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ชื่อโครงการ Synthesis and Reactivity of Copper Complexes for Oxygen Reduction

การสังเคราะห์และความว่องไวต่อปฏิกิริยาของสารประกอบเชิงซ้อนคอปเปอร์สำหรับปฏิกิริยาออกซิเจนรีดักชัน

ชื่อนิสิต นางสาวอินทุออน อารีพูนสวัสดิ์

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ปีการศึกษา 2559

คณะวิทยาศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

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By

Intuon Areepoonsawat

A Report Submitted in Partial Fulfillment of the Requirements

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By: Intuon Areepoonsawat

Accepted by Department of Chemistry, Faculty of Science, Chulalongkorn University in Partial Fulfillment of the Requirements for the Degree of Bachelor of Science Program in Chemistry

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(Associate Professor Dr. Vudhichai Parasuk)

Date..... May 2017

The quality of this report ☑ Very Good ☐ Good ☐ Fair

ชื่อโครงการ การสังเคราะห์และความว่องไวต่อปฏิกิริยาของสารประกอบเชิงซ้อนคอปเปอร์สำหรับปฏิกิริยาออกซิเจนรีดักชัน

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ภาควิชาเคมี คณะวิทยาศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ปีการศึกษา 2559

บทคัดย่อ

การเร่งปฏิกิริยารีดักชันของออกซิเจนโดยเอนไซม์ที่มีคอปเปอร์เป็นองค์ประกอบหรือสารประกอบเชิงซ้อนคอปเปอร์ที่ถูกสังเคราะห์ขึ้นเป็นหนึ่งในกระบวนการพื้นฐานที่สำคัญที่สุดและได้รับความสนใจอย่างมากเนื่องจากคุณสมบัติในการเป็นเซลล์เชื้อเพลิงของมัน ในงานวิจัยนี้เราสามารถเตรียมสารประกอบเชิงซ้อนคอปเปอร์ที่มี dipicolylamine-based เป็นลิแกนด์ รวมถึงศึกษาการเร่งปฏิกิริยาของสารประกอบเชิงซ้อนคอปเปอร์ต่อปฏิกิริยารีดักชันของออกซิเจน โดยสารประกอบเชิงซ้อนคอปเปอร์ถูกสังเคราะห์จาก **DPA** (**DPA** = 2,2′-dipicolylamine) หรือ **L** (**L** = 9-[(2,2′-dipicolylamino)methyl]anthracene) กับคอปเปอร์(II) เปอร์คลอเรต ($Cu(ClO_4)_2$) ในสารละลายไดคลอโรมีเทนและเมทานอล (CH_2Cl_2/CH_3OH) ในอัตราส่วน 1:1 โดยปริมาตร) โดยเราสามารถพิสูจน์เอกลักษณ์ของสารประกอบเชิงซ้อนคอปเปอร์ทั้ง 2 ชนิดด้วยเทคนิค mass spectrometry/(MS) elemental analysis/(EA) และ UV-vis spectroscopy และติดตามปฏิกิริยาระหว่างสารประกอบเชิงซ้อนคอปเปอร์(II) และกรดแอสคอร์บิก (ascorbic acid) ภายใต้แก๊สไนโตรเจน (nitrogen) ด้วยเทคนิค UV-vis spectroscopy โดยพบว่า มีสารประกอบเชิงซ้อนคอปเปอร์(I) เกิดขึ้นและจากผลการทดลองพบว่าแอนทราซีน (anthracene) ในสารประกอบเชิงซ้อนคอปเปอร์มีอิทธิพลอย่างมากต่อปฏิกิริยารีดักชันของคอปเปอร์(II) และความเสถียรของคอปเปอร์(I) นอกจากนี้เมื่อให้ออกซิเจน (oxygen) ลงในระบบสารประกอบเชิงซ้อน $[Cu^{I}L]^{+}$ พบว่ามีคอปเปอร์(II) เกิดขึ้นอย่างช้าๆ โดยจากผลการทดลองชี้ให้เห็นว่า $[Cu^{I}L]^{+}$ เป็นตัวกลางที่ทำให้เกิดปฏิกิริยาออกซีเจนรีดักชันได้

คำสำคัญ: ปฏิกิริยารีดักชันของออกซิเจน, สารประกอบเชิงซ้อนคอปเปอร์, เซลล์เชื้อเพลิง

Project Title Synthesis and reactivity of copper complexes for oxygen reduction

Student Name Intuon Areepoonsawat Student ID 5633174023

Advisor Name Dr. Pannee Leeladee

Department of Chemistry, Faculty of Science, Chulalongkorn University, Academic Year 2016

ABSTRACT

Oxygen reduction catalyzed by copper-containing enzymes and their synthetic analogs is one of the most fundamental processes and has gained much attention due to its application in fuel cells. In this study, two copper complexes containing dipicolylamine-based ligands were successfully prepared, and their reactivity towards oxygen reduction was examined. The Cu^{II} complexes were synthesized from reaction of **DPA** or **L** (**DPA** = 2,2′-dipicolylamine; **L** = 9-[(2,2′-dipicolylamino)methyl]anthracene) with $Cu(ClO_4)_2$ in CH_2Cl_2 /CH_3OH (1:1 v/v). The Cu^{II} products were then characterized by mass spectrometry, elemental analysis and UV-vis spectroscopy. Monitored by UV-vis, reaction of Cu^{II} complexes and ascorbic acid under nitrogen atmosphere resulted in the formation of Cu^{I} species. It was also shown that the presence of anthracene moiety in the Cu complexes has a significant influence on Cu^{II} reduction and stability of the Cu^{I} species. In addition, when $[Cu^{I}\mathbf{L}]^{+}$ was exposed to oxygen atmosphere, the Cu^{II} species was slowly regenerated. The result suggested that $[Cu^{I}\mathbf{L}]^{+}$ was capable of mediating oxygen reduction.

Keywords: Copper-containing enzyme, DPA, Copper-dioxygen intermediate, Cu-O_2 species, Oxygen reduction

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Intuon Areepoonsawat

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LIST OF ABBREVIATION

International System of Units

g	gram
L	liter
M	molar
mM	millomolar
MHz	megahertz
mL	milliliter
mmol	millimol
nm	nanometers
pH	hydrogen potential
%	percentage
Å	angstrom
λ	wavelength

CHAPTER 1

INTRODUCTION

1.1 Background

Copper containing enzymes play fundamental roles in a variety of biological functions, such as oxygen transport in the hemolymph of arthropods and mollusks namely hemocyanin (Hc); aromatic ring oxidations including tyrosinase (Tyr), catechol oxidase and quercetin 2,3-dioxygenase (QDO); the biogenesis of neurotransmitters and peptide hormones including dopamine β-monooxygenase (DβM) and peptidylglycine α-amidating monooxygenase (PHM).[1] Figure 1.1 illustrates copper containing enzymes with different structures of active-sites that can be used to activate dioxygen molecules leading to a wide range of reactivities.

Comprehension of their structures and reactivities can motivate development of catalysts for industrial applications. In fact, it is very hard to study the enzymes directly because of their high reactivities and short-lived intermediates. For this reason, copper complexes as the stable models for copper enzymes have been developed to mimic the structures and functions of the real enzymes.[2] Extensive studies investigated effects of ligand modulation on the complex reactivity. The recent results showed that different ligands resulted in changes of the structures and reactivities of copper complexes.[3] In particular, polypyridyl-based ligands expecially tripycolylamine derivatives have been typically used to form copper complexes to model copper enzymes. However, copper complexes containing dipycolylamine analogs have not been much explored.

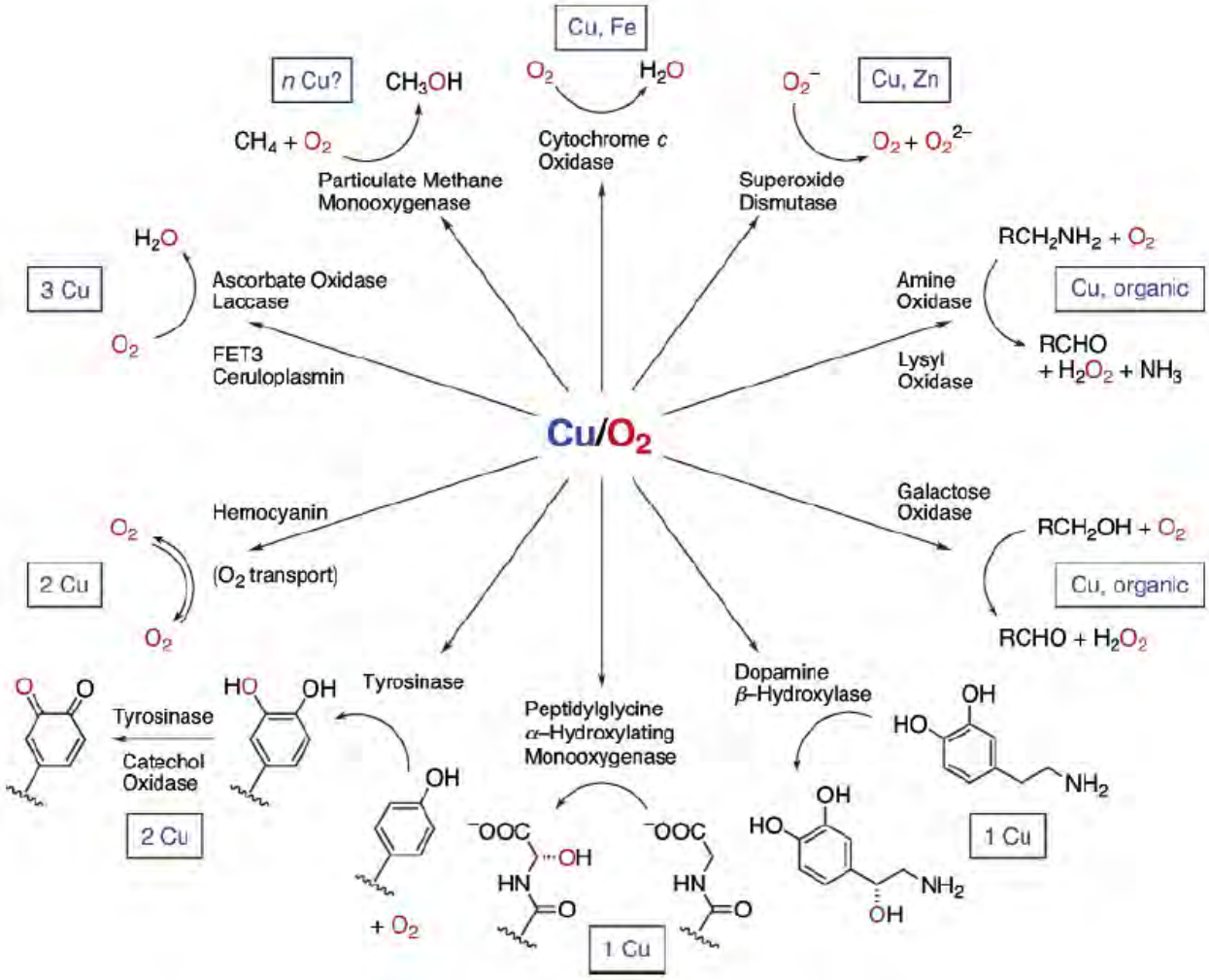


Figure 1.1. Copper containing enzymes that activate oxygen.[1]

In addition, nowadays many researches have extensively studied about non-covalent interactions of coordination compounds, such as metal-π, anion-π and π-π interactions. These non-covalent interactions could increase stability of coordination compounds.[4] Conry and co-workers successfully synthesized copper(I) complex with N,S,S-macrocyclic ligand which modified with naphthalene ring. Figure 1.2 (A) and Figure 1.2 (B) shows crystal structure of this copper complex which have intramolecular metal-π interactions between copper and naphthalene ring (Cu-arene interaction).[5-6]

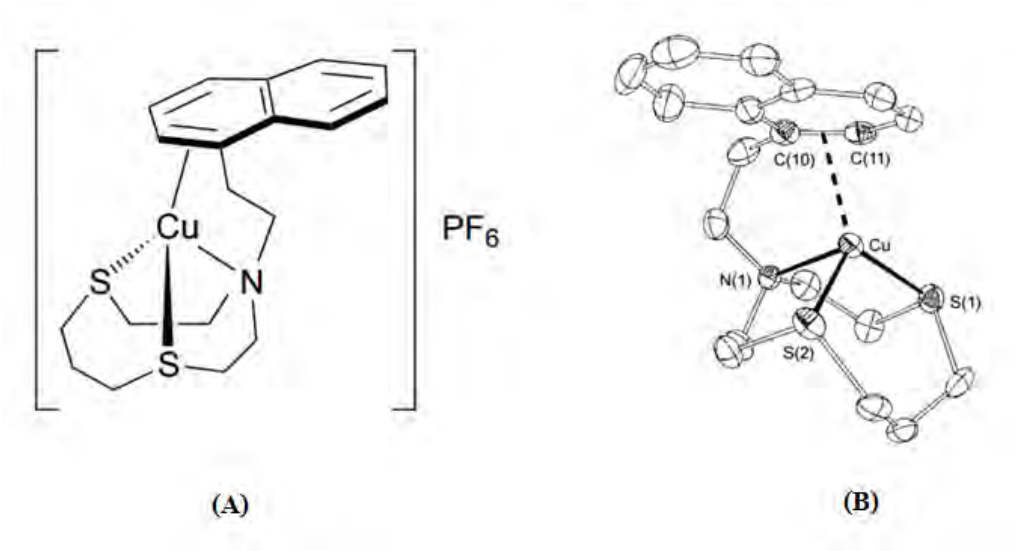


Figure 1.2. (A) Copper(I) complex with N,S,S-macrocyclic ligand and (B) its crystal structure.[5]

In this study, bioinspired-copper complexes based on dipicolylamine derivatives were synthesized, and the effect of conjugated-π system from anthracene in oxygen reduction reactivities was investigated. Moreover, ascorbic acid was used as reducing agent in this study because ascorbic acid is a natural reducing agent and it can give the electrons and protons in the system. This study will gain knowledge about structures and reactivities of bioinspired-copper complexes.

