Systems Chemistry

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Chemical Signals Turn On Guest Binding through Structural Reconfiguration of Triangular Helicates**

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Biological processes are controlled through highly complex networks of assembling and disassembling functional entities,[1,2] for example, cascades of enzymes.[1] Abiological chemical networks provide a means to study the fundamental phenomena that underpin the functioning of biochemical networks.[3] Understanding these phenomena also enables the design of increasingly intricate synthetic chemical systems with new functions.[4]

Chemical self-assembly has been employed to create architectures with increasingly intricate geometries,[5] with great strides having been made in recent years on the creation of complex three-dimensional architectures.[6] The dynamic nature of the linkages between these assemblies' building blocks opens the possibility of including these structures as parts of self-sorting multi-component systems[7] or exploring functions related to adaptation in response to chemical or physical stimuli.[8] The subcomponent self-assembly method,[9] by which complex architectures are built through simultaneous formation of metal–ligand coordinative and dynamic-covalent imine bonds,[10] enables the creation of structures that are robust, yet capable of dynamic exchange involving both kinds of labile bonds.[11] This technique has afforded a range of discrete metal–organic complexes[12] that can rearrange by taking advantage of enthalpic and entropic driving forces.[13]

Herein we describe a system based on self-assembled Zn^{II} complexes, wherein the expression of function can be controlled by chemical stimuli. The complexes are based on a C_3-symmetric ligand that forms a unique triangular triple helicate structure. This structure, upon addition of a subcomponent, is able to transform into a double helicate structure that selectively encapsulates flat, aromatic guests.

The reaction of subcomponent **A** (3 equiv), 4-methoxyaniline (**B**, 9 equiv), and zinc(II) triflimide ($Zn(NTf_2)_2$,

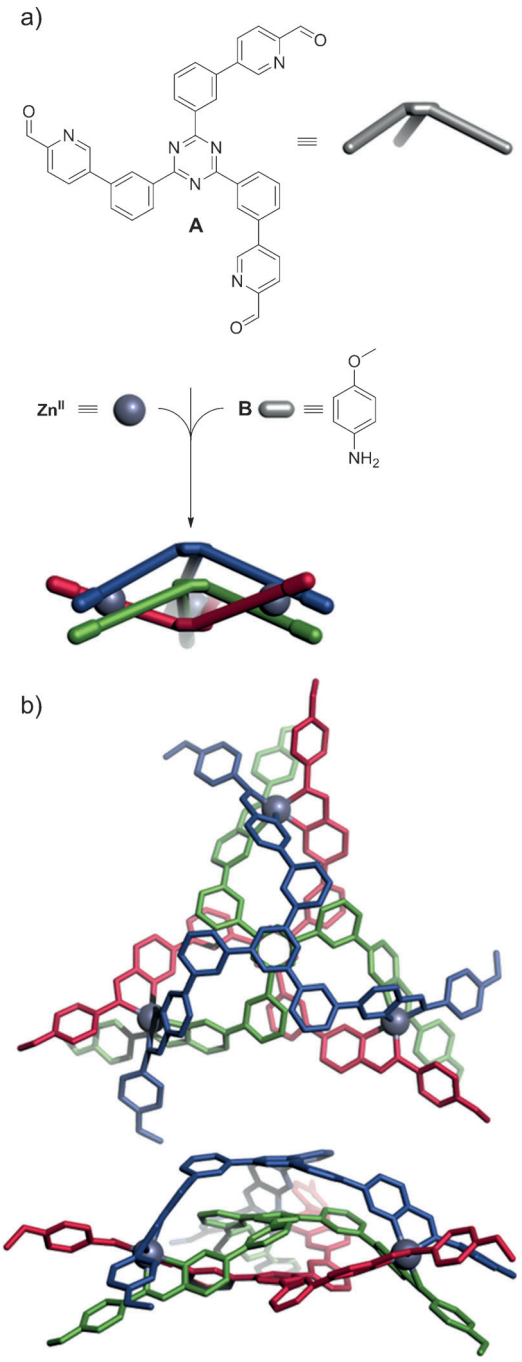

Figure 1. a) Synthesis and schematic representation of triangular triple helicate **1**. Conditions: CH_3CN, 343 K, 16 h, yield 94%. b) Front and side view of the crystal structure of $\mathbf{1}(NTf_2)_6$.[15] For clarity, hydrogen atoms and anions are omitted, and each strand is a different color.

