

## Topography of Cyclodextrin Inclusion Complexes. IV.\*

### Crystal and Molecular Structure of the Cyclohexaamylose-1-Propanol-4·8Hydrate Complex

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(Received 8 March 1974; accepted 25 March 1974)

The  $\alpha$ -CD-1-propanol-4·8hydrate complex, where  $\alpha$ -CD is cyclohexaamylose ( $\alpha$ -cyclodextrin), crystallizes in a cage-type structure with space group  $P2_12_12_1$  and cell dimensions  $a=14\cdot292$  (4),  $b=37\cdot515$  (7),  $c=9\cdot393$  (3) Å. The structure was elucidated from 5303 X-ray diffractometer data and refined by least-squares methods to  $R=7\%$ . The  $\alpha$ -CD molecule assumes the shape of a truncated cone with the larger diameter formed by the O(2), O(3) hydroxyl groups and the smaller by the O(6) hydroxyl groups. All C(6)-O(6) bonds point away from the  $\alpha$ -CD centre and one C(6)-O(6) bond is twofold disordered with site occupancies 85% and 15%. The 1-propanol molecule is oriented in the  $\alpha$ -CD void with its hydroxyl group near the O(6) side of the  $\alpha$ -CD ring and in close contact with the low occupancy site of the disordered O(6) hydroxyl group. It is itself twofold disordered with the two sites about  $60^\circ$  apart, in agreement with the  $\alpha$ -CD pseudo-hexagonal symmetry. Two of the 4·8 water of hydration molecules are also twofold disordered. From the structure of the  $\alpha$ -CD-propanol complex it appears as if in aqueous solution the 1-propanol molecule approaches the  $\alpha$ -CD ring from the O(2), O(3) side and enters the void with the hydroxyl group head on. Further results on the mechanism of adduct formation of the  $\alpha$ -CD molecule are discussed with respect to the  $\alpha$ -CD hexahydrate structure.

#### Introduction

Cyclohexaamylose ( $\alpha$ -cyclodextrin,  $\alpha$ -CD) is a macrocyclic molecule consisting of six  $\alpha(1 \rightarrow 4)$  linked glucose residues (Fig. 1). It is toroidal with an inner aperture about 5 Å in diameter, an outer diameter of 13·5 Å and a height of 8·5 Å. The hydrophilic O(6), O(2) and O(3) hydroxyl groups are located at the outside of the toroid whereas the inside of the aperture is mainly hydrophobic in character (McMullan, Saenger, Fayos & Mootz, 1973a; Thoma & Stewart, 1965; French, 1957; Cramer, 1954; Griffiths & Bender, 1973).

In aqueous solution,  $\alpha$ -CD forms inclusion complexes, the fitting of the substrate into the 5 Å-wide cavity being the only obvious requirement for inclusion (Cramer, 1954; French, 1957; Thoma & Stewart, 1965; Griffiths & Bender, 1973). The adducts can be crystallized in two major forms. In the channel-type structures the  $\alpha$ -CD rings are arranged on top of each other with the apertures forming 'endless' channels. In the cage-type structures the  $\alpha$ -CD rings are arranged crosswise with the aperture of one  $\alpha$ -CD ring blocked

at both ends by contiguous  $\alpha$ -CD molecules. Channel-type structures are preferred when adducts with long molecules or ionic substrates are crystallized; cage-type structures form with small molecular substrates (McMullan, Saenger, Fayos & Mootz, 1973a).

The crystals of one kind of cage-type structure are almost isomorphous with orthorhombic space group  $P2_12_12_1$  and cell constants similar to those given in Table 1 for the  $\alpha$ -CD-1-propanol adduct. As the arrangement of the  $\alpha$ -CD molecules determines the crystal structures of these  $\alpha$ -CD adducts the packing forces will be similar. Therefore, in this class of crystal structures differences in conformations of the  $\alpha$ -CD molecules in adducts with different substrates will reveal the influence of the substrate molecules on the geometry of the  $\alpha$ -CD molecule.

Table 1. *Crystallographic data*

Space group:	orthorhombic, $P2_12_12_1$
Cell dimensions	$a=14\cdot292$ (4) Å $b=37\cdot515$ (7) $c=9\cdot393$ (3)
Observed density (flotation method, methyl iodide/cyclohexane)	$\rho_{\text{obs}}=1\cdot468$ (2) g cm <sup>-3</sup>
Stoichiometry of complex from density:	$(C_6H_{10}O_5)_6 \cdot C_3H_8O \cdot 4 \cdot 5H_2O$
Stoichiometry of complex from X-ray data:	$(C_6H_{10}O_5)_6 \cdot C_3H_8O \cdot 4 \cdot 8H_2O$

Here we report the X-ray analysis of the  $\alpha$ -CD-1-propanol adduct. This study has been undertaken in order to investigate the interactions between the  $\alpha$ -CD

\* Part III: *Crystal and Molecular Structure of Cyclohexaamylose, the (H<sub>2</sub>O)<sub>2</sub> Inclusion Complex* [Manor & Saenger (1974). *J. Amer. Chem. Soc.* In the press].

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molecule and a polar molecule  $\text{CH}_3\text{-CH}_2\text{-CH}_2\text{-OH}$  with hydrophobic and hydrophilic ends. In previous contributions the adducts of  $\alpha$ -CD with water and iodine have been described (Manor & Saenger, 1972; McMullan, Saenger, Fayos & Mootz, 1973b) and, earlier, details of the channel-type structure of the  $\alpha$ -CD-potassium acetate complex were reported (Hybl, Rundle & Williams, 1965).

### Experimental

Large prismatic crystals of the  $\alpha$ -CD-1-propanol adduct were obtained by slowly cooling a hot, saturated solution of  $\alpha$ -CD in an aqueous 60% 1-propanol solution. The crystals were stable in air and did not decompose during data collection, in contrast to our experience with the 'isomorphous'  $\alpha$ -CD-iodine-tetrahydrate adduct (McMullan, Saenger, Fayos & Mootz, 1973b).

The crystallographic data for the  $\alpha$ -CD-propanol adduct are given in Table 1. From density measurements the composition of the crystallographic asymmetric unit was derived as  $\alpha$ -CD-1-propanol-4.5 $\text{H}_2\text{O}$  (the refined structure has a water content of 4.8 $\text{H}_2\text{O}$ ). 5303 intensities were collected on an automatic Siemens diffractometer operated in the  $\theta/2\theta$  scan mode at a minimum rate of  $1^\circ \text{min}^{-1}$  with variable scan widths and Cu  $K\alpha$  radiation,  $\lambda = 1.54182 \text{ \AA}$ . 725 of the 5303 had intensities less than twice the error,  $\sigma$ , calculated according to counting statistics, and were considered unobserved. The data were corrected for geometrical factors but not for absorption.

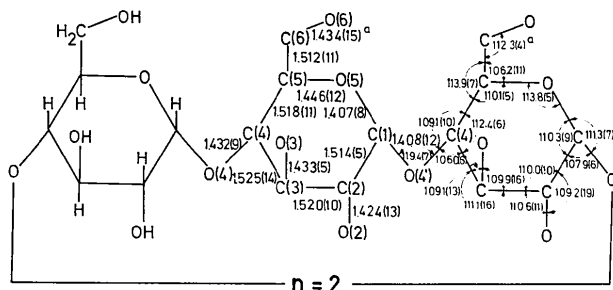


Fig. 1. Chemical structure and numbering scheme for the  $\alpha$ -CD molecule used in the text. Atom numbering scheme for  $\alpha$ -CD and for water molecules is similar to that in the  $\alpha$ -CD-iodine-tetrahydrate complex (McMullan, Saenger, Fayos & Mootz, 1973b). Bond distances (Å) and angles (°) are averaged from entries in Tables 9 and 10 (see footnote to p. 2021); standard deviations are calculated according to  $\sigma = [\sum_{i=1}^n (y_i - \bar{y})^2 / 5]^{1/2}$ . The superscript *a* indicates that in the calculation of these values glucose number 6 has not been included, owing to the disorder of atom O(6). Atom designation in the 1-propanol molecule is: O(1P)-C(1P)-C(2P)-C(3P). The bond angles and distances in the 1-propanol molecule are as follows (estimated standard deviations are given in parentheses; A and B refer to A and B sites with 85% and 15% occupancy respectively): O(1P)A-C(1P)-C(2P) 105(1)°, O(1P)B-C(1P)-C(2P) 113(2), C(1P)-C(2P)-C(3P)A 113(1)°, C(1P)-C(2P)-C(3P)B 119(4)°, O(1P)A-C(1P) 1.43(1), O(1P)B-C(1P) 1.31(3), C(1P)-C(2P) 1.56(1), C(2P)-C(3P)A 1.44(2), C(2P)-C(3P)B 1.21 C(8) Å.

