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An M_2L_4 Molecular Capsule with an Anthracene Shell: Encapsulation of Large Guests up to 1 nm

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S *Supporting Information*

ABSTRACT: A new M_2L_4 molecular capsule with an aromatic shell was prepared using two Pd(II) ions and four bisanthracene ligands. The self-assembled capsule possesses a cavity with a diameter of ∼1 nm that can encapsulate medium-sized spherical and planar molecules as well as a very large molecule (C_{60}) in quantitative yields. The encapsulated guests are fully segregated and shielded from the external environment by the large anthracene panels.

Fullerenes, the well-known class of spherical molecules composed of curved aromatic shells with diameters of ∼1 nm, are the archetypical molecular capsules.[1] Within their confines, encapsulated small molecules can exhibit unusual properties that emerge from the effects of isolation as well as interactions with the aromatic rings. However, the enclathration of guest molecules within fullerenes is nontrivial, so we designed a new molecular capsule possessing extended aromatic frameworks intended to engender unique chemical phenomena within its cavity.[2] Coordinative self-assembly is one of the most advanced methods for the facile preparation of large capsulelike supramolecules,[3] and there are many examples of coordination capsules assembled from organic ligands with small aromatic rings (e.g., benzene and naphthalene rings).[4,5] Capsules assembled from ligands with extended aromatic panels, however, remain uncommon.[6] Herein we report the preparation of a novel molecular capsule with an M_2L_4 composition bearing large aromatic panels and metal ions (Figure 1a). The large capsule cavity is fully enclosed yet can quantitatively encapsulate a variety of neutral guest molecules with diameters of up to ∼1 nm.

We focused on molecular M_2L_4 coordination cages because of their simple composition and highly symmetric structures. Accordingly, many M_2L_4 analogues have been reported since the first example by Steel et al. in 1998.[7] However, the structures typically consist of wirelike frameworks (Figure 1b), and therefore, their molecular recognition or host−guest interactions have been limited to anions or molecules with lone pairs mainly via metal coordination.[7g−i] To create a truly functional molecular host for neutral guests with various sizes and shapes,[2] we refreshed the M_2L_4 motif with the following design specifications and features: (1) extended aromatic panels were incorporated into the ligand framework to provide an aromatic shell (Figure 1a) that demarcates the enclosed cavity and facilitates stronger host−guest interactions; (2) the rigid and curved ligand was designed to give a capsule cavity that is large (∼1 nm in diameter) and suitable for the encapsulation of large guest molecules (e.g., fullerenes); and finally (3) the attachment of exterior functional groups to control the solubility and crystallinity was readily achievable.

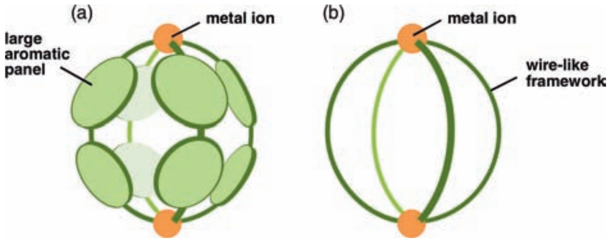

Figure 1. Cartoons of (a) the M_2L_4 capsule with large aromatic panels reported herein and (b) a previous M_2L_4 cage with a wirelike framework.

Anthracene was selected for the large aromatic panels of the ligands because it can be found in the partial structure of many fullerene frameworks. To make a curved anthracene wall, we designed the new bridging bispyridine ligand **1** having two anthracene rings connected by a *m*-phenylene spacer (Figure 2a). The phenyl−anthryl and anthryl−pyridyl bonds of ligand **1** are hindered by the ortho substituents, restricting bond rotation and forcing the aromatic subunits to adopt orthogonal conformations (Figure 2b).[8] As a result, **1** is a rigid, bent ligand with anthracene walls (Figure 2c). The two pendant methoxyethoxy groups on the *m*-phenylene ring serve to increase the solubility in protic solvents. Accordingly, the simple combination of Pd(II) ions and the ligands in a 1:2 ratio favors the exclusive formation of an M_2L_4 capsule.

