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cyclohexylurea was removed by filtration. Purification of the pentapeptide was achieved by gel permeation chromatography on Sephadex LH-20 with methanol as eluent. The product crystallized spontaneously in the glass tubes of the fraction collector (mp 187–189 °C dec); yield, 355 mg (75%). TLC: R_f(B) = 0.24; R_f(C) = 0.59; R_f(D) = 0.59. UV: A solution of 3.55 mg of the product in 5 mL of methanol (0.75 mM) at 359 nm showed an absorbance of 0.236; calculated from ϵ_{358} 320, A = 0.240.

(e) **Tyr-Gly-Gly-ATEPhe-Leu (13).** A total of 350 mg (0.37 mmol) of the protected pentapeptide was saponified with 200 μL of 2 N aqueous NaOH in 1 mL of methanol. After 1 h, the solution was neutralized with acetic acid and subjected to column chromatography on silica gel with solvent D as eluent; yield, 280 mg (81%). TLC: R_f(C) = 0.24; R_f(D) = 0.67. For removal of the residual protective groups the peptide acid was treated with 5% TFA in dichloromethane for 10 min (cleavage of the Ddz group; TLC: R_f(D) = 0.58), followed by 50% TFA in dichloromethane (cleavage of the *tert*-butyl ester; TLC: R_f(D) = 0.42). After evaporating the solvent in vacuo, the residue was purified by column chromatography on silica gel with solvent D, followed by gel permeation chromatography on Sephadex LH-20 with methanol as eluent; yield, 140 mg (83%).

Amino acid analysis: Gly 1.95 (2); Leu 1.09 (1); Tyr 1.00 (1); Phe[§] 0.51 (1) ([§]compare **12**).

The purity of the product was checked by HPLC (column, RP-8, 5 μm, 250 × 4 mm; solvent, linear gradient from 30% to 50% aqueous acetonitrile containing 0.1% TFA; gradient time, 10 min; flow rate, 1 mL/min; detection, UV at 277 and 354 nm; retention time, 6.0 min). Separation on a preparative scale could not be achieved by this gradient due to the limited solubility of the peptide in this solvent but using a 60–80% gradient of aqueous methanol containing 0.1% TFA.

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Registry No. 1, 87736-85-4; **2**, 92367-11-8; **3**, 92367-12-9; **4**, 92367-13-0; **5**, 92367-14-1; **6**, 92367-15-2; **7**, 92367-16-3; **8**, 92396-67-3; **9**, 92367-17-4; **10**, 92367-18-5; **11**, 92367-19-6; **12**, 92367-20-9; **13**, 92367-21-0; **14**, 92367-22-1; **15**, 92367-23-2; **16**, 92367-24-3; **17**, 92367-25-4; **18**, 92367-26-5; **19**, 92396-68-4; **20**, 92396-69-5; Boc-Gly-OH, 4530-20-5; H-Gly-OEt-HCl, 623-33-6; Boc-Gly-Gly-OEt, 25438-03-3; H-Gly-Gly-OEt, 627-74-7; Ddz-Tyr(Bu-*t*)-OH, 70266-05-6; Ddz-Tyr(Bu-*t*)-Gly-Gly-OEt, 92367-33-4; Boc-ATEPhe-Leu-OMe, 92367-31-2; Ddz-Tyr(Bu-*t*)-Gly-Gly-OH, 92367-30-1; H-ATEPhe-Leu-OMe, 92367-34-5; H-Leu-OMe-HCl, 7517-19-3; Ddz-Tyr(Bu-*t*)-Gly-Gly-ATEPhe-Leu-OMe, 92367-32-3; Ddz-Tyr(Bu-*t*)-Gly-Gly-ATEPhe-Leu-OH, 92367-35-6; Ddz-Asp(*t*-Bu)-OSu, 92367-27-6; Ddz-Asp(*t*-Bu)-ATEPhe-OH, 92367-28-7; Ddz-Asp(*t*-Bu)-ATEPhe-OMe, 92367-29-8; 2,2,2-trifluoro-1-(4-methylphenyl)-1-ethanone, 394-59-2; 2,2,2-trifluoro-1-(4-methylphenyl)-1-ethanone oxime, 75703-25-2; sodium diethyl acetamide malonate, 41679-89-4; L-*N*-*tert*-butoxycarbonyl-β-*tert*-butylaspartic acid, 1676-90-0.

Supplementary Material Available: Scheme and experimental details of the synthesis of D,L-*N*-acetyl-4′-(trifluoroacetyl)-phenylalanine and its oxime (7 pages). Ordering information is given on any current masthead page.

Circular and Flip-Flop Hydrogen Bonding in β-Cyclodextrin Undecahydrate: A Neutron Diffraction Study[†]

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Abstract: β-Cyclodextrin crystallizes from water in monoclinic space group $P2_1$ with a = 21.261 (6) Å, b = 10.306 (3) Å, c = 15.123 (4) Å, β = 112.3 (5)°, V = 3065.8 Å^3, Z = 2, D_x = 1.462 g/cm^3, FW = 1351.2, $(C_7H_{10}O_5)_7(11 \pm 0.5)H_2O$ per asymmetric unit. The crystal structure was initially determined from X-ray data, and H atoms were located from a 6610 neutron F_s' above σ, measured at 293 K, diffractometer equipped with a BF_3 counter, Be monochromator, λ = 1.015 Å, flux 10^6 n cm^{-2}·s^{-1}, 0.56 Å resolution, full-matrix least-squares refinement, R = 6.8%. There are 53 H bonds per asymmetric unit of which 35 are normal O—H···O and 18 are of the flip-flop type O—H···H—O, representing a statistical average O—H···O ⇌ O···H—O. The 11 water molecules are distributed over 16 positions, 8 in the cavity of β-CD (6.13 water molecules) and 8 in interstices (4.88 water molecules). Cavity waters form only 2 H bonds to enclosing β-CD and 6 contacts to neighboring β-CD. Their positions are better occupied and they are better ordered than "outside" water in interstices, an effect probably due to the hydrophobic character of the cavity. Flip-flop O—H···H—O bonds are interconnected to produce more extended systems, with one infinite flip-flop chain running through the whole crystal structure. Since the two states are energetically near-equivalent, flip-flop H bonds are entropically favored. Flip-flop bonds are also observed between all seven intramolecular, interglucose O(2), O(3) hydroxyls, O(2)—H···H—O(3), and explain the unusual conformational stiffness of β-CD in solution, compared with the more flexible α-CD which does not exhibit such flip-flop H bonds in the crystalline state. As in the α-CD·6H_2O crystal structure, β-CD·11H_2O contains some circularly closed, H-bonded systems which also involve flip-flops. Circles combined with flip-flop can form an entropically favorable system which could occur in water and in the hydration of macromolecules, i.e., β-CD·11H_2O can be considered as the frozen state of hydrated β-CD.

When starch is degraded by a special type of amylases called glucanotransferases, a family of cyclically closed oligosaccharides is obtained. They are composed of six to eight α(1–4) linked glucoses and called α-, β-, γ-cyclodextrins (α-CD, β-CD, γ-CD). Due to their annular structure, they are able to form inclusion complexes with a great variety of substrate (guest) molecules[1-5] under the proviso that the substrates are small enough to fit physically into the central cavities of the cyclodextrin rings.[1,2]

[†] Topography of Cyclodextrin Inclusion Complexes, Part 20. For Part 19 see: Betzel, Ch., et al. *J. Incl. Phenom.* **1983**, *1*, 181–191. For Part 18 see: Lindner, K.; Saenger, W. *Carbohydr. Res.* **1982** *107*, 7–16.

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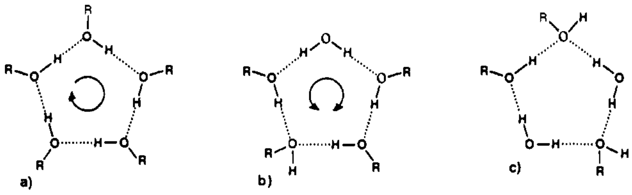

Figure 1. Definition of circularly arranged O—H···O hydrogen bonds: (a) homodromic, (b) antidromic, (c) heterodromic.

There have been many attempts to explain the driving force of this inclusion formation and to make use of cyclodextrins in research and in industry.[3-5]

Owing to their primary O(6)H and secondary O(2)H, O(3)H hydroxyl groups located on both rims of the ring-shaped cyclodextrin molecules, crystal structures in general display a great number of O—H···O hydrogen bonds. The number is even greater if the cyclodextrins are crystallized as "empty" molecules from water because water molecules are located in the cavities as included water and additionally in interstices between cyclodextrin molecules. The number of water molecules contained in crystals of cyclodextrin hydrates increases with the ring size so that chemical compositions α-CD·6H_2O, β-CD·11H_2O, and γ-CD·18H_2O are observed.

X-ray and neutron diffraction studies of α-CD·6H_2O have demonstrated the occurrence of networks of O—H···O hydrogen bonds which involve α-CD hydroxyls as well as water molecules.[6] An analysis of the hydrogen-bonding scheme has shown that the network contains several "endless" chains O—H···O—H··· with all hydroxyls pointing in the same direction (homodromic) and running through the whole crystal. These chains are formed preferentially due to the cooperative effect which increases the hydrogen-bonding affinity of an O–H group when it is in hydrogen-bonding contact.[7,8] The chains can also close up circularly with four to seven or more hydroxyls and water molecules involved. These circles constitute unique patterns in which O–H directions are all in the same direction, homodromic. Besides these, antidromic and heterodromic circles can occur which designate cases with two chains emanating from the same water molecule and colliding at one oxygen atom (anti) and cases with O–H groups in random orientation (hetero), see Figure 1.[9,10]

The crystal structure of γ-CD·18H_2O has been determined in two X-ray studies,[11] and a neutron-diffraction analysis is under way (Hingerty, Betzel, Zabel, Saenger, 1984). For β-CD hydrate, two crystal forms have been detected which differ slightly in unit cell constants and more significantly in the number of 11 and 12 water molecules associated with β-CD, as has been shown by X-ray analyses.[12,13] In order to determine the hydrogen-bonding scheme occurring in β-CD·11H_2O form I,[12] the neutron-diffraction analysis described in this work has been carried out. Some details of the hydrogen-bonding pattern were the subject of a preliminary publication.[14]

Experimental Section

β-CD was purchased from SERVA, Heidelberg. In order to reduce incoherent neutron scattering due to H atoms, all exchangeable (hydroxyl) protons of β-CD were replaced by D through repeated (three times) dissolution in D_2O and subsequent evaporation. Finally a hot, saturated, filtered solution of about 0.1 g of β-CD in 1 mL of D_2O immersed in a Dewar flask filled with hot water (~80 °C) was allowed to cool down in 3 days. The obtained stout, prismatic crystals have composition $(C_6H_7O_5D_3)_7$·(11 ± 0.5)D_2O, unit cell constants a = 21.261 (6) Å, b = 10.306 (3) Å, c = 15.123 (4) Å, β = 112.3 (5)°, space group monoclinic $P2_1$, Z = 2, D_x = 1.462g/cm³, V = 3065.8 Å³, FW = 1351.2.

A crystal of size 2 × 2 × 3 mm was sealed together with some mother liquor in a quartz capillary in order to prevent decomposition which leads to cracking of crystals if they are left in the atmosphere. When a four-circle diffractometer installed at the high-flux reactor at Oak Ridge National Laboratory was used, 8909 neutron intensity data were measured at 293 ± 2 K to a resoltuion of 0.56 Å in seven shells with use of a BF_3 counter. The flux employed was 10^6 n cm^{-2} s^{-1} at a wavelength of 1.015 Å (Be monochromator). The data were corrected empirically for absorption effects and then for Lorentz and polarization factors and were converted to F's with standard deviations calculated on the basis of counting statistics.[15] During full-matrix least-squares refinement, secondary extinction effects were corrected isotropically[16] and only a total of 6610 data of the five innermost shells with $F > \sigma(F)$ were included because the outer two shells were collected after reactor refill and the quartz capillary appeared to have leaked.

Structure Determination and Refinement. Atomic scattering lengths used in the structure factor calculations were taken from Bacon.[17] Initial difference Fourier maps were based on C and O parameters of β-CD determined in the X-ray study.[12] Since oxygen and deuterium scattering is of the same dimension, the disorder of water oxygens described in the X-ray paper and the associated disorder of water deuterium atoms produced considerable difficultly in the interpretation of neutron-scattering density.

In a series of full-matrix least-squares refinement cycles[16] followed by difference Fourier syntheses, minor sites of O and D atoms could be assigned and their coordinates and occupancies were refined. In the beginning of the refinement process, partially occupied sites of disordered D atoms were constrained so that occupancy factors added up to 1.0 for each D (or to the occupation of the bound water oxygen, if required). In the final stages of refinement, free variation of these occupation factors produced no significant deviation from ideal values, and temperature factors which were first kept isotropic were converted to and refined as anisotropic. A difference map computed at the end of the refinement process showed only random background noise which we attribute largely to incoherent scattering due to C–H hydrogen atoms. The final R factor is 6.8% for all 6610 reflection data above $\sigma(F)$.

