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Crystal structure of a new α-cyclodextrin hydrate form. Molecular geometry and packing features: disordered solvent contribution

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Abstract

The crystallographic study of a new hydrated form of α-cyclodextrin (cyclohexaamylose) is reported. $C_{36}H_{60}O_{30}\cdot 11H_2O$; space group $P2_12_12_1$ with cell constants $a=13.839(3)$, $b=15.398(3)$, $c=24.209(7)$ Å; final discrepancy index $R=0.057$ for the 5182 observed reflections and 632 refined parameters. Besides four ordered water molecules placed outside α-cyclodextrins, the structure shows regions of severely disordered solvent mainly confined in the oligosaccharide cavities. The contribution of the observed disorder has been computed via Fourier inversions of the residual electron density and incorporated into the structure factors in further refinements of the ordered part. The α-cyclodextrin molecule assumes a relaxed round shape stabilised by a ring sequence of all the six possible O2···O3 intramolecular hydrogen bonds. The four ordered water molecules take part in an extensive network of hydrogen bonds (infinite chains and loops) without modifying the scheme of intramolecular H-bonds or the (−)*gauche* conformations of O-6–H hydroxyl groups. The structure shows a new molecular arrangement, for an "empty" hydrated α-cyclodextrin, like that "brick-type" observed for α-CD in the iodoanilide trihydrate complex crystallising in an isomorphous cell.

Keywords: α-Cyclodextrin water complexes; X-ray structure; Molecular features and crystal packing; Disordered solvent contribution

1. Introduction

Cyclodextrins (CDs) have received for many years special attention for their ability to form inclusion complexes with a large variety of appropriate-size molecules [1]. Such complexes are of interest in the pharmacological industry because oligosaccharide cavities can be effectively used as vehicle for drugs. In fact, in this micro-encapsulation some drug properties such as stability, solubility and bioavailability can be enhanced and toxicity minimised [2]. Cyclodextrins are also

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extensively employed in affinity chromatography [3,4] as chiral discriminators against the optically active molecules with which they form inclusion complexes. The increasing interest in CD complexes stimulates more and more researches with different techniques. In particular, the crystallographic study can be helpful to clarify inclusion phenomena. In fact this approach is able to give a clear picture of non-covalent interactions between CD and guest molecules and also it is useful to better evaluate the contribution to the complex stability of water molecules, a recurring factor in such complexes.

On carrying out different crystallization procedures with the purpose to obtain single crystals suitable for an X-ray study of complexes between α-CD and different surfactants [5,6], some attempts, tried in the presence of ethanol and at low concentrations of guest molecules, yielded a new crystal form of empty α-CD hydrated, called form IV according to the referee's suggestion. This form is isomorphous to α-CD complexed with substituted benzene, such as the iodoanilide trihydrate complex [7,8]. The molecular and packing features of this form, which includes regions of fully disordered solvent, are discussed in the present paper.

2. Experimental

Experiments to obtain single crystals of inclusion complexes between α-CD (cyclohexaamilose from Sigma Chemical Co) and molecules containing alkylic chains (f.e. sodium hexylsulphonate, triethylhexyl-ammonium bromide, pentaoxyethylenehexyl alcohol, butylurea) were carried out by vapour phase diffusion of ethanol, as precipitant, into the aqueous solutions of α-cyclodextrin. From crystallizations at low concentrations of guest (equimolecular or a little more), single crystals grew in the form of transparent prisms unstable in air that were sealed in glass capillaries with a small amount of mother solution. Some samples were tested on an Enraf–Nonius CAD4-F diffractometer on line with a MicroVAX Digital computer using graphite monochromatized CuKα radiation. Cell dimensions of all tested crystals appeared the same within experimental error. In addition, the crystals showed similar intensity patterns ($R_{int} < 0.07$) suggesting the presence of only one crystal type, in spite of different guest molecules in the crystallization batches.

