Study of the Catalytic Abilities of Methyl-Functionalized & Dimethyl-Functionalized Iron Complexes for Proton Reduction

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Study of the Catalytic Abilities of Methyl-Functionalized & Dimethyl-Functionalized
Iron Complexes for Proton Reduction

A thesis submitted in partial fulfillment of the requirement
for the degree of Bachelor of Science in Department of Chemistry from
The College of William and Mary

by

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Accepted for Honors

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Williamsburg, VA
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Chapter 1

Introduction

1. Energy, Global Warming and Energy Crisis

Energy, the essential currency on the Earth, is indispensable in our lives. People harness energy to fuel all kinds of human activities, and ultimately, evolve our civilization. The Second Industrial Evolution, from the late 19th century into the early 20th century, booted the unprecedentedly rapid development of industrial production and scientific technologies. Consequently, fossil fuels, including coal, oil and natural gas, became the dominant energy resources to advance human progress. In 2007, The U.S. Energy information Administration (EIA) concluded that 86.4% of the primary energy consumption in the world can be sourced back to fossil fuels. To their credit, fossil fuels have several advantages. They are abundant in the worldwide, and their transportation can be done easily. Meanwhile, they are cost-efficient, as well as safe. Hence, exploitation and consumption of fossil fuels increased explosively to keep up with exponential growth of world economy and population.

Burning of fossil fuels not only releases tremendous amounts of energy, but also emits enormous quantity of greenhouse gases, such as carbon dioxide (CO₂). These greenhouse gases absorb heat radiated from the surface of the Earth, and then radiate back to the surface, causing warming of the Earth. Figure 1.1 shows a general trend of change in global surface temperature. It can be concluded that the global temperature has gone up drastically over
the past 40 years. In fact, the Earth’s average global temperature has risen by 0.8 °C since 1880. According to Global Climate Report by NOAA, the year 2019 was the second warmest year in the 140-year record, which is only 0.04 °C less than the record high value. Global climate change arisen from global warming effect causes melting cryosphere, leading to sea level rise. In addition, the Earth’s natural environment will be degraded, resulting in a loss of species diversity. Human life and prosperity will also suffer due to reduction of crop yield and polluted air. Even if all emissions of greenhouse gases were to stop today, due to the existent greenhouse gases, the Earth’s average surface temperature would climb another 0.6 °C or so over the next several decades before temperature stopped rising.

On the other hand, the unrestrained exploitation of fossil fuels leads to a foreseeable shortage of fossil fuel reservoir in the future. Figure 1.2 shows the dominance of fossil fuels in the worldwide energy consumption. According to BP Energy Outlook 2019, the largest parts of world’s primary energy consumption will still be fossil fuels, even in 2040. However, as human activities consume at a much higher rate than nature regenerates, the predictable depletion of fossil fuel reservoir becomes worrisome. From Figure 1.3, it can be concluded that all kinds of fossil fuels will be depleted in the near future.
Therefore, it is both necessary and urgent to find renewable and clean energy substitutes for human’s life and prosperity.

Thankfully, people are realizing the necessity of alternative energy. According to Key World Energy Statistics 2019 by IEA, the contribution of alternative energy has been increased 5.5% (Figure 1.4). Alternative energies, such as nuclear, hydro, biofuel and tide energies, are turning into major eco-friendly substitutes for fossil fuels. However, many of these alternative energies have serious shortcomings, preventing them from being widely used. Nuclear energy is criticized for its potential safety hazard and large startup cost, and biofuels can cause industrial pollution. Hydro and tidal energies are highly relied on geographical locations. Hence, an alternative energy, which is in adequate supply, easy to access, globally available, and safe, is the key to solve global warming and energy crisis. Consequently, solar energy becomes the optimal choice.

2. Solar Energy: The Best Solution

The Sun, the star at the center of the solar system, has been providing the Earth with incredibly huge amount of energy for nearly 4.5 billion years. The Sun’s power, about 386 billion billion mega Watts, is produced by nuclear fusion. It is estimated that the Sun will still output
energy via radiation for another 5 billion years or so. Moreover, the potential of solar energy striking the surface of the Earth is several times larger than the total world energy consumption. Obviously, solar energy is indeed ample and globally available, compared to other alternative energies.

There are in fact 3 main ways to harness solar energy: photovoltaics, solar heating & cooling, and concentrating solar power. Among these methods, photovoltaics (PV), which generate electricity directly from sunlight via an electronic process, are becoming more and more competitive due to the drastic drop of price of PV devices over the last decade. A PV cell, or solar cell, is composed of two wafers, n-type silicon layer and p-type silicon layer. When PV cells are struck by sunlight, the free electrons are excited via radiation energy. Consequently, PV cells are generating electricity, the transfer of energy due to moving electrons. PV seem to be the promising option, but, several drawbacks limit PV’s potential to meet the nowadays increasing energy demand. Besides long-time deployment of large land space and intermittency of solar energy, PV require inverters to convert DC to AC, and storage batteries for continuous electricity supply. Moreover, even today’s most efficient solar panels can only convert 22% of available energy into power. Such limitations...
prevent PV from using solar energy efficiently, and therefore, people are now paying attention on a natural solar energy converting process, photosynthesis.

