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Bispidine Copper(II) Compounds: Effects of the Rigid Ligand Backbone

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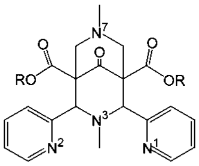
Approximative density-functional theory calculations indicate that the tetradentate ligand L (L = 2,4-bis-(2-pyridyl)-3,7-diaza-[3.3.1]-bicyclononane) enforces an unusual and strong binding of a co-ligand (substrate) to a copper(II) center. The co-ligand in $[Cu(L)(Cl)]^+$ completes a square-pyramidal coordination around copper(II) and binds in the equatorial plane rather than on the apical position. This configuration is a stable geometric isomer for the model complex $[Cu(NH_3)_2(imine)_2(Cl)]^+$, but it is disfavored by approximately 10 kJ mol^{-1} and not commonly observed for CuN_4 chromophores with a monodentate co-ligand. The equatorial coordination increases the bond energy of the copper(II)−chloride bond by approximately 80 kJ mol^{-1}, and similar results are expected for other copper(II)−L-substrate complexes, some of which show strong catalytic activity or unusual stability. Despite the enforced configuration, L does not impose significant steric strain on the copper(II) center but is well preorganized for the Jahn−Teller labile ion in this unusual geometry. The preorganization extends to the orientation of the pyridine donors (torsion angle around the copper−pyridine bond), and this seems to be of importance in the reactivity of the copper−L complexes and their derivatives.

Introduction

The enforcing of a specific coordination geometry by ligands may lead to transition-metal compounds with predictable and interesting properties, i.e., unusual spectroscopic or electrochemical properties due to the stabilization or destabilization of ground and/or excited states, catalytic activity due to the energization of a substrate by a complex fragment (entatic state[1,2]), and metal-ion selectivity by the favoring or disfavoring of the binding modes preferred by specific metal ions (ligand preorganization).[3]

Ligand-enforced coordination geometries, preorganization, and entasis are not mutually exclusive and may all be related to a match or mismatch between the size and shape of a ligand cavity and the metal-ion requirement (note that stabilization by preorganization is generally related to thermodynamics while entasis is originally defined for kinetics).[1,2,4,5] There are long and controversial arguments on the entatic state hypothesis,[1,2,4] in particular with respect to blue copper proteins.[6−8] The focal point is the question whether the trigonal-pyramidal copper(II) geometry with a cysteinate and two histidine donors, in plane with the metal center, and an axial methionine is enforced by the protein backbone or whether this is preferred by the metal center. The exciting result, relevant to the present study, is that the protein induces little strain to the copper(II) site in cupredoxines.[9,10]

Chart 1



Bis-pyridine-substituted bispidines L (L = 2,4-bis-(2-pyridyl)-3,7-diaza-[3.3.1]-bicyclononane) (see Chart 1 for the ligand backbone) are known to be rigid ligands, with structures well suited for square-pyramidal or distorted-octahedral complexes. They enforce axially elongated structures with N3 (see Chart 1 for the numbering scheme), the two pyridine groups and a substrate trans to N3 in the equatorial plane, and N7, as well as a potential sixth ligand defining the axial positions.[11−15] Therefore, L is well preorganized for Jahn−Teller active ions such as copper(II); the role of the Jahn−Teller effect in the stereocontrol of copper(II) complexes has been studied extensively.[16−18]

In square-pyramidal $[CuN_4X]^{n+}$ compounds the co-ligands X are usually coordinated at the apical position, and the [Cu-

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(L)]$^{2+}$ fragment has been designed and used to stabilize and activate the substrates X (e.g., O_2^{2-}, catecholate) in equatorial positions.[13−15] In this paper, we analyze the role of the bispidine backbone in the stabilization (preorganization) and activation (entasis) of substrates based on a density-functional theory (DFT) analysis of [Cu(L)(Cl)]$^+$ and a simplified model (see Figure 1a for a plot of the experimentally determined structure (substituents to the backbone of L omitted)).[13]

