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Dynamic Molecular Invasion into Multiply Interlocked Catenane

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Abstract: A multiply interlocked catenane with a novel molecular topology was synthesized; a phthalocyanine bearing four peripheral crown ethers was quadruply interlocked with a cofacial porphyrin dimer bridged with four alkylammonium chains. The supramolecular conjugate has two nanospaces surrounded by a porphyrin, a phthalocyanine, and four alkyl chains to accommodate guest molecules. Because the phthalocyanine is movable along the alkyl chains, it acts as an adjustable wall, permitting the invasion of large molecules to the nanospaces without spoiling the affinity of the association. The dynamic molecular invasion allowed the intercalation of dianionic porphyrins into both the nanospaces with a high affinity. A photometric titration experiment revealed the two-step inclusion phenomenon. The multiply interlocked catenane complexed with three Cu^{2+} ions, and the spin–spin interaction was switched off by the intercalation of dianionic porphyrins.

Induced fit is an important concept for protein–ligand interactions; this lowers the final-state energy by a dynamic conformational change of the host to fit the guest molecules, maximizing their affinity through enthalpy increase.[1] On the other hand, if the host has a narrow access for incorporating the guest, the transition process during the complexation requires a higher activation energy. Although the access to the host can be expanded to lower the activation energy, such as flexibility would generally decrease the affinity between the host and guest, because the flexibility causes a larger entropy loss during the complexation. Hence, to improve the accessibility of the guest to the host without losing the affinity, it would be advantageous to introduce another concept to couple with induced fit.

A molecular elevator[2,3] is a molecular machine[4–9] composed of two planar molecular components joined with more than two interlock linkages. The component with macrocyclic rings fused with a planar core can move between two competitive recognition sites through the linear threads attached on the other planar component. Strength of the interactions between the recognition sites is modulated by external stimuli such as pH switching, changing the relative position of the two planar components. However, although the macrocyclic rings are attracted to one of the recognition sites, the planar core with the rings still has the ability to move along the threads. This is because the affinity between the ring and recognition point does not help to anchor the ring at this position, but only increases the probability of the position. This flexibility of the interlock linkage satisfies the requirement of the dynamic invasion of a guest molecule. The molecular system permits the invasion of a large guest molecule by expanding the access and stabilizing the host–guest interaction by induced fit based on the interactions between the ring and recognition point (Figure 1).

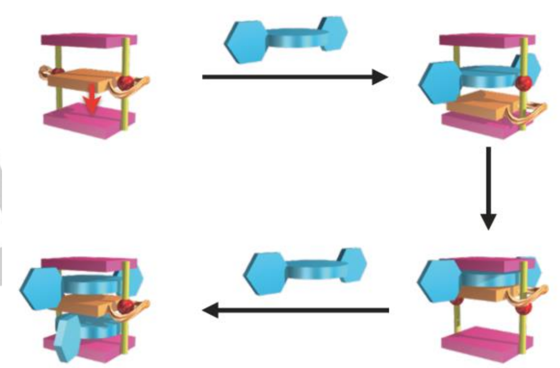

Figure 1. Schematic representation of the dynamic invasion of large guest molecules into a mechanically interlocked host.

Recently, we reported a four-fold rotaxane composed of a porphyrin with four alkylammonium chains and a phthalocyanine with four peripheral crown ethers.[10] Two porphyrinoids faced each other and formed a nanospace with four alkyl pillars in the supramolecular conjugate. In this paper, we report the structural expansion of the conjugate to a D_{4h} symmetrical mechanically interlocked molecule $[H_6\mathbf{1}\cdot 4H]^{4+}$ with a novel molecular topology (Figures 2a and 2b) and the dynamic invasion phenomenon of the multiply interlocked catenane. A phthalocyanine bearing four peripheral crown ethers was quadruply interlocked with a porphyrin dimer bridged with four alkylammonium chains in the catenane. Consequently, three π-planar components were cofacially assembled through the flexible linkages, producing two nanospaces separated by the phthalocyanine that acted as an adjustable wall along the four threads. It was envisioned that the nanospaces would accommodate planer guest molecules using π–π interactions through dynamic molecular inclusion.[11]

