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Continuing the Metalation and Ring Closure of Biliazine

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Continuing the Metalation and Ring Closure of Biliazine

Joshua Villers 4144785

Honors Project Report

Course No.: 3150:497

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Introduction

Diiminoisoindoline (DII) can be used to make multidentate isoindoline derived ligands which have shown to bind strongly to many different metal centers.¹ Chemists and researchers alike have developed methods to react DII with other compounds such as amines and amides.^{2,3} Many methods have been developed in order to prepare isoindolines including the reaction of phthalonitrile with methanol-ammonia at high temperature, with sodium amide in formamide, and with sodium methoxide-ammonia in methanol.² However, the research of chemist Ryu Soto provided a two new ways to prepare DII derivatives by reacting phthalonitrile with elemental sulfur in liquid ammonia and amines and by treating 2-cyanobenzaldehyde with primary and secondary alkylamines at room temperature.² Once discovering multiple ways to synthesize DII, researchers went on to make DII derivatives using primary amines. The method for synthesizing these derivatives is taking DII and refluxing it with two equivalents of an aryl amine in butanol or methanol.^{3,4} These reactions will typically create a bis(aryl-imino)isoindoline compound. These compounds bind readily with metal centers.⁴ These compounds can be pincer type ligands with tridentate coordination modes around metal centers. In some cases, DII forms 1:1 compounds with arylamines such as amino azoles. **Fig. 1** shows the reaction between DII and 2-aminopyrazole to create a compound considered as a semihemiporphyrine.^{3,5,6} Recently, Ziegler and coworkers showed that this compound can form a tetradentate macrocycle-like compound upon reaction with metals. This new ligand system was called biliazine.³

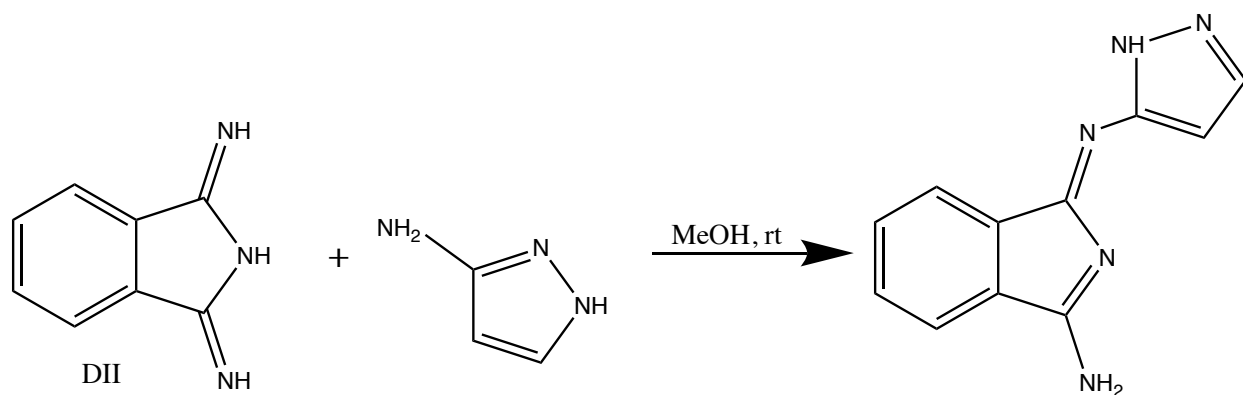


Fig. 1- The synthesis of the semihemiporphyrazine from DII and 2-aminopyrazole.

To take this chemistry one step further, in this study the 2-aminopyrazole was replaced with 3-amino-5-phenylpyrazole in an attempt to produce more soluble variants of subsequent molecules. This synthesis can be found in **Figure 2**.

