Available online at www.sciencedirect.com
SCIENCE DIRECT®
Carbohydrate Research 338 (2003) 781–785
CARBOHYDRATE RESEARCH
www.elsevier.com/locate/carres

Crystal structure of the dimeric β-cyclodextrin complex with 1,12-dodecanediol

Tzvetana Bojinova,[a] Heinz Gornitzka,[b] Nancy Lauth-de Viguerie,[a,*] Isabelle Rico-Lattes[a]

[a] *Laboratoire des Interactions Moléculaires et Réactivité Chimique et Photochimique (UMR 5623), Bâtiment 2R1, Université Paul Sabatier, 118 route de Narbonne, F-31062 Toulouse, France*
[b] *Laboratoire d'Hétérochimie Fondamentale et Appliquée (UMR 5069), Bâtiment 2R1, Université Paul Sabatier, 118 route de Narbonne, F-31062 Toulouse, France*

Received 23 November 2002; accepted 29 December 2002

Abstract

The structure of the complex of β-cyclodextrin (β-CD) with 1,12-dodecanediol has been determined at 173 K and refined to a final $R = 0.0615$ based on 22,386 independent reflections. The complex crystallizes in the triclinic space group $P\bar{1}$ with $a = 17.926(4)$, $b = 15.399(3)$, $c = 15.416(3)$ Å, $\alpha = 103.425(4)$, $\beta = 113.404(4)$, $\gamma = 98.858(4)°$, $D_c = 1.362$ Mg cm^{-3} and $V = 3651.4(13)$ Å^3 for $Z = 1$. One molecule of the diol is located as a guest in the hydrophobic cavity of a β-CD-dimer, forming a [3]pseudorotaxane. The guest molecule shows a disorder over two positions. The hydroxyl groups of the diol emerge from the primary faces of the β-CD dimer and form several hydrogen bonds with water molecules lying in the interstitial space, similarly to dimeric complexes of β-CD with other α,ω-bifunctional guests. © 2003 Elsevier Science Ltd. All rights reserved.

Keywords: β-Cyclodextrin; 1,12-Dodecanediol; Inclusion complexes; X-ray structures; [3]Pseudorotaxane

1. Introduction

Cyclomaltoheptaose (β-Cyclodextrin, β-CD) is a cyclic oligosaccharide with seven α-(1 → 4)-linked D-glucopyranose units[1,2] which is well known for its ability to form inclusion complexes with a great variety of molecules.[3,4] In the case of small guest molecules (up to nine carbon atoms and aromatic systems) a 1:1 complexation is observed. More recently, interest has focused on the cyclodextrin-based supramolecules in which long 'linear' molecules penetrate the cavities of dimeric CDs in a non-covalent way to form rotaxanes or pseudorotaxanes.[5] In rotaxanes, the linear molecule (the guest) has a bulky stopper group added to the thread's extremities to prevent its unthreading, while in pseudorotaxanes no stopper is present.[6] The overall shape and packing of the β-CD macrocycle in crystal lattices are affected by the size and character of the respective guest molecule. The elucidation of the spatial structures of inclusion complexes is essential for understanding the interactions between the three molecules and the mechanism of complex formation. Four packing modes of β-CD dimeric complexes have been observed: channel, screw-channel, chessboard, intermediate.[7]

Dimeric β-CD complexes have been reported in the literature with guests such as linear long aliphatic α,ω-dicarboxylic acids[8–10] and long linear aliphatic monocarboxylic acids.[11] The α,ω-dicarboxylic acids with 10–16 carbon atoms induce intermediate packing of the β-CD dimeric complexes, while monoacids with 12–16 C-atoms show channel type packing. With monoacids, the carboxyl groups build dimers and this effect is responsable for the formation of channels. In complexes with diacids, the carboxyl groups are fully hydrated by environmental water molecules and no direct contact is observed between the guest molecules, which explains a different type of packing. When the guest is

---

* Corresponding author. Tel.: + 33-5-61556135; fax: + 33-5-61558155
E-mail address: viguerie@chimie.ups-tlse.fr (N. Lauth-de Viguerie).

doi:10.1016/S0008-6215(03)00013-2

a long aliphatic diamine (1,12-diaminododecane), the polar groups are outside of the cavities of the CD dimer giving a intermediate type packing.[12]

In order to get more information about the influence of guest properties on crystal packing, we studied the complexation of β-CD with 1,12-dodecanediol.

