Using Phosphine Aldehydes to Generate New Transition Metal Complexes and the Synthesis of Chiral NHC-Amino Ligands

by

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A thesis submitted in conformity with the requirements for the degree of Master of Science Graduate Department of Chemistry University of Toronto

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Abstract

Several new late transition metal complexes containing P-O and P-N ligands derived from 2-dicyclohexylphosphinoacetaldehyde were synthesized. A facile one-pot template method is used for the synthesis of P-N complexes, where the phosphine aldehyde and amine can undergo a condensation reaction to form a phosphine-imine metal complex in the presence of a metal precursor. Metal complexes with phosphino-enolate, imine, and oxime ligands are synthesized. Ni(II), Pt(II), Rh(I) and Ir(I) metal centres were investigated. The Rh(I) and Ir(I) complexes contain a 1,5-cyclooctadiene ligand, thus resembling Crabtree’s hydrogenation catalyst [Ir(COD)(py)(PCy$_3$)][PF$_6$]. These complexes are also active catalysts for olefin hydrogenation. Furthermore, the synthesis of a new chiral amine functionalized NHC ligand is explored, which has potential applications as a ligand in the metal-catalyzed enantioselective hydrogenation of polar bonds. This ligand is inspired by previous achiral hydrogenation catalysts reported by Morris et al. that displayed high activity for a variety of unsaturated substrates.
Acknowledgements

I am deeply grateful to Professor Robert Morris for allowing me this wonderful opportunity to explore science in such an encouraging and motivating environment. His vast knowledge and passion for chemistry was something I had heard about even prior to arriving in Toronto, but truly it is his open-mindedness and inquisitive nature which inspires the interesting and successful research that occurs in the Morris group.

All of the Morris group members are great chemists from whom I learned much from, and thankfully, they are also wonderful individuals. I would especially like to thank Paraskevi Lagaditis for sharing her expertise and experiences for the phosphine aldehyde project and other general research problems, and Wylie O, who was instrumental in inspiring and helping me to work through the chiral amino-NHC ligand synthesis. I am sincerely thankful to have had the privilege to work with everybody in the Morris group. Thank you for your help and company: Mazharul Maishan, Alexandre Mikhailine, Demyan Prokopchuck, Jessica Sonnenberg, Peter Sues, and Weiwei Zuo.
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<td>ATH</td>
<td>asymmetric transfer hydrogenation</td>
</tr>
<tr>
<td>atm</td>
<td>atmosphere</td>
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<tr>
<td>[BARF₄]⁺</td>
<td>tetrakis[3,5-bis(trifluoromethyl)phenyl]borate</td>
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<td>ee</td>
<td>enantiomeric excess</td>
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<td>FID</td>
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<td>pyridine</td>
</tr>
<tr>
<td>SHOP</td>
<td>Shell Higher Olefin Process</td>
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<tr>
<td>tBu</td>
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<tr>
<td>tert</td>
<td>tertiary</td>
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<tr>
<td>THF</td>
<td>tetrahydrofuran</td>
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<tr>
<td>TOF</td>
<td>turnover frequency</td>
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<tr>
<td>tol.</td>
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<tr>
<td>Ts</td>
<td>$p$-toluenesulfonyl (tosylate)</td>
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<td>xs.</td>
<td>excess</td>
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Chapter 1: General Introduction

The generation of new transition metal complexes using phosphine aldehydes as ligand precursors can result in novel complexes that are catalytically active,\textsuperscript{1} or resemble known catalysts.\textsuperscript{2,3,4} Phosphine aldehydes are powerful tools for the synthesis of new catalysts due to the modularity inherent in the phosphine and aldehyde functionalities. Phosphine ligands are generally strong $\sigma$-donors with a polarizable phosphorus centre, resulting in electron donation to the metal centre, along with $\pi$-accepting properties via the back-donation of electrons from the metal $d_{\pi}$ orbitals into the phosphorus $\sigma^*$ orbital. However, the extent of these effects can be controlled by changing the substituents attached to the phosphine.\textsuperscript{5,6} By attaching the generally electron withdrawing aryl or electron donating alkyl substituents to the phosphine, the electronics of the phosphine ligand can be manipulated. Similarly, the steric crowding around the phosphine ligand can also be modified by varying these substituents.\textsuperscript{7} Cyclohexyl, isopropyl, and ortho/meta-substituted aryl substituents result in bulkier phosphines, whereas ethyl, phenyl, and para-substituted aryl substituents result in sterically unencumbered ligands. Thus, modification of the phosphine ligand provides a powerful method of controlling the reactivity of the metal complex. Aldehydes provide similar advantages by their ability to undergo condensation reactions with amines to form various imines. The steric, electronics, and denticity of the resulting imine ligand can be controlled by choosing an appropriate amine. Furthermore, using chiral amines with phosphine aldehydes provides a facile route to more complicated chiral ligands. NHCs (N-heterocyclic carbenes) are similar to phosphines in that they are neutral, strong $\sigma$-donors.\textsuperscript{8,9,10} Unlike phosphines, changing the electronics of the ligand is not as
straightforward. In order to significantly change the electronics of NHCs, a major modification of the heterocycle is often required. For example, in the case of imidazolium derived NHCs, exchanging substituents on the nitrogen atoms of the heterocycle has a significantly lower electronic effect than does changing substituents on phosphines.\textsuperscript{11,12} However, these modifications can still have significant impact on the sterics of the ligand.\textsuperscript{13} Additionally, NHCs are more environmentally friendly and less toxic than phosphorus-based ligands, which justify their recent use in place of phosphines, often resulting in higher reactivity.\textsuperscript{14,15}

Amino acids are also interesting ligand precursors for enantioselective catalysis as they are cheap and easily obtainable. Previous results from our group have demonstrated that coordination of chelating NHC-amino ligands on Ru(II) Cp* precursors produce highly active hydrogenation catalysts for polar double bonds (Figure 1.1).\textsuperscript{16} By using amino acids in place of the achiral phenylene backbone used in the original catalyst, it may be possible to induce enantioselectivity in this catalytic process.

**Figure 1.1:** Ru(II)Cp* NHC-amino precatalyst (7) active for hydrogenation of ketones, esters, and imines
1.1 Transition Metal Complexes with Chelating P-O or P-N Motifs

Chelating ligands containing a phosphine moiety and either oxygen or nitrogen donors are prominent in the design of many active catalysts. Such compounds are often active for hydrogenation catalysis,\textsuperscript{1,17,18,19} although other types of catalysis such as olefin hydroformylation,\textsuperscript{20,21,22} hydroamination,\textsuperscript{3,23,24} and oligomerization\textsuperscript{25,26,27} have been demonstrated. Inspiration for designing these chelating ligands is often based upon modifying previously known metal complexes which only contain monodentate ligands. This strategy provides many benefits to a catalyst’s activity and selectivity, such as increased catalyst lifetime, activity, regioselectivity, and also can assist in enforcing asymmetry in enantioselective processes. Difficulties arise due to the effort and time required to develop and synthesize these chelating ligands, which can require complex, multi-step organic syntheses. In the case of catalysis optimization, the catalytic conditions can be easily controlled by modifying the solvents, temperature, and concentration of reagents. However, if exploration into the modification of the ligand is necessary, the need to synthesize multiple analogues of the ligand can be time consuming. Thus, it is highly advantageous to design ligand precursors based on a modular design.

1.2 Olefin Oligomerization Catalysts in the Shell Higher Olefin Process

Examples of catalysts containing a P-O ligand are nickel(II)-based ethylene oligomerization catalysts, which are industrially important complexes used in the Shell Higher Olefin Process (SHOP).\textsuperscript{27,28} SHOP is an industrial process where ethylene is
transformed into more valuable C\textsubscript{11}-C\textsubscript{15} fatty alcohols. Initially, ethylene is oligomerized into linear \(\alpha\)-olefins, where linear oligomers containing 10-14 carbons atoms are removed by distillation. These oligomers are modified via hydroformylation to form the linear aldehydes which are then subsequently reduced to form the fatty alcohol. Oligomers that are longer or shorter than the desired length are recycled via isomerization and olefin metathesis reactions to form linear \(\alpha\)-olefins that contain 10-14 carbons atoms.

Catalysts incorporating Ni(II) often have a neutral monodentate ligand such as triphenylphosphine, which has been shown to be important in controlling the oligomer length.\textsuperscript{27} Replacement of triphenylphosphine with a less coordinating ligand or the use of a phosphine scavenger results in polymerization of ethylene. The first published synthesis of a well-defined SHOP-type catalyst based on nickel(II) with a chelating P-O ligand was by Keim \textit{et al.} in 1986.\textsuperscript{29} Ni(COD)\textsubscript{2} was reacted with a keto-stabilized phosphorus ylide via oxidative addition, resulting in oxidation of the metal center to Ni(II), reduction of the phosphorus ylide to a phosphine, and the transfer of a phenyl from the phosphorus to the nickel (Scheme 1.1). Fryzuk \textit{et al.} later developed a method of synthesizing the same precatalyst starting with a phosphine enolate proligand (Scheme 1.2) and a Ni(II) precursor.\textsuperscript{30}

\begin{center}
\textbf{Scheme 1.1:} Synthesis of SHOP-type catalyst using keto-stabilized phosphorus-ylide
\end{center}
Scheme 1.2: Synthesis of SHOP-type catalyst starting from phosphine and Ni(II) precursors

1.3 Polar Bond Hydrogenation Catalysis

Chelating P-N ligands can be found in highly active and selective catalysts involved in the hydrogenation of polar double bonds. These catalysts are important for the pharmaceutical, fragrance, and fine chemical industries. Well-known ruthenium catalysts in this field include ones by Noyori et al. (Figure 1.2), as well as highly active iron catalysts from our group (Scheme 1.4). Noyori has previously made the empirical observation that highly active catalysts in this area generally contain an N-H amino ligand and require the addition of base in order to be active, which has been coined the “NH effect”. This effect is rationalized by invoking a bifunctional mechanism through which the hydrogenation of polar bonds is proposed to take place (Scheme 1.3). The catalysis is considered bifunctional because of the ligand-metal cooperativity in the proposed mechanism. Precatalysts containing an amino ligand (A) provide the most facile route to the catalytic cycle via their deprotonation with strong base to form the amido complexes (B). Deprotonation of a proton/hydride source, such as hydrogen gas (direct hydrogenation) or isopropanol (transfer hydrogenation), by the amido ligand and the abstraction of the hydride by the metal centre results in the formation of an amino metal-hydride complex (C). This \( H^+ / H^- \) transfer to the metal complex (TSBC) may be concerted or stepwise depending on the
catalyst and reaction conditions. The reduced metal complex can then transfer its proton/hydride couple in the analogous reverse reaction to the substrate’s double bond (TS_{CB}), resulting in one catalytic turnover.

**Figure 1.2:** Transfer hydrogenation catalysts for polar bonds by Noyori *et al.* (C/S/B = catalyst/substrate/base)

**Scheme 1.3:** Bifunctional mechanism for the direct and transfer hydrogenation of polar double bonds containing an "NH" moiety
Previous work in the Morris group has demonstrated that phosphine aldehydes, when reacted in a template fashion with chiral diamines and an Fe (II) precursor, form tetradentate PNNP complexes (Scheme 1.4).\textsuperscript{1,33,38} These complexes, after reaction with CO to form a PNNP carbonyl complex, have been shown to be highly active and selective catalysts for the transfer hydrogenation of acetophenone to 1-phenylethanol. The choice of diamine backbone affected both the activity and enantioselectivity of the catalysis. When dpen was used, the catalysis was more rapid and stereoselective, whereas the saturated- and alkyl- substituted diamines were slower and less selective in the transfer hydrogenation reaction. It is very likely that the first generation Fe(II) PNNP complexes, which contain o-phenylene linkers between the phosphine and imine, catalyze the asymmetric transfer hydrogenation (ATH) of ketones via formation of Fe(0) nanoparticles coated with chiral PNNP ligand.\textsuperscript{34} The mechanistic details of the second generation Fe(II) PNNP catalyst have been explored in depth.\textsuperscript{39,40} The second generation Fe(II) PNNP catalyst is also active for the ATH of ketimines.\textsuperscript{41}

\textbf{Scheme 1.4:} 5,5,5-PNNP Fe(II) precatalyst for the highly efficient transfer hydrogenation of ketones
Other interesting work includes that of Ikariya and co-workers on an iridium catalyst containing a C-N ligand (Scheme 1.5),\textsuperscript{42} where the N-oxime ligand’s OH group acts as the proton source in place of the more conventional NH as seen in the previous examples. Their synthesis started with an Ir(III)Cp*(C, N-oxime)Cl complex, which upon deprotonation of the oxime OH by base, dimerized through O-oxime coordination to the Ir(III) centre and removal of the chloride. Subsequent reduction by iPrOH under basic conditions followed by isolation resulted in the precatalyst, a hydride bridged Ir(III) dimer and containing a proton which is hydrogen bonded between two oximate groups. In solution, it is proposed that the precatalyst splits apart heterolytically to form the active catalysts in two forms: the oxime/metal-hydride complex, and the coordinatively unsaturated oximate complex (Scheme 1.6). This catalyst, while very novel, is poorly active for the transfer hydrogenation of acetophenone and other aryl-substituted analogues when iPrOH is used as a reductant. Although several substrates go to 100% yield, it is necessary to use a S/C ratio of 20:1 (5 mol\% catalyst), and the reaction takes 15h to complete at 50 °C. Crabtree and co-workers have developed a similar Ir(III) Cp* complex containing a chelating pyridine-alkoxide ligand, where the Ir(III) and alkoxide ligand can bifunctionally split H\textsubscript{2} gas, forming an analogous dimer to one observed by Ikariya and co-workers (Figure 1.3, right).\textsuperscript{43}