Bisanthracene ligand **1** was prepared in five steps from 9-bromoanthracene in 55% overall yield using Negishi and Suzuki−Miyaura cross-coupling protocols. When ligand **1** (13.7 μmol), $PdCl_2(DMSO)_2$ (7.0 μmol), and $AgNO_3$ (14.3 μmol) were combined in DMSO-d_6 (0.5 mL) at 100 °C for 3 h, a single product, **2**, was formed quantitatively (Figure 3a), as demonstrated by NMR spectroscopy and mass spectrometry (MS).[9] In the ^{1}H NMR spectrum, the shifts of the pyridyl signals as well as the considerable upfield shift of the inner *m*-phenylene signal (H_b; $\Delta\delta = -1.15$ ppm) indicated the formation of a discrete M_2L_4 complex. At room temperature (rt), only six sharp signals in the aromatic region were observed (Figure 3c), but four additional signals appeared and sharpened at 100 °C (Figure 3d). COSY and NOESY analyses showed that the original sharp

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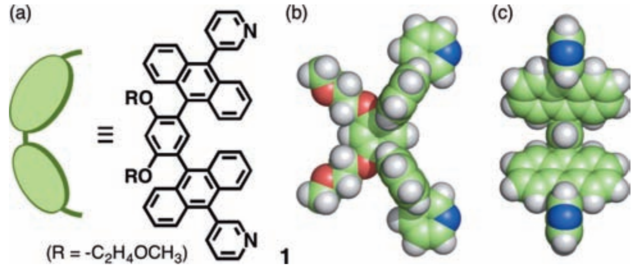

Figure 2. (a) Bridging bidentate ligand **1** and (b, c) views of the optimized structure (DFT calculation, B3LYP/6-31G* level): (b) side view; (c) front view.

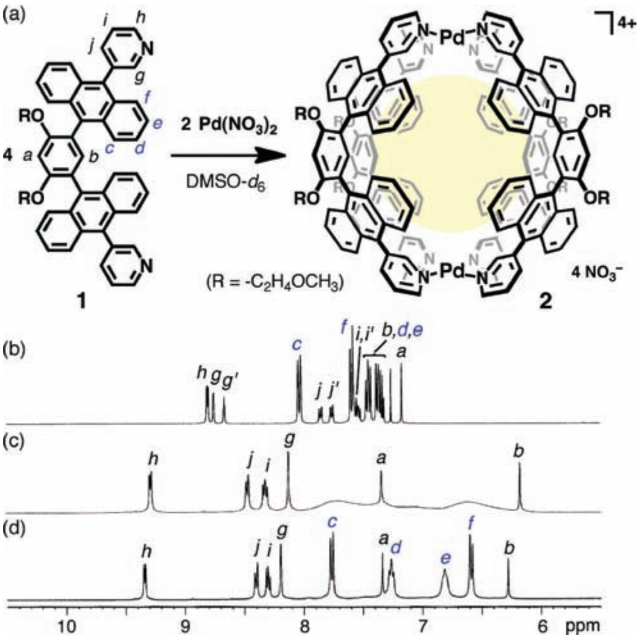

Figure 3. (a) Schematic representation of the self-assembly of molecular capsule **2**. (b–d) ^{1}H NMR spectra (400 MHz, aromatic region) of (b) ligand **1** in $CDCl_3$ at rt and of **2** in DMSO-d_6 at (c) rt and (d) 100 °C.

signals came from the pyridyl and *m*-phenylene protons ($H_{g,h,i,j}$ and $H_{a,b}$, respectively) of **2** (Figures S16 and S18 in the Supporting Information). The broadened signals came from protons located on the anthracene moieties ($H_{c,d,e,f}$) of **2**. The sharpening at higher temperatures is consistent with a tightly wound closed-shell framework wherein the cooperative motion of individual anthracene moieties is restricted and slow on the NMR time scale at room temperature. A single band with a diffusion coefficient (D) of 8.51×10^{-10} m^2 s^{-1} was present in the ^{1}H DOSY NMR spectrum, from which the diameter of the M_2L_4 complex was calculated to be ~1.5 nm (Figure S21). Prominent signals in the electrospray ionization–time of flight (ESI–TOF) MS spectrum at *m*/*z* 786.0, 1068.6, and 1634.0 were assigned to the respective $[\mathbf{2} - n\mathrm{NO_3}^-]^{n+}$ (n = 4, 3, 2) ions, corroborating the formation of a $[\mathrm{Pd(NO_3)_2}]_2\cdot(\mathbf{1})_4$ complex with a molecular weight of 3391.9 Da (Figure S22). Therefore, the formation of M_2L_4 molecular capsule **2** was well-supported by the solution-state NMR and MS studies.

