Supramolecular Structures

The Hydrophobic Effect as a Driving Force in the Self-Assembly of a [2 × 2] Copper(I) Grid**

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Dedicated to Professor Jean-Marie Lehn
on the occasion of his 65th birthday

Grid-type coordination arrays, which consist of a regular array of metal ions sandwiched between two perpendicular sets of parallel ligand molecules, have been shown a great deal of interest in recent years.[1–6] The regular spacing of metal ions and ligands results in a variety of interesting magnetic behaviors,[6–9] and also evokes the possibility of using these complexes as molecular computing elements (quantum-dot cellular automata).[10]

We report herein the preparation of a [2 × 2] copper(I) grid that possesses two novel features. Firstly, the geometry of this grid structure is atypical, not being readily predictable from

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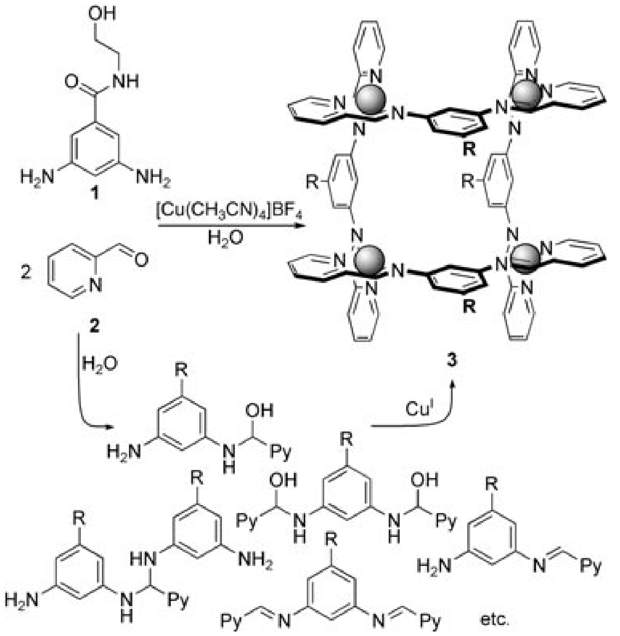
the "self-assembly instructions" encoded within the components.[11] The ligands of grids generally cross at perpendicular junctions,[6] which they cannot do in the present structure without distortion. Evidence of this distortion was noted in the crystal structure. Secondly, the self-assembly[4,5,12,13] reaction by which this grid was synthesized took place quantitatively in aqueous solution, but was not observed to occur at all in other solvents. This observation suggests that the hydrophobic effect[14] might play an essential role in directing the self-assembly process.

The mixture of diaminobenzamide **1** (0.024 mmol) with pyridinecarboxaldehyde **2** (0.049 mmol) in D_2O (0.7 mL) under an argon atmosphere gave a complex mixture of products, as observed by NMR spectroscopy. Within five minutes of addition, approximately 30% of **1** and **2** initially present had reacted; possible product structures are shown in Scheme 1. These products were not definitively characterized. However, signals corresponding to at least five distinct aminal and imine products were noted in the ^{1}H NMR spectrum. These products are capable of interconversion by carbon–nitrogen bond exchange, and thus comprise a dynamic combinatorial library.[15,16] Since diamine **1** may link two molecules of **2**, and **2** may conversely bridge two molecules of **1** in its aminal form,[16] this library could contain a limitless variety of oligomeric and cyclic structures. Our attempts to follow its evolution were hampered by the precipitation of a yellow film over the course of several hours.

The addition of $[Cu(CH_3CN)_4]BF_4$ (0.024 mmol) rapidly brought order to this complex mixture: the presence of Cu^I ions induced the formation of grid structure **3** (Scheme 1) as the unique product, thus templating[17] the formation of the corresponding bisimine ligand from the dynamic library with perfect selectivity. NOESY NMR spectra indicated that the ligand conformation was as shown in structure **3**, and electrospray mass spectra demonstrated it to be tetrameric.

X-ray crystallographic analysis confirmed the presence of this tetrameric structure in the solid state (Figure 1).[18] The complex shows a highly symmetric arrangement around a $\bar{4}$ (S_4) crystallographic axis despite the presence of the flexible hydroxyethyl substituents, which are ordered by hydrogen bonds between neighboring ligands (Figure 1, right). Although they reinforce the grid structure, these hydrogen bonds are not necessary for its formation: 3,5-diaminobenzamide also generated a grid in water when used in place of **1**, despite the fact that it is incapable of forming interligand bonds within a grid-type structure.



Scheme 1. Dynamic combinatorial library generated from an aqueous solution of diamine **1** and aldehyde **2**, and the collapse of this library into grid **3** on addition of $[Cu(CH_3CN)_4]BF_4$. Py = 2-pyridyl, R = 2-hydroxyethylcarbamoyl. Shaded spheres represent Cu^I ions.