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The multiply interlocked catenane $[H_6\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ was synthesized as summarized in Figure 2c by utilizing the four-fold rotaxane formation method reported previously.[10,12] A porphyrin template bearing four alkylammonium sidechains with terminal benzaldehyde moieties $[H_2\mathbf{3}\cdot 4H]^{4+}\cdot 4BARF^-$ was complexed with 1 equiv of a phthalocyanine bearing four peripheral 24-crown-8 units **2**, affording a four-fold pseudorotaxane. Condensation of the four terminal benzaldehyde units of the pseudorotaxane with 4 equiv of pyrrole in the presence of $BF_3\cdot OEt_2$, followed by oxidation with chloranil, successfully furnished the second porphyrin ring, simultaneously forming six macrocycles consisting of four alkyl chains and two porphyrins as the four-way nodes. Each alkyl chain went through the peripheral crown ethers on the phthalocyanine. Consequently, the phthalocyanine was entrapped in the four-pillared conjugate by multiple catenane linkages, affording $[H_6\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$. The compound showed ion peaks corresponding to the multiply interlocked molecule in the electrospray ionization time-of-flight (ESI-TOF) mass spectrum (Figure S10). Surprisingly, the ^1H-NMR spectrum indicated the highly symmetrical D_{4h} structure of $[H_6\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$, and the spectrum was assignable as one-eighth part of the entire structure of $[H_6\mathbf{1}\cdot 4H]^{4+}$ despite the intricate structure (Figures 3, S11 and S12). The simple symmetry suggests that all the alkylammonium chains of the cage were mechanically interlocked inside each crown ring on the phthalocyanine. Notably, the signals of the pyrrolic NH protons of both the porphyrin and phthalocyanine (H_a and H_α in Figure 3, respectively) showed significant high-field shifts from those of each component themselves, indicating a close cofacial stacking of the porphyrins form both sides of the phthalocyanine, because the chemical shifts of the signals have similar tendency as those of the pyrrolic NH protons of closely stacked phthalocyanines in a conjugate composed of stacked porphyrins and phthalocyanines reported previously.[10a,12] Because the length of the C10 alkyl chains connecting the porphyrins with the central phthalocyanine (~13 Å) is much longer than the stacking

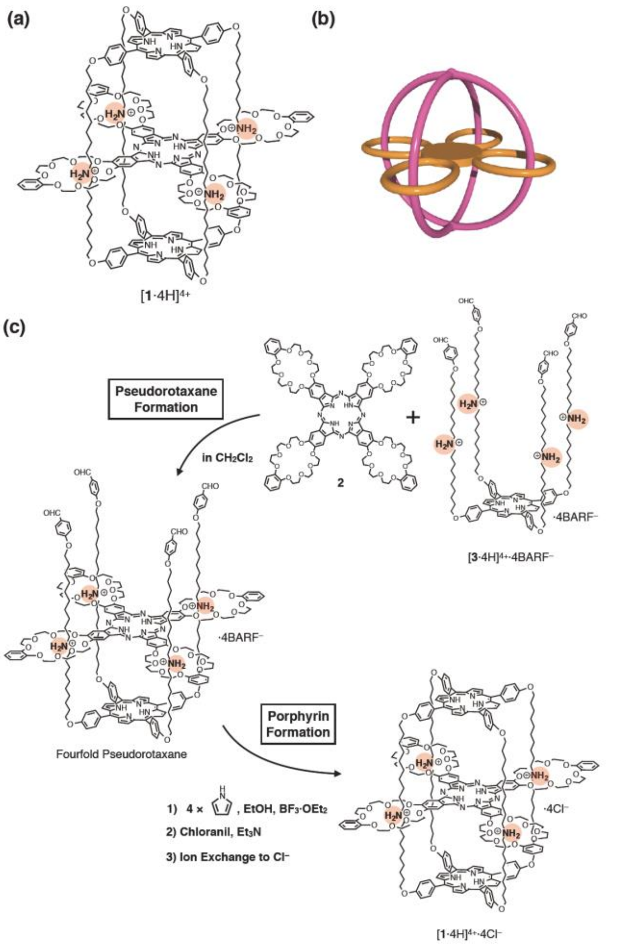

Figure 2. (a) Chemical structure of a multiply interlocked catenane $[H_6\mathbf{1}\cdot 4H]^{4+}$. (b) Generic topology of $[H_6\mathbf{1}\cdot 4H]^{4+}$. (c) Synthetic procedure of $[H_6\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$.