Crystal data and structure refinement.—From a batch containing pentaoxyethylene-hexyl alcohol as guest, a single crystal of size $0.42\times0.38\times0.35$ mm was selected for X-ray data collection. Cell constants were accurately determined by least-squares refinement of the setting angles of 25 reflections at medium θ ($23^\circ < \theta < 27^\circ$). $a = 13.839(3)$, $b = 15.398(3)$, $c = 24.209(7)$ Å, orthorhombic symmetry, space group $P2_12_12_1$ as indicated by the systematic absences. 6452 reflections were measured at room temperature, $\theta_{max} = 73^\circ$, using $\omega - 2\theta$ scan mode as suggested by peak-shape analysis. The crystal and equipment stability were checked by the intensities of four standard reflections monitored every 5 h. No significant intensity decay was observed (4% variation). After the equivalent reflections were averaged ($R_{int} = 0.04$) a set of 5843 independent reflections was obtained, 5182 of which were observed [$I \geq 2.5\sigma(I)$]. The intensities were corrected for Lorentz and polarization factors, but not for absorption effect. The structure was solved by direct methods using SIR92 package [9] and proved to be a hydrate form of α-CD without guest: four water oxygens were clearly located on a Fourier map. The refinement was carried out by full-matrix (on F) least-squares methods on positional and anisotropic temperature parameters of all 70 non-hydrogen atoms. At convergence, hydrogens were positioned (distances C–H = 1.02 and O–H = 0.96 Å) on the basis of geometrical considerations and difference Fourier map suggestions. The H-water positions could be inferred bearing also in mind the pattern of hydrogen interactions. All hydrogens were included in the refinement as fixed atoms with isotropic thermal parameters set equal to B_{eq} of the parent atom. The refinement on the 5182 observed reflections reached at the discrepancy index $R = 0.098$, with rather large e.s.d. on the structural parameters. A subsequent difference Fourier map showed limited regions of nearly homogeneous residual electron density (highest value = 3.6 e·Å^{-3}), mainly confined in the oligosaccharide cavities (see Fig. 1). This fact was interpreted as the presence of disordered solvent (water). The continuous and diffuse distribution of the electron density, without pronounced peaks, precluded to model this disorder with discrete atoms. Attempts to refine atoms with alternative site occupancies were completely unsuccessful.

Structure refinement including the disordered-solvent contribution.—For taking into account the contribution of the disordered regions, with the

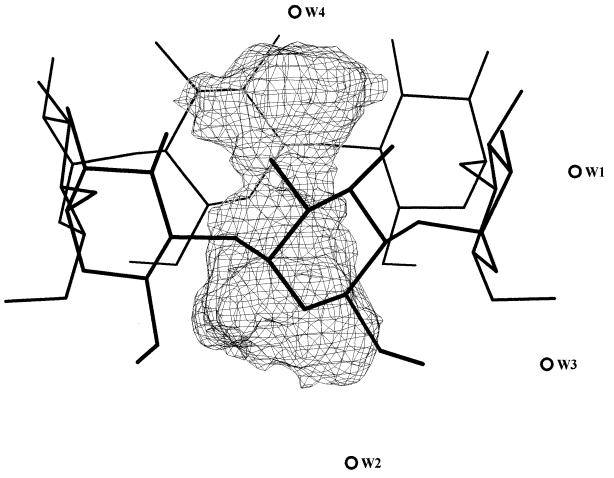

Fig. 1. Residual electron density in the α-CD cavity: the contour level is at 0.7 e/Å^3. The four ordered water molecules together with the α-cyclodextrin are shown.

purpose to better determine the ordered part of the structure and to reduce the large errors of atomic parameters, we have resorted to a procedure analogous to that used by Wehman et al. [10] and by Sluis and Spek [11]. In these methods the contribution to the structure factors of a generic disordered solvent is evaluated via discrete Fourier transforms of its residual electron density. So, the refinement of the present structure has been broken in four steps. (**1**)- Identification of the regions allowed to disordered solvent; (**2**)- Fourier inversion of the residual electron densities computed in the solvent regions; (**3**)- Standard least squares refinement of the ordered part englobing the solvent contribution, calculated by Fourier inversion, as fixed contribution to the structure factor; (**4**)- Check and modification of the hydrogen parameters following the criteria reported below. In particular, all the regions in the crystal cell that were outside the van der Waals volumes of the ordered atoms and also larger than a generic solvent with minimum radius equal 1.3 Å have been identified as solvent regions (17% in volume). The only van der Waals radius of hydroxyl and water hydrogens has been decreased of 0.4 Å with respect to the 1.2 Å value [12] considering the decrease of the interatomic distance in H-bonding interaction. The Fourier maps 2Fo-Fc were calculated using grid divisions of 0.25 Å. Negative values are set to zero. In each run the value of F(000) was optimized according with the count of electrons in the disordered areas. At convergence the F(000) value (2504) provides as the structurally independent part one α-CD molecule and 11 waters, seven of which disordered. Really, this quantity of disordered solvent is possibly overestimated, as comes out from the presence of negative values in the residual electron density. Besides, the number of disordered water molecules evaluated on the basis of the accessible volume is close to five.

All the steps were reiterated five times until convergence yielding at the end an appreciable improvement in the crystallographic discrepancy index ($R = 0.057$ instead of 0.098) and mainly the halving of the e.s.d. associated to molecular parameters.

