

Self-Assembled Cu-Based Capsule

Synthesis of a Self-Assembled Molecular Capsule that Traps Pyridine Molecules by a Combination of Hydrogen Bonding and Copper(II) Coordination**

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Molecule and molecular assemblies with cavities of different size and shape to encapsulate guest molecules have been synthesized in view of their potential use as selective hosts for anion sensing, catalysis, selective recognition, and separation of guest molecules.^[1] Rebek, Jr. and co-workers recently

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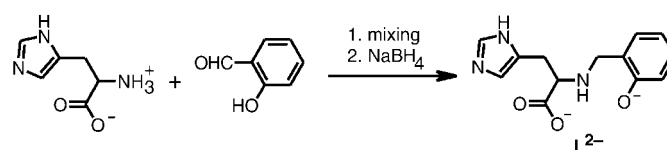
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demonstrated that the binding of a reagent inside a capsular cavity boosts the rate of a Diels–Alder reaction.^[2] The self-assembly of relatively small molecules, through hydrogen bonding, or metal–ligand interactions, proved to be very useful in forming large capsular cavities.^[1] While several capsular cavities have been synthesized by using organic frameworks (e.g. resorcinarene, calixarene),^[1] coordination complexes with a redox stable metal center,^[1] and a few with a redox active metal center,^[3] there is no report of a capsular cavity with the redox-active metal center having an available binding site inside the capsule.^[4] The synthesis of a capsular cavity with an available coordination site at redox active metal centers inside the pocket can, in principle, facilitate the study of the reactivity of the bound guest molecule inside a cavity. In our effort to synthesize a capsular cavity with a redox center, we have synthesized a self-assembled capsule of an octameric Cu^{II} coordination complex by using an easy to synthesize ligand (Scheme 1). This capsule has four guest pyridine molecules trapped inside the cavity (Figure 1), in which two of the pyridine molecules are held with a combination of hydrogen bonds and Cu^{II} coordination.

The octameric Cu^{II} complex (Figure 1) was synthesized from the tetradentate deprotonated ligand (L²⁻, Scheme 1) and the Cu^{II} salt, Cu(ClO₄)₂·6H₂O. Because of the presence of an amine hydrogen atom, an imidazole N–H group (a H-bond donor), and carboxylate oxygen atoms (a H-bond acceptor) in



Scheme 1. Synthesis of the tetradentate ligand, L²⁻.

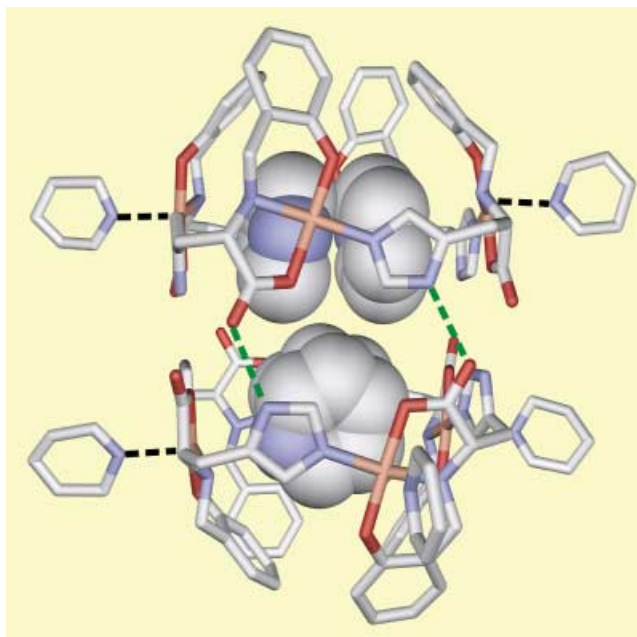


Figure 1. Molecular structure of **1**. Solvent molecules are omitted for clarity.