2. Experimental

2.1. Preparation and crystallization of the complex

Colorless crystals of the title complex were obtained from a 10^{-2} M solution of β-CD·11H$_2$O (purchased

Table 1
Crystal data and structure refinement

Empirical formula	$(C_{42}H_{70}O_{35})_2 \cdot C_{12}H_{26}O_2 \cdot (H_2O)_{29}$
Formula weight	2994.76
Temperature (K)	173(2)
Radiation wavelength (Å)	0.71073
Crystal system	triclinic
Space group	$P\bar{1}$
Unit cell dimensions	
a (Å)	17.926(4)
b (Å)	15.399(3)
c (Å)	15.416(3)
α (°)	103.425(4)
β (°)	113.404(4)
γ (°)	98.858(4)
V (Å^3)	3651.4(13)
Z	1
D_{calcd} (Mg m^{-3})	1.362
Absorption coefficient (mm^{-1})	0.124
$F(000)$	1608
Crystal size (mm)	$0.1 \times 0.4 \times 0.4$
θ Range for data collection (°)	1.41–29.36
Index ranges	$-24 \le h \le 24$, $-20 \le k \le 19$, $-19 \le l \le 21$
Reflections collected/independent	32,575/22,386
R_{int}	0.0470
Completeness to $\theta = 29.36°$	76.3%
Absorption correction	semi-empirical
Max/min transmission	1.000/0.815
Refinement method	full-matrix least-squares on F^2
Data/restraints/parameters	22,386/2362/2166
Goodness-of-fit on F^2	1.043
Final R indices $[I_o > 2\sigma(I_o)]$	$R_1 = 0.0615$, $wR_2 = 0.1442$
R indices (all data)	$R_1 = 0.0942$, $wR_2 = 0.1712$
Absolute structure parameter	0.3(9)
Largest difference peak and hole (e Å^{-3})	0.543 and −0.440
Mean shift/e.s.d.	0.018

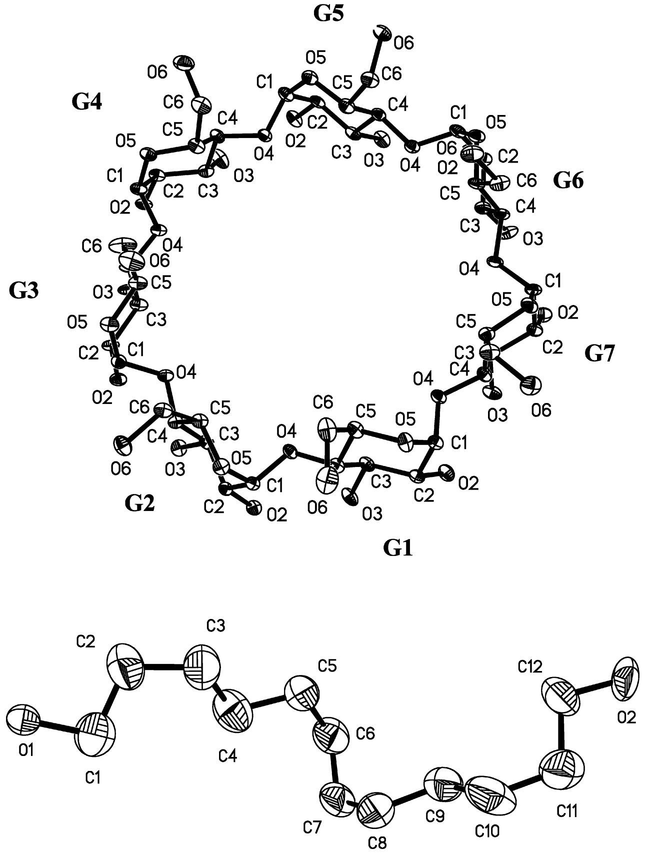

Fig. 1. The structures and numbering scheme of the β-CD and 1,12-dodecanediol molecules.

