Supramolecular assemblies built with host-stabilized charge-transfer interactions

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Host-stabilized charge-transfer (CT) interactions and supramolecular assemblies built with these interactions are described. A variety of supramolecular assemblies including polyrotaxanes, molecular necklaces, and rotaxane dendrimers were synthesized through the intramolecular or intermolecular host-stabilized CT complex formation using cucurbit[8]uril (CB[8]) and D–A molecules having both electron-donor and electron-acceptor units connected by various types of linkers. Applications, including the design and synthesis of redox-driven molecular machines such as molecular loop locks, development of redox-controllable vesicles and detection of biologically important molecules, are also described.

1. Introduction

The charge-transfer (CT) interactions or donor–acceptor interactions$^1$ between π-systems are an important class of non-covalent interactions and have been greatly exploited in the design and synthesis of self-organizing systems. In particular, the CT interactions between electron-deficient 4,4′-bipyridinium derivatives and electron-rich aromatics have been extensively used to build mechanically interlocked molecules such as rotaxanes and catenanes,$^2$ which later led to elegant studies of molecular machines and switches.$^3$ Electron-rich tetraphiafulvalene derivatives have also been incorporated into elaborate molecular systems acting as sensors or molecular switches by virtue of their ability to form CT complexes with a variety of π-electron acceptors.$^4$ The organization of alternating electron-rich and electron-deficient units has also been employed to create novel macromolecules with folded structures$^{5a–5c}$ and discotic liquid crystalline materials.$^{5d}$

Although formation of stable CT complexes in the pores of zeolites had been reported,$^6$ there was no report on stable CT complex formation in a molecular host until 2001, when we reported the first example of selective inclusion of an electron-donor and -acceptor pair in cucurbit[8]uril, driven by the strong CT interaction between the guests.$^7$ The host-stabilized CT complex formation is an interesting phenomenon in its own right but, more importantly, it offers new opportunities to construct supramolecular assemblies. Indeed, for the last several years, we and others reported a wide variety of supramolecular assemblies such as molecular necklaces, molecular loop locks, and redox controllable vesicles, based on this chemistry. This feature article focuses on supramolecular assemblies built with the host-stabilized CT interactions primarily based on our own work.

2. Host-stabilized charge-transfer interactions

2.1. Cucurbit[n]uril

The host family cucurbit[n]uril (CB[n], n = 5–10), comprising n glycoluril units,$^8$–$^{10}$ have a hydrophobic cavity and two...
identical carbonyl-laced portals, which allow them to form stable inclusion complexes with a wide variety of guest molecules.11 Going from CB[5] to CB[10], the ring size increases progressively while the height remains constant. The cavity diameter increases from 4.4 Å to 11.7 Å and the portal diameter from 2.4 Å to 10.0 Å.9 Although they share common structural features, their varying cavity and portal sizes lead to remarkable molecular recognition properties different from each other.11 For example, CB[6] forms stable 1 : 1 host–guest complexes with protonated π,ω-diaminoalkanes.10 On the other hand, CB[7] forms stable 1 : 1 complexes with larger guest molecules such as adamantylamine as well as methyl viologen dication, which are not included in CB[6]. CB[8] (Fig. 1), which has a cavity comparable to that of γ-cyclodextrin, exhibits remarkable host–guest properties different from those of the smaller homologues, including the encapsulation of two aromatic guest molecules such as naphthalene derivatives inside the cavity to form a stable 1 : 2 host–guest complex.10,12 The cavity of CB[8] is large enough to encapsulate a macrocycle such as cyclen and cyclam to form a macrocycle within a macrocycle.12a The cavity of CB[8] has been used as a reaction chamber to mediate chemical reactions such as stereospecific [2 + 2] cycloadditions.12b,c Furthermore, by encapsulation, the molecular host can stabilize otherwise unstable species. For example, methyl viologen cation radicals or tetrathiafulvalene cation radicals form stable π-dimers in the cavity of CB[8].12d,e Most remarkably, CB[8] encapsulates two different guest molecules, an electron-deficient molecule and an electron-rich molecule, inside the cavity to form a stable 1 : 1 : 1 complex, which is driven by the markedly enhanced charge-transfer (CT) interaction between the guest pair inside the hydrophobic cavity of CB[8], as described in detail in the following section.

