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Note

The dimeric complex of cyclomaltoheptaose with 1,14-tetradecanedioic acid. Comparison with related complexes

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Abstract

The structure of the complex of cyclomaltoheptaose (β-cyclodextrin, βCD) with 1,14-tetradecanedioic acid has been determined and refined to a final $R = 0.0693$ based on 9824 observed reflections. Each diacid molecule threads through two βCD monomers arranged in dimers thus, forming a [3]pseudorotaxane. The end carboxylic groups of adjacent dimers, far apart and fully hydrated, are associated indirectly through water molecules. The positioning of the carboxylic groups with respect to the βCD dimer and the H-bonds with water molecules are very similar to these of the corresponding complexes of the diacids with 12 and 13 carbon atoms. The bending in the middle of the aliphatic chain is more prominent, compared to that of the corresponding guests with less carbon atoms, thus the end carboxylic groups stay in the same height of the primary faces of the βCD dimeric complex. As a consequence of the present structure, more close contacts are observed between calculated H-atoms of the guest and O-atoms of the host inside the cavity. This bending is allowed by the width of the βCD dimer cavity at the secondary interface region.

Keywords: β-Cyclodextrin; 1,14-Tetradecanedioic acid; Dimeric inclusion complex; [3]Pseudorotaxane

1. Introduction

Cyclomaltohexaose and cyclomaltoheptaose (α- and β-cyclodextrins, αCD and βCD, respectively) enclose long aliphatic molecules forming [3]pseudorotaxanes,[1]], the [3] referring to the number of the individual molecules associated. These are supermolecules composed of two βCD macrocycles forming a dimer and one guest molecule spanning the whole length of the dimer's cavity.[2–8] The overall shape of the dimeric βCD complexes of aliphatic monocarboxylic acids and a,ω-dicarboxylic acids with 12–16 carbon atoms ([3]pseudorotaxanes) is the same.[3–6] However, their crystal packing is different. Monoacid complexes form isomorphous crystals and the [3]pseudorotaxanes stack one on top of the other and create infinite hydrophobic channels, inside of which carboxylic ends form carboxylic dimers.[3,4] In the diacids,[5,6] whose crystals are again all isomorphous, they are further apart and the carboxylic groups are fully hydrated. It has been shown by NMR spectroscopy studies on inclusion complexes

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of αCD/α,ω-bifunctional guests[7] that [3]pseudorotaxanes exist in solution as well.

In the crystalline state, the association of two βCD monomers to form a dimer involves H-bonding only between the O-3 secondary hydroxyl groups.[6] In the same report, it was shown how the dense network of complementary intra and intermolecular strong H-bonds between the secondary hydroxyl groups of the two monomers forms the intradimer interface. As a result, the βCD dimer behaves like a stable entity, in the shape of a barrel. The external side surface of the barrel is not influenced by the guest. Indeed, it was observed[9,10] that, in the dimeric βCD inclusion complexes, there exists a semi-invariant network of H-bonds around the dimers, as they interact with each other and with water molecules to form 2D layers independent of the nature of the guest. Moreover, the extensive H-bonding of secondary hydroxyls among themselves and with water molecules at the outside of the dimer does not seem to allow interaction between guests and secondary hydroxyls in the inside of the cavity. Thus the secondary interface behaves like an extension of the hydrophobic cavity of the βCD monomers and accommodates perfectly well hydrophobic parts of guest molecules. On the other hand, in the primary faces of the dimers, top and bottom of barrels, the presence of the guest is crucial because it induces or forbids interactions of these faces with the environment (primary hydroxyls and/or water molecules) depending on its nature, and thus it influences the association of the 2D layers in forming the 3D lattice.[3]