![Scheme 1.5: Ikariya's C-N oxime catalyst for the hydrogenation of ketones](image-url)
Scheme 1.6: Proposed mechanism for activation of Ikariya’s oxime containing precatalyst and its catalytic cycle

Shvo’s catalyst is another unconventional catalyst that is active for a variety of catalytic transformations (Figure 1.3, left). Of relevance is its ability to catalyze a variety of hydrogenation reactions, including alkynes, alkenes, ketones, and imines. This catalyst is highly active and is unique in that it uses the cyclopentadienone moiety instead of an amide in its bifunctional hydrogenation mechanism.
1.4 Olefin Hydrogenation Catalysis

Classic olefin hydrogenation catalysts include Wilkinson’s catalyst \((\text{RhCl}(\text{PPh}_3)_3)\)\(^{46}\) and Crabtree’s catalyst \([\text{Ir(COD)}(\text{py})(\text{PCy}_3)][\text{PF}_6]\) (Figure 1.4)\(^{47,48}\). Olefin hydrogenation was primarily accomplished by using heterogeneous catalysts until the introduction of the highly active homogenous Wilkinson’s catalyst. In this catalytic system, the \(\text{Rh(I)}\) complex is neutral, and when similar \(\text{Ir(I)}\) analogues were tested for activity, they were largely unreactive\(^{49}\). The main disadvantage of Wilkinson’s catalyst is that it is only minimally reactive with tri-substituted olefins, and mostly unreactive with tetrasubstituted olefins.

\[
\text{Cl} \quad \text{Rh} \quad \text{PPh}_3 \\
\text{Ph}_3 \text{P} \quad \text{Rh} \quad \text{PPh}_3 \\
\text{Schrock-Osborn Catalyst} \quad \text{Wilkinson's Catalyst} \\
\left[ \text{Rh(PPh}_3)_3 \right][\text{PF}_6] \\
\left[ \text{Ir(PCy}_3)_3 \right][\text{PF}_6] \\
\text{Crabtree's Catalyst}
\]

Figure 1.4: Examples of classic olefin hydrogenation catalysts
It was found later that coordinatively unsaturated cationic hydrogenation catalysts were significantly more active than their neutral counterparts, via the discovery of the rhodium-based cationic Schrock-Osborn ([Rh(COD)(PPh₃)₂][PF₆]) catalyst in 1976 (Figure 1.4), and the highly successful iridium-based Crabtree’s catalyst ([Ir(COD)(py)(PCy₃)][PF₆]) in 1977. The Shrock-Osborn catalyst was significantly faster than Wilkinson’s catalyst for the hydrogenation of terminal olefins, however it was mostly inactive for hydrogenation of disubstituted olefins. Furthermore, it was found that Schrock-Osborn catalysts with the nbd (norbornadiene) ligand were up to 100 times faster than ones with the COD (1,5-cyclooctadiene) ligand. Eventually, the same active catalyst was formed, but due to the inherent ring strain of nbd when chelated to rhodium, it was hydrogenated and released from the metal at a much higher rate than other diolefins. Crabtree’s catalyst was also a significant breakthrough, because it turned out to be more active than previous catalysts for the hydrogenation of mono- to tetrasubstituted olefins.

Since the success of Crabtree’s catalyst, numerous Ir(I) 1,5-cyclooctadiene analogues containing chelating ligands have been developed, many of which contain P-O, P-N, and P-P ligands. By switching from monodentate to chelating ligands, a higher degree of control over the ligand design was possible by incorporating different donor groups such as oxazolines and amines, or by the facile addition of chiral groups to the ligand. Examples include Pfaltz and co-workers’ highly successful Ir(I) analogues which contain chiral bidentate phosphine-oxazoline ligands. These catalysts have been shown to be highly active in the hydrogenation of tri- and tetrasubstituted unfunctionalized olefins with excellent enantioselectivity. Furthermore, it was discovered that the counteranion in cationic catalysts is very important to the catalyst’s activity. When the tetrakis[3,5-
bis(trifluoromethyl)phenyl]borate anion ([BArF₄]) was used in place of the standard [PF₆]⁻. Catalyst lifetime and activity increased dramatically. This is due to the greater delocalization of the negative charge throughout the large [BArF₄]⁻ anion and the low C-F bond polarizability, making it less coordinating.

1.5 Organization of the Thesis

Chapter 2 contains work done on the synthesis of new bidentate ligands and metal complexes. K. Park did all experimental work and A. J. Lough mounted single crystals, collected data, and solved the X-ray molecular structures. P. O. Lagaditis did preliminary work for this project, including an independent synthesis of the Ni(II)(P-O)₂ complex 2. Furthermore, she was the main contributor for the alkyl phosphonium dimer syntheses, which was used in this thesis, published in *J. Organomet. Chem.* in 2010.⁵⁹ Work done in this chapter is under submission for publication.

Chapter 3 contains work done on the synthesis of new chiral amino-functionalized NHC derived from amino acid starting materials. K. Park did all experimental work, with special thanks to W. W. N. O for sharing his expertise and insight into starting this project.
Chapter 2: Synthesis of P-O, P-N, and P-P Transition Metal Complexes Using Phosphine Aldehydes

2.1 Introduction

The use of phosphine aldehydes in the synthesis of a library of metal complexes is attractive because they allow a simple one-pot template synthesis using metal precursors and amines. Furthermore, the possibility of changing the substituents on the phosphine and the ability to condense a variety of amines on the aldehyde results in a great number of possible ligands.\(^{38}\) For example, by using amines with additional donor groups, it is possible to form a variety of bi-, tri-, and tetridentate ligands (Figure 2.1). Unfortunately the only phosphine aldehyde commercially available is 2-(diphenylphosphino)benzaldehyde which hinders our ability to modify the ring-size of the chelating ligand as well as the organic groups on the phosphine.\(^{5,6,33}\) An interesting alternative to this phosphine aldehyde is 2-(diphenylphosphino)acetaldehyde, which can be generated \textit{in situ} by the deprotonation of its “phosphonium dimer”. The synthesis of phosphonium dimers was therefore improved upon by the Morris group and the synthesis of a variety of different aryl and alkyl phosphonium dimers were explored.\(^{59}\)
These new phosphonium dimers provided us the ability to facilely change the electronics and steric on the phosphine, and thereby allowed an exploration into the role of steric and electronics in our chiral Fe(II) PNNP ketone transfer hydrogenation catalysts. A series of iron(II) carbonyl PNNP complexes with varying alkyl- and aryl-groups on the phosphines were synthesized and tested for the ATH of prochiral ketones. These new complexes were compared to the original phenyl-substituted catalyst by their catalytic activity, which was then correlated to electronic and steric parameters of each complex (Figure 2.2). CO stretching frequencies were used as the electronic parameter, where highly electron donating alkyl substituents displayed the lowest CO stretching frequencies, and highly electron withdrawing –CF₃ substituted aryl substituents displayed the highest frequencies. The Tolman cone angle was used as the steric parameter. Complexes with large Tolman cone angles, such as isopropyl, cyclohexyl, or ortho-phenyl substituted phosphines, were inactive for catalysis because the steric crowding around the metal centre obstructed its reactivity. Phosphines with highly electron-donating alkyl substituents, or electron withdrawing –CF₃ substituted aryl groups were found to be mostly inactive for catalysis.
However, phosphines with slightly more electron-donating substituents than the phenyl substituent itself resulted in a more active catalyst (i.e. para-tolyl vs. phenyl). Subtle increases in the steric by using 3,5-(CH₃)₂C₆H₃ groups resulted in better enantioselectivity. By correlating the catalyst activity with electronics and steric of the phosphines, we are able to obtain a set of data which can be used to interpolate and make further rational decisions in ligand design.

There are several synthetic advantages to generating the phosphine aldehyde *in situ* via the deprotonation of the phosphonium dimer. Due to the phosphine’s lone pair being occupied in the formation of a P-C bond in the phosphonium dimer, the protected phosphines are resilient to oxidation to form phosphine oxides. Additionally, the phosphonium dimer salts are solids making them easier to handle than the oily phosphine aldehydes. These advantages, combined with their facile synthesis, even in gram scales, and the ability to vary the phosphine substituents make them versatile compounds for the synthesis of new ligands and metal complexes.
Figure 2.2: “Volcano plot” of catalyst activity (TOF, h⁻¹) versus CO stretch (cm⁻¹) representing an electronic parameter, and Tolman cone angle (deg), a steric parameter, for precatalysts [Fe(PNNP)(CO)Br][BPh₄], where the phosphines (-PR₂) have varying substituents.⁵ R = a) para-CH₃C₆H₄, b) ortho-CH₃C₆H₄, c) 3,5-(CH₃)₂C₆H₃, d) para-CF₃C₆H₄, e) 3,5-(CF₃)₂C₆H₃, f) phenyl, g) ethyl, h) isopropyl, i) cyclohexyl

The synthesis of the P-N or other chelating ligands requires the condensation of an amine with the aldehyde functionality. However, the generation of the phosphine aldehyde and subsequent imine condensation does not generally yield the P-N proligand as an isolable product. Thus, the synthesis of metal complexes using phosphonium dimers is done in a template, one-pot synthesis. The phosphine aldehyde is generated in situ by deprotonation of the phosphonium dimer, then, in conjunction with an amine and a metal precursor it forms the ligands at the desired metal in one-pot. In this reaction, the metal acts as a Lewis acid facilitating the condensation reaction, while also acting as a thermodynamic sink via
coordination of the chelating ligand. An example of a template synthesis involving isolable intermediates is the synthesis of iron(II) PNNP complexes (Scheme 2.2). When an iron(II) precursor, diamine, and phosphine aldehyde are reacted in acetonitrile, the iron(II) bis-PNN complex is isolated as the major product. However, with additional heating, the complex forms the more thermodynamically stable iron(II) PNNP complex. Numerous unique ligands have already been explored primarily using iron(II) metal precursors, including PNNP, PNN, PNP, and PNS chelating complexes.

Scheme 2.1: The one-step synthesis of the dicyclohexylphosphonium dimer salt 1, subsequent in situ generation of phosphine aldehydes using base, and metal assisted imine condensation
In this chapter, we focus mainly on the synthesis of late transition metal complexes containing bidentate P-O or P-N ligands. The formation of phosphino-enolate, imine, and oxime ligands are presented, as well as phosphine ligands with pendant aldehydes and their intraligand aldol reactivity resulting in a diphosphine ligand. Several metal centres are explored, including Ni(II), Pt(II), Rh(I), and Ir(I), to demonstrate the template synthesis with our phosphine aldehydes are not limited to Fe(II). The Rh(I) and Ir(I) complexes contain a 1,5-cyclooctadiene ligand, therefore resembling Crabtree’s catalyst, and were tested for olefin hydrogenation.

2.2 Results and Discussion

2.2.1 Synthesis of Ni(II)-Derived Phosphino-enolate Complexes

The synthesis of the \textit{trans}-bis(phosphino-enolato)Ni(II) complex 2 was carried out by deprotection of phosphonium dimer 1 with 2 equivalents of base in toluene followed by filtration to remove KBr salt. Then coordination of the free phosphine aldehyde that was generated \textit{in situ} was achieved by addition of 1 equivalent of [Ni(H\textsubscript{2}O\textsubscript{6})][BF\textsubscript{4}]\textsubscript{2} and enough
methanol to solubilize the Ni(II) salt. The addition of 2 more equivalents of base caused the light brown reaction mixture to darken instantaneously, indicating the formation of an enolate via deprotonation of the phosphine aldehyde (Scheme 2.3). The neutral Ni(II) complex, 2, was easily isolated upon removal of solvent in vacuo as a pale brown solid obtained in 72% yield. Complex 2 is soluble in most organic solvents, including pentanes, hexanes, ethers, toluene, and DCM. Its moderate solubility in pentanes allows easy separation from salts generated in the synthesis.

**Scheme 2.3: Synthesis of Ni(II) trans-bisphosphino-enolate complex 2**

Characteristic resonances in the $^1$H NMR spectrums are the olefinic peaks at 7.08 and 3.43 ppm, with the more downfield signal displaying virtual coupling due to trans phosphine ligands. The X-ray diffraction data (Figure 2.3) shows that the trans-phosphine ligands were 180.0(1)$^\circ$ to each other, as were the trans-enolate ligands, displaying complete planarity about the Ni(II) metal centre and the atoms that are coordinated to it. The sum of the internal angles of the 5-membered ring formed by the ligand backbone and the metal centre is 540.0(9)$^\circ$, thus the complex is mostly planar. An analogous Ni(II) complex isolated by Braunstein and co-workers, which also has trans-bis(di-iso-propylphosphino-enolate) ligands derived from a ketone (Scheme 2.4) shows similar planarity displaying an O1-Ni-O2
bond angle of 180.0(1)°, and a sum for the internal angle of its metallacycle of 539.7(3)°.