2.2. Cucurbit[8]uril-stabilized charge-transfer interactions

4,4’-Bipyridinium dications (also called viologens, V2+), well-known electron-deficient molecules, have been widely incorporated into many supramolecular systems.2–4 The host–guest interaction between redox-active viologens and cyclodextrins has been extensively studied.13 While methyl viologen (MV2+) shows little interaction with β- or γ-cyclodextrin,13c it readily forms a 1 : 1 host–guest complex with CB[8] (MV2+⊂CB[8]) in water with a formation constant of 1.1 × 105 M−1.12f Furthermore, addition of 1 equivalent of an electron-rich aromatic compound such as 2,6-dihydroxynaphthalene (HN) or 1,4-dihydroxybenzene (HB), to the 1 : 1 complex of MV2+ and CB[8] results in instantaneous and quantitative formation of an inclusion complex containing the electron-donor–acceptor pair (MV2+-HN)⊂CB[8].7 Similarly, when added to the 1 : 1 complex of MV2+ and CB[8], a water-soluble tetrathiafulvalene (TTF) derivative12f forms a very stable CT complex with MV2+ inside the host.14 N,N’-Dimethyl-dipyridiliumylethylene (MPE2+), which is a stronger electron-acceptor than MV2+, not only forms a 1 : 1 complex with CB[8] but also the resulting 1 : 1 complex has higher affinity toward electron-rich guest molecules (K > ~106 M−1), resulting in a more stable ternary complex.15

Such ternary complexes are also formed exclusively when their components are mixed in a 1 : 1 : 1 ratio in aqueous solution (Scheme 1). It should be noted that electron-rich guest molecules themselves do not bind to CB[8] in the absence of an electron-acceptor. Therefore, the major driving force for the ternary complex formation appears to be strong CT interaction between an electron-donor and -acceptor pair inside the host cavity. The 1 : 1 : 1 ternary complexes exhibits a CT absorption band between 400 and 600 nm which is largely red-shifted (Δλ ~ 100 nm) with concomitant high increase in intensity compared to those of the corresponding CT complexes formed in the absence of CB[8]. Strong fluorescence quenching is also observed upon formation of the CT complexes inside CB[8]. The highly enhanced CT interaction between the two guests is probably due to their close contact within the cavity of CB[8], which has been confirmed by X-ray

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Fig. 1 Structural formula and X-ray crystal structure of CB[8]. Color codes: carbon: grey; nitrogen: blue; oxygen: red.

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The discovery of the host-stabilized CT complex formation prompted us to explore creation of elaborate supramolecular assemblies as well as recognition of biomolecules with aromatic residues based on this chemistry, as described below.

3. Supramolecular assemblies built with cucurbit[8]uril and a molecule containing both electron-donor and -acceptor units

In building novel supramolecular assemblies by exploiting the host-stabilized CT complex formation we decided to study the host–guest complex formation between CB[8] and a guest molecule (D–A molecule) having both electron-donor and electron-acceptor units connected by a suitable linker. We envisioned that several different types of supramolecular assemblies can be obtained by this process depending on the length and flexibility of the linker between the donor and acceptor units. A long and flexible linker would favor a 1 : 1 complex by the host-stabilized intramolecular CT interaction, whereas a rigid and/or short linker would lead to a 2 : 2 complex or polymer (or poly(pseudorotaxane)) by host-stabilized intermolecular CT interactions. Finally, a rigid linker with a proper angle may lead to a cyclic oligomer, which is a molecular necklace in which a number of CB[8] beads are threaded on a large “ring” formed by intermolecular CT interactions (Scheme 2). Indeed, we observed all the above supramolecular assemblies as described below in detail.

In characterizing the resulting supramolecular assemblies we used various NMR techniques extensively, including COSY and ROESY, and mass spectrometry. In particular, the pulsed field gradient (PFG) NMR technique turned out to be very useful to characterize them. It allows the measurement of the self-diffusion coefficient of a supramolecular species generated, from which we can estimate its size. Furthermore, in the case of multiple components, it provides an additional dimension to distinguish them by their mobility.

3.1. Host-stabilized intramolecular charge-transfer complexes

A D–A molecule with a flexible linker can easily fold to bring its donor and acceptor units into close proximity, resulting in the formation of a stable intramolecular CT complex inside the CB[8] cavity. The D–A molecule 12+, in which electron-donor and acceptor units are linked by a four-atom bridge, forms a 1 : 1 complex (52+) with CB[8] by intramolecular CT interaction. When 1 equivalent of CB[8] is added to the guest 12+, the solution turns violet (λmax = 566 nm), indicating the formation of a CT complex. The formation of 1 : 1 complex 52+ was further confirmed by NMR and mass...
spectroscopy. The size of $5^{2+}$ estimated by the PFG NMR technique is 1.3 times larger than that of CB[8] itself. The energy-minimized structure of $5^{2+}$ (Fig. 3) obtained by molecular modeling is consistent with the proposed structure.