Figure 2 shows the coordinate vectors[19] of the ligands present in **3**, which converge at an angle of approximately 60° in an idealized ligand geometry. The coordinate vectors of other ligands in grid complexes lie naturally parallel[1,9] or

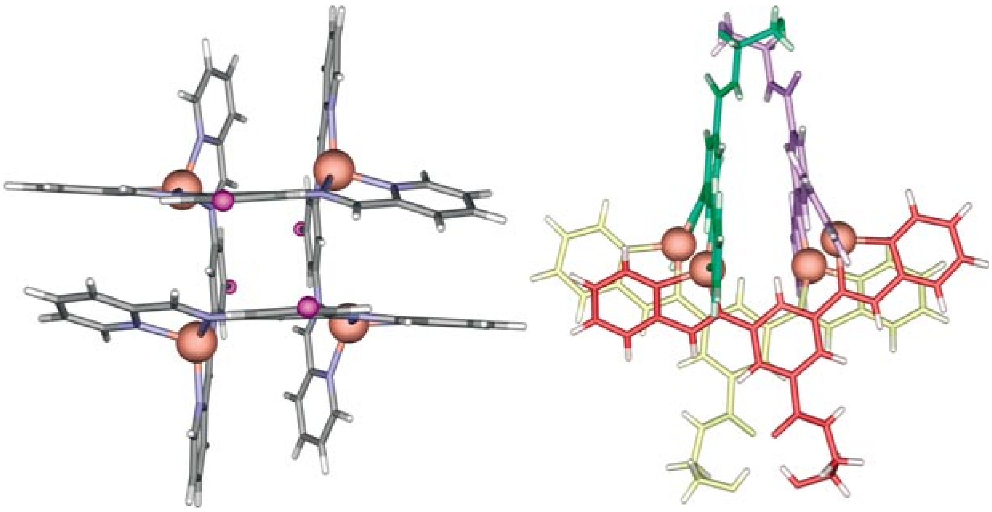


Figure 1. Views of the X-ray crystal structure of **3**. The 2-hydroxyethylcarbamoyl ($-CONHCH_2CH_2OH$) groups have been replaced by purple spheres in the right view for clarity. Each symmetry-equivalent ligand is shown in a different color in the view on the right.

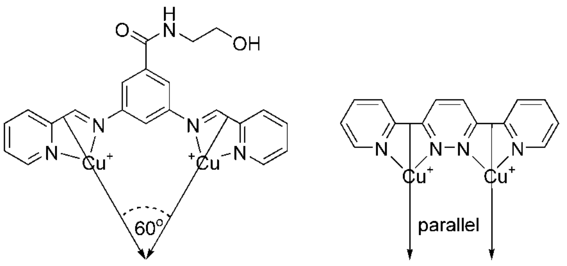


Figure 2. The coordinate vectors[19] of the ligand present in **3** and of the prototypical grid ligand reported by Youinou et al.[1]

diverge slightly.[3,8] Since the geometry of the grid enforces a parallel arrangement of the ligands, distortion must occur. This distortion is exhibited as: 1) a coordination environment around copper intermediate between tetrahedral (preferred by Cu^I ions) and see-saw (as can be seen in Figure 1, right), 2) an opening of the C_{imine}-N_{imine}-C_{phenyl} angle from an ideal 120° to 127.7°, and 3) a bending (ca. 20°) from planarity of one pyridylimino group on each ligand, thus pushing the copper ions out from the square junctions formed by the ligands (Figure 1, left). These deformations imply the presence of strain, an unusual feature for a quantitatively formed self-assembled structure.

The inference of this strain was supported by the observation that **3** did not appear to be stable in solvents other than water. The formation of **3** was not observed on mixing the precursors of **3** in acetic acid, acetonitrile, acetone, benzene, chloroform, dimethyl formamide, dimethyl sulfoxide, diethyl ether, ethanol, methanol, nitromethane, pyridine, or tetrahydrofuran. When presynthesized **3** was suspended in any of the aforementioned solvents, either it did not dissolve or decomposition was observed. Thus, despite the fact that neither Cu^I ions nor imines are commonly considered to be stable in water, we were able to detect this Cu^I-linked imine complex *uniquely* in that solvent. Our previously described[5,13] aqueous systems were stable in other solvents, and the successes of other research groups with the techniques of ligand-component self-assembly were obtained in nonaqueous solvents.[4,12]

This solvent-dependent stability is likely to be a result of two factors. Firstly, water is a poor ligand for Cu^I ions. The compact donor orbitals of H_2O overlap poorly with the diffuse acceptor orbitals of copper(I) ions, which leads to the latter's tendency to disproportionate in aqueous solution. Imine donors, in contrast, are good ligands for Cu^I ions, so much so that this metal will template their formation in water from amines and aldehydes.[13] The disassembly of complex **3** would be facilitated by a solvent that bound strongly to Cu^I ions, and is conversely hindered by the presence of a solvent which does not, thus stabilizing **3** in water. Secondly, non-aqueous solvents would be better able to solvate exposed ligand surfaces, and thus would not force the mixture of species derived from **1**, **2**, and Cu^I ions to collapse into the compact structure of **3**. This structure maximizes the favorable van der Waals interactions, including stacking interactions,[20] between the ligands while minimizing the unfavorable ligand–solvent interactions.

