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Transformative Binding and Release of Gold Guests from a Self-Assembled Cu_8L_4 Tube**

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The highly specific binding, transformation and protection of chemical compounds are functions associated with biomolecular systems' inner phases,[1] pockets of space that are well-isolated from the external environment. A growing number of abiological host molecules have been developed to emulate these functions.[2] Container molecules have been developed that can encapsulate xenon[3] and sulfur hexafluoride[4] with the specificity that hemoglobin and myoglobin exhibit when binding and transporting dioxygen within the body.[5] The ability of enzymes to transform substrates by binding to the transition state of a reaction has inspired the use of container molecules to catalyze reactions[6] and the protection of the highly reactive active sites of nitrogenases[7] from atmospheric oxidation,[8] has been mimicked, allowing sensitive compounds to be stabilized within synthetic hosts.[9]

Whereas nature makes use of narrow tubular channels for purposes ranging from carbon monoxide reduction[10] to ion transport,[11] most synthetic capsules have compact binding cavities.[2a,12] In order to investigate the specific binding and transformation of linear substrates within rigid tubular hosts, we designed and synthesized tetramine subcomponent **A** (Figure 1). Based on modeling studies[13] and our prior experience with copper(I)-templated subcomponent self-assembly,[14] we predicted **A** to have the correct geometry to assemble into a $Cu_8L_4^{8+}$ host with a narrow central channel.

Indeed, **A**, 6-methyl-2-formylpyridine and tetrakis(acetonitrile)copper(I) tetrafluoroborate reacted in the ratios shown in Figure 1 to form the deep red-purple product **1** in acetonitrile. Electrospray ionization mass spectra (ESI-MS) and elemental analysis of **1** were consistent with the formula $[Cu_8L_4](BF_4)_8$, but ^1H and ^{13}C NMR spectra indicated the presence of two distinct product structures.

Vapor diffusion of diethyl ether into an acetonitrile solution of **1** led to the isolation of opaque crystals having two different crystalline aspects. Single-crystal X-ray diffraction experiments revealed that two isomeric structures had crystallized separately, allowing the structures of both to be determined (Figure 2). In both isomers, four self-assembled ligands, each formed from one residue of **A** and four 2-formyl-6-methylpyridine residues, are observed to wrap around eight Cu^I template ions to create tube-like complexes with approximate D_{2d} and D_4 point symmetries, in which the copper(I) ions form an elongated cuboidal structures. The ligands adopt different conformations in these two diastereomers of **1**, as shown in Figure 1. In **1**-D_{2d}, the long faces of the cuboid form isosceles trapezoids, with the shorter faces forming rectangles. The parallel ligands of **1**-D_{2d} thus come together in such a way as to eliminate internal void volume, as shown in Figure 2c and d. In **1**-D_4, the cuboid approximates a right square prism in which one of the square faces is twisted by 40° with respect to the other. This ligand arrangement results in a narrow tubular channel having a radius of ca. 2.1 Å and a volume of 193 Å^3.[15] In the crystal structure two acetonitrile molecules were found encapsulated in this channel (Figure 2a and b).

The **1**-D_{2d} and **1**-D_4 diastereomers in the solid state were also observed in solution by ^1H and ^{13}C NMR spectroscopy. The different symmetries of these isomers led to different NMR peak multiplicities. Kinetic studies (described in the Supporting Information) revealed activation enthalpies and entropies of $148 \pm 5\ kJ\,mol^{-1}$ and $134 \pm 15\ J\,K^{-1}\,mol^{-1}$ respectively for the isomerization from **1**-D_4 to **1**-D_{2d}, and $85 \pm 7\ kJ\,mol^{-1}$ and $-62 \pm 21\ J\,K^{-1}\,mol^{-1}$ for the reverse transformation (from **1**-D_{2d} to **1**-D_4). The rate constants for both transformations were identical at 323 K, marking **1**-D_4 as the dominant species in solution below this temperature, and **1**-D_{2d} above.

As the interior of **1**-D_4 was observed to accommodate two acetonitrile molecules in the crystal, we reasoned that other linear guests[16] might also bind within this host. No new peaks were observed in the ^1H NMR spectrum, however, following the addition to an acetonitrile solution of **1** (1.8 mM) of either: 1) the potassium salts of $Ag(CN)_2^-$, $Cu(CN)_2^-$, CN^-, OCN^-, SCN^-, $SeCN^-$, N_3^-, H_2F^-, or F^- (1 equiv in each case), 2) CuCN, $Ni(CN)_2$, $Hg(CN)_2$, CS_2, 1,4-dichlorobut-2-yne, succinonitrile, butyronitrile, C_6F_6, or but-2-yne (5 equiv), or 3) N_2O, C_2H_4, or C_2H_2, (by bubbling the gas through the acetonitrile solution for 5 min at 25 °C), suggesting that no guest binding occurred.