To gain further insight into the nature of $5^{2+}$, we investigated the interaction of $5^{2+}$ with competing electron-donor and -acceptor molecules. When HN or MV$^{2+}$ is added to $5^{2+}$ in D$_2$O, no change in color or in $^1$H NMR spectrum is observed. However, the addition of MPE$^{2+}$, which is a stronger electron-acceptor than MV$^{2+}$, results in complete conversion of $5^{2+}$ to a ternary complex $6^{4+}$, in which MPE$^{2+}$ forms a CT complex with the naphthalene unit of $1^{2+}$, inside CB[8], by replacing the bipyridinium unit of $1^{2+}$ with MPE$^{2+}$ (Fig. 4). This experiment demonstrates that the guest in the supramolecular system changes its conformation from a folded form to an extended form in response to an external chemical stimulus.

D–A molecule $2^{2+}$, in which a but-2-enyloxy unit containing a double bond links its acceptor and donor units, also forms an intramolecular CT complex inside the cavity of CB[8] ($7^{2+}$). We had first thought that the but-2-enyloxy linker would be rigid enough to prevent the intramolecular CT complex formation inside CB[8]. However, it turned out that $2^{2+}$ folds back to form 1 : 1 complex $7^{2+}$ whose structure is similar to that of $5^{2+}$, as evidenced by NMR and ESI-mass spectrometry. In the structure of $7^{2+}$, $2^{2+}$ is folded in such a way that the inner pyridinium ring of the dipyridyliumylethylene unit interacts with the naphthalene unit inside the CB[8] cavity, as revealed by $^1$H NMR spectroscopy. These host-stabilized intramolecular CT complexes provided an insight into designing molecular machines triggered by external stimuli, as described in Section 4.

3.2. Host-stabilized intermolecular CT complexes

The introduction of a rigid and/or short linker between the donor and the acceptor units leads to a 2 : 2 complex or polymer (or poly(pseudorotaxane)) by preventing the intramolecular CT complex formation inside CB[8]. Reaction of CB[8] with D–A molecule $3^{2+}$, containing a rigid $p$-xylylene linker, resulted in quantitative formation of stable 2 : 2 complex $8^{4+}$, which was characterized by PFG NMR as well as 2D NMR spectroscopy such as COSY and ROESY. The hydrodynamic volume of $3^{2+}$ is 3.1 times that of CB[8] itself, supporting the formation of the 2 : 2 complex, which was finally confirmed by ESI-mass spectrometry. The inclusion geometry of the energy-minimized structure of $8^{4+}$ (Fig. 5) is consistent with the changes in chemical shifts of $3^{2+}$ upon complex formation, and the intermolecular NOE between the protons of the two guests. The 2-naphthol unit of one guest interacts with the terminal pyridinium unit of the dipyridyliumylethylene of the other guest molecule inside the cavity of CB[8].

On the other hand, treatment of D–A molecule $4^{2+}$, containing 4,4’-bipyridinium as an acceptor unit, with CB[8] produced a polymeric (oligomeric) species as well as a 2 : 2 complex. Upon addition of 1 equivalent of CB[8] to $4^{2+}$ in H$_2$O the color of the solution changed from yellow to red with the appearance of a strong absorption band at ~482 nm, indicating formation of a CT complex. NMR spectroscopy, using COSY, NOESY and DOSY techniques, established that the complex between CB[8] and $4^{2+}$ formed in aqueous solution (2 mM) is a mixture of a 2 : 2 complex and a
polymeric (oligomeric) species in a 3 : 2 ratio. The hydrodynamic volume of the polymeric species estimated by DOSY suggested a degree of polymerization of ~4. The failure to observe species with a higher degree of polymerization in solution was most likely due to their poor solubility.