Crystal data of the form IV α-CD hydrate including disordered solvent contribution. $C_{36}H_{60}O_{30}\cdot 11H_2O$, $Mr = 1171.03$, space group $P2_12_12_1$, cell constants: $a = 13.839(3)$, $b = 15.398(3)$, $c = 24.209(7)$ Å, $V = 5159(4)$ Å^3, $Z = 4$, $Dc = 1.508\ g\cdot cm^{-3}$, $\mu = 11.71\ cm^{-1}$. Final discrepancy index $R = \Sigma \parallel Fo| - |Fc \parallel / \Sigma |Fo| = 0.057$ for the 5182 observed reflections with $I \geq 2.5\sigma(I)$ and 632 refined parameters including extinction coefficient $g = 1.4(2) \times 10^{-7}$ [13]; $Rw = 0.066$ with $w^{-1} = [\sigma^2(Fo) + (0.02Fo)^2 + 2]$ [14]; error in an observation of unit weight $S = 0.986$; largest parameter shift/error $(\Delta/\sigma)_{max} = 0.02$; final residual electron density in the range -0.4; -0.6 e·Å^{-3}. Atomic scattering factors were taken from Cromer and Waber [15]. Enraf-Nonius *SDP* software [16] on a MicroVAX 3100 computer was used.[2]

3. Results and discussion

Molecular geometry and conformation.—Fig. 2 shows a perspective view of the final crystallographic model of the structure. Together with α-cyclodextrin, the ordered water molecules involved in hydrogen bonds (O···O distances within 3.3 Å) are shown. Positional parameters and equivalent isotropic temperature factors for the non-hydrogen atoms are given in Table 1.

The molecular geometry, on the whole, agrees well with the expected values [17,18] and, if compared with other α-CD hydrated structures [19–21], it is especially in agreement with the form III [20]. No significant discrepancy occurs among the corresponding values in glucosidic units. The glucose

[2] Structure factors, anisotropic displacement and hydrogen parameters together with molecular geometry have been deposited with the Cambridge Crystallographic Data Centre and may be required.

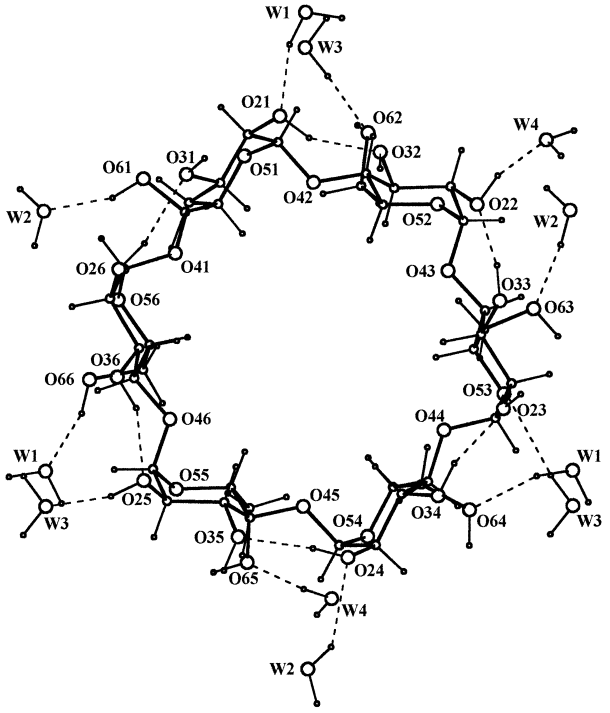

Fig. 2. Perspective view of the α-CD molecule: for clarity only oxygen atoms are labelled, the second digit indicates the glucose unit to which the atom belongs. The nearest ordered water molecules (distances within 3.3 Å) are also shown.

rings present endocyclic torsion angles within narrow ranges around the (+) or (−)*gauche* values, the deviations from expected $^4C_1$ chair conformation can be quantified by the puckering parameters [22,23] reported in Table 2. A few molecular parameters are less typical for α-CDs and more characteristic for the β-CDs [24]. The distances of C-1 and C-4 atoms from the best planes through the remaining ring atoms show a constant trend in the first five glucosic residues with C-1 more displaced with respect to C-4. These displacements are on average 0.692(4) Å for C-1 and 0.610(4) Å for C-4 in agreement with the expected values for α-CDs: 0.675 and 0.629 Å, respectively [18]. Instead, in the sixth glucose unit the trend is inverted with C-1 less displaced (0.649(4) Å) than C-4 (0.679(4) Å) according to what observed in several β-cyclodextrins [24]. Moreover, the angles at glycosyl links C-$1^{(n)}$–O-$4^{(n+1)}$–C-$4^{(n+1)}$ are in the range 118.9–119.9° and intra-residue distances O-$4^{(n)}$–O-$4^{(n+1)}$ are on average 4.23 Å, both values agree with the expected 119° and 4.23 Å for α-CDs. On the contrary, conventional 'torsion angles' (see Table 3) ϕ = O-$4^{(n)}$.....C-$1^{(n)}$–O-$4^{(n+1)}$–C-$4^{(n+1)}$ and ψ = C-$1^{(n)}$–O-$4^{(n+1)}$–C-$4^{(n+1)}$.....O-$4^{(n+2)}$, involving O-4–C-1 virtual bonds to describe the rotations of adjacent residues around the glycosyl bonds, are on average 170(6)° and −172(3)°, respectively. These values are significantly larger than the expected $\phi = 166°$ and $\psi = -169°$ for α-cyclodextrins and more similar to those occurring in β-CDs. At last the O-$2^{(n)}$–O-$3^{(n+1)}$ distances (2.87 Å on average) are more in agreement with the values in β-cyclodextrins (2.86 Å) rather than the expected 3.00 Å for α-CDs [18].