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3 equiv) resulted in the selective formation of triangular triple helicate **1** (Figure 1 a). The ^{1}H NMR spectrum of **1** is complex, with 30 signals in the aromatic region and three signals in the aliphatic region (Supporting Information, Figure S2). This crowded spectrum reflects a non-symmetrical arrangement of the three ligands in the assembly, as a symmetrical disposition would only show 11 signals in total. Two-dimensional NMR spectroscopy allowed the assignment of the peaks to three distinct ligand environments. Diffusion ordered ^{1}H NMR spectroscopy (DOSY) was consistent with the presence of a single species in solution (Figure S3). The $[Zn_3L_3]$ (where L = **A** + 3**B** − 3 H_2O) stoichiometry of the assembly was further confirmed by electrospray ionization mass spectrometry (ESI-MS; Figure S4).

The structure of **1** inferred by ESI-MS and NMR spectroscopy measurements, was further confirmed in the solid-state by single-crystal X-ray analysis (Figure 1 b).[14] The crystal structure revealed a metallosupramolecular $[Zn_3L_3]^{6+}$ triangular triple helicate, which crystallizes with C_3 point symmetry, such that only one-third of it lies in the asymmetric unit and all Zn^{II} centers are crystallographically equivalent. Three facially-coordinated Zn^{II} centers are bridged by three tris-bidentate ligands with Zn–Zn distances of 14.73 Å. Each Zn^{II} center adopts a flattened and distorted octahedral coordination geometry, and all the Zn^{II} stereocenters within one helicate share the same Δ or Λ stereochemistry. Both enantiomers are present in the crystal. Each ligand thus adopts a C_3-symmetric propeller-like helical arrangement within **1**.

The three ligands are stacked on top of each other; the centroid-centroid distances of 3.7 Å between the phenyl rings of two of the adjacent ligands are consistent with π–π stacking, leaving no void space within the structure. Two of the ligands (red and green, Figure 1) wrap around each other in a helical manner while the third ligand (blue, Figure 1) caps the top of the assembly. The central triazine rings of each ligand are vertically stacked on top of each other along the C_3 axis with centroid-centroid separations of 3.4 and 3.6 Å between adjacent ligands. Complex **1** is a new structure type; to our knowledge this is the first time a threefold-symmetric ligand has been used to build a triangular triple helicate.

The asymmetrical conformation of **1** persisted in solution upon heating to 338 K, as indicated by variable temperature NMR spectroscopy (Figure S9). Heating **1** to 363 K for 10 days also did not result in its degradation or transformation into another structure, suggesting considerable thermodynamic stability.

We explored the possibility of intercalating guests into **1**,[16] or of inducing **1** to rearrange into a suitable host through guest addition.[17] However, of the 20 guests examined (Figure S10), none led to an observable change in the ^{1}H NMR spectra, even after heating to 343 K for 15 h.

The conformation adopted by the ligands in **1** inspired the design of the $[Zn_3L'_2]$ (where L′ = **A** + 3**C** − 3 H_2O) triangular double helicate **2**, where the use of two tris-tridentate ligands instead of the three tris-bidentate ligands of **1** was envisaged to enable the inclusion of a planar guest in place of the third ligand in **1**. Host **2** (Figure 2 a) was prepared through the reaction of subcomponent **A** (2 equiv) with quinolin-8-amine (**C**, 6 equiv) and $Zn(NTf_2)_2$ (3 equiv) as confirmed by ESI-MS and NMR measurements (Figures S6–S8). The symmetry of **2** is reflected in its simple ^{1}H NMR spectrum, displaying only one set of ligand resonance signals and two-dimensional NMR spectroscopy allowed the assign-

