Investigating the Effects of Tethered, Axial Lewis Base Coordination on Rhodium(II) Paddlewheel Complexes

William A. Sheffield
wsheffie@vols.utk.edu

Follow this and additional works at: https://trace.tennessee.edu/utk_gradthes

Part of the Organic Chemistry Commons

Recommended Citation
https://trace.tennessee.edu/utk_gradthes/6254
To the Graduate Council:

I am submitting herewith a thesis written by William A. Sheffield entitled "Investigating the Effects of Tethered, Axial Lewis Base Coordination on Rhodium(II) Paddlewheel Complexes." I have examined the final electronic copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Chemistry.

Ampofo K. Darko, Major Professor

We have read this thesis and recommend its acceptance:

Shawn R. Campagna, David M. Jenkins

Accepted for the Council:

Dixie L. Thompson

Vice Provost and Dean of the Graduate School

(Original signatures are on file with official student records.)
Investigating the Role of Tethered, Axially Coordinated Lewis Bases in Rhodium(II) Paddlewheel Complexes

A Thesis Presented for the
Master of Science
Degree
The University of Tennessee, Knoxville

William Alexander Sheffield
August 2020
Copyright © 2020 William A. Sheffield
All rights reserved.
Abstract

Dirhodium(II) paddlewheel complexes are highly renowned for their use in diazo decomposition to form a metallic-carbenoid species. This species has been used for a diverse range of chemical transformations including cyclopropanation, cyclopropenation, C-H functionalization, and X-H (Si, S, O, N) insertion reactions. Modulation of these catalysts traditionally involve the exchange of bridging ligands which have profound effects on the catalyst’s reactivity, chemo, and enantioselectivity. Recent interest has turned towards modifying the axial sites present in the complex as an additional means of modulating catalytic activity. These sites normally serve as the active site of the catalyst, but coordination of Lewis Bases on one of the sites are known to be beneficial to chemo and enantioselectivity. However, a main problem encountered in this field is the lack of control of coordination to the axial site.

This work aims to examine the development of novel ligands containing a pendant chain containing a Lewis base, and their incorporation into the rhodium(II) paddlewheel scaffold. Inclusion of these tether-containing ligands allows for more direct control of the location of the Lewis base and effectively increases the local concentration of the Lewis base near the active site. Ligands derived from amino acids or amino alcohols that contained either a phosphite or a thioether moiety were synthesized and attempts to exchange onto the rhodium complex were investigated. Exchange of the phosphite containing ligands was unsuccessful due to complications with oxidation. The thioether ligands proved to be more robust in comparison with successful exchange onto the catalyst scaffold with a variety of thioether derivatives. Evaluation of these complexes in Si-H insertion and cyclopropanation reactions revealed that the presence of the tethered thioether does indeed provide a positive benefit, with increased yields as compared to a control with no tethered thioether additive.
# Table of Contents

**Chapter 1: Introduction**

1.1 Dirhodium Paddlewheel Complexes Background ........................................... 1

1.2 Dirhodium(II) carbenoid reactions ......................................................... 2

1.3 Additive Effects ....................................................................................... 3

1.4 Tethered-Complexes .............................................................................. 5

1.5 Goals of this research .......................................................................... 6

**Chapter 2: Synthesis of heteroleptic dirhodium catalysts with ligands containing a tethered Lewis base** ......................................................... 8

2.1 Background ......................................................................................... 8

2.2 Ligand Synthesis .................................................................................. 11

2.3 Carboxamidate Catalyst Synthesis ......................................................... 15

2.4 Carboxylate Catalyst Synthesis ............................................................ 22

**Chapter 3: Investigating tethered, axially coordinated thioethers to dirhodium paddlewheels and their effects on the catalyst activity** ......................................................... 25

3.1 Introduction .......................................................................................... 25

3.2 Aryl Donor-acceptor Si-H Insertion Studies ........................................... 26

3.3 Alkyl Donor-Acceptor Si-H Insertion Studies ......................................... 32

3.4 Si-H Insertion Studies Using Chiral Catalysts with Tethered Thioethers .... 35

3.5 Cyclopropanation with EDA Studies ...................................................... 39

**Chapter 4: Experimental data** ....................................................................... 41

**List of References** .................................................................................... 54

**Appendix** ................................................................................................. 61

**Vita** ........................................................................................................... 97
List of Tables

Table 2.1: Yields for ligand exchange for thioether series of catalyst-----------------------------------------------17
Table 2.2: Yields for ligand exchange of TCB catalyst--------------------------------------------------------------------22
Table 3.1: Catalyst screening of Si-H insertion of methyl phenyl diazoacetate------------------------------------27
Table 3.2: Si-H insertion substrate scope-----------------------------------------------------------------------------------29
Table 3.3: Alkyl donor/acceptor catalyst screen--------------------------------------------------------------------------32
Table 3.4: Si-H insertion using chiral catalysts-----------------------------------------------------------------------------36
Table 3.5: Si-H insertion using chiral catalysts-----------------------------------------------------------------------------37
Table 3.6: Cyclopropanation of EDA catalyst screening------------------------------------------------------------------------39
List of Figures

Figure 1.1: Example of a Dirhodium(II) complex----------------------------------------------- 1
Figure 1.2: Reactivity and selectivity trend of the bridging ligands--------------------------------------1
Figure 1.3: Different chiral Rh(II) complexes and their potential conformations-----------------------------1
Figure 1.4: Relative reactivity of diazo compounds and their subsequent carbenoid species-------------------3
Figure 1.5: A.) Naphthyridine catalyst developed by Turro. B.) Ferrocene-amide complex developed by Bera-----------------------------------------------------------------6
Figure 1.6: Bead-peptide supported rhodium catalyst with an imidazole group axially coordinated to an axial site-----------------------------------------------------------------6
Figure 2.1: Ligand backbones used in this research-----------------------------------------------------------------------------------10
Figure 2.2: Different chain lengths can be obtained depending on choice of amino acid precursor-----11
Figure 2.3: Ring size variation formed from axial coordination-----------------------------------------------------------------------------------12
Figure 2.4: (S)-Metox-----------------------------------------------------------------------------------------------------------------------------------13
Figure 2.5: 1H-NMR of 18 (top) and 19 (bottom) -----------------------------------------------------------------------------------------------------------14
Figure 2.6: Proposed interaction of sulfoxide 19-----------------------------------------------------------------------------------------------------------------------------------14
Figure 2.7: Picture of a Soxhlet apparatus------------------------------------------------------------------------------------------------------------------------------------------------------------------15
Figure 2.8: Proposed coordination of phosphite 5 ligand to Rh2(OAc)4 and the accompanying 31P-NMR--16
Figure 2.9: UV/Vis spectrum of 25 with and without Et2S and 20---------------------------------------------19
Figure 2.10: Different geometries chiral carboxamidate catalysts------------------------------------------------------------------------------------------------20
Figure 2.11: Proposed structure of 28------------------------------------------------------------------------------------------------------------------------------------------------------------------21
Figure 2.12: Different chiral phthalimide parent catalysts---------------------------------------------------------------------------------------------------23
Figure 3.1: Mixed oxazolidinate/carboxylate catalysts used to investigate Si-H insertion reactions----27
Figure 3.2: Energy levels, HOMO-LUMO gap, and orbital distribution of the HOMO and LUMO for complexes Rh2(OAc)3(Metox) and Rh2(OAc)3(2-Ox)----------------------------------------------------------------30
Figure 3.3: Different tether-containing carboxylate catalysts--------------------------------------------------------------------------------32
Figure 3.4: Proposed coordination of the diazo compound to the axial site of the complex---------------33
Figure 3.5: Different chiral dirhodium(II) catalysts----------------------------------------------------------------------------------------------------------34
Figure 3.6: Potential orientations of the tether containing ligand-----------------------------------------------------------------------------------35
Figure 3.7: Proposed structures of heteroleptic dirhodium catalysts containing a tethered thioether-----35
Figure 3.8: Proposed structure for 18------------------------------------------------------------------------------------------------------------------------------------------------------------------36
Figure 3.9: Glutamic acid-derived bis-complex 23a----------------------------------------------------------------------------------------------------------39
List of Schemes

Scheme 1.1: Proposed mechanism for diazo decomposition by Rh(II) catalysts---------------------------2
Scheme 1.2 Different reaction pathways for the rhodium-carbenoid species---------------------------2
Scheme 1.3: Coordination of exogenous ligands to axial sites----------------------------------------4
Scheme 1.4: Different pathways that can be taken when exogenous ligands are added----------------5
Scheme 2.1: Different arrangements of bis-substituted complexes----------------------------------8
Scheme 2.2: Synthesis of DPTI heteroleptic catalysts by Corey------------------------------------------9
Scheme 2.3: Selective synthesis of bis-complexes developed by Bera---------------------------------9
Scheme 2.4: Example of equatorial ligand exchange---------------------------------------------------10
Scheme 2.5: Phosphite and phosphate synthesis derived from (l)-Glutamic acid------------------------11
Scheme 2.6: Phosphite and phosphate synthesis derived from (L)-Serine-------------------------------12
Scheme 2.7: Synthesis of Glutamic acid derived thioethers--------------------------------------------13
Scheme 2.8: Oxidation of PhTCB to PhOTCB---------------------------------------------------------------14
Scheme 2.9: Synthesis of thioether series of catalysts--------------------------------------------------17
Scheme 2.10: Synthesis of the carboxamidate control catalyst-----------------------------------------18
Scheme 2.11: Synthesis of Rh$_2$(PHOX)$_3$(Metox)--------------------------------------------------------20
Scheme 2.12: Synthesis of the achiral carboxylate TCB series catalysts-------------------------------------22
Scheme 2.13: Synthesis of Rh$_2$(OAc)$_3$(PhOTCB)----------------------------------------------------------23
Scheme 2.14: Synthesis of the chiral complex Rh$_2$(PTPA)$_3$(PhTCB)--------------------------------------24
Scheme 3.1: Catalytic cycle for Si-H insertion catalyzed by Rh(II) paddlewheel catalyst-----------------26
Scheme 3.2: Hemilability of sulfur moiety allows for nucleophilic attack of diazo compound-----------28
Scheme 3.3: Proposed catalytic cycle of Si-H insertion when tethered axial coordination is present on Rh(II) complexes--------------------------------------------31
Scheme 3.4: Alternate reaction pathways of alkyl donor/acceptor diazo compounds---------------------31
Scheme 3.5: Cyclopropanation of styrene with EDA--------------------------------------------------------38
Scheme 3.6: Catalytic cycle of a dirhodium(II) catalyzed cyclopropanation reaction--------------------38
List of Abbreviations

DCM - Dichloromethane
DCE – 1,2-Dichloroethane
EDA - Ethyl 2-diazoacetate
EDG - Electron donating group
ee- enantiomeric excess
equiv - equivalent
Et₂O - diethyl ether
EtOAc – ethyl acetate
EWG - Electron withdrawing group
Fc – Ferrocene
FMO - Frontier molecular orbital
HOMO- Highest occupied molecular orbital
HPLC - High Performance Liquid Chromatography
hr - Hour
HR-MS - High Resolution Mass Spectroscopy
L – Lewis Base
LB - Lewis Base
LUMO- lowest unoccupied molecular orbital
MeCN - acetonitrile
mL - milliliter
NHC – N-heterocyclic carbene
NMR – Nuclear Magnetic Resonance
Ph - phenyl
Rh – rhodium
Rh(II)- dirhodium paddlewheel
[Rh₂(OAc)₄] – dirhodium(II) tetrakisacetate
[Rh₂(S-DOSP)₄] - dirhodium(II) tetrakis[1-[[4-dodecylphenyl]sulfonyl]-prolinate]
[Rh₂(S-MEOX)₄] – dirhodium(II) tetrakis[methyl 2-oxo-oxazolidine-4(S)-carboxylate]
[Rh₂(PTTL)₄] – dirhodium(II) tetrakis[N-phthaloxy-(S)-tertleucinate]
^Bu - tert butyl
TEA – triethyl amine
THF - Tetrahydrofuran
TLC - Thin Layer Chromatography
Ts – tosyl
Chapter 1: Introduction

1.1 Dirhodium(II) Paddlewheel Complexes Background

Dirhodium(II) complexes are bimetallic compounds consisting of four bridging ligands, two axial sites and a metal-metal bond (Figure 1.1). The arrangement of these ligands displays an octahedral geometry, giving rise to a lantern-like or paddlewheel-like shape. These complexes have been investigated for a variety of applications, including anticancer therapeutics, oxidation reactions, and most prominently diazo decomposition reactions.\cite{1-4} One of the most prominent features of these catalysts is the wide variety of bridging ligands that have been incorporated into the structural motif. By far the most prominent ligands that have been studied are carboxylates and carboxamidates. Other ligands such as phosphates and naphthyridines have also been used.\cite{4-8}

The electronic nature of the bridging ligand can have a profound effect on the catalyst by directly affecting the electrophilicity of the rhodium metal center. More electron-withdrawing ligands typically result in a more electrophilic metal center, whereas more electron-donating ligands result in less electrophilic metal centers. It is this distinct alteration that has made these catalysts so popular for their

![Figure 1.1: Example of a Dirhodium(II) complex.](image1)

![Figure 1.2: Reactivity and selectivity trend of the bridging ligands](image2)

![Figure 1.3: Different chiral Rh(II) complexes and their potential conformations.](image3)
use in diazo decomposition reactions. In general, the more electrophilic the catalyst, the more reactive the catalyst is towards facilitating diazo decomposition. Conversely, more electron donating bridging ligands tend to exhibit more selectivity towards their target products but are typically less reactive towards diazo decomposition. These changes have been observed to directly affect catalytic activity, including both chemoselectivity and regioselectivity.9,10

In addition to tuning the electronic nature of the catalyst, functionality can also be incorporated onto the backbone of these ligands. Incorporation of bulky substituents onto these backbones creates an asymmetric environment around the active site of the catalyst that influences the approach of substrates to the active site. This has a profound effect on the catalyst’s enantioselectivity, and in some cases, regioselectivity.5,11 Many different examples of these chiral Rh(II) catalysts exist, with the substituents on the bridging ligand typically adopting specific confirmations around the axial site. Some examples of carboxylate-type catalysts include Rh₂(DOSP)₄ and Rh₂(PTTL)₄, which exhibit the D₂ and C₄ type geometries, respectively (Figure 1.3). Carboxamidate type catalysts, such as Rh₂(MEOX)₄, typically exhibit the C₂ type geometry (Figure 1.3). Carboxamidate ligands, unlike carboxylate ligands, are bound through with N and O, as shown by Rh₂(MEOX)₄ (Figure 1.3). These catalysts are much more rigid as compared to the carboxylate ligands. Similar to carboxylate ligands, the arrangement of the bulkiest substituent will arise as a means of mitigating the steric interaction of ligands. However, the presence of two different atoms, specifically the O and N, binding to the rhodium metals also influence the arrangement of the bridging ligands, resulting in the C₂ conformation.

1.2 Dirhodium (II) carbenoid reactions

![Scheme 1.1: Proposed mechanism for diazo decomposition by Rh(II) catalysts.](image1)

Scheme 1.1: Proposed mechanism for diazo decomposition by Rh(II) catalysts.

![Scheme 1.2 Different reaction pathways for the rhodium-carbenoid species.](image2)

Scheme 1.2 Different reaction pathways for the rhodium-carbenoid species.
As mentioned before, one of the major features that made the rhodium(II) paddlewheels so renowned was its ability to facilitate diazo decomposition to form a metal carbenoid species (Scheme 1.1). This is believed to occur through the nucleophilic attack of the diazo compound to the rhodium metal center (Step A, Scheme 1.1). After the nucleophilic attack, electrons from the rhodium metal are believed to attack the σ* of the C-N bond to extrude N₂, resulting in the metal-carbenoid species (Step B, Scheme 1.1). It is this metal carbenoid species that can undergo a variety of reactions, such as cyclopropanation, C-H functionalization, and X-H (X = N, O, S, and Si) insertion reactions (Scheme 1.2). While there are two axial sites available, it is generally accepted that only one site forms the transient carbene species. The second site is believed to act cooperatively during a reaction by compensating for electronic changes in the other Rh atom.

Though choice of ligand for the catalyst are a dominant factor in catalyst activity, the choice of diazo substrates is also important. Diazo compounds are classified based on the functionality directly bonded to the carbon with the N₂ group, which can either be acceptors or donors. Acceptors typically consist of electron withdrawing groups resulting in a more stable diazo compound, but more reactive carbenoid species. Donor groups have the opposite effect, resulting in a less stable diazo compound and more reactive carbenoid species (Figure 1.4). The most common carbenoids typically fall in the acceptor/acceptor, donor/acceptor, and acceptor carbenes. Because of the reactivity profile differences between diazo compounds, certain diazo compounds may be more suitable for specific catalysts over others. Donor/donor diazo compounds are not typically employed for catalysis, due to their highly reactive nature. As such, most studies typically employ the other diazo compound variants.