The primary hydroxyl groups are all (−)*gauche* oriented with respect to the O-5 ring oxygens. The g^- form, with C-6–O-6 bond pointing away from the centre of cavity, is indeed preferred whenever this hydroxyl group does not take part in H-bonding with guest molecules (water or other) included within the oligosaccharide cavity.

Hydrogen bonding and crystal packing.—The geometrical details of hydrogen bonds are given in Table 4. Criteria to define D–H·····A interactions are according to refs [25,26]. A ring sequence of six intramolecular hydrogen bonds between the secondary hydroxyl groups of adjacent glucose residues stabilises the oligosaccharide conformation. The involved O-2·····O-3 intramolecular distances are in the range 2.656–3.095 Å. The presence of all the possible intramolecular H-bonds, O-2·····O-3 type, has been previously observed only in the form III [20] among the hydrated α-cyclodextrins. That is accompanied by a symmetrically round shape of the α-CD cavity (O-4–O-4 diameters in the present structure in the range 8.306–8.601 Å) and low twist of the glucose units.

Crystal packing projected onto ac plane is shown in Fig. 3. The α-CD molecules arrange with a *pseudo* hexagonal symmetry in layers parallel to *ac* plane. Each layer is formed by rows of cyclodextrins translated along the *a* direction and joined through H-bonds between O-6–H primary hydroxyls of the third and sixth residues. As shown in Fig. 4, adjacent molecular-rows of a layer exhibit CD toroids upside down (screw symmetry along *c* axis) and are interconnected by three H-bonds involving O-3–H and O-6–H groups. In particular, two H-bonds link as a dimer pairs of screw related molecules through residues 1 and 5 (O-35–H·····O-61 and O-65–H·····O-31), the third H-bond is established between O-64–H and O-32. At last, the layers are H-bonded by means of the molecules arranged on subsequent layers in head to head orientation (screw symmetry along *a* axis), while only weak interactions (O·····O distances

Table 1
Fractional coordinates and equivalent thermal parameters: $Beq = 1/3\Sigma_i\Sigma_j\beta_{ij}a_i{}^*a_j{}^*\boldsymbol{a}_i\boldsymbol{a}_j$