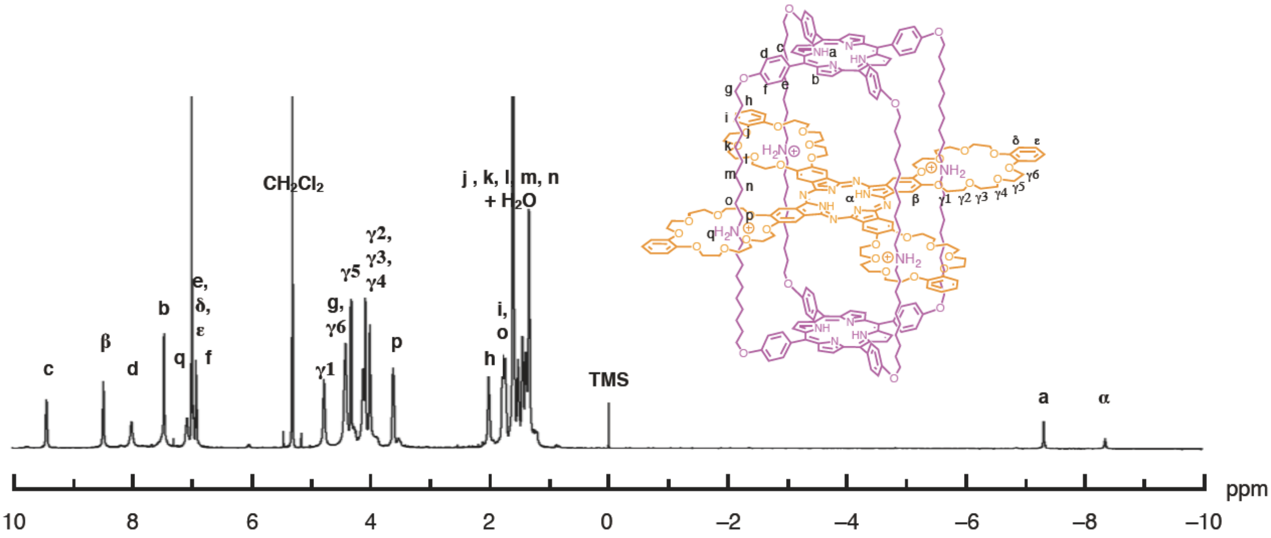

Figure 3. (a) ^1H-NMR spectrum (400 MHz) of the multiply interlocked catenane $[H_6\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ was obtained in CD_2Cl_2 at 293 K. The signals labeled with a–q can be assigned to the resonance of the porphyrin dimer quadruply connected through the alkylammonium chains (shown in pink), and the signals labeled with α–ε can be assigned to the resonances of the phthalocyanine unit (shown in orange).