Having established the existence of a polymeric species in solution, we decided to grow the poly(pseudorotaxane) on gold, which was carried out in two steps.16 We first anchored pseudorotaxane $10^{2+}$, comprising CB[8] threaded on $9^{2+}$, which contains a dipyridiumylethylene unit and a thiol terminal, on the surface. Using the immobilized pseudorotaxane as a “seed”, a linear poly(pseudorotaxane) was then grown on the surface, utilizing the host-stabilized CT interaction as “glue” (Scheme 3). After a self-assembled monolayer (SAM) of $10^{2+}$ on gold was formed by dipping a gold substrate in a solution containing $10^{2+}$, a poly(pseudorotaxane) was grown by soaking the substrate in an aqueous solution containing CB[8] and $4^{2+}$. The growth of the poly(pseudorotaxane) was monitored by reflectance FT-IR spectroscopy and the surface plasmon resonance (SPR) technique, which revealed that the growth of the poly(pseudorotaxane) on the surface can be reversibly controlled by the concentration of the monomer solution and the immersion time. The poly(pseudorotaxane) grown on gold by dipping the substrate in 1 mM monomer solution for a day has a degree of polymerization of ~4. The AFM image of the poly(pseudorotaxane) grown on gold showed large grains (Fig. 6) with a height increase of 3.9 nm, which was consistent with the IR and SPR results. This is a rare example of noncovalent polymers grown on a solid surface.

3.3. Designed self-assembly of molecular necklaces

We then extended this effort to build cyclic oligomers (molecular necklaces) via the host-stabilized intermolecular CT complex formation using a carefully designed D–A molecule.19 D–A molecule $11^{2+}$ contains a naphthalene unit and a dipyridiumylethylene unit connected by a methylene bridge. The short, bent linker prevents the intramolecular CT complex formation inside CB[8] while setting a stage for the formation of a cyclic oligomer via the host-stabilized intermolecular CT complex formation. Since the angle between the electron-donor and -acceptor units of $11^{2+}$ set by the methylene bridge is close to the vertex angle of an equilateral pentagon, we thought that five CB[8] molecules and five $11^{2+}$ molecules would form a cyclic pentamer (molecular necklace [6][MN] as shown in Scheme 4. Indeed, the D–A molecule and CB[8] self-assembled into a molecular necklace [6][MN ($12^{10+}$) quantitatively via the host-stabilized intermolecular CT interaction, which was characterized by NMR and mass spectrometry and X-ray crystallography. The NMR data hinted that the product is most likely a cyclic oligomer. The hydrodynamic volume of the complex measured by the PFG NMR technique is 8.7 times that of CB[8] itself. A molecular mechanical calculation established that a cyclic pentameric structure ([6][MN] is the most stable one (Fig. 7), which was eventually confirmed by ESI-mass spectrometry and X-ray crystallography. In the structure, five molecules of $11^{2+}$ form a cyclic framework by the intermolecular CT interaction, on which five CB[8] molecules are threaded with an arrangement reminiscent of a five-fold propeller. Despite some disorder in the cyclic framework, the X-ray crystal structure of $12^{10+}$ closely matched the calculated structure shown in Fig. 7. The molecular necklace measures ~3.7 nm in diameter and ~1.8 nm in thickness. Other molecular necklaces with different sizes, shapes, and numbers of molecular beads may be synthesized by varying the length and angle of the linker of the guest molecule.
3.4. Noncovalent synthesis of rotaxane dendrimers

Rotaxane dendrimers are dendritic molecules containing rotaxane-like mechanical bonds to link their components. Combining many attractive features of conventional dendrimers with properties that result from the mechanical bonds, they are not only structurally appealing but also hold great promise for applications in many areas including materials science. Rotaxane dendrimers are classified into three types depending on where rotaxane-like moieties appeared—Type I, II, and III rotaxane dendrimers, which incorporate rotaxane-like features at the core, terminal and branches, respectively. The synthesis of Type I and II rotaxane dendrimers is relatively straightforward, whereas that of well-defined Type III rotaxane dendrimers (Scheme 5), particularly second and higher generations, still remains challenging. Therefore, we decided to build high generation Type III rotaxane dendrimers using CB[n] as ring components.

