UC Berkeley
UC Berkeley Electronic Theses and Dissertations

Title
Nickel- and Palladium-Catalyzed Cross Coupling Reactions: Reaction Development and Mechanistic Studies

Permalink
https://escholarship.org/uc/item/85p1s81s

Author
Green, Rebecca

Publication Date
2016

Peer reviewed|Thesis/dissertation

eScholarship.org Powered by the California Digital Library
University of California

Nickel- and Palladium-Catalyzed Cross Coupling Reactions: Reaction Development and Mechanistic Studies

By

Rebecca Green

A dissertation submitted in partial satisfaction of the
requirements for the degree of

Doctor of Philosophy
in
Chemistry
in the
Graduate Division
of the
University of California, Berkeley

Committee in charge:
Professor John F. Hartwig, Chair
Professor F. Dean Toste
Professor John Arnold
Professor Alexander Katz

Spring 2016

Abstract

Nickel- and Palladium-Catalyzed Cross Coupling Reactions:
Reaction Development and Mechanistic Studies

By

Rebecca Green

Doctor of Philosophy in Chemistry

University of California, Berkeley

Professor John F. Hartwig, Chair

The following dissertation discusses the development of a nickel catalyst for the synthesis of Csp^2-Csp bonds in addition to the development and mechanistic studies of nickel and palladium catalysts for the synthesis of Csp^2-N bonds.

The first chapter is a review of the cross-coupling reactions discussed in this dissertation. Nickel and palladium will be compared with respect to physical properties and reactivity differences. The challenges associated with nickel-catalyzed cross coupling will be illustrated, while drawing analogies to analogous palladium-catalyzed reactions. The literature background for the synthesis of Csp^2-Csp bonds, catalyzed by palladium and palladium/copper catalytic systems, will be reviewed, while highlighting the challenges and limitations of the field. The field of Csp^2-N bond-forming reactions will be examined, as the differences in reactivity between nickel and palladium will be emphasized.

Chapter 2 discusses our efforts towards the development of a nickel catalyst for the development of a Csp^2-Csp bond forming reaction, performed in the absence of a copper co-catalyst.

Chapter 3 describes the development of a single-component nickel complex that catalyzes the coupling of aryl chlorides with primary alkylamines. A series of mechanistic experiments, including synthesis of catalytic intermediates and kinetic experiments, were performed to elucidate the mechanism of the reaction.

Chapter 4 discusses our report the palladium-catalyzed coupling of aryl halides with ammonia and gaseous amines as their ammonium salts. A difference in selectivity between reactions of aryl chlorides and aryl bromides was discovered and investigated.

Chapter 5 describes the development of a single-component nickel catalyst for the coupling of aryl chlorides with ammonia and ammonium sulfate to form the corresponding primary arylamines. The application of ammonium salts was extended to the coupling of gaseous amines, such as methylamine and ethylamine, which were subjected to the reaction conditions as their hydrochloride salt.

Table of Contents

Chapter 1	**Overview of Methods for Csp-Csp^2, Csp^2-N Bond Forming Reactions**	1
	1.1 Overview of Nickel-Catalyzed Cross-Coupling Reactions	2
	1.2 Methods for the Preparation of Arylalkynes	3
	1.3 Methods for the Preparation of Alkyl-Arylamines	6
	1.4 Methods for the Preparation Primary of Arylamines	9
	1.5 References	12
Chapter 2	**Development of Nickel-Catalyzed Alkynylation of Aryl Halides**	16
	2.1 Introduction	17
	2.2 Results and Discussion	18
	2.3 Conclusion	24
	2.4 Experimental	24
	2.5 References	44
Chapter 3	**Nickel-Catalyzed Amination of Aryl and Heteroaryl Chlorides and Bromides with Primary Aliphatic Amine**	46
	3.1 Introduction	47
	3.2 Results and Discussion	48
	3.3 Conclusion	66
	3.4 Experimental	67
	3.5 References	89
Chapter 4	**Palladium-Catalyzed Amination of Aryl Chlorides and Bromides with Ammonium Salts**	91
	4.1 Introduction	92
	4.2 Results and Discussion	93
	4.3 Conclusion	99
	4.4 Experimental	100
	4.5 References	115
Chapter 5	**Nickel-Catalyzed Amination of Aryl Chlorides with Ammonia or Ammonium Salts**	118
	5.1 Introduction	119
	5.2 Results and Discussion	119
	5.3 Conclusion	126
	5.4 Experimental	127
	5.5 References	175

Acknowledgements

It is quite unreal to believe that I am receiving a PhD from UC Berkeley. When I was still a naïve undergraduate, I had talked about Berkeley being my dream graduate school. However, when it came down to sending out applications, Berkeley was not on the list, to my family's surprise. I had favored UIUC, since the group that appealed the most to me was located there. However, after my acceptance letter to UIUC arrived, I heard the rumor that the professor I wanted to work for was moving to Berkeley. After meeting with him and somehow convincing him that I would be a valuable student in his group, my application to UC Berkeley was submitted – two months past the deadline. As a rather unconventional method to arrive at the university, I have always been grateful for the feeling of home it provided for just over four years. It has been nothing but a tremendous experience and I am forever thrilled at how everything ended up.

First, I would like to thank those who helped me grow as a scientist, before I even arrived at Berkeley. Daniel Rivalti and Rodrigo Mendoza-Sanchez taught me just about everything I know about organic synthesis. I am so happy to the wonderful mentorship they provided to me, despite being just an undergrad.

This degree would be nothing if not for Professor John Hartwig. I'm still not sure what he saw in me that one visit weekend in Illinois that convinced him that I should join his group as he moves to Berkeley, but I will be forever grateful. Under his patient guidance and scholarly mentorship, I learned a lot about chemistry and about how to be a successful scientist. He was always very supportive of my efforts and I appreciate him taking the time to teach me how to conduct research in an organized and informed fashion, especially as a new graduate student. I am very grateful for the opportunities to learn about many fields of organic and organometallic chemistry, through subgroup and individual meetings and catalysis lunch activities. I appreciate the effort he took to teach me how to write scientifically and how to present my research in a coherent fashion. Lastly, I want to thank him for allowing me to choose and direct my research projects, which allowed me to work on chemistry that I am passionate about.

Over my time in the Hartwig group at Berkeley, I had the pleasure of working alongside group members who were not only brilliant chemists, but also wonderful people. Thank you to some of the older graduate students, Yichen Tan, Carl Liskey, and Allie Strom, and as well as a few postdocs, Eric Simmons and Ramesh Giri, who taught me the ropes and were patient with me as I began working in the group. Thank you, Christo Sevov, for being a kind friend and an infinite source of knowledge of kinetics and mechanistic insight. You always have great insight and your friendship is something I will always treasure. To some of the "younger" graduate students, Matt Larsen, Mike Mormino, and Taegyo Lee: I had the pleasure of watching them grow during their graduate career and they have become treasured friends. Thank you to Sarah Lee, Jeff Holder, and Jason Beiger, who came to the group as postdocs with a lot of knowledge and a patient ear to listen to my problems. Mark Bartlett is a dear friend and his ability to raise such wonderful kids while being a brilliant and productive scientist is inspirational. Lastly, I have unforgettable memories from my colleagues and friends in 705: Andy Brusoe, York Schramm, and Sophie Arlow. I will always treasure all of our conversations, chemistry-related or not.

A sincere thank you goes to Micah Ziegler, one my dearest friends in the Berkeley chemistry department. I enjoy discussing chemistry with you and value all of our conversations. Thank you for always being there to help me with anything.

One more person from UC Berkeley deserves a big hug and a thank you: Anneke Runtupalit. Thank you for keeping the group functional and for helping us navigate through the bureaucracy of UC Berkeley. You are so supportive of us and are the real "group mom".

One of the things I will miss most about living in the Bay Area will be not being able to see Minh Truong on a regular basis. What are the chances we would find a "kindred spirit" when we signed up for graduate housing at Berkeley? I love discussing our cooking and baking adventures, going shopping at Anthropologie or Sur la Table, and all of our traditional holiday celebrations. Living in a six-bedroom apartment where a helmet was required to open the freezer and eggs occasionally exploded was worth it so I could meet one of my closest friends.

To my girls, Jessica Ho-Wo-Cheong and Wenwen Liu, it doesn't matter if we only see each other every once in a while, you will always have a special place in my heart, and just the thought of making s'mores and eating lava cakes brings back a rush of wonderful memories. Thank you for always making sure I stay true to myself.

Thank you to my parents for always supporting me throughout my journey to and throughout Berkeley. You taught me to be myself, to stick to my beliefs, and never to forget where I came from. Merci, maman, pour tes conseils, sa sagesse, et ton support pour ma carrière et pour nos discussions de repas et de recettes. Thanks, dad, for teaching me, among many things, that life is too short to drink cheap wine – I'm sorry it took me so long to realize it. Je vous aime fort fort fort.

Finally, I can't begin to express how grateful I am to have my husband, Patrick Fier, in my life. He is a brilliant scientist who taught me a lot about organic chemistry, but is also an incredibly kind, supportive, and loving person, and most importantly, he is my best friend. I treasure every moment we spend together and I am very excited for all of our future adventures.

CHAPTER 1

Overview of Methods for Csp-Csp^2, Csp^2-N Bond-Forming Reactions

1.1 Overview of Nickel-Catalyzed Cross-Coupling Reactions

The construction of C-C and C-heteroatom bonds are valuable reactions that provide synthetic chemists with methods for the construction of complex molecular structures in few synthetic steps. Palladium complexes have been a mainstay as reliable and active catalysts in the field of cross-coupling reactions, in which an electrophile is coupled with a nucleophile. With such high reactivity observed with the precious metal palladium, there is interest to develop catalysts based on the abundant nickel metal. At first glance, it might seem that the major difference between nickel, a first row transition metal in the group 10 series, and palladium, its second row counterpart, is the price, a reflection of its natural abundance. Although nickel and palladium are common to a period and therefore share many similarities, their differences allow each metal catalyst to be unique and therefore exhibit distinct reactivities and selectivities.[1,2]

Palladium has been extensively studied in the past four decades as a valuable catalyst for various transformations, in particular cross coupling reactions. Indeed, the discovery and development of these reactions was awarded the 2010 Nobel Prize in Chemistry. The literature of palladium-catalyzed cross-coupling reactions encompasses not only the development of highly active catalysts for the desired transformations, but also mechanistic studies on both the catalytic reactions and the elementary steps that comprise the catalytic cycle.[3,4] It was only with this crucial and deep understanding of the fundamental reactivity that new ligands and precatalysts were developed to achieve the impressive reactivity with high turnover numbers reported in the recent literature.

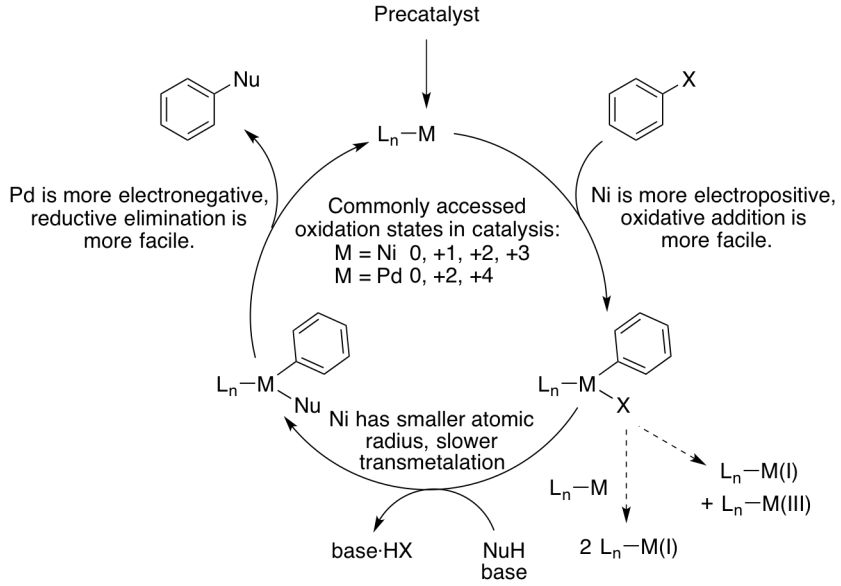
Extensive studies and applications over the past few decades have often focused on precious metals, such as palladium, due to their reliability and reactivity. Hence, a combination of the high reactivity of the complexes, numerous mechanistic experiments, and typically low sensitivity to oxygen and moisture has allowed palladium catalysis to flourish with numerous coupling reactions and with very low catalyst loadings.[5,6] Despite the low catalyst loadings required for high reactivity, the metal is not highly abundant and therefore costly. In lieu of these limitations, there is a need to develop new base metal catalysts with high reactivity, which, with the help of mechanistic studies, will be comparable to their precious metal analogs.

Given the fine balance of similarities and differences between the two metals, an opportunity presents itself not only to explore new reactivity, but also to develop new catalysts as alternatives to precious metal catalysts. These differences in reactivity are often overlooked and are therefore are summarized in Scheme 1.1.[2] In terms of physical properties, nickel has a smaller atomic radius than palladium, rendering the metal complex to be congested. However, since nickel can readily adopt a five-coordinate geometry, the rates of ligand substitution by nickel are faster than the rates of ligand substitution by palladium.[7]

Nickel is more electropositive than palladium, which in turn allows nickel to be more easily oxidized from Ni(0) to Ni(II) than palladium from Pd(0) to Pd(II). This difference is quite pronounced in the overall transformations catalyzed by nickel. For example, phenol derivatives[8-11], aryl nitriles[12], and aryl fluorides[13-15] are successful cross-coupling electrophiles with nickel. However, these are not good coupling electrophiles with palladium catalysts.

Furthermore, nickel catalysts are known to access numerous oxidation states, and proceed through radical mechanisms,[16-18] while palladium catalysts typically remain in the Pd(0)/Pd(II) oxidation states for typical cross-coupling reactions. [19]

Scheme 1.1 Comparison of Ni and Pd in Cross-Coupling Reaction Mechanism



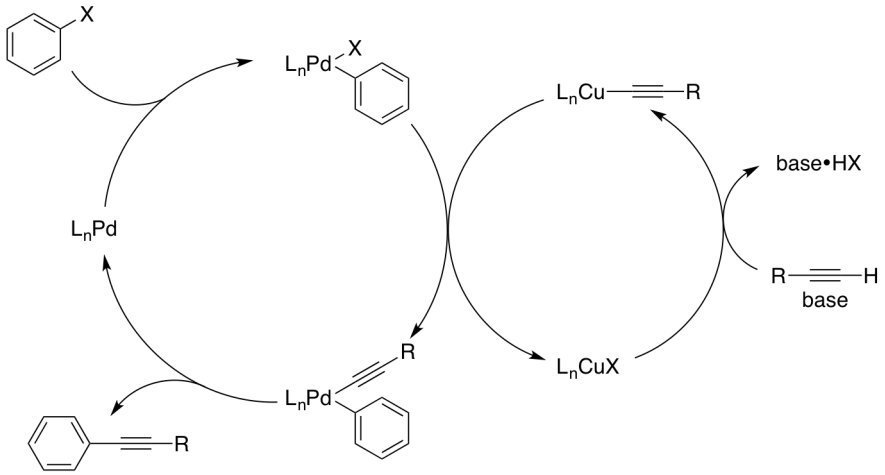
The fundamental differences between nickel and palladium are perhaps subtle, but there are a multitude of differences in reactivity. Therefore, with a greater understanding of the mechanism of the elementary steps, in parallel with the development of new catalysts, the repertoire of nickel chemistry is growing rapidly.

1.2 Methods for the Preparation of Arylalkynes

Alkynes are a prevalent functional group in pharmaceutical and agrochemical compounds, and conjugated materials. In addition, alkynes are a valuable synthetic intermediate in organic synthesis. They can be readily hydrogenated to the corresponding E- or Z-alkenes. In addition, there is vast literature on the hydrofunctionalization of alkynes to form other functional groups, such as enamines,[20,21] α,β-unsaturated esters[22] and nitriles,[23-25] and vinyl silanes.[26-29]

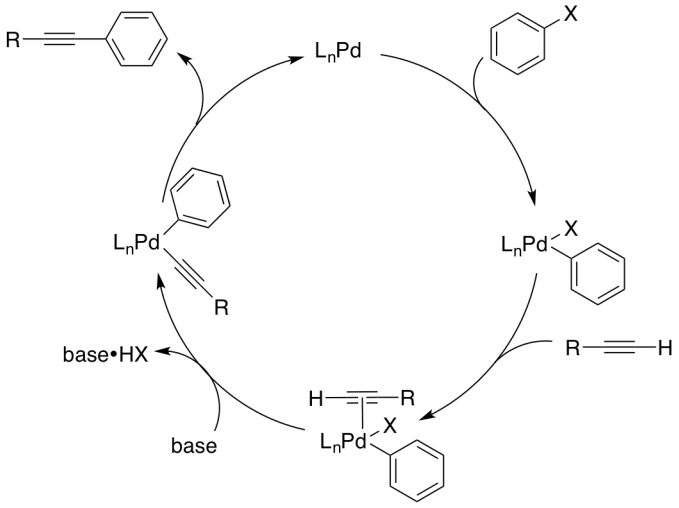
Terminal alkynes are readily prepared from aldehydes via the Corey-Fuchs reaction.[30] There are a few methods to functionalize terminal alkynes. The Csp-H bond of the terminal alkyne is quite acidic (phenylacetylene pKa = 28.8 in DMSO[31,32]) and can therefore be readily deprotonated and react with electrophiles, such as alkyl halides or carbonyl compounds, to form alkyl-substituted alkynes. Alternatively, a palladium-catalyzed cross-coupling reaction of an aryl electrophile with a terminal alkyne forms an arylalkyne.[33] Subsequently, a copper co-catalyzed variant, named the Sonogashira reaction, was introduced to increase catalyst turnover.[34] The copper co-catalyst reacts with the alkyne and base, to form an alkynyl-copper transmetalation reagent, and transfers the alkyl-moiety to the palladium(II) complex (Scheme 1.2).

Scheme 1.2 Proposed Catalytic Cycle for Pd/Cu-Catalyzed Sonogashira Reaction



Although the copper is a valuable co-catalyst to facilitate one of the elementary steps, its presence has some harmful effects on the catalytic cycle. In part, the copper-catalyzed Glaser coupling reaction is a side-reaction that has been observed in Pd/Cu-catalyzed Sonogashira reactions. In addition, alkyne oligomerization reactions consume the alkyne irreversibly. In lieu of these concerns, the copper-free Sonogashira reaction received more attention than the copper co-catalyzed variant.[35,36] In copper-free Sonogashira reactions, a vacant coordination site on the palladium (II) complex allows coordination of the alkyne via the π-bond to acidify the Csp-H bond, subsequently forming the alkynyl-Pd(II) complex after deprotonation by base (Scheme 1.3).[37]

Scheme 1.3 Proposed Catalytic Cycle for Pd-Catalyzed Sonogashira Reaction

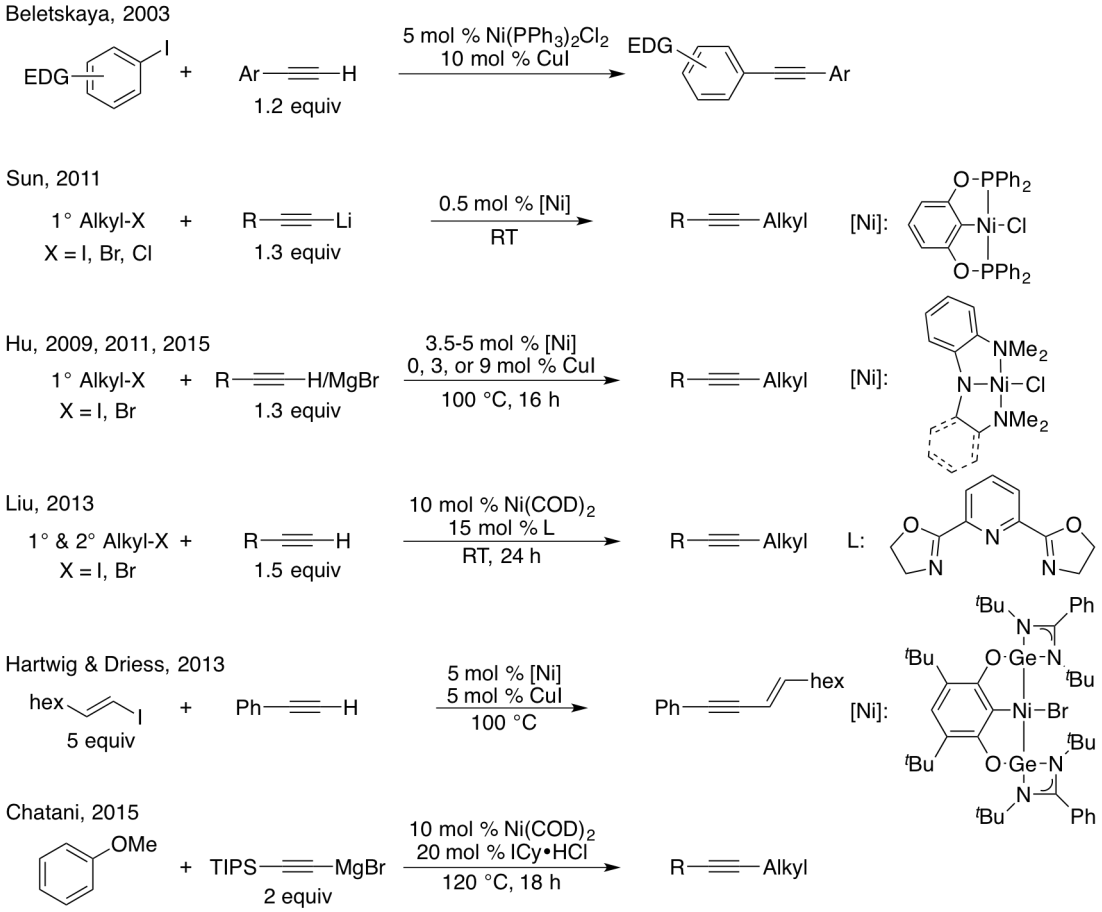


One of the major side-reactions of the Sonogashira reaction is the polymerization of the alkyne. Alkyne oligomerization can occur either by migratory insertion of an alkyne into a metal-carbon bond or by reductive coupling to a metal of low oxidation state. In some cases, when the rates of oligomerization and cross-coupling reactions are comparable, the alkyne is protected in the form of an alkynyl reagent, such as a silanol,[38-

[40] or a silane.[41] In the presence of an appropriate activating agent, an alkynyl-metal species is formed in situ. The organometallic reagent subsequently undergoes transmetalation with the palladium catalyst to afford the required Pd(II) complex to undergo reductive elimination and form the desired cross-coupled product.

Despite these advances in the development of the palladium-catalyzed Sonogashira reaction, there are few reports of a Ni-catalyzed variant. Nickel complexes are known to catalyze alkyne oligomerization reactions via cycloaddition.[42,43] Therefore, this known reactivity must be suppressed under Sonogashira coupling conditions, such that the rate of the Csp^2-Csp coupling reaction is faster than the undesired oligomerization reaction.

Scheme 1.4 Summary of Ni-Catalyzed Sonogashira Reactions



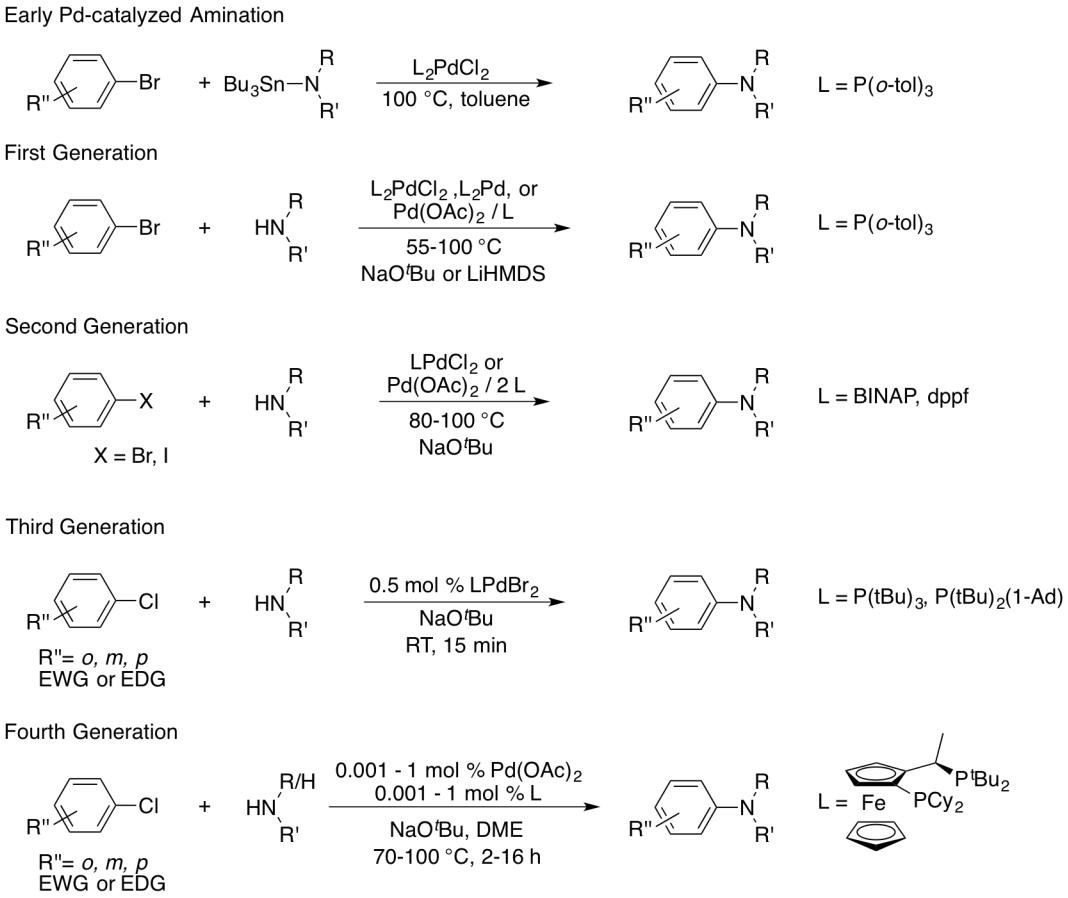
In light of these challenges, there are few reports on the Ni-catalyzed Sonogashira reaction, in particular in the absence of a copper co-catalyst. The few examples in the literature are outlined in Scheme 1.4. There are only two examples of the coupling of an aryl or vinyl electrophile with a free alkyne, both with copper co-catalysts.[44,45] The other reports in the literature are coupling reactions between an alkyl electrophile and a free alkyne[46-48] or with an alkynyl organometallic species.[49-51] There are no reports of the copper-free nickel-catalyzed coupling of an aryl electrophile with a free

alkyne. With these limitations in mind, our studies towards the development of this reaction are detailed in Chapter 2.

1.3 Methods for the Preparation of Alkyl-Arylamines

Substituted anilines are a common functional group in pharmaceutical and agrochemical compounds. Although anilines are a common functional group, the classical methods to prepare them are limited. The nitration of arenes followed by reduction requires harshly acidic reaction conditions and form genotoxic by-products, thereby limiting this method to the early stages of a synthesis. If an aniline functional group is already present in the molecule, it can be functionalized by either unselective alkylation or low-yielding reductive amination of the aniline. Anilines are frequently prepared by nucleophilic aromatic substitution of electron-deficient aryl halides. In light of these limitations, transition metal-catalyzed amination of aryl halides emerged as a powerful method to form aryl C-N bonds.[5,52,53] Indeed, the Csp^2-N bond-forming reaction is the third most frequently used reaction in medicinal chemistry.[54]

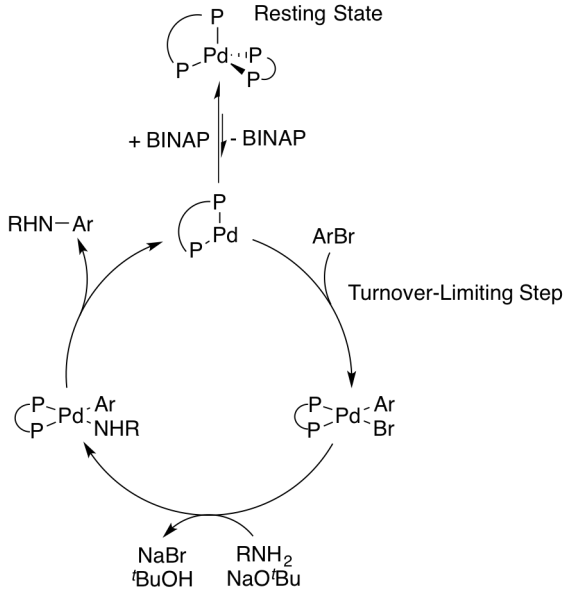
Scheme 1.5 First Reports and Improvements of the Palladium-Catalyzed Amination with Aryl Halides



The cross coupling reaction of amines with aryl electrophiles has been extensively developed with palladium catalysts. The original reports and selected improvements are shown in Scheme 1.5.

Kosugi et al. reported the first coupling of a tin amide with an aryl halide in 1983, albeit restricted to dialkylamides and electron-neutral aryl electrophiles.[55] Simultaneously, Hartwig[56] and Buchwald[57] independently reported tin-free conditions to conduct the coupling of a secondary alkylamine with an aryl bromide in the presence of a palladium catalyst ligated by tri-*ortho*-tolylphosphine. The second-generation catalyst, a palladium complex ligated by the bidentate aryl phosphine ligands such as BINAP[58,59] and dppf[60] expanded the scope of nucleophiles to include primary amines. The third-generation palladium catalysts containing bulky alkyl monodentate phosphine ligands extended the reaction scope to incorporate aryl chlorides and catalyst loadings to be lowered to 0.5 mol %; however, primary amines were not coupled effectively.[61] The fourth-generation catalysts consisted of palladium ligated by a Josiphos ligand derivative, allowing for the use of aryl and heteroaryl chlorides as electrophiles and primary amines and ammonia as nucleophiles.[62,63]

Scheme 1.6 Proposed Mechanism for the BINAP-Ligated Pd-Catalyzed Coupling of Aryl Bromides with Primary Alkylamines



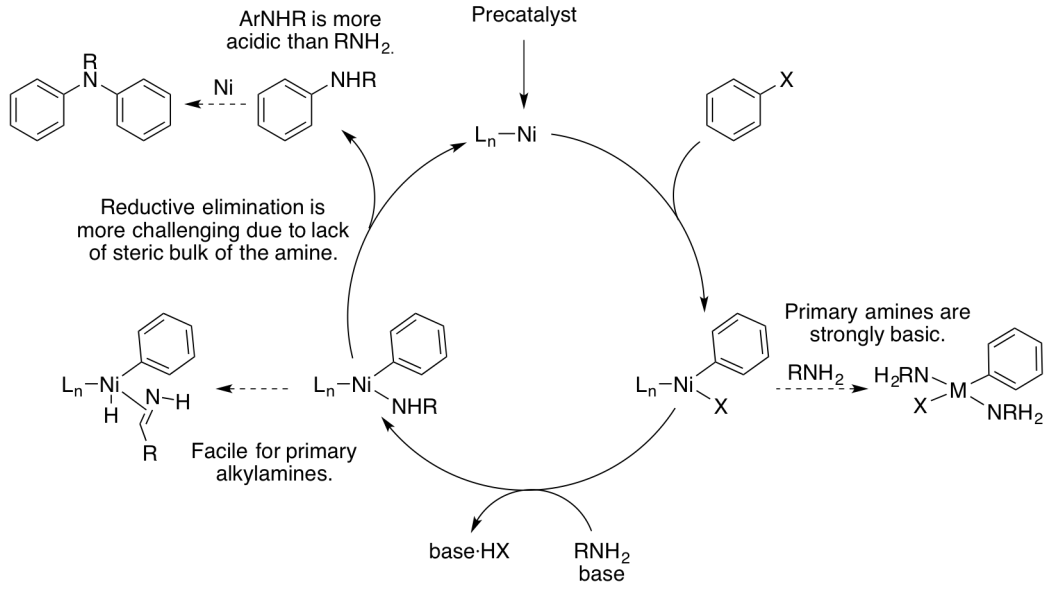
The studies towards the development of new catalysts and ligands for the transformation were conducted in parallel with mechanistic studies of the elementary steps and the catalytic cycle. Extensive studies conducted by the Hartwig, Buchwald, and Blackmond groups led to a proposed mechanism for the coupling of aryl bromides with primary alkylamines, catalyzed by a BINAP-ligated Pd(0) catalyst.[64] (Scheme 1.6) The resting state of the reaction was observed as $(BINAP)_2Pd$. The complex reversibly dissociates BINAP, as evidenced by the inverse first order kinetics measured for the ligand, to enter the catalytic cycle and form a reactive species, (BINAP)Pd. This unsaturated complex undergoes oxidative addition of the aryl bromide, which is the

turnover-limiting step of the reaction. It was demonstrated that the Pd(0) complex that reacts with the aryl bromide is not ligated by amine, but rather simply by the phosphine ligand.[65]

Despite the significant advances and efficient catalysts developed with palladium to couple aryl electrophiles with amines, nickel catalysts have not yet been shown to exhibit similar reactivity or substrate scope. Analogous to the second-generation palladium catalysts for the amination of aryl bromides, Buchwald and co-workers disclosed that dppf-ligated nickel complexes were active towards the coupling of aryl chlorides with secondary alkyl amines and anilines (Scheme 1.7).[66] This was followed up by reports by Fort on the coupling of aryl chlorides with a 2,2'-bipyridine ligated-nickel catalyst[67-69] and Knochel on the coupling of aryl chlorides with 3,5,6,8-tetrabromo-1,10-phenanthroline-ligated nickel catalyst.[70] N-heterocyclic carbenes were identified as versatile ligands for the amination of aryl chlorides,[71-74] pivalates,[75] carbamates,[76,77] sulfamates,[73,77,78] phosphates,[79] sulfonates,[80,81] and methyl ethers.[82] Recently, air-stable nickel catalysts ligated by phosphines were reported for the coupling of various aryl electrophiles.[83,84]

Despite the growing repertoire of the aryl electrophiles in the C-N coupling, the scope of the amine nucleophile has not expanded significantly beyond piperidine, morpholine, aniline, and their respective derivatives (Scheme 1.7). There are a few unique challenges that arise in the coupling of aryl electrophiles with primary alkylamines (Scheme 1.8). Firstly, the lack of steric hinderance and strong basicity allow alkylamines to coordinate and displace phosphine ligands to form amine-ligated Ni(II) complexes, which may exhibit low reactivity and/or selectivity for the desired amination reaction. Furthermore, the Ni(II) amido complex, has two easily accessible β-H atoms, rendering a facile β-H elimination reaction, which results in the formation of imine and arene.[85] In addition, the lack of steric bulk around the amino complex may retard the rate

Scheme 1.8 Challenges for Ni-Catalyzed Coupling of Aryl Electrophiles with Primary Aliphatic Amines



of reductive elimination. Lastly, the product, an aryl-alkylamine, is more acidic, and hence more reactive towards a subsequent amination reaction, than the alkylamine starting material.

Despite the aforementioned challenges on the nickel-catalyzed coupling of aryl electrophiles with primary alkylamines, our group reported a single-component nickel(0), (BINAP)Ni(η^2-NCPh) for this transformation.[86] The development of the catalyst, its reaction scope, and the mechanistic studies are discussed in Chapter 3. The single-component Ni(0) complex, although highly active, is air-sensitive. Following our report, an air-stable variant, (BINAP)Ni[$P(OPh_3)$]$_2$ was reported in the literature, but required an increased catalyst loading (5 mol %) for the reactions to occur to completion.[87]

As the field stands, the BINAP-ligated catalysts are the only nickel catalysts reported for the coupling of primary alkylamines with aryl electrophiles. The catalyst loadings are relatively low (1-4 mol %), but the catalysts are not as active as palladium catalysts for the analogous reactions (0.001-1 mol %). Our reported mechanistic studies, discussed in detail in Chapter 3, suggest that oxidative addition is the turnover-limiting step of the reaction and that displacement of the ligand by amine leads to significant amounts of catalyst decomposition. It will be crucial in the future to develop reaction conditions in which the ligand is electron-rich and strongly coordinating to promote a facile oxidative addition and that amine concentration is low to minimize catalyst decomposition.

