

## Efficient Synthesis and Characterization of Tetrakis(*p*-cyanophenyl)cavitand Based on Resorcin[4]arene

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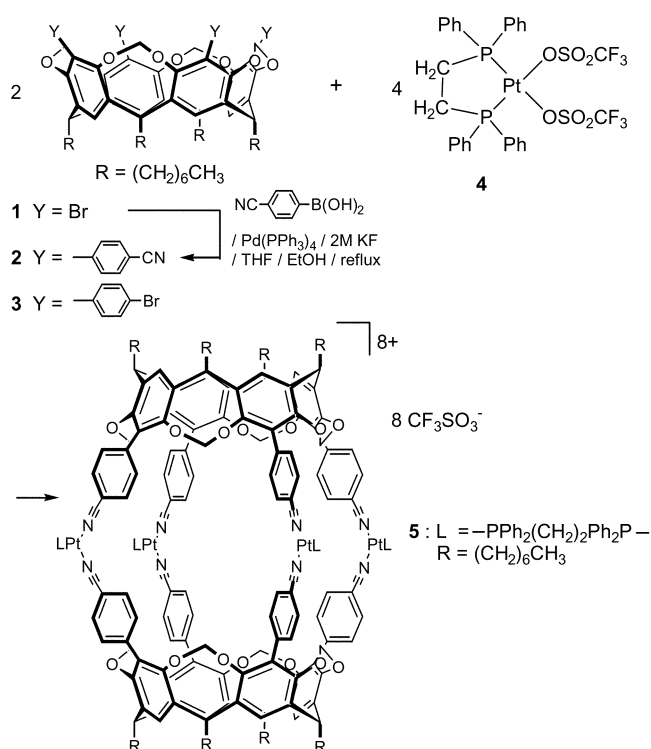
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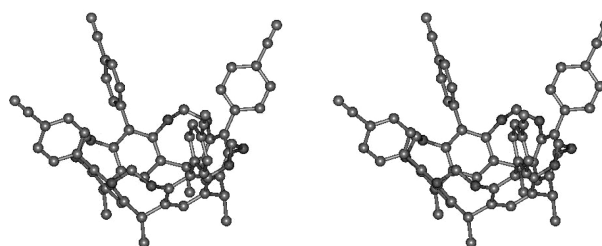
Self-assembled molecular capsules (SMC) held together by hydrogen bond or metal-ligand interaction have attracted much interest.<sup>1</sup> The hydrogen-bonded SMCs were mostly constructed by the dimerization of cyclophane-based cavitands<sup>2</sup> or molecular tweezers<sup>3</sup> capable of hydrogen-bonds complementing each other. They showed unusual molecular recognition properties and dynamic guest-exchange properties.<sup>4</sup> The SMCs by metal-ligand interaction were constructed by ordered association of organic ligands and metal ions in convergent manner.<sup>5,6</sup> But most SMCs are kinetically unstable in polar medium since they are held by the polar interactions.

Here, we report the efficient synthesis of deep-cavity tetrakis(*p*-cyanophenyl)cavitand **2** and its SMC **5** having a nanosize cavity utilizing cyano-Pt interaction.

Tetrabromocavitand **1** in Scheme 1 was synthesized by the known procedure.<sup>7</sup> Tetracyanocavitand **2** was efficiently



**Scheme 1**

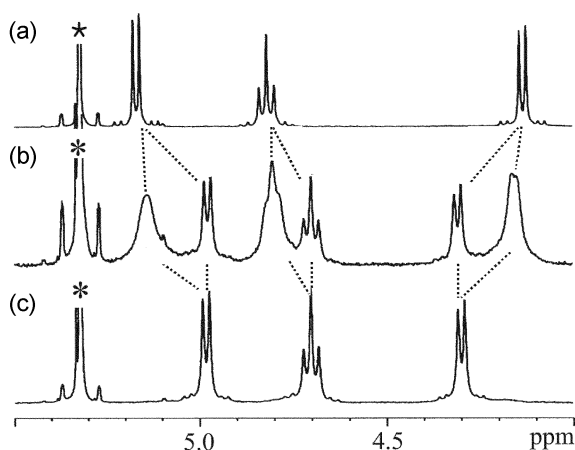


**Figure 1.** Stereo view of single X-ray crystal structure of **2**. Solvent molecules, hydrogens, and long alkyl feet are omitted for clarity.