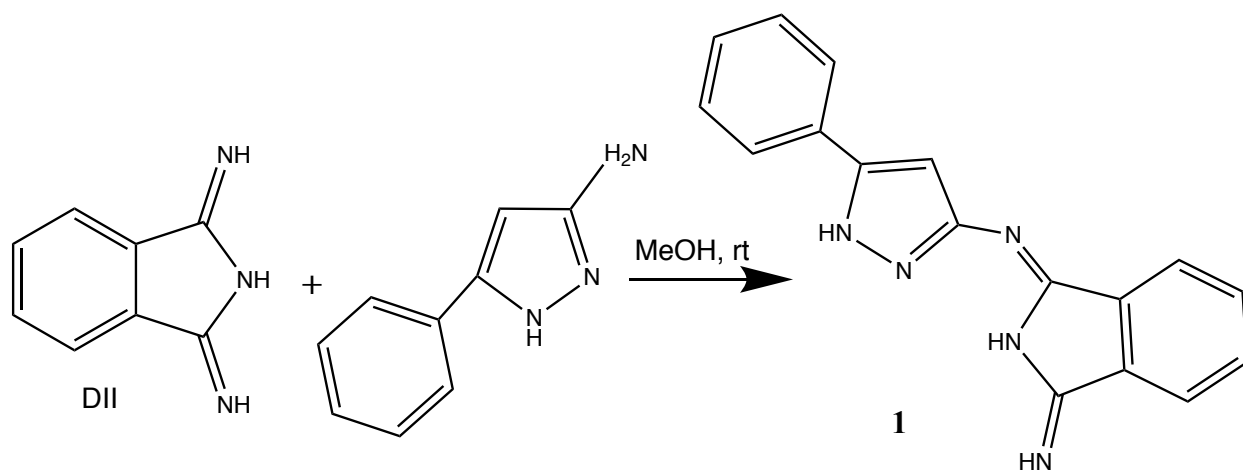


Fig. 2- The synthesis of the new compound (1) combining DII and 3-amino-5-phenylpyrazole.

In this study, we will explore the bonding capabilities of three different metal compounds with our new phenyl modified ligand. The metal reagents being used are $\text{Co}(\text{OAc})_2$, $\text{Ni}(\text{OAc})_2$, and $\text{Fe}(\text{OAc})_2$. We hypothesized that this new phenyl variant would form biliazines with these metal acetates.³

Experimental

Synthesis of $\text{Co}(\text{phenylBlzH})$ (Scheme 1): Two equivalents of compound **1** (phenyl ligand) (100 mg, 3.48×10^{-4} mol) and $\text{Co}(\text{OAc})_2$ (43.34 mg, 1.74×10^{-4} mol) were combined in a 25 mL round-bottom flask with 5 mL of DMF and a magnetic stir bar. The solution was heated with a heat gun for approximately thirty seconds in order to dissolve and was allowed to stir for 24 hours. The solution was then allowed to evaporate, and the crystals were grown with the solvent DMF. Single crystals were collected and investigated by X-ray diffraction.

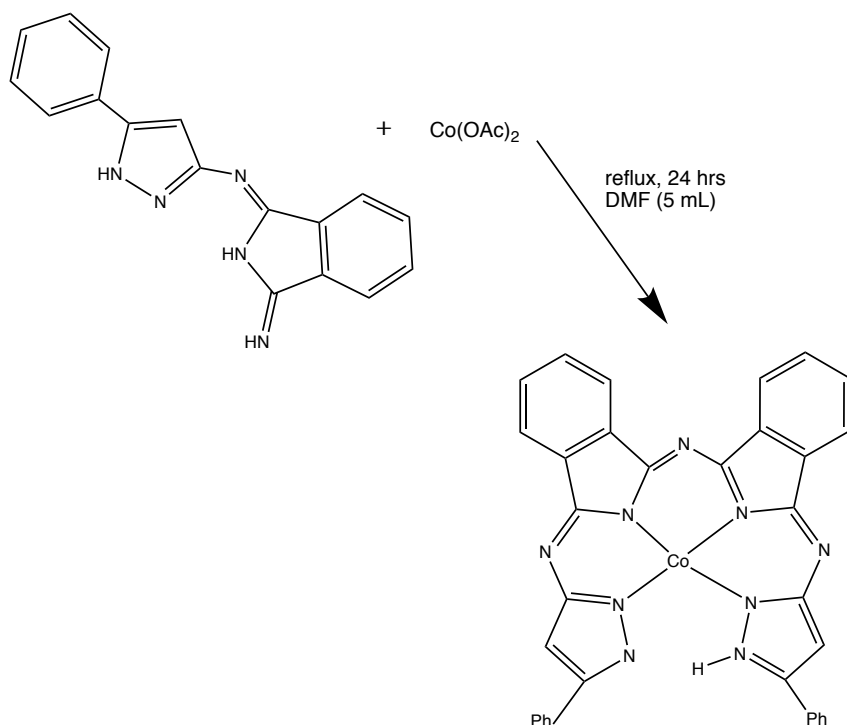
Synthesis of $\text{Ni}(\text{phenylBlzH})$ (Scheme 2): Two equivalents of compound **1** (phenyl ligand) (100 mg, 3.48×10^{-4} mol) and $\text{Ni}(\text{OAc})_2$ (30.76 mg, 1.74×10^{-4} mol) were combined in a 25 mL round-bottom flask with 5 mL of DMF and a magnetic stir bar. The solution was heated with a heat gun for approximately thirty seconds in order to dissolve and was allowed to stir for 24 hours. The solution was then allowed to evaporate, and the crystals were grown with the solvent pyridine. Single crystals were collected and investigated by X-ray diffraction.

