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CRYSTAL AND MOLECULAR STRUCTURE OF CYCLOHEPTA-AMYLOSE DODECAHYDRATE*

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ABSTRACT

β-Cyclodextrin (cyclohepta-amylose, β-CD) is a torus-shaped, cyclic heptasaccharide consisting of (1→4)-linked α-D-glucopyranosyl residues. It is able to form inclusion complexes with small molecules in aqueous solution because of its annular aperture (width, 6.2 Å). β-Cyclodextrin dodecahydrate, the "empty" β-CD, crystallises from water in space group $P2_1$, with cell constants $a = 21.29(2)$, $b = 10.33(1)$, $c = 15.10(2)$ Å, and $\beta = 112.3(5)°$. A total of 5189 X-ray counter-data were collected on a four-circle diffractometer. The crystal structure was solved on the basis of the highly isomorphous $\beta\text{-CD} \cdot 2HI \cdot 8H_2O$ adduct, and the atomic parameters were refined by the full matrix, least-squares method to $R = 7.3\%$ for all data. The crystal structure belongs to the cage type. The β-CD macrocycle exists in an open, circular conformation stabilised by intramolecular hydrogen-bonds between HO-2 and HO-3 of adjacent glucosyl residues; four of the seven HO-6 groups are in the favoured (−)*gauche* orientation with respect to O-5, two are in the (+)*gauche* orientation, and one is disordered over these two orientations. The 6.5 water molecules within the cavity are distributed over 8 sites and display extensive thermal motion which is probably correlated with statistical disorder.

INTRODUCTION

The degradation of helical starch molecules by cyclodextrin glucanotransferase from *Bacillus macerans* yields cyclodextrins (CD; cycloamyloses; Schardinger dextrins), which are cyclic oligosaccharides consisting of six or more (1→4)-linked α-D-glucopyranosyl rings. The main fractions of these oligosaccharides contain six, seven, or eight residues (α-, β- and γ-CD). The inclusion of guest molecules within the cavity of these cyclodextrins has been studied by using theoretical and physicochemical methods as well as crystallography[2,3]. The only obvious requirement for complex formation is that the guest molecule or a substantial part of it must fit geometrically into the annular void. Various effects have been discussed as the driving

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*Topography of Cyclodextrin Inclusion Complexes, Part XVII. For Part XVI, see ref. 1.

force of complexation, namely, hydrophobic, van der Waals, and dipole interactions, hydrogen bonding, and release of conformational strain energy. The last force was proposed on the basis of comparative X-ray crystallographic studies of the "empty" α-CD hexahydrate and different α-CD guest complexes[4]. Since various X-ray crystallographic structures of β-CD inclusion complexes with 4-nitroacetanilide[5], 2,5-di-iodobenzoic acid[6], 1-propanol[7,8], and 4-iodophenol[7] have been published, we have performed an X-ray structural investigation on the "empty" β-CD hydrate. A preliminary report of this study has been published[9], and we now report details of the structure determination and of the molecular geometry of the β-CD molecule.

EXPERIMENTAL

β-CD was purchased from Corn Products Development, Englewood Cliffs, N.J., and further purified by recrystallisation from 1-propanol (once) and water (twice). It crystallises from water as chunky, colorless prisms that exhibit symmetry and X-ray extinctions of space group $P2_1$. The unit-cell dimensions are $a = 21.29(2)$, $b = 10.33(1)$, $c = 15.10(2)$ Å, and $\beta = 112.3(5)°$ ($\lambda = 1.54188$ Å). The content of the asymmetric unit has been established[10] as $C_{42}H_{70}O_{35} \cdot (12.0 \pm 0.5)H_2O$, and the crystal density reported[11] as 1.43 g.cm^{-3}; the calculated density is 1.453 g.cm^{-3}. Integrated intensities of 5189 independent reflections ($2\theta_{max} = 120°$) were measured with Ni-filtered CuKα radiation, using a STOE, automatic, four-circle diffractometer. The data were collected in the θ–2θ scan mode with stationary background measurements on both sides of each scan. Reflection intensities were corrected for background, polarisation, and Lorentz effects. Only those reflections that had values of $F_o > 3\sigma(F_o)$ were included in the refinement (σ estimated[12] from counting statistics plus 3% of I_{net}).