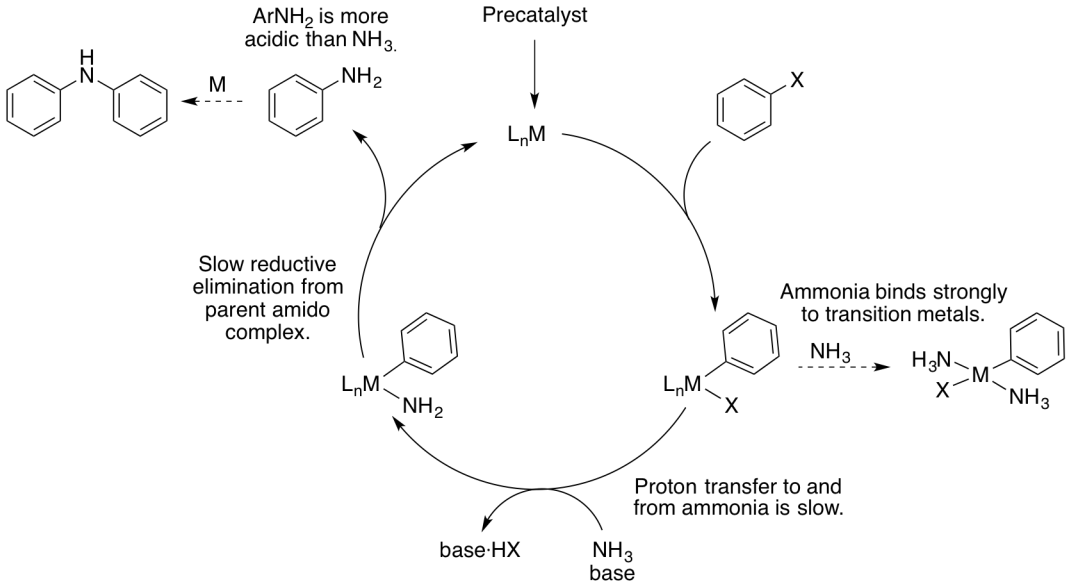
1.4 Methods for the Preparation of Primary Arylamines

1.4.1 Overview of Transition-Metal Catalyzed Synthesis of Primary Anilines

There are distinctive challenges associated with the synthesis of primary arylamines via transition-metal catalyzed C-N coupling reactions of ammonia because of the intrinsic properties of the reagent. First, because ammonia is a gas, it must be dissolved in the reaction medium for the reaction to proceed. Second, ammonia is a strongly coordinating ligand and can readily bind to metal complexes, leading to loss of reactivity and selectivity for the catalytic reaction. Third, the mild basicity and mild acidity of ammonia disfavor proton transfers to and from the reagent, which are required to form a parent amido complex. Furthermore, the lack of steric bulk around the amido complex due to the absence of substituents, leads to a slow reductive elimination. Last, the aniline product is more acidic than ammonia. Hence, the aniline product can react with aryl halide to form undesired diarylamine. These challenges are summarized in Scheme 1.9.

To avoid using ammonia as a reagent, ammonia surrogates were investigated as valuable alternatives. For example, coupling with benzophenone imine affords the N-aryl benzophenone imine, which hydrolyzes readily to the corresponding aniline and benzophenone.[66,88,89] In addition, bis(trimethylsilyl)amides,[90] amides,[91] and carbamates[92] undergo the coupling reaction to afford the protected aniline. These ammonia surrogates are summarized in Scheme 1.10.

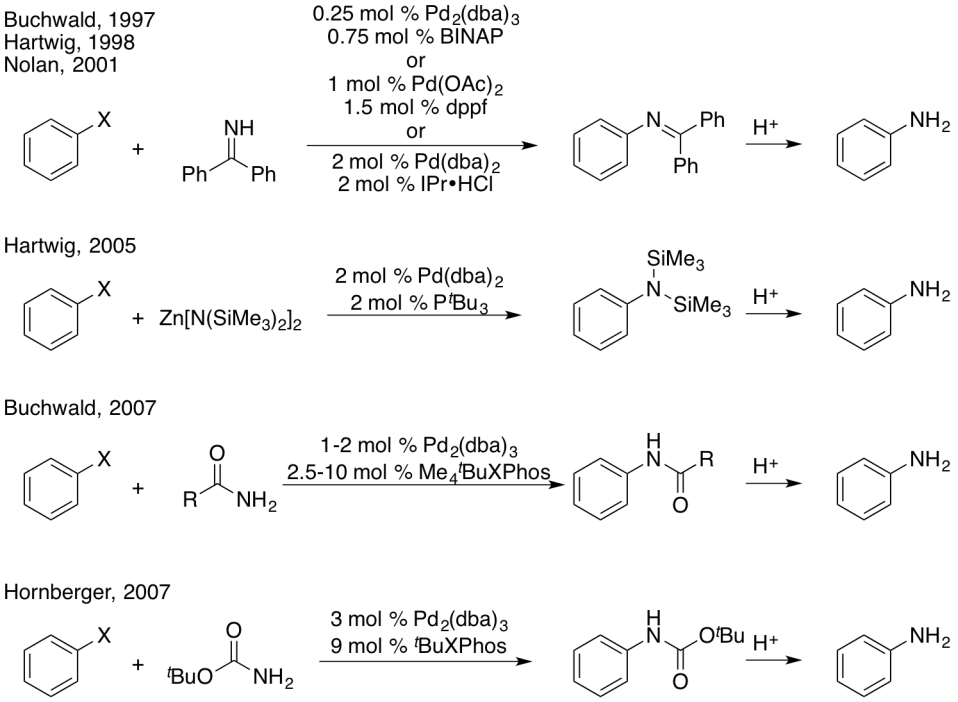
Scheme 1.9 Challenges for Transition Metal Catalyzed Coupling of Aryl Electrophiles with Ammonia



1.4.2 Overview of Pd-Catalyzed Synthesis of Anilines

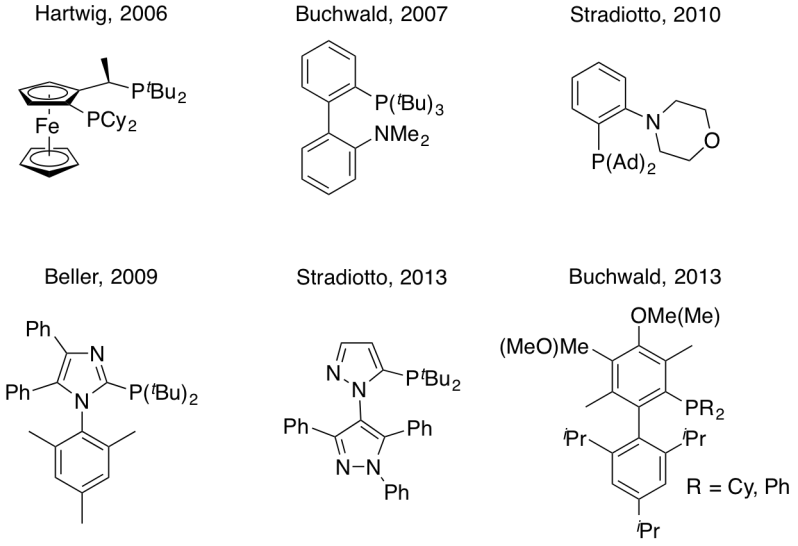
Palladium catalysts have been developed for the coupling aryl electrophiles with ammonia to form directly primary arylamines. Very sterically bulky ligands were

Scheme 1.10 Ammonia Surrogates for Pd-Catalyzed Synthesis of Primary Arylamines



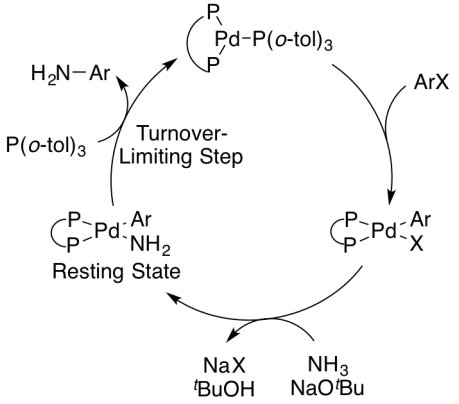
identified that promote the Pd-catalyzed coupling reaction (Scheme 1.11).[63,93-97] Diarylamine side-product was observed in these reactions, but the amount was low (5-10%).

Scheme 1.11 Ligands for Pd-Catalyzed Coupling of Aryl Electrophiles with Ammonia



Mechanistic studies helped elucidate the origin of selectivity for the coupling reaction. C-N bond-forming reductive elimination is the turnover-limiting step of the reaction catalyzed by palladium and a bisphosphine ligand (Scheme 1.12).[98] The selectivity of the amination reaction is determined by the rapid generation of the Pd(II)amido complex and its greater thermodynamic stability than the arylamido complex, not by the rate of reductive elimination. Hence, the concentration of ammonia in solution is an important variable in the reaction equation. Thus, it is not surprising that it has been reported that increased pressures of ammonia lead to higher selectivities.[63] However, the high concentration of ammonia leads to significant catalyst decomposition because the strongly coordinating ammonia displaces phosphine ligands. In the absence of the appropriate phosphine ligand, the reactivity and selectivity is compromised.

Scheme 1.12 Proposed Catalytic Cycle for Pd[P(*o*-tol)$_3$]$_2$/Josiphos-Catalyzed Coupling of Aryl Halides with Ammonia



1.4.3 Overview of Cu-Catalyzed Synthesis of Anilines

Complexes based on first row transition metal copper are valuable catalysts for C-N coupling reactions and reaction conditions have been developed to couple aryl electrophiles with numerous amine nucleophiles.[99,100] Before 2000, the reaction conditions for the Cu-catalyzed coupling of aryl electrophiles were limited to high catalyst loadings, high reaction temperatures, and limited electrophile coupling partners. The tolerance of copper catalysts to various functional groups allowed the reactions to be practical since aqueous ammonia and ammonium salts could be used as alternatives to gaseous ammonia.[101]

There are two main limitations to copper-catalyzed C-N coupling reactions: the high catalyst loading and the limited scope of amenable aryl electrophiles. Due to the low price and toxicity of copper, the high (approximately 20 mol %) catalyst loadings ligated by solvent molecules or inexpensive ligands are not detrimental to the application of the reaction on large scale. However, the requirement for activated aryl electrophiles, such as aryl iodides and heteroaryl bromides, is a limitation of copper-catalyzed coupling reactions, since they are not widely available and costly building blocks. Very recently, the Ma group reported a family of ligands that enables copper catalysts to undergo an oxidative addition of aryl chlorides in a coupling reaction with primary alkyl and aryl amines.[102] In a subsequent report, they demonstrated that these new ligands promote the coupling of aryl chlorides with either aqueous or gaseous ammonia.[103] The functional group tolerance is high due to the use of a weak base, but the presence of an *ortho*-substituent on the aryl chloride hinders reactivity.

1.4.4 Overview of Ni-Catalyzed Synthesis of Anilines

Prior to our work on Ni-catalyzed amination of aryl chlorides with ammonia and ammonium salts,[104] described in detail in Chapter 5, there were no nickel catalysts for the synthesis of primary arylamines. In conjunction with our report, Stradiotto and co-workers reported a similar catalyst for the same transformation.[105] A mixture of $Ni(COD)_2$ and Josiphos ligand CyPF-Cy (10 mol % each) afforded the primary aryl and heteroarylamines in high yields.

1.5 References

(1) Ananikov, V. P. *ACS Catal*. **2015**, *5*, 1964.
(2) Tasker, S. Z.; Standley, E. A.; Jamison, T. F. *Nature* **2014**, *509*, 299.
(3) Amatore, C.; Le Duc, G.; Jutand, A. *Chem. Eur. J.* **2013**, *19*, n.
(4) Lennox, A. J. J.; Lloyd-Jones, G. C. *Angew. Chem. Int. Ed.* **2013**, *52*, 7362.
(5) Hartwig, J. F. *Acc. Chem. Res.* **2008**, *41*, 1534.
(6) Fu, G. C. *Acc. Chem. Res.* **2008**, *41*, 1555.
(7) Peloso, A. *Coord. Chem. Rev.* **1973**, *10*, 123.

(8) Mesganaw, T.; Garg, N. K. *Org. Process Res. Dev.* **2013**, *17*, 29.
(9) Rosen, B. M.; Quasdorf, K. W.; Wilson, D. A.; Zhang, N.; Resmerita, A.-M.; Garg, N. K.; Percec, V. *Chem. Rev.* **2011**, *111*, 1346.
(10) Li, B.-J.; Yu, D.-G.; Sun, C.-L.; Shi, Z.-J. *Chem. Eur. J.* **2011**, *17*, 1728.
(11) Penney, J. M.; Miller, J. A. *Tetrahedron Lett.* **2004**, *45*, 4989.
(12) García, J. J.; Brunkan, N. M.; Jones, W. D. *J. Am. Chem. Soc.* **2002**, *124*, 9547.
(13) Tobisu, M.; Xu, T.; Shimasaki, T.; Chatani, N. *J. Am. Chem. Soc.* **2011**, *133*, 19505.
(14) Liu, X.-W.; Echavarren, J.; Zarate, C.; Martin, R. *J. Am. Chem. Soc.* **2015**, *137*, 12470.
(15) Niwa, T.; Ochiai, H.; Watanabe, Y. *J. Am. Chem. Soc.* **2015**.
(16) Tsou, T. T.; Kochi, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 6319.
(17) Cornella, J.; Gómez-Bengoa, E.; Martin, R. *J. Am. Chem. Soc.* **2013**, *135*, 1997.
(18) Schley, N. D.; Fu, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 16588.
(19) Hartwig, J. F. *Organotransition Metal Chemistry: From Bonding to Catalysis*; University Science Books, 2010.
(20) Bandar, J. S.; Pirnot, M. T.; Buchwald, S. L. *J. Am. Chem. Soc.* **2015**, *137*, 14812.
(21) Shi, S.-L.; Buchwald, S. L. *Nature Chemistry* **2015**, *7*, 38.
(22) Beller, M.; Seayad, J.; Tillack, A.; Jiao, H. *Angew. Chem. Int. Ed.* **2004**, *43*, 3368.
(23) Funabiki, T.; Yamazaki, Y.; Sato, Y.; Yoshida, S. *J. Chem. Soc., Perkin Trans. 2* **1983**, No. 9, 1915.
(24) Funabiki, T.; Sato, H.; Tanaka, N.; Yamazaki, Y.; Yoshida, S. *J. Mol. Catal.* **1990**, *62*, 157.
(25) Jackson, W. R.; Lovel, C. G. *Aust. J. Chem.* **1983**, *36*, 1975.
(26) Na, Y.; Chang, S. *Org. Lett.* **2000**, *2*, 1887.
(27) Takeuchi, R.; Tanouchi, N. *J. Chem. Soc., Chem. Commun.* **1993**, No. 17, 1319.
(28) Takeuchi, R.; Tanouchi, N. *J. Chem. Soc., Perkin Trans. 1* **1994**, No. 20, 2909.
(29) Trost, B. M.; Ball, Z. T.; Jöge, T. *J. Am. Chem. Soc.* **2002**, *124*, 7922.
(30) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, *13*, 3769.
(31) Bordwell, F. G.; Drucker, G. E.; Andersen, N. H. *J. Am. Chem. Soc.* **1986**, *108*, 7310.
(32) Matthews, W. S.; Bares, J. E.; Bartmess, J. E. *J. Am. Chem. Soc.* **1975**, *97*, 7006.
(33) Dieck, H.; Heck, F. *J. Organomet. Chem.* **1975**, *93*, 259.
(34) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, *50*, 4467.
(35) Pu, X.; Li, H.; Colacot, T. J. *J. Org. Chem.* **2013**, *78*, 568.
(36) García-Melchor, M.; Pacheco, M. C.; Nájera, C.; Lledós, A.; Ujaque, G. *ACS Catal.* **2012**, *2*, 135.
(37) Sikk, L.; Tammiku-Taul, J.; Burk, P. *Organometallics* **2011**, *30*, 5656.
(38) Denmark, S. E.; Ambrosi, A. *Org. Process Res. Dev.* **2015**, *19*, 982.
(39) Denmark, S. E.; Regens, C. S. *Acc. Chem. Res.* **2008**, *41*, 1486.
(40) Chang, S.; Yang, S.; Lee, P. *Tetrahedron Lett.* **2001**, *42*, 4833.
(41) Nishihara, Y.; Ikegashira, K.; Mori, A.; Hiyama, T. *Chem. Lett.* **1997**, No. 12, 1233.
(42) Thakur, A.; Louie, J. *Acc. Chem. Res.* **2015**, *48*, 2354.
(43) Kurahashi, T.; Matsubara, S. *Acc. Chem. Res.* **2015**, *48*, 1703.
(44) Beletskaya, I. P.; Latyshev, G. V.; Tsvetkov, A. V.; Lukashev, N. V. *Tetrahedron Lett.* **2003**, *44*, 5011.

(45) Gallego, D.; Brück, A.; Irran, E.; Meier, F.; Kaupp, M.; Driess, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 15617.
(46) Vechorkin, O.; Barmaz, D.; Proust, V.; Hu, X. *J. Am. Chem. Soc.* **2009**, *131*, 12078.
(47) Perez Garcia, P. M.; Ren, P.; Scopelliti, R.; Hu, X. *ACS Catal.* **2015**, *5*, 1164.
(48) Yi, J.; Lu, X.; Sun, Y.-Y.; Xiao, B.; Liu, L. *Angew. Chem. Int. Ed.* **2013**, *52*, 12409.
(49) Vechorkin, O.; Godinat, A.; Scopelliti, R.; Hu, X. *Angew. Chem. Int. Ed.* **2011**, *50*, 11777.
(50) Xu, G.; Li, X.; Sun, H. *J. Organomet. Chem.* **2011**, *696*, 3011.
(51) Tobisu, M.; Takahira, T.; Ohtsuki, A.; Chatani, N. *Org. Lett.* **2015**, *17*, 680.
(52) Hartwig, J. F. *Angew. Chem. Int. Ed.* **1998**, *37*, 2046.
(53) Surry, D. S.; Buchwald, S. L. *Chem. Sci.* **2011**, *2*, 27.
(54) Roughley, S. D.; Jordan, A. M. *J. Med. Chem.* **2011**, *54*, 3451.
(55) Kosugi, M.; Kameyama, M.; Migita, T. *Chem. Lett.* **1983**, No. 6, 927.
(56) Louie, J.; Hartwig, J. F. *Tetrahedron Lett.* **1995**, *36*, 3609.
(57) Guram, A. S.; Rennels, R. A.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **1995**, *34*, 1348.
(58) Wolfe, J. P.; Wagaw, S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 7215.
(59) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1144.
(60) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 7217.
(61) Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805.
(62) Shen, Q.; Shekhar, S.; Stambuli, J. P.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2005**, *44*, 1371.
(63) Shen, Q.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 10028.
(64) Shekhar, S.; Ryberg, P.; Hartwig, J. F.; Mathew, J. S.; Blackmond, D. G.; Strieter, E. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 3584.
(65) Shekhar, S.; Ryberg, P.; Hartwig, J. F. *Org. Lett.* **2006**, *8*, 851.
(66) Wolfe, J. P.; Ahman, J.; Sadighi, J. P.; Singer, R. A.; Buchwald, S. L. *Tetrahedron Lett.* **1997**.
(67) Brenner, E.; Fort, Y. *Tetrahedron Lett.* **1998**.
(68) Desmarets, C.; Schneider, R.; Fort, Y. *Tetrahedron* **2001**, *57*, 7657.
(69) Desmarets, C.; Schneider, R.; Fort, Y. *Tetrahedron Lett.* **2001**.
(70) Manolikakes, G.; Gavryushin, A.; Knochel, P. *J. Org. Chem.* **2008**, *73*, 1429.
(71) Gradel, B.; Brenner, E.; Schneider, R.; Fort, Y. *Tetrahedron Lett.* **2001**.
(72) Fan, X.-H.; Li, G.; Yang, L.-M. *J. Organomet. Chem.* **2011**, *696*, 2482.
(73) Fine Nathel, N. F.; Kim, J.; Hie, L.; Jiang, X.; Garg, N. K. *ACS Catal.* **2014**, *4*, 3289.
(74) Rull, S. G.; Blandez, J. F.; Fructos, M. R.; Belderrain, T. R.; Nicasio, M. C. *Adv. Synth. Catal.* **2015**, *357*, 907.
(75) Shimasaki, T.; Tobisu, M.; Chatani, N. *Angew. Chem. Int. Ed.* **2010**, *49*, 2929.
(76) Mesganaw, T.; Silberstein, A. L.; Ramgren, S. D. *Chem. Sci.* **2011**, *2*, 1766.
(77) Hie, L.; Ramgren, S. D.; Mesganaw, T.; Garg, N. K. *Org. Lett.* **2012**, *14*, 4182.
(78) Ramgren, S. D.; Silberstein, A. L.; Yang, Y.; Garg, N. K. *Angew. Chem. Int. Ed.* **2011**, *50*, 2171.
(79) Huang, J.-H.; Yang, L.-M. *Org. Lett.* **2011**, *13*, 3750.
(80) Gao, C.-Y.; Yang, L.-M. *J. Org. Chem.* **2008**, *73*, 1624.

(81) Iglesias, M. J.; Blandez, J. F.; Fructos, M. R.; Prieto, A.; Álvarez, E.; Belderrain, T. R.; Nicasio, M. C. *Organometallics* **2013**, *31*, 6312.
(82) Tobisu, M.; Yasutome, A.; Yamakawa, K.; Shimasaki, T.; Chatani, N. *Tetrahedron* **2012**, *68*, 5157.
(83) Park, N. H.; Teverovskiy, G.; Buchwald, S. L. *Org. Lett.* **2014**, *16*, 220.
(84) Kampmann, S. S.; Sobolev, A. N.; Koutsantonis, G. A.; Stewart, S. G. *Adv. Synth. Catal.* **2014**, *356*, 1967.
(85) Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 6054.
(86) Ge, S.; Green, R. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 1617.
(87) Kampmann, S. S.; Skelton, B. W.; Wild, D. A.; Koutsantonis, G. A.; Stewart, S. G. *Eur. J. Org. Chem.* **2015**, *2015*, 5995.
(88) Grasa, G. A.; Viciu, M. S.; Huang, J.; Nolan, S. P. *J. Org. Chem.* **2001**, *66*, 7729.
(89) Mann, G.; Hartwig, J. F.; Driver, M. S. *J. Am. Chem. Soc.* **1998**, *120*, 827.
(90) Lee, D.-Y.; Hartwig, J. F. *Org. Lett.* **2005**, *7*, 1169.
(91) Ikawa, T.; Barder, T. E.; Biscoe, M. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 13001.
(92) Bhagwanth, S.; Waterson, A. G.; Adjabeng, G. M.; Hornberger, K. R. *J. Org. Chem.* **2009**, *74*, 4634.
(93) Vo, G. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 11049.
(94) Surry, D. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 10354.
(95) Crawford, S. M.; Lavery, C. B.; Stradiotto, M. *Chem. Eur. J.* **2013**, *19*, 16760.
(96) Lundgren, R. J.; Peters, B. D.; Alsabeh, P. G.; Stradiotto, M. *Angew. Chem. Int. Ed.* **2010**, *49*, 4071.
(97) Alsabeh, P. G.; Lundgren, R. J.; McDonald, R.; Johansson Seechurn, C. C. C.; Colacot, T. J.; Stradiotto, M. *Chemistry* **2013**, *19*, 2131.
(98) Klinkenberg, J. L.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 11830.
(99) Aubin, Y.; Fischmeister, C.; Thomas, C. M.; Renaud, J.-L. *Chem. Soc. Rev.* **2010**, *39*, 4130.
(100) Shaughnessy, K. H.; Ciganek, E.; DeVasher, R. B. Denmark, S. E., Ed.; Organic Reactions: Hoboken, NJ, USA, 2014; Vol. 85, pp 1–415.
(101) Kim, J.; Chang, S. *Chem. Commun.* **2008**, No. 26, 3052.
(102) Zhou, W.; Fan, M.; Yin, J.; Jiang, Y.; Ma, D. *J. Am. Chem. Soc.* **2015**, *137*, 11942.
(103) Fan, M.; Zhou, W.; Jiang, Y.; Ma, D. *Org. Lett.* **2015**, *17*, 5934.
(104) Green, R. A.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2015**, *54*, 3768.
(105) Borzenko, A.; Rotta-Loria, N. L.; MacQueen, P. M.; Lavoie, C. M.; McDonald, R.; Stradiotto, M. *Angew. Chem. Int. Ed.* **2015**, *54*, 3773.

CHAPTER 2

Development of Nickel-Catalyzed Alkynylation of Aryl Halides

2.1 Introduction

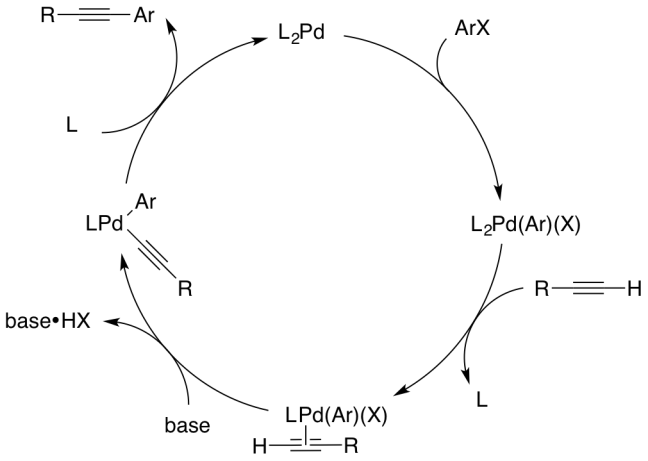
Cross-coupling reactions are powerful tools in organic chemistry, enabling new disconnections and strategies in synthetic planning. Reactions that enable carbon-carbon bond formation by cross coupling exhibit particularly high selectivity due to the pre-functionalization of the reagents. Moreover, this class of reactions allows for the late-stage coupling of two complex fragments.[1-3] In particular, palladium-catalyzed alkynylation reactions have become general and reliable methods to construct alkyne derivatives. The palladium-catalyzed alkynylation of aryl halides is the second most used catalytic carbon-carbon bond forming reactions in medicinal chemistry, after the Suzuki-Miyaura reaction.[4]

Alkynes are a prevalent functional group, both in the final product of a synthesis and as a synthetic intermediate. Partial hydrogenation of the alkyne is a powerful method for the synthesis of geometrically pure alkenes. Alkynes can also be transformed into a variety of functional groups including ketones, alkyl or alkenyl halides, vinyl metal species and alkanes.

There are few catalytic methods to prepare substituted alkynes. Terminal alkynes already present in the molecule can be used as nucleophiles in substitution reactions to derivatize the alkyne; however, this method is limited to the substitution of primary alkyl electrophiles.[5] Alkynes can be introduced into a molecule using the Corey-Fuchs reaction, starting from an aldehyde; however the use of alkyl lithium reagents and carcinogenic carbon tetrabromide limit the utility of this reaction. The metal-catalyzed alkynylation method is an efficient route to prepare diverse alkynes due to the high functional group compatibility and the mild reaction conditions.

The use of a copper co-catalyst in the Sonogashira reaction often leads to varying amounts of the homocoupled alkyne as a side-product (Glaser-Hay reaction). For example, Buchwald[6] and Ruiz[7] reported that the addition of catalytic amounts of copper salts decreased the yield of the desired cross-coupled product significantly, due to competitive alkyne homocoupling and oligomerization processes. The major side-reaction, oligomerization of the alkyne substrate, can be minimized via slow addition of the alkyne into the reaction mixture.[6]

Scheme 2.1 Proposed Mechanism for Palladium-Catalyzed Copper-Free Sonogashira Reactions



The proposed catalytic cycle of the palladium-catalyzed copper-free Sonogashira reaction is presented in Scheme 3. Both experimental[8] and DFT[9,10] studies support this catalytic cycle, which involves the oxidative addition of the aryl halide to the ligated palladium(0) complex,

followed by coordination of the alkyne. Coordination of the alkyne to palladium lowers the pK_a of the C-H bond, facilitating deprotonation by base to yield an alkynyl-palladium intermediate. The alkynyl-palladium intermediate undergoes C-C bond forming reductive elimination to yield the desired cross-coupled product and regenerate the active catalyst. The alkyne is deprotonated while π-coordinated to the palladium; thus, the alkynyl palladium intermediate is formed without the need of copper. In reactions with copper co-catalysts, alkynylcopper species are formed in the presence of base and undergo transmetalation to palladium. Copper-free palladium-catalyzed Sonogashira reactions are often performed with bulky electron-rich monodentate phosphine ligands. The use of bulky electron-rich monodentate phosphine ligands is believed to favor coordination of the alkyne by more easily forming coordinatively-unsaturated intermediates than bidentate or less-bulky ligands (Scheme 2.1).[6,7,11]

Despite the advances in palladium-catalyzed Sonogashira reactions, both with and without copper co-catalysts, the use of a nickel catalyst to achieve the same transformation has not been well developed. Nickel is significantly less expensive and more abundant than palladium. Therefore, the interest in nickel-catalyzed cross-coupling reactions has grown in recent years. However, cross-coupling reactions with nickel generally require higher catalyst loadings than reactions with palladium, due to the increased likelihood of nickel to undergo disproportionation to catalytically inactive Ni(I) species.

Currently, nickel-catalyzed Sonogashira reactions are limited to the coupling of an aryl or vinyl electrophile with a free alkyne, both with copper co-catalysts.[12,13] There are reports in the literature of coupling reactions between an alkyl electrophile and a free alkyne[14-16] or with an alkynyl organometallic species.[17-19] It should be noted that the nucleophilic substitution of a primary alkyl electrophile by an alkynyllithium reagent is a known transformation, for which a catalyst is not necessary.[5]

We report the development of the first copper-free nickel-catalyzed Sonogashira reaction of aryl chlorides and bromides with alkynes.

2.2 Results and Discussion

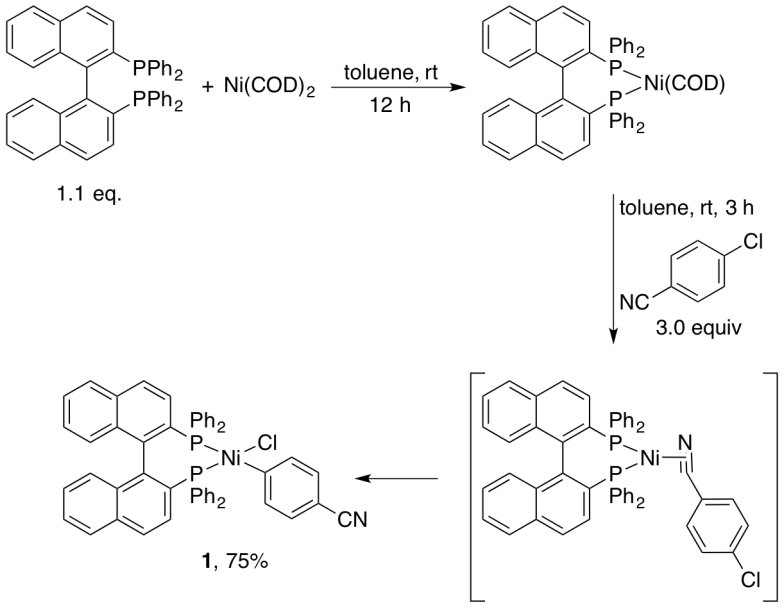
Stoichiometric Sonogashira Reactions: Free Alkyne

Our effort towards the development of nickel-catalyzed Sonogashira reactions with aryl electrophiles began by investigating the elementary steps of the proposed catalytic cycle as separate stoichiometric reactions. Our group recently reported a procedure to prepare and isolate nickel complex **1**, which is formed from oxidative addition of an aryl halide to a phosphine-ligated nickel(0) species formed *in-situ* (Scheme 2.2). [20]

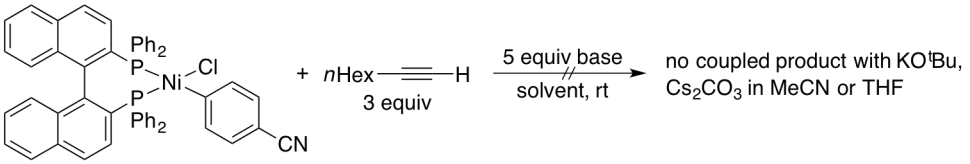
The nickel complex **1** is proposed to lie on the catalytic cycle for nickel-catalyzed alkynylation (Scheme 2.3) and was thus used to develop reaction conditions for alkyne deprotonation, transmetalation, and reductive elimination with the aryl electrophile. Among the bases added to the combination of **1** and 1-octyne, none promoted the formation of the desired cross-coupled product. (Scheme 2.3)

Complex **1** contains a bidentate phosphine ligand. This 16-electron square planar complex is unlikely to coordinate the alkyne to form an 18-electron trigonal bipyramidal complex, as suggested by preliminary results. Alternatively, the alkyne can be deprotonated by a weak base, assisted by a metal additive, prior to transmetalation to a bisphosphine-ligated nickel complex. Moreover, monophosphine-ligated nickel complexes can favor π-coordination of the

Scheme 2.2 Synthesis of (BINAP)Ni(Ar)Cl (**1**)



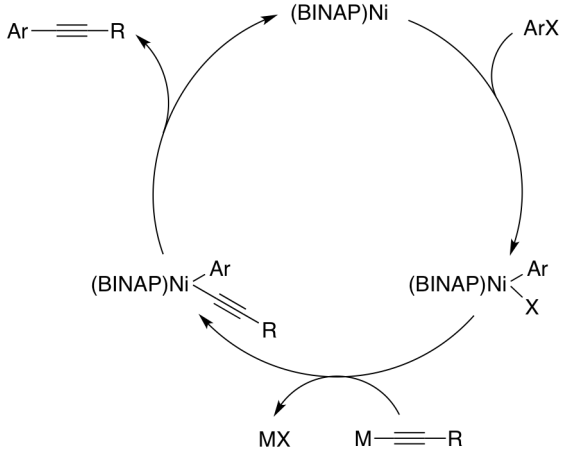
Scheme 2.3 Stoichiometric Experiments with Free Alkyne



alkyne (*vide supra*) to the nickel, followed by deprotonation by base. Methods to achieve transmetalation in the presence of a bisphosphine ligand were studied (Scheme 2.4). The resulting aryl-alkynyl nickel(II) species is proposed to undergo C-C bond-forming reductive elimination to yield the desired cross-coupled product.

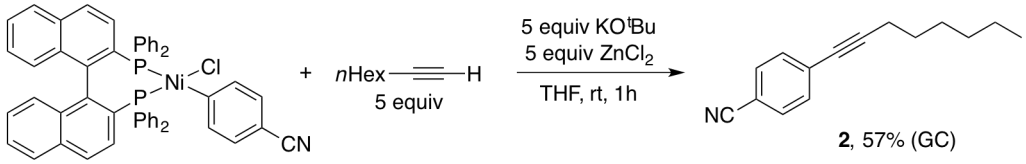
Organozinc reagents are known to undergo facile transmetalation under mild conditions without the need for additional activators. We proposed that an alkynylzinc species would undergo efficient transmetalation for our desired reaction (Scheme 2.4, M = ZnX). The alkynylzinc intermediate was prepared according to the literature procedure via addition of the alkynyllithium reagent to $ZnCl_2$, and allowed to react with nickel complex **1**.[21] Formation of the desired cross-coupled product was observed by GC-MS, along with full consumption of complex **1** within minutes, as indicated by ^{31}P NMR spectroscopy. However, the preparation of alkynylzinc reagents prior to the reaction is tedious; therefore, we proposed that the organozinc reagent could be prepared *in-situ*. Various weak bases were used to generate the alkynylzinc species *in-situ* by adding the alkyne and a base to zinc chloride. The reaction with KO^{t}Bu as the base gave the desired product in 57% yield, as determined by GC (Scheme 2.5). The alkyne reagent was almost fully consumed throughout the reaction without any side-products observed by GC. We propose that high molecular weight oligomers are being formed under the reaction conditions, a known issue with the Sonogashira cross-coupling reaction.[6]

Scheme 2.4 Proposed Catalytic Cycle For Nickel-Catalyzed Alkynylation.