3. Artificial Photosynthesis: An Inspiration from the Natural World

Photosynthesis is a process mainly used by plants to convert solar energy into chemical energy via chemical reactions. Plants absorb sunlight, using the energy from sunlight to produce carbohydrates via CO$_2$ and H$_2$O. Figure 1.6 illustrates the light-dependent reactions of photosynthesis process.$^{16}$ When sunlight strikes plants, chlorophyll absorbs energy from sunlight, losing one electron. That electron flows along the electron transport chain, leading to the reduction of NADP$^+$ to NADPH. The newly formed NADPH will participate in light-independent reactions, which lead to formation of carbohydrate products.

Taking the inspiration from plant photosynthesis to store solar energy in chemical bonds, researchers are developing artificial photosynthesis (AP) to either split water or reduce CO$_2$. From splitting of water via AP, hydrogen and oxygen gas are formed as products. A fuel cell powered by hydrogen gas is two to three times more efficient than an internal combustion engine running on gasoline, showing the high efficiency of hydrogen gas as a fuel.$^{17}$ Additionally, burning hydrogen gas produces only water and energy as products, which is not only eco-
friendly but also recyclable in AP to produce H₂ again. Thus, finding a systematic design that makes AP as efficient as possible is crucial to resolve global warming and energy crisis.

Figure 1.7 illustrates a water-splitting artificial photosynthesis system. Generally, a semiconductor membrane will convert energy of sunlight into electron/hole pairs. The photogenerated electrons and holes would be directed to opposite sides of the membrane where catalyst in contact with a water solution would produce hydrogen and oxygen. To generate an optimized AP system for water splitting, researchers designed water-splitting dye-sensitized solar cell.19
cells (WS-DSSC) toward the goal of low-cost, integrated systems for the direct conversion of solar energy to high energy density fuels. Figure 1.8 illustrates a setup of a WS-DSSC.

Conventionally, a WS-DSSC requires a monolayer of dye as photosensitizer, a semiconductor material such as TiO$_2$, and a catalyst. The dye molecules absorb photons from sunlight, exciting electrons of the outer shell. The generated electron-hole pairs are then processed by the semiconductor via passing electrons to cathode to reduce H$^+$ into H$_2$, and migrating the remaining holes to anode in order to oxidize O$_2^-$ into O$_2$. The cathodic reaction, which reduces H$^+$ into H$_2$, copes with desire of forming hydrogen gas. However, in order to drive the reaction only with the solar energy, a catalyst is the essential part.

4. Catalysts for Proton Reduction

Since the modern version of DSSC was originally coinvented by Michael Grätzel and coworkers in 1988, platinum was used to reduce protons to hydrogen gas in WS-DSSC. However, as a metal, platinum is one of the rare elements in the Earth, limiting its widespread use in catalysis. Therefore, mankind are now paying attention on more abundant metals. So far, several cobalt and nickel complexes have been tested that are active in reducing protons to hydrogen gas. For example, McNamara et al. reported a series of cobalt dithiolene complexes that are exceptionally active for catalytic reduction of protons in aqueous solvent mixtures. Our group has also reported a homogeneous nickel complex containing a bis-dithiocarbazate Schiff base ligand for the photocatalytic generation of hydrogen from aqueous solutions. Although cobalt and nickel are much more abundant than platinum, it is still of great interest to develop catalytic complexes that contain the most abundant element on the Earth, iron.
5. Iron Polypyridyl Complexes: A Family of Catalysts Incorporating Iron Center

Based on the incredible abundance of iron on Earth, synthesizing catalysts using iron immensely reduces the cost of a system for AP. Our group has synthesized a family of iron polypyridyl complexes. Figure 1.9 shows the structures of the family of iron polypyridyl complexes studied in recent year. Complex 1 is the first one synthesized by G. P. Connor and coworkers among these complexes. Complex 2 and 3 represent a group of analogues to complex 1. Complex 2 is a sulfinato derivative, and Complex 3 is a para-nitro derivative.

![Figure 1.9 Iron polypyridyl complexes](image)

**Figure 1.9** Iron polypyridyl complexes.

![Scheme 1.1](image)

**Scheme 1.1** Scheme illustrating syntheses of complexes 1, 2 and 3.
Syntheses of these three complexes follow similar processes. The overall synthetic scheme can be divided into two parts (Scheme 1.1): 1) Syntheses of polypyridyl ligands from salicylaldehyde and dipicolylamine; 2) Syntheses of iron(III) polypyridyl complexes from polypyridyl ligands and iron(III) precursor salt. Due to the chelate effect and rigidity of formed rings, the resulting iron complexes are greatly stabilized by the tetradentate polypyridyl ligands. Meanwhile, the two chlorine ligands on the complex are comparatively labile, leading to the opening of active sites for catalysis.