Final fractional atomic coordinates and occupational and equivalent isotropic temperature factors (computed from anisotropic ones) are collected in Table I. (A list of anisotropic temperature factors and structure amplitudes is in the supplementary material.) Interatomic distances and angles are entered in Table II. The atomic numbering scheme used denotes first the kind of atom (H, C, O); for hydrogens and deuteriums, which for the sake of simplicity are both called hydrogens in the following, the second letter means the covalent partner to which they are attached. The next digit (first one in parentheses) gives the atom numbering within the glucose, followed by a digit designating which of the seven glucoses in β-CD is meant (Figure 2a). Hydration water molecules are designated OW1 to OW14 in correspondence to the X-ray study.[12] An additional letter A, B, or C is used to distinguish partially occupied atomic sites or if two atoms are bound to a central atom, e.g., H_2O or CH_2.

Results and Discussion

(a) The β-CD Macrocycle. Conformational and structural parameters of the β-CD macrocycle have already been described[12] and are therefore not considered here further. The primary hydroxyl group O(62) and all H atoms bound to secondary O(2), O(3) hydroxyl groups are statistically disordered, see paragraph e. Bond angles and distances obtained by the neutron study (Table II) differ slightly from those derived on the basis of X-ray data. O–H and C–H distances are, in general, longer because neutrons locate atomic nuclei rather than electron clouds; this phenomenon has also been observed with other carbohydrate neutron and X-ray analyses.[8,18] An illustration displaying the packing of the β-CD molecules in the unit cell is given in Figure 3a.

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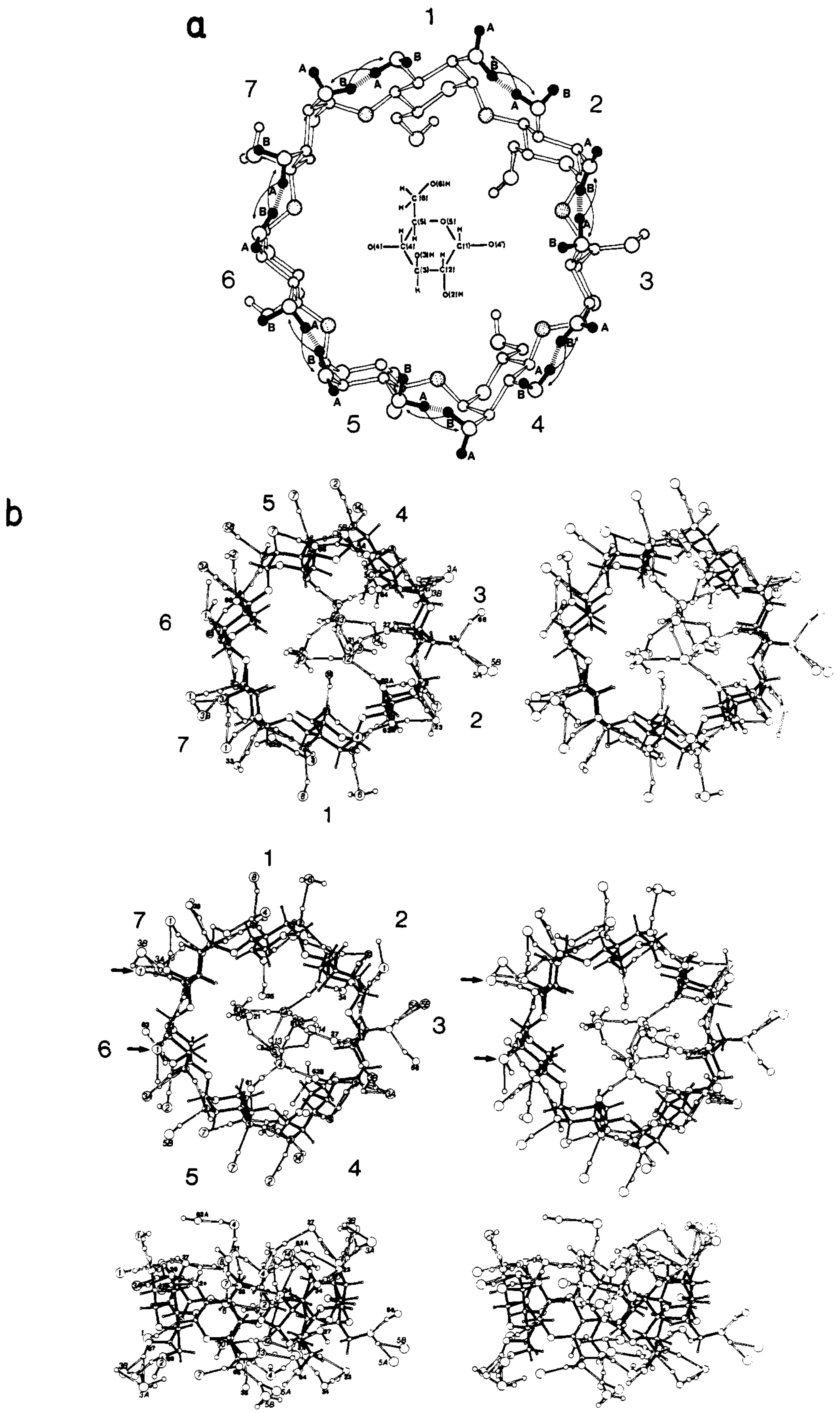


Figure 2. (a) Structure of the β-CD molecule in the crystal structure of β-CD·11H_2O. Insert shows the atomic numbering scheme used and numbers at the periphery refer to glucoses 1–7. H and C atoms are indicated by small and large spheres, glucosidic oxygens O_4 by stippling, and hydrogens attached to secondary O(2), O(3) groups are drawn solid. They are engaged in intramolecular, interglucoses flip-flop hydrogen bonds of the type O—H···H—O (arrows and |||); H-atom positions A and B cannot be occupied simultaneously and are only about half filled. (b) Stereodiagrams of β-CD and hydrogen-bonding interactions seen from the O(6) rim (top), from the O(2), O(3) rim (middle), and in a side view (bottom). Oxygen atoms of hydroxyl groups and water are indicated in italics and in normal numbers (35 representing O(3)5), and large numbers at the periphery designate glucose units. Arrows in the middle structure indicate a section of the infinite flip-flop chain (see Figure 4).

Table I. Fractional Atomic Coordinates, Occupational Parameters, and Mean Isotropic Temperature Factors B (Å^2)[a]

