

Aminotriazines as Locking Fragments in Macrocyclic Synthesis

Paul V. Bernhardt* and Elizabeth J. Hayes

Department of Chemistry, University of Queensland, Brisbane, 4072, Australia

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The macrocyclic compounds (6-(4',6'-diamino-1',3',5'-triazinyl)-1,4,6,8,11-pentaazacyclotetradecane)copper(II) triperchlorate dihydrate, $[\text{Cu}(\text{HL}^2)](\text{ClO}_4)_3 \cdot 2\text{H}_2\text{O}$, (6-(6'-amino-4'-oxo-1'-H-1',3',5'-triazinyl)-1,4,6,8,11-pentaazacyclotetradecane)copper(II) diperchlorate hydrate, $[\text{CuL}^3](\text{ClO}_4)_2 \cdot \text{H}_2\text{O}$, and [(6-(4',6'-dioxo-1'-H-1',3',5'-triazinyl)-1,4,6,8,11-pentaazacyclotetradecane)copper(II)] diperchlorate, $[\text{CuL}^4](\text{ClO}_4)_2$, have been synthesized. The macrocycles synthesized contain respectively pendant melamine, ammeline, and ammelide rings. The X-ray crystallographic analyses of $[\text{Cu}(\text{HL}^2)](\text{ClO}_4)_3 \cdot 2\text{H}_2\text{O}$, triclinic, space group $P\bar{1}$, $a = 9.489(10)$ Å, $b = 12.340(2)$ Å, $c = 24.496(4)$ Å, $\alpha = 87.74(10)^\circ$, $\beta = 85.51(10)^\circ$, $\gamma = 70.95(10)^\circ$, and $Z = 4$, and $\{[\text{CuL}^3](\text{ClO}_4)_2 \cdot \text{H}_2\text{O}\}_2$, monoclinic, space group $C2/c$, $a = 18.624(8)$ Å, $b = 17.160(2)$ Å, $c = 15.998(6)$ Å, $\beta = 117.82(2)^\circ$, and $Z = 4$, are reported. The structure of $[\text{Cu}(\text{HL}^2)](\text{ClO}_4)_3 \cdot 2\text{H}_2\text{O}$ shows the formation of linear tapes, formed by a combination of hydrogen bonds and π - π stacking interactions. The structure of $[\text{CuL}^3](\text{ClO}_4)_2 \cdot \text{H}_2\text{O}$ displays formation of dimers, formed by a coordinate bond from the oxygen in one molecule to the copper atom of another. The tautomeric forms of the ammeline and ammelide moieties have been determined. The potential of these compounds as subunits for cocrystallization has been investigated.

Introduction

Recent work in the field of crystal engineering has focused on the design of new solids with desired physical and chemical properties. By the synthesis of subunits which possess specific properties and then exploitation of intermolecular interactions such as hydrogen bonding and π - π stacking, these molecules and ions can be persuaded to form specific structural units. Once control over the crystalline form is achieved, control over such properties as thermal stability, solubility, color, and conductivity is possible.

Hydrogen bonding is one of the better understood types of noncovalent interaction that have been used by chemists in the fields of self-assembly and crystal engineering. The hydrogen bond has both strength and directionality, which makes it particularly attractive. Indeed, when suitably positioned, the number and orientation of hydrogen bond donor and acceptor sites can be used to impart "intelligence" in molecules, such that they may selectively recognize another molecule.³ Considerable work has been done on the synthesis of organic hydrogen-bonded aggregates, by the likes of Lehn,⁴ Hamilton,⁵ Desiraju,⁶ and Whitesides.⁷ Whitesides, in particular, has done

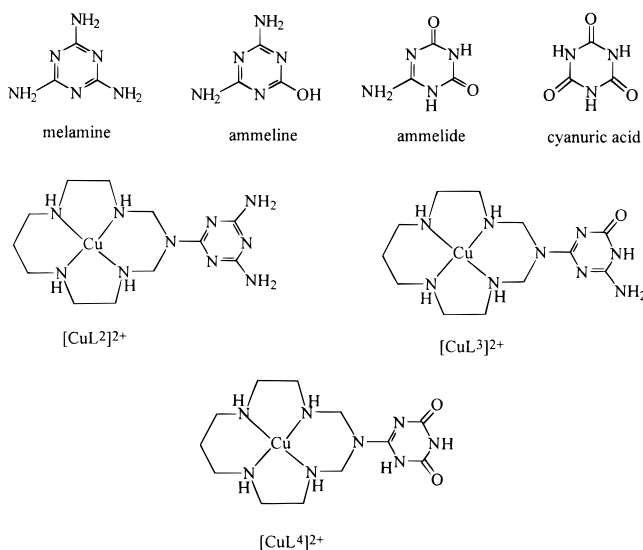
extensive study on cocrystals of melamine derivatives and barbituric acids (Chart 1), which contain extended hydrogen-bonded tapes. It is evident from such work that the hydrogen bond is an important tool in the areas of organic self-assembly, host-guest chemistry and molecular recognition. Recently, Mingos and co-workers have extended these principles to the study of metal complexes of ligands with potential hydrogen bonding groups on the periphery.⁸ Such transition metal complexes have bifunctional ligands that combine good ligating properties and hydrogen-bonding sites. The design of suitably complementary component parts can thus lead to the self-assembly of high-nuclearity complexes.