Table 1
Crystal data and structure refinement

Molecular formula	$(C_{42}H_{70}O_{35})_2\cdot C_{14}H_{26}O_4\cdot (H_2O)_{21.86}\cdot (C_2H_6O)_{0.42}$
Formula weight	2941.51
Temperature (K)	293
Radiation/wavelength (Å)	1.5418
Space group	$P1$
a (Å)	18.242(1)
b (Å)	15.492(1)
c (Å)	15.436(1)
α (°)	102.755(3)
β (°)	113.010(2)
γ (°)	99.780(3)
V (Å^3)/Z	3753.5(5)/1
D_{calcd} (Mg/m^3)	1.301
2θ Range for data collection (°)	6.4–110.06
Index ranges	$-19 \leq h \leq 19$, $-16 \leq k \leq 0$, $-15 \leq l \leq 16$
Reflections collected/independent	9833/9824
R_{int}	0.025
Solution method	isomorphous molecular replacement
Refinement method	full-matrix least-squares on F^2
Data/restraints/parameters	9824/76/1842
Goodness-of-fit on F^2	1.079
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0693$, $wR_2 = 0.1882$
R indices (all data)	$R_1 = 0.0765$, $wR_2 = 0.2021$
Largest difference peak and hole (e/Å)	0.590 and −0.465

The present contribution is part of a systematic study of βCD inclusion complexes with long aliphatic α,ω-bifunctional molecules in order to determine how the nature of the guest's terminal groups and its length influences the channel forming ability of βCD dimers.

2. Results and discussion

The inclusion complex of 1,14-tetradecanedioic acid(C_{14}) in β-cyclodextrin is composed of a dimer of βCD, through which a molecule of the aliphatic acid, disordered over two sites (a and b), has been threaded. This geometry is the same as in the corresponding βCD complexes of dodecanedioic acid(C_{12}),[6] tridecanedioic acid(C_{13}),[5] as well as the diacids with 15 and 16 carbon atoms, whose structures have not been determined but they are isomorphous so they must have the same overall shape. Crystallographic data are summarized in Table 1. The numbering scheme for the βCD molecules is given in Fig. 1; C(A or B)*mn* and O(A or B)*mn* denote the *m*th atom within the *n*th glucosidic residue (Gn) of the crystallographically independent βCD molecules A and B. The dimer's sevenfold axis forms an angle of 20° with the *a*-axis (Fig. 2). As a result, the dimers do not stack on top of each other to form channels and the primary faces are accessible to water molecules. Consequently, the carboxylic groups of the guests are displaced by about 7.5 Å and do not form direct H-bonds.

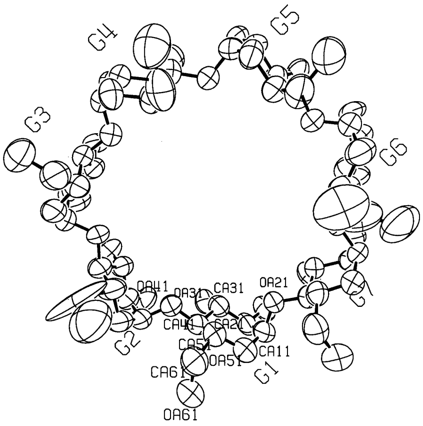


Fig. 1. ORTEP[13] diagram of βCD molecule A showing the atom numbering scheme. Displacement ellipsoids are plotted at the 50% level.

Geometry of the host.—The pyranose rings of βCD have the $^4C_1$ conformation with the (−)-gauche conformation for the primary hydroxyl groups, except for two hydroxyls of molecule A, these of residue G2 and the disordered site (OA-66b) of G6, which have the (+)-gauche conformation and point inwards. The host molecules posses near sevenfold symmetry. The values of the angle between the glucosidic oxygen atoms O-4n do not differ significantly from 128.57°, the angle of the regular heptagon, and the deviations (d) of the O-4n atoms from their optimum plane are close to zero, while the glucose units tilt very regularly towards the sevenfold axis. The conformation of each βCD macrocycle is stabilized[9] through intramolecular hydrogen bonds connecting the O-3n and O-2$(n+1)$ atoms of neighboring glucosidic units (average O-3n···O-2$(n+1)$ distances 2.79 Å). Their angles, C-3n–O-3n···O-2$(n+1)$ (average 116.4°) and O-3n···O-2$(n+1)$–C-2$(n+1)$ (average 118.5°), lie within the normal values for H-bonds. The βCD dimer is formed via OA-3n···OB-3$(8-n)$ H-bonds[6] with an average distance 2.82 Å. The angles CA-3n–OA-3n···OB-3$(8-n)$ and OA-3n···OB-3$(8-n)$–CB-3$(8-n)$ have mean values 118.5 and 118.4°, respectively.