	x	y	z	occ	B, Å^2
C(11)	0.5411 (3)	0.5314 (6)	0.0930 (3)	1.00	4.1 (1)
C(21)	0.4706 (3)	0.5028 (7)	0.0190 (4)	1.00	4.3 (2)
C(31)	0.4765 (2)	0.4142 (6)	−0.0582 (3)	1.00	3.7 (1)
C(41)	0.5248 (3)	0.4710 (6)	−0.0997 (3)	1.00	3.7 (1)
C(51)	0.5934 (3)	0.5021 (7)	−0.0197 (4)	1.00	4.7 (2)
C(61)	0.6423 (5)	0.5703 (10)	−0.0535 (7)	1.00	7.3 (3)
O(21)	0.4305 (4)	0.4424 (10)	0.0650 (5)	1.00	5.5 (2)
O(31)	0.4118 (3)	0.4025 (9)	−0.1339 (4)	1.00	4.9 (2)
O(41)	0.5335 (3)	0.3795 (6)	−0.1642 (4)	1.00	3.7 (1)
O(51)	0.5818 (4)	0.5861 (8)	0.0479 (5)	1.00	5.0 (2)
O(61)	0.7051 (9)	0.5870 (24)	0.0165 (16)	1.00	15.5 (9)
HC11	0.5392 (7)	0.6048 (12)	0.1455 (9)	1.00	5.8 (4)
HC21	0.4478 (5)	0.5942 (13)	−0.0135 (7)	1.00	5.8 (3)
HC31	0.4946 (5)	0.3213 (10)	−0.0276 (7)	1.00	4.6 (3)
HC41	0.5051 (6)	0.5632 (11)	−0.1384 (8)	1.00	5.7 (4)
HC51	0.6156 (7)	0.4102 (16)	0.0139 (10)	1.00	6.0 (4)
HC61A	0.6486 (25)	0.6695 (28)	−0.0284 (21)	1.00	11.7 (14)
HC61B	0.6500 (10)	0.5179 (21)	−0.1114 (14)	1.00	11.9 (11)
HO21A	0.3929 (10)	0.4900 (24)	0.0583 (12)	0.66	8.4 (6)
HO21B	0.4561 (10)	0.3970 (29)	0.1144 (15)	0.34	5.9 (7)
HO31A	0.4163 (5)	0.3513 (14)	−0.1842 (8)	0.58	4.8 (3)
HO31B	0.3859 (3)	0.3378 (22)	−0.1169 (18)	0.30	5.5 (5)
HO61A	0.7054 (13)	0.6650 (32)	0.0561 (19)	1.00	14.0 (11)
C(12)	0.6797 (2)	0.2870 (7)	0.4195 (3)	1.00	4.5 (1)
C(22)	0.6017 (2)	0.2759 (7)	0.3821 (3)	1.00	4.3 (1)
C(32)	0.5693 (2)	0.2933 (7)	0.2738 (3)	1.00	3.9 (1)
C(42)	0.5966 (2)	0.4156 (7)	0.2442 (3)	1.00	4.0 (1)
C(52)	0.6738 (3)	0.4107 (7)	0.2833 (4)	1.00	4.6 (1)
C(62)	0.7080 (5)	0.5246 (9)	0.2582 (7)	1.00	7.5 (3)
O(22)	0.5856 (3)	0.1553 (10)	0.4104 (5)	1.00	5.2 (2)
O(32)	0.4979 (4)	0.2935 (13)	0.2452 (6)	1.00	6.7 (3)
O(42)	0.5691 (3)	0.4160 (7)	0.1419 (4)	1.00	3.8 (1)
O(52)	0.6982 (3)	0.4016 (8)	0.3859 (5)	1.00	5.2 (2)
O(62)A	0.7828 (23)	0.5049 (22)	0.2816 (24)	0.54	14.1 (19)
O(62)B	0.6998 (11)	0.6481 (14)	0.2706 (14)	0.46	6.3 (7)
HC12	0.6996 (6)	0.2948 (15)	0.4981 (8)	1.00	6.5 (4)
HC22	0.5838 (7)	0.3521 (17)	0.4180 (9)	1.00	7.0 (4)
HC32	0.5833 (6)	0.2140 (12)	0.2394 (8)	1.00	5.0 (3)
HC42	0.5798 (7)	0.5021 (14)	0.2715 (8)	1.00	6.7 (4)
HC52	0.6889 (6)	0.3252 (14)	0.2534 (9)	1.00	5.4 (3)
HC62A	0.6885 (16)	0.5388 (32)	0.1864 (23)	1.00	15.8 (12)
HC62B	0.7035 (16)	0.6006 (19)	0.3103 (28)	0.51	8.7 (13)
HC62C	0.7700 (20)	0.5084 (24)	0.2796 (27)	0.38	9.0 (16)
HO22A	0.5438 (5)	0.1504 (14)	0.4142 (8)	0.60	5.1 (3)
HO22B	0.6138 (21)	0.0949 (37)	0.4055 (19)	0.37	8.2 (10)
HO32A	0.4782 (7)	0.3299 (20)	0.1851 (11)	0.65	7.1 (4)
HO32B	0.4875 (26)	0.3635 (26)	0.2817 (11)	0.38	6.8 (16)
HO62A	0.7761 (24)	0.4288 (21)	0.2373 (21)	0.53	8.3 (13)
HO62B	0.7246 (14)	0.6699 (42)	0.3410 (35)	0.43	9.6 (12)
C(13)	0.8609 (2)	−0.0871 (7)	0.5014 (3)	1.00	3.7 (1)
C(23)	0.7905 (2)	−0.1273 (7)	0.4982 (3)	1.00	3.9 (1)
C(33)	0.7370 (2)	−0.0378 (7)	0.4300 (3)	1.00	3.5 (1)
C(43)	0.7543 (2)	0.1015 (6)	0.4610 (3)	1.00	3.4 (1)
C(53)	0.8267 (2)	0.1336 (6)	0.4702 (3)	1.00	3.6 (1)
C(63)	0.8496 (2)	0.2656 (7)	0.5161 (4)	1.00	4.3 (1)
O(23)	0.7777 (4)	−0.2595 (8)	0.4700 (5)	1.00	4.9 (2)
O(33)	0.6720 (3)	−0.0690 (9)	0.4324 (5)	1.00	4.6 (2)
O(43)	0.7058 (2)	0.1777 (7)	0.3895 (3)	1.00	3.7 (1)
O(53)	0.8738 (2)	0.0409 (8)	0.5311 (3)	1.00	3.9 (1)
O(63)	0.8440 (4)	0.2660 (10)	0.6057 (5)	1.00	5.4 (2)
HC13	0.9010 (5)	−0.1442 (13)	0.5545 (7)	1.00	5.2 (3)
HC23	0.7901 (6)	−0.1163 (14)	0.5689 (9)	1.00	5.7 (4)
HC33	0.7357 (5)	−0.0522 (11)	0.3569 (6)	1.00	4.5 (3)
HC43	0.7503 (5)	0.1152 (12)	0.5305 (7)	1.00	4.6 (3)
HC53	0.8276 (5)	0.1334 (14)	0.3969 (7)	1.00	5.8 (3)
HC63A	0.8196 (7)	0.3395 (17)	0.4718 (11)	1.00	6.5 (4)
HC63B	0.9024 (6)	0.2793 (18)	0.5241 (10)	1.0	6.9 (4)
HO23A	0.7605 (9)	−0.3181 (17)	0.5081 (14)	0.48	5.2 (5)
HO23B	0.8071 (16)	−0.2746 (22)	0.4422 (20)	0.54	9.9 (9)
HO33A	0.6439 (6)	0.0047 (14)	0.4161 (9)	0.61	4.9 (3)
HO33B	0.6483 (21)	−0.1336 (36)	0.3850 (22)	0.37	7.9 (11)
HO63	0.8560 (6)	0.3463 (14)	0.6369 (9)	1.00	8.1 (4)
C(14)	0.9714 (2)	−0.2553 (6)	0.2631 (3)	1.00	3.1 (1)
C(24)	0.9497 (2)	−0.3522 (6)	0.3217 (3)	1.00	3.3 (1)
C(34)	0.8948 (2)	−0.2934 (6)	0.3492 (3)	1.00	3.2 (1)
C(44)	0.9187 (2)	−0.1649 (6)	0.4001 (3)	1.00	3.1 (1)
C(54)	0.9466 (2)	−0.0757 (6)	0.3435 (3)	1.00	3.4 (1)
C(64)	0.9824 (3)	0.0402 (8)	0.4007 (5)	1.00	5.6 (2)
O(24)	0.9257 (3)	−0.4678 (7)	0.2690 (5)	1.00	4.1 (2)
O(34)	0.8772 (4)	−0.3784 (10)	0.4089 (5)	1.00	5.2 (2)
O(44)	0.8609 (2)	−0.1041 (8)	0.4096 (3)	1.00	3.8 (1)
O(54)	0.9949 (2)	−0.1417 (7)	0.3159 (3)	1.00	3.5 (1)
O(64)	1.0071 (8)	0.1314 (13)	0.3455 (9)	1.00	10.3 (5)
HC14	1.0142 (5)	−0.2932 (12)	0.2454 (6)	1.00	4.6 (3)
HC24	0.9940 (5)	−0.3763 (12)	0.3867 (8)	1.00	4.5 (3)
HC34	0.8497 (5)	−0.2747 (11)	0.2823 (7)	1.00	4.2 (2)
HC44	0.9580 (5)	−0.1839 (11)	0.4719 (7)	1.00	4.5 (2)
HC54	0.9046 (5)	−0.0449 (11)	0.2792 (8)	1.00	4.9 (3)
HC64A	0.9504 (9)	0.0864 (22)	0.4326 (16)	1.00	9.2 (7)
HC64B	1.0278 (7)	0.0082 (17)	0.4593 (10)	1.00	7.5 (5)
HO24A	0.8956 (7)	−0.4441 (14)	0.2070 (13)	0.43	4.1 (4)
HO24B	0.9638 (9)	−0.5245 (20)	0.2671 (13)	0.53	5.8 (4)
HO34A	0.8456 (8)	−0.3488 (13)	0.4300 (10)	0.46	4.2 (3)
HO34B	0.8411 (13)	−0.4234 (26)	0.3702 (20)	0.56	7.9 (7)
HO64	0.9714 (43)	−0.2018 (27)	0.3241 (36)	1.00	3.6 (9)
C(15)	0.8618 (2)	−0.2231 (6)	−0.1162 (3)	1.00	3.3 (1)
C(25)	0.8554 (2)	−0.3516 (6)	−0.0707 (3)	1.00	3.5 (1)
C(35)	0.8553 (2)	−0.3295 (5)	0.0288 (3)	1.00	3.1 (1)
C(45)	0.9186 (2)	−0.2527 (5)	0.0885 (3)	1.00	2.8 (1)
C(55)	0.9204 (2)	−0.1270 (6)	0.0373 (3)	1.00	3.3 (1)
C(65)	0.9826 (3)	−0.0452 (7)	0.0894 (4)	1.00	4.5 (1)
O(25)	0.7970 (3)	−0.4177 (7)	−0.1316 (5)	1.00	4.9 (2)
O(35)	0.8533 (4)	−0.4504 (8)	0.0713 (5)	1.00	4.7 (2)
O(45)	0.9142 (2)	−0.2275 (7)	0.1778 (3)	1.00	3.2 (1)
O(55)	0.9201 (2)	−0.1560 (8)	−0.0564 (3)	1.00	3.7 (1)
O(65)	1.0431 (3)	−0.1159 (9)	0.1152 (5)	1.00	5.4 (2)
HC15	0.8694 (4)	−0.2425 (12)	−0.1827 (6)	1.00	4.9 (3)
HC25	0.8990 (6)	−0.4131 (12)	−0.0638 (8)	1.00	5.1 (3)
HC35	0.8108 (4)	−0.2723 (11)	0.0221 (6)	1.00	4.4 (2)
HC45	0.9637 (4)	−0.3099 (10)	0.0979 (5)	1.00	3.8 (2)
HC55	0.8756 (5)	−0.0708 (11)	0.0312 (7)	1.00	4.3 (2)
HC65A	0.9813 (7)	0.0387 (15)	0.0439 (11)	1.00	7.0 (4)
HC65B	0.9795 (7)	−0.0104 (14)	0.1537 (12)	1.00	6.1 (4)
HO25A	0.7606 (7)	−0.3601 (14)	−0.1619 (11)	0.58	5.2 (3)
HO25B	0.7896 (21)	−0.5000 (21)	−0.1031 (24)	0.42	13.2 (17)
HO35A	0.8730 (9)	−0.4505 (16)	0.1413 (13)	0.57	5.9 (4)
HO35B	0.7995 (14)	−0.4546 (27)	0.0556 (22)	0.44	7.7 (7)
HO65	1.0509 (5)	−0.1410 (14)	0.0552 (10)	1.00	7.7 (3)
C(16)	0.6607 (2)	0.0616 (5)	−0.3512 (3)	1.00	3.0 (1)
C(26)	0.6520 (2)	−0.0843 (6)	−0.3553 (3)	1.00	3.4 (1)
C(36)	0.6936 (2)	−0.1442 (5)	−0.2588 (3)	1.00	3.3 (1)
C(46)	0.7670 (2)	−0.1002 (5)	−0.2265 (3)	1.00	2.9 (1)
C(56)	0.7704 (2)	0.0480 (5)	−0.2266 (3)	1.00	3.1 (2)
C(66)	0.8417 (3)	0.1013 (7)	−0.2017 (4)	1.00	4.2 (1)
O(26)	0.5815 (3)	−0.1136 (8)	−0.3876 (5)	1.00	4.8 (2)
O(36)	0.6893 (4)	−0.2800 (8)	−0.2669 (6)	1.00	5.8 (2)
O(46)	0.8032 (2)	−0.1494 (6)	0.1324 (3)	1.00	3.2 (1)
O(56)	0.7310 (3)	0.0953 (7)	−0.3191 (4)	1.00	3.4 (1)
O(66)	0.8720 (4)	0.0574 (10)	−0.2641 (6)	1.00	5.6 (2)
HC16	0.6363 (5)	0.1034 (12)	−0.4249 (7)	1.00	4.5 (2)
HC26	0.6708 (6)	−0.1216 (14)	−0.4083 (7)	1.00	5.5 (3)
HC36	0.6744 (5)	−0.1134 (10)	−0.2048 (7)	1.00	4.4 (2)
HC46	0.7893 (5)	−0.1376 (11)	−0.2774 (6)	1.00	4.3 (2)
HC56	0.7511 (5)	0.0844 (11)	−0.1738 (7)	1.00	4.4 (3)
HC66A	0.8404 (9)	0.2059 (16)	−0.2007 (14)	1.00	6.8 (5)
HC66B	0.8736 (6)	0.0691 (14)	−0.1282 (8)	1.00	5.9 (3)
HO26A	0.5698 (6)	−0.2047 (17)	−0.3955 (11)	0.52	5.2 (4)
HO26B	0.5621 (9)	−0.0596 (18)	−0.3612 (15)	0.48	6.2 (5)
HO36A	0.7223 (13)	−0.3190 (19)	−0.2129 (15)	0.42	5.7 (5)
HO36B	0.7008 (16)	−0.3146 (21)	−0.3243 (21)	0.59	4.3 (8)
HO66	0.8609 (4)	0.1155 (13)	−0.3165 (8)	1.00	6.9 (3)
C(17)	0.5146 (3)	0.4120 (6)	−0.2608 (3)	1.00	3.5 (1)
C(27)	0.4751 (2)	0.2978 (6)	−0.3221 (3)	1.00	3.6 (1)
C(37)	0.5215 (2)	0.1826 (6)	−0.3056 (3)	1.00	3.1 (1)
C(47)	0.5857 (2)	0.2195 (5)	−0.3221 (3)	1.00	2.7 (1)
C(57)	0.6197 (2)	0.3402 (5)	−0.2669 (3)	1.00	2.9 (1)
C(67)	0.6741 (2)	0.3925 (6)	−0.2981 (4)	1.00	3.6 (1)
O(27)	0.4175 (4)	0.2665 (8)	−0.3016 (5)	1.00	4.7 (2)
O(37)	0.4886 (3)	0.0774 (7)	−0.3672 (5)	1.00	4.2 (2)
O(47)	0.6308 (2)	0.1118 (6)	−0.2903 (3)	1.00	2.9 (1)
O(57)	0.5711 (3)	0.4433 (6)	−0.2820 (4)	1.00	3.4 (1)
O(67)	0.6452 (3)	0.4273 (8)	−0.3972 (4)	1.00	4.9 (2)
HC17	0.4845 (6)	0.4990 (10)	−0.2754 (8)	1.00	4.8 (3)
HC27	0.4590 (5)	0.3310 (11)	−0.3967 (7)	1.00	4.8 (3)

Table I (Continued)

