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CRYSTAL STRUCTURE OF γ-CYCLODEXTRIN AT ROOM TEMPERATURE

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The crystal structure of γ-cyclodextrin 13.3 hydrate was determined by the X-ray method on the basis of the data measured at room temperature. The γ-cyclodextrin molecule is in a round shape, and is slightly distorted from the regular octagonal structure. The γ-cyclodextrin cavity includes 5.3 water molecules which occupy the 13 sites.

Cyclodextrins, which are cyclic oligosaccharides consisting of six or more D-glucose residues, form a number of inclusion complexes with a variety of guest molecules. In α- and β-cyclodextrin complexes, the conformation of the host molecules and the geometry of inclusion have been intensively investigated by the X-ray method.[1] On the other hand, only a few crystallographic studies have been reported for γ-cyclodextrin complexes. Maclennan and Stezowski[2] have determined the crystal structure of uncomplexed γ-cyclodextrin by using the data measured at 120 K. Lindner and Saenger have reported the structure of the γ-cyclodextrin–1-propanol complex.[3] We have been investigating the crystal structure of uncomplexed γ-cyclodextrin on the basis of the data measured at room temperature. In this paper, we briefly describe the crystal structure of the γ-cyclodextrin 13.3 hydrate, which is quite interesting in comparison with the structure determined at 120 K.

Crystals of the γ-cyclodextrin 13.3 hydrate were obtained 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 room temperature (*ca.* 22 °C) on a Nicolet P3/F diffractometer with graphite-monochromated CuKα radiation. 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 effect. Crystal data were as follows: $C_{48}H_{80}O_{40}\cdot 13.3H_2O$, F.W.=1536.7, monoclinic, space group $P2_1$, Z=2, a=16.847(2), b=11.098(2), c=20.271(2) Å, β=104.97(1)°, V=3661.4(8) Å^3, D_x=1.394 g·cm^{-3}. The orientation of the molecular axis of γ-cyclodextrin was deduced from a Patterson map. The atomic positions in the unit cell were determined by the trial-and-error method combined with the rotation about the molecular axis and the rigid-body least-squares technique. Water molecules and 87 hydrogen atoms were found on a difference-Fourier map. The structure was refined by the block-diagonal least-squares method to the R-value of 0.062.

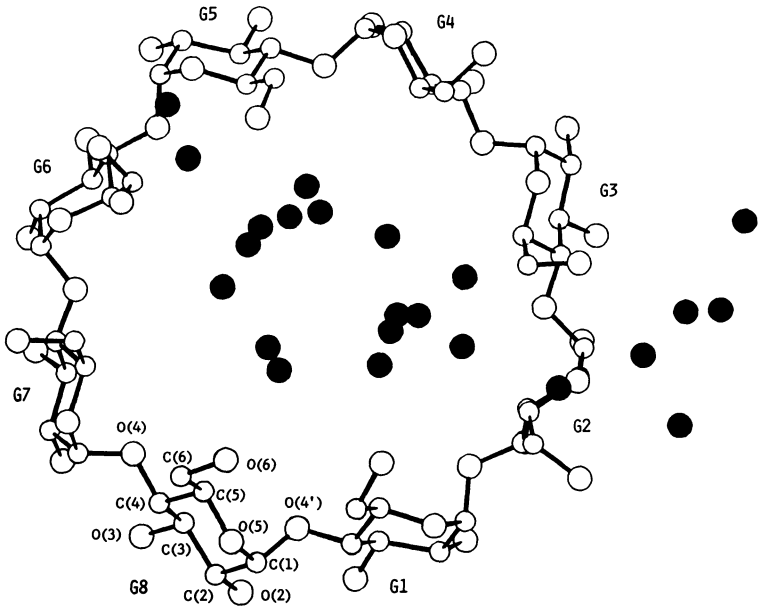

Fig. 1. The numbering scheme of γ-cyclodextrin. Water molecules are shown by full circles.