Computational Methods

DFT calculations were performed with Gaussian 98,[19] using the B3LYP functional and 6-311G(d) basis set for the metal center, 6-31G-(d) for the donor atoms, and 3-21G for all remaining backbone atoms or ADF99,[20,21] using quadruple-ζ basis sets for all atoms (frozen core approach: 2p, 2p, 1s, 1s for Cu, Cl, C, N, respectively), and the Becke Perdew functional.[22,23] No symmetry constraints were applied in the calculations with Gaussian 98; some ADF99 calculations were done with enforced C_s symmetry. All structures reported here are fully optimized without any further geometrical constraints. However, for the ADF99 calculations on [Cu(NH$_3$)$_2$(imine)$_2$(Cl)]$^+$, some of the square-pyramidal geometries with axial Cl$^-$ were initially enforced by geometrical constraints, but these were relieved for the final refinements. This was necessary since some trigonal-bipyramidal structures are also local minima. The descriptors “square pyramidal” and “trigonal bipyramidal” are not used here in an absolute sense.[24] Vibrational analyses were used to define local minima. The data discussed here are derived from the Gaussian calculations, with the exception of the Cu−Cl bonding energies and the qualitative analysis of the molecular orbital (MO) contributions along the Cu−pyridine rotation. Generally, optimized structures and energies with the two methods were close to identical. The fact that this includes optimizations with very different basis sets and functionals indicates that spin contamination is not a significant problem.

Results and Discussion

Figure 1a is a plot of the experimentally determined structure of [Cu(L)(Cl)]$^+$ (substitutents omitted); the fully optimized structure is shown in Figure 1b, and Figure 1c is an overlay of the experimental and computed structures. Relevant structural parameters are given in Table 1. There is excellent agreement between the observed and computed structures, and this is a good indication of the quality of the method, i.e., the basis sets and the functional are appropriate for the present study. The largest but still acceptable deviation (N3−Cu−Cl angle) is probably due to the substitution of the N−Me groups by N−H in the computed structure. The small deviation, with respect to the bond distance of the axially coordinated nitrogen donor, is expected for gas-phase calculations and may be attributed to differences between condensed and gas phases rather than inaccuracies due to the DFT calculation.[25,26]

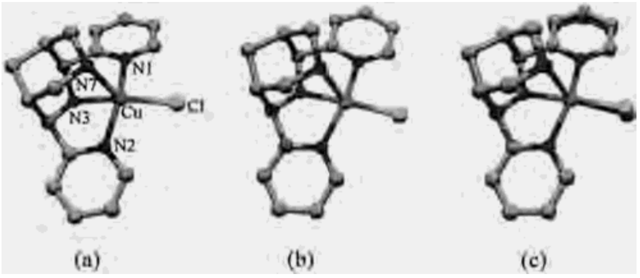

Figure 1. [Cu(L)(Cl)]$^+$: (a) experimentally determined[13] structure, (b) computed structure, (c) overlay of the experimental and computed structures. The substituents to the ligand backbone are omitted.

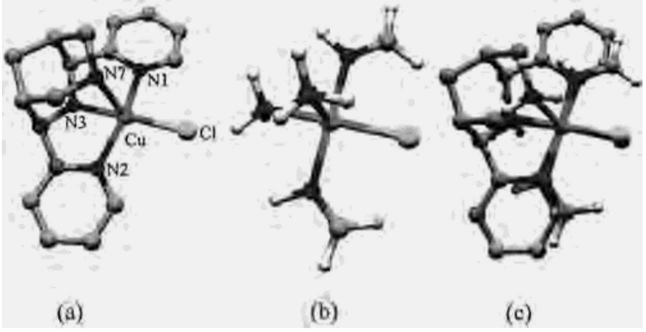

Figure 2. [Cu(L)(Cl)]$^+$: (a) computed structure (DFT in Table 1), (b) the simplified model (DFT simple in Table 1), (c) overlay of (a) and (b).

Table 1. Comparison of the Experimentally Observed and Computed Structures of [Cu(L)(Cl)]$^+$ and of the Simplified Model [Cu(NH$_3$)$_2$(imine)$_2$(Cl)]$^+$ (Distances in Å, Angles in deg)

parameter	X-ray[a]	DFT	DFT simple
Cu−N1	2.024	2.025	2.032
Cu−N2	2.020	2.025	2.032
Cu−N3	2.043	2.030	2.108
Cu−N7	2.273	2.323	2.326
Cu−Cl	2.232	2.224	2.275
N1−Cu−N2	158.1	159.0	168.3
N3−Cu−Cl	165.0	176.6	172.0
N3−Cu−N7	85.0	82.3	95.9
N1,N2−Cu−Cl	97.4	98.0	98.0
−N1−Cu−	14.9	15.0	15.0

[a] Reference 13.

