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Interaction between β-cyclodextrin and 1,10-phenanthroline: uncommon 2:3 inclusion complex in the solid state

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Abstract—The crystallographic structure of the complex formed by β-cyclodextrin with 1,10-phenanthroline has been studied by X-ray diffraction. The result shows that the complex adopts an uncommon 2:3 stoichiometry in solid state, that is, every complex unit contains three 1,10-phenanthroline molecules and two β-cyclodextrin molecules, where two 1,10-phenanthroline molecules individually occupy two cyclodextrin cavities, and the third guest molecule is located in the interstitial space between two head-to-head cyclodextrin molecules. The intermolecular hydrogen bonds between the adjacent complex units further link these individual monomers to a channel-type assembly. Furthermore, ^{1}H and 2D NMR spectroscopy has been employed to investigate the inclusion behavior between the host β-cyclodextrin and guest 1,10-phenanthroline in aqueous solution.

Keywords: Cyclodextrin; 1,10-Phenanthroline; Crystal structure; Inclusion complex

1. Introduction

Cyclic oligosaccharides consisting of six, seven, and eight α-(1→4)-linked D-glucose units, are generally known as cyclomaltooligosaccharide (cyclomaltohexaose, cyclomaltoheptaose, cyclomaltooctaose, i.e. α-, β-, and γ-cyclodextrins).[1] As illustrated in Figure 1, their exterior, bristling with hydroxyl groups like OH-6 at the primary side and OH-2 and OH-3 at the secondary side, is fairly polar; whereas the interior of the cavity coated with H-3, H-5 atoms and ether-like O-4, O-5 atoms is nonpolar.[2] This remarkable property makes cyclodextrins well known for their ability of recognizing many kinds of guests to form host–guest inclusion complexes[3–7] and construct into nanometer scale supramolecular assembly systems.[8,9]

In order to elucidate the mechanism of their intermolecular interaction and aggregation, a number of crystalline complexes of cyclodextrins were studied by X-ray crystallographic analysis with a variety of guest molecules in their intramolecular cavities.[10–14] There were abundant reports on ordinary stoichiometric 1:1, 2:1, and 1:2 complexes between host cyclodextrins and guests.[15–19] For example, Harata et al. reported a 1:2 δ-cyclodextrin/cycloundecanone complex,[20] and Caira et al. also described a 1:1 inclusion complex in triclinic

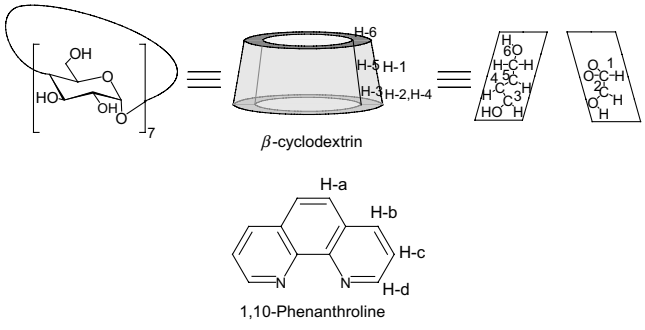

Figure 1. Chemical structures and atomic numbering of β-cyclodextrin and 1,10-phenanthroline.

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and monoclinic formed between β-cyclodextrin and methylparaben under different conditions.[21] Different from these reported complexes in which the guest molecules were almost located inside the cyclodextrin cavities, Konstantin et al. reported a crystalline complex by β-cyclodextrin with *n*-octanol and pyrene, in which the octanol molecule penetrated into the cavities of the adjacent cyclodextrin units from the primary hydroxyl side, while the pyrene molecule lied flat between two cyclodextrin molecules to form head-to-head dimers.[22]

Somewhat unexpectedly, only one 2:3 complex of β-cyclodextrin has been published up to date,[23] to the best of our knowledge, in which the cyclodextrin cavity accommodates the lipophilic side of *p*-iodophenol at its primary hydroxyl side, while another guest molecule is located between two β-cyclodextrin units. Herein, we present another sample of 2:3 inclusion complex of β-cyclodextrin with symmetrical 1,10-phenanthroline molecules in the crystalline state, in which the guest plays two significantly different roles, that is, both penetrator and linker.

2. Experimental

2.1. Crystallization

β-Cyclodextrin and 1,10-phenanthroline at 1:1 molar ratio were fully dissolved in water and ethanol separately, and then the two solutions were mixed and stirred. The resulting mixture was stored at room temperature for two weeks to provide colorless crystals suitable for X-ray crystallographic investigation.