	x	y	z	occ	B, Å^2		x	y	z	occ	B, Å^2
HC37	0.5362 (5)	0.1475 (11)	−0.2322 (7)	1.00	4.3 (2)	OW5A	0.8803 (9)	0.5041 (18)	0.7061 (13)	0.70	7.0 (4)
HC47	0.5733 (4)	0.2362 (10)	−0.3989 (6)	1.00	3.7 (2)	OW5B	0.8506 (13)	0.4667 (26)	0.7395 (17)	0.13	3.5 (6)
HC57	0.6411 (5)	0.3170 (10)	−0.1914 (6)	1.00	4.5 (2)	OW5C	0.8955 (21)	−0.3234 (30)	−0.3341 (27)	0.20	6.1 (10)
HC67A	0.7135 (6)	0.3213 (15)	−0.2833 (10)	1.00	6.0 (4)	HW5A	0.8979 (8)	0.4560 (20)	0.7798 (13)	0.60	10.7 (5)
HC67B	0.6976 (7)	0.4773 (15)	−0.2540 (11)	1.00	6.2 (4)	HW5B	0.9233 (16)	0.5522 (33)	0.6873 (20)	0.51	9.9 (8)
HO27A	0.3791 (7)	0.2997 (13)	−0.3447 (11)	0.58	5.3 (3)	HW5C	0.8617 (17)	−0.4302 (15)	−0.3068 (17)	0.47	5.9 (7)
HO27B	0.4233 (10)	0.3003 (21)	−0.2416 (23)	0.34	8.2 (9)	HW5H	0.8550 (22)	−0.3105 (21)	−0.3977 (23)	0.21	9.7 (13)
HO37A	0.4726 (10)	0.0987 (18)	−0.4356 (13)	0.46	5.6 (5)	HW5E	0.8236 (23)	0.4855 (26)	0.7670 (21)	0.22	14.2 (18)
HO37B	0.5200 (9)	0.0107 (15)	−0.3593 (16)	0.47	5.9 (5)	OW6	0.3286 (20)	0.6179 (29)	0.0524 (20)	0.88	6.7 (18)
HO67A	0.6090 (9)	0.5013 (23)	−0.4020 (20)	0.33	5.2 (6)	HW6A	0.3352 (22)	0.5978 (29)	0.1075 (30)	0.87	5.3 (12)
HO67B	0.6780 (8)	0.4774 (15)	−0.4101 (10)	0.62	6.5 (5)	HW6B	0.2852 (16)	0.5457 (28)	0.0075 (19)	0.95	5.8 (12)
OW1	0.5377 (4)	−0.3624 (7)	−0.4383 (5)	1.00	5.0 (2)	OW7	0.9303 (7)	−0.6704 (17)	0.0443 (11)	0.78	8.0 (5)
HW1A	0.5303 (7)	−0.3830 (13)	−0.5040 (13)	0.50	5.7 (4)	HW7A	0.9698 (10)	−0.6613 (21)	0.1009 (17)	0.83	10.8 (7)
HW1B	0.5620 (8)	−0.4291 (13)	−0.3916 (14)	0.60	7.7 (5)	HW7B	0.9045 (6)	−0.5967 (20)	0.0525 (8)	0.80	9.3 (5)
HW1C	0.5583 (8)	−0.2850 (15)	−0.4160 (11)	0.49	5.4 (4)	OW8	0.3042 (25)	−0.3987 (22)	0.8128 (21)	0.53	5.4 (14)
HW1H	0.5009 (21)	−0.3753 (36)	−0.4359 (22)	0.34	10.6 (15)	HW8A	0.3024 (19)	−0.3801 (20)	0.7490 (20)	0.52	11.1 (11)
OW2	0.9736 (6)	−0.1225 (13)	−0.2363 (10)	1.00	8.7 (5)	HW8B	0.3414 (16)	−0.4421 (19)	0.8354 (21)	0.61	6.3 (16)
HW2A	0.9373 (7)	−0.0628 (16)	−0.2455 (9)	0.99	9.3 (4)	OW9	0.2221 (12)	0.4892 (21)	−0.1248 (16)	0.72	9.3 (36)
HW2B	1.0027 (13)	−0.0803 (20)	−0.2546 (23)	0.44	9.4 (8)	HW9A	0.1712 (15)	0.4836 (23)	−0.1499 (26)	0.63	6.2 (14)
HW2C	0.9567 (23)	−0.2049 (22)	−0.2756 (29)	0.49	3.6 (16)	HW9B	0.2373 (19)	0.5029 (23)	−0.0529 (16)	0.75	4.7 (20)
OW3A	0.7483 (6)	0.6045 (12)	0.6079 (8)	0.71	5.4 (3)	OW10	0.2353 (15)	−0.2011 (22)	0.0467 (23)	0.81	8.1 (17)
HW3A1	0.7341 (14)	0.6568 (21)	0.6487 (26)	0.12	3.7 (7)	HW10A	0.2207 (22)	−0.1258 (16)	0.0688 (19)	0.81	11.1 (12)
HW3A2	0.7109 (25)	0.5408 (21)	0.5811 (23)	0.37	10.3 (17)	HW10B	0.2687 (16)	−0.1715 (22)	0.0191 (33)	0.82	6.7 (19)
HW3A3	0.7974 (12)	0.5717 (23)	0.6521 (13)	0.46	6.9 (6)	OW12	0.2185 (25)	0.8084 (21)	−0.1409 (23)	0.89	7.2 (20)
HW3A4	0.7442 (18)	0.6421 (23)	0.5500 (17)	0.35	6.6 (9)	HW12A	0.2483 (19)	0.7297 (19)	−0.1610 (29)	1.00	6.7 (19)
OW3B	0.6760 (28)	−0.3676 (22)	0.5065 (23)	0.28	9.9 (10)	HW12B	0.2372 (22)	0.8290 (18)	−0.0720 (30)	0.84	10.7 (17)
HW3B1	0.6392 (11)	−0.3610 (21)	0.4395 (20)	0.22	6.9 (17)	OW13	0.1168 (17)	0.6758 (20)	−0.1553 (21)	0.68	6.1 (18)
HW3B2	0.6965 (21)	−0.4200 (20)	0.4837 (21)	0.41	6.2 (8)	HW13A	0.1017 (20)	0.7172 (21)	−0.0988 (19)	0.66	5.6 (12)
OW4	0.7133 (11)	0.7976 (22)	0.1278 (17)	1.00	11.8 (8)	HW13B	0.1621 (12)	0.6697 (23)	−0.1183 (23)	0.68	6.7 (16)
HW4A	0.6693 (14)	0.8276 (22)	0.1175 (18)	0.58	9.5 (9)	OW14	0.1338 (20)	0.7968 (22)	−0.2912 (18)	0.62	6.6 (17)
HW4B	0.7187 (21)	0.7553 (20)	0.1832 (22)	0.49	14.4 (20)	HW14A	0.1083 (14)	0.8758 (13)	−0.3191 (24)	0.64	3.9 (16)
HW4C	0.7381 (21)	0.8734 (22)	0.1165 (21)	0.80	4.5 (18)	HW14B	0.0991 (24)	0.7323 (19)	−0.2906 (20)	0.61	7.3 (18)

[a] Mean $\bar{B}$'s were obtained for anisotropic B's [$\bar{B} = {}^1/_3(B_{11} + B_{22} + B_{33})$], see supplementary materials. Figures in parentheses refer to last digits given and are calculated from the least-squares correlation matrix. The mean standard deviation of occupancies for disordered atoms is 0.02. For the atomic numbering scheme, see text and Figure 1.

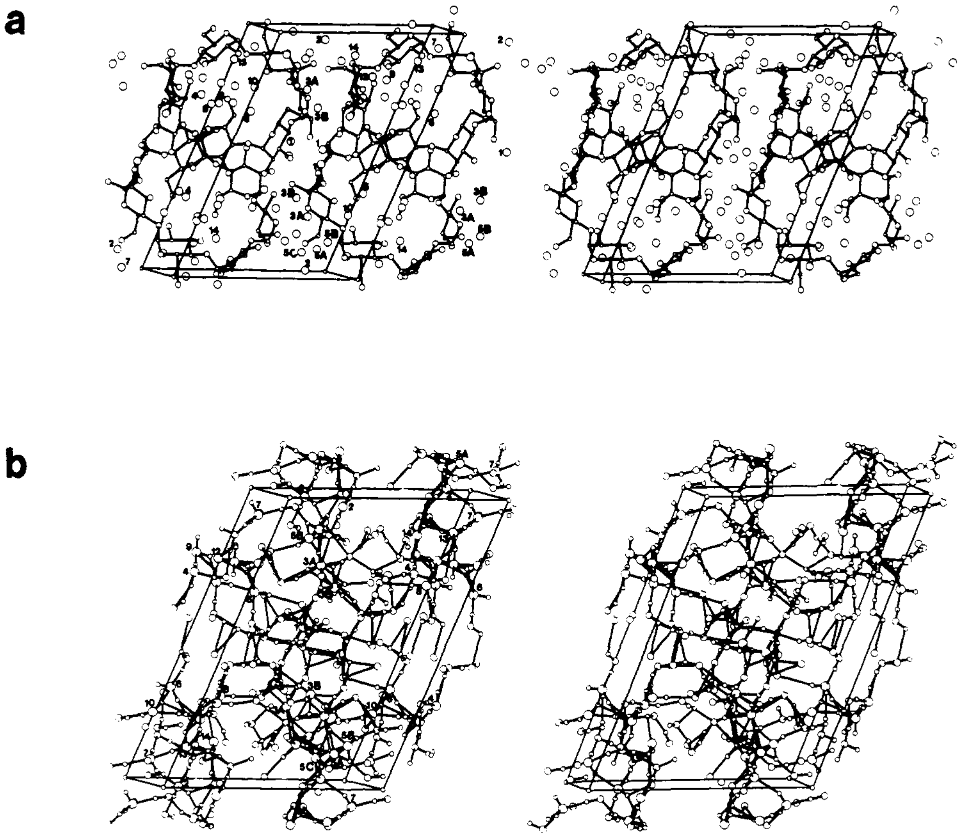


Figure 3. (a) Stereodiagram showing packing of β-CD molecules in the unit cell. (b) Same view as in part a but only O–H and water molecules are drawn and C and C–H are omitted. Solid bonds are covalent O–H and open bonds are hydrogen interactions O—H···O. In both figures, the view is down b, with a horizontal and c up.

Table II. Bond Distances (Å) and Angles (deg)[a]