To test the influence of the rigid bispidine backbone, a series of model calculations were performed on the extremely simplified model compound [Cu(NH$_3$)$_2$(imine)$_2$(Cl)]$^+$ (see Figure 2b; in some calculations, H$_2$NCH$_3$ was used instead of NH$_3$ to reduce the possibility of N−H···Cl interactions and to reduce the number of relevant isomers). The exciting result is that the fully optimized structure of the simplified chromophore is basically identical to that with the full bispidine backbone and also to the experimentally observed structure (see Figure 2 and Table 1). The rigid ligand backbone does *not* enforce a particularly distorted coordination geometry to the copper center

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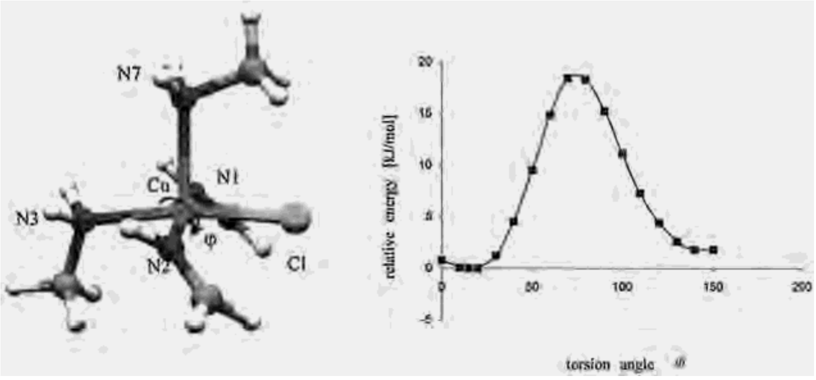

Figure 3. Computed energy barrier for the rotation of the imine donors.

but is well preorganized for the demands of copper(II) with this specific donor set and in that particular configuration.

An interesting feature is that the preorganization extends to the orientation of the imine substituents (pyridine donors in the bispidine ligand L); they are approximately coplanar to the copper(II) chromophore (see *−N1−Cu−* torsion angles in Table 1). In the free bispidine ligand L, the orientation of the pyridine groups is the only degree of freedom (*−C2−C_{py}−* torsion angle), and the coordination of the pyridine donors of L to a metal ion locks the *−N1−Cu−* torsion angles at values around 15°.

DFT calculations along this internal coordinate were used to analyze the extent of preorganization of the imine donors. There is an energy barrier of approximately 20 kJ $\mathrm{mol^{-1}}$ associated with this torsion (see Figure 3). The reason for this is not unambiguously assigned. Pyridines are primarily σ-donors and are only weak π-donors. Therefore, it is not unexpected when an analysis of the charge distribution and the relevant MOs reveals that the differences in the charge distribution are of primary importance for the orientation of the imines.

If the position α to the nitrogen donor is methylated, the imines in the model compound are rotated away from the planar conformation to an energetically less favorable position (*−N1−Cu−* torsion angle 70°). Such behavior is also observed experimentally with a bispidine ligand with 6′-methyl substituents;[14] sterically demanding co-ligands do not bind at the site trans to N3 but at the weakly coordinating apical site trans to N7. The corresponding Cu(I) complexes do not coordinate a solvent molecule as in the complexes with the parent ligand L, and more importantly, no stable Cu(II)−peroxo complexes can be detected.[14]