STRUCTURE DETERMINATION AND REFINEMENT

The structure was solved with the aid of the isomorphous complex β-CD $\cdot$ 2HI $\cdot$ 8H$_2$O, the structure of which had been solved previously with both heavy atom and direct methods (full details will be described elsewhere). The co-ordinates of all C and O atoms from β-CD $\cdot$ 2HI $\cdot$ 8H$_2$O (except solvent oxygen and O-6) were used and refined on the basis of 1149 data from β-CD hydrate (all reflections with $2\theta < 60°$). A subsequent, difference Fourier synthesis revealed the positions of the missing O-6 atoms and of four water-oxygens. Further cycles of isotropic refinement resulted in an R-value of 0.137. Progress was slowed down by the pronounced disorder of the solvent, 12.08 water molecules occupying 15 positions. After several cycles of full-matrix, least-squares refinement[13] employing individual, anisotropic temperature factors, a difference Fourier map was calculated (R-value at this stage: 0.083). Because of the disorder, no hydrogens could be located. Consequently, the calculated positions of the hydrogens bonded to carbon atoms were evaluated, and their scattering included as constant parts in the final least-squares cycles (each

TABLE I

β-CYCLODEXTRIN DODECAHYDRATE: FRACTIONAL ATOMIC COORDINATES (STANDARD DEVIATIONS IN PARENTHESES APPLY TO THE LAST DIGIT GIVEN) FOR NON-HYDROGEN ATOMS

Atom	x	y	z	*Atom*	x	y	z
C-1^1	.5407(4)	.5325(10)	.0936(6)	O-2^1	.4300(3)	.4429(7)	.0649(4)
C-2^1	.4704(4)	.5015(9)	.0190(6)	O-3^1	.4114(3)	.3989(7)	−.1347(4)
C-3^1	.4764(4)	.4122(9)	−.0586(5)	O-4^1	.5338(3)	.3759(5)	−.1631(3)
C-4^1	.5254(4)	.4723(9)	−.0996(6)	O-5^1	.5825(3)	.5853(6)	.0493(4)
C-5^1	.5942(4)	.4987(10)	−.0198(6)	O-6^1	.7043(5)	.5879(14)	.0148(9)
C-6^1	.6396(6)	.5776(16)	−.0580(9)	O-2^2	.5855(3)	.1512(7)	.4097(4)
C-1^2	.6782(4)	.2874(10)	.4200(5)	O-3^2	.4972(3)	.2969(9)	.2447(4)
C-2^2	.6030(4)	.2760(10)	.3829(5)	O-4^2	.5692(3)	.4150(6)	.1417(3)
C-3^2	.5708(4)	.2937(10)	.2741(5)	O-5^2	.6984(3)	.4024(7)	.3870(4)
C-4^2	.5963(4)	.4124(10)	.2456(5)	O-6^{2}A	.7716(7)	.5025(17)	.2806(14)
C-5^2	.6738(4)	.4096(10)	.2831(6)	O-6^{2}B	.7008(7)	.6487(15)	.2776(10)
C-6^2	.7095(6)	.5254(12)	.2595(8)	O-2^3	.7777(3)	−.2616(7)	.4699(4)
C-1^3	.8601(4)	−.0874(10)	.5017(5)	O-3^3	.6717(2)	−.0690(7)	.4319(4)
C-2^3	.7912(4)	−.1290(10)	.4990(5)	O-4^3	.7052(2)	.1770(6)	.3888(3)
C-3^3	.7371(3)	−.0399(9)	.4301(5)	O-5^3	.8740(2)	.0414(6)	.5318(3)
C-4^3	.7548(3)	.0981(9)	.4624(5)	O-6^3	.8445(3)	.2652(7)	.6083(4)
C-5^3	.8266(3)	.1351(9)	.4703(5)	O-2^4	.9259(3)	−.4692(6)	.2679(4)
C-6^3	.8492(4)	.2622(10)	.5163(6)	O-3^4	.8750(3)	−.3802(7)	.4077(4)
C-1^4	.9720(3)	−.2543(9)	.2626(5)	O-4^4	.8607(2)	−.1058(6)	.4090(3)
C-2^4	.9502(4)	−.3538(9)	.3218(5)	O-5^4	.9953(2)	−.1419(6)	.3161(3)
C-3^4	.8947(4)	−.2932(8)	.3485(5)	O-6^4	1.0017(5)	.1288(9)	.3447(7)
C-4^4	.9192(3)	−.1667(9)	.4002(5)	O-2^5	.7957(3)	−.4204(6)	−.1309(4)
C-5^4	.9457(3)	−.0775(9)	.3415(5)	O-3^5	.8530(3)	−.4513(6)	.0725(4)
C-6^4	.9822(5)	.0426(11)	.4016(7)	O-4^5	.9140(2)	−.2275(6)	.1780(3)
C-1^5	.8618(3)	−.2250(9)	−.1173(5)	O-5^5	.9201(2)	−.1556(6)	−.0567(3)
C-2^5	.8561(4)	−.3528(8)	−.0697(5)	O-6^5	1.0442(3)	−.1164(7)	.1137(4)
C-3^5	.8555(4)	−.3297(8)	.0290(5)	O-2^6	.5809(2)	−.1150(6)	−.3864(4)
C-4^5	.9181(3)	−.2544(8)	.0886(5)	O-3^6	.6896(3)	−.2828(6)	−.2648(5)
C-5^5	.9200(4)	−.1292(8)	.0369(5)	O-4^6	.8022(2)	−.1515(5)	−.1327(3)
C-6^5	.9840(4)	−.0464(10)	.0891(6)	O-5^6	.7303(2)	.0944(5)	−.3202(3)
C-1^6	.6602(4)	.0616(8)	−.3518(5)	O-6^6	.8715(3)	.0565(8)	−.2664(4)
C-2^6	.6528(4)	−.0861(8)	−.3559(5)	O-2^7	.4172(3)	.2684(7)	−.2996(4)
C-3^6	.6937(4)	−.1436(8)	−.2581(5)	O-3^7	.4873(2)	.0782(6)	−.3689(4)
C-4^6	.7669(3)	−.1008(8)	−.2271(5)	O-4^7	.6309(2)	.1116(5)	−.2896(3)
C-5^6	.7708(4)	.0474(8)	−.2248(5)	O-5^7	.5713(2)	.4434(5)	−.2825(3)
C-6^6	.8418(4)	.1003(10)	−.2019(6)	O-6^7	.6461(3)	.4245(7)	−.3964(4)
C-1^7	.5145(4)	.4135(8)	−.2601(5)	O-W-1	.5369(3)	−.3630(6)	−.4385(4)
C-2^7	.4757(4)	.2993(8)	−.3216(5)	O-W-2	1.0280(4)	−.6193(9)	.2385(5)
C-3^7	.5222(4)	.1812(8)	−.3048(5)	O-W-3A	.7469(5)	−.3978(9)	−.3954(7)
C-4^7	.5855(3)	.2181(7)	−.3222(5)	O-W-3B	.6810(21)	−.3766(40)	−.4825(32)
C-5^7	.6206(3)	.3377(8)	−.2656(5)	O-W-4	.2894(5)	.3003(10)	−.1279(8)
C-6^7	.6753(4)	.3914(8)	−.2972(5)	O-W-5A	.8817(5)	−.4914(11)	−.2946(7)
				O-W-5B	.8511(9)	−.5369(19)	−.2630(12)
				O-W-6	.3252(8)	.6015(21)	.0519(13)
				O-W-7	.9294(4)	−.6697(10)	.0469(5)
				O-W-8	.3097(11)	−.3973(18)	.8126(13)
				O-W-9	.2148(13)	−.5000(22)	.8972(27)
				O-W-10	.2295(8)	−.1763(15)	.0585(11)
				O-W-12	.2330(13)	−.1907(28)	.8602(22)
				O-W-13	.1218(11)	−.3265(25)	.8433(17)
				O-W-14	.8815(16)	.2936(21)	.3031(23)

