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# *C*-Pentyltetra(3-pyridyl)cavitand: A Versatile Building Block for the Directed Assembly of Hydrogen-Bonded Heterodimeric Capsules

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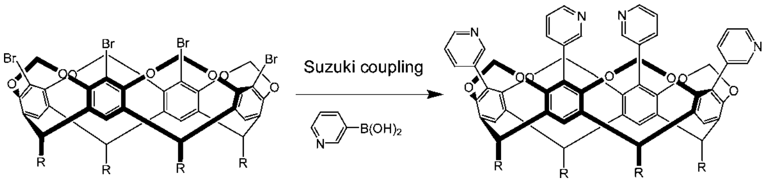
## ABSTRACT



**Hydrogen-bond-directed assembly of heterodimeric cavitand-based capsules is of considerable interest. Herein, we report the synthesis and single-crystal X-ray structure determination of a pyridyl-functionalized cavitand that contains suitable hydrogen-bond acceptor moieties for the construction of asymmetric cavitand-based capsules.**

The deliberate and predesigned assembly of individual molecular entities into larger well-defined cavities with accessible space is an area of considerable fundamental scientific interest.[1] It has been shown that encapsulation of guest molecules within a rigid interior framework can produce nanosized reaction vessels and containers that exhibit drastically different behavior from bulk-phase environments, leading to successful stabilization of highly reactive intermediates[2] and enhanced chemical reaction rates.[3]

During the past few years, a variety of homomeric capsules have been constructed from resorcinarene-based cavitands and metal ions, primarily cis-capped palladium(II) or platinum(II) ions.[4] In addition, silver(I) ions have also been employed as synthetic tools for the construction of homomeric cages.[5]

To expand the library of readily accessible and versatile building blocks for both organic and metal-containing capsules, we report the synthesis, characterization, and single-crystal X-ray structure determinations of a *C*-pentyltetra(3-pyridyl)cavitand and its tetrabromo precursor.

The synthesis of precursor **1** was achieved in good yields, following previously reported procedures.[6] Crystals suitable for single-crystal X-ray crystallography of **1** were grown by slow evaporation of an acetonitrile solution at room temperature over 24 h. The structure determination of **1**, Figure 1, shows that one guest molecule of acetonitrile is positioned at the "lower rim" of the cavitand, surrounded by the "pentyl feet".[7]

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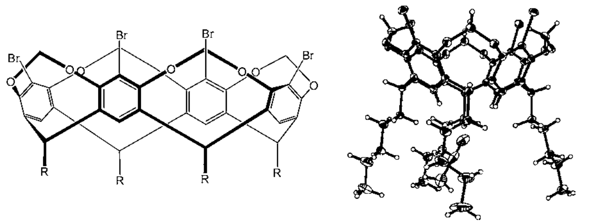

**Figure 1.** Molecular structure and thermal ellipsoids (50% probability level) of the tetrabromo cavitand in the crystal structure of **1**·acetonitrile.

The cavitands are organized into one-dimensional strands as a result of the interaction between one of the pentyl feet and the upper rim of a neighboring cavitand (Figure 2).

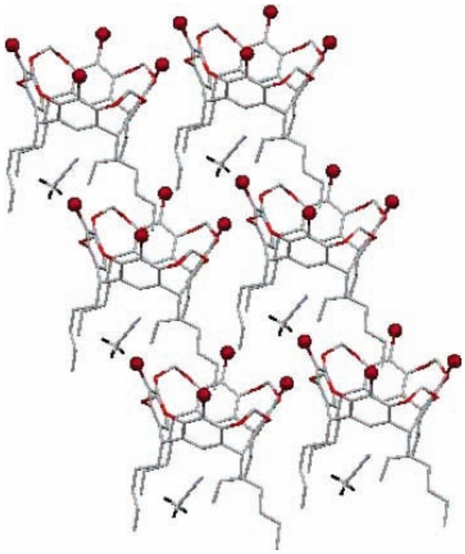

**Figure 2.** Packing of cavitand **1**·acetonitrile. The hydrogen atoms have been removed, except on the acetonitrile solvent molecules, for clarity.[8]

Cavitands in neighboring strands are arranged in antiparallel dimers organized via a pair of very short and symmetry-related Br···Br interactions (3.470 Å, Figure 3).