### 1.3 Additive Effects

One area that has recently become more focused is the coordination of molecules to the axial sites. Under ambient conditions, molecules capable of coordinating to the axial site will do so readily. During a reaction, only one site of the catalyst is used, with the distal Rh compensating for electronic changes in the active Rh. The effect of solvent coordination was evaluated through diazo decomposition studies. A notable decrease in catalytic activity was observed in the presence of coordinating solvents. This indicated that some degree of activity was influenced through the coordination of molecules to the active sites. It was determined that coordination to the axial site is controlled by an equilibrium process, with the initial coordination occurring much more favorably than the second coordination. The difference in rate is believed to be due to trans influence of the two coordinated species to the complex, resulting in a weaker interaction. Stronger σ-donating solvents bound much faster, but also resulted in decreased activity. As such, most reactions using Rh(II) catalysts are run in non-coordinating solvents, and the σ-donating species added in as an exogenous ligand in order to tune catalyst activity.
Early studies involving exogenous LBs were performed by Jessop and coworkers, who evaluated the efficiency of their catalyst performing the cyclopropanation of styrene with methyl phenyl diazoacetate. In the absence of any additives, they achieved 90% ee of the cyclopropane product, but upon adding strong σ-donating phosphines like PEt₃, the enantioselectivity decreased substantially to 21% ee.¹⁷ Even with weaker σ-donating ligands, the enantioselectivity of their catalyst suffered to some extent. Snyder and colleagues investigated the effects of axially coordinated NHCs by pre-coordinating the NHC to their catalyst, Rh₂(Piv)₄. They evaluated this complex in C-H insertion and cyclopropenation reactions, but their results were no different than when Rh₂(Piv)₄ was used with no NHC added. This indicated that at some point the NHC disassociated from the complex during catalysis.¹⁸

These early results did not seem promising for using additives to modulate catalytic activity, but later research would strongly imply that additives do have a positive benefit. Research performed by Davies and co-workers showed that σ-donating additives can provide a benefit to the catalyst. When performing the cyclopropanation of styrene with methyl phenyl diazoacetate using Rh₂(DOSP)₄, they increased the yield from 62% to 96% and enantioselectivity from 25% to 85% of the product with the addition of one equivalent of methyl benzoate.¹⁹ Other examples have also shown that axial coordination has benefitted enantioselectivity and increased yields. Zaykov and Ball illustrated this by incorporating the Rh(II) paddlewheel onto a peptide chain and used this catalyst to facilitate the Si-H insertion reaction of methyl phenyl acetate. The addition of P(OPh)₃ as an additive resulted in an increase in enantioselectivity of their catalyst by 18%.²⁰ Afonso and coworkers revisited NHC containing Rh(II) paddlewheels in C-H insertion of diazo-acetamides.²¹, ²² By incorporating phenylisopropyl groups onto the NHC, the NHC was able to remain bound to the Rh(II) complex. While yields lowered slightly, it was evident that the coordination of the NHC was influencing the catalyst in some fashion, as a new product was observed only when the NHC was coordinated to the catalyst. Though more recent studies indicate that axial coordination can play a positive role, this area of research still has many problems and questions that require answers. One problem presented by the NHC containing catalysts is the significant increase in reaction time. While affording new products, many of the examples described by Afonso took significantly longer to react compared to catalysts that did not contain NHC ligands. This is most likely a result of the strongly coordinating ligand heavily deactivating the catalyst.¹⁶ In regards to the experiments where the additive is added as an exogenous ligand, the mode of action of the additive comes into question. To favor the coordination of these additives, they are added in excess in comparison to the catalyst itself. As a result, coordination control becomes a problem. This lack of control introduces different pathways the catalyst can go, as illustrated in Scheme 1.4. If the additives bind too strongly, the catalyst is deactivated through occupation of both active sites and can no longer

Scheme 1.3: Coordination of exogenous ligands to axial sites.
catalyze reactions. Because the association/disassociation can occur at any time and is concentration dependent, the formation of the carbenoid species could occur at different rates. Consequently, any potential benefits afforded through axial coordination may not be as apparent due to the competing pathway involving catalysis with no axial coordination.

These problems beg the following questions: what is the additive doing to the catalyst and how can we obtain a more accurate representation of the role of the axially coordinated ligand? There needs to be a balance between the strength of coordination such that whatever properties are afforded through coordination can occur while simultaneously not severely deactivating the catalyst. One method that could provide answers to this problem would be to have the σ-donating species tethered to the catalyst, capable of coordinating to the axial site. This would remove the uncertainty of the location of the LB, and effectively increase the local concentration of the LB at the axial site without having to add an excess of the exogenous ligand. Likewise, one could modulate the σ-donating strength of the LB through judicious choice of specific LBs onto the ligands. For example, if a NHC is too strong of a σ-donor, other known LBs, such as phosphines or thioethers, could serve as appropriate LBs to the complexes. This would allow for a more fine-tuned approach to understanding the effects of axial coordination to the complex.

**1.4 Tethered, Lewis base-containing catalysts**

Rh(II) paddlewheel complexes can be divided into two separate classifications based on the types of ligands incorporated into the ligand scaffold: homoleptic and heteroleptic. Homoleptic complexes are those that have the same functionality present in each bridging ligand and are by far the most common type of Rh(II) complexes. Heteroleptic complexes, in comparison, have at least one bridging ligand different from the other. Rh₂(OAc)₄ and the previously mentioned chiral catalysts Rh₂(DOSP)₄ and Rh₂(MEOX)₄ would be examples of homoleptic complexes. There are examples of heteroleptic species reported in the literature.
linker to a solid support of some type.\textsuperscript{31-33} Other common practices include incorporating Rh(II) complexes into amino acid chains by exchanging the bridging ligand with amino acid residues.\textsuperscript{20,34}

Tethering a σ-donating moiety to the Rh(II) paddlewheel motif has been explored in the past. An early example of these heteroleptic complexes are the naphthyridyl complexes containing a pyridyl group synthesized by Turro (A, Figure 1.5).\textsuperscript{8} These naphthyridyl complexes were explored for their DNA binding interactions. Their studies showed that availability of the axial sites was imperative for stronger DNA binding interactions. Though these catalysts were not investigated for their catalytic efficiency in diazo decomposition, their synthesis and isolation of the tethered, axially coordinated groups was indeed possible. Bera and coworkers also utilized this naphthyridyl backbone with a ferrocene-amide functional group coordinated to the axial site (B, Figure 1.6).\textsuperscript{35} Even with both axial sites occupied, the amide functional groups were still catalytically active towards the C-H functionalization of indoles. Other variations that containing rigid functional groups near the axial site, but not bound, prevented or severely reduced catalytic activity. They proposed that the fluxional behavior of the amide group appeared to play a role in allowing catalysis to take place.

Another notable example was by Ball and coworkers, whom incorporated Rh$_2$(OAc)$_4$ onto a peptide chain by exchanging the bridging ligands with aspartic residues in the peptide chain (Figure 1.6).\textsuperscript{36} This peptide chain also contained a histidine residue near the rhodium moiety allowing coordination of the imidazole to the axial site of the rhodium complex. Using this catalyst, they achieved up to 97% ee using the axially coordinated histidine residue for the cyclopropanation of styrene with methyl phenyl diazo acetate. This was a noticeable increase in enantioselectivity compared to an analogous rhodium peptide catalyst containing a phenylalanine residue in place of the histidine residue which achieved only 51% ee.

### 1.5 Goals of this Research

The motivation for our research is to obtain a greater understanding of the role axially coordinated ligands in their influence on catalyst activity. Efficient and novel methods to incorporate these tether-containing ligands are needed to understand how the coordinated LB is interacting with the metal site. Little to no research has been dedicated to tethering phosphorus or sulfur LBs to rhodium paddlewheel complexes. Having a more concise understanding about the role of axial coordination and its effects on
catalytic activity would allow for more precise application of the catalysts towards chemical transformations. This could allow for a more fine-tuned approach towards catalyst development for application to chemical transformations. As such, this research aims to explore methods to incorporate ligands containing a σ-donating LB capable of axial coordination onto the rhodium(II) paddlewheel motif using ligand precursors described in the literatures. The main points to explore are as follows:

1.) Develop ligands containing sulfur and phosphite Lewis bases.
2.) Incorporate these LB containing ligands onto the dirhodium paddlewheel scaffold.
3.) Evaluate the effects of the LBs coordination through catalyst properties and use in reaction studies.

Chapter 2 will focus on the synthesis of the ligands and attempts to incorporate them into rhodium paddlewheel complexes. These catalysts will then be evaluated in Si-H insertion and cyclopropanation reactions as described in Chapter 3.
Chapter 2: Synthesis of heteroleptic dirhodium catalysts with ligands containing a tethered Lewis base

2.1 Background

Different methods have been investigated for the synthesis of heteroleptic rhodium paddlewheels. Typically, a new ligand is added to a solution of a rhodium paddlewheel precursor and heated, if needed, to promote exchange. The primary problem that is present in the synthesis of heteroleptic catalysts is the control of ligand displacement. The exchange process predominantly controlled by equilibrium. Removing the liberated ligand from the system pushes towards further substitution. As such, controlling stoichiometric amounts of ligand is the most common way that heteroleptic catalysts have been prepared from homoleptic parent catalysts. However, even with stoichiometric amounts of ligand, the formation of multiple products is still a common problem. As the acetate bridging ligands are displaced, the number of potential isomers that can form increase due to the lack of control over which acetate ligand is displaced. This is further compounded by the presence of the two atoms being different, as is the case with carboxamidate-type ligands (Scheme 2.1). Because of this, a series of geometric arrangements of the complex can form. Should there be chirality on the backbone of the bridging ligand, each of these isomers would have an additional conformation. To avoid this, researchers have investigated new methods for controlling ligand substitution, taking advantage of the properties of catalyst precursors.

Scheme 2.1: Different arrangements of bis-substituted complexes.
One method for selective substitution of one or two ligands was investigated by Corey. This was done by starting from a heteroleptic complex precursor containing more labile ligands, such as trifluoro acetate (Scheme 2.2). These ligands are known to disassociate more readily compared with other parent ligands, a process which was utilized to isolate both mono- and bis-substitution. The main caveat from this method stems from the added steps needed to synthesize separate precursors rather than proceeding directly from the single parent catalyst. While this method was successful in selectively targeting cis vs trans isomers, the relative orientation of the ligands, shown in Scheme 2.2, remained a problem. An alternative method developed by Bera involves starting from a hexa-coordinated rhodium(II) salt complex (Scheme 2.3). These complexes tend to favor the formation of bis-substituted complexes. Notably, the incorporation of the axial coordinating moiety was also stereospecific, with the tether being present on opposite sides of the complex.

My research aimed to investigate the feasibility of incorporating a ligand backbone containing a LB functionalized tether onto the scaffold. Ideally, the presence of the tethered LB would aide in the selective synthesis of the mono and bis substituted products. It is generally accepted that for ligand exchange to take place, the incoming ligand must approach the axial site in some fashion to initiate the exchange (Scheme 2.4). Should the exchange occur, the tethered LB should be coordinated to the axial site. Having the LB present would, in theory, inhibit further exchange as one of the axial sites would be effectively blocked. Likewise, the coordination of the LB should result in the remaining axial site becoming less electrophilic, and thus less susceptible to ligand exchange.

Based on previous studies involving axial ligands, a ligand containing either phosphorus or sulfur would serve as an ideal candidate to study. Phosphorus containing compounds, such as phosphines and phosphites, are highly versatile ligands, commonly utilized in transition metal chemistry. In addition, their coordination affinity and effects to rhodium catalysts has been previously studied. Sulfur-
containing compounds such as thioethers can also serve as a coordinating species.\textsuperscript{13,49} Though not as strong as most $\sigma$-donating phosphorus species, these would allow for a wider scope of coordination strength to the complexes. Likewise, both species can be modulated even further in their $\sigma$-donating strength by altering the functionality directly off the phosphorus or sulfur, offering a potentially wide library of ligands to study.

Two different types of equatorial ligand were explored to exchange on to the rhodium catalysts: the carbamoyl benzoate backbone and oxazolidinate backbone (Figure 2.1). These were chosen for their commercial availability and ease of synthesis from amino alcohols or amino acids. They also allow for the synthesis of a wide library of ligand derivatives that could contain a tethered LB. In my studies, a series of ligands containing Lewis bases were synthesized and evaluated for their influence in promoting ligand exchange.

![Scheme 2.4: Example of equatorial ligand exchange.](image)

![Figure 2.1: Ligand backbones used in this research.](image)
2.2 Ligand Synthesis

2.2.1 Synthesis of oxazolidinone with phosphorus containing LB

Initial studies conducted in our lab sought to use the oxazolidinone motif with some variability in the carbon chain length of the ligand (Figure 2.2). Depending on choice of starting amino acid, the chain length could easily be altered between one to three carbons, giving some flexibility in the tether. Following a modified procedure, an oxazolidinone ligand containing a phosphate or phosphite moiety was synthesized, which was derived from the amino acid (L)-glutamic acid (Scheme 2.5). The resulting oxazolidinone moiety contained a tether with a three-carbon chain length. This involved initially esterifying the carboxylic acids and subsequent amine protection to form diester carbamate in good yields (78% over two steps). The reduction of the esters was the next step, affording the diol in excellent yields. Finally, subjecting the diol to NaH resulted in the formation of the oxazolidinone.

From here, the phosphite moiety was added by phosphoramidite alcoholysis promoted by 1H-tetrazole and diisopropyl N,N dibenzyl phosphoramidite. Because of the instability of the phosphite product, purification of the product was initially difficult. Addition of triethylamine to the eluent during flash

![Scheme 2.5: Phosphite and phosphate synthesis derived from (L)-Glutamic acid.](image-url)
column chromatography proved to be sufficient in allowing isolation of the phosphite product in decent yields.  $^{31}$P-NMR indicated the presence of a single phosphorus signal at 138.8 ppm, which agrees with other phosphite compounds. While this compound was cleanly isolated, it still degraded over time. This degraded product was most likely the oxidized form of the phosphite product. The phosphate 5 was synthesized through the same procedure as the synthesis of the phosphite with the addition of the oxidant mCPBA. Yields were relatively low (28%) compared to the phosphite, due to difficulty during column purification. It had a significantly different chemical shift as compared to the phosphite ligand, -0.79 ppm, which is in agreement with other phosphate compounds. While not as strong of a σ-donor as the phosphite 4, 5 should still be able to coordinate through the double-bonded oxygen to the rhodium complex.

While this alteration of the LB does allow for direct modulation of σ-donation, a factor that does need to be considered is the chain length of the tether chain. For the LB to affect the metal center, it needs to be able to coordinate to the Rh metal. The resulting coordination of the tethered LB would result in a ring. Different sized rings exhibit various levels of angular strain, which in turn could influence the coordinating ability of the LB. With the chain length of 3, the resulting coordination of the phosphite to the rhodium complex would result in an 8-membered ring (7, Figure 2.3). Six-membered rings are very common in organic structures, and exhibit much lower angle strain compared to other ring sizes.

![Figure 2.3: Ring size variation formed from axial coordination](image)

Scheme 2.6: Synthesis of serine-derived phosphite and phosphate.
A six-membered ring could be obtained if the oxazolidinone was derived from serine rather than glutamic acid. As such, a serine derived oxazolidinone 10 was also synthesized following a known procedure in the literature (Scheme 2.6).\textsuperscript{55} (L)-Serine was esterified to form 8, which when treated with triphosgene and triethylamine affords the methyl ester oxazolidinone product 9. The reduction of the ester affords oxazolidinone 10. From there, the phosphite and phosphate derivatives, 11 and 12, were synthesized in the same manner as the glutamic variants, but with much lower yields. Though the yields were low, they afforded enough material to evaluate them for incorporation onto a dirhodium complex.

\subsection*{2.2.2 Synthesis of oxazolidinones with thioether LB}

![Figure 2.4: (S)-Metox.](image)

Other functional groups were also investigated in our group, specifically aiming to add thioether functionality to the ligands. As with the phosphite ligands, the length of the tether could be altered based on choice of starting amino acid. Oxazolidinone ligand (S)-Metox, 13, (Figure 2.4), which was obtained from Derek Cressy, was derived from the amino acid (L)-methionine following a published procedure.\textsuperscript{56}

Deriving a thioether from glutamic acid could be achieved as well.\textsuperscript{50} The alcohol was tosylated to act as a better leaving group. The thioether of interest can then be synthesized by reacting that tosylated product with an appropriate thiol and base. Attempts to synthesize a methyl variant proved to be exceedingly difficult, as a different product was also observed in the reaction. While the thioether product was present by \textsuperscript{1}H-NMR, other impurities of significant intensity were also present. A mass spectrum of the sample using DART revealed a peak that could correspond to 17 (Scheme 2.7) as well as the desired thioether product. Unfortunately, separation of these two products by column chromatography proved to be unsuccessful.

Alternatively, however, synthesis of (S)-GluPhtox (16, Scheme 2.7) was successful, using thiophenol as the thiol source with little byproduct. A plausible reason for why the impurity observed for when the methyl thiol was used could stem from the reagents being used in the reactions. Synthesis of the (S)-GluPhtox utilized a suspension of K\textsubscript{2}CO\textsubscript{3}, allowing only tiny amounts of base into the reaction. While the proton on the thiol is more acidic compared to the carbamate proton, if a strong enough base is present,

![Scheme 2.7: Synthesis of Glutamic acid derived thioethers.](image)
it is possible for the carbamate proton to be deprotonated, which could result in the side reaction product. Methane thiol is kept in a basic aqueous solution and is basic enough to deprotonate the carbamate proton. As a result of the excess base being present, it is possible that the side reaction also takes place, resulting in the formation of the bicyclic product 17.

2.2.3 Synthesis of carboxylate ligand with sulfur functional group

Much of the initial work towards developing the TCB ligand 18 was done by Dr. Brad Anderson and Jay Patel. These ligands were derived from inexpensive amino alcohols. To further expand the scope of our coordination studies, we sought to investigate sulfoxides as an alternative LB for axial coordination. Sulfoxides are somewhat unique as a coordinating species. Sulfoxides have been observed to have two different binding modes to rhodium paddlewheels, either through the oxygen or through the remaining lone pair of electrons of the sulfur. Coordination through the sulfur is common, usually observed in the crystal structures of complexes. There are examples of coordination of the oxygen to the rhodium complex, typically when the complex is electron poor. The coordination of the sulfoxide through the sulfur should be weaker in comparison to the unoxidized thioether. Should the axial coordination of the unoxidized thioether prove to be too strong, oxidizing the sulfur should weaken that coordination.

To obtain a sulfoxide derivative 19, I worked with undergrad student Kimberly Hollister to develop methods for oxidizing 18 directly. Using a modified procedure from the literature, we were successful in oxidizing the Ph-TCB ligand to the sulfoxide (Scheme 2.8). A problem that was observed in in the original procedure involved a basic workup to remove the excess acetic acid. Unfortunately, that posed

![Scheme 2.8: Oxidation of PhTCB to PhOTCB.](image)

Figure 2.5: 1H-NMR of 18 (top) and 19 (bottom).

