Available online at www.sciencedirect.com
SCIENCE DIRECT®
Carbohydrate Research 340 (2005) 513–517
Carbohydrate RESEARCH

Note

The molecular crystal structure and self-assembly behavior of 6^{I}-*O*-(3-nitrophenyl)cyclomaltoheptaose

Zhi Fan,* Zuo-Liang Jing and Chun-Hua Diao

College of Sciences, Tianjin University of Science and Technology, Tianjin 300222, PR China

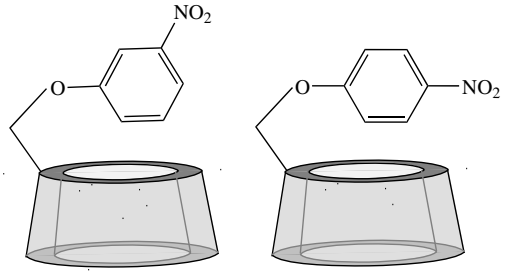
Received 19 July 2004; accepted 3 December 2004

Abstract—The mono-modified β-cyclodextrin derivative, 6^{I}-*O*-(3-nitrophenyl)cyclomaltoheptaose{mono[6-*O*-(3-nitrophenyl)]-β-cyclodextrin} was synthesized, and its crystal structure was determined by single-crystal X-ray analysis. The crystal structure suggests that the 3-nitrophenyl substituent group is inserted into the adjacent β-cyclodextrin cavity from the secondary hydroxyl side, and the molecules are stacked along the twofold screw axis to form an infinite one-dimensional polymeric chain.

Keywords: Cyclodextrin; Crystal structure; Supramolecular chemistry; Self-assembly

Cyclomaltooligosaccharides (cyclodextrins, CDs) are known to form host–guest inclusion complexes with a wide variety of guest molecules included within the hydrophobic cavities. Consequently, they are ideal prototypes for examining intermolecular interactions associated with molecular recognition and assembly.[1–4] Native β-CD and modified β-CDs are widely used in chromatographic applications and as building blocks for supramolecular structures.[5–8] Systematic crystallographic studies can provide direct access to this type of structural information.[9–11] Recently, Liu and co-workers have reported the crystal structure and self-assembly behavior of mono-modified β-CDs.[12] In that work, it was found that the self-assembling orientation, alignment, and helicity in the solid state may be influenced by tuning the pivot atom and the tether length.[12b] Yannakopoulou and co-workers have investigated the structures and preferred conformations of isomeric aminobenzoic acid-modified β-CDs by NMR spectroscopy and X-ray crystallography, respectively, in aqueous solution and the solid state,[13] which showed the influence of hydrogen bonding of the carboxyl with the hydroxyl of the β-CD on the molecular conformation. Believing crystallographic studies of appropriate β-CD supramolecular self-assemblies can provide improved insight on subtle differences in interactions of similar energy as such interactions are commonly associated with molecular recognition and self-assembly, we expanded the study to include the allotropic substituent group.

In this paper, we now report the synthesis and crystal structure of 6^{I}-*O*-(3-nitrophenyl)cyclomaltoheptaose-{mono[6-*O*-(3-nitrophenyl)]-β-CD} (**1**). By comparing the complex **1** with 6^{I}-*O*-(4-nitrophenyl)cyclomaltoheptaose{mono[6-*O*-(4-nitrophenyl)]-β-CD} (**2**) in substituent backbone functional group,[12b] we hope to gain an improved understanding of the mechanism of controlling the formation of one-dimensional polymeric chain as mediated by intermolecular interaction.