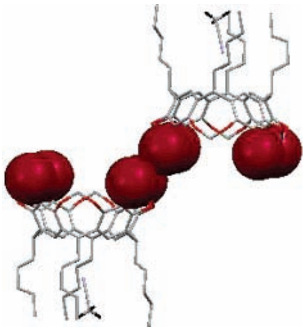

**Figure 3.** Neighboring cavitands linked through short Br···Br interactions in cavitand **1**·acetonitrile.

If **1** is recrystallized from dichloromethane, however,[9] a cavitate-type structure is formed where the guest molecule resides outside of the host cavitand framework. However, regardless of the location of the guest, neighboring hosts are arranged into one-dimensional strands where one of the pentyl feet is dipping into the upper rim of a neighboring cavitand (Figure 4).

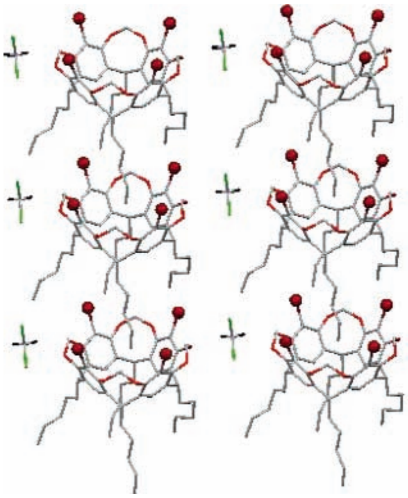

**Figure 4.** Packing of cavitand **1**·dichloromethane. The hydrogen atoms have been omitted, except from the dichloromethane solvent molecules, for clarity.

One of the “feet” of the cavitand in **1**·$CH_2Cl_2$ does display a gauche conformation; although unusual, such configurations are not rare,[10] and it is difficult to point directly to what may cause this geometry. The crystallographic screw axis is essentially perpendicular to the two 1D strands shown

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(7) Crystal data for **1**·acetonitrile: $C_{52}H_{60}Br_4O_8 \cdot C_2H_3N$, $M = 1173.69$ amu, triclinic, $P\bar{1}$, $a = 10.7767(7)$ Å, $b = 11.6740(7)$ Å, $c = 20.8192$ Å, $\alpha = 80.392(4)$, $\beta = 97.977(3)°$, $\gamma = 76.503(3)°$, $V = 2510.8(3)$ Å$^3$, $Z = 2$, $D_c = 1.552$ g cm$^{-3}$, $\mu$(Mo K$\alpha$) $= 3.261$ mm$^{-1}$, crystal size $0.30 \times 0.25 \times 0.20$ mm. Data were collected at 173 K on a Bruker SMART 1000 diffractometer using Mo K$\alpha$ radiation. A total of 18 907 reflections (1.82° $< \theta <$ 28.28°) were processed, of which 9466 were unique and significant with $I > 2\sigma(I)$. Structure solution and refinement were carried out using SHELXS-97 and SHELXL-97. $R_{int} = 0.0287$. Final residuals for $I > 2\sigma(I)$ were $R_1 = 0.0330$ and 0.0877 (GOF = 1.097).

(8) Images created using mercury 1.4.1.

(9) Crystal data for **1**·dichloromethane: $C_{52}H_{60}Br_4O_8 \cdot CH_2Cl_2$, $M = 1217.57$ amu, monoclinic, $P2(1)$, $a = 10.4432(15)$ Å, $b = 15.049(2)$ Å, $c = 16.320(2)$ Å, $\alpha = \gamma = 90°$, $\beta = 97.977(3)°$, $V = 2540.0(6)$ Å$^3$, $Z = 2$, $D_c = 1.592$ g cm$^{-3}$, $\mu$(Mo K$\alpha$) $= 3.328$ mm$^{-1}$, crystal size $0.22 \times 0.19 \times 0.02$ mm. Data were collected at 100 K on a Bruker SMART 1000 diffractometer using Mo K$\alpha$ radiation. A total of 22 914 reflections (2.39° $< \theta <$ 30.09°) were processed, of which 7209 were unique and significant with $I > 2\sigma(I)$. Structure solution and refinement were carried out using SHELXS-97 and SHELXL-97. $R_{int} = 0.735$. Final residuals for $I > 2\sigma(I)$ were $R_1 = 0.0447$ and 0.0674 (GOF = 0.735).