Both complexes display identical P1-Ni-O1 bond angles of 87.0(1)°. The C1-C2 bond length of 2 is 1.343(4) Å, which is closer to the typical bond length observed for olefins which is 1.34 Å compared to the bond length of benzene at 1.40 Å.

![Figure 2.3: ORTEP plot of the complex 2 with thermal ellipsoids drawn at the 50% probability level](image)

**Table 2.1: Selected bond distances and angles of 2**

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<tr>
<th>Angles, deg</th>
<th>Bond distances, Å</th>
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<td>Ni(1)-P(1)-C(2)</td>
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<td>P(1)-C(2)-C(1)</td>
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<td>C(2)-C(1)-O(1)</td>
<td>125.4(3)</td>
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<tr>
<td>C(1)-O(1)-Ni(1)</td>
<td>117.9(2)</td>
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The two phosphino-enolate ligands of 2 were found to coordinate trans to each other. Braunstein and co-workers have synthesized similar Ni(II) complexes containing two phosphino-enolate ligands, but generated from ketones instead of aldehydes (Scheme 2.4). They found that the diphenylphosphino-enolate ligands exclusively formed the cis isomer, the di-tert-butylphosphino-enolate ligands exclusively formed the trans isomer, and the di-iso-propylphosphino-enolate ligands formed a mixture of the trans and cis isomers. This can be rationalized by both the trans influence and steric interactions. Due to the trans influence, the trans-coordination of phosphine ligands is destabilized and thus cis-coordination is favourable only if electronic factors are considered. However, if steric energies between cis-phosphines are great enough, the ligands will then preferentially coordinate trans. Hence, in the case of the di-tert-butylphosphino-enolate ligands, the steric factors outweigh any trans influence/electronic factors. Therefore, trans- and cis-coordination of di-iso-propylphosphino-enolate ligands on nickel(II) both occur because neither steric nor electronic factors outweigh each other. The new nickel(II) complex 2 fits the pattern Braunstein observed, which is that the cyclohexyl groups are more sterically bulky than isopropyl groups, and therefore we observe the selective formation of the trans isomer. The $^{31}$P NMR spectra for the cis- and trans-di-iso-propylphosphino-enolate complexes were respectively 39.3 ppm and 50.0 ppm. The trans chemical shift is similar to the new trans complex 2, which displays a resonance in the $^{31}$P NMR spectrum at 47.6 ppm.
Scheme 2.4: Analogous Ni(II) P-O complexes synthesized by Braunstein and co-workers

When just one equivalent of phosphine aldehyde is reacted with the [Ni(OH$_2$)$_6$]$^{2+}$ precursor, no diamagnetic Ni(II) complex is detected via $^1$H and $^{31}$P NMR spectroscopy. Interestingly, when deprotected phosphine aldehyde and [Ni(H$_2$O)$_6$][BF$_4$]$_2$ were reacted, the phosphino-enolate complex 2 was the major product formed, even without the addition of 2 more equivalents of base to deprotonate the two aldehydes to enolates. The formation of the enolate, even in the absence of a stoichiometric amount of base, is likely due to the water from the hydrate salt which is basic enough to enolize the ligand. The formation of a highly $\pi$-conjugated 5-membered metallacycle, along with Ni(II) acting as a Lewis acid, stabilize the enolate. The strong conjugation in the metallacycle is evident in the X-ray data which shows that the rings are overall planar.

Due to the insolubility of Ni(II) salts in toluene, a reaction only began to take place when methanol was added, as the colourless slurry solution slowly turned brown and homogenous. However, the addition of methanol results in solubilization of the halide salts generated in the deprotection of the phosphonium aldehyde. The halide anions are then capable of forming unwanted by-products. This was avoided by carefully removing all halide
salts by filtration in the deprotection step when done in toluene, and also by using 
[Ni(OH$_2$)$_6$](BF$_4$)$_2$ which does not contain highly coordinating anions.

### 2.2.2 Synthesis of Pt(II) Derived Phosphine Aldehyde and Bisphosphino Aldehyde complexes

After the synthesis of the Ni(II) complex 2, we were interested in seeing the effects of introducing a larger d$^{10}$ metal centre. Unfortunately, isolating Pd(II) precursors proved difficult and was not pursued further. Addition of the platinum complex, Pt(COD)Cl$_2$, to the phosphine aldehyde that was generated in situ at room temperature allowed the isolation of a crude product as a white solid. The product was easily separated from salts generated in the synthesis by extraction of the solid crude product with diethyl ether. The product is also soluble in other organic solvents such as toluene, DCM and THF, but not hexanes. Analysis by $^1$H and $^{31}$P NMR spectroscopy revealed two species were formed in the reaction: the trans-phosphinoaldehyde complex, 3a, was observed as the major product (88%), and the unexpected diphosphine complex, 3b, was observed as a minor product (12%) (Scheme 2.5). They are maintained in solution as indicated by $^{31}$P{$^1$H} NMR spectroscopy where 3a gives a singlet while 3b shows two doublets with $^2$J$_{PP}$ = 16.9 Hz. The aldehyde hydrogen for 3a and 3b resonates at 9.96 and 9.52 ppm, respectively.

The structures as determined from the X-ray diffraction study are shown in Figure 2.4 and Figure 2.5. Curiously, the two molecules co-crystallized in 1:1 ratio despite the greater abundance of complex 3a in solution. The Pt-P (2.315(3) Å) and Pt-Cl (2.310(3) Å) bond lengths measured for 3a (Table 2.2) are comparable to the Pt-P bond length of 2.337(2) Å and Pt-Cl bond length of 2.317(2) Å of the complex trans-Pt(PC$_3$)$_2$Cl$_2$. The Pt-P bonds for
the *cis*-aldol complex 3b are significantly shorter at 2.258(3) Å, while the Pt-Cl bond lengths are longer at 2.367(2) Å and correlate well with the measured bond lengths of the complex Pt(dcpp)Cl₂. The differences in bond lengths are due to the high trans influence of phosphine ligands. The P1-Pt-P2 bond angle of 3b is 96.1(1)°, which is comparable to the Pt(dcpp)Cl₂ bond angle of 96.1(3)°.

Scheme 2.5: Synthesis of Pt(II) phosphino-aldehyde complexes 3a and 3b

The diphosphine ligand is the product of a novel intraligand aldol condensation reaction in presumably the *cis*-bis(phosphino-aldehyde) complex (Scheme 2.6). As it was observed from the Ni(II) complex 2, the bulky dicyclohexylphosphines preferentially coordinate trans due to steric effects. However, due to the displacement of the 1,5-cyclooctadiene ligand and the aldol reactivity that was observed, initial coordination of the phosphino-aldehyde ligands is likely *cis*. Furthermore, no exchange of the chloro ligand is observed when the bromide salt of 1 is used. Thus, it is most likely that isomerization to the *trans* phosphine complex occurs after initial *cis* coordination. Considering that a *cis*-bis(phosphino-aldehyde) intermediate is indeed formed, it is easy to believe that a
combination of the repulsion between the bulky phosphines which keeps the aldehydes close together, and the formation a six-membered metalallocyclic “transition state”, causes the aldol condensation to be very favourable. This is another example of a template-assisted ligand synthesis, because if phosphine aldehydes are reacted under various aldol condensation reaction conditions in the absence of a metal, no diphosphine compound is observed.

**Scheme 2.6:** Proposed mechanism for the formation of 3b

The reaction was started at -78 ºC and then warmed to rt to yield 70% of the trans-diphosphine complex 3b and 30% of 3a according to $^{31}$P{$^1$H} NMR spectra. This is likely due to isomerization of the initially formed cis isomer of 3a to the trans isomer, which occurs rapidly at room temperature, but at lower temperatures isomerization slows down and allows
the aldol condensation reaction to take place. When the synthesis is done in H₂O as the solvent, exclusive formation of 3a observed, as the aldol condensation reaction is suppressed.

Alternate methods toward the synthesis of the aldol condensation diphosphine ligand were attempted. The focus was to utilize a dianionic bidentate ligand to replace the chloride ligands, restricting the formation of the trans-phosphinoaldehyde. A catechol derived Pt(II) complex was synthesized and reacted with phosphine aldehydes, but it did not lead to the formation of an aldol-condensation product. A mixture of complexes 3a and 3b were reacted with silver oxalate in order to force the phosphines to coordinate in a cis fashion, however the reaction yielded an intractable mixture by NMR spectroscopy. These reactions presumably did not work due to reactivity between the basic catecholate or oxalate, and the enolizable phosphine aldehyde.
Figure 2.4: ORTEP plot of the complex 3a with thermal ellipsoids drawn at the 50% probability level

Table 2.2: Selected bond distances and angles for 3a

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**Figure 2.5:** ORTEP plot of the complex 3b with thermal ellipsoids drawn at the 50% probability level

**Table 2.3:** Selected bond distances and angles for 3b

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2.2.3 Synthesis of Neutral Rh(I) and Ir(I) Phosphino-enolate Complexes

Neutral rhodium and iridium phosphino-enolate complexes were synthesized (Scheme 2.7). The phosphine aldehyde was first generated in situ from the phosphonium dimer and base, after which the metal precursor, $[\text{M(COD)}(\mu-\text{Cl})]_2$ ($\text{M} = \text{Rh}, \text{Ir}$), was added. When additional base was added to enolize the aldehyde functionality, neutral phosphino-enolate complexes were formed. Both the rhodium and iridium complexes are moderately soluble in hexanes, making them especially easy to isolate from various salts in the mixture. The rhodium complex, 4a, was isolated in 57% yield as a yellow solid, while the iridium complex, 4b, as an orange-red solid in 57% yield.

Scheme 2.7: Synthesis of neutralRh(I) and Ir(I) phosphino-enolate complexes 4a and 4b

Structures from X-ray diffraction studies of single crystals of 4a (Figure 2.6) and 4b (Figure 2.7) show that both complexes are square planar and have comparable bond distances and angles. There is significant lengthening of the M-C bonds trans to the phosphine due to the trans influence which is also observed in Stradiotto and co-workers’ neutral Ir(P-O)COD complex.$^{54}$ The M-L bond distances for both Rh and Ir complexes are similar as was
expected due to their similar covalent radii as deduced from a study of crystallographic data. Comparisons to similar Rh\textsuperscript{20} and Ir\textsuperscript{54} P-O complexes also show comparable data.

These neutral COD complexes contain ligands similar to the highly active Crabtree’s olefin hydrogenation catalyst, [Ir(COD)(py)(PCy\textsubscript{3})][PF\textsubscript{6}]. Most cobalt group olefin hydrogenation catalysts with COD precursors are cationic, although some neutral precatalysts have been reported. Stradiotto and co-workers have reported both neutral and zwitterionic Ir(COD)(P-N)\textsuperscript{2} and neutral Ir(COD)(P-O)\textsuperscript{54} complexes active for olefin hydrogenation. These types of catalysts have also been shown to be active also for olefin hydroamination\textsuperscript{3} and hydroformylation.\textsuperscript{20} Although highly active and enantioselective catalysts already exist, investigations into neutral analogues may prove useful. Neutral catalysts can be soluble in hydrocarbon solvents instead of higher dielectric chlorinated solvents and thereby allow greener reaction conditions, as well as avoid the deactivating properties of coordinating solvents. Another advantage of developing neutral olefin hydrogenation catalysts is that there are no potential for counteranion effects and precludes the use of expensive counteranions such as [BAR\textsubscript{4}]\textsuperscript{-}.\textsuperscript{55}

The Rh complex 4\textsubscript{a} was tested for catalytic hydrogenation of stilbene and was found to be inactive. The Ir complex 4\textsubscript{b} was poorly active for stilbene hydrogenation, but found to be more active for hydrogenation of the olefinic bonds in cyclooctene and (E)-4-phenyl-3-buten-2-one (Table 2.7). When catalysis was done in DCM, significantly higher turnover frequencies were obtained than when done in hexanes. This is in contrast to Stradiotto and co-workers’ results where hexanes were found to be the best solvent for the hydrogenation of styrene. Changes in catalyst reactivity in different solvents can be ascribed to stabilization or destabilization of catalytic intermediates due to solvent coordination.
**Figure 2.6:** ORTEP plot of the complex 4a with thermal ellipsoids drawn at the 50% probability level

**Table 2.4:** Selected bond distances and angles for 4a

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<th>Angles, deg</th>
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Figure 2.7: ORTEP plot of the complex 4b with thermal ellipsoids drawn at the 50% probability level

Table 2.5: Selected bond distances and angles for 4b

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2.2.4 Synthesis of Rh(I) and Ir(I) (P-N) Complexes

The cationic iridium phosphino-imine complex 5 was synthesized using aniline as the amine source in a condensation reaction with the phosphine aldehyde (Scheme 2.8). Synthesis of P-N complexes is done in a template fashion, where the addition of the metal precursor is necessary to enable the reaction to go to completion. Addition of [NH₄][PF₆] yielded the product as the [PF₆]⁻ salt in 82% yield as air stable red crystals. Due to the acidic α-proton of the imine, if NaPF₆ or KPF₆ were used, a mixture of the cationic imine and the neutral enamido complexes were observed, presumably due to the basicity of the methanol solvent or any moisture present in the reaction mixture.