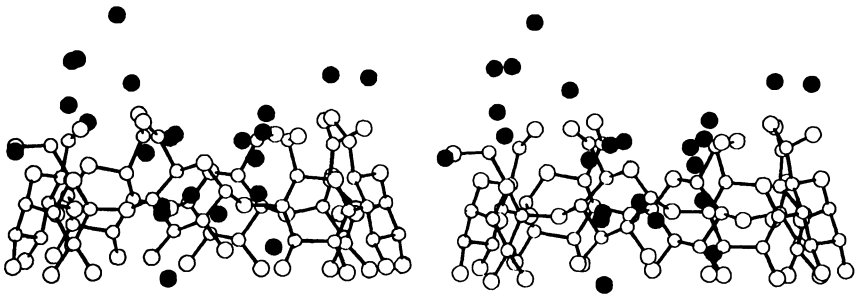

Fig. 2. A stereo-drawing of the structure. Water molecules are shown by full circles.

The γ-cyclodextrin molecule is in a round shape, but somewhat distorted from the regular octagonal structure, as shown in Figs. 1 and 2. Except for the orientation of C(6)-O(6) bonds, the eight glucose residues are in the same conformation. The planarity of C(2), C(3), C(5), and O(5) atoms and that of C(1), C(4), O(4), and O(4') atoms are fairly good; the maximum deviations from the least-squares plane are 0.05 Å for the former and 0.03 Å for the latter. The C(6)-O(6) bonds in the G1, G5, and G8 residues are in a *gauche-trans* (to C(5)-O(5) and C(5)-C(4) bonds, respectively) conformation, and those in the G2, G3, G4, and G7 residues are in a *gauche-gauche* conformation. The C(6)-O(6) bond of of the G6 residue is statistically disordered, showing *gauche-trans* and *gauche-gauche* conformations. The eight glycosidic oxygen atoms form a distorted octagon.

The radius of the octagon, which is measured from the center of gravity of the octagon to each indivivual O(4) atoms, is in the range 5.84-5.94 Å (Table 1). The planarity of the O(4) octagon is quite good; the maximum deviation of 0.196 Å is smaller than that (0.280 Å) of β-cyclodextrin.[4] The glycosidic oxygen angles are in the range 116.1-117.6°, and the average value of 116.6° is significantly greater than that of the γ-cyclodextrin–1-propanol complex (112.6°).[3] Distances between O(2) and O(3') of the adjacent glucose residue are 2.77-2.91 Å. These O(2) and O(3') atoms are linked by the intramolecular O(2)–H···O(3') or O(2)···H–O(3') hydrogen bond. The tilt-angle of each residue, which is defined as the angle made by the O(4) plane and the plane through C(1), C(4), O(4), and O(4') atoms of each residue, is in the range 2.4-23.9°. The average value of 15.2° is larger than that (12.5°) of β-cyclodextrin, but smaller than that (19.2°) of α-cyclodextrin.[5] These geometrical data indicate that the intramolecular O(2)···O(3') hydrogen bonds impose restriction on the inclination of glucose residues and make the macrocyclic ring round.

γ-Cyclodextrin molecules are stacked along the crystallographic b axis, as shown in Fig. 3, with which the O(4) plane makes an angle of 46.5°, and form a cage-type packing similar to that of β-cyclodextrin. The γ-cyclodextrin cavity includes 5.3 water molecules, which are statistically disordered and occupy 13 sites. The other water molecules are distributed in intermolecular spaces between γ-cyclodextrin molecules. When compared this structure with that determined by Maclennan *et al.*, two major differences should be pointed out. In the struc-

Table 1. Geometrical data for the γ-cyclodextrin macrocycle
The estimated standard deviations for III, IV, and V are in the range 0.01-0.02 Å