1.2 Literature reviews

Copper containing enzymes play important roles in biological processes, such as electron transfer, reversible dioxygen binding, dioxygen activation and nitrogen oxide transformations. In general, copper active-sites of the enzymes can bind and activate dioxygen molecule to operate biological activities.[7] Thus, understandings of the dioxygen activation at the active-sites of copper containing enzymes are important in learning biochemical systems. The dioxygen activation of copper containing enzymes occurs through a number of steps, i.e. binding of oxygen at the Cu(I) center and generation of copper-dioxygen ($Cu\text{-}O_2$) intermediate species including superoxo and peroxo species. Figure 1.3

shows biomimetic models, of which activation of oxygen by Cu(I) with different ligands led to several Cu-O_2 intermediate structures. The Cu-O_2 intermediate species can be investigated by spectroscopic techniques, such as UV-Vis, resonance Raman (rR) and EPR spectroscopy. In addition, computational techniques, such as TD-DFT and DFT calculations can also be used to investigate Cu-O_2 intermediate species.[8]

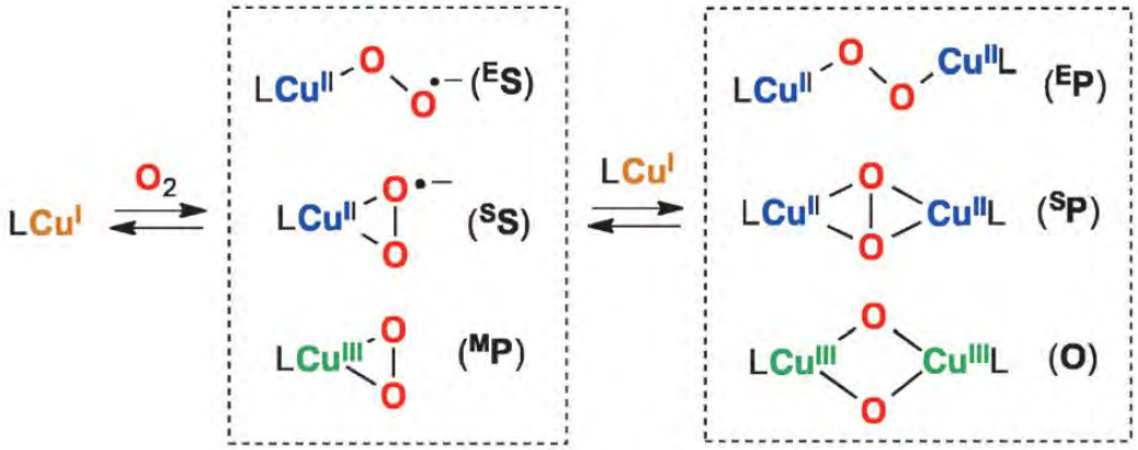


Figure 1.3. Different copper-dioxygen intermediates.[8]

Previous studies found that the different ligands could generate different structures and reactivities of Cu-O_2 intermediate species, depending on different denticity and steric effect of the ligand. In addition, ligands with different donor atoms and chelate ring sizes can affect structures and reactivities of Cu-O_2 intermediate species.[2] For example, copper complex with tetradentate ligand gives end-on Cu-O_2 intermediate species. In contrast, copper complexes with bi- or tridentate ligand gives side-on Cu-O_2 intermediate species.[8-9] Cu-O_2 species with different ligands are shown in Figure 1.4.

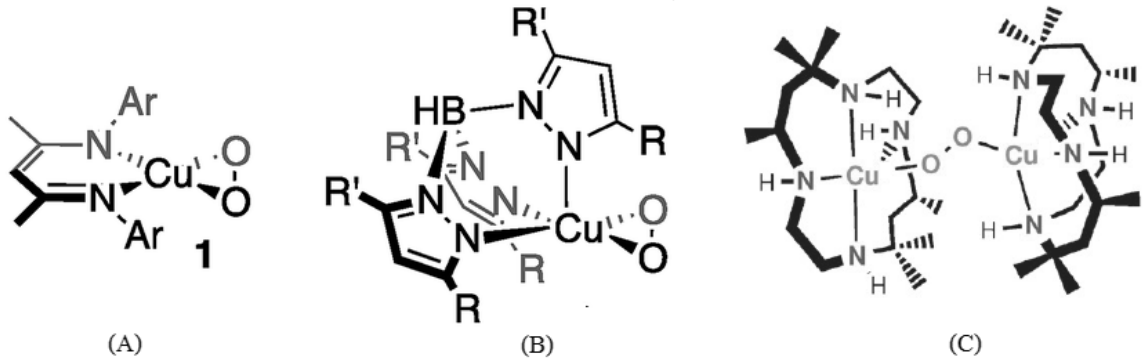


Figure 1.4. Cu-O_2 species with (A) bidentate ligand gives side-on Cu-O_2 species (B) tridentate ligand gives side-on Cu-O_2 species and (C) tetradentate ligand gives end-on Cu-O_2 species.[9]

In 2007, Cu-O_2 intermediate species have been successfully characterized and got more details about Cu-O_2 intermediate species. Cramer and Tolman reported different binding modes which related to their electronic structures. They used X-ray crystallography and EXAFS experiments to investigate Cu-O_2 intermediate species. Figure 1.5 shows comparison of the core structures of Cu-O_2 species with different ligand denticity. Figure 1.5 (A) and (B) shows the O–O distances in characteristic range of superoxo species (about1.2–1.3 Å) and Figure 1.5 (C) shows a O–O distance of peroxo species (about1.4 Å). In addition, investigation of side-on and end-on species was performed by DFT calculations. From the results, they could confirm that copper complexes with tetradentate ligands would give end-on Cu-O_2 species. In contrast, copper complexes with bi- or tridentate ligands resulted in side-on Cu-O_2 intermediates.[10]

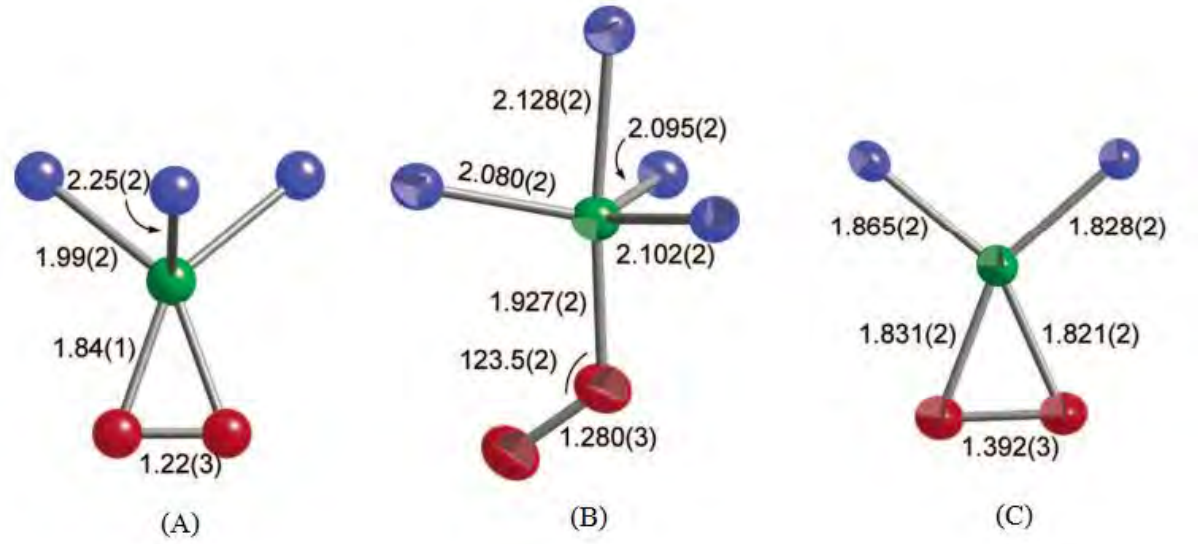


Figure 1.5. Cu-O_2 intermediate species characterized by X-ray crystallography (A) and (B) superoxo species and (C) peroxo species. Cu atoms are colored green, N atoms are blue and O atoms are red.[10]

Moreover, previous studies have shown that the several copper containing enzymes in nature could reduce oxygen to water (H_2O) or hydrogen peroxide (H_2O_2). These reactions need electrons and protons for the formation of H_2O and H_2O_2. Thus, the proton donor such as, $HClO_4$ or CF_3COOH was required in the biomimetic reaction.[11] Figure 1.6 (A) shows the example from the recent research that used $HClO_4$ as proton donors and produced H_2O via oxygen reduction reaction. The reaction was investigated by UV-Vis spectroscopy, shown in Figure 1.6. (B) and (C).

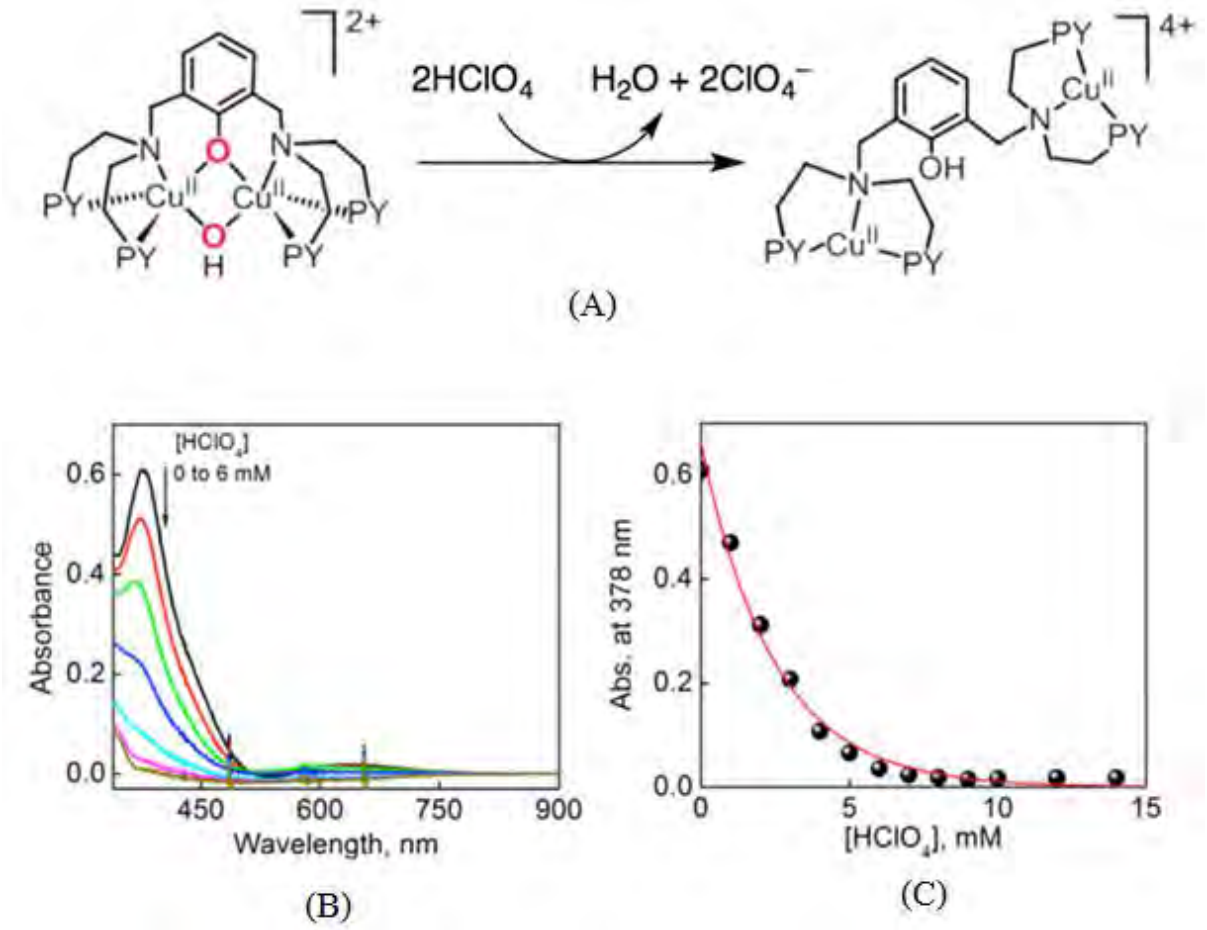


Figure 1.6. (A) The example of oxygen reduction reaction which used $HClO_4$ as proton donor and produced H_2O (B) UV–visible spectral changes at 378 nm upon addition of $HClO_4$ (C) Absorbance changes at 378 nm as $[HClO_4]$ function.[11]

For mechanistic investigation, we want a stable intermediate that can be characterized and studied the reactivity. Inspired by copper(I) ion as a capable cofactor of the ethylene receptor proteins implanted in cell membrane. In fact, their structures have not been completely characterized but it was suggested that ethylene may binds to the copper site via a copper(I)-ethylene d-π interaction, similar to synthetic copper(I) complexes that can form stable ethylene-π complexes.[5,12,13] Figure 1.7 shows example of the structure of copper(I)-ethylene complex $[MeB\{3\text{-}(CF_3)Pz\}_3]Cu(C_2H_4)$ containing the B-methylated tris (pyrazolyl)borate group that was successfully synthesized in previous study.