the ligand, we expected an interligand hydrogen-bonding network to aid in the formation of cages. Crystallization of the complex from pyridine and diethyl ether afforded deep-green crystals of $[\text{Cu}_8\text{L}_8\text{Py}_{10}]\cdot\text{Py}\cdot 3\text{MeOH}\cdot(\text{C}_2\text{H}_5)_2\text{O}$ (**1**; Py = pyridine). The complex **1** was crystallized in the space group of $P1$ (No. 1) with two slightly different cup-shaped tetrameric units in the unit cell (**1a** and **1b**).^[5] The lattice diagram shows that **1a** and **1b** are on top of each other, thus forming a capsule bound through eight hydrogen-bonding interactions between the imidazole NH groups of one tetramer and nonbonded NH groups of the other tetramer (Figure 1).^[6]

The structure of **1a** (Figure 2) is a cyclic tetramer with an imidazole “arm” from one monomeric unit coordinated to the next monomeric unit to form a cycle. The coordination geometry around the Cu^{II} center is square pyramidal with an N_3O_2 -donor environment. The four phenolate rings are organized in a manner that effectively closes one side of the square, thus making a cup shaped bottom. Two pyridine molecules are trapped inside **1a** side by side, with each N atom of the pyridine molecule oriented towards the amine N atom of the ligand. The N(trapped pyridine)–N(amine) separations (N5–N3a 2.990 Å, N6–N3c 3.025 Å) are within the range of 2.68–3.09 Å observed for $\text{N}\cdots\text{HN}$ hydrogen bonds.^[7] The space-filling model demonstrates that the two side-by-side pyridine molecules fill the cavity perfectly (Figure 2b).

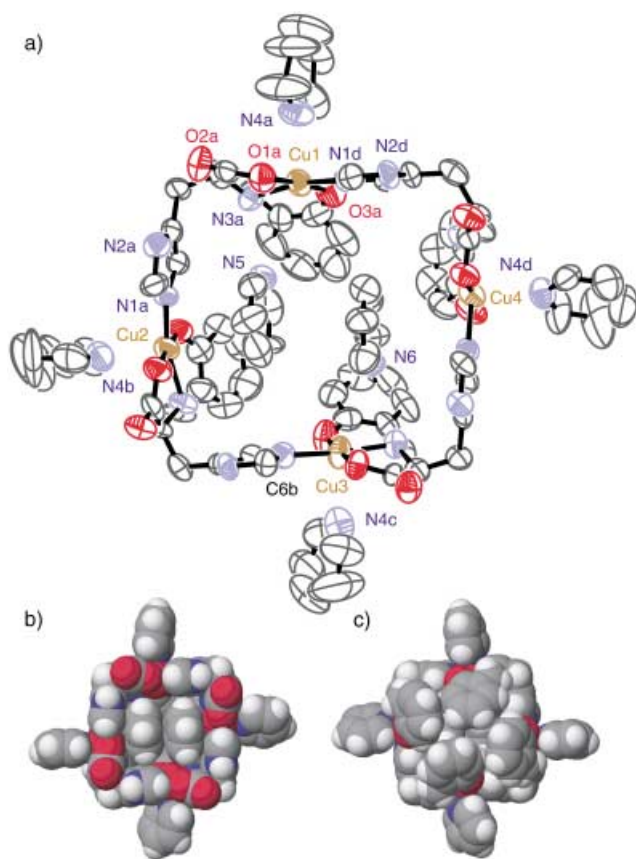


Figure 2. a) One tetrameric copper unit (**1a**, $[\text{Cu}_4\text{L}_4\text{Py}_6]$) ORTEP diagram, thermal ellipsoids set to 50% probability). b) Space-filling model of **1a** top view and c) bottom view.

