1. PRF# 59142
2. Project Title: Copper-Catalyzed Oxidative Functionalization of Unactivated Alkenes
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4. Co-Pi (if any): N/A

Narrative Report 2019

Research Progress

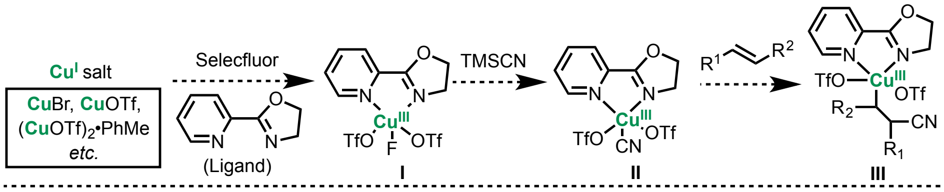

FIGURE 1: Proposed pathway for independent synthesis of Cu(III) intermediates

Our research efforts this year have focused primarily on the activities described in Aim 2 of the proposal, which centered on synthesis, isolation, and characterization of putative Cu(III) intermediates relevant to a recently discovered catalytic, branched-selective, oxidative cyanation of alkenes. Specific complexes of interest (**I–III**) are shown in Figure 1.

Stoichiometric studies were performed in an effort to synthesize model complex **I'** containing the symmetric 1,10-phenanthroline (phen) ligand (Figure 2). Reactions were performed using a variety of solvents, including acetonitrile, chloroform, DMSO and methanol in an argon glovebox. Experiments were carried out at room temperature, and crystallizations were set up at -35 °C and room temperature. Stoichiometric experiments to synthesize model complexes **II'** and **III'** were also set up independently (Figure 3). For trials to prepare complex **II'**, different combinations of ligand, copper source, and F^+ source were examined following the workflow described for complex **I'**, with the addition of TMSCN or $TMSCF_3$. Though it is not strictly relevant to catalysis, the latter reagent was tested based on the hypothesis that a $-CF_3$ ligand may stabilize a high-valent copper center to allow for isolation. For the migratory insertion complex **III'**, a less reactive (i.e., lower yielding) internal alkene substrate was used, as other substrates, such as internal alkenes, reacted rapidly to form the cyanated product under the reaction conditions, thereby hindering isolation of this model complex.

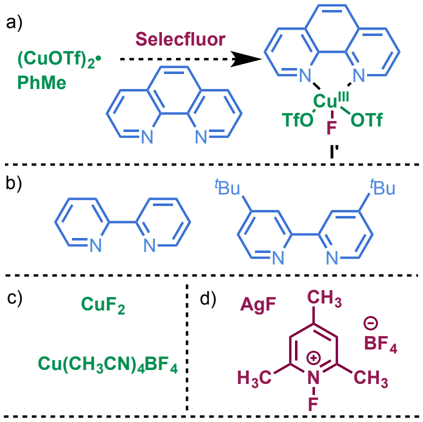

FIGURE 2: a) Stoichiometric experiments carried out for the synthesis of model complex **I'**. b) Alternate ligands examined. c) Alternate copper sources examined. d) Alternate F^+ souces examined.

As an alternate strategy, pre-ligated complex $Cu(phen)Cl_2$ was used in place of in situ formed copper(I)/ligand based on the hypothesis that a Cu(II) complex could be more easily oxidized using Selectfluor to give Cu(III) products.

Despite our best efforts, the experiments attempted thus far have failed to generate the desired Cu(III) model complexes. Instead, the new copper complexes that were isolated and characterized by X-ray crystallography all turned out to be Cu(II) complexes with different ancillary ligands depending on the reaction conditions (Figure 4).

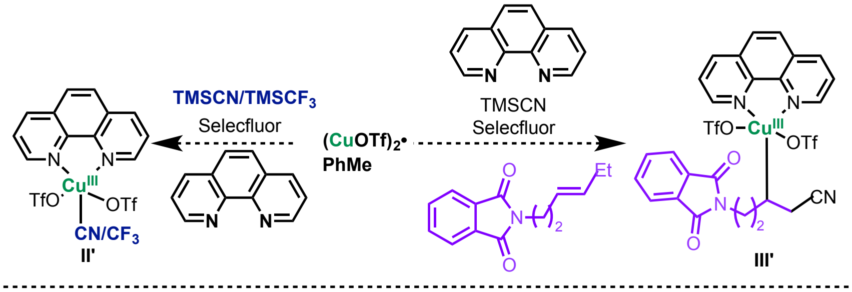

FIGURE 3: Stoichiometric experiments carried out for the synthesis of model complexes **II'** and **III'**.

Collectively these results suggest that either: the reaction conditions were insufficiently oxidizing, thereby resulting in Cu(II) complexes, or alternatively that Cu(III) intermediates were indeed formed but were too unstable and immediately underwent single-electron transfer to form the observed Cu(II) complexes. To further probe these possibilities, we will determine relevant oxidation potentials by cyclic voltammetry. Additionally we will examine more strongly coordinating tridentate ligands, Lastly, we will pursue the activities describe in the other two aims focused on optimizing the reaction conditions for alkene oxidative cyanation and discovering new transformations based on this reactivity platform.

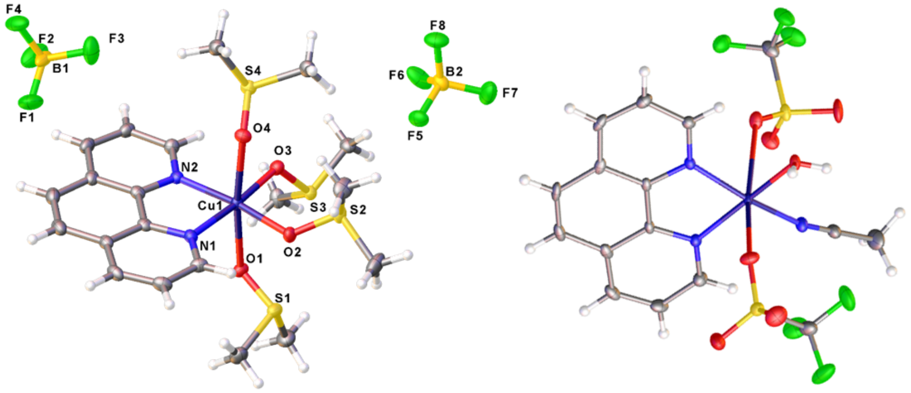

FIGURE 4: Crystal structures of isolated Cu(II) complexes: a) Cu(phen)(DMSO)$_4$(BF$_4$)$_2$; b) Cu(phen)(OTf)$_2$(H$_2$O)(CH$_3$CN)

Impact on Career and Student Training

Support for this project was invaluable for allowing the PI to pursue an early-stage idea for which there was only limited preliminary data at the time of application. These results, in turn, enabled successful applications for other early stage investigator awards, such as the 2019 Sloan Fellowship and the 2019 Camille Dreyfus Teacher-Scholar Award. The student trainee on this project has received valuable experience on fundamental coordination chemistry and inorganic synthesis that otherwise would not have been possible.