Biologically inspired Calixpyrrole ligands for nitrogen activation.

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ABSTRACT

Climate change has become one of the most important topics talked about today. A large contributor to climate change is greenhouse gas emissions coming from fossil fuels. Because of greenhouse gas emissions, the Earth's atmospheric temperature is projected to increase by 1.5˚C by the year 2040. Higher temperatures, droughts, forest fires, flooding and other natural disasters are also hypothesized to be consequences of climate change and greenhouse gas emissions. In order to halt these negative impacts, alternative fuel sources must be explored. Ammonia is a favorable choice because it will release nitrogen gas as a byproduct, and it has very similar characteristics to petroleum gas. They are both stored, transported, and handled very similarly, which would make the transition to ammonia fuels much easier. Current production of ammonia is unsustainable so new methods for making this potential fuel are needed. Many scientists have used inspiration from an enzyme called nitrogenase to design catalysts that will produce ammonia from nitrogen. There are several problems with the current nitrogen reduction catalysts. Those problems include very strong acids and reductants for proton and electron sources, as well as, relatively small amounts of ammonia. Changes must be made to increase the viability of nitrogen reduction catalysts. Inspired by literature and nature, a macrocyclic calixpyrrole ligand was synthesized containing a ferrocene backbone to aid in electron transfer. During this synthetic procedure, there was the discovery of two other ligands that could also be useful in creating catalysts for nitrogen reduction.

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Chapter One: Introduction

Introduction:

Part 1: Climate Change

During the mid-1700s, coal became a widely used fuel due to a large demand for energy sources.[1] Following the increased usage of coal, other fossil fuels were discovered. Today, fossil fuels are the world's largest energy source.[2] With a finite supply, fossil fuel reserves will be completely depleted in less than 100 years. Oil and gas are projected to be exhausted by 2042, leaving coal as the only fossil fuel supply after that.[3] As for the United States, one of the largest fossil fuel consumers, about 80% of the energy supply comes from fossil fuels.[4] While the U.S. uses a majority of their own fossil fuel supply currently, the country is predicted to use all of its coal reserves by 2088.[5] This would mean that after the supply runs out, the United States would rely solely on other countries to provide energy for the country. [3]

While the finite supply of fossil fuels is a serious problem, there are larger problems associated with fossil fuels. The burning of fossil fuels creates large amounts of waste and emits large amounts of carbon dioxide, which is a major contributor to climate change and the greenhouse effect.[6] Having large amounts of carbon dioxide in the atmosphere is detrimental to the environment. Because of the increased use of fossil fuels, the National Climate Assessment has projected the atmospheric temperature to increase 1.5˚C in as little as twenty years and about 5˚C by the end of the century.[7] The increase in atmospheric temperatures will have an effect on many different parts of the environment. For instance, because of the increase in atmospheric temperature the temperature of the oceans is increasing. Ocean temperatures have increased about 1.3˚C over the last 100 years.[7] With the concentration of carbon dioxide increasing in the atmosphere due to the release of greenhouse gases, it is reacting with sea water and creating more carbonic acid. This increase of carbonic acid is causing the pH of sea water to decrease.[8] Lower pH in sea water is damaging to many organisms in the ocean. Ocean acidification is known to be responsible for the irreversible destruction to coral reefs.[9] Not only is ocean acidification causing harm to sea water, but fresh water areas are also being affected by the increase of carbon dioxide in the air.[7] In addition to this, oxygen levels in coastal areas are declining due to the rise of sea levels and changes in precipitation and winds. This has affected many sea organisms, including whales, fish, and small microbes.[7] Another effect of rising atmospheric temperatures is the rise of sea levels. Sea levels are the highest now than they have been in almost three thousand years.[7]

Currently, sea levels have risen about 8 inches in the last 20 years. The rising coast lines are directly related to the increase of land-based ice melting.[10] At the rate that the ice is melting, it's been projected that the sea level will continue to about 4 feet by the end of this century.[7]

Temperature changes will affect more than just ocean-life. With rising temperatures, farming areas will be heavily affected. Growing seasons will increase with the increase in heat-trapping gas emissions. This will negatively affect the production because the higher temperatures will lower the quality of what is growing because the crops will not get sufficient water supply. Pollination of plants could also be affected by the higher temperatures because it will be too warm for insects to do their job. In addition to this, a longer and warmer growing season will increase the interactions of harmful bugs with people and crops, as cooler weather typically is responsible for forcing those bugs out of the area.[11] NASA has suggested that with the addition of longer growing seasons, higher temperatures will bring more droughts and harmful weather.[12] With droughts come the increased possibility of wildfires. The changes in climate have caused some of the largest wildfires in California, an example of this being the 2018 California Wildfires.[13] Hurricanes are also suggested to become significantly worse due to the changes in climate due to greenhouse gases. Because the frequency of severe hurricanes has increased over the last thirty years, it's predicted that hurricanes will continue to increase in intensity and release more precipitation.[7,12]

One way to combat these dangerous changes is by limiting the amount of fossil fuels used for energy and increasing the use of renewable energy sources. A viable renewable source that would halt climate change would be a fuel source that does not include carbon. For instance, hydrogen is ideal, but is not reasonable. Hydrogen can be produced as a fuel by an electrolytic process of splitting water into hydrogen and oxygen.[14] While this process sounds promising, the danger comes in the storage of the fuel. In order to use hydrogen as a fuel source for transportation, the fuel must be stored under large pressures. This is potentially harmful because hydrogen is very explosive. Hydrogen is a colorless and odorless gas and it is challenging to discover a leak. When there is a fire due to hydrogen gas, the flames are invisible which makes it very difficult to fight.[15] Because of the explosive capability of the fuel, different fuels must be explored.

Another fuel source that does not contain carbon is ammonia. When ammonia is burned, no greenhouse gases are emitted. In fact, using ammonia as a fuel will produce nitrogen, which can then be used again to be turned into more ammonia. Like hydrogen, the production of ammonia is very flexible as it can potentially be made using wind, water and solar sources. Unlike hydrogen, ammonia does not have explosive tendencies. Ammonia is predicted to be a successful transportation fuel because it is stored, handled and transported similar to gasoline.[16] Although ammonia has a lower energy content compared to gasoline, 11.62 MJ/liter and 31.81MJ/liter, respectively, it does have a much higher energy density than that of hydrogen (1.81 MJ/liter) at 690 bar.[17] While there are always safety concerns when using chemicals, ammonia is less harmful compared to hydrogen. Ammonia is known to have dangerous fumes, but because it is lighter than air, the fumes dissipate very quickly so humans are less likely to be affected by the fumes. In addition, there is no evidence of ammonia being a carcinogen, whereas gasoline fumes have possible carcinogenic effects.[18] Because ammonia has favorable characteristics in comparison with gasoline and hydrogen, it a promising renewable energy fuel source.

Part 2: Nitrogenase

Ammonia is also produced by prokaryotic organisms that contain the enzyme, nitrogenase, which converts nitrogen gas to ammonia. Nitrogen is used by almost all living things on Earth. Nitrogen is so abundant on Earth, as it makes up about 75% of the atmosphere.[19] The problem with nitrogen gas is that it is so chemically inert that in order for living things to make use of the gas, it must first be converted into another form. Ammonia is one of the most used forms that nitrogen gets converted to. There are three different types of nitrogenases found in different bacteria. There are the Vanadium (V), Iron (Fe) nitrogenase, and the Molybdenum (Mo) nitrogenases.[20] The most well-known and studied nitrogenase is the molybdenum nitrogenase. In this form of nitrogenase, there is an Iron (Fe) protein and Molybdenum-Iron (MoFe) protein, see Figure 1.[21] The iron protein contains an iron- sulfur ([4Fe-4S])

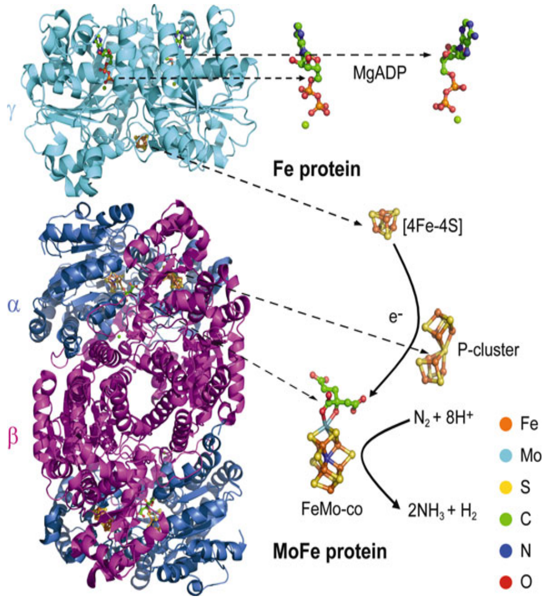


Figure 1:Iron and Molybdenum-iron proteins in nitrogenase enzyme

cluster. Along with the [4Fe-4S] cluster, MgATP molecules are used to send electrons from the iron protein to the molybdenum-iron protein. This reaction causes the transfer of electrons to the MoFe protein. In order to fully reduce N_2, eight electrons must be transferred. After the electrons arrive in the MoFe protein, they enter the P-cluster, containing a [8Fe-7S] cluster, which acts as a storage site for the electrons.[20] The electrons are then transferred from the P-cluster to the FeMo-cofactor. This is where the reduction of dinitrogen occurs, and ammonia is formed. Overall, eight protons and eight electrons are transferred to create ammonia and hydrogen gas. The exact mechanism is still under investigation.[20] Because nitrogenase is only seen in some prokaryotic organisms, production of ammonia is very low in comparison to human needs.

Part 3: Alternative Ways to Make Ammonia

With low yields of ammonia from biological sources, a large-scale production method is needed for ammonia creation. Industrially, ammonia is produced by the Haber-Bosch process. The Haber-Bosch process combines nitrogen and hydrogen to form ammonia, see Figure 2. This process is currently the way that fertilizer is produced because it has a high ammonia yield, about 98%.[22] Despite this, there are several problems with the Haber-Bosch process. To begin, the hydrogen used in combination with the nitrogen typically comes from natural gas, like methane, or petrochemicals that are often supplied by coal plants. Essentially, it takes hydrogen from "dirty fuel" to create a potential "clean fuel" in ammonia. In addition to the unsustainable hydrogen supply, in order to push the process to completion, extremely high temperatures and pressures are needed. This energy intensive process requires temperatures around 450˚C and pressures around 200 atm.[22] Because of this, it requires about 5% of all energy production. This process is not the best to use for ammonia production for renewable fuel purposes because the goals are to eliminate or reduce fossil fuel usage and to have a process that is accessible, and the Haber-Bosch process works toward neither goal.