The cyclic tetramer **1b**, is similar to **1a** (Figure 3), however, two sides of the cup bend inwardly. The trapped pyridine molecules of **1b** are coordinated to the Cu^{II} center instead of being H-bonded to the amine groups (Figure 4). This coordination of the pyridine molecule from inside the

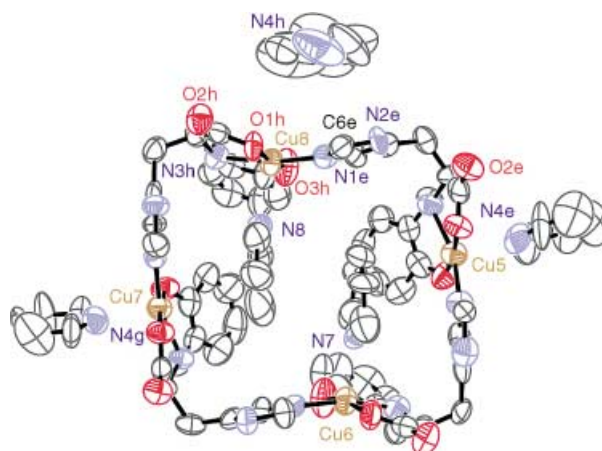


Figure 3. Tetrameric copper unit (**1b**, $[\text{Cu}_4\text{L}_4\text{Py}_4]$) ORTEP diagram, thermal ellipsoids set to 50% probability).

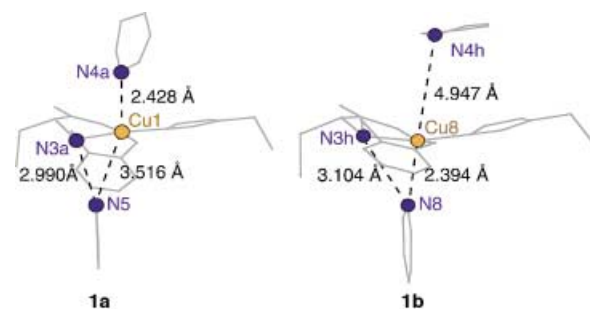


Figure 4. Part of the Cu_4L_4 unit of **1a** and **1b** showing the change in bonding interactions between trapped pyridine molecules, amine N atoms, Cu^{II} centers, and external pyridine molecules.

cavity to the Cu^{II} center results in the deviation of the Cu8 and Cu6 atoms from the plane described by O1, N3, O3, N1 towards the trapped pyridine (shift of 0.194 and 0.203 Å for Cu8 and Cu6, respectively). Consequently, there is no coordination of the external pyridine molecules to the Cu8 and Cu6 atoms, as square-pyramidal geometry is preferred for Cu^{II} complexes over octahedral geometry because of Jahn–Teller distortions. Thus, the coordination sites at the copper centers are accessible from inside the cyclic tetramer.

The two halves of the capsule exhibit contrasting binding with guest molecules. In **1a**, the Cu1 and Cu3 atoms are each coordinated by an external pyridine molecule, but not by the trapped pyridine molecules. On the other hand, in **1b** the N atom of the pyridine molecule (N8) is coordinated to Cu8 (similarly N7 to Cu6). The N8–N3h(amine) separation of 3.104 Å in **1b** is closer to $\text{N}\cdots\text{HN}$ hydrogen bonding range of 2.68–3.09 Å (Figure 4).^[7] Thus, the presence of a N–H close to the Cu^{II} center allow trapped pyridine molecules in **1b** to bind using both metal–ligand interactions and hydrogen bonding,

simultaneously. This factor makes the trapped pyridine molecules less labile compared to the external pyridine molecules as observed in the solution studies (see below). We are not aware of this type of binding in any other reported capsular cavity.

The Cu–N(external pyridine) distances in molecules **1a** and **1b** (2.4–2.5 Å, see Supporting Information) are considerably longer than Cu–N(apical pyridine) bond length of 2.17 Å in [Cu(Cyclops)Py] ClO₄^[8] (Cyclops = difluoro-3,3'-(trimethylenedinitrilo)bis(2-butanoneoximato)borate) and 2.12, 2.13 Å in Cu₂(OAc)₄Py₂^[9] but within the range of 2.6–2.8 Å for apical Cu–N^[10] bond lengths. This makes the externally bound pyridine molecules particularly labile.