TABLE II

OCCUPATION FACTORS OF DISORDERED O-6 AND OF WATER OXYGENS

Atom	*Occupancy*[a]	*Atom*	*Occupancy*[a]
O-6^{2}A	0.50(2)	O-W-6	1.0
O-6^{2}B	0.50(2)	O-W-7	1.0
O-W-1	1.0	O-W-8	0.59(3)
O-W-2	1.0	O-W-9	0.90(4)
O-W-3A	0.71(3)	O-W-10	1.0
O-W-3B	0.29(2)	O-W-12	0.96(4)
O-W-4	1.0	O-W-13	0.93(4)
O-W-5A	0.61(4)	O-W-14	0.64(3)
O-W-5B	0.24(3)		

[a] Standard deviations in parentheses refer to the last significant digit.

hydrogen atom was assigned the isotropic temperature factor of the atom to which it was bonded). The refinement converged at a final, residual R-value of 0.073. Fractional co-ordinates of the non-hydrogen atoms are listed in Table I. Table II presents atomic occupation factors, and Table III bond lengths and angles*.

RESULTS AND DISCUSSION

Glucopyranose conformation. Bond lengths and angles. — At first, the structure of β-CD may be treated as consisting of seven independent glucopyranosyl residues, all in the $^4C_1$ conformation (Fig. 1). Table III states the average over all seven independent observations of a particular bond within a glucosyl residue. Perhaps the relatively short distances C-1–C-2 and C-3–C-4 in glucosyl residue 2 are due to the disorder of atom O-6 of the same residue, or they may reflect problems in refinement associated with the disorder of the included water molecules. The comparison of average values of bond lengths and angles with average values stated[4] for α-CD yields no significant differences between glucosyl residues of β-CD and α-CD. The only possible exception is the glucosidic angle C-4–O-4–C-1, which appears to be slightly smaller for β-CD dodecahydrate (117.7 ±1.0°) than for the average α-CD structure (119.0 ±0.3°; ref. 4). The significance of these values, however, must be assessed as soon as more data on β-CD structures are available.

Torsion angles as stated in Table IV are by no means unusual if compared to the values found for α-CD structures. The only significant difference from other α-CD structures is in the orientations of the C-6–O-6 bonds. These are generally turned "away" from the center of the ring with torsion angles O-5–C-5–C-6–O-6

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*Tables containing positions of calculated C–H hydrogen atoms and anisotropic temperature factors of C and O atoms and structure amplitudes are deposited with and can be obtained from: Elsevier Scientific Publishing Company, BBA Data Deposition, P.O. Box 1527, Amsterdam, The Netherlands. Reference should be made to No. BBA/DD/199/*Carbohydr. Res.*, 99 (1982) 103–115.