The synthesis of metal complexes as building blocks, as opposed to organic molecules, presents many opportunities. Factors such as oxidation state and coordination preferences of different transition metals may present ways in which the network design may be influenced.⁹ In addition, intermolecular interactions between metal centers provide motivation for the study of such compounds. It has been shown that magnetic^{10,11} and photophysical¹² interactions between metal centers can be propagated through hydrogen bonds. The use of hydrogen

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Chart 1



bonding to control the self-assembly of metal complexes is therefore appealing since the hydrogen bonds can both control the assembly of the components and then provide a pathway for transmitting interactions between them.¹³

The aminotriazines such as melamine, ammeline, and ammelide engage in extensive hydrogen bonding.⁴ These primary amino groups offer themselves as locking fragments for closure of a macrocyclic ring in a basic template synthesis. A coordinated amine reacts with an aldehyde to form a coordinated imine, which is then susceptible to nucleophilic attack by a primary amine.¹⁴ Macrocycles bearing such a pendent group possess a hydrogen-bonding face, and as such represent possible components for the self-assembly of multinuclear aggregates.

Experimental Section

Safety Note. All preparative work was carried out in the fume hood. Perchlorate salts are potentially explosive. Although no problems were experienced with the compounds synthesized, they should only be handled in small quantities, never scraped from sintered glass frits, nor heated in the solid state.

3,7-Diaza-1,9-nonanediamine (L¹),¹⁵ ammeline,¹⁶ and ammelide¹⁷ were synthesized according to published methods.

(6-(4',6'-Diamino-1',3',5'-triazinyl)-1,4,6,8,11-pentaazacyclotetradecane) copper(II) Triperchlorate Dihydrate, [Cu(HL²)](ClO₄)₃·2H₂O. L¹ (1.81 g, 11.3 mmol) was dissolved in methanol (200 cm³). Cu(NO₃)₂·3H₂O (2.48 g, 10.3 mmol), triethylamine (2.03 g, 20 mmol), and 37% aqueous formaldehyde (2.0 cm³, 26 mmol) were added, and the mixture stirred and brought to reflux. A solution of melamine (1.56 g, 12.4 mmol) in aqueous methanol (1:1, v/v; 100 cm³) was added dropwise over about 1 h. The mixture was refluxed for 11 days. The formation of a macrocyclic species was tested for by addition of acid to a small aliquot. Persistence of a pink color indicated formation of a macrocycle. The resulting solution was cooled and filtered and sorbed onto a Sephadex C-25 cation-exchange resin (Na⁺ form). The product eluted second from the column (after [CuL¹]²⁺) with 0.2 M NaClO₄ solution (λ_{max} 518 nm), and concentration of this solution to ca. 50 mL

produced a pink solid upon standing. This was collected by filtration, washed with EtOH, and air-dried (0.69 g, 9%). Several crops were obtained from the filtrate. Recrystallization from dilute aqueous perchloric acid produced crystals suitable for X-ray diffraction. Calcd for C₁₂H₃₁Cl₃CuN₁₀O₁₄: C, 20.35; H, 4.27; N, 19.78. Found: C, 19.9; H, 4.1; N, 19.2. The nonprotonated compound, [CuL²](ClO₄)₂·2H₂O, was synthesized using the same procedure. Dark pink crystals formed directly from the concentrated solution (pH 7). Electronic spectrum (H₂O): λ_{max} 514 nm, ε 89 M⁻¹ cm⁻¹. Anal. Calcd for C₁₂H₃₀Cl₂CuN₁₀O₁₀: C, 23.67; H, 4.97; N, 23.01. Found: C, 23.9; H, 4.7; N, 23.3.