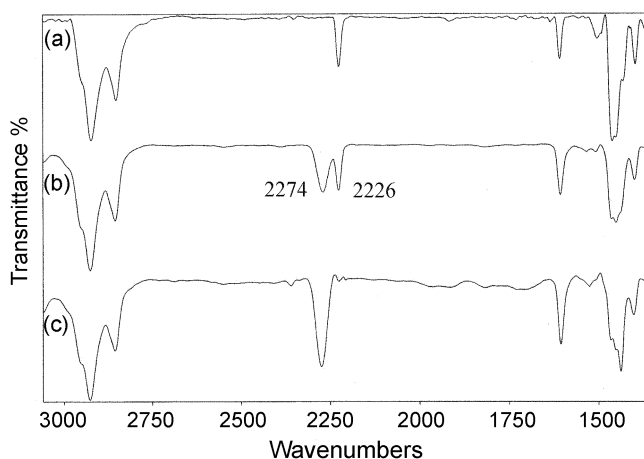
obtained in 88% yield by Pd-catalyzed Suzuki coupling reaction of tetrabromocavitand **1** with 4-cyanophenyl boronic acid in a mixture of 2 M KF, EtOH, and THF at reflux under argon for 3 days. Dalcane et al synthesized tetracyanocavitand **2** (R = pentyl or undecyl)<sup>6d</sup> in < 34% yield from the corresponding tetrabromide **3**<sup>8</sup> which was obtained by 7-step synthesis from 1,3-dimethoxybenzene. Square planar *cis*-Pt bis(triflate) complexes **4** was prepared by the reaction of the corresponding PtCl<sub>2</sub> complex with AgOTf.<sup>6b,9</sup> SMC **5** was assembled by mixing cavitand **2** with **4** in a 1 : 2 molar ratio at room temperature in a nonpolar solvent such as CHCl<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>, or tetrachloroethane.

Single-crystal X-ray analysis of tetracyanocavitand **2** showed a well-defined nanosize deep cavity (Figure 1). The average diameters defined as the distance between two nitrogens and two methine carbons are 16.0 and 7.2 Å, respectively. The depth of the cavity defined as the distance between the two best planes of four nitrogens and four methine carbons is 9.6 Å.

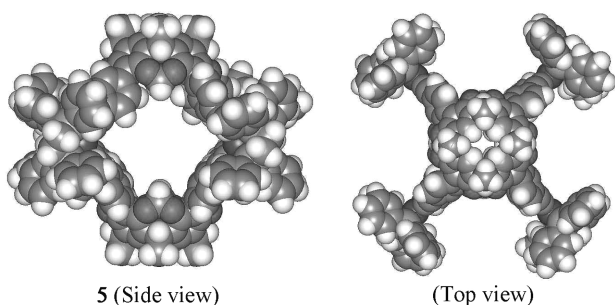
Figure 2 shows the changes of chemical shifts of dioxymethylene (doublets at 5.22 and 4.17 ppm) and of methine (triplet at 4.82 ppm) hydrogens of tetracyanocavitand **2** (Figure 2a) or those of SMC **5** (Figure 2c) upon metal-ligand interaction. When mixing 1 : 1 of **2** and **4**, these proton peaks of free cavitand **2** and SMC **5** (doublets at 4.98 and 4.30 ppm, triplet at 4.70 ppm) appeared separately in a 1 : 1 ratio (Figure 2b), which shows that SMC **5** is kinetically stable on an <sup>1</sup>H NMR time scale. When the ratio of **2** : **4** reached 1 : 2, the peaks of free cavitand **2** disappeared completely and only those of SMC **5** remained. The simple patterns of <sup>1</sup>H NMR peaks for the 1 : 2 mixture of two



**Figure 2.** Partial  $^1\text{H}$  NMR spectra ( $[\text{2}] = 3 \text{ mM}$  in  $\text{CD}_2\text{Cl}_2$ , 400 MHz, 298 K): (a) **2**, (b)  $[\text{2}]:[\text{4}] = 1:1$ , (c)  $[\text{2}]:[\text{4}] = 1:2$ . Symbols (\*) designate the proton of residual  $\text{CH}_2\text{Cl}_2$ .