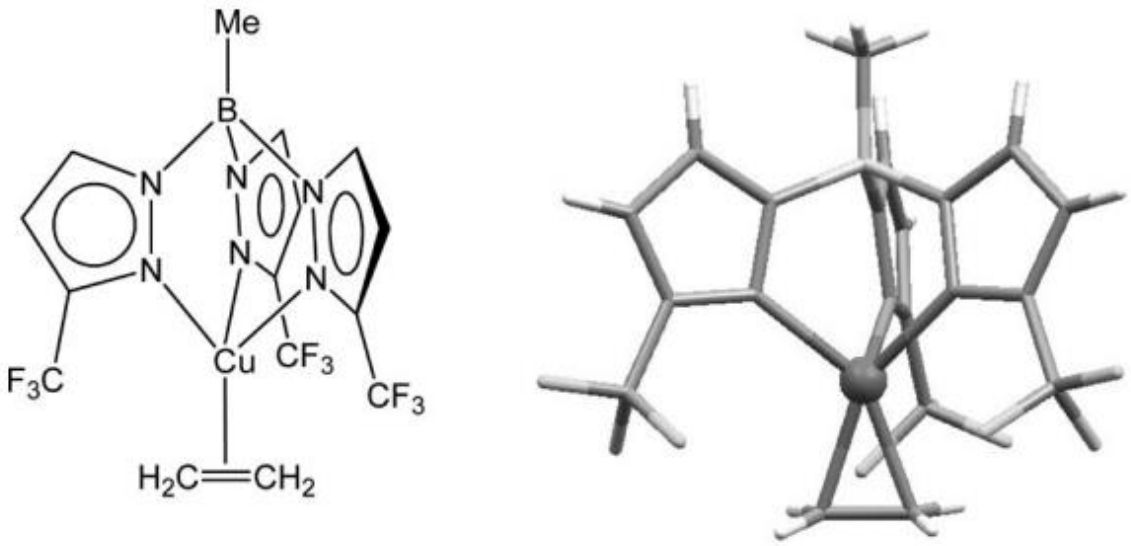


Figure 1.7. Copper(I)-ethylene complex [MeB{3-(CF_3)Pz}$_3$]Cu-(C_2H_4).[13]

Moreover, Osako and co-worker successfully synthesized and characterized copper complexes with bis[2-(2-pyridyl)ethyl]amine tridentate series which are shown in Figure 1.8. The results showed that structure and reactivity of Cu-O_2 intermediate depended on metal-π interaction between the copper ion and the phenyl ring; the stronger metal-π interaction, the less oxygen reduction reactivity.[13-14] Thus, π-conjugated derivatives may be a good choice to produce stable Cu-O_2 intermediate species.

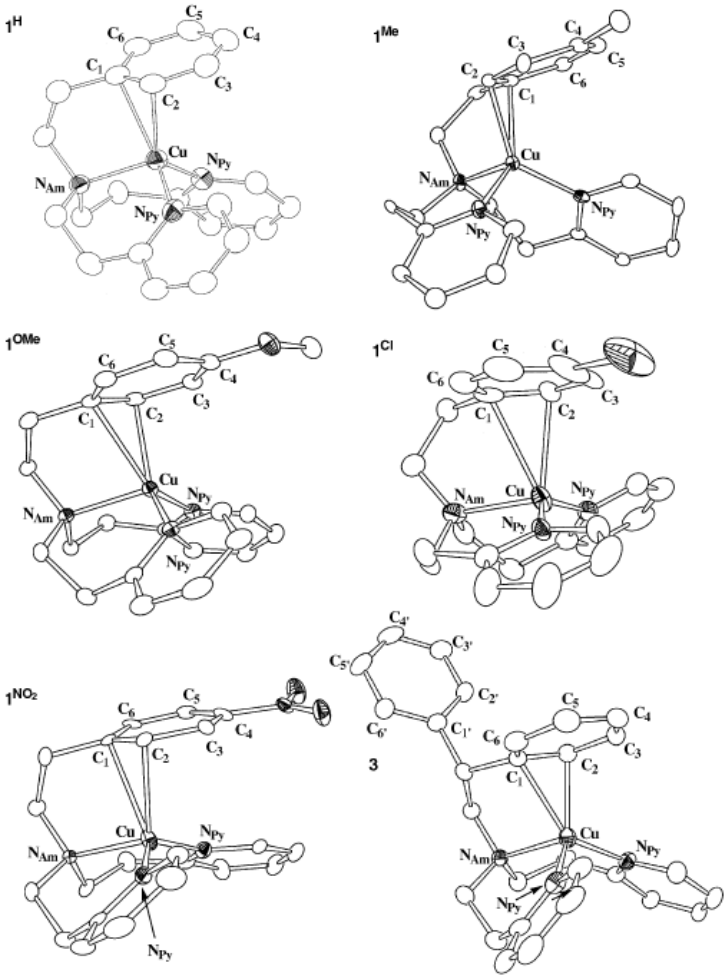


Figure 1.8. Crystal structures of copper(I) complexes with bis[2-(2-pyridyl)ethyl]amine tridentate series.[14]

In addition, there has been reported about intramolecular **π-π** interactions between anthracene and polypyridal amine in a dinuclear copper complex based on two tripodal tris(2-pyridylmethyl)amine (TMPA). The result showed intramolecular **π-π** interactions when the anthracene was modified in their structure. In contrast, the intramolecular **π-π** interaction in the dinuclear copper complex with benzene-based linker was not presented. All results were confirmed by crystal structure in Figure 1.9. Moreover, recent results showed that anthracene had intramolecular non-covalent interactions which could control stability of molecule activation.[8,15] From that reason, anthracene was the linker part to show different reactivity in this study.

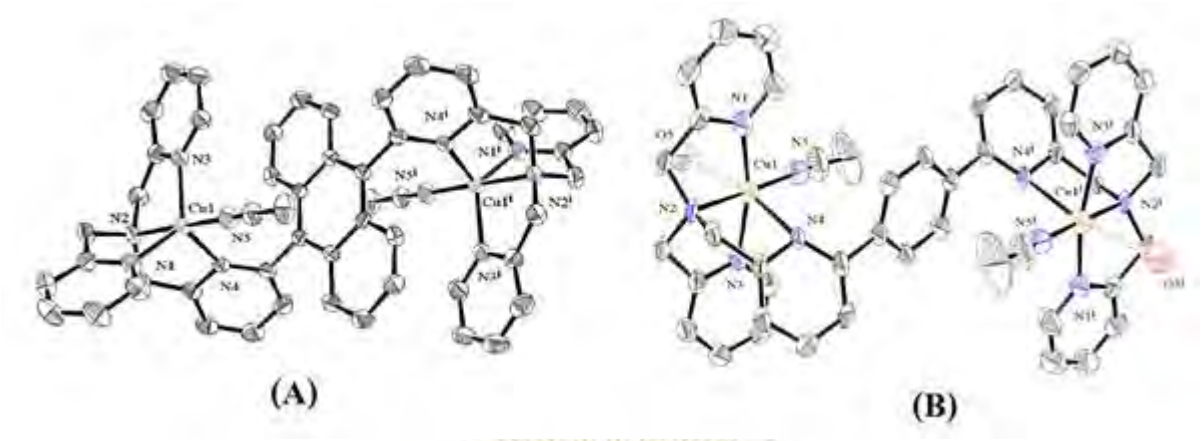


Figure 1.9. Crystal structures of dinuclear copper complex (A) with anthracene linker and (B) with phenyl linker.[15]

Herein, we synthesized copper complexes with dipicolylamine derivatives and examined the effect of conjugated-π system from anthracene in oxygen reduction reactivity. The copper complexes were characterized by ^{1}H-NMR, Mass spectrometry and Elemental analysis. The reactivity was investigated by UV-Vis spectroscopy. This study would provide more understanding about copper complexes with dipicolylamine and motivate development of catalysts based on non-precious metal complexes.

1.3 Objectives

1. To synthesize and characterize dipicolylamine-based ligands and their Cu(II) complexes.

2. To investigate the effect of π-conjugated moiety (anthracene) on stability of Cu(I) complexes.

3. To study reactivity of the Cu(I) complex toward oxygen reduction.

CHAPTER 2

MATERIALS AND METHODS

2.1 Materials and instruments

All chemicals and solvents were purchased from TCI and Merck. All UV-Visible measurements were carried out using a Varian Cary 50 probe UV-Visible spectrophotometer. ^{1}H-NMR spectra were recorded on 400 MHz Varian Mercury or 400 MHz Bruker spectrometer at 298 Kelvin. All solvents were dried with molecular sieves prior to use. All glassware used in the experiments were rinsed with acetone and dried prior to use.

2.2 Methods

2.2.1 Ligand synthesis

Bis-pyridin-2-ylmethylamine (**DPA**) and 10-bis[2,2'-(dipicolylamino)methyl]anthracene (**L**) were synthesized according to previously described or using similar synthetic procedures.[17-19]

Synthesis of the pyridine-2-ylmethylpyridin-2-ylmethyleneamine (1)

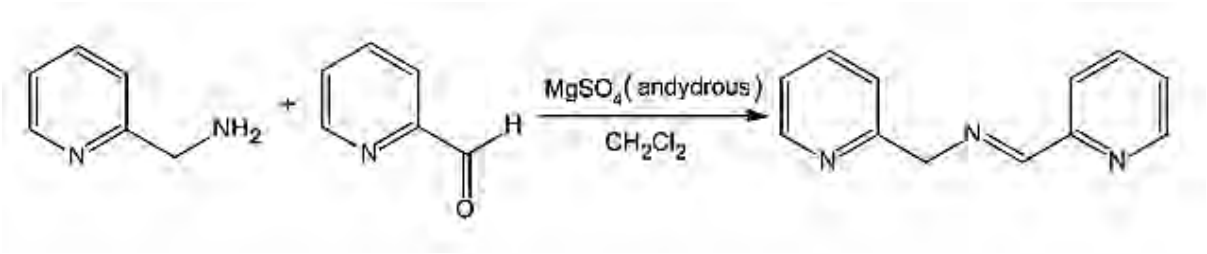


Figure 2.1. Synthesis of pyridine-2-ylmethylpyridin-2-ylmethyleneamine (**1**).

To a suspension of anhydrous magnesium sulfate (2.78 g, 23.1 mmol) in dichloromethane (15.2 mL). Next, 2-pyridinecarboxaldehyde (0.48 mL, 4.67 mmol) was added and then 2-(aminomethyl) pyridine (0.44 mL, 4.62 mmol) was added. After stirred at

room temperature under nitrogen gas for 3 hours, the suspension was filtered and washed with dichloromethane (19 mL). The solvent in crude product was removed by vacuum evaporator. Yellow solid (1.079 g, 6.03 mmol) was obtained.

Synthesis of the Bis-pyridin-2-ylmethylamine (DPA)

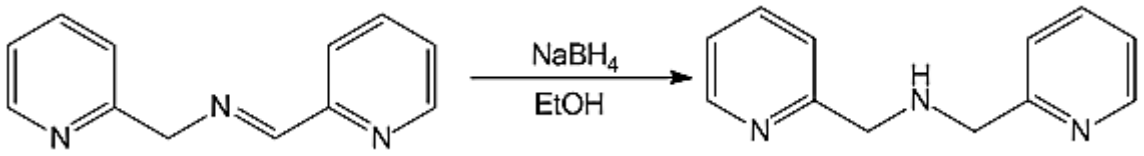


Figure 2.2. Synthesis of bis-pyridin-2-ylmethylamine (**DPA**).

The pyridine-2-ylmethylpyridin-2-ylmethyleneamine (1) (1.079 g, 6.03 mmol) was dissolved in acetonitrile (7.4 mL, 231.4 mmol) and cooled the solution to 5 °C. After that, acetic acid (0.4 mL, 6.81 mmol) dissolved in ethanol in one portion was added. The yellow solution was obtained and then added a suspension of sodium borohydride (1.01 g, 26.83 mmol) over a period of 1 hour at 5 °C. Strong bubbling was observed during the addition in concomitance with the precipitation of a white solid. The color of the solution changed from yellow into bright red by the end of addition. Next, the solution was stirred at room temperature for 16 hours, 12 M hydrochloric acid (10.6 mL, 245.2 mmol) was then added and the solution was heated at 60 °C for 2 hours until no more gas was evolved. The white precipitate was filtered and the solvent was removed by a rotary evaporator. Next, the precipitate was re-dissolved in water (70 mL). After that, the yellow aqueous solution was basified by addition of sodium sulfate anhydrous (3.22 g, 80.5 mmol) with efficient cooling and red oil separated immediately. It was extracted with ether three times. The ether extracts were dried over sodium sulfate anhydrous. Finally, the solvent was removed by vacuum evaporator and red oil (0.806 g, 65 %) was obtained.