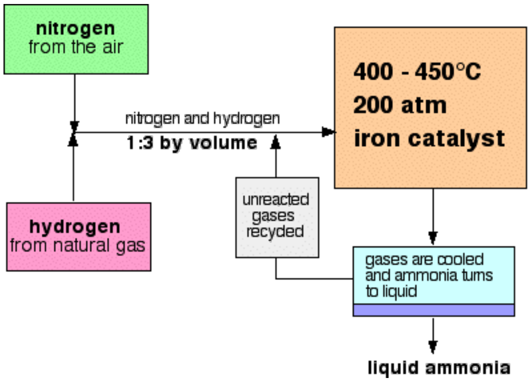


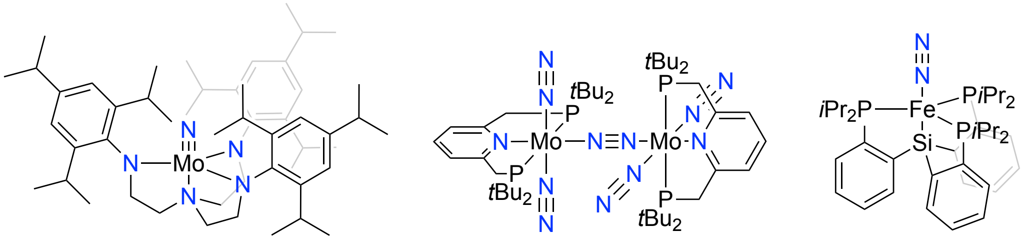
Figure 2: Simplified scheme of Haber-Bosch process

Due to the limitations of the Haber Bosch process, many groups have looked to nitrogenase for inspiration in the development of nitrogen reduction catalysts. Some of the groups that have researched nitrogen reduction catalysts include the Schrock, Peters and Nishibayashi groups.

Schrock and co-workers have synthesized several molybdenum complexes that can reduce nitrogen. Their complexes contain a single molybdenum center with a $[HIPTN_3N]^{3-}$ ligand, see Figure 3a. When testing the catalytic ability of the complexes, only 7-8 equivalents were able to be formed.[23] One of their catalysts was triamidoamine complex with a single molybdenum center. They used a strong lutidinium acid, {2,6-lutidinium}{BAr′4}, as their proton source and decamethylchromocene as the electron source when testing the catalytic activity of the molybdenum complex.[24] From this experiment, they determined that approximately 8 equivalents of ammonia were formed.[25] This had an efficiency of about 66% in relation to the reducing equivalents. This means that what is not being used to create ammonia, is being used to form hydrogen. They attempted previously to use a ligand that contained hexamethylterphenyl and one that contained hexa-*tert*-butylterphenyl as different variations, but determined that those complexes were inactive in producing ammonia from nitrogen.[26] Later, the Schrock group synthesized another single molybdenum complex with a pyridine diamindo ligand.[27] When they tested the catalytic abilities of the complex, it was found that there were 10 equivalents of ammonia that formed when decamethylcobaltocene were used as an electron source and Ph_2NH_2OTf as a proton source.[27]

Another group that synthesized nitrogen reduction catalysts with a single metal center was the Peters group. This group synthesized a catalyst with a single iron center that had a phosphine and boron containing ligand, see Figure 3c. Their catalyst needed a very strong acid and reductant, like $[H(OEt_2)_2][BAr^F_4]$ and potassium graphene.[28] Although these are both very harsh, they were successful in creating 84 equivalents of ammonia, which was a large amount compared to other complexes.[29] Later, they used this as inspiration to add osmium to their ligand. Another change they made was that they used a weaker acid, $[H_2NPh_2][OTf]$, instead of the stronger $[H(OEt_2)_2][BAr^F_4]$, and instead of potassium graphene, they used decamethylcobaltocene. These changes resulted in the production of about 120 equivalents on ammonia during the catalytic cycle.[30]

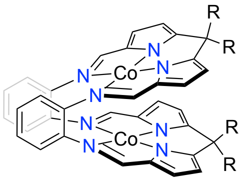
Influenced by previously made catalysts, Nishibayashi and his group synthesized a molybdenum complexes using PNP-pincer ligands, see Figure 3b. With the use of potassium graphene and $[H(OEt_2)_2][BAr^F{}_4]$, their initial catalyst was able to create around 14 equivalents of ammonia.[31] Changing things up, this group also worked on a bimetallic complex that split apart during catalysis, using two molybdenum centers and PCP-pincer ligands. They used lutidinium acid, [LuH]OTf in combination with decamethylchromocene to give a total turnover number of 47 for their catalyst.[32]



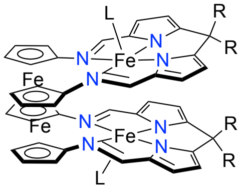
3a: Schrock **3b: Nishibiyashi** **3c: Peters**

Figure 3: Some examples of previously synthesized Nitrogen Reduction catalysts

While all of the abovementioned catalysts have shown success in nitrogen reduction, improvements are needed because of the incredibly harsh reductants and acids that must be used. This would cause large amounts of waste during large scale reactions because large amounts of ammonia are not generated in relation to the amount of acid and reductant required in the reaction.



4a: Love Calixpyrrole



4b: Proposed Calixpyrrole

Figure 4: Calixpyrrole Complexes

Taking inspiration from porphyrin chemistry and the work done by previous research groups, the Love group synthesized a bimetallic calixpyrrole catalyst, see Figure 4a. This dicobalt catalyst was successful in oxygen reduction.[33] Mechanistic pathways for two electron and four electron transfer have been observed with the cofacial calixpyrrole catalyst.[33]

Considering the improvements that are needed in nitrogen reduction catalysts and the advancements made with the bi-metallic calixpyrrole oxygen reduction catalyst brought the idea to create multimetallic calixpyrrole complexes that could potentially be used for nitrogen reduction. Instead of the o-phenylenediamine used by the Love group, a ferrocene backbone would be used on the calixpyrrole ligand which should increase the electron pool of the entire system and allow multi-electron transfer, see Figure 4b. With the calixpyrrole ligand architecture and the use of the ferrocene backbone, there would be a total of four metal centers for electron transfer. This should improve the amount of ammonia that can be formed during a catalytic procedure because the previous nitrogen reduction catalysts only utilized one or two metal centers.

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Chapter Two: Synthesis of Calixpyrrole Ligands

Introduction:

The natural way of converting nitrogen to ammonia is through nitrogenase, an enzyme in some prokaryotic organisms. Nitrogenase makes ammonia in very small amounts due to the fact that it is only present in small numbers of organisms. This inspired the industrial process of creating ammonia; the Haber Bosch process. While the Haber Bosch process is successful in creating large amounts of ammonia, it also creates large amounts of waste and requires excessive heat and pressure in order for the process to proceed.[1] Because of that research groups have been working on synthetic catalysts that can reduce nitrogen and form ammonia.

Some of the work done by the Schrock group included a dinitrogen reduction catalyst with a single molybdenum center.[2] Their work showed that they created a catalyst that could successfully reduce nitrogen to ammonia, but there were several problems. To start, after the complex was synthesized, catalysis needed to be tested. In order to do that, lutidinium BAr^F_4 was needed as the proton source and the electron source was decamethylchromacene.[2] Lutidinium was used because it is a weaker acid and the $BAr^F_4{}^-$ was chosen because it is so large that it would likely not interact with the metal. The electron source, decamethylchromacene, was used because there were previous studies that it could reduce $Mo(NH_3)Bar^F_4$ to $Mo(NH_3)$, when used in benzene.[3] It was determined that 7-8 equivalents of ammonia were formed with these conditions.[2] Schrock's group has experimented with other ligands as well, but those did not show high turnover numbers.[4]

Also using a single metal center was the Peters group. They used a single iron center instead of molybdenum.[5] Because of the work done by the Schrock group, the Peters group used lutidinium acid for their proton source and decamethylchromocene. Their work showed better results when using a stronger acid in combination with either decamethylchromacene or decamethylcobaltocene.[5] These changes resulted in a turnover number of 84. Prior to this, one of the highest turnover numbers reported for a single iron center catalytic complex was only around 64.[6] Because of the success from the iron complex, the Peters group synthesized analogous osmium and ruthenium complexes. Decamethylcobaltocene and triflic acid were used with the osmium complex to test its catalytic capabilities. Switching to an osmium complex showed great results with a turnover number around 120.[7] The ruthenium complex showed to be a viable catalyst, but the results were not as successful as previous recorded.

Another group working on nitrogen reduction is the Nishibayashi group. Following the iron catalyst trend of the Peters group, the Nishibayashi group also synthesized an iron complex with a PNP-pincer ligand. Originally, they attempted using decamethylcobaltocene and 2,6-lutidinium trifluromethanesulfonate ([LutH]OTf) for their catalytic reactions.[8] They found no ammonia production under these conditions. These results made them rethink their procedure, so they considered the conditions completed by the Peters group in their previous research.[9] Nishibayashi and coworkers switched up their procedure by using potassium graphite, KC_8, as the electron source and $[H(OEt_2)_2]Bar^F_4$ as the proton source. Using 200 equivalents of reductant and 184 equivalents of acid, the highest amount of ammonia equivalents was 14.3.[8] In addition to an iron complex with a PNP-pincer ligand, Nishibayahsi and co-workers have previously worked on dimolybdenum complexes that could reduce nitrogen.[10] With the use of lutidinium acid and cobaltocene, the bi-metallic complexes had turnover numbers up to 23, which are not as high as some of the other nitrogen reducing catalysts.

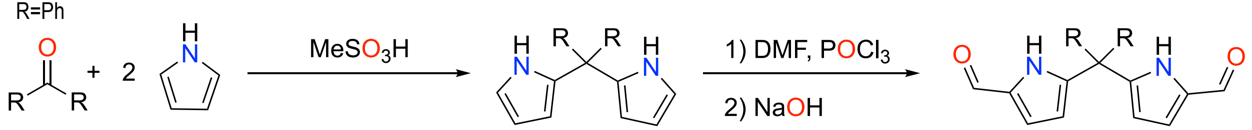
The Love Group synthesized a bimetallic calixpyrrole catalyst that was used for oxygen reduction.[11] To synthesize their macrocycle ligand, they used a *o*-phenylenediamine as the backbone, along with 5,5-Diformyl-2,2-diphenyldipyrromethane to complete the ligand.[12] This Pac-man structure showed the ability to incorporate two metal centers into the ligand. With the addition of cobalt to the macrocycle ligand, the catalyst had the ability to reduce oxygen.[11]

Using inspiration from the bimetallic macrocycle made by the Love group, and the success of the aforementioned groups working on nitrogen reduction, came the idea to create a calixpyrrole catalyst with a ferrocene backbone that can be used for nitrogen reduction. In order to start the project, the calixpyrrole ligand needed to be synthesized first.