![Scheme 2.8: Synthesis of cationic Ir(I) phosphino-imine complex 5](image)

Changing the amine in the condensation reaction from aniline to hydroxylamine resulted in the formation of phosphino-oxime complexes 6a and 6b (Scheme 2.9). These complexes were formed as the [PF₆]⁻ salts, where the rhodium complex 6a was isolated as a yellow solid in 70% yield, and the iridium complex 6b as an orange solid in 97% yield. They have two potentially acidic protons on the backbone and oxime oxygen. The rhodium complex 6a was crystallized and examined by X-ray diffraction (Figure 2.8). The C(1)-C(2)
bond distance for the ligand backbone is 1.483(3) Å, which is longer than the bond distances of the enolate complexes, and characteristic of a C-C single bond.

**Scheme 2.9:** Synthesis of cationic Rh(I) and Ir(I) phosphino-oxime complexes 6a and 6b

Phosphine-oxime ligands are uncommon in literature, with the closest examples being bidentate phosphine-oxide, oxime ligands. In particular, Wan and co-workers have used chelating phosphine oxide and N-oxime ligands with Cu(I) for N-arylation of alkylamines and N-H containing heterocycles,\(^{67}\) as well as aryl iodide and thiol coupling.\(^{68}\) No well-defined metal complexes have been isolated in these studies. These new phosphine-oxime complexes present new possibilities in catalyst design. An example of a catalyst containing an oxime ligand is the bifunctional ketone transfer hydrogenation catalyst by Ikariya and co-workers\(^{42}\), which contains a C-N ligand and a Cp* ligand on Ir(III) (Scheme 1.5).

Preliminary tests on the new Rh(I) and Ir(I) oxime complexes for the transfer hydrogenation of acetophenone showed no activity.
**Figure 2.8:** ORTEP plot of the complex 6a with thermal ellipsoids drawn at the 50% probability level

**Table 2.6:** Selected bond distances and angles for 6a

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<th>Angles, deg</th>
<th>Bond distances, Å</th>
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<tr>
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<td>Rh(1)-N(1)-C(2) 124.5(1)</td>
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<tr>
<td>C(1)-C(2) 1.483(3)</td>
<td>N(1)-O(1) 1.423(2)</td>
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</table>
2.2.5 Hydrogenation Catalysis with Rh(I) and Ir(I) Complexes 4-6

The catalytic hydrogenation of olefins was attempted with the neutral complexes 4a and 4b, and the cationic complexes 5, 6a, and 6b (Table 2.7). Stilbene was used as the initial olefin substrate; however, attempted catalysis with complexes 4-6 was slow and incomplete. Activity was observed for the hydrogenation of cyclooctene with catalysts 4 and 5, where both Rh(I) and Ir(I) neutral catalysts were faster than the cationic catalyst 5. Cationic metal centres are often thought to be optimal for catalytic activity, especially in the case of poorly coordinating unfunctionalized tri- and tetrasubstituted olefins, as they may have greater affinity for the olefins. However, with less substituted olefins such as cyclooctene, it is possible that this is not a major factor. A previous study by Pfaltz and co-workers on counteranions has shown that the use of hexafluorophosphate anions are suboptimal for cationic Ir(I) olefin hydrogenation catalysts and resulted in slower turnover and more rapid catalyst death when compared to the larger and less coordinating [BARF]⁻ anion. The neutral complexes 4a and 4b do not have counteranions and thus have the potential to avoid this problem.

The Rh(I) complex 4a is more active for the hydrogenation of cyclooctene in hexanes than in DCM, whereas the Ir(I) complex 4b had the reverse activity. One possible explanation is after the COD ligand dissociates after hydrogenation, the Rh(I) metal centre is more Lewis acidic than the Ir(I) metal centre. This difference renders Rh(I) to have a higher affinity for DCM coordination and thereby cause a greater hindering of substrate coordination. It may also be possible that the Ir(I) catalyst is more prone to catalyst deactivation through oligomerization of the active catalyst than the Rh(I) catalyst, and DCM coordination is able to stabilize and maintain the active catalyst in solution.
Phosphino-oxime complexes 6a and 6b were mostly inactive for the hydrogenation of olefins and acetophenone. This was expected, as they are coordinatively unsaturated hydrogenation catalysts with coordinating alcohol or amine groups on the ligand. Hence their inactivity is likely due to a deactivation pathway involving the formation of dimers or other oligomers. Furthermore, catalysts 4-5 are selective for olefin hydrogenation over carbonyl groups, as demonstrated by the selective hydrogenation of 4-phenyl-3-buten-2-one to 4-phenyl-2-butane.

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<th>conv. (%)</th>
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2.2.6 Summary and Conclusions

Facile, one-pot methods for the synthesis of bidentate P-O, P-P and P-N complexes, some of which were catalytically active for the hydrogenation of C=C double bonds, were developed based on the utility of the phosphino aldehyde ligand precursor. A Ni(II) complex containing two bidentate phosphino-enolate ligands coordinated \textit{trans} to each other was synthesized. This complex may be of interest for further investigations towards the synthesis of an ethylene oligomerization catalyst, as Fryzuk and co-workers have published a method of forming active olefin oligomerization catalysts from similar starting materials.\textsuperscript{30} Also, a novel method of generating a diphosphine ligand containing a pendant aldehyde in a template method is presented using Pt(II) as the metal precursor. These ligands have potential for tethering metal complexes to heterogeneous materials making them more recyclable, or may be further transformed through functionalization of the alkene or aldehyde in the ligand backbone to generate more interesting ligands. Rh(I) and Ir(I) complexes have been synthesized based on Crabtree’s iridium catalyst design. The neutral Ir(I) complex 4b shows moderate activity for the hydrogenation of disubstituted olefins. However it is less active with the more sterically hindered stilbene. It was surprising that 4b was found to be more active than the cationic Ir(I) phosphino-imine complex considering that most catalysts of this design are cationic and contain a P-N ligand. Lastly, novel cationic Rh(I) and Ir(I) phosphino-oxime complexes 6 were synthesized and characterized. These complexes have
potential for a variety of catalytic processes, in particular for the bifunctional hydrogenation of polar bonds, where the oxime may act as a proton source in the proton/hydride transfer from the metal complex to the double bond. However, initial tests with acetophenone did not support this hypothesis.

2.3 Experimental Section

2.3.1 General Considerations

All of the preparations and manipulations, unless otherwise stated, were carried out under a nitrogen or argon atmosphere using standard Schlenk-line and glovebox techniques. Dry and oxygen-free solvents were used unless otherwise stated. The synthesis of the bromide salt of dicyclohexylphosphonium dimer 1 was synthesized according to literature procedures.59 The synthesis of the chloride salt of 1 only requires the replacement of bromoacetaldehyde diethyl acetal with chloroacetaldehyde diethyl acetal. All other reagents and solvents were purchased from commercial sources and were used as received. Deuterated solvents were purchased from either Cambridge Isotope Laboratories or Sigma Aldrich, and degassed and dried over molecular sieves prior to use. NMR spectra were recorded on a Varian Mercury 400 MHz or Bruker Avance 400 MHz spectrometer. 1H and 13C{1H} NMR spectra were referenced relative to their respective partially deuterated solvent peaks. All 31P chemical shifts were measured relative to 85% phosphoric acid as an external reference. The electrospray ionization mass spectrometry (ESI-MS) data were collected on an AB/Sciex QStar mass spectrometer with an ESI source and the DART-MS data were collected on a JEOL AccuTOF-DART mass spectrometer with a DART-ion source (no solvent is required).
Elemental analyses were performed using a Perkin-Elmer 2400 CHN elemental analyzer at the Department of Chemistry at the University of Toronto. Single-crystal X-ray diffraction data were collected using a Nonius Kappa-CCD diffractometer with Mo Kα radiation ($\lambda = 0.71073$ Å). The structures were solved and refined using SHELXTL V6.1.

### 2.3.2 Synthesis and Characterization

**Bis(dicyclohexylphosphinoacetaldehyde enolato)nickel (2).** A vial was charged with dicyclohexylphosphinoaldehyde chloride dimer 1 (26 mg, 0.047 mmol), KOtBu (11 mg, 0.094 mmol) and toluene (2 mL). The mixture was stirred for 10 min, yielding a white suspension. Solids were filtered off through Celite, and [Ni(H2O)6][BF4]2 (16 mg, 0.047 mmol) and methanol (1 mL) were added to the reaction mixture resulting in a brown solution. Upon addition of additional KOtBu (11 mg, 0.094 mmol) solution darkened slightly and was stirred overnight. The volatiles were removed *in vacuo*, and the brown residue extracted with pentanes (3 x 2 mL) until only white solids were left. Filtration of the mixture through Celite and removal of pentanes *in vacuo* afforded the product as a brown solid. Yield: 72% (25 mg). Crystals of 2 suitable for X-ray diffraction studies were grown by the slow evaporation of hexanes. $^1$H NMR (400 MHz, CD$_2$Cl$_2$): $\delta$ 7.08 (m, 1H, H/C=O), 3.43 (d, $J_{HH} = 3.13$ Hz, 1H, H/C=P), 2.60 (m, 2H, H$_2$C$_c$y), 1.97-1.67 (m, 8H, H$_2$C$_c$y), 1.70 – 1.60 (m, 2H, H$_c$C$_c$y-P), 1.52-1.20 (m, 10H, H$_c$C$_c$y). $^{13}$C {$^1$H} NMR (100 MHz, CD$_2$Cl$_2$): $\delta$ 175.66 (t, $J_{CP} = 4.4$ Hz, C=O), 76.79 (dd, $J_{CP} = 25.0$ Hz, 27.9 Hz, C-P), 35.92 (t, $J_{CP} = 12.5$ Hz, C$_c$y-P), 29.53 (s, C$_c$y), 27.90 (t, $J_{CP} = 2.2$ Hz, C$_c$y), 26.82 (m, C$_c$y), 25.85 (s, C$_c$y). $^{31}$P {$^1$H} NMR (161 MHz, CD$_2$Cl$_2$): $\delta$ 47.57 (s). Anal. Calcd for C$_{28}$H$_{48}$O$_2$P$_2$Ni: C, 62.59; H, 9.00. Found: C, 62.11; H, 9.55. MS (ESI, methanol/water; $m/z^+$): 537.3 ([C$_{28}$H$_{49}$O$_2$P$_2$Ni]$^+$).
Bis(dicyclohexylphosphinoacetaldehyde)dichloroplatinum (3a, 3b). A vial was charged with dicyclohexylphosphinoaldehyde chloride dimer 1 (33 mg, 0.060 mmol), KOTBu (13 mg, 0.12 mmol) and toluene (2 mL). The mixture was stirred for 10 min, yielding a white suspension. 1,5-Cyclooctadiene dichloroplatinum (23 mg, 0.060 mmol) was weighed directly into the vial, and stirred overnight. The resulting pale yellow solution was filtered through Celite to remove salts and dried in vacuo to yield the product as a white solid. Yield: 98% (44 mg).

Through NMR analysis, it was shown that 88% of the recovered product was the trans phosphinoaldehyde complex 3a, and 12% was the cis aldol condensation product 3b. When the same reaction was attempted at -78 ºC for 1 h, and then slowly warmed to room temperature, the reaction yielded only 30% 3a and 70% 3b.

Recrystallization in DCM and hexanes yielded crystals containing a molecule of 3a and a molecule of 3b per unit cell.

3a:

$^1$H NMR (300 MHz, CD$_2$Cl$_2$): $\delta$ 9.96 (t, $^3J_{HH} = 3.2$ Hz, 1H, HC=O), 3.20 (m, 2H, H$_2$C-P), 2.09 (m, 2H, HC$_{cy}$-P), 1.93-1.15 (m, 20H, H$_2$C). $^{13}$C{$^1$H} NMR (100 MHz, CD$_2$Cl$_2$): $\delta$ 198.74 (s, C=O), 32.69 (t, $J_{CP} = 10.3$ Hz, C-PC$_{cy}$2), 32.30 (t, $J_{CP} = 14.7$ Hz, P-C$_{cy}$), 28.80 (s, C$_{cy}$), 28.42 (s, C$_{cy}$), 27.32 (m, C$_{cy}$), 26.64 (s, C$_{cy}$). $^{31}$P{$^1$H} NMR (121 MHz, CD$_2$Cl$_2$): $\delta$ 15.40 (s). Anal. Calcd for C$_{28}$H$_{50}$Cl$_2$O$_2$P$_2$Pt: C, 45.04; H, 6.75. Found: C, 45.50; H, 6.84. MS (DART; $m/z^+$): 710.3 ([C$_{28}$H$_{50}$ClO$_2$P$_2$Pt]$^+$).

