ORGANIC LETTERS

2011
Vol. 13, No. 15
3916–3919

Scaffolding a Cage-Like 3D Framework by Coordination and Constitutional Dynamic Chemistry

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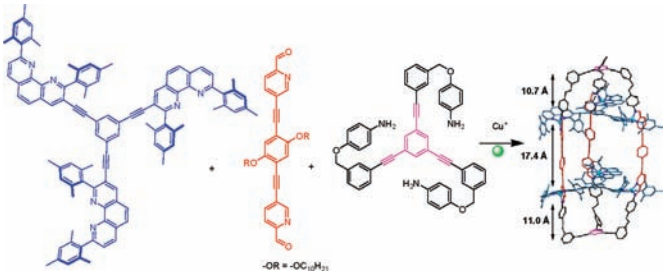
Received May 27, 2011

ABSTRACT



By exploiting the supramolecular assistance of a sterically encumbered phenanthroline-Cu^{+} motif, we report on the self-assembly of a trigonal nanoprism, its post-self-assembly functionalization, and transformation into a cage-like 3D framework with distinct compartments.

Self-assembled cages and capsules have received huge attention over the past two decades because of their well-defined nanocavities, capable of performing fascinating functions, such as the highly selective encapsulation of guest species,[1] modulation of guest reactivity,[2] catalysis,[3] etc. Obviously, their full utility depends on the size and nature of the cavity, but equally on features of the self-assembly protocol. Small manipulations in building blocks may alter the state of assembly, thereby offering different properties.[4] For practical matters, the majority of all known cages and capsules are formed via the dimerization of concave self-complementary building blocks.[5] Hence, new developments toward structurally multifarious cages may offer additional venues to useful functions.[6] Herein, we describe the post-self-assembly functionalization of a trigonal nanoprism and its transformation into a new class of cage-like 3D frameworks with three compartments via constitutionally dynamic imine bond formation. In order to perfect the methodology, full orthogonality of various processes,[7] such as heteroleptic complex formation along the HETPHEN concept,[8] "proof read for errors" via reversible imine bond formation, and dynamic nanoaggregate formation, need to be amalgamated in a one-pot

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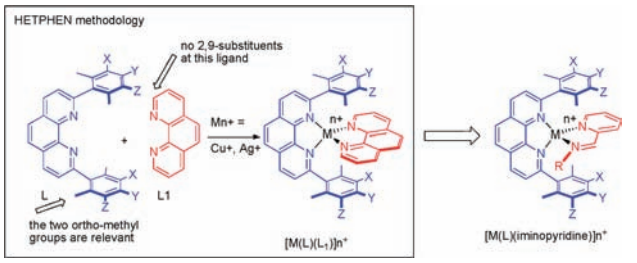
10.1021/ol201440a
Published on Web 06/28/2011

process. To the best of our knowledge, the framework constitutes the first example of a 3D metal-coordination driven cage with three compartments.

Scheme 1. Illustration of the HETPHEN Concept[8] and Its Extention to Heteroleptic Complexes Involving the Iminopyridine Ligand

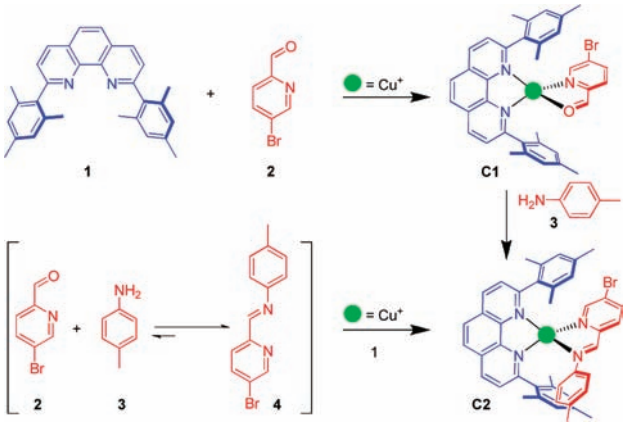


Over years, heteroleptic copper(I) bisphenanthroline complexes have been prepared in our group using the HETPHEN concept (Scheme 1). As a result of a finely tuned balance of steric and electronic effects, emerging from the two bulky diaryl substituents of phenanthroline **L**, the thermodynamically controlled, exclusive formation of the heteroleptic complex is warranted despite the fact that it is kinetically labile. The latter property has been essential for the use of this complex motif in the construction of a wide number of dynamic supramolecular structures.[9]