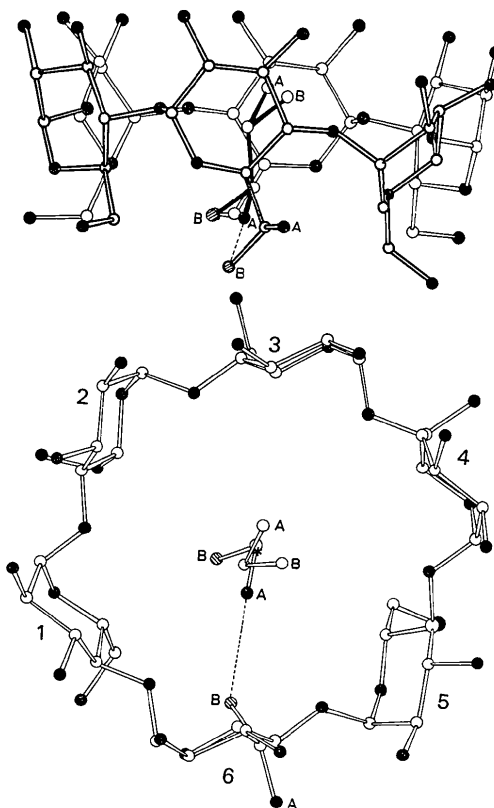


Fig. 2. Projection of the  $\alpha$ -CD-1-propanol complex on the best plane through the six O(4) atoms, viewed from the O(2), O(3) side. The glucose numbering scheme used in the text is indicated. Carbon atoms are drawn as open circles, oxygen atoms as solid circles. \* marks the centre of the O(4) hexagon. Disordered sites of the O(6) atom and of the 1-propanol molecule are indicated as A and B.

The structure solution was based on the assumption that the  $\alpha$ -CD torus would be in a similar location and conformation to that of the 'isomorphous' iodine adduct (McMullan, Saenger, Fayos & Mootz, 1973b). The positions of the carbon and oxygen atoms, except O(6) of the  $\alpha$ -CD molecule from the iodine adduct, were utilized with the  $\alpha$ -CD-1-propanol data and refined in two cycles of full-matrix least-squares calculations with data limited to  $2\theta \leq 80^\circ$ . A Fourier synthesis based on the phases thus obtained revealed the positions of all the O(6) atoms, of the water oxygen atoms and of the 1-propanol carbon and oxygen atoms. Refinement continued with assignment of the disordered 1-propanol and water atoms in the isotropic refinement cycles. The non-hydrogen atoms were refined anisotropically and the positions of the hydrogen atoms attached to the carbon atoms were calculated and included in the last cycle with an average isotropic temperature factor  $B = 3.0 \text{ \AA}^2$ . In this last cycle the average parameter shifts were less than  $\frac{1}{3}$  of the average errors determined from the correlation matrix. The final  $R$  [ $= \sum (|F_o| - |F_c|) / \sum |F_o|$ ] is 7.0%. The quantity minimized was  $\sum w(|F_o| - |F_c|)^2$  with  $w$  proportional

to the reciprocal of  $\sigma$ ; atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1968).

### Results and discussion

Fig. 1 gives the nomenclature. Atoms in the text are numbered with two figures, the first (in parentheses) designating atoms within glucose units, the second the glucose number in the macrocycle; the glucose numbers 1  $\rightarrow$  6 follow clockwise when the molecule is viewed from the O(2), O(3) side (Fig. 2). Final atomic parameters are given in Table 2 with standard deviations

as obtained from the diagonal elements of the least-squares variance-covariance matrix. Table 3 contains the observed and calculated structure factors.\*

Details of the geometry of the  $\alpha$ -CD-1-propanol adduct are described in Tables 4 to 10 and in Figs. 1 to 7.\* Standard deviations are given in parentheses where appropriate. Intermolecular distances less than 3.0 Å indicate hydrogen-bonding contacts in Figs. 5, 6 and 7.

\* Tables 3, 9 and 10 have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30425 (26 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 2. Fractional atomic coordinates multiplied by  $10^4$  and anisotropic temperature factors for the non-hydrogen atoms

Temperature factors are in the form  $T = \exp[-\frac{1}{4}(h^2 B_{11} a^{*2} + k^2 B_{22} b^{*2} + l^2 B_{33} c^{*2} + 2hk B_{12} a^* b^* + 2hl B_{13} a^* c^* + 2kl B_{23} b^* c^*)]$ .  
The occupancy factors are listed in the column headed OC.

