

The Structure of the First Supramolecular α -Cyclodextrin Complex with an Aliphatic Monofunctional Carboxylic Acid

Saddys Rodríguez-Llamazares,^[a] Nicolás Yutronic,^{*[a]} Paul Jara,^[a] Ulli Englert,^{*[b]} Michael Noyong,^[b] and Ulrich Simon^[b]

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The crystal structure of the supramolecular complex between α -cyclodextrin and decanoic acid was determined: The aliphatic chain of the carboxylic acid is threaded through a head-to-head dimer of two cyclodextrin residues, resulting in a 1:2 stoichiometry. Head-to-head orientation is also ob-

served between neighboring complexes. The overall degree of hydration with 25 water molecules per supramolecular complex is remarkably high.

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Introduction

Cyclodextrins (CDs) are doughnut-shaped cyclic oligosaccharides with a central hydrophobic cavity that can enclose one or several molecules bonded by noncovalent interactions. The major driving forces of the formation of CD inclusion compounds are hydrophobic and van der Waals interactions between the inner surface of the CD ring and the hydrophobic sites on the guest.^[1] CDs are widely used in pharmaceutical science, catalysis, separation technology, and more recently in the field of chemical nanostructures.^[1,2]

It has already been reported that α -CD forms three types of structural packing: the so-called “cage-type”, “layer-type”, and “channel-type”.^[1] For the channel structure, two possible arrangements of the α -CD hosts exist, namely head-to-tail and head-to-head orientation. Complexes with 2:1 stoichiometry between the α -CD host and guest molecules with an extended hydrocarbon chain have been studied by NMR spectroscopy^[3] and powder XRD. Valeric acid,^[4] 1-octanol,^[4] dialkylamine,^[5] and lauric acids^[6] represent examples for guest molecules that form channel inclusion compounds of hexagonal symmetry with α -CD. In contrast, the α -CD adducts with the linear aliphatic bifunctional compounds 1,12-diaminododecane^[7] and 12-aminododecanoic acid^[8] crystallize to form pseudorotaxanes and have successfully been characterized by single-crystal X-ray diffraction. Despite extensive research, it has not yet been possible to determine the structure of α -CD complexes with linear aliphatic monofunctional guests. In this contribution,

we report the first results in this context obtained on the 2:1 complex of α -CD and decanoic acid. In the solid state, the supramolecular aggregate adopts a structure of surprising complexity^[9] and crystallizes in the approximate stoichiometry (dec-acid)(α -CD)₂·25H₂O, **1**.^[10]

Results and Discussion

The high content of solvent water is reflected in the pronounced sensitivity of the crystals with respect to desolvation. The unit cell is large due to the presence of 4 independent cyclodextrin dimers, each of which is associated to a decanoic acid molecule and a total of ca. 100 independent water molecules. Despite the limited resolution of our diffraction data, the head-to-head orientation within the cyclodextrin dimers and the presence of the decanoic acid molecule in the pseudochannels was unambiguously established. The arrangement of these residues in one of four independent but similar supramolecular complexes is depicted in Figure 1.

The guest is fully enclosed in the α -CD dimer, and the carboxylic group is located on the primary hydroxy side. The accuracy of displacement parameters in the structure of **1** should not be overestimated; however, a consistent feature among the aliphatic chains of all four symmetrically independent decanoic residues lies in the fact that the two carbon atoms in the middle of the chain, the ones between the two carbohydrate subunits, are associated with relatively high displacement parameters. The position of these atoms is less well-defined. We note that guest folding in the middle of the dimers was observed in the crystal structure of the β -CD/1,14-tetradecanedioic acid complex.^[13]

The α -CD molecules possess a near sixfold symmetry, and the mean value of the angle between the glycosidic oxygen atoms is almost 120°, the angle in a regular hexagon.

[a] Departamento de Química, Facultad de Ciencias, Universidad de Chile, Casilla 653, Santiago, Chile

[b] Institute of Inorganic Chemistry, RWTH Aachen University, Landoltweg 1, 52074 Aachen, Germany
Fax: +49-241-8092288
E-mail: ullrich.englert@ac.rwth-aachen

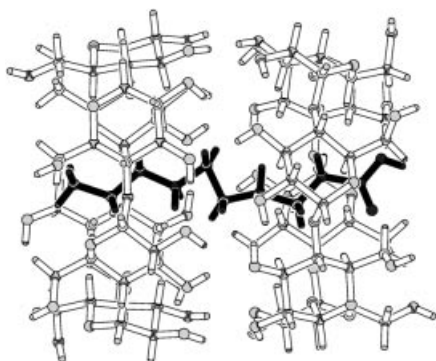


Figure 1. A molecule of decanoic acid (black) threaded through an α -CD dimer.

The conformation of the α -CD monomer is stabilized by intramolecular H-bonds between neighboring secondary hydroxy groups with average distances of 2.80(6) Å (range 2.69–2.95 Å). Similar distances of 2.78(2) Å (range 2.74–2.82 Å) were reported for the β -CD dimer complexes;^[14] this fact indicates that the stabilization in both dimer structures is approximately the same.

The two α -CD residues forms head-to-head dimers through six H-bonds with an average intermolecular distance of 2.83(3) Å (range 2.77–2.89 Å). The dimers are slightly displaced towards each other in the crystallographic c and a axes, which results in a pseudochannel structure (Figure 2).