X-ray crystallographic analysis provided the final evidence for the formation of an M_2L_4 molecular capsule. Pale-yellow single crystals of capsule **2** were obtained by slow concentration of a MeOH/H_2O solution,[9] and X-ray crystallographic analysis revealed that four curved ligands **1** bridge two Pd atoms to provide the expected M_2L_4 structure with a virtual D_4 symmetry (Figure 4). Each Pd atom has the standard square-planar geometry and is bound by the four pyridines in a twisted conformation that brings the anthracene panels into contact and couples their restricted motion, as observed in the broadened ^{1}H NMR spectrum at room temperature (Figure 3c). The large interior cavity of the capsule, with a volume of ~580 Å^3,[10] is defined by a Pd–Pd distance of 1.36 nm and a 1.12 nm diagonal between the opposing *m*-phenylene hydrogen atoms (H_b). Solvent molecules (seven MeOH and one H_2O) and a counteranion (NO_3^-) were present within the cavity. We emphasize that the eight anthracene panels of **2** form a roughly spherical aromatic shell, fully enclosing and segregating the cavity interior from the exterior environment (Figure 4b).

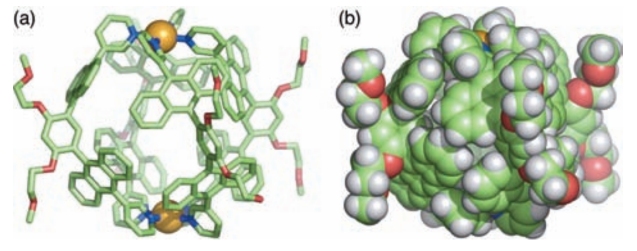

Figure 4. X-ray crystal structure of molecular capsule **2**: (a) ball-and-stick representation without the hydrogen atoms (yellow balls represent Pd atoms); (b) space-filling representation. The counteranion and solvent molecules have been omitted for clarity.

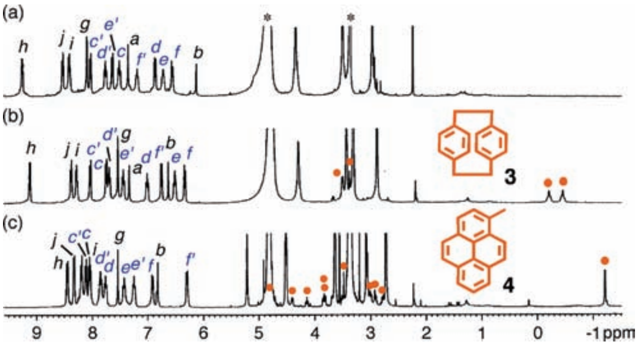

Figure 5. ^{1}H NMR spectra (400 MHz, 2:1 CD_3OD/D_2O, rt) of (a) capsule **2**, (b) the $\mathbf{2}\supset\mathbf{3}$ complex, and (c) the $\mathbf{2}\supset(\mathbf{4})_2$ complex (orange ●, signals from encapsulated guest **3** or **4**; *, solvent signals).

Molecular capsule **2** presents an isolated hydrophobic cavity suitable for encapsulating guest molecules through hydrophobic interactions. The solubility of capsule **2** in aqueous solution is increased because of the pendant hydrophilic chains, and the ^{1}H NMR spectrum in 2:1 CD_3OD/D_2O revealed desymmetrization of the host framework. The anthracene protons H_{c-f} split into eight sharp signals from 6.55 to 8.02 ppm (Figure 5a), which suggests the anthracene panels of **2** were tightly wound, compressing the capsule and decreasing the hydrophobic surface area presented. When a slight excess of [2,2]paracyclophane (**3**), a spherical guest with a diameter of 0.67 nm, was suspended in the CD_3OD/D_2O solution (6.0 mM) of capsule **2** at 60 °C for 3 h, the 1:1 host–guest complex $\mathbf{2}\supset\mathbf{3}$ was obtained in nearly quantitative yield, as revealed by NMR and MS analyses (Figures S24–S26).