Complexes 1, 2, and 3 were proved to be electrocatalytically active for proton reduction by lowering the activation energy. To test their electrocatalytic abilities, cyclic voltammetry (CV) was used.

6. Cyclic Voltammetry and Metrics to Measure Electrocatalytic Abilities of Catalysts

As a powerful electrochemical technique to investigate redox processes of molecular species, CV is invaluable in studying electron transfer-initiated chemical reactions, including catalysis.26 The current density throughout the whole scan, and catalytic behavior of the investigated molecules, are recorded. Figure 1.10 shows the CVs of 1, 2 and 3 in acetonitrile (CH₃CN) upon incremental addition of trifluoroacetic acid (TFA). In each one, the CV in black demonstrates a reversible redox couple of complex in the absence of acid, indicating that Fe³⁺ gets reduced into Fe²⁺ and then gets oxidized back to Fe³⁺. Upon addition of TFA, an irreversible reduction event, as known as catalytic wave, occurs at a certain potential (-1.17 V vs SCE for 1, -
1.57 V vs Fc/Fc for 2, and -1.18 V vs Fc/Fc for 3), indicating the catalytic reduction of protons to hydrogen gas.23-25

With the application of CV, several metrics are quantified to distinguish electrocatalytic abilities of those complexes. First of all, overpotential (\( \mu \)), defined as the difference between the applied potential and the standard for the formation of product from substrate, indicates the additional potential needed to drive a reaction at a specific rate.27 In other words, overpotential is the energy barrier that a catalytic event need to overcome. The overpotential of 1 is 660 mV in CH\(_3\)CN, whereas 2 has the overpotential of 800 mV, which indicates that 2 catalyzes proton reductions less thermodynamically favorably than 1. Complex 3 has an overpotential of 300 mV, which seems more thermodynamically favorable than 1. Due to the electron-withdrawing nitro group para to the oxygen on the phenolate group of complex 3, iron center of 3 becomes more electron-deficient, further lowering the energy required for proton reduction.

Secondly, to kinetically quantify catalysis, TOF (turnover frequency) is introduced to characterize the catalytic activity. TOF is defined as the number of moles of product evolved per
unit of time per mole of catalyst, describing the activity of catalysts. TOFs are calculated using the following expression:

\[
\frac{i_{\text{cat}}}{i_p} = \frac{n}{0.4463} \sqrt{\frac{RTk_{\text{obs}}}{Fv}}
\]

(1)

Where \(n\) is the number of electrons in each catalyzed reaction, \(R\) is the gas constant, \(T\) is temperature in Kelvin, \(F\) is the Faraday constant and \(v\) is the scan rate (V s\(^{-1}\)). Solving \(k_{\text{obs}}\) gives the TOF in s\(^{-1}\). Based on Equation 1, getting the value of \(\frac{i_{\text{cat}}}{i_p}\) is necessary for calculating TOF. \(i_{\text{cat}}\) is the peak current of the catalytic wave, and \(i_p\) is the peak current of the system without proton source. For complex 1, the maximum TOF is 1210 s\(^{-1}\) in CH\(_3\)CN, meaning that complex 1 is highly active as the catalyst for proton reduction. Interestingly, complex 1 is even more active in the presence of water, with the maximum TOF of 2850 s\(^{-1}\). Complex 2, with the maximum TOF of 3300 s\(^{-1}\), is more active than complex complex 1. Complex 3, which has the lowest overpotential, has comparatively smaller \(\text{TOF}_{\text{max}}\) (550 s\(^{-1}\)).

The aforementioned iron complexes are electrochemically active. This family of iron polypyridyl complexes reveal a promising blueprint of constructing an iron-based AP system, which is both stable and active. However, there is a room for improving the understanding of ligand effects on catalytic abilities of iron complexes. More studies are carried out in our group, including researches on the common starting material, dipicolylamine (DPA).
7. Back to Starting Material: Simplification of Designing of Iron Complexes

![Crystal structure of complex 1 via X-ray crystallography. Color code: iron, orange; oxygen, red; chlorine, green; nitrogen, blue; carbon, black. Hydrogen atoms have been omitted for clarity.]