	glucose unit								
	1	2	3	4	5	6	7	mean	σ
(A) Bond Distances									
C(1)-C(2)	1.518 (7)	1.538 (7)	1.536 (7)	1.519 (8)	1.522 (8)	1.514 (8)	1.534 (7)	1.526	0.010
C(2)-C(3)	1.525 (8)	1.525 (6)	1.521 (7)	1.509 (7)	1.523 (7)	1.519 (6)	1.508 (8)	1.518	0.009
C(3)-C(4)	1.512 (9)	1.525 (9)	1.512 (9)	1.519 (9)	1.524 (7)	1.517 (7)	1.526 (8)	1.519	0.006
C(4)-C(5)	1.531 (7)	1.518 (7)	1.528 (6)	1.523 (8)	1.516 (8)	1.529 (8)	1.518 (7)	1.523	0.006
C(5)-C(6)	1.499 (9)	1.504 (9)	1.520 (9)	1.500 (9)	1.512 (7)	1.517 (7)	1.507 (8)	1.508	0.008
mean	1.517	1.522	1.523	1.514	1.519	1.519	1.517		
σ	0.012	0.012	0.009	0.009	0.005	0.006	0.013		
C(1)-O(5)	1.409 (9)	1.400 (9)	1.387 (8)	1.397 (7)	1.405 (7)	1.426 (7)	1.396 (9)	1.403	0.012
C(1)-O(4)	1.407 (9)	1.406 (9)	1.399 (7)	1.423 (7)	1.398 (8)	1.404 (7)	1.400 (7)	1.405	0.009
C(2)-O(2)	1.432 (9)	1.399 (9)	1.422 (9)	1.416 (9)	1.407 (8)	1.419 (8)	1.413 (9)	1.415	0.011
C(3)-O(3)	1.420 (6)	1.411 (9)	1.431 (8)	1.406 (9)	1.410 (9)	1.405 (9)	1.426 (8)	1.416	0.010
C(4)-O(4)	1.418 (9)	1.430 (7)	1.413 (7)	1.434 (8)	1.413 (7)	1.427 (6)	1.425 (7)	1.423	0.008
C(5)-O(5)	1.431 (9)	1.439 (9)	1.434 (8)	1.419 (8)	1.446 (7)	1.415 (6)	1.438 (8)	1.432	0.011
C(6)-O(6)	1.362 (9)	1.51 (5)A 1.31 (2)B	1.406 (9)	1.480 (9)	1.398 (9)	1.406 (9)	1.431 (8)	1.427	0.050
mean	1.411	1.427	1.413	1.425	1.411	1.415	1.418		
σ	0.0024	0.038	0.017	0.027	0.016	0.010	0.016		
(B) Bond Angles									
C(1)-C(2)-C(3)	109.4 (5)	111.6 (5)	108.9 (5)	109.7 (5)	110.6 (4)	110.3 (4)	109.5 (4)	110.0	0.9
C(2)-C(3)-C(4)	110.8 (5)	110.2 (4)	109.6 (4)	110.2 (4)	109.2 (4)	113.3 (5)	110.3 (5)	110.5	1.3
C(3)-C(4)-C(5)	110.1 (4)	109.6 (5)	111.6 (5)	111.6 (4)	109.3 (3)	109.9 (4)	112.4 (4)	110.6	1.2
C(4)-C(5)-C(6)	113.7 (6)	115.5 (6)	111.8 (5)	112.1 (5)	113.5 (4)	113.8 (4)	112.4 (4)	113.3	1.3
mean	111	111	110	111	111	112	111		
σ	2	3	1	1	2	2	1		
C(2)-C(1)-O(5)	109.7 (5)	110.0 (5)	109.7 (5)	109.9 (8)	110.2 (4)	110.6 (4)	110.9 (5)	110.1	0.5
C(2)-C(1)-O(4)	108.9 (5)	109.0 (5)	107.8 (4)	108.4 (4)	108.9 (5)	111.4 (4)	108.7 (5)	109.0	1.1
C(1)-C(2)-O(2)	109.2 (5)	108.0 (4)	109.9 (6)	110.5 (5)	109.5 (4)	108.8 (5)	111.2 (5)	109.6	1.1
C(3)-C(2)-O(2)	110.5 (6)	111.7 (5)	111.7 (4)	110.1 (5)	112.7 (5)	113.3 (5)	110.7 (6)	111.5	1.1
C(2)-C(3)-O(3)	109.3 (5)	108.7 (6)	108.9 (5)	110.5 (6)	109.3 (5)	109.1 (5)	111.4 (4)	109.6	1.0
C(4)-C(3)-O(3)	107.5 (5)	113.3 (7)	109.3 (5)	109.8 (5)	111.3 (4)	110.5 (5)	109.3 (5)	110.1	1.8
C(3)-C(4)-O(4)	108.4 (5)	106.0 (5)	105.7 (4)	107.3 (4)	107.2 (4)	108.2 (4)	106.2 (4)	107.0	1.1
C(5)-C(4)-O(4)	110.4 (5)	110.8 (5)	111.4 (5)	109.0 (5)	110.7 (5)	111.4 (4)	109.6 (3)	110.5	0.9
C(4)-C(5)-O(5)	108.6 (6)	108.1 (6)	110.2 (5)	110.9 (5)	109.4 (5)	109.6 (4)	110.9 (4)	109.7	1.1
C(6)-C(5)-O(5)	106.9 (7)	108.3 (6)	106.3 (4)	106.6 (5)	107.4 (5)	106.2 (5)	106.0 (5)	106.8	0.8
C(5)-C(6)-O(6)	113.6 (1)	114 (1)A 128 (1)B	108.2 (6)	113.1 (7)	112.6 (6)	112.9 (5)	110.2 (4)	114.1	6.0
mean	109	111	109	110	110	110	110		
σ	2	6	2	2	2	2	2		
C(4)-O(4)-C(1)′	119.8 (5)	119.1 (6)	119.1 (6)	118.7 (4)	119.0 (4)	118.3 (5)	118.7 (4)	119.0	0.5
C(1)-O(5)-C(5)	114.1 (7)	114.3 (6)	112.3 (5)	115.4 (4)	113.9 (5)	113.6 (5)	114.9 (5)	114.1	1.0
mean	117	117	116	117	116	116	117		
σ	4	3	5	2	4	3	3		
O(5)-C(1)-O(4)′	112.2 (6)	110.9 (6)	111.4 (6)	110.1 (5)	110.7 (5)	111.4 (4)	111.5 (5)		
(C) Bond Distances									
C(1)-H(1)	1.11 (1)	1.10 (1)	1.09 (1)	1.11 (1)	1.10 (1)	1.12 (1)	1.07 (1)	1.10	0.02
C(2)-H(2)	1.09 (1)	1.10 (2)	1.08 (2)	1.10 (1)	1.09 (1)	1.09 (1)	1.10 (1)	1.09	0.01
C(3)-H(3)	1.07 (1)	1.07 (1)	1.11 (1)	1.11 (1)	1.09 (1)	1.09 (1)	1.09 (1)	1.09	0.02
C(4)-H(4)	1.11 (1)	1.10 (2)	1.10 (1)	1.11 (1)	1.09 (1)	1.11 (1)	1.10 (1)	1.10	0.01
C(5)-H(5)	1.09 (2)	1.09 (2)	1.12 (1)	1.09 (1)	1.09 (1)	1.09 (1)	1.08 (1)	1.09	0.01
C(6)-H(6)A	1.08 (3)	1.01 (3)	1.09 (2)	1.08 (1)	1.06 (2)	1.11 (1)	1.10 (2)	1.07	0.03
C(6)-H(6)B	1.09 (3)	1.14 (4)	1.05 (2)	1.08 (3)	1.10 (2)	1.08 (2)	1.07 (2)	1.08	0.03
C(6)-H(6)C		1.24 (4)							
O(2)-HO(2)A	0.88 (2)	0.91 (1)	1.00 (2)	0.94 (2)	0.94 (2)	0.97 (2)	0.90 (1)	0.93	0.04
O(2)-HO(2)B	0.87 (2)	0.88 (4)	0.89 (4)	1.01 (2)	0.99 (3)	0.87 (2)	0.93 (3)	0.92	0.06
O(3)-HO(3)A	0.96 (2)	0.92 (2)	0.94 (2)	0.90 (2)	0.98 (2)	0.94 (2)	0.98 (2)	0.94	0.03
O(3)-HO(3)B	0.96 (2)	0.98 (3)	0.97 (3)	0.90 (3)	1.08 (3)	1.05 (4)	0.93 (2)	0.98	0.06
O(6)A-HO(6)A	1.00 (4)	1.01 (4)	0.94 (2)	1.01 (6)	1.01 (2)	0.95 (2)	1.07 (2)	1.00	0.04
O(6)A-HO(6)B							0.95 (2)		
O(6)B-HO(6)B		1.02 (5)							
(D) Bond Angles									
HC1-C(1)-C(2)	111.4 (8)	108.6 (9)	110.8 (8)	111.5 (8)	109.0 (8)	109.8 (7)	111.8 (6)	110.4	1.3
HC1-C(1)-O(5)	105.7 (9)	106.6 (9)	105.7 (7)	106.6 (7)	106.1 (7)	105.7 (7)	104.9 (9)	105.9	0.6
HC1-C(1)-O(4)′	108.9 (8)	111.7 (9)	111.3 (8)	110.3 (6)	111.8 (6)	111.0 (7)	109.0 (8)	110.4	1.2
HC2-C(2)-C(1)	108.0 (8)	107.0 (8)	108.5 (8)	108.8 (7)	109.1 (8)	107.7 (9)	105.4 (7)	107.8	1.3
HC2-C(2)-O(2)	110.5 (9)	108.1 (9)	109.0 (9)	108.4 (8)	106.6 (8)	107.9 (7)	109.8 (7)	108.6	1.3
HC2-C(2)-C(3)	109.1 (8)	110.3 (8)	108.8 (9)	109.4 (8)	108.3 (7)	108.6 (7)	110.1 (8)	109.2	0.8

Table II (Continued)

	glucose unit								
	1	2	3	4	5	6	7	mean	σ
				(D) Bond Angles					
HO2A-O(2)-C(2)	112 (2)	115 (1)	119 (1)	108 (1)	111 (1)	116 (1)	112 (1)	113	4
HO2B-O(2)-C(2)	111 (2)	110 (3)	103 (2)	113 (1)	112 (2)	109 (1)	109 (2)	110	3
HO2A-O(2)-HO2B	128 (2)	132 (3)	130 (2)	112 (2)	121 (3)	122 (2)	108 (2)	122	9
HC3-C(3)-C(2)	109.1 (7)	109.6 (7)	108.8 (7)	107.8 (7)	108.5 (6)	110.7 (6)	110.1 (8)	109.2	1.0
HC3-C(3)-O(3)	110.5 (8)	108.6 (9)	109.8 (7)	110.0 (7)	110.2 (8)	108.9 (8)	106.9 (8)	109.3	1.3
HC3-C(3)-C(4)	109.7 (8)	106.3 (9)	110.3 (8)	108.3 (7)	108.3 (7)	107.8 (6)	108.8 (6)	108.5	1.3
HO3A-O(3)-C(3)	109 (1)	109 (1)	109 (1)	116 (1)	115 (1)	110 (1)	114 (1)	112	3
HO3B-O(3)-C(3)	109 (1)	106 (3)	112 (3)	106 (2)	99 (2)	112 (2)	109 (1)	108	5
HO3A-O(3)-HO3B	94 (2)	98 (2)	105 (2)	81 (3)	103 (2)	104 (2)	104 (2)	98	9
HC4-C(4)-C(3)	111.7 (9)	110.2 (9)	108.6 (8)	108.9 (8)	109.3 (6)	109.3 (6)	110.0 (6)	109.7	1.0
HC4-C(4)-O(4)	109.2 (8)	110.3 (8)	111.1 (7)	109.5 (7)	110.6 (5)	110.8 (6)	109.7 (7)	110.2	0.7
HC4-C(4)-C(5)	106.9 (7)	109.8 (8)	109.3 (6)	110.4 (7)	109.7 (7)	108.2 (7)	108.9 (6)	109.0	1.2
HC5-C(5)-C(4)	107.3 (8)	108.1 (7)	108.0 (6)	108.4 (8)	107.9 (7)	108.1 (7)	108.6 (7)	108.1	0.4
HC5-C(5)-O(5)	110.7 (9)	110.6 (9)	111.3 (8)	108.5 (8)	110.6 (7)	110.9 (7)	108.6 (7)	110.2	1.1
HC5-C(5)-C(6)	109.4 (9)	106.1 (9)	109.3 (9)	110.2 (8)	108.1 (7)	108.2 (7)	110.3 (7)	108.9	1.5
HC6A-C(6)-C(5)	109 (3)	110 (2)	107.7 (9)	109 (1)	108 (1)	108 (1)	109 (1)	109	0.8
HC6B-C(6)-C(5)	112 (1)	101 (2)	110.2 (9)	110 (1)	108 (1)	110 (1)	109 (1)	109	0.4
HC6C-C(6)-C(5)		113 (2)							
HC6A-C(6)-O(6)A	70 (2)*	104 (3)	111 (1)	105 (1)	107 (1)	108 (1)	111 (1)	108	3
HC6B-C(6)-O(6)A	106 (1)	107 (2)	111 (1)	113 (1)	113 (1)	111 (1)	112 (1)	110	3
HC6C-C(6)-O(6)B		106 (1)							
HC6A-C(6)-HC6B	135 (3)	122 (3)	109 (1)	106 (1)	108 (1)	107 (1)	106 (1)	113	11
HOA-O(6)A-C(6)	110 (2)	95 (4)	112 (1)	104 (5)	109 (1)	109 (1)	105 (2)	106	6
HO6B-O(6)B-C(6)		109 (3)							
HO6B-O(6)A-C(6)							107 (1)		

(E) Bond Distances and Angles for Water Molecules

OW1-HW1A	0.97 (2)	HW1A-OW1-HW1B	115 (2)
OW1-HW1B	0.98 (2)	HW1A-OW1-HW1C	117 (2)
OW1-HW1C	0.91 (2)	HW1A-OW1-HW1H	103 (3)
OW1-HW1H	0.81 (5)	HW1B-OW1-HW1C	107 (1)
		HW1B-OW1-HW1H	95 (3)
		HW1C-OW1-HW1H	118 (3)
OW2-HW2A	0.96 (2)	HW2A-OW2-HW2B	105 (2)
OW2-HW2B	0.88 (4)	HW2A-OW2-HW2C	112 (3)
OW2-HW2C	1.02 (3)	HW2B-OW2-HW2C	111 (4)
OW3A-HW3A1	0.95 (4)	HW3A1-OW3A-HW3A2	104 (3)
OW3A-HW3A2	0.99 (4)	HW3A1-OW3A-HW3A3	105 (2)
OW3A-HW3A3	1.06 (2)	HW3A1-OW3A-HW3A4	116 (3)
OW3A-HW3A4	0.93 (3)	HW3A2-OW3A-HW3A3	119 (2)
		HW3A2-OW3A-HW3A4	97 (3)
		HW3A3-OW3A-HW3A4	116 (3)
OW3B-HW3B1	1.01 (4)	HW3B1-OW3B-HW3B2	88 (4)
OW3B-HW3B2	0.85 (6)		
OW4-HW4A	0.94 (4)	HW4A-OW4-HW4B	99 (4)
OW4-HW4B	0.91 (4)	HW4A-OW4-HW4C	106 (3)
OW4-HW4C	0.99 (4)	HW4B-OW4-HW4C	130 (3)
OW5A-HW5A	1.14 (3)	HW5A-OW5A-HW5B	115 (2)
OW5A-HW5B	1.16 (4)	HW5A-OW5A-HW5C	125 (3)
OW5A-HW5C	0.77 (3)	HW5B-OW5a-HW5C	86 (4)
OW5B-HW5A	0.96 (3)	HW5A-OW5B-HW5E	117 (4)
OW5B-HW5E	0.85 (6)		
OW5C-HW5H	1.03 (5)		
OW6-HW6A	0.82 (5)	HW6A-OW6-HW6B	103 (5)
OW6-HW6B	1.18 (4)		
OW7-HW7A	0.95 (2)	HW7A-OW7-HW7B	99 (2)
OW7-HW7B	0.97 (3)		
OW8-HW8A	0.97 (5)	HW8A-OW8-HW8B	100 (6)
OW6-HW8B	0.86 (5)		
OW9-HW9A	1.00 (4)	HW9A-OW9-HW9B	106 (4)
OW9-HW9B	1.02 (3)		
OW10-HW10A	0.94 (4)	HW10A-OW10-HW10B	106 (4)
OW10-HW10B	1.00 (6)		

Table II (Continued)

(E) Bond Distances and Angles for Water Molecules			
OW12–HW12A	1.14 (6)	HW12A–OW12–HW12B	113 (4)
OW12–HW12B	0.99 (5)		
OW13–HW13A	1.11 (5)	HW13A–OW13–HW13B	96 (4)
OW13–HW13B	0.91 (4)		
OW14–HW14A	0.98 (3)	HW14A–OW14–HW14B	106 (5)
OW14–HW14B	1.00 (5)		

[a] Standard deviations given in parentheses. Mean values for rows and columns are calcualted according to $\sigma = [\sum_{i=1}^{m}(y_i - \bar{y}_m)^2/m - 1]^{1/2}$ where $\bar{y}$ = mean value of observations y_i and m = number of observations.

