

## Pseudorotaxanes of $\beta$ -Cyclodextrin with Diamino End-functionalized Oligo-phenyl and -benzyl Compounds in Solution and in the Solid State

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### Abstract

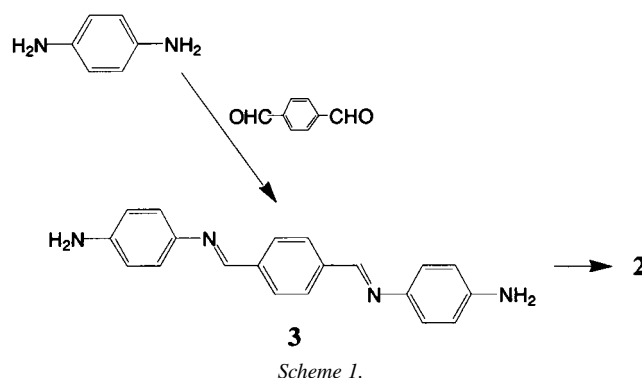
$\beta$ -Cyclodextrin forms a 1:1 host:guest inclusion complex ([2]pseudorotaxane) with 4-[2-(4-aminophenyl)ethyl]-benzenamine (**1**) in water as determined by 1D and 2D NMR experiments. In the crystalline state, the structure of the complex has revealed a 2:2 stoichiometry, with two  $\beta$ CD molecules forming head-to-head dimers by H-bonds between the secondary O3 hydroxyl groups and enclosing two molecules of the guest. The packing mode of the present complex is encountered for the first time, since it does not belong to any of the four known packing types of the dimeric  $\beta$ CD inclusion complexes. On the other hand,  $N^1, N^4$ -bis(4-aminophenyl)-1,4-benzenedimethanamine (**2**), which is longer than **1** by a phenylene diamine unit, has not afforded any crystals, at present, however it threads into  $\beta$ CD in aqueous solution forming most probably [2]- and [3]pseudorotaxanes. The solution structures and the equilibria in this system are investigated.

### Introduction

It has been of general interest to study the ability of long bifunctional molecules [1–3] to thread CD rings along their skeleton. This process can impose further order on the macrocycle, by sequential threading of CD rings to form pseudorotaxanes and provide the ability of stoppering via the guest's end-functional groups to afford rotaxanes [4–5]. We have already described the formation [3] and equilibria [3, 6] in solution of several long aliphatic diamines, diacids and aminoacids, and discussed the prerequisites for crystal engineering in the solid state [7]. Here we expand the studies to diamines having phenyl and benzyl backbones, such as 4-[2-(4-aminophenyl)ethyl]-benzenamine (**1**) and  $N^1, N^4$ -bis(4-aminophenyl)-1,4-benzenedimethanamine (**2**) (Scheme 1).

### Experimental

$N^1, N^4$ -bis(4-aminophenyl)-1,4-benzenedimethanamine (**2**). 1,4-Phenylenediamine (9.733 g, 90 mmoles) was dissolved in abs. ethanol (100 ml) and a solution of terephthalaldehyde (2.012 g, 15 mmoles) in abs. ethanol (100 ml), with 2–3 drops of glacial acetic acid dissolved, was gradually added under stirring and nitrogen. The mixture was left to agitate at ambient temperature for 14 h. Vacuum filtration and successive washings with n-pentane and abs. ethanol, followed