#### Cyclohexaamylose molecule

	$x/a$	$y/b$	$z/c$	$B_{11}$	$B_{22}$	$B_{33}$	$B_{12}$	$B_{13}$	$B_{23}$	OC
C(1)1	7926 (4)	2315 (1)	104 (6)	3.8 (2)	2.1 (2)	3.4 (2)	-0.1 (2)	0.0 (2)	0.1 (2)	1.00
C(2)1	8496 (4)	2157 (1)	-1094 (5)	3.2 (2)	2.4 (2)	2.9 (2)	-0.2 (2)	0.1 (2)	0.4 (2)	1.00
C(3)1	9052 (3)	1840 (1)	-528 (5)	2.7 (2)	2.2 (2)	2.7 (2)	-0.2 (1)	0.2 (2)	0.2 (1)	1.00
C(4)1	9597 (3)	1934 (1)	792 (6)	3.2 (2)	1.9 (2)	3.0 (2)	-0.5 (1)	0.2 (2)	0.2 (1)	1.00
C(5)1	9024 (4)	2134 (1)	1895 (6)	3.6 (2)	2.5 (2)	2.7 (2)	-0.5 (2)	0.4 (2)	-0.5 (2)	1.00
C(6)1	9581 (4)	2284 (1)	3114 (6)	4.1 (2)	3.0 (2)	3.2 (2)	-0.1 (2)	0.0 (2)	-0.1 (2)	1.00
O(2)1	7906 (3)	2043 (1)	-2244 (4)	4.4 (2)	3.5 (1)	3.3 (2)	-0.0 (1)	-0.2 (1)	-0.0 (1)	1.00
O(3)1	9682 (3)	1720 (1)	-1609 (4)	3.8 (2)	3.6 (1)	3.0 (1)	-0.1 (1)	0.1 (1)	-0.3 (1)	1.00
O(4)1	9885 (3)	1598 (1)	1399 (4)	3.3 (1)	2.5 (1)	3.0 (1)	-0.4 (1)	0.2 (1)	0.2 (1)	1.00
O(5)1	8531 (3)	2425 (1)	1212 (4)	4.1 (2)	2.2 (1)	3.6 (2)	-0.2 (1)	-0.0 (1)	-0.4 (1)	1.00
O(6)1	10438 (3)	2456 (1)	2656 (5)	4.9 (2)	4.4 (1)	5.1 (2)	-0.9 (2)	-0.9 (2)	-0.8 (2)	1.00
C(1)2	4557 (4)	1904 (1)	1787 (7)	3.2 (2)	2.2 (2)	3.5 (2)	0.3 (2)	-0.1 (2)	0.4 (2)	1.00
C(2)2	4742 (4)	1884 (1)	197 (6)	3.2 (2)	3.0 (2)	3.1 (2)	-0.1 (2)	-0.1 (2)	0.5 (2)	1.00
C(3)2	5783 (4)	1841 (1)	-70 (6)	3.7 (2)	2.7 (2)	2.3 (2)	0.3 (2)	-0.2 (2)	0.3 (2)	1.00
C(4)2	6310 (3)	2141 (1)	701 (5)	3.0 (2)	2.4 (2)	2.6 (2)	0.3 (1)	0.3 (2)	-0.1 (1)	1.00
C(5)2	6040 (4)	2170 (1)	2247 (6)	3.5 (2)	3.3 (2)	2.7 (2)	0.3 (2)	0.6 (2)	-0.1 (2)	1.00
C(6)2	6434 (5)	2501 (2)	2973 (7)	4.4 (3)	4.9 (2)	3.9 (3)	-0.0 (2)	0.3 (2)	-0.9 (2)	1.00
O(2)2	4230 (3)	1598 (1)	-436 (4)	4.1 (2)	3.8 (1)	3.7 (3)	-0.1 (1)	-0.9 (1)	0.4 (1)	1.00
O(3)2	5962 (3)	1859 (1)	-1569 (4)	4.1 (2)	4.0 (2)	2.8 (1)	-0.0 (1)	0.4 (1)	0.0 (1)	1.00
O(4)2	7289 (2)	2053 (1)	588 (4)	3.0 (1)	2.3 (1)	3.4 (1)	-0.1 (1)	0.6 (1)	0.4 (1)	1.00
O(5)2	5029 (3)	2194 (1)	2382 (4)	3.7 (1)	2.8 (1)	3.7 (2)	0.3 (1)	0.7 (1)	-0.4 (1)	1.00
O(6)2	6284 (3)	2813 (1)	2154 (5)	5.1 (2)	3.3 (1)	5.1 (2)	-0.5 (1)	0.7 (2)	-0.9 (1)	1.00
C(1)3	4049 (4)	800 (1)	5251 (6)	2.5 (2)	2.1 (2)	3.1 (2)	0.3 (2)	0.4 (2)	0.4 (2)	1.00
C(2)3	3689 (4)	757 (1)	3755 (6)	2.7 (2)	2.2 (2)	3.3 (2)	0.4 (2)	-0.5 (2)	-0.1 (2)	1.00
C(3)3	4204 (4)	996 (1)	2723 (6)	2.7 (2)	2.4 (2)	2.8 (2)	0.4 (2)	0.3 (2)	-0.0 (2)	1.00
C(4)3	4184 (4)	1381 (1)	3272 (6)	2.4 (2)	2.4 (2)	2.7 (2)	0.5 (1)	0.3 (2)	-0.0 (2)	1.00
C(5)3	4486 (4)	1409 (1)	4803 (6)	3.1 (2)	2.3 (2)	3.2 (2)	-0.0 (2)	0.0 (2)	0.1 (2)	1.00
C(6)3	4302 (4)	1773 (1)	5446 (6)	4.1 (2)	2.5 (2)	3.6 (2)	0.1 (2)	-0.3 (2)	-0.6 (2)	1.00
O(2)3	3801 (3)	388 (1)	3366 (5)	4.1 (2)	2.4 (1)	4.8 (2)	-0.1 (1)	-0.9 (2)	-0.3 (1)	1.00
O(3)3	3787 (3)	990 (1)	1344 (4)	4.1 (2)	3.6 (1)	2.9 (1)	0.6 (1)	-0.4 (1)	-0.4 (1)	1.00
O(4)3	4825 (2)	1577 (1)	2397 (4)	3.0 (1)	2.8 (1)	3.2 (1)	0.8 (1)	0.5 (1)	0.6 (1)	1.00
O(5)3	3958 (3)	1160 (1)	5675 (4)	3.0 (1)	2.4 (1)	2.8 (1)	0.6 (1)	0.4 (1)	-0.2 (1)	1.00
O(6)3	3345 (3)	1885 (1)	5280 (5)	5.1 (2)	3.1 (1)	4.8 (2)	0.9 (1)	0.9 (2)	0.2 (1)	1.00
C(1)4	7065 (3)	159 (1)	7326 (5)	2.5 (2)	1.9 (1)	2.0 (2)	0.1 (1)	-0.1 (1)	0.1 (1)	1.00
C(2)4	6426 (3)	-75 (1)	6437 (5)	2.6 (2)	2.0 (2)	2.2 (2)	0.3 (1)	-0.0 (2)	-0.1 (1)	1.00
C(3)4	5816 (3)	152 (1)	5495 (5)	2.5 (2)	1.8 (2)	2.1 (2)	0.0 (1)	0.1 (2)	0.1 (1)	1.00
C(4)4	5314 (4)	452 (1)	6310 (5)	2.7 (2)	1.9 (2)	2.0 (2)	0.2 (1)	0.2 (2)	0.0 (1)	1.00
C(5)4	5981 (3)	650 (1)	7320 (5)	2.8 (2)	1.9 (1)	2.4 (2)	0.1 (1)	-0.1 (2)	0.0 (1)	1.00
C(6)4	5484 (4)	877 (1)	8392 (6)	3.9 (2)	2.6 (2)	3.5 (2)	0.8 (2)	-0.3 (2)	-0.9 (2)	1.00
O(2)4	7013 (2)	-304 (1)	5643 (4)	2.9 (1)	2.4 (1)	3.5 (1)	0.4 (1)	-0.1 (1)	-0.9 (1)	1.00
O(3)4	5129 (2)	-70 (1)	4813 (4)	2.8 (1)	2.2 (1)	2.9 (1)	-0.1 (1)	-0.6 (1)	-0.4 (1)	1.00
O(4)4	4993 (2)	697 (1)	5261 (3)	2.3 (1)	2.6 (1)	2.4 (1)	0.6 (1)	0.2 (1)	0.6 (1)	1.00
O(5)4	6530 (2)	400 (1)	8143 (3)	2.7 (1)	2.6 (1)	1.8 (1)	0.5 (1)	-0.1 (1)	-0.3 (1)	1.00
O(6)4	4862 (3)	671 (1)	9286 (4)	4.2 (2)	4.0 (2)	2.7 (1)	0.9 (1)	0.9 (1)	-0.2 (1)	1.00
C(1)5	10375 (3)	644 (1)	5831 (5)	2.6 (2)	3.0 (2)	2.0 (2)	-0.3 (1)	-0.3 (2)	0.1 (1)	1.00
C(2)5	10241 (5)	244 (2)	5844 (8)	3.3 (3)	3.2 (3)	2.3 (3)	0.4 (3)	0.4 (3)	0.3 (2)	1.00
C(3)5	9191 (4)	160 (1)	5749 (5)	2.8 (2)	2.2 (2)	2.3 (2)	-0.3 (1)	0.3 (2)	-0.2 (2)	1.00

Table 2 (cont.)

C(4)5	8630 (3)	373 (1)	6811 (6)	2·1 (2)	2·0 (2)	2·6 (2)	-0·3 (1)	-0·2 (2)	-0·2 (2)	1·00
C(5)5	8886 (3)	766 (1)	6800 (5)	2·7 (2)	2·2 (2)	2·1 (2)	-0·1 (1)	0·1 (1)	-0·2 (1)	1·00
C(6)5	8452 (4)	979 (1)	8011 (5)	3·1 (2)	2·0 (2)	2·4 (2)	-0·2 (2)	0·0 (2)	-0·4 (2)	1·00
O(2)5	10734 (3)	94 (1)	4680 (5)	3·6 (2)	3·7 (1)	4·9 (2)	0·5 (1)	0·9 (2)	-0·3 (1)	1·00
O(3)5	9067 (2)	-214 (1)	5979 (4)	3·1 (1)	2·2 (1)	3·2 (1)	0·1 (1)	0·1 (1)	-0·3 (1)	1·00
O(4)5	7668 (2)	339 (1)	6418 (3)	2·1 (1)	2·4 (1)	2·0 (1)	-0·2 (1)	-0·2 (1)	0·3 (1)	1·00
O(5)5	9872 (2)	811 (1)	6918 (3)	2·8 (1)	3·3 (1)	1·9 (1)	-0·9 (1)	0·0 (1)	-0·4 (1)	1·00
O(6)5	8803 (3)	873 (1)	9357 (4)	4·0 (2)	2·7 (1)	2·3 (1)	-0·6 (1)	0·4 (1)	-0·2 (1)	1·00
C(1)6	10852 (4)	1529 (1)	1531 (5)	2·8 (2)	3·2 (2)	2·6 (2)	-0·6 (2)	-0·0 (2)	0·3 (2)	1·00
C(2)6	11000 (3)	1145 (1)	1077 (5)	2·6 (2)	3·3 (2)	2·2 (2)	-0·6 (2)	0·3 (2)	-0·0 (2)	1·00
C(3)6	10498 (4)	892 (1)	2091 (5)	2·7 (2)	2·6 (2)	2·1 (2)	-0·4 (1)	0·2 (2)	-0·1 (1)	1·00
C(4)6	10736 (4)	976 (1)	3643 (5)	2·9 (2)	2·6 (2)	2·1 (2)	-0·5 (2)	-0·1 (2)	0·1 (2)	1·00
C(5)6	10632 (4)	1372 (1)	3971 (5)	3·1 (2)	3·0 (2)	2·1 (2)	-0·6 (2)	-0·3 (2)	-0·3 (2)	1·00
C(6)6	11001 (4)	1482 (1)	5407 (6)	4·1 (2)	3·4 (2)	2·6 (2)	-0·6 (2)	-0·1 (2)	-0·2 (2)	1·00
O(2)6	10656 (3)	1091 (1)	-311 (4)	4·1 (2)	4·1 (2)	2·1 (1)	-0·2 (1)	0·0 (1)	-0·3 (1)	1·00
O(3)6	10749 (3)	529 (1)	1840 (4)	4·1 (2)	2·8 (1)	2·8 (1)	0·2 (1)	-0·1 (1)	-0·3 (1)	1·00
O(4)6	10100 (2)	771 (1)	4467 (4)	2·4 (1)	3·0 (1)	2·2 (1)	-0·6 (1)	0·1 (1)	0·4 (1)	1·00
O(5)6	11160 (3)	1578 (1)	2941 (4)	3·5 (2)	3·7 (1)	2·7 (1)	-0·6 (1)	-0·2 (1)	-0·2 (1)	1·00
O(6)6A	11963 (4)	1353 (1)	5563 (6)	4·3 (2)	5·1 (2)	4·3 (2)	-0·8 (2)	-0·9 (2)	-0·5 (2)	0·85
O(6)6B	10384 (22)	1840 (7)	5781 (31)	5·1 (15)	3·4 (13)	3·0 (13)	0·2 (10)	-0·9 (11)	-0·9 (10)	0·25