2.2. X-ray data

Final lattice parameters are given in Table 1 along with other information on data collection structure refinement. Data collection was done on a standard Siemens SMART CCD area detector system equipped with a normal focus molybdenum target X-ray tube (Mo Kα radiation $\lambda = 0.71073$ Å) operated at 2.0 kW (50 kV, 40 mA) and a graphite monochromator. The final *R* value was not particularly precise because of the background arising from the aqueous solution and the glass tube as well as slow airslaking.

2.3. NMR studies

^{1}H NMR spectra were recorded with a Varian Mercury VX300 instrument at 298K in a deuterium oxide solution. Tetramethylsilane was used as reference and no correction was made for susceptibility of the capillary. ROESY spectrum was performed in D_2O at 298 K with a mixing time of 400 ms.

Table 1. Crystal data and structure refinement for β-cyclodextrin/1,10-phenanthroline complex

Empirical formula	$(C_6H_{10}O_5)_7 1.5(C_{12}H_8N_2)9.25H_2O$
Formula weight	1571.93
Temperature (K)	293(2)
Wavelength, λ Mo Kα (Å)	0.71073
Crystal system, space group	Monoclinic, C2
Unit cell dimensions	$A = 19.68(2)$ Å
	$B = 24.18(3)$ Å, $\beta = 115.38(2)°$
	$C = 17.794(19)$ Å
Volume (Å^{-3})	7649(14)
Z	4
D_{calcd} (Mg/m^{-3})	1.365
Absorption coefficient (mm^{-1})	0.118
F(000)	3342
Crystal size (mm)	$0.30 \times 0.25 \times 0.20$
Range for data collection, θ (°)	1.27–26.40
Limiting indices (°)	$-19 \leqslant h \leqslant 24$
	$-30 \leqslant k \leqslant 28$
	$-22 \leqslant l \leqslant 20$
Reflections collected/unique	21743/13838 [R(int) = 0.1116]
Completeness to $\theta = 25.00$	98.9%
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	13838/639/1127
Goodness-of-fit on F^2	1.058
Final *R* indices [$I > 2\sigma I$)]	$R_1 = 0.1462$, $wR_2 = 0.3200$
R indices (all data)	$R_1 = 0.2850$, $wR_2 = 0.3944$
Largest diff. Peak and hole (e Å^{-3})	0.972 and −0.527

3. Results and discussion

3.1. Crystal structure

A view of the β-cyclodextrin/1,10-phenanthroline complex is presented in Figure 2. Each glucose residue of β-cyclodextrin has the usual $^4C_1$ chair conformation, and each β-cyclodextrin has an approximate 7-fold axis maintaining the round shape of the macrocycle. Contrary to the general 1:1 inclusion complexes formed between cyclodextrin and other guest molecules, where the guest only penetrates the hydrophobic cavity of

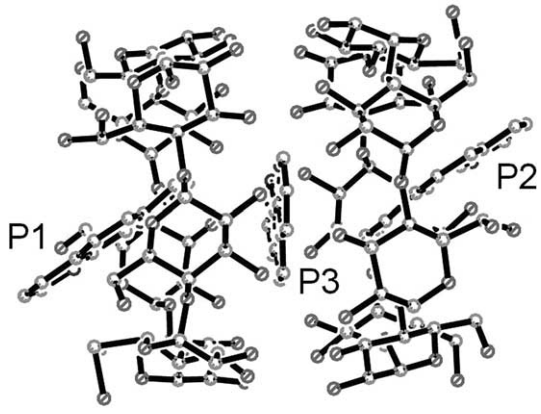

Figure 2. View of 2:3 β-cyclodextrin/1,10-phenanthroline inclusion complex.

cyclodextrin from either its primary or secondary face,[10] the main feature of the complex is that it adopts an uncommon 2:3 host–guest stoichiometry, that is, every complex unit contains three 1,10-phenanthroline molecules and two β-cyclodextrin molecules with a dihedral angle between the heptagons formed by the seven glycosidic oxygen atoms in β-cyclodextrins of 178.9°. Figure 2 shows that two 1,10-phenanthroline molecules (P1 and P2) individually occupy two cyclodextrin cavities with an angle of 31.7° to the C_7 axis of cyclodextrin, while the third guest molecule (P3) is located in the interstitial space between two head-to-head cyclodextrin molecules, and the corresponding angles between the C_7 axis of cyclodextrin and P3 plane are 89.3° and 89.2°, respectively. The dihedral angle between P1 (or P2) plane and P3 plane is 57.9°. The guest with the two positions of β-cyclodextrin mentioned above are both disordered over two sites (with occupation of 50% individually).