(6-(6'-Amino-4'-oxo-1'-H-1',3',5'-triazinyl-4'-one)-1,4,6,8,11-pentaazacyclotetradecane)copper(II) Dipperchlorate Hydrate, [CuL³](ClO₄)₂·H₂O. L¹ (1.82 g, 11.4 mmol) was dissolved in methanol (200 cm³). Cu(NO₃)₂·3H₂O (2.41 g, 10 mmol), NaOH (0.76 g, 19 mmol), and 37% aqueous formaldehyde (2.0 cm³, 26 mmol) were added, and the mixture stirred and brought to reflux. A solution of ammeline (1.52 g, 12 mmol) and NaOH (0.51 g, 12.75 mmol) in aqueous methanol (1:1, v/v; 100 cm³) was added dropwise over 20 min. The mixture was refluxed for 45 h. The solution was filtered and sorbed onto a Sephadex C-25 cation-exchange resin (Na⁺ form). The product eluted from the column with 0.1 M NaClO₄ solution, and concentration of this solution produced a pink solid (0.47 g, 8%), which was recrystallized from water to produce dark pink crystals suitable for X-ray diffraction. These were collected by filtration, washed with EtOH, and air-dried. Electronic spectrum (H₂O): λ_{max} 514 nm, ε 95 M⁻¹ cm⁻¹. Anal. Calcd for C₁₂H₂₇Cl₂CuN₉O₁₀: C, 24.35; H, 4.60; N, 21.30. Found: C, 24.0; H, 4.4; N, 21.3.

(6-(4',6'-Dioxo-1'-H-1',3',5'-triazinyl)-1,4,6,8,11-pentaazacyclotetradecane) copper(II) Dipperchlorate, [CuL⁴](ClO₄)₂. L¹ (1.84 g, 11.5 mmol) was dissolved in methanol (200 cm³). Cu(NO₃)₂·3H₂O (2.41 g, 10 mmol), NaOH (0.76 g, 19 mmol), and 37% aqueous formaldehyde (2.0 cm³, 26 mmol) were added, and the mixture was stirred and brought to reflux. A slurry of ammelide (1.14 g, 8.9 mmol) in water (100 cm³) was added dropwise over about 10 min. The mixture was refluxed for 5.5 h. The resulting solution was cooled and filtered and sorbed onto a Sephadex C-25 cation-exchange resin (Na⁺ form). The desired product eluted first, with 0.15 M NaClO₄. Concentration to ca. 50 cm³ gave a purple solid (0.23 g, 4%). Electronic spectrum (H₂O): λ_{max} 518 nm, ε 112 M⁻¹ cm⁻¹. Anal. Calcd for C₁₂H₂₄Cl₂CuN₈O₁₀: C, 25.07; H, 4.21; N, 19.50. Found: C, 26.0; H, 4.4; N, 20.1.

1:1 [CuL³](ClO₄)₂-Barbituric Acid Adduct. [CuL²](ClO₄)₂·2H₂O (10⁻⁴ mol) and barbituric acid (5 × 10⁻⁵ mol) were dissolved in ca. 5 cm³ of acetonitrile in a test tube. The test tube was placed in a jar of hexane. Dark pink crystals formed by vapor diffusion. Anal. Calcd for C₁₆H₃₀Cl₂CuN₁₂O₁₁: C, 27.41; H, 4.31; N, 23.98. Found: C, 27.4; H, 4.6; N, 24.2. Infrared: 3403, 3225, 1700, 1696, 1684, 1648, 1569, 1560, 811 cm⁻¹.

Physical Methods. Solution UV-visible spectra were measured on a Perkin-Elmer Lambda 12 spectrophotometer. DC normal and differential pulse polarography were performed using an EG&G PARC model 303 dropping Hg electrode. A Pt wire auxiliary and an Ag/AgCl reference electrode were used. A BAS 100B/W potentiostat was employed. Cyclic voltammetry was performed using a static mercury drop electrode. All solutions for electrochemistry were 0.1 M in NaClO₄ and were purged with N₂ before measurement. The stoichiometry of each electron-transfer process was established by wave-height comparisons with known one-electron redox processes. Potentiometric titrations of acidified (HClO₄) aqueous solutions (0.1 M Et₄NClO₄) of complexes were carried out at 298 K with a Metrohm 665 Dosimat and an Orion model 720A pH meter, using Et₄NOH as the base. Data were analyzed with the program TITFIT.¹⁸ Electron paramagnetic resonance spectra of frozen solutions (1:2 DMF/water, 77 K) were measured on a Bruker ER200 D spectrometer. Spin Hamiltonian parameters were obtained by spectral simulation using EPR50F.¹⁹

Structure Analyses. Cell constants were determined by a least-squares fit to the setting parameters of 25 independent reflections

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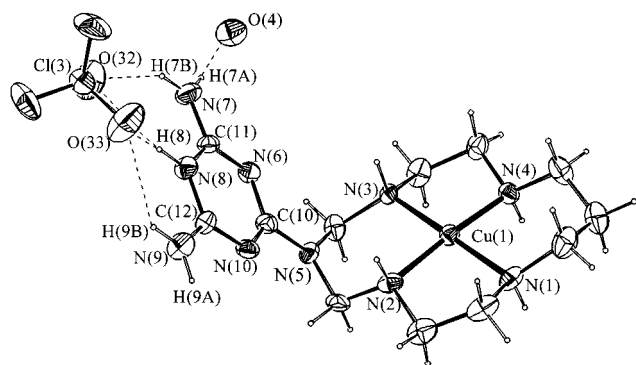
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Table 1. Crystal Data