As a part of this effort, we decided to synthesize a dendritic [10]pseudorotaxane, or a second generation Type III pseudorotaxane dendrimer, in which the ring components reside on the branches, by combining the remarkable host–guest behavior of CB[6] and CB[8]. As shown in Scheme 6, the strategy for the construction of a dendritic [10]pseudorotaxane using noncovalent interactions involves (1) threading a CB[8] bead onto each of three electron-deficient “arms” of a triply branched core to make a [4]pseudorotaxane, or G1 pseudorotaxane dendrimer, (2) at the same time synthesizing a triply branched wedge ligand containing one electron-donor “arm” and two amine “arms” on each of which a CB[6] bead is threaded, and (3) linking the first generation (G1) pseudorotaxane dendrimer with three of the wedge ligands via CB[8]-stabilized CT interactions to form a dendritic [10]pseudorotaxane, or G2 Type III pseudorotaxane dendrimer (Fig. 8). The triply branched core molecule 13 contains a trans-1,2-bis(1-methyl-4-pyridinio)ethylene unit (as an acceptor) on each branch. Stirring a mixture of 13 and three equivalents of CB[8] in water resulted in formation of stable [4]pseudorotaxanes (14), which may be considered as a G1 pseudorotaxane dendrimer. Stirring an aqueous solution containing 15 and 2 equivalents of CB[6] yields the wedge ligand 16 in which a CB[6] bead is threaded onto each of the protonated diaminobutane units. Finally, mixing 14 with 3 equivalents of 16 produced dendritic [10]pseudorotaxane (or G2 pseudorotaxane dendrimer) 17, which was characterized by UV-visible and NMR spectroscopy. The dendritic [10]pseudorotaxane was the first example of a G2 Type III-A (pseudo) rotaxane dendrimer in which 13 molecular components are held together by noncovalent interactions. Since the host-stabilized CT interaction is weakened by reduction of electron-acceptor units or oxidation of electron-donor units, the dendritic [10]pseudorotaxane is disassembled upon addition of redox stimuli.

4. Molecular machines based on the CT complex formation inside CB[8]

The interplay between the redox and inclusion processes of host-stabilized CT complexes has been studied and exploited in designing molecular machines.
4.1. Interconversion of hetero- and homo-guest pair inclusion in CB[8]

One-electron reduction of MV$^{2+}$ leads to cation radical MV$^{+}$, which has moderate tendency to dimerize and therefore exists as a monomer and a dimer in equilibrium in aqueous solution. However, one-electron reduction of MV$^{2+}$ in the presence of CB[8] results in the rapid generation of 2:1 inclusion complex (MV$^{+}$)$_2$·CB[8], comprising a dimer of the monocation radical MV$^{+}$ encapsulated in CB[8]. The dimerization constant of MV$^{+}$ in the presence of equimolar CB[8] is estimated to be $2 \times 10^7$ M$^{-1}$, which is about 10$^5$ times larger than that of MV$^{+}$ alone in aqueous media.$^{12d}$

As described in section 2, MV$^{2+}$ and HN form a stable CT complex inside the CB[8] cavity to form the stable 1:1 complex (MV$^{2+}$·HN)·CB[8]. However, treatment of a 1:1 mixture of MV$^{2+}$ and the ternary complex with a reducing agent such as sodium dithionite (Na$_2$S$_2$O$_4$) resulted in near-quantitative formation of 2:1 inclusion complex (MV$^{+}$)$_2$·CB[8], and free HN (Scheme 7). This guest exchange is completely reversible since electrochemical oxidation reinstates the hetero-guest pair inclusion complex and MV$^{2+}$. This result demonstrated the reversible conversion of hetero- and homo-guest pair inclusion inside CB[8] triggered by a redox stimulus. The redox-coupled guest exchange process was also investigated by cyclic voltammetry and spectroelectrochemistry, which suggested that the reduction of (MV$^{2+}$·HN)·CB[8] initially generates the one-electron reduced species containing MV$^{+}$ and HN encapsulated in CB[8], which then reacts with free MV$^{+}$ to undergo the rapid guest exchange leading to (MV$^{+}$)$_2$·CB[8] and free HN.

As described in Section 2, TTF derivatives readily form a stable CT complex with MV$^{2+}$ inside CB[8] ((MV$^{2+}$·TTF)·CB[8]) in aqueous solution. Recently, we also reported the first stable π-dimer of TTF cation radical encapsulated in the cavity of CB[8] ((TTF$^{+}$)$_2$·CB[8]), which has been isolated at room temperature and fully characterized.$^{12f}$ Furthermore, the ternary complex (MV$^{2+}$·TTF)·CB[8] is reversibly converted to (MV$^{+}$)$_2$·CB[8] + 2TTF or (TTF$^{+}$)$_2$·CB[8] + 2MV$^{2+}$ upon reduction or oxidation, respectively.$^{14}$ The interconversion of hetero- and homo-guest pair inclusion in CB[8] provided an operating principle of molecular machines triggered by redox stimuli as described below.