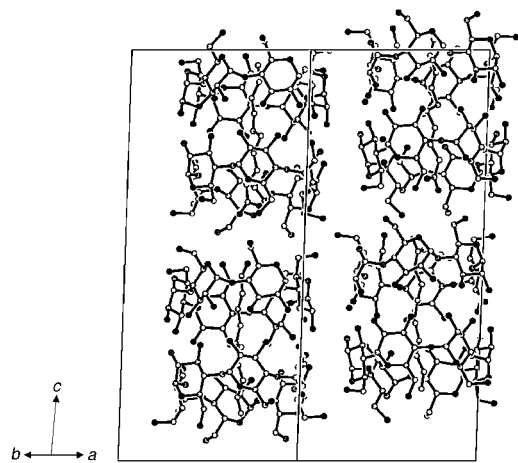


Figure 2. Packing of the dimers in **1** along the $[-1-10]$ direction. Water molecules are omitted for clarity.

The guest orientation is head to head, but no direct H-bonding occurs between the carboxyl groups of two consecutive dimers. They interact, however, through hydrogen bonds with two intervening water molecules along the c axis. Additional hydrogen bonds in the distance range 2.69–2.84 Å stabilize the intercolumn structure as shown in Figure 3.

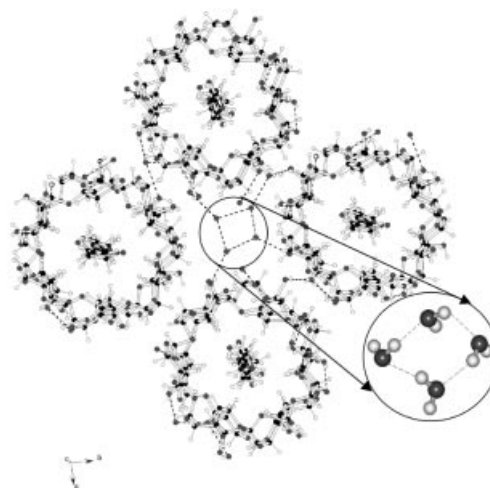


Figure 3. Packing of the dimers along the $[-1-10]$ direction. Water molecules are omitted for clarity.

Conclusions

For methyl orange, the influence of this guest molecule on the host structure of the α -CD inclusion compound was reported.^[14] The crystal exhibits a head-to-tail channel structure in which α -CD rings are stacked along the c axis. However, when 1,12-diaminododecane^[7] is included into α -CD, the amine nitrogen atoms protrude from the primary hydroxy side of the α -CD dimer. They link to primary hydroxy oxygen atoms of a neighboring carbohydrate residue and thus prevent stacking of the dimers along the channel. In contrast to these cases, our result shows that a pseudochannel structure with a head-to-head orientation is induced by a guest molecule with a long aliphatic chain that is entirely included in the α -CDs dimer.

Experimental Section

(dec-acid)(α -CD)₂·25H₂O (1): Compound **1** was synthesized from decanoic acid and a saturated solution of α -CD in water at room temp. The guest-to- α -CD molar ratio used in the experiment was 10:1, greater than the stoichiometric ratio. A mixture of α -CD (0.50 g, 0.51 mmol) in water (10 mL) and decanoic acid (0.9 mL, 4.66 mmol) was stirred for 30 min. In the course of several days, well-formed colorless crystals were obtained by slow solvent evaporation at room temp.

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- [9] To the best of our knowledge, **1** is associated with the largest asymmetric unit reported to date in the Cambridge Structural Database for a cyclodextrin structure. Earlier examples for hydrated cyclodextrin structures that crystallize in space groups of low symmetry with large unit cells comprise: a) K. Harata, H. Akasaka, T. Endo, H. Nagase, H. Ueda, *Chem. Commun.* **2002**, 1968–1969; b) K. Gessler, I. Uson, T. Takaha, N. Krauss, S. M. Smith, S. Okada, G. M. Sheldrick, W. Saenger, *Proc. Natl. Acad. Sci. USA* **2002**, *96*, 4246–4251; c) K. Benner, P. Klüfers, J. Schuhmacher, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 743–745.
- [10] Single crystals of complex **1** instantaneously undergo desolvation; a colorless platelet of approximate dimensions $0.40 \times 0.15 \times 0.03 \text{ mm}^3$ was covered with a thin layer of vacuum grease, rapidly mounted in a cryo loop and immediately exposed to a cold stream of N_2 . The structure was solved by dual space methods as implemented in SHELXD;^[11] the best solution was associated with a correlation coefficient of 79.85 and allowed to locate most atoms of the eight symmetrically independent cyclodextrin moieties. The structure model was completed by difference Fourier syntheses and refined on F^2 with SHELXL.^[12] Resolution of the diffraction data and accuracy of geometric parameters are limited, and no H atoms could be associated with the solvent molecules. No attempt was made to refine part of the structure model with anisotropic displacement parameters, and no split positions for water oxygen were assigned. H atoms associated with CD and decanoic acid were included as riding in standard geometry. Crystallographic data for **1**: $(\text{C}_{36}\text{H}_{60}\text{O}_{30})_2 \cdot (\text{C}_{10}\text{H}_{20}\text{O}_2) \cdot 25\text{H}_2\text{O}$, $M = 2568.34$, triclinic, $P1$ (no. 1), $T = 120 \text{ K}$, $a = 19.7161(11) \text{ \AA}$, $b = 19.7424(12) \text{ \AA}$, $c = 31.8334(19) \text{ \AA}$, $\alpha = 82.839(2)^\circ$, $\beta = 80.158(2)^\circ$, $\gamma = 86.721(3)^\circ$, $V = 12105.2(12) \text{ \AA}^3$, $Z = 4$, $D_{\text{calcd.}} = 1.409 \text{ Mg m}^{-3}$, $\mu(\text{Mo-K}\alpha) = 0.129 \text{ mm}^{-1}$, $2\theta_{\text{max}} = 45^\circ$, $wR_2 = 0.3546$ (31550 data for 2708 variables), $R_1 = 0.1566$ (21017 observed data). $S = 1.108$. CCDC-634928 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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