

## Metallo-Supramolecular Assembly

## Hampered Subcomponent Self-Assembly Leads to an Amino Ligand: Reactivity with Silver(I) and Copper(II)

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**Abstract:** Insight into the ineffectiveness of a subcomponent self-assembly procedure between 4-aminopyridine (4-apy) and pyridine-2-carbaldehyde (2-pyA) led to a new amino ligand (L). The combination of L with Ag<sup>I</sup> gave a 2D luminescent network, in which the silver ions have a distorted triangular-pyramidal coordination geometry. The amino ligand is stable in acetonitrile and DMSO but decomposes in alcohol solvents. Moreover, we found

that Cu<sup>II</sup> also induced the decomposition of L, which led to Cu(pic)<sub>2</sub>, {[Cu(4-apy)<sub>4</sub>](ClO<sub>4</sub>)<sub>2</sub>}, and an unprecedented {[Cu<sub>4</sub>(pic)<sub>4</sub>(OH)<sub>2</sub>(H<sub>2</sub>O)<sub>6</sub>](ClO<sub>4</sub>)<sub>2</sub>} tetramer based on Cu<sup>II</sup> ions and picolinic acid (Hpic) generated in situ. The decomposition pathway of L was clarified by a combination of single-crystal XRD analysis, NMR spectroscopy, and ESI-MS.

## Introduction

The development of metallo-supramolecular architectures has allowed chemists to explore key issues such as self-assembly, self-organization, self-sorting, and molecular recognition.<sup>[1]</sup> Metal–ligand interactions are directional: metallo-supramolecular chemistry allows the partial design and hence control of the resulting products thanks to coordination bonds that act as an organizing algorithm for the self-assembly protocol. In the last few years, the subcomponent self-assembly route has been established as a powerful tool to produce coordination-driven assemblies.<sup>[2]</sup> In particular, Nitschke and co-workers have largely explored and developed this route to produce metallo-supramolecular capsules and other architectures as prototypes of complex and dynamic systems.<sup>[3]</sup> The subcomponent approach is based on a metal-templated reaction to produce imine bonds. In this way, complex structures can be generated from simple molecular precursors such as amines, aldehydes, and metal salts. The presence of a metal atom assures stabilization of the imine bonds. However, amino and hemiamino are in equilibrium with the metal-stabilized imine species<sup>[2a]</sup> and can also be isolated as metal complexes.<sup>[4]</sup> Recently, the first example of an anion-controlled metal-templated synthesis of an amino–(bis)imine Fe<sup>II</sup> complex was reported.<sup>[5]</sup> Again, amino and hemiamino-based dynamic combinatorial libraries (DCLs) have been developed through Zn<sup>II</sup>-templated reactions.<sup>[6]</sup> Herein, we report an example for which metal-templated subcomponent self-assembly fails. This ineffectiveness is ascribed

to the electron-withdrawing effect of the pyridine group in the 4-aminopyridine used for the sub-component route. Accurate analysis of the system allowed us to identify and then synthesize a new amino ligand used to generate a 2D Ag-based network. The ligand was found to decompose in the presence of Cu<sup>II</sup> and in alcohol solvents. In situ Cu<sup>II</sup>-assisted decomposition led to an unprecedented tetramer based on picolinic acid. The decomposition pathway was clarified by a combination of single-crystal XRD analysis, NMR spectroscopy, and ESI-MS.

## Results and Discussion

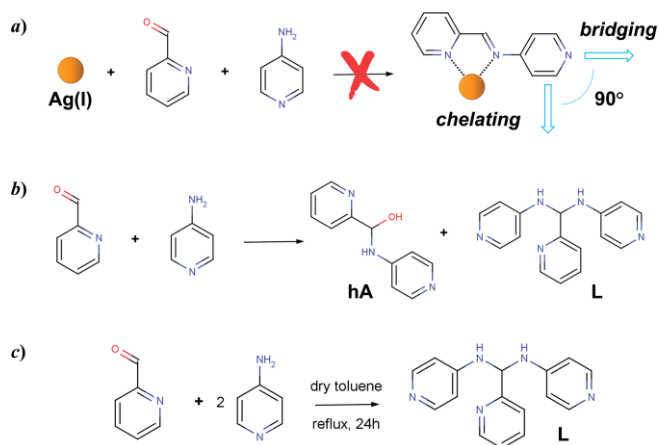
We are very interested in the design and development of discrete coordination-driven boxes and capsules and to exploit the potential of confined supramolecular environments.<sup>[7]</sup> In this context, to produce a metallo-supramolecular “corner” for the design of new coordination-driven vessels, we decided to explore the sub-component self-assembly route through condensation of 4-aminopyridine (4-apy) and pyridine-2-carbaldehyde (2-pyA) (Scheme 1a).