By mimicking the active site of hydrogenase enzymes, complexes 1, 2 and 3 demonstrate a successful platform to design catalytic-active iron complexes. Figure 1.11 shows the crystal structure of complex 1 as a distorted octahedral. By pinching the iron center, the polypyridyl ligand opens up space around iron center as probable catalytic sites, facilitating catalytic reactions. However, researchers in our group are investigating the feasibility of simplifying polypyridyl ligands to modified DPA ligands. So far, an iron complex synthesized from DPA and iron(III) salt has been reported to be catalytic active on proton reduction (Figure 1.12). This iron complex, originally as a catalyst for oxygen reduction, shows a promising activity on proton reduction. It is proposed that removal of benzyl derivatives and resulting third chlorine ligand release more space around iron center, generating more possible sites for catalysis. Therefore, the
rate of catalysis will be promoted. By regarding [Fe(DPA)Cl₃] as the parent complex, various
derivatives can be built up for further comparisons of catalytic performance.

8. Methyl-Functionalized & Dimethyl-Functionalized Iron Complexes

Complex 1 through 4 together show the effect of linking DPA with benzyl derivatives on
catalytic performance. However, limited studies have been carried out on modifying DPA itself.
Two new complexes, 5 and 6, are proposed to be synthesized as derivatives of the parent
complex 4. Structure of 5 and 6 are shown in Figure 1.1. By adding methyl group(s) to the
ortho position of the pyridine ligand(s), we are using complex 5 and 6 to probe the role of steric
hinderance at the site of catalysis plays. We hypothesize that methyl-functionalized and
dimethyl-functionalized iron polypyridyl complexes are more active electrocatalysts for proton
reduction compared to their parent complex 4.
Chapter 2

Syntheses and Characterization of Methyl-Functionalized & Dimethyl-Functionalized Iron Complexes

1. Introduction

As mentioned in the previous chapter, a bis(2-pyridylmethyl)amine Fe(III) complex (4) is an active electrochemical catalyst. Aiming to investigate the effects of steric hinderance on catalysis, we proposed to synthesize two derivatives of the complex 4. In this chapter, attempts of syntheses of 5 and 6, shown in Figure 2.1, are described. Electrochemical characterization of 5 is also discussed.

2. Materials and Methods

2.1 Materials

All experiments were carried out using standard Schlenk techniques under an Ar atmosphere unless otherwise indicated. All chemicals used in the syntheses and instrumental analysis were purchased from Fisher Scientific, Alfa Aesar, TCI (Tokyo Chemistry Industry), Sigma-Aldrich, and Acros Organics, and used without further purifications unless otherwise
indicated. Dry solvents were retrieved from SPBT-103 Bench Top Solvent Purification System by LC Technology. Post synthetic purifications with column chromatography used silica gel and TLC plates from Sorbtech, and sand, white quartz from Sigma-Aldrich. Crystallization of metal complexes used solvents from Fisher Scientific and Honeywell.

2.2 Instrumentation

$^1$H and $^{13}$C NMR spectra were recorded on an Agilent 400MR DD2 spectrometer operating in the pulse Fourier transform mode. Chemical shifts are referenced to residual solvent. Electrochemical experiments were operated under an Ar atmosphere using CH instruments 620D potentiostat. Cyclic voltammograms were acquired using a standard three-electrode electrochemical cell. The reference electrode was a saturated calomel electrode (SCE) unless otherwise indicated. Prior to every acquisition, the working electrode (glassy carbon) and the auxiliary/counter electrode (platinum) were polished using water-alumina slurry (DI water+0.05 µm alumina power) on a cloth-covered polishing pad, followed by rinsing with DI water and acetonitrile. Ferrocene was included in all measurements as an internal standard to correct drifting of reference electrode.

2.3 Syntheses

2.3.1 Synthesis of $1$-(6-methylpyridin-2-yl)-$N$-(pyridin-2-ylmethyl)methanamine ($L_1$)

![Scheme 2.1](image)