	x	y	z	*B*eq		x	y	z	*B*eq
C11	0.4442(3)	0.0033(3)	0.6077(2)	2.84(8)	C14	0.5594(3)	−0.0444(4)	0.1677(2)	3.8(1)
C21	0.3836(3)	−0.0772(3)	0.6162(2)	2.70(8)	C24	0.6258(4)	−0.1236(4)	0.1680(2)	4.5(1)
C31	0.3302(3)	−0.1004(3)	0.5637(2)	2.80(8)	C34	0.6742(3)	−0.1325(3)	0.2236(2)	3.54(9)
C41	0.2744(3)	−0.0229(3)	0.5420(2)	2.75(8)	C44	0.7277(3)	−0.0484(3)	0.2371(2)	2.96(8)
C51	0.3332(4)	0.0609(3)	0.5405(2)	3.16(9)	C54	0.6646(3)	0.0316(3)	0.2310(2)	3.25(9)
C61	0.2729(4)	0.1419(3)	0.5318(2)	4.1(1)	C64	0.7213(4)	0.1162(3)	0.2339(2)	4.2(1)
O21	0.4419(2)	−0.1484(2)	0.6361(1)	3.14(6)	O24	0.5698(3)	−0.1999(3)	0.1546(2)	8.7(1)
O31	0.2630(2)	−0.1694(2)	0.5731(1)	3.59(6)	O34	0.7408(3)	−0.2025(2)	0.2214(2)	5.39(9)
O41	0.2474(2)	−0.0459(2)	0.4867(1)	2.97(6)	O44	0.7574(2)	−0.0543(2)	0.2934(1)	3.14(6)
O51	0.3831(2)	0.0729(2)	0.5928(1)	3.27(6)	O54	0.6160(3)	0.0305(2)	0.1772(1)	3.91(7)
O61	0.1936(3)	0.1465(3)	0.5685(2)	5.38(9)	O64	0.8125(3)	0.1109(3)	0.2061(2)	5.37(9)
C12	0.7963(3)	0.0025(3)	0.5215(2)	3.37(9)	C15	0.2060(3)	−0.0303(3)	0.2510(2)	2.96(8)
C22	0.7689(4)	−0.0728(3)	0.5592(2)	3.55(9)	C25	0.2297(4)	−0.1101(3)	0.2161(2)	3.28(9)
C32	0.6616(4)	−0.0861(3)	0.5575(2)	3.14(8)	C35	0.3373(4)	−0.1242(3)	0.2146(2)	3.39(9)
C42	0.6111(3)	−0.0032(3)	0.5736(2)	2.78(8)	C45	0.3898(3)	−0.0419(3)	0.1977(2)	3.16(8)
C52	0.6465(3)	0.0737(3)	0.5395(2)	3.14(8)	C55	0.3566(3)	0.0378(3)	0.2307(2)	3.28(9)
C62	0.6082(5)	0.1591(3)	0.5601(3)	5.0(1)	C65	0.3953(4)	0.1228(3)	0.2081(3)	4.6(1)
O22	0.8164(3)	−0.1508(2)	0.5395(1)	4.63(7)	O25	0.1830(3)	−0.1846(2)	0.2386(1)	3.78(7)
O32	0.6325(3)	−0.1504(2)	0.5968(2)	4.56(8)	O35	0.3613(3)	−0.1936(2)	0.1770(1)	4.73(8)
O42	0.5109(2)	−0.0151(2)	0.5640(1)	2.95(6)	O45	0.4906(2)	−0.0559(2)	0.2099(1)	3.82(7)
O52	0.7499(2)	0.0789(2)	0.5399(1)	3.66(6)	O55	0.2531(2)	0.0437(2)	0.2290(1)	3.28(6)
O62	0.6217(3)	0.1667(2)	0.6178(2)	6.3(1)	O65	0.3914(3)	0.1287(3)	0.1493(2)	5.35(9)
C13	0.8553(3)	−0.0457(3)	0.3065(2)	3.42(9)	C16	0.1508(3)	−0.0321(3)	0.4694(2)	3.15(8)
C23	0.8832(4)	−0.1182(3)	0.3444(2)	3.56(9)	C26	0.1205(4)	−0.1134(3)	0.4372(2)	3.36(9)
C33	0.8255(3)	−0.1115(3)	0.3975(2)	3.16(8)	C36	0.1762(4)	−0.1197(3)	0.3834(2)	3.14(9)
C43	0.8365(3)	−0.0224(3)	0.4235(2)	2.86(8)	C46	0.1702(3)	−0.0349(3)	0.3508(2)	2.82(8)
C53	0.8180(4)	0.0485(3)	0.3816(2)	3.59(9)	C56	0.2023(4)	0.0408(3)	0.3870(2)	3.23(9)
C63	0.8413(6)	0.1389(4)	0.4036(2)	5.7(1)	C66	0.1932(5)	0.1295(3)	0.3599(2)	4.5(1)
O23	0.8646(3)	−0.1988(2)	0.3168(1)	4.76(8)	O26	0.1344(3)	−0.1899(2)	0.4693(1)	4.03(7)
O33	0.8585(3)	−0.1791(2)	0.4340(1)	4.02(7)	O36	0.1320(3)	−0.1879(2)	0.3520(1)	4.51(8)
O43	0.7664(2)	−0.0168(2)	0.4669(1)	3.24(6)	O46	0.2373(2)	−0.0449(2)	0.3059(1)	2.81(5)
O53	0.8748(3)	0.0354(2)	0.3331(1)	3.94(7)	O56	0.1421(3)	0.0425(2)	0.4359(1)	3.70(6)
O63	0.9352(4)	0.1456(3)	0.4255(2)	6.7(1)	O66	0.0927(5)	0.1489(3)	0.3494(2)	8.8(1)
OW1	1.0083(4)	0.1162(4)	0.2491(2)	7.4(1)	OW3	0.5024(4)	0.1714(6)	0.7104(3)	15.3(2)
OW2	1.0040(4)	0.1454(5)	0.5330(2)	9.1(2)	OW4	0.9447(5)	−0.2145(5)	0.6099(3)	11.9(2)

Table 2
Ring conformations

Atomic sequence	$\theta(^\circ)$	Q(Å)	$\varphi(^\circ)$	Displacement (Å)	
				C1	C4
O51-C11·····C51	8.7(4)	0.548(4)	60(3)	0.692(4)	−0.576(4)
O52-C12·····C52	6.1(5)	0.562(4)	96(4)	0.687(4)	−0.626(4)
O53-C13·····C53	6.0(5)	0.565(5)	57(4)	0.695(5)	−0.622(4)
O54-C14·····C54	6.7(5)	0.568(4)	81(4)	−0.702(5)	0.616(4)
O55-C15·····C55	6.2(4)	0.555(4)	43(4)	−0.684(4)	0.610(4)
O56-C16·····C56	4.1(5)	0.568(5)	313(6)	−0.649(4)	0.679(4)