As shown in Figure 3, every head-to-head complex unit is stabilized by five hydrogen bonds between the secondary hydroxyl groups ($d_{O21B\cdots O21D} = d_{O21A\cdots O28C} = 2.876$ Å, $d_{O37B\cdots O31D} = d_{O37A\cdots O31C} = 2.884$ Å, $d_{O31B\cdots O37D} = d_{O31A\cdots O37C} = 2.884$ Å, $d_{O33B\cdots O35D} = d_{O33C\cdots O35A} = 2.919$ Å, and $d_{O35B\cdots O33D} = d_{O33A\cdots O35C} = 2.919$ Å). Simultaneously, no hydrogen bond exists between the N atoms of the 1,10-phenanthroline (P1, P2, and P3) at the two different positions and the neighboring hydroxyl groups of cyclodextrins. In addition, a lot of water molecules are found in this crystal structure, and some of them form hydrogen bonds with the hydroxyl groups of cyclodextrins. The origin of this uncommon 2:3 stoichiometric inclusion complex of β-cyclodextrin with 1,10-phenanthroline may be attributed to the almost planar shape like pyrene[22] of the guest, so it can lie flat between two β-cyclodextrin molecules. At the same time, its symmetrical quasi-linear structure enables it to penetrate the cyclodextrin cavity.

A more interesting structural feature of the crystal is that the β-cyclodextrin/1,10-phenanthroline complex dimers are aligned along the *z*-axis, forming a channel-type superstructure. As shown in Figure 3, though no π–π interactions between the two parallel 1,10-phenanthrolines in the two adjacent complex units can be observed, one crucial hydrogen bond between the primary hydroxyl groups of cyclodextrin ($d_{O61E\cdots O61C} = 2.595$ Å) links the adjacent complex units into a channel-type structure. As can be seen from Figure 4, the channel-type structure can further extend to a more sophisticated level through hydrogen-bonding interactions between water molecules and the hydroxyl groups of cyclodextrins.

3.2. NMR study

^{1}H NMR spectrometry has been widely used to give evidence for inclusion complex of cyclodextrin in solution.[24,25] It is well known that cyclodextrin possesses outer-surface (H-2 and H-4) and inner-surface (H-3 and H-5) protons, and the H-6 protons are situated at the

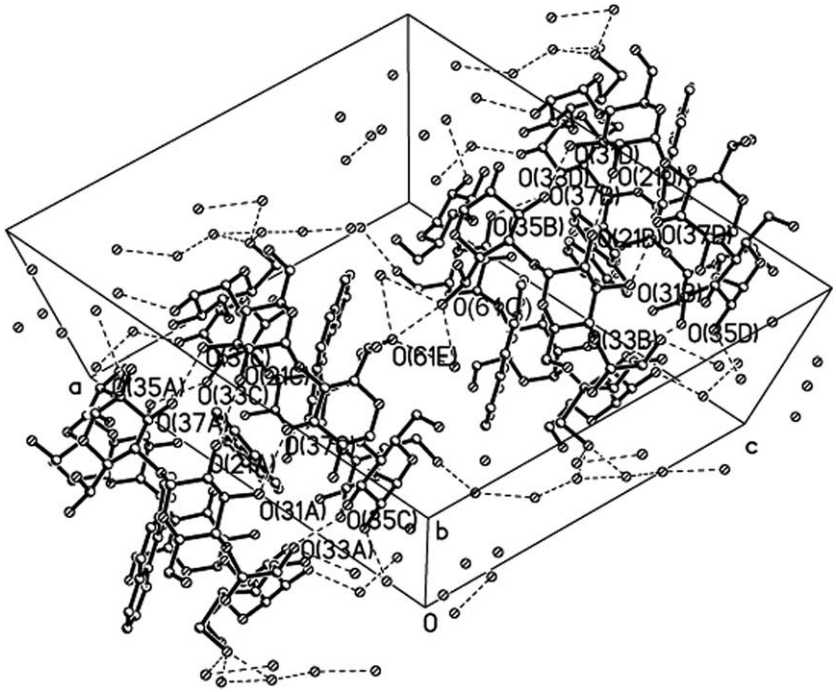

Figure 3. Channel structure of β-cyclodextrin/1,10-phenanthroline; view is approximately along the *y*-axis. The hydrogen bonds are outlined by dashed lines.