by drying, afforded a pure yellow solid (m.p. 200–201°C), the bis-Schiff base **3** (Scheme 2), in 91% yield. This was dissolved (0.472 g, 1.5 mmoles) in THF (40 ml) and NaBH<sub>4</sub> (2.134 g, 56 mmoles) was added in one portion, followed by gradual addition of abs. ethanol (40 ml). The mixture was heated under reflux for 4 h. Cooling, addition of H<sub>2</sub>O (70 ml), reduction of the volume to about 50 ml, vacuum filtration, washing with abs. ethanol and air drying, afforded a light red solid, 69% yield, m.p. 137.5–138°C; <sup>1</sup>H NMR (500 MHz, DMSO-d<sub>6</sub>, 298 K):  $\delta$  = 7.26 (s, 4H, *Hc*), 6.36 (s, 8H, *Ha* and *Hb*), 5.25 (t, *J* = 6.2 Hz, 2H, –NH–), 4.18 (s, 4H, –NH<sub>2</sub>), 4.09 (d, *J* = 6.2 Hz, 4H, –CH<sub>2</sub>–); <sup>13</sup>C NMR (62.9 MHz, DMSO-d<sub>6</sub>, 298 K):  $\delta$  = 140.0 (C-2), 139.0 (C-3), 138.9 (C-6), 127.1 (C-5), 115.3 (C-4), 113.7 (C-1), 47.5 (–CH<sub>2</sub>–); IR (KBr): 3377 and 3392 cm<sup>–1</sup> (–NH and –NH<sub>2</sub>), disappearance of peaks at 1614 and 1633 cm<sup>–1</sup> (–C=N–); MS: *m/e* = 318 (M<sup>+</sup>, 64%).

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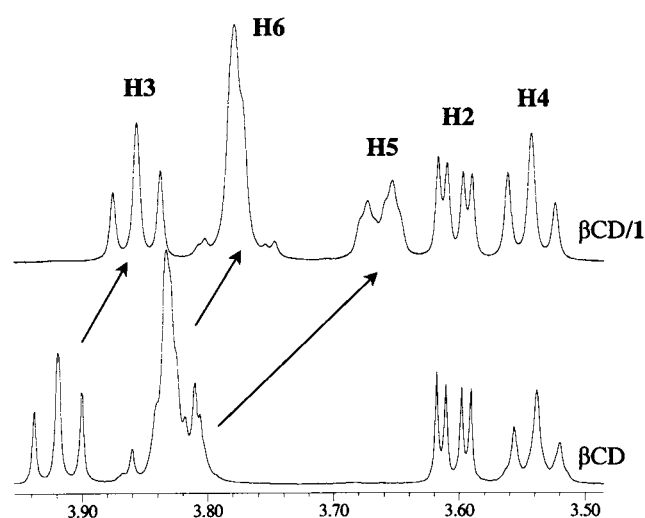
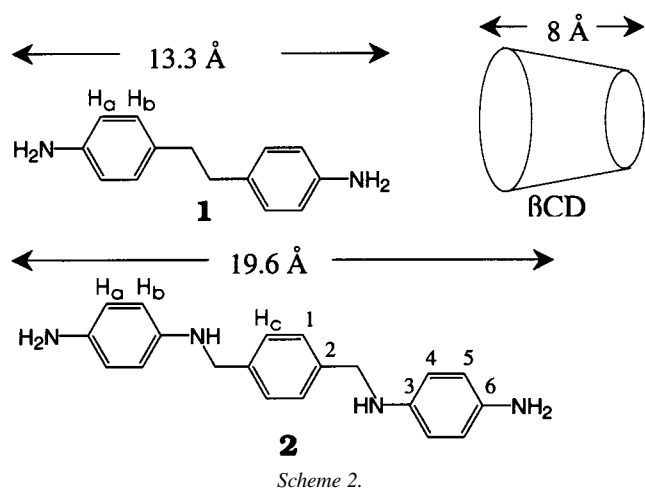


Figure 1. Partial  $^1\text{H}$  NMR spectra in  $\text{D}_2\text{O}$  of  $\beta\text{CD}$  and  $\beta\text{CD}/\mathbf{1}$ .