The charm of using imine bond formation at metal ions lies in the fact that it involves the coupled formation of a covalent C=N and a new coordinative (nitrogen−metal) bond, establishing both the new ligand and complex at the same time.[10] As a consequence, the metal ion directed and templated synthesis of imine bonds has been employed in the creation of a good number of complex structures, such as macrocycles,[7a,11] helicates,[12] cages,[13] rotaxanes,[14] catenanes,[15] grids,[16] and Borromean links.[17] Extending the homoleptic $[M(iminopyridine)_m]^{n+}$ motif to constitutionally dynamic heteroleptic $[M(\mathbf{L})(iminopyridine)]^{n+}$ complexes (Scheme 1) should even further increase our options for highly intricate and diverse structures.[18]

For a start, we envisaged that already a precursor to the iminopyridine such as 5-bromo-pyridine-2-carbaldehyde (**2**) may combine with 2,9-dimesityl[1,10]phenanthroline (**1**) and Cu^+ to the heteroleptic copper(I) complex **C1** (Scheme 2). Indeed, quantitative formation of **C1** was immediately observed upon addition of **2** to a solution of **1** and $[Cu(CH_3CN)_4]PF_6$ in CD_2Cl_2 as evidenced from spectroscopic data (see Supporting Information). As a result of the complexation of **2** to Cu^+, the aldehyde functionality should become even more susceptible toward nucleophilic reagents, such as amines. Indeed, addition of *p*-toluidine (**3**) to a solution of **C1** (Scheme 2) led to quantitative formation of the iminopyridine ligand **4** at the Cu^+ center, thereby furnishing the heteroletic complex **C2**, as confirmed by spectroscopic evidence (see Supporting Information).

Scheme 2. Synthesis of Heteroleptic Complexes **C1** and **C2**



To gain additional mechanistic insight into the formation of the iminopyridine ligand at the phenanthroline-Cu^+ center, some model experiments were carried out. In a first set of experiments, both **2** and **3** were taken in a 1:1 ratio in an NMR tube and dissolved in CD_2Cl_2. The ^1H NMR of the resulting solution showed that **4** emerged in a typical equilibrium with both starting materials, **2** and **3**, (**4**:**2**:**3** ≈ 1:0.1:0.1; based on integration in the ^1H NMR) remaining constant over 3 days after mixing (see Supporting Information). Upon addition of 1 equiv of $[Cu(CH_3CN)_4]PF_6$ and **1** each, a red solution formed instantaneously. A ^1H NMR measurement confirmed the clean formation of **C2** (Scheme 2). Thus, the metal ion, acting as both catalyst and binding "glue" to the emergent ligand, drives the formation of **4** to completion.

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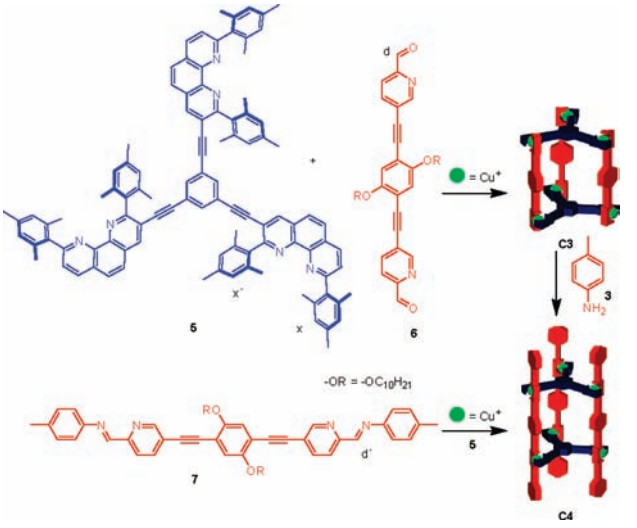
In principle, any HETPHEN phenanthroline loaded with a coordinatively unsaturated metal ion will assist in the fabrication of iminopyridine ligand(s). Therefore, we installed three shielded phenanthroline units as in ligand **5**. Two pyridine-2-carbaldehyde units were set up in **6**. The latter was readily accessible via a Sonogashira cross-coupling reaction between 5-ethynyl-pyridine-2-carbaldehyde and 1,4-bis(decyloxy)-2,5-diiodobenzene (see Supporting Information). The alkoxy groups were introduced for higher solubility.