3b:

$^1$H NMR (300 MHz, CD$_2$Cl$_2$): $\delta$ 9.52 (m, HC=O), 7.94 (m, 1H, HC=C), 2.98 (m, 4H, H$_2$C-P), 1.93-1.15 (m, 20H, H$_2$C). $^{31}$P{$^1$H} NMR (121 MHz, CD$_2$Cl$_2$): $\delta$ 32.88 (d, $J_{PP} = 16.9$ Hz), 9.91 (d, $J_{PP} = 16.9$ Hz).
(1,5-Cyclooctadiene)(dicyclohexylphosphinoacetaldehyde enolato)rhodium (4a). A vial was charged with dicyclohexylphosphinoaldehyde chloride dimer 1 (26 mg, 0.047 mmol), KOtBu (10 mg, 0.094 mmol) and toluene (2 mL). The mixture was stirred for 20 min, yielding a white suspension. Cyclooctadiene rhodium chloride dimer (23 mg, 0.047 mmol) was weighed directly into the vial, and stirred briefly, followed by addition of KOtBu (10 mg, 0.094 mmol). The yellow solution was stirred at room temperature for 2.5 h. The yellow solution was filtered through Celite to remove salts and dried in vacuo to yield the product as a yellow solid. The product was recrystallized by slow diffusion of methanol into a DCM solution of the product. Yield: 97% (46 mg). Bright yellow crystals of 4a suitable for X-ray diffraction studies were grown from slow diffusion of methanol into a hexane solution of the product. $^1$H NMR (400 MHz, CD$_2$Cl$_2$): $\delta$ 7.35 (dt, $^3J_{HH} = 3.7$ Hz, $^2J_{HP} = 39.3$ Hz, 1H, H-C-O), 4.91 (m, 2H, H=C=CH), 3.75 (m, 2H, H=C=CH), 3.49 (dd, $^3J_{HH} = 1.8$ Hz, $^2J_{HH} = 3.7$ Hz, 1H, H=CH), 2.36-2.14 (m, 4H, COD H$_2$C), 2.06-1.92 (m, 4H, COD H$_2$C), 1.70-1.79 (m, 2H, HC=C), 1.38-1.03 (m, 10H, H$_2$C). $^{13}$C$^\{^1^H\}$ NMR (100 MHz, CD$_2$Cl$_2$): $\delta$ 177.35 (d, $^2J_{CP} = 15.4$ Hz, C=O), 101.64 (dd, $J = 8.1$ Hz, 10.3 Hz, COD C=C trans-P), 78.55 (dd, $^1J_{CP} = 14.8$ Hz, C=C-P), 66.85 (d, $^1J_{RhC} = 13.2$ Hz, COD C=C cis-P), 34.01 (dd, $^2J_{RhC} = 1.5$ Hz, $^3J_{CP} = 24.9$ Hz COD CH$_2$), 33.63 (d, $^2J_{RhC} = 2.9$ Hz, COD CH$_2$), 28.69 (d, $J_{CP} = 3.67$ Hz, C$_{Cy}$), 28.47 (d, $J_{CP} = 3.67$ Hz, C$_{Cy}$), 27.46 (s, C$_{Cy}$), 27.35 (d, $J_{CP} = 16.1$ Hz, C$_{Cy}$), 27.35 (d, $J_{CP} = 13.20$ Hz, C$_{Cy}$), 26.80 (d, $J_{CP} = 1.47$ Hz, C$_{Cy}$). $^{31}$P$^\{^1^H\}$ NMR (161 MHz, CD$_2$Cl$_2$): $\delta$ 44.92 (d, $^1J_{RhP} = 155.0$ Hz). Anal. Caled for C$_{22}$H$_{36}$OPRh: C, 58.67; H, 8.06. Found: C, 57.64; H, 8.10. MS (ESI, methanol/water; m/z): 451.2 ([C$_{22}$H$_{37}$OPRh]$^+$).

(1,5-Cyclooctadiene)(dicyclohexylphosphinoacetaldehyde enolato)iridium (4b). A vial was charged with dicyclohexylphosphinoaldehyde chloride dimer 1 (26 mg, 0.047 mmol), KOtBu (10 mg, 0.094 mmol) and toluene (2 mL). The mixture was stirred for 20 min, yielding a white suspension. Cyclooctadiene iridium chloride dimer (32 mg, 0.047 mmol) was weighed directly into the vial, and stirred briefly, followed by addition of KOtBu (10 mg, 0.094 mmol). The dark red solution was stirred at
room temperature overnight. The red solution was filtered through Celite to remove salts and dried *in vacuo* to obtain the crude product as a dark red sticky solid. The solid was washed with a few drops of Et₂O several times to yield an orange solid. The product was recrystallized by slow diffusion of methanol into a DCM solution of the product. Yield: 45% (23 mg). Red crystals of 4b suitable for X-ray diffraction studies were grown from slow diffusion of methanol into a hexane solution of the product. ¹H NMR (400 MHz, CD₂Cl₂): δ 7.54 (dd, 3 J₃HH = 4.1 Hz, 3 J₃HP = 34.0 Hz, 1H, HC-O), 4.60 (m, 2H, COD HC=CH), 3.80 (t, 3 J₃HH = 4.1 Hz, 1H, HC-P), 3.58 (m, 2H, COD HC=CH), 2.31 – 2.16 (m, 2H, H₃C₂-P), 2.15 – 1.13 (m, 28H, H₂C). ¹³C¹¹H¹ NMR (100 MHz, CD₂Cl₂): δ 180.21 (d, 2 JCP = 13.2 Hz, C-O), 89.14 (d, 2 JCP = 11.7 Hz, COD C=C trans-P), 82.64 (d, 1 JCP = 48.4 Hz, C=C-P), 50.65 (s, COD C=C cis-P), 34.44 (d, 3 JCP = 13.2 Hz, COD CH₂), 34.58 (s, COD CH₂), 34.02 (s, H₃C₂-P), 27.36 (d, JCP = 12.5 Hz, Cₐ), 27.28 (d, JCP = 11.0 Hz, Cₐ), 26.73 (d, JCP = 1.5 Hz, Cₐ). ³¹P¹¹H¹ NMR (161 MHz, CD₂Cl₂): δ 37.42 (s). Anal. Calcd for C₂₂H₃₆OPIr: C, 48.96; H, 6.72. Found: C, 48.62; H, 6.94. MS (ESI, methanol/water; m/z): 541.2 ([C₂₂H₃₇OPIr]⁺).

(1,5-Cyclooctadiene)(N-phenyldicyclohexylphosphinoacetimine)iridium hexafluorophosphate (5). A vial was charged with dicyclohexylphosphinoaldehyde bromide dimer (38 mg, 0.060 mmol), KOrBu (13 mg, 0.116 mmol), aniline (12 mg, 0.129 mmol) and toluene (2 mL). The mixture was stirred for 30 minutes, yielding a yellow solution. Cyclooctadiene iridium chloride dimer (40 mg, 0.060 mmol), NH₄PF₆ (20 mg, 0.120 mmol) and methanol (1 mL) was then added directly into the vial to form a bright red/orange solution. The solution was stirred at room temperature overnight and the solvent removed *in vacuo*. The resulting red solid was dissolved in cold DCM and filtered through Celite to remove any insoluble salts. The solvent was removed and washed several times with pentanes. The filtrate was dried *in vacuo* to yield the product as a red solid. Yield: 82% (75 mg). ¹H NMR (400 MHz, CD₂Cl₂): δ 8.15 (dt, 3 J₃HH = 2.3 Hz, 3 J₃HP = 22.7 Hz, 1H, HC=N), 7.43 – 7.09 (m, 5H, H₈Ph), 3.83 (br s, 4H, COD CH₂), 3.11 (dd, 3 J₃HH = 2.3 Hz, 2 J₃HP = 8.2 Hz, 1H, H₂C-P), 2.28 – 1.23 (m, aliphatic H). ¹³C¹¹H¹ NMR (100 MHz, CD₂Cl₂): δ 149.76 (s, HC=N), 129.03 (s, C₆Ph), 128.06 (s, C₆Ph), 122.82 (s, C₆Ph), 68.95 (bs,
COD C=C), 35.59 (d, \(^1J_{CP} = 23.5\) Hz, C-P), 35.48 (d, \(^1J_{CP} = 22.7\) Hz, C-P), 31.89 (s, CH\(_2\)), 29.30 (s, CH\(_2\)), 28.82 (s, CH\(_2\)), 27.26 (d, \(^1J_{CP} = 10.3\) Hz, CH\(_2\)), 26.49 (d, \(^1J_{CP} = 1.5\) Hz, CH\(_2\)).

\(^{31}\)P \(^1\)H NMR (161 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 47.81 (s), -144.38 (septet, \(J = 711\) Hz, PF\(_6\)). Anal. Calcd for C\(_{28}\)H\(_{42}\)F\(_6\)NP\(_2\)Ir: C, 44.20; H, 5.56; N, 1.84. Found: C, 41.88; H, 5.57; N, 1.85. (ESI, methanol/water; \(m/z^+\)): 616.3 ([C\(_{28}\)H\(_{42}\)NPIr]').

\(\text{1,5-Cyclooctadiene}(\text{dicyclohexylphosphinoacetaldehyde oxime})\text{rhodium hexafluorophosphate (6a). A vial was charged with dicyclohexylphosphinoacetaldehyde chloride dimer (33 mg, 0.060 mmol), KOtBu (13 mg, 0.120 mmol) and toluene (2 mL). The mixture was stirred for 10 minutes, yielding a white suspension. Hydroxylammonium chloride (6 mg, 0.080 mmol), KOtBu (9 mg, 0.080 mmol) and methanol (2 mL) was added and stirred for 20 minutes. Cyclooctadiene rhodium chloride dimer (20 mg, 0.040 mmol) and NaPF\(_6\) (16 mg, 0.094 mmol) was then weighed directly into the vial forming a yellow solution. The solution was stirred at room temperature overnight and the solvent removed in vacuo. The resulting red solid was dissolved in DCM and filtered through Celite to remove any insoluble salts. The filtrate was dried in vacuo to yield the product as a yellow solid. Yellow crystals of 6a suitable for X-ray diffraction studies were grown from slow diffusion of pentanes into a DCM solution of the product. Yield: 70% (36 mg). \(^1\)H NMR (400 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 9.17 (bs, 1H, N-OH), 8.00 (m, 1H, HC=N), 5.57 (br s, 2H, COD CH\(_2\)), 4.45 (m, 2H, COD CH\(_2\)), 2.65 (dd, \(^3J_{HH} = 2.7\) Hz, \(^2J_{HP} = 8.8\) Hz, 1H, H\(_2\)C-P), 2.47 – 1.10 (m, aliphatic H). \(^{13}\)C \(^1\)H NMR (100 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 164.73 (t, \(J = 5.1\) Hz, C=N), 106.38 (dd, \(J = 7.3\) Hz, 8.8 Hz, COD C=C), 79.08 (d, \(^1J_{RHC} = 11.7\) Hz, COD C=C), 34.30 (dd, \(^2J_{RHC} = 1.8\) Hz, \(^1J_{CP} = 21.3\) Hz, C\(_{cy}\)P), 32.55 (d, \(J = 2.9\) Hz, COD CH\(_2\)), 29.07 (d, \(J = 2.2\) Hz, CH\(_2\)), 28.80 (d, \(J = 1.5\) Hz, COD CH\(_2\)), 28.49 (s, CH\(_2\)), 27.34 (d, \(^1J_{CP} = 21.3\) Hz, H\(_2\)C-P), 26.90 (d, \(J = 11.0\) Hz, CH\(_2\)), 26.28 (d, \(J = 1.5\) Hz, CH\(_2\)). \(^{31}\)P \(^1\)H NMR (161 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 50.90 (d, \(^1J_{RHP} = 149.4\) Hz), -144.20 (p, \(^1J_{PP} = 711\) Hz, PF\(_6\)). Anal. Calcd. for C\(_{22}\)H\(_{38}\)FNO\(_2\)Rh: C, 43.22; H, 6.26; N, 2.29. Found: C, 44.31; H, 5.97; N, 2.43. MS (ESI, methanol/water; \(m/z^+\)): 466.2 ([C\(_{22}\)H\(_{38}\)NOPRh]').
(1,5-Cyclooctadiene)(dicyclohexylphosphinoacetaldehyde oxime)iridium hexafluorophosphate (6b). A vial was charged with dicyclohexylphosphinoaldehyde chloride dimer (26 mg, 0.047 mmol), KOrBu (10 mg, 0.094 mmol) and toluene (2 mL). The mixture was stirred for 10 minutes, yielding a white suspension. Hydroxylammonium chloride (7 mg, 0.094 mmol), KOrBu (10 mg, 0.094 mmol) and methanol (2 mL) was added and stirred for 20 minutes. Cyclooctadiene iridium chloride dimer (31 mg, 0.047 mmol) and NaPF₆ (16 mg, 0.094 mmol) was then weighed directly into the vial forming a bright red/orange solution. The solution was stirred at room temperature overnight and the solvent removed in vacuo. The resulting red solid was dissolved in DCM and filtered through Celite to remove any insoluble salts. The filtrate was dried in vacuo to yield the product as a red solid. Yield: 97% (46 mg)

1H NMR (400 MHz, CD₂Cl₂): δ 11.07 (bs, 1H, N-OH), 8.71 (broad d, 3JHP = 23.9 Hz, 1H, HC=N), 4.97 (broad s, 2H, COD HC=CH), 4.29 (broad s, 2H, COD HC=CH), 2.78 (d, 3JHH = 8.0, 2H, H₂C-P), 2.31-1.08 (m, aliphatic H). 13C {¹H} NMR (100 MHz, CD₂Cl₂): δ 188.39 (d, 2JCp = 6.6 Hz, C=N), 90.16 (s, COD C=C), 60.31 (s, COD C=C), 34.92 (d, 1JCp = 26.4 Hz C-P), 34.57 (d, JCP = 26.4 Hz, C-P), 32.31 (s, CH₂), 28.79 (d, JCP = 2.2 Hz, CH₂), 28.74 (s, CH₂), 27.00 (d, JCP = 12.5 Hz, CH₂), 26.86 (d, JCP = 11.0 Hz, CH₂), 26.26 (d, JCP = 1.5 Hz, CH₂). 31P {¹H} NMR (161 MHz, CD₂Cl₂): δ 45.34 (s), -144.41 (p, J = 711 Hz). Anal. Calcd for C₂₂H₃₈NOP₂Ir: C, 37.71; H, 5.47; N, 2.00. Found: C, 38.94; H, 5.50; N, 2.35. MS (ESI, methanol/water; m/z⁺): 556.2 ([C₂₂H₃₈NOPIr]⁺).