Part 1: Synthesis of Calixpyrrole Ligand and Discovery of Half Ligand

The first step in synthesizing the targeted calixpyrrole ligand was to make 5,5-Diformyl-2,2-diphenyldipyrromethane. This molecule acts as the “top” and “bottom” of the ligand. This aldehyde was chosen because the Love group showed promising results with this analog for oxygen reduction.[12] A multi-step literature procedure was followed, see Scheme 1.

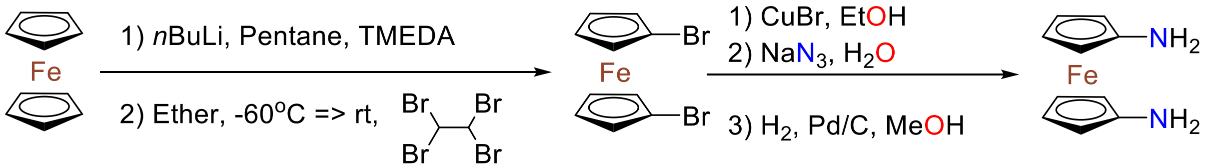
Scheme 1: Synthesis of 5,5-diformyl-2,2-diphenyldipyrromethane



First, 2,2-diphenyldipyrromethane was made with pyrrole, benzophenone, and methanesulfonic acid.[12,13] The synthesis of this molecule was confirmed by proton nuclear magnetic resonance, ^1H NMR spectroscopy. After the 2,2-diphenyldipyrromethane was made, it was combined with dimethylformamide, phosphorus oxychloride, and sodium hydroxide to make 5,5-diformyl-2,2-diphenyldipyrromethane, in a Vilsmeier-Haack reaction.[12] ^1H NMR spectroscopy was also used to confirm the synthesis of 5,5-diformyl-2,2-diphenyldipyrromethane**.**

The Love group used *o*-phenylenediamine for the backbone of the calixpyrrole that they synthesized.[12] The targeted ligand will be different because it will contain a ferrocene backbone, instead of a benzene ring. In order to incorporate the ferrocene backbone, 1,1’-diaminoferrocene needed to be made, shown in Scheme 2.

Scheme 2: Initial synthesis of 1,1’-diaminoferrocene



To make dilithioferrocene, ferrocene was reacted with *n*-Butyllithium and tetramethylethylenediamine in pentane.[14] Due to the sensitive nature of the dilithioferrocene, its purity was not confirmed by ^1H NMR spectroscopy, but all impurities could be purified out in the next step. Following the synthesis of dilithioferrocene, dibromoferrocene was made by reacting dilithioferrocene with tetrabromoethane in ether at -60˚C for six hours. The synthesis of dibromoferrocene was confirmed using ^{1}H NMR spectroscopy. After that, a copper catalyzed coupling reaction with sodium azide was used to yield diazidoferrocene, which was then used in the final step with hydrogen gas and palladium on carbon. 1,1'-diaminoferrocene was purified and isolated from methanol.[15] A clean product was collected and verified using ^{1}H NMR spectroscopy, see Figure 5

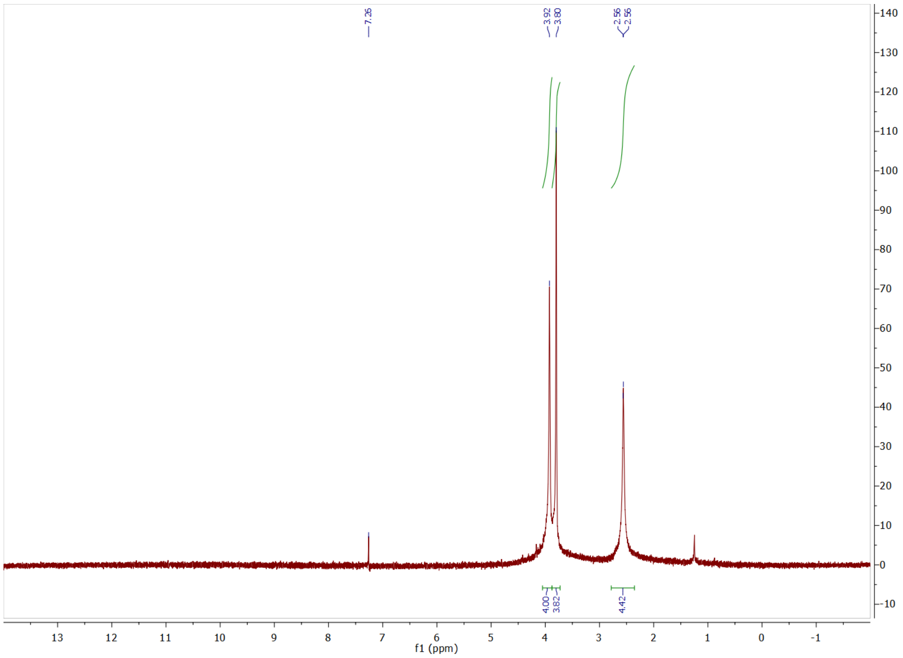
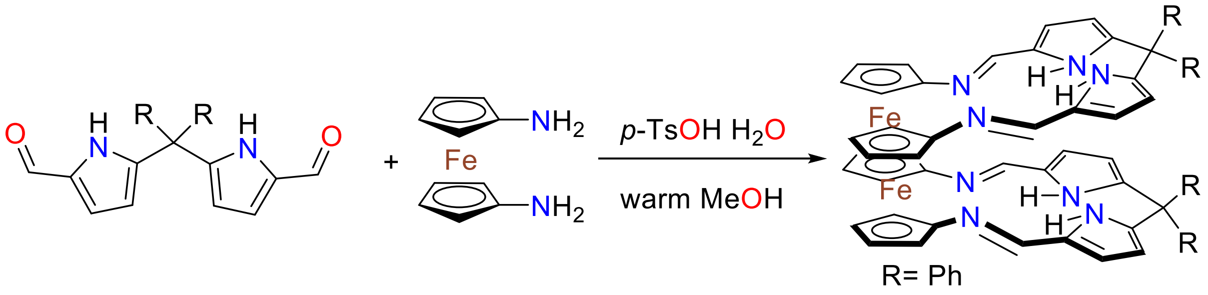


Figure 5: 1H NMR of 1,1'-diaminoferrocene in C6D6 solvent

This procedure often failed to generate a clean product with a decent yield because there was difficulty reproducing the copper catalyzed azide coupling step. Because of that, alternative synthetic routes were explored. As before, dilithioferrocene was made with the same procedure. Then, using a safer procedure with a more protected azide, 1,1'-bis(azido)ferrocene was synthesized from dilithioferrocene and triisyl azide, following literature procedures.[16,17] With the addition of triphenylphosphine, the 1,1'-bis(azido)ferrocene was converted into 1,1'-Bis(*N*-triphenylphosphoranilideneamino)ferrocene.[17] This could then be heated in the presence of water and recrystallized from methanol to give diaminoferrocene crystals. This procedure was more successful than the previous because it created 1,1'-diaminoferrocene in much greater yields. This was particularly wasteful because the starting material, dibromoferrocene, of the first method gave a low yield as well. By starting with dilithioferrocene, a reaction that generally has high yield, there is already less product lost throughout the reaction.

Initially, attempts that closely followed the procedure performed by Love and coworkers to isolate the desired calixpyrrole ligand were performed, equal parts of 5,5-diformyl-2,2-diphenyldipyrromethane and diaminoferrocene were reacted in methanol with *p*-toluenesulfonic acid[12].

Scheme 3: Synthesis of Calixpyrrole Ligand



When one drop of acid was added, a black tar like substances appeared in the flask. This result led to the determination that the ferrocene starting material was electron rich enough that acid was not needed to initiate the reaction. The reaction was attempted again without adding acid. After taking the ^{1}H NMR spectrum, many peaks appeared in the imine region (8.00ppm to 8.5ppm), as well as the ferrocene region (3.25ppm to 4.50ppm), see Figure 6.

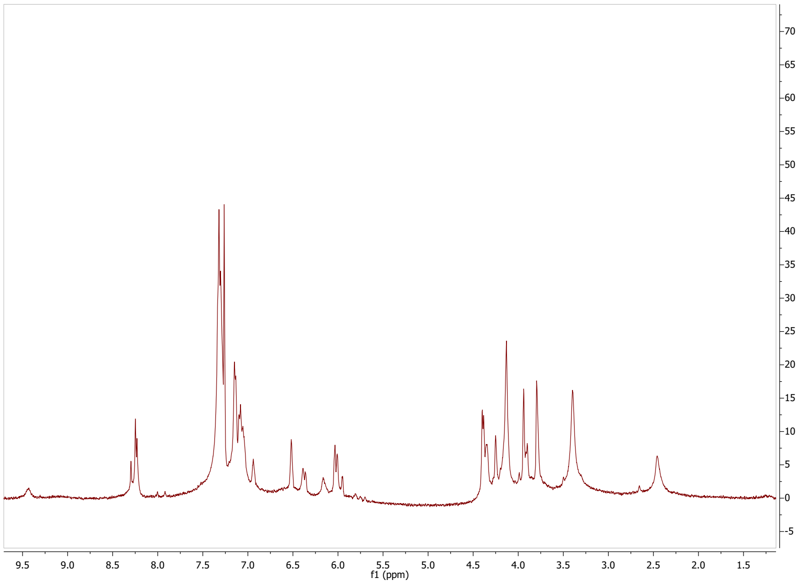


Figure 6: 1H NMR of initial Calixpyrrole reaction in CDCl3 solvent

This suggested that there were multiple products present in the sample. The challenge came when trying to determine which imine peak was associated with which ferrocene peak, and which was the desired product. The table below demonstrates the first four attempts of synthesizing the targeted ligand and focusing on the significant peaks in the spectra, peaks around 8.00-8.30 ppm correspond to the imine region.

