Articles

Structurally Reinforced Tetraazamacrocyclic Complexes

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The reaction between alkyl or aryl aldehydes and macrocyclic ligands with pendant amine groups produced imidazolidine-containing bi- or tricyclic ligands. The copper complexes of three of these ligands were structurally characterized: $[CuL^3Cl]\cdot 3H_2O$ (triclinic, $P\bar{1}$, $a = 10.041(2)$ Å, $b = 10.172(1)$ Å, $c = 11.202(1)$ Å, $\alpha = 92.07(1)°$, $\beta = 96.76(2)°$, $\gamma = 92.99(1)°$, $Z = 2$), $[Cu(H_2L^4)Cl]Cl\cdot 2H_2O$ (monoclinic, $P2_1/n$, $a = 15.159(5)$ Å, $b = 10.645(1)$ Å, $c = 19.094(6)$ Å, $\beta = 93.78(1)°$, $Z = 4$), $[CuL^5]\cdot 2H_2O\cdot NaNO_3$ (monoclinic, $P2_1/n$, $a = 10.649(8)$ Å, $b = 7.261(2)$ Å, $c = 15.25(1)$ Å, $\beta = 94.77(4)°$, $Z = 2$). The conformational rigidity and stereochemical activity of these macrocycles and their complexes are discussed in comparison with close analogues.

Introduction

Our group has reported previously the synthesis of structurally reinforced tetraazamacrocyclic ligands containing fused imidazolidine rings, by the reaction of the diamino-substituted macrocyclic complex $[CuL^2]^{2+}$ with formaldehyde in aqueous solution.[1] This reaction involves an intramolecular cyclization of the uncoordinated pendent amine and an adjacent coordinated secondary amine, leading to both tri- (L^6) and tetracyclic products (L^7) (Chart 1). At the time, we noted that incorporation of methylene links between the pendent amine the coordinated secondary amine resulted in a ligand with greatly reduced conformational flexibility, and the physical properties of the resulting Cu^{II} complexes differed significantly from those of the parent macrocyclic complexes. This is a consequence of both alkylation of a secondary amine, which is known to significantly affect the donor capacity of the amine, and steric constraints imposed by the fused five-membered ring. This reaction offers a new route toward functionalized ligands by employing aldehydes (other than formaldehyde) with active groups, that may become incorporated into the macrocycle. In addition, bridging the pendent amines of either L^1 or L^2 to an adjacent secondary amine via an aminal link locks the pendent group in a predetermined and stereochemically rigid conformation.

We report now the metal-free synthesis of further examples of this class of modified ligands, where substituents are attached to the aminal carbon, by reaction of L^1 and L^2 with both alkyl and aryl aldehydes. These imidazolidines are stereochemically active and are of pharmacological interest as α-adrenergic receptor agonists.[2] There is also interest in their use in synthesis as *N*,*N*′-bisacylimidazolidines.[3,4] There are several examples of imidazolidine-containing complexes in the literature,[5] mostly involving salicylaldehyde or similar aldehydes. These cyclic aminals are considered to be relatively stable, though they can be readily hydrolyzed by aqueous acids.[6] This work describes the synthesis and isolation of three macropolycyclic complexes, $[CuL^3Cl]^+$, $[Cu(H_2L^4)Cl]^+$, and $[CuL^5]$, which have been characterized both spectroscopically and by crystal structure analyses. Some anomalous trends in their visible and electron spin resonance spectroscopy are discussed, as well as the exceptional stability of $[CuL^5]$. We are unaware of any examples of structural characterization of imidazolidines derived from glyoxylic acid (HO_2CCHO), and thus this paper presents the first structurally characterized example of this class of imidazolidines.

