



# Exploration of copper(II) complexes as oxidation catalysts: Strategies for the construction of heterogeneous catalysts

Jeffrey J. Bodwin\*, Kevin P. Schultze, Tracy J. Kurtz, Nivedha Manohar, Rachel P. Branson, and Deborah L. Pestka  
Department of Chemistry, Minnesota State University Moorhead, 1104 7th Avenue South, Moorhead, MN 56563



## Abstract:

Copper(II) complexes have been shown to catalyze a variety of oxidation reactions in biological and non-biological systems. The utility of these catalysts could be increased by designing systems in which the catalyst is heterogeneous through inclusion of the catalyst on a surface or as part of an organic or inorganic polymer. This work is aimed at screening a number of different copper(II) complexes for catalytic function and exploring modifications to their ligand peripheries which will allow these catalysts to be immobilized. Ligand families will range from classic ligands such as salen to more novel ligands with pyridine, amide and other donors and resolved chiral centers. This range of complexes has the potential to catalyze a number of specific and selective oxidations, although preliminary screening will focus on the oxidation of veratryl alcohol.

## Introduction:

Very few chemical feedstocks are useful as collected, either from the ground in the case of fossil fuels, or from "natural" products such as biomass. One of the more useful organic transformations to perform on these raw materials is oxidation because it can be the first step in a variety of synthetic pathways that lead to commercially useful materials. Although oxidation can be accomplished with a variety of chemical reagents, many of those oxidants pose environmental and safety questions that are increasingly difficult to answer. In addition, many good oxidants take a "big hammer" approach to oxidation; they are "good" oxidants largely because they are very active/reactive and can result in numerous over-oxidation products and other side products. In an effort to make oxidation chemistry more "green", a tremendous effort has gone into development of catalysts that allow milder conditions, offer higher selectivity, and generate less waste and less toxic waste.

One of the inspirations for rationally designed oxidation catalysts is the variety of metalloenzymes that perform exquisitely selective and controlled oxidations in biological systems. By their very nature, catalytically active sites that exist in living organism must be not only effective at oxidation, but must be selective and relatively non-toxic. Taking the lead from biological systems, many groups have looked at model compounds that contain many of the first-row transition metals as well as some others. Of particular interest to our group are metalloenzymes and models that use copper(II) as the active site of oxidative catalysis. Copper(II) was selected for a number of reasons:

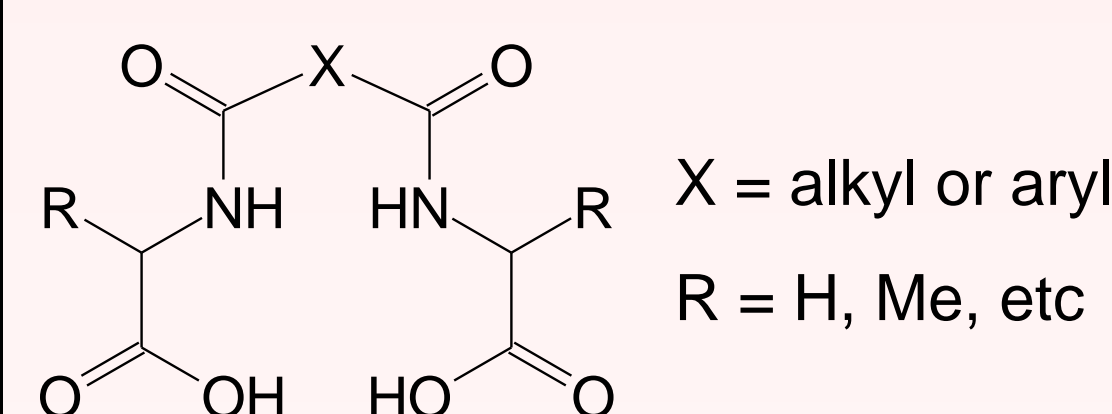
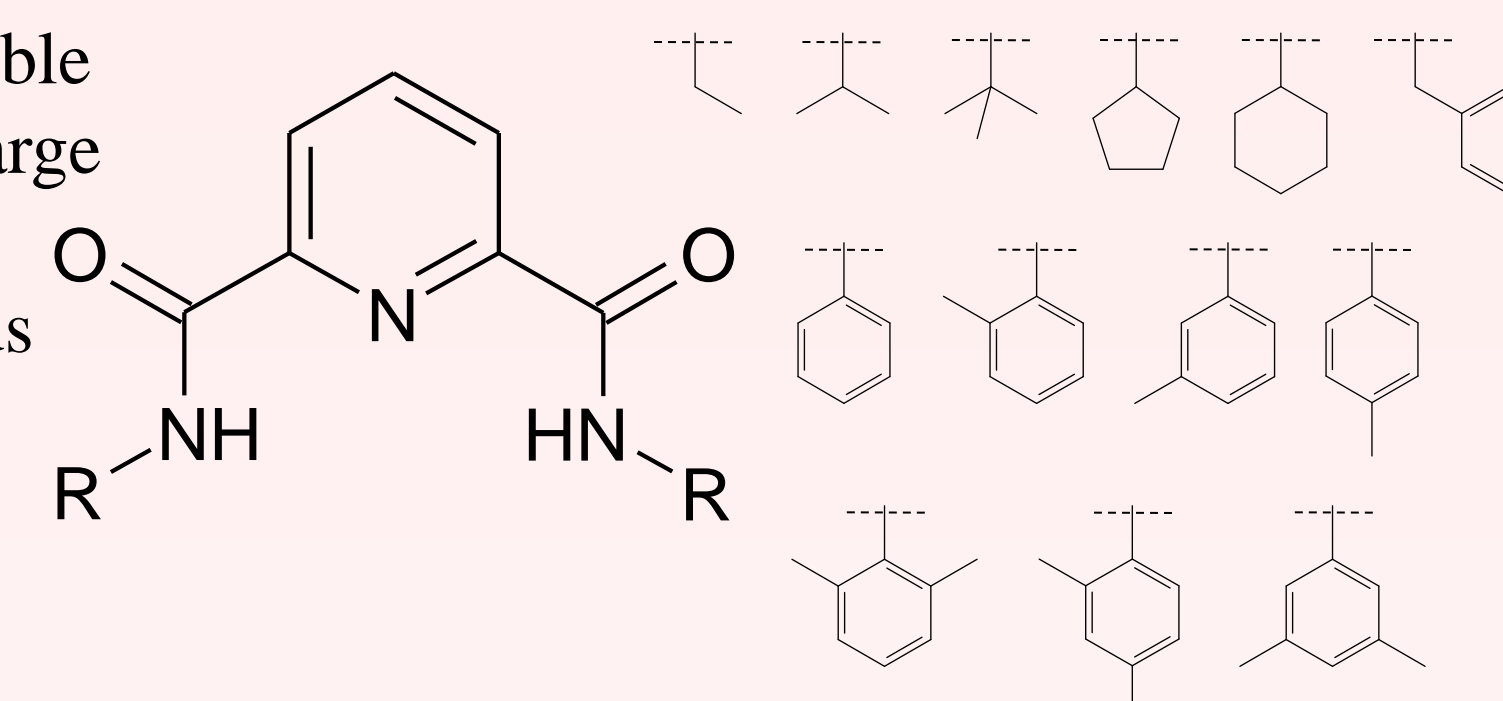
1. Copper(II) is a relatively well-behaved transition metal ion. It will bind a variety of donor atoms, the redox activity of copper(II) complexes is less complex than many 1<sup>st</sup>-row transition metals, and the coordination geometry of copper(II) complexes is relatively predictable but is variable enough to allow significant alteration during catalysis.
2. Although extremely complex and challenging ligands *can* be used, copper(II) allows the complexity of the ligand to be tailored to the ability of the students performing the research. All of these research students will be undergraduates and many of them are interested in starting research in their first or second year, often before they have any significant exposure to organic chemistry and the associated laboratory techniques. By starting students out with "simple" ligands, they are able to make substantive contributions to the overall goal of the project from their earliest exposure, and as they progress through their classes the syntheses and expectations can be increased accordingly.
3. Copper(II) has a number of spectroscopic handles that can be studied with the facilities available at an undergraduate institution. Elemental analysis, thermal analysis, X-ray diffraction studies and other techniques are essential to this research and samples can be sent out for external analysis, but students are also able to explore the nature and behavior of their products by FTIR, UV-Vis, NMR, CV, etc. in house.
4. Copper(II) complexes can be synthesized without rigorous air-free, anhydrous or other restrictions. Similar to the ligand considerations above, this allows students at all levels to participate and contribute more readily than if all syntheses and manipulations had to be carried out in Schlenk-ware or an inert atmosphere box.
5. Numerous literature precedents are available for students to explore. This allows the research student a little more freedom in developing his or her own niche within the overall project.

