Potential Use of Transition Metal Complexes Consisting of Poxal-derived Schiff Bases and Amino Acids as Anti-Cancer Drugs

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Introduction

2-Pyridinecarboxaldehyde N-oxide, also known as poxal, is capable of forming Schiff bases with amino acids through condensation. It has been proven that these Schiff bases possess a significant role in biological systems when paired with transition metals, specifically copper(II) complexes. Schiff bases derived from poxal (**c**) and amino acids in comparison to those derived from salicylaldehyde (**a**) or 2-pyridinecarboxaldehyde (**b**) (Figure 1) provide a third nitrogen donor atom rather than an oxygen donor atom after deprotonation. When forming complexes with transition metals, ligands **b** and **c** form complexes with M^{2+} that require either an anionic ligand or counter anion in order to form a neutral complex while ligand **a** does not. Ligands **a** and **c** have the same sequence of donor atoms, ONO, and are able to form same-sized metallocycles while ligand **b** forms two five-membered metallocycles with its NNO donor atom sequence (Figure 2). Studies have shown that salicylaldehyde Schiff-base complexes **d** have antimicrobial amongst other biological activities, indicating that complexes of type **f** may have similar biological properties due to the similarities in structure despite their different charges. Therefore, copper(II) complexes of type **f** were of particular interest in Adrian Humboldt's preliminary study.[1] Our current goal was to optimize the synthesis of complexes and to scale it up to produce sufficient amounts of materials for their full biological activity testing.

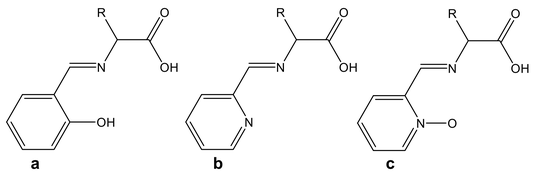


Figure 1: Structure of Schiff bases derived from salicylaldehyde (**a**), 2-pryidinecarboxaldehyde (**b**) and poxal (**c**)

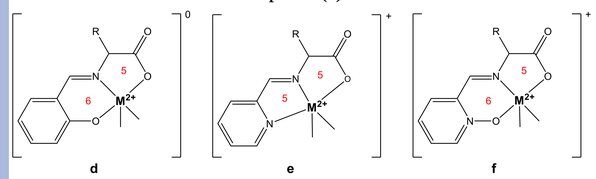


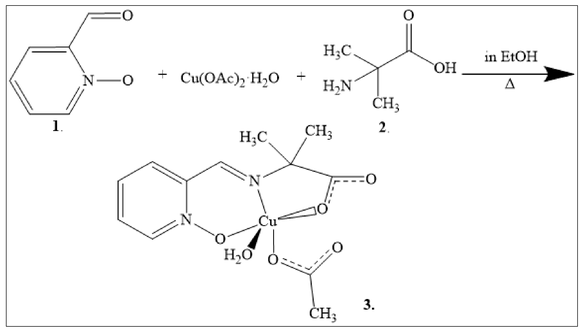
Figure 2: Structure of M^{2+} complexes with the Schiff bases from Figure 1. Red number is the size of metallocycle formed.

Objectives

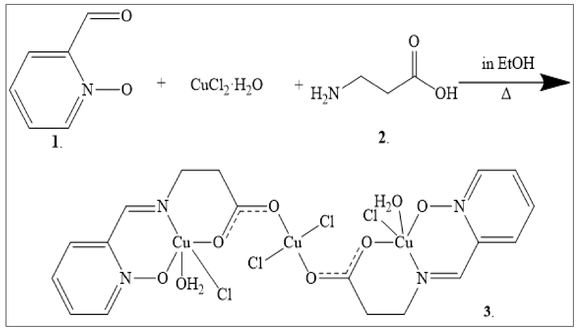
1. Reproduce and optimize syntheses of five Cu(II) complexes.

2. Obtain at least 0.500 g of each complex for biological testing.

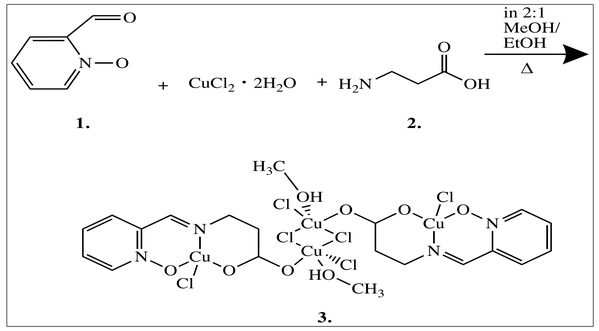
Preliminary Results → Intended Schemes for Complexes 1-3, 6 and 7 as proposed by Adrian Humboldt