Experimental Section

6-Methyl-1,4,8,11-tetraazacyclotetradecane-6-amine pentahydrochloride ($L^1\cdot 5HCl$) and *trans*-6,13-dimethyl-1,4,8,11-tetraazacyclotetradecane-6,13-diamine hexahydrochloride ($L^2\cdot 6HCl$) were prepared as previously described.[7,8] Glyoxylic acid monohydrate was washed with

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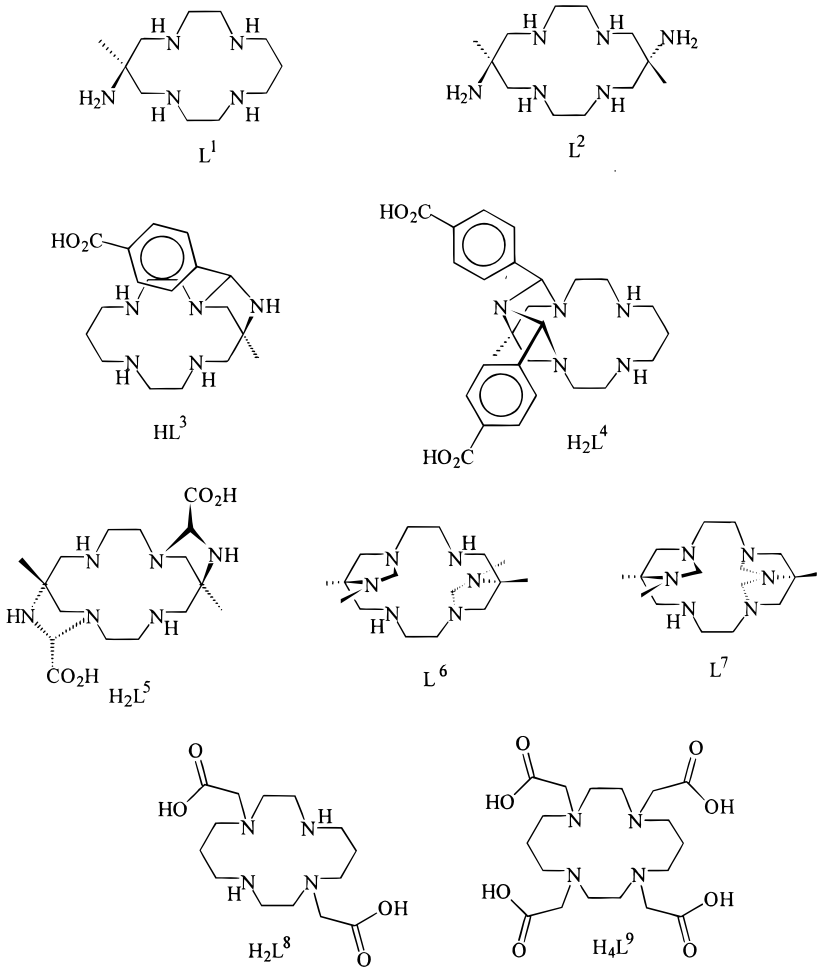
Chart 1



diethyl ether and filtered before use. All other chemicals were obtained commercially and used without further purification.

L^1·5HCl (2.0 g) was suspended in 100 cm^3 of absolute EtOH. Triethylamine (2.45 g, 5 equiv) was added and the solution stirred until all of the ligand hydrochloride had dissolved. 4-Carboxybenzaldehyde (0.73 g, 1 equiv) was added, followed by 5 g of $MgSO_4$ (anhydrous), and the solution was refluxed for 4 h. In an initial experiment, the solution was cooled to room temperature and 1.7 g of $NaBH_4$ was added portionwise. In later experiments, the $NaBH_4$ was omitted with no effect on the final yield of products. An excess of $Cu(NO_3)_2$·$2.5H_2O$ (1.50 g) was added, and the solution was stirred. The solution was filtered to remove $MgSO_4$, and triethylamine was removed from the filtrate by rotary evaporation. The solution was diluted with water to 5 L and applied to a Sephadex cation exchange column (Na^+ form). A pink-colored solution was not retained by the column upon water being added (band 1), but was not present in sufficient quantity to allow isolation of a solid. A solution of 0.2 M NaCl adjusted to pH 8 with Na_2CO_3 was applied to the column, and two bands rapidly eluted using this solution (bands 2 and 3). A fourth band was slower to elute and was found to be unreacted $[CuL^1]^{2+}$. A compound precipitated on the column but eluted with 0.2 M NaCl/5% acetic acid (band 5).

The summary of the column chromatography is as follows.

Band 1: minor band, charge-neutral, λ_{max} 515 nm.

Band 2: minor band, λ_{max} 513 nm.

Band 3: major band, λ_{max} 507 nm, $[CuL^3]^+$ (32% of total complexed Cu^{II}).