## 1-Propanol molecule

C(1P)	7509 (7)	1477 (2)	4753 (10)	7·9 (5)	5·6 (4)	5·4 (4)	0·7 (3)	-0·9 (4)	0·0 (3)	1·00
C(2P)	7732 (8)	1264 (3)	3364 (13)	8·4 (5)	6·7 (4)	8·4 (6)	-0·9 (4)	0·7 (5)	0·0 (4)	1·00
C(3P)A	6991 (11)	1028 (4)	2948 (17)	6·9 (8)	8·4 (8)	8·4 (8)	-0·9 (6)	-0·5 (7)	-0·9 (7)	0·80
C(3P)B	7618 (57)	944 (21)	3347 (92)	7·6 (42)	6·9 (41)	6·9 (43)	-0·2 (31)	-0·9 (36)	-0·2 (34)	0·20
O(1P)A	8386 (6)	1621 (2)	5191 (9)	7·0 (4)	7·9 (4)	7·5 (4)	-0·2 (3)	0·9 (4)	-0·9 (3)	0·80
O(1P)B	7845 (21)	1802 (8)	4730 (33)	7·9 (17)	6·8 (15)	6·4 (16)	-0·2 (12)	0·5 (13)	-0·2 (12)	0·20

## Water molecules

O(W1)A	2432 (8)	1682 (3)	8974 (14)	4·9 (3)	6·7 (3)	7·1 (3)	-0·1 (2)	0·5 (3)	0·5 (3)	0·50
O(W1)B	2343 (21)	836 (8)	8355 (35)	6·4 (15)	7·1 (16)	7·1 (17)	-0·5 (11)	0·5 (13)	-0·2 (13)	0·20
O(W2)	2937 (5)	396 (2)	8561 (9)	5·9 (4)	6·7 (4)	6·5 (4)	0·9 (3)	-0·9 (3)	-0·5 (3)	0·80
O(W3)	2383 (4)	2309 (2)	3305 (7)	6·5 (3)	6·5 (3)	7·2 (3)	-0·5 (2)	0·4 (3)	0·9 (3)	1·00
O(W4)A	2663 (8)	1701 (3)	7909 (13)	5·8 (5)	7·0 (5)	6·2 (5)	0·5 (4)	-0·5 (5)	-0·5 (5)	0·50
O(W4)B	2076 (5)	1020 (2)	8018 (7)	4·6 (5)	5·4 (5)	4·6 (6)	0·9 (4)	0·9 (5)	0·7 (5)	0·80
O(W5)	2454 (4)	150 (1)	1521 (6)	5·4 (2)	7·1 (3)	5·6 (2)	-0·2 (2)	-0·9 (2)	-0·9 (2)	1·00

Table 4. Geometrical data for the hexagon described by the O(4) atoms

## (a) O(4)···O(4) distances in the six glucose units

Glucose number		Distance (Å)
1	O(4)6···O(4)1	4·247
2	O(4)1···O(4)2	4·155
3	O(4)2···O(4)3	4·298
4	O(4)3···O(4)4	4·267
5	O(4)4···O(4)5	4·194
6	O(4)5···O(4)6	4·250
Mean = 4·24 ± 0·07 Å		

## (b) Diagonal O(4)···O(4) distances (Å)

O(4)1···O(4)4	8·572
O(4)2···O(4)5	8·465
O(4)3···O(4)6	8·353
Mean = 8·46 ± 0·1 Å	

## (c) Angles

O(4)6···O(4)1···O(4)2	119·3°
O(4)1···O(4)2···O(4)3	119·2
O(4)2···O(4)3···O(4)4	121·7
O(4)3···O(4)4···O(4)5	117·6
O(4)4···O(4)5···O(4)6	120·7
O(4)5···O(4)6···O(4)1	120·8
Mean O(4)···O(4)···O(4) angle = 119·9 ± 0·9°	

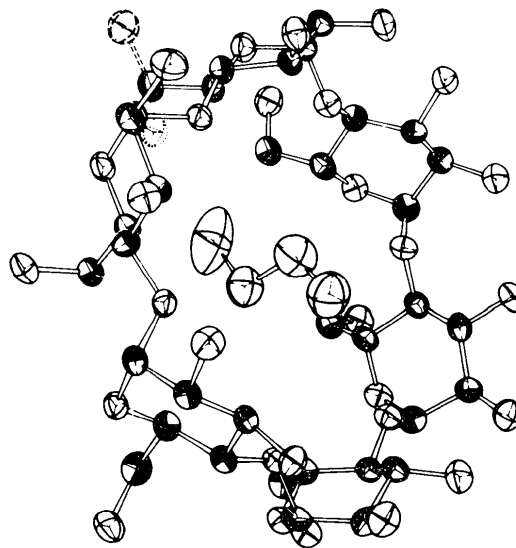
Fig. 3. View of the  $\alpha$ -CD-1-propanol complex along the crystallographic  $b$  axis with 50% probability thermal ellipsoids drawn (Johnson, 1965). The 1-propanol molecule is indicated only with its 80% occupancy site.

Table 5. Deviations of atoms (Å) from individual glucose least-squares planes defined by atoms C(2), C(3), C(5), O(5)

Glucose unit:	1	2	3	4	5	6
C(1)	-0.692	-0.674	-0.668	-0.670	-0.648	-0.668
C(2)	-0.014	0.000	0.008	0.012	-0.019	-0.024
C(3)	0.013	0.000	0.007	0.012	0.018	0.023
C(4)	0.576	0.626	0.618	0.580	0.593	0.619
C(5)	-0.014	0.000	-0.008	-0.012	-0.020	-0.024
C(6)	0.679	0.746	0.747	0.753	0.683	0.660
O(2)	-0.701	-0.643	-0.733	-0.760	-0.781	-0.752
O(3)	0.806	0.758	0.782	0.801	0.795	0.820
O(4)	0.232	0.408	0.372	0.195	0.303	0.375
O(5)	0.015	0.000	0.008	0.013	0.021	0.025
O(6)	2.124	2.143	2.144	2.130	2.002	2.089
O(4')	-2.025	-2.019	-2.003	-1.997	-2.015	-2.006

Table 6. Dihedral angles (°) in glucose units

The angles  $A-B-C-D$  are defined as zero when the bonds  $A-B$  and  $C-D$  are *cis* planar. They are counted positive when, looking along the central  $B-C$  bond, the far bond is rotated clockwise with respect to the near bond.