	[Cu(HL ²)](ClO ₄) ₃ ·2H ₂ O	{[Cu(L ³)](ClO ₄) ₂ ·H ₂ O} ₂
formula	C ₁₂ H ₃₁ Cl ₃ CuN ₁₀ O ₁₄	C ₂₄ H ₅₄ Cl ₄ Cu ₂ N ₁₈ O ₂₀
<i>a</i> , Å	9.489(1)	18.624(8)
<i>b</i> , Å	12.340(2)	17.160(2)
<i>c</i> , Å	24.496(4)	15.998(6)
α , deg	87.74(1)	
β , deg	85.51(1)	117.82(2)
γ , deg	70.95(1)	
<i>V</i> , Å ³	2702.6(7)	4522(3)
<i>Z</i>	4	4
fw	709.36	1183.74
space group	<i>P</i> 1̄ (No. 2)	<i>C</i> 2/ <i>c</i> (No. 15)
<i>T</i> , °C	23	23
λ , Å	0.710 73	0.710 73
ρ_{calcd} , g cm ⁻³	1.743	1.739
μ , cm ⁻¹	11.87	12.72
<i>R</i> (<i>F</i> _o), ^a <i>wR</i> ₂ (<i>F</i> _o ²) ^b	0.0921, 0.2744 ^c	0.0898, 0.2344 ^d

^a $R(F_o) = \sum ||F_o| - |F_c|| / \sum |F_o|$. ^b $wR_2(F_o^2) = (\sum w(F_o^2 - F_c^2) / \sum wF_o^2)^{1/2}$. ^c $w = (\sigma^2(F_o^2) + (0.0981P)^2 + 48.53P)^{-1}$. ^d $w = (\sigma^2(F_o^2) + (0.0981P)^2 + 48.53P)^{-1}$, where $P = 1/3[\max(F_o, 2.0)] + 2/3F_c^2$.

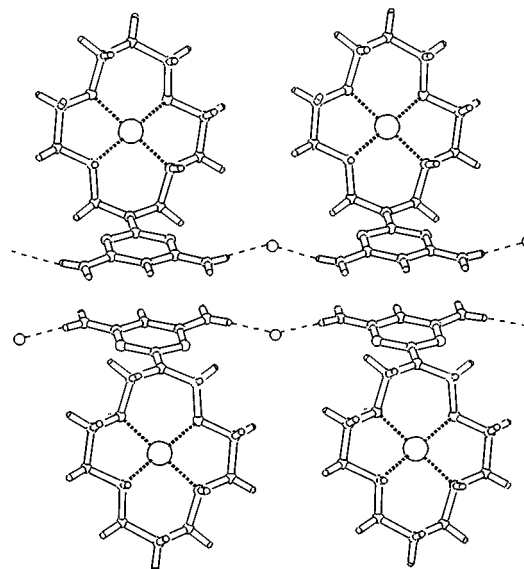
**Figure 1.** View of the [Cu(HL²)]³⁺ cation (30% probability ellipsoids shown).

measured on an Enraf-Nonius CAD4 four-circle diffractometer employing graphite-monochromated Mo K α radiation (0.710 73 Å) and operating in the ω -2 θ scan mode within the range $2 < 2\theta < 50^\circ$. Data reduction and empirical absorption corrections (ψ -scans) were performed with the XTAL²⁰ package. For [Cu(HL²)](ClO₄)₂·2H₂O, 9499 unique reflections were measured of which 4918 were considered observed ($F_o > 2\sigma$), whereas for {[Cu(L³)](ClO₄)₂·H₂O}₂ 3957 reflections were measured of which 2881 were observed.

Structures were solved by heavy-atom methods with SHELXS-86²¹ and refined by full-matrix least-squares analysis with SHELXL-93.²² All non-H atoms were refined with anisotropic thermal parameters, except for disordered O-atoms. These were refined with partial occupancies and isotropic thermal parameters. Noncoordinated water H-atoms were not modeled. Drawings of molecules were produced with the programs PLUTON²³ and PLATON.²⁴ Crystal data are listed in Table 1.