Table 1: Reaction conditions for targeted ligand

Synthesis Attempt	Diaminoferrocene to Diformyldiphenyldipyrromethane Mole Ratio	Solvent (mass ratio)	Duration of Reaction (Days)	Temp. of Reaction (˚C)	Imine Peaks (ppm)
1	1:1	2 equiv MeOH	1	40	8.3, 8.25, 8.23, 8.00, 7.92
2	2:1	1 equiv MeOH	1	Room	8.23, 8.22, 8.18, 8.17, 8.14
3	1:1	1 equiv MeOH	1	Room	8.12, 8.03, 7.96
4	1:1	1 equiv MeOH	3	Room	8.19, 8.15

6*	1:1	1 equiv CH_3CN	3	Room	8.10

Because there were so many imine peaks, it was impossible to decipher what the products actually were. This meant that adjustments were needed. Spectra of the reaction mixture showed that there was some leftover 5,5-diformyl-2,2-diphenyldipyrromethane starting material, so in hopes of having all of the starting materials react, more diaminoferrocene was used in Attempt 2. The amount of solvent was also decreased in the hopes that concentrating the reaction would allow the reaction to go to completion and the temperature was decreased to room temperature to better monitor the reaction. After the second attempt, there were still many imine peaks, so more conditions needed to be changed. In the third attempt, the amount of diaminoferrocene was decreased so that equal parts of stating materials were used. This showed much progress because the number of imine peaks decreased. At this point, the next step was to increase the reaction time. It was believed that the reaction conditions were mostly correct for this type of reaction, but further investigation needed to be made to determine why there were still several imine peaks. So, the reaction was run for three days instead of one day. This resulted in a decrease in the number of imine peaks. Looking back at the reaction mixtures, there was always leftover starting material as a byproduct. This showed that methanol was unable to give a clean reaction. The multiple imine peaks suggested that the reaction could be occurring too quickly and uncontrolled. Because of this, the solvent was changed to acetonitrile. As the starting materials had different solubilities in the new solvent. 5,5’-diformyl-2,2’-diphenyldipyrromethane was only partially soluble and it was thought that this could control the experiment more by making it more dilute. After adjusting the solvent to acetonitrile and taking examining the ^{1}H NMR spectra of Attempt 6, there was one imine peak, shown in Figure 7.

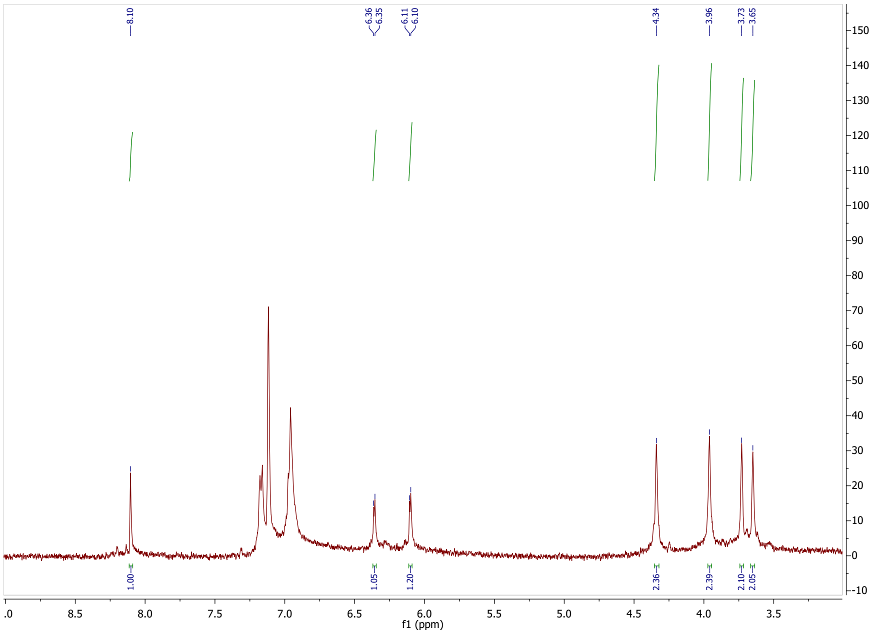


Figure 7: 1H NMR of Trial 6 product (Half Ligand) in C6D6 solvent

Because there was only one imine peak evident, that was good evidence that only one molecule existed in the product. To further investigate this, the ferrocene region was also examined. Due to the structure of the desired molecule, the integration of the spectrum should show a one to one ratio for imine to each of the four ferrocene peaks, so a 1:1:1:1:1 ratio. When examining this NMR spectrum, there was a 1:2:2:2:2 ratio which suggested that it was not the targeted molecule. This ratio suggested that only one half of the ligand was synthesized, see Figure 8.

For future use in this report, this compound will be referred to as the "half" ligand. The peaks in the spectrum suggested the synthesis of a clean product. The yield recorded for this reaction was about 4% making the reaction unrealistic to continue on a large scale, so the procedure needed to be adjusted in order to increase the yield.

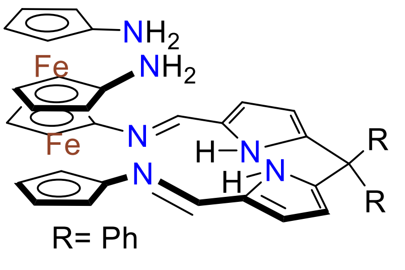


Figure 8: Proposed structure of Half Ligand

Table 2: Adaption of "Half" Ligand procedure

Reaction Number	Diaminoferrocene to Diformyldiphenyldipyrromethane Mole Ratio	Duration of Reaction (Days)	Temp. of Reaction (˚C)	Yield
138	2:1	7	40	9.5%
139	2:1	2	40	6.14%
145	1.5:1	2	40	N/A
147	1.5:1	2	35	15.16%
148	1.75:1	2	40	N/A
149*	1.5:1	1 2 1	45 Room 45	21.6%
150	1.5:1	2	45	5.22%
151	1.5:1	2	45	N/A
153	1.5:1	2	50	N/A
154	1.5:1	14	Room	N/A
155	1.5:1	1 1 1	45 Room 45	N/A

After examining what was left as side product from the original "half" ligand procedure, it was determined that there was a lot of 5,5'-Diformyl-2,2'-diphenyldipyrromethane leftover, so the ratio of diaminoferrocene was increased to 2:1 to push the reaction to completion. The temperature stayed the same, and the duration of the reaction was adjusted to seven days in reaction 138. While this successfully increased the yield to 9.5%, there was a problem because two of the variables were adjusted making it difficult to determine the reason behind the increased yield. Learning from that mistake, the reaction conditions were kept the same except for the duration of the reaction. This caused the yield to go down. Continuing with this, the duration stayed at 2 days, but the ratio of starting materials was adjusted in Experiment 145. This resulted in a yield that was unmeasurable because the product was unable to be isolated cleanly. In the next reaction, the temperature was lowered to 35˚C and all other conditions from the previous reaction remained the same. Experiment 147 had resulted in an increased yield of 15.16%, which was the highest seen at that time. Before making the final assumption that the successful ratio was 1.5:1 of diaminoferrocene, a new ratio of 1.75:1 was tested. Experiment 148 was completed with a 1.75:1 ratio of diaminoferrocene to 5,5-diformyl-2,2-diphenyldipyrromethane, the duration stayed at 2 days, and the temperature returned back to 40˚C. A yield was unable to be determined because a single product was unable to be isolated. These results confirmed that the most successful ratio of starting materials was 1.5:1 diaminoferrocene to 5,5-diformyl-2,2-diphenyldipyrromethane. So, in order to further increase the yield, the temperature and duration was adjusted. The most successful trial came during Experiment 149, but the problem was that the power went out during the reaction so the exact amount of time that it was heated and not heated was estimated. Finally, the most successful yield obtained in the experiment was 21.6%.

During this time of adjusting the procedures, the procedure for purifying the product was adjusted too. Originally, the product was purified with acetonitrile and methanol by stirring for several hours in the given solvent. Because the solvent used in the reaction was acetonitrile, washing the solid product with that solvent did not do much to the product. When methanol was used, it typically caused many small peaks to appear in the imine region. Different solvents were also tested. DME was determined successful in isolating the targeting imine peak if there were several in the region. After stirring in DME for several hours, the targeted product with an imine peak in the desired area was isolated in the filtrate. Ether was also used to dissolve excess diaminoferrocene starting material, while giving a solid product. Together, DME and ether were used to try to recrystallize the product, but no crystals were successfully grown.

Going back to the original goal of the project, a full calixpyrrole ligand with ferrocene backbone, the discovery of the "half" ligand changed the approach for accessing the full ligand. The thought was that in order to successfully synthesize the "full" ligand, first the "half" ligand needed to be generated then the reaction could be pushed to completion. In order to control the speed of the reaction, acetonitrile was used first to slow the reaction and methanol was predicted to increase the speed of the reaction for the second set of coordination.

Table 3: Synthesis of Full Calixpyrrole Ligand

Synthesis Attempt	**Diaminoferrocene to Diformyldiphenyldipyrromethane Mole Ratio**	**CH_3CN to MeOH Mass Ratio**	**Duration of Reaction (Days)**	**Temp. of Reaction (˚C)**	**Imine Peaks (ppm)**
7	1:1	1:0 1:0 1:1	1-CH_3CN 3- CH_3CN 1-MeOH	35 Room Room	8.34, 8.3, 8.26, 8.23
8	1:1	1:1	1- CH_3CN 2- CH_3CN & MeOH	37	8.28

The first attempt of doing a two-step reaction, Attempt 7 in Table 3, showed many imine peaks but instead of being near 8.0-8.20 ppm, all of the peaks were near 8.3 ppm. This indicated that something was different about the reaction. Because there were still multiple peaks, and a single peak was not isolable, adjustments needed to be made. In the next attempt, instead of adding the acetonitrile and methanol sequentially, it was decided to add equal parts at the same time to allow them to react. This resulted in the appearance of one single peak at 8.28 ppm. The ^{1}H NMR spectrum was further examined in the ferrocene region and it was determined that the single imine peak at 8.28 ppm corresponded to the ferrocene peaks at 4.23 ppm, 3.86 ppm, 3.30 ppm, and 3.09 ppm, shown in Figure 9. The integration ratio between the one imine peak and four ferrocene peaks had a ratio of 1:1:1:1:1, meaning there was one imine proton for each ferrocene proton. This result matched what was predicted to occur.

