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# Bis(molecular tube)s: Supramolecular Assembly of Complexes of Organoselenium-Bridged β-Cyclodextrins with Platinum(IV)

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## ABSTRACT

**A novel supramolecular assembly, bis(molecular tube)s composed of complexes of organoselenium-bridged β-cyclodextrins and platinum(IV) ion, have been fabricated via the pseudorotaxane with poly(propylene glycol) and characterized by $^1$H NMR, TEM, and AFM images, etc.**

Molecular recognition and molecular self-assembly are currently being extensively studied in chemical and biological systems.[1] Recently, Ghadiri et al.[2] reported the construction of open-ended hollow nanotubes based on the self-assembly of cyclic peptide subunits, which display good channel-mediated ion-transport activity with rates exceeding $10^7$ ions per second, rivaling the performance of many naturally occurring counterparts. Such molecular assemblies should find use in medicine and material science. Nolte and co-workers[3] reported the self-assembling of crown ether-substituted phthalocyanines into columnar supramolecular architectures having a length of several micrometers. The most interesting applications are in the field of one-dimensional transport of energy, charge, and ions. In the meanwhile, Harada et al.[4] reported a molecular tube, composed of cyclodextrin molecules linked by covalent bonds. Ooya et al.[5] reported the synthesis of a similar biodegradable polyrotaxane for the use in drug delivery systems, in which cyclodextrins were used as drug carriers. Here, we report a novel molecular assembly—bis(molecular tube)s of β-cyclodextrin derivatives containing selenium and platinum. It is well-known that some *cis*-platinum complexes are successful anticancer agents, and organoselenium compounds were suggested as repressors of human immunodeficiency virus (HIV) transcription.[6] Therefore, the nano assembly reported here might have important potential application in drug delivery systems.

The assembly was prepared according to the procedures shown in Scheme 1. As shown in Scheme 1, β-cyclodextrin was converted to mono[6-*O*-(*p*-toluenesulfonyl)]-β-cyclodextrin. Subsequently, this intermediate reacted with 1,2-diselenacyclopentane in a mixture of *N*,*N*-dimethylformamide and ethanol in the presence of sodium borohydride to give organoselenium-bridged bis(β-cyclodextrin) **1**.[7] Thermal analysis (or calorimetric measurement) and $^1$H NMR spectra clearly indicated that β-cyclodextrin dimer **1** forms a complex with Pt(IV). The stoichiometric quantity of the **1**−Pt(IV) complexes formed was determined as 2:1 by conductometric titrations, using mixtures of **1** and $PtCl_4$ of various molar ratios ranging from 10:1 to 1:10.[7] The complexation of β-cyclodextrin dimer **1** and Pt(IV) affords a favorable orientation for the **1**−Pt(IV) complexes to form a pseudorotaxane with linear polymeric chain, i.e., poly(propylene glycol) (PPG, average molecular weight: 2000). The pseudorotaxane can be converted to rotaxane **2** by the esterification of the terminal hydroxyl groups of the included PPG with 3,5-dinitrobenzoic acid. Bis(molecular tube)s **3** was obtained by cross-linking the adjacent cyclodextrin rings with epichlorohydrin and removal of the polymeric chain through the hydrolysis of the terminal ester groups.[8]

The assembling behavior of **1** with PPG was invesitgated in situ by using $^1$H NMR sepctroscopy. To the solution of **1**−Pt(IV) complexes in $D_2O$ was added PPG, and then 3,5-dinitrobenzoic acid, recording the chemical shift changes. As shown in Figure 1, the characteristic upfield shifts of cyclodextrin's $H_3$ and $H_5$ signals upon the inclusion complexation from $\delta$ 3.8−3.9 to 3.4−3.7 indicate the formation of a rotaxane-type complex with PPGs penetrating through the cyclodextrin cavity. Molecular weight of assembly **2** determined by the end-group assay[9] is $2.2 \times 10^4$, indicating