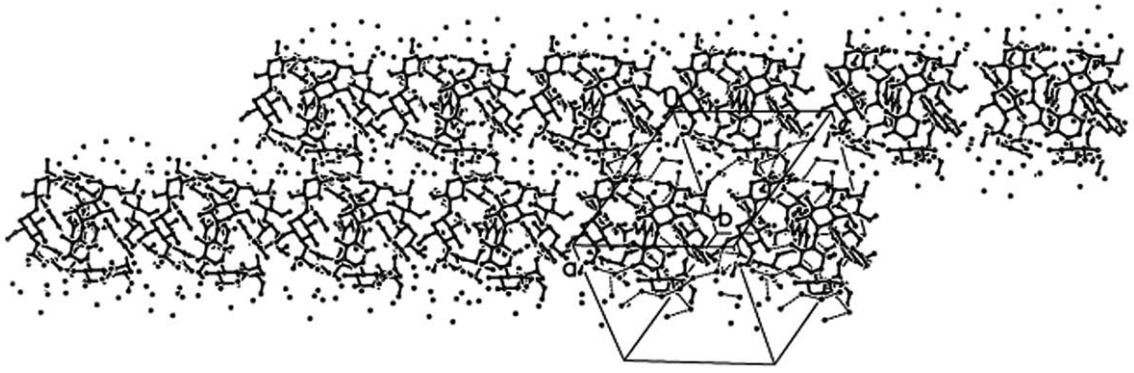

Figure 4. View of assembly formed by β-cyclodextrin/1,10-phenanthroline complex units.

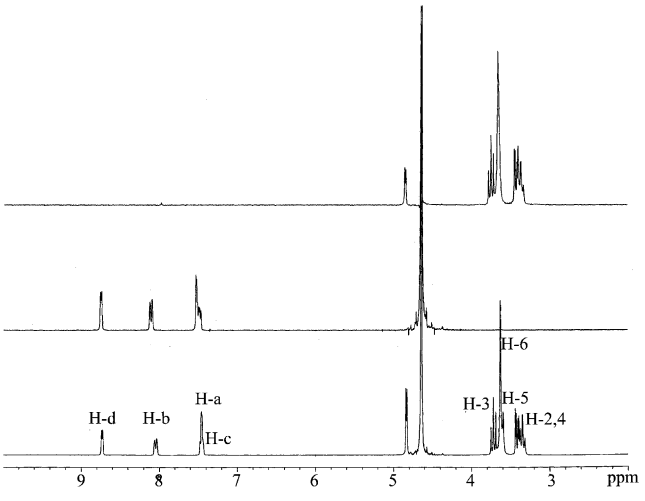

Figure 5. 300 MHz ^{1}H NMR spectra of β-cyclodextrin (5.0×10^{-3} M), 1,10-phenanthroline (5.0×10^{-3} M), and their mixture at the same concentration in D_2O.

primary side of the cyclodextrin cavity (Fig. 1). The inclusion complexation of a guest molecule into the cyclodextrin cavity will result in changes of the chemical shifts of guest protons,[26–28] and these change of the protons inside and/or outside the cyclodextrin cavity can be used to analyze the formation of inclusion complex between cyclodextrin with the guest.[29]

For the sake of comparison, the spectra of β-cyclodextrin and 1,10-phenanthroline as well as their mixture at the same concentration are shown in Figure 5, while the spectral characteristics of β-cyclodextrin and 1,10-phenanthroline are shown in Table 2.

As can be seen from Table 2, in the presence of 1,10-phenanthroline, a negligible effect is observed on the cyclodextrin protons H-1, H-2, and H-3. In contrast, protons H-4, H-5, and H-6 exhibit substantial changes, and they undergo relatively strong shielding exceeding 0.05 ppm. The facts that the chemical shifts of H-5 (0.06 ppm) and H-6 (0.07 ppm) are greater than that of H-3 (0.03 ppm) demonstrate that the guest should be included into the cyclodextrin cavity from its primary side. Unfortunately, the reason of the abnormal change of H-4 is not clear. On the other hand, substantial differences of the guest are also found in the presence of β-cyclodextrin. The chemical shifts of the protons of a, b positions in the phenanthroline ring are upfield ($\Delta\delta = -0.06$ to 0.07 ppm), whereas the other protons are almost not affected. This phenomenon indicates that the hydrogen atoms of a, b positions in the phenanthroline ring are more affected by its surrounding environment than that of c, d positions, which is consistent with the crystal structure.

Furthermore, 2D NMR experiment provides further information about the β-cyclodextrin/1,10-phenanthroline inclusion complex in solution. As illustrated in Figure 6, the ROESY spectrum of the complex displays clear cross-peaks between the H-3, H-5 protons of cyclodextrin, which are located inside the cyclodextrin cavity, and the H-d protons of 1,10-phenanthroline (peaks A and B). On the other hand, some weaker cross-peaks between the H-a, H-b, and H-c protons of 1,10-phenanthroline and H-3 protons at the secondary side of cyclodextrin can also be observed. These phenomena jointly indicate that the 1,10-phenanthroline molecules are included in the cyclodextrin cavity, or located near to the secondary side of cyclodextrin parallelly. In addition, the Job's plot shows the maximum at a molar fraction of 0.4 (Fig. 7), confirming the formation of 2:3 host/guest inclusion complex between β-cyclodextrin and 1,10-phenanthroline, which is consistent with the crystal structure obtained in solid state.