^{1}H-NMR (400 MHz, $CDCl_3$): δ 3.99 (s, 4H), 7.17 (d, 2H), 7.37 (t, 2H), 7.66 (t, 2H), 8.57 (d, 2H)

Synthesis of the 10-bis[2,2-(dipicolylamino)methyl]anthracene (L)

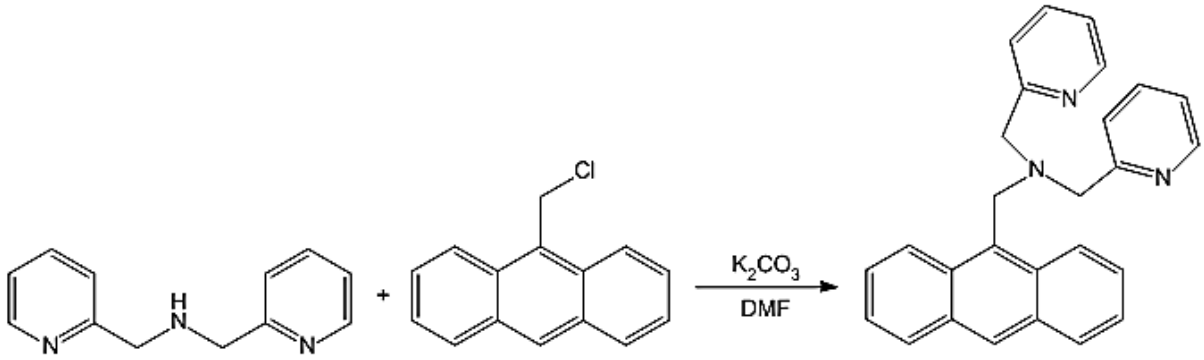


Figure 2.3. Synthesis of 10-bis[2,2-(dipicolylamino)methyl]anthracene (**L**).

To a solution of 9-bis(chloromethyl)anthracene (1.00 g, 4.40 mmol), **DPA** (1.05 g, 5.20 mmol) and potassium carbonate (2.43 g, 1.70 mmol) in anhydrous DMF (6.8 mL) was added dropwise a solution of potassium iodide (0.73 g, 4.40 mmol) in DMF (3.6 mL) over 1 hour at room temperature. After the solution was stirred at room temperature for 30 minutes, 1M hydrochloric acid added and then ethyl acetate was used to wash the solution. The aqueous layer was alkalized with 4 M sodium hydroxide and extracted three times with ethyl acetate–tetrahydrofuran solution (1:1). The combined organic layers were washed with water and followed by drying over magnesium sulfate anhydrous. After that, the solvent was removed by a rotary evaporator. The residue was washed with a small amount of methanol. Next, the product was recrystallized by acetate–tetrahydrofuran solution to give 10-bis[2,2'-(dipicolylamino)methyl]anthracene (**L**) (0.91 g, 2.33 mmol, 53 %) as a pale yellow powder.

^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 4H), 4.68 (s, 2H), 7.11 (m, 2H), 7.32 (d, 2H), 7.47 (m, 2H), 7.58 (m, 4H), 7.96(d, 2H), 8.37 (d,2H), 8.39 (s, 1H), 8.50 (d, 2H)

2.2.2 Copper(II) complex synthesis

Synthesis of the copper(II) complex with ligand DPA (CuDPA)

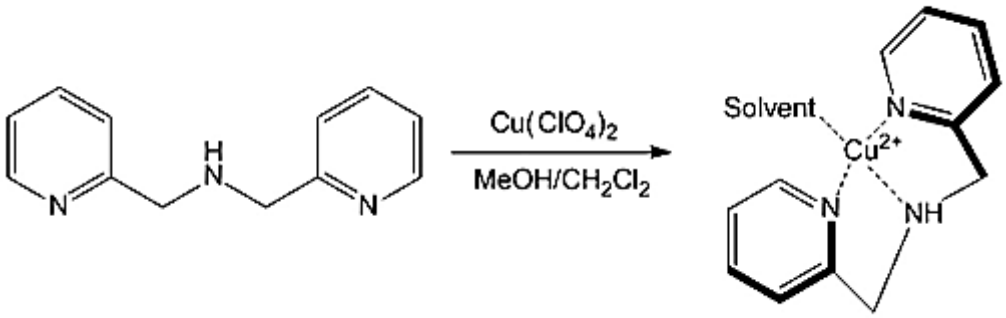


Figure 2.4. Synthesis of $[Cu^{II}\mathbf{DPA}]^{2+}$.

Aqueous solution of copper(II) perchlorate 2 mL (0.55 g, 1.48 mmol) was added dropwise in **DPA** (0.2 g, 1.00 mmol) in dichloromethane (2 mL) and then the mixture was stirred at room temperature for 30 minutes. After that, the product was precipitated and filtered. Finally, the blue solid of Cu**DPA** (0.149 g, 0.32 mmol, 32 %) was obtained. The Cu(II) product, Cu**DPA** was further characterized by UV-Vis, mass spectrometry (MS) and elemental analysis (EA).

MALDI-TOF MS (m/z) of $[Cu\mathbf{DPA}\text{-}H]^{+}$: 261.234

"Calcd (found) of $C_{12}H_{15}Cl_2CuN_3O_9$: %C = 30.04 (30.34), %H = 3.15 (3.05), %N = 8.76 (8.72)"

Synthesis of the copper(II) complex with ligand L (CuL)

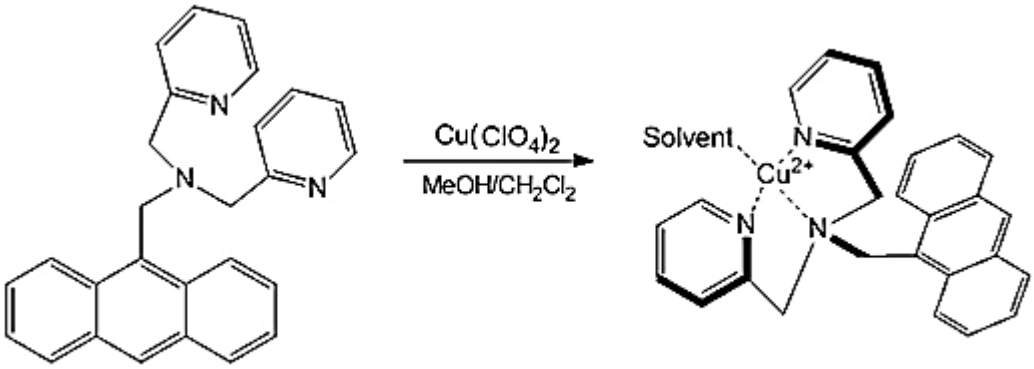


Figure 2.5. Synthesis of $[Cu^{II}L]^{2+}$.

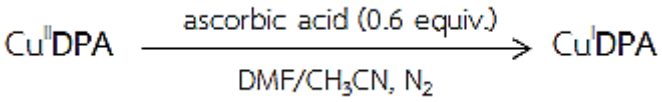
Aqueous solution of copper(II) perchlorate 2 mL (0.29 g, 0.74 mmol) was added dropwise into 10-bis[2,2'(dipicolylamino)methyl]anthracene (**L**) (0.10 g, 0.27 mmol) in dichloromethane and then the mixture was stirred at room temperature for an hour. The green solid was obtained. Finally, the residue was recrystallized with methanol to give Cu**L** (0.128 g, 0.19 mmol, 70 %) as a green solid. Successful preparation of Cu**L** was confirmed by UV-Vis and mass spectrometry (MS).

MALDI-TOF MS (m/z) of $[Cu\mathbf{L}]^{+}$: 551.006

2.2.3 Reduction of Cu^{II} complexes with ascorbic acid

Solvent (acetonitrile) was deoxygenated by bubbling with nitrogen for an hour prior to use.

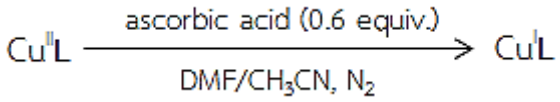
Reaction of Cu^{II}DPA and ascorbic acid



The Cu^{II}**DPA** complex (2 mM, 4.01 mmol) in CH_3CN 2.00 mL was reduced to Cu^{I}**DPA** complex by 0.6 equivalent ascorbic acid (0.048 M, 2.38 mmol) in 5% DMF/CH_3CN. The

reactions of the Cu^{II}**DPA** complex was carried out in a 10 mm path quartz cell equipped with a stir bar and capped with a rubber septum. After addition of ascorbic acid, the disappearance of the absorption band of Cu^{II}L at 603 nm was monitored by UV-Vis spectroscopy for 22 hours.

Reaction of of Cu^{II}L and ascorbic acid

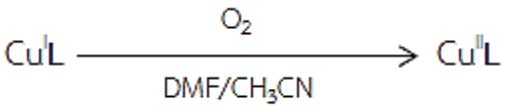


The Cu^{I}**L** complex was prepared from Cu^{II}**L** complex (2 mM, 3.77 mmol) in CH_3CN 2.00 mL and 0.6 equivalent ascorbic acid (0.048 M, 2.38 mmol) in 5% DMF/CH_3CN. The reactions of the Cu^{II}**L** complex was also carried out in a 10 mm path quartz cell equipped with a stir bar and capped with a rubber septum. After addition of ascorbic acid, the reaction was monitored from the absorption band of Cu^{II}**L** at 585 nm by UV-Vis spectroscopy for an hour.

UV-vis titration

The stoichiometric ratio between Cu^{II}**L** and ascorbic acid in the reaction was determined by UV-vis titration. The Cu^{II}**L** (2 mM, 3.77 mmol) was dissolved in CH_3CN 2.00 mL and the Cu^{II}**L** solution was placed in a 10 mm path quartz cell equipped with a stir bar and capped with a rubber septum. Ascorbic acid (0.04 M, 0.48 mmol, 0.1 equiv.) in 5% DMF/CH_3CN was added into solution 10 times and the formation of Cu^{I}**L** was followed by UV-vis spectroscopy via the absorption band at 585 nm.

2.2.4 Reactivity of Cu^{I} complex toward oxygen reduction



First, The $Cu^{I}L$ complex was generated from $Cu^{II}L$ complex (2 mM, 3.77 mmol) in CH_3CN 2.00 mL by addition of 0.6 equivalent ascorbic acid (0.048 M, 2.38 mmol) in 5% DMF/CH_3CN. The solution was carried out in a UV-Vis cell with 10 mm path quartz cell equipped with a stir bar and capped with a rubber septum. The disappearance of the absorption band of $Cu^{II}L$ at 585 nm was monitored by UV-Vis spectroscopy. Next, oxygen gas was continuously provided to generate $Cu^{II}L$ species. Formation of the $Cu^{II}L$ complex was determined by monitoring the appearance of the absorption band at 585 nm from UV-Vis spectroscopy for 48 hours.

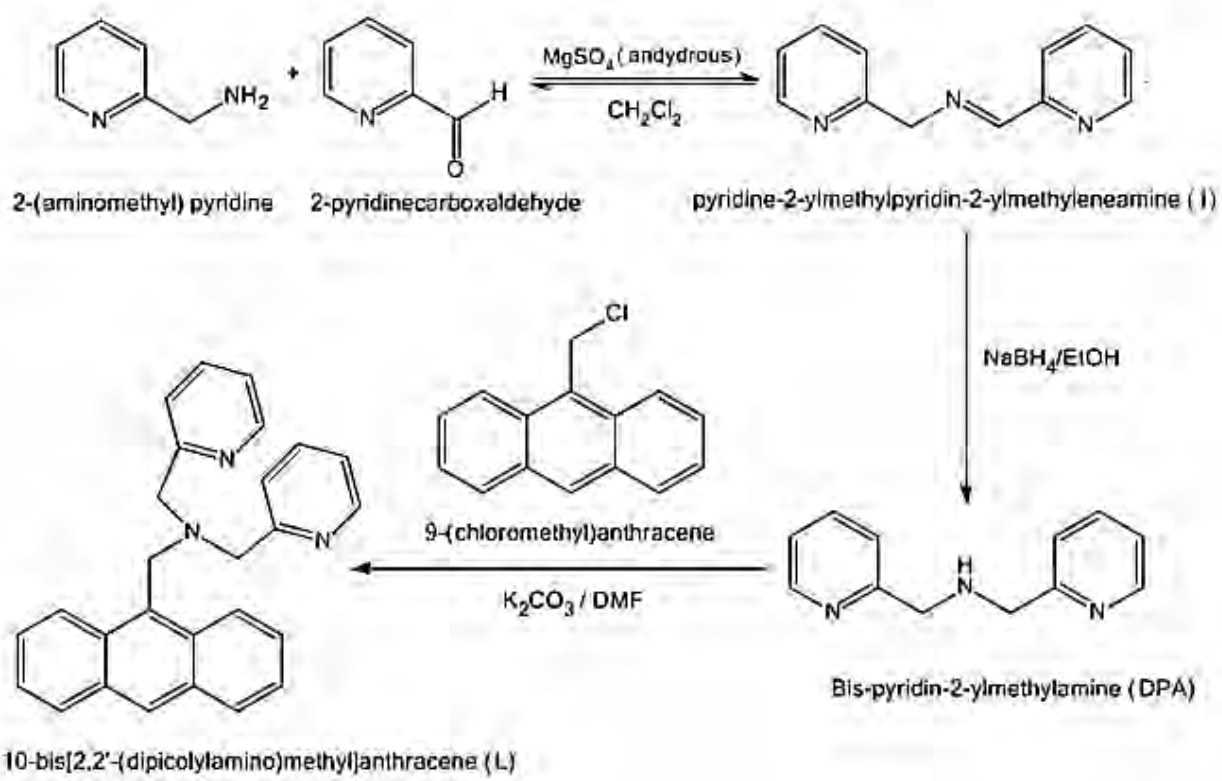
CHAPTER 3

RESULTS AND DISCUSSION

3.1 Preparation of the copper complexes

3.1.1 Ligand synthesis and characterization

First, bis-pyridin-2-ylmethylamine (**DPA**) and 10-bis[2,2′-(dipicolylamino)methyl] anthracene (**L**) were synthesized according to previous studies or using modified synthetic procedures.[17-19] The synthetic route is shown in Scheme 3.1.