This structure is thus held together through the cooperative interplay of three distinct self-assembly processes: the formation of strong, covalent $C{=}N$ bonds, as well as weaker, dative N–Cu bonds, and finally the diffuse yet necessary "compression" applied by the hydrophobic effect.[14] The use of the hydrophobic effect as it applies to both metals and ligands represents a new means of control within the field of metallo-organic self-assembly, thus complimenting its use in other contexts.[21] We are continuing to investigate the ways in which an aqueous reaction medium may allow for the construction of new kinds of assemblies, as well as the novel properties that might be engendered by the presence of strain.

Experimental Section

3: Compound **1** (0.0277 g, 0.14 mmol), **2** (0.0303 g, 0.28 mmol), and water (5 mL) were added to a 50-mL Schlenk flask. The flask was then sealed, and the atmosphere was purified of dioxygen by three evacuation/argon-fill cycles. When the solution was homogeneous, $[Cu(CH_3CN)_4]BF_4$ (0.0446 g, 0.14 mmol) was added, which immediately dissolved to give a violet-black solution. The atmosphere was once more purified of dioxygen by three evacuation/argon-fill cycles, and the reaction was kept at room temperature overnight without stirring. Volatiles were then removed under dynamic vacuum to give **3** in a yield of 0.073 g (99 %) as a violet crystalline product, which was pure by NMR spectroscopic analysis. Following the above procedure and starting with a copper concentration of 2.45×10^{-2} M, X-ray quality single crystals (which were also used for the elemental analysis) of **3** were isolated when the solvent was decanted instead of evaporated. ^{1}H NMR (500 MHz, 300 K, D_2O, referenced to 2-methyl-2-propanol at 1.24 ppm as the internal standard): $\delta = 9.24$ (s, 8H, imine), 8.22 (d, $J = 1.7$ Hz, 8H, 2,6-phenylamide), 7.94 (d, $J = 7.7$ Hz, 8H, 3-pyridyl), 7.84 (m, 12H, 4-pyridyl, 4-phenylamide), 7.77 (d, $J = 5$ Hz, 8H, 6-pyridyl), 7.26 (dt, $J = 5.5$ Hz, J = 1.1 Hz, 8H, 5-py), 3.95 (t, $J = 5.5$ Hz, 8H, hydroxyethylcarbamoyl), 3.74 (t, $J = 5.5$ Hz, 8H, hydroxyethylcarbamoyl); ^{13}C NMR (125.77 MHz, 300 K, D_2O, referenced to the methyl groups of 2-methyl-2-propanol at 30.29 ppm as internal standard): $\delta = 168.1$, 160.3, 149.9, 149.0, 147.6, 139.7, 137.6, 129.7, 129.6, 129.4, 118.6, 59.7, 43.1; ESI-MS: $m/z = 436.3$ $[CuL]^+$, 961.2 $[Cu_2L_2{+}BF_4]^+$, 1484.1 $[Cu_3L_3{+}2\,BF_4]^+$, 2009.9 $[Cu_4L_4{+}3\,BF_4]^+$; elemental analysis calcd for $C_{84}H_{76}N_{20}O_8Cu_4B_4F_{16}\cdot H_2O\cdot CH_3CN$: C 47.95, H 3.79, N 13.65; found: C 47.93, H 4.10, N 13.73.

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[18] Crystallographic data for **3**: $[\mathrm{Cu}(\mathrm{C_{21}H_{19}N_5O_2})]_4(\mathrm{BF_4})_4\cdot 2\mathrm{H_2O}\cdot\mathrm{CH_3CN}$; prism $0.18\times0.18\times0.23$ mm; tetragonal, $I4_1/a$ (no. 88); $M_r=2172.3$; $Z=4$; $a=14.6561(3)$, $c=43.9683(14)$ Å, $V=9444.4(5)$ Å^3; $\rho_{\mathrm{calcd}}=1.528\ \mathrm{g\,cm^{-3}}$; $2\theta_{\max}=52.0°$; $\mathrm{Mo_{K\alpha}}$ radiation ($\lambda=0.71073$ Å); ϕ scans of 0.5°; 37767 reflections measured at 200 K, 4601 unique reflections of which 2653 were observables ($|F_o|>4\sigma(F_o)$); $4.4<2\theta<52.0°$. Data were corrected for Lorentz and polarization effects and for absorption ($T_{\min}$, $T_{\max}=0.8230$, 0.8523). The structure was solved by direct methods (SIR97).[22] All calculations were performed with the XTAL system.[23] Full-matrix least-squares refinement based on F using weights of $1/(\sigma^2(F_o)+0.00015(F_o^2))$ gave final values $R=0.036$, $\omega R=0.037$, and $S=1.73(2)$ for 391 variables and 2914 contributing reflections. The maximum Δ/σ on the last cycle was 0.004. Min./max. residual electron density corresponded to $0.76/-0.46\ \mathrm{e^-\,Å^{-3}}$. Hydrogen atoms of the complex were placed in calculated positions except OH and NH groups, for which hydrogen atoms were observed and refined with restraints on bond lengths. CCDC-242577 (**3**) 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).

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