	I[a]	II[b]	III[c]		IV[d]		V[e]
Residue	d/Å	ϕ/°	l/Å	O(4)···O(4')	l/Å	O(2)···O(3')	l/Å
G1	-0.051	16.8	5.84	O(4,G1)-O(4,G2)	4.59	O(2,G1)-O(3,G2)	2.91
G2	0.172	2.4	5.88	O(4,G1)-O(4,G8)	4.55	O(2,G8)-O(3,G1)	2.87
G3	0.012	23.7	5.90	O(4,G2)-O(4,G3)	4.45	O(2,G2)-O(3,G3)	2.77
G4	-0.196	4.9	5.84	O(4,G3)-O(4,G4)	4.46	O(2,G3)-O(3,G4)	2.77
G5	0.085	23.7	5.88	O(4,G4)-O(4,G5)	4.47	O(2,G4)-O(3,G5)	2.83
G6	0.050	13.5	5.80	O(4,G5)-O(4,G6)	4.49	O(2,G5)-O(3,G6)	2.80
G7	0.051	12.9	5.94	O(4,G6)-O(4,G7)	4.57	O(2,G6)-O(3,G7)	2.85
G8	-0.123	23.9	5.94	O(4,G7)-O(4,G8)	4.43	O(2,G7)-O(3,G8)	2.78
Average	0.111[f]	15.2	5.88	Average	4.50	Average	2.82

a) The deviation of O(4) atoms from the least-squares plane through the O(4) octagon. b) The tilt-angle of each residue. c) The distance from the center of gravity of the O(4) octagon to each O(4) atom. d) The O(4)···O(4') distance between adjacent glucose residues. e) The distance between O(2) and O(3') of the adjacent glucose residue. f) The root-mean-square deviation.

ture at 120 K, (1) seventeen water molecules are found, and (2) one glucose residue is statistically disordered. In the present structure, however, the number of water molecules is 13.3, and all glucose residues are well ordered, although the average temperature factor (7.0 $\mathring{A}^2$) of the C(1), C(2), C(3), C(4), C(5), and O(5) of the G8 residue is larger than the corresponding values, 4.1-5.1 $\mathring{A}^2$, of the other residues. These differences may be ascribed to the smaller thermal motion of water molecules at 120 K and/or the different condition of crystallization. The full explanation, however, is difficult at this stage. The water molecules in the γ-cyclodextrin cavity is characterized by the high degree of disorder, which is more remarkable than that found in the β-cyclodextrin dodecahydrate. Most of such disordered water molecules are not fully hydrogen-bonded, and seems to be in a "activated state",[6] which may play an important role in the complex formation of γ-cyclodextrin with guest molecules.

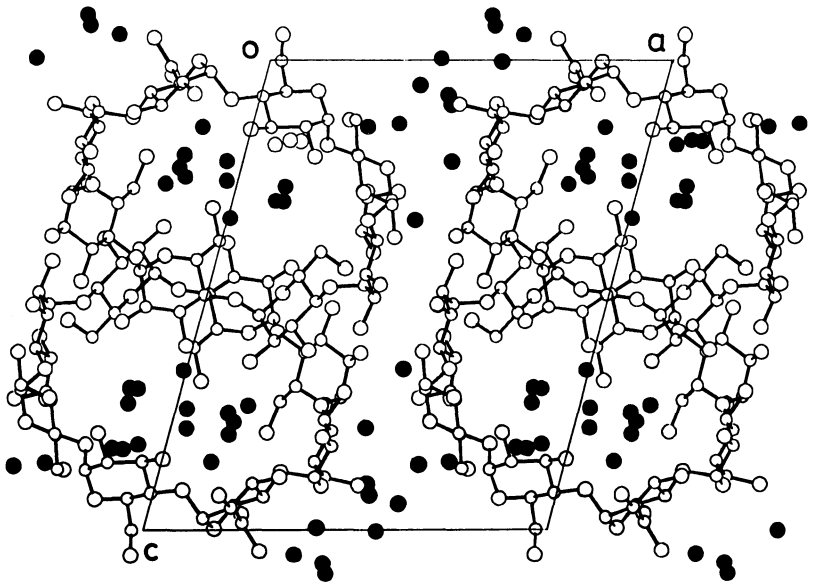

Fig. 3. The crystal structure viewed along the b axis. Water molecules are shown by full circles.

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