Scheme 3.1. Synthesis of ligands used in this study.

All ligands in this study including bis-pyridin-2-ylmethylamine (**DPA**) and 10-bis[2,2′-(dipicolylamino)methyl]anthracene (**L**) were characterized by ^{1}H-NMR.

^{1}H-NMR spectrum in Figure 3.1 confirmed the structure of **DPA** which resembled the spectrum in a previous study.[20] ^{1}H-NMR (400 MHz, $CDCl_3$): δ, 3.99 (s, 4H), 7.17 (d, 2H), 7.37 (t, 2H), 7.66 (t, 2H), 8.57 (d, 2H)

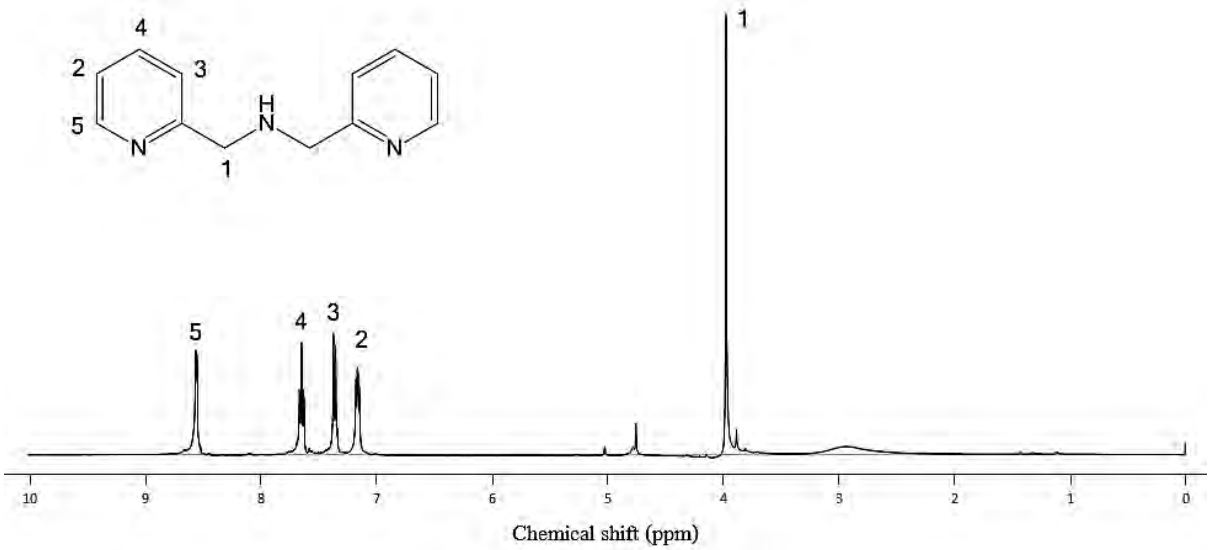


Figure 3.1. ^{1}H-NMR spectrum of **DPA**.

^{1}H-NMR spectrum in Figure 3.2 confirmed the structure of ligand **L**, corresponding to the reported structure.[19] ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.88 (s, 4H), 4.68 (s, 2H), 7.11 (m, 2H), 7.32 (d, 2H), 7.47 (m, 2H), 7.58 (m, 4H), 7.96(d, 2H), 8.37 (d,2H), 8.39 (s, 1H), 8.50 (d, 2H)

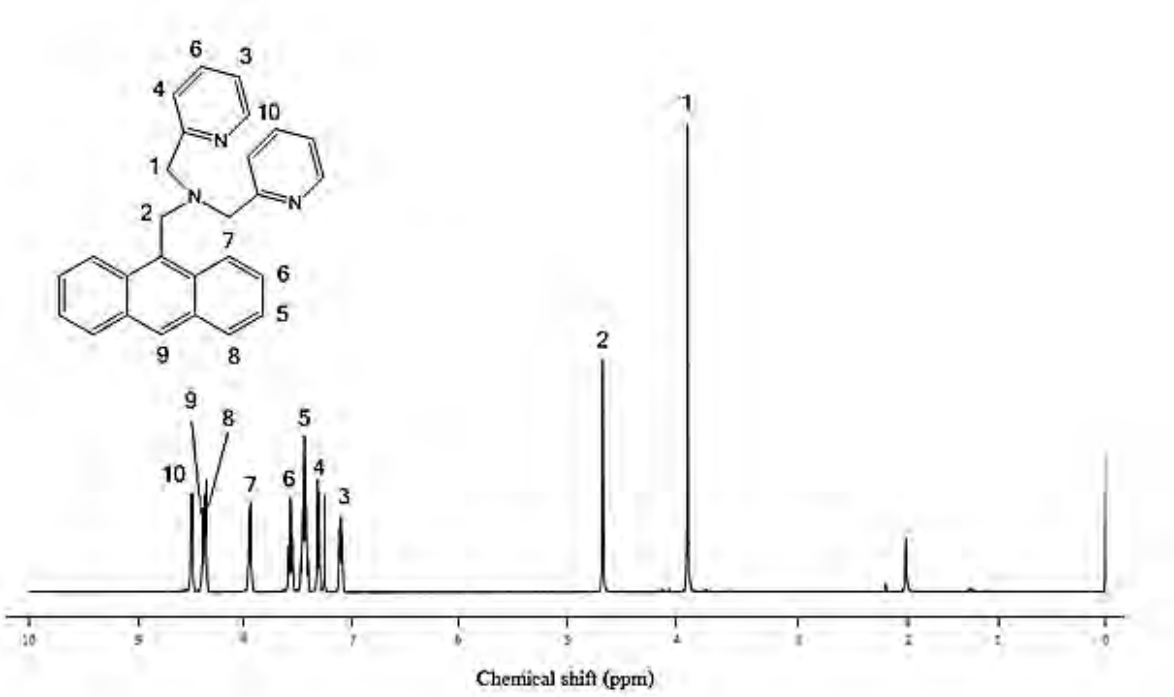
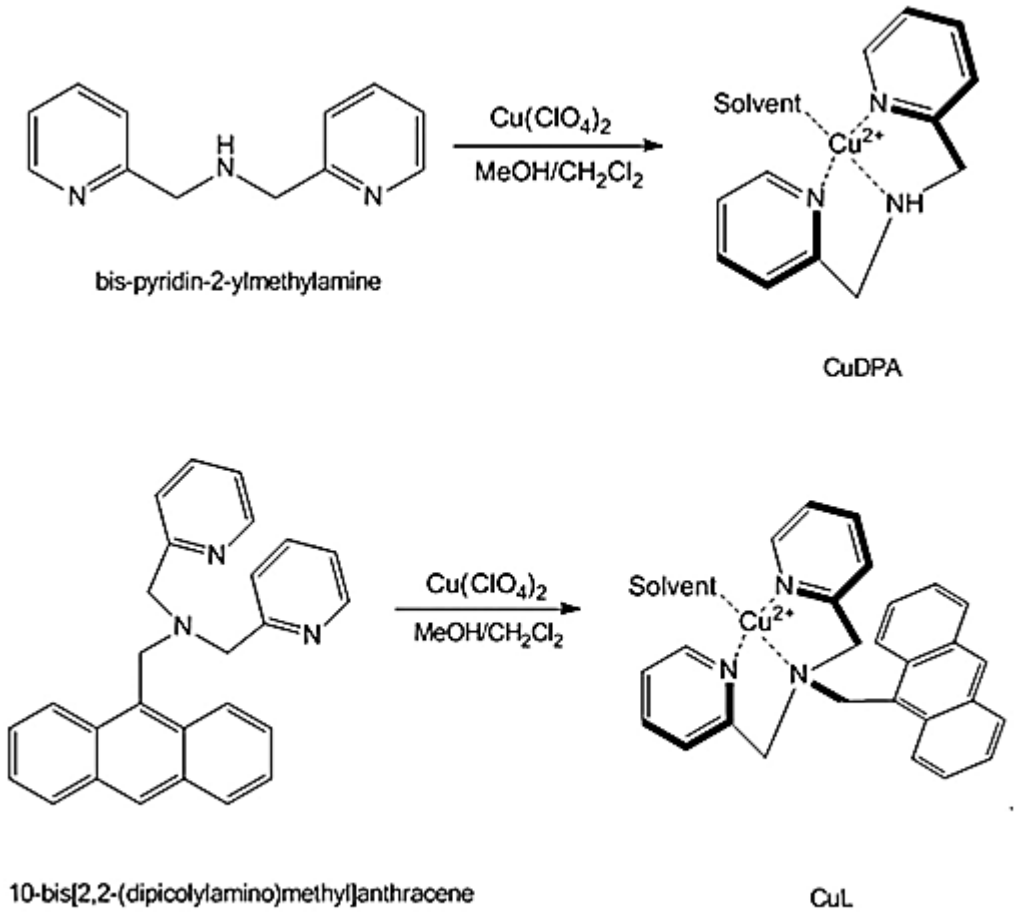


Figure 3.2. ^{1}H-NMR spectrum of ligand **L**.

3.1.2 synthesis of copper(II) complexes

Next step, we prepared copper(II) complexes from our synthesized ligands as shown in Scheme 3.2.



Scheme 3.2. Synthesis of copper complexes.

Cu**DPA** was characterized by matrix assisted laser desorption ionization-time of flight mass spectrometry (MALDI-TOF MS) (Figure 3.3). The signal centered at m/z 261.234 corresponded to $[Cu\mathbf{DPA}\text{-}H]^+$ and the signal centered at m/z 378.576 corresponded to $[Cu\mathbf{DPA}+(ClO_4)+H_2O]^+$. All results confirmed our successful preparation of Cu^{II}**DPA**.

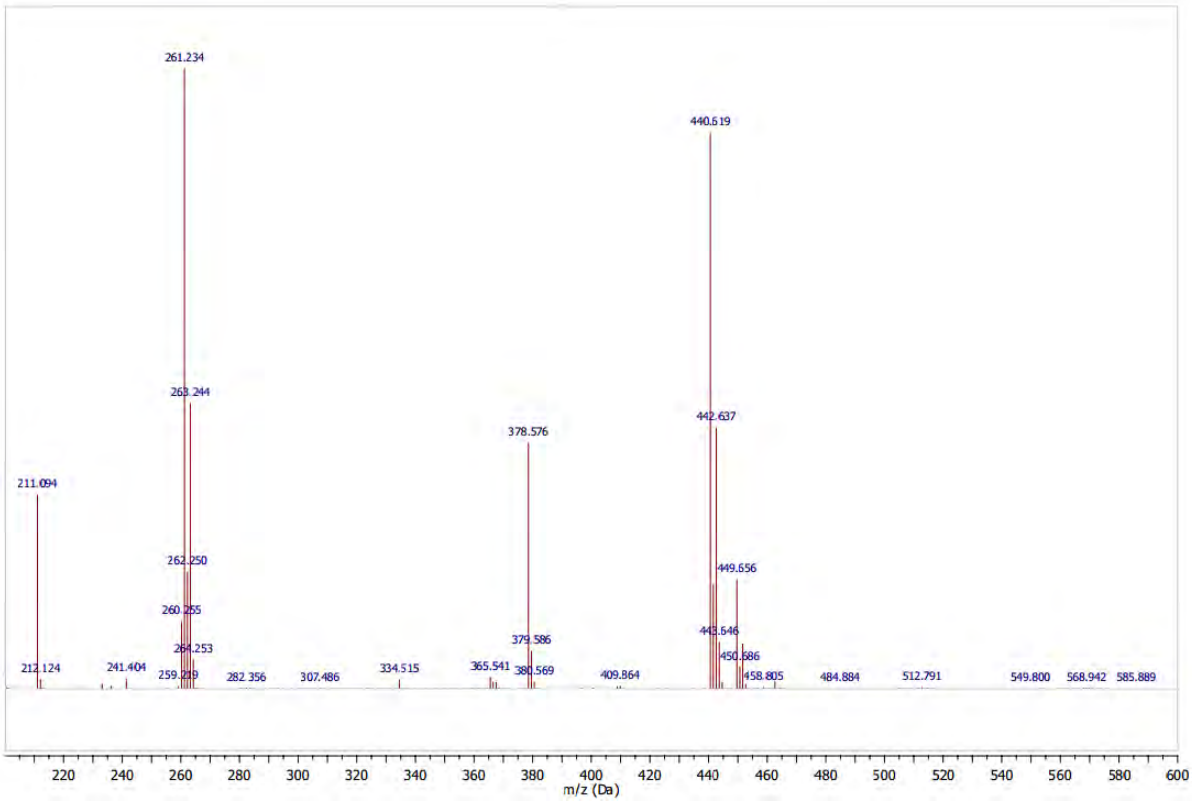


Figure 3.3. MALDI-TOF MS spectrum of Cu**DPA**.