Scheme 3. Synthesis of Nanoprisms **C3** and **C4**



In our initial experiment, ligands **5** and **6** as well as $[Cu(CH_3CN)_4]PF_6$ were mixed in a 2:3:6 ratio in CD_2Cl_2 (Scheme 3) to afford instantaneously a dark red solution. The product was characterized without any further purification by ESI-MS, NMR, and elemental analysis. The ESI-MS spectrum exhibited three major peaks (Figure S29 in Supporting Information) at 1051.7, 1350.9, and 1849.4 Da for $[Cu_6(\mathbf{5})_2(\mathbf{6})_3](PF_6)^{5+}$, $[Cu_6(\mathbf{5})_2(\mathbf{6})_3](PF_6)_2{}^{4+}$, and $[Cu_6(\mathbf{5})_2(\mathbf{6})_3](PF_6)_3{}^{3+}$ pointing to the assembly **C3**. ^{1}H NMR, ^{13}C NMR, ^{1}H$-^1$H COSY, and diffusion-ordered spectroscopy (DOSY) NMR further supported the structural assignment. ^{1}H NMR showed a diagnostic upfield shift of the mesityl protons x, x′ in **C3** (δ = 6.68 ppm) as compared to those in free **5** (δ = 6.93 and 6.94 ppm) and of aldehyde protons d (δ = 9.64 ppm) as compared to those in free **6** (δ = 10.09 ppm). An intimate $\pi-\pi$ stacking between the mesityl groups of **5** and the pyridine-2-carbaldehyde unit of **6** may be responsible for such shift in the ^{1}H NMR of **C3**.[8] In principle, four sets of mesityl resonances would be expected in **C3** due to their difference in chemical and spatial environment. However, experimentally only one set was well resolved. Finally, the exclusive formation of **C3** in solution was confirmed by a single diffusion coefficient in the DOSY NMR. As so far any attempt to grow single crystals of **C3** was met with failure, MM^+ force-field computations on **C3** provided some insight into the nanoprism structure. Taking the Cu^+-Cu^+ distance as a measure, the two panels in nanoprism **C3** are separated by 16.8 Å in the energy-minimized structure (Figure S32 in Supporting Information).

The six terminal aldehyde groups of **C3** are an interesting starting point for the post-self-assembly functionalization as indicated in Scheme 2. Indeed, nanoprism **C4** with its six constitutionally dynamic imine sites (Scheme 3) was cleanly obtained upon addition of 6 equiv of **3** to a solution of **C3** in CD_2Cl_2, as evidenced by ESI-MS, NMR, and elemental analysis (see Supporting Information). For example, in the ESI-MS no signals corresponding to **C3** were observed, only peaks being in full agreement with the newly formed nanoprism **C4**, i.e., at 941.7, 1159.0, and 1485.0 Da (Figure S30 in Supporting Information), representing $[Cu_6(\mathbf{5})_2(\mathbf{7})_3]^{6+}$, $[Cu_6(\mathbf{5})_2(\mathbf{7})_3]PF_6{}^{5+}$, and $[Cu_6(\mathbf{5})_2(\mathbf{7})_3](PF_6)_2{}^{4+}$.