Despite these other guests' failure to bind, the addition of $KAu(CN)_2$ to an acetonitrile solution of **1** produced a new host–guest complex **2**, as identified by NMR spectroscopy (Figure S40, Supporting Information) and ESI-MS. Mass spectra indicated that the dicyanoaurate adduct of **1** was not a simple 1:1 complex, however, but rather that the guest species was the complex anion $Cu(Au(CN)_2)_2^-$, leading to the formulation of **2** as $[Cu(Au(CN)_2)_2 \subset \mathbf{1}\text{-}D_4]^{7+}$ (Figure 3). The

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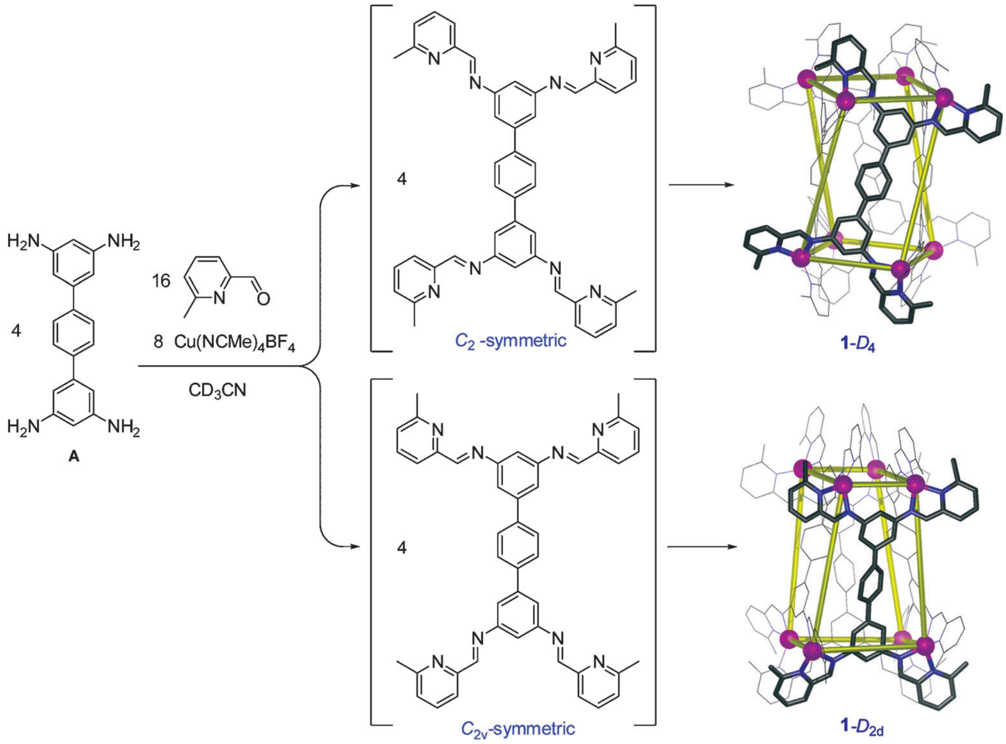

Figure 1. Formation of the two diastereoisomers of Cu_8L_4 complex **1**, **1**-D_4 and **1**-D_{2d}, by subcomponent self-assembly.[17]

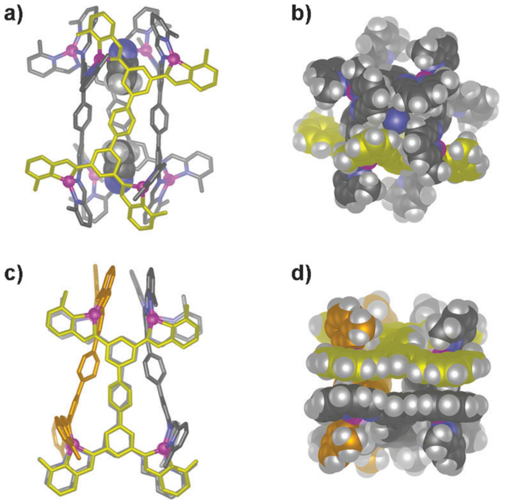

Figure 2. Crystal structures of the two diastereoisomers of **1**. All views omit solvent molecules and anions, and non-space-filling views omit hydrogen atoms, for clarity. a, b) **1**-D_4, with one ligand highlighted and the two encapsulated acetonitrile molecules emphasized as space-filling representations: a) side view down the pseudo-C_2 axis; b) space-filling representation of top view down the pseudo-C_4 axis. c, d) **1**-D_{2d} with two ligands of different orientations highlighted in lighter shades: c) view down the pseudo-mirror plane; d) space-filling representation of view down the pseudo-C_2 axis.