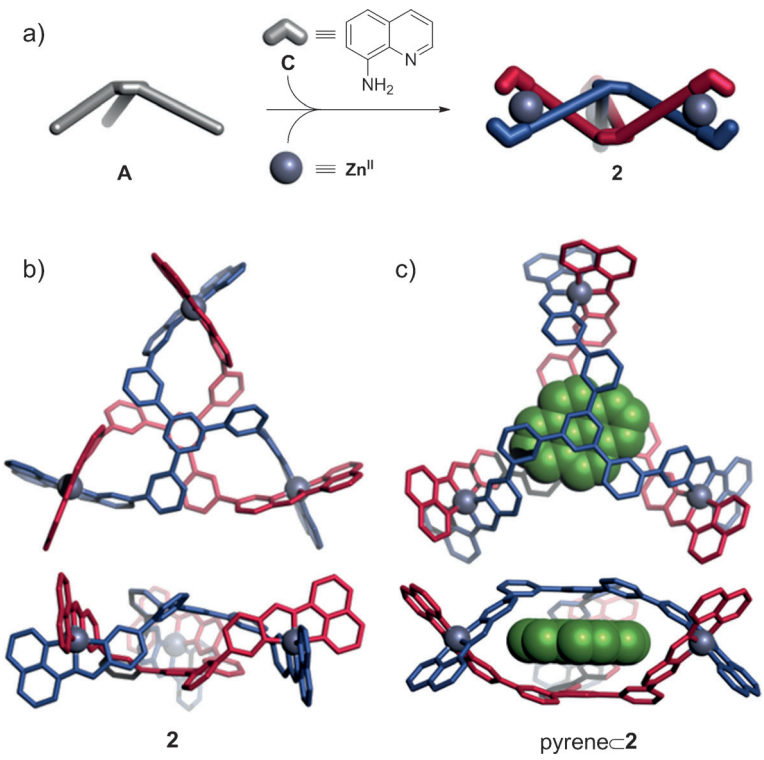

Figure 2. a) Synthesis and schematic representation of triangular double helicate **2**. Conditions: CH_3CN, 343 K, 18 h, yield 95%. b) and c) Front and side view of the MM2-optimized structures of **2** and pyrene⊂**2**. For clarity, hydrogen atoms are not shown, and each strand is a different color.

Table 1: Guests explored for the triangular double helicate **2**.

Guest	Encapsulation[a]
anthracene	yes
pyrene	yes
perylene	yes
coronene	yes
1,3,5-trimethoxybenzene	yes
naphthalene-1,5-diol	yes
2,2′-(((naphthalene-1,5-diylbis(oxy))bis(ethane-2,1-diyl))bis(oxy))diethanol	yes
fluorescein	yes
triphenylene-2,3,6,7,10,11-hexaol	yes
2,4,6-tri(pyridin-2-yl)-*s*-triazine	yes
triptycene	no
C_{60}	no
cyclohexane	no
cyclodecane	no

[a] Monitored by ^{1}H NMR spectroscopy and ESI-MS.

ment of all the signals of triangular double helicate **2**. The presence of only a single species in solution was further confirmed by DOSY NMR spectroscopy (Figure S7).

Figure 2b shows the MM2 optimized structure of helicate **2**. The two ligands are twisted around each other giving rise to a D_3-symmetric structure, consistent with the simple ^{1}H NMR spectrum of **2**.[18]

The distance between the centroids of the two outer triazine rings in the crystal structure of **1** was measured to be 7.0 Å. It was therefore hypothesized that the space between the ligands in **2** could provide a cavity with enough space to accommodate planar aromatic guest molecules.[16] Table 1 lists all of the prospective guest molecules tested. In all cases where host–guest complexation was inferred to occur, shifts in signals of the ^{1}H NMR spectra of both host and guest were observed (Figures S15–S24), consistent with fast guest exchange on the ^{1}H NMR time scale. ESI-MS spectra showed ions corresponding to guest⊂**2** complexes (Figures S33–S39) indicating that the structure of **2** remains intact upon encapsulation of the guest molecules. Conversely, none of the molecules inferred not to bind to **2** (Table 1), were observed to form adducts detectable by ESI-MS or ^{1}H NMR spectroscopy. Both electron-rich and electron-deficient polycyclic aromatic guests were observed to bind to **2**, whereas non-planar (triptycene and C_{60}) and non-aromatic (cyclohexane and cyclodecane) molecules showed no evidence of interaction.

To rule out the possibility of the guests interacting with the exterior of the triangular double helicate **2** by π–π stacking instead of being incorporated within the cavity, we further explored the behavior of the complex pyrene⊂**2**. A Job plot verified the 1:1 binding stoichiometry (Figure S40) and the binding constant was determined to be $1240 \pm 80\,\text{M}^{-1}$ in acetonitrile by means of ^{1}H NMR titration, with data fitting well to a one-to-one binding model (Figure S41). Increasing the polarity of the solvent through addition of methanol did not change the ^{1}H NMR spectrum of pyrene⊂**2** (Figure S42). These results are consistent with the formation of a pyrene⊂**2** inclusion complex; further evidence for 1:1 guest binding is presented in the Supporting Information (sections 3.2 and 4.7).