Band 4: major band, λ_{max} 510 nm, $[CuL^1]^{2+}$ (14% of total complexed Cu^{II}).

Band 5: major band, λ_{max} 537 nm, $[Cu(H_2L^4)]^{2+}$ (54% of total complexed Cu^{II})

The products from bands 1 and 2 were not identified.

$[CuL^3Cl]$·$3H_2O$. Band 3 was concentrated on a rotary evaporator; then slow evaporation afforded dark purple crystals suitable for X-ray diffraction. (Found: C, 44.68; H, 7.20; N, 13.55. Calcd for $C_{19}H_{40}ClCuN_5O_5$: C, 44.09; H, 7.79; N, 13.53.) UV/vis: λ_{max}, nm (ϵ, L mol^{-1} cm^{-1}) 507 (144), 231 (13 900), shoulder 272 (9480).

HL^3. Ca. 0.05 g of $[CuL^3Cl]$·$3H_2O$ was dissolved in 0.75 cm^3 of D_2O. Na_2S·$9H_2O$ was added in small portions until the solution was no longer purple. The solution was filtered to remove precipitated CuS, and the filtrate was used directly for NMR measurements. NMR (D_2O): ^1H, δ 1.25 (s, 3H, Me); 1.76 (mult, 2H), 2.15−2.80 (mult, 15H including AB doublet at 2.30 ppm), 3.39 (AB doublet, 1H) 4.20 (s, 1H), 4.80 (HDO), 7.55−7.92 (AA′BB′, 4H). ^{13}C: 25.38 (CH_3), 27.76 ($CH_2CH_2CH_2$), 46.58, 47.35, 47.74, 48.82, 48.92, 49.23, 57.39 ($HNCH_2C$−), 59.57 (quaternary C), 61.67 (−CH_2− imidazolidine ring), 81.97 (HNCHRN), 127.65, 129.27, 141.28 (Ar *C*), 148.78 (Ar CCO_2H), 180.65 (CO_2H).

$[Cu(H_2L^4)Cl]Cl$·$2H_2O$. The eluate from band 4 was concentrated to ca. 100 cm^3, and purple crystals, which formed overnight, were collected by filtration. (Found: C, 48.39; H, 6.02; N, 10.02. Calcd for $C_{27}H_{35}Cl_2CuN_5O_4$·$2.5H_2O$: C, 48.18; H, 5.99; N, 10.40.) UV/vis: (pH 1.6): λ_{max}, nm (ϵ, L mol^{-1} cm^{-1}) 535 (264), 280 (15 200), 233 (25 600). (The visible spectrum was recorded in a solution of pH 1.60, by addition of 1 M HCl to a suspension of the complex. The compound is sparingly soluble in neutral or basic aqueous solution.) $[Cu(H_2L^4)Cl]Cl$·$2H_2O$ could not be demetalated using Na_2S·$9H_2O$, because of the formation of an insoluble sulfide salt of the complex.

$[CuL^5]$·$2H_2O$·$NaNO_3$. A procedure analogous to that described above was used for the reaction of L^1 and glyoxylic acid monohydrate. $Cu(NO_3)_2$·$2.5H_2O$ was added to the reaction mixture, the solution filtered, and the filtrate diluted to ca. 5 L. The solution was applied to a Sephadex cation exchange column (Na^+ form). A blue solution (λ_{max}

Table 1. Crystal Data

	$[CuL^3Cl]\cdot 3H_2O$	$[Cu(H_2L^4)Cl]Cl\cdot 2H_2O$	$[CuL^5]\cdot 2H_2O\cdot NaNO_3$
space group	$P\bar{1}$ (No. 2)	$P2_1/n$ (No. 14)	$P2_1/n$ (No. 14)
formula	$C_{19}H_{36}ClCuN_5O_5$	$C_{27}H_{42}Cl_2CuN_5O_6$	$C_{16}H_{32}CuN_7NaO_9$
a, Å	10.041(2)	15.159(5)	10.649(8)
b, Å	10.172(1)	10.645(1)	7.261(2)
c, Å	11.202(1)	19.094(6)	15.25(1)
α, deg	92.07(1)		
β, deg	96.76(2)	93.78(1)	94.77(4)
γ, deg	92.99(1)		
V, Å^3	1133.6(3)	3074.4(1)	1175(1)
ρ_{calc}, g cm^{-3}	1.504	1.435	1.563
fw	513.52	664.07	553.02
Z	2	4	2
μ, cm^{-1}	11.22	9.32	10.09
temp, K	293	293	293
λ, Å	0.710 73	0.710 73	0.710 73
N	3976	5379	2075
N_0 ($F > 2\sigma$)	3283	3356	1606
$2\theta_{max}$, deg	50	50	50
$R(F_o)$, wR2(F_o^2)[a]	0.0805, 0.1956	0.0403, 0.1046	0.0652, 0.1675