Glucose unit:	1	2	3	4	5	6
C(1)-C(2)-C(3)-C(4)	-51.2	-53.7	-52.7	-50.3	-49.2	-50.2
C(2)-C(3)-C(4)-C(5)	47.3	51.6	50.2	46.0	47.9	48.9
C(3)-C(4)-C(5)-O(5)	-48.6	-52.1	-51.8	-47.0	-50.8	-55.2
C(4)-C(5)-O(5)-C(1)	58.5	58.0	58.4	57.5	58.6	60.9
C(5)-O(5)-C(1)-C(2)	-65.2	-62.1	-61.1	-62.9	-62.6	-63.5
O(5)-C(1)-C(2)-C(3)	59.2	59.7	58.0	57.4	56.0	56.9
O(5)-C(5)-C(6)-O(6)	-78.3	-73.2	-67.1	-61.7	-56.4	-68.6 (85.3)†
C(4)-C(5)-C(6)-O(6)	44.2	47.8	53.3	59.5	65.9	52.0 (-154.1)†
C(2)-C(1)-O(4')-C(4')*	-128.4	-126.9	-130.4	-138.2	-124.8	-137.4
C(1)-O(4')-C(4')-C(3')*	129.9	131.4	127.5	113.9	149.2	118.7
C(2)-C(1)-O(4')-C(4')*	-128.4	-126.9	-130.5	-138.3	-124.8	-137.4
O(5)-C(1)-O(4')-C(4')*	111.3	111.0	110.0	100.4	112.1	102.1
C(1)-O(4')-C(4')-C(5')*	-108.4	-107.2	-112.2	-124.6	-89.7	-119.4
O(2)-C(2)-C(3)-O(3)	65.5	62.9	67.8	69.5	68.6	68.5
C(3)-C(4)-C(5)-C(6)	-170.4	-170.9	-169.4	-165.2	-170.7	-170.7

\* Primed atoms belong to glucose of next higher number on cyclic permutation.

† Value in parentheses for *B* site, without parentheses for *A* site.

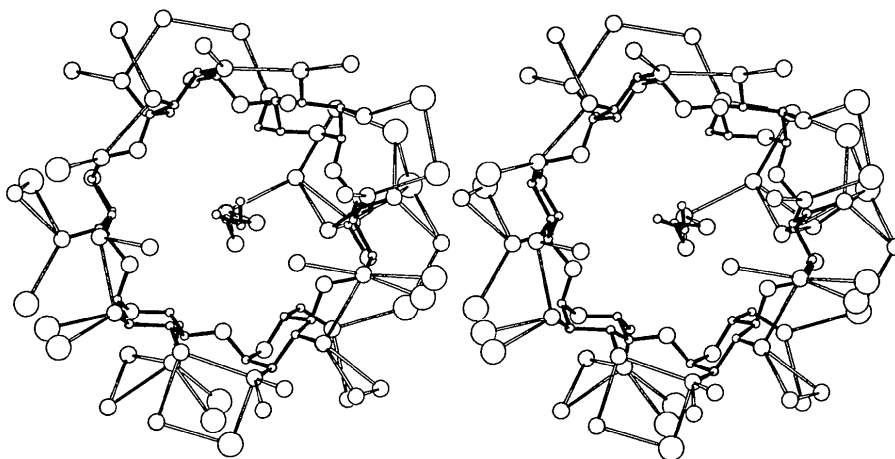


Fig. 4. A stereo view of the  $\alpha$ -CD-1-propanol complex with all  $O \cdots O$  contacts  $< 3.0 \text{ \AA}$ . Small, medium and large circles represent carbon atoms, hydroxyl groups of  $\alpha$ -CD and of 1-propanol and water molecules respectively. Heavy and light bonds indicate covalent bonding and close contacts  $< 3.0 \text{ \AA}$ .

Table 7. Deviations of atoms ( $\text{\AA}$ ) from the least-squares plane defined by the six O(4) atoms

The equation of this plane is  $0.071X + 0.653Y + 0.754Z - 6.054 = 0$  with  $X, Y, Z$  parallel to the crystallographic  $a, b, c$  axes respectively.

	Glucose unit					
	1	2	3	4	5	6
O(4)	-0.144	0.131	-0.003	-0.113	0.103	0.026
C(1)	0.493	0.338	0.037	0.246	0.709	-0.123
C(4)	0.218	0.326	0.070	0.064	0.564	0.009
C(6)	2.719	2.829	2.584	2.598	2.879	2.524
O(2)	-1.839	-2.020	-2.332	-2.088	-1.417	-2.519
O(3)	-2.000	-2.008	-2.292	-2.296	-1.422	-2.363

### Conformation of the glucose residues

The six glucose residues are in the usual  $C_1$  chair conformation and exhibit similar conformational parameters. The  $O(4) \cdots O(4)$  distance of a glucose residue is a sensitive measure of its conformation. In this  $\alpha$ -CD molecule the distances are nearly identical,  $4.24 \pm 0.07 \text{ \AA}$  (Table 4), and comparable to the value assumed for  $\beta$ -amylose (Zugenmaier & Sarko, 1973).

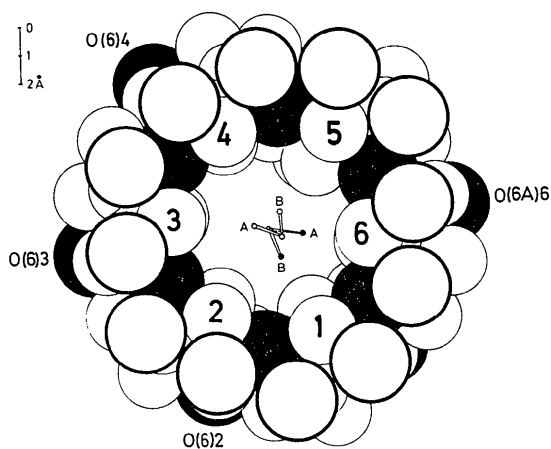


Fig. 5. The  $\alpha$ -CD molecule of the  $\alpha$ -CD-1-propanol complex drawn with van der Waals radii taken from Pauling (1960); view is from the O(2), O(3) side. O(2), O(3) atoms are drawn with heavy lines, O(4) and O(6) are shaded. Numbering 1 to 6 refers to glucose units and is indicated on hydrogen atoms attached to C(3).

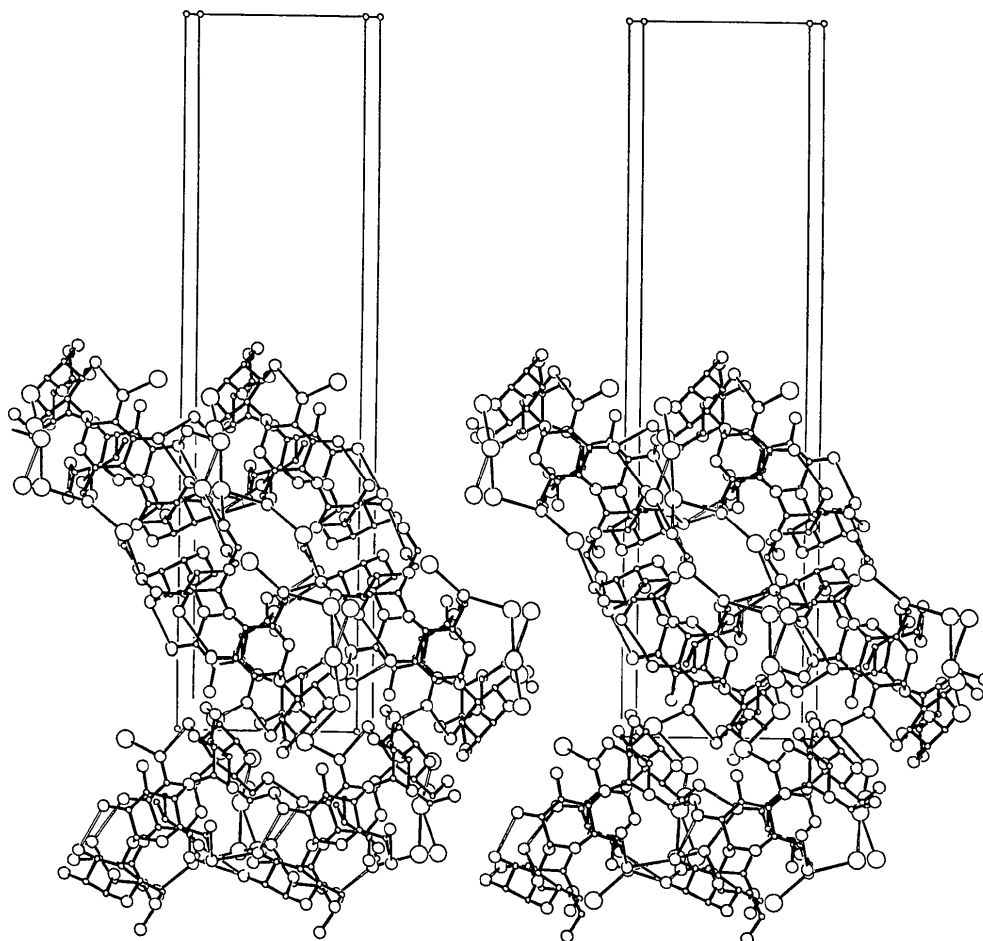


Fig. 6. A stereoscopic representation of part of the unit-cell content. Atoms and bonds are indicated as in Fig. 4.