In particular, we decided to use templating metal ions such as Ag<sup>I</sup> and Cu<sup>II</sup>. Ag<sup>I</sup> has already proved to be a well-suited metal for a “corner ligand” such as 4-(2-pyridyl)pyrimidine that leads to molecular squares, rectangles, and infinite helical chains depending on the used anion.<sup>[8]</sup> On the other hand, we envisaged that by using Cu<sup>II</sup> the chelating moieties would be able to coordinate the equatorial positions of the metal centers, whereas the axial positions would be prone to expand the metal coordination through the bridging group of the “corner ligand”. A mixture of 4-apy, 2-pyA, and AgClO<sub>4</sub> (molar ratio 1:1:1) in CD<sub>3</sub>CN at 50 °C was monitored by NMR spectroscopy. Overnight heating, as well as longer reaction times (up to 1 week), did not lead to the imine product. The NMR spectrum only showed the signals of unreacted 4-apy and 2-pyA, along with very small traces of unidentified products. Hence, we analyzed the reac-

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Scheme 1. (a) Proposed (but ineffective) design of a coordination-driven corner by sub-component self-assembly. (b) Observed products from the reaction of 4-apy and 2-pyA in hot acetonitrile. (c) Synthesis of aminal L.

tion between 4-apy and 2-pyA in the absence of silver ions. A previous study claimed that the reaction between 4-apy and 2-pyA did not give any condensation products.<sup>[9a]</sup> On the contrary, the same study demonstrated that the reaction of 2-pyA with the 2-aminopyridine or 3-aminopyridine isomer led to the formation of an aminal species. However, thin-layer chromatography (TLC) of the 4-apy/2-pyA mixture in acetonitrile at 50 °C, and at reflux after 4, 6, and 24 h, evidenced the presence of two products (very light spots, low concentrations), which suggested that condensation was activated by higher temperatures. The two products were identified by ESI-MS and NMR spectroscopy (see Section S1.2 in the Supporting Information) as a hemiaminal and an aminal species, (pyridin-2-yl)[(pyridin-4-yl)amino]methanol (hA) and 1-(pyridin-2-yl)-*N,N'*-bis(pyridin-4-yl)methanediamine (L), respectively (Scheme 1b). TLC also revealed the same light spots for the reaction performed at 50 °C in the presence of Ag<sup>I</sup> (subcomponent route). By performing the condensation in hot dry toluene, with a molar ratio of 1:1, aminal L was obtained in good yield (ca. 50 %), as confirmed by NMR spectroscopy. The yield could be improved (75 % after purification) by heating 4-apy and 2-pyA in dry toluene at reflux under argon for 24 h with the correct molar ratio (2:1; Scheme 1c). The NMR spectrum of pure L allowed us to unambiguously identify the low-intensity signals from the reaction of 4-apy, 2-pyA, and AgClO<sub>4</sub> (molar ratio 1:1:1) in CD<sub>3</sub>CN (50 °C) as the aminal species L. Compound L is insoluble in chlorinated solvents, poorly soluble in acetonitrile and acetone, and soluble in alcohols (MeOH and EtOH), DMSO, and hot toluene. It is well known that the reactivity of aromatic rings is significantly affected by substituent groups through electron-donating or electron-withdrawing effects. It was previously demonstrated that the electronic effects of the *para* substituent of aniline could be used to orchestrate subcomponent substitution reactions of imine-based Cu<sup>I</sup> complexes.<sup>[10]</sup> In particular, limited amounts of imines were formed in the Cu<sup>I</sup>-templated synthesis with electron-withdrawing-group-substituted 4-nitroaniline. Again, in the absence of Cu<sup>I</sup>, this aniline did not form the imine. Similarly, two recent dynamic covalent reaction (DCR) studies on imine species derived from 2-pyA and aromatic