4.2. Molecular loop-lock: a redox-driven molecular machine

The discovery of the redox-coupled guest-exchange process prompted us to design and synthesize a redox-driven molecular machine behaving as a molecular loop lock that can be "locked" and "unlocked" with a key and a redox stimulus (Scheme 8).$^{22}$ The D–A molecule 18$^{3+}$ contains a naphthalene-2-yloxy (Np) unit and a viologen (V$^{2+}$) unit linked to each other by a flexible tether, along with a bulky cationic "stopper" unit. Treatment of 18$^{3+}$ with 1 equivalent of CB[8] in aqueous solution resulted in exclusive formation of the stable 1:1 complex 19$^{3+}$ through the intramolecular CT complex formation between the Np and V$^{2+}$ units inside CB[8] with the formation of a molecular loop$^{15}$ with a "closed" or "folded" conformation (Scheme 8). The NMR spectrum of 19$^{3+}$ is not affected by addition of 1 equivalent of MV$^{2+}$, indicating that the 1:1 host–guest complex formed by the intramolecular CT interaction is much more stable than the ternary complex formed by the intermolecular CT interaction between the Np unit of 18$^{3+}$ and MV$^{2+}$ inside CB[8].

However, electrochemical reduction of the solution containing 19$^{3+}$ and 1 equivalent of MV$^{2+}$ resulted in formation of the ternary complex 20$^{3+}$ (Scheme 8) in which the one-electron reduced viologen unit of 18$^{2+}$ interacts with MV$^{+}$ inside CB[8] as confirmed by UV-visible spectroscopy. NMR spectroscopy also revealed that the Np unit is now located outside CB[8], which means that 20$^{3+}$ has an "open" or "unfolded" conformation. Introduction of O$_2$ into the solution of 20$^{3+}$ regenerates 19$^{3+}$ and MV$^{2+}$. Taken together, 19$^{3+}$ with a "closed" conformation is converted to 20$^{3+}$ with an "open" conformation upon reduction in the presence of MV$^{2+}$, and the process can be reversed by oxidation. This system thus behaves as a molecular loop lock that can be "locked" and "unlocked" with a key and a redox stimulus (Scheme 8), where 19$^{3+}$ and 20$^{3+}$ represent the locked and unlocked states, respectively, and MV$^{2+}$ plays the role of the key which is activated by reduction. One may regard it as a "safeguarded" lock since it requires not only a key but also an activation process to open.

4.3. Molecular loop-lock with a built-in key

A molecular loop lock with a built-in key was also designed and synthesized (Scheme 9).$^{23}$ The D–A molecule 21$^{3+}$ contains a naphthalene unit and a viologen unit linked to each other by a rigid phenanthroline unit. In addition, another

![Scheme 7](image_url) Interconversion of hetero- and homo-guest pair inclusion in CB[8] triggered by a redox stimulus.

![Scheme 8](image_url) Formation of molecular loop lock 19$^{3+}$ (locked state) and redox-induced formation of ternary complex 20$^{3+}$ (unlocked state) along with an illustration of the working mode of a molecular loop lock with a key.
viologen unit, which behaves as a key, is linked to the above-mentioned viologen unit by a flexible tether. Treatment of $21^{4+}$ with 1 equivalent of CB[8] results in formation of the stable 1 : 1 complex $22^{4+}$, with a folded conformation, through the intramolecular CT interaction between the naphthalene and viologen units inside the host ("closed" or "locked" state). The "locked" and "unlocked" states of the molecular loop lock with a built-in key can be controlled by a redox stimulus. Two-electron reduction of $22^{4+}$ results in formation of $23^{3+}$, with intramolecular pairing of the viologen cation radical units inside CB[8], leaving the naphthalene unit outside CB[8] ("open" or "unlocked" state). This process is reversible; upon oxidation, $22^{5+}$, with a "locked" conformation, is regenerated.

### 4.4. Molecular machines based on TTF and viologen

As described in Section 4.1, electron-deficient MV$^{2+}$ and electron-rich TTF derivatives form a stable CT complex inside CB[8], which undergoes a guest exchange reaction upon reduction or oxidation. Based on this observation, a molecular machine working in response to reduction as well as oxidation was designed. The D–A molecule $24^{2+}$ contains TTF and viologen (V$^{2+}$) units connected by the penta(ethylene glycol) chain. When 1 equivalent of CB[8] is added to $24^{2+}$, the V$^{2+}$ and TTF units of $24^{2+}$ form a stable intramolecular CT complex inside CB[8] as expected. Reduction or oxidation of the 1 : 1 complex $25^{2+}$ generates a radical cation of the viologen unit or TTF unit, respectively, which then rapidly dimerize to form an intermolecular 2 : 1 inclusion complex, $(24$-$V^{+2}$)$2$-$CB[8]$ ($26^{2+}$) or $(24$-$TTF^{+2}$)$2$-$CB[8]$ ($27^{2+}$), respectively, with a conformational change from a folded form to an extended form (Scheme 10). For example, treatment of $25^{2+}$ with Fe(ClO$_4$)$_3$ in aqueous solution results in formation of the ternary complex $27^{2+}$, in which the TTF radical cation units of two D–A molecules form a dimer inside CB[8] as confirmed by the appearance of the new absorption bands characteristic of a CB[8]-stabilized TTF radical cation dimer. Similarly, reduction of $25^{2+}$ with sodium dithionite (Na$_2$S$_2$O$_4$) produces the 2 : 1 inclusion complex $26^{2+}$.