Results

Crystal Structures. The X-ray crystal structural analysis of [Cu(HL²)](ClO₄)₂·2H₂O (Figure 1) revealed the unit cell to contain two independent macrocycles, with the perchlorate anions and water molecules positioned at general sites. Three

**Figure 2.** Molecular tapes of [Cu(HL²)]³⁺.**Table 2.** Selected Bond Lengths (Å) and Angles (deg) for [Cu(HL²)](ClO₄)₃

Cu(1)–N(1)	2.017(11)	C(10)–N(5)	1.37(2)
Cu(1)–N(2)	2.019(11)	C(10)–N(6)	1.33(2)
Cu(1)–N(3)	2.010(10)	C(10)–N(10)	1.31(2)
Cu(1)–N(4)	2.008(10)	C(11)–N(6)	1.33(2)
H(7A)···O(4)	2.06	C(11)–N(7)	1.29(2)
H(7B)···O(32)	2.31	C(11)–N(8)	1.34(2)
H(8)···O(32)	2.23	C(12)–N(8)	1.39(2)
H(8)···O(33)	2.29	C(12)–N(9)	1.29(2)
H(9A)···O(4)	2.14	C(12)–N(10)	1.31(2)
H(9B)···O(33)	2.54		
N(6)–C(10)–N(10)	127.4(12)	C(10)–N(10)–C(12)	118.0(12)
N(8)–C(11)–N(6)	121.0(12)	C(12)–N(8)–C(11)	120.5(11)
N(10)–C(12)–N(8)	118.2(12)	C(11)–N(6)–C(10)	114.7(11)

of the perchlorate anions exhibit disorder about a chlorine–oxygen axis. A melamine ring N-atom was found to be protonated, which is consistent with published structures of protonated melamine and its derivatives.^{25–28} A perchlorate anion is located close to the melamine ring, between the two unbound primary amines, supporting this assignment. H(8) forms hydrogen bonds to two of the oxygen atoms in the perchlorate anion located near the melamine ring. Each of these oxygens also forms a hydrogen bond to a proton on the primary amines, H(9B) and H(7B). The other proton on the primary amine in turn forms a hydrogen bond to a water molecule (Figure 1). The melamine ring is situated perpendicularly to the plane of the macrocyclic ring. Selected bond lengths and angles are shown in Table 2.

This series of hydrogen bonds results in the formation of extended chains along the *a* axis, in which each residue is linked by water molecules (Figure 2). A π – π stacking interaction is also evident in this structure. Melamine rings of two adjacent molecules stack on top of each other, with a distance of 3.47 Å between them. Both independent cations adopt similar H-bonded chains.

The structural analysis of {[Cu(L³)](ClO₄)₂·H₂O}₂ showed the unit cell to contain four dimers, each situated on a 2-fold axis (Figure 3). The pendent ammine groups are again at right angles to the plane of the macrocyclic ring. An interesting feature is the formation of a coordinate bond from the oxygen in the ammine moiety to the copper atom of another molecule,

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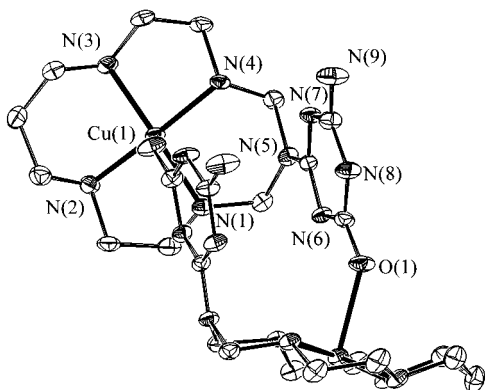


Figure 3. View of the $\{[\text{CuL}^3]\}_2^{4+}$ cation (30% probability ellipsoids shown).

Table 3. Selected Bond Lengths (Å) and Angles (deg) for $\{[\text{CuL}^3](\text{ClO}_4)_2 \cdot \text{H}_2\text{O}\}_2$

Cu(1)–N(1)	2.051(5)	C(11)–N(6)	1.348(8)
Cu(1)–N(2)	2.003(5)	C(11)–N(8)	1.408(9)
Cu(1)–N(3)	2.011(6)	C(11)–O(1)	1.228(8)
Cu(1)–N(4)	2.010(5)	C(12)–N(7)	1.314(9)
C(10)–N(5)	1.356(8)	C(12)–N(8)	1.345(9)
C(10)–N(6)	1.343(8)	C(12)–N(9)	1.320(9)
C(10)–N(7)	1.338(8)	Cu(1)–O(1) ^a	2.288(5)
N(6)–C(10)–N(7)	127.1(6)	C(10)–N(7)–C(12)	115.9(5)
N(7)–C(12)–N(8)	121.8(6)	C(12)–N(8)–C(11)	120.6(5)
N(8)–C(11)–N(6)	118.0(5)	C(11)–N(6)–C(10)	116.4(5)
C(11) ^a –O(1) ^a –Cu(1)	137.3(4)		

^a Symmetry transformation: $-x + 1/2, y, -z + 1/2$

resulting in dimer formation. π – π stacking interactions are also present, with a distance of 3.66 Å between ring faces in the dimers. This interaction may, in part, be responsible for holding the two molecules in place. Selected bond lengths and angles are shown in Table 3.