These results suggest that each step of the proposed catalytic cycle in Scheme 2.4 occurs at room temperature. To investigate if this reaction would occur with a catalytic amount of nickel, excess *p*-chlorobenzonitrile and 1-octyne were added to the reaction. However, the reaction did not occur catalytically; the yield of the cross-coupled product was only 3% with 10 mol % catalyst loading.

Scheme 2.5 Stoichiometric Experiment with Alkynylzinc



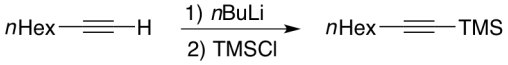
The catalyst turnover might be inhibited by coordination of the reaction product to the Ni(0) intermediate. Benzonitriles are known to coordinate to (BINAP)Ni(0).[20] Since the product contains both a nitrile and an alkyne, an off-cycle Ni(0) complex may be formed. Such a coordination would hinder the oxidative addition of the subsequent aryl halide to the low valent (BINAP)Ni(0) species.

Stoichiometric Sonogashira Reactions: Protected Alkyne Nucleophiles

High concentrations of terminal alkynes in the reaction mixture increase the rates of competitive side-reactions, notably the formation of oligomers. To address this issue, a series of alkyne derivatives were prepared that could be transformed into the free alkyne *in-situ*.

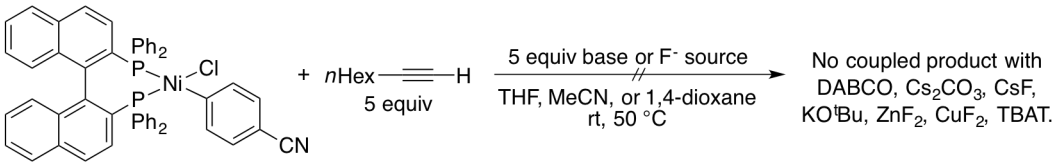
Silyl protecting groups are commonly installed onto terminal alkynes in syntheses due to the acidity and reactivity of the C-H bond of acetylenes. Silyl protected alkynes have been used in palladium-catalyzed alkynylation reactions. Silanols[22,23] and trimethylsilyl-protected alkynes[24] have been shown to undergo cross-coupling in the presence of an activating agent, such as fluoride[23], silanoates[22], or a copper salt[24], through the intermediacy of a free alkynyl metal species. Latent nucleophile **3** was subjected to alkynylation-reaction conditions with **1**. Multiple bases and fluorides were screened, with and without added zinc chloride as a transmetallating agent. However, none of these reactions formed the cross-coupled product, as indicated by GC analysis (Scheme 2.7).

Scheme 2.6 Synthesis of TMS-Protected Alkyne



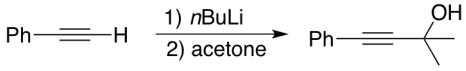
3, 60%

Scheme 2.7 Stoichiometric Reactions with TMS-Protected Alkyne



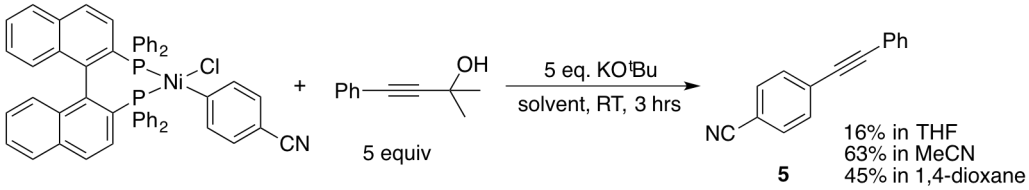
We chose to investigate protected alkyne **4** as a masked alkyne, which was prepared by the addition of an alkynyllithium reagent to acetone to form adduct **4** (Scheme 2.8).[25] The free alkyne can be revealed in the presence of a strong base at elevated temperatures. An aryl analogue of **4** has been used in palladium-catalyzed cross-coupling, in which the metal complex first coordinates to the alcohol, followed by a β-carbon elimination to release acetone and form the aryl-palladium intermediate.[26] We proposed that a similar approach could be extended from the aryl nucleophile to the alkynyl nucleophile. Although removal of the acetone adduct from the alkyne moiety typically requires the use of a strong base at elevated temperatures, we proposed that the presence of nickel as a Lewis acid would lower the barrier for this process. Therefore, to maintain the mild conditions developed thus far for the other elementary steps of the catalytic cycle, we conducted these reactions at ambient temperature. Propargylic alcohol **4** was studied in stoichiometric reactions, and numerous bases and additives were evaluated to promote transmetalation. As shown in Scheme 2.9, only reactions with potassium *tert*-butoxide yielded any desired cross-coupled product at ambient temperature.

Scheme 2.8 Synthesis of Acetone Adduct of Phenylacetylene



4, 95%

Scheme 2.9 Stoichiometric Reactions with Acetone Adduct of Phenylacetylene



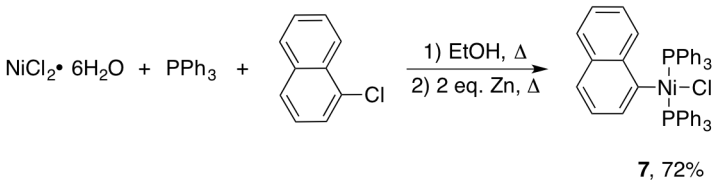
5

The addition of zinc chloride, however, diminished the yield significantly, affording only trace amounts of the desired product, and **4** depleted at a faster rate in the presence of zinc chloride than in the absence of the added zinc salt. Presumably, the deprotection of **4** to form free alkyne can occur while the alcohol is either coordinated to the nickel or the zinc complexes in solution, followed by β-carbon elimination.

Stoichiometric Sonogashira Reactions: Monodentate Phosphine Ligands

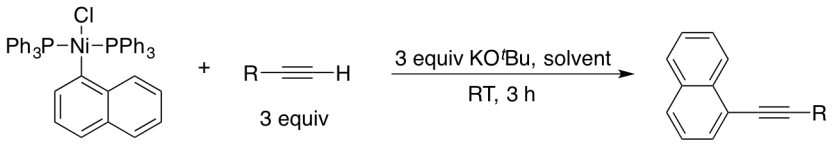
Monodentate-phosphine-nickel-aryl-halide complexes have been reported in the literature and used as the catalyst source in other nickel-catalyzed transformations.[27] Complex **7** was prepared according to literature procedure[28] (Equation 8), and is proposed to be an intermediate in the proposed Sonogashira reaction. Numerous reaction conditions were evaluated with **7**, by varying the alkyne, the base, and the solvents. Of the bases subjected to the reaction conditions, KO^{t}Bu was the only one that yielded the cross-coupled product in high yield (Equation 9). However, advancing from stoichiometric quantities of complex **7** to catalytic amounts, the yield of the cross-coupled product never surpassed that of the catalyst loading.

Scheme 2.10 Synthesis of $(PPh_3)_2Ni(1\text{-naphthyl})(Cl)$



7, 72%

Scheme 2.11 Stoichiometric Reactions with $(PPh_3)_2Ni(1\text{-naphthyl})(Cl)$ and Alkynes



7 **8**

R = Ph (**8a**)	R = nHex (**8b**)
69% (1,4-dioxane)	75% (MeCN)
49% (THF)	72% (THF)
46% (MeCN)	65% (toluene)
29% (toluene)	

To identify suitable ligands for the nickel-catalyzed alkynylation of aryl chlorides, a high-throughput screen of 96 reactions catalyzed by nickel complexes containing monodentate phosphine ligands was conducted on a 10 μmol scale. The high-throughput screen was conducted with 1-chloronaphthalene as the electrophile and KO^{t}Bu as the base. Four solvents (THF, MeCN, 1,4-dioxane, and toluene) were screened, along with 12 monophosphine ligands possessing a range of steric and electronic properties. In addition, both 1-octyne and phenylacetylene were evaluated as coupling partners.

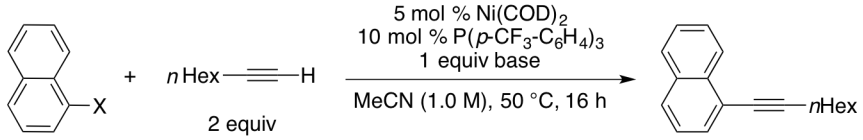
Analysis of each reaction showed that the reaction of 1-chloronaphthalene and 1-octyne was catalyzed by a combination of 5 mol % $Ni(COD)_2$ and 10 mol % $P(p\text{-}CF_3\text{-}C_6H_4)_3$ in 24% yield. In addition to increasing the yield of the cross-coupled product, relative to reactions with PPh_3 as a ligand, the amount of product from oligomerization of the alkyne was also reduced. This result suggests that reductive coupling of the alkyne, a process that leads to alkyne oligomerization, is minimized with the electron-deficient nickel complex.

Although the reactions of the high-throughput experiment were not heated, the reaction plate was warmer than ambient temperature due to the stirring apparatus. Upon subsequent

experiments, the reaction temperature, base, concentration were evaluated and the findings are summarized in Scheme 2.12.

In the high-throughput experiment, the $Ni(COD)_2$ and ligands were premixed, and this procedure was replicated in the optimization experiments. The duration of the premixing affected

Scheme 2.12 Evaluation of Reaction Components



base	X = Cl	X = Br	Notes
KO^{t}Bu	25%	33%	
NaO^{t}Bu	45%	61%	
NaO^{t}Bu	68%	71%	20 mol % ligand

the yields and led to inconsistent results. Thus, it was postulated that a preformed nickel complex would eliminate such inconsistent results. Therefore, the nickel complex $Ni[P(p\text{-}CF_3\text{-}C_6H_4)_3]_3$ was prepared as shown in Scheme 2.13, and characterized by elemental analysis and X-ray crystallography (Figure 2.1).

Scheme 2.13 Synthesis of $Ni[P(p\text{-}CF_3\text{-}C_6H_4)_3]_3$

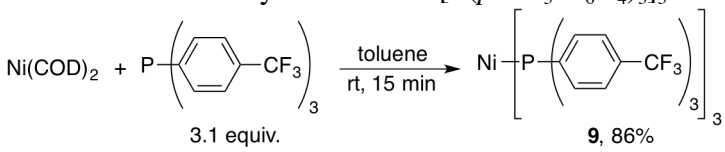
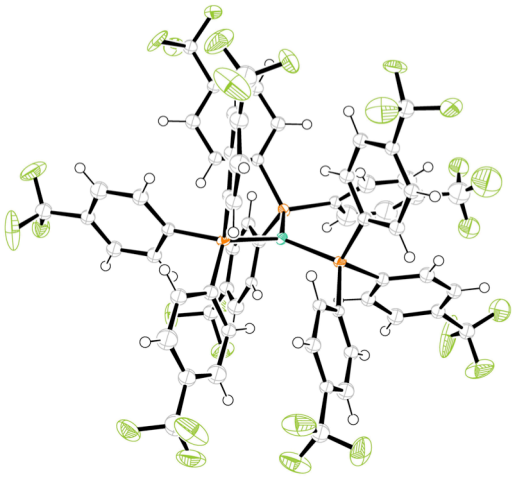
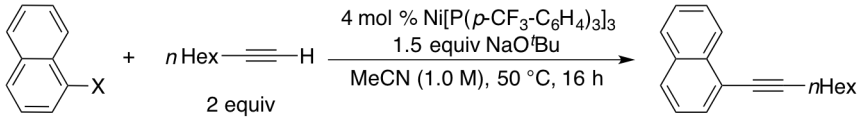


Figure 2.1 X-ray Crystal Structure of $Ni[P(p\text{-}CF_3\text{-}C_6H_4)_3]_3$



With the new precatalyst in hand, it was subjected to our reaction conditions. The yields were consistent from run to run and yielded the substituted alkyne in higher yields than a combination of $Ni(COD)_2$ and the ligand (Figure 2.14).

Scheme 2.14 Alkynylation Reactions Catalyzed by Ni[P(*p*-CF_3-C_6H_4)$_3$]$_3$



X = Cl 66%
X = Br 83%

2.3 Conclusion

The development of nickel-catalyzed Sonogashira reaction began with studies on the transmetalation and reductive elimination of alkynes to an isolated BINAP-ligated nickel(II) complex. However, attempts to make the reaction catalytic with complex 1 were unsuccessful. Suppression of alkyne oligomerization was attempted with the alkyne derivatives, yet the use of these derivatives produced similar or worse yields of reactions ran with the free alkyne. We proposed that monodentate phosphine ligands could dissociate to form unsaturated complexes that would bind alkynes, facilitating deprotonation. The activity of monodentate phosphine ligands was investigated with $(PPh_3)_2$Ni(1-naphthyl)(Cl). With PPh_3 as the ligand, no catalytic activity was observed. However, 96-well-plate-high-throughput-ligand screen revealed that the electron-deficient P(*p*-CF_3-C_6H_4)$_3$ reduced oligomerization of the alkyne and promoted the activity of the nickel complex for catalytic coupling. Further optimization and the synthesis of the isolated Ni[P(*p*-CF_3-C_6H_4)$_3$]$_3$ nickel complex allowed for the cross-coupling of 1-chloronaphthalene and 1-octyne in 83% yield with 4 mol % catalyst loading at 50 °C.

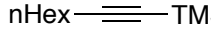
2.4 Experimental

General

All manipulations were conducted under an inert atmosphere with a nitrogen-filled glovebox unless otherwise noted. All reactions were conducted in oven-dried 4-mL or 20-mL vials fitted with a Teflon-lined screw cap under an atmosphere of nitrogen unless otherwise noted. Nickel complexes [*rac*-BINAP]Ni(Cl)(C_6H_4-4-CN) (**1**)[20] and *trans*-chloro(naphthyl)bis(triphenylphosphine)nickel(II) (**7**)[28] were prepared according to literature procedure and the ^{31}P NMR shifts compared to those documented. All other reagents were purchased from commercial suppliers and used as received. GC yields were determined via comparison of the signal to the internal standard (dodecane) added at the beginning of the reaction. A calibration curve was prepared by isolating desired cross-coupled products from palladium-catalyzed reaction conditions reported in the literature.[11] Organic extracts were dried over sodium sulfate (Na_2SO_4) and concentrated by rotary evaporation. Flash column chromatography was performed on Silicycle Siala-P silica gel. The products were visualized by UV light and stained with potassium permanganate ($KMnO_4$). NMR spectra were acquired on 400 or 600 MHz Bruker instruments at the University of California. NMR spectra were processed with iNMR 4.2.0 (Mestrelab Research). Chemical shifts are reported in ppm and referenced to residual solvent peaks ($CHCl_3$ in $CDCl_3$: 7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C) or to an external standard (85% H_3PO_4 for ^{31}P). Coupling constants are reported in hertz. All GC-MS analyses were conducted with an

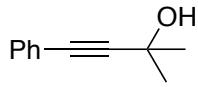
Agilent 6890N GC equipped with an HP-5 column (25 m x 0.20 mm ID x 0.33 μm film) and an Agilent 5973 Mass Selective Detector. The temperature for each run was held at 50 °C for 2 min, ramped from 50 °C to 300 °C at 40 °C/min, and held at 300 °C for 5 min. All GC analyses were conducted with an Agilent 7890 GC equipped with an HP-5 column (30m x 0.2 mm ID x 0.33 μm film). The injector temperature was 300 °C with a 2.1 mL/min He carrier gas flow. Unless otherwise noted, the temperature for each run was held at 100 °C for 3 mins, ramped from 100 °C to 300 °C at 40 °C/min, and held at 300 °C for 2.5 min.

Trimethyl(1-octynyl)silane (**3**)



A dry 50 mL round-bottom flask was charged with 1-octyne (1.0 mL, 0.75 g, 6.8 mmol) and THF (8 mL) under a N_2 atmosphere using a Schlenk manifold. The solution was cooled to -78 °C for the slow addition of *n*BuLi (2.8 mL, 2.5 M, 7.0 mmol). The mixture was stirred at 0 °C for 30 min, followed by the drop-wise addition of TMSCl (0.86 mL, 1.08 g, 9.95 mmol). The resulting solution was stirred at ambient temperature for 30 min prior to the solvent being removed *in vacuo*. The white reside was suspended in H_2O (20 mL) and the product extracted with hexanes (3 × 20 mL). The combined organic layers were dried and evaporated to yield a yellow oil (731.4 mg, 4.010 mmol, 59%). ^{1}H-NMR (400 MHz; $CDCl_3$): δ 2.25 (t, *J* = 7.2 Hz, 2H), 1.54 (q, *J* = 7.5 Hz, 2H), 1.44-1.30 (m, 6H), 0.93 (t, *J* = 6.9 Hz, 3H), 0.18 (q, *J* = 3.8 Hz, 8H). ^{13}C{^{1}H} NMR (101 MHz; $CDCl_3$): δ 107.8, 84.3, 31.3, 28.6, 28.5, 22.5, 19.9, 14.0, 0.2.

2-methyl-4-phenylbut-3-yn-2-ol (**4**)



A dry 50 mL round-bottom flask was charged with phenylacetylene (1.0 mL, 0.94 g, 9.1 mmol) and diethyl ether (15 mL) under a N_2 atmosphere using a Schlenk manifold. The mixture was cooled to -78 °C for the slow addition of *n*BuLi (3.7 mL, 2.5 M, 9.3 mmol), then stirred at 0 °C for 20 min. A solution of acetone (0.75 mL, 0.59 g, 10. mmol) in diethyl ether (10 mL) was added slowly to the solution and the resulting mixture stirred at ambient temperature for 2 hours. The reaction was quenched with saturated $NH_4Cl_{(aq)}$(15 mL) and the product extracted (3 × 20 mL) with diethyl ether. The combined organic layers were dried and evaporated. The product was purified by flash column chromatography (5%→10% EtOAc in Hexanes) and isolated a pale yellow oil (1.4 g, 8.7 mmol, 95%). ^{1}H-NMR (400 MHz; $CDCl_3$): δ 7.42 (d, *J* = 0.9 Hz, 2H), 7.31-7.29 (m, 3H), 2.13 (s, 1H), 1.62 (s, 6H). ^{13}C{^{1}H} NMR (101 MHz; $CDCl_3$): δ 131.8, 128.4, 122.9, 93.9, 82.3, 65.8, 31.6.

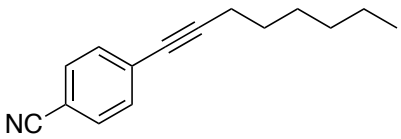
General procedure for palladium-catalyzed cross-coupling for GC standards [11]

A vial was charged with $[(allyl)PdCl]_2$ (3 mol %) and the aryl bromide (1.0 equiv). The P^tBu_3 (12 mol %) dissolved in MeCN (0.5 M) was added, followed by sequential additions of the alkyne (1.2 equiv) and DABCO (2.0 equiv). The solution was stirred at ambient temperature for 12 hrs. The mixture was quenched with H_2O (10 mL), and the product extracted with ethyl acetate (3 × 15 mL). The combined organic layers were dried and evaporated. The residue was purified by flash column chromatography.

General procedure for nickel-mediated Sonogashira reactions

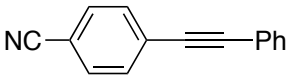
A vial was charged with the alkyne (5.0 equiv), base (5.0 equiv), additive (5.0 equiv), [*rac*-BINAP]Ni(Cl)(C_6H_4-4-CN) (11.0 mg, 0.133 mmol, 1.0 equiv), and solvent (0.02 M). The reaction was stirred either at ambient temperature or 50 °C. Reactions were quenched with H_2O (1 mL), and the product extracted with ethyl acetate (2 mL). An aliquot from the organic phase was filtered through silica, followed by GC analysis.

4-(oct-1-yn-1-yl)benzonitrile (**2**)



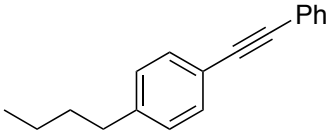
Purified by flash column chromatography (5% EtOAc in Hexanes). Prepared on 2.0 mmol scale. Isolated as a pale yellow oil (275.9 mg, 1.306 mmol, 65%). ^{1}H-NMR (400 MHz; $CDCl_3$): δ 7.55 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 2.41 (t, *J* = 7.1 Hz, 2H), 1.60 (quintet, *J* = 7.4 Hz, 2H), 1.43 (dt, *J* = 14.5, 7.1 Hz, 2H), 1.35-1.25 (m, 4H), 0.89 (t, *J* = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz; $CDCl_3$): δ 132.2, 132.0, 129.3, 118.8, 110.9, 95.9, 79.6, 31.5, 28.74, 28.55, 22.7, 19.7, 14.2.

4-(phenylethynyl)benzonitrile (**5**)



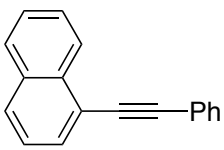
Purified by flash column chromatography (5% → 10% EtOAc in Hexanes). Prepared on 1.0 mmol scale. Isolated as a pale yellow powder. (83.6 mg, 0.411 mmol, 41%). ^{1}H-NMR (400 MHz; $CDCl_3$): δ 7.64-7.59 (m, 4H), 7.55 (dd, *J* = 6.6, 3.1 Hz, 2H), 7.38 (dd, *J* = 5.0, 1.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz; $CDCl_3$): δ 132.4, 132.4, 132.2, 129.5, 128.9, 128.6, 122.6, 118.9, 111.8, 94.2, 88.1.

1-butyl-4-(phenylethynyl)benzene (**6**)



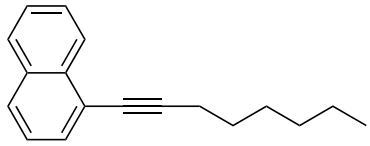
Purified by flash chromatography (2% EtOAc in hexanes). Prepared on 0.992 mmol scale. Isolated as a colorless oil (89.4 mg, 0.382 mmol, 38%). ^{1}H-NMR (400 MHz; $CDCl_3$): δ 7.52-7.50 (m, 2H), 7.43 (d, *J* = 8.2 Hz, 2H), 7.33-7.31 (m, 3H), 7.16-7.14 (m, 2H), 2.61 (t, *J* = 7.7 Hz, 2H), 1.58 (d, *J* = 7.6 Hz, 2H), 1.34 (dd, *J* = 14.9, 7.4 Hz, 2H), 0.92 (t, *J* = 7.3 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz; $CDCl_3$): δ 143.5, 131.7, 131.6, 128.6, 128.5, 128.2, 123.6, 120.5, 89.7, 88.8, 35.8, 33.6, 22.5, 14.1

1-(phenylethynyl)naphthalene (**8a**)



Purified by flash chromatography (1% EtOAc in hexanes). Prepared on 1.00 mmol scale. Isolated as a yellow oil (201.9 mg, 0.8844 mmol, 88%). ^{1}H-NMR (600 MHz, $CDCl_3$): δ 8.50 (d, *J* = 8.4 Hz, 1H), 7.91-7.85 (m, 2H), 7.82 (t, *J* = 8.9 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 2H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.56 (dt, *J* = 9.4, 5.7 Hz, 1H), 7.53-7.48 (m, 1H), 7.45-7.39 (m, 3H).

1-(oct-1-yn-1-yl)naphthalene (**8b**)



Purified by flash chromatography (1→2% EtOAc in hexanes). Prepared on 1.00 mmol scale. Isolated as a yellow oil (144.0 mg, 0.6093 mmol, 61%). ^{1}H-NMR (400 MHz; $CDCl_3$): δ 8.36-8.34 (m, 1H), 7.82 (s, 1H), 7.78 (d, J = 8.3 Hz, 1H), 7.63-7.61 (m, 1H), 7.58-7.48 (m, 2H), 7.40 (s, 1H), 2.57 (t, J = 7.1 Hz, 2H), 1.72-1.70 (m, 2H), 1.59-1.51 (m, 2H), 1.37 (dd, J = 7.3, 3.6 Hz, 4H), 0.95-0.91 (m, 3H). ^{13}C-NMR (101 MHz, $CDCl_3$): δ 133.66 (s, 1C), 133.34 (s, 1C), 130.09 (s, 1C), 128.31 (s, 1C), 127.99 (s, 1C), 126.58 (s, 1C), 126.46 (s, 1C), 126.33 (s, 1C), 125.37 (s, 1C), 121.96 (s, 1C), 95.73 (s, 1C), 78.72 (s, 1C), 31.56 (s, 1C), 29.05 (s, 1C), 28.87 (s, 1C), 22.77 (s, 1C), 19.90 (s, 1C), 14.24 (s, 1C).

General Procedure for the 96-well plate screen

Experiments were run on a 10 μmol scale (0.1 M) with 5% catalyst loading and 10% ligand loading. Plating of reagents was performed as follows: reagents were placed into solution, each vial was charged with the desired amount, and the solvent was removed under a N_2 blow-down solvent evaporation apparatus. Phosphines were dissolved in dichloroethane and plated in solution. Soluble solid reagents were dissolved in THF and plated in solution. Liquid reagents were added to the desired reaction solvent. The order of addition performed is listed as follows: phosphines (1 μmol), $Ni(COD)_2$ (0.5 μmol), base (20 μmol), $ZnCl_2$ (0.5 μmol), liquid reagents (aryl bromide and alkyne, 10 μmol each) and solvent. The vials were sealed with a Teflon film, 2 sheets of rubber, and a metal plate. The reaction was stirred at 50 °C for 12 hours prior to quenching with 100 μL dH_2O. The internal standard (dodecane, 10 μmol) was added in EtOAc (315 μL). The plate was sealed and the contents shaken. The plate was left to rest and settle for 3 hours and the supernatant organic layer removed for GC analysis. The temperature for each run began at 175 °C, ramped from 175 °C to 300 °C at 40 °C/min, and held at 300 °C for 0.875 min.

Preparation of $Ni[P(p\text{-}CF_3\text{-}C_6H_4)_3]_3$ (**9**)

A vial equipped with a stir bar was charged with $Ni(COD)_2$ (55.0 mg, 0.200 mmol) and $P(p\text{-}CF_3\text{-}C_6H_4)_3$ (289.0 mg, 0.620 mmol), dissolved in toluene (2 mL). The red mixture was stirred at ambient temperature for 20 minutes, when a red precipitate was observed. To the solution was added 15 mL pentane and the precipitate was collected via filtration, and rinsed with pentane (3 x 5 mL). The red powder was dried under vacuum to yield the title compound (252 mg, 0.173 mmol, 86%). Elemental Analysis: Calculated: 51.91% C, 2.49% H. Found: 52.13% C, 2.41% H. Crystallization of compound 9 for X-ray analysis: A saturated solution of the compound in toluene was placed in 4 mL vial. This vial was placed in a 20 mL vial containing pentane. Slow diffusion of pentane at -30 °C afforded crystals suitable for single-crystal X-ray diffraction analysis.

General Procedure for Nickel-Catalyzed Sonogashira reaction

A vial equipped with a stir bar was charged with nickel catalyst **9** (4%), the aryl chloride (0.200 mmol, 1 equiv), the alkyne (0.400 mmol, 2 equiv), and NaO^tBu (0.240 mmol, 1.2 equiv). The mixture was dissolved in toluene (0.2 mL, 1.0 M) and stirred at 50 °C for 5 hours. The mix-

ture was quenched with H_2O (1.0 mL) and extracted with EtOAc (2.5 mL). An aliquot of the organic phase was filtered through silica for GC analysis.

X-ray crystallographic data for of Ni[P(*p*-CF_3-C_6H_4)$_3$]$_3$ (9)

A red needle 0.10 x 0.02 x 0.01 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using phi and omega scans. Crystal-to-detector distance was 60 mm and exposure time was 30 seconds per frame using a scan width of 1.0°. Data collection was 98.2% complete to 25.00° in q. A total of 6792 reflections were collected covering the indices, 0<=*h*<=34, 0<=*k*<=21, 0<=*l*<=14. 6927 reflections were found to be symmetry independent, with an R_{int} of 0.2379. Indexing and unit cell refinement indicated a primitive, orthorhombic lattice. The space group was found to be Pna2(1) (No. 33). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SIR-2011) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-97). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-97.

Empirical formula C63 H36 F27 Ni P3
Formula weight 1457.54
Temperature 100(2) K
Wavelength 0.71073 Å
Crystal system Orthorhombic
Space group Pna2(1)
Unit cell dimensions a = 28.400(2) Å a= 90°.
b = 17.8476(14) Å b= 90°.
c = 11.6588(8) Å g = 90°.
Volume 5909.4(8) Å^3
Z 4
Density (calculated) 1.638 Mg/m^3
Absorption coefficient 0.537 mm^{-1}
F(000) 2920
Crystal size 0.10 x 0.02 x 0.01 mm^3
Crystal color/habit red needle
Theta range for data collection 1.43 to 25.40°.
Index ranges 0<=h<=34, 0<=k<=21, 0<=l<=14
Reflections collected 6792
Independent reflections 6927 [R(int) = 0.2379]
Completeness to theta = 25.00° 98.2 %
Absorption correction Semi-empirical from equivalents
Max. and min. transmission 0.9946 and 0.9482
Refinement method Full-matrix least-squares on F^2
Data / restraints / parameters 6927 / 1 / 531
Goodness-of-fit on F^2 1.028
Final R indices [I>2sigma(I)] R1 = 0.0907, wR2 = 0.1349

R indices (all data) R1 = 0.1620, wR2 = 0.1628
Absolute structure parameter 0.11(4)
Largest diff. peak and hole 0.807 and -0.702 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for hartwig19. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	7944(4)	6707(7)	725(10)	16(3)
C(2)	8342(4)	6537(7)	86(11)	19(3)
C(3)	8312(4)	6434(7)	-1106(12)	26(3)
C(4)	7884(4)	6547(8)	-1616(12)	30(3)
C(5)	7496(4)	6755(8)	-1012(13)	34(4)
C(6)	7526(4)	6827(8)	164(11)	24(3)
C(7)	7849(5)	6465(9)	-2906(14)	45(4)
C(8)	8188(3)	5847(6)	2696(11)	18(3)
C(9)	8186(4)	5249(7)	1946(12)	25(3)
C(10)	8296(4)	4524(7)	2301(12)	31(3)
C(11)	8409(4)	4411(7)	3434(11)	21(3)
C(12)	8416(4)	4987(7)	4216(12)	25(3)
C(13)	8309(4)	5705(7)	3851(11)	23(3)
C(14)	8504(4)	3614(8)	3824(12)	29(3)
C(15)	7466(4)	6856(7)	2965(11)	21(3)
C(16)	7083(3)	6388(7)	2669(12)	25(3)
C(17)	6660(5)	6408(9)	3257(13)	39(4)
C(18)	6617(4)	6889(8)	4177(12)	28(3)
C(19)	6983(4)	7334(8)	4536(13)	35(3)
C(20)	7408(4)	7327(7)	3886(10)	21(3)
C(21)	6158(5)	6927(10)	4809(15)	41(4)
C(22)	9371(4)	7388(7)	4290(10)	20(3)
C(23)	9813(4)	7109(7)	4579(11)	22(3)
C(24)	9912(4)	6951(7)	5740(11)	22(3)
C(25)	9576(4)	7054(8)	6572(12)	25(3)
C(26)	9125(4)	7316(8)	6269(12)	31(3)
C(27)	9031(4)	7468(6)	5135(10)	16(3)

C(28)	9680(4)	6881(8)	7777(12)	28(3)
C(29)	9556(4)	6964(7)	1987(10)	17(3)
C(30)	9931(4)	7133(8)	1254(11)	23(3)
C(31)	10152(4)	6563(7)	667(12)	25(3)
C(32)	10005(4)	5833(7)	779(11)	19(3)
C(33)	9647(4)	5657(8)	1521(11)	24(3)
C(34)	9426(4)	6229(7)	2116(11)	20(3)
C(35)	10246(4)	5221(8)	128(12)	22(3)
C(36)	9576(3)	8524(6)	2652(11)	18(3)
C(37)	9520(5)	8956(8)	1696(13)	35(4)
C(38)	9730(5)	9643(9)	1549(14)	42(4)
C(39)	10003(4)	9919(8)	2383(14)	33(3)
C(40)	10109(6)	9505(10)	3361(16)	62(5)
C(41)	9878(5)	8819(10)	3462(14)	50(4)
C(42)	10238(6)	10690(10)	2257(17)	57(5)
C(43)	8469(4)	9641(6)	2804(10)	19(3)
C(44)	8500(4)	10349(6)	2322(12)	24(3)
C(45)	8704(4)	10932(7)	2925(11)	22(3)
C(46)	8868(4)	10818(7)	4004(11)	22(3)
C(47)	8839(4)	10128(7)	4529(13)	29(3)
C(48)	8645(4)	9536(7)	3859(11)	23(3)
C(49)	9049(5)	11466(8)	4703(12)	29(3)
C(50)	8161(4)	8990(7)	607(10)	18(3)
C(51)	7866(4)	9510(7)	100(11)	23(3)
C(52)	7831(4)	9544(7)	-1120(11)	20(3)
C(53)	8097(4)	9052(8)	-1774(11)	19(3)
C(54)	8395(4)	8547(8)	-1271(11)	21(3)
C(55)	8426(4)	8505(7)	-83(11)	21(3)
C(56)	8034(5)	9045(9)	-3045(12)	30(4)
C(57)	7563(3)	8996(6)	2578(11)	14(2)
C(58)	7205(4)	8644(7)	1932(10)	17(3)
C(59)	6738(4)	8697(7)	2305(11)	22(3)
C(60)	6626(4)	9112(7)	3243(10)	18(3)
C(61)	6979(4)	9461(8)	3881(12)	28(3)
C(62)	7437(4)	9406(7)	3511(10)	20(3)
C(63)	6123(5)	9184(8)	3676(13)	31(3)

F(1)	7986(3)	7059(5)	-3485(7)	41(2)
F(2)	7411(3)	6322(7)	-3265(8)	81(4)
F(3)	8122(4)	5898(6)	-3279(8)	82(4)
F(4)	8109(3)	3236(5)	4012(10)	76(4)
F(5)	8753(4)	3236(6)	3076(8)	79(4)
F(6)	8736(3)	3570(4)	4789(7)	38(2)
F(7)	6173(3)	7319(6)	5763(8)	61(3)
F(8)	5821(3)	7210(6)	4151(8)	76(4)
F(9)	6007(3)	6226(5)	5085(8)	51(3)
F(10)	9438(3)	7302(5)	8524(7)	52(3)
F(11)	9558(3)	6176(5)	8065(8)	49(2)
F(12)	10132(3)	6950(6)	8036(7)	64(3)
F(13)	10586(2)	4892(5)	758(7)	42(2)
F(14)	9954(3)	4666(4)	-184(8)	49(3)
F(15)	10467(2)	5450(4)	-826(6)	33(2)
F(16)	10212(5)	11084(9)	3240(14)	52(5)
F(17)	10709(5)	10606(9)	2144(13)	46(5)
F(18)	10075(8)	11067(13)	1390(20)	103(8)
F(16A)	10540(10)	10850(17)	3060(30)	87(11)
F(17A)	10418(7)	10818(13)	1251(19)	50(8)
F(18A)	9914(7)	11231(12)	2220(20)	49(7)
F(19)	9330(4)	11254(5)	5555(10)	90(4)
F(20)	8710(3)	11852(6)	5218(9)	71(3)
F(21)	9285(3)	11951(5)	4114(8)	62(3)
F(22)	7987(3)	9728(5)	-3505(7)	56(3)
F(23)	8390(3)	8715(5)	-3607(6)	40(2)
F(24)	7647(3)	8675(6)	-3377(8)	62(3)
F(25)	5824(2)	8801(6)	3012(8)	62(3)
F(26)	6064(3)	8953(6)	4704(8)	59(3)
F(27)	5981(3)	9875(5)	3593(12)	86(4)
P(1)	8043(1)	6816(2)	2283(3)	15(1)
P(2)	9228(1)	7667(2)	2806(3)	16(1)
P(3)	8182(1)	8821(2)	2154(3)	15(1)
Ni(1)	8489(1)	7756(1)	2477(1)	14(1)

Bond lengths [Å] and angles [°].