[a] $R(F_o) = \sum||F_o| - |F_c||/(\sum|F_o|)$. $wR2(F_o^2) = [\sum w(F_o^2 - F_c^2)/(\sum wF_o^2)]^{1/2}$. $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$. $P = {}^1/_3\max(F_o^2,0) + {}^2/_3F_c^2$.

557 nm) was not retained by the column and was collected by washing the column with water. The solution was concentrated on the rotary evaporator, and slow evaporation over a period of several weeks led to the formation of X-ray quality crystals, of a deep purple color. Later crops afforded a purple powder (yield 25%). (Found: C, 32.22; H, 6.24; N, 13.93. Calcd for $C_{16}H_{28}CuN_6O_4\cdot 6H_2O\cdot NaCl$: C, 32.11; H, 6.74; N, 14.04.) UV/vis: λ_{max}, nm (ϵ, L mol^{-1} cm^{-1}) 544 (79), 263 (7900).

Physical Methods. Solution UV/vis spectra were measured on a Beckman DU 7500 spectrometer. Nuclear magnetic resonance (NMR) spectra were measured at 200 (^{1}H) and 50.3 MHz (^{13}C) on a Bruker AC200 spectrometer. Spectra were referenced with tetradeuterated sodium trimethylsilylpropionate (TSP) or 1,4-dioxane (^{13}C), and all chemical shifts are cited versus trimethylsilane. EPR spectra of all Cu^{II} complexes were measured on a Bruker ER200 D spectrometer as frozen 1 mM solutions (1:2 DMF:water, 77 K), except for the sparingly soluble $[Cu(H_2L^4)Cl]Cl\cdot 2H_2O$, where a saturated solution was used, with an increased gain and number of scans. Spin Hamiltonian parameters were obtained by spectral simulation.[9]

X-ray Crystal Structure Analyses. Intensity data for the compounds were measured on an Enraf-Nonius CAD4 four-circle diffractometer using graphite-monochromated Mo Kα radiation (λ 0.710 73 Å) in the $\omega-2\theta$ scan mode. Lattice dimensions were determined by a least-squares fit of the setting parameters of 25 independent reflections. Data reduction and empirical absorption corrections were performed with the XTAL package.[10] No absorption correction was applied to the data for $[CuL^3Cl]\cdot 3H_2O$. Structures were solved by heavy-atom methods with SHELXS-86[11] and refined by full-matrix least-squares analysis with SHELXL97.[12] All non-H atoms were refined with anisotropic thermal parameters. Crystallographic data are given in Table 1 and selected bond lengths appear in Tables 2−4. The atomic nomenclature is defined in Figures 1−3, drawn with the graphics program PLATON.[13]

Results and Discussion

There is considerable interest in the modification of polyazamacrocyclic ligands for their use in chemical sensing, pharmaceutical applications, and their attachment to biological molecules. Consideration of these approaches shows that theyrely generally upon the N-substitution of expensive parent macrocycles, often requiring selective protection and deprotection regimes. It is for these reasons that we have begun to investigate the modification of the macrocyclic ligands L^1 and L^2, formed by inexpensive metal template reactions. It was

Table 2. Selected Bond Lengths (Å) and Angles (deg) for $[CuL^3Cl]\cdot 3H_2O$

Cu(1)−N(1)	2.006(4)	Cu(1)−N(4)	2.065(4)
Cu(1)−N(3)	2.026(4)	Cu(1)−Cl(1)	2.603(1)
Cu(1)−N(2)	2.040(4)		
N(1)−Cu(1)−N(3)	170.9(1)	N(2)−Cu(1)−N(4)	172.0(1)
N(1)−Cu(1)−N(2)	84.9(2)	N(1)−Cu(1)−Cl(1)	97.1(1)
N(3)−Cu(1)−N(2)	94.5(2)	N(3)−Cu(1)−Cl(1)	92.0(1)
N(1)−Cu(1)−N(4)	93.6(2)	N(2)−Cu(1)−Cl(1)	90.4(1)
N(3)−Cu(1)−N(4)	85.8(2)	N(4)−Cu(1)−Cl(1)	97.5(1)