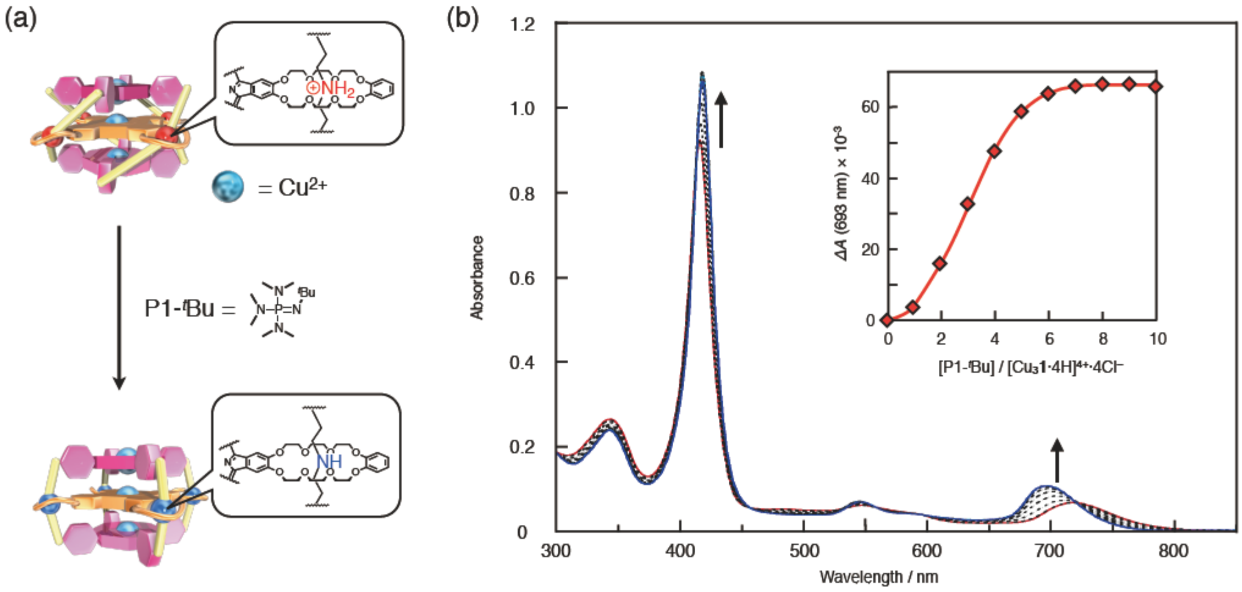

Figure 4. (a) Schematic representation of the deprotonation of the ammonium ions of the trinuclear Cu(II) complex $[Cu_3\mathbf{1}\cdot 4H]^{4+}$. (b) Spectral change during the addition of 0–10 equiv of phosphazene P1-^{t}Bu base. $[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ was dissolved in CH_2Cl_2 at a concentration of 2 μM at 293 K. Inset: Titration curve monitored by the absorption change at 693 nm.

distance between a porphyrin and phthalocyanine (3–4 Å), the alkyl chains should be bent or twisted along the stacking axis in CH_2Cl_2. The D_{4h} symmetrical ^{1}H-NMR spectrum in CD_2Cl_2 indicates that each component moves faster compared to the NMR timescale at room temperature. It is probable that the flexible interlocked linkages in $[H_6\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ also enhance the dynamic conformational change in the solution.

Because of the stacking interactions between the phthalocyanine and porphyrins, the UV–visible spectrum of $[H_6\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ in CH_2Cl_2 showed a significant bathochromic shift and broadening of the Q-bands of the phthalocyanine unit and a hypsochromic shift of the Soret band of the porphyrin units as shown in Figure S13. Similar spectral features were observed in the UV–visible spectrum of $[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ in CH_2Cl_2 (red line in Figure S14), and a close stacking between the Cu-phthalocyanine and Cu-porphyrins in $[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ is expected. In fact, a distinct spin–spin interaction was observed between the three Cu^{2+} spins in $[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ in the continuous-wave electron paramagnetic resonance (CW-EPR) spectrum of $[Cu_3\mathbf{1}\cdot 4H]^{4+}$ in a frozen CH_2Cl_2 solution measured at 4 K (Figure 5a). The quartet state (S = 3/2) in the ground state was evidenced by the temperature dependence of the signals from 4 K to 40 K and explains the ferromagnetic interaction among the three radicals on the Cu centers (Figure S15). The interactions between the ammonium ions and the crown ethers in the catenane were stabilized by the electrostatic interactions between the positive charge on the ammonium ion and the slightly negative core of the crown ether derived from the dense ether oxygens as well as by the hydrogen bonding arising from the ammonium ion to the lone pairs of the oxygen atoms.[13,14] Therefore, deprotonation of the ammonium ions would result in a relational change of the porphyrins and phthalocyanine in the conjugate. The addition of a phosphazene base (P1-^{t}Bu) caused significant spectral changes in the UV–visible absorption spectra of the trinuclear Cu^{2+} complex ($[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$) in CH_2Cl_2 (Figure 4). As the concentration of P1-^{t}Bu against $[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ was increased, the intensity of the Q-bands of the phthalocyanine and the Soret bands of the porphyrins gradually increased with hypsochromic and bathochromic shifts, respectively. These changes can also be attributed to the changes in the stacking structure in $[Cu_3\mathbf{1}\cdot 4H]^{4+}$ caused by the deprotonation of the ammonium protons, affording the fully deprotonated species $Cu_3\mathbf{1}$. Apparent isosbestic points on the spectra and sigmoidal shape of the titration curve indicate that the deprotonation of the ammonium ions of $[Cu_3\mathbf{1}\cdot 4H]^{4+}$ occurred in a concerted fashion. The CW-EPR spectrum of $Cu_3\mathbf{1}$ was reproducible in a simulation as the S = 1/2 pattern in the ground state resulted from the alternation of one of the three spins to antiferromagnetic (Figures 5b and S16). The deprotonation led to only a small change in the distance between the metal centers within the boundary, where significant dipole interactions were observed between the electron spins (at the zero-field splitting parameter D = 25 mT), but the orbital overlapping of the three Cu(II) complexes dynamically changed between ferromagnetic and antiferromagnetic interactions. Hence, it can be concluded that the deprotonation induced the rotation or slipping in the stacking of the complexes, thus increasing the orbital overlapping between the radicals (Figure 5c).