## Results and discussion

### A. 4-[2-(4-aminophenyl)ethyl]benzenamine (**1**)

Diamine **1** readily complexes with  $\beta\text{CD}$  as indicated by the observation of large chemical shifts of the cavity protons in the  $^1\text{H}$  NMR spectra (Figure 1) and the detection of intermolecular interactions in the ROESY spectrum (Figure 2). Specifically, in Figure 2a, there are strong interactions of the  $-\text{CH}_2-$  groups of **1** with all cavity protons, indicating (i) virtual threading of **1** inside the cavity and (ii) possible *bending* of the ethylene part. In Figure 2b, we observe slightly weaker interactions of  $\text{H}_a$ , than of  $\text{H}_b$  (Scheme 1) with the cavity protons, indicating that  $\text{H}_a$  atoms are probably located at the rims of the  $\beta\text{CD}$  cup. The solid crystalline complex, after dissolution in  $\text{DMSO}-d_6$ , showed a 1:1 stoichiometry.

X-ray analysis of the crystalline complex provided the supramolecular structure of the adduct. The  $\beta\text{CD}$  host, forming head-to-head dimers by H-bonding between the O3 hydroxyl groups [8] encloses two guest molecules. The dimers of  $\beta\text{CD}$  form C-centered layers in all dimeric complexes. The packing, however, of the layers to form the 3D lattice varies depending on the guest [7]. Up to now four packing modes of dimeric  $\beta\text{CD}$  complexes have been en-

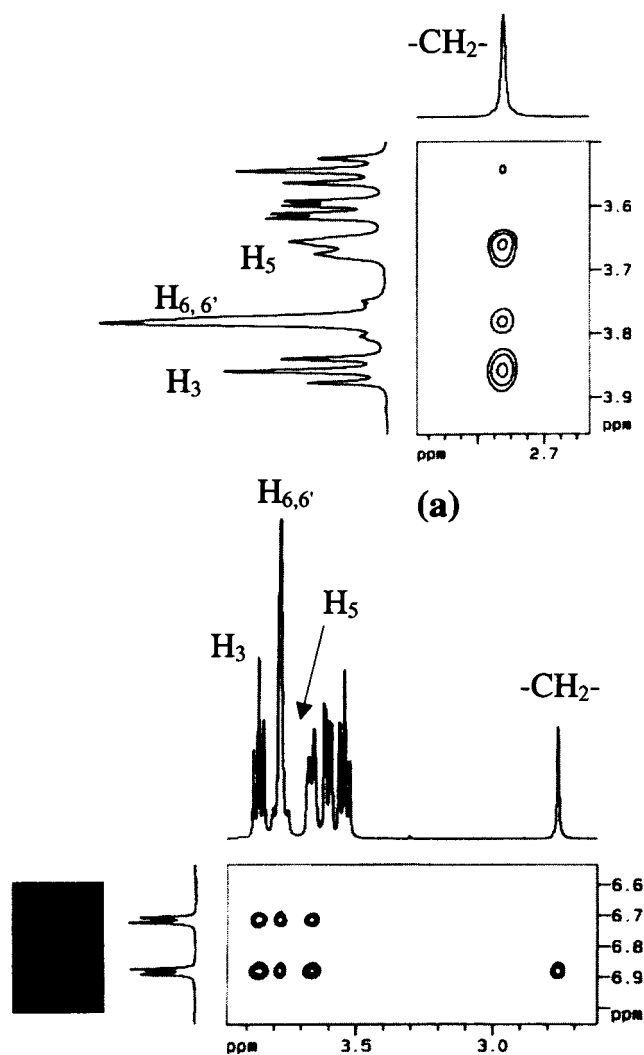


Figure 2. 2D ROESY spectrum (500 MHz) of  $\beta\text{CD}/\mathbf{1}$  in  $\text{D}_2\text{O}$ .

countered [9]. The present structure is a new packing mode and does not belong to any of them. Two kinds of  $\beta\text{CD}$  dimers exist in the lattice differing only in the conformation of the guest (Figure 3). The latter has an extended conformation in the one kind of dimers, whereas in the other the guest is in a puckered (bent) conformation, disordered over two positions. The guest molecules of both types exhibit  $\pi$ - $\pi$  interactions inside the  $\beta\text{CD}$  cavity.