**Figure 3.** Thin film FT-IR spectra of (a) **2**, (b)  $[\text{2}]:[\text{4}] = 1:1$ , (c) **5** ( $[\text{2}]:[\text{4}] = 1:2$ ).



**Figure 4.** Energy minimized structure of **5**.

compounds, **2** and **4**, confirm the SMC structure of a  $D_{4h}$  symmetry shown in Scheme 1.

Figure 3 shows the partial FT-IR spectra of SMC **5**. When the molar ratio of **2** : **4** was 1 : 1, two stretching bands of cyano group at  $2226 \text{ cm}^{-1}$  for cavitand **2** and  $2274 \text{ cm}^{-1}$  for SMC **5** were observed. When the molar ratio of **2** : **4** was 1 : 2, only the stretching band at  $2274 \text{ cm}^{-1}$  for SMC **5** was observed. These results also support the  $D_{4h}$  symmetry of SMC **5**.

An energy minimized structure of **5** using the Cerius2 program with the CFF95 force field was shown in Figure 4.<sup>10</sup> The side view of **5** shows rather large portals through which potential guests can transport without high energy barrier.

In conclusion, the deep-cavity tetracyanocavitand **2** was efficiently synthesized and its self-assembled molecular capsule (SMC) **5** by Pt-cyano interaction were observed in nonpolar solvents. The solution behaviors of the nano-size SMC depending on the polarity and size of solvent, temperature, and the chelate on Pt complex are being studied.

## Experimental Section

Solvents and all commercially available reagents were used without any purification. Melting points were determined using an Electrothermal IA9100 apparatus without calibration.  $^1\text{H}$  NMR spectra were recorded at 400 MHz on a Bruker Avance 400 spectrometer. Infrared spectra were recorded on a Mattson 3000 spectrometer. FAB-MS spectra were measured on a JMS-700 Mstatopm spectrometer. Elemental analyses were performed on CE Instrument EA 1110 CHNS-Porapack PQS column.

**Tetrakis(*p*-cyanophenyl) cavitand 2:** To 4-cyanophenyl bionic acid (1.77 g, 12.05 mmol) and  $\text{Pd}(\text{PPh}_3)_4$  (139 mg, 0.12 mmol) under an argon atmosphere were added argon-saturated THF (50 mL), added argon-saturated EtOH (10 mL), added argon-saturated aqueous 2 M KF (30 mL), and tetrabromo cavitand **1** (3 g, 2.41 mmol). The mixture was stirred at refluxing temperature for 3 days. After cooling to room temperature and evaporation solvents, the residue was dissolved with  $\text{CH}_2\text{Cl}_2$ . The organic solvents were washed with  $\text{H}_2\text{O}$ , and dried over  $\text{MgSO}_4$ . After concentration of solvents, the residue was purified by silica gel column chromatography eluted with Hexane:EtOAc (3:1) and poured into EtOH to give pure **2** as a white solid (2.83 g, 88%): mp > 280 °C (dec). FAB+ MS  $m/z$  1334 ( $\text{M}^+$  10%). Anal. calcd for  $\text{C}_{62}\text{H}_{64}\text{O}_{12}$ : C, 74.38; H, 6.44. Found: C, 74.06; H, 6.35%.  $^1\text{H}$  NMR (400.1 MHz,  $\text{CDCl}_3$ , 25 °C):  $\delta = 7.62$  (d, 8H,  $J = 8.4 \text{ Hz}$ ,  $\text{CNAr}$ ), 7.37 (s, 4H,  $\text{ArH}$ ), 7.15 (d, 8H,  $J = 8.4 \text{ Hz}$ ,  $\text{CNAr}$ ), 5.22 (d, 4H,  $J = 6.8 \text{ Hz}$ , outer  $\text{OCH}_2\text{O}$ ), 4.82 (t, 4H,  $J = 8.0 \text{ Hz}$ , methine), 4.17 (d, 4H,  $J = 6.8 \text{ Hz}$ , inner  $\text{OCH}_2\text{O}$ ), 2.34 (m, 8H  $\text{CH}_2(\text{CH}_2)_5\text{CH}_3$ ), 1.48–1.32 (m, 40H,  $(\text{CH}_2)_5\text{CH}_3$ ), 0.91 (t, 12H,  $J = 6.8 \text{ Hz}$ ,  $(\text{CH}_2)_6\text{CH}_3$ );  $^{13}\text{C}$  NMR (100.6 MHz,  $\text{CDCl}_3$ , 25 °C):  $\delta = 152.3$ , 138.9, 138.6, 131.7, 130.8, 127.8, 120.9 (Ar), 118.6 (ArCN), 111.3 (Ar), 100.5 ( $\text{OCH}_2\text{O}$ ), 37.0 (CH), 31.9, 30.3, 29.8, 29.4, 27.9, 22.7 ( $\text{CH}_2$ ), 14.1 ( $\text{CH}_3$ ); IR (KBr):  $2226 \text{ cm}^{-1}$  (CN).