The crystals desolvate rapidly and loose crystallinity on isolation. The elemental analysis matches with the formula [Cu₈L₈Py₄(H₂O)₈]. Thermogravimetric analysis (TGA) exhibits a curve that corresponds to a weight loss of 5.3% in the 30–110°C range and a further 11.4% loss in the 180–230°C temperature range, which corresponds to the removal of eight water and four pyridine molecules (expected total of 15.1%). We believe that these pyridine molecules are those that were trapped inside the cavity. The room temperature magnetic moment is less than that expected for a *S* = 1/2 system, which indicates the possible presence of antiferromagnetic coupling between the Cu^{II} centers.

The electrospray ionization mass spectra of **1** in MeOH shows the presence of a Cu₄L₄ unit, but no peak was observed corresponding to the pyridine adduct. This is not surprising as the hydrogen-bonding network holding the two halves of the capsule open up in a protic solvent such as MeOH, and the trapped pyridine molecules axially coordinated to the kinetically labile Cu^{II} center are replaced by solvent molecules. Thus, the Cu₄L₄ units are stable in MeOH. The EPR spectrum of **1** in MeOH at 77 K is typical for a distorted square pyramidal geometry around a Cu^{II} center.^[11]

In conclusion, we have synthesized a new self-assembled capsule by using an easy to synthesize ligand, and a Cu^{II} salt. The capsule has enough space inside to accommodate four pyridine molecules. The capsule has both H-bonds and kinetically labile Cu^{II} centers which are available for binding from inside the cavity. Thus, we have observed a novel guest binding inside the cavity that uses both hydrogen bonds and metal coordination at the same time.

Experimental Section

Elemental analysis calcd (%) for **1** Cu₈(C₁₃H₁₃N₃O₃)₈·(C₅H₅N)₄·8H₂O: C 48.94, H 4.64, N 12.88; found: C 48.68, H 4.51, N 12.92. IR (KBr, $\tilde{\nu}$): 1615(sh), 1596(s) cm⁻¹ $\tilde{\nu}$ (COO)_{asym}; 1388(s) cm⁻¹ $\tilde{\nu}$ (COO)_{sym}. *A*_M: (MeOH) 2 S cm⁻² mol⁻¹. ESI-MS(+) in MeOH for {[Cu₄(L)₄] + H}⁺; *m/z* calculated 1291.1, found 1290.8; UV/Vis: λ_{\max} [nm] (ϵ [M⁻¹ cm⁻¹]/Cu: in pyridine: 416 (520), 668 (170); in MeOH: 273 (5700), 382 (920), 686 (150). EPR: powder; 300 K 2.116 (isotropic), 77 K, 2.118 (isotropic); MeOH, 77 K, *g*_{||} = 2.253, *g*_⊥ = 2.060, *A*_{||} = 175 G. μ_{eff} (powder, 298 K); 1.63 μ_{B} /Cu.

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Keywords: amino acids · cavitand · copper · hydrogen bonds · self-assembly

