



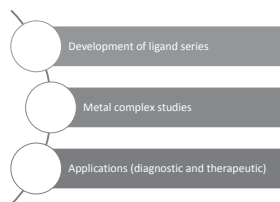
Functional modifications and electronic influences on tetra-aza macrocyclic Cu(II) complexes

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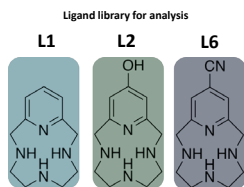
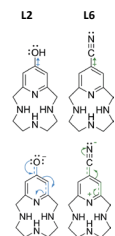
ABSTRACT

A library of novel tetra-aza macrocyclic molecules, specifically 3,6,9,15-tetraazabicyclo[9.3.1]pentadeca-1(15),11,13-triene derivatives, capable of chelating metal ions *in vivo* have been synthesized. Applications of these complexes are currently being pursued as a 1) therapeutic, focusing on radical scavenging and metal chelation, and 2) diagnostic tool such as magnetic resonance imaging (MRI) contrast agents when complexed with specific metal ions. However, a full study of the electronic effects imparted by substitution to the pyridyl moiety and the subsequent impact on the metal center have not been explored. The objective of the present study is to characterize metal complexes of four tetra-aza macrocyclic metal chelating molecules. The pyridyl functional groups studied include: **A**) unmodified pyridyl (**L1**), **B**) *p*-hydroxyl (**L2**), and **C**) *p*-nitrile modified pyridyls (**L6**) on a pycen base structure. Notable progress has been made in developing an optimal procedure for obtaining copper (II) complexes. Analysis of the resulting copper (II) complex of the *p*-nitrile tetra-aza macrocycle (**L6**) indicate a six-coordinate metal center based on X-ray diffraction, UV-visible spectroscopy and electrochemistry help to confirm donor strength among the ligand series as well as a comparison to other tetra-aza macrocycles of interest.

INTRODUCTION



Induction and resonance effects



	Inductive Effect	Resonance Effect	Hammett σ Parameter
L1	-	+	0
L2	-	+	-0.341
L6	-	-	+0.657

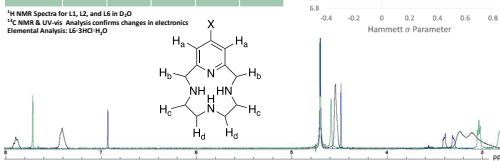
+ donating; - withdrawing

PROJECT OBJECTIVES

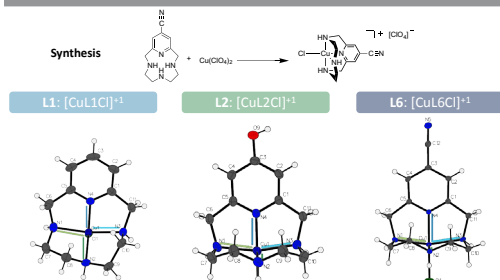
- Assess **L6** ligand synthesis by ^1H and ^{13}C NMR, UV-visible spectroscopy, and elemental analysis;
- Develop a chelation procedure and crystal growth method of **L6** with copper(II) perchlorate;
- Characterize **L6**-Cu(II) crystal by single-crystal X-ray diffraction, UV-vis, cyclic voltammetry;
- Compare electronic influences to the fully characterized **L1**-Cu(II), **L2**-Cu(II), and **L6**-Cu(II) complexes.

CHARACTERIZATION OF L6

^1H NMR	X	H_a	H_b	H_c	H_d
L1		7.91 (1H)	7.44 (2H)	4.56 (4H)	3.27 (4H)
L2	OH	6.92 (2H)	4.48 (4H)	3.40 (4H)	3.30 (4H)
L6	CN	7.71 (2H)	4.59 (4H)	3.03 (4H)	2.82 (4H)



SINGLE CRYSTAL X-RAY DIFFRACTION

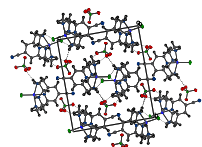


Bond Lengths	L1 ¹	L2 ¹	L6
N5 - C12	-	-	114
C12 - C3	-	-	145
N4 - Cu	195	193	196
N3 - Cu	207	207	208
N1 - Cu	206	208	208
N2 - Cu	215	217	220
C1 - Cu	224	222	227
τ	0.63	0.07	0.18

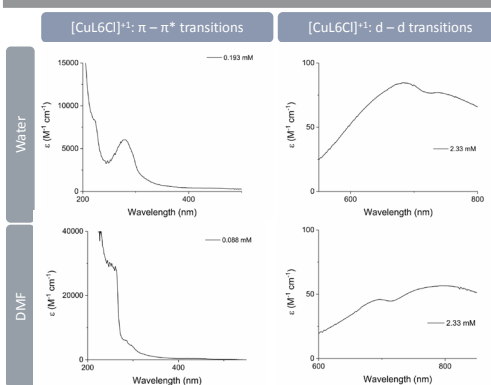
Crystal Isolation and Packing of **L6**: $[\text{CuL6Cl}]^{+1}$

Green block-like crystals were grown by slow evaporation of water.

Monoclinic P2₁/n ($\text{C}_{12}\text{H}_{14}\text{N}_4\text{CuCl}_2\text{O}_4$)
 $a = 7.198$ $\alpha = 90^\circ$ $V = 1626$
 $b = 15.970$ $\beta = 98.49^\circ$ $Z = 2$
 $c = 14.304$ $\gamma = 90^\circ$



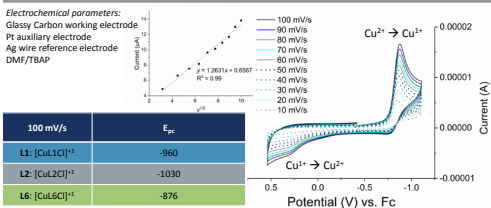
UV-VISIBLE SPECTROSCOPY



λ_{max}/nm ($\epsilon/M^2\text{cm}^{-1}$)	Abs. 1	Abs. 2	Abs. 3
L1: $[\text{CuL1Cl}]^{+1}$	261 (4353)	275 - 330 (sh)	713 (249)
L2: $[\text{CuL2Cl}]^{+1}$	249 (8779)	284 - 330 (sh)	699 (107)
L6: $[\text{CuL6Cl}]^{+1}$	221 (sh)	280 (4540)	684 (86)

sh = shoulder; all values reported in table were completed in water.

ELECTROCHEMISTRY



CONCLUSIONS

- Successful synthesis, purification, and characterization of **L6** $3\text{HCl} \cdot \text{H}_2\text{O}$;
- Reproducible chelation procedure and crystal growth achieved;
- Electronic influences compared among **L1**, **L2**, and **L6** Cu(II) complexes indicate that the electron withdrawing nature of the cyano group on **L6** imparts significant structural and electrochemical differences.

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