Molecular Capsules

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A Molecular Capsule Network: Guest Encapsulation and Control of Diels–Alder Reactivity**

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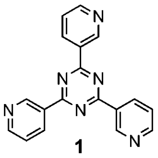
The environments isolated within the cavities of molecular capsules[1] display distinctly different properties from that of the bulk solvent and unusual chemical events can be observed within such cavities: e.g., the stabilization of short-lived intermediates, the acceleration of reaction rates, and the fixation of metastable conformations.[2–4] To date, the chemistry of molecular encapsulation has been developed primarily in solution and scant attention has been paid to molecular encapsulation occurring in the solid or crystalline state.[5] To transfer the wealth of solution-state molecular host-guest chemistry into the solid, crystalline state,[6,7] we designed an infinite network of molecular capsules based upon M_6L_4 octahedral coordination capsules formed by triazine ligand **1** with 90° metal hinges.[8] When the metal centers are shared between neighboring capsule units, a network of molecular hosts arises. Herein, we report the preparation and encapsulation properties of a cobalt(II) coordination network consisting of an infinite array of M_6L_4 molecular capsules. Just as in solution, the solid-state network of molecular hosts encapsulates various guest molecules; however, now the encapsulation behavior can be readily observed by X-ray diffraction analysis owing to the high crystallinity of the network solid. New solid-state host properties were observed and, unlike in solution, the homodimerization of cyclopetadiene by Diels–Alder reaction[9] was suppressed within the capsule.



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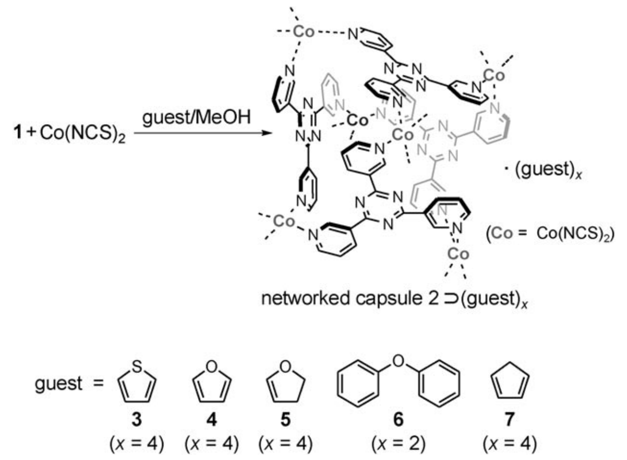
Networked capsule **2** was prepared by slowly layering a methanol solution of Co(NCS)$_2$ onto a thiophene (**3**)/methanol solution of tris(3-pyridyl)triazine (**1**).Pale red crystals of the network capsule had formed after 2 days; these crystals were isolated by filtration in 60% yield (Scheme 1). Elemental analysis of the as-synthesized **2** showed a formula of $\{[(\mathrm{Co(NCS)_2})_3(\mathbf{1})_4]\cdot(\mathbf{3})_6\cdot(\mathrm{MeOH})_5\cdot(\mathrm{H_2O})\}_n$. X-ray single-crystal analysis revealed that network solid **2** consisted of an infinite array of M_6L_4 capsules, with each cobalt(II) corner shared between adjacent capsules.[10,11] In each M_6L_4 capsule subunit, four thiophene guests (**3**) exist and interact with the four panel ligand **1** via aromatic-aromatic interactions: 3.5 Å interplanar distance (Figure 1). To emphasize the molecular host behavior of this infinite network solid, we denote this complex by $\mathbf{2}\supset(\mathbf{3})_4$. The gaps between adjacent ligand panels are smaller than the thiophene and, hence, the four guest molecules are fully enclathrated.



Scheme 1. Synthesis of networked capsule **2** with various guests.

To our delight, near-identical capsule-networks crystallized when we employed furan (**4**), 2,3-dihydrofuran (**5**), and diphenyl ether (**6**) instead of thiophene in 38, 35, and 67% yield, respectively (Figure 2). X-ray analysis confirmed that the obtained crystals possessed the same M_6L_4 capsule framework as $\mathbf{2}\supset(\mathbf{3})_4$. Four molecules of **4** and **5** were encapsulated to give infinite $\mathbf{2}\supset(\mathbf{4})_4$ and $\mathbf{2}\supset(\mathbf{5})_4$ complexes, whereas only two molecules of the larger diphenyl ether guest (**6**), were co-enclathrated in a tennis-ball orientation to give $\mathbf{2}\supset(\mathbf{6})_2$. The solvent involved in crystallization for the layer-diffusion method can dramatically affect the solid-state structures of the coordination-network complexes; however, network capsule **2** provided a rather rare example where an identical network framework crystallized regardless of the "co-solvent" guest.