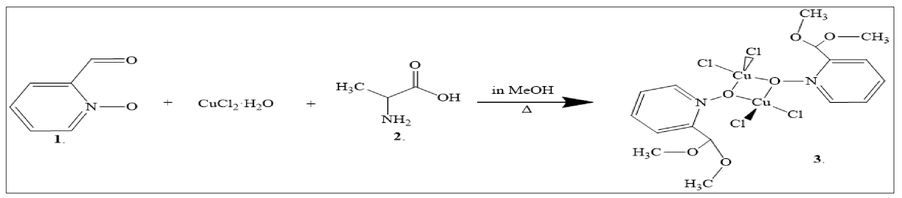
Scheme 1: Synthesis of coordination complex 1
1. poxal, 2. 2-aminoisobutyric acid, 3. $[Cu(L^1)(Oac)(H_2O)] \cdot H_2O$



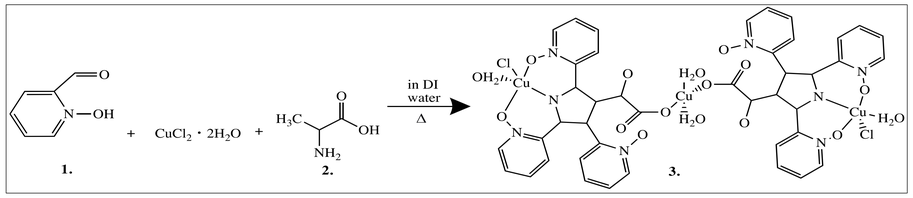
Scheme 2: Synthesis of coordination complex 2
1. poxal, 2. beta-alanine, 3. $[Cu_3(L^2)Cl_4(H_2O)_2]$



Scheme 3: Synthesis of coordination complex 3
1. poxal, 2. beta-alanine, 3. $[Cu_4(L^2)_2Cl_6(MeOH)_2]$



Scheme 4: Synthesis of coordination complex 6
1. poxal, 2. alpha-alanine, 3. $[Cu_2(L^4)Cl_4]$



Scheme 5: Synthesis of coordination complex 7
1. poxal, 2. alpha-alanine, 3. $[Cu_3(L^5)_2Cl_2(H_2O)_4] \cdot 2.6H_2O$

Our Results

Multiple syntheses were preformed for complexes 1, 2, 3, 6 and 7. The syntheses for complexes 2 and 6 were able to be replicated, resulting in the formation of the desired product (yields: 0.9519 g and 0.0262 g respectively). Complex 2 was confirmed using infrared spectroscopy (Figure 3) while complex 6 was confirmed using X-ray crystallography (Figure 4). All syntheses for complexes 1 and 3 yielded products that were different from those Adrian previously synthesized. The syntheses for complex 7 did not result in the formation of product.

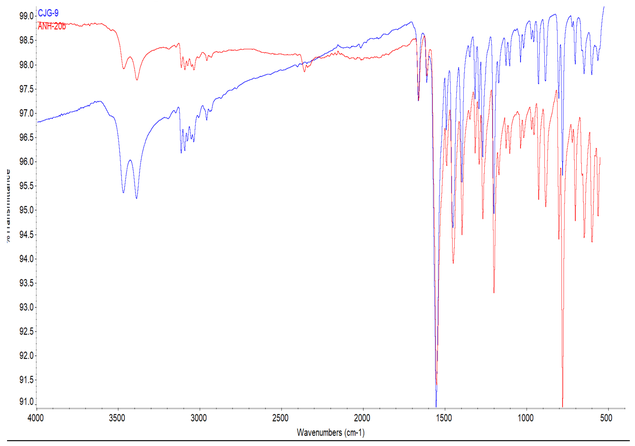


Figure 3: IR spectra of complex 2. The red line is the IR spectrum for our synthesis. The blue line is the IR spectrum for Adrian's synthesis.

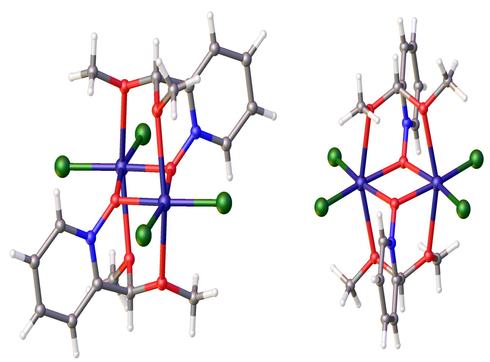


Figure 4: Two views of crystal structure of complex 6 from our synthesis

Conclusion/Project Outlook

Successful synthesis of compounds 2 and 6 were proven through IR and X-ray crystallography. However, inconsistences in Adrian's procedure and our intended compounds need to be further identified. The crystals synthesized that do not match IR spectra should be elucidated further to find the crystal structure. Also, finding a reproducible method for getting the novel crystals should be investigated further.

Acknowledgements

Juniata College Department of Chemistry and Biochemistry
Adrian Humboldt as his thesis guided this research

References

[1] Humboldt, A. Synthesis and characterization of potentially biologically active transition metal complexes with Schiff bases derived from 2-pyridinecarboxaldehyde N-oxide and amino acids. thesis, (bachelor thesis), 2019.