1 **2**

* Corresponding author. Fax: +86 22 23001002; e-mail: zhifan@public.tpt.tj.cn

0008-6215/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2004.12.004

Table 1. The crystal data, experimental and refinement parameters of **1**

	Compound **1**
Molecular formula	$C_{48}H_{73}NO_{37}{\cdot}8.75H_2O$
M_r (g mol^{-1})	1413.71
Crystal system	Monoclinic
Space group	*P*2(1)
Z	4
a (Å)	16.402(6)
b (Å)	13.830(5)
c (Å)	29.579(11)
β (°)	101.732(7)
V (Å^3)	6569(4)
ρ_{calcd} (g cm^{-3})	1.429
F (000)	3006
Absorption coefficient (mm^{-1})	0.129
Crystal size (mm)	$0.22 \times 0.20 \times 0.18$
Range scanned *θ* (°)	1.63–26.42
Data/restraints/parameters	25,181/211/1874
Final *R* indices [$I > 2\sigma(I)$]	0.0909
R Indices (all data)	$R1 = 0.2095$, $wR2 = 0.2371$
Largest diff. peak and hole (e Å^{-3})	0.520 and −0.281

The geometrical data are given in Table 1, and parameters describing the macrocyclic conformation of **1** and **2** are presented in Table 2. All glucose residues of the complexes are in the usual $^4C_1$ chair conformation. The original skeleton of the macrocyclic moiety with an approximate sevenfold axis and a round shape is not significantly changed when bearing a substituent group, as observed in other 6-mono-modified β-CDs.[9e]

In molecular structure of **1**, seven glycosidic oxygen atoms (O4), which are nearly coplanar within the deviation of 0.2409 Å, showing an irregular plane. The dihedral angle between phenyl ring and the plane of glycosidic oxygen atoms (O4) is 44°, and the substituent group directs away from the center of the β-CD ring and extends in a direction parallel to the macrocyclic ring, as shown in Figure 1.

Seven glycosidic oxygen atoms (O4) of molecular structure of **2** are coplanar within 0.0738 Å, showing good planarity compared with **1**. The dihedral angle

Table 2. Geometrical data describing the β-CD unit of the compounds

	O4(*n*)–O4(*n* − 1) (Å)	O4(*n*)–O4(*n* + 1)–O4(*n* + 2) (°)	C4(*n*)–O4(*n*)–C1(*n* + 1) (°)	Tilt angle[a] (°)	Deviation of O(4) atom (Å)[b]
Compound **1**					
G1	4.303	125.7	119.5	4.7	−0.1223
G2	4.430	131.7	118.8	16.8	0.2748
G3	4.411	125.2	117.7	11.1	0.0955
G4	4.175	126.9	119.8	23.2	−0.4506
G5	4.348	131.0	118.3	9.6	0.2211
G6	4.330	127.1	117.9	28.0	0.2516
G7	4.374	127.9	118.9	16.6	−0.2702
Compound **2**					
G1	4.416	126.4	118.9	20.1	−0.1032
G2	4.419	127.2	119.6	2.0	0.0049
G3	4.225	130.2	120.5	18.6	−0.0156
G4	4.331	131.3	120.7	10.8	0.1067
G5	4.447	122.4	117.7	2.5	−0.1069
G6	4.370	130.9	120.3	16.0	−0.0327
G7	4.290	130.7	114.8	9.5	0.1468

[a] The tilt angle is defined as an angle made by the O(4) plane and the plane through C(1), C(2), O(4), and O(4)′.
[b] The deviation of each of O(4) atom from the plane through seven O(4) atoms.

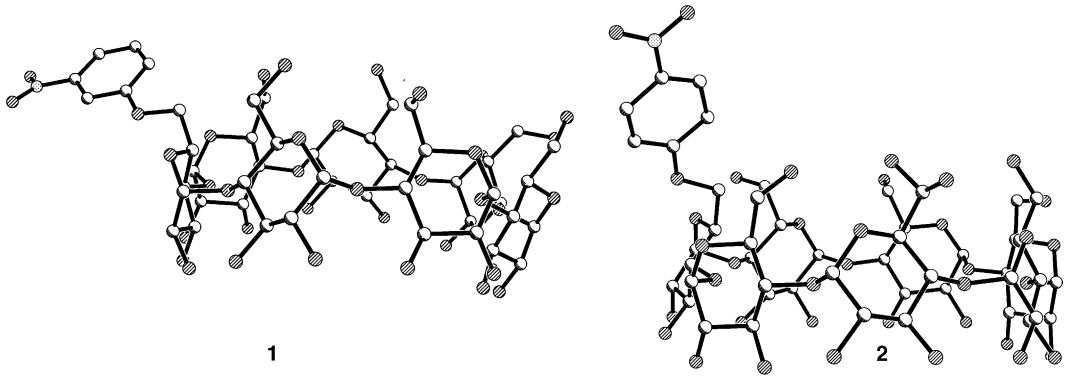


Figure 1. The molecular structure of **1** and **2**.

