FUNDAMENTAL STUDIES OF CARBON OXYGEN BOND ACTIVATION IN NICKEL DIPHOSPHINE ETHER COMPLEXES

AND

METALLOMACROCYCLES AS LIGANDS: SYNTHESIS AND CHARACTERIZATION OF ALUMINUM-BRIDGED BISGLYOXIMATO COMPLEXES OF IRON AND COBALT

Thesis by
Paul Kelley

In Partial Fulfillment of the Requirements
for the Degree of Doctor of Philosophy

CALIFORNIA INSTITUTE OF TECHNOLOGY
Division of Chemistry and Chemical Engineering
Pasadena, California
2014
(Defended on April 10, 2014)

© 2014
Paul Kelley
All Rights Reserved

“See! Caltech made you happy.”

-Agnes Tong

ACKNOWLEDGEMENTS

Graduate school can be a series of trials, most of these trials are too much for a single being to handle alone. Fortunately no one has to undertake these tasks alone. Family, mentors, and friends are all critical to ones success in graduate school. Admittingly, without these forementioned resources I would have never been able to complete my PhD. It is to them that I owe my success. I would like to thank my mentors, friends, and family and anyone I may not list in the following statement. I want you to know that you have all touched my life in a special way and I am glad to have met you.

Thank you.

Prof. Theodor Agapie, I need to thank you first of all for taking me into your group back in 2008. It has been a long journey. In your group, I have had the opportunity to work on many projects and explore many different areas of chemistry and I thank you for that. Throughout my years at Caltech you have been a source of guidance and inspiration both in and out of the lab. Theo, I cannot thank you enough for the support you have given me. I will always remember my first years in lab and how you worked beside me teaching me how to use a schlenk line. Thank you for all that you taught me about inorganic and organometallic chemistry. Thank you for all the time you have taken pouring over my many presentations and teaching me how to be a respectable presenter. I thank you for all the times you allowed me to TA 102 with you. The lessons I learned from watching you teach and craft that class will be invaluable to me in the future, and I thank you for the time that you spent imparting that to me. I am also grateful that I got to observe (and partake) in the development and management of a newly founded research group. I would be lying if I said I didn't enjoy helping to build the Agapie group. Most of all, thank you for teaching me how to be a scientist and an overall better person, your rigor and passion for chemistry will always inspire me.

Prof. John Bercaw, thank you so much for being the chair of my thesis committee. Your advice and guidance has got me out of a rut numerous times. To the other members of my committee, Profs. Jonas C. Peters and Greg C. Fu, thank you for all your honest feedback on my scientific endeavors. Your words inside and outside my meetings helped me feel that you are genuinely invested in my development as a scientist. Thank you both for coming back to Caltech!

Many thanks to the members of the Gray group who provided a tremendous amount of time and effort in helping me when I was working on a bioinorganic project. Similarly I need to thank the members of the Bercaw group who provided advice and help on numerous occasions. Alex Miller, Ian Tonks, Paul Oblad, and Ted Weintrob thank you for all your help. The Bercaw group shrunk significantly near the end of my PhD studies. However, what the group lacked in size was made up with character and heart. Tom Teets, Dave Leitch, and Aaron Sattler, thank you all for making so many BP meetings enjoyable, and I wish you all luck in your careers!

Most of my time at Caltech was spent with my homies, by that I mean the Agapie group. I have spent many years with this group of people, I have shared their success and failures, while I can maybe convince myself that I helped them all in some fashion during their journeys, I feel what I may have done for them pales in comparison to what they have done for me.

Thanks to all my box mates of the past and present Jessica Sampson, Justin Henthorn, Josh Wiensch, and Madalyn Radlauer for putting up with me. I have always enjoyed the chemistry you guys would produce and I know you will keep up the good work! Maddy kudos to you for being an awesome safety officer, keeping us safe, and encouraging us to get regular healthy hours of sleep, I will always miss your peppy and chipper attitude. Sibo thanks for all your support over the years, thanks for all your comments, experimental suggestions, and just being overall helpful when I was in a scientific rut. Emily Tsui thanks for being an awesome friend all these years, hopefully we can continue the party in our postdocs! To Sandy, you will always be the best of the best to me. Thanks for all your help, from those early years of the bioinorganic projects to now. Davide thanks for all your hard work in making our group parties enjoyable! Thanks for all your tireless work as our dungeon master in our grand D&D adventure! The time when we encountered the Gnolls in our campaign is one of my top 5 greatest moments in graduate school. Thank you for that. Jacob thanks for always being a great guy, from your taste in music, to the kind words you would say sometimes, to that time your unbuttoned my shirt, thanks for all that! (Some more than others though…) Guy A. Edouard thanks for being an awesome co-worker! I really enjoyed working with you and still wake up in a cold sweat sometimes due to that paper we co-authored, but at least we both now know the source of the hydrogen! Justin Henthorn thanks for being a great bay mate. You would always remind me when my bay was getting to dirty by cleaning yours first, oh the shame. Guy, Justin, and Josh Wiensch thanks for allowing me to hang out with you guys I will always remember the lunches that we would get… I felt like a Goon. Kyle Horak, thanks for being an awesome friend, although you never answer my text messages ☹. Kyle, never forget your style, for it is uniquely your own. Buss thanks for being a fun guy to hang around you will always be my Boo. To all the first years, the most painful thing about moving on is that I won't get to hang out and see what you guys come up with. Good luck to all three of you in your amazing Agapie group journey! I'm certain we will meet again at a conference or something I look forward to all the chemistry you guys do!