In both nanoprism structures, the three phenanthroline units of **5** may take either a clockwise or anticlockwise orientation, leading to two stereoisomers of **C3** and **C4**: one with the same orientation of both **5** units (C_{3h}) and the other with an opposite sense of orientation (D_3). Notably, other arrangements of **5** are precluded due to a large steric hindrance between neighboring phenanthroline units.

The ^{1}H NMR spectrum of **C4** is broad and rather complicated as both diastereomers exhibit some different sets of signals. Notably, in the ^{1}H NMR spectrum of **C4**, the resonance of the aldehyde (d) protons (δ = 9.64 ppm for **C3**) was absent, whereas a new resonance at δ = 8.33 ppm appeared due to the imine protons (d′). The resonance of the mesityl (x, x′) protons in **C4** was observed as a multiplet in the region of δ = 6.47−6.20 ppm, (compared to δ = 6.68 ppm for **C3**) suggesting enhanced $\pi-\pi$ stacking between mesityl groups of **5** and the iminopyridine units of **7**. The DOSY NMR spectrum showed a single diffusion coefficient for both diastereomers, one more time confirming the exclusive formation of the nanoprism structure **C4**.

To fabricate a doubly capped cage assembly from **C3**, a tritopic end-cap with terminal amino groups was considered. Hyperchem computations using the MM^+ force-field suggested that compound **8** may be well suited for such process; see Figure 1. The capping agent **8** was thus synthesized by a Sonogashira cross-coupling of 1,3,5-triiodobenzene and 4-(3-ethynyl-benzyloxy)aniline (see Supporting Information). Finally, **5**, **6**, **8**, and $[Cu(CH_3CN)_4]PF_6$ were mixed in a 2:3:2:6 ratio and refluxed for 3 days in acetonitrile/DCM (6:1). After obtaining a reddish brown solution from the initial yellow one, the mixture was analyzed by spectroscopic techniques. To our delight, the ESI-MS spectrum (Figure S31 in Supporting Information) showed only peaks representing the doubly capped cage **C5**. Its formation was corroborated by the presence of three major peaks at 1081.9, 1327.2, and 1694.7 Da representing $[Cu_6(\mathbf{5})_2(\mathbf{9})]^{6+}$ (**9**: macrobicycle), $[Cu_6(\mathbf{5})_2(\mathbf{9})]PF_6{}^{5+}$, and $[Cu_6(\mathbf{5})_2(\mathbf{9})](PF_6)_2{}^{4+}$, respectively. The experimental isotopic splitting pattern of the major peak is in full agreement with the calculated splitting pattern (Figure 2).[19]

(19) The metallosupramolecular coordination ensures the exclusive formation of the constitutionally dynamic covalent macrobicycle **9** with six iminopyridine binding motifs (**9** = $(\mathbf{6})_3(\mathbf{8})_2 - 6H_2O$).

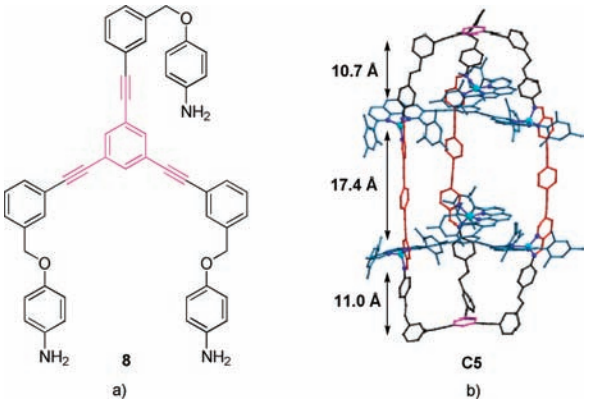


Figure 1. (a) Chemical structure of **8**. (b) Energy-minimized (MM^+) structure of **C5** with anticlockwise orientation of both ligands **5**. Counter anions and alkoxy groups are omitted for clarity.

Importantly, the choice of solvent proved to be crucial. Under similar reaction conditions with DCM as the only solvent, some brown precipitation was observed that could not be solubilized even at higher temperature upon addition of acetonitrile. The insolubility did not allow any further characterization of the precipitated compound(s), but it is reasonable to assume that some oligomeric products were formed.