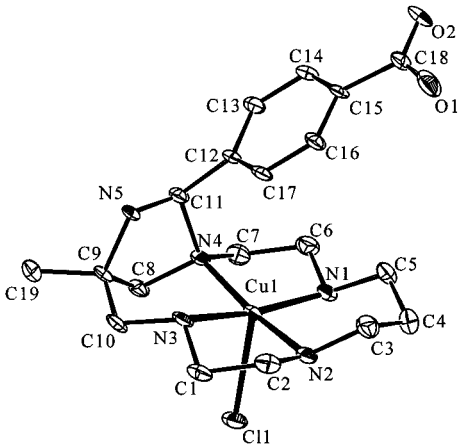


Figure 1. Drawing of $[CuL^3Cl]$; 30% probability ellipsoids shown. H atoms and solvent molecules have been omitted for clarity.

Table 3. Selected Bond Lengths (Å) and Angles (deg) for $[Cu(H_2L^4)Cl]Cl\cdot 2H_2O$

Cu(1)−N(4)	2.009(3)	Cu(1)−N(2)	2.066(3)
Cu(1)−N(3)	2.016(3)	Cu(1)−Cl(1)	2.603(1)
Cu(1)−N(1)	2.053(3)		
N(4)−Cu(1)−N(3)	97.2(1)	N(1)−Cu(1)−N(2)	90.6(1)
N(4)−Cu(1)−N(1)	85.5(1)	N(4)−Cu(1)−Cl(1)	96.4(1)
N(3)−Cu(1)−N(1)	170.0(1)	N(3)−Cu(1)−Cl(1)	86.8(1)
N(4)−Cu(1)−N(2)	170.3(1)	N(1)−Cu(1)−Cl(1)	102.55(9)
N(3)−Cu(1)−N(2)	85.3(1)	N(2)−Cu(1)−Cl(1)	93.17(9)

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Table 4. Selected Bond Lengths (Å) and Angles (deg) for $[CuL^5]\cdot 2H_2O\cdot NaNO_3$

Cu(1)−N(2)	2.025(4)	Cu(1)−O(1)	2.339(4)
Cu(1)−N(1)	2.032(4)	N(1)−C(5)	1.469(6)
N(1)−Cu(1)−N(2)	86.5(2)	N(1)−Cu(1)−O(1)	79.2(1)
N(2)−Cu(1)−O(1)	91.8(2)		

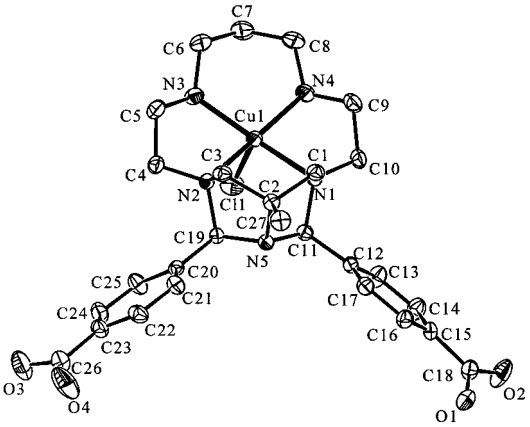


Figure 2. Drawing of $[Cu(H_2L^4)Cl]^+$; 30% probability ellipsoids shown. H atoms and solvent molecules have been omitted for clarity.