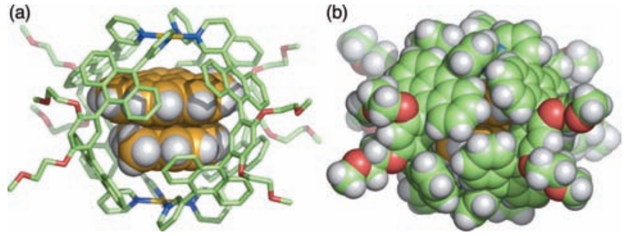

Figure 6. X-ray crystal structure of the **2**⊃(**4**)$_2$ complex: (a) stick (**2**) and space-filling (**4**) representation; (b) space-filling representation of **2**⊃(**4**)$_2$. The anions and solvent molecules have been omitted for clarity.

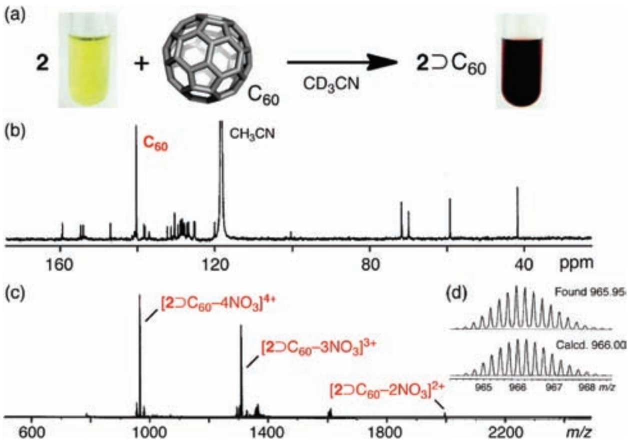

Figure 7. (a) Schematic representation of the quantitative encapsulation of C_{60} by molecular capsule **2** in CD_3CN. (b) ^{13}C NMR (100 MHz, CD_3CN, rt) and (c) ESI−TOF MS spectra (CH_3CN) of the **2**⊃C_{60} complex. (d) Expansion and simulation of the [**2**⊃C_{60} − 4NO_3^-]$^{4+}$ signals.

The methylene ^{1}H NMR signals of the encapsulated **3** were desymmetrized and strongly shifted upfield to −0.19 and −0.44 ppm ($\Delta\delta_{max}$ = −3.5 ppm) (Figure 5b).[9] Capsule **2** also bound 2 equiv of the large, planar guest molecule 1-methylpyrene (**4**) to give the complex **2**⊃(**4**)$_2$ in quantitative yield. Sets of methyl and aromatic ^{1}H NMR signals of **4** were found at −1.25 and 2.75−4.82 ppm, respectively, indicative of encapsulation by **2** (Figure 5c). The methyl ^{1}H NMR signal exhibited a huge upfield shift ($\Delta\delta$ = −4.2 ppm) due to enhanced shielding by the aromatic anthracene panels. The aromatic signals of **2** underwent a slight shift, but the symmetry of the capsule framework remained unchanged after guest encapsulation.[9] Quantitative formation of a 1:2 host−guest complex was confirmed by ^{1}H NMR integration and ESI−TOF MS analysis: only signals at m/z 894.0, 1212.7, and 1850.0, assigned to the [**2**⊃(**4**)$_2$ − $n$$NO_3^-$]$^{n+}$ (n = 4, 3, 2) species, respectively, were observed (Figure S29).

The detailed molecular structure of **2**⊃(**4**)$_2$ was confirmed by X-ray crystallographic analysis.[9] The crystal structure shows two stacked molecules of **4** with an interplanar distance of 3.5 Å resting between the two Pd(II) centers (Figure 6a). The stacked dimer interacts with the framework of **2** through complementary CH−π interactions: CH(**4**)−π(anthracene) and CH(pyridine)−π(**4**). The large planar guests (**4**)$_2$ are fully shielded by the anthracene framework of capsule **2** (Figure 6b,c).