## Ligand Families:

Initial efforts in this research are intended to screen a variety of ligand types in an effort find favorable candidates for further study as oxidation catalysts. We have focused on a few classes of ligands.

### Pyridine bis-amide ligands:

This class of ligands offers a variety of readily available (and inexpensive) starting materials. This allows a large library of potential catalysts to be synthesized for screening. In reported studies, nitrogen-donor ligands have been shown to be excellent candidates for the oxidation of veratryl alcohol.

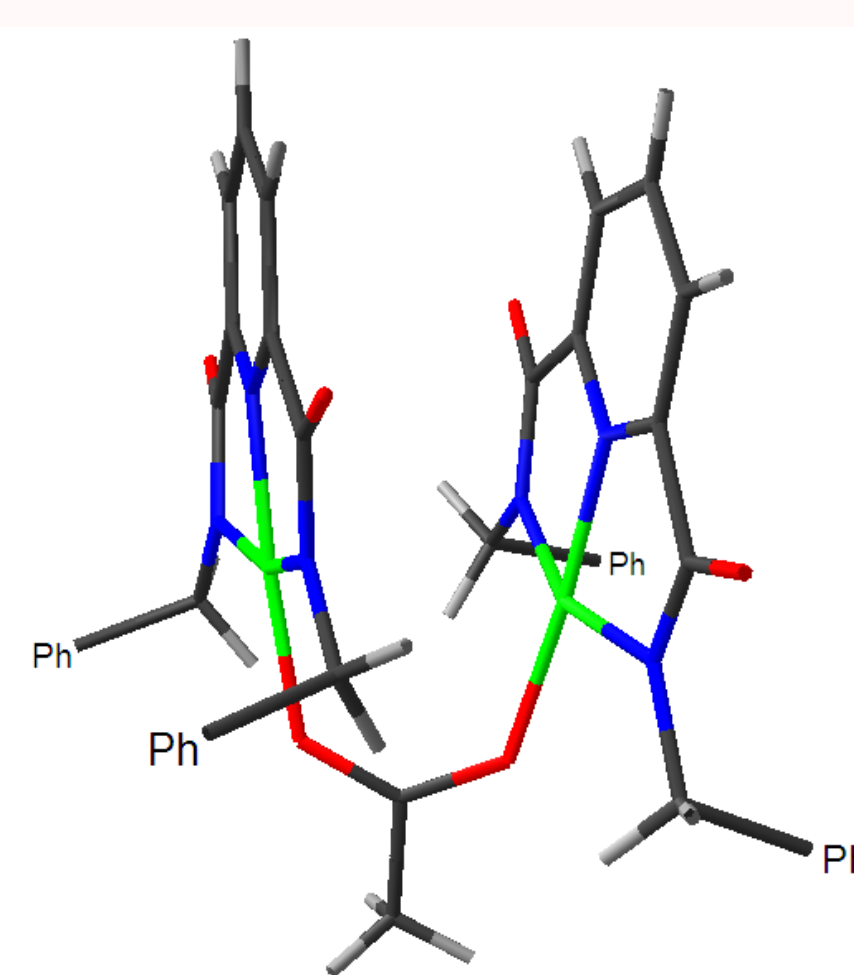
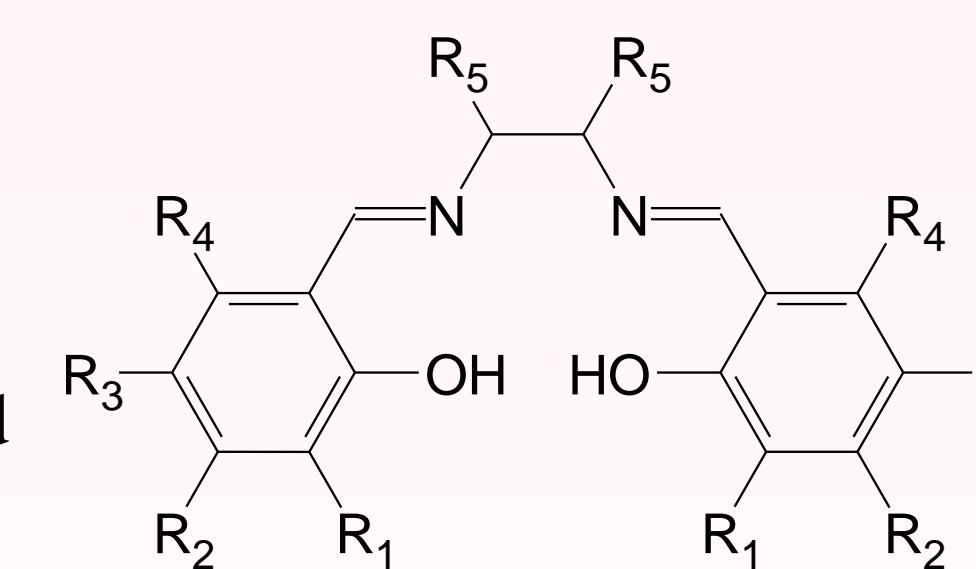