H-bonding network and solvent molecules.—The βCD dimers form 2D layers in the $[b, c]$ plane.[9,10] There are seven direct H-bonds among hydroxylic groups of adjacent host dimers (Table 2(a)), of which six bind hydroxyl groups in the 2D layers: Three along the c-axis, OA-27···OB-25, OA-63···OA-67 and OB-61···OB-65 and three along the b-axis, OA-25···OB-27, OB-63···OB-67 and OA-65···OA-61. Four of the above bonds, OA-27···OB-25, OA-25···OB-27, OA-63···OA-67 and OB-63···OB-67, are observed in all dimeric βCD complexes irrespective of the crystal packing and they characterize the 2D layers. The layers stack in the intermediate packing mode[9] with the centers of consecutive dimers laterally shifted by 6.0 Å. The seventh direct H-bond, OA-62···OB-62, is the only one between βCD dimers of adjacent 2D layers, as in the other inclusion complexes packed in the intermediate mode, and it involves OA-62 pointing inwards both in this structure and in structures C_{12} and C_{13}, thus justifying the inwards orientation of this hydroxyl. This direct H-bond does not occur in the case of the long aliphatic monocarboxylic acids which pack in channels.[3]

There are 19 water molecules in the asymmetric unit distributed over 32 sites around the βCD dimer and 30 of them are within H-bonding distance from oxygen atoms of the hydroxylic groups as shown in Table 2(b). The water sites have been labeled from the number of the closest oxygen atom to which they are H-bonded. H-bonding distances 2.40–3.14 Å and angles C–O(H)···O(water) of 90–130° are assumed in order to compare with other published structures with related guest molecules. The angle range, although quite wide, is justifiable because of the usual disorder accompanying water molecules and the inability to locate their H-atoms.[9] Finally, one ethanol molecule with occupancy of 42% has been found in the crystal lattice but no participation in the H-bonding scheme has been detected up to 3.14 Å. However, it forms a very weak H-bond with the primary hydroxyl OB-66 of βCD (3.48 Å).

Guest geometry and interactions with its environment.—Both orientations of the guest have a bend in the middle of the aliphatic chain (Fig. 3). The width of the βCD cavity, particularly in the secondary interface, allows this, since in analogous inclusion complexes of α-cyclodextrin[7,8] the aliphatic chain has a regular zig–zag shape and it is not disordered. Comparing the guest geometry in the present structure with that of the aliphatic diacids in C_{12}[6] and C_{13},[5] we note the following: The sum of distances d_1 and d_2 (Scheme 1 and Table 3), which are the mean distances of the two carboxylic oxygen atoms from the planes formed by the glucosidic atoms O-4 of the closest βCD monomers, does not increase as the number of the carbon atoms of the guest increases (Table 3). Thus, although the length of the guest increases, its polar ends do not protrude more from the βCD primary faces, because its aliphatic middle part curls and bends more inside the cavity. Indeed, in the present structure there exist ten distances in the range 2.60–2.99 Å between calculated H-atoms of the guest (exclusively at the middle of the aliphatic chain) and O-atoms of the host in the interior of the cavity as compared to three for the C_{12} (2.78–2.89 Å) and two for the C_{13} acid (2.83–2.95 Å).