Several trials to stopper the  $\beta\text{CD}/\mathbf{1}$  adduct did not afford the desired rotaxane. As the crystal structure shows, the end- $\text{NH}_2$  groups are not really available for solid-state reaction (due to the dimer and channel formation) with e.g., aldehydes; on the other hand, in the solution the semirotaxane formation is more likely due to accessibility of only one  $-\text{NH}_2$  group at a time, however, formation of a rotaxane and fast unthreading cannot be excluded. Figure 4a illustrates the attempted stoppering of the complex via formation of a double Schiff base **4** by reaction with naphthalene salicylaldehyde, either in solution, in the melt or in the solid state. Less than 17% of the semirotaxane **5** was formed, which gradually (4 days) unthreaded to its components,  $\beta\text{CD}$  and **4** (Figure 4b).

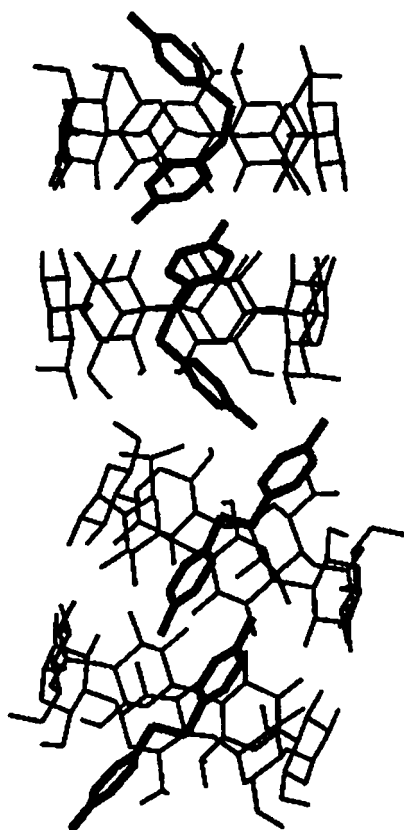
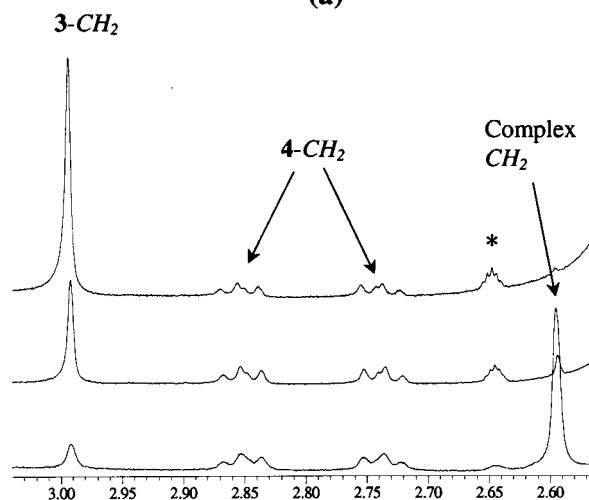
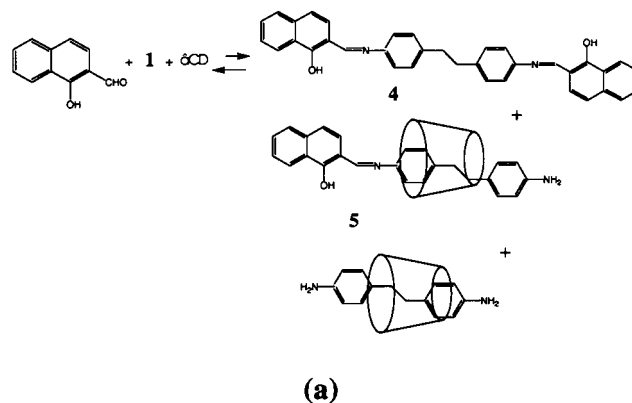


Figure 3. Crystal structure of the  $\beta$ CD/1 complex, showing the two kinds of guests.