> 3.4 Å) are present between the molecules head to tail arranged (screw symmetry along *b* axis). The four ordered water molecules, placed outside the void of α-CD torus, are each involved in three H-bonds (double donor an single acceptor) except W-4 whose H′ hydrogen points at the disordered region. The connectivity diagram of H-bonding interactions (Fig. 5) shows the presence of both the motifs, infinite chain and loops, typical of cyclodextrin hydrate crystals [25]. W-2 and W-4 are also connected to disordered region forming a virtual infinite chain: ·····O-22→W-4→disordered region→W-2→O-63·····.

The α-CD arrangement is like that observed in the *p*-iodoanilide trihydrate complex that crystallises in an isomorphous unit cell [7]. This ''brick

Table 3
Conventional torsion angles about the glycosyl bonds (°)

	ϕ		ψ
O41–C11-O42–C42	174.3(7)	C11–O42-C42–O43	−170.9(6)
O42–C12-O43–C43	−179.8(8)	C21–O43-C43–O44	−175.7(6)
O43–C13-O44–C44	166.1(8)	C31–O44-C44–O45	−175.8(6)
O44–C14-O45–C45	167.4(8)	C41–O45-C45–O46	−171.9(6)
O45–C15-O46–C46	172.4(7)	C51–O46-C46–O41	−172.8(6)
O46–C16-O41–C41	161.1(5)	C61–O41-C41–O42	−165.8(7)

type'' packing [18,27] presents cyclodextrin cavities blocked on both ends by rims of molecules arranged in the adjacent layers. This packing type is analogous to the 'class 2A' channel structures [27] and the present structure could be also described as a *pseudo* 'channel type' with two different types of channels, as schematised in Fig. 6. One type (***A***) is formed outside the CD cavities and holds two of the ordered water molecules. The other type (***B***) involves alternately inside and outside the cavities of α-cyclodextrins and includes disordered solvent regions together with the remaining two ordered waters. However the channels present between the ordered waters short narrowing sections, diameter 2 Å, that not permit the free transfer of guest molecules.

In conclusion, on the basis of geometrical and conformational features, the present structure is an

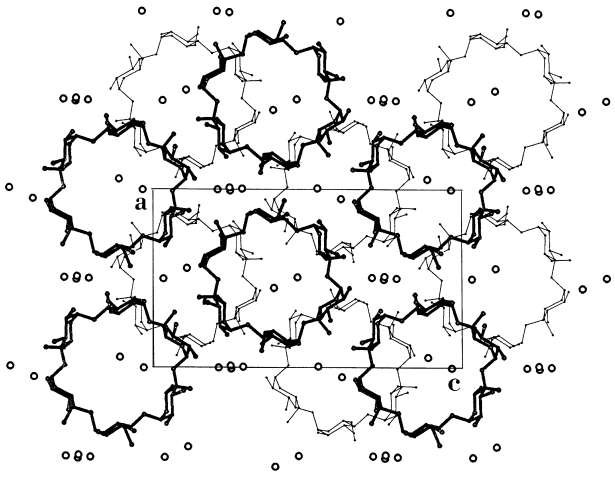

Fig. 3. Molecular packing projected onto *ac* plane. Thick and thin lines indicate two subsequent α-CD layers along the *b* axis.

example, together with the form III α-CD hydrate [20], of intermediate round α-CD in the relaxed shape suitable to form an inclusion complex, according to the mechanism proposed by Saenger et al. [18,21]. The α-cyclodextrin takes a symmetrical conformation and its extended round-shape is stabilised by all the six intramolecular H-bonds without particular tilt of one of the glucosyl residues. The relaxed structural form of α-CD is considered a transition state ready for complex