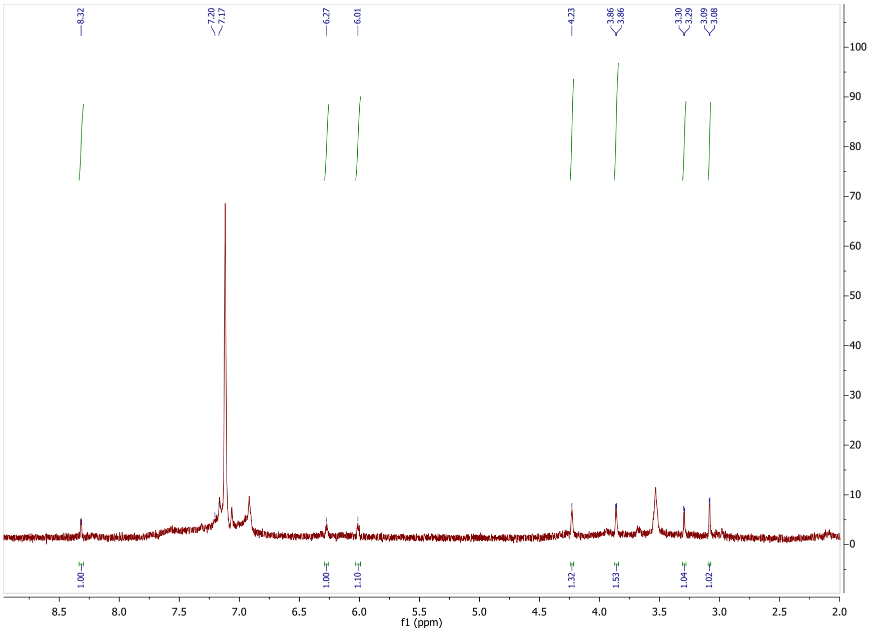


Figure 9: 1H NMR of Full Calixpyrrole ligand in C6D6 solvent

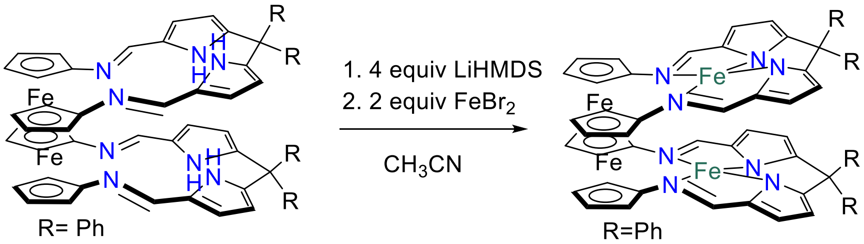
Throughout the synthesis of the calixpyrrole ligand, different purification and crystallization methods were explored in order to obtain as much of a clean product as possible. Similar to the "half" ligand procedure, acetonitrile and methanol were used first when purifying, by stirring for several hours in attempt to isolate a clean spectrum without excess peaks. Pure methanol was used in an attempt to finish the reaction if the starting materials, 5,5'-diformyl-2,2'-diphenyldipyrromethane and diaminoferrocene were evident. It was mentioned above that methanol was no longer used during the reaction because it caused the reactants to interact too readily, but when using methanol during purification it often caused any unreacted starting material to react. After methanol was used, the product would stir in acetonitrile over night to clean up any extra imine peaks that were not desired, and the product was found in the filtrate. The yield of the targeted calixpyrrole ligand only reached a maximum of about 4.16%. At this time, the best way to purify the full calixpyrrole ligand was to wash with acetonitrile.

In order to confirm the structure of the full ligand, attempts to crystallize the product were carried out. Growing a crystal of the product could provide a 3-dimensional structure of what was synthesized. Crystal growth was attempted by dissolving portions of the product in dichloromethane, chloroform, benzene, and tetrahydrofuran. There were two samples of each solvent prepared. Then, the vials were placed in larger vials that contained either ether or pentane.

While the results showed that there was no crystal growth with any of the samples, the results did show that the product was sensitive to chloroform. When chloroform was added to the product, the bright red color slowly turned brown. After several hours, the entire sample was a dark, murky brown.

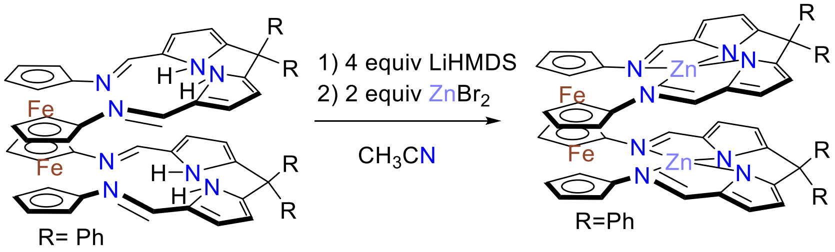
Because a clean product was seen in the ^{1}H NMR, the next step , installing metal centers in the ligand, was investigated. For the initial investigation, iron was added to the ligand. The reaction is shown in Scheme 4.

Scheme 4: Insertion of Iron to Calixpyrrole ligand



This experiment did not provide much information due to the paramagnetic nature of the resulting iron complex. Crystallization was attempted using the same solvents as above, except for chloroform, but no crystals grew. Because no conclusions were made from the experiment, it was decided to take a step back. The reaction was attempted again, but instead of inserting iron, zinc was chosen instead. Zinc was chosen as the metal to insert because as a d^{10} all of the d-orbital electrons would be completely paired, meaning it could only generate diamagnetic products. The reaction conditions were similar to the iron reaction which are shown in the scheme below.

Scheme 5: Insertion of Zinc to Calixpyrrole ligand



The ^{1}H NMR spectrum showed a slight shift in the imine peak from 8.3 ppm to 8.11 ppm in Figure 10.

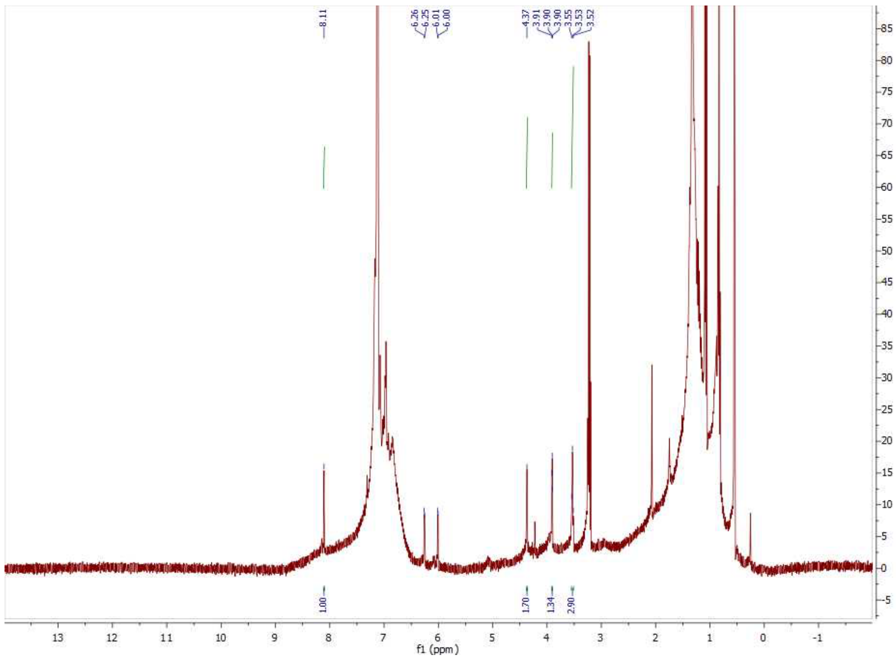
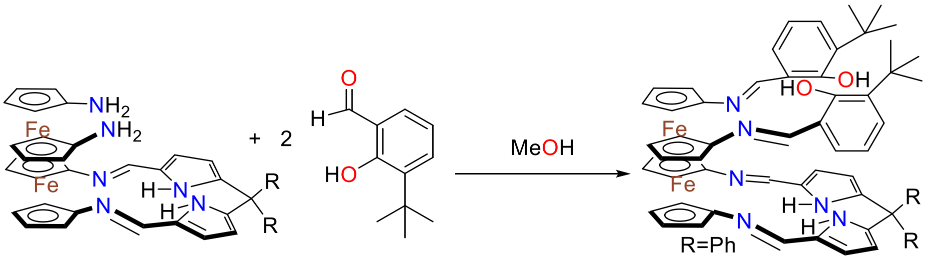


Figure 10: 1H NMR of possible Zinc Complex in C6D6 solvent

Part 2: A Mixed Ligand System

At this point in the project, there was evidence for the synthesis of two ligands; a full calixpyrrole ligand and a "half" calixpyrrole ligand. With a clean "half" calixpyrrole ligand isolated the possibility of adding a different top to the half ligand arose. The unique thing about having a different "top" and "bottom" to the calixpyrrole ligand is that there could be the potential of installing two *different* metals in the mixed calixpyrrole ligand. This could allow for unique electron transfer properties. In order to do this, a functional group other than a pyrrole group needed to be chosen to act as the "top" of the ligand. The molecule that was selected for this part of the project was 3-*tert*butylsalicylaldehyde, see Scheme 6. This was chosen because it was readily available and was predicted to react cleanly with the "half ligand".

Scheme 6: Synthesis of Half ligand with Salicylaldehyde “top”



This reaction was only completed once but had promising results as shown by the ^{1}H NMR spectrum, see Figure 11. The ^{1}H NMR spectrum showed two imine peaks at 8.26 ppm and 8.13 ppm, and there was also a small shift in the ferrocene peaks from the “half” ligand, which was to be expected. The yield was not recorded for this reaction because it was performed on small scale and all of the complete product was used for the ^{1}H NMR spectrum. The results from this reaction suggested that there was a way to add different molecules to the “half” calixpyrrole ligand in order to generate mixed ligand systems.