The molecular host properties of capsule **2** encouraged us to examine the encapsulation of C_{60}. Black C_{60} powder (3 equiv based on **2**) was suspended in a CD_3CN solution of **2** (4.5 mM) at 80 °C for 3 h. The color of the solution dramatically changed from pale-yellow to red-purple (Figure 7a), even though C_{60} is insoluble in acetonitrile.[11] The appearance of a new broadened absorption band at 500−600 nm in the UV−vis spectrum,[9] corresponding to a typical charge-transfer band for C_{60} due to π-stacking interactions, substantiated the encapsulation of C_{60} by capsule **2**. A single ^{13}C NMR signal at 141.2 ppm was easily observed; no signal for free C_{60} was detected (Figure 7b). The upfield shift of this signal ($\Delta\delta$ = ~2 ppm relative to C_{60} in DMSO) provided further evidence for the encapsulation of C_{60}. ESI−TOF MS analysis unambiguously confirmed the **2**·C_{60} product composition with a molecular weight of 4109.0 Da ([**2**⊃C_{60} − $n$$NO_3^-$]$^{n+}$ with n = 4, 3, 2) (Figure 7c,d). Peaks corresponding to either the empty capsule or free C_{60} were not observed, reflecting the high stability of the **2**⊃C_{60} complex. Furthermore, the isolated **2**⊃C_{60} composite remained intact over several weeks in CH_3CN at room temperature. The **2**⊃C_{60} complex is soluble in various organic solvents, and while encapsulated within capsule **2**, very high concentrations (~20 mM) of C_{60} in MeOH or 2:1 MeOH/H_2O were obtained.[11,12] Notably, capsule **2** showed selective molecular recognition capabilities and could bind only C_{60} of complementary size and shape from a mixture of C_{60} and C_{70}.[13]

In summary, we have designed and prepared a new M_2L_4 molecular capsule with a spherical aromatic shell using two Pd(II) ions and four bisanthracene ligands. The self-assembled capsule possesses a cavity with a diameter of ~1 nm that is capable of encapsulating not only medium-sized spherical ([2,2]paracyclophane) and planar (1-methylpyrene) molecules but also a very large molecule (C_{60}) in quantitative yields. It is worthy of note that these molecular recognitions typically were not found for previous M_2L_4 coordination cages with wirelike frameworks. The encapsulated guest molecules are fully segregated and shielded from the external environment by the large aromatic panels. The pendant hydrophilic chains endow enhanced solubility and facilitate the remarkable solubilization of encapsulated fullerene C_{60} in protic solvents. This new class of molecular hosts with extended aromatic π surfaces holds great promise, and potential new properties and chemical reactions in their large cavities are currently under investigation.[14]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information. Experimental procedures, physical properties, and crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) See the Supporting Information.

(10) The cavity size of **2** ($\sim$580 Å^3) is smaller than that of previous large coordination capsules [e.g., $\sim$900 Å^3 (ref 5b), $\sim$1150 Å^3 (ref 5d), 1340 Å^3 (ref 6c), and $\sim$2700 Å^3 (ref 5e)], but **2** shows good ability to encapsulate large guest molecules, as discussed in detail later in the manuscript.

(11) The solubility of C_{60} in MeCN or MeOH is extremely low (< 0.0013 mM). See: Ruoff, R. S.; Tse, D. S.; Malhotra, R.; Lorents, D. C. *J. Phys. Chem.* **1993**, *97*, 3379–3383.

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(13) The binding preference of capsule **2** for the guests employed here is **4** > C_{60} > **3** ≫ C_{70}. Investigations of further molecular recognition (e.g., organometallic and chiral guests) and the mechanisms of guest binding and release are currently being studied in our group. Guests **3** and **4** are almost insoluble in a 2:1 MeOH/H_2O solution.

(14) M_2L_4 capsule **2** and the host−guest complexes exhibited no emission because of the heavy atom effect of the Pd(II) ions. For details, see: Li, Z.; Kishi, N.; Hasegawa, K.; Akita, M.; Yoshizawa, M. *Chem. Commun.* DOI: 10.1039/C1CC12946E, submitted.