**X-ray Structure of 2:**  $\text{C}_{97}\text{H}_{118}\text{Cl}_6\text{N}_4\text{O}_{12}$ ,  $M = 1744.65$ , colorless needle  $0.55 \times 0.35 \times 0.18 \text{ mm}^3$ , monoclinic  $\text{C2}/c$ ,  $a = 39.778(3)$ ,  $b = 21.2022(13)$ ,  $c = 22.0087(14) \text{ \AA}$ ;  $\alpha = 90^\circ$ ,  $\beta = 98.776(10)^\circ$ ,  $\gamma = 90^\circ$ ;  $V = 18344(2) \text{ \AA}^3$ ,  $Z = 8$ ,  $\rho_{\text{calcd}} = 1.263 \text{ mg/m}^3$  (including solvent),  $\mu$  (Mo-K $\alpha$ ,  $\lambda = 0.71073 \text{ \AA}$ ) =  $0.250 \text{ mm}^{-1}$ ; 58078 measured reflections, 22052 unique of which 7700 observables [ $I > 2\sigma(I)$ ]. The structure was solved by direct methods and refined by full-matrix least

squares calculations with SHELXTL. The final  $R1 = 0.1515$ ,  $wR2 = 0.4074$  for 7700 reflections of  $I > 2\sigma(I)$ ; measurements: Brukers SMART CCD equipped with a graphite crystal incident-beam monochromator. Crystallographic data for cavitand 2 have been deposited with the Cambridge Crystallographic Data Center as supplementary publication numbers CCDC250107. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

**SMC 5**:  $^1\text{H NMR}$  (400.1 MHz,  $\text{CD}_2\text{Cl}_2$ , 25 °C):  $\delta = 7.92$ -7.17 (m, 120H,  $\text{PPh}_2$ ,  $\text{CNArH}$  and  $\text{ArH}$ ), 4.98 (d, 8H,  $J = 7.2$  Hz, outer  $\text{OCH}_2\text{O}$ ), 4.70 (t, 8H,  $J = 7.6$  Hz, methine), 4.30 (d, 8H,  $J = 7.2$  Hz, inner  $\text{OCH}_2\text{O}$ ), 2.87 (bd, 16H,  $J = 19.6$  Hz,  $\text{PCH}_2\text{CH}_2\text{P}$ ), 2.32 (bs, 16H  $\text{CH}_2(\text{CH}_2)_5\text{CH}_3$ ), 1.47-1.33 (m, 80H,  $(\text{CH}_2)_5\text{CH}_3$ ), 0.92 (t, 24H,  $J = 6.8$  Hz,  $(\text{CH}_2)_6\text{CH}_3$ ).

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