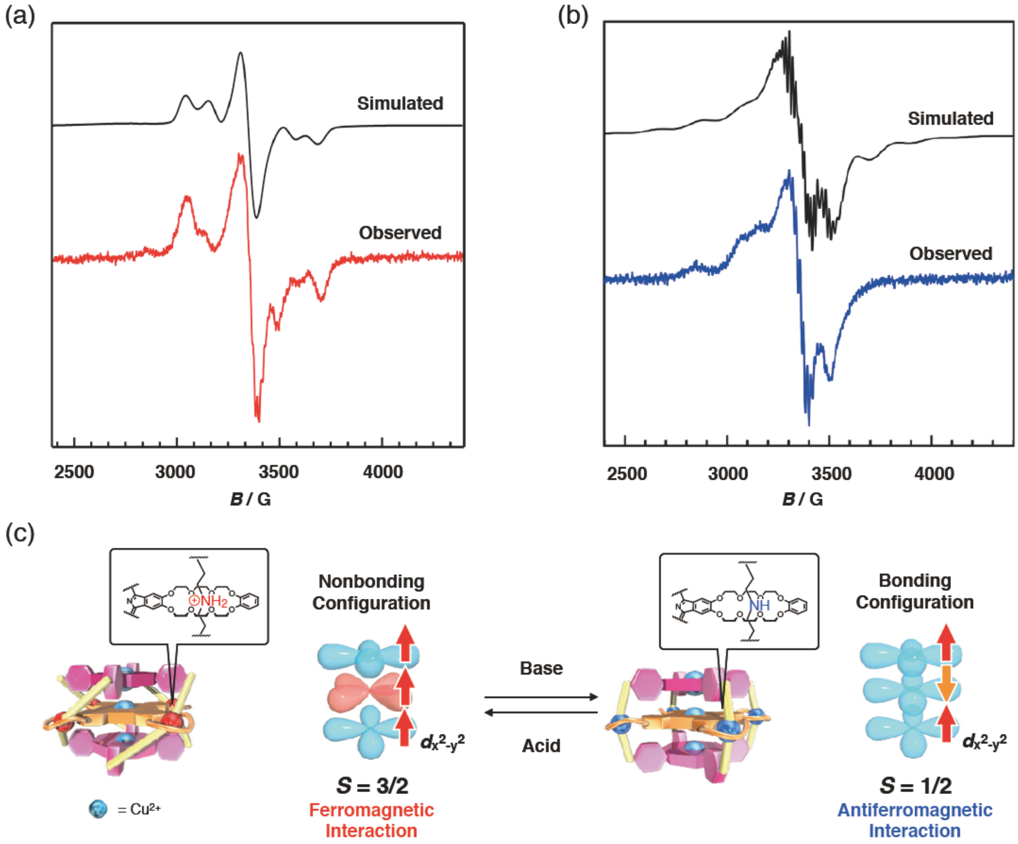

Figure 5. (a) Experimental (red curve) and simulated (black curve) ESR spectra of the trinuclear Cu(II) complex $[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ in the absence of phosphazene base (P1-^{t}Bu) in CH_2Cl_2 at 4 K ($[[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-]$ = 500 μM). (b) Experimental (blue curve) and simulated (black curve) ESR spectra of $[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ in the presence of 8 equiv of phosphazene base (P1-^{t}Bu) in CH_2Cl_2 at 4 K ($[[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-]$ = 500 μM). (c) Schematic representation of the spin–spin interaction of the d_{x2-y2} orbitals inside the multiply interlocked catenane before and after the deprotonation of ammonium ions.

