
G2	5.88	G6	5.81
G3	5.90	G7	5.94
G4	5.84	G8	5.94

a) The estimated standard deviation is 0.01 Å.

II. O(4)···O(4′) Distance between Adjacent Glucose Residues[a)]

Distance (l/Å)		Distance (l/Å)	
O(4,G1)···O(4,G8)	4.54	O(4,G4)···O(4,G5)	4.48
O(4,G1)···O(4,G2)	4.59	O(4,G5)···O(4,G6)	4.48
O(4,G2)···O(4,G3)	4.46	O(4,G6)···O(4,G7)	4.58
O(4,G3)···O(4,G4)	4.46	O(4,G7)···O(4,G8)	4.43

a) The estimated standard deviation is 0.01 Å.

III. O(2)···O(3′) Distances between Adjacent Glucose Residues[a)]

Distance (l/Å)		Distance (l/Å)	
O(2,G1)···O(3,G2)	2.91	O(2,G4)···O(3,G5)	2.83
O(3,G1)···O(2,G8)	2.88	O(2,G5)···O(3,G6)	2.81
O(2,G2)···O(3,G3)	2.77	O(2,G6)···O(3,G7)	2.84
O(2,G3)···O(3,G4)	2.76	O(2,G7)···O(3,G8)	2.77

a) The estimated standard deviation is 0.01 Å.

IV. Torsion Angle Index[a)]

Residue	Index (ϕ/°)	Residue	Index (ϕ/°)
G1	99.8	G5	112.0
G2	107.0	G6	97.0
G3	113.1	G7	120.4
G4	119.9	G8	116.5

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

V. Tilt Angle[a)]

Residue	Tilt angle (ϕ/°)	Residue	Tilt angle (ϕ/°)
G1	16.6	G5	18.4
G2	−2.5	G6	13.4
G3	23.8	G7	12.7
G4	4.8	G8	23.6

a) The tilt angle is defined as the angle made by the plane through the eight O(4) atom and the plane through C(1), C(4), O(4), and O(4′) of each residue.

VI. Deviation of O(4) Atoms from Their Least-Squares Plane

Atom	Deviation (d/Å)	Atom	Deviation (d/Å)
O(4,G1)	0.054	O(4,G5)	−0.077
O(4,G2)	−0.173	O(4,G6)	−0.046
O(4,G3)	−0.005	O(4,G7)	−0.056
O(4,G4)	0.192	O(4,G8)	0.126

bonds are found. These hydrogen bonds may maintain the round structure of γ-cyclodextrin.

The crystal structure is shown in Figs. 3 and 4. γ-Cyclodextrin molecules are stacked along the crystallographic b axis, showing a packing feature similar to the cate-type packing found in the crystal of uncomplexed β-cyclodextrin.[10] The plane through eight O(4) atoms makes an angle of 46.5° with the b axis. As the result, adjacent two molecules along the b axis are laterally shifted each other by about half a molecule.

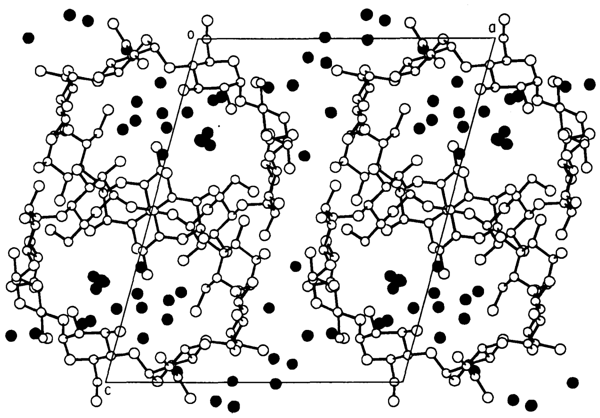

Fig. 3. The crystal structure viewed along the b axis. Water molecules are shown by full circles.

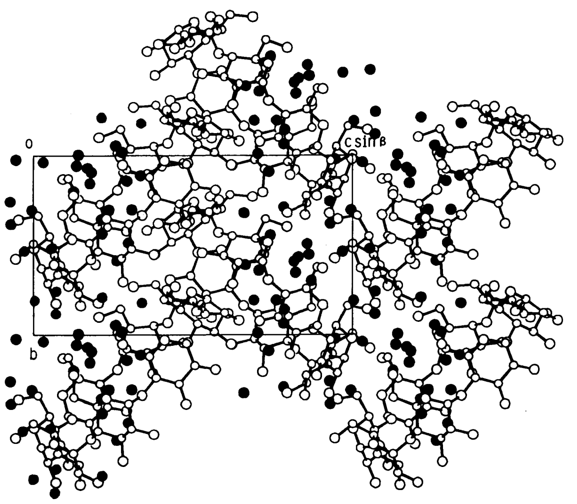

Fig. 4. The crystal structure viewed along the a axis. Water molecules are shown by full circles.

Both ends of the γ-cyclodextrin cavity are blocked by adjacent molecules. Owing to the incomplete blockade, however, the cavity is not closed. A narrow channel runs through the inside of the macrocycle stacked along the b axis. This channel is filled with water molecules as shown in Fig. 4. The G7 and G8 residues are partially inserted into the adjacent γ-cyclodextrin ring from the O(2), O(3) side, and form hydrogen bonds with included W6, W15, W18, and W23 water molecules.

The asymmetric unit of the crystal contains 14.1 water molecules, which are distributed over 23 sites. γ-Cyclodextrin includes 7.1 water molecules which occupy 14 sites. It is obvious that water molecules within the cavity can not fully form hydrogen bonds. These water molecules are arranged in the limited accommodation space so that they can form no ideal geometry of hydrogen bonding. Although it is not possible to discuss the details of hydrogen-bonding scheme because most of hydrogen atoms of water molecules were not located on the difference-Fourier map, most of hydroxyl groups of γ-cyclodextrin are hydrogen-bonded to water molecules located outside the cavity and form hydrogen-bond network in the crystal.