Moreover, elemental analysis (EA) was used to determine percentage of carbon, hydrogen and nitrogen in samples. In this study, we also used elemental analysis to confirm the purity of copper complexes. The EA data was in agreement with our proposed structure of $[C_{12}H_{15}CuN_3](ClO_4)_2$

Cu**L** was characterized by MALDI-TOF MS (Figure 3.4). The signal centered at m/z 451.873 corresponded to $[Cu\mathbf{L}]^{+}$. Next, the signal centered at m/z 551.006 corresponded to $[Cu\mathbf{L}+(ClO_4)]^{+}$, confirming our successful preparation of $Cu^{II}\mathbf{L}$.

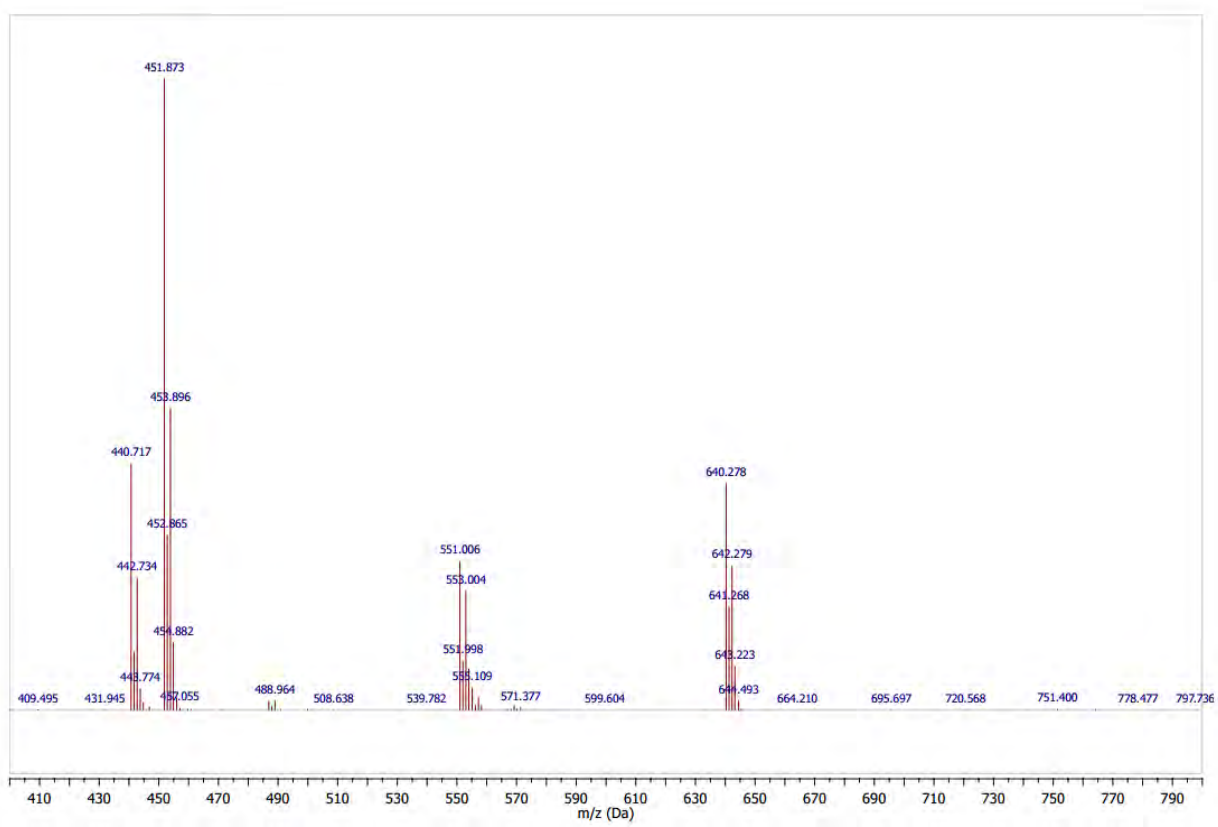


Figure 3.4. MALDI-TOF MS spectrum of Cu**L**.

3.2 Optical Characterization

Copper complexes typically exist in two states including Cu^{I} and Cu^{II}. These two states of copper complexes exhibit different electron configuration in Figure 3.5. The Cu^{I} species possess d^{10} configuration and is diamagnetism. On the other hand, the Cu^{II} species exhibit d^{9} configuration and is paramagnetism.

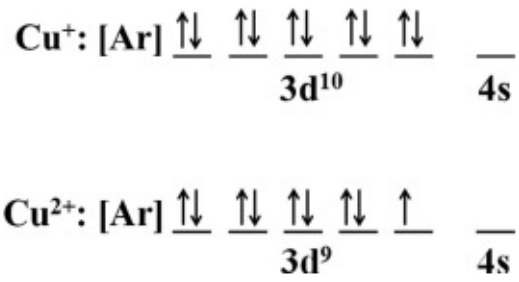
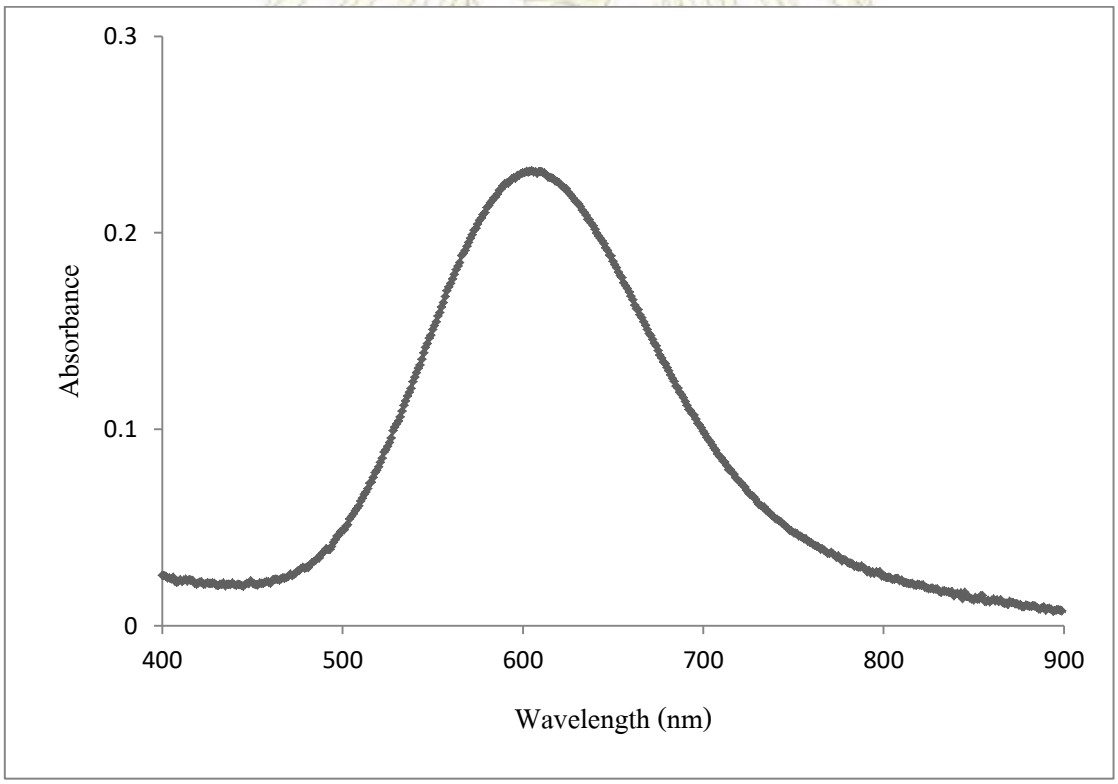
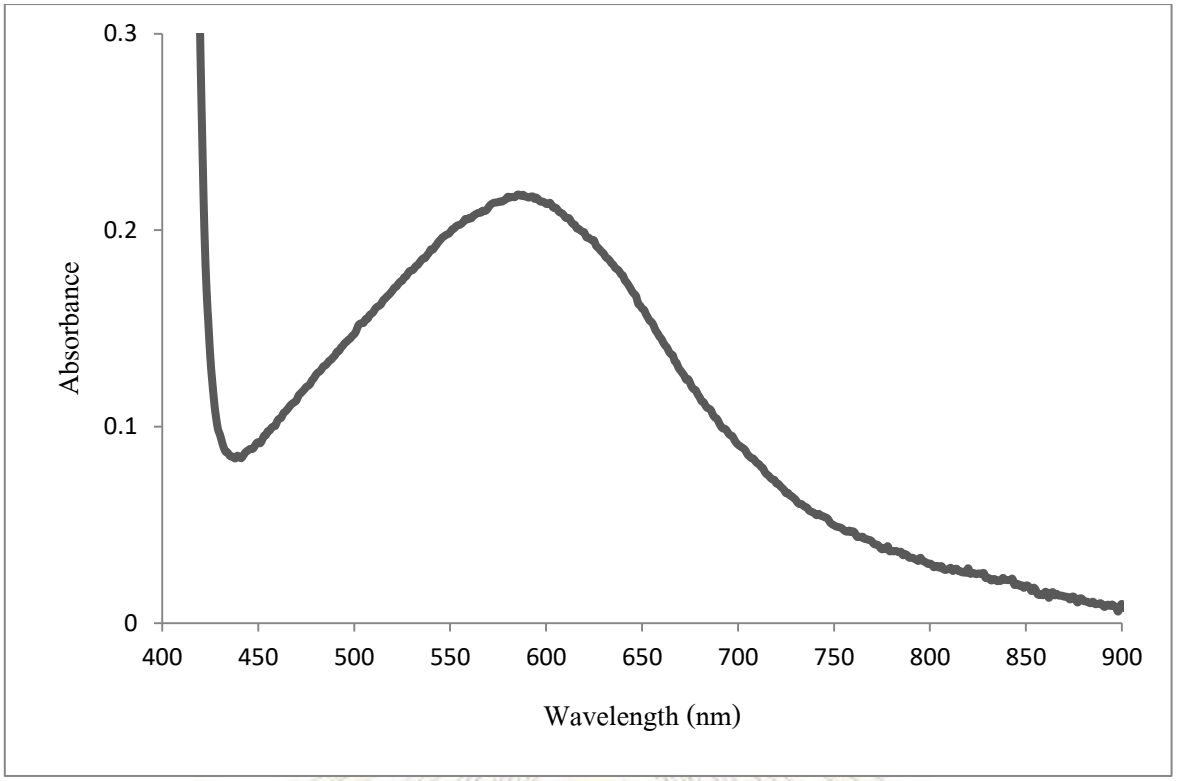


Figure 3.5. The electron configuration of Cu^{I} and Cu^{II}.

In this study, UV-Visible spectroscopy was used to characterize two states of copper complexes. Only Cu^{II} complexes with one unpaired electron showed the d-d band in UV-Vis spectrum. This is because the unpaired electron can transferred from a lower energy d orbital to a higher energy d orbital by absorption of appropriate energy. On the contrary, Cu^{I} complexes with d^{10} configuration possess completely filled orbitals, hence no d-d transition. UV-Vis spectra of Cu^{II}**DPA** and Cu^{II}**L** are shown in Figure 3.6.



(A)



(B)

Figure 3.6. UV-Vis spectra (A) Cu^{II}**DPA** and (B) Cu^{II}**L** in acetronitrile.

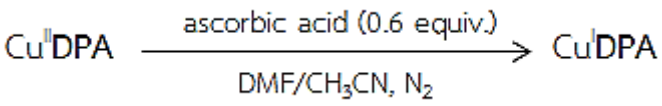
3.3 Reduction of Cu^{II} complex with ascorbic acid

UV-Vis spectra in Figure 3.6 showed the absorption bands about 600 nm of Cu^{II} complexes. In this study, we needed to generate Cu^{I} species which served as the reactive species for oxygen reduction. Therefore, we firstly tested the reduction of Cu^{II} to Cu^{I} by addition of 0.6 equivalent ascorbic acid under nitrogen gas because we speculated Cu^{II} complex was reduced by ascorbic acid on 1:0.5 ratios. Ascorbic acid was chosen because ascorbic acid is a natural reducing agent. Moreover, it could give electrons and protons in the system.

3.3.1 Reduction of Cu^{II}DPA with ascorbic acid

First, we added 0.6 equivalent ascorbic acid (dissolved in 5% DMF/CH_3CN) into 2 mM Cu^{II}**DPA** solution. The results showed that the blue solution of Cu^{II}**DPA** was changed to pale

blue. UV-Vis spectroscopy was used to monitor the reaction via the absorption band at 603 nm. After addition of ascorbic acid (0.6 equivalent) into Cu^{II}**DPA** solution (2 mM), the absorption band of Cu^{II}**DPA** decreased slowly. After 22 hours, the absorption band still remained and did not decrease anymore. This suggested that reduction of Cu^{II}DPA was not complete and reaction between Cu^{II}DPA and ascorbic acid was very slow. From this result, we speculated that Cu^{I}**DPA** might be unstable so after reduction process it was oxidized to Cu^{II}**DPA** immediately.



