

Designed Self-Assembly of Molecular Necklaces Using Host-Stabilized Charge-Transfer Interactions

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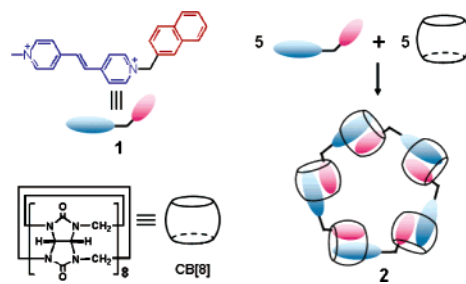
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The creation of nanoscale molecular or supramolecular architectures that have specific structures, properties, and functions has been of great interest in recent years.¹ In particular, the efficient synthesis of interlocked molecules² such as catenanes and rotaxanes has attracted much attention due not only to their aesthetic appeal but also to their potential applications in nanotechnology.³ Thanks to various template strategies developed during the last two decades, the synthesis of such topologically intriguing supermolecules is now much more feasible than before.² However, the synthesis of some classes of interlocked molecules still remains challenging, which includes molecular necklaces in which a number of small rings are threaded onto a large ring. The conventional covalent synthesis of molecular necklaces generally leads to a mixture of products; therefore, a desired molecular necklace is obtained in a low yield after a laborious separation procedure.^{4,5} Several years ago, we developed a noncovalent synthetic strategy for molecular necklaces based on the transition metal directed self-assembly⁶ and successfully synthesized molecular necklaces [4]MN and [5]MN,⁷ in which three and four small rings, respectively, are threaded onto a large ring, in high yields without laborious purification.^{2e,8}

A member of the host family cucurbit[*n*]uril, cucurbit[8]uril (CB[8]),⁹ which has a cavity comparable to that of γ -cyclodextrin, exhibits remarkable host–guest properties¹⁰ including the encapsulation of a pair of electron-rich and electron-deficient guest molecules inside the cavity to form a stable 1:1:1 complex,^{10b} which is driven by the markedly enhanced charge-transfer (CT) interactions between the guests inside the hydrophobic cavity of CB[8]. This discovery led us to build several novel supramolecular assemblies such as redox-controllable vesicles^{10c} and molecular loops^{10d,e} using the host-stabilized CT interactions. We then decided to extend this effort to build molecular necklaces. Here, we report a novel approach to the noncovalent synthesis of molecular necklaces using the host-stabilized intermolecular CT complex formation, and the first quantitative self-assembly of a molecular necklace [6]MN from 10 components.

Our strategy involves the host–guest complex formation between CB[8] and a guest molecule in which an electron donor and an electron acceptor unit are connected by a rigid linker with a proper angle, to form a cyclic oligomer (molecular necklace) through the host-stabilized intermolecular CT complex formation. A properly designed guest molecule should prevent the intramolecular CT complex formation^{10d} inside CB[8] while maintaining a bent shape to set a stage for the formation of a cyclic oligomer via the host-stabilized intermolecular CT complex formation. With this idea in

Scheme 1



mind, we designed the guest molecule **1** containing a naphthalene unit and a dipyrilidiumylethylene unit connected by a methylene bridge. Because the angle between the electron donor and acceptor units of **1** set by the methylene bridge is close to the vertex angle of an equilateral pentagon, we thought that five CB[8] molecules and five **1** molecules would form a cyclic pentamer (molecular necklace [6]MN) as shown in Scheme 1. Indeed, this novel approach successfully led to the quantitative self-assembly of the first molecular necklace [6]MN.

The addition of 1 equiv of CB[8] to **1** dissolved in water resulted in the appearance of a strong absorption at 330 nm, indicating the host-stabilized charge-transfer complex formation. The ¹H NMR spectrum of the solution (Figure 1) showed only one set of concentration-independent signals, indicating the quantitative self-assembly of a single supermolecule with a highly symmetric structure. Slow diffusion of ethanol vapor into the solution produced **2** as yellow brick-shaped crystals in 86% yield.¹¹

Product **2** was characterized by various NMR methods including COSY, NOESY, and pulsed-field gradient (PFG) NMR techniques. As seen in Figure 1, the signals for the terminal pyridylum (*b*, *c*), ethylene (*d*, *e*), and naphthalene (*i*–*n*) protons shift upfield relative to those in the free guest, whereas those for the methylene (*h*) and inner pyridylum (*f*, *g*) protons shift downfield. In addition, the signals for pyridylum protons (*b*, *c*, *f*, *g*) in the complex are split into two sets. Strong negative NOE cross-peaks were observed even at 40 °C (Figure S2). The terminal methyl protons, *a*, show the intermolecular NOE cross-peaks with the methylene protons, *h*, and two naphthalene protons, *i* and *o*, of another guest molecule, in accord with the CT interactions between two guests inside the CB[8] cavity. The methylene protons of CB[8] interact, in an intermolecular fashion, with inner pyridinium protons, *f*, and the naphthalene proton, *k*, of **1**. The hydrodynamic volume of **2** measured by the PFG NMR technique (Figure S3)¹² is 8.7 times that of CB[8] alone. The much higher spin–lattice relaxation times (*T*₁) of the CB[8] protons in **2** as compared to those of free CB[8]

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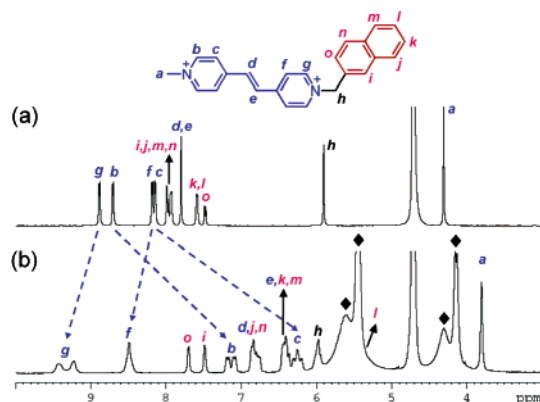


Figure 1. ^1H NMR spectra of **1** in D_2O (a) before and (b) after addition of 1 equiv of CB[8] (♦) at 25°C .