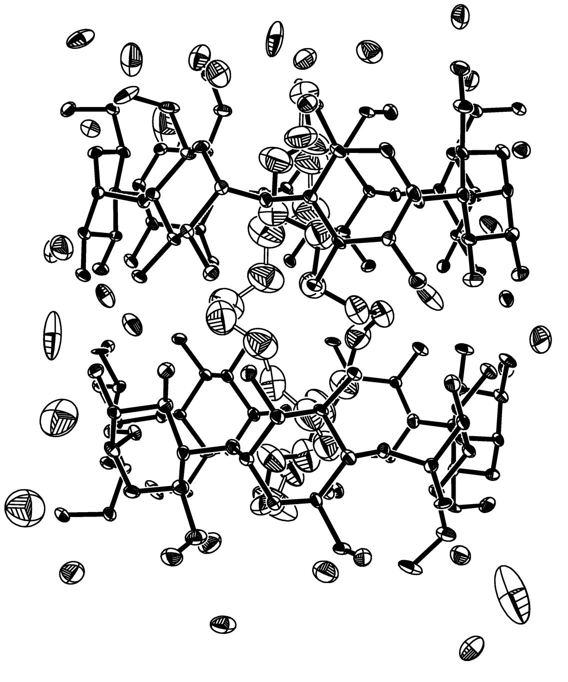

Fig. 2. X-ray structure of the 2:1 host–guest inclusion complex between β-CD and 1,12-dodecanediol.

Table 2
Direct hydrogen bonds within β-CD dimers

OAmn···OB$m'n'$	Distance (Å)
OA31···OB37	2.782
OA34···OB34	2.809
OA36···OB32	2.761
OB31···OA37	2.768
OB33···OA35	2.696
OB35···OA33	2.679

from Roquette, France; water content determined by TGA and Karl–Fischer measurements) in pure water to which 1,12-dodecanediol (purchased from Aldrich) was added in a host–guest molar ratio of 1:2. The suspension obtained was stirred at 60 °C for 2 h and was allowed to cool to room temperature (rt). After 7 days at rt, colorless crystals were formed.

2.2. X-Ray measurements, determination and refinement of the structure

All data were collected at low temperatures (173 K) on a Bruker-AXS CCD-1000 diffractometer with Mo K$_\alpha$ radiation ($\lambda = 0.71073$ Å). Crystal data are summarized in Table 1. All attempts failed to determine the crystal structure by conventional direct methods,[13] but we were able to solve the structure by an 'ab initio' real/reciprocal space recycling procedure implemented in SHELXD.[14] The structure was refined on F^2,[15] and all non-hydrogen atoms were treated anisotropically. The crystallographic unit contains one 2:1 host–guest complex (dimeric complex). A disorder of the diol was refined anisotropically with the help of ADP and distances restraints. The numbering scheme for the host and guest molecules is given in Fig. 1: C(A or B) *mn* and O(A or B) *mn* denotes the *m*th atom within the *n*th glucosidic residue (**Gn**) of the β-CD monomers A and B.

3. Results and discussion

3.1. Structure of the inclusion complex

β-CD and 1,12-dodecanediol form a 2:1 host–guest inclusion complex (Fig. 2). The crystallographically independent β-CD molecules A and B form head-to-head dimers (in almost perfect sevenfold symmetry) via direct hydrogen bonds between the O(3) secondary hydroxyl groups OA3n···OB3($8-n$) (mean distance 2.749 Å and range 2.679–2.809 Å) (Table 2), as frequently observed for this kind of supramolecular complexes.[7] The guest molecule lies across the length of the β-CD dimer, forming a [3]pseudorotaxane.