Figure 2.6: Proposed interaction of sulfoxide 19.
problem for our ligand, due to the presence of the carboxylic acid. We found that it was more effective to remove the remaining acetic acid in vacuo. The sulfoxide product 19 exhibit unique $^1$H-NMR splitting patterns not observed in the starting material 18. As shown in Figure 2.5, the $^1$H-NMR of the methylene protons adjacent to the sulfur and the geminal methyl groups all have shifted slightly. Interestingly, unlike the unoxidized form, the signals also split, suggesting they are in different chemical environments. This unique splitting could possibly be due to the presence of the sulfoxide. A HSQC of sulfoxide 19 supports that the signals correspond to protons on the same carbon for the methylene position. Another plausible reason for this phenomenon could be the coordination of the oxygen from the sulfoxide to the proton of the amide (Figure 2.6).\(^{59}\) This coordination would result in a 6-membered ring, and if rigid enough, would place the protons of the methylene position in unique chemical environments.

### 2.3 Carboxamidate Catalyst Synthesis

#### 2.3.1 Catalyst Synthesis with Phosphorus-containing Ligands

With the carboxamidate ligands in hand, we sought to explore different methods to promote ligand exchange, starting with the phosphite containing ligands. Phosphite ligands were chosen for their potential benefits as observed in the literature.\(^{20}\) Furthermore, we hypothesized that coordination through the axial site could effectively protect the phosphorus atom from potential oxidation. The most common method to promote ligand exchange from Rh$_2$(OAc)$_4$, especially in the case of homoleptic complexes, is with a Soxhlet apparatus (Figure 2.7). Heating the reaction mixture promotes ligand exchange, resulting in liberation of one of the acetate ligands in the form of acetic acid. The liberated acetic acid forms an azeotrope with the solvent and then condenses in the Soxhlet apparatus. A thimble in the Soxhlet typically will contain Na$_2$CO$_3$-sand mixture which reacts with the acetic acid to form sodium bicarbonate and sodium acetate. This remains trapped in the thimble, while the solvent returns to the reaction mixture. This takes advantage of Le Chatelier’s Principle to shift the equilibrium in favor of promoting ligand exchange.

Unfortunately, all attempts utilizing the Soxhlet extractor to promote ligand exchange of Rh$_2$(OAc)$_4$ with either of the phosphite containing ligands failed. Upon mixing of the Rh$_2$(OAc)$_4$ and phosphite ligand, either the glutamic derived 4 or serine derived phosphite 11, a distinct orange color formed, which was

![Figure 2.7: Picture of a Soxhlet apparatus.](image)
believed to be the coordination of the phosphorus to the rhodium axial site. Upon heating the solution, however, the color returned to a green hue typical of these reactions, indicating the disassociation of the phosphite ligand. Whatever products that may have formed during the reaction were either not stable or decomposed during the reaction. An $^1$H-NMR of the mixture was not clear due to numerous signals, making it difficult to distinguish any notable peaks. No $^{31}$P-NMR signal pertaining to the phosphite was present. Instead, signals appearing in the range of 10 to -5 ppm were present. This was a sign that the phosphite was either oxidized or possibly decomposing, indicated by the multiple phosphorus signals in the $^{31}$P-NMR. Isolation of any of the products proved to be exceedingly difficult as well.

Because the potential for oxidation appeared to be high, attempts were made to promote exchange using either phosphate ligand 5 or 12 under the same conditions. These attempts also proved to be unsuccessful. In the attempted purification when ligand 12 was used, only signals belonging to the phosphate moiety could be distinguished by $^1$H-NMR. This was also corroborated with the $^{31}$P-NMR containing a single signal in the region where phosphates are typically observed. This could have possibly resulted from the hydrolysis of the phosphate from the oxazolidinone ligand. This material is normally a white solid, but the isolated fractions was a yellow-orange residue. The color of the material could indicate there may be some metal species present. However, based on the $^1$H-NMR and $^{31}$P-NMR alone, it is does not appear that ligand exchange has occurred.

Due to the problems encountered using a Soxhlet extractor to promote ligand exchange, an alternative method was investigated. Rather than chlorobenzene, a relatively non-coordinating solvent, these reactions were also conducted in 1,4 dioxane in the presence of the mild base triethylamine. Efforts to promote ligand exchange were attempted using both 4 and 11 at various temperatures. 1,4-Dioxane was chosen due to its similarity to THF in term of coordination affinity to rhodium but had a higher boiling point which meant that a higher temperature could be utilized if needed. However, as with the attempts with the Soxhlet extractor, the phosphite ligand was still oxidized to the phosphate. The rate appeared to vary based on temperature, occurring very rapidly at elevated temperatures and more slowly at room temperature.

However, unlike with the Soxhlet extractor, the crude material was cleaner for both the $^1$H-NMR and $^{31}$P-NMR. The $^1$H-NMR had signals that more closely matched to the phosphate ligand and Rh$_2$(OAc)$_4$, and the $^{31}$P-NMr had a single signal pertaining to what was most likely the phosphate. However, at room temperature, though ligand exchange was unable to be observed, a new signal in the $^{31}$P-NMR was observed in the NMR. A doublet of doublets at 30 ppm for 5 and 32 ppm for 12 in the $^{31}$P-NMR agrees

![Figure 2.8: Proposed coordination of phosphite 5 ligand to Rh$_2$(OAc)$_4$ and the accompanying $^{31}$P-NMR.](image-url)
with the literature for a singly coordinated phosphorus atom to a rhodium paddlewheel complex.\textsuperscript{60} Both the serine and glutamic derived phosphite exhibited this splitting, but the serine derived species was more prominent in the crude mixture. The axially coordinated species of ligand 5 and Rh\textsubscript{2}(OAc)\textsubscript{4} was able to be isolated via column chromatography, but integration of the \textsuperscript{1}H-NMR suggests no ligand exchange occurred (Figure 2.8). Likewise, the isolated species oxidized over time. Because of this instability and propensity for oxidation, we decided to move forward with ligands that were less susceptible to oxidation.

\subsection*{2.3.2 Catalyst Synthesis with Sulfur-containing Ligands}

Because of the problems encountered when trying to promote ligand exchange with the phosphorus-containing ligands and their inherent instability, we decided to investigate the more stable sulfur-containing ligands. Initial attempts in our group were successful in exchanging the (S)-Metox ligand on to the rhodium using a 1:1 ratio of ligand to rhodium catalyst via the Soxhlet method.\textsuperscript{61} Though these attempts targeted the formation of the mono-substituted 20, a mixture of bis isomers, 21a/b were isolated as well. Because the mechanism for ligand exchange is believed to also be equilibrium-based, using a lower amount of ligand to maximize the amount of 20 produced was hypothesized to aid in that endeavor. The exchange process does appear to hit a certain threshold before subsequent exchange takes place. Interestingly, the ratio of the two isomers typically comes to about 1.5:1 between the two isomers. Without a crystal structure, it is not possible to identify which isomer is in abundance by \textsuperscript{1}H-NMR alone. However, it is likely that the \textit{cis} isomer is in excess over the \textit{trans}. After the first exchange has occurred, there is one acetate ligand \textit{trans} to the oxazolidinone ligand and two acetate ligands \textit{cis} to it. Statistically, the \textit{cis} product should be in abundance, as the chance for that ligand to be exchanged is doubled compared to the \textit{trans} ligand. However, the ratio of products is not 2:1 for \textit{cis} to \textit{trans}. This

\begin{table}[h]
\centering
\begin{tabular}{cccccc}
\hline
Entry & Ligand equiv & n & R & Mono-complex Yield [%] & Bis-complex Yield [%] \textsuperscript{[a]} \\
\hline
1 & 1 & 1 & Me & 44\textsuperscript{[b]} & 28\textsuperscript{[b]} \\
2 & 2.5 & 1 & Me & 29 & 20 \\
3 & 1 & 2 & Ph & -- & 11 \\
4 & 2 & 2 & Ph & -- & 75 \\
\hline
\end{tabular}
\caption{Yields for ligand exchange for thioether series of catalysts. Only one \textit{cis} isomer of the bis-adducts is shown.}
\end{table}

\textsuperscript{[a]} Yield is based on combination of both \textit{cis} and \textit{trans} isomers.  
\textsuperscript{[b]} Yields from literature.
could be due to *trans* influence of the oxazolidinone ligand destabilizing the *trans* acetate ligand, resulting in that acetate becoming more labile. This would allow the exchange to occur more feasibly.

A previous study by Doyle on monitoring ligand exchange also agrees with this distribution of products.\(^{42}\) Because of the reaction being controlled by equilibrium, adding more equivalents of ligand should favor the formation of the bis complexes. As such, 2.5 equivalents of (S)-Metox ligand were used to promote ligand exchange (Scheme 2.9). However, attempts to isolate the bis-products cleanly proved to be challenging. Due to the excess (S)-Metox ligand being present, removal of the ligand from the bis-complexes required multiple purification attempts by column chromatography. As a result, much of the bis products were lost. These complexes were able to be isolated separately, obtaining an 8% yield for what is believed to be the *trans* isomer 21b and a 12% yield of the *cis* isomer 21a for a 20% total yield overall (Entry 2, Table 2.1). It is possible that too much ligand being present may inhibit ligand exchange, similar to how coordinating solvent inhibits ligand exchange.\(^{16}\) Though isolation of the bis products was challenging, an adequate amount of mono-species was also isolated in a 29% yield (Entry 2, Table 2.1).

When 1 equivalent of (S)-GluPhpto (16) was utilized under similar conditions as (S)-Metox, different results for the product distribution were observed. The formation of mono-complex 22 was not observed during the reaction. Instead, the ligand exchange appeared to proceed directly to the bis adducts 23a/b (Entry 3, Table 2.1). When 2 equivalents of ligand were used, the exchange also proceeded directly to the bis complex, giving a 75% overall of the bis complexes 23a/b, with a 2:1 between the two isomers (Entry 4, Table 2.1). The *cis* and *trans* isomers were able to be separated much more easily as compared to complexes 21a and 21b via column chromatography. Like with complexes 21a/b, the *cis* isomer is most likely the major isomer due to the statistical ratio of ligands that could be exchanged. An interesting difference between 21a/b and 23a/b is the chemical shift of the acetate ligands. The acetate signals for complexes 21a/b appears around 1.91-1.89 ppm, whereas complexes 23a/b signals appear around 1.74-1.71 ppm. The reason for this difference remains unclear. A crystal structure should provide more insight on the ligand interactions with the catalyst, which may explain the observed chemical shift differences.

### 2.3.3 Carboxamidate Control Catalyst Synthesis

To obtain a more accurate understanding for what the role of the tethered thioether was, we needed a control catalyst that did not contain a tethered thioether. Unfortunately, \(\text{Rh}_2(\text{OAc})_4\) would not serve as a good comparison, due to the different bridging ligands. Ideally, a heteroleptic complex with a single
oxazolidinate ligand would serve as an ideal comparison. Conveniently, 2-oxazolidinone, 24, is a commercially available compound. However, synthesis of this heteroleptic oxazolidinate/carboxylate complex proved to be quite challenging. Few carboxamidate/carboxylate heteroleptic catalysts are reported in the literature, mostly stemming from the harsh conditions typically employed to promote ligand exchange, including lengthy times at elevated temperatures. This was evident in my initial attempts to synthesize the mono-oxazolidinone product 25, as no product was observed under the same conditions for the exchange of (S)-Metox. This does indicate that the sulfur of the tethered thioether is providing aid during the exchange to some degree. One possibility could be by allowing coordination to occur more readily. Having the thioether present may allow for closer interaction of the ligand to the metal center which may aid in facilitating the ligand exchange process.

An alternative route for synthesizing rhodium complexes used a microwave reactor. A benefit of using this method would allow for a significant decrease in the time it would take to promote the exchange by running the reaction at a higher temperature. Unfortunately, attempts to synthesize 25 with 1 equivalent of ligand 24 was not successful, with little to no exchange appeared to take place. Increasing the ligand amount to 10 equivalents did allow for exchange to occur. As a result, the mono-species was able to be isolated at 32% yield, as well as a mixture of what is believed to be further substituted products which were unable to be isolated (Scheme 2.10).

We determined that complex 25 would serve as a good control to compare to 20 due to its similar heteroleptic nature. Adding Et₂S would allow us to mimic 20 with the thioether coordination. A UV/Vis spectrum (Figure 2.9) of complex 25 was obtained with and without the coordination of the Et₂S and was compared to 20. Without any additives, 25 has a quite different λ_max of the π* to σ* at 637 nm compared to 20 at 572 nm. However, adding one equivalent of Et₂S to 25, the λ_max of this complex was 576 nm, almost identical to 20.

![Figure 2.9: UV/Vis spectrum of 25 with and without Et₂S and 20.](image)
2.3.4 Chiral Carboxamidate Catalyst Synthesis

![Different geometries chiral carboxamidate catalysts.](Image)

As mentioned before, one of the renowned properties of these rhodium catalysts is the ability to induce chirality in various reactions. This induction is predominantly controlled by the ligand sphere surrounding the axial site. When different moieties are present around the axial site, the approach of the incoming diazo will change to favor fewer steric interactions. Starting from Rh$_2$(OAc)$_4$, allowed us to gauge what kind of conditions and effect the presence of the tethered LB had on the catalyst during the exchange. Ultimately, other ligands containing some type of moiety on the backbone would need to be present to induce chirality in the insertion product.

Synthesizing a chiral complex that contained a chiral environment, however, has other problems not present in the achiral catalyst synthesis; specifically, the starting point for which to begin the exchange. Previously, we sought only to exchange one or two acetate groups, where the tether-containing ligand was the only substrate of interest. Now, a second competing ligand is also present. To minimize competing substrates exchanging on the catalyst by starting with rhodium acetate, it would be more efficient to exchange a ligand starting from a parent complex. As mentioned previously, carboxamidate-type catalysts form a variety of products as ligand exchange takes place. Over time, they ultimately settle in the (2,2)-cis arrangement, which is believed to be the thermodynamic product (Figure 2.10). However, during the ligand exchange process, multiple arrangements are present. This indicates that these carboxamidate-type ligands can exchange with other carboxamidate ligands. Likewise, Doyle reported the successful synthesis of a heteroleptic carboxamidate catalyst in 2002, indicating that this is indeed possible. As such, I hypothesized should be possible exchange a ligand from the parent complex.

To test this theory, Rh$_2$(PHOX)$_4$·4ACN, 27, was synthesized following a literature procedure (Scheme 2.11). This catalyst was chosen because the parent ligands contained an oxazolidinone backbone and
because of the availability of ligand 26 in our lab. Unlike when starting from rhodium acetate, the liberated ligand is not removed from the system, but remains in solution. Ideally, should ligand exchange take place, the presence of the tether should impede the exchange of the liberated parent ligand. To monitor these reactions, TLC was used, but it was difficult to make any confirmation if new spots were forming due to small $R_f$ differences. Instead, these reactions were monitored by HPLC. This proved fruitful, as two new signals were present on the chromatogram. Unfortunately, purification was quite difficult, as the separation of the parent complex from the product was not efficient. To maximize efficiency, I utilized an HPLC to monitor small-scale reactions under different conditions to evaluate the optimal conditions to promote ligand exchange. Based on these results, 2 equivalents of (S)-Metox ligand 13 appeared to give the largest amount of 28 relative to remaining starting material 27. Excess ligand above 2 equivalents appeared to inhibit ligand displacement, even after 24 hours.

By refluxing 27 in chlorobenzene with two equivalents of (S)-Metox ligand, we were able to promote ligand exchange and isolate 28 in 30% yield. The other observed product was difficult to isolate due to degradation. Unlike the previous achiral catalysts and parent catalyst 27, the $^1$H-NMR of 28 was much more complex. With the presence of the (S)-Metox ligand, the catalyst would have a $C_1$ symmetry with each of the remaining parent ligands now in a unique chemical environment. This results in all ligands having their own unique signals on the $^1$H-NMR. When evaluating the signals present in the spectrum, the signals for ligand 13 were present in similar locations to the achiral complex 20 except for the methyl attached to the sulfur. A singlet much further upfield at 1.12 ppm was present and integrated to three. We postulated that this was due to the anisotropic effects of the phenyl rings on the other bridging ligands (Figure 2.11). A crystal structure would be needed to confirm the structure of the catalyst, but unfortunately, attempts thus far to obtain one have not been successful.
2.4 Carboxylate Catalyst Synthesis

2.4.1 Synthesis of carboxylate catalysts with sulfur functionalized tether

Unlike carboxamidate-based catalysts, carboxylate catalysts undergo exchange much more rapidly. Performing ligand exchange reaction using a Soxhlet proved to be somewhat problematic, as the reaction ended up difficult to purify and yields were quite low. As a result, an alternative method following a similar procedure proposed by Corey using NaHMDS in THF proved to be successful.\(^{43, 61}\)

Unlike the Soxhlet method, the acetate ligand is not being removed from the reaction system. Instead, the base is deprotonating the carboxylate ligand, in theory allowing it to exchange more readily. To reduce the likelihood of the base coordinating to the axial site, an extremely bulky base, NaHMDS was used. This proved to be successful in the synthesis of 28 and 29a/b, but still in low yields (Entry 1, Table 2.2). In the literature, this method was used for imidazolidinone ligand, which does require a strong base to deprotonate the imidazolidinone proton. Because our ligand is a carboxylate, I hypothesized that such a strong base was not necessary to promote the same reaction. Using a weaker bulky base, such as Hünig’s base, we would be able to promote ligand displacement while minimizing the degradation of the ligand and catalyst.\(^{63}\) This method provided a significantly more efficient and facile way of synthesizing the mono and bis TCB complexes, 28 and 29a/b (Scheme 2.12). Attempts using either chlorobenzene or DCE as the solvent with 1.1 equivalents of ligand, the ligand is nearly completely consumed. When refluxed in chlorobenzene, the exchange process occurs in a comparable manner to the carboxamidate series, where the second substitution appears to occur quite readily compared to the first. This is indicated by the much higher yield of the bis complexes (Entry 2, Table 2.2). Refluxing in DCE afforded more of the mono-product (Entry 3, Table 2.2), but a moderate amount

**Scheme 2.12: Synthesis of the achiral carboxylate TCB series catalysts.**

**Table 2.2: Yields for ligand exchange of TCB catalyst.**

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Base</th>
<th>28 Yield [%]</th>
<th>29a/b Yield [%][a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>THF</td>
<td>NaHMDS</td>
<td>25[b]</td>
<td>12[b]</td>
</tr>
<tr>
<td>2</td>
<td>Chlorobenzene</td>
<td>Hünig’s base</td>
<td>26</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>DCE</td>
<td>Hünig’s base</td>
<td>36</td>
<td>43</td>
</tr>
</tbody>
</table>

[a] Yield is based on combination of both cis and trans isomers.