In the multiple catenane, although the phthalocyanine is closely stacked with the porphyrins, the caged structure has a high potential to be a molecular host for functionalized molecular assemblies. The multiple catenane has the structural features of a host for anionic porphyrins, because it has four ammonium moieties and a couple of cages surrounded by a porphyrin, a phthalocyanine, and four alkyl pillars. Planer anionic porphyrins could be captured into the cages by a combination of π–π stacking and electrostatic interactions. Moreover, the most salient feature of the cages is the frontages that are flexibly extensible by the molecular-elevator motion of the phthalocyanine on the alkylammonium rails. Figure 6 shows the photometric titration of the multiple catenane $[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ with 5,15-bis(4-sulfonatophenyl)-10,20-diphenylporphyrin (*trans*-TPPdiS^{2-}) with a large π-planer structure and two anions. *Trans*-TPPdiS^{2-} is slightly larger for sliding into the cage through the window, because the peripheral phenyl rings are orthogonal to the porphyrin plane. However, the addition of an increasing amount of *trans*-TPPdiS^{2-} from 0 to 1 equiv against $[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ (2 μM) caused a spectral change with hyperchromic shifts in the Q-bands of the phthalocyanine unit and the spectra through isosbestic points. Furthermore, subsequent addition of 1 to 2 equiv of *trans*-TPPdiS^{2-} resulted in a different course of spectral change with hypochromic shifts of the Q-bands and the spectra through other isosbestic points. Linear titration curves were obtained in each step as shown in the inset of Figure 6. These results indicate that *trans*-TPPdiS^{2-} was able to slip into the cage and quantitatively complexed with $[Cu_3\mathbf{1}\cdot 4H]^{4+}$ in a stepwise manner to form a stable 1:2 complex even in this highly diluted condition, which indicates two binding events were not cooperative, but the first guest affected the second binding. It is reasonable to consider that the frontages of the cages extended flexibly to adapt the penetration of the guests. Although the guest inclusion process does not need deprotonation from ammonium moieties, the first hyperchromic shifts remind the spectral change in Figure 4(b). It is probably because geometrical correlation of the guest and phthalocyanine is similar with the porphyrin-phthalocyanine interaction in $[Cu_3\mathbf{1}]$. The second hypochromic shifts can be attributed to the tight stacking of the *trans*-TPPdiS^{2-} to the phthalocyanine. These spectral changes provide a description of the stacking interactions affecting the phthalocyanine.

To clarify the intercalation phenomenon of *trans*-TPPdiS^{2-}, the EPR spectrum of the complex was obtained in frozen dichloromethane at 4 K (Figure S17). In sharp contrast to the spectrum in the absence of *trans*-TPPdiS^{2-}, the spectrum of $[Cu_3\mathbf{1}\cdot 4H]^{4+}$:*trans*-TPPdiS^{2-} = 1:2 complex showed a typical doublet (S = 1/2) pattern corresponding to the isolated spins of the Cu^{2+} ions, indicating negligible spin–spin interactions between the three Cu^{2+} spins owing to the accommodation of two *trans*-TPPdiS^{2-} in the two different nanospaces of $[Cu_3\mathbf{1}\cdot 4H]^{4+}$. Thus, we demonstrated the discrete quintuple arraying of porphyrinoids through dynamic molecular incorporation into the flexible and adaptable cages in the