Synthesis of $\text{Fe}(\text{phenylBlzH})$ -oxo-dimer (Scheme 3): Two equivalents of Compound **1** (phenyl ligand) (100 mg, 3.48×10^{-4} mol) and $\text{Fe}(\text{OAc})_2$ (30.27 mg, 1.74×10^{-4} mol) were combined in a 25 mL round-bottom flask with 5 mL of DMF and a magnetic stir bar. The solution was heated with a heat gun for approximately thirty seconds in order to dissolve and was allowed to stir for

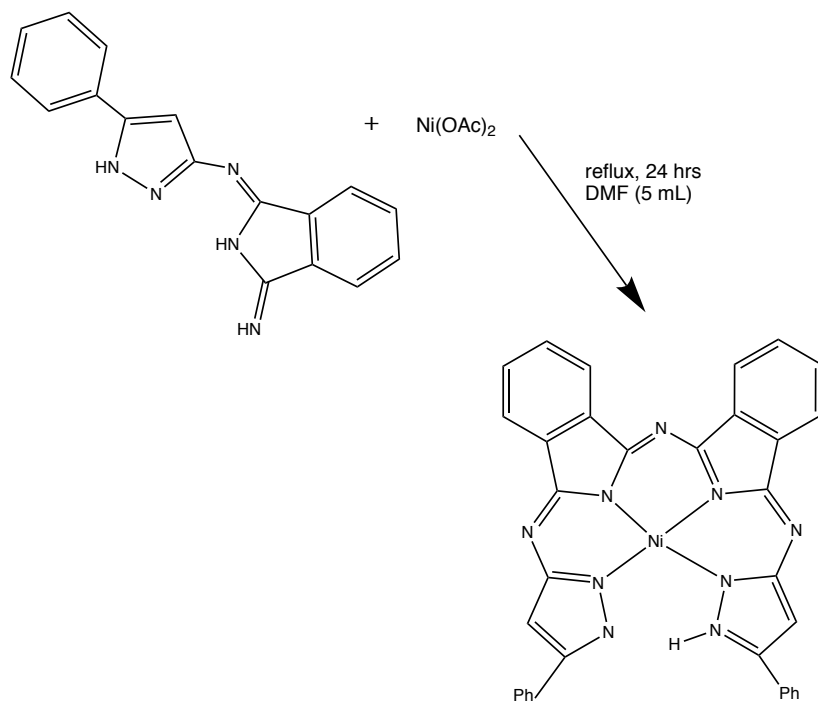
24 hours. The solution was then allowed to evaporate, and the crystals were grown with the solvent DMF. Single crystals were collected and investigated by X-ray diffraction.