[b] Yields from literature.
of the bis complexes still formed. The substantially higher yield of the bis complex when refluxing in chlorobenzene was used is most likely due to the increased temperature of the reaction as compared to DCE.

The sulfoxide ligand 19 was subjected to similar conditions in DCE to promote ligand exchange (Scheme 2.13). Unlike with the unoxidized ligand 18, some type of degradation was observed during the exchange by TLC. Isolation of this product proved to be difficult, but we were able to obtain a 41% yield of the mono-complex 30. The mono-complex exhibited similar splitting patterns as the ligand but shifted slightly downfield compared to the free ligand. The most dramatic difference being the location of the geminal dimethyl, which was split much more significantly compared to the free ligand.

### 2.4.2 Chiral Carboxylate Catalyst Synthesis

Synthesis of chiral carboxylate-containing catalysts was also investigated. The phthalimide-based catalysts developed by Hashimoto served as good candidates due to their ease of synthesis. The parent catalysts that were chosen were tetrakis[N-phthaloyl-(S)-phenylalaninato] dirhodium (Rh₂(PTPA)₄) and tetrakis[N-phthaloyl-(S)-tert-leucinate] diroodium (Rh₂(PTTL)₄) (Figure 2.12). These phthalimide catalysts also exhibit unique properties in their structural geometry in the solid state and in solution. The
Rh$_2$(PTPA)$_4$ in the solid state adopts the $\alpha$, $\alpha$, $\beta$, $\beta$ geometry, resulting in $C_2$ symmetry. Unlike carboxamidate catalysts which are much more rigid and locked in their geometry, the phthalimide ligands are much more fluxional in nature. This is observed in the $^1$H-NMR for 31, in which the signals are significantly broadened. Rh$_2$(PTTL)$_4$, 32, is more atypical compared to most other carboxylate catalysts. It adopts an ‘all up’ $\alpha, \alpha, \alpha, \alpha$ geometry in the solid state (Figure 2.12). There is evidence that in solution the ligands exhibit some fluxional behavior, but it is significantly less compared to the Rh$_2$(PTPA)$_4$ catalyst. Like with the carboxamidate catalysts, there are examples in the literature that describe exchanging one of the ligands to synthesize a heteroleptic catalyst.

Attempts to exchange ligand 18 followed a similar procedure to the achiral species using Hünig’s base to help promote the exchange (Scheme 2.13). Monitoring the reaction by TLC indicated the formation of a new product. The resulting isolated product was a shiny, powdery, blue-green solid (33, Scheme 2.11). Unlike the parent complex 31, when the product was dissolved in deuterated chloroform, the $^1$H-NMR had significantly sharper signals. This indicates that the complex has become much more rigid as compared to the parent complex. Upon dissolving the product in deuterated acetonitrile, the $^1$H-NMR signals become significantly sharper. Like the chiral carboxamidate complex, the $^1$H-NMR is much more complex compared to the achiral variant. What is unique about the spectrum, however, is the chemical shift of the geminal methyl groups on the PhTCB ligand. In the achiral complex 28, the $^1$H-NMR signal of the geminal methyl groups overlap, appearing as one signal. For the isolated complex 33, two signals were present with a 1 to 1 ratio to one another, which I believe are the geminal methyl groups. The separation of the signals could be due to anisotropic effects from the various aromatic rings present on the structure. An HSQC of the complex agrees with this hypothesis as both signals both are associated with a similar carbon signal, despite being so different in the $^1$H-NMR.

Attempts to exchange with the Rh$_2$(PTTL)$_4$ parent catalyst proved to be more difficult. Monitoring the reaction by TLC indicated the formation of a new species. The formation of this new species occurred more slowly compared to when Rh$_2$(PTPA)$_4$ was used. Unfortunately, isolation of the product proved to be unsuccessful. A likely reason for this could be that the new spot was a result of axial coordination of the ligand with no equatorial displacement. Upon trying to isolate the newly formed spot, the ligand may have disassociated from the complex.

Scheme 2.14: Synthesis of the chiral complex Rh$_2$(PTPA)$_3$(PhTCB).
Chapter 3: Investigating tethered, axially coordinated thioethers to dirhodium paddlewheels and their effects on the catalyst activity

This chapter contains material originally published by William Sheffield, Anthony Abshire, and Ampofo Darko:


William Sheffield performed all synthesis and characterization, wrote the manuscript, and assembled the supporting information document. Anthony Abshire performed all calculations. Ampofo Darko supervised writing of the manuscript and provided conceptualization for the project.

3.1 Introduction

The focus of this research aimed to elucidate the potential role of the tethered thioether and the effects afforded from its coordination to the catalyst. Early work in our group involved exploring the use of these tether-containing catalysts and evaluated their efficacy in rudimentary cyclopropanation reactions. In this study, the TCB series of catalysts could catalyze the cyclopropanation of the electron deficient donor-acceptor diazo substrate, even outperforming rhodium acetate, indicating that the tethered thioether was providing some type of benefit. Conversely, the oxazolidinate Metox series severely underperformed as compared to the TCB series and even rhodium acetate. Because not every catalyst is necessarily suited for every reaction, we hypothesized that this choice of diazo may not have been the ideal for that series of catalysts. Carboxamidate catalysts are typically less reactive compared to carboxylate catalysts, due to the intrinsic electronic nature of the equatorial ligands. Specifically, the more electron-donating oxazolidinone ligands donate more electron density into the rhodium metal centers. This directly affects the catalytic activity by decreasing the electrophilicity of the catalyst. This decrease in electrophilicity results in a lower susceptibility to nucleophilic attack by diazo compounds. We hypothesized that this series of catalyst would be more suitable with more reactive substrates, specifically more reactive diazo compounds and reactive heteroatom substrates. For that reason, Si-H insertion reactions in conjunction with more reactive donor-acceptor diazo compounds were chosen for these studies.
3.2 Aryl Donor-Acceptor Silyl-hydrogen Insertion Studies

3.2.1 Silyl-hydrogen insertion reaction

Si-H insertion is one of the many reactions that the reactive rhodium carbene species can insert into. Organosilicon compounds are highly versatile species that have a variety of applications. These range from acting as protecting groups, synths for synthesis for more complex molecules, and even as isosteres for medicinal compounds. As such, having different methods for incorporating organosilanes on to organic scaffolds is highly advantageous. One such method involves inserting into the Si-H bond. Rh(II)-catalyzed Si–H insertion with diazo compounds was first reported by Doyle in 1988. The currently accepted catalytic cycle is shown in Scheme 3.1. Formation of the rhodium carbenoid species occurs in the first part of the reaction. This occurs through the initial attack of the diazo compound to an open rhodium axial site and is followed by the extrusion of $N_2$ resulting in the carbenoid species (A and B, Scheme 3.1). From here, the silyl substrate is believed to approach the carbenoid species, step C, forming the transient intermediate D. The mechanism for the insertion into the Si-H bond is considered to be analogous to that of a C-H insertion, in which the insertion occurs in a concerted, asynchronous manner. Since then, Rh$_2$(OAc)$_4$ and other Rh(II) catalysts have been shown to give high yields and enantioselectivity of silyl-insertion products. Among the previous reports, only a study by Ball and Zaykov has considered the influence of axial coordination on the outcome of Si–H insertion. In this article, the authors used kinetic studies to prove that axial coordination of triphenylphosphite improved enantioselectivity of silane insertion with methyl phenyl diazoacetate using dirhodium peptide complexes. Our interests in utilizing tethered thioether ligands in Rh(II) catalysts led us to further explore the effects of axial coordination in silyl-insertion reactions. Different donor/acceptor diazo compounds and silyl substrates were evaluated to obtain a greater understanding.

![Scheme 3.1: Catalytic cycle for Si-H insertion catalyzed by Rh(III) paddlewheel catalyst.](image-url)
of the role tethered thioether and elucidate any benefits and downfalls of tethering a thioether to the catalyst.

3.2.2 Results and Discussion

![Figure 3.1: Mixed oxazolidinate/carboxylate catalysts used to investigate Si-H insertion reactions.](Image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>[Rh]</th>
<th>Temp. [°C]</th>
<th>Solvent</th>
<th>Yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>25</td>
<td>CH₂Cl₂</td>
<td>73</td>
</tr>
<tr>
<td>2</td>
<td>2a/2b</td>
<td>25</td>
<td>CH₂Cl₂</td>
<td>16</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td>25</td>
<td>CH₂Cl₂</td>
<td>70</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>40</td>
<td>CH₂Cl₂</td>
<td>84</td>
</tr>
<tr>
<td>5</td>
<td>2a/2b</td>
<td>40</td>
<td>CH₂Cl₂</td>
<td>25</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td>40</td>
<td>CH₂Cl₂</td>
<td>72</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>0</td>
<td>CH₂Cl₂</td>
<td>50</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td>25</td>
<td>Toluene</td>
<td>78</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td>60</td>
<td>Toluene</td>
<td>89</td>
</tr>
<tr>
<td>10</td>
<td>2a/2b</td>
<td>60</td>
<td>Toluene</td>
<td>74</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
<td>60</td>
<td>Toluene</td>
<td>77</td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>60</td>
<td>Toluene</td>
<td>79</td>
</tr>
</tbody>
</table>

[a] Yields are reported as averages of two runs and were determined by ²H NMR using mesitylene as an internal standard.  
[b] Reaction had diazo remaining 2 hours after start of reaction.  
[c] Yields in parentheses are when diethyl sulfide (2 mol-%) was included as an additive.  
[d] Separately, 2a and 2b gave average yields of 70 and 73 %, respectively.  
[e] (S)-MeTOX ligand (2 mol-%) was included as an additive.

Initial catalyst evaluation was conducted using dimethylphenylsilane and methyl phenyl diazoacetate (4a). Complex 1 was able to efficiently catalyze the carbene insertion into the Si–H bond in ambient conditions with a 73 % yield in dichloromethane (DCM). Upon subjecting the complexes 2a and 2b to the same conditions, only 16 % yield of the product was observed, even two hours after diazo addition was complete. Complex 3 provided a 70 % yield of silane 5a under these conditions and a 72 % yield when 2 mol% of diethyl sulfide was added. Performing the reaction in refluxing DCM further improved the yield for complex 1 to 84 % and for 2a/2b to 25 %, but the yields for complex 3 did not improve, even when dimethyl sulfide was added (Table 3.1, entries 4–6). Cooling to 0 °C was detrimental to the performance of complex 1, reducing 6a yield to 50 % (Table 3.1, entry 7). Changing solvents to toluene and raising the temperature to 60 °C gave the best yield for complex 1 (89 %, Table 1, entry 9), and were used as the optimal conditions to further evaluate the performance of complexes 2a/2b and 3. For 2a/2b, the optimal conditions dramatically increased the yield of silane 5a to 74 % (Table 3.1, entry 10).
The observation that \( \textbf{2a} \) and \( \textbf{2b} \) were more active at elevated temperatures is a strong indication of ligand hemilability.\textsuperscript{77} Presumably, the displacement of the thioether ligand by diazo \( \textbf{4a} \) becomes more facile at higher temperatures, enabling catalysis in complexes \( \textbf{2a} \) and \( \textbf{2b} \) (Scheme 3.2). Complex \( \textbf{1} \) already possesses an open site, allowing it to react much more readily at lower temperatures. Subjecting \( \textbf{3} \) to the optimized conditions only marginally improved its yield of \( \textbf{5a} \) (77 % yield, Table 3.1, entry 11), which was lower than the yield with complex \( \textbf{1} \) (compare entries 9 and 11 in Table 3.1). The addition of 2 mol% of diethyl sulfide or (S)-Metox ligand to complex \( \textbf{3} \) did not significantly improve yields for \( \textbf{5a} \) (Table 1, entries 11 and 12). The UV/Vis results suggested that complex \( \textbf{3} \) with diethyl sulfide should have similarly reactivity to complex \( \textbf{1} \). However, the results at higher temperature imply that the diethyl sulfide additive is too weakly coordinated to be of any benefit, indicating that tethering the thioether to the catalyst is most beneficial at elevated temperatures.

With optimal conditions in hand, we investigated the scope of the Si–H insertion reaction in the presence of the tethered thioether. Keeping diazo \( \textbf{4a} \) constant, we tested complexes \( \textbf{1}–\textbf{3} \) with a series of silyl substrates but observed essentially comparable yields between them. Complex \( \textbf{1} \) was the best catalyst for most substrates tested, but only marginally (\( \textbf{5b}–\textbf{e} \), Table 3.2, entries 1–12). With the exception of triphenyl silane, the silanes in the scope are considered to be more reactive than dimethylphenylsilane.\textsuperscript{70} Thus, it seems that the reactive nature of these silanes outweigh any potential benefits in yield afforded by the tethered thioether moiety.

We also sought to investigate the effects afforded from the tethered thioether when electronics were perturbed on the diazo compound and found more notable differences. When a strong withdrawing group is present on the phenyl ring, \( \textbf{1} \) has lower activity when compared to \( \textbf{3} \). However, as the donating ability of the diazo became stronger, complex \( \textbf{1} \) began to perform more effectively (\( \textbf{5f}–\textbf{h} \), Table 3.2, entries 13–18). There was also a larger change in yield when compared to changes in yield for complex \( \textbf{3} \). For example, the difference in yield of products \( \textbf{5f} \) and \( \textbf{5g} \) was 24 % for complex \( \textbf{1} \) (Table 3.2, compare entries 13 and 15), while the difference in yield for the same substrates was 8 % for complex \( \textbf{3} \) (Table 3.2, compare entries 14 and 16). This indicates a greater selectivity for diazo compounds when the tethered thioether group is present.
The enhanced selectivity could be due to the effects that coordinated LBs have on the frontier molecular orbitals on the dirhodium paddlewheel complex. Having ligands coordinated at axial sites has been previously examined computationally in studies that suggest a dramatic increase in the energy of the LUMO of the complex.\(^{78}\) An analysis of the frontier molecular orbitals of complex 1 and 3 seem to agree
with this. When the tethered thioether is present, the LUMO energy level is increased by 1.21 eV (≈ 28 kcal/mol, Figure 3.2), along with an increased HOMO-LUMO gap (5.56 eV for 3 vs. 6.47 eV for 1, Figure 3.2). Consequently, the initial step of the nucleophilic attack of the diazo onto the rhodium center is expected to be more difficult (step a, Figure 3). This may explain the improved yields at elevated temperatures. The result that complex 1 is still active, albeit less so, at 0 °C suggests that the activity of the complex is more nuanced. Using Berry’s three-center/four electron bonding model as an inspiration, it's plausible that the labile nature of the thioether coordination allows an elongation of the Rh–S bond to compensate for the binding of the diazo compound, which could lower the barrier for the first step (step a, Scheme 3.3). The thioether ligand can then contract its Rh–S bond to donate electron density to the metal center, facilitating nitrogen extrusion and lengthening the Rh–C bond of the resulting carbene (step b, Scheme 3.3). This “push-pull” relationship of axial ligands on the Rh paddlewheel scaffold has been previously invoked to explain results when N-heterocyclic carbenes are used as axial ligands in diazo-mediated reactions. We hypothesize that the same relationship exists in our system, but with the key modification of introducing flexibility through tethered coordination of weakly coordinating thioether ligands. The more rigid ligand system used in this study can only “flex” so far, however, and cannot adequately accommodate less nucleophilic diazo compounds such as 4b. This agrees with the results shown in Table 3.2, as 1 performed worse than 3 in the production of 5f. As the substituent on the phenyl ring of the diazo becomes more donating, as in diazo 4d, the benefits of the thioether are more pronounced due to a better reactivity match. As such, more work in understanding the effects of axially coordinated thioethers is still needed.
3.3 Alkyl Donor-Acceptor Silyl-hydrogen Insertion Studies

3.3.1 Alkyl Diazo Substrates

To expand our knowledge from our experiments in the Si-H insertion reactions, we decided to explore alkyl donor-acceptor diazo substrates as a potential route that our catalysts could be applicable for. Alkyl donor acceptors should be more reactive as compared to the aryl donor acceptors. A potential problem unique to alkyl donor-acceptor diazo compounds arises from the presence of hydrogens alpha to near the carbene center. The presence of this hydrogen allows for an alternative reaction pathway to form an alkene via β-hydride migration/elimination (Scheme 3.4). This side reaction has been observed in the past and is a competing pathway that can occur during the catalysis. Two factors that have been determined to play a role in mitigating the migration: temperature and the bridging ligands present on the catalyst. Temperature has been shown to play a major role with colder temperature decreasing the likelihood of the migration from taking place, followed by choice of ligand. Likewise, heteroatom-hydrogen insertions have shown success in outcompeting β-hydride migration due to their more reactive nature. There have been examples of Si-H insertion catalyzed by Rh(II) paddlewheel
complexes using α-alkyl diazo acetates that have been reported in the literature. As such, we sought to investigate what effects afforded from the presence of the thioether-functionalized tether would have on the catalysis.

### 3.3.2 Results and Discussion

Initial catalyst screening was conducted at room temperature with the slow addition of ethyl ethyl diazo acetate, 6, to form silane product 7. Initial screening in DCE at room temperature using $\text{Rh}_2\text{(OAc)}_4$ and our catalysts resulted in relatively low yields (entries 1-6, Table 3.3). Catalysts 9 and 11 both performed the with 41% yield compared to $\text{Rh}_2\text{(OAc)}_4$, which had a yield of 26% (entries 1, 3, and 5, Table 3.3). Catalyst 11 was also evaluated in DCM which showed comparable results to DCE (entry 7, Table 3.3). Because temperature has also been reported a prominent factor towards avoiding β-hydride migration, the Si-H insertion using 11 was conducted at -75 °C. As expected, the yield increased dramatically to 72% (entry 8, Table 3.3). However, during the addition of the diazo compound, no bubble formation of $\text{N}_2$ was observed during the addition, unlike entries 1-7. Instead, the solution turned a red/brown color, drastically different than the diazo substrate and catalyst.