### 5. Other applications of the host-stabilized CT interactions

The host-stabilized CT complex formation not only provided an operating principle of molecular machines, but also found other applications such as the development of smart materials and detection of biologically important molecules.

#### 5.1. Hierarchical self-assembly of vesicles triggered by CT complex formation in a host

We recently demonstrated the hierarchical self-assembly of giant vesicles triggered by the formation of a CT complex inside CB[8]. When a long alkyl tail is tethered to viologen, the viologen part of the guest forms a stable CT complex with an electron-donor molecule such as HN inside the CB[8] cavity, leaving the alkyl tail extended into the solution (Scheme 11). For example, sonication of an equimolar mixture of CB[8], a viologen with a long alkyl chain ($28^{2+}$), and HN in water produces a violet turbid solution with a broad absorption band centered at ~550 nm, indicating the formation of a CT complex inside CB[8] ($29^{2+}$), which was further confirmed by NMR and mass spectrometry. The SEM images of the complex $29^{2+}$ show relatively large spherical objects with diameters of 0.02–1.2 µm, which turned out to be vesicles (Fig. 9). The vesicles are exceptionally robust as they maintain the spherical shape even under the SEM experiment conditions. Their hollow structures were confirmed.

![Scheme 10](image1)

**Scheme 10** Formation of intramolecular CT complex $25^{2+}$ (folded) inside CB[8], and its conversion to intermolecular 2 : 1 inclusion complex $(24$-$MV^{+2}$)$2$-$CB[8]$ ($26^{2+}$) or $(24$-$TTF^{+2}$)$2$-$CB[8]$ ($27^{2+}$) upon reduction or oxidation, respectively.

![Scheme 11](image2)

**Scheme 11** Formation of a stable ternary complex $29^{2+}$.
high-resolution TEM. Encapsulation of a fluorescent dye within the interior of the vesicles, which can be visualized by confocal microscopy, provides another evidence for the vesicle formation. Although the exact mechanism of the hierarchical self-assembly is not clear, the first step involves the formation of a ternary complex from the viologen derivative with a tail, HN and CB[8], which behaves as a supramolecular amphiphile with a large polar head group and a hydrophobic tail, which in turn self-assembles into a large vesicle. Since the ternary complex is stabilized by CT interaction of an electron-donor–acceptor pair inside the host, redox chemistry can be used to trigger the collapse of the vesicles. Addition of cerium(IV) ammonium nitrate oxidizes HN to the quinone, which disrupts the CT complex and results in the collapse of the vesicles, which was confirmed by SEM. This supramolecular, redox-controllable vesicle system may find useful applications in many areas including development of smart materials and drug delivery.

5.2. Recognition of biologically important molecules using the host-stabilized CT interactions

The design of artificial receptors capable of recognizing biologically important molecules in aqueous solution is an important problem in the chemical and biomedical sciences. The unique phenomenon of the CT complex formation inside CB[8] can be utilized for the detection of biologically important molecules containing aromatic side chains. We have shown that small biomolecules with aromatic residues form stable ternary complexes with an electron-acceptor molecule and CB[8] that are easily recognized by the pronounced color development as well as fluorescence quenching owing to the CT interaction. Aromatic amino acids, tyrosine and tryptophan, and dopamine form stable CT complexes (K ≈ 10^−10 M^−1) with MV^2+ inside CB[8], as indicated by color, UV-visible, emission and ^1^H NMR spectral changes (Fig. 10). The 1 : 1 inclusion complex MPE^2+⊂CB[8] binds the biomolecules more tightly than MV^2+⊂CB[8]. For example, the binding affinity of the former (K_a ≈ 2.9 × 10^5 M^−1) to tryptophan is around 6 times higher than that of the latter (K_a ≈ 5.1 × 10^4 M^−1), as measured by isothermal titration calorimetry (ITC) in aqueous solution. Similarly, stable complex formation with neurotransmitters such as epinephrine and serotonin was also observed. Recently, the potential of MV^2+⊂CB[8] to recognize specific amino acids and peptides was further examined by Urbach et al. The binding affinities of MV^2+⊂CB[8] to the natural aromatic amino acids were measured using ITC in a pH 7.0 buffer, which showed that MV^2+⊂CB[8] binds tryptophan (K_a = 4.3 × 10^4 M^−1) selectively over phenylalanine and tyrosine with 8-fold and 19-fold specificity, respectively. No binding was observed for histidine. They also tested the recognition of specific tripeptides by MV^2+⊂CB[8], which showed that MV^2+⊂CB[8] binds to N-terminal tryptophan residues with higher binding affinity than C-terminal or internal tryptophan residues: it binds Trp–Gly–Gly (K_a = 1.3 × 10^5 M^−1) with 6-fold and 40-fold specificity over Gly–Trp–Gly, and Gly–Gly–Trp, respectively. They suggested that peptide recognition is mediated by the electrostatic charge(s) proximal to the indole. The complex formation is accompanied by the growth of a visible CT band and quenching of indole fluorescence. These optical properties, combined with the stability and selectivity of this system, make this system potentially useful in sensing and separating specific peptides.