(b) Disorder of Water Molecules. There are 11 ± 0.5 water molecules per β-CD in this crystal structure. They are distributed over 16 sites, with only three of them fully occupied. The other sites are filled statistically with between 0.13 and 0.89 water molecules (Table I). Their distribution in cavities and interstices between β-CD molecules will be described in the next paragraph.

Compared with the X-ray study where 12 ± 0.5 water molecules were located, the present investigation accounts for one water less. This finding may be explained with inaccuracies in structure determination because most of the water molecule positions are only partially occupied. In addition, it is known that the number of water molecules in the β-CD crystal (and the volume of the unit cell) is largely dependent on crystallization and history of the crystals.[13] Thus, differential scanning calorimetry showed that within 4 weeks, transition occurs between two β-CD hydrate forms. This is of relevance to the present study because measurement of neutron data took about 4 months, and 2 months elapsed after crystal growth before data collection was started. During data collection, no obvious phase transition took place because the three reference reflections were constant with time.

An overall view of the hydrogen-bonding scheme in the crystal structure of β-CD·11H_2O is displayed in Figure 3b. The complexity of the situation is enormous. Compared with the smaller α-CD·6H_2O where all water molecules are well ordered and a rather clear hydrogen-bonding pattern is apparent, the disordered water molecules in β-CD·11H_2O produce a messy picture. This is especially obvious at several junction points formed by disordered water molecules W3 and W5, where hydrogen-bonding interactions cluster together.

In total, there are 106 hydrogen bonds per unit cell or 53 per asymmetric unit which are considered here further. Of these, 35 are of the type O—H···O and are listed in Table IIIA with all the respective geometrical characteristics. However, there are 18 hydrogen bonds of type O—H···H—O which deserve more interest and will be described in greater detail in the next sections of this paper.

(c) Water Molecules in Intramolecular Cavities and in Intermolecular Interstices. One of the main characteristics of cyclodextrins is that the insides of their cavities are hydrophobic due to the occurrence of C–H hydrogens and of glucosidic, ether-like O(4) oxygens whereas they are hydrophilic at the periphery because the rims are lined with primary and secondary hydroxyl groups. When β-CD molecules pack together in the crystal lattice, interstices are formed which do not display such clearly defined hydrophobic and hydrophilic areas but are, in general, more hydrophilic in character. The question arises whether the water molecules enclosed within the β-CD cavity and those located in interstices reflect these differences.

Out of the total of 11 water molecules per β-CD, 6.13 are located in the cavity and distributed over 8 positions, with only OW4 fully occupied and the others (OW6, OW8, OW9, OW10, OW12, OW13, OW14) in the range 0.53–0.89, average occupation 0.766. Only OW9 and OW13 are hydrogen bonded exclusively to other included water molecules; the others form hydrogen bonds to β-CD hydroxyls. OW8—H···O(43) is a rare situation where a glucosidic oxygen accepts a hydrogen bond with an H···O distance of 2.12 (3) Å, Table III.

Of the 4.88 water molecules located in 8 interstitial sites, two (OW1, OW2) are fully occupied, the others (OW3A, OW3B, OW5A, OW5B, OW5C, OW7) in the range 0.13–0.78, average 0.35. Two of these (OW1, OW3A) display 4 bound H atoms and one (OW2) 3 bound H atoms, indicating that even under disorder conditions water molecules do not rotate freely.

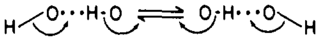
These data show that, on average, positions of water molecules located in the hydrophobic β-CD cavity are more densely populated and better ordered compared with the interstices between β-CD molecules which are predominantly of hydrophilic character. We cannot assess whether this also holds for β-CD dissolved in water and if so whether the difference in density would contribute to the driving force of inclusion formation.

(d) Flip-Flop Hydrogen Bonds. In β-CD·11H_2O, 18 hydrogen bonds are of type O—H···H—O. In these, the oxygens are in the normal distance range of 2.7–3.0 Å for O—H···O bonds,[8] and the H···H distances lie between 0.86 and 1.15 Å. They are much shorter than the 2.4 Å expected from the sum of van der Waals radii,[20] i.e., only one H atom can be engaged in hydrogen-bonding contact at a given time. This is also suggested by occupational parameters for these H atoms which are in all cases around 0.5.

The O—H···H—O hydrogen bond can be interpreted as average over two states

$$\mathrm{O{-}H{\cdots}O \rightleftharpoons O{\cdots}H{-}O}$$

We assume that transition from one state into the other is not by tunneling of the hydrogen over the hump in a double minimum potential but rather by rotation of hydroxyl groups:



Comparable schemes have been observed previously in ice and in ice clathrates.[21,22] In ice, the disordered H atoms are only 0.74 Å apart and account for the residual entropy.[22,23] The situation in ice and in ice clathrates, however, is *very* different from that found in β-DC·11H_2O. This is because the high-symmetry space groups and special positions of water molecules in ice and ice clathrates *require* disorder of this kind with H positions exactly half-occupied. In β-CD·11H_2O, no such restrictions apply and all hydrogen bonds of type O—H···H—O are formed without symmetry constraints.

In the O—H···H—O hydrogen bonds observed in β-CD·11H_2O, two alternative possibilities of arrangement occur and are in many cases assocated with larger systems. Therefore, we have chosen the term "flip-flop" to properly describe this phenomenon.[14]

Let us look at a few situations where "flip-flop" hydrogen bonds are connected as illustrated in Figure 5. Water molecule W2 displays three hydrogen-atom positions of which two are about half and one is fully occupied (A = 0.44; B = 0.48; C = 0.99); the oxygen atom is at full occupancy, Table I. This water molecule is in normal hydrogen-bonding contact O—H···O with water W7 and hydroxyl O(66) and in flip-flop O—H···H—O contact with hydroxyl O(24) which is also connected with hydroxyl O(35), and the latter hydrogen bonds to hydroxyl O(61). In the chain W2···O(24)···O(35)···O(61), flip-flop hydrogens designated A and

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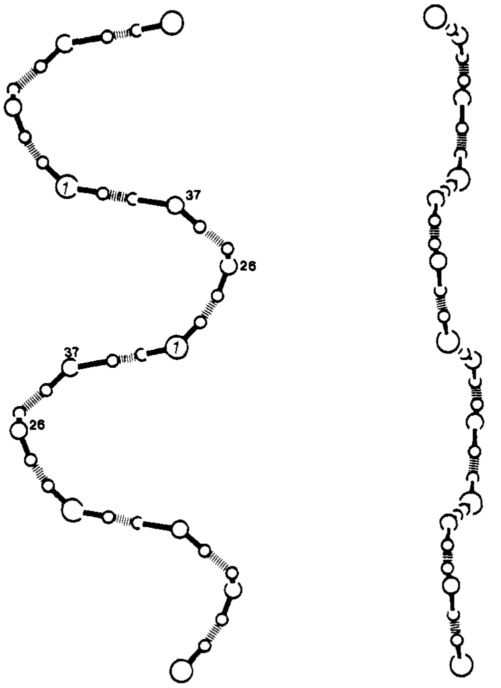

Figure 4. Two views of the flip-flop chain consisting entirely of O—H···H—O interactions and running through the whole crystal structure. It is composed of water molecule 1 and hydroxyl groups O(3)7 and O(2)6, indicated as 1, 37, and 26. The operation of the 2_1 axis at $a = c = {}^1/_2$ produces the endless chain.

B are about half occupied and *only* hydrogens A *or* hydrogens B can be presented at the same time as indicated in Figure 5, I and II. As a consequence, two chains of the form O···O—H···O—H···O—H···O ⇌ O···H—O···H—O···H—O···O must exist in equilibrium; if only one O–H group flips from one hydrogen-bonding position into the other, the whole chain has to reverse in a concerted, cooperative manner.

Do we really have a dynamical equilibrium or do we observe statistical disorder? To find out which situation prevails, we have carried out differential scanning calorimetry on crystalline powder of β-CD·11H_2O.[13] An exothermic process was observed at −46 °C which we tentatively interpret as ordering of dynamically disordered flip-flops into one or the other form. Additional evidence has been provided by a recent neutron-diffraction study carried out at 120 K which demonstrated that of the 18 flip-flop hydrogen bonds, 14 had disappeared and reappeared after the mixture was warmed up to room temperature (Zabel, Mason, and Saenger, in preparation for 1985). Final confirmation of the dynamic situation will be provided by inelastic neutron-scattering experiments which are planned for the near future.

(e) The β-CD Macrocycle Is Stabilized by Intramolecular Flip-Flop Hydrogen Bonds. Thus far, X-ray and neutron-diffraction studies on α-, β-, and γ-cyclodextrins showed that the O(2)···O(3) distances between adjacent glucoses in cyclodextrin macrocycles are, on average, in the range 2.7–3.0 Å. Therefore, interglucose (intramolecular) hydrogen bonds can form which were characterized in a few α-CD systems.[6,24,25] For β- and γ-CD, however, hydrogen atoms could not be located from X-ray data and the hydrogen-bonding patterns remained obscure.

In the present β-CD·11H_2O complex, the interglucose O(2)···O(3) distances are in the range 2.796 (9)–2.974 (13) Å (Table IIIB), with an average of 2.88 Å slightly longer than the 2.75 to 2.80 Å obtained in a survey of 365 O—H···O hydrogen bonds.[26] All associated hydrogen atoms are located, and it is surprising to find that all seven intramolecular, interglucose O(2)···O(3) hydrogen bonds are of the flip-flop type O(2)—H···H—O(3), Figure 2, a and b. This means that each O(2) and O(3) hydroxyl group is engaged in interglucose hydrogen bonding and, moreover, forms hydrogen bonds with "external" hydroxyl groups and water molecules. In addition, there are close contacts between hydrogen atoms in O(2), O(3) flip-flops and the neighboring glucosidic O(4) atoms, in the range 2.23 (5)–2.58 (2) Å. These distances are slightly shortened compared to the van der Waals H···O distance of 2.6 Å,[20] yet distinctly shortened if Allinger's minimum contact distances, 3.15 Å for H···O, are considered.[27] In any case, the close proximity of O(2), O(3) hydrogen atoms and glucosidic O(4) oxygens indicates a mutual attraction which appears to be due to the sterically favorable arrangement of atoms and to the chemical properties of the half-acetal O(4) oxygen atoms. In addition, the flip-flop hydrogen bonds will be promoted by the slightly acidic p*K* values of the secondary O(2), O(3) hydroxyl groups, 12.2, which encourages hydrogen bond formation.[28,29]

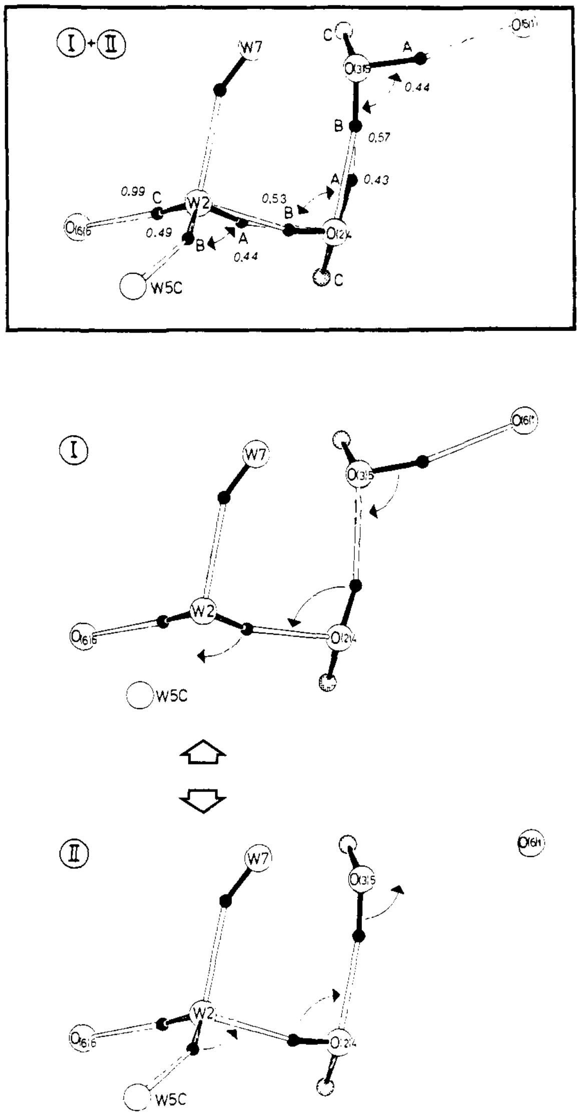

Figure 5. View of a flip-flop system with O—H···H—O bonds (top) and deconvolution into two states (I and II) having normal hydrogen bonds O—H···O. Small (black), medium (stippled), and large (open) circles represent H, C, and O atoms, covalent bonds are drawn solid, and H bonds are drawn as open lines. Occupational factors of H atoms are indicated by italics in the top picture. Curved arrows indicate how O–H groups rotate to go from one flip-flop state (I) to the other (II) and vice versa. Note that in the structure at the top, only H-atom positions A *or* B can be filled and that a change A ⇌ B has to proceed in a concerted, cooperative jump.