amines pointed out the possibility to control the equilibrium mixture through substituent effects.<sup>[6a,11]</sup> For instance, electron-withdrawing groups such as CN and NO<sub>2</sub> facilitate the formation of aminal species over imine products.<sup>[6a]</sup> Again, it was reported that only trace amounts of products (aminal 4 %, hemiaminal ether 2 %, and imine 9 %) were observed in the reaction of 2-pyA, 4-nitroaniline, and ethanol.<sup>[11]</sup> On the other hand, the reaction between 2-pyA and aniline or aromatic amines with electron-donating and weak electron-withdrawing *para* substituents led to the formation of imine species as major products.<sup>[6a,10,11]</sup> The pyridine group has withdrawing character comparable to that of the nitro group. We postulate that the subcomponent self-assembly route in the case of 4-apy is hampered by the electron-withdrawing effect of pyridine.

The obtained aminal was treated at room temperature with AgClO<sub>4</sub> in acetonitrile in the absence of light. The presence of silver ions highly increased the solubility of L in acetonitrile, likely as a result of Ag–L coordination. Single crystals of a coordination polymer with the formula {[AgL(CH<sub>3</sub>CN)](ClO<sub>4</sub>)<sub>n</sub>} (1) were obtained (yield 70 %) after 2 weeks. The obtained assembly was found to form a 2D network, in which the Ag<sup>I</sup> ion has a distorted triangular-pyramidal coordination geometry (Figure 1b). Three independent L molecules coordinate to the metal ion at the equatorial positions (Ag–N 2.23–2.35 Å), whereas one acetonitrile molecule coordinates to the metal atom at the apical position (Ag–N 2.63 Å). The 2D network is supported by the formation of two different rings, as shown in the simplified structure (Figure 1c). The smaller is a 4-ring composed of two Ag<sup>I</sup> ions and two independent ligands with a  $\pi$ – $\pi$  stacking interaction between two pyridine moieties (centroid–centroid distance 3.53 Å, shift distance 1.12 Å; Figure 1d). The larger is an 8-ring composed of four Ag ions and four independent ligands, with an average ring diameter of 15 Å. The combination of these structural features leads to a network of topological type

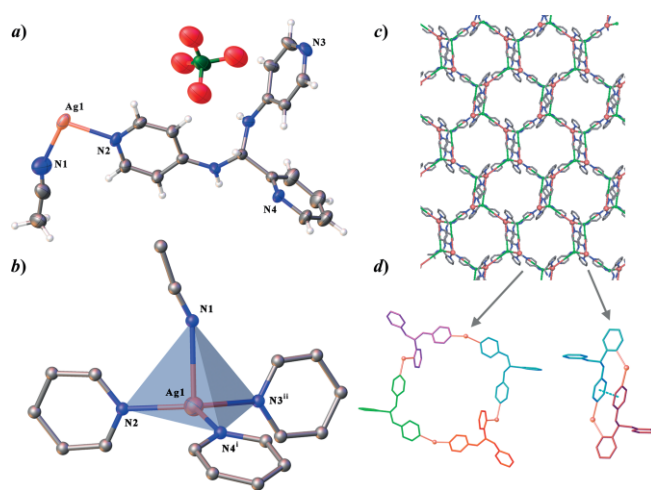


Figure 1. (a) Asymmetric unit in compound 1; disordered atoms are omitted. Color code: Ag, orange; Cl, green; O, red; N, blue; C, gray; H, white. (b) Coordination polyhedron of the Ag ion; selected bond lengths [Å]: Ag1–N1 2.629(12), Ag1–N2 2.232(7), Ag1–N3<sup>ii</sup> 2.277(7), Ag1–N4<sup>i</sup> 2.355(8) (symmetry operations: i: –1/2 + x, 3/2 – y, 1/2 + z; ii: 2 – x, 1 – y, 1 – z). (c) Simplified structure overlapped with the real one (Ag, orange; L centroid, green). (d) 8-ring and dimeric pocket forming the 4-ring (cyan dashed line:  $\pi$ – $\pi$  stacking).