Kaifer et al. reported the recognition of neurotransmitters such as dopamine using the host-stabilized CT interaction. The 1 : 1 inclusion complex MDAP^2+⊂CB[8] (MDAP^2+ = 2,7-dimethyldiazapyrenium; Scheme 1) was used as a “fluorescent host” to bind substrates with aromatic residues. The presence of CB[8] markedly increased the sensitivity of the MDAP^2+ probe for the detection of catechol and dopamine. Increased fluorescence quenching in the presence of the host may be explained by static quenching due to the short lifetime of the excited state of the diazapyrenium dication and the close proximity to the π-donor inside the hydrophobic cavity of CB[8]. To explore further the sensing ability of the MDAP^2+⊂CB[8] inclusion complex, they fabricated a fluorescent sensor by anchoring a DAP^2+ derivative on the surface of silica nanoparticles and investigated the response of the fluorescent nanoparticles to dopamine and catechol in the presence and absence of CB[8]. Resembling the results...
obtained in solution, the observed level of fluorescence quenching was considerably more pronounced when CB[8] was present. Thus, this supramolecular host system may be useful for sensitive fluorescence detection of catecholamines and related neurotransmitters.

6. Summary and outlook
In this feature article we described the host-stabilized CT interactions and supramolecular assemblies built with these interactions. Particularly, the CB[8]-stabilized CT complexes are thermodynamically stable, but can be readily disassembled into their components when treated with redox stimuli. The high thermodynamic stability of the CB[8]-stabilized CT interactions allowed us to build various supramolecular assemblies ranging from molecular necklaces to vesicles. Furthermore, the reversibility of the CT complex formation inside CB[8] led us to design redox-driven molecular machines such as molecular loop locks based on this chemistry. It has also been demonstrated that the host-stabilized CT interactions are useful in the detection of biologically interesting molecules containing aromatic residues. Very recently, Mori et al. reported that, upon formation of an intramolecular CT complex inside the CB[8] cavity, a chiral D–A molecule greatly enhances the anisotropy factor due to the confinement of the guest in the host,29 which suggests that the host-stabilized CT interactions may be useful in chiral recognition as well.

Using carefully designed components one may be able to design and create other elaborate supramolecular assemblies in the solid state, on surfaces as well as in solution, based on the CB[8]-stabilized CT interactions. For example, sophisticated molecular machines with unidirectional rotatory motion, and/or working on surfaces may be developed. The work described here can be extended further using other host systems such as CB[10]30 and coordination nanocages31 that can accommodate two (or more) π-conjugated molecules to form a stable CT complex. In fact, Fujita et al. recently reported stacking of two or more large π-conjugated molecules within organic-pillared coordination cages, stabilized by CT interactions.30 The use of CB[10] with a large cavity and functionalized CB[8] with tailored properties31 may provide a new dimension to the chemistry of the host-stabilized CT interactions. The application perspectives of supramolecular assemblies based on host-stabilized CT interactions are great. For example, the polyrotaxanes built with the host-stabilized CT interactions may display interesting electrical and optical properties. The redox-controllable vesicles may find useful applications in the development of smart materials and drug delivery. The studies of the molecular machines may lead to the development of new sensors and actuators. Practical sensors detecting biogenic molecules such as neurotransmitters may be developed. With these exciting developments and perspectives, the future of the chemistry of the host-stabilized CT interactions looks bright.

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