between phenyl ring and the plane of glycosidic oxygen atoms (O4) is 53.4°. The substituent group in **2** extends along the side of the β-CD ring and is inclined to the perpendicular axis to the O(4) atoms plane to make the hydrophobic cavity small at the primary hydroxyl side.

Comparison of the molecular structure reveals that the difference of the molecular conformation results from the position of the nitro group. To form a one-dimensional polymeric chain, the location of the adjacent β-CDs must be adjusted to favor the inclusion of the substituent group in the β-CD cavity. As a result, the position of the nitro group in the nitrophenyl-β-CD gives rise to quite different space groups, and, notably, a different molecular conformation for them.

The packing arrangements of the two complexes are shown in Figure 2. In the two complexes, the substituent group successively penetrates into the adjacent β-CD cavity from the secondary side to form an extended one-dimensional helical columnar superstructure. The substituent group is located at the center of the adjacent β-CD ring and fully occupies the cavity. Thus each molecule behaves as both host and guest.

The molecules of crystal **1** are aligned on a twofold screw axis parallel to the *b* crystal axis, and the inclusion of the substituent group of the symmetry-related mate forms polymeric-like columns. The aromatic group in **1** is deeply included into the hydrophobic cavity of an adjacent β-CD and makes an angle of 53.2° with the O(4) atoms plane of the adjacent β-CD. The dihedral angle of the O(4) atoms plane between the adjacent β-CD is 57.5°. The position of the substituent group in the adjacent β-CD cavity can be adjusted to maximize the van der Waals contacts with the inside wall of the β-CD, critically depending on the flexibility of the ether bond linking the phenyl ring and β-CD. Interestingly, the phenyl ring is fully inserted in the adjacent β-CD cavity while one nitro group oxygen atom, O(36), is hydrogen bonded to a primary hydroxyl group of the same β-CD ($d_{[H29A\cdots O36C]}$ = 2.508 Å, $\Phi_{[C29A-H29A\cdots O36C]}$ = 149.9°). As a result, the position of the 3-nitrophenyl group within the β-CD cavity is determined by the host–guest interactions that include the van der Waals contacts and hydrogen bonds (Table 3) between the substituent group and β-CD. At the same time, the helical column is stabilized by the hydrogen bonds formed between the primary and secondary hydroxyl groups of the adjacent β-CD or through intervening water molecules.

In the crystal of **2** the substituent group is deeply included into the hydrophobic cavity of an adjacent β-CD and makes an angle of 59.6° with the O(4) atoms plane of the adjacent β-CD. The dihedral angle of the O(4) atoms plane between the adjacent β-CD is 38.0°. The crystal has three twofold screw axes, and the adjacent helical column that is symmetry-related by another twofold screw axis is extended in the same direction. The nitro group linked to the benzene ring, not only protrudes from the primary hydroxyl side, but also further interacts with the secondary hydroxyl of the third β-CD by hydrogen bonding ($d_{[H31C\cdots O2B]}$ = 2.420 Å, $\Phi_{[O31C-H31C\cdots O2B]}$ = 169.3°), forming a zigzag structure. On the other hand, the glucosyl O-atom accepts one of the aromatic hydrogens to form a hydrogen bond ($d_{[H74D\cdots O43B]}$ = 2.459 Å, $\Phi_{[C74D-H74D\cdots O43B]}$ = 169.3°). These two independent hydrogen-bonding interactions fix the position and orientation of the substituent of **2** in the self-assembling structure.

