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X-Ray structure of the δ-cyclodextrin complex with cycloundecanone

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The crystal structure of the δ-cyclodextrin complex with cycloundecanone shows a channel-type structure consisting of head-to-head dimer units that include four guest molecules.

Cyclodextrins are cyclic oligosaccharides consisting of six or more α-1,4-linked glucose units. These macrocyclic compounds are well known for their ability of forming inclusion complexes in solution and/or in solid state.[1] X-Ray analysis has revealed the structures of a number of crystalline complexes of α-, β-, and γ-cyclodextrin that consist of six, seven, and eight glucose units, respectively, and accommodate a variety of guest molecules in their intramolecular cavity.[2] However, we have no direct evidence of inclusion complexes being formed for larger cyclodextrins. Recently, Ueda and his co-workers have reported the complex formation of δ-cyclodextrin with some macrocyclic compounds[3] and fullerenes.[4] Those bulky guest molecules with round or spherical shape have been expected to be well fitted to the large annular cavity of δ-cyclodextrin. These complexes were precipitated from an aqueous solution and examined by powder X-ray diffraction and DSC analysis. A single crystal suitable for X-ray analysis was obtained for the complex with cycloundecanone. Here, we present its crystal structure that demonstrates the formation of an inclusion complex.

The crystal structure revealed the 1 : 2 stoichiometry of host and guest molecules. The asymmetric unit contains four δ-cyclodextrin molecules and eight cycloundecanone molecules. This huge structure with a formula weight of 8037.3 Dalton was solved by direct methods and refined by the full-matrix least-squares method.[5] As shown in Fig. 1, two δ-cyclodextrin molecules form a head-to-head dimer with their secondary hydroxyl sides facing each other. The dimer structures are supported by many hydrogen bonds between secondary hydroxyl groups. This barrel-like structure of the δ-cyclodextrin dimer creates a large cylindrical cavity that accommodates four cycloundecanone molecules. At the primary hydroxyl side of each δ-cyclodextrin ring, one guest molecule is located parallel to the δ-cyclodextrin ring, thus, capping both ends of the dimer cavity. The inner cavity of the dimer is occupied by two guest molecules which are facing each other and situated perpendicularly to the δ-cyclodextrin ring. These guest molecules are arranged with complicated disorder and their structures were modeled to fit the doughnut-shaped electron density. The two independent dimer units are stacked to form a cylindrical structure with the length of 33 Å, which is the repetition unit of the channel extending along the crystallographic *c* axis.

The δ-cyclodextrin ring has pseudo nine-fold symmetry as shown in Fig. 2, The nine glycosidic O-4 atoms form a nonagon with a radius of 6.7 Å and a side length of 4.6 Å. These atoms are coplanar with a root-mean-square deviation of 0.054 Å from their least-squares plane. No significant structural difference was observed among four independent δ-cyclodextrin molecules. The macrocyclic structure is stabilized by the intramolecular hydrogen bonds between hydroxyl groups, O-3H and O-2H of the next glucose unit which are in the region of about 2.8 Å. The uncomplexed δ-cyclodextrin molecule is elliptically distorted in the crystalline state and the cavity is narrower than that expected from its ring size.[6] The O-4 atoms that form a warped nonagon are considerably deviated from their least-squares plane with the root-mean-square deviation of 0.80 Å. The tilt angle[7] of each glucose unit is in the range from 11.2° to 60.7° and some glucose units are sharply inclined against the molecular plane to reduce the vacant cavity. The present structure shows that the inclusion of cycloundecanone caused the induced-fit structural change to make the macrocyclic ring symmetrical. The cycloundecanone ring that is fitted to the narrower side of the host cavity supports to maintain the round structure of δ-cyclodextrin.

The head-to-head channel type structure has also been observed in crystalline complexes of α-, β-, and γ-cyclodextrin. A prominent characteristic of this packing form is to accommodate guest molecules that are larger than the single cavity of cyclodextrins. On the other hand, crystal structures have shown that the larger cyclodextrins in the uncomplexed state are not in the round shape and their slit-like cavity is narrow.[8,9] However, our present results demonstrate the possibility of forming