4.8<sup>2</sup>-fes, with Ag and L as nodes (Figure 1c).<sup>[12]</sup> Upon treating the three building blocks through a one-pot reaction (AgClO<sub>4</sub>, 4-apy, 2-pyA) in CD<sub>3</sub>CN at 82 °C for 12 h, the aminal ligand was formed only in trace amounts. This is coherent with the results of the reaction between 4-apy and 2-pyA in MeCN at reflux temperature (Section S1.2), for which the reaction led to the partial formation of aminal L and hA as a byproduct. Moreover, analysis of the one-pot reaction (Section S1.5) by NMR spectroscopy evidenced that the amount of L formed was considerably smaller in the presence of Ag<sup>+</sup> ions. As shown by NMR spectroscopy, the metal ions coordinate to the nitrogen atoms of the starting material (pyridine and –NH<sub>2</sub> group), and this may affect the formation of L.

Ligand L and coordination polymer **1** both exhibit luminescence at room temperature upon excitation in the UV and visible regions. We observed visible emission from both compounds (see Figure 2); the corresponding bands present a similar profile, and they are centered in the green region. The maximum emission of ligand L (ca. 530 nm) is slightly blueshifted relative to the maximum emission of silver compound **1** (ca. 560 nm). On the other hand, the emission band of L is overlapped with that of **1** in the red region, and it is broader in the blue region, which results in a larger bandwidth.

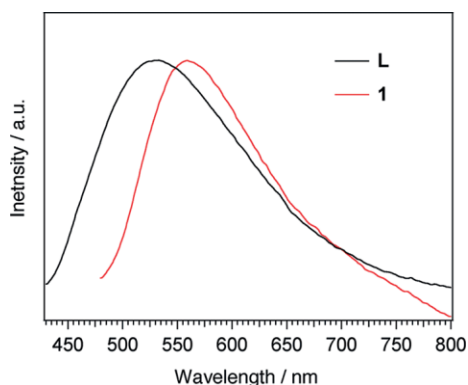


Figure 2. Emission spectra of L and **1** in the solid state at room temperature.

Upon treating L with Cu<sup>II</sup>, the ligand decomposed and underwent oxidation to give the picolinate anion (pic) and 4-apy. The same behavior was observed in the one-pot reaction of Cu<sup>II</sup>, 2-pyA, and 4-apy. We succeeded in isolating the decomposition products of L as single crystals of Cu<sup>II</sup> complexes through a set of different crystallization conditions (Figure 3). Degradation of the aminal ligand in the presence of transition metals was already observed.<sup>[13]</sup> Moreover, 2-pyA with Cu<sup>II</sup> was used as a source of different ligands through in situ reactions such as the Cannizzaro reaction, aldol and nucleophilic addition to give the picolinate anion, *gem*-diol and hemiacetal species.<sup>[14]</sup> From the reaction of L with Cu(ClO<sub>4</sub>)<sub>2</sub> in acetonitrile, single crystals of {[Cu(4-apy)<sub>4</sub>(CH<sub>3</sub>CN)<sub>2</sub>](ClO<sub>4</sub>)<sub>2</sub>} (yield 70 %) were isolated (see the Supporting Information). On the contrary, from alcohol or DMSO solutions we isolated copper picolinate species. In particular, the major product (yield 90 %) was the well-known Cu(pic)<sub>2</sub> complex (Figure 3a), along with a minor tetrameric product (yield 4 %) of formula {[Cu<sub>4</sub>(pic)<sub>4</sub>(OH)<sub>2</sub>(H<sub>2</sub>O)<sub>6</sub>](ClO<sub>4</sub>)<sub>2</sub>} (**2**) (Figure 3b,c).