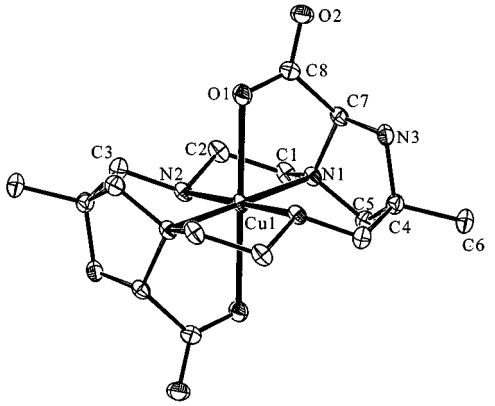


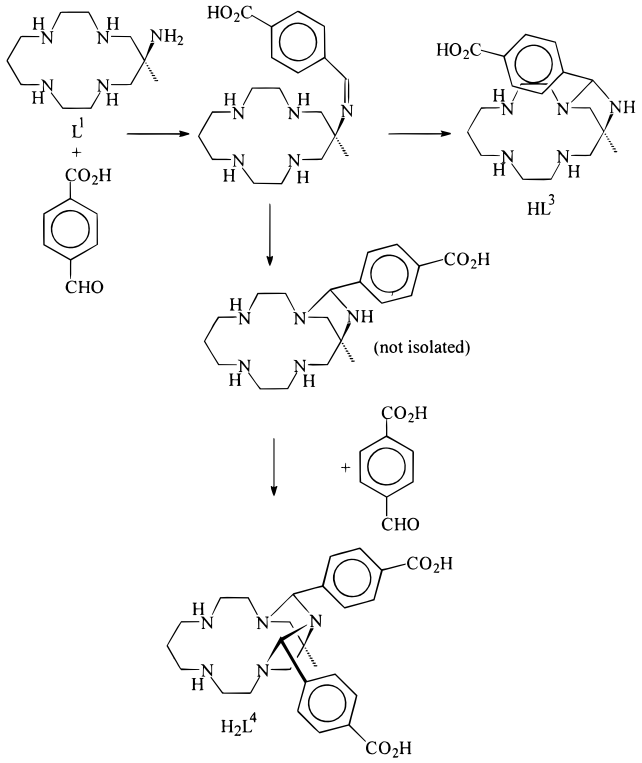
Figure 3. Drawing of $[CuL^5]$; 30% probability ellipsoids shown. H atoms and solvent molecules have been omitted for clarity.

hoped that the primary amine or amines of these ligands would be capable of being modified specifically by reductive alkylation using aldehydes, which would provide suitable functional groups for possible further derivatization.

The reaction of 4-carboxybenzaldehyde with L^1 proceeded readily in ethanol solution, but in situ reduction of the imine intermediate using sodium borohydride did not occur. The major product isolated was not the 4-carboxybenzylated ligand, but instead the imine intermediate underwent intramolecular condensation with one of the secondary amines of the macrocyclic ring, as shown in Scheme 1, to form HL^3. Indeed an additional product was identified where two imidazolidine rings had formed, H_2L^4, despite the aldehyde and L^1 being reacted in a 1:1 ratio. Analogous reactions were seen when $[CuL^2]^{2+}$ was reacted with aqueous formaldehyde.[1] In the present instance, imidazolidine complexes are not formed when these less reactive substituted aldehydes are reacted with the copper complexes of L^1 or L^2.

The crystal structure of $[CuL^3Cl]\cdot 3H_2O$ (Figure 1) revealed a square pyramidal coordination geometry, with one chloro and four nitrogen donors. Selected bond lengths and angles appear in Table 2. There are significant differences in the four Cu−N bond distances. As expected, the tertiary amine Cu−N(4) distance is the longest of the four. The distortion induced by

Scheme 1



the presence of the imidazolidine ring is reflected in the N−Cu−N bond angles. N(1)−Cu−N(3) has an angle of 170.7°. The remaining nitrogen, N(5), is precluded from binding to the metal center by the rigid nature of the five-membered imidazolidine ring. The Cu atom is displaced 0.152 Å from the least-squares plane defined by the four nitrogen donors, in the direction of the axial ligand. The chloro ligand completes the coordination sphere by forming a bond to the metal at a distance of 2.603(1) Å. In the imidazolidine ring, the C−N bond further away from the metal is shorter (1.447(6) Å as compared to 1.506(5) Å). This has been observed previously in other macrocyclic systems possessing an N−C−N group.[14,15] The configuration of the aminal carbon is such as to have the 4-carboxybenzyl group positioned over the macrocyclic ring, blocking access to the remaining axial site of the metal. The Cu−H(17) distance is 2.74(1) Å.