Further, the deviations of atoms C(1) and C(4) from the 'best' planes defined by the four atoms C(2), C(3), C(5), O(5) are similar in the six glucoses (Table 5) and the endocyclic dihedral angles do not deviate by more than  $\pm 4^\circ$  from the mean dihedral angles (Table 6).

The orientations of the six C(6)–O(6) bonds are defined by the dihedral angles O(5)–C(5)–C(6)–O(6) and C(4)–C(5)–C(6)–O(6) which in all cases are in the (–)gauche, (+)gauche range. These angles show up to  $11^\circ$  deviation from the mean, a consequence of the hydrogen bonding in which all the O(6) hydroxyl groups are involved. The O(6) hydroxyl group is twofold disordered with site *A*, occupancy 80%, away from the centre of the molecule like the other five O(6) atoms and site *B*, occupancy 20%, towards the centre and in close contact with the 1-propanol molecule (Fig. 2 and Table 6).

### Conformation of the macrocycle

The  $\alpha$ -CD molecule consists of two types of cyclic structures: one, the glucose units, the other the ar-

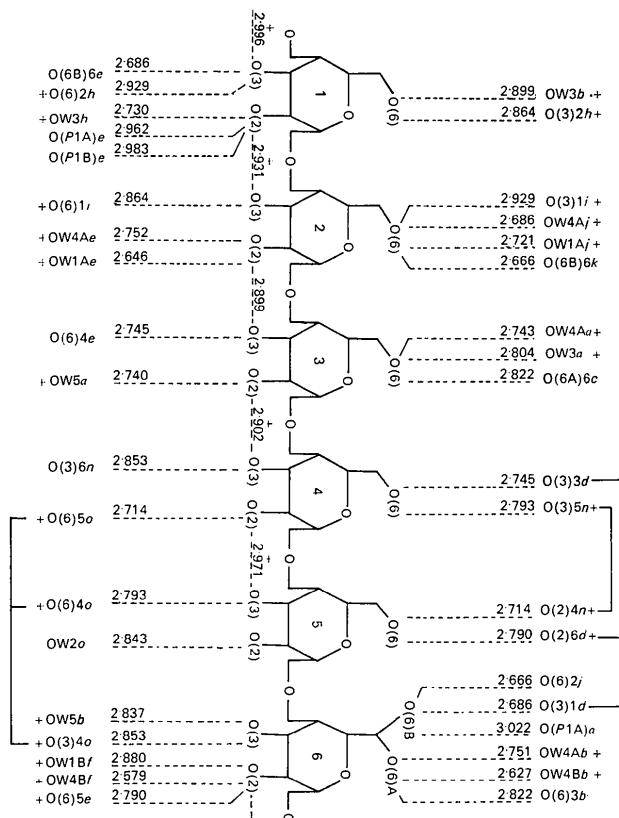
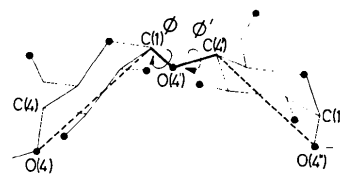


Fig. 7. A schematic representation of Fig. 4, indicating O...O distances (Å) and, in the letters after atomic designations, symmetry transformations. These transformations are: (a)  $x, y, z$ ; (b)  $1+x, y, z$ ; (c)  $-1+x, y, z$ ; (d)  $x, y, 1+z$ ; (e)  $x, y, -1+z$ ; (f)  $1+x, y, -1+z$ ; (g)  $-1+x, y, 1+z$ ; (h)  $\frac{1}{2}+x, \frac{1}{2}-y, -z$ ; (i)  $-\frac{1}{2}+x, \frac{1}{2}-y, -z$ ; (j)  $\frac{1}{2}+x, \frac{1}{2}-y, 1-z$ ; (k)  $-\frac{1}{2}+x, \frac{1}{2}-y, 1-z$ ; (l)  $\frac{1}{2}-x, -y, \frac{1}{2}+z$ ; (m)  $\frac{1}{2}-x, -y, -\frac{1}{2}+z$ ; (n)  $1\frac{1}{2}-x, -y, \frac{1}{2}+z$ ; (o)  $1\frac{1}{2}-x, -y, -\frac{1}{2}+z$ . Bonds marked '+' were similarly observed in the  $\alpha$ -CD-iodine tetrahydrate adduct.

Table 8. Dihedral angles ( $^\circ$ )  
O(4) $n$ ...C(1) $n$ –O(4) $n+1$ –C(4) $n+1$   
and C(1) $n$ –O(4) $n+1$ –C(4) $n+1$ ...O(4) $n+2$   
to describe relative orientations of two adjacent glucose units about the common glycosidic linkage

For definition of dihedral angles, see Table 6.



O(4)1...C(1)1–O(4)2–C(4)2	169.6	} $\phi$
O(4)2...C(1)2–O(4)3–C(4)3	170.6	
O(4)3...C(1)3–O(4)4–C(4)4	168.4	
O(4)4...C(1)4–O(4)5–C(4)5	159.3	
O(4)5...C(1)5–O(4)6–C(4)6	171.1	
O(4)6...C(1)6–O(4)1–C(4)1	160.8	
C(1)1–O(4)2–C(4)2...O(4)3	–169.1	} $\phi'$
C(1)2–O(4)3–C(4)3...O(4)4	–167.1	
C(1)3–O(4)4–C(4)4...O(4)5	–171.4	
C(1)4–O(4)5–C(4)5...O(4)6	–183.5	
C(1)5–O(4)6–C(4)6...O(4)1	–149.5	
C(1)6–O(4)1–C(4)1...O(4)2	–179.6	

rangement of the six glucoses to form the  $\alpha$ -CD macrocycle. While the glucose units appear to be relatively rigid, the macrocycle is more flexible as each of the glucose units can rotate individually about the glycosidic C(4)–O(4)–C(1') bonds, primed and unprimed atoms designating adjacent glucose units. The geometry of the macrocycle is described by the coplanarity of the six O(4) atoms, by the dihedral angles involving the six glycosidic bonds and by the O(4)...O(4) distances across the macrocycle.

The O(4) atoms are roughly coplanar with a maximum deviation of 0.144 Å from their common mean plane (Table 7). As the atoms bonded to the O(4) atoms, C(1') and C(4), are located on the same side of this plane as atoms C(6) with only C(1)6 as exception, the macrocycle toroid assumes the shape of a truncated cone with the wide aperture at the O(2), O(3) side of the molecule and the smaller aperture at the O(6) side (Fig. 2).

Although the O(4) atoms of the macrocycle are almost coplanar, the toroid is by no means ideal. A projection onto the best plane defined by the six O(4) atoms (Fig. 2), reveals that the six-membered rings of glucoses 3, 4 and 6 are roughly perpendicular to this plane while glucoses 2, 1 and 5 are inclined by an increasing angle, the O(6) side nearer to the molecular axis, the O(2), O(3) side further apart. This tilt of the glucoses is also obvious from the deviations of the C(1) and C(4) atoms from the best plane through atoms O(4): the C(1) and C(4) atoms of glucoses 3, 4, 6 are nearer to this plane than atoms C(1) and C(4) of glucoses 2, 1 and 5.

That glucoses 1 and 5 are more inclined than the other four glucoses is also apparent from a comparison of the dihedral angles around the glucosidic bonds,  $C(1)-O(4')-C(4')-C(3')$ ,  $C(1)-O(4')-C(4')-C(5')$  and  $C(2)-C(1)-O(4')-C(4')$ ,  $O(5)-C(1)-O(4')-C(4')$  (Table 6): the entries listed under glucose numbers 4 and 6 (those adjacent to 5 and 1) differ significantly from the other four values. The same trend is indicated by the dihedral angles  $O(4)n \cdots C(1)n-O(4)n+1-C(4)n+1$  and  $C(1)-O(4)n+1-C(4)n+1 \cdots O(4)n+2$  (Table 8).