presence of bridging cyanides was confirmed by the observation of two C≡N resonances in the infrared spectrum (2144 and 2190 cm^{-1}) at higher wavenumbers than free dicyanoaurate (2142 cm^{-1}).[18]

When a 1:1 stoichiometry of $KAu(CN)_2$:**1** was employed, the Cu^I required to generate the $Cu(Au(CN)_2)_2^-$ guest was obtained through decomposition of a portion of the host molecules present. This partial host consumption was indicated by the appearance of free 6-methyl-2-formylpyridine, which was observed by ^1H NMR in proportion to the amount of **2** produced, together with **2**, **1**-D_4, and **1**-D_{2d} in solution (Figure S22). When host **1**, $KAu(CN)_2$, and $Cu(CH_3CN)_4BF_4$ were mixed in a 1:2:1 ratio, host decomposition was suppressed; analysis of the product of this reaction enabled the calculation of the stability constant of **2** to be $1.21 \times 10^9\,M^{-3}$.

Further evidence for the structure of **2** was provided through its preparation from ^{13}C-labeled $KAu(CN)_2$. In the ^{13}C NMR spectrum (Figure S26), the ^{13}C-labeled guest gave rise to a pair of coupled doublets ($^2J_{C\text{-}C} = 47.6$ Hz), consistent with the two inequivalent carbon environments of the NC-Au-CN-Cu-NC-Au-CN anion observed in solution, whereas free $KAu(^{13}CN)_2$ showed one singlet. The addition of excess $KAu(^{13}CN)_2$ allowed for the observation of both $[Cu(Au(^{13}CN)_2)_2\subset$**1**-$D_4]^{7+}$ and free $KAu(^{13}CN)_2$ simultaneously.

When $KAu(^{13}CN)_2$ and $Cu(CH_3CN)_4BF_4$ were mixed in a molar ratio of 2:1 in CD_3CN or dimethylsulfoxide (DMSO) in the absence of **1** an insoluble precipitate formed and only free dicyanoaurate was observed in solution; no evidence of $Cu(Au(CN)_2)_2^-$ was observed. This observation suggests that the linear binding pocket of **1**-D_4 served as a protective cover for the complex $Cu(Au(CN)_2)_2^-$ anion, suppressing the formation of cyanide-bridged insoluble polymeric and oligomeric species.[18,19] In seeking thermodynamic equilibrium, this host–guest system may thus be observed not only to stabilize an otherwise inaccessible guest,[9] but to generate an optimal guest from amongst the different possibilities latent

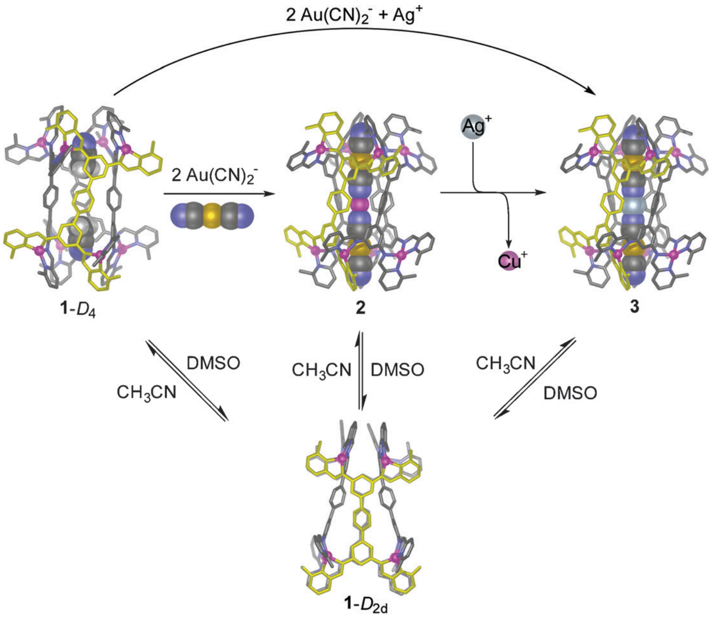

Figure 3. Transformations between host and host–guest complexes.

in the system, although this guest has no observed independent existence.