There are two distinct void spaces in the crystal network of **2**. The first is the cavity defined by the M_6L_4 molecular capsules; here, guest molecules are tightly packed and their orientations are constrained. Second, the interstitial void

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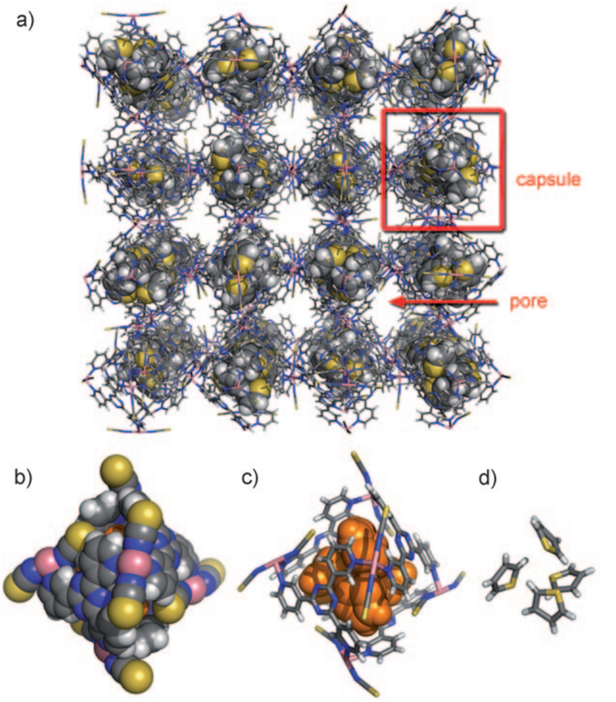

Figure 1. a) Crystal packing of **2**⊃(**3**)$_4$. One capsule is marked with a red square. b) CPK and c) stick models of the M$_6$L$_4$ capsule where the thiophene guests are shown in orange. d) The orientation of encapsulated thiophene molecules.

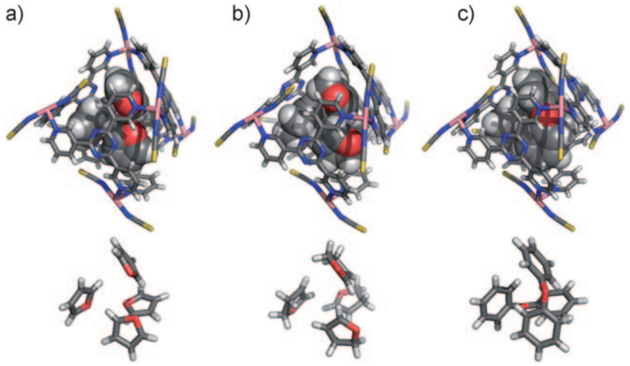

Figure 2. X-Ray crystal structures of a) **2**⊃(**4**)$_4$, b) **2**⊃(**5**)$_4$, and c) **2**⊃(**6**)$_2$. (top: capsule unit, bottom: orientations of the encapsulated guest molecules).

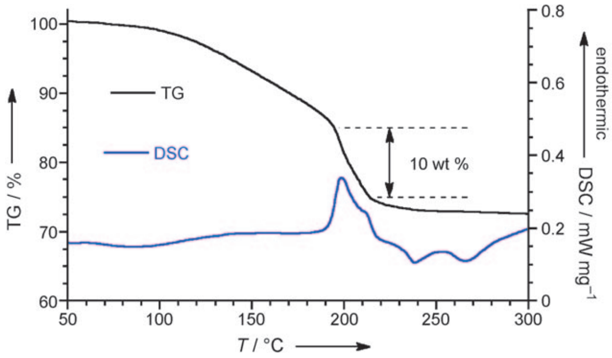

Figure 3. TG-DSC curves of **2**⊃(**3**)$_4$.

between capsules in the infinite array of M$_6$L$_4$ hosts forms a three-dimensional pore (Figure 1). On the basis of elemental and X-ray analyses, as-synthesized network **2**⊃(**3**)$_4$ contains a total 28 wt % of guest molecules, where thiophene (**3**) in the M$_6$L$_4$ capsules and the interstitial pores account for 10 wt % and 18 wt %, respectively.

In the interstitial pores, guest molecules showed much higher mobility and volatility (Figure 3). The thermogravimetric (TG) curve shows a gentle 17 % weight loss from 50 °C to 200 °C, followed by a steep 10 % weight loss between 200 and 220 °C; the initial loss is attributed to guest evaporation from the pores whilst the guest molecules inside the M$_6$L$_4$ capsules remaineded trapped until 200 °C. Differential scanning calorimetry (DSC) analysis revealed a sharp endothermic peak at 198 °C, which corresponded to a large entropy gain upon guest molecules escaping from the capsules. Similar characteristic weight losses and endothermic peaks (at ca. 200 °C) were recorded for network capsules **2**⊃(**4**)$_4$, **2**⊃(**5**)$_4$, and **2**⊃(**6**)$_4$ (see the Supporting Information). Guests **3**–**5** have boiling points below 84 °C yet remained enclathrated within the molecular capsules at up to 200 °C. In all cases, the total weight losses observed by TG analysis were consistent with those estimated from X-ray and elemental analyses.