As mentioned above, the dihedral angle of the plane of the O(4) atoms between the adjacent β-CD in **1** is larger than that in **2**, resulting in the fact that the molecule of **1** may contain more water molecules (8.75 H_2O in **1**, and 5 H_2O in **2** per molecule, respectively). The additional water molecules in the hydrophilic interface binding environment participate in interactions with β-CD molecules, typically by bridging hydroxyl groups of neighboring β-CD molecules, which contribute to stabilization of the polymeric-like column. On the other hand, the depth of the substituent group in the adjacent β-CD is different. The center of phenyl ring exceeds the plane of the O(4) atoms of the adjacent β-CD by 0.16 Å for **1** in comparison with 0.36 Å for **2**, which results from the hydrogen bonds between nitro oxygen atom and different hydroxyl groups.

When comparing the positions and orientations of the substituent groups in the β-CD cavities, it should be noted that the slight variation in the self-assembly behavior caused by the substituent group depends on the host–guest interaction because the geometry of intermolecular inclusion is mainly regulated by the shape and size of the rigid group. This indicates that we can use the position of the substituent group as an additional convenient and reliable tool for designing and constructing desired supramolecular structures and functions.

1. Experimental

1.1. General methods

NMR spectra were recorded in D_2O on a Varian Mercury VX300. Elemental analyses was performed on a Perkin–Elmer 240 instrument. X-ray intensity data were collected on a standard Siemens SMART CCD Area Detector System equipped with a normalfocus molybdenum-target X-ray tube operated at 2.0 kW (50 kV, 40 mA) and a graphite monochromator. The structure was solved using the direct method and refined by the full-matrix least-squares method (Siemens SHELXTL, version 5.04). Reagent grade β-CD (Shanxi Biochemical Reagent Works) was recrystallized twice