The diazo substrate 6 normally is a yellow color, and in the case of catalyst 11, normally a green/blue color. Upon warming the reaction to room temperature, bubbles began to form, and the reaction turned back to the green color of the catalyst. A plausible reason through possible coordination of the diazo to the axial site (Figure 3.4). A crystal structure of a diazo compound coordinated through the nitrogen of the diazo compound to the axial site of a dirhodium(II) catalyst was isolated by Fürstner in 2016. In their study, they rationalized that the steric bulk of their catalyst prevented the subsequent

---

Table 3.3 Alkyl donor/acceptor catalyst screen.

<table>
<thead>
<tr>
<th>Entry</th>
<th>[Rh]</th>
<th>Temp. [°C]</th>
<th>Solvent</th>
<th>Yield [%](^a)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$\text{Rh}_2\text{(OAc)}_4$</td>
<td>25</td>
<td>DCE</td>
<td>26</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>25</td>
<td>DCE</td>
<td>18</td>
</tr>
<tr>
<td>3</td>
<td>9</td>
<td>25</td>
<td>DCE</td>
<td>41</td>
</tr>
<tr>
<td>4</td>
<td>10</td>
<td>25</td>
<td>DCE</td>
<td>36</td>
</tr>
<tr>
<td>5</td>
<td>11</td>
<td>25</td>
<td>DCE</td>
<td>41</td>
</tr>
<tr>
<td>6</td>
<td>12a/b</td>
<td>25</td>
<td>DCE</td>
<td>17</td>
</tr>
<tr>
<td>7</td>
<td>11</td>
<td>25</td>
<td>DCM</td>
<td>43</td>
</tr>
<tr>
<td>8</td>
<td>11</td>
<td>-75</td>
<td>DCM</td>
<td>72</td>
</tr>
<tr>
<td>9</td>
<td>11</td>
<td>-75</td>
<td>DCM</td>
<td>72(^c)</td>
</tr>
<tr>
<td>10</td>
<td>9</td>
<td>-75</td>
<td>DCM</td>
<td>65(^c)</td>
</tr>
<tr>
<td>11</td>
<td>11</td>
<td>-20</td>
<td>DCM</td>
<td>73</td>
</tr>
<tr>
<td>12</td>
<td>$\text{Rh}_2\text{(OAc)}_4$</td>
<td>-75</td>
<td>DCM</td>
<td>68(^c)</td>
</tr>
<tr>
<td>13</td>
<td>8</td>
<td>-75</td>
<td>DCM</td>
<td>87</td>
</tr>
<tr>
<td>14</td>
<td>8</td>
<td>-75</td>
<td>DCM</td>
<td>85(^c)</td>
</tr>
</tbody>
</table>

\(a\) Yields determined by GC using a dodecane internal standard.
\(b\) Diazo 6 was added at 3 mL/hr
\(c\) Addition of the diazo was added in one portion by syringe.

---

Figure 3.3: Different tether-containing carboxylate catalysts.
diazo decomposition. In our case, the coordination of the sulfur could be inhibiting the extrusion of nitrogen. In our proposed mechanism (Scheme 3.3), elevated temperatures allow the sulfur to ‘pull’ away from the rhodium metal more easily. The lower temperature could be reducing or inhibiting the previously described ‘pulling’ action of the sulfur (Step B, Scheme 3.3) keeping it closer in proximity to the rhodium metal. As a result, the diazo compound is not able to overcome the energetic barrier of the catalyst.

Because of this lowered activity, the concentration of the diazo solution builds up in solution. Thus, upon warming, the catalyst can facilitate the extrusion of N₂ and subsequent Si-H insertion. To test this hypothesis, rather than a slow addition, the diazo was added in one portion to the catalyst solution, and it turned the same red-brown color. Allowing the reaction mixture to warm to room temperature resulted in a similar yield to when the diazo was added with a syringe pump (entry 9, Table 3.3). Catalyst 9 also performed similarly to 11, including similar color changes and N₂ gas formation (entry 10). In both reactions, bubble formation began to form while the solution was still cold. Catalyst 11 was conducted at -20 °C with the slow addition of diazo 6 (entry 11, table 3.3). In this case, the color change was not observed, but bubble formation was much slower. However, it obtained a comparable yield to when the diazo was added in one portion at -75 °C. Rh₂(OAc)₄ was subjected to the rapid addition conditions and obtained a slightly lower yield compared to catalyst 11 (entry 12, Table 3.3). However, a factor to consider when comparing Rh₂(OAc)₄ to catalysts 9 and 11 is the phenyl ring present on the bridging ligand. Phenyl rings are more electron donating compared to the methyl group on Rh₂(OAc)₄.

As such, catalyst 8 was subjected to the slow and rapid addition of diazo 6 at -75 °C and obtained yields at 87% and 85%, respectively (entries 13 and 14, Table 3.3).

Based on these results, temperature does indeed play a significant role in reducing the likelihood of β-hydride migration. As mentioned before, previous work by Taber showed that carboxamidate catalysts performed much more poorly compared to carboxylate catalysts in avoiding β-hydride migration. This would agree with the observed results with 1 performing the worst at room temperature. Taber described that both the steric bulk of the ligands and the earliness vs lateness of the transition state of the carbenoid play a role towards β-hydride elimination. Specifically, if the ligands contain sufficiently bulky groups, the resulting carbenoid would increase in length to avoid steric interaction. This lengthening of the carbenoid results in a higher propensity for β-hydride elimination. In our previously proposed mechanism (Scheme 3.3), after the extrusion of nitrogen to form the carbenoid (step B), the sulfur donates more electron density to the metal center. As consequence, this would lengthen the Rh-C bond of the resulting carbene. The stronger the donation of electron density, the longer the Rh-C bond, which in turn, promotes more β-hydride elimination. This trend is indeed apparent in our results,
as shown by catalyst 9 having the lowest yield (65%) of silane 6, followed by catalyst 10 (73%), and finally catalyst 6 which contains no thioether (83%). The oxidized state of the sulfur in catalyst 10 should result in a weaker coordination to the metal center, thus less electron donation into the metal center. Consequently, the carbenoid should be less likely to undergo β-hydride elimination, resulting in the slight increase in yield of silane 6.

3.4 Silyl-hydrogen Insertion Studies Using Chiral Catalysts with Tethered Thioethers

3.4.1 Chiral Catalysts

As mentioned previously, one of the primary reasons that made Rh(II) paddlewheels so famous was their ability to produce enantioenriched products. This is heavily controlled by the inclusion of substituents on the bridging ligand backbones. These groups arrange themselves around the active sites, creating an asymmetric environment around the active site. This arrangement influences the approach of substrates, orienting them to minimize steric interactions with the substituents on the ligands. Some examples of chiral catalysts that have been used to promote Si-H insertion include Rh\(_2\)(DOSP)\(_4\), Rh\(_2\)(MEOX)\(_4\), and Rh\(_2\)(PTTL)\(_4\) as well other variations of chiral catalysts (Figure 3.5).\(^{67, 72-74, 91}\)

As mentioned before, a challenge in the synthesis of heteroleptic complex containing chiral ligands is maintaining a chiral environment around the active site. Losing the symmetry around the active site can result in a drastic decrease in enantioselectivity.\(^94\) However, should the addition of the new ligand maintain the asymmetric environment around the axial site, enantio-induction can still be achieved. For example, Fox synthesized a heteroleptic catalyst Rh\(_2\)(PTTL)\(_3\)(TPA) derived from Rh\(_2\)(PTTL)\(_4\). This heteroleptic catalyst was able to maintain a similar ligand sphere orientation as Rh\(_2\)(PTTL)\(_4\) and was capable of achieving higher enantioselectivity.\(^30\) Ligand exchange was successful with both Rh\(_2\)(PHOX)\(_4\), 13, and Rh\(_2\)(PTPA)\(_4\), 14, (Figure 3.5). Both catalysts exhibit C\(_2\) symmetry (15, Figure 3.6). Depending on the orientation of the tether-containing ligand, two different orientations can be observed (16 and 17).

![Diagram of catalysts](image-url)
Ideally, the conformation of 17 would be most beneficial for these catalysts, as the asymmetric environment surrounding the remaining axial site would still be maintained.

Additionally, these catalysts were also selected based on previous research towards Si-H insertion. Complex 14 serves as a suitable candidate to evaluate the effects of incorporating a thioether tether in a tetrakis carboxamidate catalyst. Though this catalyst was not used for Si-H insertion reactions, it is very similar in structure compared to Rh$_2$(MEOX)$_4$, which was previously evaluated in catalyzing the Si-H insertion of methyl phenyl diazoacetate by Doyle in 1996 (Figure 3.5). These catalysts typically require heat to become more active. Though these catalysts did not perform as well enantioselectivity compared to Hashimoto’s catalysts, it still should allow us to obtain a better understanding of the interactions of the thioether tether. Rh$_2$(PTPA)$_3$ has been used for Si-H insertion in a study by Hashimoto. It achieved yields up to 86% and %ee up to 74%. Using 13 as a standard, we can directly compare 15 (Figure 3.7) to 13 to observe any major changes in a reactivity and enantioselectivity. As such, both Rh$_2$(PHOX)$_3$(Metox), 18, and Rh$_2$(PTPA)$_3$(PhTCB), 19, (Figure 3.7) were evaluated for their efficiency at catalyzing the Si-H insertion of methyl phenyl acetate.
3.4.2 Results and Discussion

18 and 13 were subjected to similar conditions for Si-H insertion used in the achiral catalyst study. Catalyst 18 achieved a 49% yield and a 26% ee (Entry 1, Table 3.4). While this yield and enantioselectivity is not entirely unexpected, it is important to note that this is an improvement to 13 (entry 2, Table 3.4). Not only did incorporating the tether increase the yield, it also increased the enantioselectivity. As of now, it is not fully understood how exactly the thioether is altering the catalyst to increase both its reactivity and enantioselectivity. Unlike the achiral catalysts, having different functionality present on the other bridging ligands brings into question potential steric interactions. For example, the $^1$H-NMR signal of what is believed to be the methyl attached to the sulfur is drastically altered in comparison to the achiral catalyst. This could possibly be due to neighboring aryl ring. The methyl group could be interacting with the pi-cloud of the aromatic ring, causing the $^1$H-NMR signal to be shifted upfield (Figure 3.7). Because of this interaction, there could be a slight conformation change in the other ligands, resulting in a change to the ligand sphere on the active side.

Additionally, an electronic perturbation caused by the sulfur coordination could be affecting how the carbene is stabilized, similar to our proposed model in Scheme 3.3. The increase in yield agrees with the results observed in the achiral catalyst studies. However, more work is needed to be conducted to fully understand what factors are at play. Obtaining a crystal structure of the complex would elucidate more clearly if any changes to the structure were induced by the presence of the tether.

Unlike 13, Rh$_2$(PTPA)$_4$, 14, was previously described by Hashimoto. As such, 19 was evaluated under the same conditions as reported in the literature.$^{74}$ Initial studies were conducted under the optimal conditions for the 14 catalyst at -78 °C with the slow addition of the diazo substrate. Unfortunately, 19 underperformed in the enantioselective induction of silyl product 20 at 20% ee, compared to Rh$_2$(PTPA)$_4$ reported value of 68%. An observation noticed in the reaction, however, was a distinct color change from blue green to red for complex 19 upon addition of the diazo to the catalyst. Upon complete addition of the diazo, the solution was an orange/yellow color, presumed to be a saturation of diazo compound. It was not until the solution warmed up to room temperature that the extrusion of N$_2$ was observed and the blue-green color of the solution returned, indicating the consumption of the diazo substrate was complete. Conversely, Rh$_2$(PTPA)$_4$ appeared to immediately consume the diazo as it was

---

Table 3.4: Si-H insertion using chiral catalysts.

<table>
<thead>
<tr>
<th>Entry</th>
<th>[Rh]</th>
<th>Yield [%][a]</th>
<th>ee [%][b]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>18</td>
<td>47</td>
<td>26</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>29</td>
<td>13</td>
</tr>
</tbody>
</table>

[a] Yields determined by NMR with a mesitylene internal standard. [b] %ee determined by HPLC.

Figure 3.8: Proposed structure for 18.
added to the solution and no apparent color change was observed. These changes in color appeared to be similar to color changes observed in the studies on the alkyl donor/acceptor studies mentioned previously (Section 3.3.2). A similar process could be occurring here, where the diazo substrate is coordinating through the nitrogen of the diazo to the catalyst, inhibiting diazo decomposition. Consequently, the concentration of diazo substrate would build up in solution. As the reaction warms up, the catalyst would then consume the diazo to facilitate the insertion reaction. Due to being a warmer temperature, the catalyst reacts more rapidly, resulting in a lower enantioselectivity.

Another factor to consider, like with 18, the incorporation of the tethered ligand could be altering the ligand sphere of the complex. 14, in the solid state exists in the α, α, β, β geometry, and in solution is much more fluxional as indicated by the $^1$H-NMR. Incorporation of the thioether ligand appears to increase the rigidity of the catalyst, indicated by sharper signals in the $^1$H-NMR. However, the lower enantioselectivity could be a result of the orientation of the remaining ligands around the active site. Whatever this new conformation is, it is clearly not suitable for creating an asymmetric environment around the active site. However, there is clearly some type of interaction between the remaining phthalimide ligands and the thioether-containing ligand. Obtaining a crystal structure of this complex could shed light on what this interaction is. With that information, we can choose a more suitable parent catalyst to take advantage of that interaction. As it stands, more work is needed to develop more effective chiral catalysts containing a functionalized tether.

Table 3.5: Si-H insertion using chiral catalysts.

<table>
<thead>
<tr>
<th>Entry</th>
<th>[Rh]</th>
<th>Yield [%][a][b]</th>
<th>ee [%][c]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>14</td>
<td>30</td>
<td>60%</td>
</tr>
<tr>
<td>2</td>
<td>19</td>
<td>50</td>
<td>20%</td>
</tr>
</tbody>
</table>

[a] Isolated yield. [b] Reactions not duplicated. [c] %ee determined by chiral HPLC.
3.5 Cyclopropanation with Ethyl Diazo Acetate

3.5.1 Cyclopropanation background

From our Si-H studies, we learned that the oxazolidinate catalysts clearly performed better with more reactive diazo compounds. However, because of the highly reactive nature of the silane substrates in the Si-H insertion reactions, the overall scope of exploring the effects afforded by the thioether is somewhat limited. As such, we decided to revisit cyclopropanation reactions, using the more reactive diazo compound ethyl diazo acetate. Cyclopropanes are 3-membered rings consisting of carbon. The highly strained nature of these moieties offers unique properties not typically observed in hydrocarbon compounds. These properties range from increased lipophilicity, metabolic stability, and brain permeability. As such, cyclopropyl rings have been incorporated in numerous pharmaceutical drugs. Different methods have been utilized to synthesize cyclopropanes, such as the Simmons-smith reaction or thermal decomposition of diazo compounds in the presence of an olefin. Metal-catalyzed decomposition of diazo compounds have been widely explored, including rhodium(II) paddlewheels. By far, one of the most explored diazo substrates used for cyclopropanation is ethyl diazo acetate (EDA), 21. The catalytic cycle for the cyclopropanation catalyzed by a rhodium(II) paddlewheel complex follows a similar pathway as the Si-H insertion (Scheme 3.5). The initial steps involve the nucleophilic attack of the diazo to the metal, which then extrudes N\textsubscript{2} to form the reactive carbenoid intermediate B. The alkene approaches the carbenoid end-on, resulting in the cyclopropanation of the olefin. The
cyclopropanation step, D, has been proposed to be nonsynchronous, but occurs very rapidly, with a slight charge build up on the olefin in the transition state.

In these studies, the more reactive acceptor diazo compound ethyl diazo acetate (EDA, 21 Scheme 3.6) was chosen to be used in the cyclopropanation study. Unlike the donor/acceptor diazo compound variants, the cyclopropanation of carbenoids derived from EDA and other acceptor type diazo compound are not typically stereoselective.101 This is partially due to how the alkene approaches the carbenoid species.100 Additionally, due to the increased reactivity of the resulting carbenoid species, dimerization of 21 is often a competing reaction. To mitigate the dimerization of EDA, excess olefin is often added to favor cyclopropanation. With the understanding that incorporation of our thioether tether increases catalyst selectivity, we sought to investigate whether it would be possible to selectively cyclopropanate EDA over dimerization with stoichiometric amounts of olefin.

3.5.2 Results and discussion

Based on our observations of our catalysts increased reactivity with more reactive diazo compounds, the initial investigation into cyclopropanation of EDA began using only 1 equivalent of styrene under similar conditions to my group’s previous work.61 Due to the success in the TCB series of catalysts in the previous cyclopropanation reaction, that series of catalyst was studied first. Initial studies, however, were difficult to get consistent results of the cyclopropane and dimer products by 1H-NMR, possibly due to volatility of the product. Using a GC allowed for more consistent results. Like the previous studies, our tether containing catalysts 9 and 10 both out-performed Rh2(OAc)4 and the control catalyst 8 (entries 1-4, Table 3.6). This was a very promising start, prompting exploring the use of our other catalysts. To our surprise, catalyst 1 outperformed both catalysts 9 and 10 (Entry 5, Table 3.6), quite different from our previous study. From there, my colleagues have pursued on exploring other

<table>
<thead>
<tr>
<th>Entry</th>
<th>[Rh]</th>
<th>Yield 22 [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rh2(OAc)4</td>
<td>42</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>54</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>58</td>
</tr>
<tr>
<td>4</td>
<td>8</td>
<td>38</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>64[b]</td>
</tr>
<tr>
<td>6</td>
<td>23</td>
<td>35</td>
</tr>
<tr>
<td>7</td>
<td>23</td>
<td>93[c]</td>
</tr>
</tbody>
</table>

[a] Yields determined by GC with a mesitylene standard. [b] Reaction performed by Derek Cressy. [c] 1.7 equiv of 21 used.
carboxamidate catalyst derivatives in an effort to maximize the cyclopropyl product 22. In that spirit, I tested the bis complex 23a in the cyclopropanation reaction. Under the same conditions, 23a only achieved a 35% yield (Entry 6, Table 3.6). However, when 1.7 equivalents of EDA was added to the reaction solution rather than 1 equivalent, catalyst 23a obtained a surprisingly high yield of 93% (entry 7, Table 3.6). This was quite interesting, as just using only 1 equivalent of EDA resulted in a much lower yield. Very few examples in the literature have investigated using excess diazo compound in cyclopropanation reactions, especially with dirhodium(II) complexes. As such, the reason for this dramatic change in yield is not yet understood. Being that it is much easier to synthesize the bis-complexes over the mono-complexes, this may pave a new route for catalyst utility. As it stands, more research in using excess diazo is needed to fully understand what exactly is at play.

