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Combining Dynamic Heteroleptic Complex Formation with Constitutional Dynamic Synthesis: A Facile Way to M_3LL' Cage Assemblies

Jian Fan,[†] Jan W. Bats,[‡] and Michael Schmittel*,[†]

[†]*Center for Micro- and Nanochemistry and Engineering, Organische Chemie I, Universität Siegen, Adolf-Reichwein-Strasse, 57068 Siegen, Germany, and* [‡]*Institut für Organische Chemie und Chemische Biologie, Johann Wolfgang Goethe-Universität, Max-von-Laue-Strasse 7, D-60438 Frankfurt am Main, Germany*

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The quantitative preparation of heteroleptic copper(I) complexes arising from a combination of 2,9-diarylphenanthrolines and iminopyridines (Schiff bases) is described. This strategy was applied to construct mono- and binuclear complexes but equally a discrete three-dimensional M_3LL' cage. By means of a constitutional dynamic synthesis, the heteroleptic aggregates were equally prepared from four-component mixtures using the copper(I) center as a catalyst for the in situ generation of the iminopyridine ligands.

Interest in hollow structures (cages, polyhedra, and capsules) arises because of not only the complexity and beauty of these structures but also their potential applications in the areas of separation, encapsulation, and catalysis.[1] In the past decade, a large number of polynuclear complexes $M_xL_yL'_z$ have been synthesized by combining organic ligands and transition-metal salts.[2] Notably, the heteroleptic cage structure M_3LL' has rarely been reported up to now.[3] Because the M_3LL' cage is comprised of only two ligands, this structure represents, from a complexity point of view, the simplest type of a heteroleptic cage; however, the strict geometric requirements such as the size-match and shape similarity of the ligands to minimize strain and stress within such a cage make it a rather difficult topology. Herein, we demonstrate a facile approach to the M_3LL' cage structure based on two developments that will be detailed below: (i) a protocol to prepare dynamic heteroleptic mono- and polynuclear $[Cu(phen^1)(iminopyridine)]^+$ complexes and (ii) a four-component self-assembly procedure combining heteroleptic complex formation with constitutional dynamic imine bond formation.

The quantitative formation of a dynamic heteroleptic complex necessitates the preferential selection of two or more types of ligands from a mixture while avoiding the formation of alternative homoleptic complexes.[4] Over the years, our group has developed a powerful strategy to construct dynamic heteroleptic metal complexes, such as tetracoordinated $[M(phen^1)(phen^2)]^{n+}$ and $[M(phen^1)(bipy)]^{n+}$ as well as pentacoordinated $[M(phen^1)(terpy)]^{n+}$ motifs (phen = phenanthroline, bipy = 2,2′-bipyridine, and terpy = terpyridine).[5−7] All of these heteroleptic motifs are based on the use of a bulky 2,9-diarylphenanthroline, such as **L1** (Chart 1). The principal structural and bonding features are as follows: (i) the combination of the ligand **L1** and the metal ion will generate a $[M(\mathbf{L1})]^{n+}$ unit but not a homoleptic complex $[M(\mathbf{L1})_2]^{n+}$ because of the steric hindrance between the bulky aryl substituents of **L1**. As a result, the metal ion is "frustrated" and readily

*To whom correspondence should be addressed. E-mail: schmittel@chemie.uni-siegen.de.

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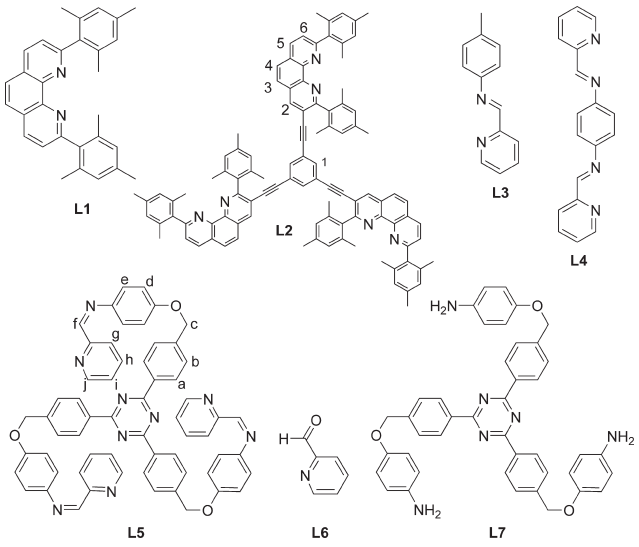
Chart 1. Ligands Chosen for the Present Study