Scheme 2.1 Synthesis of $1$-(6-methylpyridin-2-yl)-$N$-(pyridin-2-ylmethyl)methanamine
Scheme 2.1 illustrates the synthetic scheme of 1-(6-methylpyridin-2-yl)-N-(pyridin-2-ylmethyl)methanamine. This procedure was a reductive alkylation of amines adapted from a modified published literature procedure. The whole reaction was divided into two steps: 1) Formation of an imine intermediate from nucleophilic addition of a primary amine to the carbonyl group of an aldehyde; 2) Reduction of the imine intermediate by sodium borohydride (NaBH₄). Namely, 2-pyridylmethlamine (1.375 g, 12.5 mmol) was dissolved in 25 mL of MeOH. The solution mixture was then transferred into a 100 mL Schlenk tube. 6-methyl-2-pyridylmethylcarboxyaldehyde (1.5 g, 12.5 mmol) was added into the Schlenk tube to start nucleophilic addition reaction. The reaction mixture was stirred for 1 hour at room temperature. The reaction vessel was then put in an ice bath to be cooled down to 0 °C. Due to the strong reactivity of sodium borohydride (NaBH₄), addition of sodium borohydride (375 mg, 10 mmol) into the reaction vessel was carried out slowly. The resulting reaction mixture was then stirred for another 1 hour at room temperature. Concentrated hydrochloric acid was then added to the reaction mixture until the pH of the reaction mixture became 1 to decompose an excess of sodium borohydride. The solvent of reaction mixture was evaporated partly with a rotary evaporator and 100 mL aqueous solution of Na₂CO₃ was then added to the residual reaction mixture to make the reaction mixture basic. The resulting mixture was then extracted with DCM (3*50 mL). The collected organic layers were washed with brine and then dried with sodium sulfate followed by gravity filtration. Solvent was removed with a rotary evaporator to yield a dark amber oil (2.25 g, 10.5 mmol, 84% yield). ¹H NMR (CDCl₃): δ 8.55 (d, 1H), δ 7.64 (dt, 1H), δ 7.52 (t, 1H), δ 7.36 (d,1H), δ 7.13-7.17 (m, 2H), δ 7.01 (d, 1H), δ 4.00 (s, 2H), δ 3.95 (s, 2H), δ 2.53 (s, 3H). The full spectrum is included in Figure A1.
2.3.2 Synthesis of 1-(6-methylpyridin-2-yl)-N-(pyridin-2-ylmethyl)methanamine Fe(III) chloride ([FeCl₃(L₁)])

\[
\begin{align*}
\text{[FeCl₃(L₁)]} &= \text{[FeCl₃(L₁) + FeCl₃·6H₂O → MeOH, r.t.]}
\end{align*}
\]

[FeCl₃(L₁)] was synthesized using a modified literature procedure. Namely, L₁ (200 mg, 0.94 mmol) was dissolved in 10 mL of MeOH. The solution mixture was transferred into a 200 mL Schlenk tube. FeCl₃·6H₂O (253.4 mg, 0.94 mmol) was then dissolved in 10 mL of MeOH and the resulting bright yellow solution was added into the Schlenk tube. The resulting dark amber solution mixture was then stirred for 1 hour at room temperature. After allowing the reaction to cool down for 45 minutes in an ice bath, the reaction mixture was filtered under vacuum, washed with cold MeOH and Et₂O. Both filtrate and filtration residue were kept. After vacuum filtration, the filtrate was transferred into a vial and evaporated 2/3 of the solvent with a rotary evaporator. The vial was then chilled at 10 °C for precipitation. Collected precipitate was crystallized via vapor diffusion crystallization.
2.3.3 Synthesis of bis((6-methylpyridin-2-yl)methyl)amine (L2)

Scheme 2.3 illustrates the synthetic scheme of bis((6-methylpyridin-2-yl)methyl)amine.

This procedure was adapted from a modified published literature procedure. The synthetic process involves an Sn2 nucleophilic substitution to convert (6-methylpyridin-2-yl)methanol to 2-(chloromethyl)-6-methylpyridine, following by another Sn2 nucleophilic substitution to convert 2-(chloromethyl)-6-methylpyridine to 4-methyl-N,N-bis((6-methylpyridin-2-yl)methyl)benzenesulfonamide. Deprotection reaction is then carried out to remove the tosyl group. Due to the hygroscopy, (6-methylpyridin-2-yl)methanol (1.2 g, 9.8 mmol) was weighed and then added to a dry 100 mL 3-neck round bottom flask very quickly. The flask was then put under vacuum to dry the reagent. Meanwhile, 30 mL of dichloromethane was degassed with argon for 15 minutes. The degassed dichloromethane was transferred into the round bottom flask using a cannula under air-free conditions. Thionyl chloride (3.6 mL, 50.3 mmol) was then added dropwise to the reaction vessel with the mixture. The resulting clear solution was stirred and refluxed (45 °C) for 1 hour. After allowing the reaction to cool down to room temperature, the solution was evaporated to dryness with a rotary evaporator and then 100 mL of 2 M sodium carbonate was added to the residue. The resulting mixture was extracted with DCM (3*70 mL). The collected organic layers were washed with brine solution and then dried with potassium carbonate following by gravity filtration to yield a light amber solution. Solvent was evaporated with a rotary evaporator to yield a pink oil (883.2 mg, 6.2 mmol, 63% yield). $^1$H NMR (CDCl3):
δ 7.60 (t, 1H), δ 7.28 (d, 1H), δ 7.09 (d, 1H), δ 4.64 (s, 2H), δ 2.56 (s, 3H). The full spectrum is included in Figure A2.