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Table III. Distances (Å) and Angles (deg) for Hydrogen Bonding and Water Coordination (Standard Deviations Are Given in Parentheses)

(A) Geometries of Hydrogen-Bonding Interactions[a]

donor H atom acceptor	symm code	O···O	O—H···O	H···O	
O(21)—HO21A···OW6	(55501)	2.78 (4)	168 (2)	1.88 (4)	**
O(21)—HO21B···O(32)	(55501)	2.97 (1)	166 (2)	2.12 (3)	**
O(31)—HO31A···O(27)	(55501)	2.94 (1)	171 (1)	1.99 (2)	**
O(31)—HO31B···OW4	(64502)	2.91 (3)	141 (2)	2.09 (3)	**
O(61)—HO61A···OW4	(55501)	2.71 (3)	175 (3)	1.71 (4)	
O(22)—HO22A···OW1	(65502)	2.82 (1)	173 (1)	1.91 (2)	**
O(22)—HO22B···O(33)	(55501)	2.89 (1)	161 (3)	2.04 (4)	**
O(32)—HO32A···O(21)	(55501)	2.97 (1)	165 (2)	2.06 (2)	**
O(62)—HO62A···OW12	(64501)	2.93 (5)	164 (5)	1.95 (5)	
O(62)B—HO62B···O(23)	(56501)	2.99 (2)	170 (4)	1.98 (4)	
O(23)—HO23A···OW3A	(54501)	2.77 (2)	162 (2)	1.81 (3)	
O(23)—HO23A···OW3B	(55501)	2.67 (6)	136 (2)	1.86 (6)	
O(23)—HO23B···O(34)	(55501)	2.89 (1)	156 (2)	2.05 (4)	**
O(33)—HO33A···O(22)	(55501	2.89 (1)	168 (1)	1.97 (2)	**
O(33)—HO33B···O(27)	(64502)	2.74 (1)	163 (4)	1.81 (3)	**
O(63)—HO63···OW5A	(55501)	2.83 (2)	177 (2)	1.90 (2)	
O(63)—HO63···OW5B	(55501)	2.86 (3)	147 (2)	2.02 (3)	
O(24)—HO24A···O(35)	(55501)	2.80 (1)	158 (2)	1.90 (2)	**
O(24)—HO24B···OW2	(74502)	2.86 (2)	168 (2)	1.87 (3)	**
O(34)—HO34A···O(23)	(55501)	2.89 (1)	172 (1)	1.99 (2)	**
O(34)—HO34B···O(62)A	(54501)	2.49 (3)	166 (4)	1.61 (4)	
O(25)—HO25A···O(36)	(55501)	2.83 (1)	157 (2)	1.91 (2)	**
O(35)—HO35A···O(24)	(55501)	2.80 (1)	167 (2)	1.83 (2)	**
O(35)—HO35B···O(61)	(54501)	2.96 (2)	164 (3)	1.91 (3)	
O(65)—HO65···OW7	(75502)	2.74 (2)	174 (1)	1.73 (2)	
O(26)—HO26B···O(37)	(55501)	2.89 (1)	167 (1)	1.79 (2)	**
O(26)—HO26A···OW1	(55501)	2.74 (1)	164 (3)	1.91 (3)	**
O(36)—HO36A···O(25)	(55501)	2.80 (1)	163 (3)	1.89 (2)	**
O(36)—HO36B···OW3A	(54401)	2.90 (2)	160 (2)	1.89 (4)	**
O(66)—HO66···O(63)	(55401)	2.82 (1)	164 (1)	1.90 (2)	
O(27)—HO27A···O(33)	(65502)	2.74 (1)	153 (1)	1.92 (2)	**
O(27)—HO27B···O(31)	(55501)	2.94 (1)	164 (2)	2.03 (3)	**
O(37)—HO37A···OW1	(65402)	2.85 (1)	167 (2)	1.88 (2)	**
O(37)—HO37B···O(26)	(55501)	2.89 (1)	161 (2)	1.99 (2)	
O(67)—HO67A···OW1	(56501)	3.04 (1)	169 (2)	1.98 (2)	
O(67)—HO67B···OW3B	(56401)	2.78 (4)	136 (2)	2.02 (3)	
O(67)—HO67B···OW3A	(55401)	2.83 (1)	159 (2)	1.93 (2)	
OW1—HW1A··O(37)	(64402)	2.85 (1)	177 (1)	1.88 (2)	**
OW1—HW1B···O(57)	(54501)	2.97 (1)	153 (2)	2.07 (2)	
OW1—HW1C···O(26)	(55501)	2.74 (1)	167 (1)	1.84 (2)	**
OW1—HW1H···O(22)	(64502)	2.82 (1)	160 (4)	2.04 (5)	**
OW2—HW2A···O(66)	(55501)	2.75 (2)	176 (2)	1.80 (2)	
OW2—HW2B···O(24)	(75502)	2.86 (2)	168 (3)	1.99 (3)	**
OW2—HW2C···OW5C	(55501)	2.71 (3)	154 (5)	1.76 (5)	
OW3A—HW3A1···O(36)	(56601)	2.90 (2)	163 (2)	1.97 (4)	**
OW3A—HW3A2···O(67)	(55601)	2.83 (1)	148 (3)	1.94 (5)	**
OW3A—HW3A3···OW5A	(55501)	2.82 (2)	169 (2)	1.78 (3)	
OW3A—HW3A3···OW5B	(55501)	2.72 (3)	151 (2)	1.74 (3)	
OW3A—HW3A4···O(23)	(56501)	2.77 (2)	153 (3)	1.91 (3)	**
OW3B—HW3B2···O(52)	(54501)	3.14 (4)	152 (4)	2.36 (3)	
OW4—HW4A···O(31)	(65502)	2.91 (3)	164 (3)	1.99 (3)	**
OW4—HW4B···O(62)B	(55501)	2.76 (3)	160 (4)	1.88 (4)	
OW5A—HW5A···O(65)	(75602)	2.85 (2)	156 (2)	1.77 (2)	
OW5A—HW5B···O(64)	(75602)	3.08 (3)	179 (2)	1.91 (4)	
OW5B—HW5E···O(25)	(56601)	2.87 (3)	153 (4)	2.08 (4)	
OW5C—HW5H···O(23)	(55401)	3.13 (3)	171 (3)	2.11 (3)	

Table III (Continued)

(A) Geometries of Hydrogen-Bonding Interactions[a]

donor H atom acceptor	symm code	O···O	O—H···O	H···O	
OW6—HW6B···OW9	(55501)	3.07 (3)	146 (3)	2.02 (3)	**
OW7—HW7A···OW2	(74502)	2.88 (2)	159 (3)	1.98 (3)	
OW7—HW7B···O(35)	(55501)	2.92 (2)	179 (2)	1.94 (2)	
OW8—HW8A···O(43)	(64602)	3.10 (2)	174 (3)	2.12 (3)	
OW8—HW8B···O(31)	(54601)	2.94 (4)	161 (3)	2.04 (3)	
OW9—HW9A···OW13	(55501)	2.85 (4)	154 (3)	2.28 (4)	**
OW9—HW9B···OW6	(55501)	3.07 (3)	130 (3)	2.31 (4)	**
OW10—HW10A···O(25)	(55501)	3.15 (4)	170 (4)	2.33 (6)	
OW10—HW10B··OW12	(56501)	2.72 (5)	107 (3)	2.25 (6)	**
OW12—HW12A···OW8	(56401)	3.06 (6)	176 (3)	1.92 (6)	
OW12—HW12B···OW10	(56501)	2.72 (5)	148 (4)	1.84 (6)	**
OW13—HW13A···OW7	(66602)	2.76 (4)	157 (2)	1.71 (4)	
OW13—HW13B···OW9	(55501)	2.85 (4)	120 (3)	2.28 (3)	**
OW14—HW14A···O(24)	(66502)	2.81 (3)	136 (3)	2.03 (3)	
OW14—HW14B···OW13	(55501)	2.55 (5)	111 (3)	2.02 (4)	

(B) Intramolecular, Interglucosidic Flip-Flop Hydrogen Bonds between Adjacent O(2)–O(3) Hydroxyl Groups[b]

	O···H	O···H	H···H	O···O	O···H···O	
1. O(21)···HO(21)B···O(32)	0.874 (24)	2.120 (28)	1.208 (30)	2.974 (13)	165.8 (24)	0.343
O(21)···HO(32)A···O(32)	0.922 (19)	2.065 (19)	1.208 (30)	2.974 (13)	168.6 (20)	0.654
						0.997
2. O(22)···HO(22)B···O(33)	0.886 (44)	2.042 (41)	1.106 (42)	2.892 (13)	160.5 (35)	0.367
O(22)···HO(33)A···O(33)	0.939 (16)	1.968 (17)	1.106 (42)	2.892 (13)	167.6 (14)	0.614
						0.981
3. O(23)···HO(23)B···O(34)	0.891 (39)	1.922 (42)	1.184 (36)	2.871 (11)	156.4 (23)	0.539
O(23)···HO(34)A···O(34)	0.901 (20)	1.992 (20)	1.184 (36)	2.871 (11)	172.1 (15)	0.463
						1.002
4. O(24)···HO(24)A···O(35)	0.943 (16)	1.924 (16)	0.926 (24)	2.796 (9)	157.7 (16)	0.434
O(24)···HO(35)A···O(35)	0.979 (19)	1.833 (17)	0.926 (24)	2.796 (9)	167.4 (18)	0.572
5. O(25)···HO(25)A···O(36)	0.942 (15)	1.914 (15)	0.980 (15)	2.804 (10)	156.5 (17)	0.575
O(25)···HO(36)A···O(36)	0.939 (21)	1.892 (22)	0.980 (15)	2.804 (10)	163.3 (25)	0.417
						0.992
6. O(26)···HO(26)B···O(37)	0.875 (24)	2.083 (21)	1.160 (28)	2.889 (11)	152.7 (17)	0.476
O(26)···HO(37)B···O(37)	0.935 (19)	1.990 (23)	1.160 (28)	2.889 (11)	160.6 (22)	0.472
						0.948
7. O(27)···HO(27)B···O(31)	0.934 (37)	2.032 (38)	1.073 (38)	2.940 (12)	163.6 (23)	0.344
O(27)···HO(31)A···O(31)	0.960 (16)	1.987 (16)	1.073 (38)	2.990 (12)	171.3 (12)	0.584
						0.928
	0.923 (32)	1.983 (81)	1.091 (106)	2.881 (65)	163.2 (59)	0.979 (29)

(C) Coordination Angles (deg) at Water Molecules

OW1	O(26)–OW1–O(22)	97.7 (3)	OW3B	O(67)–OW3B–O(52)	89.4 (13)
	O(26)–OW1–O(37)	113.9 (3)			
	O(26)–OW1–O(57)	117.2 (3)	OW4	O(61)A–OW4–O(62)B	92.2 (10)
	O(26)–OW1–O(67)	117.5 (3)		O(61)–OW4–O(31)	118.4 (8)
	O(22)–OW1–O(37)	110.1 (3)		O(62)B–OW4–O(31)	79.2 (9)
	O(22)–OW1–O(57)	83.0 (3)			
	O(22)–OW1–O(67)	133.4 (4)	OW5A	O(63)–OW5A–O(65)	94.2 (6)
	O(37)–OW1–O(57)	124.7 (3)		O(63)–OW5A–O(64)	108.2 (8)
	O(37)–OW1–O(67)	83.8 (3)		O(65)–OW5A–O(64)	102.0 (6)
	O(57)–OW1–O(67)	112.5 (4)			
			OW5B	O(65)–OW5B–OW3A	167.3 (12)
OW2	OW5C–OW2–O(66)	98.6 (9)		O(65)–OW5B–O(63)	98.7 (9)
	OW5C–OW2–OW7	118.0 (9)		O(65)–OW5B–O(25)	90.2 (8)
	OW5C–OW2–O(24)	132.4 (12)		OW3A–OW5B–O(63)	92.9 (7)
	O(66)–OW2–O(24)	101.2 (5)		OW3A–OW5B–O(25)	82.3 (8)
	O(66)–OW2–OW7	118.8 (7)		O(63)–OW5B–O(25)	149.0 (11)
	O(24)–OW2–OW7	88.9 (5)			
			OW5C	OW2–OW5C–OW3A	134.5 (16)
				OW2–OW5C–O(23)	117.2 (11)
OW3A	OW5B–OW3A–O(23)	117.8 (8)			
	OW5B–OW3A–O(67)	94.4 (7)	OW6	OW10–OW6–O(21)	176.5 (14)
	OW5B–OW3A–O(36)	99.3 (7)		OW10–OW6–OW9	89.0 (12)
	O(23)–OW3A–O(67)	134.4 (4)		O(21)–OW6–OW9	94.3 (10)
	O(23)–OW3A–O(36)	124.2 (5)			
	O(23)–OW3A–OW5A	96.7 (6)	OW7	OW13–OW7–OW2	76.6 (7)
	OW5A–OW3A–O(67)	112.4 (5)		OW13–OW7–O(35)	90.4 (8)
	OW5A–OW3A–O(36)	113.5 (6)		OW2–OW7–O(35)	86.8 (6)