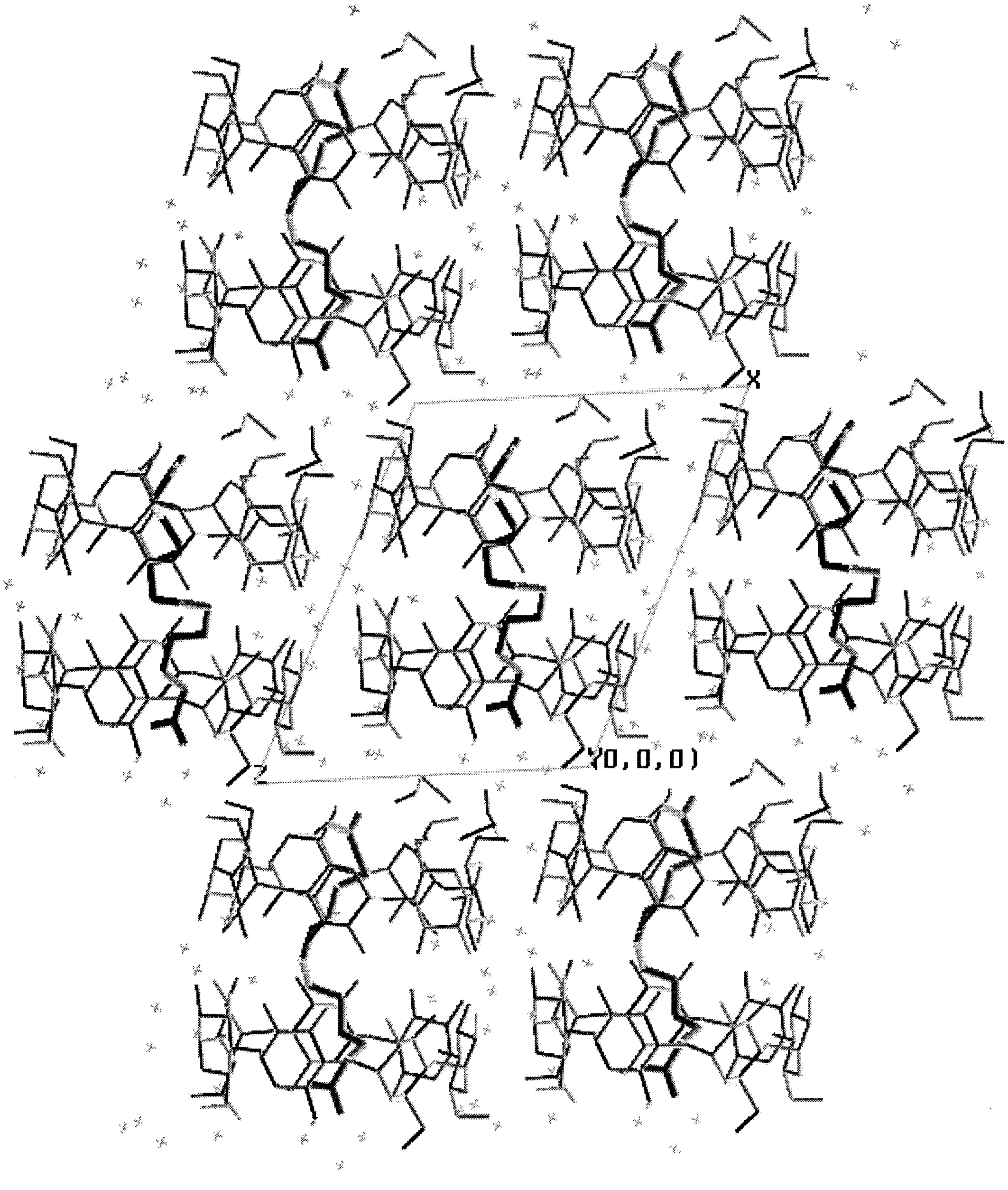


Fig. 2. The packing of the βCD-1,14-tetradecanedioic acid complex molecules. The two disordered positions of the diacids are shown (bold) in the different layers. Water molecules are shown as stars and the ethaanol molecule (occupancy 42%) as wireframe in the lattice.