TABLE III

BOND LENGTHS (Å) AND ANGLES (deg.); STANDARD DEVIATIONS ARE OF THE ORDER OF 0.014 Å FOR BOND LENGTHS AND 0.8° FOR BOND ANGLES

Bond	D-*Glucosyl residue*								
	1	*2*	*3*	*4*	*5*	*6*	*7*	*Mean*	*σ*
C-1–C-2	1.525	1.387	1.514	1.545	1.530	1.533	1.533	1.524	0.019
C-2–C-3	1.535	1.531	1.531	1.520	1.515	1.520	1.526	1.526	0.008
C-3–C-4	1.531	1.470	1.508	1.510	1.510	1.512	1.516	1.508	0.019
C-4–C-5	1.525	1.526	1.536	1.527	1.519	1.534	1.526	1.528	0.006
C-5–C-6	1.535	1.530	1.478	1.558	1.545	1.518	1.523	1.527	0.025
C-1–O-5	1.411	1.416	1.400	1.394	1.424	1.428	1.409	1.411	0.011
C-1–O-4	1.428	1.434	1.428	1.426	1.419	1.408	1.417	1.421	0.008
C-2–O-2	1.430	1.441	1.434	1.424	1.445	1.451	1.441	1.438	0.009
C-3–O-3	1.430	1.459	1.435	1.440	1.428	1.441	1.440	1.439	0.010
C-4–O-4	1.440	1.451	1.456	1.446	1.414	1.433	1.424	1.438	0.015
C-5–O-5	1.467	1.454	1.450	1.419	1.441	1.451	1.467	1.450	0.017
C-6–O-6	1.402	1.258 A 1.331 B	1.430	1.405	1.393	1.422	1.428	1.384	0.060
Angle									
C-1–C-2–C-3	110.3	111.8	108.5	108.4	111.0	109.7	110.3	110.0	1.2
C-2–C-3–C-4	109.4	110.5	108.5	110.1	109.3	109.2	109.4	109.5	0.6
C-3–C-4–C-5	110.5	110.0	112.3	110.7	108.9	109.8	112.6	119.7	1.3
C-4–C-5–C-6	110.6	117.5	113.2	110.8	113.6	113.9	112.9	113.2	2.3
C-2–C-1–O-5	110.5	111.2	111.2	109.8	109.8	109.2	109.7	110.2	0.8
C-2–C-1–O-4	107.7	108.8	108.0	110.7	108.3	109.1	107.0	108.5	1.2
C-1–C-2–O-2	109.5	108.8	111.0	110.5	108.1	107.2	110.1	109.5	1.2
C-3–C-2–O-2	110.9	110.5	110.8	110.3	111.5	109.0	110.3	110.5	0.8
C-2–C-3–O-3	109.5	108.6	110.2	110.3	109.3	109.0	109.9	109.5	0.6
C-4–C-3–O-3	108.3	111.5	108.5	110.1	111.0	110.0	109.6	109.9	1.2
C-3–C-4–O-4	105.3	107.0	105.2	106.5	107.9	106.8	106.1	106.4	1.0
C-5–C-4–O-4	108.9	109.3	109.4	108.2	110.3	109.8	108.0	109.1	0.8
C-4–C-5–O-5	107.4	107.3	108.3	110.6	110.6	107.8	109.9	108.8	1.5
C-6–C-5–O-5	104.2	106.5	105.7	105.9	105.9	105.6	104.8	105.5	0.8
C-5–C-6–O-6	108.5	111.2 A 125.4 B	110.1	110.3	113.1	113.1	109.6	112.7	6.4
C-4–O-4–C-1	116.0	118.9	117.4	118.8	118.0	117.1	117.9	117.7	1.0
C-1–O-5–C-5	114.2	112.9	114.6	114.2	113.5	113.8	114.6	114.0	0.6
O-5–C-1–O-4	110.4	109.8	111.5	110.0	110.0	111.3	111.8	110.8	0.8

corresponding to (—)*gauche*. In the β-CD dodecahydrate, two C-6–O-6 bonds are rotated "inward" [(+)*gauche*], while one O-6 is twofold disordered over (—)*gauche* and (+)*gauche* (Fig. 2). The O-6 atoms in (+)*gauche* orientation take part in hydrogen bonding with water molecules included in the cavity (Fig. 2). The endocyclic torsion angles all show *gauche* conformation; the difference between angles with C-3 or C-4 as the central atom and angles with C-1 or C-2 as central atom are not as significant as observed[2] for α-CD structures. Angles with O-5 as central atom, ~60°,