Discussion

The present X-ray analysis has shown that the γ-cyclodextrin molecule is round and rather symmetrical. When compared this structure with the structure reported by Maclennan and Stezowski,[3] a major difference is that one glucose residue is disordered in the structure at 120 K. In the structure at room temperature, however, all glucose residues are well ordered although the average temperature factor of the G8 residue is ca. twice greater than the average value of the other residues. This difference may be ascribed to the different conditions of data measurements and/or crystallization.

Table 3 gives some geometrical parameters to compare the macrocyclic conformation among three cyclodextrins. The glycosidic oxygen angle does not significantly change among these cyclodextrins, and is in good agreement with the O(4) angle found in maltosides.[12–14] This indicates that the effect of cyclization on the O(4) angle is small. A difference is found in the

Table 3. Comparison of Average Values of Some Geometrical Parameters Describing the Macrocyclic Conformation[b)]

	α-Cyclodextrin	β-Cyclodextrin	γ-Cyclodextrin
O(2)···O(3′) distance (l/Å)	3.3(0.6)	2.9(0.1)	2.8(0.1)
O(4)···O(4′) distance (l/Å)	4.3(0.1)	4.4(0.1)	4.5(0.1)
O(4) angle (ϕ/°)	118(1)	118(1)	117(1)
Planarity of the O(4) polygon (d/Å)[a)]	0.084	0.178	0.110
Torsion-angle index (ϕ/°)	127(9)	120(7)	111(9)
Tilt-angle (ϕ/°)	19(12)	12(10)	14(9)

a) The root-mean-square deviation from the least-squares plane through the O(4) polygon. b) Standard deviations are given in parentheses.

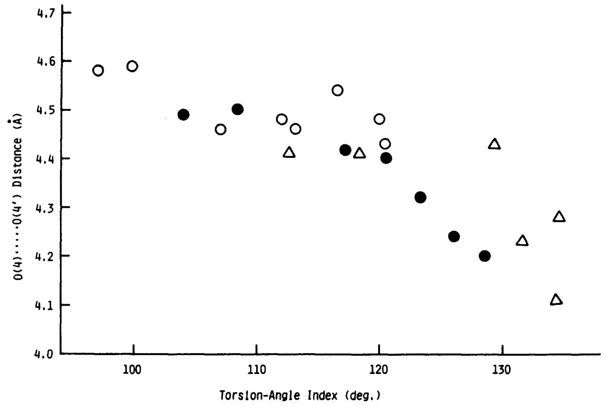

Fig. 5. Plot of the O(4)···O(4′) distance between adjacent glucose residues against the torsion angle index: α-cyclodextrin (△), β-cyclodextrin (●), and γ-cyclodextrin (○).

O(4)···O(4′) distance and the torsion-angle index. The average O(4)···O(4′) distance increases with the increasing number of the glucose residues, while the average torsion-angle index decreases. Figure 5 shows that the O(4)···O(4′) distance and the torsion angle index are in the limited region depending on the size of the macrocycle. Since the O(4) atoms of γ-cyclodextrin are aligned on a circle with the radius larger than the radius of the other cyclodextrins, the greater O(4)···O(4′) distance is necessary to avoid the unfavorable distortion of the glycosidic linkage. The change of the O(4)···O(4′) distance can be easily derived by the small change of the endocyclic conformation angle of the pyranose ring, as indicated by the correlation between the O(4)···O(4′) distance and the torsion-angle index.

The O(2)···O(3′) distance indicates that the intramolecular hydrogen bond becomes stronger in order of α-, β-, and γ-cyclodextrin. The α-cyclodextrin ring is remarkably distorted and two intramolecular hydrogen bonds are disrupted because of the sharp inclination of glucose residues. Chako and Saenger[15] have also reported that the uncomplexed α-cyclodextrin, crystallized in the presence of $BaCl_2$, is more symmetrical with the six O(2)···O(3′) hydrogen bonds. In that case, however, the average O(4)···O(4′) distance is decreased to 4.234 Å and the glycosidic oxygen angle is somewhat increased (118.4°), suggesting that the strain is imposed on the macrocycle although such strain energy may be compensated by the formation of additional two hydrogen bonds. In β-cyclodextrin and γ-cyclodextrin, the radius of the macrocycle is so large that the macrocyclic ring can be symmetrical and also in the relaxed state.

The G7 and G8 residues are found to be partially inserted into the cavity of the adjacent γ-cyclodextrin, which is related by the two-fold screw axis. Such close contact between host molecules has not been observed in other cyclodextrin crystals since the diameter of the cavity is too small to allow the penetration of the glucose moiety. The effective space of the γ-cyclodextrin cavity to accommodate water molecules becomes considerably smaller than the expected space from the radius of the macrocycle. The interesting fact is that the temperature factor of the G8 residue is significantly larger than the temperature factor of the other residues. This may be ascribed to the limited hydrogen-bonding contacts of the G8 residue in the hydrophobic environment. The O(2,G8)H and O(3,G8)H hydroxyl groups form hydrogen bonds with W15 and W18, respectively, which have relatively low occupation factor (0.25 and 0.55, respectively). Moreover, no intramolecular hydrogen bond is observed between O(2,G7)H and O(3,G8)H hydroxyl groups. This indicates that hydrogen bonds, especially intramolecular hydrogen bonds, play an important role to maintain the rigid structure of cyclodextrins.

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