3.6 Conclusion

With this research, I have shown that incorporating a thioether tether onto a dirhodium complex does have positive influence in catalyst activity. Likewise, matching catalyst to diazo substrate is important in obtaining positive results. However, much more work is needed to fully understand the role of LB functionalized tethers in dirhodium(II) complexes. Much of the work shown in this thesis has set the foundation for future directions catalyst development can go, particularly towards chiral catalyst development. In the future, should someone establish new efficient ways to incorporate tether containing ligands on to catalysts, the phosphorus-containing ligands may be able to be revisited using those new methods. Conversely, other stronger σ-donating ligands can be incorporated into our ligand motif.
Chapter 4: Experimental Section

General Procedures

Unless otherwise noted, all reagents were used as received from the manufacturer without further purification. Reactions were carried out under an N\textsubscript{2} atmosphere using Schlenk techniques and either flame or oven dried glassware unless otherwise indicated. Dried hexanes, THF, diethyl ether, DCM, and ACN were dried with columns packed with alumina using an Inert\textsuperscript{®} PureSolv Micro Solvent Purification System and stored over molecular sieves. Reactions were monitored using thin layer chromatography (TLC) on Sorbent Technologies Silica XG TLC Plates. Column chromatography was performed using 60 Å, 40-63 μm flash silica, 60 Å, 63-200 μm gravity silica from Sorbent Technologies, or SiliaBond Cyano 60 Å, 40-63 μm silica from Silicycle when indicated. Microwave-assisted reactions were carried out in a closed vessel using a Biotage Initiator+ microwave reactor monitoring the reaction by equipped IR sensor. \textsuperscript{1}H and \textsuperscript{13}C NMR spectra were recorded on a Varian Mercury Vx 300 MHz or Varian VNMR 500 MHz spectrometers. Signals were referenced by residual solvent signal for \textsuperscript{1}H-NMR (CHCl\textsubscript{3} = 7.26 ppm, acetone = 2.05 ppm, MeCN = 1.94 ppm) and \textsuperscript{13}C-NMR (CHCl\textsubscript{3} = 77.16 ppm, acetone = 206.26 ppm, MeCN = 1.32 ppm). The mass spectra were obtained using either an Exactive Plus OrbitrapTM Mass Spectrometer (Thermo Scientific, San Jose, CA, USA) via direct injection or with a JEOL AccuTOF Mass Spectrometer fitted with a DART interface, run in positive mode when indicated. Chiral HPLC analysis was performed on a Shimadzu LC-2030 Prominence-i instrument.

2.2 Ligand Synthesis

General:

Ligand (S)-4-(2-(methylthio)ethyl)-2-oxazolidinone ((S)-Metox 13) was obtained from Derek Cressy and used as is. Ligand 2-((2-methyl-1-(phenylthio)propan-2-yl)carbamoyl)benzoic acid (PhTCB 18) was obtained from Dr. Brad Anderson and used as is. (S)-4-(3-hydroxypropyl)oxazolidin-2-one, 3, was prepared from glutamic acid using a modified procedure from the literature.\textsuperscript{50} Compounds 8 through 10 were synthesized from (L)-Serine following an established procedure.\textsuperscript{55} Compounds 1-5, 11-12, 14, 16, and 19 were synthesized following modified procedures.\textsuperscript{50, 53, 58} 2-(1,3-dioxoisooindolin-2-yl)-3-phenylpropanoic acid, PTPA ligand, was synthesized following a similar procedure described by Hashimoto and the 1\textsuperscript{H}-NMR compared to the literature.\textsuperscript{102, 103}

Dimethyl (ethoxycarbonyl)-L-glutamate (1)

Acetyl chloride (31 mL, 0.436 mol) was added dropwise to methanol (170 mL) at 0°C. (L)-Glutamic (20 g, 0.136 mmol) was added in one portion to the reaction at 0°C and refluxed for 3 hours. The reaction was cooled to room temperature, concentrated, and diluted with deionized water (267 mL). Sodium bicarbonate (59.47 g, 0.708 mol) followed by ethyl chloroformate (15.37 g, 0.142 mmol) were each added to the reaction mixture at 0°C. The reaction mixture was stirred at room temperature for 8 hours. The reaction was then extracted with 70 mL of ethyl acetate 4 times and washed with deionized H\textsubscript{2}O and saturated NaCl. The solution was dried over Na\textsubscript{2}SO\textsubscript{4} and the solvent removed \textit{in vacuo}. Diester 1 was obtained as a clear viscous oil (26.47 g, 0.107 mol, 78%). \textsuperscript{1}H NMR (300 MHz, Chloroform-\textit{d}) \& 5.29 (d, J = 8.2 Hz, 1H), 4.39 (t, J = 6.6 Hz, 1H), 4.11 (q, J = 7.1 Hz, 2H), 3.74 (s, 3H), 3.67 (s, 3H), 2.50 – 2.31 (m, 2H), 2.20 (dtd, J = 14.9, 7.5, 5.1 Hz, 1H), 2.06 – 1.88 (m, 1H), 1.28 – 1.20 (m, 3H).

Ethyl (S)-(1,5-dihydroxypentan-2-yl) carbamate (2)

Diester 1 (5.45 g, 0.022 mol) was dissolved in 44 mL of MeOH under ambient conditions and cooled in an ice bath. Sodium borohydride (5.003 g, 0.132 mol) was added slowly to the reaction mixture,
monitoring by TLC. Once 2 is no longer present, reaction was quenched with acetic acid and concentrated down. The crude material was purified by column chromatography using flash silica (10%MeOH/DCM) to afford product 2 as a white solid (3.99 g, 0.209 mol, 94%). $^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 6.71 (d, 1H), 4.54 (t, $J = 5.6$ Hz, 1H), 4.32 (t, $J = 5.1$ Hz, 1H), 3.94 (q, 2H), 3.40 – 3.26 (m, 4H), 3.21 (m, 1H), 1.57 – 1.28 (m, 3H), 1.22 (m, 1H), 1.13 (t, 3H).

(S)-4-(3-hydroxypropyl) oxazolidin-2-one (3)

Compound 2 (3.80 g, 0.0199 mol) was added to a 3-neck flask and dissolved in 53 mL of dry THF. The solution was then cooled in an ice-bath. Sodium Hydride (60% w/w in mineral oil, 0.406 mol) was added portion-wise to the reaction and stirred for 2 hours at room temp, followed by one hour at reflux. The reaction was quenched with 2M HCl to pH of ~4-5, concentrated to remove THF, and re-dissolved in MeOH. This solution was dried with Na$_2$SO$_4$, filtered, and concentrated to afford the crude product as an oil. Crude product was purified by column (eluent 10%MeOH/DCM) to afford 3 as a white solid (2.310 g, 0.0159 mol, 80%). $^1$H NMR (500 MHz, DMSO-d$_6$) $\delta$ 7.70 (s, 1H), 4.42 (t, 1H), 4.34 (t, 1H), 3.86 (dd, $J = 8.5$, 6.0 Hz, 1H), 3.73 (dqd, $J = 8.3$, 6.1, 1.0 Hz, 1H), 3.37 (m, 2H), 1.50 – 1.39 (m, 3H), 1.42 – 1.29 (m, 1H).

(S)-dibenzyl (3-(2-oxooxazolidin-4-yl) propyl) phosphite (4)

Oxazolidinone 3 (0.200 g, 1.38 mmol) was added to a Schlenk flask, followed by dibenzyl N,N-diisopropyl phosphoramidite (0.7139 g, 2.07 mmol) by syringe. 1-H-tetrazole (3-4% w/v, 4.13 mmol) was added to reaction mixture by syringe slowly, immediately resulting in a cloudy solution. Reaction was stirred at room temperature overnight. The following day, mCPBA was added in one portion (0.594 g, 3.45 mmol) and the reaction stirred for 10 minutes. Reaction mixture was diluted with 15 mL of EtOAc and washed 2 times with 15 mL of NaHSO$_3$. The pooled aqueous was extracted 3 times with 10 mL of EtOAc. All organic layers were combined and dried with MgSO$_4$. The crude mixture was concentrated by rotary evaporation and purified by column chromatography (flash silica, 100%EtOAc) to afford phosphate product 5 as a colorless oil (0.154 g, 0.380 mmol, 28%). $^1$H NMR (500 MHz, Chloroform-d) $\delta$ 7.55 – 7.16 (m, 10H), 5.62 (s, 1H), 5.10 – 4.97 (m, 4H), 4.40 (t, $J = 8.4$ Hz, 1H), 4.01 – 3.93 (m, 2H), 3.91 (dd, $J = 8.6$, 6.0 Hz, 1H), 3.82 – 3.73 (m, 1H), 1.64 – 1.49 (m, 4H). $^{13}$C NMR (126 MHz, Chloroform-d) $\delta$ 159.29, 135.68, 128.67, 128.63, 128.03, 69.92, 69.46, 69.42, 66.99, 66.95, 51.84, 31.34, 25.83, 25.78. $^{31}$P NMR (202 MHz, Chloroform-d) $\delta$ -0.79.

(R)-dibenzyl ((2-oxooxazolidin-4-yl) methyl) phosphite (11)

Oxazolidinone 10 (0.200 g, 1.71 mmol) was added to a Schlenk flask, followed by dibenzyl N,N-diisopropyl phosphoramidite (0.885 g, 2.57 mmol) by syringe. 1-H-tetrazole (3-4% w/v, 5.13 mmol) was
added to reaction mixture by syringe slowly, immediately resulting in a cloudy solution. Reaction was stirred at room temperature overnight. The reaction was then concentrated down, and purified by column chromatography (flash silica, 5:45:50 TEA:EtOAc:Hexanes) to afford phosphite product 11 as a clear colorless oil (0.1912 g, 0.529 mmol, 31%). 

1H NMR (500 MHz, Chloroform-d) δ 7.42 – 7.26 (m, 9H), 5.41 (d, J = 8.9 Hz, 4H), 4.35 (t, J = 8.7 Hz, 1H), 4.04 (dd, J = 5.0 Hz, 1H), 3.85 (ddd, J = 8.9, 5.0, 0.9 Hz, 1H), 3.79 – 3.66 (m, 2H).

13C NMR (126 MHz, Chloroform-d) δ 159.02, 137.78 (d, J = 4.5 Hz), 128.58 (d, J = 1.7 Hz), 128.06 (d, J = 1.4 Hz), 127.62 (d, J = 3.3 Hz), 66.67, 65.00 (d, J = 2.4 Hz), 64.90 (d, J = 2.3 Hz), 63.43, 63.37, 52.40 (d, J = 4.8 Hz).

31P NMR (202 MHz, Chloroform-d) δ 140.13.

(R)-dibenzyl ((2-oxooxazolidin-4-yl) methyl) phosphate (12)

Oxazolidinone 10 (0.200 g, 1.71 mmol) was added to a Schlenk flask, followed by dibenzyl N,N-diisopropyl phosphoramidite (0.7139 g, 2.57 mmol) by syringe. 1-H-tetrazole (3-4% w/v, 5.13 mmol) was added to reaction mixture by syringe slowly, immediately resulting in a cloudy solution. The reaction was stirred at room temperature for 3.5 hours, and then mCPBA (0.737 g, 4.27 mmol) was added in one portion and the reaction stirred for 10 minutes. Reaction mixture was diluted with 15 mL of EtOAc and washed 2 times with 15 mL of NaHSO₃. The pooled aqueous was extracted 3 times with 10 mL of EtOAc. All organic layers were combined and dried with MgSO₄. The crude mixture was concentrated down and purified by column chromatography (flash silica, 100%EtOAc) to afford phosphate product 12 as a clear colorless oil (0.130 g, 0.345 mmol, 20%). 

1H NMR (500 MHz, Chloroform-d) δ 7.44 – 7.28 (m, 9H), 5.51 (s, 1H), 5.05 (qdd, J = 11.7, 9.2, 4.1 Hz, 4H), 4.39 – 4.31 (m, 1H), 4.03 – 3.96 (m, 1H), 3.25 (dd, J = 6.2, 5.1 Hz, 2H), 1.79 – 1.58 (m, 4H).

13C NMR (126 MHz, Chloroform-d) δ 158.58, 135.42, 135.36, 128.89 (d, J = 1.9 Hz), 128.73 (d, J = 1.2 Hz), 128.22, 128.17, 69.90 (t, J = 5.5 Hz), 67.96 (d, J = 5.7 Hz), 66.05, 51.78, 51.72. 

31P NMR (202 MHz, Chloroform-d) δ -0.83.

(S)-3-(2-oxooxazolidin-4-yl) propyl 4-methylbenzenesulfonate (14)

Oxazolidinone 6 (3.424 g, 0.0236 mol) was added to a 250 mL Schlenk flask and dissolved in 30 mL of dry DCM and cooled down in an ice bath. TEA (4.774 g, 0.0472 mol) was added by syringe to the reaction mixture, followed by Tosyl chloride (5.396 g, 0.0283 mol) which was added portion-wise. The reaction was slowly warmed to room temperature and stirred overnight. 80 mL of dH₂O was added to the reaction mixture, and the organic layer collected. The organic layer was washed with 40 mL of deionized H₂O and the aqueous layers were pooled together. The aqueous layers were then extracted 2 times with 40 mL of DCM. The organic layers were combined and dried with Na₂SO₄, filtered, and concentrated down resulting in a dark yellow oil. The crude material was purified by column chromatography (100% EtOAc) to afford a sticky solid. This sticky solid was recrystallized by dissolving in boiling EtOAc and adding hexanes just until solid began to precipitate, then was placed in the freezer overnight. A white precipitate formed and was filtered and washed with ice cold 25% EtOAc/hex to afford product 14 as a white solid. 

1H NMR (500 MHz, Chloroform-d) δ 7.80 – 7.75 (m, 2H), 7.38 – 7.34 (m, 2H), 4.47 (t, J = 8.5 Hz, 1H), 4.06 (dd, J = 6.2, 5.1, 2.3 Hz, 2H), 3.98 (dd, J = 8.7, 5.9 Hz, 1H), 3.89 – 3.84 (m, 1H), 2.46 (d, J = 0.8 Hz, 3H), 1.79 – 1.58 (m, 4H). 

13C NMR (126 MHz, Chloroform-d) δ 159.50, 145.08, 132.79, 129.96, 127.87, 69.91, 69.47, 51.80, 51.42, 24.71, 21.65.

(S)-4-(3-(phenylthio) propyl) oxazolidin-2-one (16)

Under ambient conditions, potassium carbonate (0.139 g, 1.00 mmol) added to a 25 mL round bottom flask and suspended in 1.5 mL of acetone. Thiophenol (0.221 g, 2.00 mmol) was then added to the round bottom by syringe. Tosylate 14 (0.300 g, 1.00 mmol) was then added in one portion to the suspension, and the reaction mixture was gently refluxed for 24 hrs. Reaction was cooled close to room temperature, and solvent was removed till the volume was reduced by half. To the mixture, 10 mL of deionized H₂O was added, and the resulting solution was then extracted 3 times with 3 mL of DCM. The
organic layers were pooled together and washed with brine, dried with Na$_2$SO$_4$, and solvent removed by rotary evaporation. Crude material was purified by column chromatography using flash silica (2.5% MeOH/DCM) to afford 16 as a colorless oil (0.130 g, 0.549 mmol, 55%). $^1$H NMR (500 MHz, Chloroform-d) $\delta$ 7.34 – 7.25 (m, 4H), 7.22 – 7.14 (m, 1H), 6.60 (s, 1H), 4.44 (t, $J = 8.5$ Hz, 1H), 3.97 (dd, $J = 8.6$, 6.1 Hz, 1H), 3.89 – 3.80 (m, 1H), 2.99 – 2.87 (m, 2H), 1.77 – 1.65 (m, 3H), 1.68 – 1.55 (m, 1H). $^{13}$C NMR (126 MHz, Chloroform-d) $\delta$ 160.10, 135.87, 129.40, 128.99, 128.98, 126.21, 70.13, 52.22, 34.15, 33.37, 24.66.

**PhOTCB ligand 2-((2-methyl-1-(phenylsulfinyl) propan-2-yl) carbamoyl) benzoic acid (19)**

Compound 18 (0.150 g, 0.455 mmol) and Na$_2$WO$_4$·2H$_2$O (0.0045 g, 0.0137 mmol) were added to a reaction vial under ambient conditions. 0.45 mL of glacial acetic acid was added to the reaction mixture, followed by 0.045 mL of 30% H$_2$O$_2$ (1.365 mmol). The solution was stirred for 3 minutes and then diluted with 10 mL of dH$_2$O. The resulting aqueous solution was extracted 3 times with 3 mL of EtOAc and the organic layers were pooled together. The organic layer was then dried, filtered, and concentrated to afford an oil. To the oil, 2 mL of diethyl ether was added resulting in the formation of a white precipitate. The vessel was then concentrated _in vacuo_ to remove the solvent for 30 minutes. This process was repeated twice to afford 19 a free-flowing white powder (0.131 g, 0.379 mmol, 67% yield). $^1$H NMR (500 MHz, Chloroform-d) $\delta$ 7.90 (dd, $J = 7.8$, 1.3 Hz, 1H), 7.67 – 7.53 (m, 3H), 7.51 – 7.39 (m, 5H), 7.25 (s, 1H), 3.51 (d, $J = 13.8$ Hz, 1H), 3.08 (d, $J = 13.7$ Hz, 1H), 1.63 (d, $J = 7.5$ Hz, 6H).