The effects of encapsulation were clearly demonstrated by the suppression of the dimerization of cyclopentadiene (**7**) within the capsule. A solution of Co(NCS)$_2$ was layered onto a methanol solution of freshly prepared **7** and ligand **1** and, after 40 hours, capsule network **2** containing guests **7** and **8** was isolated in 35 % yield. The remaining supernatant contained **7** and **8** in a 64:36 ratio, thus indicating that dimerization occurred under the reaction conditions.[12] Nevertheless, only monomer **7** was observed in the M$_6$L$_4$ capsules by X-ray crystallographic analysis: four cyclopentadiene monomers were located within the capsules (Figure S3 in the Supporting Information). The snug fit and restricted conformations presumably inhibited an orientation that was favorable for dimerization. The entrapped monomer **7** was

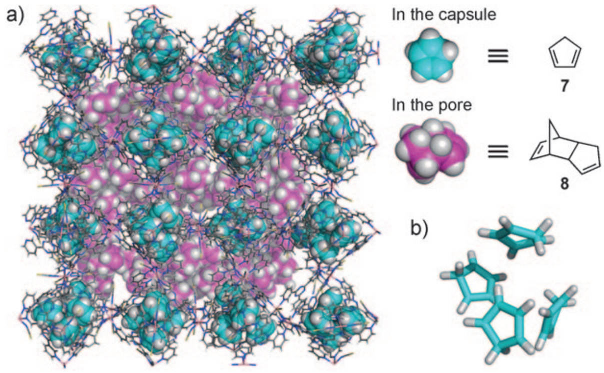

Figure 4. a) Network structure of **2**⊃(**7**)$_4$ after heating at 40 °C in freshly distilled cyclopentadiene (**7**) for 1 day. The encapsulated guest **7** and dimer **8** in the pore are shown in blue and pink, respectively. b) The orientations of four cyclopentadiene molecules (**7**) in a M$_6$L$_4$ capsule.

thermally stable and dimerization to afford **8** was completely suppressed in the capsule, even after heating the crystal at 40 °C for 1 day. In contrast, only dimer **8** was located within the interstitial pores in the crystallographic analysis (Figure 4).[13] The enrichment of dimer **8** in the pores is attributable to the acceleration of the reaction in the pore or selective inclusion of the dimer from the bulk solution.

In summary, we have demonstrated that network capsule **2** can be reproducibly synthesized with a variety of guest molecules. TG analysis showed that the capsule retains guest molecules at up to 200 °C, far above the boiling points of the guests. Within the molecular capsule, monomeric cyclopentadiene (**7**) was isolated and remarkably stable. The capsule network **2** provides a unique opportunity to transfer solution state host–guest chemistry into the solid-state and engender new encapsulation phenomena.

Experimental Section

Synthesis of network capsule $\mathbf{2}\supset(\mathbf{3})_4$: A solution of 2,4,6-tris(3-pyridyl)-1,3,5-triazine (**1**; 6.3 mg, 20 μmol) in a mixture of thiophene (**3**; 4.0 mL) and methanol (1.0 mL) was placed in a test tube (inner diameter 1 cm, height 10 cm). Absolute methanol (0.2 mL) was layered onto the top of the solution as a buffer. Then, a solution of $Co(NCS)_2$ (10.5 mg, 60 μmol) in methanol (1.0 mL) was carefully layered on the top of the resultant solution, and the test tube was allowed to stand at room temperature for 2 days. The title network crystallized on the glass surface of the test tube and was collected by filtration and dried at RT under reduced pressure (0.5 mmHg) for 15 min. (60 % yield, 7.6 mg; averaged value over 5 batches.) Elemental analysis: calculated for $\{[(Co(SCN)_2)_3(\mathbf{1})_4]\cdot 6.0(\mathbf{3})\cdot 5.0(MeOH)\cdot 1.0(H_2O)\}_n$: C 52.29, H 3.86, N 17.10; found: C 52.01, H 3.68, N 16.82 IR (KBr): $\tilde{\nu} = 3345$ (m), 3062 (m), 2069 (s, SCN st.), 1586 (s), 1525 (s), 1422 (m), 1364 (s), 1318 (m), 1194 (m), 1029 cm^{-1} (m).

CCDC 782803 ($\mathbf{2}\supset(\mathbf{3})_4$), 782804 ($\mathbf{2}\supset(\mathbf{4})_4$), 782805 ($\mathbf{2}\supset(\mathbf{5})_4$), 782806 ($\mathbf{2}\supset(\mathbf{6})_2$), 782807 ($\mathbf{2}\supset(\mathbf{7})_4$ as-synthesized), and 782808 ($\mathbf{2}\supset(\mathbf{7})_4$ after heating at 40 °C) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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[11] 64 M_6L_4 units were found in the cubic lattice of network **2**, which are classified into two types; 48 of the 64 M_6L_4 units form a capsule shape, and the other 16 units are open-mouthed octahedral cages in which guest molecules were not trapped (for detailed structures, see the Supporting Information).

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[13] For the as-synthesized $\mathbf{2}\supset(\mathbf{7})_4$, the ratio of **7**/**8** in the crystal was shown to be 38:62 from the crystal structure, but was estimated to be 56:44 by NMR analysis of the guests extracted from the crystals (after acid decomposition of the crystal). Presumably, monomer **7** also existed in the interstitial pores to some extent but could not be located by crystallography because of disorder.