A combination of ^{1}H NMR, ^{1}H$-^1$H COSY, and DOSY NMR spectroscopy finally verified the formation of cage **C5**. In the ^{1}H NMR, some of the phenanthroline protons appeared in two sets, pointing toward the existence of two diastereomers in solution, as for **C4**. The ratio of the two diastereomers (2:1) was determined from the integration of the two sets, with the C_{3h} isomer being lower in energy according to MM^+ computations. Indicatively, the resonances of the mesityl protons in **C5** showed a significant upfield shift and were split in four sets, appearing at δ = 5.92, 6.13, 6.22, and 6.57 ppm, suggesting an intimate stacking between the mesityl group of **5** and the iminopyridine units of the macrobicyclic ligand **9**. Finally, exclusive formation of **C5** in solution was confirmed by a single diffusion coefficient in the DOSY NMR spectroscopy. The experimental hydrodynamic diameter derived therefrom is in good agreement with the MM^+ computed one (23.6 vs 23.0 Å, see Supporting Information).

The slow evaporation of acetonitrile from a solution of **C5** produced very tiny crystals that immediately became amorphous when taken out from the mother liquor. Unfortunately, all attempts of X-ray analysis for such tiny crystals under solution were met with failure. Moreover, all efforts with various solvent(s) to obtain larger single crystals of **C5** remained unsuccesful. MM^+ forced-field computations on **C5** provided some insight into the distorted cage-like structure. Taking the Cu^+-Cu^+ distance in the energy-minimized structure as a measure, the average distance between two anticlockwise-oriented **5** units in the cage is 17.4 Å. The two units **8** are separated from the near-by unit **5** by 11.0 or 10.7 Å, taking the central phenyl ring in **5** and **8** as reference for the distance measurement. In principle, the two distinct spaces with different voids (V_L = 4500 Å^3 and V_s = 940 Å^3) are available in **C5** for inclusion of different guest molecules.

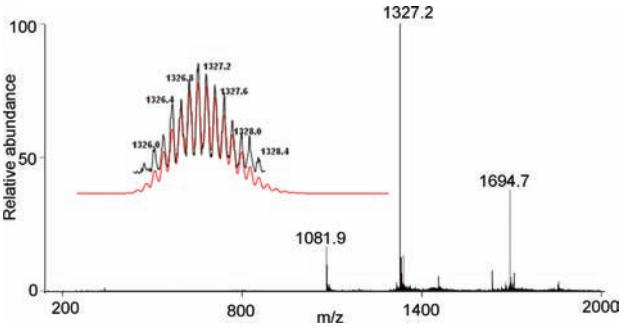


Figure 2. ESI-MS of the cage **C5**. Inset: Experimental (black line) and calculated (red line) isotopic distribution of $[Cu_6(\mathbf{5})_2(\mathbf{9})(PF_6)]^{5+}$.

In conclusion, we have utilized the supramolecular assistance of a sterically encumbered tris(phenanthroline-Cu^+) unit for the exclusive formation of self-assembled nanoprisms and a cage with a high level of constitutional control. The fidelity of the methodology depends on the mutual allegiance of constitutionally dynamic imine bond formation and heteroleptic complex formation in a one-pot process. The spectroscopic data evidence the exclusive formation of all supramolecular structures in solution. Further applications of this methodology to construct other fascinating architectures and the use of nanoprism **C3** and **C4** and cage **C5** in host–guest chemistry are in progress.

Acknowledgment. We are thankful to the Deutsche Forschungsgemeinschaft, the AvH foundation (J.F.), and the University of Siegen for financial support. We thank Dr. S. Khatua/University of Siegen for assistance with the drawings. This publication is dedicated to Prof. Dr. Dr. h.c. G. Bringmann/Würzburg on the occasion of his 60th birthday.

Supporting Information Available. Experimental procedures and spectroscopic data for **6**, **8**, and all complex assemblies. Energy minimized structures for **C3**, **C4**, and **C5** This material is available free of charge via the Internet at http://pubs.acs.org.