Table 2
Hydrogen bonds of the βCD-1,14-tetradecanedioic acid complex

O*mn*···O*m*′*n*′	O*mn*···O*mn*′	C*mn*–O*mn*···O*mn*′		O*mn*···O*mn*′–C*mn*′	
	Distance (Å)	Angle (°)		Angle (°)	
(a) Direct hydrogen-bonds between dimers					
OB-25···OA-27^{I}	2.773(6)	110.3(4)		109.4(4)	
OA-67···OA-63^{ii}	2.780(9)	127.5(5)		109.2(5)	
OB-65···OB-61^{i}	2.94(1)	128.1(5)		108.6(5)	
OB-27···OA-25^{iii}	2.771(9)	111.5(4)		107.1(4)	
OB-67···OB-63^{iii}	2.811(9)	130.2(5)		110.1(5)	
OA-65···OA-61^{iv}	2.91(1)	128.2(5)		107.9(5)	
OA-62···OB-62^{v}	2.76(1)	127.3(5)		98.0(5)	
Molecule A	Distance (Å)	Angle (°)	Molecule B	Distance	Angle
(b) Hydrogen-bonds between βCD hydroxyls, OA(B)nm and water molecules, OnmA(B)					
OA-21···O-21A	2.67(1)	108.1(5)	OB-21···O-21B	2.72(1)	109.5(5)
OA-22 ···O-22A	2.74(2)	99.7(4)	OB-22···O-22B	2.75 (2)	97.9(4)
OA-23···O-23A	2.94(2)	109.6(4)	OB-23···O-23B	2.80(2)	109.7(4)
OA-24···O-24A	2.75(1)	98.2(6)	OB-24···O-24B	2.74(2)	95.6(6)
OA-26···O-26A	2.77(4)	102.5(4)	OB-26···O-26B	2.92(4)	102.8(2)
			OB-26···O-21B	3.12(3)	121.0(5)
OA-34···O-22A	2.87(2)	110.0(6)	OB-34···O-22B	2.82(2)	110.6(7)
OA-35···O-21A	2.90(1)	116.3(4)	OB-35···O-21B	2.92(1)	118.7(4)
OA-36···O-24A	2.86(1)	112.2(4)	OB-36···O-24B	2.92(1)	109.4(4)
OA-61···O-61A_1	2.72(1)	116.6(4)	OB-61···O-61B	2.85(2)	103.0(4)
OA-61···O-61A_2	2.76(2)	103.5(4)	OB-61···O-64B	2.75(1)	117.3(4)
OA-61···O-64B_2	2.66(4)	99.7(5)			
OA-62···O-67B	2.79(1)	106.2(9)	OB-62···O-61A_1	2.74(1)	103.5(4)
OA-63···O-63A	2.74(3)	113.7(4)	OB-63···O-67A	2.78(1)	103.5(4)
			OB-63···O-66B_2	3.05(4)	118.3(5)
OA-64···O-64A_1	2.68(6)	128.3(6)	OB-64···O-64B_1	2.74(1)	114.0(6)
OA-64···O-64A_2	2.70(4)	112.0(5)	OB-64···O-64B_2	2.52(4)	120.1(5)
OA-64···O-61A_1	2.74(1)	107.2(5)			
OA-65···O-65A	2.75(1)	125.2(6)	OB-65···O-65B	2.76(1)	124.7(6)
OA-66b···O-66A_1	2.8(1)	106(2)	OB-66···O-66B_1	2.37(5)	136.8(8)
OA-66b···O-66A_2	2.83(9)	107(1)	OB-66···O-66B_2	2.66(6)	108.0(8)
OA-66b···O-66A_3	3.01(4)	141(2)	OB-66···O-66B_3	3.01(7)	101.0(8)
OA-66b···O-66A_4	3.11(4)	103(2)			
OA-66a···O-63A	2.91(2)	113(1)			
OA-67···O-67A	2.72(1)	121.0(4)	OB-67···O-67B	2.73(4)	125.1(3)
Molecule a	Distance (Å)	Angles (°)	Molecule b	Distance (Å)	Angles (°)
(c) Hydrogen bonds between guest's carboxylic groups and water molecules					
O-1a···O-66A_2	3.11(7)	120.1(3)	O-1b···O-66A_2	2.82(6)	107(3)
O-1a···O-66A_3	3.28(7)	137.1(5)			
O-2a···O-61B	2.75(5)	121.6(1)	O-2b···O-61B	3.19(5)	126.2(1)
			O-2b···O-66A_2	3.23(6)	88.8(3)
O-3a···O-63A	3.04(2)	96.6(1)	O-3b···O-64A_1	3.22(5)	128.5(2)
O-3a···O-66A_4 [a]	2.16(1)	100(2)	O-3b···O-63A	3.23(5)	129.7(1)
O-4a···O-W4	3.02(7)	114(8)	O-4b···O-66A_1	2.7(1)	155.6(9)
O-4a···O-66A_4	2.578	165.8			

(i) x, y, $z-1$; (ii) x, y, $z+1$;(iii) x, $y-1$, z; (iv) x, $y+1$, z; (v) $x+1$, $y+1$, $z+1$.

[a] Since the occupancies of guests a or b, O-66A-4 are 50%, the molecules might not coexist.