**2-(1,3-dioxoisoindolin-2-yl)-3-phenylpropanoic acid (PTPA ligand) synthesis**

(L)-Phenylalanine (2.50 g, 0.0151 mol) and phthalic anhydride (2.242 g, 0.0154 mol) were added to a 100 mL 3-neck flask that was outfitted with a short-path distillation apparatus with a 50 mL round bottom collecting flask. Dry toluene (60 mL) was added to the 3-neck, followed by triethylamine (0.153 g, 0.00151 mol). Reaction mixture was heated to reflux, then increased to 135 °C until solvent began to distill at a slow constant rate for 40 minutes. After the 40 minutes, reaction was cooled to room temperature and 15 mL of 5% HCl was added in one portion, followed by 10 mL of deionized H$_2$O. The reaction mixture was then poured into a separatory funnel, and the organic layer was removed. The aqueous layer was extracted 2 times with EtOAc. The organic layer was pooled together, washed with brine, and then dried with Na$_2$SO$_4$. Solvent was removed by rotary evaporation resulting a white solid. This solid was recrystallized by dissolving in boiling EtOAc. Once dissolved, adding in hexanes until solid precipitated and persisted. The vessel was covered and allowed to settle overnight, resulting in large, needle-like crystals. The crystals were collected by Büchner funnel. The filtrate was collected, concentrated by rotary evaporation and the resulting solid was re-subjected to recrystallization again. Both recrystallization products were combined and resulted in a white crystalline solid (3.3872 g, 0.0115 mol, 76%). $^1$H NMR (300 MHz, Chloroform-d) $\delta$ 7.83 – 7.73 (m, 2H), 7.72 – 7.64 (m, 2H), 7.25 – 7.07 (m, 5H), 5.31 – 5.15 (m, 1H), 3.66 – 3.55 (m, 2H).

### 2.3 Carboxamidate Catalyst Synthesis

Catalysts 20 and 21a/b were confirmed by comparing $^1$H-NMR to the literature values. Procedures for ligand exchange using a Soxhlet apparatus was modified from past methods developed by Doyle. Rh$_2$(PHOX)$_4$, 27, was synthesized following a known procedure.
Axially coordinated Glutamic-derived phosphite 5 to dirhodium acetate (Figure 2.8)

To an oven dried reaction vial under N$_2$, Rh$_2$(OAc)$_4$ (0.0048 g, 0.0109 mmol) was added to the vial under a positive flow of N$_2$ followed by 2 mL of 1,4 dioxane. 1.34 mL from a stock solution (prepared under ambient conditions) containing a 1:1 mixture of phosphite 5 (0.0084 g, 0.0218 mmol) and triethylamine (0.0022 g, 0.0218 mmol) was added to the reaction vial. The reaction mixture stirred at room temperature, while being monitored by HPLC. After 72 hours, the reaction mixture was concentrated down and purified by column chromatography (5%MeOH/DCM). Isolated 1.3 mg of a purple residue believed to be the pendant coordination of the ligand to the rhodium complex. $^1$H NMR (500 MHz, Chloroform-$d$) δ 7.47 (m, 4H), 7.40 – 7.31 (m, 6H), 5.34 – 5.25 (m, 4H), 4.40 – 4.34 (m, 1H), 4.24 (m, 2H), 3.89 (m, 2H), 1.95 (s, 2H), 1.89 (s, 12H), 1.77 – 1.58 (m, 3H). $^{31}$P NMR (202 MHz, Chloroform-$d$) δ 30.33 (dd, $J$ = 149.2, 49.7 Hz).

Axially coordinated Serine-derived phosphite 11 to dirhodium acetate

To an oven dried reaction vial under N$_2$, Rh$_2$(OAc)$_4$ (0.010 g, 0.0226 mmol) was added to the vial under a positive flow of N$_2$ followed by 2 mL of 1,4 dioxane. 1.0 mL from a stock solution (prepared under ambient conditions) containing a 1:1 mixture of phosphite 11 (0.009 g, 0.0249 mmol) and triethylamine (0.0025 g, 0.0249 mmol) was added to the reaction vial. The reaction mixture stirred at room temperature for 24 hours monitored by HPLC, then concentrated in vacuo. A crude $^{31}$P-NMR was taken of the sample in CDCl$_3$ under ambient conditions. $^{31}$P NMR (202 MHz, Chloroform-$d$) δ 31.98 (dd, $J$ = 146.8, 49.9 Hz), -0.12.

Procedure for Ligand exchange of dirhodium acetate with (S)-Metox

To a three-neck round bottom flask, fitted with a Soxhlet apparatus with a thimble containing an oven-dried 2:1 mixture of Na$_2$SO$_4$ to sand (by volume), was added dirhodium acetate (0.100 g, 0.226 mmol) and (S)-Metox ligand 13 (0.0912 g, 0.565 mmol). Dry chlorobenzene (20 mL) was added via syringe to dissolve the reagents. The reaction was heated to 155 °C for eight hours, allowed to cool, and stir at room temperature overnight. The reaction mixture was then concentrated in vacuo and purified by column chromatography to afford the mono-substitution product 20 and both bis-substitution products 21a and 21b. The $^1$H-NMR of these products were compared to their literature value to confirm their identity.

[Rh$_2$(OAc)$_3$(Metox)] (20)

Isolated as a purple solid (0.0352 g, 0.0648 mmol, 29%). $^1$H NMR (500 MHz, Chloroform-$d$) δ 4.40 (t, $J$ = 7.6 Hz, 1H), 3.77 – 3.63 (m, 2H), 3.09 – 2.96 (m, 2H), 2.54 (s, 3H), 2.06 (m, 1H), 1.99 (s, 3H), 1.95 – 1.88 (m, 1H), 1.88 (s, 3H), 1.86 (s, 3H).

Cis-[Rh$_2$(OAc)$_2$(Metox)$_2$] (21a)

Isolated as a red solid (0.0206 g, 0.0320 mmol, 12%). $^1$H NMR (500 MHz, Chloroform-$d$) δ 4.28 (t, $J$ = 7.6 Hz, 2H), 3.75 – 3.56 (m, 4H), 3.23 (ddd, $J$ = 13.2, 5.6, 2.0 Hz, 2H), 2.98 (ddd, $J$ = 13.2, 12.0, 2.4 Hz, 2H), 2.63 (s, 5H), 1.93 (t, $J$ = 2.7 Hz, 1H), 1.91 (s, 7H), 1.90 – 1.82 (m, 1H).
trans-[Rh₂(OAc)₂(Metox)₂] (21b)

Isolated as a red solid (0.0084 g, 0.0130 mmol, 8%). ¹H NMR (500 MHz, Chloroform-d) δ 4.30 (t, J = 7.8 Hz, 2H), 3.73 – 3.52 (m, 4H), 3.14 – 3.02 (m, 4H), 2.61 (s, 6H), 1.96 (dtd, J = 14.3, 9.8, 4.5 Hz, 1H), 1.90 (s, 8H), 1.87 (ddd, J = 4.8, 3.0, 1.7 Hz, 1H).

Procedure for Ligand exchange of Rh₂(OAc)₄ with (S)-GluPhtox 23a/b

[Rh₂(OAc)₂((S)-GluPhtox)₂] (23a/b)

Dirhodium acetate (0.075 g, 0.170 mmol) and (S)-GluPhtox ligand 16 (0.0805 g, 0.339 mmol) were added to a Schlenk flask. Dry chlorobenzene (15 mL) was added via syringe to dissolve the reagents. Under a positive flow of nitrogen, the Schlenk flask was fitted with a Soxhlet apparatus with a thimble containing an oven-dried 2:1 by volume mixture of Na₂SO₄ to sand. The reaction was refluxed for 20 hours, allowed to cool, and stir at room temperature overnight. The reaction mixture was then concentrated in vacuo and purified by column chromatography to afford a mixture of the bis-substitution products 23a and 23b as a red/purple solid (0.0853 g, 0.128 mmol, 75%). ¹H NMR (300 MHz, Chloroform-d) δ 7.86 – 7.76 (m, 4H), 7.34 (m, 6H), 4.40 (t, J = 8.5 Hz, 2H), 3.85 – 3.55 (m, 7H), 3.46 (m, 2H), 2.28 (s, 2H), 2.06 – 1.77 (m, 4H), 1.74 (s, 3H), 1.71 (s, 3H), 1.68 – 1.55 (m, 4H).

Cis-[Rh₂(OAc)₂((S)-GluPhtox)₂] (23a)

Isolated as a shiny red/purple solid. ¹H NMR (500 MHz, Chloroform-d) δ 7.83 – 7.78 (m, 4H), 7.37 – 7.28 (m, 6H), 4.40 (dd, J = 9.2, 7.9 Hz, 2H), 3.81 (dtd, J = 9.4, 7.3, 2.1 Hz, 2H), 3.69 (dd, J = 8.0, 7.2 Hz, 2H), 3.62 (ddd, J = 11.9, 8.9, 2.6 Hz, 2H), 3.46 (ddd, J = 12.4, 8.6, 2.5 Hz, 2H), 2.29 (m, 1H), 2.01 – 1.92 (m, 1H), 1.74 (s, 6H), 1.68 – 1.57 (m, 4H). ¹³C NMR (126 MHz, Chloroform-d) δ 188.85, 167.80, 134.27, 131.58, 128.60, 127.53, 72.18, 61.79, 36.80, 36.64, 26.31, 23.41.

Synthesis [Rh₂(OAc)₃(2-Ox)] (25)

To four separate 2-5 mL microwave reactor vials, dirhodium tetraacetate (0.025 g, 0.057 mmol) and 2-oxazolidinone (0.049 g, 0.57 mmol) were added. 1,2-Dichloroethane (5 mL) was then added to the vial, rinsing the sides of the vial of any solid material. A cap was then crimped onto the vial and placed in the microwave reactor. The reactor was set to the following parameters: fixed hold time of 10 minutes; 1-minute pre-stir; low absorbance; temperature 190 °C. After the reaction was complete and cooled, the contents of the microwave vials were combined, and volatiles were removed in vacuo. Purification by column chromatography using gravity silica gel with 1:1 CH₃CN:toluene afforded compound 3 along with a mixture of other ligand substitution products. Compound 25 was obtained as a purple solid (40 mg, 0.066 mmol, 32% yield) ¹H-NMR (500 MHz, Chloroform-d) δ 4.32 (t, J = 8.4 Hz, 2H), 3.71 (dd, J = 8.9, 7.9 Hz, 2H), 2.44 (s, 6H), 2.06 (s, 3H), 1.91 (s, 6H). ¹³C-NMR (126 MHz, Chloroform-d) δ 191.90, 190.17, 168.93, 65.62, 49.55, 24.00, 23.43. HRMS (obtained using OrbitrapTM) [M+H]+ m/z calcd for C₁₁H₁₆N₂O₈Rh₂([Rh₂(OAc)₃(2-Ox)-CH₃CN]): 510.9045; found: 510.9084.

Synthesis of complex [Rh₂(POX)₃(Metox)] (28)

Rh₂(POX)₄-4ACN (27) (0.020 g, 0.0196 mmol) was added to a 3-neck round-bottom flask was outfitted with a condenser. Ligand 13 (0.0065 g, 0.0403 mmol) was added to the round by rinsing 8 mL of dry chlorobenzene the ligand into the round bottom. The reaction mixture was heated to reflux and stirred at that temperature for 7 hours. It was then concentrated in vacuo. The crude mixture was purified by
column chromatography (100% EtOAc), afforded a red/purple solid. Rinsing this solid with boiling toluene afforded product 28 as a blue solid (0.0050 g, 0.00588 mmol, 30% yield). $^1$H-NMR (500 MHz, Chloroform-d) δ 7.50 – 7.43 (m, 2H), 7.46 – 7.37 (m, 1H), 7.40 – 7.33 (m, 2H), 7.36 – 7.30 (m, 2H), 7.33 – 7.27 (m, 3H), 7.26 – 7.12 (m, 4H), 6.92 – 6.84 (m, 2H), 4.93 (dd, $J = 9.2, 7.4$ Hz, 1H), 4.61 (dd, $J = 9.3, 8.0$ Hz, 1H), 4.51 (t, $J = 8.4$ Hz, 1H), 4.48 – 4.39 (m, 1H), 4.18 (dd, $J = 8.3, 2.2$ Hz, 1H), 4.07 – 4.00 (m, 2H), 3.92 (dd, $J = 9.6, 7.8$ Hz, 1H), 3.77 – 3.67 (m, 2H), 3.58 (t, $J = 7.9$ Hz, 1H), 2.57 (dd, $J = 14.3, 5.8, 2.0$ Hz, 1H), 1.66 (m, 1H), 1.12 (s, 3H).

General Information for carboxylate-based catalysts

$^{1}$H NMR (500 MHz, Chloroform-d) δ 8.16 (m, 2H), 7.83 (m, 1H), 7.62 (m, 4H), 7.48 – 7.42 (m, 1H), 7.39 – 7.32 (m, 2H), 5.83 (s, 1H), 4.43 (d, $J = 13.8$ Hz, 1H), 1.93 (s, 7H), 1.73 (s, 6H), 1.30 (s, 3H). $^{13}$C NMR (126 MHz, Chloroform-d) δ 191.74, 170.29, 132.29, 131.57, 129.79, 129.56, 129.05, 127.09, 126.72, 66.05, 53.02, 29.68, 29.11, 28.70, 23.74.

Synthesis of $[^{1}]$Rh$_2$(PTPA)$_4$ (31)

The procedure for synthesizing Rh$_2$(PTPA)$_4$ adopted from the method described by Hashimoto for the synthesis of Rh$_2$(PTTL)$_4$.$^{102}$ Rh$_2$(OAc)$_4$ (0.100 g, 0.226 mmol) and PTPA ligand (0.3341 g, 1.131 mmol) were added to a 2-neck round bottom outfitted with a short path condenser and round bottom flask. Dry chlorobenzene (5 mL) was added by syringe and the reaction mixture heated to 150 °C for three hours. Reaction mixture was cooled to room temperature and stirred at room temperature overnight. Reaction was concentrated in vacuo then dissolved in 20 mL of EtOAc. The solution was washed twice with 7 mL of saturated NaHCO$_3$, once with brine, and then dried with Na$_2$SO$_4$. The organic layer was then filtered, concentrated by rotary evaporation, and purified by column chromatography (50% EtOAc/hexane gradient to 75% EtOAc/hexanes) to afford a green/blue residue. This residue was
dissolved in boiling EtOAc. Hexanes was added just until solids began to precipitate and persist. The solution was covered with a watch glass and allowed to slowly evaporate overnight to afford $\text{Rh}_2(\text{PTPA})_2\cdot2\text{EtOAc}$ as shiny green crystals (0.2013 g, 0.129 mmol, 57%). Note: Due to fluxional nature of ligands, determination of the amount of EtOAc present was based on aromatic proton signals. $^1\text{H NMR}$ (300 MHz, Chloroform-$d$) $\delta$ 7.62 (m, 12H), 7.16 (m, 24H), 5.36 (s, 1H), 4.13 (q, $J = 7.1$ Hz, 4H), 3.40 (s, 1H), 2.04 (s, 6H), 1.25 (t, $J = 7.1$ Hz, 6H).

$[\text{Rh}_2(\text{PTPA})_3(\text{PhTCB})]$ (33)

$\text{Rh}_2(\text{PTPA})_4\cdot2\text{EtOAc}$ (0.0287 g, 0.0184 mmol) was added to a Schlenk flask followed by 8 mL of dry DCE and then heated to reflux. A solution of PhTCB (0.0066 g, 0.0201 mmol) and Hunig’s base (0.0026 g, 0.0201 mmol) was prepared in dry DCE was being used and added to the solution of $\text{Rh}_2(\text{OAc})_4$. This mixture was refluxed for 3 hours and then cooled to room temp. The reaction mixture was then concentrated in vacuo and purified by column chromatography (2.5% MeOH/DCM) to afford the product as a blue/green solid (0.0134 g, 0.00946 mmol, 51%). $^1\text{H NMR}$ (500 MHz, Acetonitrile-$d_3$) $\delta$ 7.82 – 7.69 (m, 8H), 7.65 (m, 4H), 7.51 (d, $J = 7.4$ Hz, 1H), 7.48 – 7.35 (m, 3H), 7.27 – 7.06 (m, 15H), 6.88 (d, $J = 6.7$ Hz, 3H), 6.17 (s, 1H), 5.03 (ddd, $J = 20.1$, 11.8, 4.3 Hz, 3H), 3.75 (s, 2H), 3.46 (ddd, $J = 13.8$, 8.6, 4.4 Hz, 3H), 1.49 (s, 3H), 1.33 (s, 3H). $^{13}\text{C NMR}$ (126 MHz, Acetonitrile-$d_3$) $\delta$ 189.34, 168.04, 167.93, 138.68, 135.38, 132.33, 130.82, 130.03, 129.96, 129.63, 129.36, 129.29, 128.92, 127.66, 127.56, 127.50, 124.23, 124.14, 60.96, 55.26, 54.95, 35.86, 35.66, 27.95, 27.79, 21.15.

**General Procedure for Aryl Si-H insertion reactions**

Diazo compound (0.4 mL, 0.114 mmol) from a 0.284 M stock solution was added in one portion to an 8 mL reaction vial containing silane (0.125 mmol, 1.1 equiv) and rhodium catalyst (2 mol%) under ambient conditions. The vial was immediately capped and placed in a pre-heated well plate set to 60 °C and stirred for 30 minutes. Excess solvent was removed by rotary evaporation and the crude material was dissolved in chloroform-$d$. Mesitylene (0.114 mmol, 1.0 equiv) was added as an internal standard. Yields were obtained via $^1\text{H-NMR}$. Chemical shifts of known Silyl products were as reported in literature.\[^{104, 105}\]

**Aryl Si-H insertion reaction product yield calculations**

Normalized integration of the methyl proton signal of mesitylene (2.28 ppm) was compared to the integration of the protons assigned to the methyl ester of the products. For products $5e$ and $5g$ which had overlapping signals for the methyl ester and methine proton of the stereocenter, the integration of mesitylene was compared to the combined area of both the methyl ester and methine proton signals. For products $5c$ and $5d$, the integration of mesitylene was compared to the methine proton signal. For product $5e$, the integration of mesitylene was compared to the methyl signal of the isopropyl group.