The structures of the guest⊂**2** complexes were investigated using molecular modeling (Figure S49). As an example, pyrene⊂**2** is shown in Figure 2c. The MM2 optimized structure of pyrene⊂**2** allows us to infer that **2** is indeed able to accommodate aromatic guest molecules such as pyrene. The dynamic nature of the coordinative bonds together with the flexibility of subcomponent **A** enable **2** to adopt a conformation containing a void space able to adapt to accommodate a guest molecule.[16]

Building on prior work on imine exchange,[13,19] we envisaged that double helicate **2** could also be formed by subcomponent substitution, starting from triple helicate **1**. The addition of stoichiometric amounts of quinolin-8-amine (**C**, 9 equiv) and $Zn(NTf_2)_2$ (1.5 equiv) to a solution of **1** in acetonitrile afforded helicate **2**. This transformation is driven by the displacement of 4-methoxyaniline (**B**) for quinolin-8-amine (**C**), in analogous fashion to previously reported transformations, where differences in the electronic and steric properties of various amines, together with the chelate effect, were utilized as driving forces for imine exchange.[13]

Based on this behavior we have built a simple chemical network, where chemical signals trigger a functional response. As shown in Figure 3, the action of chemical stimuli (**C** and Zn^{II}) resulted in the transformation of **1** into **2**, which is able to adapt its cavity in the presence of an aromatic guest to effect guest intercalation. The conversion from **1** into guest⊂**2** (where pyrene was used as a representative guest, Figure 3) can be achieved along three pathways: 1) a direct transformation from triple helicate **1** to guest⊂**2** triggered by the addition of **C**, additional Zn^{II}, and guest at once; 2) a two-step transformation where **2** is formed as the intermediate upon addition of **C** and Zn^{II} to **1**. The subsequent addition of guest, as a second stimulus, brought about encapsulation. Finally, 3) a two-step transformation in which a mixture of **1** and pyrene is considered the first stage. Only after addition of **C** and Zn^{II}, was pyrene encapsulated in a pyrene⊂**2** complex. This third pathway illustrates the chemical orthogonality of the system's processes of imine exchange and guest binding. Each step in the dynamic system was monitored by ^{1}H NMR spectroscopy and inferred to have reached equilibrium after 24 h at 298 K (Figures S51–S53).

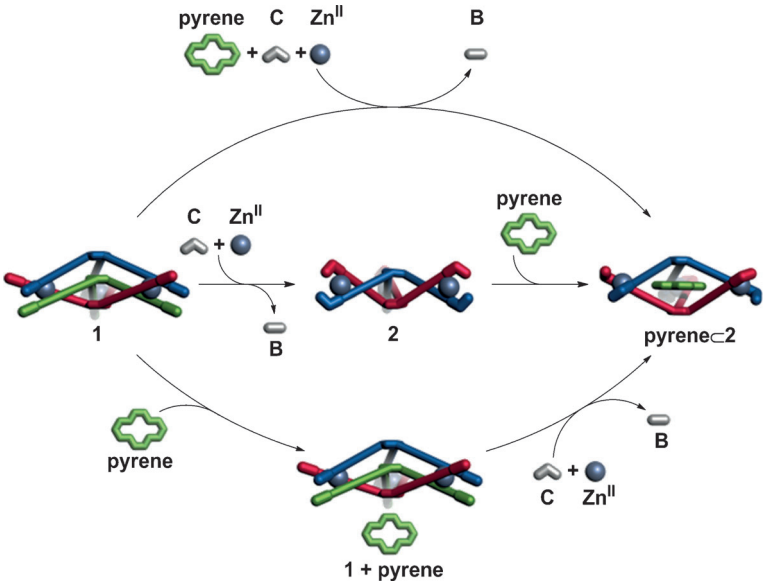

Figure 3. Schematic representation of the dynamic system of transformations linking the triangular triple helicate **1** to the host–guest complex pyrene⊂**2**.

In summary, a triangular triple helicate **1**, representing a new structure type, has been prepared from Zn^{II} and a threefold-symmetric trialdehyde subcomponent. The dynamic nature of the linkages holding **1** together has allowed the creation of a simple system of assembled structures whose

function is controlled by external stimuli. Through subcomponent substitution, triple helicate **1** transformed into double helicate **2**, which has the ability to adapt its conformation in the presence of planar aromatic guest molecules. It was found that **2** forms 1:1 complexes with a range of aromatic guest molecules which have been characterized by ^{1}H NMR spectroscopy and ESI-MS. Current efforts are focused upon the use of such triggered guest binding phenomena as parts of more complex and functional chemical networks, in particular where such transformations might be undertaken reversibly.

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