Physical Properties. Infrared spectroscopy is a good indicator of incorporation of melamine into the macrocyclic ring. Melamine has several very distinctive vibrations, including the region from 3450 to 3125 cm^{-1} , which contains the N–H stretching absorptions. A second region, from 1670 to 1430 cm^{-1} , consists of three or four quite intense signals, corresponding to the in-plane vibrations of the triazine ring. A third distinctive band, due to an out-of-plane motion of the ring, can be found just beyond 830 cm^{-1} .²⁹ All of these are present in the infrared spectrum of $[\text{CuL}^2]^{2+}$, as well as the signals due to the macrocyclic ring e.g. C–H stretches.

The EPR spectrum of $[\text{CuL}^2]^{2+}$, at a concentration of 10 mM, was typical of a Cu^{II} d^9 system, showing two sets of four lines due to hyperfine coupling with the copper nucleus. Simulation yielded the parameters shown in Table 4, where || refers to the alignment of the magnetic field parallel to the z axis, i.e. perpendicular to the macrocyclic plane. The spectra of $[\text{CuL}^2]^{2+}$, $[\text{CuL}^3]^{2+}$, and $[\text{CuL}^4]^{2+}$, at either 1 or 10 mM, were identical. This indicates that all species exist in solution as mononuclear complexes.

The electrochemical reductions of $[\text{CuL}^2]^{2+}$, $[\text{CuL}^3]^{2+}$, and $[\text{CuL}^4]^{2+}$ were all found to be irreversible two-electron processes on a mercury working electrode and occurred at similar potentials (Table 4). The protonation constants of the pendent triazine rings varied quite significantly across the series of compounds reported here. The $\text{p}K_a$ of $[\text{CuL}^2]^{2+}$ was found to be 4.2, which is lower than that of melamine itself (5.35). A lowering of $\text{p}K_a$ values was also noticed for $[\text{CuL}^3]^{2+}$ ($\text{p}K_a$ 8.5,

Table 4. Physical Data

	$[\text{CuL}^2]^{2+}$	$[\text{CuL}^3]^{2+}$	$[\text{CuL}^4]^{2+}$
λ_{max} (nm)	518	514	518
ϵ ($\text{M}^{-1} \text{cm}^{-1}$)	87	95	112
$\text{p}K_a$	4.2	2.4, 8.5	<2.0
g_{\parallel}	2.186	2.186	2.186
g_{\perp}	2.045	2.045	2.045
A_{\parallel} (G)	201	201	201
A_{\perp} (G)	22	22	22
$E_{1/2}$ (mV vs Ag/AgCl)	–760	–720	–780
infrared (cm^{-1})	3439	3383	1738
	3172	3177	1699
	1557	1749	1652
	1489	1648	1586
	1456	1597	
	810		

2.4), compared to ammeline ($\text{p}K_a$ 9.4, 4.5). No $\text{p}K_a$ values could be determined for $[\text{CuL}^4]^{2+}$.