The system's ability to discriminate between Au(CN)$_2^-$ Ag(CN)$_2^-$ is also remarkable. We hypothesize that Ag(CN)$_2^-$ is not a competent guest for **1** because of the ability of silver(I) to adopt a wide range of coordination geometries, whereas gold(I) complexes tend to adopt a linear 2-coordinate geometry.[20]

Although no evidence of interaction was observed between KAg(CN)$_2$ and **1**, Ag^I was able to take the place of the central Cu^I ion within **2** to generate complex **3**, [Ag(Au(CN)$_2$)$_2$⊂**1**-D_4]. This complex could be prepared under identical conditions to those used to make **2** when AgBF$_4$ was substituted for Cu(CH$_3$CN)$_4$BF$_4$. The titration of AgBF$_4$ into an acetonitrile solution of **2** resulted in the displacement of Cu^I by Ag^I within the guest, allowing the stability constant of $4.2\times10^{10}\,\text{M}^{-3}$ for **3** to be obtained, 34 times greater than that of **2**; the larger Ag^I center appears better stabilized by van der Waals contacts and favorable interactions with the π-electron density[21] of the host framework than the smaller Cu^I. The ^{13}C NMR spectrum of **3** prepared using ^{13}C-labeled dicyanoaurate was consistent with a NC-Au-CN-Ag-NC-Au-CN guest structure, wherein the signals of the carbon atoms closest to silver were further split due to coupling to the NMR-active silver centers (Figures S34 and S35).

The addition of excess KAu(CN)$_2$ to **1** did not result in generation and encapsulation of the Au(Au(CN)$_2$)$_2^-$ guest; only [Cu(Au(CN)$_2$)$_2$⊂**1**-D_4]$^{7+}$ was observed, followed by precipitation of the complex once five equivalents had been added. The use of other Au$^+$ precursors with less strongly bound ligands is under investigation.

When dissolved in DMSO, complexes **1**, **2**, and **3** were observed to transform into **1**-D_{2d}, with disappearance of all **1**-D_4 and its guest complexes, as shown in Figure 3. The complex guests of **2** and **3** were not stable in DMSO solution; dissolution of **2** or **3** prepared with ^{13}C-labeled Au(CN)$_2^-$ in DMSO gave only a simple ^{13}C NMR signal corresponding to free Au(CN)$_2^-$. Evaporation of the DMSO and addition of acetonitrile resulted in the partial regeneration of **1**-D_4 and **2** or **3** along with insoluble material which we infer to be oligomer or polymer generated from Au(CN)$_2^-$.[18,19c] We attribute the instability of the host–guest complexes **2** and **3** in DMSO to the greater ability of this more polar solvent to solvate the separated **1**$^{8+}$ and Au(CN)$_2^-$ ions; less-polar acetonitrile would be expected to favour the ion pairing required for host–guest complex formation. DMSO also appears too large to fit into the cavity of **1**-D_4, thus depriving this diastereomer of the inner-cavity solvation that likely stabilizes it in acetonitrile.

Host **1** thus displays an ability to bind gold with high affinity and remarkable selectively, not through simple encapsulation of Au(CN)$_2^-$, but by transforming this anion into an optimal guest that is not observed in the host's absence. This behavior emerges from the complex interactions of the parts of a system, as it reconstitutes itself for binding during the process of thermodynamic equilibration. This process comprises several distinct chemical events, including 1) the elimination of the D_{2d} isomer of **1**, the cavity of which is too small, 2) the consumption of part of the host, if required, to provide a necessary copper(I) building block for the optimal guest, and 3) the construction of this optimal guest by arranging two dicyanoaurate units around a single linearly coordinated copper(I) or silver(I) ion. This adaptive response to perturbation is much less complex than what is observed in biological systems, but the response nonetheless occurs at a system-wide level and achieves the potentially useful function of tight and selective binding of dicyanoaurate, a substrate of considerable economic value. Given current record gold prices, the ability to specifically bind and release dicyanoaurate, the form in which gold is extracted from ores in modern mines,[22] might allow for economic and environmental benefits to be realized during the extraction and refining of this increasingly useful metal.[23]

CCDC 846044 and 846045 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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