The ^{1}H NMR spectrum of the demetalated macrocycle $(L^3)^-$ (as its Na^+ salt) shows the expected AB pattern from the methylene group in the five-membered imidazolidine ring. One part of the resulting AB coupling pattern is seen at 3.39 ppm, and the other is at 2.30 ppm. A singlet is observed at 4.20 ppm, due to the hydrogen attached to the aminal tertiary carbon. The ^{13}C NMR spectrum shows the asymmetry of the macrocycle, 12 resonances being seen in the alkyl region of the spectrum (90 to 0 ppm) whereas only 8 would be expected for the macrocycle alkylated only at the pendent nitrogen atom. The resonance at 81.9 ppm is characteristic of an aminal carbon, which is expected to fall in the range 70−80 ppm.[16] Importantly, no decomposition of the metal free ligand was found over a period of several weeks.

The crystal structure of $[Cu(H_2L^4)Cl]Cl\cdot 2H_2O$ (Figure 2) shares a number of features common with that of $[CuL^3Cl]\cdot$

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Table 5. Spectroscopic Parameters for Copper Complexes of Imidazolidine-Containing and Other Tetraazamacrocycles

complex	$g_{\|\|}$	$A_{\|\|}$ (G)	$g_{\perp}$	$A_{\perp}$ (G)	λ_{max} (ϵ L mol^{-1} cm^{-1})	ref
[CuL^{3}Cl]	2.172	201.0	2.037	23.8	507 (144)	this work
[Cu(H$_2$L^4)Cl]$^+$	2.192	188.0	2.0375	23.84	535 (264)	this work
[CuL^5]	2.192	188.0	2.0375	23.84	544 (66.7)	this work
[Cu(cyclam)]$^{2+}$	2.186	199.7	2.049	39.80	513 (100)	23, 24
[Cu(Me$_4$cyclam)$^{2+}$	2.240	154.1	2.072	51.67	650 (275)	25

3H$_2$O. Again, the metal atom is five-coordinate, with a N$_4$Cl coordination sphere. There is less distortion of the macrocyclic ring due to the more symmetrical nature of the macrocyclic ligand, with the Cu−N distances separating into two pairs; the tertiary amines forming bonds approximately 0.04 Å longer than those of the secondary amines. The chloro ligand occupies an axial site, at a distance from the copper slightly longer than that observed in [CuL^{3}Cl]·3H$_2$O. The copper atom is displaced 0.166 Å from the least-squares plane defined by the four nitrogen donors toward the chloro ligand. This is a slightly larger distance than for the complex containing only one imidazolidine ring. The presence of the two five-membered rings (with N(5) being common to both rings) precludes coordination in the remaining axial site. The configurations of the aminal carbons (C(11) and C(19)) lead to 4-carboxybenzyl groups that point away from the macrocyclic ring. Both carboxyl groups are protonated.

The synthesis was also extended to the reaction of glyoxylic acid with the diamino-substituted macrocycle L^2. The close approach of the phenyl ring to the metal atom in [CuL^{3}Cl] suggested the design of a ligand where the close proximity of a functional group could force coordination in the axial site of a metal. Reaction of glyoxylic acid with L^2 proceeded to give H$_2$L^5 as the major product, even when the aldehyde was reacted with the ligand in a 1:1 ratio. The product was isolated as its copper complex, using cation exchange chromatography to separate the neutral copper complex from charged byproducts and starting material.

The crystal structure of [CuL^5]·2H$_2$O·NaNO$_3$ reveals a centrosymmetric complex (Figure 3). The complex has a tetragonally elongated octahedral structure, with a coordination sphere consisting of pairs of symmetry-related secondary amines, tertiary amines, and carboxylate oxygens. The nitrogen atoms occupy the equatorial plane, with the coordinated carboxylate oxygens occupying the two axial sites. The four Cu−N bond lengths are the same within experimental error. Both carboxylate groups are forced to coordinate because of the configuration of the tertiary C atoms, which places them in close proximity of the metal. The Cu−O distance is within the range expected for axially bound carboxylates (2.30−2.40 Å).[17] For comparison, the analogous distance in [CuL^8] (H$_2$L^8 = 1,4,8,11-tetraazacyclotetradecane-1,8-diacetic acid) is slightly shorter at 2.263 Å.[18] The Cu−O distances in [CuL^9]$^{2-}$ (H$_4$L^9 = 1,4,8,11-tetraazacyclotetradecane-*N*,*N*′,*N*″,*N*‴-tetraacetic acid), which shares the distorted *trans*-octahedral geometry, are 2.302(5) and 2.278(6) Å.[19] The coordinated O atoms are laterally displaced from axial coordination sites, the angle N(1)−Cu−O(1) of 79.2° illustrating this. This feature is also observed in the copper complex of (L^8)$^{2-}$. The two aminal N−C bonds (N(1)−C(7) and N(5)−C(7)) are of the same length within experimental error, whereas it has usually been observed that the bond further from the metal is slightly shorter.