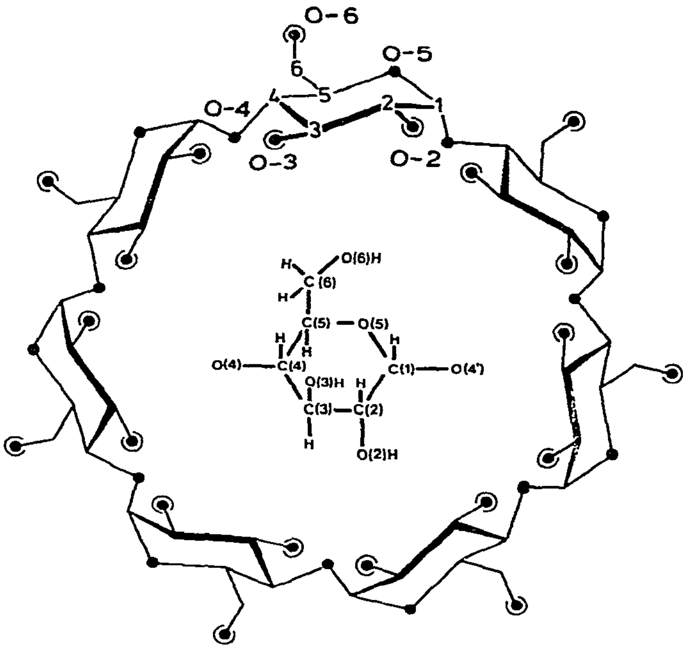

Fig. 1. Chemical structure and numbering of the atoms in β-cyclodextrin: ●, oxygen atoms; ◉, hydroxyl groups.

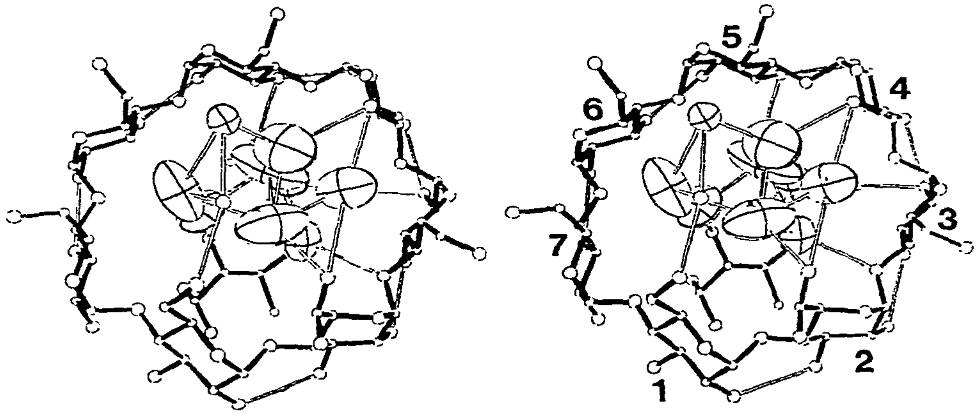

Fig. 2. Stereoview of the β-CD molecule in the dodecahydrate complex, viewing on the plane of the O-4 atoms. Water molecules included in the cavity are also drawn.

are greater than the others, ~55°. ϕ and ψ torsion angles in α- and β-CD are comparable[4].

The geometrical data for the glucosyl residues are displayed in Table V. If we compare the average deviations of atoms C-1 and C-4 from the planes through atoms C-2, C-3, C-5, and O-5 [Table V, *A*; 0.661(15) and −0.675(54) Å] with corresponding data[4] for α-CD (0.675 and −0.629 Å), a general trend is observed, although the

TABLE IV

SELECTED TORSION ANGLES (deg.); STANDARD DEVIATIONS ARE OF THE ORDER OF 1.0°

Torsion angle	D-*Glucosyl residue*								
	1	*2*	*3*	*4*	*5*	*6*	*7*	*Mean*	*σ*
C-1-C-2-C-3-C-4	−53.3	−50.7	−56.3	−55.5	−55.9	−56.4	−54.6	−54.7	2.1
C-2-C-3-C-4-C-5	56.2	55.4	55.8	53.5	56.7	57.8	52.4	55.4	1.9
C-3-C-4-C-5-O-5	−58.3	−60.7	−54.1	−53.3	−58.3	−58.7	−51.9	−56.5	3.3
C-4-C-5-O-5-C-1	62.1	63.0	56.7	59.0	60.2	62.0	56.9	60.0	2.6
C-5-O-5-C-1-C-2	−61.1	−59.4	−61.1	−62.0	−57.6	−61.5	−60.4	−60.4	1.5
O-5-C-1-C-2-C-3	55.2	51.4	59.1	58.8	55.3	57.1	58.4	56.5	2.7
O-5-C-5-C-6-O-6	70.9	70.5 A −66.1 B	−63.0	64.6	−70.9	−61.1	−60.8	—	—
O-2-C-2-C-3-O-3	66.7	65.5	62.9	61.7	60.8	64.5	63.2	63.6	2.1
C-1-O-4′-C-4′-C-3′[a]	134.3	139.9	115.2	131.5	127.0	129.7	120.5	128.3	8.3
O-5-C-1-O-4′-C-4′[a]	110.6	115.0	103.0	120.0	110.9	107.6	102.5	109.9	6.3
C-1-O-4′-C-4′-C-5′[a]	−106.5	−99.3	−125.7	−109.7	−113.9	−109.4	−121.0	−112.2	8.9
C-2-C-1-O-4′-C-4′[a]	−128.7	−123.1	−134.6	−120.2	−129.2	−131.8	−137.3	−129.3	6.0
O-4···C-1-O-4′-C-4′[a] (θ)	169.3	174.8	163.1	177.8	169.8	166.7	161.0	168.9	6.0
C-1-O-4′-C-4′···O-4″[a] (ψ)	−163.3	−160.7	−184.2	−167.6	−172.7	−169.8	−179.1	−171.1	8.4

[a] Primed atoms belong to the D-glucosyl residue of next, higher number.