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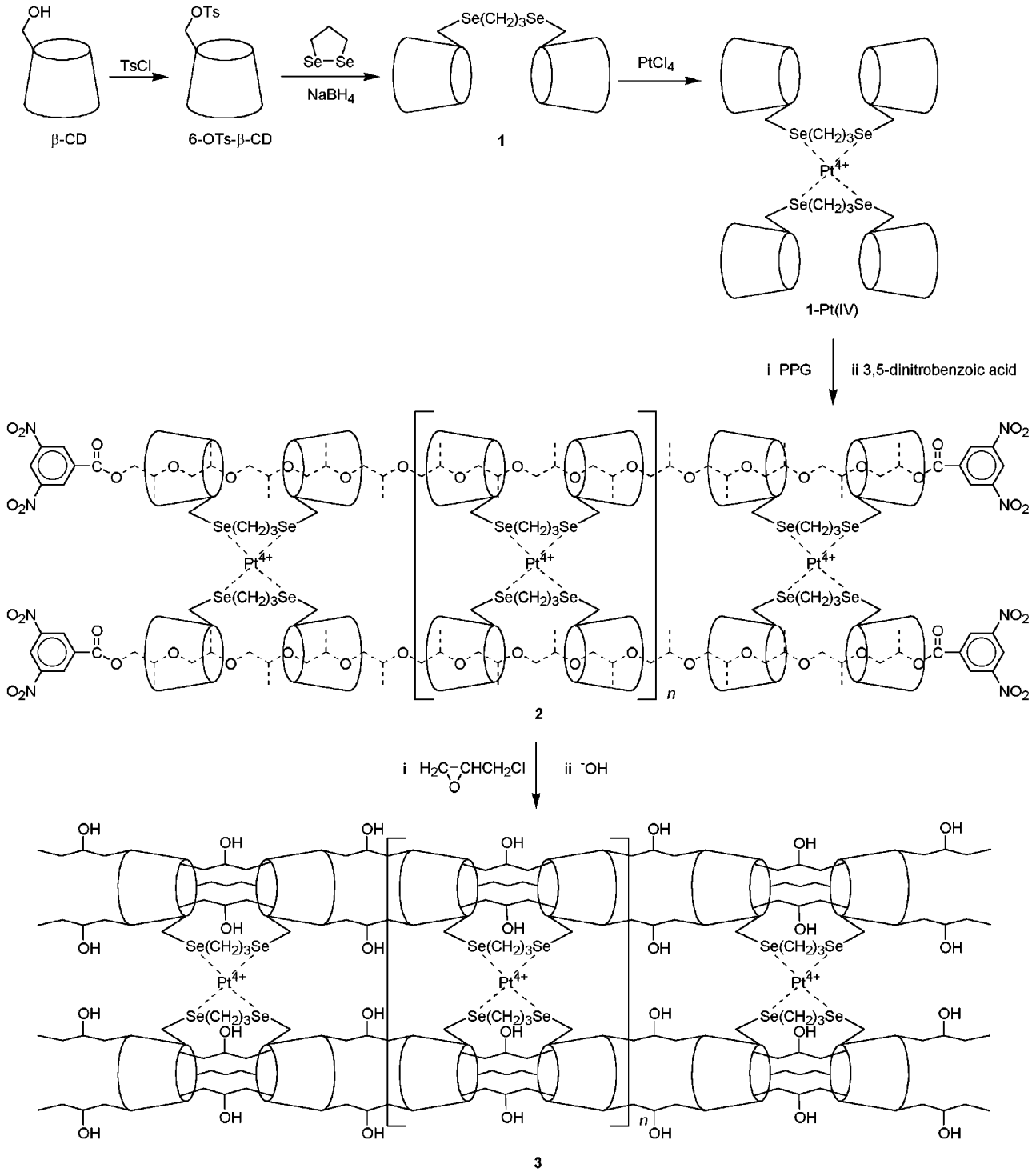
**Scheme 1**




that 4 units of **1**-Pt(IV) complexes were assembled by adding PPG as a template to the supramolecule.