C(1)-C(6)	1.372(15)	C(16)-H(16)	0.9500
C(1)-C(2)	1.388(15)	C(17)-C(18)	1.380(19)
C(1)-P(1)	1.849(12)	C(17)-H(17)	0.9500
C(2)-C(3)	1.405(18)	C(18)-C(19)	1.374(17)
C(2)-H(2)	0.9500	C(18)-C(21)	1.499(18)
C(3)-C(4)	1.366(17)	C(19)-C(20)	1.425(16)
C(3)-H(3)	0.9500	C(19)-H(19)	0.9500
C(4)-C(5)	1.359(18)	C(20)-H(20)	0.9500
C(4)-C(7)	1.51(2)	C(21)-F(7)	1.315(18)
C(5)-C(6)	1.381(18)	C(21)-F(8)	1.328(16)
C(5)-H(5)	0.9500	C(21)-F(9)	1.362(17)
C(6)-H(6)	0.9500	C(22)-C(27)	1.385(15)
C(7)-F(1)	1.315(17)	C(22)-C(23)	1.392(15)
C(7)-F(2)	1.337(16)	C(22)-P(2)	1.846(12)
C(7)-F(3)	1.348(17)	C(23)-C(24)	1.412(17)
C(8)-C(9)	1.379(16)	C(23)-H(23)	0.9500
C(8)-C(13)	1.412(18)	C(24)-C(25)	1.373(17)
C(8)-P(1)	1.842(12)	C(24)-H(24)	0.9500
C(9)-C(10)	1.394(17)	C(25)-C(26)	1.410(16)
C(9)-H(9)	0.9500	C(25)-C(28)	1.469(19)
C(10)-C(11)	1.375(18)	C(26)-C(27)	1.376(17)
C(10)-H(10)	0.9500	C(26)-H(26)	0.9500
C(11)-C(12)	1.374(17)	C(27)-H(27)	0.9500
C(11)-C(14)	1.516(18)	C(28)-F(12)	1.323(13)
C(12)-C(13)	1.384(17)	C(28)-F(10)	1.340(14)
C(12)-H(12)	0.9500	C(28)-F(11)	1.349(15)
C(13)-H(13)	0.9500	C(29)-C(34)	1.370(16)
C(14)-F(6)	1.307(15)	C(29)-C(30)	1.399(16)
C(14)-F(5)	1.312(15)	C(29)-P(2)	1.831(12)
C(14)-F(4)	1.327(14)	C(30)-C(31)	1.377(17)
C(15)-C(20)	1.373(17)	C(30)-H(30)	0.9500
C(15)-C(16)	1.413(15)	C(31)-C(32)	1.374(17)
C(15)-P(1)	1.823(12)	C(31)-H(31)	0.9500
C(16)-C(17)	1.383(16)	C(32)-C(33)	1.371(16)

C(32)-C(35)	1.497(17)	C(48)-H(48)	0.9500
C(33)-C(34)	1.385(16)	C(49)-F(21)	1.292(15)
C(33)-H(33)	0.9500	C(49)-F(20)	1.326(15)
C(34)-H(34)	0.9500	C(49)-F(19)	1.328(16)
C(35)-F(15)	1.341(14)	C(50)-C(51)	1.382(16)
C(35)-F(14)	1.342(13)	C(50)-C(55)	1.401(16)
C(35)-F(13)	1.348(14)	C(50)-P(3)	1.829(12)
C(36)-C(37)	1.364(18)	C(51)-C(52)	1.426(17)
C(36)-C(41)	1.381(18)	C(51)-H(51)	0.9500
C(36)-P(2)	1.831(11)	C(52)-C(53)	1.387(17)
C(37)-C(38)	1.374(19)	C(52)-H(52)	0.9500
C(37)-H(37)	0.9500	C(53)-C(54)	1.369(17)
C(38)-C(39)	1.339(19)	C(53)-C(56)	1.492(17)
C(38)-H(38)	0.9500	C(54)-C(55)	1.390(17)
C(39)-C(40)	1.39(2)	C(54)-H(54)	0.9500
C(39)-C(42)	1.54(2)	C(55)-H(55)	0.9500
C(40)-C(41)	1.39(2)	C(56)-F(22)	1.339(16)
C(40)-H(40)	0.9500	C(56)-F(23)	1.339(15)
C(41)-H(41)	0.9500	C(56)-F(24)	1.341(15)
C(42)-F(18)	1.30(3)	C(57)-C(62)	1.360(16)
C(42)-F(16A)	1.30(3)	C(57)-C(58)	1.412(15)
C(42)-F(17A)	1.30(3)	C(57)-P(3)	1.853(10)
C(42)-F(18A)	1.33(3)	C(58)-C(59)	1.400(14)
C(42)-F(16)	1.35(2)	C(58)-H(58)	0.9500
C(42)-F(17)	1.35(2)	C(59)-C(60)	1.359(16)
C(43)-C(48)	1.341(16)	C(59)-H(59)	0.9500
C(43)-C(44)	1.387(15)	C(60)-C(61)	1.394(16)
C(43)-P(3)	1.838(12)	C(60)-C(63)	1.520(17)
C(44)-C(45)	1.383(16)	C(61)-C(62)	1.373(15)
C(44)-H(44)	0.9500	C(61)-H(61)	0.9500
C(45)-C(46)	1.357(17)	C(62)-H(62)	0.9500
C(45)-H(45)	0.9500	C(63)-F(26)	1.279(16)
C(46)-C(47)	1.378(17)	C(63)-F(27)	1.301(16)
C(46)-C(49)	1.505(18)	C(63)-F(25)	1.337(15)
C(47)-C(48)	1.425(17)	P(1)-Ni(1)	2.114(3)
C(47)-H(47)	0.9500	P(2)-Ni(1)	2.141(3)

P(3)-Ni(1)	2.124(4)

C(6)-C(1)-C(2)	118.9(12)
C(6)-C(1)-P(1)	125.7(9)
C(2)-C(1)-P(1)	115.3(8)
C(1)-C(2)-C(3)	120.6(11)
C(1)-C(2)-H(2)	119.7
C(3)-C(2)-H(2)	119.7
C(4)-C(3)-C(2)	117.8(12)
C(4)-C(3)-H(3)	121.1
C(2)-C(3)-H(3)	121.1
C(5)-C(4)-C(3)	122.3(14)
C(5)-C(4)-C(7)	119.1(13)
C(3)-C(4)-C(7)	118.5(13)
C(4)-C(5)-C(6)	119.4(13)
C(4)-C(5)-H(5)	120.3
C(6)-C(5)-H(5)	120.3
C(1)-C(6)-C(5)	120.8(12)
C(1)-C(6)-H(6)	119.6
C(5)-C(6)-H(6)	119.6
F(1)-C(7)-F(2)	105.6(13)
F(1)-C(7)-F(3)	105.6(12)
F(2)-C(7)-F(3)	106.9(14)
F(1)-C(7)-C(4)	114.4(14)
F(2)-C(7)-C(4)	113.0(13)
F(3)-C(7)-C(4)	110.8(14)
C(9)-C(8)-C(13)	117.9(11)
C(9)-C(8)-P(1)	124.0(9)
C(13)-C(8)-P(1)	118.1(9)
C(8)-C(9)-C(10)	121.9(13)
C(8)-C(9)-H(9)	119.0
C(10)-C(9)-H(9)	119.0
C(11)-C(10)-C(9)	118.3(13)
C(11)-C(10)-H(10)	120.9
C(9)-C(10)-H(10)	120.9
C(12)-C(11)-C(10)	122.0(13)
C(12)-C(11)-C(14)	120.0(11)

C(10)-C(11)-C(14)	117.9(12)
C(11)-C(12)-C(13)	119.1(12)
C(11)-C(12)-H(12)	120.5
C(13)-C(12)-H(12)	120.5
C(12)-C(13)-C(8)	120.8(13)
C(12)-C(13)-H(13)	119.6
C(8)-C(13)-H(13)	119.6
F(6)-C(14)-F(5)	105.6(11)
F(6)-C(14)-F(4)	104.8(12)
F(5)-C(14)-F(4)	107.7(13)
F(6)-C(14)-C(11)	113.8(12)
F(5)-C(14)-C(11)	112.2(12)
F(4)-C(14)-C(11)	112.2(11)
C(20)-C(15)-C(16)	117.4(11)
C(20)-C(15)-P(1)	118.2(9)
C(16)-C(15)-P(1)	124.1(10)
C(17)-C(16)-C(15)	122.1(13)
C(17)-C(16)-H(16)	118.9
C(15)-C(16)-H(16)	118.9
C(18)-C(17)-C(16)	118.5(13)
C(18)-C(17)-H(17)	120.7
C(16)-C(17)-H(17)	120.7
C(19)-C(18)-C(17)	122.0(12)
C(19)-C(18)-C(21)	118.8(13)
C(17)-C(18)-C(21)	119.2(12)
C(18)-C(19)-C(20)	118.2(14)
C(18)-C(19)-H(19)	120.9
C(20)-C(19)-H(19)	120.9
C(15)-C(20)-C(19)	121.5(12)
C(15)-C(20)-H(20)	119.2
C(19)-C(20)-H(20)	119.2
F(7)-C(21)-F(8)	108.0(13)
F(7)-C(21)-F(9)	107.5(13)
F(8)-C(21)-F(9)	105.0(12)
F(7)-C(21)-C(18)	114.3(13)

F(8)-C(21)-C(18)	111.1(13)
F(9)-C(21)-C(18)	110.4(13)
C(27)-C(22)-C(23)	119.6(11)
C(27)-C(22)-P(2)	119.0(8)
C(23)-C(22)-P(2)	121.4(9)
C(22)-C(23)-C(24)	118.9(11)
C(22)-C(23)-H(23)	120.6
C(24)-C(23)-H(23)	120.6
C(25)-C(24)-C(23)	120.8(11)
C(25)-C(24)-H(24)	119.6
C(23)-C(24)-H(24)	119.6
C(24)-C(25)-C(26)	120.0(13)
C(24)-C(25)-C(28)	120.5(11)
C(26)-C(25)-C(28)	119.5(12)
C(27)-C(26)-C(25)	118.8(12)
C(27)-C(26)-H(26)	120.6
C(25)-C(26)-H(26)	120.6
C(26)-C(27)-C(22)	121.9(11)
C(26)-C(27)-H(27)	119.0
C(22)-C(27)-H(27)	119.0
F(12)-C(28)-F(10)	107.3(11)
F(12)-C(28)-F(11)	106.2(11)
F(10)-C(28)-F(11)	103.2(10)
F(12)-C(28)-C(25)	113.2(11)
F(10)-C(28)-C(25)	113.6(11)
F(11)-C(28)-C(25)	112.5(12)
C(34)-C(29)-C(30)	118.5(12)
C(34)-C(29)-P(2)	117.6(9)
C(30)-C(29)-P(2)	123.9(10)
C(31)-C(30)-C(29)	119.5(12)
C(31)-C(30)-H(30)	120.3
C(29)-C(30)-H(30)	120.3
C(32)-C(31)-C(30)	120.9(12)
C(32)-C(31)-H(31)	119.6
C(30)-C(31)-H(31)	119.6

C(33)-C(32)-C(31)	120.2(12)
C(33)-C(32)-C(35)	119.4(12)
C(31)-C(32)-C(35)	120.3(11)
C(32)-C(33)-C(34)	118.9(12)
C(32)-C(33)-H(33)	120.6
C(34)-C(33)-H(33)	120.6
C(29)-C(34)-C(33)	121.9(11)
C(29)-C(34)-H(34)	119.0
C(33)-C(34)-H(34)	119.0
F(15)-C(35)-F(14)	106.8(11)
F(15)-C(35)-F(13)	104.5(9)
F(14)-C(35)-F(13)	105.5(10)
F(15)-C(35)-C(32)	114.3(11)
F(14)-C(35)-C(32)	113.2(10)
F(13)-C(35)-C(32)	111.8(11)
C(37)-C(36)-C(41)	114.6(12)
C(37)-C(36)-P(2)	119.3(10)
C(41)-C(36)-P(2)	126.0(11)
C(36)-C(37)-C(38)	123.8(14)
C(36)-C(37)-H(37)	118.1
C(38)-C(37)-H(37)	118.1
C(39)-C(38)-C(37)	119.3(15)
C(39)-C(38)-H(38)	120.4
C(37)-C(38)-H(38)	120.4
C(38)-C(39)-C(40)	121.6(15)
C(38)-C(39)-C(42)	120.8(15)
C(40)-C(39)-C(42)	117.5(14)
C(39)-C(40)-C(41)	115.8(16)
C(39)-C(40)-H(40)	122.1
C(41)-C(40)-H(40)	122.1
C(36)-C(41)-C(40)	124.7(16)
C(36)-C(41)-H(41)	117.7
C(40)-C(41)-H(41)	117.7
F(18)-C(42)-F(16A)	133(2)
F(18)-C(42)-F(17A)	49.4(14)

F(16A)-C(42)-F(17A)	110(2)
F(18)-C(42)-F(18A)	49.5(14)
F(16A)-C(42)-F(18A)	109(2)
F(17A)-C(42)-F(18A)	96.4(19)
F(18)-C(42)-F(16)	111.8(18)
F(16A)-C(42)-F(16)	46.3(14)
F(17A)-C(42)-F(16)	134.2(19)
F(18A)-C(42)-F(16)	67.5(15)
F(18)-C(42)-F(17)	109.6(18)
F(16A)-C(42)-F(17)	56.0(15)
F(17A)-C(42)-F(17)	62.7(14)
F(18A)-C(42)-F(17)	139.3(18)
F(16)-C(42)-F(17)	101.2(15)
F(18)-C(42)-C(39)	112.6(18)
F(16A)-C(42)-C(39)	115(2)
F(17A)-C(42)-C(39)	114.5(18)
F(18A)-C(42)-C(39)	110.7(14)
F(16)-C(42)-C(39)	111.3(15)
F(17)-C(42)-C(39)	109.8(14)
C(48)-C(43)-C(44)	118.4(12)
C(48)-C(43)-P(3)	115.6(9)
C(44)-C(43)-P(3)	126.0(9)
C(45)-C(44)-C(43)	120.4(12)
C(45)-C(44)-H(44)	119.8
C(43)-C(44)-H(44)	119.8
C(46)-C(45)-C(44)	120.2(13)
C(46)-C(45)-H(45)	119.9
C(44)-C(45)-H(45)	119.9
C(45)-C(46)-C(47)	121.7(13)
C(45)-C(46)-C(49)	120.3(12)
C(47)-C(46)-C(49)	117.8(12)
C(46)-C(47)-C(48)	116.3(13)
C(46)-C(47)-H(47)	121.9
C(48)-C(47)-H(47)	121.9
C(43)-C(48)-C(47)	123.0(12)

C(43)-C(48)-H(48)	118.5
C(47)-C(48)-H(48)	118.5
F(21)-C(49)-F(20)	105.6(12)
F(21)-C(49)-F(19)	106.1(12)
F(20)-C(49)-F(19)	104.2(13)
F(21)-C(49)-C(46)	113.8(12)
F(20)-C(49)-C(46)	113.4(11)
F(19)-C(49)-C(46)	113.0(12)
C(51)-C(50)-C(55)	119.6(12)
C(51)-C(50)-P(3)	123.6(10)
C(55)-C(50)-P(3)	116.5(9)
C(50)-C(51)-C(52)	119.8(12)
C(50)-C(51)-H(51)	120.1
C(52)-C(51)-H(51)	120.1
C(53)-C(52)-C(51)	118.9(12)
C(53)-C(52)-H(52)	120.5
C(51)-C(52)-H(52)	120.5
C(54)-C(53)-C(52)	121.2(12)
C(54)-C(53)-C(56)	119.6(13)
C(52)-C(53)-C(56)	119.2(12)
C(53)-C(54)-C(55)	120.1(12)
C(53)-C(54)-H(54)	120.0
C(55)-C(54)-H(54)	120.0
C(54)-C(55)-C(50)	120.3(12)
C(54)-C(55)-H(55)	119.8
C(50)-C(55)-H(55)	119.8
F(22)-C(56)-F(23)	106.2(11)
F(22)-C(56)-F(24)	104.5(11)
F(23)-C(56)-F(24)	105.2(12)
F(22)-C(56)-C(53)	113.7(13)
F(23)-C(56)-C(53)	113.6(12)
F(24)-C(56)-C(53)	112.8(12)
C(62)-C(57)-C(58)	118.4(10)
C(62)-C(57)-P(3)	123.7(8)
C(58)-C(57)-P(3)	117.8(9)

C(59)-C(58)-C(57)	119.1(11)
C(59)-C(58)-H(58)	120.4
C(57)-C(58)-H(58)	120.4
C(60)-C(59)-C(58)	120.6(11)
C(60)-C(59)-H(59)	119.7
C(58)-C(59)-H(59)	119.7
C(59)-C(60)-C(61)	120.3(11)
C(59)-C(60)-C(63)	122.2(11)
C(61)-C(60)-C(63)	117.4(11)
C(62)-C(61)-C(60)	118.8(13)
C(62)-C(61)-H(61)	120.6
C(60)-C(61)-H(61)	120.6
C(57)-C(62)-C(61)	122.7(12)
C(57)-C(62)-H(62)	118.7
C(61)-C(62)-H(62)	118.7
F(26)-C(63)-F(27)	109.6(14)
F(26)-C(63)-F(25)	107.1(12)
F(27)-C(63)-F(25)	104.2(12)
F(26)-C(63)-C(60)	114.0(11)
F(27)-C(63)-C(60)	110.2(12)
F(25)-C(63)-C(60)	111.2(12)
C(15)-P(1)-C(8)	97.2(5)
C(15)-P(1)-C(1)	107.2(5)
C(8)-P(1)-C(1)	101.1(6)
C(15)-P(1)-Ni(1)	117.4(4)
C(8)-P(1)-Ni(1)	125.7(4)
C(1)-P(1)-Ni(1)	106.2(4)
C(36)-P(2)-C(29)	104.3(5)
C(36)-P(2)-C(22)	101.5(6)
C(29)-P(2)-C(22)	101.1(6)
C(36)-P(2)-Ni(1)	116.8(4)
C(29)-P(2)-Ni(1)	117.1(4)
C(22)-P(2)-Ni(1)	113.8(4)
C(50)-P(3)-C(43)	106.8(6)
C(50)-P(3)-C(57)	101.8(5)

C(43)-P(3)-C(57)	100.1(5)
C(50)-P(3)-Ni(1)	109.6(4)
C(43)-P(3)-Ni(1)	117.3(4)
C(57)-P(3)-Ni(1)	119.5(4)
P(1)-Ni(1)-P(3)	116.53(13)
P(1)-Ni(1)-P(2)	123.20(14)
P(3)-Ni(1)-P(2)	119.97(14)

Anisotropic displacement parameters ($Å^2 x\ 10^3$). The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
F(1)	53(5)	45(6)	27(5)	7(5)	-5(4)	-24(4)
F(2)	73(6)	140(11)	28(6)	1(7)	-19(5)	-72(7)
F(3)	165(11)	52(7)	28(6)	-6(5)	-8(6)	45(7)
F(4)	54(5)	34(5)	139(11)	39(7)	-37(6)	-18(5)
F(5)	162(10)	40(6)	34(6)	3(5)	24(6)	49(6)
F(6)	46(5)	32(5)	36(5)	4(4)	-5(4)	0(4)
F(7)	48(5)	80(7)	56(6)	9(7)	27(5)	18(5)
F(8)	31(4)	116(9)	82(8)	63(8)	14(5)	33(5)
F(9)	33(4)	58(6)	62(7)	15(6)	19(4)	-3(4)
F(10)	77(6)	57(7)	22(5)	-4(5)	1(4)	22(5)
F(11)	77(6)	26(5)	43(6)	17(5)	-17(5)	-11(5)
F(12)	44(5)	116(9)	32(5)	26(6)	-18(4)	-30(6)
F(13)	41(4)	43(6)	43(5)	9(5)	5(4)	27(4)
F(14)	38(4)	27(5)	82(7)	-34(5)	9(4)	2(4)
F(15)	41(4)	31(5)	27(5)	-2(4)	11(4)	6(4)
F(19)	135(9)	23(6)	113(10)	-4(6)	-103(8)	-6(6)
F(20)	61(6)	59(7)	94(9)	-58(7)	28(6)	-27(5)
F(21)	75(6)	40(6)	70(8)	-22(6)	15(6)	-30(5)
F(22)	118(8)	43(6)	8(4)	6(5)	2(5)	33(6)
F(23)	49(5)	52(6)	19(4)	9(5)	15(4)	25(4)
F(24)	52(5)	86(8)	47(6)	-16(6)	-14(5)	-2(5)
F(25)	25(4)	95(8)	65(7)	-20(6)	9(4)	-9(5)

F(26)	33(4)	99(8)	46(6)	20(6)	12(4)	10(5)
F(27)	41(5)	37(6)	180(12)	17(7)	45(6)	17(5)
P(1)	15(1)	17(2)	13(2)	-5(2)	0(1)	0(1)
P(2)	14(1)	16(2)	17(2)	4(2)	1(1)	0(1)
P(3)	17(1)	16(2)	13(2)	0(2)	1(1)	1(1)
Ni(1)	14(1)	13(1)	15(1)	-1(1)	-2(1)	0(1)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3).

	x	y	z	U(eq)
H(2)	8638	6490	459	23
H(3)	8579	6291	-1544	31
H(5)	7208	6851	-1397	40
H(6)	7254	6962	591	29
H(9)	8106	5334	1165	30
H(10)	8293	4119	1772	37
H(12)	8493	4893	4996	30
H(13)	8318	6108	4383	27
H(16)	7118	6049	2047	29
H(17)	6405	6097	3031	47
H(19)	6954	7639	5200	42
H(20)	7657	7656	4094	25
H(23)	10045	7027	4004	26
H(24)	10215	6771	5949	26
H(26)	8889	7385	6837	37
H(27)	8725	7634	4924	19
H(30)	10032	7637	1162	27
H(31)	10410	6676	178	30
H(33)	9553	5151	1626	29
H(34)	9177	6109	2627	24
H(37)	9325	8771	1099	42
H(38)	9681	9919	863	50
H(40)	10324	9679	3924	74

H(41)	9933	8534	4137	59
H(44)	8380	10435	1573	28
H(45)	8730	11414	2583	27
H(47)	8943	10051	5294	35
H(48)	8639	9046	4175	27
H(51)	7688	9843	562	27
H(52)	7629	9898	-1477	24
H(54)	8581	8224	-1735	25
H(55)	8628	8146	263	25
H(58)	7281	8374	1255	21
H(59)	6497	8441	1899	26
H(61)	6904	9731	4559	34
H(62)	7674	9665	3924	24

2.5 References

(1) Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, *107*, 874.
(2) Doucet, H.; Hierso, J.-C. *Angew. Chem. Int. Ed.* **2007**, *46*, 834.
(3) Negishi, E.-I.; Anastasia, L. *Chem. Rev.* **2003**, *103*, 1979.
(4) Roughley, S. D.; Jordan, A. M. *J. Med. Chem.* **2011**, *54*, 3451.
(5) Stork, G.; Borch, R. *J. Am. Chem. Soc.* **1961**, *86*, 1.
(6) Gelman, D.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2003**, *42*, 5993.
(7) Ruiz, J.; Cutillas, N.; López, F.; López, G.; Bautista, D. *Organometallics* **2006**, *25*, 5768.
(8) Ljungdahl, T.; Bennur, T.; Dallas, A.; Emtenäs, H.; Mårtensson, J. *Organometallics* **2008**, *27*, 2490.
(9) García-Melchor, M.; Pacheco, M. C.; Nájera, C.; Lledós, A.; Ujaque, G. *ACS Catal.* **2012**, *2*, 135.
(10) Sikk, L.; Tammiku-Taul, J.; Burk, P. *Organometallics* **2011**, *30*, 5656.
(11) Soheili, A.; Albaneze-Walker, J.; Murry, J. A.; Dormer, P. G.; Hughes, D. L. *Org. Lett.* **2003**, *5*, 4191.
(12) Beletskaya, I. P.; Latyshev, G. V.; Tsvetkov, A. V.; Lukashev, N. V. *Tetrahedron Lett.* **2003**, *44*, 5011.
(13) Gallego, D.; Brück, A.; Irran, E.; Meier, F.; Kaupp, M.; Driess, M.; Hartwig, J. F. *Journal of the …* **2013**.
(14) Vechorkin, O.; Barmaz, D.; Proust, V.; Hu, X. *J. Am. Chem. Soc.* **2009**, *131*, 12078.
(15) Perez Garcia, P. M.; Ren, P.; Scopelliti, R.; Hu, X. *ACS Catal.* **2015**, *5*, 1164.
(16) Yi, J.; Lu, X.; Sun, Y.-Y.; Xiao, B.; Liu, L. *Angew. Chem. Int. Ed.* **2013**, *52*, 12409.
(17) Vechorkin, O.; Godinat, A.; Scopelliti, R.; Hu, X. *Angew. Chem. Int. Ed.* **2011**, *50*, 11777.

(18) Xu, G.; Li, X.; Sun, H. *J. Organomet. Chem.* **2011**, *696*, 3011.
(19) Tobisu, M.; Takahira, T.; Ohtsuki, A.; Chatani, N. *Org. Lett.* **2015**, *17*, 150113095731002.
(20) Ge, S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 16330.
(21) King, A. O.; Negishi, E.; Villani, F. J., Jr; Silveira, A., Jr. *J. Org. Chem.* **1978**, *43*, 358.
(22) Denmark, S. E.; Regens, C. S. *Acc. Chem. Res.* **2008**, *41*, 1486.
(23) Chang, S.; Yang, S.; Lee, P. *Tetrahedron Lett.* **2001**, *42*, 4833.
(24) Nishihara, Y.; Ikegashira, K.; Mori, A.; Hiyama, T. *Chemistry Letters* **1997**, No. 12, 1233.
(25) Spee, M. P. R.; Boersma, J.; Meijer, M. D.; Slagt, M. Q.; van Koten, G.; Geus, J. W. *J. Org. Chem.* **2001**, *66*, 1647.
(26) Terao, Y.; Wakui, H.; Satoh, T.; Miura, M.; Nomura, M. *J. Am. Chem. Soc.* **2001**, *123*, 10407.
(27) *Nickel-Catalyzed Cyanation of Aromatic Halides*; Advances in Chemistry Series: Washington, D. C., 1974; Vol. 132, pp 252–273.
(28) De Roma, A.; Yang, H.-J.; Milione, S.; Capacchione, C.; Roviello, G.; Grassi, A. *Inorg. Chem. Commun.* **2011**, *14*, 542.

CHAPTER 3

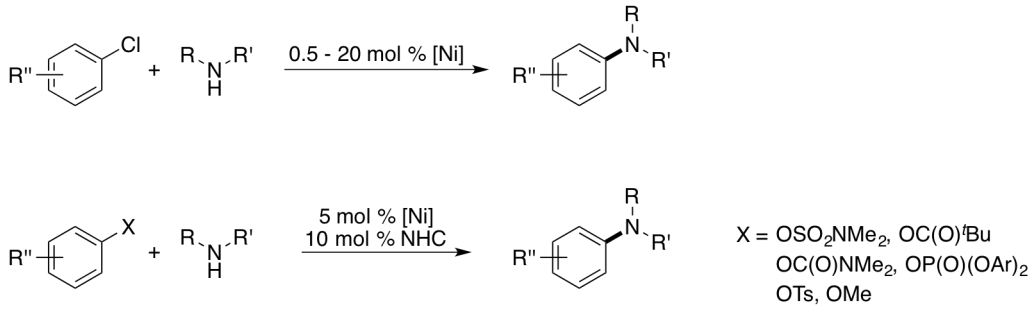
Nickel-Catalyzed Amination of Aryl and Heteroaryl Chlorides and Bromides with Primary Aliphatic Amines

3.1 Introduction

Transition-metal-catalyzed aminations of aryl halides are one of the most powerful methods to construct arylamines.[1] The development of methods to couple aryl halides with amines has been studied extensively in the past decade. Most studies have focused on palladium and copper complexes as catalysts. Palladium-catalyzed reactions occur with a broad scope of both coupling partners, high functional group tolerance, and very good selectivity for monoarylation of the amine nucleophile.[2,3] However, this scope is accomplished at a price. Both the palladium metal and the ligands used for this reaction are costly, and the ligand is difficult to recycle.

For these reasons, much interest has been paid recently to develop catalytic reactions with first-row metal complexes that are typically catalyzed by precious metals. For example, copper complexes have been studied extensively for the coupling of aryl iodides, and to a lesser extent aryl bromides, with nitrogen nucleophiles.[4] Yet, the scope of such coupling with electron-rich bromoarenes, ortho-substituted bromoarenes, unactivated aryl chlorides, and heteroaryl halides is limited. Many of the first-row metals are more electropositive than those of the second row and form electron-rich low-valent species.

Scheme 3.1 Previous Work for Nickel-Catalyzed C-N Coupling Reactions.



Indeed, nickel complexes have been shown to catalyze the amination of aryl halides and phenol derivatives (Scheme 3.1).[5-24] Such nickel-catalyzed amination reactions could be more practical than palladium-catalyzed aminations on large scale because the metal is much less expensive, and much simpler ligands on the nickel center are needed for the catalyst to react with aryl chlorides. For example, Hidai showed over 40 years ago that $Ni(PPh_3)_4$ adds phenyl chloride at room temperature to form $(PPh_3)_2Ni(Ph)(Cl)$.[25] However, the scope of nickel-catalyzed aminations of aryl halides has been limited to the coupling of secondary alkylamines and arylamines.[11-19] Primary alkylamines, one of the most significant classes of amines for such cross coupling, have been shown to couple only with activated aryl chlorides.[11,17]

In addition to the limitations on the scope of the coupling of aryl halides with amines, the mechanism of the coupling of aryl halides with amines catalyzed by nickel complexes has not been studied. Many papers cite the potential of Ni(I) intermediates,[26] either as part of a one-electron redox events or as part of a mechanism involving Ni(I) and Ni(III) intermediates. In contrast, the mechanism for the palladium-catalyzed amination of aryl electrophiles has been studied in detail, including the kinetic behavior of the catalytic reaction and stoichiometric reactions of isolated intermediates.[27-30] Such

studies have not been conducted on nickel-catalyzed couplings to form C-N bonds, but are particularly important if one is to determine how to create catalysts of nickel that are as long-lived as those of palladium and that react with similarly broad scope.

Here, we present the first nickel-catalyzed aminations of unactivated aryl chlorides with primary aliphatic amines. The reaction occurs with aryl and heteroaryl chlorides and bromides catalyzed by a single-component BINAP-ligated nickel(0) precursor. Kinetic studies have been conducted on the reaction, and studies on the relative rates of the reaction with various isolated nickel complexes have been conducted. These studies rule out a catalytic cycle occurring through a Ni(I) halide intermediate and are consistent with a Ni(0)/Ni(II) catalytic cycle for the amination of aryl chlorides and aryl bromides, which react with different Ni(0) species.

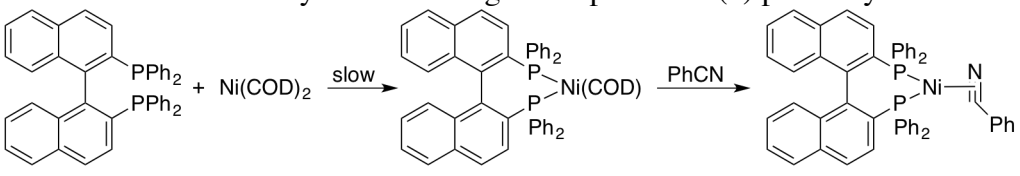
3.2 Results and Discussion

3.2.1 Evaluation of Different Ligands for the Ni-Catalyzed Amination Reaction

We initiated our studies of nickel-catalyzed amination of aryl chlorides with primary aliphatic amines by studying the reaction between 3-chloroanisole and octylamine. We investigated nickel complexes generated in situ from $Ni(COD)_2$ and various phosphine ligands as catalysts. These results are listed in Table 3.1. These reactions were conducted with NaO^tBu as base in toluene at 50 °C. Reactions catalyzed by the combination of $Ni(COD)_2$ and monophosphines, such as PPh_3 and PCy_3, afforded only trace amounts of the desired amine product. Similar results (< 5% conversion and < 2% yield) were obtained for reactions catalyzed by the combination of $Ni(COD)_2$ (1 mol %) and dppe, dppp, or dppb (1 or 2 mol %). However, reactions catalyzed by the combination of $Ni(COD)_2$ and dppf or BINAP gave significant amounts of product (16–67%).

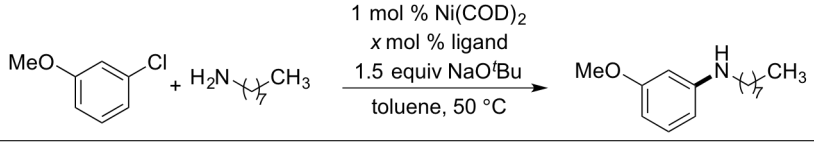
The displacement of COD from $Ni(COD)_2$ by BINAP is slow. Therefore, we wanted to create a single-component Ni(0) complex that was not ligated by COD (Scheme 3.2). We found that substitution of bidentate ligand COD by monodentate ligand PhCN formed a catalyst, **1**, that afforded the amination reaction product in 92% yield. An explanation for the high activity of this catalyst will be revealed during the presentation of our mechanistic studies.

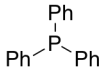
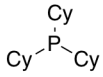
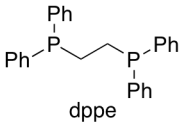
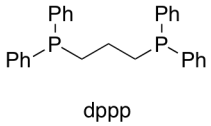
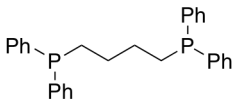
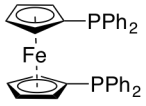
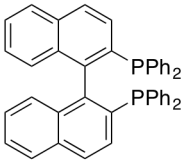
Scheme 3.2 Synthesis of single-component Ni(0) precatalyst



1, 92%

Table 3.1 Evaluation of Nickel Precursors and Ligands for Amination of 3-Chloroanisole with Octylamine[a]



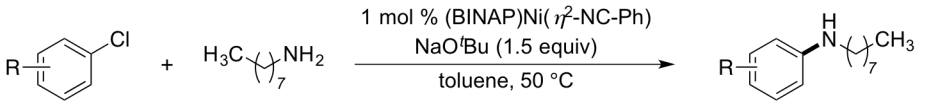
		 dppe	 dppp
x = 2 < 5% conv. 3% yield	*x* = 2 < 5% conv. 3% yield	*x* = 1 < 5% conv. < 2% yield	*x* = 1 < 5% conv. < 2% yield
x = 4 < 5% conv. < 2% yield	*x* = 4 < 5% conv. < 2% yield	*x* = 2 < 5% conv. < 2% yield	*x* = 2 < 5% conv. < 2% yield
 dppb	 dppf	 BINAP	
x = 1 < 5% conv. < 2% yield	*x* = 1 31% conv. 16% yield	*x* = 1 71% conv. 66% yield	
x = 2 < 5% conv. < 2% yield	*x* = 2 44% conv. 32% yield	*x* = 2 75% conv. 67% yield	

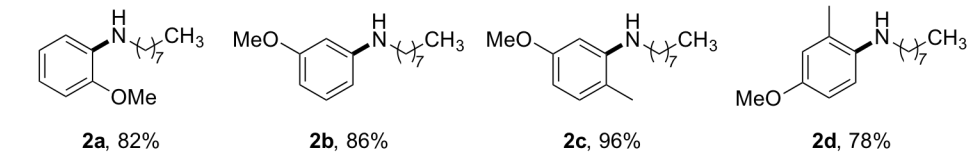
[a] Conditions: 3-chloroanisole (0.400 mmol), octylamine (0.600 mmol), NaO^{t}Bu (0.600 mmol), 24 h; Conversion and yield were determined by GC analysis using dodecane as internal standard.
[b] [Ni^0] = (BINAP)Ni(η^2-NCPh).