*B. N<sup>1</sup>,N<sup>4</sup>-bis(4-aminophenyl)-1,4-benzenedimethanamine (2)*

The title compound (Scheme 1) could, in principle, thread two  $\beta$ CD rings, forming primarily a [3]pseudorotaxane in solution, and hopefully, in the solid state. Condensation of 1,4-phenylene diamine and terephthalaldehyde and subsequent reduction with sodium borohydride afforded **2** (Scheme 2), which was identified by its spectroscopic data ( $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, IR, MS). Compound **2** was found to complex with  $\beta$ CD in buffered  $\text{D}_2\text{O}$  solution (pH 7.3), as indicated by the observed  $^1\text{H}$  shifts of both the host and the guest (Figure 5a). The stoichiometry of the  $\beta$ CD/**2** complex was found to be a mixture of 1:1 and 2:1, as suggested by the Job plots (Figure 6) and the titration diagrams (Figure 7). The latter were not completed due to solubility problems. It is worth noting that the  $^1\text{H}$  NMR spectrum of free **2** in  $\text{D}_2\text{O}$  instead of the expected first order type-peaks for Ha and Hb shows a large wide peak at 6.7 ppm (Figure 5a, bottom left), which covers the other peaks. This arises from a particular conformation (or aggregation) that **2** adopts in  $\text{D}_2\text{O}$ , since this particular peak increases with time, after dissolving **2** in  $\text{D}_2\text{O}$ , and is not the result of some kind of degradation, as was verified by spectra in other solvents. The presence of  $\beta$ CD modifies this conformation (aggregation) (Figure 5a, top left) and Ha, Hb appear as two first-order doublets. This phenomenon must be, at least in part, responsible for the “irregular” inversion points in the Job plots (see Figure 6a, 6b), which do not correspond to a single clear stoi-



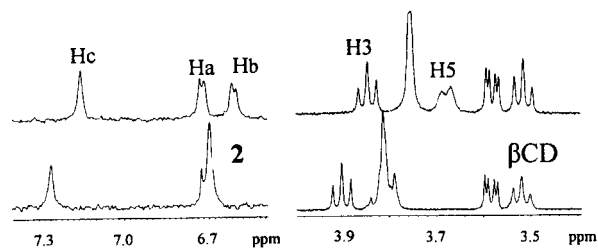
(b)

Figure 4. Attempted formation of a rotaxane of  $\beta$ CD/1 by naphthalene salicylaldehyde stoppering. (b)  $-\text{CH}_2-$ -region of the  $^1\text{H}$  NMR spectrum (DMSO- $d_6$ ) of  $\beta$ CD/1 complex + 6 equivs naphthalene salicylaldehyde; \*  $^{13}\text{C}$  satellite from solvent peak. The spectra were acquired in 4 day-intervals, the stop spectrum being the last.