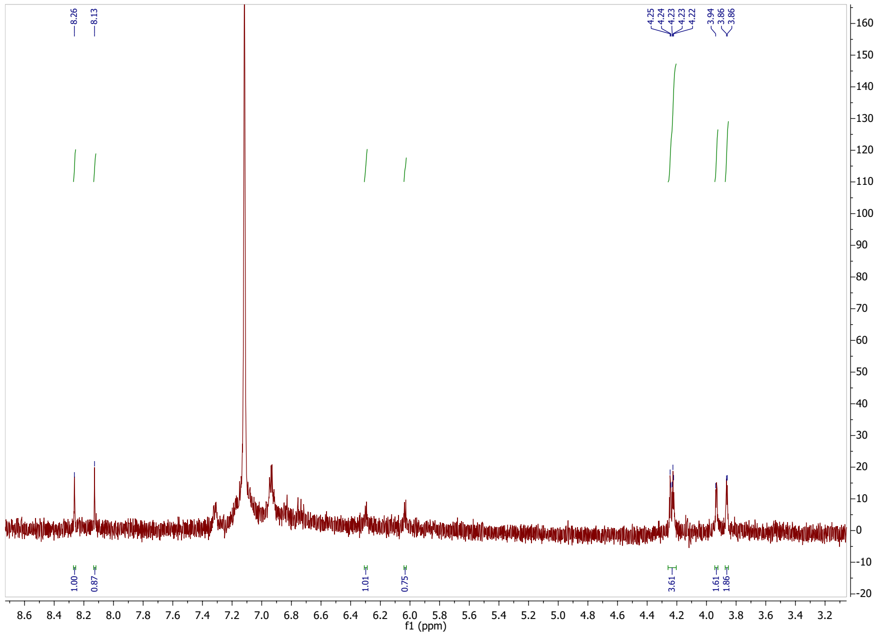


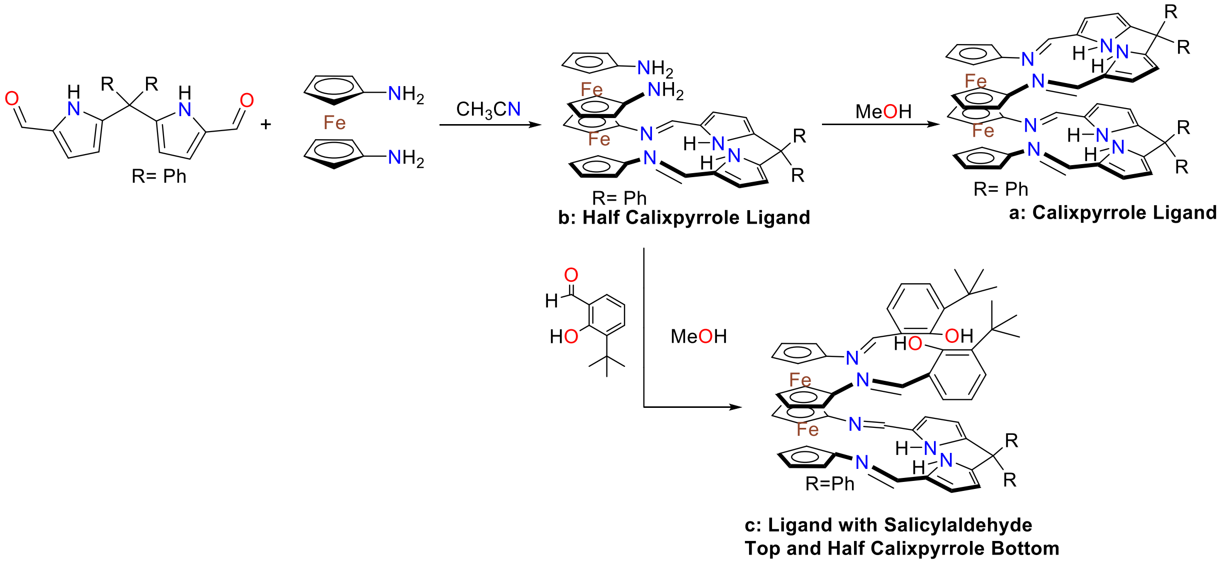
Figure 11: 1H NMR of mixed ligand system in C6D6 solvent

Throughout this project three different ligands can be and were synthesized. The next step would be to insert metals into the ligands to investigate whether or not it is possible, and how develop a general procedure to do it.

Conclusion:

In order to synthesize the targeted calixpyrrole ligand two starting materials were synthesized; 5,5'-Diformyl-2,2'-diphenyldipyrromethane and 1,1'-diaminoferrocene. 5,5'-diformyl-2,2'-diphenyldipyrromethane was made using simple literature procedures, while there was some difficulty when synthesizing 1,1'-diaminoferrocene. Much time was spent throughout the project discovering a new synthetic route for generating 1,1'-diaminoferrocene. After the 1,1'-diaminoferrocene was synthesized, the next step required determining a method of combining 5,5'-diformyl-2,2'-diphenyldipyrromethane and diaminoferrocene to create the ligand. During this process, the discovery of a "half" ligand was made. Reactions were done to increase the yield of the "half" ligand. Alterations to the procedure were made to increase the yield of the new "half" ligand molecule. This work lead to a new approach in synthesizing the original targeted calixpyrrole ligand. Rather than doing the entire procedure all at once, it was broken down to a multi-step procedure, see Scheme 7.

Scheme 7: Synthetic route of developing three Calixpyrrole ligands



With the success that came from the "half" ligand, it was decided to add a different molecule to the "top" of the ligand. 3-*tert*butylsalicylaldehyde was chosen as the "top" of the "half" ligand. The resulting mixed ligand is important because it opens the door of potentially adding two different metal centers to the ligand. This chapter demonstrated the ability to synthesize, purify, and characterize via ^{1}H NMR spectroscopy three different calixpyrrole ligands that have the potential to be used as nitrogen reduction catalysts.

General Considerations:

Solvents used for these reactions were purified used LC Technology Solutions Solvent Purification System. Standard purification methods were used to dry and degas solvents, such as methanol and ethanol, that were not able to be used in the purification system.

To achieve a nitrogen atmosphere, a Vacuum Atmosphere Company, VAC, glovebox was filled with nitrogen gas and used. In addition, Schlenk-line techniques were practiced in reactions where extreme heating or cooling was required. To achieve an argon environment, a Vacuum Atmosphere Company, VAC, glovebox was filled with argon gas and used.

^{1}H NMR spectra were recorded on a Varian 400 MHz NMR spectrometer, a Bruker 400 MHz NMR spectrometer, and a Bruker 600 MHz NMR spectrometer. Data was plotted in parts per million, ppm, in relation to a reference residual solvent peak of either $CDCl_3$ (7.26ppm) or C_6D_6 (7.16ppm).

All reagents were purchased commercially and used as received unless specified otherwise.

1,1'-Diaminoferrocene: In a nitrogen atmosphere, 5.54 g $Fe(CpN{=}PPh_3)_2$ was stirred in ~300 mL toluene. 2.7 mL of water was degassed for 30 minutes and added to the reaction which was refluxed overnight. The reaction was cooled, and the solvent was evaporated under reduced pressure. The product was dissolved in ~20-30 mL MeOH, stirred for 15 min., and then filtered through Celite. The filtrate was cooled to -30˚C for several days for crystallization. The crystals that formed were isolated by filtration, then washed with very small amounts of cold MeOH. The yellow gold crystals were dried under vacuum and weighed. The product was confirmed via ^{1}H NMR spectroscopy, which matched literature values. The filtrate from the crystals was concentrated and recrystallized to yield multiple crops of the product. Yield: 0.738 g.

Full Calixpyrrole Ligand: Under a nitrogen atmosphere, 0.2208 g of 1,1'-diaminoferrocene was stirred in a round bottom flask with 15 mL of acetonitrile. Slowly, 0.3635 g of 5,5'-diformyl-2,2'-diphenyldipyrromethane in 40 mL of acetonitrile was added over a 15-minute period. The reaction was then stirred overnight at 37˚C. The next day, 10 mL of methanol was added to the reaction to stir for a day. Upon completion, the solvent was evaporated and equal parts of CH_3CN and MeOH were added to the reaction flask, 30 mL each. The reaction was stirred for another night before the solvent was evaporated under reduced pressure. The product was washed with acetonitrile, then stirred in diethyl ether. The mixture was filtered, and the filtrate was recrystallized from DME and diethyl ether. The reaction yielded a red solid. Yield: 4.16%

Half Calixpyrrole Ligand: Under a nitrogen atmosphere, 0.1028 g of 1,1'-diaminoferrocene was combined with 0.1133 g of 5,5'-Diformyl-2,2'-diphenyldipyrromethane and 21 mL of acetonitrile. The reaction was stirred at 45˚C for 2 days. The reaction was then filtered. The filtrate was evaporated under reduced pressure and stirred in ether. It was then filtered and the solid was isolated as a red solid. Yield: 21.8%

Half Calixpyrrole – Half Salicylaldehyde Ligand (Mixed Ligand): Under a nitrogen atmosphere 0.02232 mL of 3-*tert*-butylsalicylaldehyde was stirred with 0.0341 g of half calixpyrrole ligand and 0.0497 g of barium triflate in 5 mL of methanol. The reaction was stirred over-night and evaporated to give a red powder.

Iron Calixpyrrole Complex: Under a nitrogen atmosphere, 0.0481 g of ferrocene-linked calixpyrrole ligand was dissolved in 3 mL in acetonitrile. In a separate vial, 0.04585 g of lithium bis(trimethylsilyl)amide was dissolved in 1 mL acetonitrile. The LiHMDS solution was then added dropwise to the calixpyrrole ligand solution and stirred for 5 minutes. In a different vial, 0.0195 g of iron (II) dibromide was dissolved in 1 mL in acetonitrile. The $FeBr_2$ solution was added dropwise to the calixpyrrole and LiHMDS mixture. The mixture was stirred over-night and solvent was evaporated. The reaction yielded a red solid.

Zinc Calixpyrrole Complex: Under a nitrogen atmosphere, 0.0293 g of ferrocene-linked calixpyrrole ligand was combined with 0.0183 g of LiHMDS and 1 mL of acetonitrile. The reaction was stirred for one hour. In a separate vial, 1 mL of acetonitrile was added to 0.0129 g of zinc bromide. The zinc solution was added dropwise to the calixpyrrole mixture and stirred overnight. The reaction was filtered the next day and the solid was isolated. The product was a red solid.

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Chapter Three: Conclusion and Future Work

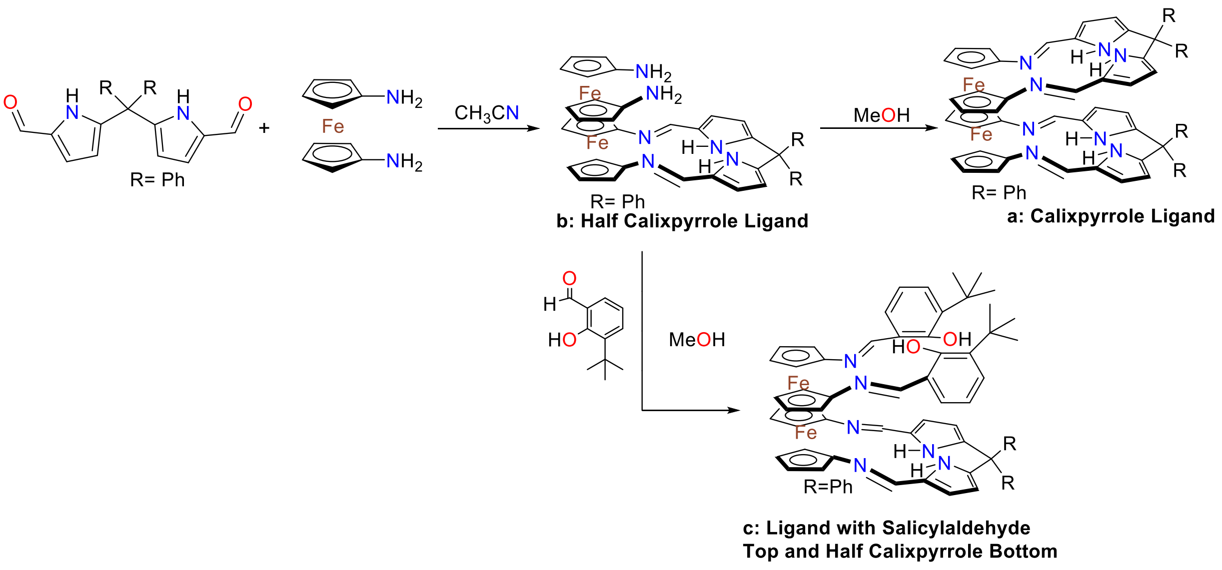
Conclusions:

In summary, the work shown in the previous chapter is the first critical step toward the synthesis of nitrogen reduction catalysts. These types of catalysts are needed to combat the negative impacts of carbon emissions due to the burning of fossil fuels.[1] Measures have been taken to synthesize nitrogen reduction catalysts that have the ability to form ammonia because the natural way, through nitrogenase, does not produce enough for human use and the industrial way, through the Haber-Bosch process, requires incredibly high temperatures and pressures and produces large amounts of waste.[2] Several research groups have created catalysts that have the ability to form ammonia, but in low quantities. For instance, the Schrock group has synthesized several catalysts containing single molybdenum centers, but only had turnover numbers as high as 10.[3,4] The molybdenum center mimicked the molybdenum iron protein that is present in nitrogenase.[5] Even more so, Peters and co-workers found success using iron centered nitrogen reduction catalyst that had the ability to create 14 equivalents of ammonia.[6] Having an iron center closely related to the structure of nitrogenase because there is an iron protein and a molybdenum iron protein.[5] The Peters group also updated their iron complex by changing a ligand and changing the metal center to osmium. They found great success with the osmium complex they synthesized with 120 equivalents of ammonia being formed.[7] Another group that had success in creating nitrogen reduction catalysts was the Nishibayashi group. This group created an iron centered ligand with a PNP-ligand and was able to obtain about 14 equivalents of ammonia.[8] Later, they synthesized a bi-metallic complex with molybdenum. The two metals in this catalyst split apart during the catalytic cycle to produce 47 equivalents of ammonia.[9] These are some of the catalysts that showed activity for nitrogen reduction similar using similar metals as nitrogenases. Unfortunately, these catalysts have relatively low turnover numbers meaning they would not be viable for creating a large amount of ammonia for human use.