3.2.2 Scope of the Ni-Catalyzed Amination of Aryl Chlorides with Primary Aliphatic Amines.

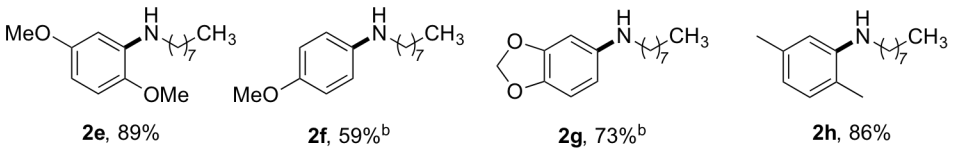
With an active catalyst in hand and reliable conditions identified for this Ni-catalyzed amination, we studied the scope of aryl chlorides that undergo these amination reactions, and the results are summarized in Table 3.2. In general, a range of electron-rich (**2a**–**2e**), electron-neutral (**2h**), and electron-deficient (**2i**–**2l**) aryl chlorides coupled with octylamine in high yields (76–96%) under the developed conditions with 1 mol % nickel complex **1**. For very electron-rich aryl chlorides, 4 mol % of the catalyst was required to obtain modest to good yields (**2f** and **2g**). For these two reactions, aryl chlorides were not fully converted, and only trace amounts (< 5%) of biaryl compounds were detected by GC analysis. Mono-*ortho*-substituted aryl chlorides reacted in high yields (**2a**, **2c**–**2e**, **2h**, and **2j**). However, di-*ortho*-substituted aryl chlorides, such as 2-chloro-1,3-dimethylbenzene, did not couple with octylamine under the developed conditions.

Table 3.2 Nickel-Catalyzed Amination: Aryl Chloride Scope[a]

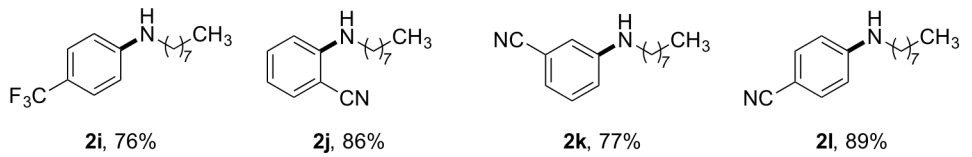




2a, 82% **2b**, 86% **2c**, 96% **2d**, 78%



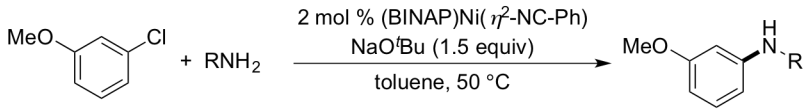
2e, 89% **2f**, 59%[b] **2g**, 73%[b] **2h**, 86%

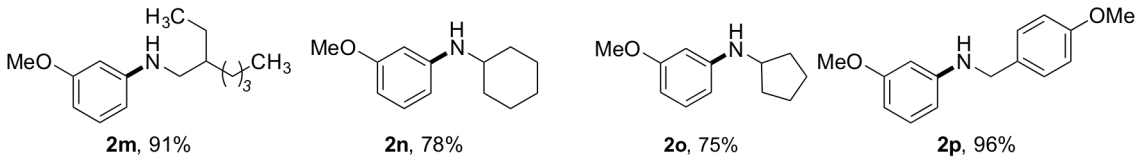


2i, 76% **2j**, 86% **2k**, 77% **2l**, 89%

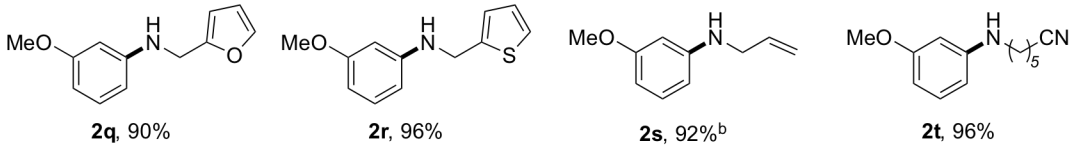
[a] Conditions: ArCl (0.400 mmol), octylamine (0.600 mmol), (BINAP)Ni(η^2-NCPh) (4.0 μmol, 1 mol %), NaO^{t}Bu (0.600 mmol), toluene (1 mL), temperature: 50 °C; reaction time: 24 h;
[b] (BINAP)Ni(η^2-NCPh) (16.0 μmol, 4 mol %).

Table 3.3 Nickel-Catalyzed Amination: Primary Amine Scope[a]

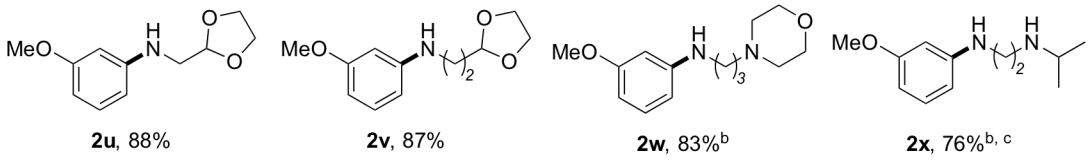




2m, 91% **2n**, 78% **2o**, 75% **2p**, 96%



2q, 90% **2r**, 96% **2s**, 92%[b] **2t**, 96%



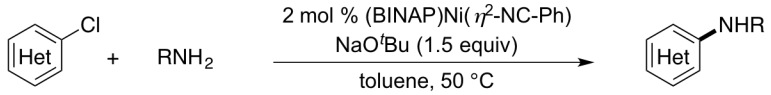
2u, 88% **2v**, 87% **2w**, 83%[b] **2x**, 76%[b, c]

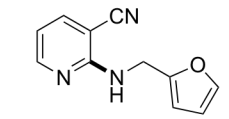
[a] Conditions: 3-chloroanisole (0.400 mmol), primary amine (0.600 mmol), (BINAP)Ni(η^2-NCPh) (8.0 μmol, 2 mol %), NaO^{t}Bu (0.600 mmol), toluene (1 mL), temperature: 50 °C; reaction time: 24 h;
[b] 80 °C; [c] (BINAP)Ni(η^2-NCPh) (16.0 μmol, 4 mol %).

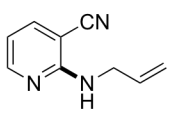
The scope of primary amines was studied by conducting the amination reactions of 3-chloroanisole catalyzed by 2 mol % complex **1**. The results of this study are summarized in Table 3.3. In general, a variety of primary aliphatic amines underwent this amination process in good to excellent isolated yields (75–96%).

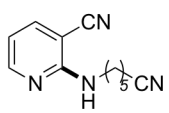
The steric bulk of the alkyl group of the primary amines significantly influenced the yields of these reactions. The reactions of an amine containing a primary alkyl group (**2m**) afforded the product in higher yield than the reactions of amines containing a secondary alkyl group (**2n** and **2o**), although the primary amines containing a secondary alkyl group still coupled with aryl chlorides in good yield. However, the amination of 3-chloroanisole with primary amines containing a tertiary alkyl group, such as *tert*-butylamime and tert-amylamine, gave only trace amounts of the desired products. Amines containing aryl (**2p**), heteroaryl (**2q** and **2r**), allyl (**2s**), and cyano (**2t**) groups

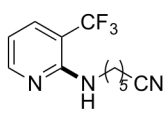
Table 3.4 Nickel-Catalyzed Amination of Heteroaryl Halides with Primary Amines[a]

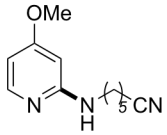


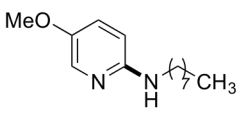

3a, 81%

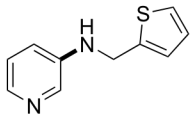

3b, 63%

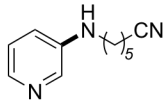

3c, 76%

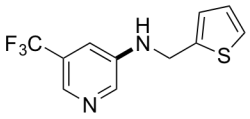

3d, 64%[b]

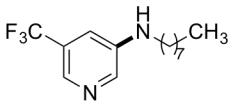

3e, 57%[c]

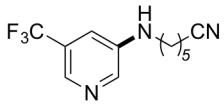

3f, 89%[c]

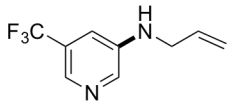

3g, 81%

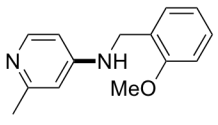

3h, 67%

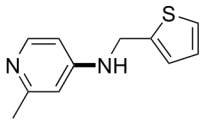

3i, 94%

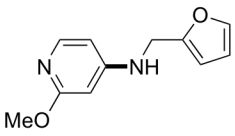

3j, 94%

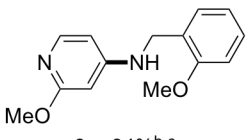

3k, 83%

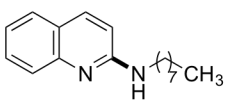

3l, 82%

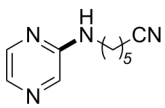

3m, 85%

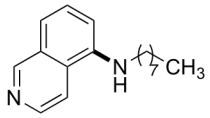

3n, 76%

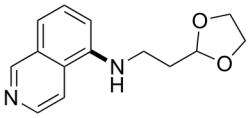

3o, 96%[c]


3p, 94%[b,c]


3q, 76%


3r,80%[b,c]


3s, 94%


3t, 91%[b,c]

[a] Conditions: 3-chloroanisole (0.400 mmol), primary amine (0.600 mmol), (BINAP)Ni(η^2-NCPh) (8.0 μmol, 2 mol %), NaO^{t}Bu (0.600 mmol), toluene (1 mL), temperature: 50 °C; reaction time: 24 h; [b] 80 °C; [c] (BINAP)Ni(η^2-NCPh) (16.0 μmol, 4 mol %).

reacted in high yields (90–96%). Primary amines bearing 1,3-dioxolane (**2u** and **2v**) and morpholine (**2w**) moieties also reacted in high yields (83–88%). The reaction of *N*-isopropylethylenediamine, a substrate containing both primary and secondary amines, occurred selectively at the primary amine, leaving the secondary amine intact (**2x**).

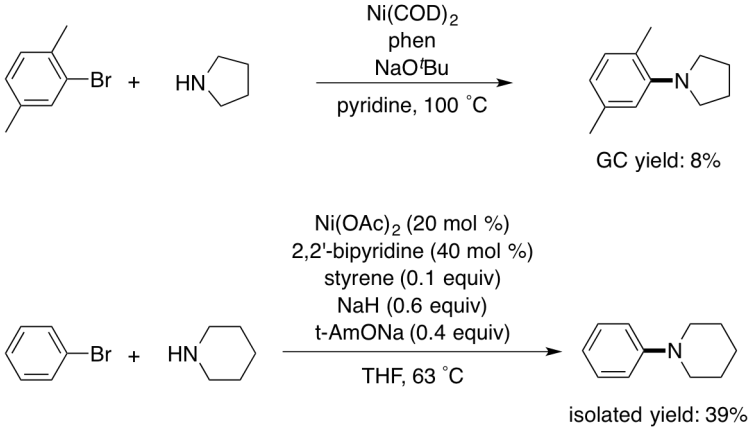
Nitrogen-containing heterocycles containing amino substituents are of particular importance for pharmaceutical applications. However, the C-N coupling reactions between nitrogen-containing heteroaryl electrophiles and primary amines are challenging, presumably because of the coordinating properties of both pyridines and primary amines. Such coupling reactions have been achieved only with palladium and copper catalysts.[31-35] Nickel catalysts have been reported for the amination of heteroaryl chlorides, but the amine nucleophiles are limited to secondary amines.[21]

Cross-coupling reactions between nitrogen-containing heteroaryl chlorides and primary amines catalyzed by 2 mol % of complex **1** are summarized in Table 3.4. The scope of heteroaryl chlorides that underwent this amination reaction encompassed a range of 2-pyridyl (**3a**–**3f**), 3-pyridyl (**3g**–**3l**), and 4-pyridyl (**3m**–**3p**) chlorides containing electron-donating groups (Me and OMe) and electron-withdrawing groups (CN and CF_3). In general, these reactions afforded the corresponding heteroaryl alkylamine in good to excellent isolated yields (57–96%, average yield: 81%). This amination also occurred in high yields with 2-chloroquinoline (**3q**) and 2-chloropyrazine (**3r**). 5-Chloroisoquinoline also reacted in high yields (**3s** and **3t**). The scope of primary amines that underwent reactions with chloropyridines was similar to that of the reactions of 3- chloroanisole described in Table 3.3.

3.2.3 Nickel-Catalyzed Amination of Aryl Bromides

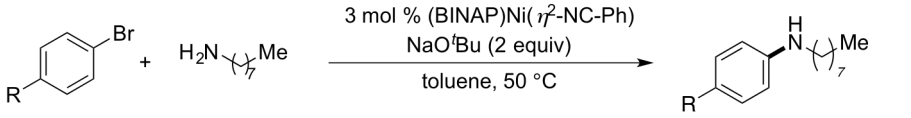
Compared to the well-established palladium-catalyzed amination of aryl bromides, the nickel-catalyzed amination of aryl bromides has been less studied, and conditions for coupling of aryl bromides with amines by nickel catalysts have not been identified. Only two examples of nickel-catalyzed amination of aryl bromides have been published,[11,12] and these two reactions occurred in poor yields (Scheme 3.3). Having identified conditions for the nickel-catalyzed amination of aryl chlorides, we tested these conditions for the coupling of aryl bromides with primary amines.

Scheme 3.3 Prior Studies on Nickel-Catalyzed Amination of Aryl Bromides



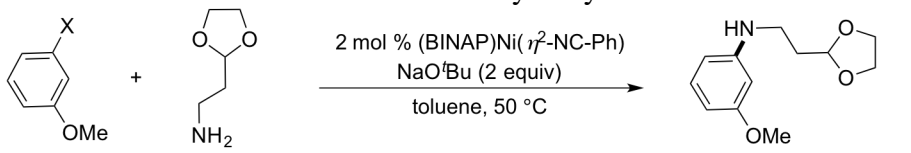
The amination of aryl bromides catalyzed by benzonitrile adduct **1** in toluene with NaO^{t}Bu base occurred in good yields in some cases, but the scope of the reaction was limited. Bromobenzene and 4-bromobenzotrifluoride reacted with octylamine in high GC-yields (98% and 94%, respectively) under conditions listed in Table 3.2 with 3 mol % complex **1** (Scheme 3.4). However, 3-bromoanisole coupled with 2-(1,3-dioxolan-2-yl)ethan-1-amine in only 55% GC-yield, whereas the reaction of the same amine with 3-chloroanisole afforded the desired product in 87% isolated yield (Scheme 3.5). This limited scope for amination of aryl bromides may stem from the faster thermal decomposition of arylnickel(II) bromide species to nickel(I) bromide, relative to the rate of decomposition of arylnickel(II) chloride.[36]

Scheme 3.4 Ni-Catalyzed Amination of Bromobenzene and 4-Bromobenzotrifluoride with Octylamine



Yield determined by GC
R = H, 98%
R = CF_3, 94%

Scheme 3.5 Ni-Catalyzed Amination of Functionalized ArCl and ArBr with Funcitonalized Primary Alkylamine



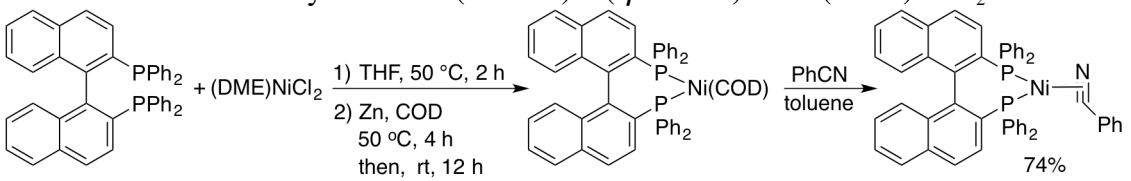
X = Br, GC yield: 55%
X = Cl, isolated yield: 87%

3.2.4 Improved Synthesis of (BINAP)Ni(η^2-NCPh) from the Air-Stable Nickel Precursor (DME)$NiCl_2$

The catalyst precursor employed in this study is a single-component nickel(0) complex (BINAP)Ni(η^2-NCPh) (**1**). Previously, we reported the synthesis of this nickel complex by substitution of the 1,5-cyclooctadiene in Ni(COD)$_2$ by BINAP, and benzonitrile (Scheme 3.2).[36] To avoid using the thermally labile, air- and moisture-sensitive Ni(COD)$_2$, we developed a new synthesis (Scheme 3.6) of this complex starting from the air-stable nickel precursor (DME)$NiCl_2$. Reaction of (DME)$NiCl_2$ with 1 equivalent of BINAP in THF at 50 ºC afforded (BINAP)$NiCl_2$, which was then reduced by zinc metal in the presence of COD. ^{31}P NMR analysis of this reaction indicated a clean formation of (BINAP)Ni(COD). The byproduct $ZnCl_2$ was removed by washing the reaction mixture with degassed aqueous NaOH. At this stage, all the volatile components of the reaction mixture were removed under vacuum. The residue was suspended in

toluene and then allowed to react with benzonitrile. This reaction sequence afforded (BINAP)Ni(η^2-NCPh) in 74% overall yield.

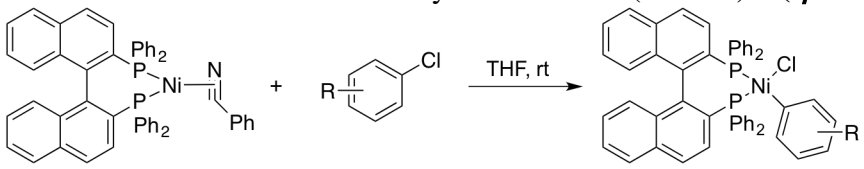
Scheme 3.6 Synthesis of (BINAP)Ni(η^2-NCPh) from (DME)$NiCl_2$



3.2.5 Synthesis of BINAP-ligated Arylnickel Chloride Complexes by Oxidative Addition of Aryl Chlorides to (BINAP)Ni(η^2-NCPh)

Arylnickel halide complexes are important intermediates in nickel-catalyzed cross-coupling reactions. In general, arylnickel halides ligated by monophosphines are synthesized by oxidative addition reactions of aryl halides to $Ni(PR_3)_x$ (R = alkyl or aryl),[37-39] but arylnickel halides ligated by bisphosphines are prepared by ligand substitution reactions between monophosphine-ligated arylnickel halide complexes with bisphosphines.[40] The direct oxidative addition of aryl halides to bisphosphine-ligated Ni(0) has rarely been investigated, mainly due to the lack of bisphosphine-ligated Ni(0) precursors that can react with aryl halides at ambient temperature. Our group recently reported the synthesis of BINAP-ligated arylnickel halide complexes by reactions of aryl halides with (BINAP)Ni(COD) in the presence of catalytic amounts of benzonitrile, and we identified (BINAP)Ni(η^2-NCPh) as the active Ni(0) species.[36] In our communication on the nickel-catalyzed asymmetric α-arylation of ketones, we reported just the reaction of electron-deficient 4-chlorobenzotrifluoride with this newly defined Ni(0) precursor **1** and no isolation of the products. Here we show the results of the reactions of complex **1** with electronically varied aryl chlorides.

Scheme 3.7 Oxidative Addition of Aryl Chlorides to (BINAP)Ni(η^2-NCPh)

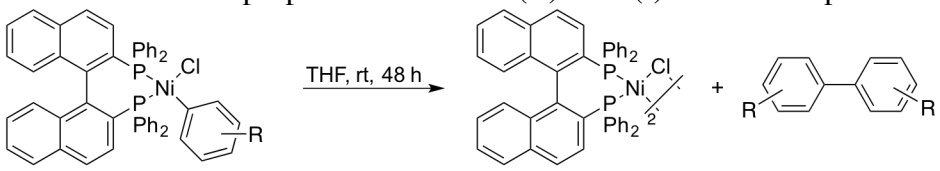


4, R = H 76%
5, R = 3-OMe 81%
6, R = 4-CN 88%
7, R = 4-CF_3 89%

Electron-neutral and electron-deficient aryl chlorides reacted smoothly with Ni(0) complex **1** in THF at room temperature, to afford the arylnickel(II) chloride complexes **4**–**7** in 76–89% isolated yields (Scheme 3.7). These complexes are stable in the solid state at ambient temperature for at least six months without noticeable decomposition. However, upon standing in THF solution at room temperature for about 48 h, they fully

decomposed to $[(BINAP)Ni(\mu\text{-}Cl)]_2$ (**8**) with concomitant release of biaryls, as detected by GC-MS analysis. The isolated yields for this reaction were about 70% (Scheme 3.8).

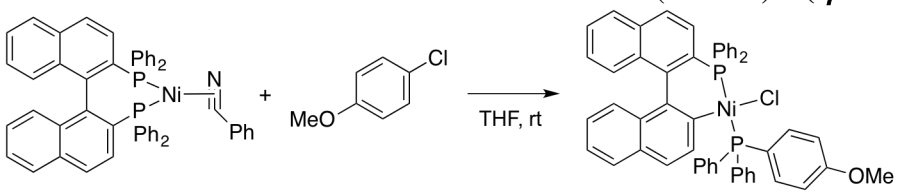
Scheme 3.8 Disproportionation of Ni(II) to Ni(I) Dimer Complexes



4–7 **8**, 70%

However, the reaction of electron-rich 4-chloroanisole with complex **1** in THF did not form the arylnickel chloride complex resulting from simple oxidative addition, as determined by ^{31}P NMR spectroscopy. Instead, two mutually *trans* phosphine resonances (doublets at 24.2 and 14.4 ppm with J_{PP} = 352 Hz) were observed. Single-crystal X-ray diffraction of the isolated material (Figure 3.1) showed that this product is complex **9**, shown in Scheme 3.9.

Scheme 3.9 Oxidative Addition of 4-Chloroanisole to (BINAP)Ni(η^2-NCPh)



9, 64%

Complex **9** contains a coordinated monophosphine ligand $Ph_2P(C_6H_4\text{-}4\text{-}OMe)$ and a six-membered nickelacyclic structure. Nickelacyclic complex **9** contains a small dihedral angle between the two naphthyl groups of 63°, and the nickel center consists of a distorted square planar geometry. Complex **9** is formed by P-C bond cleavage of the

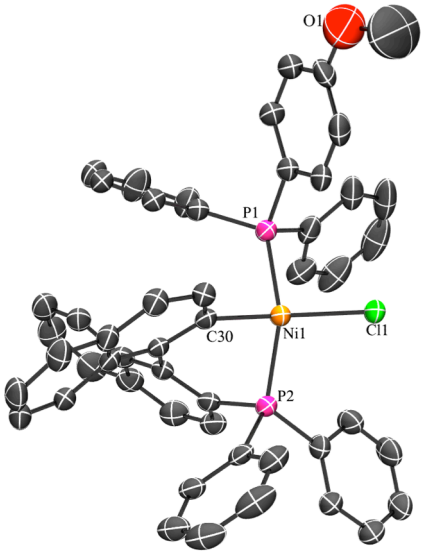


Figure 3.1 Molecular structure of the nickelacyclic compound **9**. All the ellipsoids are drawn at the 50% probability and all the hydrogen atoms are omitted for clarity.

BINAP backbone after the initial formation of BINAP-ligated arylnickel chloride complex (BINAP)NiCl(C_6H_4-4-OMe). Similar P-C bond cleavage of the BINAP backbone in a BINAP-ligated phenylpalladium bromide complex was reported by our group previously.[41]

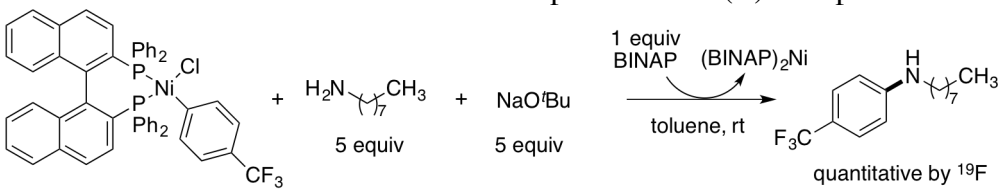
Complex **9** was subjected to the reaction conditions described in Table 3.2 to verify its catalytic competence. Only trace (< 5% by GC analysis) amounts of the amination product were formed. Thus, the formation of catalytically inactive complex **9** by the reaction of 4-chloroanisole and nickel precursor **1** explained the high catalyst loading required for the amination of electron-rich 4-chloroanisole.

3.2.6 Identification of Catalytically Active Species: (BINAP)Ni^{II}(Cl)(Ar) or [(BINAP)Ni^{I}(μ-Cl)]$_2$?

The oxidation state of the nickel intermediates in the aminations of aryl halides with amines is ambiguous, and pathways involving both Ni(0)/Ni(II) and Ni(I)/Ni(III) couples have been proposed for these reactions.[11,17] With isolated, BINAP-ligated Ni(0), Ni(I) halide dimer, and ArNi(II) halide complexes in hand, we were able to assess precisely the competence of these complexes to be intermediates in the amination reaction.

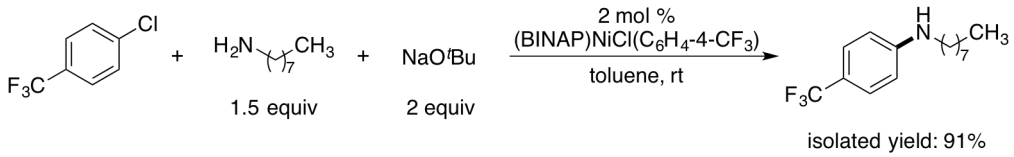
To do so, we conducted the reaction of the isolated (BINAP)NiCl(C_6H_4-4-CF_3) (**7**) with octylamine and NaO^{t}Bu in the presence of 1 equiv of BINAP to trap a Ni(0) product (Scheme 3.10). This reaction afforded *N*-octyl-4-(trifluoromethyl)aniline in quantitative yield in less than 5 min at room temperature, as indicated by ^{19}F NMR spectroscopic analysis.

Scheme 3.10 Stoichiometric Competence of Ni(II) Complex



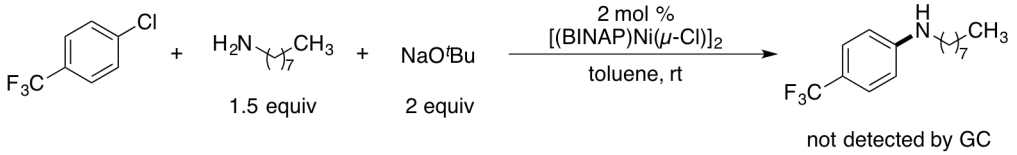
In addition, we conducted the amination reaction of 4-chlorobenzotrifluoride with octylamine in the presence of NaOtBu catalyzed by 2 mol % of (BINAP)NiCl(C6H4-4-CF3) at room temperature (Scheme 3.11). Full conversion of 4-chlorobenzotrifluoride was achieved in 2 h, and this reaction afforded N-octyl-4-(trifluoromethyl)aniline in 91% isolated yield. The same reaction catalyzed by 2 mol % of [(BINAP)Ni-μ-Cl]2 did not afforded any amination product (Scheme 3.12). These results show clearly that the

Scheme 3.11 Catalytic Competence of Ni(II) Complex



BINAP-ligated arylnickel(II) chloride compound is kinetically and chemically competent to be an intermediate in the catalytic process and the BINAP-ligated nickel(I) halide is not.

Scheme 3.12 Catalytic Competence of Ni(I) Dimer

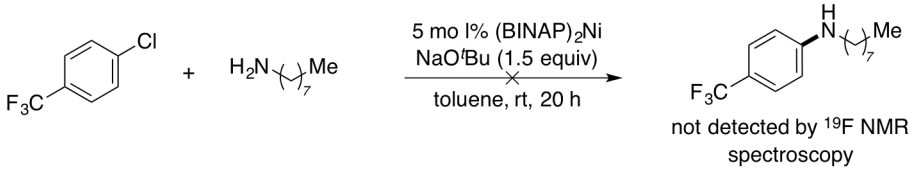


3.2.7 Identity of Nickel Species in the Catalytic Reaction Mixture

To identify the resting state of the catalyst in this nickel-catalyzed amination reaction, we monitored by $^{31}P\{^{1}H\}$ NMR spectroscopy the reaction of 4-chlorobenzotrifluoride with octylamine in the presence of NaO^{t}Bu catalyzed by 2 mol % of (BINAP)Ni(η^2-NCPh) (**1**) at room temperature. During the first 50% conversion of 4-chlorobenzotrifluoride, only (BINAP)Ni(η^2-NCPh) was observed. However, during the second 50% conversion, a new species corresponding to a $^{31}P\{^{1}H\}$ NMR resonance at δ 31.7 ppm gradually accumulated. This new species is $(BINAP)_2Ni$, as determined by independently preparing this complex by reduction of $(DME)NiCl_2$ with Zn metal in the presence of 2 equivalents of BINAP in THF and comparing the ^{31}P NMR chemical shift.

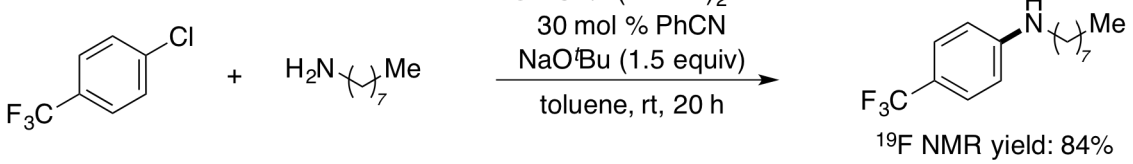
To test the catalytic activity of $(BINAP)_2Ni$ for this amination process, we conducted the reaction of 4-chlorobenzotrifluoride with octylamine catalyzed by 5 mol % of $(BINAP)_2Ni$ in the presence of NaO^{t}Bu at room temperature. This reaction did not afford detectable amounts of the amination product (Scheme 3.13). This result is consistent with the early report that $(BINAP)_2Ni$ does not undergo oxidative addition with aryl chlorides or bromides at ambient temperatures.[36]

Scheme 3.13 Catalytic Competence of $(BINAP)_2Ni$



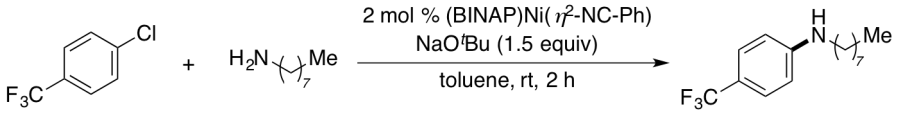
The same reaction catalyzed by 5 mol % $(BINAP)_2Ni$ in the presence of a catalytic amount of PhCN (30 mol %) afforded the amination product in 84% yield in 20 h (Scheme 3.14). For comparison, we conducted the same reaction catalyzed by only 2 mol % (BINAP)Ni(η^2-NCPh). This reaction afforded the amination product in almost

Scheme 3.14 Catalytic Competence of $(BINAP)_2Ni$ in the Presence of PhCN



quantitative yield in 2 h at room temperature (Scheme 3.15). Thus, (BINAP)Ni(η^2-NCPh) is a more active catalyst than the combination of $(BINAP)_2Ni$ and PhCN.

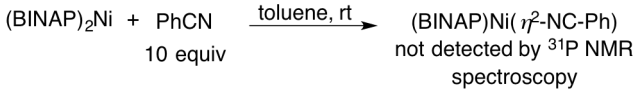
Scheme 3.15 Catalytic Reaction with Model Substrate



^{19}F NMR yield: quantitative

To assess the origin of the effect of benzonitrile on the rate of the catalytic reaction, we performed the stoichiometric reactions of $(BINAP)_2Ni$ with benzonitrile and of (BINAP)Ni(η^2-NCPh) with BINAP. The reaction of $(BINAP)_2Ni$ with 10 equiv of benzonitrile did not form detectable amounts of (BINAP)Ni(η^2-NCPh), as determined by ^{31}P NMR spectroscopy (Scheme 3.16). The reaction of (BINAP)Ni(η^2-NCPh) with 1 equivalent of BINAP afforded $(BINAP)_2Ni$ quantitatively at ambient temperature (Scheme 3.17).

Scheme 3.16 Stoichiometric Reaction of $(BINAP)_2Ni$ with PhCN



Scheme 3.17 Stoichiometric Reaction of (BINAP)Ni(η^2-NCPh) with BINAP

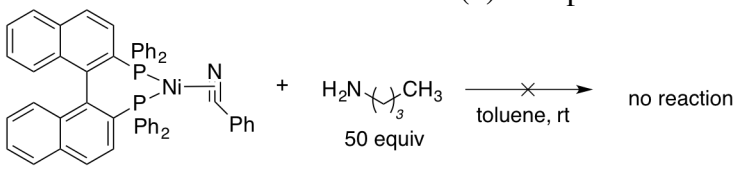
Based on these stoichiometric reactions and the catalytic reactions in Schemes 3.13 and 3.14), we conclude that the formation of $(BINAP)_2Ni$ is reversible in the presence of benzonitrile, but the equilibrium lies largely on the side of $(BINAP)_2Ni$ and free nitrile.

3.2.8 Formation of Bis(amine)-Ligated Arylnickel Chloride

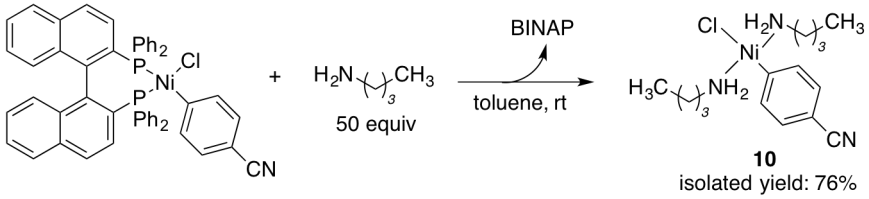
The formation of bis(amine)-ligated palladium complexes was reported as one possible pathway for deactivation of the catalyst in the palladium-catalyzed aminations of aryl halides.[42] These bis(amine)-complexes have been prepared and well characterized. Formation of analogous bis-amine complexes of nickel was proposed to explain the much lower reactivity of primary aliphatic amines than that of cyclic secondary aliphatic amines and anilines in the nickel-catalyzed amination reaction.[17] However, these bis(amine)-ligated nickel complexes have never been prepared and characterized. In the nickel-catalyzed amination of aryl chlorides with primary amines catalyzed by (BINAP)Ni(η^2-NCPh), we observed the formation of $(BINAP)_2Ni$. The stoichiometry of this conversion indicates that there are nickel complexes lacking BINAP ligand in the reaction mixture. Thus, we studied the ligand substitution reactions between primary aliphatic amines and BINAP-ligated Ni(0) and BINAP-ligated Ni(II) complexes.

The reaction of (BINAP)Ni(η^2-NCPh) with 50 equivalents of *n*-butylamine in toluene did not form any new nickel species, and free BINAP was not detected by ^{31}P NMR spectroscopy (Scheme 3.18). This result is consistent with the affinity of the electron-rich Ni(0) center for softer, p-accepting ligands.[43] However, the reaction of (BINAP)NiCl(C_6H_4-4-CN) with 50 equivalents of *n*-butylamine afforded free BINAP and *trans*-(*n*-butylamine)$_2$NiCl(C_6H_4-4-CN) (**10**) (Scheme 3.19). Complex **10** was isolated in 76% yield.