TABLE V

GEOMETRICAL DATA FOR THE D-GLUCOSYL RESIDUES[a]

	Atom	D-*Glucosyl residue*								
		1	*2*	*3*	*4*	*5*	*6*	*7*	*Mean*	σ
A.	C-2	0.016(4)[b]	0.034(5)	0.005(4)	0.003(3)	0.010(4)	−0.001(5)	−0.013(4)	—	—
	C-3	−0.015(4)	−0.033(5)	−0.005(4)	−0.003(3)	−0.010(4)	0.001(4)	0.012(4)	—	—
	C-5	0.016(4)	0.035(5)	0.005(5)	0.003(3)	0.010(4)	−0.001(5)	−0.012(4)	—	—
	O-5	−0.017(4)	−0.036(5)	−0.006(5)	−0.004(4)	−0.011(4)	0.001(5)	0.013(4)	—	—
	C-1	0.654(11)	0.618(14)	0.663(12)	0.683(8)	0.653(10)	0.681(11)	0.672(10)	0.661	0.015
	C-4	−0.694(12)	−0.688(14)	−0.660(12)	−0.650(9)	−0.698(10)	−0.706(12)	−0.628(11)	−0.675	0.054
B.		112.3(2)	106.5(2)	85.3(2)	103.6(2)	103.5(2)	92.2(2)	94.9(2)	99.8	9.3
C.		52.2(9)	56.4(9)	49.0(8)	46.0(7)	55.7(9)	53.3(9)	46.2(8)	51.3	4.3
D.		51.8(9)	50.2(9)	51.3(8)	53.7(7)	50.3(9)	52.2(9)	52.4(8)	51.7	1.2
E.		82.9(3)	89.6(3)	120.6(3)	97.9(2)	95.9(3)	109.5(2)	110.3(2)	101.0	13.1
F.		2.868(13)	2.865(11)	2.862(13)	2.875(14)	2.862(11)	2.838(11)	2.850(14)	2.860	0.012
G.		−1.7(13)	1.4(13)	1.3(13)	−1.8(12)	−1.9(15)	−2.2(14)	−3.0(11)	−1.1	1.8

[a] Key: *A*, Distances (Å) of atoms from the least-square planes defined by the atoms C-2, C-3, C-5, and O-5. *B*, Dihedral angles (deg.) between the planes defined in *A* and the plane of all seven O-4 atoms. *C*, Dihedral angles (deg.) between the planes defined in *A* and the planes defined by C-3, C-4, and C-5. *D*, Dihedral angles (deg.) between the planes defined in *A* and the planes defined by O-5, C-1, and C-2. *E*, Dihedral angles (deg.) between the planes defined by O-4, C-6, and O-4′ and the plane of all O-4 atoms. *F*, C-1 ··· C-4 distance (Å) within a D-glucosyl residue. *G*, Torsion angles (deg.) O-4′–C-1 ··· C-4–O-4.
[b] Standard deviations obtained from the least-squares correlation matrix are given in parentheses and apply to the last digit.

TABLE VI

GEOMETRICAL DATA FOR THE HEPTAGON DESCRIBED BY THE O-4 ATOMS[a]

	D-*Glucosyl residue*								
	1	*2*	*3*	*4*	*5*	*6*	*7*	*Mean*	σ
A. Distance (Å) $O\text{-}4_n \cdots O\text{-}4_{n+1}$	4.405(8)	4.502(7)	4.318(9)	4.201(9)	4.489(7)	4.400(7)	4.236(9)	4.364	0.117
B. Distance (Å) $O\text{-}4_n \cdots O\text{-}4_{n+2}$	8.082(7)	8.005(8)	7.536(9)	7.806(8)	8.194(7)	7.620(9)	7.738(8)	7.854	0.246
C. Distance (Å) $O\text{-}4_n \cdots O\text{-}4_{n+3}$	10.158(7)	9.606(9)	9.424(9)	10.164(7)	9.906(8)	9.366(9)	9.872(8)	9.758	0.327
D. Angle (deg.) $O\text{-}4_n \cdots O\text{-}4_{n+1} \cdots O\text{-}4_{n+2}$	130.1(2)	130.3(2)	124.4(2)	127.8(2)	134.4(2)	123.8(1)	127.1(2)	128.3	3.7
E. Distance of $O\text{-}4_n$ from the least-squares plane defined by the O-4 atoms	0.145(5)	0.152(5)	−0.188(5)	−0.110(5)	0.280(5)	−0.055(5)	−0.224(4)	—	—
F. Distance (Å) $O\text{-}2_n \cdots O\text{-}3_{n+1}$	2.955(9)	2.861(9)	2.855(10)	2.768(7)	2.780(7)	2.904(8)	2.876(9)	2.857	0.066