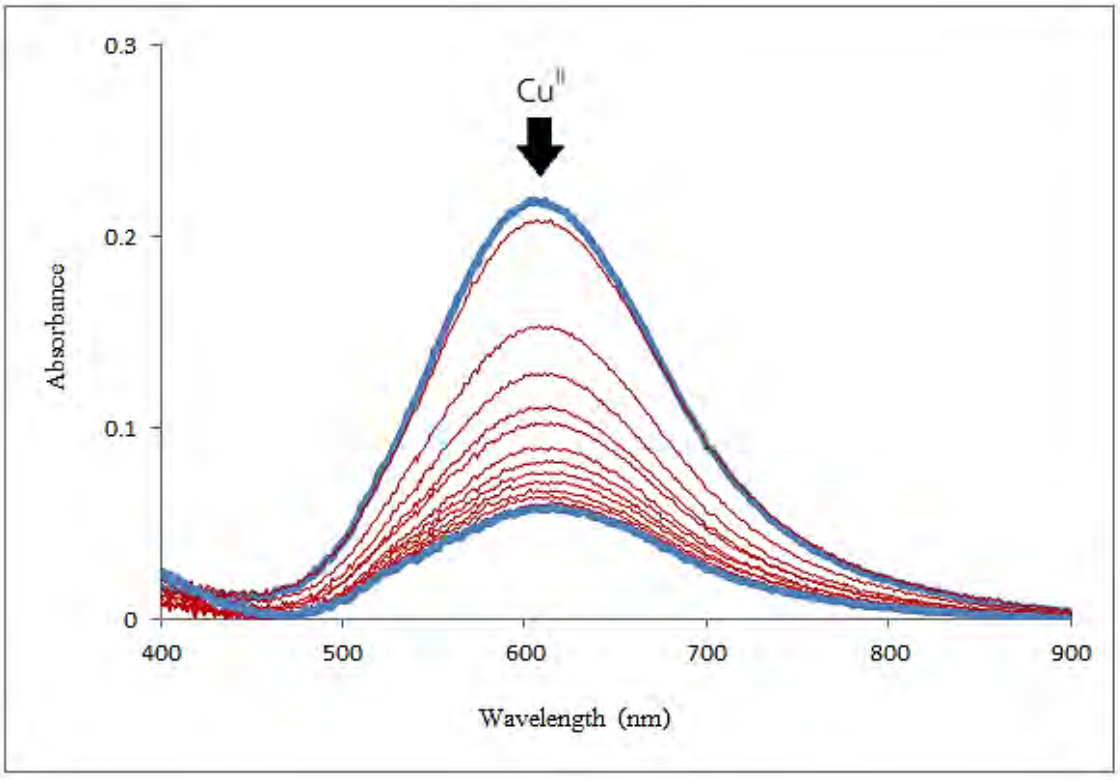


Figure 3.7. UV-Vis spectra changes after addition of ascorbic acid (0.6 equiv.) into Cu^{II}**DPA** solution (2 mM) for 22 hours.

3.3.2 Reduction of $Cu^{II}L$ with ascorbic acid

First, we added 0.6 equivalent ascorbic acid (dissolved in 5% DMF/CH_3CN) into 2 mM $Cu^{II}L$ solution. The results showed that the blue solution of $Cu^{II}L$ was changed to pale yellow solution of $Cu^{I}L$. UV-Vis spectroscopy was also used to monitor the reaction via the absorption band at 585 nm. Figure 3.7 showed UV-Vis spectra changes after addition of ascorbic acid (0.6 equiv.) into $Cu^{II}L$ solution (2 mM) for an hour. Decrease in absorption at 585 nm indicated that $Cu^{II}L$ was completely reduced to $Cu^{I}L$ for an hour.

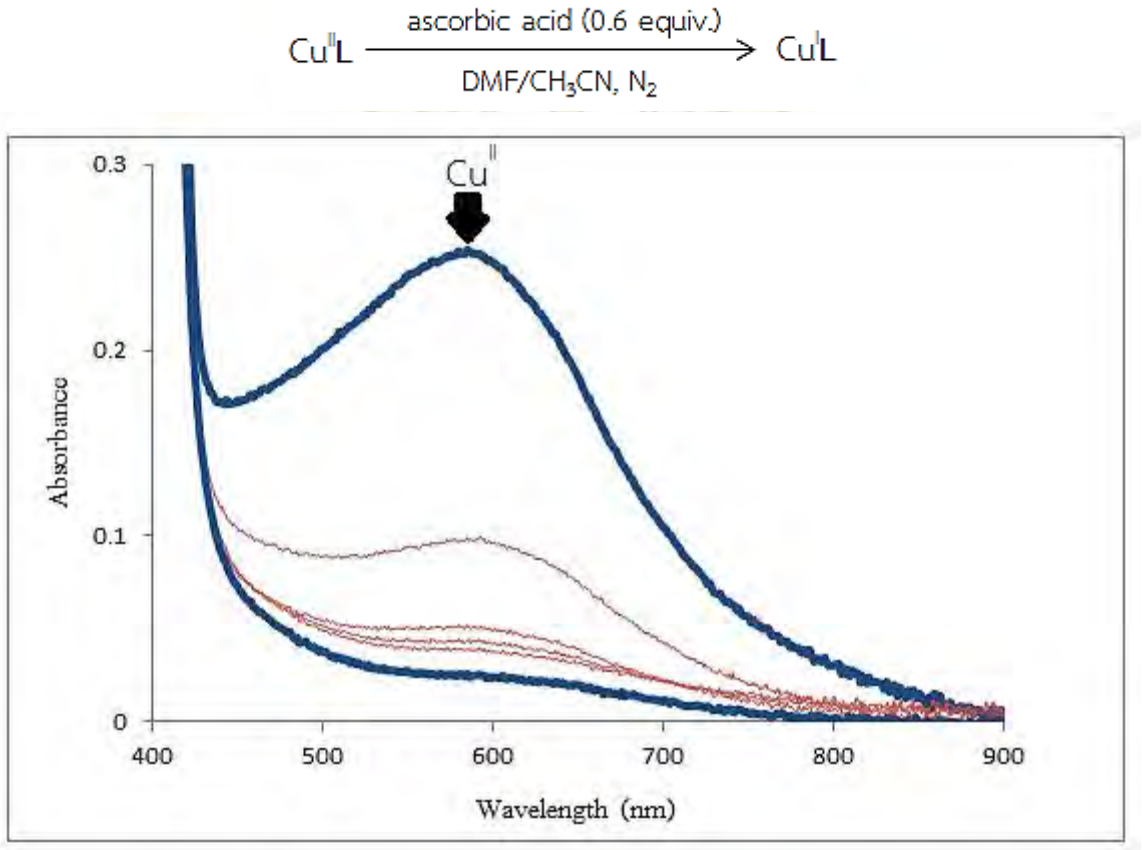
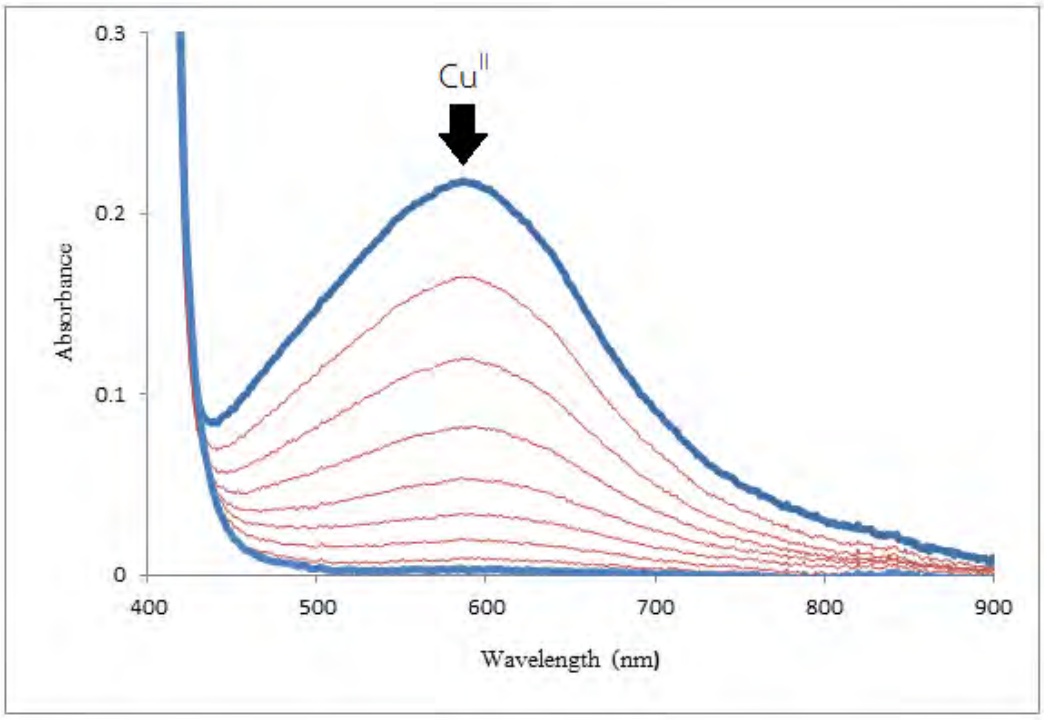
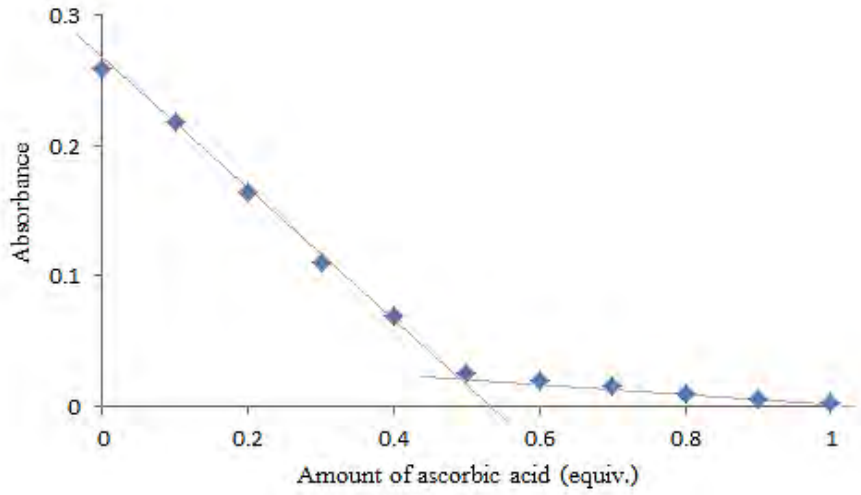


Figure 3.8. UV-Vis spectra changes after addition of ascorbic acid (0.6 equiv.) into $Cu^{II}L$ solution (2 mM).

In addition, we observed the reaction by UV-Vis titration. Figure 3.9 showed that the absorption band of $Cu^{II}L$ completely disappeared when 0.5 equivalent of ascorbic acid was added. It suggested that $Cu^{II}L$ could be reduced to $Cu^{I}L$ by ascorbic acid via 2-electron process.



(A)

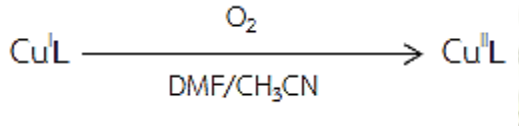


(B)

Figure 3.9. (A) UV-Vis spectra changes upon addition of ascorbic acid (0-1.0 equiv.) to Cu^{II}**L** solution (2 mM) in DMF/CH_3CN. (B) Plot of Absorbance at 585 nm vs equiv. of ascorbic acid added.

Comparison of the reactivity between 0.6 equivalents ascorbic acid and 2mM Cu^{II}**DPA** or Cu^{II}**L**, the reduction of Cu^{II}**DPA** was slow and was not complete. In contrast, Cu^{II}**L** was completely reduced to Cu^{I}**L** for an hour. This suggested that the effect of π-conjugated moiety from anthracene derivative in ligand **L** could stabilize Cu^{I}**L** so that Cu^{I}**L** had higher stability than Cu^{I}DPA due to metal- π interaction (anthracene).[13,14,21]

3.4 Reactivity of Cu^{I} complexes toward oxygen reduction



First, we prepared Cu^{I}**L** complexes by reaction of Cu^{II}**L** with ascorbic acid under nitrogen gas. Figure 3.9 showed that Cu^{II}**L** was completely reduced to Cu^{I}**L** when 0.5 equivalent of ascorbic acid was added. Figure 3.10. showed UV-Vis spectra changes upon addition of ascorbic acid (0.6 equiv. to ensure a complete formation of Cu^{I}**L**) to solution (2 mM) in DMF/CH_3CN. After that, Cu^{I}**L** could react with oxygen that we flowed into the system. Cu^{II}**L** was regenerated together with the pale yellow was returned to pale blue solution of Cu^{II}**L** slowly. Figure 3.11 showed UV-Vis spectra changes when introducing oxygen to Cu^{I}**L** solution (2 mM) in DMF/CH_3CN. The spectrum showed that the Cu^{I}**L** was oxidized to return to Cu^{II}**L** due to increasing of the absorption band at 585 nm of Cu^{II}**L** when time passed. This indicated that Cu^{I}**L** is capable of mediating oxygen reduction. However, the rate of oxygen activation by Cu^{I}**L** was quite slow. Further modification of the ligand might help to increase the reactivity toward oxygen reduction.[22-23]