Scheme 3.18 Stoichiometric Reaction of Ni(0) Complex with Octylamine

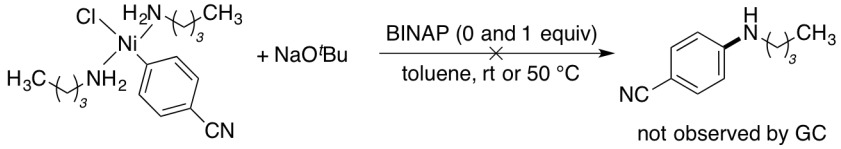


Scheme 3.19 Stoichiometric Reaction of Ni(II) Complex with Octylamine



With the bis(amine)-ligated complex **10** in hand, we tested its potential to serve as an intermediate in the amination reaction. We conducted the reaction of **10** with 2 equivalents of NaO^{t}Bu in the presence or in the absence of 1 equivalent of BINAP (Scheme 3.20). These two reactions did not form the desired amination product. This result indicates that the formation of bis(amine)-ligated nickel complexes is one possible pathway for decomposition of the nickel catalyst.

Scheme 3.20 Stoichiometric Competence of Ni(II) Bis-amine Complex



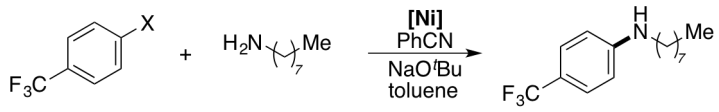
3.2.9 Kinetic Studies on Nickel-Catalyzed Amination of Aryl Chlorides

After identifying the resting state of the nickel catalyst and possible paths for catalyst deactivation, we sought to identify the rate-limiting step for this nickel-catalyzed amination process. To do so, we measured the dependence of the initial rates of the amination reaction on the concentrations of each reagent under conditions in which the other reagents were present in large excess.

We choose the reaction of 4-chlorobenzotrifluoride with octylamine in the presence of NaO^{t}Bu for the kinetic studies because this reaction occurred at ambient temperature, and we were able to monitor the reaction conveniently by both ^{31}P and ^{19}F

NMR spectroscopy (Scheme 3.21). Furthermore, no background nucleophilic aromatic substitution reaction was observed for this aryl chloride and octylamine in the presence of NaO^{t}Bu.

Scheme 3.21 Reaction Scheme for Kinetic Experiments



X = Cl, **[Ni]** = complex **7**
X = Br, **[Ni]** = complex **11**

For the initial rates to be a valid method for kinetic analysis of this reaction, all reagents must be soluble in the reaction medium, and no induction period can be present. The single-component catalyst precursor **1** is only marginally soluble in the reaction medium. Thus, we used (BINAP)NiCl(C_6H_4-4-CF_3) (**7**) as the source of nickel for our kinetic experiments because it dissolves in seconds once mixed with other reagents. Benzonitrile was added to the reaction mixture to trap the BINAP-ligated Ni(0) species to form (BINAP)Ni(η^2-NCPh), which had been identified as the catalyst resting state. In the absence of benzonitrile, the irreversible formation of $(BINAP)_2Ni$ occurs quickly. Benzonitrile (10 equiv relative to complex **7**) was added so that catalyst decomposition was not observed by ^{31}P NMR spectroscopy over the time of the kinetic experiments.

The kinetic behavior was assessed for the coupling of 4-chlorobenzotrifluoride with octylamine catalyzed by the combination of complex **7** in the presence of PhCN and NaO^{t}Bu at room temperature (eq. 8). The initial rates were measured by ^{19}F NMR spectroscopy using 4-OCF_3-anisole as the internal standard. The rate of the amination reaction was determined by measuring the formation of *N*-octyl-4-(trifluoromethyl)aniline with respect to time. The plots of concentrations of *N*-octyl-4-(trifluoromethyl)aniline *vs* time at various concentrations of each reagent are shown in Figures 3.4-3.8 in the Experimental Section (Section 3.4). The plots of the initial rates of the reaction *vs* the concentrations of the catalyst, aryl chloride, and benzonitrile are shown in Figure 3.2.

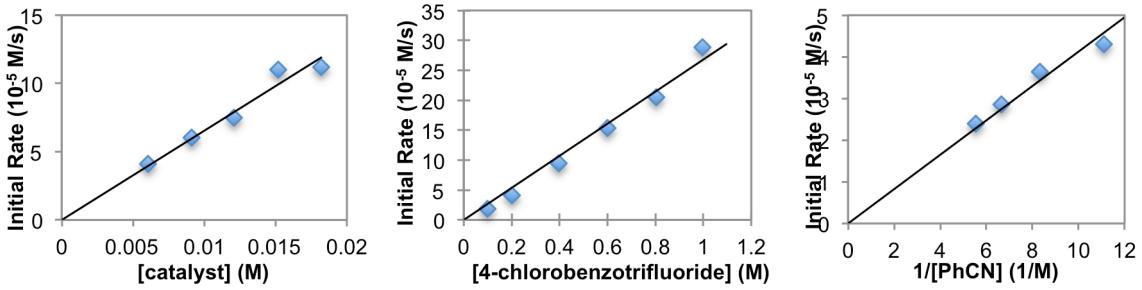


Figure 3.2 Plots of initial rates *vs* concentration of catalyst, aryl chloride, and benzonitrile for the amination of 4-chlorobenzotrifluoride (0.10–1.0 M) with *n*-octylamine (0.30 M) catalyzed by (BINAP)NiCl(C_6H_4-4-CF_3) (0.0060–0.018 M) in the presence of benzonitrile (0.090–0.180 M) and NaO^{t}Bu (0.30 M) at room temperature.

The kinetic analysis showed that this nickel-catalyzed amination reaction of aryl chloride is first order in the nickel catalyst, first order in aryl chloride, and inverse first order in PhCN. The remaining reagents, NaO^{t}Bu and amine, did not affect the initial rate of the reaction. These data indicate that oxidative addition of the aryl chloride to (BINAP)Ni(0), formed by reversible dissociation of PhCN from the catalyst resting state (BINAP)Ni(η^2-NCPh), is the turnover-limiting step in the amination reaction.

3.2.10 Kinetic Studies on Nickel-Catalyzed Amination of Aryl Bromides

The mechanism of palladium-catalyzed cross-coupling reactions with aryl halides as electrophiles has been extensively studied. These studies reveal that the halide identity has a dramatic effect on the mechanism for the oxidative addition of aryl halides to Pd(0) species. The additions of the less reactive aryl chlorides occurs through lower-coordinated Pd(0) intermediate than the additions of more reactive aryl iodides.[44] However, such mechanistic data has not been gained for the nickel-catalyzed amination of aryl halides.

Because the BINAP- and PhCN-ligated Ni(0) complex **1** catalyzes the amination of both aryl chlorides and aryl bromides, we can compare directly the kinetics and mechanism of the amination reactions of aryl chlorides and aryl bromides catalyzed by this nickel system. To do so, we conducted kinetic experiments on the amination of aryl bromides that were similar to those we conducted on the amination of aryl chlorides.

We monitored by ^{31}P NMR spectroscopy the reaction of 4-bromobenzotrifluoride with octylamine catalyzed by (BINAP)Ni(η^2-NCPh) in the presence of NaO^{t}Bu at room temperature. As was the case in the reactions of chloroarenes, (BINAP)Ni(η^2-NCPh) was identified as the resting state of the catalyst in the reaction of 4-bromobenzotrifluoride with octylamine.

Kinetic studies were conducted on the reaction of 4-bromobenzotrifluoride with octylamine catalyzed by (BINAP)NiBr(C_6H_4-4-CF_3) (**11**) in the presence of added PhCN (Scheme 3.21). The initial rates were measured for various concentrations of each reagent while keeping the other reagents in excess. The plots of concentrations of *N*-octyl-4-

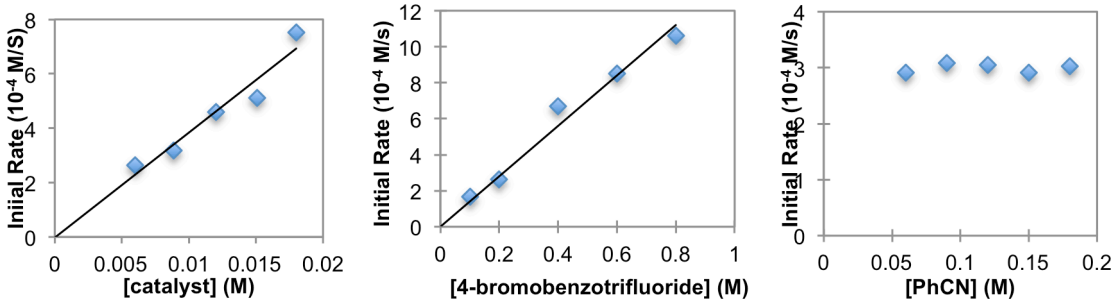


Figure 3.3 Plots of initial rates *vs* concentration of catalyst, aryl bromide, and benzonitrile for the amination of 4-bromobenzotrifluoride (0.10–0.80 M) with *n*-octylamine (0.30 M) catalyzed by (BINAP)NiCl(C_6H_4-4-CF_3) (0.0060–0.018 M) in the presence of benzonitrile (0.090–0.180 M) and NaO^{t}Bu (0.30 M) at room temperature.

(trifluoromethyl)aniline *vs* time at various concentrations of each reagent are shown in Figures 3.10-3.14 in the Experimental Section (Section 3.4). The plots of the initial rates of the reaction *vs* the concentrations of the catalyst, aryl chloride, and benzonitrile are shown in Figure 3.3.

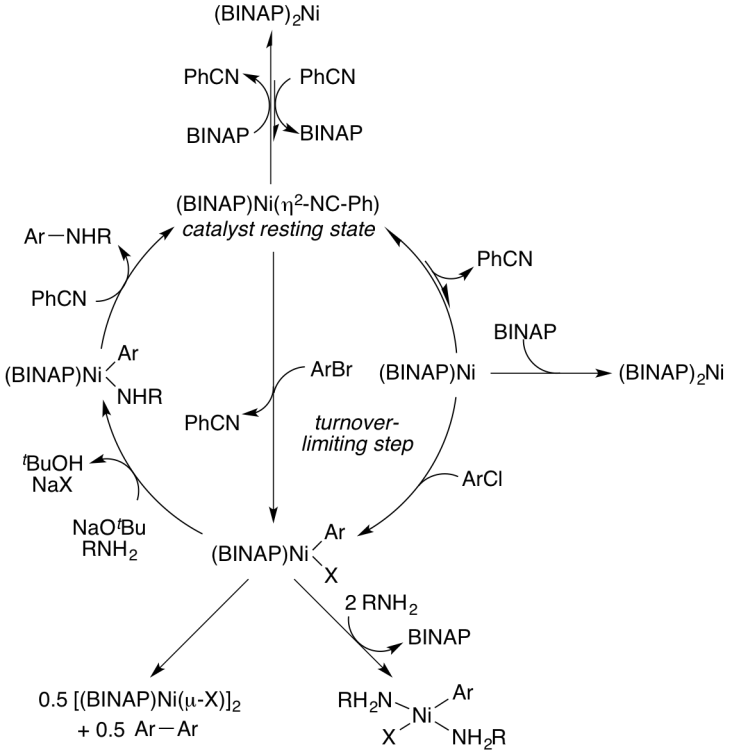
Like the amination of 4-chlorobenzotrifluoride, the amination of 4-bromobenzotrifluoride with octylamine is first order in the nickel catalyst, first order in aryl halide, zero order in NaO^{t}Bu, and zero order in amine. In contrast to the reaction of 4-chlorobenzotrifluoride, which is inverse first order in PhCN, the amination of aryl bromide is zero order in PhCN. This order in PhCN, in combination with the first order in aryl bromide, indicates that the oxidative addition of (BINAP)Ni(η^2-NCPh) occurs without dissociation of PhCN and is the turnover-limiting step for the amination of aryl bromides. The different reactivity of aryl halides with BINAP-ligated nickel complexes of different coordination number parallels a trend in oxidative addition to Pd(0) complexes noted in the introduction to this section.[44]

3.2.11 Overall Mechanism of Nickel-Catalyzed Amination of Aryl Chlorides and Aryl Bromides

Based on the stoichiometric reactions of the isolated BINAP-ligated arylnickel halides with primary amines in the presence of base and the conducted kinetic studies, we propose a catalytic cycle depicted in Scheme 3.22 for the nickel-catalyzed amination of aryl chlorides and aryl bromides reported in this chapter. The observed first order rate-dependence on the concentrations of both the catalyst and aryl halides indicates that the oxidative addition of aryl halides to BINAP-ligated Ni(0) species to form (BINAP)NiAr(X) (X = Cl or Br) is the turnover-limiting step for both amination processes. This BINAP-ligated arylnickel(II) halide complex subsequently reacts with primary amine and NaO^{t}Bu to form an arylnickel amido complex, followed by reductive elimination of the *N*-alkyl aniline product in the presence of PhCN to regenerate (BINAP)Ni(η^2-NCPh), which was confirmed as the catalyst resting state.

Interestingly, different rate-dependences on the concentration of PhCN were observed for this nickel-catalyzed amination of aryl chlorides and aryl bromides. The reaction of aryl chlorides is inverse first order in PhCN, whereas the reaction of aryl bromides is zero order in PhCN. These reaction orders indicate that aryl chlorides and aryl bromides react with different nickel(0) species. The aryl chlorides react after reversible dissociation of PhCN from (BINAP)Ni(η^2-NCPh) to form the lower-coordinate nickel(0) species (BINAP)Ni(0) to form the BINAP-ligated arylnickel(II) chloride complex. However, the aryl bromides react directly with (BINAP)Ni(η^2-NCPh) to form BINAP-ligated arylnickel(II) bromide complex and the nitrile dissociates during or immediately after the oxidative addition process. One could imagine the zero-order dependence on added PhCN could indicate that dissociation of this ligand is rate limiting, but the first-order dependence of the reaction on the aryl bromide is inconsistent with this proposal.

Scheme 3.22 Proposed Catalytic Cycle for the Nickel-Catalyzed Amination of Aryl Chlorides and Bromides.



In addition to the steps within the catalytic cycle that form the arylamine product, there are several pathways that generate catalytically inactive nickel species. The reaction of (BINAP)NiAr(Cl) with amine RNH_2 forms the catalytically inactive $(RNH_2)_2$NiAr(Cl) and free BINAP. The released free BINAP in the reaction mixture traps the (BINAP)Ni(0) fragment generated by dissociation of PhCN from (BINAP)Ni(η^2-NCPh) or reductive elimination of *N*-alkyl aniline from the BINAP-ligated arylnickel(II) amido complex to form $(BINAP)_2$Ni. $(BINAP)_2$Ni does not undergo oxidative addition of the aryl halide and does not catalyze the amination reaction. However, it can be reactivated by PhCN. Thermal decomposition of (BINAP)NiAr(X) (Ar = electron-neutral and electron-rich aryl groups) affords the catalytically inactive $[(BINAP)Ni(\mu\text{-}X)]_2$ with concomitant formation of biaryl. For the amination of electron-rich aryl chlorides, P-C bond cleavage of the BINAP backbone is another potential pathway for the deactivation of the nickel catalyst. Indeed, this complex was observed to accumulate (approximately 6.4 mM of the 16 mM concentration of initial catalyst) during the reaction of 4-chloroanisole with octylamine.

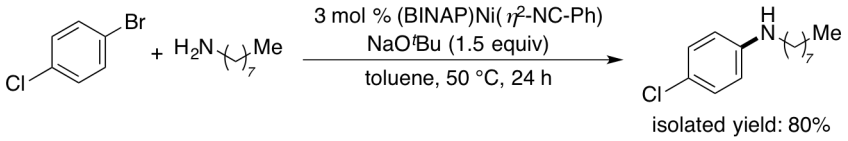
3.2.12 Competition Experiments

To gain information on the relative rates of the amination of aryl chlorides and aryl bromides and the effect of temperature and concentration of PhCN on the selectivity of the amination reaction for an aryl chloride versus an aryl bromide, we conducted a

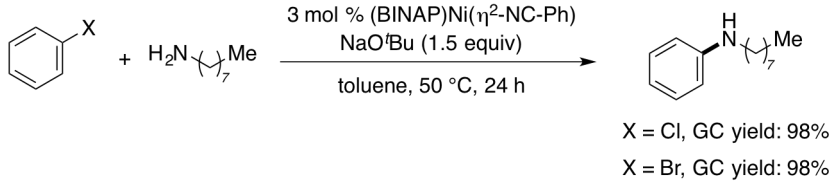
series of reactions with an aryl halide containing both chloride and bromide and a mixture of aryl halides in the presence of various amount of PhCN at room temperature or 50 °C.

The amination of 1-bromo-4-chlorobenzene with octylamine catalyzed by 3 mol % of (BINAP)Ni(η^2-NCPh) at 50 °C occurred selectively at the C-Br bond, and the product of the reaction at the C-Cl bond was not detected by GC-MS analysis. The product *N*-octyl-4-chloroaniline was isolated in 80% yield. (Scheme 3.23). However, side-by-side reactions of chlorobenzene and bromobenzene under the same conditions occurred in the same GC yield (98%) (Scheme 3.24).

Scheme 3.23 Intramolecular Competition Experiment

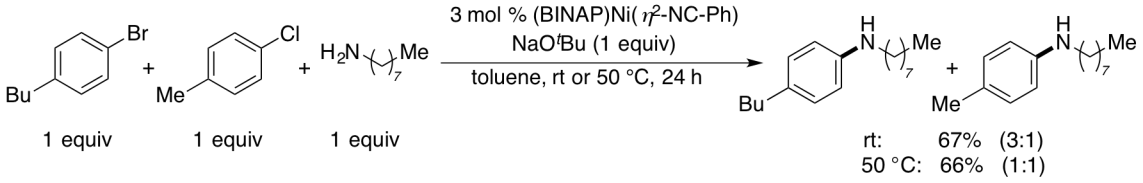


Scheme 3.24 Side-by-side Reactions of Chlorobenzene and Bromobenzene



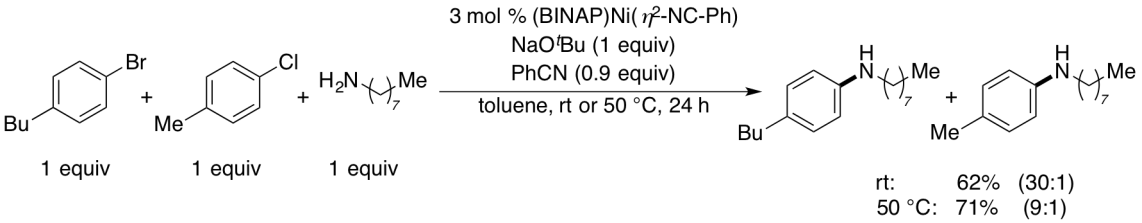
The amination of equal amounts of 1-bromo-4-butylbenzene and 4-chlorotoluene with octylamine catalyzed by 3 mol % of (BINAP)Ni(η^2-NCPh) was conducted at both room temperature and 50 °C (Scheme 3.25). At both temperatures, these reactions occurred in similar yields, but with different selectivity. At room temperature, 1-bromo-4-butylbenzene was converted selectively over 4-chlorotoluene, and a product ratio of 3:1 was obtained. However, at 50 °C, 1-bromo-4-butylbenzene and 4-chlorotoluene converted equally. Compared with the full selectivity for amination of the C-Br bond in 1-bromo-4-chlorobenzene (Scheme 3.23), the decreased selectivity for amination of the C-Br bond over the C-Cl bond in different haloarenes might stem from irreversible or nearly irreversible binding of the haloarene to Ni(0) to form an arene π-complex prior to cleavage of the carbon-halogen bond. This preferential intramolecular oxidative addition has recently been observed for the Ni-catalyzed Kumada cross-coupling reactions and chain-growth polymerizations.[45]

Scheme 3.25 Intermolecular Competition Experiment



To evaluate the effect of PhCN on the selectivity between the amination of an aryl chloride and an aryl bromide, we conducted the amination of equal amount of 1-bromo-4-butylbenzene and 4-chlorotoluene with octylamine catalyzed by 3 mol % of (BINAP)Ni(η^2-NCPh) in the presence of 0.9 equivalent of PhCN (relative to octylamine) (Scheme 3.26). Because our kinetic studies revealed different dependences of the reaction rate on PhCN for this nickel-catalyzed amination (inverse first order and zero order on PhCN for the reaction of aryl chloride and aryl bromide, respectively), we considered that an increased selectivity for the conversion of aryl bromide over aryl chloride would be observed for reaction conducted with higher concentrations of PhCN than for reaction conducted with lower concentrations of PhCN.

Scheme 3.26 Intermolecular Competition Experiment in the Presence of PhCN



Consistent with this prediction, the selectivity was higher (30:1 for the reaction at room temperature and 9:1 for the reaction at 50 °C) for the amination of 1-bromo-4-butylbenzene versus the amination of 4-chlorotoluene for reactions run with higher concentrations (from 0.004 M to 0.18 M) of benzonitrile at both room temperature and 50 °C for 24 h. These data show that the difference in M(0) species that adds the different aryl halides can be used to beneficially affect selectivity.

3.2.13 Comparison to Prior Ni Systems for Aryl Halide Amination.

Several first-row metal complexes catalyze cross coupling reactions, and many catalyze the coupling of certain classes of chloroarenes. However, no first row metal complex has been shown to catalyze the coupling of primary alkylamines with chloroarenes. Copper complexes couple bromoarenes and iodoarenes with primary amines, but they do not catalyze the coupling of chloroarenes with primary amines.

Previously, the combination of $Ni(COD)_2$ and dppf was shown to couple an electron-poor chloroarene with a primary amine, but this catalyst did not couple unactivated chloroarenes with primary amines.[11] A set of preliminary studies we conducted have shown that the complexes (dppf)Ni(COD) or $(dppf)_2Ni$ generated in situ by the reaction of $Ni(COD)_2$ and dppf do not add aryl chlorides at ambient temperature, and the reaction of chloroarene with (dppf)Ni(COD) or $(dppf)_2Ni$ at elevated temperatures forms (dppf)Ni(I)Cl and biaryl.

This formation of $(dppf)_2Ni(0)$ and (dppf)Ni(I)Cl at the elevated temperatures required for oxidative addition of chloroarene to occur, likely prevented productive coupling reactions with unactivated chloroarenes. These observations further illustrate the importance of the nitrile-ligated precursor with the general formula $L_2Ni(\eta^2$-NCPh).

Nickel complexes of *N*-heterocyclic carbenes have been shown to couple aryl chlorides and sulfonates with secondary amines and with arylamines, but not primary alkylamines. Mechanistic studies on the reactions of secondary amines catalyzed by the complexes of *N*-heterocyclic carbenes are too limited to determine the origin of their lack of reactivity with primary amines, but recent studies have shown that the arylnickel halide complexes containing hindered *N*-heterocyclic carbenes are not formed by the reaction of $(IMes)_2Ni(0)$ with chlorobenzene, bromobenzene, and iodobenzene.[46] Instead, Ni(I) species are formed, and this formation of Ni(I) complexes could either constitute the pathway for catalyst decomposition or a mechanism for reaction with this catalyst involving odd-electron nickel intermediates.

3.3 Conclusion

We have shown that nickel complexes containing common aryl bisphosphine ligands can catalyze the coupling of aryl chlorides and bromides with primary amines. In particular, we have shown that the mixed Ni(0) species (BINAP)Ni(η^2-NCPh) containing one bisphosphine and one side-bound nitrile is a particularly active catalyst for the coupling of chloroarenes with primary amines and is more active than the related $(BINAP)_2Ni$ catalyst. A range of electronically varied aryl halides and nitrogen-containing heteroaryl chlorides, including pyridine, quinoline, and isoquinoline derivatives, couple with a variety of aliphatic primary amines in high isolated yields. Several aspects of the current system lead to the ability of this first-row metal system to catalyze this class of amination reaction. In general, we attribute the high yields for these amination reactions to the facile oxidative addition of aryl chlorides and heteroaryl chlorides to the (BINAP)Ni(η^2-NCPh) precatalyst at ambient temperatures.

Detailed studies on the mechanism of the amination reaction have been conducted. The following conclusions about the mechanism of this coupling process have been drawn from these studies:

1. The oxidative addition of aryl chlorides to (BINAP)Ni(η^2-NCPh), together with the stoichiometric reactions of (BINAP)NiAr(Cl) with primary aliphatic amines in the presence of base, support a reaction pathway involving a Ni(0)/Ni(II) couple in the catalytic cycle.
2. The oxidative addition of aryl chlorides and heteroaryl chlorides to the single-component nickel precursor (BINAP)Ni(η^2-NCPh) at ambient temperatures prevents the formation of inactive Ni species.
3. Ni(I) intermediates, which have been observed in oxidative addition studies to phosphine-ligated Ni(0) complexes, appear to result from decomposition of the Ni(II) product of oxidative addition as opposed to forming from one-electron pathways for oxidative addition to Ni(0).[26]
4. The reaction of (BINAP)Ni(η^2-NCPh) with electron-rich aryl chlorides, such as 4-chloroanisole, leads to the P-C bond cleavage of the backbone of BINAP and forms the nickel complex **9** containing two monophosphine ligands. The formation of the catalytically inactive complex **9** explains the high catalyst loading required for the amination of electron-rich aryl chlorides.

5. Mechanistic and kinetic studies revealed that the turover-limiting step of these nickel-catalyzed aminations of aryl chlorides is oxidative addition of the aryl chloride to (BINAP)Ni(0), which is formed by dissociation of PhCN from the catalyst resting state (BINAP)Ni(η^2-NCPh).
6. Mechanistic and kinetic studies imply that the turover-limiting step of the reactions of aryl bromides is also oxidative addition, but that aryl bromide reacts with a different nickel species, of composition (BINAP)Ni(NCPh) containing a bound nitrile.
7. The formation of catalytically inactive bis(amine)-ligated Ni(II) species $(RNH_2)_2NiAr(Cl)$, Ni(I) species $[(BINAP)Ni(\mu\text{-}Cl)]_2$, and bis-BINAP-ligated Ni(0) species $(BINAP)_2Ni$ are the major pathways for catalyst inactivation.
8. Further studies to improve the lifetime of the Ni-bisphosphine catalysts, to determine the mechanism by which the phosphine-ligated Ni(I) species form as a means to prevent this detrimental path, and to determine if Ni(I) complexes are generated during oxidative addition of haloarenes will be the subject of future studies.

3.4 Experimental

General Remarks

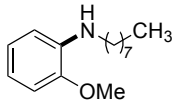
All the manipulations were performed in a nitrogen-filled glovebox, unless mentioned otherwise. THF, toluene, benzene, and pentane were purified by passing the degassed solvents (N_2) through a column of activated alumina (solvent purification system purchased from Innovative Technologies, Newburyport, MA). $(DME)NiCl_2$ and *rac*-BINAP were purchased from Strem Chemical Co. and used as received. All other chemicals were used as received from commercial resources. ^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectra were recorded using a Varian 400 MHz, 500 MHz, or 600 MHz NMR spectrometer. ^1H NMR spectra were referenced to resonances of the residual protons in the deuterated solvents; and $^{31}P\{^1H\}$ NMR shifts were reported in parts per million relative to an 85% H_3PO_4 external standard. Silica gel chromatography was performed using a Teledyne Isco Combiflash® R_f system with Redi*Sep* Gold™ columns. Elemental analyses were performed at Microanalysis Laboratory in the University of California, Berkeley. HR-MS analyses were performed at QB3/Chemistry Mass Spectrometry Facility in the University of California, Berkeley.

Division of labor: The catalyst and reaction conditions were developed by Dr. Shaozhong Ge. The substrates in Tables 3.2 and 3.3 were isolated and characterized by Dr. Shaozhong Ge. The substrates in Table 3.4 were isolated and characterized by Rebecca Green. The stoichiometric experiments were performed by both Dr. Shaozhong Ge and Rebecca Green. The kinetic analysis and competition experiments were performed by Rebecca Green.

General Procedure for the Amination Reactions of Aryl and Heteroaryl Chlorides with Primary Aliphatic Amines

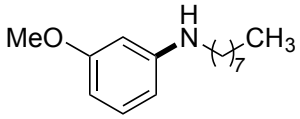
In a drybox, a 4-mL screw-capped vial was charged with (rac-BINAP)Ni(η^2-NCPh), NaO^{t}Bu (57.7 mg, 0.600 mmol), aryl chloride (0.400 mmol), amine (0.600 mmol), a magnetic stirring bar, and toluene (1.0 mL). The vial was sealed with a cap containing a PTFE septum and removed from the drybox. The reaction mixture was stirred at 50 ºC for 24 h and then cooled to room temperature. The mixture was quenched with H_2O (0.5 mL) and extracted with Et_2O (3 × 3 mL). To the etheral extract, silica (4 mL) was added and all the volatiles were removed under reduced pressure. The crude product was purified with a CombiFlash system with 5-70% ethyl acetate in hexanes as eluent. The conditions for chromatography and data for characterization of the products are given below.

2-Methoxy-*N*-octylaniline (2a)



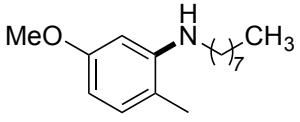
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.92 (td, *J* = 7.6, 1.2 Hz, 1H), 6.81 (dd, *J* = 7.9, 1.0 Hz, 1H), 6.71 (dd, *J* = 7.7, 1.4 Hz, 1H), 6.69–6.62 (m, 1H), 4.23 (broad s, 1H), 3.89 (s, 3H), 3.16 (t, *J* = 7.2 Hz, 2H), 1.84–1.60 (m, 2H), 1.54–1.21 (m, 10H), 0.95 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 146.7, 138.4, 121.2, 116.0, 109.7, 109.2, 55.3, 43.7, 31.8, 29.5, 29.4, 29.3, 27.3, 22.7, 14.1.

3-Methoxy-*N*-octylaniline (2b)



This reaction was conducted with 1 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10 (t, *J* = 8.1 Hz, 1H), 6.29 (dd, *J* = 8.1, 2.1 Hz, 1H), 6.25 (dd, *J* = 8.1, 2.1 Hz, 1H), 6.19 (t, *J* = 2.2 Hz, 1H), 3.80 (s, 3H), 3.66 (broad s, 1H), 3.11 (t, *J* = 7.1 Hz, 2H), 1.73–1.52 (m, 2H), 1.50–1.16 (m, 10H), 0.93 (t, *J* = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 160.8, 149.9, 129.9, 105.9, 102.0, 98.5, 55.0, 43.9, 31.8, 29.5, 29.4, 29.3, 27.2, 22.7, 14.1.

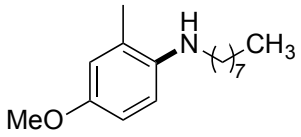
5-Methoxy-2-methyl-*N*-octylaniline (2c)



This reaction was conducted with 1 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (4 g column, 100:0→85:15 hexanes/EtOAc). The title compound was isolated in 96% yield as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.78–6.70 (m, 2H), 6.62–6.56 (m, 1H), 3.78 (s, 3H), 3.13 (t, *J* = 7.1 Hz, 2H + 1H N*H*), 2.17 (s, 3H), 1.81–1.55 (m, 2H), 1.49–1.21 (m, 10H), 0.94 (t, *J* = 6.9 Hz, 3H). ^{13}C{^{1}H}

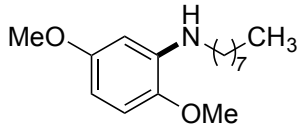
NMR (101 MHz, $CDCl_3$) δ: 151.4, 140.8, 123.5, 116.9, 111.5, 110.7, 55.7, 44.8, 31.8, 29.7, 29.5, 29.3, 27.3, 22.7, 17.7, 14.1.

4-Methoxy-2-methyl-*N*-octylaniline (2d)



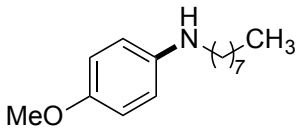
This reaction was conducted with 1 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (4 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated in 79% yield as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (d, J = 7.6 Hz, 1H), 6.26 (s, 1H), 6.24 (d, J = 2.5 Hz, 1H), 3.83 (s, 3H), 3.71–3.29 (broad s, 1H), 3.18 (t, J = 7.2 Hz, 2H), 2.12 (s, 3H), 1.78–1.58 (m, 2H), 1.47–1.24 (m, 10H), 0.96 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 159.7, 147.6, 130.5, 114.6, 100.6, 97.3, 55.4, 44.2, 32.1, 30.0, 29.8, 29.7, 29.6, 27.5, 23.0, 16.9, 14.4.

2,5-Dimethoxy -*N*-octylaniline (2e)



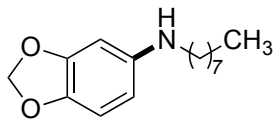
This reaction was conducted with 1 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (4 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated in 89% yield as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.68 (d, J = 8.6 Hz, 1H), 6.25 (d, J = 2.9 Hz, 1H), 6.16 (dd, J = 8.6, 2.9 Hz, 1H), 4.24 (s, 1H), 3.82 (s, 3H), 3.79 (s, 3H), 3.12 (t, J = 7.2 Hz, 2H), 1.74–1.59 (m, 2H), 1.49–1.24 (m, 10H), 0.93 (t, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 154.79, 141.39, 139.50, 109.63, 98.06, 97.84, 77.35, 77.03, 76.71, 55.86, 55.38, 43.54, 31.81, 29.39, 29.36, 29.23, 27.19, 22.63, 14.07.

4-Methoxy-*N*-octylaniline (2f)



This reaction was conducted with 4 mol % (*rac*-BINAP)Ni(η^2-N≡CPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 59% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.80 (d, J = 8.8 Hz, 2H), 6.60 (d, J = 8.9 Hz, 2H), 3.76 (s, 3H), 3.32 (broad s, 1H), 3.07 (t, J = 7.1 Hz, 2H), 1.71–1.53 (m, 2H), 1.48–1.21 (m, 10H), 0.91 (t, J = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 151.9, 142.9, 114.8, 114.0, 55.8, 45.0, 31.8, 29.7, 29. 5, 29.3, 27.2, 22.7, 14.1.

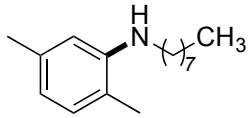
***N*-Octylbenzo[*d*][1,3]dioxol-5-amine (2g)**



This reaction was conducted with 4 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system

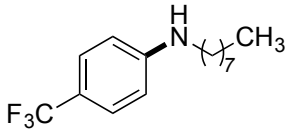
(12 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated as a white solid in 73% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.67 (d, J = 8.3 Hz, 1H), 6.25 (d, J = 2.2 Hz, 1H), 6.05 (dd, J = 8.3, 2.3 Hz, 1H), 5.86 (s, 2H), 3.41 (broad s, 1H), 3.04 (t, J = 7.1 Hz, 2H), 1.67–1.50 (m, 2H), 1.47–1.18 (m, 10H), 0.91 (t, J = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 148.3, 144.4, 139.3, 108.6, 104.2, 100.5, 95.8, 45.0, 31.8, 29.6, 29.4, 29.3, 27.2, 22.7, 14.1.

2,5-Dimethyl-*N*-octylaniline (**2h**)



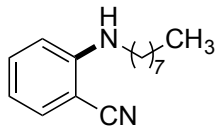
This reaction was conducted with 1 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→95:5 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.00 (d, J = 7.4 Hz, 1H), 6.53 (d, J = 7.5 Hz, 1H), 6.51 (s, 1H), 3.48 (broad s, 1H), 3.20 (t, J = 7.1 Hz, 2H), 2.37 (s, 3H), 2.16 (s, 3H), 1.80–1.65 (m, 2H), 1.56–1.26 (m, 10H), 0.97 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 146.2, 136.7, 129.8, 118.6, 117.2, 110.5, 44.0, 31.9, 29.6, 29.4, 29.3, 27.3, 22.7, 21.6, 17.0, 14.1.