3.2. Geometry of the host

As shown in Table 3, the β-CD molecules possess a near sevenfold symmetry. The values of the angles

Table 3
β-CD macrocycle characteristics

Residue	D [a] (Å)	φ [b] (°)	d [c] (Å)	D [d] (Å)	Torsion angle (°) C4n–C5n–C6n–O6n
Molecule A					
G1	4.26	124.8	−0.014	2.776	65.66
G2	4.52	131.0	−0.010	2.825	−176.82
G3	4.25	129.5	0.034	2.854	54.92
G4	4.39	126.2	−0.024	2.878	57.41
G5	4.33	129.7	−0.004	2.851	56.47
G6	4.04	128.6	0.013	2.820	−179.98
G7	4.39	130.0	0.006	2.687	54.01
Molecule B					
G1	4.34	129.1	+0.014	2.797	63.81
G2	4.32	123.7	−0.012	2.823	58.60
G3	4.52	132.9	−0.025		52.27
G4	4.28	128.8	0.052	2.794	53.68
G5	4.45	126.1	−0.033	2.825	54.33
G6	4.30	128.3	−0.003	2.719	−170.89
G7	4.47	131.1	0.007	2.776	53.70

[a] Distances between atoms O4n···O4($n+1$).

[b] Angles between atoms O4($n-1$) ···O4n···O4($n+1$).

[c] Deviations (Å) from the least-squares optimum plane of the seven O4n atoms.

[d] Intramolecular hydrogen-bond distances between O3n···O2($n+1$).

between the glucosidic oxygen atoms O-4($n-1$)···O-4n···O-4($n+1$) do not differ significantly from 128.57° (in-between 126.1 and 132.9°), the ideal value for an angle of a regular heptagon, denoting that the cavity is not distorted due to inclusion. The deviations of the O-4n atoms from their optimum plane are close to zero, while the glucose units tilt regularly towards the sevenfold axis. The O-4n···O-4($n+1$) distances vary between 4.04 and 4.52 Å. The regular conformation of the β-CD macrocycles remains undistorted because of the intramolecular hydrogen bonds connecting the secondary hydroxyl groups O-3n and O-2($n+1$) of neighboring glucosidic units (Table 3) (average O-3n···O-2($n+1$) distance 2.802 Å, range 2.687–2.878 Å) similar to other β-CD dimeric complexes[9] and to the α-CD dimeric complex with the 1,12-diaminododecane.[12]

3.3. Geometry of the guest

The diol molecule is encapsulated in the hydrophobic dimeric cavity with the hydroxyl groups emerging from the primary faces of the β-CD dimer. It shows a disorder over two positions with occupancy factors of 40 and 60% (Fig. 2). The length of the β-CD dimer is about 15 Å,[11] which is shorter than the extended conformation (zig-zag) of an aliphatic chain with 12 carbon atoms. The hydroxyl groups of the guest do not extend beyond the primary hydroxyl O atoms of the β-CD dimer. The disorder of the guest is probably due to the quite wide cavity of the β-CD, especially in the middle of the dimer and to the fact that there is a kind of bond between the polar extremities of the diol and the OH-groups of the dimer surfaces via water molecules (Table 4). Similar motifs have been observed in the literature for the dimeric β-CD complexes with guests such as long aliphatic monocarboxylic acids and α,ω-dicarboxylic acids[8,9,11]

Table 4
Hydrogen bonds between guest's hydroxyl groups and water molecules

Omn···O$m'n'$	Distance (Å)
Position a	
O-1a···W61B	2.783
O-2a···W1	2.756
W2···O-2a	2.714
W3···O-1a	2.816
Position b	
O-1b···W66A	2.691
O-2b···W1	2.682
W2···O-2b	2.596
W66B···O-1b	2.785

[a] a or b denote the two positions of guest.

Table 5
Hydrogen bonds between hydroxyl groups of adjacent β-CD dimers

Omn···Omn'	Distance (Å)
OA63···OA67	2.763
OB61···OB65	2.847
OA27···OB25	2.825
OA65···OA61	2.871
OB63···OB67	2.709
OA62···OB62	2.706