In a somewhat related field, the Love group synthesized a co-facial calixpyrrole catalyst that contained cobalt in order to reduce oxygen to water. Their work showed high yields and a way to facilitate multielectron transfer for the purpose of oxygen reduction.[10] Because of the success that group had, the idea came to create a nitrogen reducing co-facial calixpyrrole complex. In order to do that, a new calixpyrrole ligand needed to be synthesized. The targeted ligand had a ferrocene backbone that should facilitate multi-electron transfer, as it has a larger electron pool then the arene-linked ligand used by the Love group. In order to do this work, the starting materials needed to be synthesized. The starting materials used were 1,1'-diaminoferrocene and 5,5'-diformyl-2,2'-diphenyldipyrromethane. Following the procedure developed by the Love group, adjustments were made to make the targeted ferrocene-linked ligand. After the synthesis was determined, purification steps were investigated. During the synthesis of the targeted ligand, there was the discovery of a "half" ligand. Unfortunately, the yield for this compound was very low, so the reaction conditions were adjusted to increase the yield. Lastly, because there was only one 5,5'-diformyl-2,2'-diphenyldipyrromethane group added to one side of the 1,1'-diaminoferrocene backbone, that left space to attach other functional groups to the other side. Adding another group could enhance or change the activity of the ligand and in turn, give different catalytic results. Because of that, 3-*tert*-butylsalicylaldehyde was added to the "half" ligand to create a "half" calixpyrrole/half salicylaldehyde ligand. Because of the two different functional groups, there is the possibility to synthesize a mixed metal system. With a system like this, molybdenum and iron could be inserted to make the complex closely related to the molybdenum iron protein that is present in nitrogenase.

This work showed that the procedure for generating the targeted calixpyrrole ligand could be broken into a multi-step process. This multistep process allowed for the synthesis of other ligands, such as a "half" ligand and a mixed ligand system. See Scheme 8**.**

Scheme 8: Multistep route for the development of three novel ligand systems



The results from this work suggested that three different calixpyrrole ligands were synthesized. Moving forward, these ligands could to be used to generate complexes for nitrogen reduction. In order to test their catalytic abilities, their reduction potentials must be measured and compared to determine which would provide the best results. In addition, the ligands themselves could be tuned in order to adjust reduction potentials. Preliminary work has already been done in varying the structure of the calixpyrrole ligands.

Future Work:

Part 1: Generating Complexes with the Three Novel Ligands and Testing Catalytic Activity

This project has the ability to move in many different directions. Initially, full characterization using ^{13}C, COSY, and HMQC NMR spectroscopy, as well as, elemental analysis and x-ray crystallography should be completed, in addition to confirming the yields of the full calixpyrrole ligand, "half" calixpyrrole ligand, and the mixed ligand system.

After the yields are determined and the full characterization of the molecules is completed, the next step of the project can proceed. This will involve the insertion of a metal. Zinc will be used initially because it is a d^{10} metal, so any resulting complex will be diamagnetic, which would allow for NMR characterization. Using LiHMDS, zinc bromide, and the desired ligand in acetonitrile, zinc should be coordinated, see Figure 12.

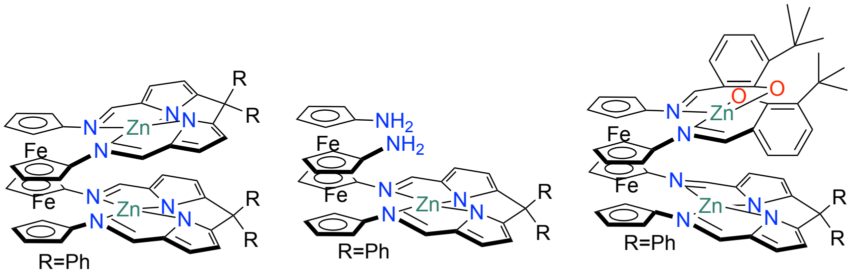


Figure 12: Structures of possible Zinc complexes

This step was previously attempted using the full calixpyrrole ligand but was not repeated. It must be attempted again to ensure reproducibility. Future studies are needed to determine the exact procedure. After zinc has been successfully inserted into the ligands, then the reduction potentials should be examined, using cyclic voltammetry. This will give baseline reduction potentials for the ligand with a non-redox active metal center. The functional groups on the ligands can be adjusted to tune the electronic structures of the complexes to give different reduction potentials.

When it is proven that a metal, zinc, can be added to the ligands, the next step will be to add other metals to the ligands, see Figure 13. There are several reasons to use iron and molybdenum. To start, they are both very abundant and affordable. Moreover, using these metals will mimic the active sites in nitrogenase enzymes. For instance, using iron would mimic the iron-only protein and using molybdenum would mimic the iron molybdenum cofactor in the MoFe protein.[5] This cofactor is thought to involve one or more metal centers and molybdenum acts as a site for N_2 binding and several of the bond breaking and bond making steps during nitrogen activation. Using a similar procedure to the insertion of zinc, iron dichloride or molybdenum trichloride and LiHMDS should be used with the ligands to coordinate the metal. Adjustments can be made after examining the results to determine an exact procedure.

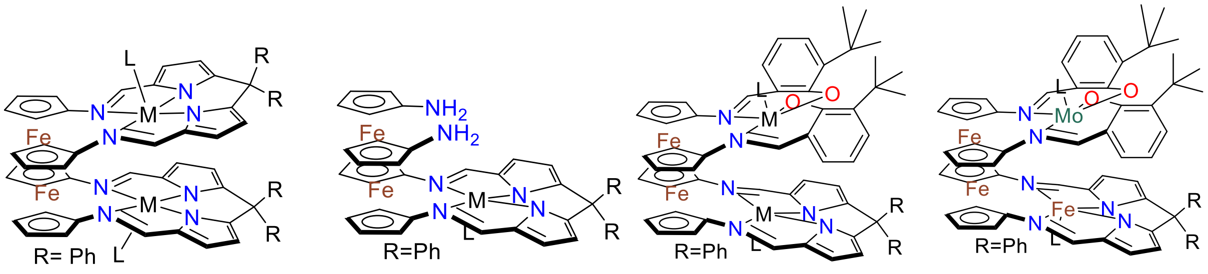


Figure 13: Proposed Iron and Molybdenum complexes

When the new metal complexes are isolated and characterized, their electrochemistry should be explored. The reduction potentials should be studied and fine-tuned by adjusting the different ligands attached to the metal. For instance, electron donating ligands, like PPh_3 or pyridine, and electron withdrawing ligands, like CO or $P(OR)_3$, should be tested. The reduction potentials will be informative in indicating which complexes will be suited for nitrogen reduction. In order to predict which will be most promising for nitrogen reduction, the reduction potentials should be below the thermodynamic reduction potential of nitrogen, +0.092V. [11]

Following the selection of complexes based on reduction potential, catalytic experiments should be carried out. Initial catalytic conditions should follow the procedures established by the Peters group and be adjusted from there. The Peters group used two main methods. One method included the use of a strong acid and reductant, $HBAr^F_4/KC_8$, where $HBAr^F_4 = [H(Et_2O)_2][BAr^F_4]$ and BAr^F_4

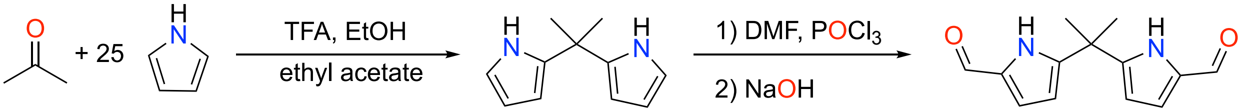
= tetrakis (3,5-bis(trifluoromethyl)phenyl) borate.[12] A milder version of this reaction was reported using $Cp^*_2Co/[Ph_2NH_2][OTf]$ or $Cp^*_2Co/[PhNH_3][OTf]$, where Cp* = pentamethylcyclopentadiene and OTf = trifluoromethanesulfonate.[6,12] The Peters group monitored their experiments using UV-Vis spectroscopy, NMR spectroscopy and magnetic susceptibility. In addition, they used Mössbauer spectroscopy to measure the different oxidation states of the metal during the catalytic cycle. In the case of this project, samples will need to be sent out for Mössbauer spectroscopy, so catalytic studies using this tool are less feasible.

Peters and co-workers also modified their procedure for electrocatalysis by using $Cp^*_2Co^+$ as an additive to shuttle electrons from an electrode to their iron catalyst.[13] Because the proposed catalysts in this project contain ferrocene backbones, they should be more amendable for electrocatalysis. As such, these catalytic systems will not need additives for electrocatalysis.

Part 2: Varying the Substituents Between Pyrrole Donors

Changing the substituents used on the pyrrole ligands could have a significant impact on the reduction potentials of the complexes and thus catalysis. Taking inspiration from the Love group which used both phenyl and methyl substituents when synthesizing calixpyrrole ligands for oxygen reduction catalysts, it was decided to synthesize a calixpyrrole ligand with a methyl group as well.[14] In order to do this, a multi-step procedure was need for synthesizing 5,5'-diformyl-2,2'-dimethyldipyrromethane. First, 2,2'-dimethyldipyrromethane was made using pyrrole and acetone.[15]

Scheme 9: Synthesis of 5,5'-diformyl-2,2'-dimethyldipyrromethane

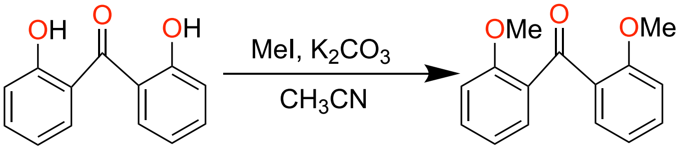


When 2,2'-dimethyldipyrromethane was synthesized following literature procedures and confirmed by ^1H NMR in addition with dimethylformamide and phosphorus oxychloride to make 5,5'-diformyl-2,2'-dimethyldipyrromethane.[16] There was some difficulty in this reaction came during the purification process. A bulb to bulb distillation was needed to isolate a clean product.