***N*-Octyl-4-(trifluoromethyl)aniline** (**2i**)



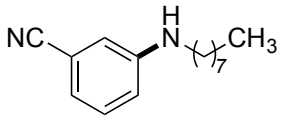
This reaction was conducted with 1 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, J = 8.5 Hz, 2H), 6.60 (d, J = 8.5 Hz, 2H), 3.97 (s, 1H), 3.14 (t, J = 7.1 Hz, 2H), 1.75–1.54 (m, 2H), 1.51–1.19 (m, 10H), 0.92 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 150.9, 126.6 (q, J = 3.8 Hz), 125.1 (q, J = 270 Hz), 118.3(q, J = 32.5 Hz), 111.6, 43.5, 31.8, 29.4, 29.3, 29.3, 27.1, 22.7, 14.1.

2-(Octylamino)benzonitrile (**2j**)



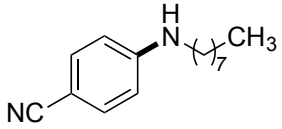
This reaction was conducted with 1 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48–7.26 (m, 2H), 6.82–6.44 (m, 2H), 4.54 (s, 1H), 3.18 (t, J = 7.0 Hz, 2H), 1.76–1.57 (m, 2H), 1.40 –1.13 (m, 10H), 0.90 (t, J = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 150.4, 134.2, 132.7, 118.0, 116.1, 110.5, 95.3, 43.3, 31.8, 29.3, 29.2, 29.1, 27.0, 22.6, 14.1.

3-(Octylamino)benzonitrile (**2k**)



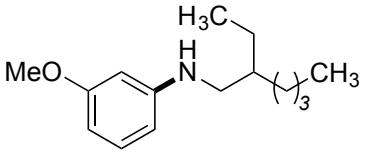
This reaction was conducted with 1 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 77% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20 (t, *J* = 8.2 Hz, 1H), 6.92 (d, *J* = 7.5 Hz, 1H), 6.82–6.73 (m, 2H), 3.91 (s, 1H), 3.09 (dd, *J* = 12.7, 6.8 Hz, 2H), 1.72–1.53 (m, 2H), 1.51–1.16 (m, 10H), 0.89 (t, *J* = 6.7 Hz, 3H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 148.6, 129.8, 120.2, 119.6, 117.0, 114.5, 112.8, 43.5, 31.8, 29.3, 29.2, 29.1, 27.0, 22.6, 14.1.

4-(Octylamino)benzonitrile (**2l**)



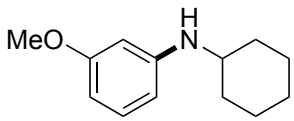
This reaction was conducted with 1 mol % (*rac*-BINAP)Ni(η^2-N≡CPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash sysntem (12 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated as a white solid in 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, *J* = 8.8 Hz, 2H), 6.58 (d, *J* = 8.8 Hz, 2H), 4.27 (s, 1H), 3.17 (t, *J* = 7.2 Hz, 2H), 1.78–1.55 (m, 2H), 1.51–1.15 (m, 10H), 0.92 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 151.4, 133.7, 120.6, 112.0, 98.3, 43.3, 31.8, 29.3, 29.2, 29.1, 27.0, 22.6, 14.1.

***N*-(2-Ethylhexyl)-3-Methoxyoctylaniline** (**2m**)



This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (t, *J* = 8.1 Hz, 1H), 6.35–6.22 (m, 2H), 6.20 (t, *J* = 2.2 Hz, 1H), 3.81 (s, 3H), 3.70 (broad s, 1H), 3.04 (d, *J* = 6.2 Hz, 2H), 1.68–1.52 (m, 1H), 1.50–1.20 (m, 9H), 1.02–0.82 (m, 5H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 160.8, 150.1, 129.9, 105.8, 101.9, 98.4, 55.0, 46.9, 39.0, 31.3, 29.7, 28.9, 24.4, 23.1, 14.1, 10.9. HR-MS (ESI) exact mass calcd for $C_{15}H_{26}NO$: m/z 236.2009 ($[M+H]^+$). Found: 236.2006 ($[M+H]^+$).

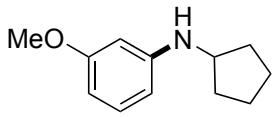
***N*-Cyclohexyl-3-Methoxyaniline** (**2n**)



This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 63% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (t, *J* = 8.1 Hz, 1H), 6.32–6.20 (m, 2H), 6.17 (t, *J* = 2.2 Hz, 1H), 3.79 (s, 3H), 3.57 (broad s, 1H), 3.33–3.18 (m, 1H), 2.15–2.00 (m, 2H), 1.87–1.72 (m, 2H), 1.72–1.56 (m,

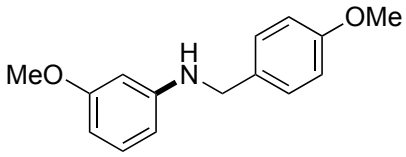
1H), 1.48–1.31 (m, 2H), 1.31–1.06 (m, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 Hz, $CDCl_3$): δ 160.8, 148.7, 129.9, 106.3, 101.7, 99.0, 55.0, 51.7, 33.4, 25.9, 25.0.

N-Cyclopentyl-3-Methoxyaniline (2o)



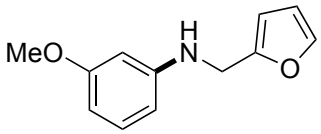
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-N≡CPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash sysntem (12 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 74% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (t, *J* = 8.1 Hz, 1H), 6.26 (dd, *J* = 11.2, 9.2 Hz, 2H), 6.19 (s, 1H), 3.86–3.76 (s, 4H), 3.69 (broad s, 1H), 2.16–1.94 (m, 2H), 1.82–1.69 (m, 2H), 1.69–1.57 (m, 2H), 1.56–1.41 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 Hz, $CDCl_3$): δ 160.7, 149.4, 129.8, 106.4, 101.8, 99.0, 55.0, 54.6, 33.5, 24.0.

3-Methoxy-*N*-(4-methoxybenzyl)aniline (2p)



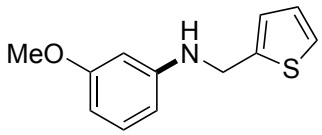
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-N≡CPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash sysntem (4 g column, 100:0→30:70 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.7 Hz, 2H), 7.13 (t, *J* = 8.1 Hz, 1H), 6.96–6.88 (m, 2H), 6.32 (dddd, *J* = 18.4, 11.0, 5.6, 5.0 Hz, 2H), 6.24 (t, *J* = 2.3 Hz, 1H), 4.27 (s, 2H), 4.03 (broad s, 1H), 3.84 (s, 3H), 3.80 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 161.1, 159.1, 149.9, 131.6, 130.2, 129.1, 114.3, 106.2, 102.8, 99.1, 55.5, 55.3, 48.0.

N-(Furan-2-ylmethyl)-3-methoxyaniline (2q)



This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→80:20 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 1.4 Hz, 1H), 7.13 (t, *J* = 8.1 Hz, 1H), 6.40–6.22 (m, 5H), 4.33 (s, 2H), 4.07 (broad s, 1H), 3.80 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 Hz, $CDCl_3$): δ 160.7, 152.6, 149.0, 141.8, 129.9, 110.3, 107.0, 106.1, 103.0, 99.1, 55.0, 41.3.

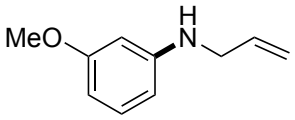
3-Methoxy-*N*-(thiophen-2-ylmethyl)aniline (2r)



This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→80:20 hex-

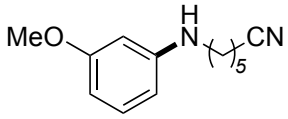
anes/EtOAc). The title compound was isolated as a slightly yellow liquid in 96% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.15 (t, *J* = 8.1 Hz, 1H), 7.07–7.04 (m, 1H), 7.01 (dd, *J* = 5.0, 3.5 Hz, 1H), 6.40–6.31 (m, 2H), 6.28 (t, *J* = 2.3 Hz, 1H), 4.52 (d, *J* = 0.5 Hz, 2H), 4.12 (s, 1H), 3.80 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.0, 149.3, 143.1, 130.3, 127.1, 125.3, 124.9, 106.5, 103.4, 99.4, 55.3, 43.7.

_N_-Allyl-3-methoxyaniline (2s)



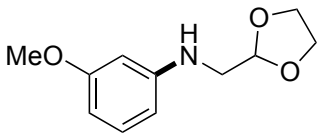
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→90:10 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 92% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.12 (t, *J* = 8.1 Hz, 1H), 6.32 (dd, *J* = 8.1, 2.1 Hz, 1H), 6.28 (dd, *J* = 8.1, 1.8 Hz, 1H), 6.22 (t, *J* = 2.2 Hz, 1H), 6.07–5.88 (m, 1H), 5.36–5.27 (m, 1H), 5.24–5.16 (m, 1H), 3.85 (broad s, 1H), 3.80 (s, 3H), 3.78 (t, *J* = 1.4 Hz, 1H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 160.7, 149.4, 135.3, 129.9, 116.2, 106.1, 102.5, 98.9, 55.0, 46.5.

6-((3-Methoxyphenyl)amino)hexanenitrile (2t)



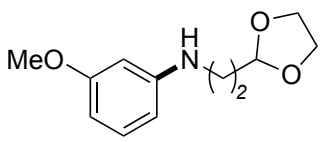
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (4 g column, 100:0→30:70 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (t, *J* = 8.1 Hz, 1H), 6.28 (dd, *J* = 8.1, 2.2 Hz, 1H), 6.23 (dd, *J* = 8.0, 1.9 Hz, 1H), 6.16 (t, *J* = 2.2 Hz, 1H), 3.78 (s, 3H), 3.68 (broad s, 1H), 3.12 (t, *J* = 6.9 Hz, 2H), 2.35 (t, *J* = 7.0 Hz, 2H), 1.75–1.60 (m, 4H), 1.60–1.47 (m, 2H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 160.7, 149.5, 129.9, 119.6, 105.8, 102.2, 98.5, 55.0, 43.4, 28.6, 26.1, 25.1, 17.0. HR-MS (ESI) exact mass calcd for $C_{13}H_{19}N_2O$: m/z 219.1492 ($[M+H]^+$). Found: 219.1490 ($[M+H]^+$).

_N_-((1,3-Dioxolan-2-yl)methyl)-3-methoxyaniline (2u)



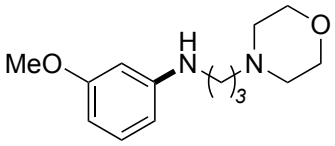
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→20:80 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (dd, *J* = 10.6, 5.5 Hz, 1H), 6.35 – 6.26 (m, 2H), 6.24 (t, *J* = 2.3 Hz, 1H), 5.11 (t, *J* = 4.1 Hz, 1H), 4.09 – 3.97 (m, 3H), 3.97 – 3.88 (m, 2H), 3.78 (s, 3H), 3.34 (d, *J* = 4.1 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 161.0, 149.6, 130.2, 106.4, 103.2, 102.6, 99.4, 65.4, 55.3, 46.9. HR-MS (ESI) exact mass calcd for $C_{11}H_{16}NO_3$: m/z 210.1125 ($[M+H]^+$). Found: 210.1124 ($[M+H]^+$).

_N_-(2-(1,3-Dioxolan-2-yl)ethyl)-3-methoxyaniline (2v)



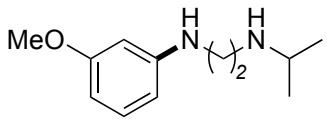
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→70:30 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 89% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (t, *J* = 8.1 Hz, 1H), 6.27 (t, *J* = 9.3 Hz, 2H), 6.19 (s, 1H), 5.00 (t, *J* = 4.4 Hz, 1H), 4.16 (broad s, 1H), 4.07–3.94 (m, 2H), 3.94–3.82 (m, 2H), 3.78 (s, 3H), 3.27 (t, *J* = 6.5 Hz, 2H), 2.02 (dd, *J* = 11.1, 6.2 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 160.7, 149.7, 129.9, 105.9, 103.6, 102.3, 98.6, 64.9, 55.0, 39.1, 32.9. HR-MS (ESI) exact mass calcd for $C_{12}H_{18}NO_3$: m/z 224.1281 ([M+H]$^+$). Found: 214.1279 ([M+H]$^+$).

3-Methoxy-*N*-(3-morpholinopropyl)aniline (**2w**)



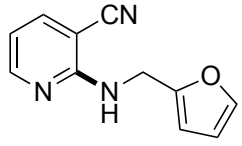
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) at 80 ºC and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→40:60 (90% hexanes + 10%Et_3N)/EtOAc). The title compound was isolated as a slightly yellow liquid in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (t, *J* = 8.1 Hz, 1H), 6.26 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.23 (dd, *J* = 8.1, 2.0 Hz, 1H), 6.16 (d, *J* = 2.1 Hz, 1H), 4.62 (broad s, 1H), 3.78 (s, 3H), 3.74 (t, *J* = 4.6 Hz, 4H), 3.18 (t, *J* = 6.4 Hz, 2H), 2.48 (t, *J* = 6.6 Hz, 6H), 1.80 (p, *J* = 6.5 Hz, 2H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 160.8, 150.0, 129.8, 105.9, 101.9, 98.5, 67.0, 57.5, 55.0, 53.7, 43.2, 25.3.

***N*^{1}-Isopropyl-*N*^{2}-(3-methoxyphenyl)ethane-1,2-diamine** (Table 3, **2x**)



This reaction was conducted with 4 mol % (*rac*-BINAP)Ni(η^2-N≡CPh) at 80 ºC and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→30:70 (90% hexanes + 10%Et_3N)/EtOAc). The title compound was isolated as a slightly yellow liquid in 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.09 (t, *J* = 8.1 Hz, 1H), 6.33–6.24 (m, 2H), 6.20 (t, *J* = 2.1 Hz, 1H), 4.13 (s, 1H), 3.78 (s, 3H), 3.21 (dd, *J* = 10.8, 5.3 Hz, 2H), 2.91–2.84 (m, 2H), 2.84–2.75 (m, 1H), 1.08 (d, *J* = 6.3 Hz, 6H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 160.8, 149.9, 129.9, 106.1, 102.4, 98.8, 55.0, 48.6, 46.2, 44.1, 23.1.

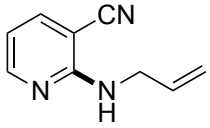
2-((Furan-2-ylmethyl)amino)nicotinonitrile (**3a**)



This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-N≡CPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash sysntem (12 g column, 100:0→70:30 hexanes/EtOAc). The title compound was isolated as a white solid in 81% yield. ^{1}H NMR (400 MHz,

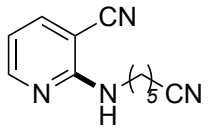
$CDCl_3$) δ 8.39–8.24 (m, 1H), 7.66 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.38 (d, *J* = 0.8 Hz, 1H), 6.63 (dd, *J* = 7.4, 5.1 Hz, 1H), 6.40–6.20 (m, 2H), 5.50 (s, 1H), 4.71 (d, *J* = 5.5 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.0, 152.8, 151.7, 142.5, 141.6, 116.8, 112.7, 110.6, 107.8, 92.0, 38.4.

2-(Allylamino)nicotinonitrile (3b)



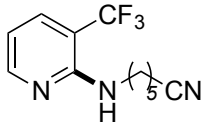
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→70:30 hexanes/EtOAc). The title compound was isolated as a yellow liquid in 63% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.29 (dd, *J* = 4.9, 1.8 Hz, 1H), 7.65 (dd, *J* = 7.6, 1.9 Hz, 1H), 6.61 (dd, *J* = 7.6, 5.0 Hz, 1H), 6.08–5.85 (m, 1H), 5.29 (broad s, 1H, overlap with dd at δ 5.26), 5.26 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.18 (dd, *J* = 10.3, 1.3 Hz, 1H), 4.15 (tt, *J* = 5.6, 1.4 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.5, 153.1, 141.6, 134.5, 117.1, 116.8, 112.4, 91.9, 43.9.

2-((5-Cyanopentyl)amino)nicotinonitrile (3c)



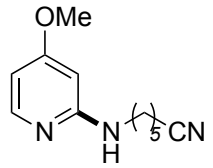
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→40:60 hexanes/EtOAc). The title compound was isolated as a yellow liquid in 76% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.25 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.62 (dd, *J* = 7.6, 1.9 Hz, 1H), 6.57 (dd, *J* = 7.6, 5.0 Hz, 1H), 5.19 (broad s, 1H), 3.60–3.38 (m, 2H), 2.36 (t, *J* = 7.1 Hz, 2H), 1.80–1.59 (m, 4H), 1.58–1.44 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.6, 153.0, 141.6, 119.9, 117.1, 112.1, 91.6, 41.2, 29.0, 26.2, 25.3, 17.3. HR-MS (ESI) exact mass calcd for $C_{12}H_{15}N_4$: m/z 215.1291 ($[M+H]^+$). Found: 215.1290 ($[M+H]^+$).

6-((3-(Trifluoromethyl)pyridin-2-yl)amino)hexanenitrile (3d)



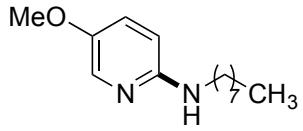
The reaction was conducted with 2% (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 hr at 80 °C. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→50:50 hexanes/EtOAc). The title compound was isolated as a pale yellow liquid in 64% yield. ^1H NMR (400 MHz, $CDCl_3$): δ 8.23 (dd, *J* = 4.9, 0.8 Hz, 1H), 7.60 (t, *J* = 0.8 Hz, 1H), 6.58 (ddd, *J* = 7.6, 5.0, 0.7 Hz, 1H), 4.86 (s, 1H), 3.50 (td, *J* = 7.0, 5.6 Hz, 2H), 2.34 (t, *J* = 7.1 Hz, 2H), 1.68 (t, *J* = 8.3 Hz, 4H), 1.53 (s, 2H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 154.5, 151.6, 135.0, 134.9 (q, J_{CF} = 5.1 Hz), 124.5 (q, J_{CF} = 271 Hz), 119.5, 111.2, 108.4 (q, J_{CF} = 31.2 Hz), 40.9, 28.7, 26.0, 25.1, 17.0.

6-((4-Methoxypyridin-2-yl)amino)hexanenitrile (3e)



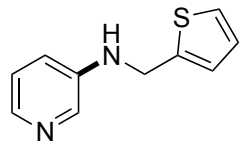
The reaction was conducted with 4% (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 hr at 50 °C. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→40:60 hexanes/EtOAc). The title compound was isolated as a dark yellow liquid in 57% yield. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.89 (d, *J* = 5.9 Hz, 1H), 6.18 (dd, *J* = 5.9, 2.2 Hz, 1H), 5.82 (d, *J* = 2.1 Hz, 1H), 4.63 (d, *J* = 0.2 Hz, 1H), 3.77 (s, 3H), 3.24 (q, *J* = 6.4 Hz, 2H), 2.33 (t, *J* = 7.1 Hz, 2H), 1.72–1.61 (m, 4H), 1.57–1.51 (m, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 167.2, 160.56, 149.2, 119.6, 101.1, 90.3, 54.9, 41.8, 28.7, 26.1, 25.1, 17.1. HR-MS (ESI) exact mass calcd for $C_{12}H_{18}N_3O$: m/z 220.1444 ([M+H]$^+$). Found: 220.1442 ([M+H]$^+$).

5-methoxy-N-octylpyridin-2-amine (3f)



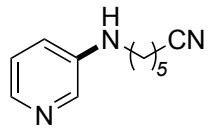
The reaction was conducted with 4% (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 hr at 50 °C. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→50:50 hexanes/EtOAc). The title compound was isolated as a beige solid in 89% yield. ^{1}H NMR (400 MHz; $CDCl_3$): δ 7.79 (d, *J* = 2.7 Hz, 1H), 7.09 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.34 (d, *J* = 8.9 Hz, 1H), 3.75 (s, 3H), 3.18 (t, *J* = 7.1 Hz, 2H), 1.58 (s, 2H), 1.27–1.25 (m, 10H), 0.86 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 154.3, 148.6, 133.7, 125.6, 106.9, 56.6, 43.1, 31.9, 29.7, 29.4, 29.3, 27.2, 22.7, 14.1. HR-MS (ESI) exact mass calcd for $C_{14}H_{25}N_2O$: m/z 237.1961 ([M+H]$^+$). Found: 237.1958 ([M+H]$^+$).

***N*-(Thiophen-2-ylmethyl)pyridin-3-amine (3g)**



This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→20:80 (10% (Et_3N in hexanes)/EtOAc). The title compound was isolated as a yellow solid in 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 2.1 Hz, 1H), 7.99 (d, *J* = 4.2 Hz, 1H), 7.22 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.08 (dd, *J* = 8.2, 4.7 Hz, 1H), 7.04–6.99 (m, 1H), 6.99–6.95 (m, 1H), 6.92 (ddd, *J* = 8.3, 2.8, 1.3 Hz, 1H), 4.51 (d, *J* = 4.2 Hz, 2H), 4.34 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 143.8, 142.3, 139.6, 136.6, 127.2, 125.6, 125.1, 124.0, 119.2, 43.27.

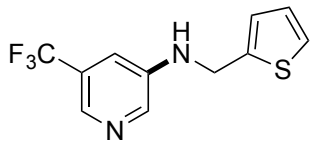
6-(Pyridin-3-ylamino)hexanenitrile (3h)



This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→20:80 (10% (Et_3N in hexanes)/EtOAc). The title compound was isolated as an off-white solid in 67% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 2.2 Hz, 1H), 7.91 (d, *J* = 4.2 Hz, 1H), 7.05 (dd, *J* = 8.3, 4.7 Hz, 1H), 6.83 (ddd, *J* = 8.3, 2.7, 1.1 Hz, 1H), 3.90 (s, 1H), 3.11 (t, *J* = 6.8 Hz, 2H), 2.34 (t, *J* = 7.0 Hz, 2H), 1.75–1.59

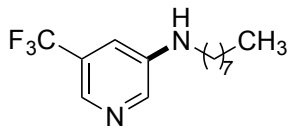
(m, 4H), 1.59–1.44 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.5, 138.7, 136.1, 124.0, 119.8, 118.5, 43.3, 28.8, 26.4, 25.3, 17.3. HR-MS (ESI) exact mass calcd for $C_{11}H_{16}N_3$: m/z 190.1339 ($[M+H]^+$). Found: 190.1337 ($[M+H]^+$).

_N_-(Thiophen-2-ylmethyl)-5-(trifluoromethyl)pyridin-3-amine (3i)



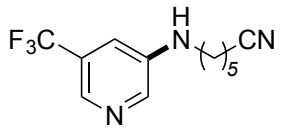
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→50:50 hexanes/EtOAc). The title compound was isolated as a yellow solid in 76% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 2H), 7.25 (dd, J = 5.1, 1.2 Hz, 1H), 7.09 (s, 1H), 7.05–7.01 (m, 1H), 6.98 (dd, J = 5.1, 3.5 Hz, 1H), 4.74 (s, 1H), 4.54 (d, J = 5.3 Hz, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 143.6, 141.0, 139.5, 135.5 (q, J_{CF} = 4.3 Hz), 127.4, 127.1 (q, J_{CF} = 32.3 Hz), 126.1, 125.5, 124.0 (q, J_{CF} = 273 Hz), 115.0 (q, J_{CF} = 3.6 Hz), 43.0. HR-MS (ESI) exact mass calcd for $C_{11}H_{10}F_3N_2S$: m/z 259.0511 ($[M+H]^+$). Found: 259.0508 ($[M+H]^+$).

_N_-Octyl-5-(trifluoromethyl)pyridin-3-amine (3j)



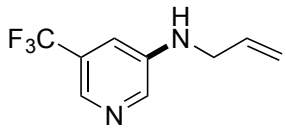
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→70:30 hexanes/EtOAc). The title compound was isolated as a white solid in 94% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.23–8.01 (m, 2H), 6.97 (s, 1H), 4.14 (s, 1H), 3.17–3.08 (m, 2H), 1.72–1.56 (m, 2H), 1.47–1.17 (m, 10H), 0.87 (t, J = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.5, 139.3, 134.49 (q, J = 4.3 Hz), 127.15 (q, J = 32.1 Hz), 124.12 (q, J = 273 Hz), 114.04 (q, J = 3.6 Hz), 43.6, 32.1, 29.6, 29.5, 29.4, 27.3, 22.9, 14.3. HR-MS (ESI) exact mass calcd for $C_{14}H_{22}F_3N_2$: m/z 275.1730 ($[M+H]^+$). Found: 275.1727 ($[M+H]^+$).

6-((5-(Trifluoromethyl)pyridin-3-yl)amino)hexanenitrile (3k)



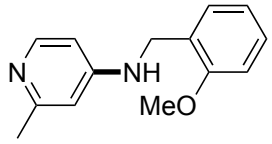
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-N≡CPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash sysntem (12 g column, 100:0→60:40 (10% Et_3N in hexanes)/EtOAc). The title compound was isolated as a yellow liquid in 83% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.16–8.10 (m, 2H), 6.97 (s, 1H), 4.33 (s, 1H), 3.24–3.04 (m, 2H), 2.36 (t, J = 6.9 Hz, 2H), 1.75–1.62 (m, 4H), 1.60–1.45 (m, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 144.3, 139.2, 134.5 (d, J_{CF} = 4.2 Hz), 127.1 (d, J_{CF} = 32.1 Hz), 124.0 (d, J_{CF} = 273 Hz), 119.8, 114.1 (q, J_{CF} = 3.7 Hz), 43.1, 28.5, 26.4, 25.3, 17.4. HR-MS (ESI) exact mass calcd for $C_{12}H_{15}F_3N_3$: m/z 258.1213 ($[M+H]^+$). Found: 258.1210 ($[M+H]^+$).

N-Allyl-5-(trifluoromethyl)pyridin-3-amine (3l)



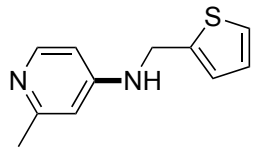
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→60:40 hexanes/EtOAc). The title compound was isolated as a yellow liquid in 93% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22–8.11 (d, J = 3.0 Hz, 2H), 7.00 (s, 1H), 5.97–5.83 (m, 1H), 5.37–5.12 (m, 2H), 4.41 (s, 1H), 3.76–3.90 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 144.1, 139.5, 134.9 (d, J = 4.3 Hz), 127.1 (d, J = 32.3 Hz), 124.0 (d, J = 273 Hz), 133.9, 117.5, 114.7 (d, J = 3.7 Hz), 46.0. HR-MS (ESI) exact mass calcd for $C_9H_{10}F_3N_2$: m/z 203.0791 ($[M+H]^+$). Found: 203.0789 ($[M+H]^+$).

N-(2-Methoxybenzyl)-2-methylpyridin-4-amine (3m)



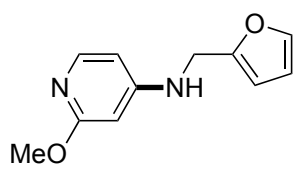
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→40:60 (10% Et_3N in hexanes)/EtOAc). The title compound was isolated as a yellow solid in 96% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, J = 5.7 Hz, 1H), 7.29–7.09 (m, 2H), 6.96–6.75 (m, 2H), 6.33 (d, J = 2.0 Hz, 1H), 6.29 (dd, J = 5.7, 2.2 Hz, 1H), 4.88 (t, J = 5.3 Hz, 1H), 4.33 (d, J = 5.9 Hz, 2H), 3.84 (s, 3H), 2.37 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.6, 157.5, 154.2, 149.5, 128.8, 128.8, 126.3, 120.7, 110.5, 106.9, 105.6, 55.5, 42.2, 24.7. HR-MS (ESI) exact mass calcd for $C_{14}H_{17}N_2O$: m/z 229.1335 ($[M+H]^+$). Found: 229.1332 ($[M+H]^+$).

2-Methyl-*N*-(thiophen-2-ylmethyl)pyridin-4-amine (3n)



The reaction was conducted with 2% (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 hr. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→20:80 (10% NEt_3 in hexanes)/EtOAc). The title compound was isolated as a dark yellow oil in 76% yield. Prepared on 0.404 mmol scale. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.08 (d, J = 5.7 Hz, 1H), 7.21 (d, J = 5.0 Hz, 1H), 6.98 (s, 1H), 6.95 (dd, J = 5.8, 2.3 Hz, 1H), 6.36 (s, 1H), 6.32 (d, J = 5.7 Hz, 1H), 4.85 (s, 1H), 4.50 (d, J = 5.5 Hz, 2H), 2.39 (s, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 158.6, 153.3, 149.4, 141.5, 127.0, 125.4, 124.9, 106.8, 105.5, 42.0, 24.5. HR-MS (ESI) exact mass calcd for $C_{11}H_{13}N_2S$: m/z 205.0794 ($[M+H]^+$). Found: 205.0791 ($[M+H]^+$).

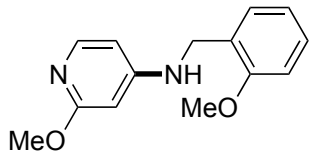
N-(Furan-2-ylmethyl)-2-methoxypyridin-4-amine (3o)



The reaction was conducted with 4% (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 hr. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→40:60 hexanes/EtOAc). The title compound

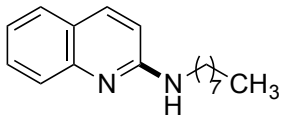
was isolated as a yellow liquid in 96% yield. ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.78 (d, *J* = 5.8 Hz, 1H), 7.34 (s, 1H), 6.30 (s, 1H), 6.21 (d, *J* = 1.9 Hz, 1H), 6.17 (d, *J* = 5.7 Hz, 1H), 5.90 (s, 1H), 4.70 (s, 1H), 4.27 (d, *J* = 5.6 Hz, 2H), 3.86 (d, *J* = 25.7 Hz, 3H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 165.6, 155.3, 151.4, 146.7, 142.2, 110.4, 107.4, 104.5, 91.2, 53.1, 40.1. HR-MS (ESI) exact mass calcd for $C_{11}H_{13}N_2O_2$: m/z 205.0972 ([M+H]$^+$). Found: 205.0969 ([M+H]$^+$).

2-Methoxy-*N*-(2-methoxybenzyl)pyridin-4-amine (3p)



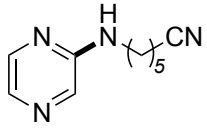
The reaction was conducted with 4% (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 hr at 80 °C. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→40:60 hexanes/EtOAc). The title compound was isolated as a colorless liquid in 94% yield. ^{1}H NMR (600 MHz; $CDCl_3$): δ 7.77 (d, *J* = 5.9 Hz, 1H), 7.23 (t, *J* = 9.5 Hz, 2H), 6.88 (t, *J* = 11.1 Hz, 2H), 6.17 (dd, *J* = 5.9, 1.7 Hz, 1H), 5.88 (d, *J* = 1.6 Hz, 1H), 4.71 (d, *J* = 5.2 Hz, 1H), 4.31 (d, *J* = 5.9 Hz, 2H), 3.84 (d, *J* = 10.9 Hz, 6H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 165.7, 157.3, 155.9, 146.6, 128.7, 126.1, 120.5, 110.34, 104.6, 91.0, 55.3, 53.1, 42.3. HR-MS (ESI) exact mass calcd for $C_{14}H_{17}N_2O_2$: m/z 245.1285 ([M+H]$^+$). Found: 245.1281 ([M+H]$^+$).

***N*-Octylquinolin-3-amine (3q)**



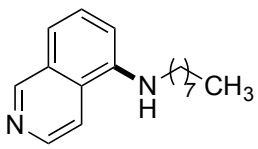
This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→40:60 hexanes/EtOAc). The title compound was isolated as a yellow liquid in 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.9 Hz, 1H), 7.70 (d, *J* = 8.3 Hz, 1H), 7.58 (d, *J* = 7.9 Hz, 1H), 7.56–7.49 (m, 1H), 7.24–7.16 (m, 1H), 6.63 (d, *J* = 8.9 Hz, 1H), 4.84 (s, 1H), 3.47 (dd, *J* = 12.8, 7.0 Hz, 2H), 1.81–1.52 (m, 2H), 1.52–1.16 (m, 10H), 0.90 (t, *J* = 6.8 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 157.4, 148.4, 137.5, 129.8, 127.7, 126.3, 123.6, 122.1, 111.3, 42.1, 32.1, 30.0, 29.7, 29.6, 27.4, 23.0, 14.4.

6-(Pyrazin-2-ylamino)hexanenitrile (3r)



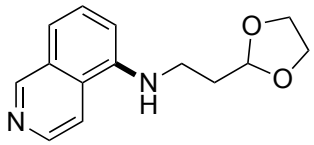
This reaction was conducted with 4 mol % (*rac*-BINAP)Ni(η^2-NCPh) at 80 ºC and the reaction time was 24 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→40:60 hexanes/EtOAc). The title compound was isolated as a white solid in 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.05 (d, *J* = 8.4 Hz, 2H), 6.58 (d, *J* = 8.4 Hz, 2H), 3.53 (m, 1H), 3.14 (t, *J* = 6.8 Hz, 2H), 2.37 (t, *J* = 7.0 Hz, 2H), 1.81–1.49 (m, 6H). ^{13}C{^{1}H} NMR (100.6 Hz, $CDCl_3$): δ 146.1, 133.1, 128.5, 119.6, 112.8, 28.8, 27.9, 26.2, 25.2, 17.1.

_N_-Octylisoquinolin-5-amine (3s)



This reaction was conducted with 2 mol % (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 12 h. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→80:20 hexanes/EtOAc). The title compound was isolated as an off-white solid in 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (s, 1H), 8.46 (d, *J* = 6.0 Hz, 1H), 7.55 (d, *J* = 6.0 Hz, 1H), 7.45 (t, *J* = 7.9 Hz, 1H), 7.32–7.24 (m, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 4.40 (s, 1H), 3.23 (dd, *J* = 12.2, 7.0 Hz, 2H), 1.86–1.65 (m, 2H), 1.52–1.16 (m, 10H), 0.90 (t, *J* = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 153.2, 143.0, 142.2, 129.6, 128.4, 126.1, 115.9, 113.6, 107.6, 44.3, 32.1, 29.7, 29.5 (two peaks overlap), 27.6, 22.9, 14.4. HR-MS (ESI) exact mass calcd for $C_{17}H_{25}N_2$: m/z 257.2012 ([M+H]$^+$). Found: 257.2011 ([M+H]$^+$).

_N_-(2-(1,3-Dioxolan-2-yl)ethyl)isoquinolin-5-amine (3t)



The reaction was conducted with 4% (*rac*-BINAP)Ni(η^2-NCPh) and the reaction time was 24 hr at 80 °C. This crude product was purified by silica gel chromatography with a CombiFlash system (12 g column, 100:0→40:60 (10% NEt_3 in hexanes)/EtOAc). The title compound was isolated as a yellow liquid in 91% yield. ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.15 (s, 1H), 8.47 (d, *J* = 6.0 Hz, 1H), 7.55 (d, *J* = 6.0 Hz, 1H), 7.46 (t, *J* = 7.9 Hz, 1H), 7.29 (d, *J* = 8.1 Hz, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 5.20 (s, 1H), 5.07 (t, *J* = 4.2 Hz, 1H), 4.05-4.01 (m, 2H), 3.95-3.90 (m, 2H), 3.41 (d, *J* = 1.2 Hz, 2H), 2.19 (td, *J* = 6.1, 4.3 Hz, 2H). ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ 152.8, 142.8, 141.9, 129.3, 128.2, 126.1, 115.7, 113.5, 107.1, 104.0, 65.0, 39.3, 32.2. HR-MS (ESI) exact mass calcd for $C_{14}H_{17}N_2O_2$: m/z 245.1285 ([M+H]+). Found: 245.1283 ([M+H]+).

General Procedure for the Oxidative Addition of (rac-BINAP)Ni(η^2-NCPh) to Aryl Chlorides

A suspension of (*rac*-BINAP)Ni(η^2-N≡CPh)(toluene) (88.0 mg, 0.100 mmol) and ArCl (1.00 mmol) in THF (2 mL) was stirred until the suspension became a clear solution. Pentane was added until it started to form precipitate and the mixture was filtered. Upon standing in a freezer at -30 ºC for 12 h, crystalline material formed and the liquid was decanted. The solid was dried under vacuum to give the corresponding arylnickel chloride complex. The characterizations of these complexes were listed below.