accessible for an additional, but "slim", ligand **L** (for example, pyridine, phenanthroline, or terpyridine); (ii) the $\pi-\pi$ interaction between the 2,9-diaryl substituents of **L1** and ligand **L** stabilizes the heteroleptic combination; (iii) the geometric arrangement of **L1** and **L** in $[M(\mathbf{L1})(\mathbf{L})]^{n+}$ provides a versatile platform for the construction of a 90° angular motif. The power of this concept was convincingly demonstrated by the clean and quantitative preparation of nanosized heteroleptic supramolecular assemblies, such as heteroleptic nanogrids,[8] triangles,[9] nanoprisms,[4h,10] molecular wheels,[11] porphyrin stacks,[12] etc.[13]

The field of constitutional dynamic chemistry (CDC) was reviewed recently by several authors.[14] It comprises two subfields, dynamic noncovalent (supramolecular) and dynamic covalent chemistry, with the latter being a much younger topic. Constitutional dynamics involves continuous equilibration of all components through dissociation and reconstitution as governed by the global thermodynamics of the total system.[15]

At first, the reaction between $[Cu(CH_3CN)_4]PF_6$, **L1**, and the iminopyridines **L3** and **L4** was investigated, resulting in the quantitative formation of two heteroleptic complexes, $[Cu(\mathbf{L1})(\mathbf{L3})]PF_6$ (**1**) and $[Cu_2(\mathbf{L1})_2(\mathbf{L4})](PF_6)_2$ (**2**). Because of $\pi-\pi$ interactions between the iminopyridine and phenanthroline in **1** and **2**, the ^{1}H NMR resonances of the mesityl Ar−H protons in **1** (δ = 6.49 and 6.26 ppm) and **2** (δ = 6.41 and 6.25 ppm) show diagnostic upfield shifts as compared to that in the free ligand **L1** (δ = 6.93 ppm). The structures of both

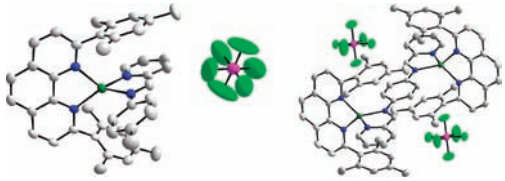


Figure 1. Crystal structure of compounds **1** (left) and **2** (right). H atoms and solvent molecules are omitted for clarity.

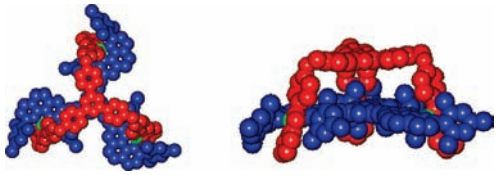


Figure 2. Hyperchem structure of the cage (left, top view; right, side view; phenanthroline, blue; Schiff base motifs, red; copper, green).

complexes were confirmed by single-crystal X-ray analysis, as depicted in Figure 1.[16] In **1** and **2**, each Cu^+ ion is tetrahedrally coordinated by two N atoms of the iminopyridine and two N atoms of phenanthroline **L1**, with the planes of both components being essentially perpendicular to each other. In compound **2**, both phenanthroline units are located parallelly at the opposite sides of ligand **L4**, with the distance between the two copper(I) ions amounting to 8.65 Å. On the basis of this result, we concluded that bulky 2,9-diaryl-substituted phenanthroline and pyridine Schiff base motifs can be used for the efficient construction of heteroleptic complexes.

In the following, the utility of the above concept for a higher-order aggregate was challenged by preparing a M_3LL' cage. The synthetic strategy was to keep intact the angular coordination motif of the phenanthroline and iminopyridine ligands around the copper(I) center, as established in **1** and **2**. Accordingly, the cage structure **3**, shown in Figure 2, was designed on the basis of molecular modeling studies (MM^+ in Hyperchem) that suggested the preparation of tris(phenanthroline) **L2** and tris(iminopyridine) **L5** as constituents for the assembly process.