The degree of cross-linking, *m*, a molar ratio of the cross-linking residue to the block residue, was determined from the result of the elemental analysis of **3** by using

$$C\,(\%) = \frac{2 \times [12.011 \times (42 \times 2 + 3 + 3m)]}{2m \times M_{\mathrm{PPR}} + 2M_{\mathrm{bCD}} + M_{\mathrm{PtCl_4}}} \times 100\% \quad (1)$$

where *m* denotes the degree of cross-linking, $M_{\mathrm{PPR}}$, $M_{\mathrm{bCD}}$, and $M_{\mathrm{PtCl_4}}$ indicate the molecular weights of cross-linking propylene residue, bridged $\beta$-cyclodextrins, and $PtCl_4$, respectively. The numerator of eq 1 contains the summation in atomic weight of all carbon atoms of one block of the molecular assembly.[10] From the equation, the value of *m* is obtained as 6. This indicates any two adjacent cyclodextrin rings were cross-linked by three propylene residues, as shown in Scheme 1.

The product **3**, which is soluble in water, dimethylformamide, and dimethyl sulfoxide, was characterized by $^1$H NMR,

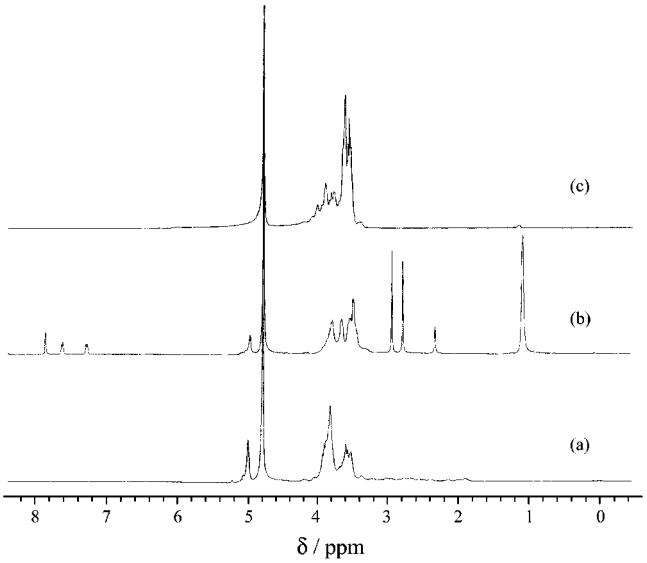



**Figure 1.** $^1$H NMR spectra of (a) $\beta$-cyclodextrin dimer **1**, (b) rotaxane **2**, and (c) bis(molecular tube)s **3**.

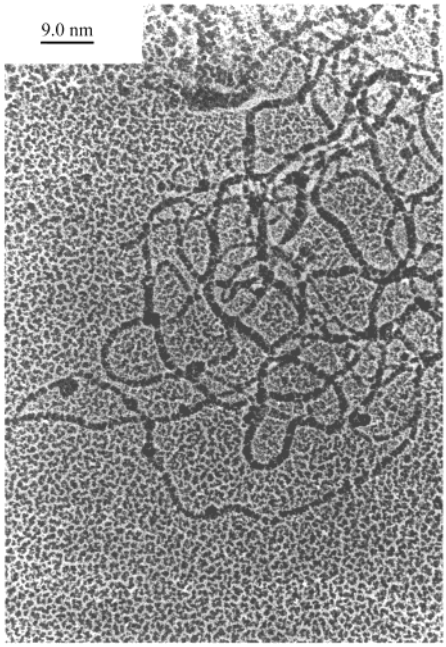



**Figure 2.** TEM spectrum of bis(molecular tube)s **3**.

IR, and UV spectroscopy. The $^1$H NMR spectrum of **3** in $D_2O$ clearly demonstrates the absence of the capping dinitrobenzoate groups and the presence of the linker's methylene and methine protons at $\delta$ 3.5−3.7 nm. The UV spectral examinations down to 250 nm also support the complete removal of the chromophoric dinitrobenzoyl group.

The solution of bis(molecular tube)s **3** was kept transparent at tempeartures from 25 to 80 °C, indicating that the assembly obtained is not a simple aggregate but possesses homogeneity with a rigid structure, as shown in Scheme 1.