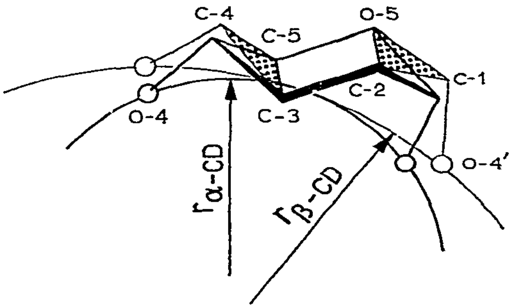

Fig. 3. Mechanical model of the distortion of the D-glucosyl residue in β-CD. Due to the larger radius r_β of the β-CD macrocycle as opposed to α-CD, the D-glucosyl residue is stretched and C-4 moves away from the plane C-2, C-3, C-5, O-5, whereas C-1 moves towards it (pointed areas).

standard deviations are high. In going from α-CD to β-CD, C-4 moves further away from, and C-1 approaches, this plane. These movements can be understood on the basis of a simple mechanical model, because the glucosyl residue in β-CD is aligned on a circle with larger radius compared to that for α-CD (Fig. 3).

French and Murphy[14] have made predictions concerning the geometry of the glucosyl residue within β-CD and the structure of the molecule itself. The C-1–C-4 distance of 2.86 ±0.01 Å is in good agreement with the 2.88 ±0.03 Å given by French and Murphy (Table V, *F*). Their value of 2.75 Å for the mean O-2···O-3' distance is at the lower end of the observed scale (Table VI, *F*), while the O-4···O-4' distance prediction of 4.40 Å is good (Table VI, *A*) as well as their estimation of the rotation of the glucosyl residue with respect to the O-4 plane (their angle θ corresponds to entry *E* in Table V, decreased by 90°): 15° predicted, 11.0 ±13.1° observed. The computer-modelling for β-CD must be considered to be rather successful.

The β-cyclodextrin macrocycle. — The β-CD macrocycle in β-CD dodecahydrate is conical in shape, with the heptagon formed by the seven O-4 atoms being surprisingly regular (Table VI). The sides of the heptagon are 4.36 ±0.12 Å, and the angles O-4···O-4···O-4 128.3 ±3.7°, corresponding to 128.6° for an ideal heptagon. The largest deviation of an O-4 atom from the common least-squares plane (Table VI) is 0.28 Å, which is not more than found[4] for most α-CD structures. The values for ϕ and ψ (Table IV) and for the angle between the plane of the O-4 atoms and the planes defined by O-4, C-6, and O-4' (Table V, *E*) do not show large deviations from the mean values and indicate an open, circular conformation rather than the collapsed conformation found in the α-CD hydrates[1,15].

The conformation of the macrocycle is stabilised through a ring of hydrogen bonds between secondary hydroxyl groups O-2···O-3 (Fig. 1 and Table VII), with all O-2···O-3 distances lying in the normally accepted range of 2.7–3.0 Å. Since hydrogen atoms could not be located, the directional sense of the hydrogen bonds cannot be assigned.

Packing scheme. — The packing of the β-CD molecules is displayed in Fig. 4. Since the void of each individual β-CD molecule is blocked on both ends by symmetry-

TABLE VII

HYDROGEN-BONDING DISTANCES OF β-CD DODECAHYDRATE. SYMMETRY CODE AS GIVEN IN ORTEP[18]

Atoms A	Atoms B	Distance (Å)	Symmetry code
O-2^{1}	O-W6	2.712(20)	
	O-3^{2}	2.955(9)	
O-3^{1}	O-W4	2.827(12)	
	O-2^{7}	2.876(9)	
	O-W8	2.905(21)	56401
O-6^{1}	O-W4	2.752(18)	65502
	O-3^{5}	2.974(12)	56501
O-2^{2}	O-W1	2.804(9)	65502
	O-3^{3}	2.861(9)	
O-6^{2}A	O-3^{4}	2.604(16)	56501
	O-W12	2.891(37)	65602
O-6^{2}B	O-W4	2.822(20)	65502
	O-2^{3}	2.889(15)	56501
	O-2^{7}	2.931(17)	65502
O-2^{3}	O-W3B	2.700(51)	55601
	O-W3A	2.750(13)	55601
	O-3^{4}	2.855(10)	
O-3^{3}	O-2^{7}	2.741(8)	64502
O-5^{3}	O-6^{6}	3.073(9)	55601
O-6^{3}	O-6^{6}	2.781(10)	55601
	O-W5B	2.787(21)	56601
	O-W5A	2.866(13)	56601
O-2^{4}	O-W14	2.751(28)	54501
	O-3^{5}	2.768(7)	
	O-W2	2.840(11)	
O-6^{4}	O-W14	2.935(33)	
	O-W13	3.082(22)	65602
O-2^{5}	O-3^{6}	2.780(7)	
	O-W5B	2.934(23)	
	O-W10	2.987(18)	64502
O-3^{5}	O-W7	2.892(12)	
O-6^{5}	O-W5B	2.626(16)	75502
	O-W7	2.746(12)	75502
	O-W5A	2.887(12)	75502
O-2^{6}	O-W1	2.739(8)	
	O-3^{7}	2.904(8)	
O-3^{6}	O-W3A	2.937(14)	
O-6^{6}	O-W2	2.714(11)	75502
O-3^{7}	O-W1	2.820(8)	65402
O-5^{7}	O-W1	2.961(8)	56501
O-6^{7}	O-W3B	2.683(48)	56501
	O-W3A	2.760(9)	56501
	O-W1	3.082(9)	56501
O-W2	O-W7	2.901(10)	
O-W3A	O-W5B	2.758(18)	
	O-W5A	2.856(13)	
O-W4	O-W9	2.717(30)	56401