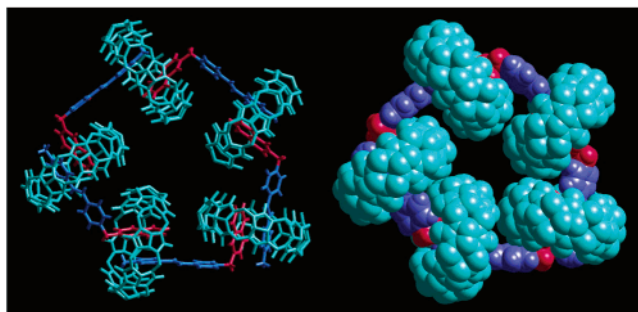


Figure 2. Energy-minimized structure of molecular necklace **2** shown in stick and space-filling models. Hydrogen atoms in CB[8] are omitted.

reflect a highly rigid structure of **2**. Taken together, the NMR data suggest that **2** is most likely a cyclic oligomer (or molecular necklace) formed by the host stabilized intermolecular CT interactions.

A molecular mechanical calculation¹³ established that a cyclic pentameric structure ([6]MN) is the most stable one for **2**. The energy-minimized structure of **2** shown in Figure 2 is congruent with all of the NMR data described above. In the structure, five molecules of **1** form a cyclic framework by the intermolecular CT interactions, on which five CB[8] molecules are threaded with an arrangement reminiscent of a five-fold propeller. The molecular necklace measures ~ 3.7 nm in diameter and ~ 1.8 nm in thickness. The formation of a cyclic tetramer or hexamer from **1** and CB[8] is unlikely due to their high strain energy. The cyclic pentameric nature of **2** was eventually confirmed by ESI-mass spectrometry where multiply charged ions of the parent complex, as well as its fragments, were observed (Figure S4). Attempts to confirm the structure of **2** by X-ray crystallography were hampered by low diffraction intensity and inherent disorder in the cyclic framework.¹⁴ Nevertheless, the preliminary X-ray data revealed that the arrangement of the five CB[8] molecules in **2** (Figure S5) closely matches that in the calculated structure shown in Figure 2.

In summary, we present a novel approach to the noncovalent synthesis of molecular necklaces using host-stabilized CT complex formation and successfully demonstrate for the first time the quantitative self-assembly of a molecular necklace [6]MN using carefully designed components. By varying the length and angle of the linker, we should be able to synthesize a variety of molecular necklaces with different sizes, shapes, and number of molecular beads. Such designed self-assembly of topologically intriguing

supramolecules may provide insight into the construction of nanoscale objects with well-defined structures and functions.

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Supporting Information Available: Description of experimental procedures, spectroscopic data, and preliminary X-ray crystallographic study (PDF and CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (11) To a solution of **1** (19 mg, $41\ \mu\text{mol}$) in H_2O (2 mL) was added CB[8]· $\text{H}_2\text{SO}_4\cdot 20\text{H}_2\text{O}$ (64 mg, $49\ \mu\text{mol}$). The resulting yellowish solution was filtered, and ethanol vapor was allowed to diffuse into the solution. Yellow, brick-shaped crystals began to form within a week. The crystalline product **2** was collected, washed with ethanol, and dried (66 mg, 86%). ESI-MS: m/z 1430.4 ($2 - 6\text{NO}_3^-$)⁶⁺, 1217.2 ($2 - 7\text{NO}_3^-$)⁷⁺, 1057.5 ($2 - 8\text{NO}_3^-$)⁸⁺, 933.1 ($2 - 9\text{NO}_3^-$)⁹⁺. Anal. Calcd for $(\text{C}_{360}\text{H}_{350}\text{N}_{170}\text{O}_{80})^{10+}\cdot 10(\text{NO}_3^-)\cdot 60(\text{H}_2\text{O})\cdot 5(\text{C}_2\text{H}_5\text{OH})$: C, 43.28; H, 4.91; N, 24.55. Found: C, 43.00; H, 4.68; N, 24.37.
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- (13) Molecular mechanics calculations were carried out using Chem2.
- (14) We have checked more than 50 single crystals of **2** and collected diffraction data on more than 10 occasions. Although the diffraction intensity was extremely weak in most cases, a set of consistent unit cell parameters was determined, and, in one case, we were able to obtain the structural solution where the asymmetric unit contains one-half the whole molecule of **2** which is related to the other half by mirror plane symmetry along the equator of the pentameric circle. The low diffraction intensity and inherent disorder in the guest molecules hampered locating the anions and many atoms of the guest molecules; current isotropic refinement converged to $R_1 = 0.2000$. Further refinement of the structure and attempts to grow better quality crystals are in progress. For more details, see Supporting Information.

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