Table 4
Hydrogen-bonding geometry

D–H·····A (Å)	D·····A (Å)	H·····A (Å)	D–H·····A (°)	Acceptor symmetry
O21-H·····O32	2.804(5)	1.91	154	x,y,z
O31-H·····O33	2.687(4)	1.91	136	x−1/2,−1/2−y,1−z
O61-H·····OW2	2.760(7)	1.84	159	x−1,y,z
O22-H·····OW4	2.649(7)	1.73	160	x,y,z
O32-H·····O26	2.934(4)	1.98	170	1/2+x,−1/2−y,1−z
O62-H·····O66	2.975(6)	2.01	179	1/2+x,1/2−y,1−z
O23-H·····O21	2.825(5)	1.87	173	1/2+x,−1/2−y,1−z
O33-H·····O22	2.656(5)	1.71	166	x,y,z
O63-H·····O66	2.854(7)	1.91	167	1+x,y,z
O42-H·····O35	2.937(6)	2.00	165	x,y,z
O34-H·····O23	2.875(5)	1.95	161	x,y,z
O64-H·····O32	2.818(5)	1.91	157	3/2−x,−y,z−1/2
O25-H·····OW3	2.662(7)	1.74	160	1/2−x,−y,z−1/2
O35-H·····O61	2.828(5)	1.90	163	1/2−x,−y,z−1/2
O65-H·····O31	2.891(5)	2.05	145	1/2−x,−y,z−1/2
O26-H·····O31	3.095(5)	2.16	165	x,y,z
O36-H·····O25	2.836(5)	1.94	155	x,y,z
O66-H·····OW1	2.740(7)	1.82	160	x−1,y,z
OW1-H·····O64	2.904(7)	1.98	162	x,y,z
OW1-H′·····O21	2.864(6)	1.93	162	3/2−x,−y,z−1/2
OW2-H·····O63	2.773(7)	1.84	162	x,y,z
OW2-H′·····O24	3.226(8)	2.42	141	3/2−x,−y,1/2+z
OW3-H·····O62	2.784(8)	1.83	176	x,y,z
OW3′-H′·····O23	3.194(7)	2.23	177	3/2−x,−y,1/2+z
OW4-H·····O65	2.794(8)	1.85	167	3/2−x,−y,1/2+z

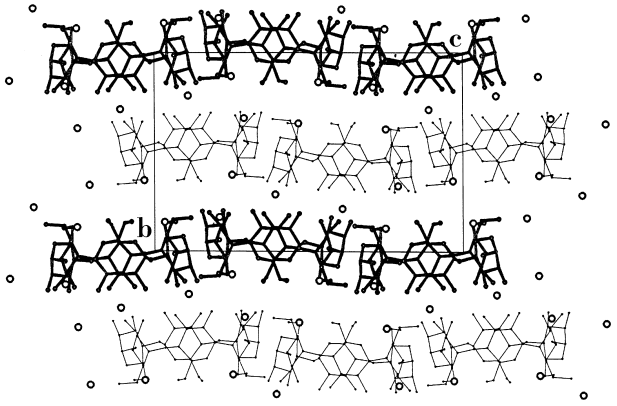

Fig. 4. Molecular arrangement seen along the *a* axis. In each layer α-CD toroids are overturned alternately.

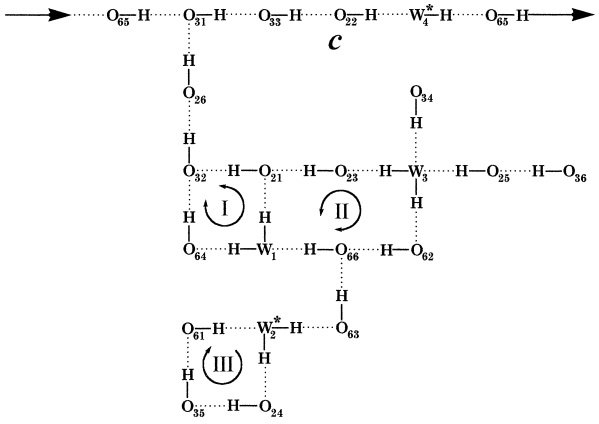

Fig. 5. Connectivity diagram of hydrogen bonding showing an infinite homodronic chain (***C***) running along the *a* axis with screw symmetry and three loops: antidromic four membered (I) fused with an antidromic six membered (II), homodromic four membered cycle (III). The waters with asterisk are connected also to disordered region forming a virtual infinite homodronic chain running with screw symmetry along the *c* axis.

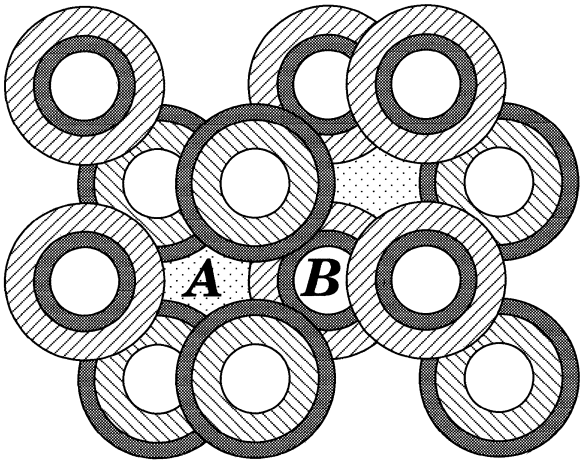

Fig. 6. Schematic drawing showing the two different *pseudo*-channels, ***A*** and ***B*** type.

formation ('induced-fit' type) and appears not to crystallise from pure water but needs presence of salt (form III) or organic molecule (present form IV). An explanation for this molecular arrangement can be tried assuming that the guest substance is present during crystal nucleation and determines the conformational change of α-cyclodextrin, as well as the molecular arrangement in the solid state. During the growth of crystals the guest is displaced by water, probably due to low concentration of guest in the crystallisation batches and not highly specific host–guest interactions. The water is however obliged to arrange in a space already moulded by the guest molecule (before present in the crystal nucleation) and can fill it only partially and in a random way.