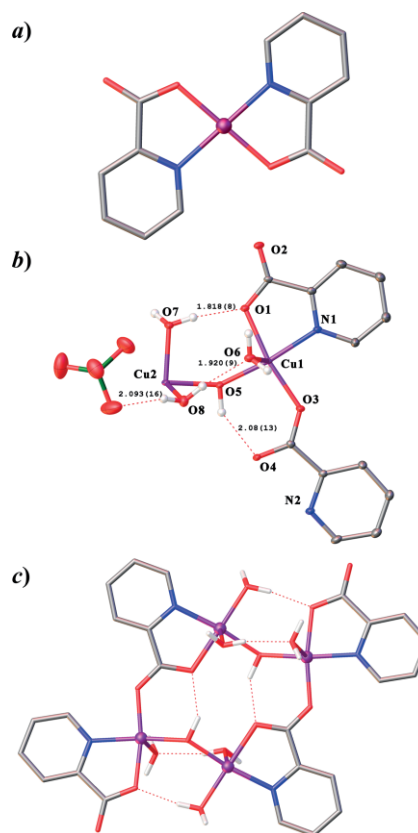


Figure 3. (a) Cu(pic)<sub>2</sub>. (b) Asymmetric unit in compound **2**. (c) Tetrameric unit of compound **2**. Color code: Cu, purple; Cl, green; O, red; N, blue; C, gray; H, white; dashed red line, H-bond; 4-apy and picolinate H atoms are omitted.

It is noteworthy that **2** was obtained only through the in situ degradation of L, as every effort to synthesize it from picolinate acid and a Cu<sup>II</sup> source gave Cu(pic)<sub>2</sub> exclusively. This unprecedented tetramer displays two different picolinate coordination modes: one anion acts as an N,O chelating ligand, and the other one acts either as an N,O chelating ligand and as a bridging ligand. In the asymmetric unit, **2** shows two independent Cu<sup>II</sup> centers (Figure 3b), both with a distorted square-pyramidal coordination geometry. In the equatorial positions, Cu1 is coordinated by one chelating picolinate anion (Cu1–O1 1.98, Cu1–N1 1.99 Å), one bridging OH group (Cu1–O5 1.92 Å), and the oxygen atom of a bridging picolinate anion (Cu1–O3 1.96 Å). The apical position is occupied by a water molecule (Cu1–O6 2.40 Å). Cu2 is coordinated by two water molecules, one axial and one equatorial (Cu2–O8 2.48 Å and Cu2–O7 1.97 Å, respectively), one bridging OH group (Cu2–O5 1.93 Å), and one N,O chelating picolinate anion (Cu2–O4 1.99, Cu2–N2 1.98 Å). Moreover, the presence of coordinating water molecules and hydroxy groups (Figure 3b,c) set up large arrays of strong intratetramer H-bonds (1.82–2.08 Å) along with inter-tetramer (1.87–2.04 Å) and tetramer-perchlorate anion H-bonds (2.09 Å).

The behavior of L in the presence of Cu<sup>II</sup> led us to analyze the stability of the ligand further. Aminal species are known to be quite sensitive to hydrolysis; however, in the solid state, L was found to be stable for several months. Dissolved in aceto-