Results and Discussion

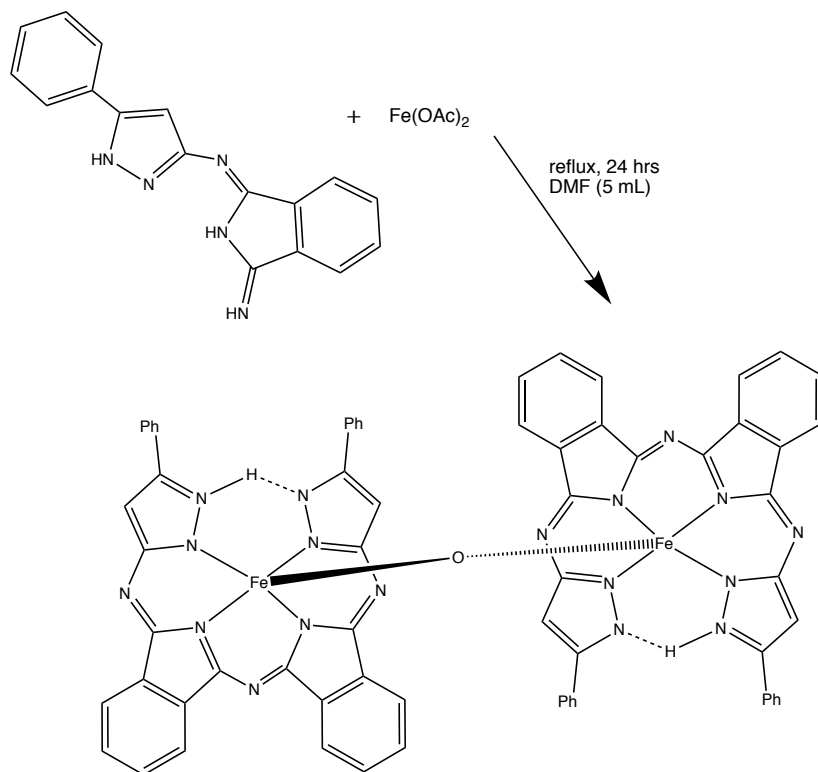
In the synthesis of these three phenyl modified biliazines, a variety of solvents were used in order to obtain the best yield of crystals. Methanol seemed to be the best solvent option according to past research within the Ziegler research group, however, in this case DMF proved to be the best solvent for fully dissolving the phenyl ligand as well as growing crystals.³ Pyridine was also used for the Ni and Fe reactions but proved to be less effective than DMF in fully dissolving the phenyl ligand. The phenyl biliazines formed from Ni and Co turned out as expected, but the Fe derivative of the phenyl biliazine formed the μ -oxo-dimer which was unexpected. Schemes for the synthesis of the three phenyl biliazines are shown below (**Schemes 1-3**).



Scheme 1: The reaction for the synthesis of Co(phenylBlzH). The crystal structure for this product is depicted in **Figure 5**.



Scheme 2: The reaction for the synthesis of Ni(phenylBlzH). The crystal structure for this product is depicted in **Figure 6**.



Scheme 3: The reaction for the synthesis of Fe(phenylBlzH)-oxo-dimer. The crystal structure for this product is depicted in **Figure 7**.

We attempted to make a variety of metal derivatives of biliazine, but most were unsuccessful because the crystal size was too small to be characterized thoroughly. Although it is very likely that the other metal biliazines were synthesized, there is no way to know for sure without proper characterization. Some of these attempts include the original reaction from the Ziegler research group in which the aminopyrazole ligand was combined with multiple metal acetates and refluxed in methanol for 24 hours.³ The attempted metal acetates using that method in this research include $\text{Mn}(\text{OAc})_2$, AgOAc , $\text{Zn}(\text{OAc})_2$, and $\text{Cu}(\text{OAc})_2$. An attempt to make the chromium derivative of biliazine was attempted using the same method in which CrCl_3 and

Cr(CO)₆. In terms of the new phenylpyrazole ligand reaction method developed in this research, other metal acetates were attempted as well including Mn(OAc)₂ and Cu(OAc)₂.