- [1] Selected review articles on supramolecular cages and capsules: a) P. J. Stang, B. Olenyuk, *Acc. Chem. Res.* **1997**, *30*, 502; b) J. Rebek, Jr., *Acc. Chem. Res.* **1999**, *32*, 278; c) A. Jasat, J. C. Sherman, *Chem. Rev.* **1999**, *99*, 931; d) S. R. Seidel, P. J. Stang, *Acc. Chem. Res.* **2002**, *35*, 972; e) F. Hof, S. L. Craig, C. Nuckolls, J. Rebek, Jr., *Angew. Chem.* **2002**, *114*, 1556; *Angew. Chem. Int. Ed.* **2002**, *41*, 1489; f) M. Fujita, *Chem. Soc. Rev.* **1998**, *27*, 417; g) M. Fujita, K. Umamoto, M. Yoshizawa, N. Fujita, T. Kusukawa, K. Biradha, *Chem. Commun.* **2001**, 509.
- [2] a) J. Kang, G. Hilmersson, J. Santamaria, J. Rebek, Jr., *J. Am. Chem. Soc.* **1998**, *120*, 3650; b) J. Kang, J. Santamaria, G. Hilmersson, J. Rebek, Jr., *J. Am. Chem. Soc.* **1998**, *120*, 7389.
- [3] a) O. D. Fox, N. K. Dalley, R. G. Harrison, *J. Am. Chem. Soc.* **1998**, *120*, 7111; b) O. D. Fox, N. K. Dalley, R. G. Harrison, *Inorg. Chem.* **1999**, *38*, 5860; c) O. D. Fox, N. K. Dalley, R. G. Harrison, *Inorg. Chem.* **2000**, *39*, 620; d) O. D. Fox, J. F. Y. Leung, J. M. Hunter, N. K. Dalley, R. G. Harrison, *Inorg. Chem.* **2000**, *39*, 783.
- [4] There are few macrocyclic coordination complexes with available metal coordination sites inside the macrocycle. Cu^{II}; A. W. Maverick, F. E. Klavetter, *Inorg. Chem.* **1984**, *23*, 4129. Co^{II}; A. W. Schwabacher, J. Lee, H. Lei, *J. Am. Chem. Soc.* **1992**, *114*, 7597. With redox inactive Zn^{II}, review; “Templating, Self-assembly, and Self-organization”: M. Fujita in *Comprehensive Supramolecular Chemistry*, Vol. 9 (Eds.: J.-P. Sauvage, M. W. Hosseini), Pergamon, Oxford, **1996**, chap. 7.
- [5] The crystal was mounted with mother liquor inside the capillary for data collection. Crystal structure analysis of **1**: C₁₆₆H₁₈₁Cu₈N₃₅O₂₈, *M*_r = 3622.8, deep-green crystal 0.3 × 0.3 × 0.2 mm³, triclinic *P*1 (No. 1), *a* = 16.845(4), *b* = 18.268(4), *c* = 20.167(4) Å; α = 92.507(4), β = 112.207(4), γ = 105.636(4)°; *V* = 5459(2) Å³, *Z* = 1, ρ_{calcd} = 1.102 Mg m⁻³, MoK α radiation, λ = 0.71073 Å, measured reflections 60205, unique reflections 44425, temperature 293(2) K. Data were collected on a Bruker Smart CCD Area Detector system with graphite monochromator. The structure was solved by direct methods and refined on *F*² by full-matrix-block least squares (G. M. Sheldrick, SHELXL-97, University of Göttingen, Göttingen (Germany), **1997**). In refinement, data/restraints/parameters are 44425/3/2046. The final *R*1 = 0.0868, *wR*2 = 0.2164 (*I* > 2 σ (*I*)); *R*1 = 0.2725, *wR*2 = 0.2890 (all data), GOF on *F*² = 0.730. CCDC-197602 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB21EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).
- [6] The (imidazole) N–H⋯O(carboxylate) separations in **1** are between 2.69 and 2.78 Å. Reported range 2.69–2.98 Å: a) S. M. Couchman, J. C. Jeffery, M. D. Ward, *Polyhedron* **1999**, *18*, 2633; b) K. Sakai, K. Matsumoto, *J. Am. Chem. Soc.* **1989**, *111*, 3074.
- [7] a) M. B. Ferrari, G. G. Fava, M. Lanfranchi, C. Pelizzi, P. Tarasconi, *J. Chem. Soc. Dalton Trans.* **1991**, 1951; b) R. Anulewicz, I. Wawer, T. M. Krygowski, F. Männle, H. Limbach, *J. Am. Chem. Soc.* **1997**, *119*, 12223.
- [8] O. P. Anderson, A. B. Packard, *Inorg. Chem.* **1980**, *19*, 2123.
- [9] G. A. Barclay, C. H. L. Kennard, *J. Chem. Soc.* **1961**, 5244.
- [10] “Tables of Interatomic Distances and Configuration in Molecules and Ions,” *Chem. Soc. Special Publ.* No.11.
- [11] U. Sakaguchi, A. W. Addison, *J. Chem. Soc. Dalton Trans.* **1979**, 600.