**Methyl 2-(cyclohexyldimethylsilyl)-2-phenylacetate ($5c$)**

Scale-up synthesis of product $6c$ was performed in order to obtain a pure sample of $5c$. $\text{Rh}_2(\text{OAc})_4$ (2.5 mg, 5.68 μmol) and dimethylphenyl silane (0.0444g, 0.312 mmol) were added to a round bottom under ambient conditions. Diazo $4a$ (0.0500 g, 0.284 mmol) dissolved in 1 mL of methylene chloride was added and the reaction mixture was stirred for 30 minutes. Solvent was then removed by rotary evaporation and the crude material was purified by column chromatography using flash silica gel. Compound $6c$ was isolated as a colorless oil. $^1\text{H-NMR}$ (500 MHz, CDCl$_3$) $\delta$ 7.35 – 7.32 (m, 2H), 7.30 – 7.25 (m, 3H), 7.19 –
7.14 (m, 1H), 3.68 (s, 3H), 3.51 (s, 1H), 1.75 – 1.59 (m, 6H), 1.26 – 1.02 (m, 5H), 0.65 (tt, J = 12.4, 3.0 Hz, 1H), 0.04 (s, 3H), -0.09 (s, 3H). 13C NMR (126 MHz, CDCl3) δ 173.76, 136.79, 128.54, 128.24, 125.70, 51.48, 43.68, 28.07, 28.03, 27.44, 27.30, 26.95, 24.41, -5.93, -5.95. HRMS (DART in positive mode) [M+H]^+ m/z calcd for C17H26O2Si: 291.1736, found: [M+H]^+ = 291.1777.

Methyl 2-(dimethyl(phenyl)silyl)-2-(4-nitrophenyl)acetate (5f)

p-Nitrophenyl methyl diazo acetate (4d) (0.0251g, 0.114 mmol) was added to a reaction vial containing dimethyl phenyl silane (0.0170 g, 0.125 mmol) and Rh2(OAc)4 (1.0 mg, 2.28 μmol). Methylene chloride (0.4 mL) was added by syringe to the reaction mixture and stirred for 30 minutes at 40 °C. Solvent was then removed via rotary evaporation to provide compound 5f (71% by 1H-NMR, 0.081 mmol) and a mixture of byproducts. Attempts to isolate 5f resulted in decomposition of the product during purification. The presence of 5f within the crude mixture was also detected by mass spectrometry. HRMS (DART in positive mode) [M+H]^+ m/z calcd for C17H19NO4Si: 330.1117, found: [M+H]^+ = 330.1110.

General Procedure for Alkyl Si-H insertion reactions

Dimethyl phenyl silane (0.228 mmol, 2 equiv) and dirhodium catalyst (2 mol %) were added to a 8 mL reaction vial with 0.1 mL of solvent under ambient conditions. The vial was capped and stirred for five minutes. If the reaction was run at cold temperatures, the vial was placed in the cooling bath (dry ice and acetone for -75 °C or ice, salt, and MeOH for -20 °C) for the 5 minutes of stirring. The diazo compound 6 (0.3 mL, 0.114 mmol) from a 0.3775 M stock solution was added by syringe at 3 mL/hr. A needle was inserted through the cap of the reaction during the addition of diazo and was removed upon complete addition. After 30 minutes, reaction was warmed to room temperature, checked by TLC, and diluted with 1.1 mL of solvent. 20 μL of dodecane was added as an internal standard and stirred. The solution was withdrawn into a 1 mL syringe and filtered through a Nylon66 0.2 μm syringe filter into a 2 mL glass GC vial. Yields were determined by gas chromatography using an internal standard of the silane product and dodecane as the internal standard.

Procedure for Aryl Si-H insertion reactions using Chiral Carboxamidate catalysts

Methyl phenyl diazo acetate (0.3 mL, 0.0851 mmol) added to an 8 mL reaction vial by pipet under ambient conditions. Dimethyl phenyl silane (0.125 mmol, 1.1 equiv) was then added to the reaction vial. The catalyst (2 mol%) was dissolved in 0.1 mL of DCM and added to the reaction vial in one portion. The vial was immediately capped and placed in a pre-heated well plate set to 60 °C and stirred for 30 minutes. Reactions were then removed from the heat and excess solvent was removed by rotary evaporation. The crude material was dissolved in chloroform-d and Mesitylene (0.0851 mmol, 1.0 equiv) was added as an internal standard. Yield was obtained via 1H-NMR. Solvent was then removed by rotary evaporation and purified by column chromatography (10%EtOAc/hexanes). Enantiomeric excess was determined using HPLC (Column: Cellulose 1; solvent: 3% IPA/hex; flow rate at 1 mL/hr, detection at 254 nm).
**Procedure for Aryl Si-H insertion reactions using Chiral Carboxylate catalysts**

Chiral dirhodium catalyst (0.5 mol %) was added to a reaction vial under ambient conditions. 2.1 mL of DCM was added by syringe, followed by dimethyl phenyl silane (0.567 mmol, 2 equiv). The reaction mixture was then cooled in a dry ice/acetone bath for at least 5 minutes. A solution methyl phenyl diazacetate (0.7 mL, 0.284 mmol) was added by syringe to the reaction mixture at 1.4 mL/hr. Once addition was complete, the reaction mixture stirred at the cold temperature for 30 minutes and then was warmed to room temperature. The reaction mixture was checked by TLC and then solvent was removed by rotary evaporation and the crude product purified by column chromatography (10%EtOAc/hex). Enantiomeric excess was determined using HPLC (Column: Cellulose 1; solvent: 10% IPA/hex; flow rate at 1 mL/hr, detection at 254 nm).

**General Procedure for the Cyclopropanation of 1 Equivalent of Styrene**

Under an atmosphere of N$_2$ a 25 mL Schlenk flask equipped with a magnetic stir bar was flame dried and charged with styrene (0.19 mL, 1.7 mmol, 1.0 equiv.), catalyst (2 mol%), and 1,2-dichloroethane (DCE) (0.5 mL). The solution was then brought to the desired temperature, followed by slow addition of ethyl diazoacetate (1.7 mL, 0.17 mmol, 1.0 equiv.) by syringe pump (1 mL/hr). Once addition was complete, 16.54 μL of mesitylene standard was added to the reaction mixture and stirred. The solution was then eluted through a Nylon66 0.2 μm syringe filter into a 2 mL glass GC vial. Yields were determined by gas chromatography using a multiple point internal standard of the cyclopropyl product and mesitylene as the internal standard.

**UV-Visible Spectra and Details**

All data was obtained using a Cary 100 spectrometer using a scan rate of 10 nm/s from 200-900 nm. Samples were run using paired quartz cuvettes with a pathlength of 10 mm. The raw data for each sample was normalized by dividing by the highest absorbance in the data set.

**Computation data**

All geometry optimizations were completed on Gaussian 09 and implemented the density functional theory M06-2X functional with the def2-TZVP basis set. An ultrafine integration grid was utilized as well as tight convergence criteria. Frequency calculations were performed to verify the stationary points on the potential energy surface were in fact ground state minima. Compound 3 did exhibit a negative frequency at -20.1475 cm$^{-1}$ but is still believed to be the ground state structure. Orbital visualizations were completed with ChemCraft.

Rh$_2$(OAc)$_3$(2-Ox) at M06-2X/def2-TZVPP level of theory

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>-0.016540000</td>
<td>0.010927000</td>
</tr>
<tr>
<td>45</td>
<td>-0.461287000</td>
<td>0.008315000</td>
</tr>
<tr>
<td>8</td>
<td>-0.178051000</td>
<td>2.054805000</td>
</tr>
<tr>
<td>8</td>
<td>-0.581628000</td>
<td>2.050158000</td>
</tr>
<tr>
<td>8</td>
<td>0.115171000</td>
<td>-2.036900000</td>
</tr>
<tr>
<td></td>
<td>5.067030000</td>
<td>5.175467000</td>
</tr>
<tr>
<td>---</td>
<td>-------------</td>
<td>-------------</td>
</tr>
<tr>
<td></td>
<td>-4.655284000</td>
<td>1.210042000</td>
</tr>
<tr>
<td>7</td>
<td>1.945972000</td>
<td>0.140641000</td>
</tr>
<tr>
<td>6</td>
<td>-0.411801000</td>
<td>2.630517000</td>
</tr>
<tr>
<td>6</td>
<td>-0.066790000</td>
<td>-2.615069000</td>
</tr>
<tr>
<td>6</td>
<td>-0.470341000</td>
<td>-4.132644000</td>
</tr>
<tr>
<td>5</td>
<td>0.003832000</td>
<td>-4.116727000</td>
</tr>
<tr>
<td>6</td>
<td>-2.827920000</td>
<td>-0.165159000</td>
</tr>
<tr>
<td>6</td>
<td>-4.305137000</td>
<td>-0.299217000</td>
</tr>
<tr>
<td>6</td>
<td>2.300040000</td>
<td>0.120479000</td>
</tr>
<tr>
<td>6</td>
<td>4.256077000</td>
<td>0.199229000</td>
</tr>
<tr>
<td>6</td>
<td>3.121333000</td>
<td>-0.052125000</td>
</tr>
<tr>
<td>5</td>
<td>0.492541000</td>
<td>4.507973000</td>
</tr>
<tr>
<td>5</td>
<td>-1.234223000</td>
<td>4.473030000</td>
</tr>
<tr>
<td>5</td>
<td>-0.655647000</td>
<td>4.505478000</td>
</tr>
<tr>
<td>5</td>
<td>0.629869000</td>
<td>-4.434737000</td>
</tr>
<tr>
<td>5</td>
<td>0.384838000</td>
<td>-4.498843000</td>
</tr>
<tr>
<td>5</td>
<td>-0.999322000</td>
<td>-4.505080000</td>
</tr>
<tr>
<td>5</td>
<td>-4.564779000</td>
<td>-1.356014000</td>
</tr>
<tr>
<td>5</td>
<td>-4.555732000</td>
<td>0.058286000</td>
</tr>
<tr>
<td>5</td>
<td>-4.860975000</td>
<td>0.237281000</td>
</tr>
<tr>
<td>5</td>
<td>5.067030000</td>
<td>-0.520629000</td>
</tr>
<tr>
<td>5</td>
<td>4.655284000</td>
<td>1.210042000</td>
</tr>
<tr>
<td>5</td>
<td>3.143422000</td>
<td>-1.066342000</td>
</tr>
<tr>
<td>5</td>
<td>3.148861000</td>
<td>0.654227000</td>
</tr>
</tbody>
</table>

**Rh₂(OAc)₃MeOX at M06-2x/def2-TZVPP level of theory**
45  0.110178000  0.469143000  -0.339391000
45  -1.392523000  -1.102604000  0.652879000
  7  1.570391000  -0.866713000  0.026877000
  8  0.129835000  -2.539477000  0.675646000
  6  1.262354000  -2.070508000  0.465482000
  8  2.352868000  -2.833922000  0.713630000
  6  3.486023000  -2.090046000  0.254778000
  6  2.988288000  -0.643534000  0.240691000
  1  3.743959000  -2.427026000  -0.752879000
  1  4.316220000  -2.269465000  0.932175000
  6  3.647708000  0.257837000  -0.788911000
  1  3.141139000  -0.191301000  1.231319000
  6  3.238597000  1.724701000  -0.635857000
  1  3.422163000  -0.105758000  -1.794828000
  1  4.730527000  0.195183000  -0.656333000
16  1.646416000  2.064853000  -1.432827000
  1  3.974773000  2.385679000  -1.091152000
  1  3.140910000  1.983665000  0.419966000
  6  1.195703000  3.598015000  -0.607816000
  1  0.199642000  3.851920000  -0.962325000
  1  1.900428000  4.384733000  -0.867910000
  1  1.162513000  3.431597000  0.467031000
  8  -1.522117000  1.757465000  -0.595552000
  8  -2.834703000  0.361511000  0.562234000
  6  -2.618418000  1.429546000  -0.064571000
  6  -3.769396000  2.388867000  -0.216465000
  1  -4.192106000  2.254654000  -1.212552000
  1  -3.415429000  3.413407000  -0.136437000
  1  -4.536393000  2.181423000  0.522942000
| 8  | -0.311998000 | -0.410398000 | -2.149324000 |
| 8  | -1.895993000 | -1.715682000 | -1.246325000 |
| 8  | -0.761536000 | -0.358924000 | 2.486858000  |
| 6  | -1.226868000 | -1.279948000 | -2.215674000 |
| 6  | -1.516753000 | -1.859312000 | -3.574330000 |
| 1  | -0.875451000 | -2.730541000 | -3.712009000 |
| 1  | -1.289318000 | -1.135643000 | -4.351413000 |
| 1  | -2.551743000 | -2.183772000 | -3.628360000 |
| 8  | 0.457040000  | 1.266781000  | 1.535949000  |
| 6  | -0.033938000 | 0.658253000  | 2.536031000  |
| 6  | 0.275790000  | 1.235808000  | 3.892048000  |
| 1  | -0.374027000 | 2.096867000  | 4.050954000  |
| 1  | 1.305918000  | 1.581588000  | 3.927132000  |
| 1  | 0.084709000  | 0.500978000  | 4.667469000  |
References:


41. Ahsan, M. Q.; Bernal, I.; Bear, J. L., Reaction of Rh$_2$(OOCCH$_3$)$_4$ with Acetamide - Crystal and Molecular-Structure of [Rh$_2$(HNOCCCH$_3$)$_4$ - 2H$_2$O] - 3H$_2$O. *Inorganic Chemistry* 1986, 25 (3), 260-265.


49. Clark, R. J. H.; Hempleman, A. J.; Dawes, H. M.; Hursthouse, M. B.; Flint, C. D., Dirhodium(II,II) tetra-acetate complexes with axially co-ordinated triphenylstibine, triphenylarsine, and dibenzyl sulphide ligands. The syntheses, properties, and X-ray crystal structures of [Rh2(O2CMe)4(SbPh3)2], [Rh2(O2CMe)4(AsPh3)2], and [Rh2(O2CMe)4(S(CH2Ph)2)2]. *Journal of the Chemical Society, Dalton Transactions* 1985, (9), 1775-1780.


Appendix

Example of HPLC trace for monitoring Ligand exchange of \( \text{Rh}_2(\text{PHOX})_4 \) and \( (S)-\text{Metox} \)

HPLC (Column: Luna C-18 column; solvent: 75\% MeCN with 0.1\%TFA/MeOH, 25\%Water with 0.1\%TFA; flow rate at 1 mL/hr, detection at 254 nm).

11.5 minute mark – \( \text{Rh}_2(\text{PHOX})_4 \)

15.3 minute mark - \( \text{Rh}_2(\text{PHOX})_3(\text{Metox}) \)

**Microwave Reactor Reaction Profile**

**Note:** Only one reaction profile is shown here. This is the microwave reactor profile for the synthesis of \( \text{Rh}_2(\text{OAc})_3(2-\text{Ox}) \) \textbf{25}.

**Experiment:** ws546-mono2ox

**User:** Cressy

**Processed:** 2019.01.13 13:07:23

**Reaction Status**

1  OK
2  OK
3  OK
4  OK

**Reaction 1**

**Processed:** 2019.01.13 13:07:41

**Status:** OK

**Absorption level:** Low
Vial type: 2.0-5.0 ml
Pre-stirring: 60
Initial power: 0
Dynamic deflector optimization: On

<table>
<thead>
<tr>
<th>Step</th>
<th>Time</th>
<th>°C</th>
<th>bar</th>
<th>W</th>
<th>FHT</th>
<th>Cooling</th>
<th>Stir Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>00:10:00</td>
<td>190</td>
<td>Off</td>
<td>Off</td>
<td>On</td>
<td>Off</td>
<td>600</td>
</tr>
</tbody>
</table>

Temperature (°C)

Pressure (bar)

Power (W)
NMR Spectra

$^1$H-NMR (500 MHz, Acetone-$d_6$)
$^{31}$P-NMR (500 MHz, Acetone-$d_6$)
$^1$H-NMR (500 MHz, CDCl$_3$)
\[ ^{13} \text{C-NMR (500 MHz, CDCl}_3 \text{)} \]
$^{31}P$-NMR (500 MHz, CDCl$_3$)
$^{1}H$-NMR (500 MHz, CDCl$_3$)
$^{13}$C-NMR (500 MHz, CDCl$_3$)
$^3$P-NMR (500 MHz, CDCl$_3$)
$^{1}H$-NMR (500 MHz, CDCl$_3$)
$^{13}$C-NMR (500 MHz, CDCl$_3$)
$^{31}$P NMR (500 MHz, CDCl$_3$)

12
**1H-NMR (500 MHz, CDCl₃)**

- **1.73 ppm**
- **1.79 ppm**
- **0.72 ppm**
- **1.00 ppm**
- **2.90 ppm**
- **4.43 ppm**
$^{1}H$-NMR (500 MHz, CDCl$_3$)

19
$^{13}$C-NMR (500 MHz, CDCl$_3$)
Structure from Figure 2.8
$^1$H-NMR (500 MHz, CDCl$_3$)
Structure from Figure 2.8

$^{31}\text{P-NMR (500 MHz, CDCl}_3\text{)}$
23a/b

$^1$H-NMR (500 MHz, CDCl$_3$)

grease
$^{13}$C-NMR (500 MHz, CDCl$_3$)
25

$^1$H-NMR (500 MHz, CDCl$_3$)

* = Toluene

H$_2$O
$^{13}$C-NMR (500 MHz, CDCl$_3$)

* = Toluene
28

$^1$H-NMR (500 MHz, CDCl$_3$)
$^{1}$H-NMR (500 MHz, CDCl$_3$)
$^{13}$C-NMR (500 MHz, CDCl$_3$)
$^1$H-NMR (500 MHz, CD$_3$CN)
$^{13}$C-NMR (500 MHz, CD$_3$CN)
5c

$^1$H-NMR (500 MHz, CDCl$_3$)
$^{13}$C-NMR (500 MHz, CDCl$_3$)

5c
$^1$H-NMR (500 MHz, CDCl$_3$)
$^{13}$C-NMR (500 MHz, CDCl$_3$)
Vita

William A. Sheffield is originally from Metairie, LA where he graduated high school from Brother Martin in 2009. He then attended Louisiana State University where he obtained his Bachelor of Science in Chemistry with a concentration in Biology in 2014. William began his graduate career at the University of Tennessee Knoxville in August 2014, joining the Darko Group studying dirhodium paddlewheel complexes.