Both ¹H and ¹³C NMR were conducted for the phenylpyrazole (**Figure 3, 4**). In the hydrogen NMR spectrum, distinct peaks can be seen at 7.07, 7.29, 7.42, 7.58, and 7.76 ppm. These peaks coordinate with the peaks for the hydrogen atoms surrounding the phenyl ring in the compound of 1-phenylpyrazole. In the ¹³C NMR spectrum, a distinct peak can be seen at 97.13 ppm which correlates to the double-bonded carbon atom next to the amino group in the pyrazole. The carbon atoms in the phenyl ring show up at 121.14, 124.72, 128.59, and 134.54 ppm. The carbon atom that correlates to the amino carbon shows up at 140.71 ppm. All of these peaks correspond with the carbon atoms in the compound of 5-amino-1-phenylpyrazole.

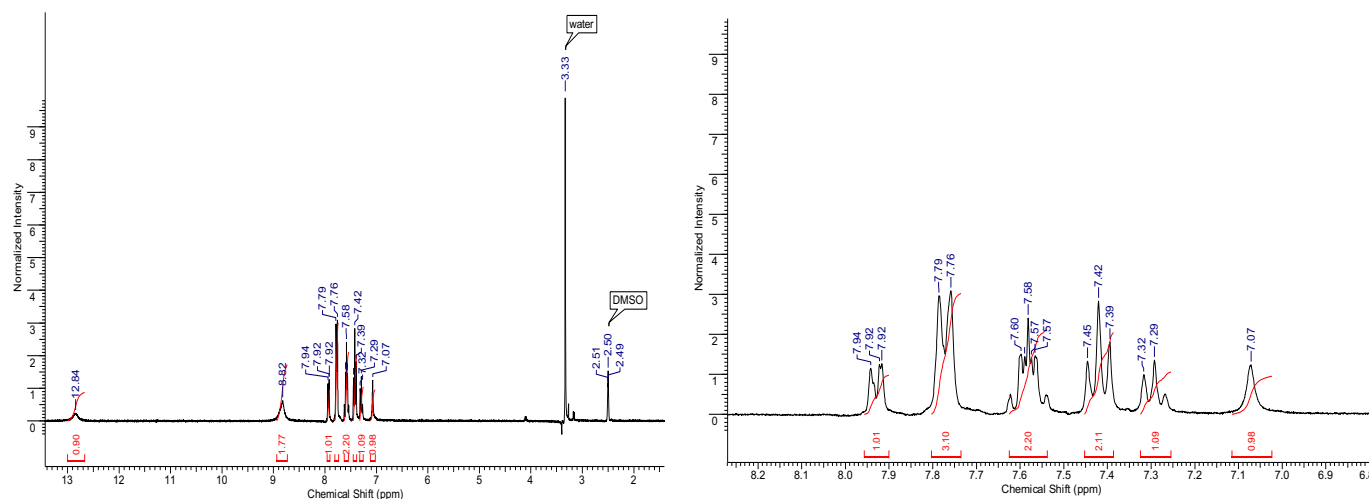


Fig. 3- ¹H NMR (300 MHz) of 3-amino-5-phenylpyrazole in d₆-DMSO.