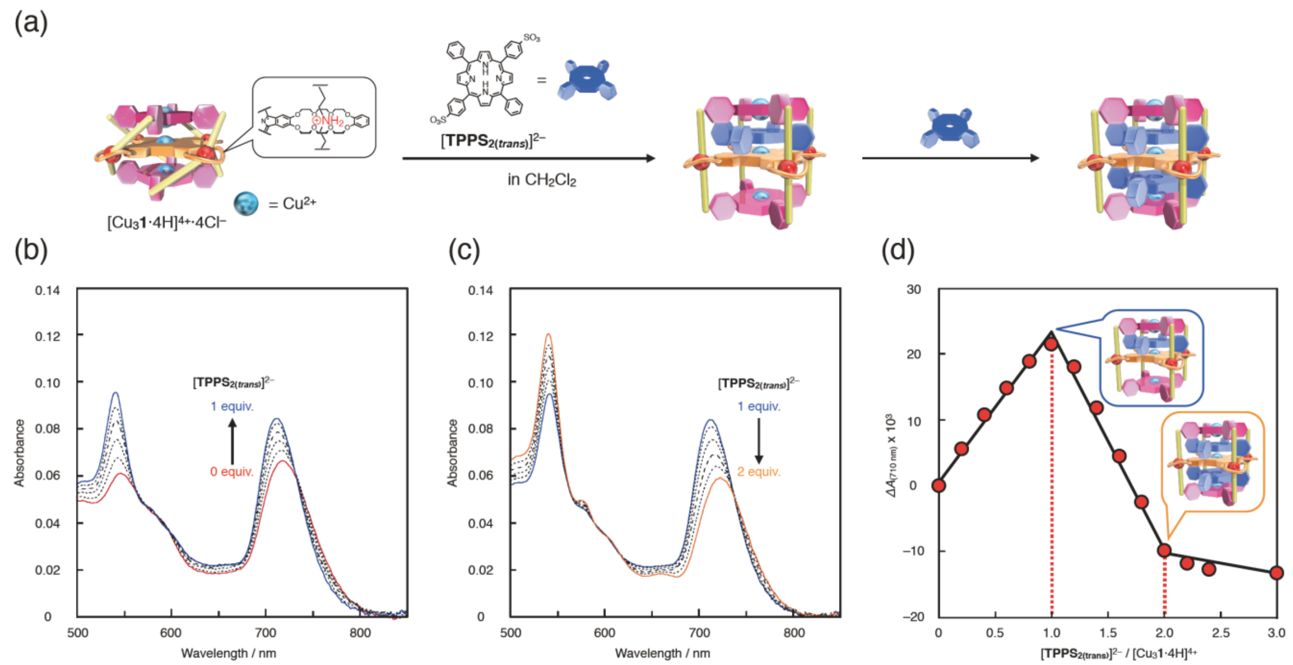

Figure 6. (a) Schematic representation of the complexation of $[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ with two dianionic porphyrins. (b) UV–visible spectral change of the trinuclear Cu(II) complex $[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ (2 μM) during the addition of 0–1 equiv of a dianionic porphyrin *trans*-TPPdiS^{2-}. (c) UV–visible spectral change of the trinuclear Cu(II) complex $[Cu_3\mathbf{1}\cdot 4H]^{4+}\cdot 4Cl^-$ (2 μM) during the addition of 1–2 equiv of a dianionic porphyrin *trans*-TPPdiS^{2-} in CH_2Cl_2 at 293 K. (d) Titration curve monitored by the absorption change at 710 nm.

multiple interlocked catenane and strong interactions among the porphyrinoid components as evidenced from the UV–visible spectra.

In conclusion, we constructed a new molecular topology consisting of multiply interlocked catenanes $[H_6\mathbf{1}\cdot 4H]^{4+}$ and $[Cu_3\mathbf{1}\cdot 4H]^{4+}$, where a phthalocyanine bearing four peripheral crown ethers was entrapped in a quadruply interlocked structure in a pillared conjugate consisting of two porphyrins joined with four alkylammonium chains, affording two symmetrical cages. The linkages composed of crown ethers and alkylammonium chains provide important mechanisms for both the dynamic conformational transition triggered by external stimuli and dynamic molecular invasion using the movable phthalocyanine as an adjustable wall. The former dynamic function resulted in the switching of the spin–spin interaction of the trinuclear Cu(II) complex by inducing rotation in the tacking of the supramolecular conjugate. The latter dynamic invasion phenomenon is based on the electrostatic and π–π interactions via keeping the window open compensated by the positional flexibility of the crown ethers on the alkylammonium chains. Commonly, in molecular inclusion phenomena or molecular recognition processes, flexibility on the molecular size or shape of a host molecule is incompatible with a high affinity of association and accuracy of selectivity. However, the interlock system accommodates the size of a guest molecule without affecting the affinity of the association. This approach could expand the design of molecular host–guest systems.

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Keywords: Catenane, Rotaxane, Molecular Cage, Molecular Inclusion

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COMMUNICATION

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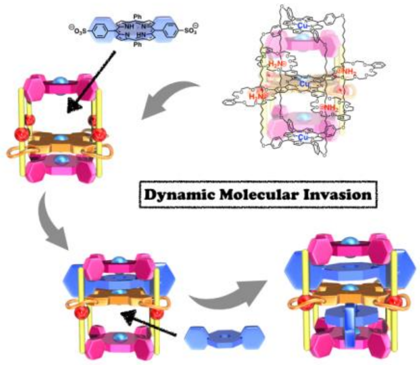

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