2.3.3 Catalysis

Hexanes and DCM were dried and degassed following standard procedures. All of the substrates were vacuum-distilled, dried over activated molecular sieves, and stored under argon prior to use. All of the hydrogenation runs were performed at constant pressures using a stainless steel 50 mL Parr hydrogenation reactor. The temperature was maintained at 35°C using a constant temperature water bath. The reactor was flushed several times with hydrogen gas at 2-4 bar prior to the addition of catalyst/substrate and base solutions.
In a typical run (Table 2.7, Entry 1), the catalyst 4a (6 mg, 13.3 µmol) and cyclooctene (146 mg, 1.33 mmol) were dissolved in DCM (16 g) (or 10 g hexanes) under an argon atmosphere. The catalyst/substrate solution was taken up by a syringe and needle in the glovebox. The needles were stoppered and the syringes were taken to the reactor. The solutions were then injected into the reactor against a flow of hydrogen gas. The hydrogen gas was adjusted to the desired pressure (35 bar). Small aliquots of the reaction mixture were quickly withdrawn with a syringe and needle under a flow of hydrogen at timed intervals by venting the Parr reactor at reduced pressure. Alternatively, small aliquots of the reaction mixture were sampled from a stainless steel sampling dip tube attached to a modified Parr reactor. The dip tube was 30 cm in length with an inner diameter of 0.01 in., and a swing valve was attached to the end of the sampling tube. Three small aliquots of sample were thereby withdrawn quickly at timed intervals by opening the swing valve, and the first two aliquots were discarded. All samples were diluted to a total volume of approximately 2 mL using oxygenated THF prior to GC analyses.

A Perkin-Elmer Clarus 400 chromatograph equipped with a chiral column (CP chirasil-Dex CB 25 m × 2.5 mm) and an auto-sampling capability was used for gas chromatography (GC) analyses. Hydrogen was used as a mobile phase at a column pressure of 5 psi with a split flow rate of 50 mL/min. The injector temperature was 250°C and the FID temperature was 275°C. All of the conversions are reported as an average of two GC runs. The reported conversions were reproducible.

The substrate, product, oven temperature (T) and the retention times for the substrate ($t_s$) and product ($t_p$) are as follows:

Cyclooctene, cyclooctane, $T = 105 ^\circ C$, $t_s = 5.15$ min, $t_p = 5.38$ min
trans-4-phenyl-3-buten-2-one, 4-phenyl-2-butanone, $T = 125 ^\circ C$, $t_s = 21.95$ min, $t_p = 11.42$ min
Stilbene, bibenzyl, $T = 200 ^\circ C$, $t_s = 5.08$ min, $t_p = 3.73$ min
Chapter 3: Synthesis of Chiral Amino-Functionalized Imidazolium Salts and their Coordination to Ru(II) Cp* Precursors

3.1 Introduction

The main research focus in our group in recent years has been in the development of new and improved homogenous catalysts for the hydrogenation of polar double bonds, including those of ketones, esters, imines, and nitriles. Ruthenium(II) and iridium(III) based catalysts containing N-heterocyclic carbene (NHC) and amino ligands, and iron(II) catalysts containing PNNP phosphino-imine ligands have been reported by our group as particularly active ketone hydrogenation catalysts. While the iron(II)-based catalysts are able to impart enantioselectivity to the hydrogenation product, the ruthenium(II) based catalyst is able to hydrogenate more difficult substrates such as esters and imines, but not enantioselectively.

Despite the multitude of known catalysts for the hydrogenation of polar double bonds, there is always a demand for more effective, cost-efficient, and environmentally-friendly catalysts. One way to improve upon previous catalysts is to change the donor group of the ligand. It is known that amino-groups are important for the generation of effective polar bond hydrogenation catalysts due to the “NH effect”. However, a relatively recent trend in catalyst design has been to replace the prevalent phosphine moiety with NHC ligands. NHCs are versatile ligands that can take the place of phosphine ligands, as they are both strong σ-donors and generally act as spectator ligands. Although NHC are often considered to be a more air, moisture, and heat stable replacement for tertiary phosphines, it has been shown that they can in many cases improve the activity of the catalyst by its
replacement of the phosphine.\textsuperscript{10} In addition, entirely organic ligands avoid problems associated with toxic phosphorus starting materials.

In terms of catalyst improvement, it is also important to consider the substrate scope. To improve the applicability of catalysts in general, it is essential to increase the catalyst’s tolerance for various functional groups. This is particularly important for applicability of the catalyst in the synthesis of larger, more complex molecules in both academic and industrial settings. The use of NHC ligands might increase the varieties of unsaturated molecules that can be hydrogenated. Ketones and aldehydes are generally the easiest substrates to hydrogenate. However, the hydrogenation of prochiral ketone substrates leads to chiral alcohol products; therefore, an improvement in the catalyst enantioselectivity is an important goal. The hydrogenation of esters and amides is significantly more difficult, but the catalysis need not be enantioselective.

### 3.1.1 General Synthesis and Coordination of NHC

The synthesis of NHC metal complexes usually requires first the synthesis of the corresponding ligand precursor, then the formation of the carbene by various methods, and then its subsequent coordination. The NHC precursors most commonly used in late transition metal chemistry are 5-membered heterocycles, including those derived from imidazoles, dihydroimidazoles, and triazoles (Figure 3.1).\textsuperscript{76} In our group, we have worked extensively with imidazole-based NHCs. Thus we will focus on their synthesis and chemistry in this chapter.
Symmetric imidazolium salts can be synthesized through a one-pot condensation reaction using a primary amine, glyoxal (or 1,2-diketones), and paraformaldehyde (Scheme 3.1). The synthesis of asymmetric imidazolium salts can be achieved by first synthesizing the asymmetric imidazole using either a modified Debus-Radziszewski, or a Van Leusen imidazole synthesis. The modified Debus-Radziszewski reaction requires a primary amine, an ammonium source, glyoxal/1,2-diketone, and paraformaldehyde to be reacted in one-pot to form the imidazole (Scheme 3.2). The Van Leusen imidazole synthesis is the reaction of aldimines with tosylmethyl isocyanide under basic conditions to form the imidazole. This synthesis was later modified to a two-step reaction where the aldimine is generated in situ, called the Van Leusen three-component reaction (Scheme 3.3). The resulting N-substituted imidazolium salt can then undergo a substitution reaction with an alkylating agent to form the asymmetric imidazolium salt. This can also be done by acquiring commercially available mono-N-substituted imidazoles and reacting it with an appropriate alkylating agent/electrophile (Scheme 3.2).

\[
2 \text{RNH}_2 + \text{CO} + \text{HCHO} + \text{HX} \rightarrow \text{RN} \cdots \text{N} \cdots \text{RN} \]  

Scheme 3.1: General synthesis of symmetrical imidazolium salts
Scheme 3.2: General synthesis of asymmetrical imidazolium salts

Scheme 3.3: Van Leusen three-component reaction

New methods for the coordination of NHC to transition metals are continuously being developed in order to increase the efficiency of NHC coordination, and to increase the scope of different NHC and metal precursors available for the formation of new NHC-metal complexes. The most straightforward method of NHC coordination is through deprotonation of the imidazolium salt and its subsequent coordination.81 The free carbene may be isolated in some cases, or reacted in situ with the metal precursor if the free carbene is unstable (Scheme 3.4). This method is only viable if there are no-base sensitive functional groups on
the ligand precursor, as imidazolium salts (pKa ~24 in DMSO) require a very strong base to deprotonate. Other methods for the formation of the free carbene include thermal decomposition of alcohol,\textsuperscript{82} CO\textsubscript{2},\textsuperscript{83} chloroform,\textsuperscript{84} or pentafluorobenzene adducts.\textsuperscript{85}

**Scheme 3.4:** Deprotonation of imidazolium using a strong base and then coordination of the NHC to a metal

![Scheme 3.4: Deprotonation of imidazolium using a strong base and then coordination of the NHC to a metal](attachment:image)

**Scheme 3.5:** Formation of an NHC-silver complex with Ag\textsubscript{2}O and subsequent transmetallation of the carbene to the desired metal centre

![Scheme 3.5: Formation of an NHC-silver complex with Ag\textsubscript{2}O and subsequent transmetallation of the carbene to the desired metal centre](attachment:image)

If the imidazolium salt is base sensitive, using silver(I) oxide (Ag\textsubscript{2}O) as a mild base and transmetalating agent can be successful (Scheme 3.5).\textsuperscript{8} The imidazolium salt is deprotonated by the oxide, forming water. If the counter-anion forms an insoluble silver salt, such as silver halides, it precipitates out as a silver salt which can be removed through filtration. The formation of an NHC-silver complex is driven by the formation of the strong NHC-silver bond. The complex can be isolated, or used \textit{in situ} for the transmetalation of the
NHC to the desired metal center. Two disadvantages of this method are the cost of the silver reagent and light sensitivity of the NHC-silver complex.

3.1.2 Ru(II) NHC-Amine Catalysts for Hydrogenation of Polar Double Bonds

Our group previously discovered the highly active catalyst 

\[ \text{[RuCp}^\ast(NHC(C_6H_4CH_2NH_2))(\text{py})][\text{PF}_6] \]

which is active for the hydrogenation of ketones and esters (Figure 3.2). To synthesize the amino-functionalized NHC ligand, 2-cyanophenylimidazole is first synthesized following literature procedures (Scheme 3.6).\(^8\) The subsequent \(N\)-alkylation or \(N\)-arylation forms the nitrile functionalized imidazolium salt.\(^8\) Then, in an elegant one-pot reaction, the reduction of the nitrile and formation of the transmetalating agent is carried out using \(\text{NiCl}_2\) as the metal precursor and excess \(\text{NaBH}_4\) as the reducing agent to form the \(\text{Ni(NHC-NH}_2)_2\) complex.\(^8\) Lastly, the ligand is transmetalated to \(\text{RuCp}^\ast(\text{COD})\text{Cl}\) and stirred in excess pyridine to afford the precatalyst \(7\). The \(p\)-cymene complex \(8\), \[ \text{[Ru}(p\text{-cymene})(NHC(C_6H_4CH_2NH_2))(\text{Cl})][\text{PF}_6] \], has also been synthesized using \[ \text{[Ru}(p\text{-cymene})\text{Cl}_2]_2 \] as the Ru(II) precursor.\(^8\)
Scheme 3.6: Synthesis of 7 and its ligand precursor

Figure 3.2: [RuCp*(NHC(C₆H₄CH₂NH₂))(py)][PF₆] 7, [Ru(p-cymene)(NHC(C₆H₄CH₂NH₂))(Cl)][PF₆] 8, and [Ru(p-cymene)(NHC(CH₂)₂NH₂)(Cl)][PF₆] 9, respectively

In an attempt to explore the effect of ring size for these series of Ru(II) catalysts, the 5-membered amino-functionalized NHC complex was synthesized. Due to synthetic difficulties, only the complex [Ru(p-cymene)(NHC(CH₂)₂NH₂)(Cl)][PF₆] 9 was prepared. To contract the ring size, the phenylene backbone was removed in favour of the saturated
ethylene backbone. The synthesis of this ligand precursor was achieved by the substitution of 2-chloroammonium with excess 1-methylimidazole to form the dicationic imidazolium salt (Scheme 3.7). The NHC was coordinated to [Ru(\(\rho\)-cymene)Cl\(_2\)]\(_2\) using Ag\(_2\)O as the base/transmetalating agent.

![Scheme 3.7: Synthesis of amino-functionalized NHC with ethylene backbone](image)

Of the Ru(II) amino-NHC complexes developed in our group, catalyst 7 was the most active. This precatalyst had a maximum turnover frequency (TOF) of 17600 h\(^{-1}\) for the hydrogenation of acetophenone at 25 °C and 8 bar H\(_2\), which are considered to be relatively mild conditions. It was also active for ester and imine hydrogenation. Catalyst 9 was appreciably less active for the hydrogenation of acetophenone, with a maximum TOF of 595 h\(^{-1}\) under much harsher conditions, requiring 50 °C and 25 bar H\(_2\). The analogous \(\rho\)-cymene complex 8 containing the phenylene backbone in the ligand was even less active at 50 °C and 25 bar H\(_2\), resulting in a TOF of 213 h\(^{-1}\).

The main differences in the catalytic activities of these compounds are speculated to be due to whether the active catalyst’s metal centre is cationic or neutral\(^{70,89}\). That is, when the Ru(II) complex contains the anionic Cp* ligand, the active catalyst is neutral and electron rich thus increasing the hydricity of the metal-hydride. When the Ru(II) complex contains a neutral arene ligand such as \(\rho\)-cymene, the active catalyst is cationic and the hydricity of the metal-hydride bond is decreased, resulting in higher energy barriers that must be overcome during catalysis. A similar effect is observed both experimentally and computationally when
Ir(III) is used in place of Ru(II) in a Cp* complex. The active catalyst for the Ir(III) system is cationic, resulting in diminished hydricity in comparison to the neutral Ru(II) catalyst.