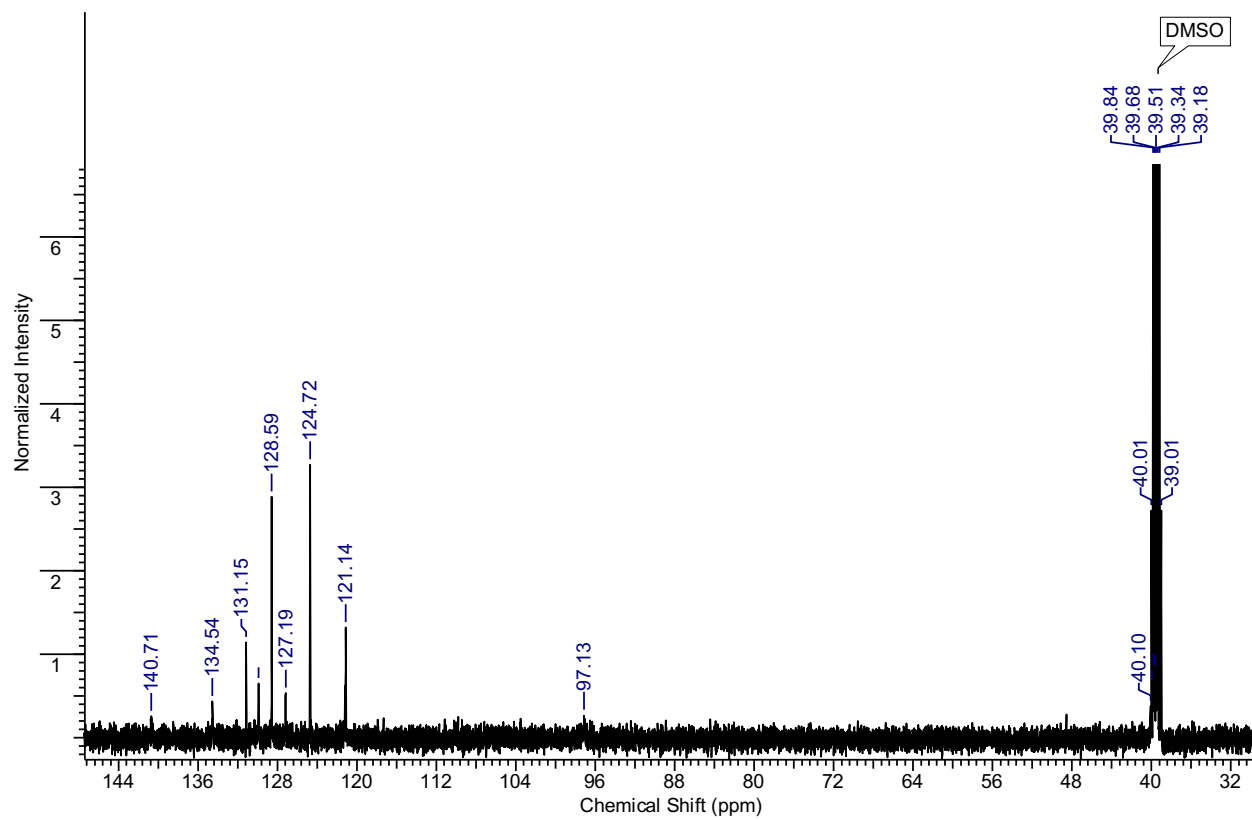


Fig. 4- $^{13}\text{C}\{^1\text{H}\}$ NMR (125 MHz) of 3-amino-5-phenylpyrazole in d_6 -DMSO.

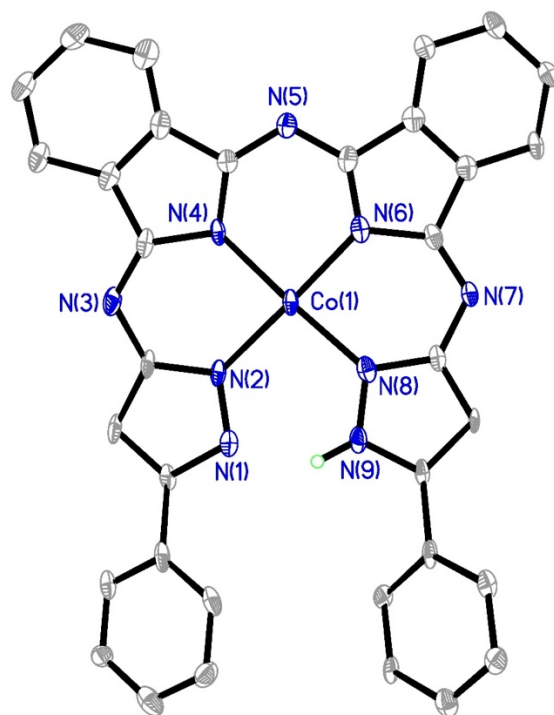


Fig. 5- The structure of Co(phenylBlzH) with 35% thermal ellipsoids. Hydrogen atoms on carbon and oxygen positions have been omitted for clarity.