The pink oil product (883.2 mg, 6.2 mmol) was then dissolved in diethyl ether and the resulting solution was added to a 250 mL Schlenk tube. The reaction vessel was put under vacuum to make sure that the pink product was dried completely. K₂CO₃ (1.7 g, 12.4 mmol) and p-TsNH₂ (537 mg, 3.1 mmol) were then added to the Schlenk tube. The reaction vessel was then degassed and backfilled with argon. 100 mL of dry CH₃CN was retrieved from SPBT-103 Bench Top Solvent Purification System by LC Technology and then transferred into the Schlenk tube. The resulting mixture was stirred and refluxed (87 °C) for 18 hours under argon. After evaporation of CH₃CN by the rotary evaporator, the residue was diluted with 100 mL of DI water and extracted with dichloromethane (3*50 mL). The collected organic layer was washed with brine and dried over sodium sulfate following by gravity filtration. The solvents were removed under vacuum to yield a solid residue. This residue was then dissolved in 25 mL of sulfuric acid and stirred for 2 hours at 115 °C. After allowing the reaction to cool down to room temperature, the solution was added to 100 mL of ice water, neutralized with 2 M NaOH and extracted with DCM (3*50 mL). The collected organic layer was washed with brine, dried with sodium sulfate and filtered to yield a clear yellow solution. Removing organic solvent leaves a yellow oil. The crude product was purified using column chromatography technique in 9:1 DCM : MeOH on silica gel to afford a yellow oil product (37.5 mg, 0.16 mmol, 1.7% yield). ¹H NMR (CDCl₃): δ 7.53 (t, 2H), δ 7.16 (d, 2H), δ 7.02 (d, 2H), δ 3.96 (s, 4H), δ 2.53 (s, 6H). The full spectrum is included in Figure A3.
3. Results and Discussion

3.1 Synthesis of Complex 5

3.1.1 Synthesis of L1

The initial procedure of synthesizing L1 was adapted from the other published literature. It involves a tosyl group protection of the amine, following by a nucleophilic substitution, and then a deprotection to remove tosyl group. However, the overall reactions takes more than 24 hours. And additionally, the deprotection of tosyl group, like synthesis of L2, may not be carried out completely and therefore results in unwanted side products. Hence, a more efficient and productive procedure was adapted, as introduced in section 1 of chapter 2.

3.1.2 Crystallization of 5

![Figure 2.2](left) Liquid-liquid diffusion crystallization. (right) Vapor diffusion crystallization.

The crystallization of complex 5 was initially carried out by liquid-liquid diffusion crystallization. DCM and diethyl ether constitute a binary solvent system, where DCM, which is denser, is on the bottom. However, no quality crystals formed under this condition. Therefore, vapor diffusion was attempted to grow crystals. It was proposed that diethyl ether, as the precipitant, would diffuse over the gas phase into DCM which is the solvent dissolving complex 5. This gas phase diffusion would lead to oversaturation, nucleation and, if all goes well, crystallization. As expected, growth of crystals was satisfactory. Solving the X-ray crystal structures of this compound is currently under investigation.
3.2 Synthesis of Complex 6

3.2.1 Synthesis of L2

As mentioned in section 1, synthesis of L2 involves two consecutive S$_{N}$2 nucleophilic substitution reactions. The second one, which involves in p-TsNH$_2$ and 2-(chloromethyl)-6-methylpyridine, leads to the formation of 4-methyl-$N,N$-bis((6-methylpyridin-2-yl)methyl)benzenesulfonamide. The deprotection of tosyl group requires a harsh condition (concentrated H$_2$SO$_4$, 115 °C). Like synthesis of L1, deprotection in this synthesis frequently results in a mixture containing the desired product and unwanted side products. Scheme 2.4 demonstrates the unwanted product, 4-methyl-$N,N$-bis((6-methylpyridin-2-yl)methyl)benzenesulfonamide, of a deprotection of tosyl group. Figure A4 shows the $^1$H NMR evidence, proving that the deprotection was carried out incompletely.

Besides the incompletion of deprotection, low reaction yield was another major issue limiting the overall efficiency of this synthesis. Although it has been proved that L2 has been successfully synthesized and purified (Figure A3), the yield of overall reactions, as denoted in section 1, is 1.7%, which is insignificant compared to 37.8% yield from literature.
3.3 Electrochemical Analysis of Complex 5 by Cyclic Voltammetry (CV)

3.3.1 Determination of Overpotential ($\mu$)

In many cases, an acid (AH) and its conjugate base (A-) form stable adducts (AHA-) through hydrogen bonding. This phenomenon is called homoconjugation. Due to the tendency of trifluoroacetic acid to exhibit homoconjugation in acetonitrile, calculation of overpotential ($\mu$) is complicated. TFA was chosen as the proton source for the previously reported systems owing to its low background reduction. On the other hand, TFA was used in this project to directly compare complex 5 with previously reported catalysts (1~4). Here, overpotential was determined by calculating the difference between the half-wave potential of catalytic reduction ($E_{1/2}$) and the reference potential ($E_{\text{ref}}$), which takes homoconjugation into account.