This distillation needed to be monitored and could not be left overnight unattended, so this process often took several days and sometimes up to a week to complete. No further work was done on the methyl substituent due to time constraints. The methyl substituted pyrrole ligand should be further developed and used to make a full ligand complex, half ligand complex, and possibly a mixed ligand complex. For the mixed ligand complex, the methyl substituted ligand could be used with the salicylaldehyde used in the previous chapter or could be used with the phenyl substituted pyrrole ligand.

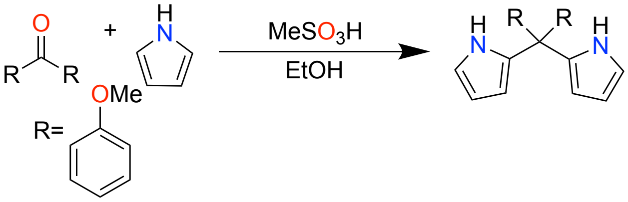
Another variation that was considered was a phenyl group with an *ortho*-methoxy substituent. This type of ligand was considered because the Schrock group had previously synthesized a nitrogen reduction catalyst with methoxy substituents.[17] It had the ability to facilitate proton-coupled electron transfer. The synthesis of the methyoxy substituent was attempted first, in hopes to eventually get to the an aldehyde using a Vilsmeier-Haack reaction. This synthesis was exceptionally challenging, and overall unsucessful after several attempts. In order to make the methoxy substituen, first 2,2'-dimethoxybenzophenone was made by reacting methyl iodide and 2,2'-dihydroxybenzophenone, see Scheme 10.[18] It matched literature values for ^{1}H NMR spectroscopy and was used in subsequent steps.

Scheme 10: Synthesis of 2,2'-dimethoxybenzophenone



The next step included 2,2'-dimethoxybenzophenone and pyrrole in the presence of methanesulfonic acid, shown in Scheme 11.

Scheme 11: Attempted synthesis of dimethoxyphenyldipyrromethane

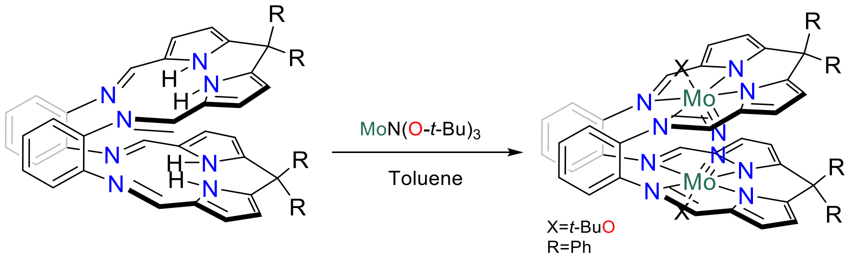


This step was unsuccessful because a black, tar-like substance was generated using this procedure. After several attempts at this reaction, no progress was made. Moving forward, a new procedure should be used to synthesize an *ortho*-methoxy substituted pyrrole ligand. Changing the acid used, or the amount of acid used, could potentially change the results of this reaction.

Part 3: Inserting Different Metals into the Arene-linked Calixpyrrole Ligand

Originally, the Love group inserted cobalt into their ligand, to make an oxygen reduction catalyst. Adding molybdenum, instead of cobalt, however, could make the calixpyrrole complex active for nitrogen reduction. This idea is supported by the structure of nitrogenase, which contains a molybdenum-iron cofactor that is used for electron transfer. Preliminary results in this began with the Love calixpyrrole ligand which was synthesized using literature procedures.[20] The calixpyrrole ligand was combined with $MoN(O\text{-}t\text{-}Bu)_3$, molybdenum nitride tris(*tert*-butoxyide), in toluene in an attempt to add molybdenum to the calixpyrrole ligand, see Scheme 12.

Scheme 12: First attempt of Molybdenum insertion with Love Calixpyrrole ligand



Based on the ^{1}H NMR spectra, it did not appear that the reaction was successful.

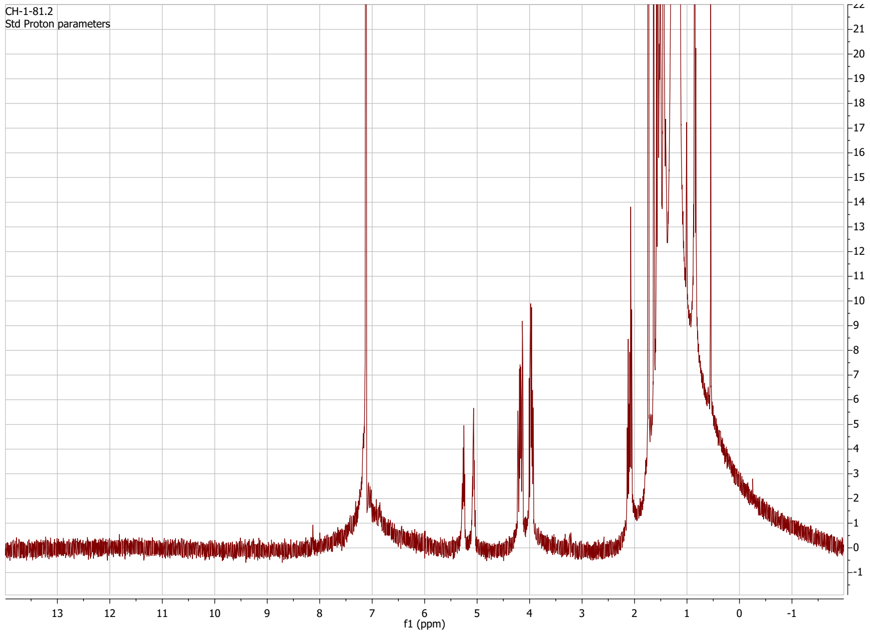
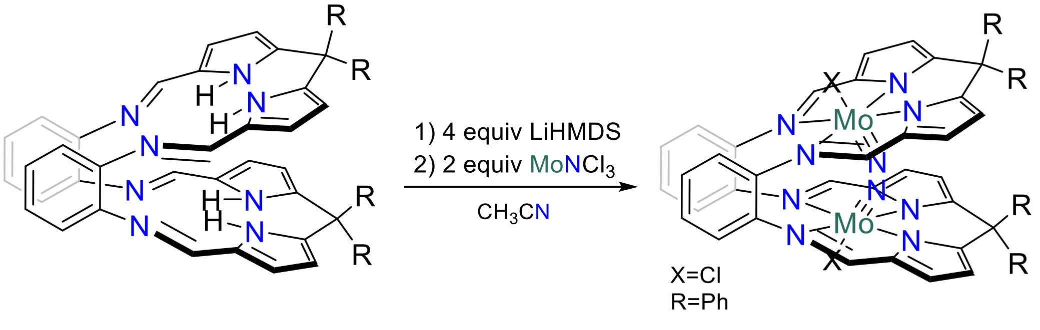


Figure 14: 1H NMR of Molybdenum Complex using Arene-linked Ligand in C6D6 solvent

After several attempts resulted in failure, a new method was tested. This time, the calixpyrrole ligand was reacted with LiHMDS and $MoNCl_3$, molybdenum nitride trichloride, in acetonitrile, see Scheme 13. Results from this reaction were inconclusive due to the decomposition of the product in deuterated benzene and chloroform, but there were several color changes which suggested that some sort of reaction occurred.

Scheme 13: Second attempt of Molybdenum insertion with Love Calixpyrrole ligand



Moving forward, the reaction should be completed again, and the stability of the complex in different solvents should be investigated. After a suitable solvent is discovered for NMR spectroscopy, then a spectrum should be collected. The results from this testing would assist in determining a solvent system for crystallization. Crystallization should be attempted to determine a three-dimensional structure of the molecule. Moving forward, if this reaction should not produce defined results, different molybdenum sources should be attempted with either a CO ligand or a phosphorus ligand. Using a CO ligand would allow for IR spectroscopy to be used to determine if there was a reaction that occurred. The benefit of using a phosphorous ligand on the molybdenum would be taking a phosphorus NMR spectrum could provide insight into the reaction progress.

General Considerations:

Solvents used for these reactions were purified used LC Technology Solutions Solvent Purification System. Standard purification methods were used to dry and degas solvents, such as methanol and ethanol, that were not able to be used in the purification system.

To achieve a nitrogen atmosphere, a Vacuum Atmosphere Company, VAC, glovebox was filled with nitrogen gas and used. In addition, Schlenk-line techniques were practiced in reactions where extreme heating or cooling was required. To achieve an argon environment, a Vacuum Atmosphere Company, VAC, glovebox was filled with argon gas and used.

^{1}H NMR spectra were recorded on a Varian 400 MHz NMR spectrometer, a Bruker 400 MHz NMR spectrometer, and a Bruker 600 MHz NMR spectrometer. Data was plotted in parts per million, ppm, in relation to a reference residual solvent peak of either $CDCl_3$ (7.26ppm) or C_6D_6 (7.16ppm).

All reagents were purchased commercially and used as received unless specified otherwise.

Insertion of Mo into the Calixpyrrole Ligand (Attempt 1): Under an argon atmosphere, 0.0508 g of MoNO-*t*-Bu_3 was added to 0.0777 g of the phenyl-substituted calixpyrrole ligand with 3-5 mL of toluene (enough to dissolve). The solution was heated at 60°C and stirred for 3 days. The product was filtered and washed with small amounts of toluene and filtrate waws evaporated. The solid product was washed with ether.

Insertion of Mo into the Calixpyrrole Ligand (Attempt 2): Under an argon atmosphere, 3 mL of acetonitrile was added to 0.958 g of phenyl-substituted calixpyrrole ligand. In a separate vial, 10 mL of acetonitrile was added to 0.7623 g of LiHMDS. The LiHMDS mixture was added dropwise to calixpyrrole ligand mixture. The reaction was stirred for one hour. In a separate vial, 2 mL of acetonitrile was added to 0.4672 g $MoNCl_3$ then that mixture was added, dropwise, to the calixpyrrole mixture and stirred overnight. Solvent was evaporated. The residue was dissolved in THF and stirred for two days. The precipitate was filtered off and the filtrate dried under vacuum.

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