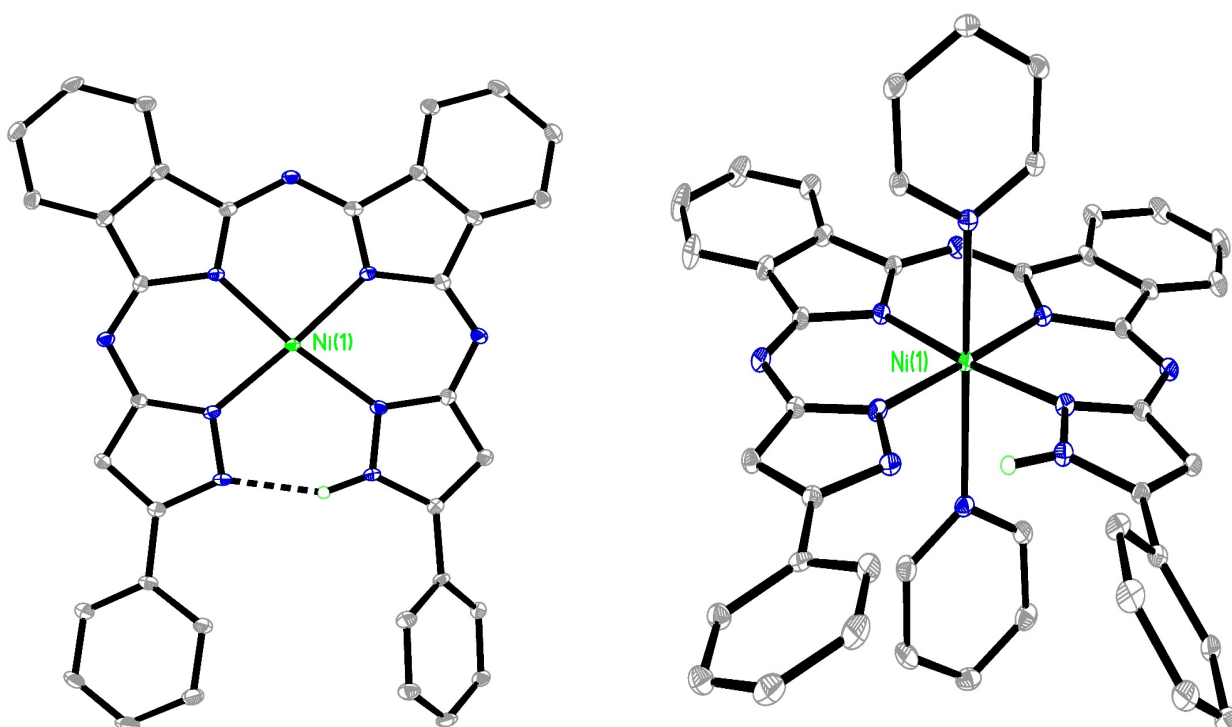


Fig. 6- (On the left) The structure of Ni(phenylBlzH) with 35% thermal ellipsoids. Axial pyridine ligands and hydrogen atoms on carbon and oxygen positions have been omitted for clarity. (On the right) The structure of Ni(phenylBlzH) with 35% thermal ellipsoids. Hydrogen atoms on carbon and oxygen positions have been omitted for clarity.