For ester hydrogenation, [RuCp*(NHC(C₆H₄CH₂NH₂))(py)][PF₆] (7), and similar achiral catalysts, are sufficient; for catalysis resulting in an achiral product, activity and cost are the main factors in determining a catalyst’s value. However, for ketone and imine hydrogenation, substrates are often prochiral, providing the opportunity for asymmetric hydrogenation to produce desirable enantiopure alcohols and amines. Thus, one of the next steps in the improvement of these Ru(II)-based catalysts is to incorporate chiral groups in an attempt to make the catalysis enantioselective. For this purpose, modifications to add chirality to the phenylene-linked NHC-amine ligand are impractical. The ethylene-backbone ligand, however, is much more modular, and contains starting materials that can be exchanged for cheap chiral molecules such as amino acid derivatives.

When 3-(ethylammonium)-1-methylimidazolium dichloride was tried as the ligand precursor in the synthesis of Ru(II) Cp* complexes, irreversible S-coordination of DMSO occurred to the metal centre (Scheme 3.8). Hydrogenation of acetophenone with this DMSO complex was unsuccessful. In the synthesis of the metal complex, DMSO was necessary to solubilize the dicationic ligand precursor. Thus, to remove DMSO from the synthesis, we also aimed to make the ligand precursor more soluble by adding a non-polar chiral group onto the ethylene backbone.
Scheme 3.8: Unexpected $S$-coordination of DMSO in the attempted synthesis of RuCp*(NHC(CH$_2$)$_2$NH$_2$)I

3.1.3 Synthesis of Chiral Amino-Functionalized Imidazolium Salt

To improve upon the 3-(ethylammonium)-1-methylimidazolium dichloride ligand precursor, we aimed to add non-polar groups to the ligand precursor in order to make it more soluble in organic solvents. As well, it would be highly advantageous to add a sufficiently large chiral group to the backbone in order to induce chirality in the hydrogenation of ketones. We planned to modify the ethylene backbone by replacing it with amino acid derivatives, where its carboxylic acid functionality would be transformed into an imidazolium. In determining which amino acid would be appropriate to use, we chose ones without additional coordinating groups, and that are sufficiently bulky to induce enantioselectivity. From previous studies done on our iron(II) PNNP complexes, we knew that when 1,2-diphenylethlenediamine (dpen) was used as the diamine backbone of the ligand, enantioselectivity and activity were the highest. Thus, we initially chose to use a phenylglycine derivative for our initial ligand synthesis. Other interesting amino acid precursors include valine and proline, which have bulky aliphatic groups and also a more rigid backbone in the case of proline.

The most direct route to an amino-functionalized NHC from an amino acid would be the reduction of the carboxylic acid, then the transformation of the alcohol to a good leaving
group. The amine would have to be protected in order to reduce its nucleophilicity, as 1-methylimidazole is a poor nucleophile and would be outcompeted in the substitution reaction by the amine, resulting in unwanted side-reactions. First, phenylglycine was reduced to phenylglycinol with LiAlH₄ in THF under refluxing conditions (Scheme 3.9). The reduction of phenylglycine was a straightforward one-step reaction of a modified literature procedure, that yielded the aminoalcohol product in 68% yield. Although phenylglycinol is commercially available, it is ~10 times more expensive than its amino acid precursor. The amino-group was then BOC protected following a literature preparation using 1 equivalent of di-tert-butyl dicarbonate and excess triethylamine in THF. The N-BOC-protected phenylglycinol 10 was synthesized in 89% yield. The alcohol group was then converted to the tosylate 11 in 70% yield using 1 equivalent of tosyl chloride and triethylamine in DCM.

Scheme 3.9: Synthesis of N-BOC protected, O-tosylated, phenylglycinol derived electrophile 11
The imidazolium precursor 11 was reacted with 1-methylimidazole in toluene at 80 °C for 24-48 h, yielding 1-methylimidazolium tosylate as the major product, along with some minor peaks that may be the desired amino-functionalized imidazolium salt (Scheme 3.10). The precursor 11 was also reacted with potassium imidazolide, which was generated in situ with potassium hydride and imidazole, yielding the expected imidazole substituted N-BOC-phenylglycinol derivative, and the same minor peaks as the assumed amino-functionalized imidazolium salt from the previous reaction. Further reaction of the imidazole substituted N-BOC-phenylglycinol derivative with strong electrophiles [Me₃O][BF₄] or CH₃I resulted in a mixture of several products.

The reactions of 11 with both 1-methylimidazole and potassium imidazolide yielded the same minor products. Upon further search of the literature, it was found that N-BOC-protected aminoalcohols can undergo an intramolecular cyclization reaction when heated or under basic conditions (Scheme 3.10). The speculated mechanism is similar to the deprotection mechanism of the BOC protecting group. However, instead of elimination of both isobutene and CO₂, only isobutene is eliminated, and the resulting intermediate carbamate complex reacts with the tosylate, forming a cyclic carbamate. The net reaction also yields tosyllic acid, which explains the appearance of 1-methylimidazolium tosylate as the major product.
Scheme 3.10: Unwanted intramolecular cyclization reaction observed in the attempted substitution reaction of 11 with 1-methylimidazole

A phthalimide protecting group approach was attempted instead (Scheme 3.11). Following literature procedures, phenylglycinol was reacted neat with 1 equivalent of phthalic anhydride at 140 °C, yielding the phthalimide protected product 12 in 86% yield. The high temperature was necessary to melt the solid phthalic anhydride and evaporate the water by-product. The phthalimide 12 was then tosylated using tosyl chloride in pyridine, yielding the tosylate 13 in 98% yield. Tosylation using triethylamine as the base resulted in poor yield and multiple products; hence neat pyridine was used as the base and solvent. When 13 was reacted with 1-methylimidazole under various conditions, a mixture of products was observed. The major product was once again 1-methylimidazolium tosylate, however some of the expected 1-methylimidazole substituted product 14 was observed. The best yield (30%) was obtained when 13 was reacted in a small scale reaction (0.2 g 13) with excess 1-methylimidazole neat at 80 °C. The N-protected ligand precursor 14 was then deprotected with hydrazine monohydrate in wet ethanol, yielding the ligand precursor 15 in
73% yield. Characteristic $^1$H NMR signals were observed for the imidazolium C-H, a singlet at 9.86 ppm, and two triplets at 7.02 ppm and 6.93 ppm. The new ligand precursor 15 was found to be soluble in chlorinated solvents and acetonitrile, thus solving the insolvability issue with the previously generated ligand with the ethylene backbone.

**Scheme 3.11:** Synthesis of the amino-functionalized imidazolium ligand precursor 15

The low yielding substitution reaction of 13 with 1-methylimidazole is speculated to be due to a side reaction involving the elimination of the tosylate (Scheme 3.12). This is
more evident in the reaction of 13 and potassium phthalide, where near stoichiometric conversion of 13 to the elimination product, N-(1-phenylethenyl)phthalimide, is observed. The weak SN2 reactivity can be attributed to 1-methylimidazole being a poor nucleophile, the tosylate on 13 being inaccessible to the nucleophile, and the acidity of the proton alpha to the phenyl and phthalimide group. The reaction requires both significant heating and reaction time because imidazoles are relatively bulky nucleophiles and good leaving groups. Also, the formation of the charged imidazolium is unfavourable. Furthermore, both the phenyl and phthalimide groups vicinal to the tosylate are sterically bulky, and hinder nucleophilic attack into the C-O σ*-orbital by the imidazole. Lastly, the electron withdrawing properties of the phenyl and phthalimide groups make the proton alpha to them acidic enough to promote the unwanted E2 reaction. Because the elimination product, N-(1-phenylethenyl)phthalimide, is also a suitable electrophile for the synthesis of 14 with 1-methylimidazole, and the product 14 can also eliminate 1-methylimidazole to form N-(1-phenylethenyl)phthalimide in the reverse reaction, it is highly likely that the substitution reaction yields 15 as a racemic mixture.

Scheme 3.12: Unwanted elimination reactivity of 13 in the synthesis of 14
3.1.4 Synthesis and Catalysis of RuCp*(NHC-NH2)(X)

The synthesis of the Ru(II) Cp* complex 16 was done via a modified procedure used to synthesize \([\text{RuCp}^*\text{(NHC-NH2)(S-DMSO)}][\text{X}]\). The ligand precursor 15 was dissolved in acetonitrile and added to a solution of 1.6 equivalents of Ag2O, 1 equivalent of RuCp*(COD)Cl, and excess KI. After stirring overnight, the desired metal complex 16 was isolated as a green solid (Scheme 3.13). The Cp* and amino-NHC ligand can be seen in the \(^1\text{H}\) NMR spectra and ESI-MS. Characteristic \(^1\text{H}\) NMR peaks include the methyl groups of Cp* at 1.62 ppm, the methyl group on the imidazolium at 3.86 ppm, and the imidazolium C-H as a pair of doublets at 6.77 ppm and 6.92 ppm. ESI-MS reveals the presence of a \([\text{RuCp}^*\text{(NHC-NH2)}]^+\) fragment. Thus, it is not for certain whether the complex exists as a neutral complex with an iodo ligand or as a salt with acetonitrile coordination.

![Scheme 3.13: Coordination of 15 to RuCp*(COD)Cl using Ag2O to form the precatalyst 16](image)

Due to the high chance of racemization of the ligand precursor during its synthesis, the precatalyst 16 is most likely a mixture of two enantiomers (Scheme 3.13). Furthermore, even if it is assumed that an enantiopure ligand was used during synthesis, there is the
possibility of two different diastereomers forming (Scheme 3.14). Initially, coordination of the ligand can occur in two ways, resulting in two different chiral-at-metal stereoisomers; however, due to the amino acid derived chiral centre on the ligand, the two stereoisomers are diastereomers. Fortunately only one product was observed in the NMR, however it is unclear which isomer was generated. Synthesis of a similar compound by Arena et al. revealed that a mixture of diastereomers was first formed which, over time, isomerized to one diastereomer. The isomer where the phenyl group on the chelating ligand points away from the bulky aryl ligand was favoured over the other isomer where the phenyl group was closer to the aryl ligand.\textsuperscript{94} This is likely the case with 16, as the phenyl group on the ligand will want to orient itself away from the \textit{Cp*}, which is even more sterically bulky than the arene ligands used in the previous example.

\textit{Scheme 3.14:} Only one diastereomer is observed in the synthesis of 16

Hydrogenation of acetophenone was attempted with 16, where the catalyst loading was done under the assumption that the catalyst was the neutral iodo complex. The catalyst and substrate was injected as a THF solution into the reactor under 25 bar H\textsubscript{2} at 50 °C, with injection of KO\textsubscript{t}Bu in THF immediately following. A catalyst:base:substrate (C:B:S) ratio of 1:7.5:1500 was used, resulting in 98% conversion after 1 h. The TOF measured was 2565 h\textsuperscript{−1}, much faster than the [Ru(\textit{p}-cymene)(NHC(CH\textsubscript{2})\textsubscript{2}NH\textsubscript{2})(Cl)][PF\textsubscript{6}] catalyst 9 which had a TOF
of 595 h\(^{-1}\), but significantly slower than the \([\text{RuCp}^*(\text{NHC( C}_6\text{H}_4\text{CH}_2\text{NH}_2))(\text{py})][\text{PF}_6]\) catalyst 7, which had a TOF of 17600 h\(^{-1}\) under much milder conditions. Insignificant enantioselectivity (2%) was obtained in the 1-phenylethanol product.

**Table 3.1:** Direct hydrogenation of acetophenone with new Ru(II) precatalyst 13, compared to previous generations of Ru(II) NHC-amino catalysts

<table>
<thead>
<tr>
<th>Catalyst</th>
<th>C/B/S</th>
<th>Temp (°C)</th>
<th>(P(\text{H}_2)) (bar)</th>
<th>Solvent</th>
<th>Conv.</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>1:8:1500</td>
<td>50</td>
<td>25</td>
<td>THF</td>
<td>98%</td>
<td>1h</td>
</tr>
<tr>
<td>7</td>
<td>1:8:2515</td>
<td>25</td>
<td>8</td>
<td>THF</td>
<td>98%</td>
<td>0.5h</td>
</tr>
<tr>
<td>9</td>
<td>1:8:600</td>
<td>50</td>
<td>25</td>
<td>THF</td>
<td>99%</td>
<td>2h</td>
</tr>
</tbody>
</table>
3.1.5 Summary and Conclusions

The syntheses of new amino acid derived amino-imidazolium salts were explored. It was shown that the addition of more non-polar groups onto the ligand made it significantly more soluble in a variety of organic solvents such as acetonitrile and other chlorinated solvents. Unfortunately, poor yields and possible racemization in the substitution reaction of 13 with 1-methylimidazole makes phenylglycinol a poor choice of amino acid. Replacing the phenyl group with a less electron withdrawing aliphatic group may make the elimination reaction less favourable by decreasing the backbone acidity. Thus valine or isoleucine are attractive alternatives to use as the starting amino acid. Furthermore, isoleucine has an additional chiral group which would result in the formation of diastereomers instead of enantiomers were the ligand to epimerize as suspected with phenylglycine, and thus be detectable by NMR.