What is the role of the bispidine backbone? Although it does not lead to significant steric strain, it enforces a square-pyramidal configuration with a free in-plane site for the coordination of a substrate. There are six stable square-pyramidal configurations for a $[\mathrm{Cu(NH_3)_2(imine)_2(X)}]^{n+}$ chromophore. These have all been located and fully optimized (note that there are also stable trigonal-bipyramidal configurations but they are not discussed here). The isomer which corresponds to the configuration found in $[\mathrm{Cu(L)(Cl)}]^{+}$ is, as expected (see Introduction), less stable than structures with axial $\mathrm{Cl^-}$, and in fact, it is the least stable configuration (see Table 2). Although the energies from the gas-phase calculation are not directly related to solution equilibria, the data of Table 2 suggest that the role of the bispidine backbone is to enforce a configuration which otherwise would not be accessible, i.e., there is no hope of being able to experimentally prove the structure in Figure 2b. This configuration seems to be crucial for the stabilization and activation of the substrate. This also emerges from the computed metal−chloride bond distances and dissociation energies (see Table 2). The energy differences from the gas-phase calculations will be partly compensated by solvent effects in solution. However, the results emphasize the role of the configuration at the metal center.

Table 2. Computed Relative Stabilities, Cu−Cl Bond Energies, and Cu−Cl Distances of the Six Isomers of $[\mathrm{Cu(NH_3)_2(imine)_2(Cl)}]^{+}$

isomer	E_{tot} (kJ $\mathrm{mol^{-1}}$)	E_{Cu-Cl} (kJ $\mathrm{mol^{-1}}$)	Cu−Cl (Å)
amine^{ax} trans^{a}	0	0	2.3
amine^{ax} cis	−8	−3	2.3
Cl^{ax} trans	−11	+76	2.5
Cl^{ax} cis	−7	+77	2.5
imine^{ax} trans	−11	−13	2.3
imine^{ax} cis	−6	−4	2.3

[a] "Bispidine" configuration.

Table 3. Comparison of Computed $[\mathrm{Cu(NH_3)_2(imine)_2(X)}]^{n+}$ Chromophores in Their "Bispidine" Configuration (amine^{ax} trans, see Table 2; Distances in Å, Angles in deg)

parameter	X = Cl	X = NH_3	X = OH^-	X = OOH^-	X = OO^-
Cu−N1	2.032	2.045	2.060	2.063	2.054
Cu−N2	2.032	2.045	2.060	2.073	2.054
Cu−N3	2.108	2.053	2.073	2.093	2.148
Cu−N7	2.326	2.361	2.356	2.342	2.296
Cu−X	2.275	2.054	1.871	1.886	1.968
N3···N7	3.294	3.241	3.215	3.280	3.347
N1−Cu−N2	168.3	169.7	162.7	164.4	158.2
N3−Cu−X	172.0	170.6	175.0	179.4	178.2
N3−Cu−N7	95.9	94.2	92.9	95.2	97.7
N1,N2−Cu-X	98.0	89.4	90.0	89.4	88.7
N1−Cu−	15.0	5.7	12.9	13.8	32.4
O−O				1.457	1.284
Cu−O−O				102.9	114.4
N7−Cu−O−O				168.9	1.3
Cu−O−O−H				129.1	

$[\mathrm{Cu(L)(Cl)}]^{+}$ is experimentally easily available and well characterized. Therefore, chloride was chosen as the co-ligand in the present study. However, if chloride is substituted by ammonia, hydroxide, hydroperoxide, or superoxide, the structure of the $[\mathrm{Cu(NH_3)_2(imine)_2(X)}]^{n+}$ chromophore in the "bispidine" configuration (amine^{ax} trans in Table 2) remains basically constant (see Table 3). This is evidence for the interpretation that the general result of this study, i.e., that bispidines enforce a nearly unstrained but unusual and interesting geometry on copper(II), may be transferred to other co-ligands or substrates.

Conclusion

The bis-pyridyl-substituted bispidine L does not induce steric strain to a copper(II) chloride fragment but yields a coordination geometry which is close to a local minimum on the energy surface of the backbone-free complex $[Cu(NH_3)_2(imine)_2(Cl)]^+$. The rigidity of the backbone excludes any other configuration around the metal center, which would bind Cl^- or other substrates less efficiently. Therefore, in terms of the structures of the active sites, L is comparable to proteins which lead to entatic states. Our experimental results with one of the most stable μ-peroxo-dicopper(II) compounds[13] and various structurally characterized catechole oxidase mimic intermediates[15] support this interpretation and point to further applications of metal complexes with coordinated L derivatives.

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(27) Reference 27.