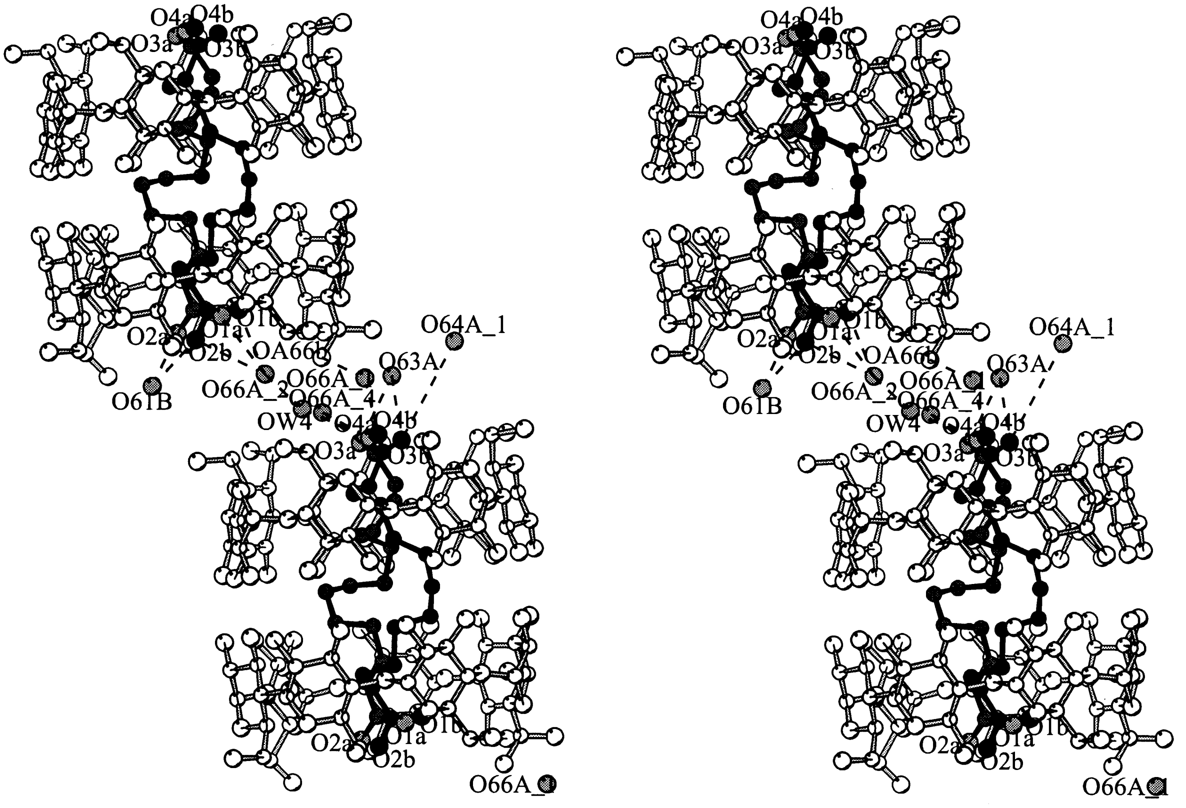
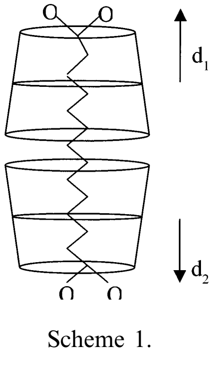


Fig. 3. Stereo view (drawn by program MOLSCRIPT[14]) of the hydrogen-bonding around the carboxylic groups in the interface of two layers of dimers. Both positions of the guest are shown. OA-66b is the only disordered primary hydroxylic group of βCD.

The carboxylic groups of the guest in its two disordered positions are stabilized by multiple H-bonds with water molecules intervening between the dimers along the *a*-axis (Table 2(c)). No direct H-bonding is observed between the carboxyls of two consecutive complexes as in the case of the aliphatic monoacids. Nevertheless, they interact via a chain of two water molecules in one of the primary interfaces (O-4a···OW-4···O-66A_2···O-1b), as shown in Fig. 3. At the alternative interface, carboxylic oxygen atoms O-1a (or O-2a) and O-4b (or O-3b) are not connected through water molecules, instead O-4b interacts via water O-66A_1 with the disordered hydroxyl group OA-66b. This explains why this second hydroxyl points toward the interior of the cavity. The same network of hydrogen bonds is also formed at the primary interfaces of the corresponding diacid complexes C_{12} and C_{13} around the carboxylic groups.