Figure 2.3 illustrates an example of determining overpotential based on derived CVs. In this study, $E_{\text{ref}}$ was defined as the reference potential of 10 mM TFA in acetonitrile. The literature value of $E_{\text{ref}}$ was found to be -0.68 V vs. Fc+/Fc. $E_{1/2}$ of proton reduction event at $v = 200$ mV/s after the addition of 8.8 mM TFA is -1.43 V vs. Fc+/Fc (Figure A5). The overpotential was then calculated to be approximately equal to:

![Graph showing cyclic voltammetry with overpotential calculation](image)
\[ \mu = (E_{\text{ref}} - E_{1/2}) = (-0.68 \text{ V}) - (-1.43 \text{ V}) = 750 \text{ mV} \]

### 3.3.2 Calculation of Turnover Frequency (TOF) using \( i_c/i_p \)

![Figure 2.4 CVs of 0.3 mg 1 in 5 mL CH\(_3\)CN before (blue) and after (black) the addition of 0.0264 M TFA in the presence of 0.1 M TBAPF\(_6\) at a rate of 10 V/s.23](image)

Typically, TOF is calculated using the obtained \( i_c/i_p \) from experiment using the equation below\(^{23}\):

\[
\frac{i_{\text{cat}}}{i_p} = \frac{n}{0.4463} \sqrt{\frac{RTk_{\text{obs}}}{Fv}}
\]

Figure 2.4 demonstrates how to use \( i_p \) and \( i_c \) values for calculating TOF.\(^{23}\) For a sample calculation of TOF, please see below Figure A5. TOF (\( k_{\text{obs}} \)) of complex 5 in CH\(_3\)CN at a scan rate of 200 mV/s was found to be 31.6 s\(^{-1}\)

### 3.3.3 Study of Proton Concentration Dependence ([TFA]) and Catalytic Mechanism

Upon addition of trifluoroacetic acid (TFA) in CH\(_3\)CN, a catalytic wave was observed at -1.23 V vs. SCE (-1.61 V vs. Fc+/Fc). When more acid is added, a larger current enhancement is
observed (Figure A5). A linear relationship between $i_c$ and [TFA] suggests a second-order dependence on proton concentration (Figure 2.5).

Upon addition of trifluoroacetic acid (TFA), a shift in the redox couple for Fe(III)/Fe(II) is observed for complex 5 from 0.13 V to 0.08 V vs. SCE, indicating that a new complex is formed upon addition of acid (Figure A5). Therefore, the catalyst operates under a mechanism where protonation is the first step (C) followed by subsequent reduction (E). The overall mechanism of catalysis is proposed to be either CECE or CEEC. It is also possible that the catalytic mechanism is more complicated than what we can deduced from CV alone.

3.3.4 Comparison Between Complex 5 and Previously Reported Complexes (1-4)

Table 2.1 summarize several important merits that characterize each of the complex (1~5).

Table 2.1 Summary of electrocatalytic proton reduction of 2 mM catalysts upon addition of 8.8 mM TFA in CH3CN,23-25,28
<table>
<thead>
<tr>
<th>Catalyst</th>
<th>$i_c/i_p$</th>
<th>$E_{cat}$ (H+/H2) (V vs. Fc+/Fc)</th>
<th>Overpotential (mV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.8</td>
<td>-1.57</td>
<td>660</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>-1.57</td>
<td>800</td>
</tr>
<tr>
<td>3</td>
<td>5.3</td>
<td>-1.18</td>
<td>300</td>
</tr>
<tr>
<td>4</td>
<td>6.8</td>
<td>-1.6</td>
<td>800</td>
</tr>
<tr>
<td>5</td>
<td>9.0</td>
<td>-1.61</td>
<td>750</td>
</tr>
</tbody>
</table>

Compared with complex 4, complex 5 has comparatively low overpotential (750 mV). In addition, based on the value of $i_c/i_p = 9.0$, it is safe to say that complex 5 is highly active for proton reduction. The higher $i_c/i_p$ of 5 suggests that steric bulk at the active site of the catalyst may increase the overall catalytic activity of this system. Therefore, it can be hypothesized that the elimination of hydrogen from the catalyst could be the slow step in catalysis.
Chapter 3
Project Outlook and Future Directions

1. Introduction

Due to the low yield of synthesizing L₂, proposed complex 6 is not yet achieved. Complex 5 is successfully synthesized and investigated through electrochemistry. Some promising results are obtained. In this chapter, conclusion and future work (synthesis and analysis) of this project will be discussed.