(10) See CSD ref codes, e.g., FEBVUE, FESMEW, FEXFIY, LIFNUJ, and TUTYEM.

in Figure 4, which means that the cavitands are not all pointing in the same direction.

Two symmetry-related pairs of Br···Br interactions, 3.349 and 3.676 Å, respectively, also play an important role in positioning adjacent cavitands into an extended up-and-down arrangement (running parallel with *a*) (Figure 5).

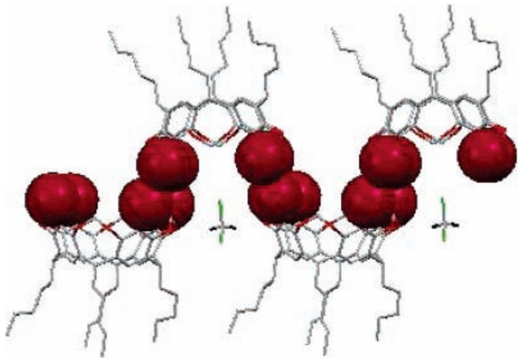
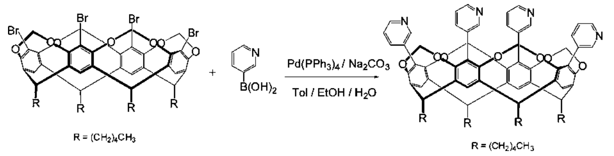


**Figure 5.** Adjacent hosts in cavitand **1**·dichloromethane linked via multiple Br···Br interactions.

The desired pyridyl-functionalized cavitand was synthesized by a palladium-catalyzed Suzuki–Miyaura cross-coupling reaction[11] of cavitand **1** and excess 3-pyridyl boronic acid[12] under a basic media (Scheme 1). The target compound was purified by silica gel column chromatography and recrystallized from acetonitrile yielding ~87% of pure py-cavitand **2**.

**Scheme 1.** Synthesis of *C*-Pentyltetra(3-pyridyl)cavitand (**2**)



It should be noted that cavitands similar to **2**, *C*-heptyltetra-(3-pyridyl)- and *C*-phenylethyltetra(3-pyridyl)cavitands, have been reported in the literature;[13] however, overall yields of these cavitands were 23% and 20%, respectively. In those cases, the synthesis was achieved by converting a tetrabromo cavitand to the desired tetraboronic acid followed by reaction with 3-bromopyridine.

Good quality crystals of the *C*-pentyltetra(3-pyridyl)-cavitand were obtained by slow evaporation at room temperature of an acetonitrile solution of **2**.[14] The structure determination of **2**, Figure 6, shows one py-cavitand and three acetonitrile molecules, although the asymmetric unit contains only one-half cavitand and three-halves solvent molecules.

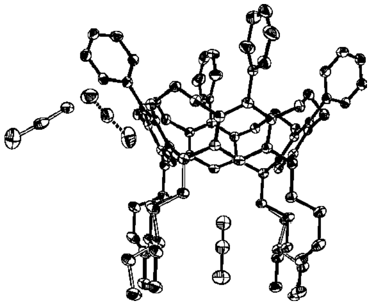


**Figure 6.** Thermal ellipsoid plot (50% probability level) of py-cavitand **2**·acetonitrile.

Cavitand **2** was also crystallized from methanol by slow evaporation at room temperature over 36 h.[15] The asymmetric unit contains two py-cavitands and seven methanol solvent molecules (Figure 7).