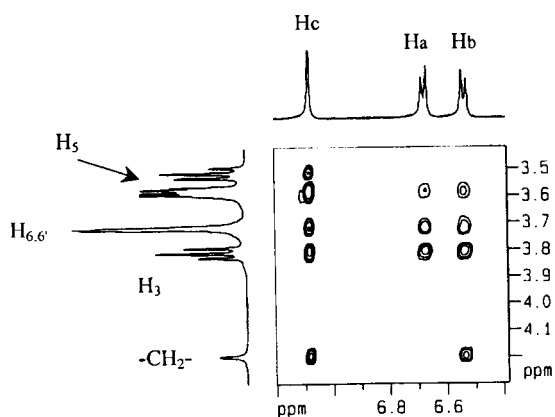
chiometry. The intermolecular correlations between the host and the guest are shown in the 2D ROESY spectrum (Figure 5b). Interaction of  $\text{CH}_2$ -groups with Hc (expected, 3-bonds apart), but also with Hb (4-bonds apart), indicates possible bending of **2**. The very strong interaction of the central ring hydrogen atoms (Hc) with all cavity protons, that may arise from both 1:1 and 2:1 adducts, suggests very tight positioning in the cavity. The end rings' Ha must be practically outside the  $\beta$ CD cone in the 1:1 case, and the observed correlations with the cavity protons must be due to the 2:1 adduct. Attempts to crystallize the complex did not succeed. There was no indication of complex formation between **2** and  $\alpha$ CD, permethylated  $\alpha$ CD and permethylated  $\beta$ CD by  $^1\text{H}$  NMR spectroscopy. Rotaxation of these compounds using various stopper molecules is under investigation.

#### Acknowledgments

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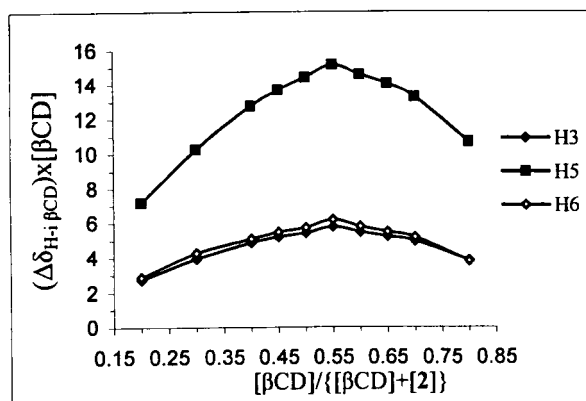


(a)

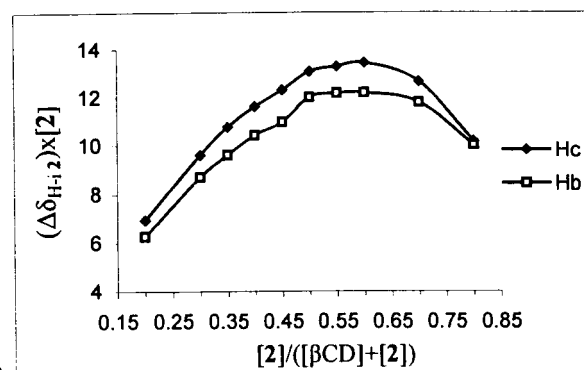


(b)

Figure 5. (a)  $^1\text{H}$  NMR spectra of free **2** and free  $\beta\text{CD}$  (bottom) and mixed (top) and (b) 2D ROESY spectrum of  $\beta\text{CD}/\mathbf{2}$ .



(a)



(b)

Figure 6. Job plot diagrams of (a)  $\beta\text{CD}$  (b) **2**.

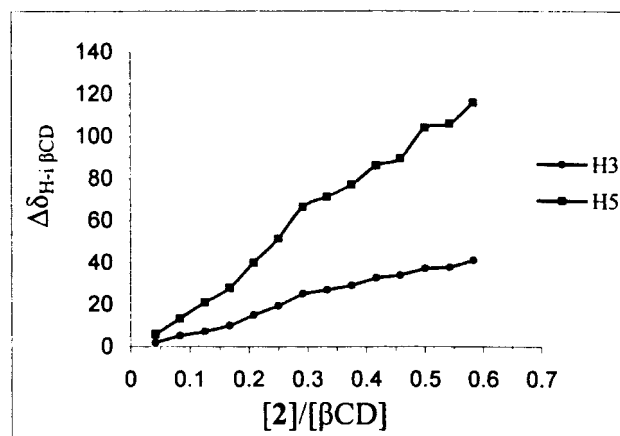


Figure 7. Mole ratio diagram of  $\beta\text{CD}/\mathbf{2}$ .

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