Thanks also to Dr Dave Herbert for all you input during my studies of the nickel diphosphine chemistry. Po-Heng Lin thanks you so much for having a great sense of humor and always being your jolly self.

Many thanks to the exceptional staff at Caltech with whom, I had a chance to interact. Thank you Drs. Scott Virgil, Dave VanderVelde, Larry Henling, Mona Shahgholi, and the late Mike Day. You guys provided so much support to me over the years and I wouldn't have been able to make it here without you.

Thanks to all my friends and family who helped me when I was not in lab. Many thanks especially to my friends from other groups mainly Peter Agbo, Ryan Henning, and Joey Varghese thanks so much for being great to just hang out with! I am certain there are other people I am not listing and for all those, from me to you, "You are awesome!"

Many thanks to the Caltech Center for Diversity and their amazing staff! I unfortunately only became envolved in the CCD near the end of my PhD studies, mostly due to the urging of Agnes Tong.

I also would like to thank my good friend Agnes Tong. While there are many things I need to thank you for I am going to list the ones I feel are most important.

Agnes you have always been there for me when I have felt like I had no one to turn to. For issues I would encounter at Caltech or issues at home you were always there and I felt like I could talk to you about it and for that I thank you. Thank you for all the administrative help you have given me over the years of my PhD study and making things so much easier to understand. Interestingly, you were the only person who ever asked me wether I was attracted to females and I thank you for that. I thank you for making me question myself and become more truthful to myself. Thank you Agnes for always being there for me and simply being someone I could always talk to. Thanks for being someone I could confide in, someone who would actually listen. Agnes you have helped me through so much and you will always (along with Sandy and Emily) rank with the best of the best, thank you so much for being my friend.

ABSTRACT

In order to develop better catalysts for the cleavage of aryl-X bonds fundamental studies of the mechanism and individual steps of the mechanism have been investigated in detail. As the described studies are difficult at best in catalytic systems, model systems are frequently used. To study aryl-oxygen bond activation, a terphenyl diphosphine scaffold containing an ether moiety in the central arene was designed. The first three chapters of this dissertation focus on the studies of the nickel complexes supported by this diphosphine backbone and the research efforts in regards to aryl-oxygen bond activation.

Chapter 2 outlines the synthesis of a variety of diphosphine terphenyl ether ligand scaffolds. The metallation of these scaffolds with nickel is described. The reactivity of these nickel(0) systems is also outlined. The systems were found to typically undergo a reductive cleavage of the aryl oxygen bond. The mechanism was found to be a subsequent oxidative addition, β-H elimination, reductive elimination and (or) decarbonylation.

Chapter 3 presents kinetic studies of the aryl oxygen bond in the systems outlined in Chapter 2. Using a series of nickel(0) diphosphine terphenyl ether complexes the kinetics of aryl oxygen bond activation was studied. The activation parameters of oxidative addition for the model systems were determined. Little variation was observed in the rate and activation parameters of oxidative addition with varying electronics in the model system. The cause of the lack of variation is due to the ground state and oxidative addition transition state being affected similarly. Attempts were made to extend this study to catalytic systems.

Chapter 4 investigates aryl oxygen bond activation in the presence of additives. It was found that the addition of certain metal alkyls to the nickel(0) model system lead to an increase in the rate of aryl oxygen bond activation. The addition of excess Grignard reagent led to an order of magnitude increase in the rate of aryl oxygen bond activation. Similarly the addition of $AlMe_3$ led to a three order of magnitude rate increase. Addition of $AlMe_3$ at -80 °C led to the formation of an intermediate which was identified by NOESY correlations as a system in which the $AlMe_3$ is coordinated to the ether moiety of the backbone. The rates and activation parameters of aryl oxygen bond activation in the presence of $AlMe_3$ were investigated.