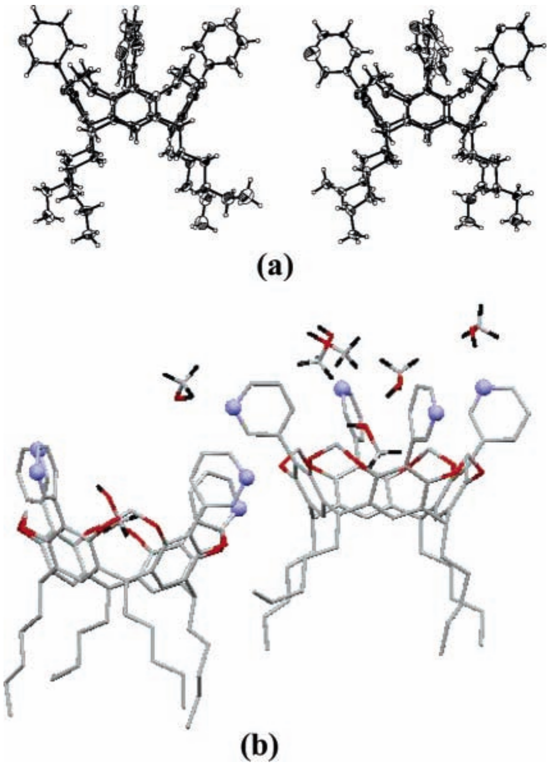


**Figure 7.** (a) Thermal ellipsoid plots (50% probability level) of the two independent py-cavitands in the crystal structure of **2**·methanol. The seven methanol solvent molecules have been omitted for clarity. (b) Asymmetric unit of **2**·methanol with the hydrogen atoms removed, except on the methanol solvent molecules, for clarity. The pyridyl nitrogen atoms are represented as light-blue spheres.

The improved synthetic route presented herein means that the py-decorated cavitand **2** is readily available in large

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quantities which offers new opportunities for preparing heterodimeric capsules using: (1) complementary hydrogen-bond functionalities on different host molecules and (2) transition metals as tools for the assembly of homomeric capsules. It is also noteworthy that intermolecular halogen···halogen interactions can play important roles in organizing relatively large molecules such as the tetrabromo-substituted host presented herein.

The noncovalent assembly of heterodimeric capsules may be somewhat hampered because the four nitrogen atoms on the rim display orientations that may result in polymeric networks instead of the desired discrete heterodimeric capsules. However, heterotopic assembly can be achieved under suitable reaction conditions,[13,16] and thus, the py-cavitand **2** presented provides more opportunities for the construction of asymmetric dimeric capsules that contain two different guests.

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**Supporting Information Available:** Detailed experimental procedures and characterization of compounds **1** and **2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) Crystal data for **2**·acetonitrile: $C_{72}H_{76}N_4O_8 \cdot 3C_2H_3N$, $M = 1248.53$ amu, tetragonal, $P4(3)2(1)2$, $a = b = 18.3708(7)$ Å, $c = 19.8745(15)$ Å, $\alpha = \gamma = \beta = 90°$, $V = 6707.4(6)$ Å$^3$, $Z = 4$, $D_c = 1.236$ g cm$^{-3}$, $\mu$(Mo Kα) $= 0.080$ mm$^{-1}$, crystal size $0.24 \times 0.10 \times 0.10$ mm. Data were collected at 100 K on a Bruker SMART APEX 1000 diffractometer using Mo Kα radiation. A total of 30 563 reflections ($1.87° < \theta < 28.31°$) were processed, of which 3614 were unique and significant with $I > 2\sigma(I)$. Structure solution and refinement were carried out using SHELXS-97 and SHELXL-97.[17] $R_{int} = 0.0582$. Final residuals for $I > 2\sigma(I)$ were $R_1 = 0.0514$ and 0.1353 (GOF = 1.059).

(15) Crystal data for **2**·methanol: $2C_{72}H_{76}N_4O_8 \cdot 7CH_3OH$ , $M = 2475.03$ amu, monoclinic, $P2(1)/n$, $a = 23.3560(16)$ Å, $b = 22.1519(16)$ Å, $c = 25.5165(16)$ Å, $\alpha = \gamma = 90°$, $\beta = 93.302(4)°$, $V = 13164.5(15)$ Å$^3$, $Z = 4$, $D_c = 1.249$ g cm$^{-3}$, $\mu$(Mo Kα) $= 0.084$ mm$^{-1}$, crystal size $0.45 \times 0.25 \times 0.10$ mm. Data were collected at 153 K on a Bruker SMART APEX 1000 diffractometer using Mo Kα radiation. A total of 59 710 reflections ($1.23° < \theta < 26.48°$) were processed, of which 8691 were unique and significant with $I > 2\sigma(I)$. Structure solution and refinement were carried out using SHELXS-97 and SHELXL-97. $R_{int} = 0.1700$. Final residuals for $I > 2\sigma(I)$ were $R_1 = 0.0929$ and 0.2680 (GOF = 0.957).

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