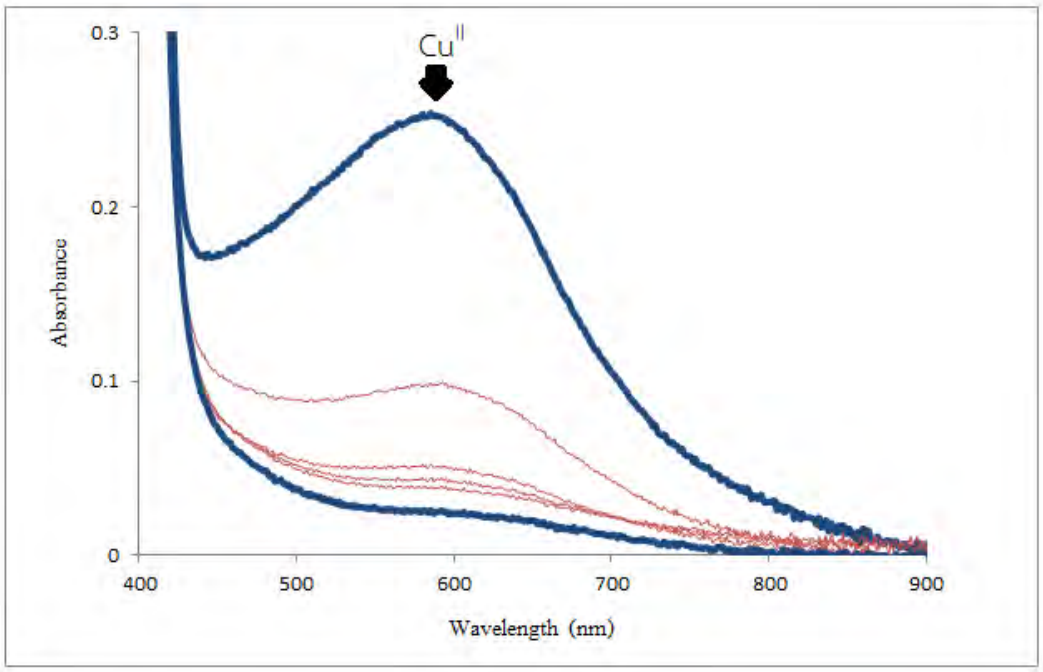


Figure 3.10. UV-Vis spectra changes upon addition of ascorbic acid (0.6 equiv.) to Cu^{II}**L** solution (2 mM) in DMF/CH_3CN.

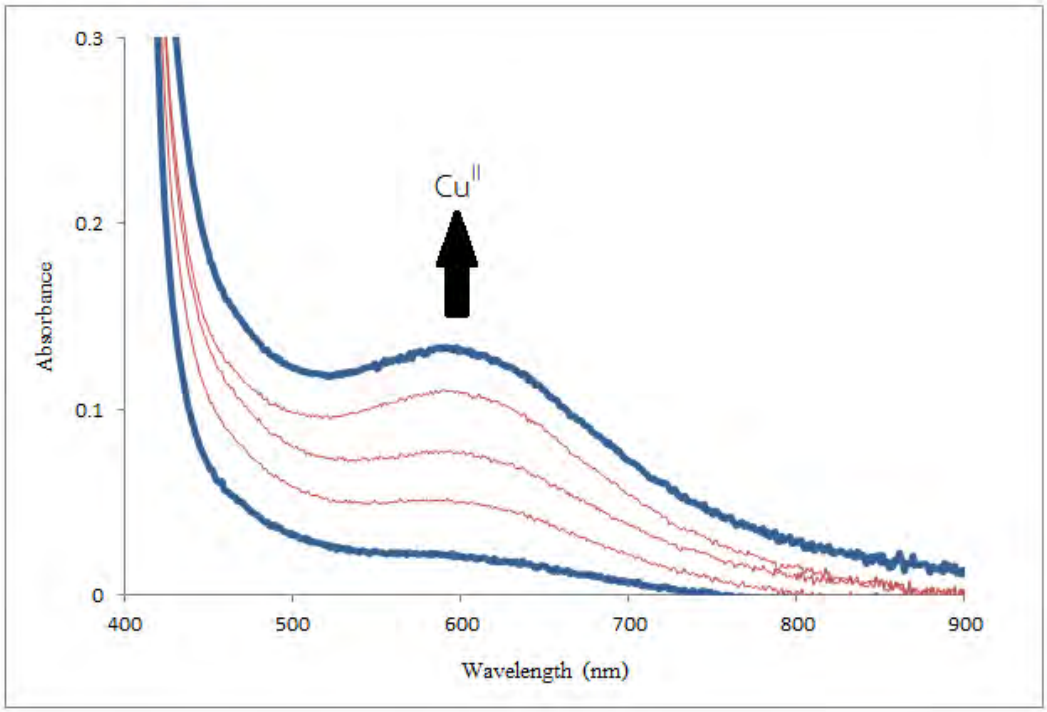


Figure 3.11. UV-Vis spectra changes when introducing oxygen to Cu^{I}**L** solution (2 mM) in DMF/CH_3CN.

CHAPTER 4

CONCLUSION

In summary, two dipicolylamine-based ligands including 2,2′-dipicolylamine (**DPA**) and 9-[(2,2'-dipicolylamino)methyl]anthracene (**L**) were successfully synthesized and were characterized by ^{1}H-NMR. Next, $[Cu^{II}\mathbf{DPA}]^{2+}$ and $[Cu^{II}\mathbf{L}]^{2+}$ were successfully synthesized and were characterized by mass spectrometry, elemental analysis, and UV-vis spectroscopy. Upon addition of ascorbic acid to Cu^{II} complexes in DMF/CH_3CN, a color change was observed, indicating that a new species was formed. Monitored by UV-vis, reduction of $[Cu^{II}\mathbf{DPA}]^{2+}$ to $[Cu^{I}\mathbf{DPA}]^{+}$ by ascorbic acid was much slower than that of $[Cu^{II}\mathbf{L}]^{2+}$. This result suggested that the presence of anthracene moiety may facilitate the Cu^{2+} reduction process. It was also found that $[Cu^{I}\mathbf{L}]^{+}$ was significantly more stable than $[Cu^{I}\mathbf{DPA}]^{+}$, highlighting the effect of anthracene moiety on the stability of the Cu^{I} complexes. Furthermore, new $[Cu^{I}\mathbf{L}]^{+}$ was found to be relatively stable under anaerobic condition at room temperature. When exposed to O_2 atmosphere, the Cu^{II} complex was regenerated which suggested that $[Cu^{I}\mathbf{L}]^{+}$ could reduce O_2 and may be further developed for catalytic O_2 reduction.

REFERENCES

(1) Lewis, E. A.; Tolman, W. B. Reactivity of Dioxygen-Copper Systems. *Chem. Rev.* **2004**, *104*, 1047-1076.

(2) Mirica, L. M.; Otteneaelder, X.; Stack, T. D. P. Structure and Spectroscopy of Copper–Dioxygen Complexes. *Chem. Rev.* **2004**, *104*, 1013-1045.

(3) Garcia-Bosch, I.; Cowley, R. E.; Diaz, D. E.; Siegler, M. A.; Nam, W.; Solomon, E. I.; Karlin, K. D. Substrate and Lewis Acid Coordination Promote O–O Bond Cleavage of an Unreactive $L_2Cu^{II}_2(O_2^{2-})$ Species to Form $L_2Cu^{III}_2(O)_2$ Cores with Enhanced Oxidative Reactivity. *J. Am. Chem. Soc.* **2016,** *22*, 5133-5137.

(4) Nugent, J. W.; Lee, H.; Lee H. S.; Reibenspies, J. H.; Hancock, R. D. The Effect of **π** Contacts between Metal Ions and Fluorophores on the Fluorescence of PET Sensors: Implications for Sensor Design for Cations and Anions. *Inorg. Chem*. **2014**, *53,* 9014-9026.

(5) Hitomi, Y.; Nagai, T.; Kodera, M. A Silver Complex with an N,S,S-Macrocyclic Ligand Bearing an Anthracene Pendant Arm for Optical Ethylene Monitiring. *Chem. Commun.* **2012,** *48,* 10392-10394

(6) Striejewske, W. S.; Conry, R. R. Synthesis of Copper(I) Complexes with a Novel Naphthyl-Appended Macrocyclic Ligand, Including the Crystal and Molecular Structure of the First Copper(i)–h2-naphthyl Complex. *Chem. Commun.* **1998**, 555-556.

(7) Hatcher, L. Q.; Vance, M. A.; Sarjeant, A. N.; Solomon, E. I.; Karlin, K. D. Copper-Dioxygen Adducts and the Side-on Peroxo Dicopper(II)/Bis(μ-oxo) Dicopper(III) Equilibrium: Significant Ligand Electronic Effects. *Inorg. Chem.* **2006,** *45,* 3004-3013.

(8) Garcia-Bosch, I.; Cowley, R.; Díaz, D.; Siegler, M.; Nam, W.; Solomon, E.; Karlin, K., Dioxygen Activation by a Macrocyclic Copper Complex Leads to a Cu_2O_2 Core with Unexpected Structure and Reactivity. *Chem. Eur. J.* **2013**, *22* (15), 5133-5137.

(9) Gomila, A.; Poul, N. L.; Kerbaol, J.; Cosquer, N.; Triki, S.; Douziech, B.; Conan, F.; Mest, Y. L. Electrochemical Behavior and Dioxygen Reactivity of Tripodal Dinuclear Copper Complexes Linked by Unsaturated Rigid Spacers. *Dalton Trans*. **2013,** *42*, 2238-2253.

(10) Cramer, C. J.; Tolman, W. B.; *Acc. Chem. Res.* **2007,** *40,* 601-608.

(11) Das, D.; Lee, Y.; Ohkubo, K.; Nam, W,; Karlin, K. D.; Fukuzumi, S. Acid-Induced Mechanism Change and Overpotential Decrease in Dioxygen Reduction Catalysis with a Dinuclear Copper Complex. *J. Am. Chem. Soc*. **2013,** *135,* 4018-4026.

(12) Dias, H. V. R.; Wu, J. Structurally Characterized Coinage-Metal–Ethylene Complexes. *Eur. J. Inorg. Chem*. **2008**, *4*, 509-522.

(13) Hirsch, J.; George, S. D.; Solomon, E. I.; Hedman, B.; Hodgson, K. O.; Burstyn, J. N. Raman and Extended X-ray Absorption Fine Structure Characterization of a Sulfur-Ligated Cu(I) Ethylene Complex: Modeling the Proposed Ethylene Binding Site of Arabidopsis thaliana ETR1. *Inorg. Chem.* **2001**, *40*, 2439-2441.

(14) Osako, T.; Tachi, Y.; Doe, M.; Shiro, M.; Ohkubo, K.; Fukuzumi, S.; Itoh, S. Quantitative Evaluation of d-**π** Interaction in Copper(I) Complexes and Control of Copper(I)-Dioxygen Reactivity. *Chem. Eur. J.* **2004,** *10,* 237-246.

(15) Zhu, L.; Santos, O. D.; Koo, C. W.; Rybstein, M.; Pape, L.; Canary, J. W. Geometry-Dependent Phosphodiester Hydrolysis Catalyzed by Binuclear Copper Complexes. *Inorg. Chem.* **2003**, *42*, 7912–7920.

(16) Kalin, K. D.; Kaderli, S.; Zuberbu A. D. Kinetics and Thermodynamics of Copper(I)/Dioxygen Interaction. *Acc. Chem. Res.* **1997,** *30*, 139-147

(17) Incarvito, C.; Lam, M.; Rhatigan, B.; Rheingold, A. L.; Qin, C. J.; Gavrilova, A. L.; Bosnich, B. Bimetallic Reactivity, preparations, properties and structures of complexes formed by unsymmetrical binucleating ligands bearing 4- and 6-coordinate sites supported by alkoxide bridges. *J. Chem. Soc., Dalton Trans***.** **2001**, *23*, 3478-3488.

(18) Miller, M.W.; Amidon, R.W.; Tawney, P.O. Some meso-substituted anthracenes. I. 9,10-Bis-(chloromethyl)-anthracene as a synthetic intermediate. *J. Am. Chem. Soc*. **1955**, *77*, 2845–2848.

(19) Ojida, A.; Mito-oka, Y.; Inoue, M.; Hamachi, I. First artificial receptors and chemosensors toward phosphorylated peptide in aqueous solution. *J. Am. Chem. Soc.* **2002**, *124*, 6256–6258.

(20) Jing, C.; Shi, L.; Liu, X.; Long, Y. A Single Gold Nanorod as a Plasmon Resonance Energy Transfer Based Nanosenor for High-Sensitivity Cu(II) Detection. *Analyst.* **2014**, *24*, 6435-6439.

(21) Osako, T.; Tachi, Y.; Taki, M.; Fukuzumi, S.; Itoh, S. Modulation of Coordination Chemistry in Copper(I) Complexes Supported by Bis[2-(2-pyridyl)ethyl]amine-Based Tridentate Ligands. *Inorg. Chem.* **2001**, *40*, 6604-6609.

(22) Nugent, J. W.; Reibenspies, J. H.; Hancock, R. D. Controlling the Fluorescence Response of PET Sensors via the Metal-Ion π-Contacting Ability of the Fluorophore: Coumarin, a Weaker π Contacter. *Inorg. Chem*. **2015**, *54*, 9976-9988.

(23) Osako, T.; Terada, S.; Tosha, T.; Nagatomo, S.; Furatachi, H.; Fujinami, S.; Kitagawa, T.; Suzuki, M.; Itoh, S. Structure and Dioxygen-reactivity of Copper(I) Complexes Supported by Bis(6-methylpyridin-2-ylmethyl)amine Tridentate Ligands. *Dalton Trans*. **2005**, *21*, 3514-3521.

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