The O(4) atoms form an almost regular hexagon with the  $O(4) \cdots O(4)$  distances as sides. Geometrical data are listed in Table 4 and the centre of the hexagon is indicated in Fig. 2 by an asterisk. The  $O(4) \cdots O(4) \cdots O(4)$  angles approach  $120^\circ$  very closely, and the diagonals deviate from the mean,  $8.46 \text{ \AA}$ , by not more than  $\pm 0.1 \text{ \AA}$  (Table 4).

#### Bond distances and angles

Individual bond distances and angles are given in Tables 9 and 10;\* average values are listed in Fig. 1. A statistical analysis of bond angles and distances was carried out for the  $\alpha$ -CD-hexahydrate structure (Manor & Saenger, 1974). It is common to both structures and to the  $\alpha$ -CD-iodine-tetrahydrate complex (McMullan, Saenger, Fayos & Mootz, 1973*b*) that the  $C(5)-O(5)$  bonds are longer than the  $C(1)-O(5)$  bonds, that the angles  $C(5)-C(6)-O(6)$ , average  $112^\circ$ , are greater than the other  $C-C-C$  or  $C-C-O$  angles which are close to the tetrahedral value  $109^\circ$ , and that the angles with atoms O(5) and O(4) as vertex,  $114^\circ$  and  $119^\circ$ , are larger than those usually observed for unstrained  $C-O-C$  linkages.

Noteworthy is the exceptionally obtuse angle  $C(4)-O(4)-C(1')$  of  $119^\circ$  which has been observed in all the  $\alpha$ -CD structures. Similar angles were found in the di- and trisaccharides methyl- $\beta$ -maltopyranoside,  $117.6^\circ$  (Chu & Jeffrey, 1967), cellobiose,  $116.7^\circ$  (Brown, 1966), maltose,  $117.2^\circ$  (Quigley, Sarko & Marchessault, 1970), and in raffinose,  $122^\circ$  (Berman, 1970). In all these cases, the hydrogen atoms attached to the C(4) and C(1') atoms are eclipsed and, thus, repel each other, which might cause the increased  $C(4)-O(4)-C(1')$  angle. On the other hand, when the hydrogen atoms are staggered this angle appears smaller and assumes a value closer to the tetrahedral as in the glucose- $O-CH_3$  group of methyl- $\beta$ -maltopyranose,  $113.2^\circ$  (Chu & Jeffrey, 1967), in the melibiose- $O-C(6)H_2$ -glucose linkage,  $111.4^\circ$ , of raffinose (Berman, 1970) and in sucrose,  $114.3^\circ$  (Brown & Levy, 1973).

Bond angles and distances in the 1-propanol molecule are less accurately determined owing to the twofold disorder.

#### Geometry of the 1-propanol inclusion

The 1-propanol molecule is located in the void of the  $\alpha$ -CD macrocycle with the  $CH_3-CH_2-CH_2-OH$

chain oriented along the axis of the  $\alpha$ -CD toroid. The 1-propanol molecule is twofold disordered, with site *A* occupied 80%, site *B* 20%. The disorder can be described by a rotation of the 1-propanol molecule of nearly  $60^\circ$  about its central  $C(1P)-C(2P)$  bond. In the *A* and *B* sites, the 1-propanol molecule is in *trans* conformation, with dihedral angles of  $165.7^\circ$  for the *A* site and  $166.4^\circ$  for the *B* site.

Owing to the disorder, the hydroxyl and methyl groups in the 1-propanol molecule could not be assigned on the basis of electron density distribution but intermolecular distances had to be taken into consideration. Atom  $O(1P)A$  is in rather short contact ( $3.022 \text{ \AA}$ ) with the  $O(6)6B$  atom of the enclosing  $\alpha$ -CD molecule and with the  $O(2)1$  atom of a contiguous  $\alpha$ -CD molecule ( $2.962 \text{ \AA}$ ). Atom  $O(1P)B$  is not in contact with a hydroxyl group of the confining  $\alpha$ -CD molecule but is  $2.983 \text{ \AA}$  from the  $O(2)1$  atom (Fig. 4). As these distances are rather uncertain owing to the disorder of the 1-propanol molecule and the  $O(6)6$  hydroxyl group, it remains an open question whether or not these short contacts are hydrogen bonds. The  $C(3P)A$ ,  $C(3P)B$  sites both represent the methyl group of the 1-propanol since they are at distances greater than  $3.6 \text{ \AA}$  from other nonbonded atoms. This nearest-contact analysis suggests that the 1-propanol molecule is oriented in the  $\alpha$ -CD void with its  $O(1P)A$ ,  $O(1P)B$  hydroxyl group towards the O(6) side of the  $\alpha$ -CD macrocycle.

It is a peculiar feature of the  $O(1P)A \cdots O(6)6B$  short contact that both partners are statistically disordered, with occupancies of 80% for  $O(1P)A$  and of 15% for  $O(6)6B$ . The  $O(6)6A$  hydroxyl group in the 85% occupancy site is hydrogen bonded to two disordered water molecules  $O(W4)A$  and  $O(W4)B$  with 50% and 80% occupancy and at  $2.751$  and at  $2.627 \text{ \AA}$ , respectively.

A disorder similar to that observed around the  $O(6)6$  hydroxyl group in the  $\alpha$ -CD-1-propanol adduct was not observed in the iodine and water adducts where all atomic sites are fully occupied. It is conceivable that in solution the enclosed 1-propanol molecule is in hydrogen-bonding contact with water molecules and with at least one of the  $O(6)$  hydroxyl groups of the enclosing  $\alpha$ -CD molecule. This  $C(6)-O(6)$  bond must be rotated towards the centre of the  $\alpha$ -CD macrocycle in order to allow the hydrogen bond to form. When the adduct crystallizes, one can envisage the 1-propanol  $\cdots O(6)$  hydrogen bond partially breaking down, probably because of the hydrogen bonds which can be formed with neighbouring hydroxyl groups within the crystal structure.

If the  $\alpha$ -CD-1-propanol adduct had crystallized in an isotropic arrangement with all six glucoses equivalent, the 1-propanol molecule would have been sixfold disordered. As, however, the environment in space group  $P2_12_12_1$  is anisotropic and the geometry of the void is not hexagonal but rather an elongated ellipse (Fig. 5), only twofold disorder is observed. From the

\* See footnote to p. 2021.



directions of the two sites of the disordered molecule, it is clear that this peculiar disorder did not occur accidentally. As mentioned, the *A* and *B* sites of the 1-propanol molecule make an angle of about 60° and (Fig. 2) are arranged such that they fit into orientations of maximum spatial width of the  $\alpha$ -CD void; *i.e.* they are aligned along the approximate diagonals through atoms C(1), C(2), O(5) of glucoses 3 and 6 for the *A* site and through the same atoms of glucoses 1 and 4 for the *B* site (Figs. 2 and 5). This regularity suggests that in solution also these and the remaining diagonal between glucoses 2 and 5 of the  $\alpha$ -CD molecule are occupied statistically by 1-propanol molecules.

#### Crystal packing and hydrogen-bonding scheme

The crystal structure of the  $\alpha$ -CD-1-propanol adduct is almost isomorphous with the crystal structure of the  $\alpha$ -CD-iodine-tetrahydrate adduct (McMullan, Saenger, Fayos & Mootz, 1973*b*). The  $\alpha$ -CD molecules are arranged similarly in the two  $P2_12_12_1$  unit cells and produce a fish-bone type pattern which is typical for space groups with screw axial symmetry (Fig. 6). As the cell dimensions, however, vary from  $a=14.292$ ,  $b=37.515$ ,  $c=9.393$  Å in the 1-propanol adduct to  $a=14.240$ ,  $b=36.014$ ,  $c=9.558$  Å in the iodine adduct, differences must occur in the details of the molecular packing, especially in the formation of hydrogen bonds between the  $\alpha$ -CD molecules themselves and between the  $\alpha$ -CD molecules and water of hydration molecules. The differences in the two structures reside not only in the different substrates but also in the water content: 4 water molecules per  $\alpha$ -CD molecule in the iodine complex *versus* 4.8 water molecules in the 1-propanol complex. Furthermore, all atomic sites are fully occupied in the iodine adduct but five atoms are two-fold disordered in the 1-propanol adduct: two atoms of 1-propanol, one atom of the  $\alpha$ -CD macrocycle and two water molecules.