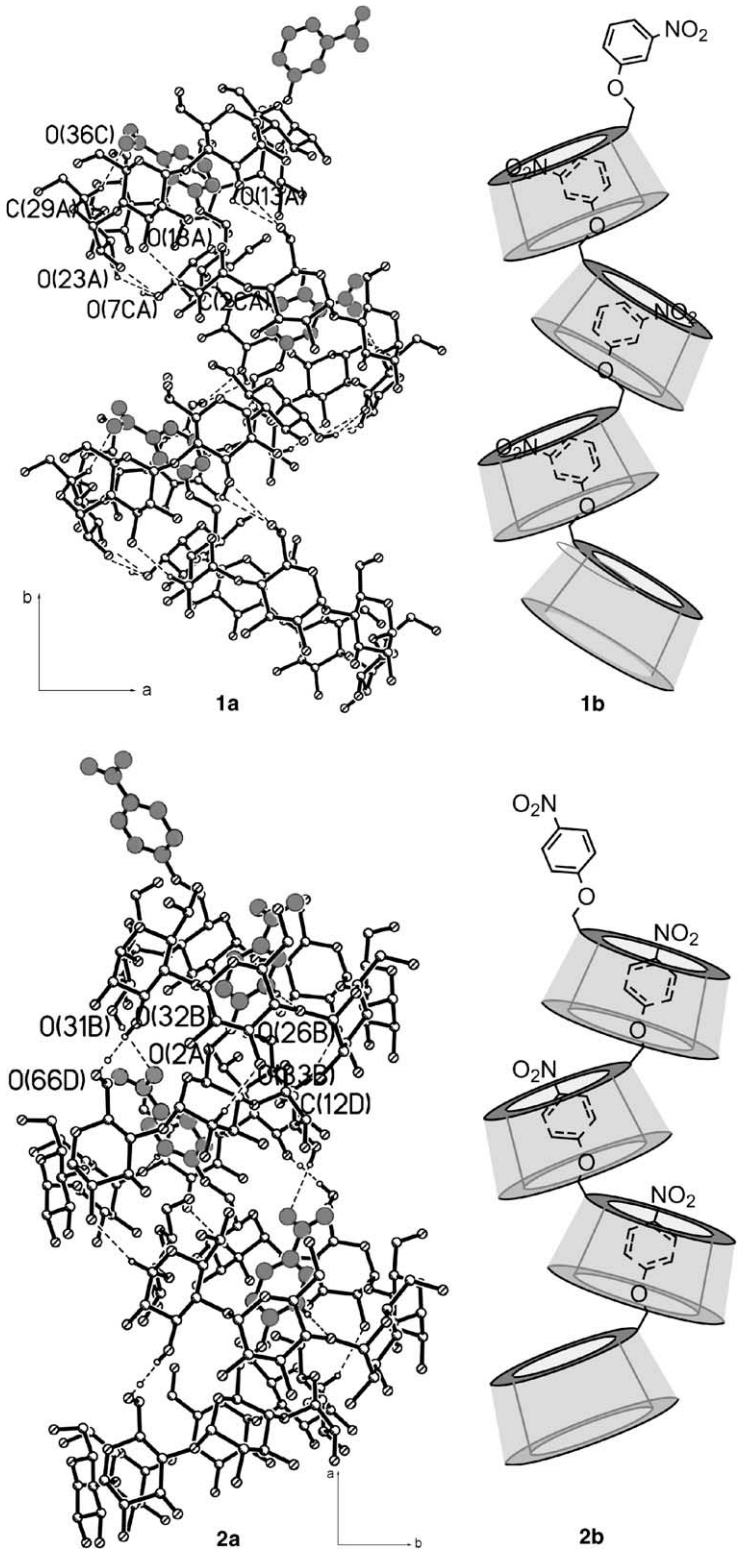


Figure 2. The one-dimensional helical superstructures of the complexes **1** and **2**. The column is located on a twofold screw axis. (a) Helical columnar structure; (b) schematic representation of packing.

from water and dried in vacuo at 95 °C for 24 h prior to use. *N*,*N*-Dimethylformamide (DMF) was dried over calcium hydride for 2 days and then distilled under a reduced pressure prior to use. K_2CO_3 (Shanghai Reagent Works) was dehydrated by heating at 200 °C in an oven.

Table 3. Parameters for selected hydrogen-bonding interactions observed in **1** and **2**

Interaction[a]	Distance (Å)[b]	Angle (°)
Compound **1**		
C29A–H29A···O36C	2.508	149.9
O7CA–H7CA···O23A	2.503	139.1
C2CA–H2AD···O18A	2.494	163.9
Compound **2**		
O32B–H32D···O66A	2.018	160.5
C74D–H74D···O43B	2.459	169.3
O66D–H66L···O32B	1.997	179.4
C27D–H27G···O33B	2.574	165.4
C12D–H12D···O26B	2.557	140.9

[a] A, B, and C denote the monomer serial number in the arrangement of the compounds.
[b] Heavy atom to H atom.

1.2. Preparation of 6^{I}-*O*-(3-nitrophenyl)cyclomaltoheptaose (1)

To a solution of 3-nitrophenol (0.52 g, 3 mmol) in dry DMF (10 mL) was added anhyd K_2CO_3 (0.4 g, 3 mmol). The mixture was stirred for 5 h at room temperature under nitrogen, to which 6-*O*-(*p*-toluenesulfonyl)-β-CD (1.9 g, 1.5 mmol) in dry DMF (20 mL) was added dropwise with stirring. The solution was heated to 80 °C for 96 h. The resultant solution was evaporated under a reduced pressure to give yellow powder, which was dissolved in a minimum amount of hot water, and then the solution was poured into acetone (200 mL). The crude product obtained was purified on a Sephadex G-25 column, recrystallized twice from water, and then dried in vacuo to give pure **1** (46% yield). ^{1}H NMR (D_2O, ppm) 3.2–4.6 (m, 42H), 4.7–4.9 (m, 7H), 7.2–7.3 (d, 1H), 7.3–7.5 (m, 1H), 7.5–7.7 (m, 2H). Anal. Calcd for $C_{48}H_{73}NO_{37}\cdot 8H_2O$: C, 41.17; H, 6.36. Found: C, 41.37; H, 6.24.

Crystals of **1** was obtained from aqueous solution. A small amount of the compound was dissolved in hot water to make a saturated solution, which was then cooled to room temperature. After the precipitates were removed by filtration, the resultant solution was kept at room temperature for several weeks. The crystal formed was collected along with its mother liquor for X-ray crystallographic analysis.