Discussion

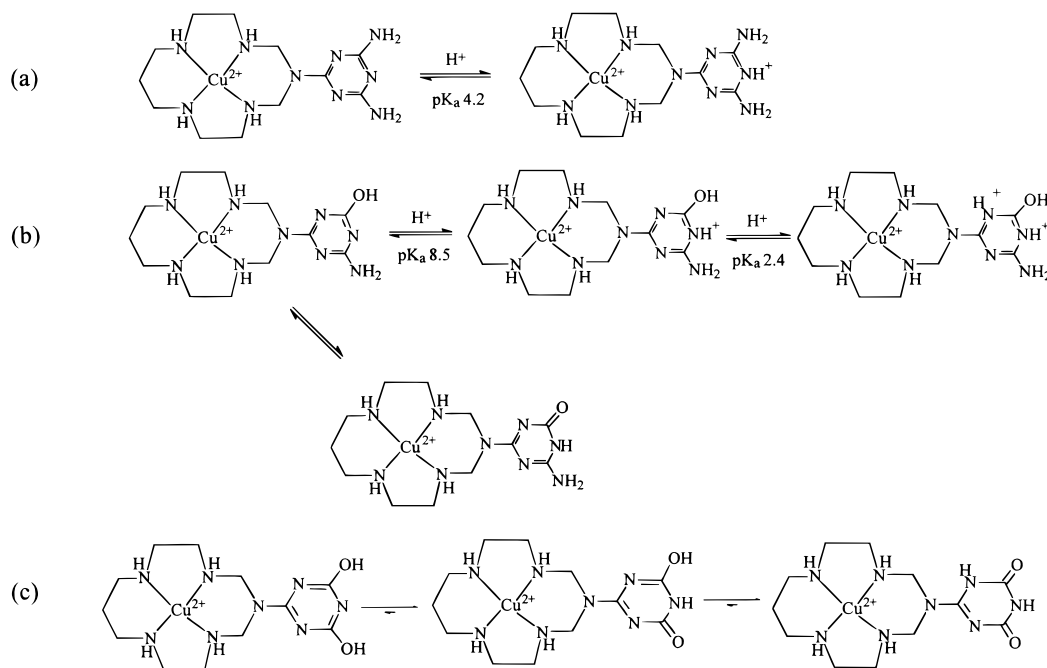
Melamine itself is a planar molecule, which is consistent with its aromaticity. This also accounts for the high thermal stability of the ring.³⁰ Upon protonation, the π -electron density delocalization causes the positive charge to be distributed almost uniformly among the protonated nitrogen and the three primary amines, giving each a partial positive charge and favoring their involvement in hydrogen-bond interactions.²⁸ In the structure of $[\text{Cu}(\text{HL}^2)]^{3+}$, the proton on the ring nitrogen forms a bifurcated hydrogen bond to two of the oxygen atoms in the perchlorate. Each of these forms a hydrogen bond to one of the protons on a primary amine, resulting in a zigzag arrangement. The primary amines also form hydrogen bonds to a water molecule. This series of hydrogen bonds results in the formation of hydrogen-bonded tapes, in which residues are linked by water molecules (see Figure 2). These molecular tapes stack by means of a π – π interaction. The aromatic melamine rings of two chains overlap, with a face-to-face distance of 3.47 Å. This is consistent with other examples of π – π stacking, in which rings are ~ 3.4 Å apart.^{31,32}

The observed crystal structure for the protonated $[\text{Cu}(\text{HL}^2)]^{3+}$ cation suggests that it has considerable potential for hydrogen bonding with other molecules. It represents a hydrogen bond donor–donor–donor (DDD) pattern. The proton can be easily removed ($\text{p}K_a$ 4.2) to leave $[\text{CuL}^2]^{2+}$, which has a donor–acceptor–donor (DAD) hydrogen-bonding face. These properties bode well for control of the assembly and disassembly of possible aggregates. Simple protonation of the ring nitrogen, achievable merely by changing the pH, will lead to a change in D–A pattern, which will disrupt interactions between previously complementary molecules. Thus modifying the pH can lead to the control of aggregate formation.

Ammeline is the first product of the acid hydrolysis of melamine.³³ The template synthesis of the macrocycle produced a complex which was quite similar to $[\text{CuL}^2]^{2+}$ in its physical

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Scheme 1



properties. In this case, however, the assignment of the hydrogen bond donor–acceptor pattern depends on which tautomeric form of the ammeline moiety is present. (Scheme 1b). The enol form of the ammeline ring represents a DAD pattern, similar to that present in the melamine macrocycle. The keto form, on the other hand, has a DAA motif. The difficulty therefore lies in determining whether the ammeline moiety of [CuL³]²⁺ contains either a hydroxyl or a carbonyl group and, of course, whether the dominant tautomer is the same in both the solid state and in solution.

The crystal structure alone indicates that the ammeline ring is present in the keto form. The structure of ammeline itself, in either tautomer, is unknown. However, several structures of ammeline ethers have been reported.³⁴ These exhibit C–O bond lengths in the range 1.320–1.358 Å, which is significantly longer than the bond length in the macrocycle (1.228 Å), which is typical of a C=O bond length. The assignment of the keto form of [CuL³]²⁺ in the solid state is supported by its infrared spectrum, in which a carbonyl peak is observed at 1749 cm⁻¹. This peak is well clear of the triazine/NH₂ region (1670–1430 cm⁻¹). This peak is absent in the spectrum of [CuL²]²⁺.

Although the ammeline ring exists in the keto form in the solid state, the solution behavior appears to be different. The EPR spectrum is characteristic of a mononuclear d⁹ system and is identical to that of [CuL²]²⁺, suggesting that the dimers are not present in solution. The identification of two protonation constants for [CuL³]²⁺ indicates that the more basic enol form plays a major role in the solution structure of this complex (Scheme 1b). The tautomerism of ammeline may also have a bearing on the assembly and disassembly of aggregates such as the dimer identified in the solid-state structure. A change in tautomer changes the hydrogen-bonding pattern and thus disrupts complementary interactions. Factors that traditionally dictate the dominant tautomer, such as temperature, may be able to be used to control aggregate formation.