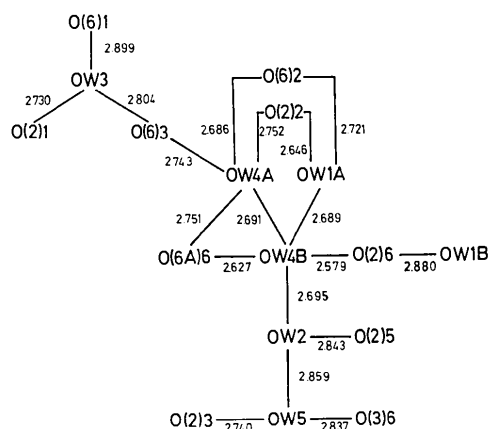


Fig. 8. A scheme of the water  $\cdots$  water contacts in the  $\alpha$ -CD-1-propanol-4.8 hydrate structure. Note the proximity of the disordered sites of water molecules *W*1 and *W*4. *W*5 was not observed in the 'isomorphous'  $\alpha$ -CD-iodine-tetrahydrate structure.

Of the 43 intermolecular contacts  $<3.0$  Å depicted in Fig. 7, 30 are similar to those observed in the  $\alpha$ -CD-iodine adduct, if the two sites of twofold-disordered water molecules are considered as one site. As hydrogen atoms of hydroxyl groups were not located in the two structures, donor and acceptor groups of possible hydrogen bonds cannot be defined. It is clear from Fig. 7 that 'new' hydrogen bonds or short  $O\cdots O$  contacts in the 1-propanol complex have formed to the 1-propanol hydroxyl group in the two sites  $O(1P)A$  and  $O(1P)B$ . The  $O\cdots O$  short contacts or hydrogen bonds are shown in Figs. 4, 6 and 7 where all atoms within a sphere of 3 Å from  $\alpha$ -CD hydroxyl groups are drawn; ether oxygen atoms are only rarely involved in hydrogen bonding and therefore short contacts to atoms O(4) and O(5) have not been taken into consideration. The water molecules and the  $\alpha$ -CD hydroxyl groups form a network of hydrogen bonds which extends throughout the whole crystal structure (Fig. 8).

The  $\alpha$ -CD molecules are arranged in a fish-bone pattern. Cages form owing to the closure of the  $\alpha$ -CD void at both ends by contiguous, symmetry-related molecules, the symmetry operations involved being mainly *c*-axis translations and screw rotations parallel to *c*. Direct contacts between  $\alpha$ -CD molecules are indicated in Fig. 7 by a jaw at the O(2), O(3) side of glucoses 4, 5 and 6 which are in close contact with another  $\alpha$ -CD molecule related by  $\frac{3}{2}-x, -y, -\frac{1}{2}+z$  and, in addition, by jaws at the O(6) side of the same glucoses which are in contact with two  $\alpha$ -CD molecules related by  $x, y, 1+z$  and by  $\frac{3}{2}-x, -y, \frac{1}{2}+z$ .

#### Conclusions

Thus far, three inclusion complexes of  $\alpha$ -CD have been described: the potassium acetate, the iodine and the water adducts.

The  $\alpha$ -CD-potassium acetate adduct with reported composition  $\alpha$ -CD-1.54 (potassium acetate)-9.7  $H_2O$  crystallizes in a channel-type structure with a crystallographic dyad coinciding with the channel and with the  $\alpha$ -CD molecular axis, and thus half an  $\alpha$ -CD molecule constitutes the asymmetric unit. The  $\alpha$ -CD molecules are arranged on top of each other and hydrogen-bonded *intramolecularly* through  $O(2)\cdots O(3)$  and *intermolecularly* through  $O(6)\cdots O(2)$ , with all six C(6)-O(6) bonds in a *gauche-trans* conformation. It appears as if the conformation of the  $\alpha$ -CD molecule in this peculiar crystal structure is largely determined by packing forces and is not representative of the  $\alpha$ -CD molecular species occurring in aqueous solution.

The other three crystal structures of the iodine, the water and the present 1-propanol complexes have space group  $P2_12_12_1$  with one  $\alpha$ -CD molecule per asymmetric unit. The  $\alpha$ -CD molecules appear to assume a conformation which is less restricted by crystal packing forces and more likely to be the conformation or one of the conformations occurring in aqueous solution.

An interesting feature emerges when the  $\alpha$ -CD-substrate complexes with space group  $P2_12_12_1$  are compared: in the water adduct which might be representative of the  $\alpha$ -CD molecule actually present in aqueous solution, an unusual conformation was observed with two of the six O(5)-C(5)-C(6)-O(6) and C(4)-C(5)-C(6)-O(6) dihedral angles being (+)-*gauche-trans* instead of the usual (-)-*gauche-(+)-gauche* arrangement and the two attached glucose residues being much more tilted towards the  $\alpha$ -CD torus axis than the other four, resulting in a rather strained conformation with a higher potential energy than that found in the other crystal structures of  $\alpha$ -CD adducts (Manor & Saenger, 1974). In the iodine, the 1-propanol and the methanol and krypton adducts with  $\alpha$ -CD (Saenger & Noltemeyer, to be published), the  $\alpha$ -CD molecules assume an almost circular, nearly hexagonal, more highly symmetrical conformation with less conformational energy than in the adduct with water. The reduction of conformational energy associated with the repulsion of water from the void of the  $\alpha$ -CD molecule and the inclusion of a substrate molecule other than water suggest a mechanism for the  $\alpha$ -CD inclusion process which is in agreement with data from spectroscopic measurements (Rees, 1970) and an extension of an earlier proposal (Cramer, Saenger & Spatz, 1967). Furthermore, this mechanism explains the hitherto unknown driving force towards inclusion formation: mainly a change in conformational energy of the  $\alpha$ -CD molecule, with the hydrogen bonding, van der Waals and entropy contributions of less importance (Manor & Saenger, 1974; Griffiths & Bender, 1973).

It is obvious from the details of the  $\alpha$ -CD-1-propanol adduct that the 1-propanol hydroxyl group is near the  $\alpha$ -CD O(6) side. This mutual, specific orientation of the two molecules suggests that, in aqueous solution, the  $\alpha$ -CD molecule is anisotropic towards the approaching and then enclosed substrate molecule; *i.e.* the  $\alpha$ -CD O(6) side is different from the O(2), O(3) side. Otherwise, the 1-propanol molecule should have been enclosed less specifically and disordered with about equal distribution of the 1-propanol hydroxyl group near the O(6) side and near the O(2), O(3) side.

Furthermore, it appears as if the 1-propanol molecule approaches the  $\alpha$ -CD torus from the O(2), O(3) side and enters with its hydroxyl group ahead. These conclusions follow from purely geometrical considerations: in the  $\alpha$ -CD-water adduct (Manor & Saenger, 1974), the species present in aqueous solution, the O(6) side is almost closed owing to the (+)-*gauche-trans* orientation of two C(6)-O(6) bonds but wide open at the O(2), O(3) side. Therefore, a substrate could enter more easily from the latter side. Upon insertion of a 1-propanol molecule into the  $\alpha$ -CD void, it can reorient itself with respect to the three possible  $\alpha$ -CD diagonals

defined by atoms C(1), C(2), O(5) through rotations about the  $\alpha$ -CD molecular axis. On the other hand, an inversion of the orientation, *i.e.* with the 1-propanol hydroxyl group near the O(2), O(3) side of the  $\alpha$ -CD molecule, would require a dissociation and reformation of the complex. The geometry of the reaction of  $\alpha$ -CD with 1-propanol at least forms the most stable, crystallizable complex. However, one cannot exclude on the basis of this X-ray study alone that, in solution, a complex with the 1-propanol hydroxyl group near the  $\alpha$ -CD O(2), O(3) side could occur, at least in minor quantities.

R. K. McMullan wishes to acknowledge a grant from the Alexander von Humboldt Stiftung. The computations were performed at computing centres in Braunschweig, Darmstadt and Göttingen and were supported in part by the Deutsche Forschungsgemeinschaft, which also provided the diffractometer.

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