### Linked bis-amido acid ligands:

These ligands have the potential to produce a huge library of compound with peripheral modifications, "R", limited only by the availability of amino acid precursors. The nature of the linking group, "X", can also be used to tune various aspects of these complexes. Because these ligands are constructed of biologically ubiquitous donors, they also have the potential to be directly analogous to copper(II)-containing metalloenzymes such as methane monooxygenase and galactose oxidase.

### Salen-type ligands:

Salen-type ligands have been used to bind nearly every metal on the Periodic Table and studied as structural and/or functional models of many metalloenzymes. This is a nice control as it is very well studied and the behavior of Cu(II)-salen complexes is fairly well understood. Salen-type ligand synthesis can also be widely modified to match the level of student, from products that crystallize out of stirred solution to those that require strictly anhydrous conditions.

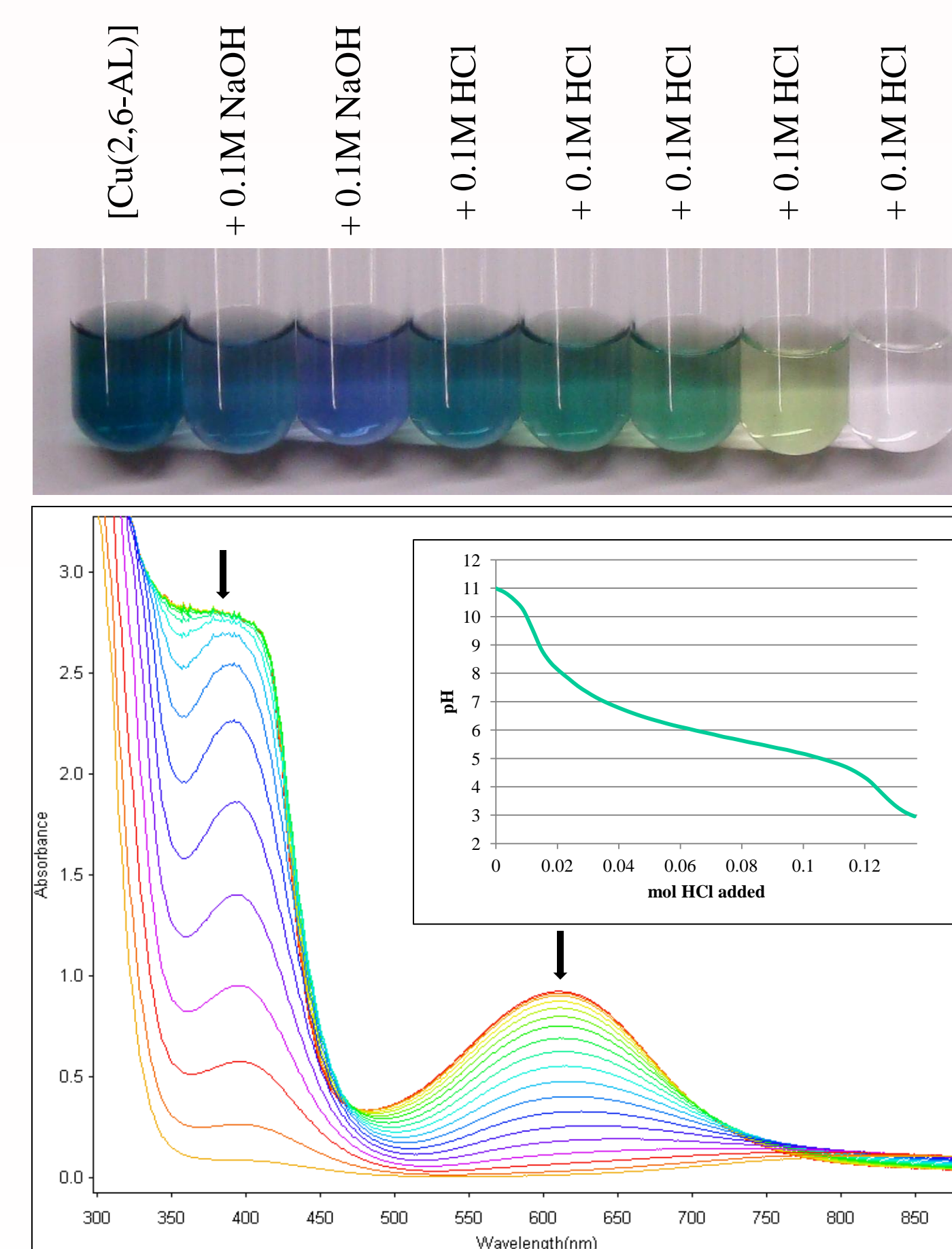
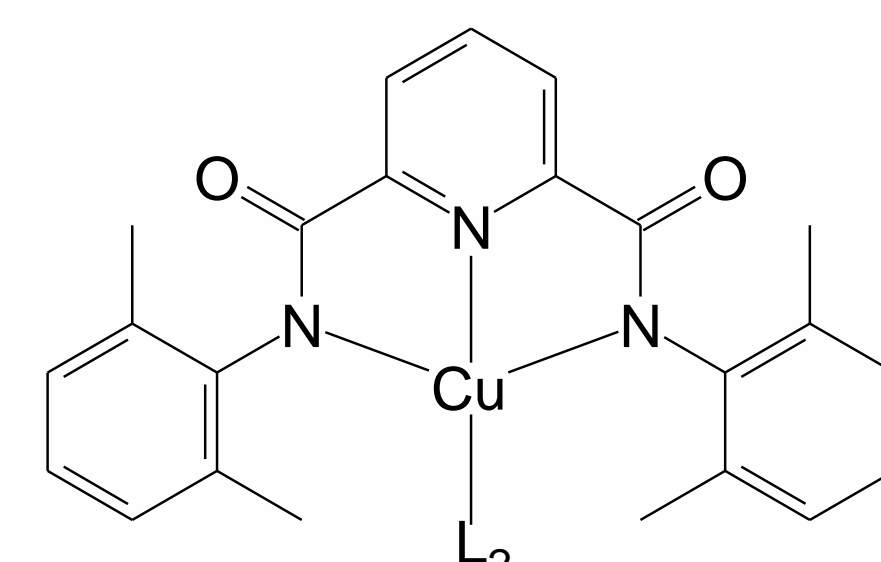