TABLE VII

Atoms		*Distance (Å)*	*Symmetry code*
A	*B*		
O-W6	O-W9	2.810(31)	56401
	O-W10	3.096(27)	56501
O-W7	O-W13	2.816(30)	64602
O-W8	O-W12	2.939(38)	
	O-W9	2.967(45)	
O-W9	O-W13	2.564(33)	
O-W10	O-W12	3.026(39)	55401
O-W12	O-W13	2.679(38)	
	O-W14	2.733(36)	64602
O-W13	O-W14	2.513(49)	64602

related molecules, this structure belongs to the cage type previously described for α-CD[15-17], but not yet observed for β-CD. The hydrogen-bonding scheme within the crystal is explained by Table VII and Fig. 2. As none of the hydroxyl hydrogen atoms could be located, the assignment of hydrogen bonds in cases where rather long O···O distances are observed is not certain. Hydrogen-bond lengths vary from 2.513 to 3.096 Å.

Water inclusion. — The water included in the cavity is characterised by its high degree of disorder; 6.5 water molecules are distributed statistically over eight sites (Fig. 2). The remaining water (5.5 molecules) occupies eight sites between symmetry-related β-CD molecules. Based on distance criteria, several of these sites cannot be occupied simultaneously. Especially within the cavity, co-ordination of the water molecules is not "ideal" at all; only O-W1 shows the usual tetrahedral arrangement of donor and acceptor groups around the water (O···O-W1···O angles range

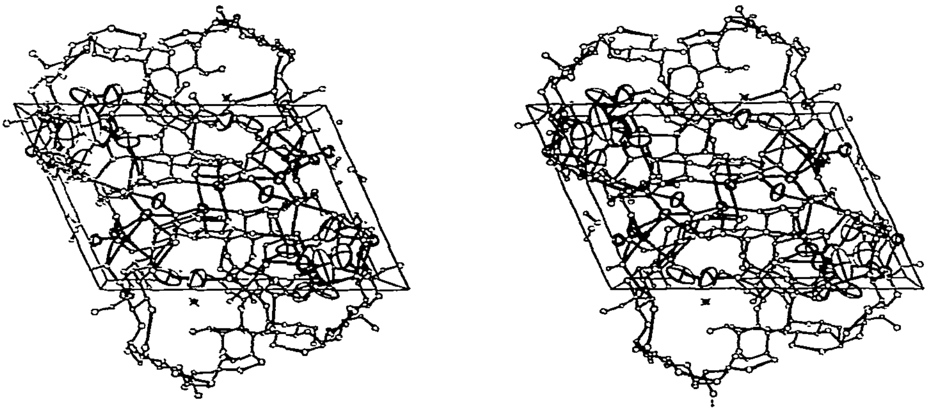

Fig. 4. Stereo-plot of the unit cell of β-CD dodecahydrate, viewing down the crystallographic *b*-axis. The stars indicate the center of the O-4 plane of a β-CD macrocycle.

from 91 to 141°), while others have even more distorted tetrahedra (O-W2, O-W4) and three or even five neighbours within suitable distances. As the hydrogen-bond donor and acceptor sites are satisfied for only one of the water molecules (O-W1) and the others are not, one would call these water molecules "activated". When expelled by a guest molecule, they become part of the bulk water and gain hydrogen-bonding energy, thus lowering their intrinsically high potential energy.

Mechanism of β-CD inclusion formation. — The "induced-fit" type mechanism of complexation can be ruled out for β-CD because, even in the "empty" water complex, the β-CD macrocycle exists in an open, round state as opposed to α-CD hydrate, where a collapsed conformation is observed[1,4,15]. As far as other mechanisms suggested for inclusion formation are concerned, this study cannot clear up how far hydrophobic forces, van der Waals interaction between guest and host, and entropy gain upon expulsion of included "activated water" are involved.

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