2. Project Conclusion

We report that a methyl-functionalized iron polypyridyl complex 5 that is active for proton reduction. It is inexpensive and synthesized in good yield. Complex 5 has proven to be highly active for proton reduction, with $i_c/i_p = 9.0$, $\mu = 750$ mV and $k_{obs} = 31.6$ s⁻¹ at the scan rate of 200 mV/s. Functionalization via adding methyl group on the pyridine ring facilitates the catalysis of proton reduction by increasing the steric hinderance at the active site of the catalyst. Therefore, it is proposed that the slow step in catalysis must be the elimination of hydrogen from the catalyst. A bulky active site would make catalysis happen faster. However, CV analysis on complex 5 is not complete. This includes the scan rate test, complex concentration study, and studies on catalytic behavior of complex 5 in aqueous solution.

On the other hand, synthesis of the dimethyl-functionalized iron polypyridyl complex 6 failed due to the low yield of synthesizing ligand L₂. Because the amount of purified L₂ was not enough, further complexation between iron(III) salt and L₂ was not able to be carried out.

Due to the outbreak of COVID-19, research laboratories were shut down at the beginning of March. As a result, repetitive synthesis of L₂ was not carried out. Full characterizations of
complex 5, including mass spectrometry, X-ray crystallography, $^{13}$C NMR, etc., were also not finished. Based on the significance of these two complexes, it is of interest to fully characterize these complexes and carry out a more thorough electrochemical analysis.

3. **Future Work**

The key to the success of this project is to synthesize 1-(6-methylpyridin-2-yl)-N-(pyridin-2-ylmethyl)methanamine (L₁) and bis((6-methylpyridin-2-yl)methyl)amine (L₂). Since a considerable amount of L₁ has been synthesized, future synthesis should be focused on synthesizing L₂. Once a decent amount of L₂ is synthesized, complexation can be carried out with iron(III) salt and L₂. Crystals can be formed via vapor diffusion crystallization, as mentioned in section 1, chapter 2.

Besides synthesis, a series of instrumental investigations should be carried out. We plan to use X-ray crystallography to elucidate the crystal structures of complexes 5 and 6. Furthermore, electrochemistry will be implemented by cyclic voltammetry (CV) to test their electrocatalytic abilities in both organic and aqueous solutions. After investigation of their electrocatalytic activities, it is of interest to determine if these complexes would be active in a photocatalytic system. It may be possible to pair the catalyst with a reducing chromophore such as fluorescein or Ru(bpy)$_{3}^{2+}$. With the presence of sacrificial donor, such as triethylamine, hydrogen evolution can be tested upon irradiation of lights.

4. **Impacts & Significance of Project**

This project aims at expanding our knowledge about how to design catalysts for hydrogen generation. From what we have gotten in this project, adding steric bulk to the active
site of iron catalysts generates more active catalysts. Combining this result with conclusions from previous studies, we see that a qualified catalyst should have both an enough steric bulk at the active site and a low thermodynamic barrier for carrying out catalysis. This helps us to find the direction to synthesize suitable catalysts in developing devices for AP.
Appendix

Figure A1 $^1$H NMR spectrum of L₁
Figure A2: $^1$H NMR spectrum of 2-(chloromethyl)-6-methylpyridine
Figure A3: 1H NMR spectrum of L2
Figure A4: $^1$H NMR spectra of crude product of L2 after column chromatography: (upper) collected fraction 4 through 9, (lower) collected 10 (total 24 fractions collected).
Sample Calculation of TOF:

From the CV data:

\[ i_p = 3.46 \times 10^{-6} \, \text{A} \]

\[ i_c = 3.10 \times 10^{-5} \, \text{A} \]

Correction of \( i_p \) for dilution\(^{36} \):

\[ i_p \times \frac{vol_i}{vol_f} \rightarrow (3.46 \times 10^{-6}) \times \frac{5 \, \text{mL}}{5.04 \, \text{mL}} = 3.43 \times 10^{-6} \]

Calculation of \( i_c/i_p \):

\[ \frac{3.10 \times 10^{-6}}{3.43 \times 10^{-6}} = 9.03 \]

Calculation of TOF (\( k_{obs} \)):

\[ k_{obs} = \left( \frac{i_c}{i_p} \times \frac{0.4463}{n} \right)^2 \left( \frac{F \nu}{RT} \right) \rightarrow k_{obs} = \left( 9.03 \times \frac{0.4463}{2} \right)^2 \left( \frac{96485 \times 0.2}{8.314 \times 298} \right) = 31.6 \, \text{s}^{-1} \]
Figure A6 CVs of 5 upon addition of 0 mM TFA (black), 2.2 mM TFA (blue), 4.4 mM TFA (red), 6.6 mM TFA (green), 8.8 mM TFA (yellow), 11.0 mM TFA (purple) and 13.2 mM TFA (brown) at a scan rate of 200 mV s⁻¹. Ferrocene was added as an internal standard.
References


Tridentate bis (2-pyridylmethyl) amine iron catalyst for electrocatalytic proton reduction. *Inorganica Chimica Acta*, 503, 119394.


35. DiRisio, R. J., Armstrong, J. E., Frank, M. A., Lake, W. R., & McNamara, W. R.