In summary, we have determined the crystal structure of the complex formed by β-cyclodextrin and 1,10-phenanthroline with an uncommon 2:3 stoichiometry. Every complex unit contains three 1,10-phenanthroline molecules and two β-cyclodextrin molecules, where the guest molecules occupy two absolutely different positions. The intermolecular hydrogen bonds between the adjacent complex units further link these individual monomers to a channel-type assembly. Furthermore, the results obtained from ^{1}H and 2D NMR spectra and Job plot jointly indicate that the complex adopts the

Table 2. The chemical shifts (δ) of β-cyclodextrin, 1,10-phenanthroline, their mixture at the same concentration and the corresponding changes

		β-cyclodextrin	1,10-phenanthroline	β-cyclodextrin + 1,10-phenanthroline	
	m	δ	δ	δ	$\Delta\delta$
H-1	d	4.85		4.83	−0.02
H-2	dd	3.44		3.42	−0.02
H-3	dd	3.75		3.72	−0.03
H-4	dd	3.40		3.35	−0.05
H-5	m	3.66		3.60	−0.06
H-6	dd	3.66		3.59	−0.07
H-a	s		7.53	7.46	−0.07
H-b	d		8.10	8.04	−0.06
H-c	m		7.49	7.47	−0.02
H-d	d		8.75	8.73	−0.02

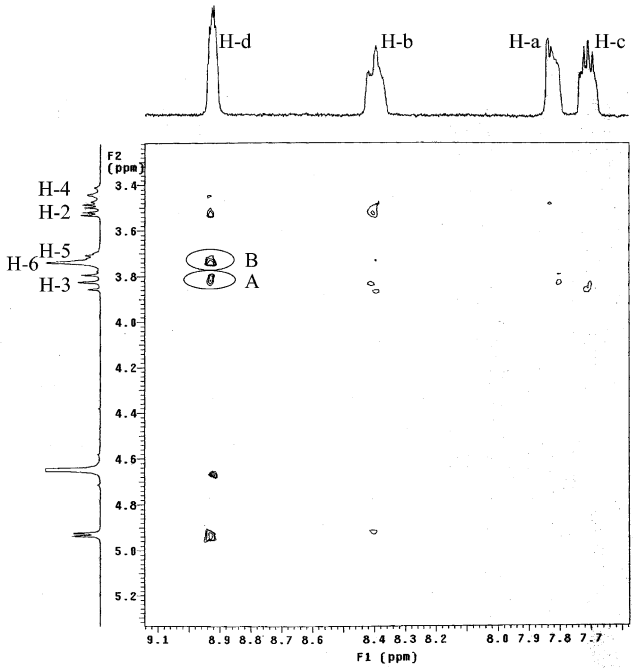

Figure 6. 2D ROESY spectrum of β-cyclodextrin/1,10-phenanthroline complex (7.0×10^{-3} M) in D_2O with a mixing time of 400 ms.

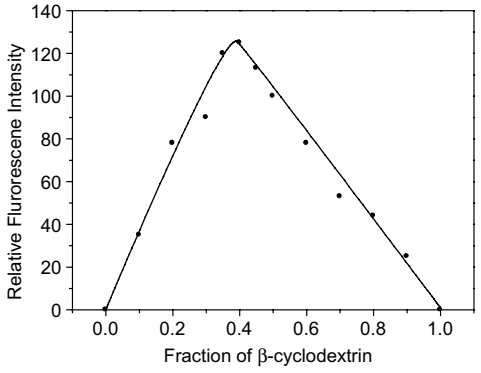

Figure 7. Continuous variation plot of the β-cyclodextrin/1,10-phenanthroline system ([β-cyclodextrin] + [1,10-phenanthroline] = 3.0×10^{-6} M) in aqueous solution.

same 2:3 stoichiometry and the 1,10-phenanthroline molecules are included in the cyclodextrin cavity in aqueous solution. These observations are useful not only for understanding the supramolecular aggregation phenomena, but also for designing novel molecular assembly of cyclodextrins and functional guests.

4. Supplementary material

CCDC-221781 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: +44-1223-336-033; or deposit@ccdc.cam.ac.uk).

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