Supplementary data

Complete crystallographic data for the structural analyses for compounds **1** and **2** have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 245064 (for **1**) and CCDC No. 196194 (for **2**). Copies of this information may be obtained free of charge from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 336033, deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk). Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2004.12.004.

References

1. Kano, K.; Hasegawa, H. *J. Am. Chem. Soc.* **2001**, *123*, 10616–10627.
2. Rekharsky, M. V.; Inoue, Y. *Chem. Rev.* **1998**, *98*, 1875–1917.
3. Corradini, R.; Dossena, A.; Impellizzeri, G.; Maccarrone, G.; Marchelli, R.; Rizzarelli, E.; Sartor, G.; Vecchio, G. *J. Am. Chem. Soc.* **1994**, *116*, 10267–10274.
4. Wenz, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 803–822.
5. Armstrong, D. W.; Ward, T. J.; Armstrong, R. D.; Beesley, T. E. *Science* **1996**, *232*, 1132–1135.
6. Armspach, D.; Ashton, P. R.; Moore, C. P.; Spencer, N.; Stoddart, J. F.; Wear, T. J.; Williams, D. J. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 854–858.
7. (a) Liu, Y.; Zhao, Y.-L.; Zhang, H.-Y.; Song, H.-B. *Angew. Chem., Int. Ed.* **2003**, *42*, 3260–3263; (b) Liu, Y.; Li, L.; Fan, Z.; Zhang, H.-Y.; Wu, X.; Guan, X.-D.; Liu, S.-X. *Nano Lett.* **2002**, *2*, 257–261.
8. Lahav, M.; Ranjit, K. T.; Willner, I. *Chem. Commun. (Cambridge)* **1997**, 259–260.
9. (a) Lindberg, B.; Lindberg, J.; Pitha, J.; Rao, C. T.; Harada, K. *Carbohydr. Res.* **1991**, *222*, 113–119; (b) Harada, K.; Trinadha, C.; Pitha, J. *Carbohydr. Res.* **1993**, *247*, 83–89; (c) Harada, K.; Takenaka, Y.; Yoshida, N. *J. Chem. Soc., Perkin Trans. 2* **2001**, 1667–1673; (d) Mentzafos, D.; Terzis, A.; Coleman, A. W.; de Rango, C. *Carbohydr. Res.* **1996**, *282*, 125–135; (e) Harada, K. *Chem. Rev.* **1998**, *98*, 1803–1827.
10. (a) Giastas, P.; Eliadou, K.; Plyta, Z. F.; Yannakopoulou, K.; Mavridis, I. M. *Carbohydr. Res.* **2004**, *339*, 1189–1194; (b) Corradini, R.; Dossena, A.; Marchelli, R.; Panagia, A.; Sartor, G.; Saviano, M.; Lombardi, A.; Pavone, V. *Chem. Eur. J.* **1996**, *2*, 373–381; (c) Liu, Y.; You, C.-C.; Zhang, M.; Weng, L.-H.; Wada, T.; Inoue, Y. *Org. Lett.* **2000**, *2*, 2761–2763.
11. (a) Udachin, K. A.; Ripmeester, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 1080–1081; (b) Udachin, K. A.; Wilson, L. D.; Ripmeester, J. A. *J. Am. Chem. Soc.* **2000**, *122*, 12375–12376.
12. (a) Liu, Y.; Fan, Z.; Zhang, H.-Y.; Diao, C.-H. *Org. Lett.* **2003**, *5*, 251–254; (b) Liu, Y.; Fan, Z.; Zhang, H.-Y.; Yang, Y.-W.; Ding, F.; Liu, S.-X.; Wu, X.; Wada, T.; Inoue, Y. *J. Org. Chem.* **2003**, *68*, 8345–8352.
13. Eliadou, K.; Giastas, P.; Yannakopoulou, K.; Mavridis, I. M. *J. Org. Chem.* **2003**, *68*, 8550–8557.