## Copper complexes:

At this point, we have had the most success with the pyridine bis-amide ligand family. Early syntheses focused on the benzyl derivative which ultimately formed X-ray quality crystals. Determination of the structure showed that this complex exists as an acetate bridged dimer in the solid state. Although this complex was readily synthesized, solubility and stability issues precluded significant further study. In an effort to address these problems, various aniline derivatives were explored.

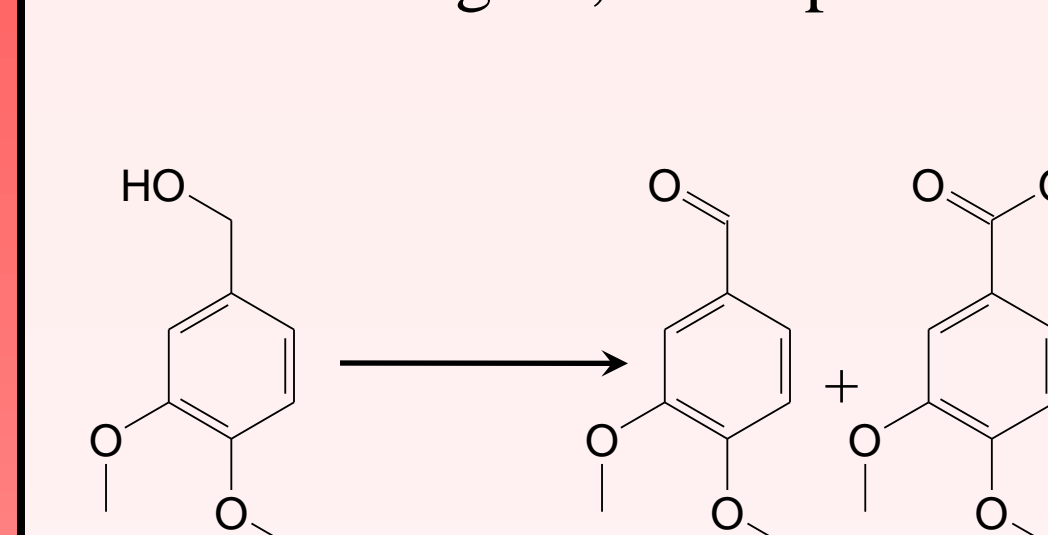
After some initial complications with ligand syntheses, these aniline-based ligands resulted in a number of complexes with similar properties, as expected.

The copper complex of the pyridine-bis-2,6-dimethylaniline derived ligand displays interesting behavior upon pH change. When the complex as synthesized is dissolved and acidified, the color progressively disappears. This color change is reversible upon addition of base. The nature of this color change is currently being investigated further.