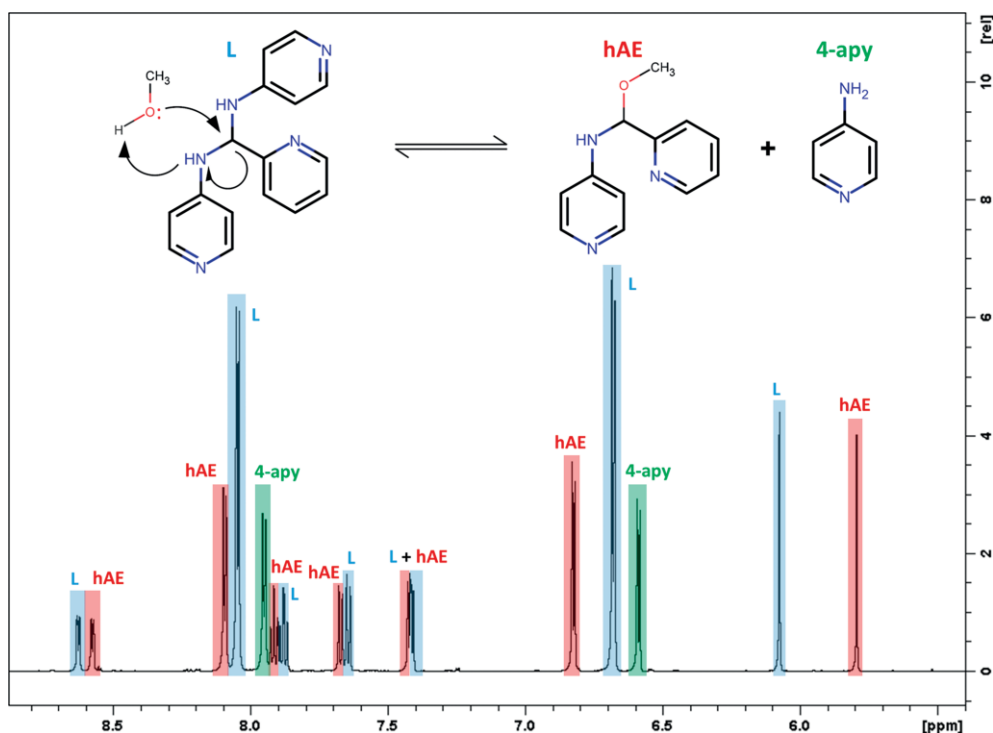


Figure 4.  $^1\text{H}$  NMR (600 MHz,  $\text{CD}_3\text{OD}$ , 25  $^\circ\text{C}$ ) spectrum of L after 12 h. Color code: L, light blue; hemiaminal ether (hAE), red; 4-apy, green.

nitrile or DMSO, L was stable, and TLC showed only one spot. On the contrary, if dissolved in alcohol, after a few hours, TLC revealed the presence of three spots, which suggested ligand decomposition. Analysis of L by NMR spectroscopy after 12 h in deuterated methanol confirmed that the ligand underwent nucleophilic hydrolysis promoted by methanol to give starting 4-apy and the hemiaminal ether *N*-[methoxy(pyridin-2-yl)methyl]pyridin-4-amine (hAE). Figure 4 shows the NMR spectrum in  $\text{CD}_3\text{OD}$  along with a suggested mechanism for the degradation of L. Area integration confirmed that the ratio between hAE and 4-apy was ca. 1:1, as expected according to the suggested decomposition pathway. On the contrary, the NMR spectrum in  $[\text{D}_6]\text{DMSO}$  does not show any degradation. The same findings were confirmed by ESI-MS. The spectrum recorded in acetonitrile gives the  $[\text{L} + \text{H}^+]$  signal ( $m/z = 278.1$ ) along with fragmentation products (see the Supporting Information). As-prepared methanol solutions of L did not show any degradation product, but after 24 h the signal of the hemiaminal ether hAE was clearly detectable ( $[\text{hAE} + \text{H}^+]$ ,  $m/z = 216.0$ ).

## Conclusions

Insight into the ineffectiveness of the subcomponent self-assembly procedure among  $\text{Ag}^I$ , 2-pyA, and 4-apy led to a new aminal ligand L. Ligand L was synthesized in high yield and was treated with silver ions to give **1**. The aminal was found to be unstable in alcohol solvents and in the presence of  $\text{Cu}^{II}$ , and its decomposition pathway was unraveled. From the in situ degradation of L,  $\text{Cu}^{II}$  tetramer **2** was isolated. Moreover, we demonstrated that the condensation of 2-pyA and 4-apy (at 50 and

80  $^\circ\text{C}$ , with or without Ag ions) gave a mixture of the two reactants, hemiaminal hA, and aminal L in low yield. The ineffectiveness of the subcomponent self-assembly process was ascribed to the electron-withdrawing effect of the pyridine group in 4-apy. This finding is very intriguing, as it opens the possibility to exploit the behavior of 4-apy to obtain new aminal products with other aldehyde species. We are currently exploring this possibility to obtain new multidentate pyridine-based ligands and coordination-driven architectures through reaction with different metal ions.

CCDC 1487013 (for **1**), 1487014 (for **2**), and 1487015 (for **3**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

**Supporting Information** (see footnote on the first page of this article): Experimental, spectral, and crystallographic data.

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**Keywords:** Self-assembly · N ligands · Aminals · Copper · Silver

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