The last two chapters involve the study of metalla-macrocycles as ligands. Chapter 5 details the synthesis of a variety of glyoxime backbones and diphenol precursors and their metallation with aluminum. The coordination chemistry of iron on the aluminum scaffolds was investigated. Varying the electronics of the aluminum macrocycle was found to affect the observed electrochemistry of the iron center.

Chapter 6 extends the studies of chapter 5 to cobalt complexes. The synthesis of cobalt dialuminum glyoxime metal complexes is described. The electrochemistry of the cobalt complexes was investigated. The electrochemistry was compared to the observed electrochemistry of a zinc analog to identify the redox activity of the ligand. In the presence of acid the cobalt complexes were found to electrochemically reduce protons to dihydrogen. The electronics of the ancillary aluminum ligands were found to affect the potential of proton reduction in the cobalt complexes. These potentials were compared to other diglyoximate complexes.

TABLE OF CONTENTS

LIST OF FIGURES

Chapter 2

Chapter 3

Chapter 4

Chapter 5

Chapter 6

LIST OF SCHEMES

Chapter 2

Chapter 3

Chapter 4

Chapter 5

Chapter 6

LIST OF TABLES

Chapter 3

Chapter 4

Chapter 6

CHAPTER 1

General Introduction

This dissertation is focused on two main areas, specifically the study of aryl oxygen bond activation in a nickel(0) diphosphine terphenyl ether complex and the study of aluminum glyoxime macrocycles and the effects of sterics and electronics on the coordination and chemistry of the central metal center.

The efficient elaboration of aryl oxygen bonds to a variety of functional groups is emerging as a versatile tool in organic methodology. One very important use of aryl oxygen moieties is for the facile modification of arene rings. These substituents can be introduced into the aromatic ring via a number of pathways, notably electrophilic aromatic substitution. One widely used example is for the lithiation of arene rings where the aryl-lithium salt can be quenched with an electrophilic species leads to derivertization of the ring.

Although the utility of aryl oxygen groups cannot be understated, their removal is not straightforward. The aryl oxygen bond is strong and hence resists efforts at its activation. Some catalytic systems have been developed albeit the systems typically suffer from low turnover and low rates. Another utility of this cleavage is in cross coupling. Cross coupling of aryl ethers allows for the utilization of phenolic precursors in organic synthesis. While catalytic systems have been developed few in-depth mechanistic studies have been done on the reactivity of aryl oxygen bonds with nickel.

While few experimental studies had been done some computational studies had been undertaken where it was found that a nickel arene interaction was of present prior to the activation of the aryl oxygen bond. Our group has been focusing on several novel terphenyl diphosphine scaffolds. These terphenyl diphosphines were found to encourage metal arene interactions with a variety of metals. Given that the ligands predisposed the metal to interact with the arene we envisioned observing intramolecular reactivity with an ether moiety in close proximity with the central arene ring. Hence we come to the main ligand of this thesis. We developed a diphosphine terphenyl containing an ether moiety in the central arene of the terphenyl. Using this novel diphosphine studies were undertaken to gain mechanistic insight into the mechanism of aryl oxygen bond activation. From this system, in collaboration with my colleagues Sibo Lin and Guy A. Edouard, a mechanism for the reductive cleavage of aryl oxygen bond was able to be worked out, which we were able to extend to catalytic systems.

From there I directed myself to studies on the effect of electronics in aryl oxygen bond activation (Chapter 3). I was able study the rate of oxidative addition in great detail in variants of the nickel diphosphine discussed in chapter two. I was able to show that the rates and kinetics of oxidative addition are not affected significantly by the electronics of the ether. This is proposed to result from similar changes in the energy of the fround and transition states. Attempts were made to extend these studies to actual catalytic systems however due to the complexity of the systems the conclusions were always less than satisfying.

However, during the kinetic studies I was able to observe the acceleration of aryl oxygen bond activation in the presence of Lewis metal alkyls. Through careful low temperature studies we were able to ascertain that the Lewis acidic metal is coordinated to the ether moiety. The rate was found to show a dependence on Lewis acidic metal alkyl hinting a much more complicated mechanism.

The second part of my thesis deals with the study of iron and cobalt glyoxime complexes. What sets these compounds apart is the large aluminum linker between the glyoximes. The aluminum linkers and the ancillary ligands on the aluminum were found to affect the chemistry and geometry of the metal center. The structural and electrochemical parameters of the iron complex were investigated. Analogous cobalt complexes were studied for proton reduction as a function of the aluminum linkers.