Ammelide is the second hydrolysis product of melamine. It has chemical properties quite different from those of ammeline, resembling cyanuric acid more in its behavior. It is therefore more likely to favor a diketo tautomeric structure.²⁹ This is important since, once again, the tautomeric form will determine the molecule's hydrogen bonding motif. As can be seen in Scheme 1c, there are actually three possible tautomeric forms of ammelide. A carbonyl peak at 1738 cm⁻¹ in the infrared spectrum, similar to that found for [CuL³](ClO₄)₂·H₂O, is consistent with the diketo form being present. No pK_a values could be determined potentiometrically for [CuL⁴]²⁺, implying that the solution structure is the same as the solid state. This supports the assignment of the more acidic diketo tautomer in solution as well as in the solid state.

Cocrystallization. The process of cocrystallization is a delicate one that is dependent upon many factors. An important starting point is to choose appropriate complementary subunits, to direct the self-assembly process. The melamine macrocycle, [CuL²]²⁺, on which cocrystallization studies were centered, presents a DAD face, in which the primary amine groups act as hydrogen bond donors and the ring nitrogen acts as a hydrogen bond acceptor. The other two ring nitrogens are unable to engage in hydrogen bonding due to the steric constraints of the nearby macrocyclic ring. It is expected that the melamine macrocycle would cocrystallize with such molecules as cyanuric acid and barbituric acid, which both represent ADA motifs. Cocrystals of the type ADA–DAD should therefore result. These molecules actually present several possible faces for hydrogen bonding, and could therefore form adducts of varying stoichiometries. For example, cyanuric acid could cocrystallize with up to three molecules of [CuL²]²⁺.

The cocrystallization of [CuL²]²⁺ with barbituric acid was successful, with microanalysis and infrared spectroscopy consistent with the formation of a 1:1 adduct. Crystals were obtained by vapor diffusion of hexane into an acetonitrile solution containing a ratio of 2:1 [CuL²]²⁺ to barbituric acid. These crystals were not of X-ray quality but exhibited properties distinct from a simple mixture of the two compounds. The infrared spectrum clearly shows peaks belonging to both the

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melamine macrocycle and the barbituric acid group. Most notable of these is a cluster of quite intense peaks at around 1700 cm^{-1} , which can be attributed to the carbonyl groups of barbituric acid. These are at slightly lower wavenumber than in barbituric acid itself, where they occur at about $1770\text{--}1716\text{ cm}^{-1}$. This shift could be attributed to hydrogen-bonding effects, since hydrogen bonding to a carbonyl group causes a shift to lower frequency by $40\text{--}60\text{ cm}^{-1}$. Similarly, the N–H stretching frequencies suggest the presence of hydrogen bonding. These signals usually occur in the region $3500\text{--}3400\text{ cm}^{-1}$ but are lowered upon hydrogen bonding by about 150 cm^{-1} . The broad nature of these bands indicates strong hydrogen-bonding interactions.³⁵

An interesting aspect of this result is that despite the fact that $[\text{CuL}^2]^{2+}$ and barbituric acid were present in the ratio of 2:1, only a 1:1 adduct formed. Barbituric acid has two ADA faces, which would prove complementary to the melamine moiety. However, many factors may conspire against the formation of such an array. For example, steric effects are quite important, and considering the nonplanarity of the $[\text{CuL}^2]^{2+}$ cation, interactions between the macrocyclic rings in a 2:1 aggregate may be unfavorable. The lower solubility of barbituric acid may also prevent the formation of aggregates of greater stoichiometry.

Conclusions

Template syntheses of 14-membered macrocyclic copper complexes were devised, in which 1,3,5-triazines were used as

locking fragments. The crystal structures of $[\text{Cu}(\text{HL}^2)]^{3+}$ and $[\text{CuL}^3]^{2+}$ both revealed noncovalent interactions to be important in network design. Both structures showed $\pi\text{--}\pi$ stacking, and the structure of $[\text{Cu}(\text{HL}^2)]^{3+}$ also showed extensive hydrogen bonding between the melamine group, perchlorate anions, and water molecules. The tautomeric forms of $[\text{CuL}^3]^{2+}$ and $[\text{CuL}^4]^{2+}$ were determined, to assign the molecules' hydrogen-bonding motifs. Both $[\text{CuL}^3]^{2+}$ and $[\text{CuL}^4]^{2+}$ were found to exist in the keto form in the solid state. These molecules, along with $[\text{CuL}^2]^{2+}$, contain different hydrogen bond donor–acceptor patterns and as such represent useful components for noncovalent self-assembly. Solid-state studies on association revealed the formation of a 1:1 $[\text{CuL}^2]^{2+}$ –barbituric acid adduct.

Future investigations will involve cocrystallization and association of the compounds reported here in both the solid state and in solution.

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Supporting Information Available: Crystallographic data, in CIF format, are available on the Internet only. Access information is given on any current masthead page.

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