The flexible $-CH_2-O-$ linkage in ligand **L5** was introduced not only to match the size of ligand **L2** but also to reduce, to a certain degree, the potential strain around the metal coordination sites in the final structure **3**. The resulting cage **3** should be chiral because the three phenanthroline units of ligand **L2** may take either a clockwise or anticlockwise conformation, resulting in two enantiomeric assemblies. Obviously, other phenanthroline conformations are precluded because of a large steric hindrance between neighboring phenanthrolines. Hence, a chiral C_3-symmetric cage should be the only possible assembly.

Tris(phenanthroline)s **L2** was synthesized by a Sonogashira cross-coupling of 1,3,5-triiodobenzene and the terminal alkynylphenanthroline unit, with the latter having been

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(16) Crystal data for **1**: M = 858.36, monoclinic, a = 25.050(3) Å, b = 16.122(3) Å, c = 23.306(2) Å, β = 121.126(8)°, U = 8057.2(18) Å^3, T = 171(2) K, space group $C2/c$, Z = 8, ρ_{calcd} = 1.415 g cm^{-3}, μ = 0.649 mm^{-1}, reflections collected 58 708, independent 9297, R1 = 0.0534, wR2 = 0.1279 [$I > 2\sigma(I)$], GOF = 1.032. Crystal data for **2**: M = 1706.29, monoclinic, a = 10.3929(9) Å, b = 27.050(3) Å, c = 13.6162(13) Å, β = 97.990(7)°, U = 3790.8(6) Å^3, T = 170(2) K, space group $P2_1/n$, Z = 2, ρ_{calcd} = 1.495 g cm^{-3}, μ = 0.825 mm^{-1}, reflections collected 55 611, independent 8738, R1 = 0.0440, wR2 = 0.0987 [$I > 2\sigma(I)$], GOF = 1.029.

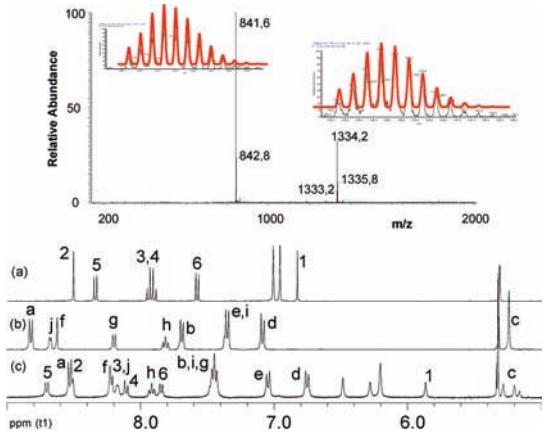

Figure 3. Top: ESI-MS spectrum of complex **3** with isotopic splitting (red: simulated isotopic splitting). Bottom: Partial ^{1}H NMR (400 MHz, 298 K) spectra of ligand **L2** in CD_2Cl_2 (a), **L5** in CD_2Cl_2 (b), and cage complex **3** in CD_2Cl_2/CD_3CN (3:1, v/v) (c).

prepared according to our published procedure.[17] Tris(iminopyridine) **L5** was prepared in three steps starting with 4-(bromomethyl)benzonitrile. Cyclization of benzonitrile led to formation of the central triazine ring, and then a nucleophilic substitution reaction between 4-aminophenol and 2,4,6-tris[4-(bromomethyl)phenyl]-1,3,5-triazine gave **L7**. Condensation of the tris(amine) **L7** and pyridine-2-carbaldehyde **L6** furnished **L5**. Ligands **L2** and **L5** were fully characterized by ^{1}H and ^{13}C NMR, electrospray ionization mass spectrometry (ESI-MS), and elemental analysis.

The heteroleptic cage **3** ($[Cu_3(\mathbf{L2})(\mathbf{L5})](PF_6)_3$) was synthesized in a clean manner by mixing $[Cu(CH_3CN)_4]PF_6$, **L2**, and **L5** in a 3:1:1 ratio in dichloromethane (DCM)/acetonitrile (3:1, v/v), as evidenced by a neat set of signals in the ESI-MS spectrum and sharp resonances in the ^{1}H NMR spectrum (Figure 3). When solely **L2** and $[Cu(CH_3CN)_4]PF$ were mixed together in DCM/acetonitrile, a yellow solution was obtained. The color of this solution changed immediately to dark red upon the addition of ligand **L5**. The recorded UV−vis spectrum of **3** showed a weak, but characteristic absorption around 503 nm due to the metal-to-ligand charge-transfer transition, indicating the formation of the heteroleptic Cu^+ complex.