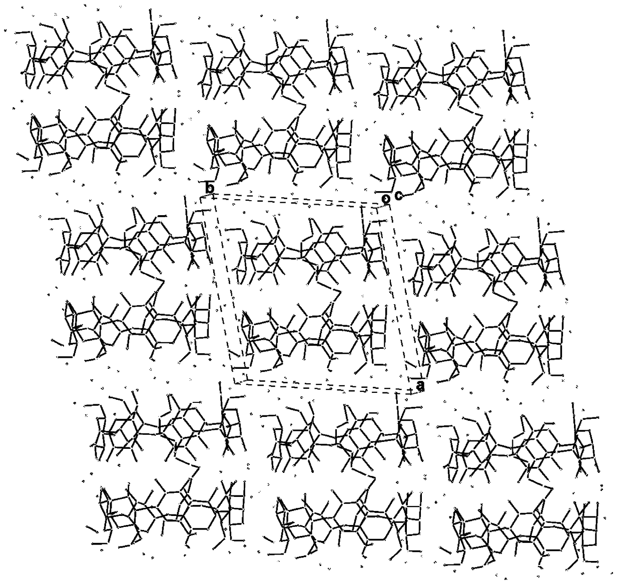

Fig. 3. Crystal packing of the dimeric inclusion complex. The guest molecule is disordered over two positions bending in the same direction.

3.4. Crystal packing

The water sites were labelled by the number of the closest oxygen atom to which they are forming H-bonds. At the primary hydroxyl level, adjacent β-CD dimers interact via hydrogen bonds, of which five bind hydroxyl groups in the 2D layer (Table 5): three along the c axis OA63···OA67 (H-atom not located), OB61···OB65 and OA27···OB25, two along the b axis, OA65···OA61 and OB63···OB67. The OA62···OB62 hydrogen bond differs between layers. In the low-temperature structure, there are 29 water molecules per asymmetric unit, distributed over 32 sites and 20 form hydrogen bonds with the hydroxyl groups of β-CD molecules and of the guest. The smallest distance between hydroxyl groups of different guest molecules is about 7.5 Å, which shows clearly the absence of direct interaction between these molecules. The dimers pack in layers shifted laterally by 20 Å along the a axis therefore, they do not stack on top of each other to form channels (Fig. 3). As observed for the corresponding diacids,[7] the centers of consecutive dimers are shifted laterally by 6.2 Å giving a packing of intermediate type (IM).

4. Supplementary material

CCDC 197537 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgements

We are grateful to Dr Alain Milius (SEPPIC, France) for starting this project and for fruitful discussions. We thank SEPPIC and ADEME (France) for financial support of this work.

References

1. Wenz, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 803–822.
2. Saenger, W. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 344–362.
3. Szejtli, J. *Cyclodextrin Technology*; Kluwer Academic: Dordrecht, The Netherlands, 1988.
4. Harata, K. *Chem. Rev.* **1998**, *98*, 1803–1827.
5. Nepogodiev, S. A.; Stoddart, J. F. *Chem. Rev.* **1998**, *98*, 1959–1976.
6. Amabilino, D. B.; Stoddart, J. F. *Chem. Rev.* **1995**, *95*, 2725–2828.
7. Mentzafos, D.; Mavridis, I. M.; Le Bas, G.; Tsoucaris, G. *Acta Crystallogr., Sect. B* **1991**, *47*, 746–757.
8. Makedonopoulou, S.; Mavridis, I. M. *Acta Crystallogr., Sect. B* **2000**, *56*, 322–331.
9. Makedonopoulou, S.; Tulinsky, A.; Mavridis, I. M. *Supramol. Chem.* **1999**, *11*, 73–81.
10. Makedonopoulou, S.; Mavridis, I. M. *Carbohydr. Res.* **2001**, *335*, 213–220.
11. Makedonopoulou, S.; Papaioannou, J.; Argyroglou, J.; Mavridis, I. M. *J. Incl. Phenom. Macrocyclic Chem.* **2000**, *36*, 191–215.
12. Rontoyianni, A.; Mavridis, I. M. *Supramol. Chem.* **1999**, 213–218.
13. Sheldrick, G. M. *Acta Crystallogr., Sect. A* **1990**, *46*, 467–473.
14. Sheldrick, G. M.; Hauptman, H. A.; Weeks, C. M.; Miller, R.; Usón, I. In *International Tables for Crystallography*; Arnold, E.; Rossmann, M., Eds.; Kluwer Academic Publishers: Dordrecht, 2001; Vol. F, pp 333–351.
15. Sheldrick, G.M., SHELXL-97, Program for Crystal Structure Refinement, University of Göttingen, 1997.