Table III (Continued)

(C) Coordination Angles (deg) at Water Molecules					
OW8	OW9–OW8–O(31)	98.8 (9)	OW10	OW6–OW10–OW8	82.0 (15)
	OW9–OW8–OW12	71.3 (16)			
	OW9–OW8–O(43)	133.1 (14)	OW12	OW10–OW12–O(62)A	138.0 (12)
	O(31)–OW8–OW12	153.2 (13)		OW10–OW12–OW8	111.1 (18)
	O(31)–OW8–O(43)	101.6 (14)		O(62)A–OW12–OW8	99.0 (18)
	OW12–OW8–O(43)	103.1 (10)			
			OW13	OW14–OW13–OW7	114.0 (11)
OW9	OW8–OW9–OW13	103.9 (12)		OW14–OW13–OW9	96.6 (16)
	OW8–OW9–OW6	75.3 (11)		OW9–OW13–OW7	137.2 (12)
	OW13–OW9–OW6	97.0 (11)			
			OW14	OW13–OW14–O(24)	96.7 (14)

[a] H bonds marked with two asterisks take part in flip–flop hydrogen bonds. Symmetry codes are as used in ORTEP.[33] Contacts that appeared too long to be considered as hydrogen bonds are HO32B···O(37), 2.51 (4) Å; angle O(3)2—HO32B···O(37) = 153 (3)°, HO25B···OW10 = 2.38 (3) Å; HO25B···O(3)5 = 2.51 (3) Å; angle O(25)–HO25B···OW10 = 175 (4)°; and O(25)–HO25B···O(35) = 100 (3)°. [b] Mean values are given in the last row. In the last column, occupation parameters for H atoms (see Table I) and their sum for each O–H group or water molecule are presented. O···O···O and angle (deg).

The situation is very different in the hydrate of the smaller α-cyclodextrin, α-CD·6H_2O, where no flip-flop hydrogen bonds occur. This might be due to the lack of disorder in this crystal structure and to the smaller ring size which increases curvature and leads to widening of O(2)···O(3) distances, average 3.00 Å.[30] Hydrogen bonds are, therefore, weaker compared to β-CD. As a consequence, in α-CD·6H_2O, the α-CD macrocycle even collapses such that four O(2)···O(3) hydrogen bonds in the distance range 2.82–3.03 Å are formed whereas two are broken (O(2)···O(3) separation 3.35 and 4.67 Å). The distortion is not apparent if α-CD includes a guest molecule, a finding also in agreement with circular dichroism studies. The latter indicated that α-CD in aqueous solution undergoes conformational change when binding a guest whereas β-CD always adopts a "round" structure.[31] Moreover, H/D exchange experiments suggested that the O(2), O(3) hydroxyl protons are more accessible in α-CD than in β-CD and pointed again to the higher stability of the O(2)···O(3) hydrogen bonds in β-CD.[28,32]

(f) An Endless Flip-Flop Chain. In crystal structures exhibiting many hydrogen bonds of type O—H···O, it is frequently observed that chains of these bonds run from one unit cell to the next and through the whole crystal. As also observed in the α-CD·6H_2O crystal, these chains are predominantly of the homodromic type, i.e., all O-H···O—H···O—H hydroxyls point in the same direction because of the cooperative effect.

Such a chain is also apparent in β-CD·11H_2O. It is formed by water molecule OW1 in contact with hydroxyls O(26) and O(37) which belong to the *same* β-CD, i.e., the chain sequence is OW1···O(26)···O(37)···OW1···O(26)···O(37)···OW1···. The endless character of the chain is produced by operation of the 2_1 screw axis which runs parallel to *b* and through the center of the unit cell.

The most interesting feature of this chain is, however, that all hydrogen bonds are of the flip-flop type. This means that we observe a system ···H—O—H···H—O—H···H—O—H···H—O—H··· which is due to an average of the two situations ···O—H···O—H···O—H··· and ···H—O···H—O···H—O···. This flip-flop chain is illustrated in Figure 4. Needless to say, as already described, the transition from one hydrogen bond chain direction to the reverse one is cooperative and has to be performed in a concerted action.

(g) Circularly Arranged Hydrogen Bonds. As mentioned in the introduction, in the α-CD·6H_2O crystal structure circular arrangements of hydrogen-bonded hydroxyl groups were found to constitute a particular structural motif. In the β-CD·11H_2O crystal, again several circular arrangements are observed which, however, also include flip-flop hydrogen bonds. Two of these, illustrated in Figure 6, a and b, represent four- and nine-membered rings.

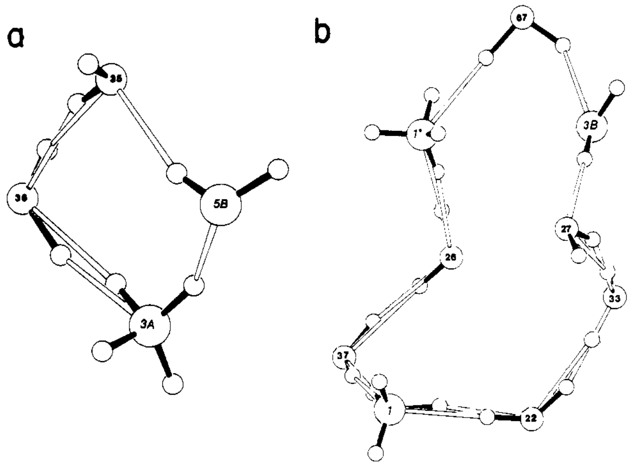

Figure 6. Two circular arrangements (a, b) of hydrogen bonds, with hydroxyl O and water O indicated by spheres of increasing size. Covalent bonds are drawn solid and hydrogen bonds by open lines. The numbering scheme is as described in Figure 2. In both circles, flip-flop hydrogen bonds occur, and in the nine-membered circle (b), hydroxyl group O(6)7 closes the circle only on time average; at a certain time, only one of the two hydrogen bonds (O(6)7—H···O(3B) or O(6)7—···O(1)) is formed.

The four-membered ring consists of two partially occupied water molecules W3A and W5B and of two hydroxyl groups O(2)5 and O(3)6. Since flip-flop bonds are involved, two systems of hydrogen bonds are possible. In one, a homodromic arrangement is obvious with all hydrogen positions A filled whereas hydrogen positions B lead to an antidromic circle with the two hydrogen-bonded chains O—H···O—H···O—H emanating from the double donor OW3A and colliding at the double acceptor O(25).

In the nine-membered circle, three water molecules are present of which two, OW1 and OW1s, are symmetry related. Hydroxyl group O(67) is in a special position because it only apparently closes the ring. In fact, the circle is open at O(67) and only the flip-flop action of this hydroxyl group closes the ring on the time average.

(h) Conclusions. This neutron-diffraction study again demonstrates that (except in simple cases) hydrogen-bonding schemes cannot be assigned with confidence if only oxygen atoms are located from X-ray diffraction data. The complexity of the hydrogen-bonding scheme encountered in β-CD·11H_2O can be broken down into a few clearly defined motifs:

(i) A cluster of eight sites filled with 6.13 disordered water molecules is enclosed within the β-CD cavity. These water molecules are in normal hydrogen-bonding contact with themselves, with enclosing β-CD (only 2 contacts!) and with neighboring β-CD.

(ii) Water molecules located in β-CD interstices are more disordered than those in cavities with 4.88 waters distributed over

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8 sites. It appears that hydrophobic surrounding (in the cavity) has an ordering effect on water molecules, or leads to better formed hydrogen bonds.

(iii) There are 18 flip-flop hydrogen bonds of type O—H···H—O which might be associated with the disorder of water molecules encountered in this crystal structure. Probably the disorder of water molecules in the β-CD cavities as well as in interstices is the releasing factor. Because flip-flops in a system $O—H\cdots O \rightleftharpoons O\cdots H—O$ represent two energetically near-equivalent states, they are entropically favorable.

(iv) Flip-flops are interconnected to form larger systems. The largest one is an endless flip-flop chain running through the crystal structure (due to the 2_1 screw operation).

(v) The seven interglucose, intramolecular O(2)···O(3) hydrogen bonds in β-CD are all of the flip-flop type. They stabilize the "round" structure of the β-CD macrocycle. Therefore, β-CD adopts the same conformation whether "empty" or filled with guest molecules, in contrast to α-CD which collapses if "empty".

(vi) As observed in the α-CD·6H_2O crystal structure, there are again some circularly arranged hydrogen bonds which, in this case, also involve flip-flops.

(vii) Flip-flops can be a general structural feature in starch and in other polymer carbohydrates exhibiting suitably positioned hydroxyl groups. In addition, they will occur in water, and if they are combined with circular hydrogen bonded systems, a dynamical, entropically favorable picture can be envisaged. Flip-flops will also play a role in the hydration of macromolecules, and the β-CD·11H_2O crystal structure can be considered as the frozen state of hydrated β-CD.

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Supplementary Material Available: Tables containing anisotropic temperature factors and structure amplitudes (45 pages). Ordering information is given on any current masthead page.

Stereoelectronic Probes on the Electronic Configuration of Imidyl Radicals: Decompositions of *N*-Bromo-7,8-dichloro-*cis*-bicyclo[4.2.0]octane-*endo,cis*-7,8-dicarboximide

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Abstract: The decomposition of the title *N*-bromide **2** in methylene chloride was investigated by direct photolysis of this compound and by the bromine atom initiated reaction in which two reacting radicals, in addition to bromine atoms, were shown to be involved in the formation of brominated and ring-opened products. The product distribution studies show that both processes lead to the generation of the imidyl radical which undergoes ring opening and intermolecular hydrogen abstraction but does not abstract the endo-C_3–H intramolecularly. The Σ electronic configuration was assigned to the imidyl radical. The second radical was generated from the interaction of a bromine atom with **2** but not in the photodecomposition in the presence of bromine atom scavengers. It undergoes intramolecular functionalization at the C_3 position specifically but no ring opening reactions. A radical complex of a bromine atom with **2** (or bromine with the imidyl radical) is proposed as the second reacting radical which is simultaneously in equilibrium with *N*-bromide **2** and the imidyl radical. The observed product distributions are rationalized with the equilibria under the reaction conditions. Because the interaction of trichloromethyl radicals as well as bromine atoms with *N*-bromide **2** generates the imidyl radical, this radical is believed to be the ground-state species from energetic considerations.

Introduction

Recent disputes[1–4] over whether one or two succinimidyl radicals serve as the intermediates in NBS decomposition have opened up a new stage of development in this field. While both Skell's[1–3] and Walling's[4] groups agree that two radical species are required to explain the chain propagations, some of their actual experimental data, such as the primary deuterium isotope effects and reaction rate constants, show wide discrepancies. These discrepancies have led to two alternative opinions as to the identity of the two radicals. On the basis of an impressive amount of self-consistent data, Skell's group regarded the two radical chain carriers to be the Π (the ground state) and Σ (the lowest excited state)[2] electronic configuration of the succinimidyl radical; the former operated in NBS–Br_2 (or NBS–$BrCCl_3$) and the latter in NBS–olefin systems.[1–3] Contrary to Skell's experimental results, Walling found that the kinetic deuterium isotope effects and the rate constants of rearrangements and hydrogen abstraction were comparable for the two radical species.[4] The latter concluded that only one succinimidyl radical, that of the ground state but not

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[1] Skell, P. S.; Tlumak, R. L.; Seshadri, S. *J. Am. Chem. Soc.* **1983**, *105*, 5125.

[2] Tlumak, R. L.; Day, J. C.; Slanga, J. P.; Skell, P. S. *J. Am. Chem. Soc.* **1982**, *104*, 7257.

[3] Tlumak, R. L.; Skell, P. S. *J. Am. Chem. Soc.* **1982**, *104*, 7267.

[4] Walling, C.; El-Taliawi, G. M.; Zhao, C. *J. Am. Chem. Soc.* **1983**, *105*, 5119.

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