The single set of phenanthroline and iminopyridine signals in the ^{1}H NMR spectrum of **3** points to the existence of a single cage structure. The singlet at $\delta = 5.24$ ppm assigned to the methylene ($-CH_2-$) protons of free **L5** is split in **3** into two doublets (δ = 5.30 and 5.18 ppm; J = 14.4 Hz), as is expected for a C_3-symmetric chiral assembly (Figure 2, bottom), because now the protons are diastereotopic. The resonances of mesityl protons (δ = 6.48, 6.28, and 6.20 ppm) in cage **3** show significant upfield shifts, compared to the corresponding resonances of free **L2** ($\delta = 6.95$ and 6.93 ppm), suggesting intimate $\pi-\pi$ stacking between the mesityl groups and the iminopyridine ligands. Hence, in **3** the three iminopyridines of **L5** are located in the notch of the 2,9-diarylphenanthroline units of **L2**, as observed in **1** and **2**.

The ESI-MS spectrum exhibited two main peaks, one at 814.6 Da and the other at 1334.2 Da, representing the 3+ and 2+ charged species. As such, the peaks correspond to $[Cu_3(\mathbf{L2})(\mathbf{L5})]^{3+}$ and $[Cu_3(\mathbf{L2})(\mathbf{L5})(PF_6)]^{2+}$, respectively. Their isotopic splitting fully agreed with those from simulations. Further confirmation of the structure of **3** was received from two-dimensional NOESY and DOSY experiments. In the NOESY (figure on p S17 in the Supporting Information), the CH_3 proton of **L2** is strongly correlated with the j-H of the pyridine moiety. In the DOSY spectrum, only one set of signals was observed, suggesting the exclusive formation of $[Cu_3(\mathbf{L2})(\mathbf{L5})](PF_6)_3$. The computed structure of cage **3** reveals a Cu−Cu distance of 16 Å and a height of ca. 7 Å. Hence, small aryl-based compounds may readily encapsulate within this cage via $\pi-\pi$ interactions.

While ample work has been published on CDC, many fewer results have been reported on the application of two archetypically different bonding schemes, i.e., one from the realm of noncovalent interactions and the other from the territory of reversible covalent bonds. A breakthrough paper was published in 2001 on double-level orthogonal dynamic combinatorial libraries using simultaneously noncovalent coordination chemistry and reversible >C=N− bond formation to generate mononuclear cobalt complexes,[18] culminating in recent years in the beautiful work on self-sorting in polynuclear complexes, such as metal helicates.[19] Spectacular cases combining metal coordination with imine bond formation were those elaborated by Lehn, Stoddart, and Severin, leading to metallosupramolecular grids, macrocyclic rings, rotaxanes, and spectacular ring systems.[20]

It was thus of interest to test whether cage **3** may also be prepared via parallel tris(imine) formation from **L6** and **L7** and heteroleptic aggregation, with copper(I) ions acting as the catalyst and as the coordination center. While the reaction of **L1** and **L6** with *p*-methylaniline or 1,4-diaminobenzene in the presence of $[Cu(CH_3CN)_4]PF_6$ furnished **1** (>99%) and **2** (~60%) with excellent to moderate success, the reaction of **L2**, **L6**, **L7**, and $[Cu(CH_3CN)_4]PF_6$ in a 1:3:1:3 ratio proceeded in a clean manner (>95% yield). The combination of dynamic heteroleptic aggregation and constitutional dynamic synthesis thus provides a facile approach to **3** and possibly to related structures by the simple modification of **L6**.

In conclusion, the present strategy has led consequentially from the use of a heteroleptic iminopyridine/phenanthroline metal unit in a mononuclear complex to its implementation into a three-dimensional cage. Moreover, cage **3** was prepared in a four-component reaction, in which tris(iminopyridine) was formed in a constitutional dynamic synthesis. Further applications of this approach to construct highly ordered heteroleptic structures and to use this cage as a host are in progress.

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Supporting Information Available: Syntheses and characterization data of ligands and complexes and crystallographic information (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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