The red-shifted visible absorption maximum of [CuL^5] (544 nm), compared to [CuL^1]$^{2+}$ (510 nm), is evidence for retention of the solid-state coordination sphere in solution. The extreme resistance of [CuL^5] to demetalation using Na$_2$S provides further evidence for this, the complex being stable for several weeks. Indeed, for the metal to be released from the center of the macrocycle, it would first be necessary to hydrolyze one of the imidazolidine rings. This is hindered by coordination of the tertiary amine, which lessens its reactivity. The pendent amines are unable to bind to the central metal because of the rigid five-membered ring. The 1,8 disubstitution pattern of the secondary amines in cyclam and its analogues (cyclam = 1,4,8,11-tetraazacyclotetradecane) is more commonly observed than 1,4 or 1,11 patterns.[20,21]

It is generally possible to relate the degree of distortion of the CuN$_4$ chromophore to parameters derived from the electron paramagnetic resonance (EPR) spectrum. The molecular g values and hyperfine constants are related to the energies of the d−d electronic transitions.[22] A weaker ligand field is consistent with larger $g_{\|\|}$ and smaller $A_{\|\|}$ values. This is demonstrated quite clearly for the tetracyclic [Cu(H$_2$L^4)Cl]$^+$ by $g_{\|\|}$ and $A_{\|\|}$ values which differ significantly from those of related complexes not containing imidazolidine rings (Table 5). The complex containing only one imidazolidine ring represents an interesting situation. The $g_{\|\|}$ value of 2.172 is smaller than that obtained for the unsubstituted analogue [Cu(cyclam)]$^{2+}$ (cyclam = 1,4,8,11-tetraazacyclotetradecane), which implies a stronger ligand field. The $A_{\|\|}$ values are comparable to those of the nonalkylated tetraazamacrocyclic complexes. For comparison, the values for the copper complexes of cyclam[23,24] and *N*,*N*′,*N*″,*N*‴-tetramethylcyclam[25] have also been placed in the table.

The visible maxima of these imidazolidine-containing Cu(II) complexes bear no clear relationship to the degree of alkylation. This is consistent with the EPR parameters. Generally, the visible maxima of complexes shift to longer wavelength as the number of tertiary amine donors increases. However, the extinction coefficients for the visible maxima of these complexes do increase by ca. 60 L mol^{-1} cm^{-1} for every additional imidazolidine ring.

Conclusions. Our previous work with 2-unsubstituted imidazolidines has been extended to the preparation of macrocyclic complexes where the imidazolidine ring contains either aryl or other substituents attached to the aminal carbon. In the case of aryl substituents, the large substituent groups block access to one of the axial sites on the metal, resulting in 5-coordinate

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square-pyramidal complexes. The formation of five-membered rings with an attached carboxylic acid group results in an extremely stable Cu(II) complex.

These results show that the introduction of fused, five-membered imidazolidine rings into preexisting macrocycles such as L^1 and L^2 offers a stable, stereochemically rigid and active pendent group attached to the ligand. The benefits of preorganizing the orientation of the pendent group attached to macrocyclic ligand framework are many. In complexes of all ligands reported in this work, the binding mode and disposition of the active pendent ligands are fixed. This is important if communication between the metal ion within the macrocyclic ring and pendent group is sought, which of course will be distance-dependent. To this end we are currently pursuing compounds similar to those reported herein with photoactive and metal ion receptor groups, where effective through-space interaction between the pendent group and the metal ion in the macrocyclic ligand is crucial.

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Supporting Information Available: Full crystal and refinement data, tables of thermal parameters, H-atom positional parameters, bond lengths and angles and unit cell diagrams. This material is available free of charge via the Internet at http://pubs.acs.org.

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