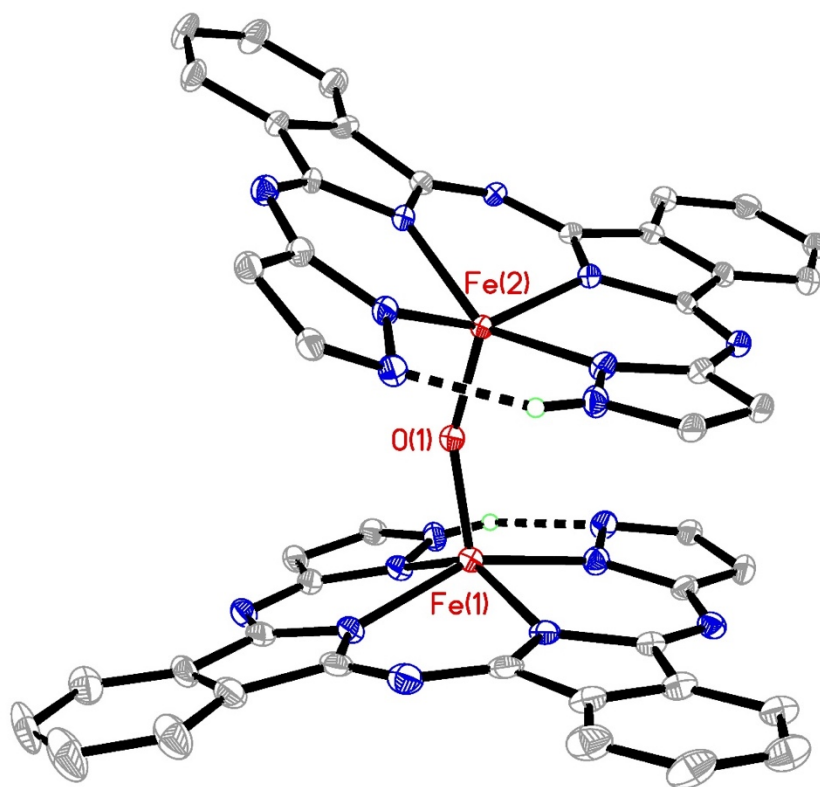


Fig. 7- The structure of the Fe(phenylBlzH) oxo-dimer with 35% thermal ellipsoids. The phenyl groups and hydrogen atoms on carbon and oxygen positions have been omitted for clarity.

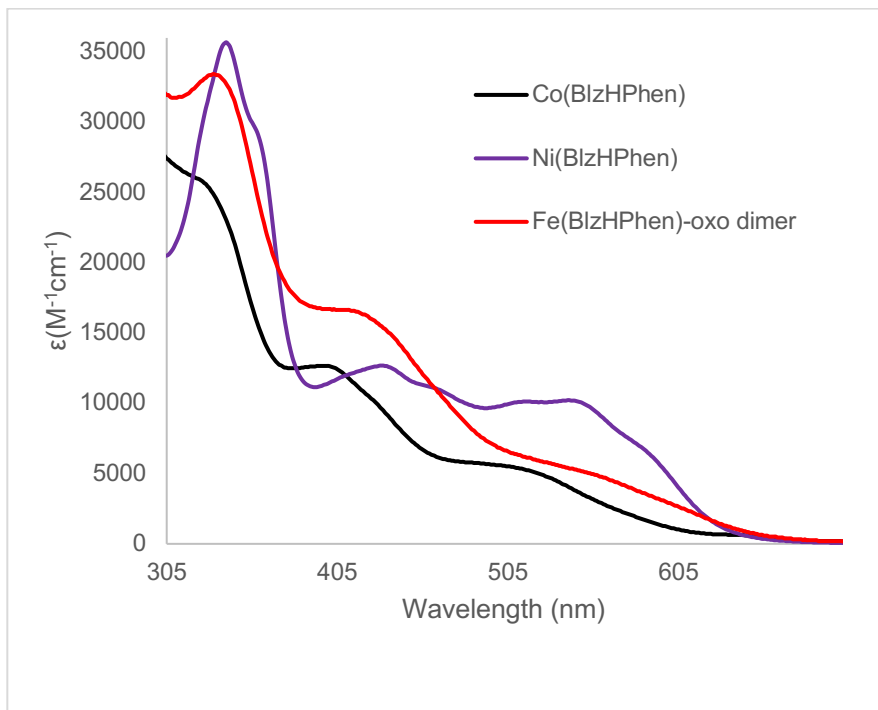


Fig. 8- The UV-visible spectra of the phenyl biliazine metal complexes in DMF solution.

Conclusion

Throughout the semester, different phenyl modified biliazines have been synthesized using techniques developed by Ziegler with the goal of seeing which metal compounds could be derived. This was done with the hope that learning more about different macrostructures of biliazine and different compounds would help to further the understanding of how metals react with biliazine.

Results show that the phenyl pyrazole derivative biliazine compounds allowed for the growth of bigger crystals to be analyzed. It also proved that Fe and Ni compounds can be made using this phenyl pyrazole method. This could lead to more research into what other metals could be used to create new biliazine compounds. A good place to start would be with Mn and Cr. We

were unable to get these two metals to bind in the right way, but there is surely opportunity in that direction. Plenty of research is left untouched when it comes to the different compounds that can be created using biliazine.

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