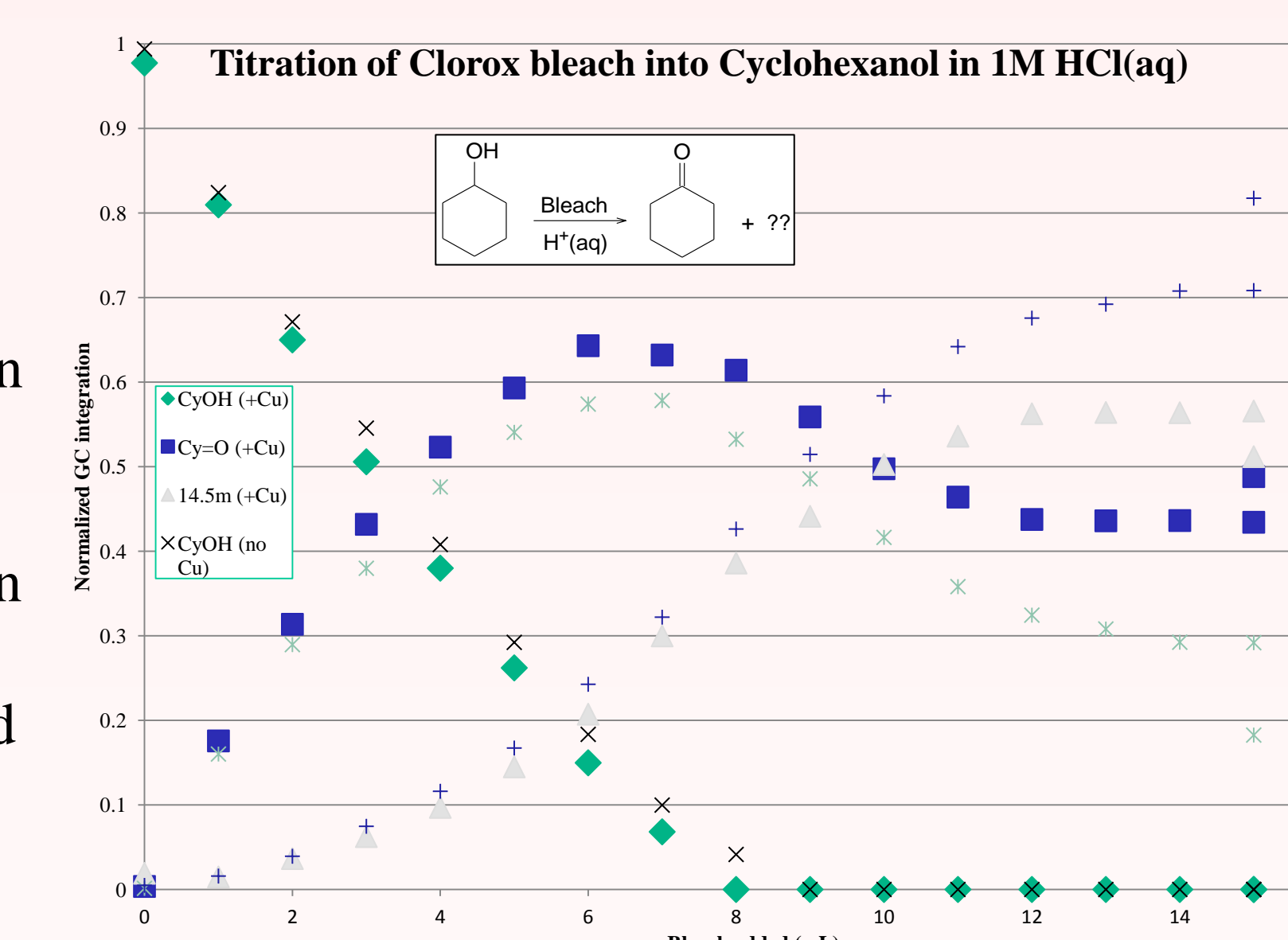
## Oxidation of Organic Substrates:

The short term goal of this research is the synthesis of a copper(II) complex that can act as an oxidation catalyst. There is significant literature precedence for these types of oxidations under a variety of conditions with a variety of oxidants. One interesting target is veratryl alcohol, which is often used as a model for lignin, a component of wood fiber.