Furthermore, transmission electron microscopy (TEM)[11] gives more information about the actual shape of the bis(molecular tube)s. The TEM image clearly verifies the formation of bis(molecular tube)s. As is well-known, the

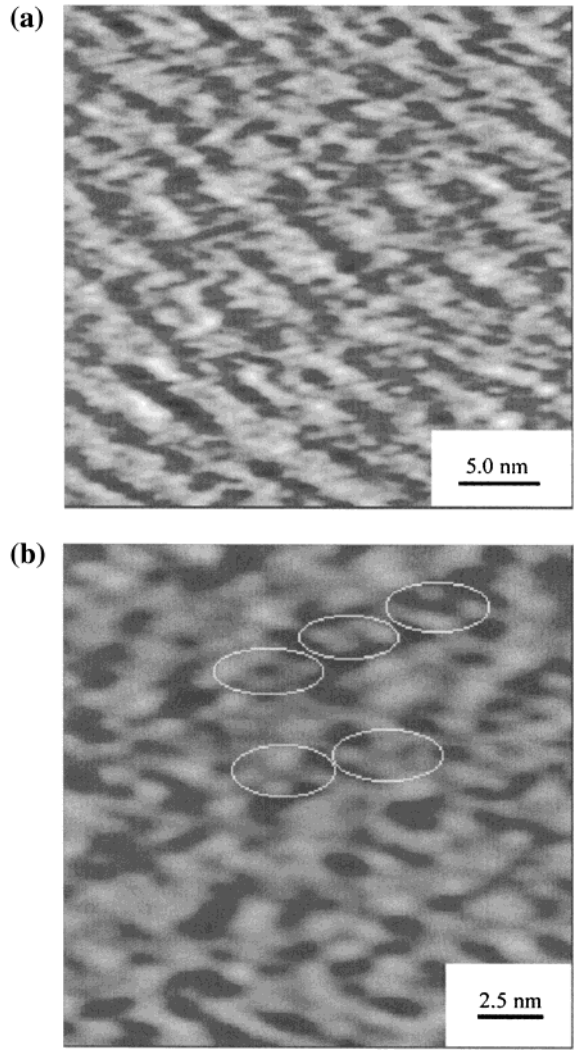



**Figure 3.** AFM spectrum of bis(molecular tube)s **3**: (a) tubular structure; (b) rectangles composed of four $\beta$-cyclodextrin units.

diameter of the $\beta$-cyclodextrin's periphery is about 1.54 ± 0.04 nm and the height of the torus is about 0.79 nm.[12] Thus, we may conclude that the width of a single strand of the bis(molecular tube)s is about 1.5 nm, whereas that of the whole bis(molecular tube)s is on the scale of 3 nm. Just as we can see from Figure 2, the observed result is consistent with the theoretical value. In other words, the wider parts correspond to the top view of bis(molecular tube)s, while the narrower parts correspond to the side view.

Atomic force microscopy (AFM) was also performed to further characterize the structure of bis(molecular tube)s **3**.[13] From Figure 3a, we may note that there exist lots of anomalous tubes on the substrate, which is in accord with the result of TEM. According to the size and shape, in the figure one bright dot corresponds to a $\beta$-cyclodextrin unit and the distances between two adjacent bis(molecular tube)s are roughly 4.0 nm. To visualize the detailed structure, a sectional picture is shown in Figure 3b. Interestingly, it may be noted from Figure 3b that four $\beta$-cyclodextrin units form a distorted rectangular block. The average distance between two adjacent $\beta$-cyclodextrin units is about 1.6 nm, closely related to the summation of two $\beta$-cyclodextrin's radii.

However, the average distances between two diagonal $\beta$-cyclodextrin units are somewhat different, i.e., 2.5 and 1.2 nm, respectively. We could conclude herein that two bridged bis($\beta$-cyclodextrin)s construct a nonplanar distorted rectangle via coordination with Pt(IV). Consequently, the blocks exhibit different topologies in Figure 3a,b. From Figure 3b, it may also be noted that several blocks connect to form a double-strand catena, in which the distance between the centers of two adjacent blocks is about 3.8 nm. Although the samples deposited on the substrate afforded multilayers and the tubes overlapped and intersected in the AFM pictures, these results clearly indicate that bis(molecular tube)s were obtained from the present synthetic strategy. Endeavors to explore the application of bis(molecular tube)s are currently in progress.