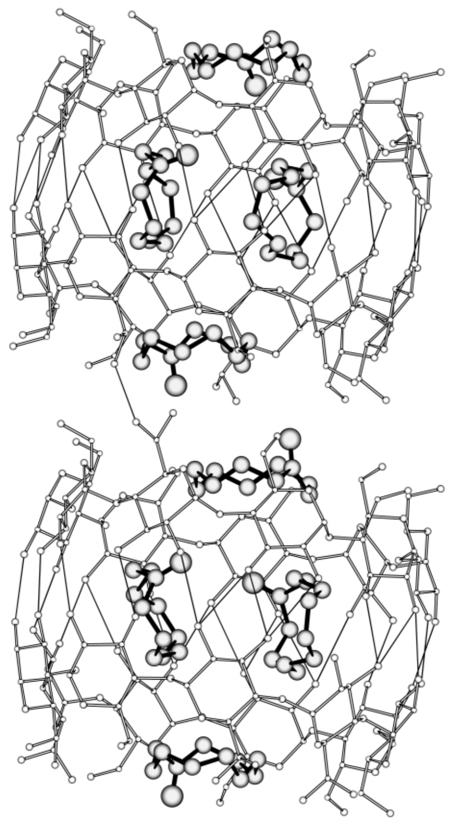

Fig. 1 Structure of the asymmetric unit of the crystalline complex of δ-cyclodextrin with cycloundecanone. The cycloundecanone molecules are shaded. Thin lines denote the intermolecular hydrogen bonds between δ-cyclodextrin molecules. The two guest molecules located at the center of the barrel-like structure of the δ-cyclodextrin dimer are two-fold disordered. The molecules of the alternative site are not shown for clarity.

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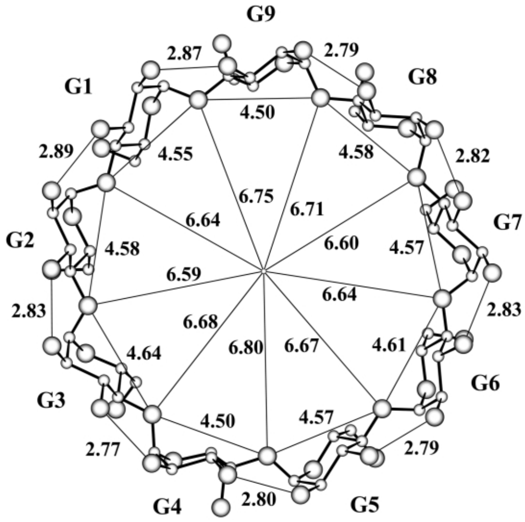

Fig. 2 The structure of one of the four independent δ-cyclodextrin molecules. Thin lines denote the radius and side of the nonagon composed of glycosidic O-4 atoms and hydrogen bonds between the O-2H hydroxyl group and the O-3H hydroxyl group of the adjacent glucose unit. The radius of the nonagon was drawn from the center of gravity of nine O-4 atoms to each O-4 atom.

inclusion complexes with guest molecules as large as will fit the round cavity created by the induced-fit structural change.

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Notes and references

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5 Crystals were obtained at room temperature by the slow evaporation of a solution containing δ-cyclodextrin and an excess amount of cycloundecanone. X-Ray experiments were carried out at 290 K on a Bruker SMART6000 diffractometer with CuKα radiation from a MAC Science M06X rotating anode generator equipped with Osmic Confocal Max-Flux Optics. Intensity data of 12 7078 reflections were measured to 0.89 Å resolution and were merged to a set of 28 172 independent reflections with R_{merge} of 0.031. The structure was solved by the direct method using the program SnB (R. Miller, S. M. Gallo, H. G. Khalak and G. W. Weeks, SnB: Structure Determination Package User's Manual for Version 1.5.0, Hauptman-Woodward Medical Research Institute, Buffalo, USA, 1994) and refined by the full-matrix least-squares method (G. M. Sheldrick, SHELX-97: Program for Crystal Structure Refinement, University of Göttingen, Germany, 1997) to the *R* value of 0.082 for all reflections and 4995 parameters. Coordinates of the hydrogen atoms of methine and methylene groups of δ-cyclodextrin were calculated and included in the structure factor calculation with an isotropic temperature factor that was 1.5 times larger than that of bonded carbon atoms. The asymmetric unit contained four δ-cyclodextrin, eight cycloundecanone, and 49.4 water molecules. Restraints were applied for bond distances, angles, and carbonyl planes for the structure of cycloundecanone and for temperature factors of all atoms. Occupancy factors of water molecules were refined in the least-squares calculation. *Crystal data*: $4C_{54}H_{90}O_{45}\cdot 8C_{11}H_{20}O\cdot 49.4H_2O$, M = 8037.3, monoclinic, space group $P2_1$, Z = 2, a = 32.537(4), b = 19.013(2), c = 33.136(6) Å, β = 98.42(1)°, V = 20277(6) Å^3, D_c = 1.316 g cm^{-3}, μ = 1.12 mm^{-1}. CCDC 186988. See http://www.rsc.org/suppdata/cc/b2/b205249k/ for crystallographic files in .cif or other electronic format.

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