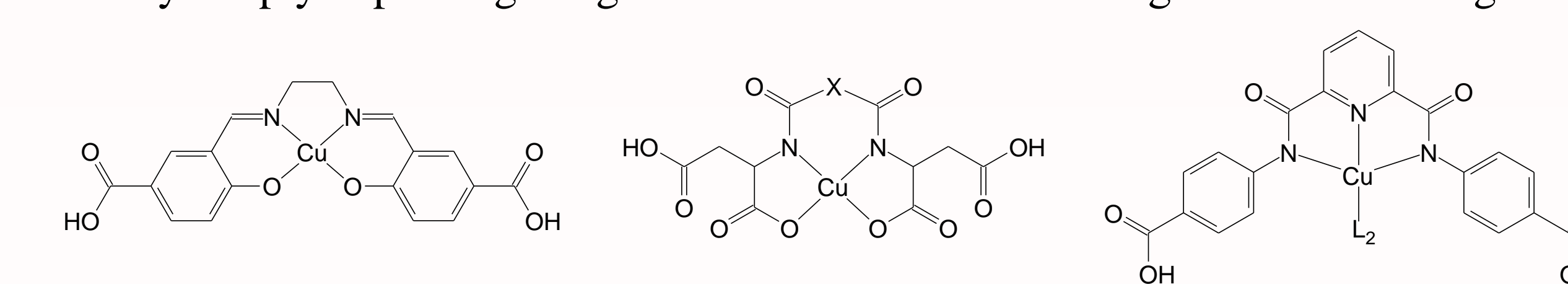
Veratryl alcohol and its aldehyde oxidation product have some very convenient spectroscopic handles to follow the oxidation. One of the most convenient methods of analysis is GC; however, analysis by GC suffers from the fact that any over-oxidation leads to veratric acid which is not sufficiently volatile for analysis by standard GC. This can be addressed by conversion of to the methyl ester, but adds an additional step to the catalyst evaluation process.

Another convenient oxidation substrate is cyclohexanol. Cy-OH can be oxidized with standard household bleach, and the products of multiple oxidations can be detected by GC, making it an ideal substrate for further study. In examining control reactions, it was determined that bleach is a sufficiently strong oxidant to form a significant fraction of a second oxidation product (likely the cyclic ether product). Furthermore, the presence of Cu(II) ions (added as CuCl<sub>2</sub>•2H<sub>2</sub>O) appears to inhibit the second oxidation, an interesting observation that warrants further study.



## Designing and Building the Heterogeneous Catalyst:

After a promising oxidation catalyst is identified, this work will move on to the design of a porous metal-organic framework that uses the active catalyst complex as a component of the framework. This will require modification of the ligand periphery with secondary donors that will support formation of the 3-dimensional coordination network. These modifications will have to be compatible with the formation of the copper(II) complex. This discrimination can be accomplished by hard/soft acid-base character or by simply exploiting the geometric constraints of the ligand's chelate rings.



## References:

- Kervinen, K. Studies on Veratryl Alcohol Oxidation Catalyzed by Co(salen) Type Complexes and Molecular Oxygen in Aqueous Solution. Ph.D. Dissertation, University of Helsinki, Helsinki, Finland, 2005.
- Korpi, H.; Sippola, V.; Filpponen, I.; Sipila, J.; Krause, O.; Leskela, M.; Repo, T. *Applied Catalysis A: General* **2006**, *302*, 250.
- Nayak, M.; Koner, R.; Lin, H.H.; Florke, U.; Wei, H.H.; Mohanta, S. *Inorganic Chemistry* **2006**, *45*, 10766.
- Lamour, E.; Rourier, S.; Bernier, J.L.; Cateau, J.P.; Bailly, C.; Vezin, H.; *J. Am. Chem. Soc.* **1999**, *121*, 1868.
- Berse, C.; Piche, L.; Lachance, L.; Laflamme, L. "The preparation of succinamide peptides, *J. Org. Chem.*, **1962**, *27*, 3489.
- Stevens, R.V.; Chapman, K.T.; Weller, H.N. "Convenient and Inexpensive Procedure for Oxidation of Secondary Alcohols to Ketones" *J. Org. Chem.* **1980**, *45*, 2030.
- Wasilke, Julia-Christina; Wu, Guang; Bu, Xianhui; Kehr, Gerald; Erker, Gerhard. "Ruthenium Carbene Complexes Featuring a Tridentate Pincer-type Ligand" *Organometallics* **2005**, *24*, 4289-4297.
- Manabendra, Ray; Subhashis, Mukerjee; Rabindranath, Mukherjee "Manganese(III) complexes of 1,2-bis(2-pyridinecarboxamido)benzene: synthesis, spectra, and electrochemistry" *J. Chem. Soc., Dalton Trans.* **1990**, 3635 - 3638

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