3. Experimental

Crystallization of the complex.—The complex was prepared by adding 1,14-tetradecanedioic acid to an aqueous solution of βCD, to a 2.5:1 host–guest ratio. The precipitate was redissolved in a mixture of water and EtOH at 70 °C and was allowed to return to rt over a period of 6 days at the end of which colorless crystals were formed.



Scheme 1.

Table 3
Sum of the average distances of the carboxylic oxygen atoms from the O-4 mean planes of the closest βCD monomer

Guest	Molecule a	d_1	d_2	Molecule b	d_1	d_2
C_{12}^{6}	5.2	3.85 (1)	1.35 (1)	4.91	3.07 (1)	1.83 (1)
C_{13}^{5}	5.59	3.64 (2)	1.86 (2)	5.07	3.09 (2)	1.98 (2)
C_{14}	4.96	2.92 (2)	2.04 (2)	4.88	2.90 (2)	1.98 (2)

X-ray structural analysis.—The crystals were colorless intergrown plates but it was possible to obtain a single crystal by separating the plates into thinner ones. A single crystal of dimensions 0.5 × 0.5 × 0.2 mm was enclosed in a glass capillary and data were collected at ambient temperature from a Syntex four-cycle $P2_1$ diffractometer using Cu K_α radiation ($\lambda = 1.5418$ Å). The cell dimensions were obtained by least-square analysis of 52 reflections in the range $24 < 2\theta < 54°$. A hemisphere of data was collected by the $\theta - 2\theta$ scan mode to $2\theta \approx 110°$ with a speed of 4.5°/min. Three standard reflections, monitored every 97 reflections, showed no decay in intensity during data collection. The structure was solved using the skeleton coordinates of the isomorphous inclusion complex of βCD with 1,13-tridecanedioic acid.[5] The remaining host atoms, followed by the solvent molecules, were found by consecutive difference Fourier calculations. The structure was refined isotropically by full-matrix least-squares (SHELX-97)[11] to an R-factor 13.7%. One primary oxygen atom of the βCD was disordered. Anisotropic thermal parameters were assigned to all C-6 and O-6 atoms of the host, as well as the O-atoms of the water molecules at that point and calculated hydrogen atoms were introduced to the βCD with temperature factors of 1.2 of the corresponding atoms to which they were bonded. More water positions were revealed, as the refinement continued up to R-factor 10.6% and a difference Fourier map revealed the guest atoms. Four distinct lobes appeared to be the positions of the carboxylic oxygen atoms in each side of the cyclodextrin dimer indicating a disordered guest molecule. Alkyl chain atoms were also found but the resulting geometries were distorted, because some atoms in the two orientations of the guest were close together. Thus from the existing peaks, two models for the guest were generated (guest-a and guest-b) and their geometries were optimized by fitting in the difference Fourier map using the graphics program ‘O’.[12] Then a rigid body refinement of the guest followed and the occupancy factors of guest molecules a and b were refined to 51 and 49%, respectively. All guest atoms were left isotropic and calculated hydrogen atoms were added to the carbon atoms. No further refinement of the guest was done except for the isotropic temperature factors at the end of the whole procedure. The full-matrix least-squares refinement continued to a final R factor of 0.0693.

4. Concluding remarks

Aliphatic a,ω-diacids with 12–16 carbon atoms form [3]pseudorotaxanes with βCD that pack in the same way in the crystalline state: their end carboxylic groups are fully hydrated and they associate indirectly through water molecules. The H-bonds with water molecules are the same for inclusion complexes of diacids with 12, 13 and 14 carbon atoms. Moreover, the positioning of the carboxylic groups at the primary faces of the βCD dimers is very close for the three complexes. It seems that the very dense network of H-bonds formed by the carboxylic groups at the observed positions offers high stabilization and forces the aliphatic part of the molecules, especially at the middle, to bend more as the number of carbon atoms increases. This is indicated by the increased number of contacts between host–guest in the case of the C_{14} complex. This bending is possible due to the width of the βCD cavity at the secondary interface region.

5. Supplementary material

Full crystallographic details have been deposited with the Cambridge Crystallographic data Centre, deposition no. CCDC 166671. The data may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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