References

[1] (a) W. Saenger, Chemical and physical studies on cyclodextrin inclusion compounds, in O. Huber and J. Szejtl (Eds.), *Proceedings of the Fourth International Symposium on Cyclodextrins*, Kluwer, Dordrecht, 1988, pp. 159–164: (b) W. Saenger, *Agnew. Chem. Int. Ed. Engl.*, 19 (1980) 344–362.

[2] G. Wenz, *Angew. Chem. Int. Ed. Engl.*, 33 (1994) 803–822.

[3] Song Li and W.C. Purdy, *Chem. Rev.* 92 (1992) 1457–1470 and references therein cited.

[4] F.P. Tomasella, P. Zuting, and L.J. Cline Love, *Supramolecular Chem.*, 1 (1992) 25–30.

[5] O. Ortona, L. Paduano, L. Costantino, and V. Vitagliano, *J. Mol. Liquids*, 63 (1995) 291–297.

[6] D. Ciccarelli, L. Paduano, L. Costantino, O. Ortona, and V. Vitagliano, *J. Mol. Liquids*, 75 (1998) 169–180.

[7] W. Saenger, K. Beyer, and P.C. Manor, *Acta Crystallogr., Sect. B*, 32 (1976) 120–128.

[8] K. Harata, *Bull. Chem. Soc. Japan*, 52 (1979) 2451–2459.

[9] A. Altomare, G. Cascarano, C. Giacovazzo, and A. Guagliardi, *J. Appl. Cryst.*, 26 (1993) 343–350.

[10] E. Wehman, G. van Koten, J.T.B.H. Jastrzebski, M.A. Rotteveel, and C.H. Stam, *Organometallics*, 7 (1988) 1477–1485.

[11] P. van der Sluis and L. Spek, *Acta Crystallogr., Sect. A*, 46 (1990) 194–201.

[12] L. Pauling, *The Nature of the Chemical Bond*, 1960, Cornell University Press, Ithaca, N.Y.

[13] G.H. Stout and L.H. Jensen, *X-ray Structure Determination*, Macmillan, New York, 1968, pp. 409–412.

[14] R.C.G. Killean and J.L. Lawrence, *Acta Crystallogr., Sect. B*, 25 (1969) 1750–1752.

[15] D.T. Cromer and J.T. Waber, *International Tables for X-ray Crystallography*, Vol. IV, Kynoch Press, Birmingham 1974 (present distributor Kluwer Academic Publishers, Dordrecht, The Netherland).
[16] B.A. Frenz and Associates, Inc., *SDP Structure Determination Package*, College Station, TX, and Enraf-Nonius, Delft, The Netherlands, 1985.
[17] W. Saenger, Environmental Effects on Molecular Structure and Properties, in B. Pullman (Ed.), *The Jerusalem Symposia on Quantum Chemistry and Biochemistry, VIII*, Dordrecht, The Netherlands, 1976, pp. 265–305.
[18] W. Saenger, Structural aspects of cyclodextrins and their inclusion complexes, in J.L. Atwood. J.E.D. Davies and D.D. MacNicol (Eds.), *Inclusion Compounds*, Vol. 2, Academic Press, London, 1984, pp. 232–259.
[19] B. Klar, B. Hingerty, and W. Saenger, *Acta Crystallogr., Sect. B*, 36 (1980) 1154–1165.
[20] K.K Chacko and W. Saenger, *J. Am. Chem. Soc.*, 103 (1981) 1708–1715.
[21] K. Lindner and W. Saenger, *Acta Crystallogr., Sect. B*, 38 (1982) 203–210.
[22] D. Cremer and J.A. Pople, *J. Am. Chem. Soc.*, 97 (1975) 1754–1758.
[23] J.A. Jeffrey and J.H. Yates, *Carbohydr. Res.* 74 (1979) 319–322.
[24] K. Lindner and W. Saenger, *Carbohydr. Res.* 99 (1982) 103–115.
[25] G.A. Jeffrey and W. Saenger, *Hydrogen Bonding in Biological Structures*, Springer–Verlag, Berlin, 1991.
[26] T. Steiner and W. Saenger, *Carbohydr. Res.*, 259 (1994) 1–12: *Carbohydr. Res.*, 266 (1995) 1–3.
[27] R.K. McMullan, W. Saenger, J. Fayos, and D. Mootz, *Carboydr. Res.*, 31 (1973) 37–46.