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## References

(1) (a) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1304−1319. (b) Lehn, J.-M. *Supramolecular Chemistry*; VCH: Weinhein, 1995. (c) Philp, D.; Stoddart, J. F. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1154−1196.

(2) (a) Ghadiri, M. R.; Granja, J. R.; Buehler, L. K. *Nature* **1994**, *369*, 301−304. (b) Hartgerink, J. D.; Granja, J. R.; Milligan, R. A.; Ghadiri, M. R. *J. Am. Chem. Soc.* **1996**, *118*, 43−50. (c) Kennan, A. J.; Haridas, V.; Severin, K.; Lee, D. H.; Ghadiri, M. R. *J. Am. Chem. Soc.* **2001**, *123*, 1797.

(3) (a) van Nostrum, C. F.; Pichen, S. J.; Schouten, A.-J.; Nolte, R. J. M. *J. Am. Chem. Soc.* **1995**, *117*, 9957−9965. (b) van Nostrum, C. F.; Nolte, R. J. M. *Chem. Commun.* **1996**, 2385−2392.

(4) (a) Harada, A.; Li, J.; Kamachi, M. *Nature* **1992**, *356*, 325−327. (b) Harada, A.; Li, J.; Kamachi, M. *Nature* **1993**, *364*, 516−518.

(5) (a) Ooya, T.; Mori, H.; Terano, M.; Yui, N. *Macromol. Rapid Commun.* **1995**, *16*, 259−263. (b) Watanabe, J.; Ooya, T.; Yui, N. *Chem. Lett.* **1998**, 1031−1032.

(6) Taylor, E. W.; Ramanathan, C. S.; Jalluri, R. K.; Nadimpalli, R. G. *J. Med. Chem.* **1994**, *37*, 2637−2654.

(7) Liu, Y.; You, C.-C.; Chen, Y.; Wada, T.; Inoue, Y. *J. Org. Chem.* **1999**, *64*, 7781−7787.

(8) Detail synthetic procedure: An aqueous solution of PPG was added to a saturated aqueous solution of **1** (2.58 g, 1 mmol) and platinum chloride (0.168 g, 0.5 mmol) with a molar ratio of 2:1 with stirring for 0.5 h at room temperature. Then 3,5-dinitrobenzoic acid (0.60 g, 50 mmol) dissolved in ether was added. After stirring for 24 h, epichlorohydrin (0.56 g, 6 mmol) and 25% aqueous NaOH solution (50 mL) were added to the solution, and the mixture was stirred for additional 36 h. The resultant mixture was neutralized with HCl, purified by column chromatography on Sephadex G-25, and evaporated under reduced pressure to dryness to give **3**. Anal. Calc for $C_{105}H_{168}O_{76}Se_2(PtCl_2)_{0.5}(H_2O)_{30}$: C, 36.58; H, 6.72. Found: C, 36.72; H, 6.69.

(9) Harada, A.; Li, J.; Kamachi, M. *J. Am. Chem. Soc.* **1994**, *116*, 3192−3196.

(10) Sugiura, I.; Komiyama, M.; Toshima, N.; Hirai, H. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 1643−1651.

(11) Transmission electron microscopy (TEM) examination was performed on a Philips EM-400ST transmission electron microscope (80 keV). The sample for the transmission electron microscope was prepared as follows. The bis(molecular tube)s-containing aqueous solution (1 mM) was dropped on a carbon-coated copper grid (230 mesh), which was allowed to dry under ambient conditions. Then the grids were moved into a Hitachi HUS-5GB high-vacuum evaporator to obtain the TEM sample.

(12) Szejtli, J. *Chem. Rev.* **1998**, *98*, 1743−1753.

(13) A Digital Instruments NanoscopeIII was used with head D and commercial standard silicon nitride cantilevers and tips. The spring constant was 0.12 N/m. The forces were set at 10−30 nN throughout the investigation in constant height mode and at ambient atmosphere. The aqueous sample in the concentration of $10^{-4}$ M was deposited onto a freshly cleaned surface of mica, which was incubated for several minutes to let the water volatilize and then used for the measurement. Image processing was done with NanoscopeIII software by mixed illumination and color coding for height for best apperance.

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