Were an efficient synthesis of chiral amino-imidazolium salts achieved, it would be a valuable tool in the synthesis of a wide array of metal complexes. Coordination to iron (II) is an obvious next step, as it would benefit by reduced costs, toxicity, and environmental impact. Indeed, the synthesis of an iron catalyst with amino acid derived chiral ligands would result in a highly economical and attractive catalyst. The fact that the NHC precursor is functionalized with an amino group is especially interesting to our group. As previously explored in Chapter 2, the template synthesis of phosphine aldehydes with amines is a powerful tool to synthesize various metal complexes. Exploration of tridentate P-N-C or other similar complexes would be interesting in light of recent developments in the synthesis of other similar tridentate iron (II) hydrogenation catalysts.
3.2 Experimental Section

3.2.1 General Considerations

All of the preparations and manipulations, unless otherwise stated, were carried out under a nitrogen or argon atmosphere using standard Schlenk-line and glovebox techniques. Dry and oxygen-free solvents were used unless otherwise stated. All reagents and solvents were purchased from commercial sources and were used as received. Deuterated solvents were purchased from either Cambridge Isotope Laboratories or Sigma Aldrich, and degassed and dried over molecular sieves prior to use. NMR spectra were recorded on a Varian Mercury 400 MHz or Bruker Avance 400 MHz spectrometer. $^1$H and $^{13}$C {$^1$H} NMR spectra were referenced relative to their respective partially deuterated solvent peaks. All $^{31}$P chemical shifts were measured relative to 85% phosphoric acid as an external reference. The electrospray ionization mass spectrometry (ESI-MS) data were collected on an AB/Sciex QStar mass spectrometer with an ESI source and the DART-MS data were collected on a JEOL AccuTOF-DART mass spectrometer with a DART-ion source (no solvent is required). Elemental analyses were performed using a Perkin-Elmer 2400 CHN elemental analyzer at the Department of Chemistry at the University of Toronto.

3.2.2 Synthesis and Characterization

(R)-Phenylglycinol. Lithium aluminium tetrahydride (5.0 g, 0.13 mol) was weighed into a 500 mL 2-neck round-bottom flask in the glovebox, and suspended in THF (250 mL). The flask was attached to a condenser under N$_2$ pressure and a glass stopper in the fume hood. The mixture was stirred and cooled to 0°C, then phenylglycine (10.0 g, 0.066 mol) was added slowly. The mixture turned green, and as gas formation slowed, the reaction was warmed to room temperature, and was refluxed overnight. The reaction mixture was cooled to rt, then quenched with saturated aqueous K$_2$CO$_3$ in a water bath under N$_2$ flow. Et$_2$O was added until phase separation was visible, then the organic layer removed. The aqueous layer was extracted with Et$_2$O (5 x 30 mL) and dried with anhydrous K$_2$CO$_3$. The ether solution was filtered and solvent removed in vacuo.
to yield \((R)-\text{phenylglycinol}\) as a yellow/white solid. Yield: 68% yield (6.2 g) \(^1\text{H}\) NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.39-7.26 (m, 5H, Ph), 4.06 (dd, \(J_{HH} = 4.3\) Hz, 8.22 Hz, 1H, HC(NH\(_2\))Ph), 3.75 (dd, \(J_{HH} = 4.7\) Hz, 11.0 Hz, 1H, HCH’), 3.56 (dd, \(J_{HH} = 8.2\) Hz, 10.6 Hz, 1H, H’CH), 1.66 (bs, 3H, NH\(_2\), OH).

\((R)-N-(2\text{-hydroxy-1-phenylethyl})\text{phthalimide (12).} (R)-\text{Phenylglycinol (4.00 g, 29.2 mmol)}\) and phthalic anhydride (4.30 g, 29.2 mmol) were added to a flask at 145\(^\circ\)C and stirred for 5 hours. The crude mixture was cooled to rt and dissolved in chloroform. The mixture was purified via silica gel chromatography (3:1 CHCl\(_3\):ethyl acetate, \(rf = 0.4\)). The solvent was removed in vacuo and the product was isolated as a yellow oil. Yield: 86% (6.68 g) \(^1\text{H}\) NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.86 (m, 2H, phthalimide), 7.73 (m, 2H, phthalimide), 7.49 – 7.28 (m, 5H, Ph), 5.49 (dd, \(J_{HH} = 5.1\) Hz, 9.0 Hz, 1H, HC(NR\(_2\))Ph), 4.65 (m, 1H, HCH’), 4.26 (m, 1H, H’CH), 2.43 (m, 1H, OH).

\((R)-N-(1\text{-phenyl-2-tosylethyl})\text{phthalimide (13).} \) The \(N\)-protected phenylglycinol phthalimide (6.68 g, 25 mmol) was dissolved in pyridine (10 mL) and at 0\(^\circ\)C with stirring, tosyl chloride (6.2 g, 32.5 mmol) was added. The reaction mixture was allowed to warm to room temperature slowly, and reacted overnight. Upon completion, H\(_2\)O was added to precipitate the product as a white oil. The product was washed with 10% aqueous citric acid solution (2 x 50 mL), H\(_2\)O (2 x 50 mL). The oil was dried under vacuum overnight to yield the product as a white solid. Yield: 98% (10.333 g) \(^1\text{H}\) NMR (400 MHz, CDCl\(_3\)): \(\delta\) 7.71 (m, 2H, phthalimide), 7.64 (m, 2H, phthalimide), 7.64 (d, \(J_{HH} = 8.6\) Hz, 2H, tosyl CA\(_r\)-H), 7.37 – 7.20 (m, 5H, Ph), 7.16 (d, \(J_{HH} = 8.6\) Hz, 2H, tosyl CA\(_r\)-H), 5.51 (dd, \(J_{HH} = 5.1\) Hz, 10.2 Hz, 1H, H(\(\text{NR}_2\))HC), 5.16 (t, \(J_{HH} = 10.6\) Hz, 1 H, HCH’), 4.51 (dd, \(J_{HH} = 5.5\) Hz, 10.6 Hz, 1H, H’CH), 2.33 (s, 3H, tosyl-CH\(_3\)).
1-methyl-2-(2-phenyl-2-(isoindole-1,3-dione)ethyl)imidazolium tosylate (14). The N-protected phenylglycinol tosylate 13 (200 mg, 0.475 mmol) and 1-methylimidazole (250 mg, 3.00 mmol) was refluxed for 24 h. The crude product was mixed with toluene causing phase separation. The toluene layer was removed and the residue was dissolved in H$_2$O, then NaHCO$_3$ was added until gas evolution ceased. The aqueous layer was extracted with DCM (6 x 30mL), the organic layer was dried with Na$_2$SO$_4$, and the solvent removed in vacuo. The product was washed vigorously with toluene (2 x 30 mL) and dried in vacuo to yield the product was a white solid. Yield: 30% (71 mg).

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 10.08 (s, 1H, imidazolium C-H), 7.79 (m, 2H, phthalimide), 7.72 (m, 2H, phthalimide), 7.77 (d, $J_{HH} = 8.2$ Hz, 2H, tosyl C$_{Ar}$-H), 7.56 – 7.30 (m, 5H, Ph), 7.16 (t, $J_{HH} = 1.6$ Hz, 1H, imidazolium C-H), 7.12 (d, $J_{HH} = 7.8$ Hz, 2H, tosyl C$_{Ar}$-H), 7.08 (t, $J_{HH} = 1.6$ Hz, 1H, imidazolium C-H), 5.83 (dd, $J_{HH} = 6.3$ Hz, 10.2 Hz, 1H, HC(NR$_2$)Ph), 5.44 (dd, $J_{HH} = 9.8$ Hz, 13.7 Hz, 1 H, H'CH$^+$), 5.25 (dd, $J_{HH} = 6.3$ Hz, 14.1 Hz, 1H, H'CH), 3.98 (s, 3H, imid-CH$_3$), 2.32 (s, 3H, tosyl-CH$_3$).

Methyl-2-(2-phenyl-2-aminoethyl)imidazolium tosylate (15). The N-protected imidazolium salt (150 mg, 0.298 mmol) and excess hydrazine monohydrate (4 mL) was stirred in 95% ethanol (15 mL), and heated at 50 °C overnight. The solvent was removed in vacuo and the residue was re-suspended in DCM or chloroform. Insolubles were filtered off and the filtrate was concentrated under vacuum to yield the product as white solid. Yield: 94% (50 mg). $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 9.87 (s, 1H, imidazolium C-H), 7.83 (d, $J_{HH} = 8.2$ Hz, 2H, tosyl C$_{Ar}$-H), 7.35 – 7.30 (m, 5H, Ph), 7.17 (d, $J_{HH} = 7.8$ Hz, 2H, tosyl C$_{Ar}$-H), 7.07 (t, $J_{HH} = 2.0$ Hz, 1H, imidazolium C-H), 6.93 (bs, 1H, imidazolium C-H), 4.50 (m, 2 H, HCH$^+$), 4.44 (dd, $J_{HH} = 5.5$ Hz, 11.4 Hz, 1H, HC(NR$_2$)Ph), 3.94 (s, 3H, imid-CH$_3$), 2.56 (bs, 3H, NH$_2$), 2.37 (s, 3H, tosyl-CH$_3$). MS (ESI, methanol/water; $m/z^+$): 202.1 ([C$_{12}$H$_{16}$N$_3$]$^+$).
[Ru(η⁵-C₅(CH₃)₅)(C–NH₂)I] (16). A Schlenk flask was charged with silver(I) oxide (19 mg, 0.080 mmol), RuCp*'(COD)Cl (20 mg, 0.054 mmol), and sodium iodide (127 mg, 0.81 mmol) in acetonitrile (1 mL) with molecular sieves (3 Å). A solution of the imidazolium salt (22 mg, 0.054 mmol) in acetonitrile (2 mL) was also prepared under an argon atmosphere. This was added to the reaction mixture containing silver(I) oxide, RuCp*'(COD)Cl, and sodium iodide in acetonitrile. The reaction mixture was stirred at 25°C, protected from light for 20 hrs. After the reaction had gone to completion, the resulting mixture was filtered through a pad of Celite. The solvent was then removed in vacuo to yield a dark red solid. This was washed with toluene (2 × 1 mL) and diethyl ether (2 × 1 mL) then dried in vacuo to yield the product as a red solid. Yield: 66% (20 mg). ¹H NMR (400 MHz, CD₂Cl₂): δ 7.37 – 7.14 (m, 5H, Ph), 6.92 (d, JHH = 1.8 Hz, 1H, imid-H), 6.77 (d, JHH = 1.8 Hz, 1H, imid-H), 3.91 (dd, JHH = 10.4 Hz, 13.3 Hz, 1H), 3.86 (s, 3 H, imid-CH₃), 3.73 (m, 1H), 3.29 (m, 1H), 1.62 (s, 5 H, Cp*). MS (ESI, methanol/water; m/z): 438.1 [M – I-]+, 470.1 [M – I- + MeOH]+.

3.2.3 Catalysis

Tetrahydrofuran that was used for all of the catalytic runs for H₂-hydrogenation was stirred over sodium for 2-3 days under argon, and distilled from sodium benzophenone ketyl prior to use. All of the substrates were vacuum-distilled, dried over activated molecular sieves, and stored under argon prior to use. All of the hydrogenation runs were performed at constant pressures using a stainless steel 50 mL Parr autoclave. The temperature was maintained at 50°C using a constant temperature water bath. The reactor was flushed several times with hydrogen gas at 2-4 bar prior to the addition of catalyst/substrate and base solutions.

The catalyst 13 (3 mg, 5.3 µmol) and acetophenone (959 mg, 8.0 mmol), and potassium tert-butoxide (5 mg, 0.040 mmol) were dissolved in THF (5 mL and 2 mL, respectively) under an argon atmosphere. The catalyst/substrate and base solutions were taken up by means of two separate syringes and needles in a glovebox. The needles were stoppered and the syringes were taken to the reactor. The solutions were then injected into
the reactor against a flow of hydrogen gas. The hydrogen gas was adjusted to the desired pressure (25 bar). Small aliquots of the reaction mixture were quickly withdrawn with a syringe and needle under a flow of hydrogen at timed intervals by venting the Parr reactor at reduced pressure. Alternatively, small aliquots of the reaction mixture were sampled from a stainless steel sampling dip tube attached to a modified Parr reactor. The dip tube was 30 cm in length with an inner diameter of 0.01 in., and a swing valve was attached to the end of the sampling tube. Three small aliquots of sample were thereby withdrawn quickly at timed intervals by opening the swing valve, and the first two aliquots were discarded. All samples were diluted to a total volume of approximately 2 mL using oxygenated THF prior to GC analyses.

A Perkin-Elmer Clarus 400 chromatograph equipped with a chiral column (CP chiral-Dex CB 25 m × 2.5 mm) and an auto-sampling capability was used for gas chromatography (GC) analyses. Hydrogen was used as a mobile phase at a column pressure of 5 psi with a split flow rate of 50 mL/min. The injector temperature was 250°C and the FID temperature was 275°C. All of the conversions are reported as an average of two GC runs. The reported conversions were reproducible.

The substrate, product, oven temperature (T) and the retention times for the substrate ($t_s$) and product ($t_p$) are as follows:

Acetophenone, 1-phenylethanol, T = 130 °C, $t_s = 4.72$ min, $t_p = 7.60$, 8.09 min.
References