(*rac*-BINAP)NiCl(C_6H_5) (**4**). Isolated as a yellow crystalline solid in a THF-solvated form. Yield: 65.6 mg, 75.7 μmol, 76%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42–8.07 (m, 2H), 8.06–7.82 (m, 2H), 7.81–7.61 (m, 2H), 7.59–7.27 (m, 8H), 7.25–7.01 (m, 8H), 6.99–6.70 (m, 7H), 6.69–6.10 (m, 8H). ^{31}P NMR (162 MHz, $CDCl_3$) δ 30.32 (broad s), 15.00 (broad s). Anal. Calcd for $C_{50}H_{37}ClNiP_2(C_4H_8O)$: C, 74.89; H, 5.24. Found: C, 74.66; H, 4.91.

(*rac*-BINAP)NiCl(C_6H_4-3-OMe) (**5**) Isolated as a orange crystalline solid. Yield: 66.6 mg, 80.8 μmol, 81%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.38–7.93 (m, 3H), 7.92–7.42 (m, 10H), 7.42–7.17 (m, 7H), 7.17–6.82 (s, 8H), 6.81–6.32 (m, 7H), 6.29–6.06 (m, 1H), 3.61 (s, 3H). ^{31}P NMR (162 MHz, $CDCl_3$) δ 29.62 (broad s), 14.81 (broad s). Anal. Calcd for $C_{51}H_{39}ClNiOP_2$: C, 74.34; H, 4.77. Found: C, 74.12; H, 5.03.

(*rac*-BINAP)NiCl(C_6H_4-4-CF_3) (**6**) Isolated as a orange crystalline solid. Yield: 76.6 mg, 88.9 μmol, 89%. ^{1}H NMR (500 MHz, CD_2Cl_2): δ 8.20 (broad s, 1H), 7.97 (broad s, 2H), 7.89 (broad s, 1H), 7.67 (broad s, 5H), 7.55 (broad s, 6H), 7.39 (broad s, 3H), 7.00 (broad s, 9H), 6.70 (broad s, 4H), 6.54 (broad s, 3H). ^{31}P{^{1}H} (202.2 MHz, CD_2Cl_2): δ 31.45 (d, J_{PP} = 32.0 Hz), 16.54 (d, J_{PP} = 32.0 Hz). Anal. Calcd for $C_{51}H_{36}ClF_3NiP_2$: C, 71.07; H, 4.21. Found: C, 70.90; H, 4.35.

(*rac*-BINAP)NiCl(C_6H_4-4-CN) (**7**) Isolated as a orange crystalline solid. Yield: 71.9 mg, 87.8 μmol, 88%. ^{1}H NMR (500 MHz, CH_2Cl_2): δ 8.19 (broad s, 1H), 7.99 (broad s, 2H), 7.88 (broad s, 1H), 7.74–7.30 (m, 14H), 7.28–6.84 (m, 11H), 6.73 (broad s, 4H), 6.57 (broad s, 3H). ^{31}P{^{1}H} NMR (202.2 MHz, CH_2Cl_2): δ 31.4 (d, J_{PP} = 34.9 Hz), 16.7 (d, J_{PP} = 34.9 Hz). Anal. Calcd for $C_{51}H_{36}ClNNiP_2$: C, 74.80; H, 4.43; N, 1.71. Found: C, 74.59; H, 4.23; N, 1.69.

Synthesis of Compound 9 (Oxidative Addition of 4-Chloroanisole to (rac-BINAP)Ni(η^2-NCPh).

A suspension of (*rac*-BINAP)Ni(η^2-N≡CPh)(toluene) (351 mg, 0.400 mmol) and 4-chloroanisole (570 mg, 4.00 mg) in THF (3.0 mL) was stirred at room temperature until it became a clear solution. Pentane (3.0 mL) was added with vigorous stirring and the resulting suspension was stirred for 1 h. The precipitate was collected by filtration and dried under vacuum. This crude material was purified by recrystallization (slow vapor diffusion of pentane to a concentrated THF solution of the crude material) at room temperature. Compound **9** was isolated as its THF-solvated form (229 mg, 0.256 mmol, 64%) as a red crystalline solid. Some of these crystals were suitable for X-ray analysis. Some of these crystals were suitable for X-ray analysis. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11–7.99 (broad s), 7.98–7.80 (m, 2H), 7.79–7.18 (m, 20H), 7.17-6.98 (m, 6H), 6.96–6.84 (m, 2H), 6.83–6.45 (m, 5H), 2.21 (s, 3H). ^{31}P NMR (162 MHz, THF): δ 24.2 (d, J = 352 Hz), 14.4 (d, J = 352 Hz). Calcd for $C_{51}H_{39}ClNiOP_2(C_4H_8O)$: C, 73.72; H, 5.29. Found: C, 73.47; H, 5.16.

Synthesis of (n-Butyl-NH_2)$_2$NiCl(C_6H_4-4-CN) (10)

To a suspension of (*rac*-BINAP)NiCl(C_6H_4-4-CN) (410 mg, 0.500 mmol) in toluene (1.5 mL), was added n-butylamine (365 mg, 5.00 mmol) and the resulting mixture was stirred for 2 h at room temperature. The mixture was filtered and the solid was washed with pentane (2 mL). The filtrate was combined and kept at 0 °C for 30 min and then filtered. Upon standing in the freezer at -30 °C for 12 h, colorless crystalline solid formed and the liquid was decanted. The solid was dried under vacuum to give the title compound as a

white solid (131 mg, 0.382 mmol, 76%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 7.6 Hz, 2H), 7.19 (d, J = 7.6 Hz, 2H), 2.63–2.35 (m, 4H), 1.58–1.37 (m, 4H), 1.32–1.14 (m, 8H), 0.84 (t, J = 7.3 Hz, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 164.0, 136.2, 132.7, 128.2, 107.1, 42.9, 34.1, 19.6, 13.5. This compound decomposes during purification by recrystallization, which makes it impossible to get a sample with sufficient purity for elemental analysis.

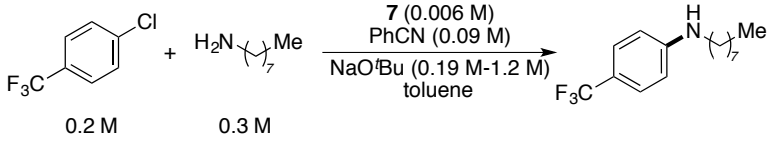
Kinetic Data for the Amination Reaction of 4-Chlorobenzotrifluoride with Octylamine

General Procedure to Acquire Kinetic Data

A 4-mL oven-dried vial was charged with (*rac*-BINAP)NiCl(C_6H_4-4-CF_3) and NaO^{t}Bu, and sealed with a screw-cap equipped with a PTFE-lined septum. A separate vial was charged with 4-chlorobenzotrifluoride, octylamine, 4-trifluoromethoxylanisole (as an internal standard), and toluene. The reactions were run under a dilution factor of 2 from the standard reaction conditions. An oven-dried NMR tube was capped with a septum under an inert atmosphere. Prior to insertion of the sample in the spectrometer, the liquid reagents were transferred to the vial containing the solid reagents with a syringe. Upon mixing of the reagents, the timer was started. The vial was vigorously shaken to solubilize the reagents. Once homogeneous, an aliquot of the solution was transferred to the NMR tube with a syringe. The NMR tube was immediately inserted into the spectrometer probe and acquisition was initiated. The ^{19}F NMR spectrum was acquired every minute for 7 minutes. The concentration of *N*-octyl-4-trifluoromethylaniline was plotted with respect to time. The initial kinetic profile plots do not go through zero, since the added catalyst is after the turnover-limiting step of the reaction.

A change in concentration of the reagent was accompanied by a change in rate for the nickel catalyst, the 4-chlorobenzotrifluoride, and benzonitrile. The reaction was shown to be first order in catalyst and aryl chloride, but inverse first order in benzonitrile. The halt of the reaction with 6 equivalents of NaO^{t}Bu is likely due to the high viscosity of the reaction and the inability to the stir the reaction during the acquisition.

Figure 3.4 Initial Kinetic Profile with Varying Amount of NaO^{t}Bu



NaOtBu (M)	Initial Rate (M/s)
0.190	4.60×10^{-5}
0.300	4.12×10^{-5}
0.600	4.55×10^{-5}

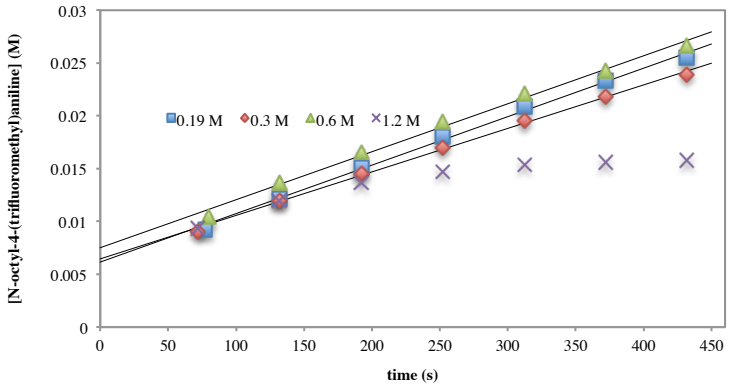
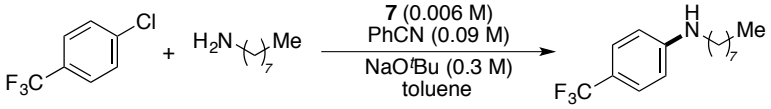


Figure 3.5 Initial Kinetic Profile with Varying Amount of 4-Chlorobenzotrifluoride



0.1 M - 1.0 M 0.3 M

ArCl (M)	Initial Rate (M/s)
0.0997	1.86×10^{-5}
0.202	4.12×10^{-5}
0.397	9.44×10^{-5}
0.600	1.53×10^{-4}
0.802	2.05×10^{-4}
0.996	2.88×10^{-4}

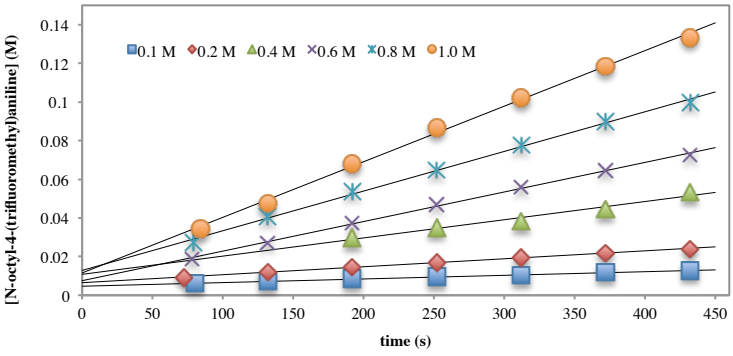
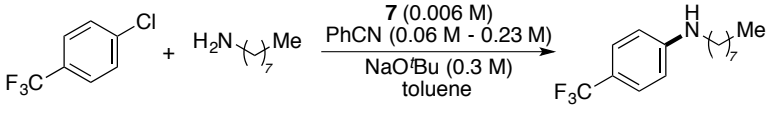


Figure 3.6 Initial Kinetic Profile with Varying Amount of Benzonitrile



0.2 M 0.3 M

PhCN (M)	Initial Rate (M/s)
0.060	4.80×10^{-5}

0.090	4.31×10^{-5}
0.120	3.65×10^{-5}
0.150	1.71×10^{-4}
0.180	1.43×10^{-4}
0.230	1.36×10^{-4}

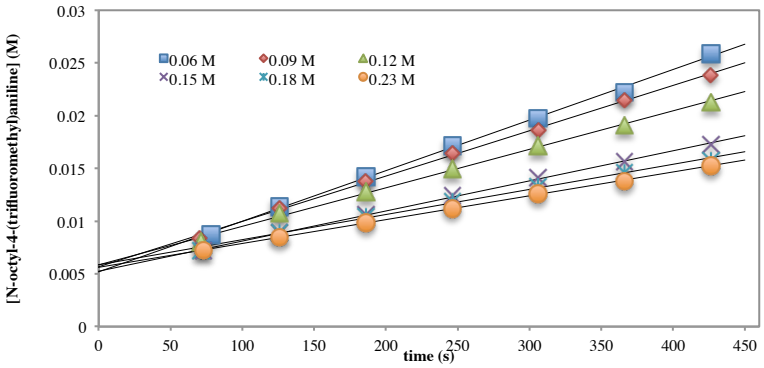
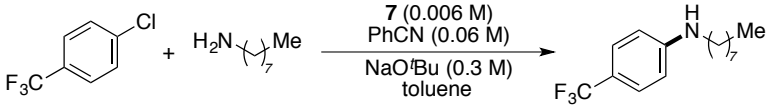


Figure 3.7 Initial Kinetic Profile with Varying Amount of Octylamine



0.2 M 0.3 M - 1.2 M

octylamine (M)	Initial Rate (M/s)
0.300	4.12×10^{-5}
0.600	3.56×10^{-5}
0.120	4.23×10^{-5}

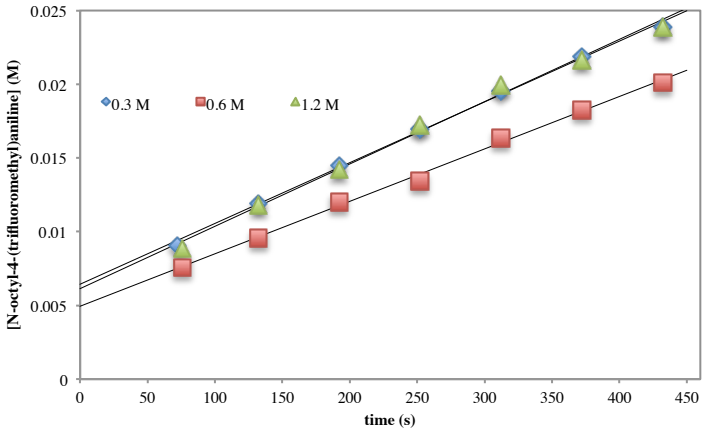
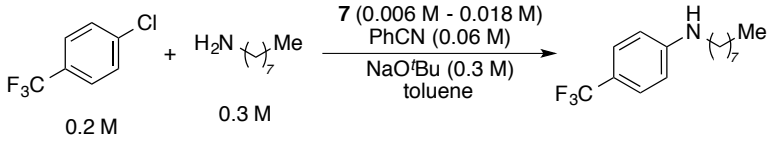
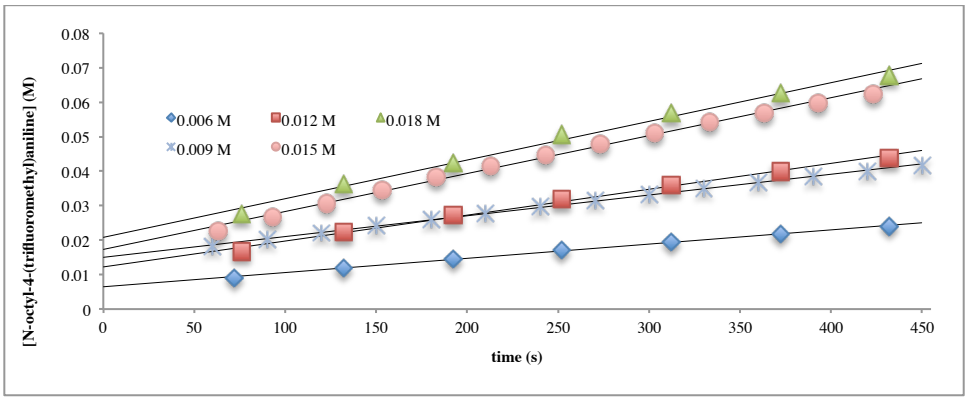


Figure 3.8 Initial Kinetic Profile with Varying Amount of Nickel Catalyst

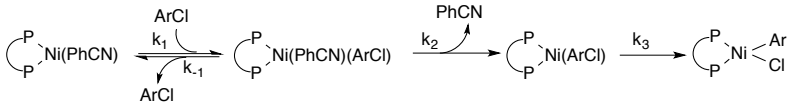


Catalyst loading (M)	Initial Rate (M/s)
6.1×10^{-3}	4.12×10^{-5}
9.1×10^{-3}	6.01×10^{-5}
1.21×10^{-2}	7.50×10^{-5}
1.52×10^{-2}	1.10×10^{-4}
1.82×10^{-2}	1.12×10^{-4}



Associative vs. Dissociative Oxidative Addition of Aryl Chloride:

Associative mechanism and proposed rate equation:



$$rate = \frac{k_1 k_2 [Ni][ArCl]}{k_{-1} + k_2} \qquad \frac{1}{rate} = \left(\frac{k_{-1}}{k_1 k_2 [Ni]}\right)\left(\frac{1}{[ArCl]}\right) + \left(\frac{1}{k_1 [Ni]}\right)\left(\frac{1}{[ArCl]}\right)$$

A plot of 1/rate vs. 1/[ArCl] would exhibit a y-intercept of zero and a slope independent on the concentration of benzonitrile

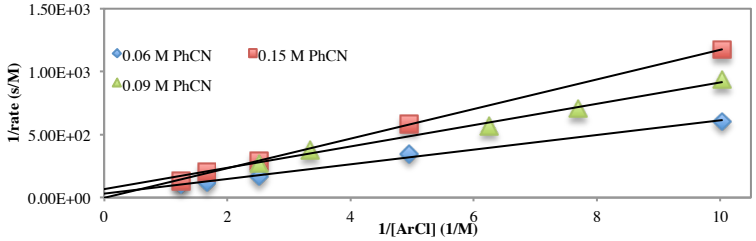
Dissociative mechanism and proposed rate equation:

$$rate = \frac{k_1 k_2 [Ni][ArCl]}{k_{-1}[PhCN] + k_2 [ArCl]} \qquad \frac{1}{rate} = \left(\frac{k_{-1}[PhCN]}{k_1 k_2 [Ni]}\right)\left(\frac{1}{[ArCl]}\right) + \left(\frac{1}{k_1 [Ni]}\right)$$

A plot of 1/rate vs. 1/[ArCl] would exbihit a y-intercept of non-zero value and a slope dependent on the concentration of benzonitrile

The initial rates of the reaction at varying aryl chloride concentrations were measured at multiple concentrations of benzonitrile. The following plot was assembled to fit the two models above:

Figure 3.9 Determination of Mechanism of Oxidative Addition

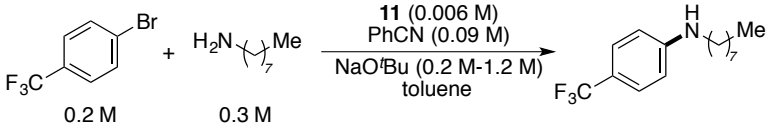


The slopes of the lines of the graph above are clearly dependent on the concentration of benzonitrile. The value of the y-intercept is of increased error and the dependence of the slope upon the concentration of benzonitrile was taken as evidence for a dissociative oxidative addition reaction.

Kinetic Data for the Amination of 4-Bromobenzotrifluoride with Octylamine

The general procedure is identical to that for the aminationof 4-chlorobenzotrifluoride with octylamine. The rate of the reaction increased from aryl chlorides to aryl bromides. Therefore, the acquisition of spectra was performed every 30 seconds for 4.5 mins. The number of points used for the plot of the initial kinetic profile may have been cut due to loss of linearity since at the given concentration of catalyst, the reaction was too fast.

Figure 3.10 Initial Kinetic Profile with Varying Amount of NaO^{t}Bu



NaOtBu (M)	Initial Rate (M/s)
0.200 M	3.11×10^{-4}
0.300 M	2.64×10^{-4}
0.600 M	2.67×10^{-4}
1.20 M	1.96×10^{-4}

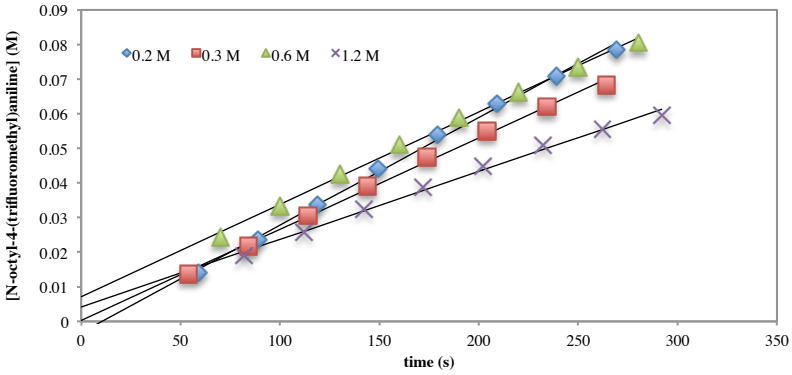
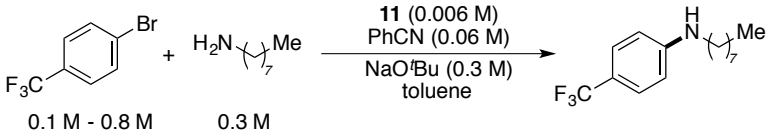


Figure 3.11 Initial Kinetic Profile with Varying Amount of 4-Bromobenzotrifluoride



0.1 M - 0.8 M 0.3 M

ArBr (M)	Initial Rate (M/s)
0.100	1.66×10^{-4}
0.200	2.64×10^{-4}
0.400	6.68×10^{-4}
0.600	8.50×10^{-4}
0.800	1.06×10^{-3}

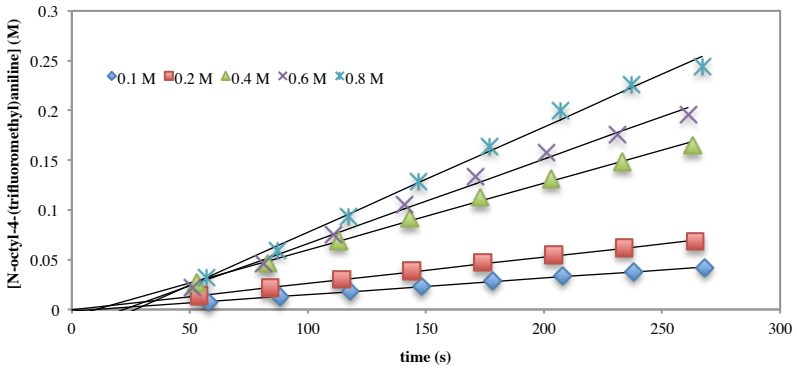
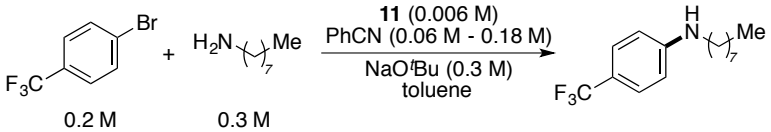


Figure 3.12 Initial Kinetic Profile with Varying Amount of Benzonitrile



0.2 M 0.3 M

PhCN (M)	Initial Rate (M/s)
0.060	2.91×10^{-4}
0.090	3.08×10^{-4}

0.120	3.05 x 10^{-4}
0.150	2.91 x 10^{-4}
0.180	3.03 x 10^{-4}

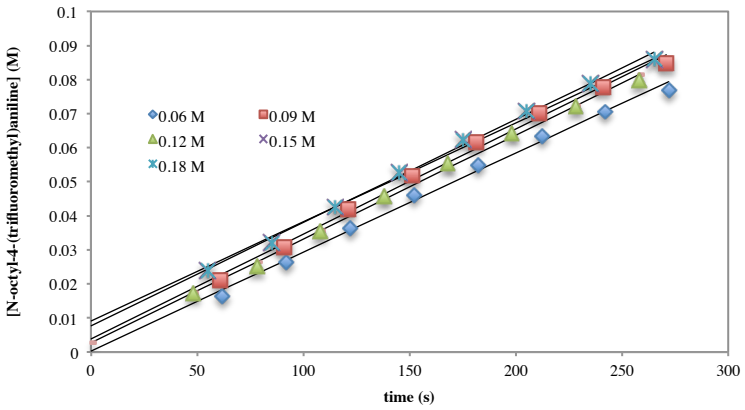
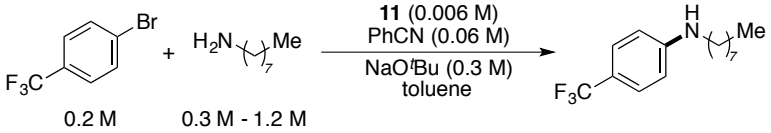


Figure 3.13 Initial Kinetic Profile with Varying Amount of Octylamine



0.2 M 0.3 M - 1.2 M

octylamine (M)	Initial Rate (M/s)
0.300	2.64 x 10^{-4}
0.600	2.82 x 10^{-4}
0.120	3.37 x 10^{-4}

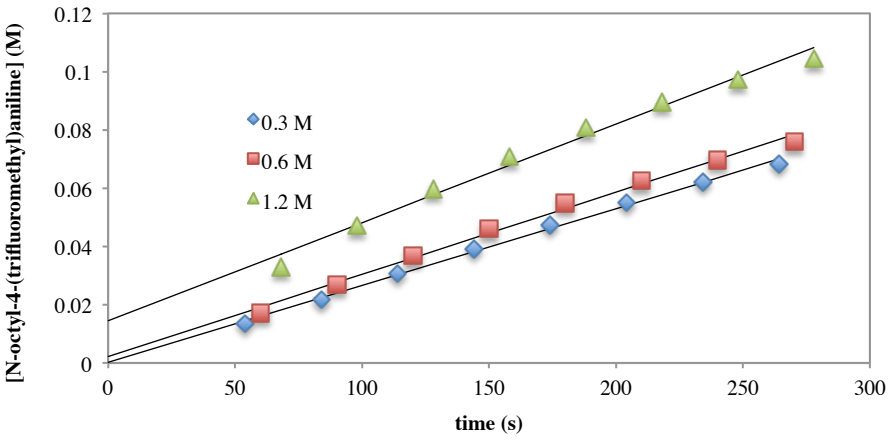
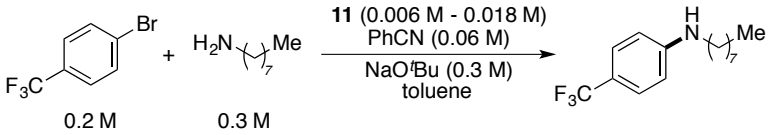
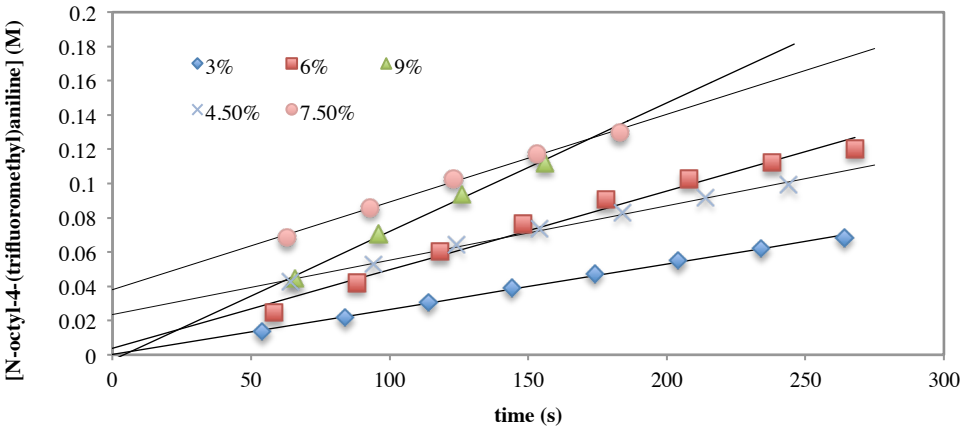


Figure 3.14 Initial Kinetic Profile with Varying Amount of Catalyst Loading



Catalyst loading (M)	Initial Rate (M/s)
6.1×10^{-3}	2.64×10^{-4}
9.1×10^{-3}	3.18×10^{-4}
1.21×10^{-2}	4.59×10^{-4}
1.52×10^{-2}	5.12×10^{-4}
1.82×10^{-2}	7.51×10^{-4}



3.5 References

Reproduced with permission from Journal of the American Chemical Society.
Copyright 2014 American Chemical Society. "Controlling First-Row Catalysts: Amination of Aryl and Heteroaryl Chlorides and Bromides with Primary Aliphatic Amines Catalyzed by a BINAP-Ligated Single-Component Ni(0) Complex"
Ge, S.; Green, R.A.; Hartwig, J.F. *J. Am. Chem. Soc.* **2014**, *136*, 1617.

(1) Ricci, A. *Modern Amination Methods*; Wiley, 2008.
(2) Hartwig, J. F. *Acc. Chem. Res.* **2008**, *41*, 1534.
(3) Surry, D. S.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2008**, *47*, 6338.
(4) Ma, D.; Cai, Q. *Acc. Chem. Res.* **2008**, *41*, 1450.
(5) Hie, L.; Ramgren, S. D.; Mesganaw, T.; Garg, N. K. *Org. Lett.* **2012**, *14*, 4182.
(6) Iglesias, M. J.; Blandez, J. F.; Fructos, M. R.; Prieto, A.; Álvarez, E.; Belderrain, T. R.; Nicasio, M. C. *Organometallics* **2012**, *31*, 6312.
(7) Ilies, L.; Matsubara, T.; Nakamura, E. *Org. Lett.* **2012**, *14*, 5570.
(8) Kuhl, S.; Fort, Y.; Schneider, R. *J. Organomet. Chem.* **2005**, *690*, 6169.

(9) Martin, A. R.; Makida, Y.; Meiries, S.; Slawin, A. M. Z.; Nolan, S. P. *Organometallics* **2013**, DOI: 10.1021/om4004863.
(10) Mesganaw, T.; Garg, N. K. *Org. Process Res. Dev.* **2012**, *17*, 29.
(11) (a) Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 6054. (b) Park, N. H.; Teverovskiy, G.; Buchwald, S. L. *Org. Lett.* **2014**, *16*, 220.
(12) Brenner, E.; Fort, Y. *Tetrahedron Lett.* **1998**, *39*, 5359.
(13) Brenner, E.; Schneider, R.; Fort, Y. *Tetrahedron* **1999**, *55*, 12829.
(14) Brenner, E.; Schneider, R.; Fort, Y. *Tetrahedron Lett.* **2000**, *41*, 2881.
(15) Desmarets, C.; Schneider, R.; Fort, Y. *Tetrahedron Lett.* **2000**, *41*, 2875.
(16) Desmarets, C.; Schneider, R.; Fort, Y. *Tetrahedron Lett.* **2001**, *42*, 247.
(17) Desmarets, C.; Schneider, R.; Fort, Y. *J. Org. Chem.* **2002**, *67*, 3029.
(18)Omar-Amrani, R.; Thomas, A.; Brenner, E.; Schneider, R.; Fort, Y. *Org. Lett.* **2003**, *5*, 2311.
(19) Chen; Yang, L.-M. *J. Org. Chem.* **2007**, *72*, 6324.
(20) Gao, C.-Y.; Yang, L.-M. *J. Org. Chem.* **2008**, *73*, 1624.
(21) (a) Manolikakes, G.; Gavryushin, A.; Knochel, P. *J. Org. Chem.* **2008**, *73*, 1429. (b) Iglesias, M. J.; Prieto, A.; Nicasio, M. C. *Adv. Synth. Catal.* **2010**, *352*, 1949. (c) Fan, X.-H.; Li, G.; Yang, L.-M. *J. Organomet. Chem.* **2011**, *696*, 2482.
(22) Shimasaki, T.; Tobisu, M.; Chatani, N. *Angew. Chem. Int. Ed.* **2010**, *49*, 2929.
(23) Mesganaw, T.; Silberstein, A. L.; Ramgren, S. D.; Nathel, N. F. F.; Hong, X.; Liu, P.; Garg, N. K. *Chem. Sci.* **2011**, *2*, 1766.
(24) Ramgren, S. D.; Silberstein, A. L.; Yang, Y.; Garg, N. K. *Angew. Chem. Int. Ed.* **2011**, *50*, 2171.
(25) Hidai, M.; Kashiwagi, T.; Ikeuchi, T.; Uchida, Y. *J. Organomet. Chem.* **1971**, *30*, 279.
(26) Tsou, T. T.; Kochi, J. K. *J. Am. Chem. Soc.* **1979**, *101*, 6319.
(27) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1995**, *117*, 4708.
(28) Widenhoefer, R. A.; Buchwald, S. L. *Organometallics* **1996**, *15*, 2755.
(29) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1997**, *119*, 8232.
(30) Shekhar, S.; Ryberg, P.; Hartwig, J. F.; Mathew, J. S.; Blackmond, D. G.; Strieter, E. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2006**, *128*, 3584.
(31) Shafir, A.; Lichtor, P. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 3490.
(32) Shen, Q.; Ogata, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 6586.
(33) Liu, Z.-J.; Vors, J.-P.; Gesing, E. R. F.; Bolm, C. *Adv. Synth. Catal.* **2010**, *352*, 3158.
(34) Liu, Z.-J.; Vors, J.-P.; Gesing, E. R. F.; Bolm, C. *Green Chem.* **2011**, *13*, 42.
(35) Maiti, D.; Fors, B. P.; Henderson, J. L.; Nakamura, Y.; Buchwald, S. L. *Chem. Sci.* **2011**, *2*, 57.
(36) Ge, S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 16330.
(37) Hernández, M.; Miralrio, G.; Arévalo, A.; Bernès, S.; García, J. J.; López, C.; Maitlis, P. M.; del Rio, F. *Organometallics* **2001**, *20*, 4061.
(38) Retbøll, M.; Edwards, A. J.; Rae, A. D.; Willis, A. C.; Bennett, M. A.; Wenger, E. *J. Am. Chem. Soc.* **2002**, *124*, 8348.
(39) Zeller, A.; Herdtweck, E.; Strassner, T. *Eur. J. Inorg. Chem.* **2003**, *2003*, 1802.
(40) Liao, X.; Weng, Z.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 195.

(41) Alcazar-Roman, L. M.; Hartwig, J. F.; Rheingold, A. L.; Liable-Sands, L. M.; Guzei, I. A. *J. Am. Chem. Soc.* **2000**, *122*, 4618.
(42) Widenhoefer, R. A.; Buchwald, S. L. *Organometallics* **1996**, *15*, 3534.
(43) Orpen, A. G.; Connelly, N. G. *Organometallics* **1990**, *9*, 1206.
(44) Barrios-Landeros, F.; Carrow, B. P.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 8141.
(45) Bryan, Z. J.; Mcneil, A. J. *Chem. Sci.* **2013**, *4*, 1620.
(46) Zhang, K.; Conda-Sheridan, M.; R. Cooke, S.; Louie, J. *Organometallics* **2011**, *30*, 2546.

CHAPTER 4

Palladium-Catalyzed Amination of Aryl Chlorides and Bromides with Ammonium Salts

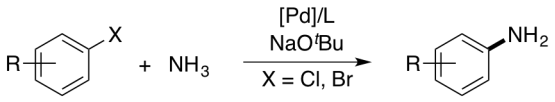
4.1 Introduction

The transition-metal catalyzed amination of aryl electrophiles has become a useful method to construct arylamines. However, the coupling of ammonia is less developed than the coupling of alkylamines, and several properties of ammonia make the coupling of this reagent more challenging than the coupling of alkylamines. Ammonia is a good σ-donor and binds more strongly to metals than do alkyl amines, and this binding can lead to catalyst deactivation. In addition, the moderate basicity and low acidity of ammonia disfavor proton exchanges to or from this reagent. Finally, the aniline formed in the reaction of an aryl halide with ammonia is also a reagent for coupling with aryl halides. Therefore, the product of the coupling of ammonia competes with ammonia as the nucleophile, giving rise to mixtures of mono- and diarylamines.[1-3]

In addition to these chemical properties, the physical properties of ammonia make it a challenging coupling partner to use in palladium-catalyzed chemistry. Because it is a gas at ambient temperature and pressure, reactions performed with anhydrous ammonia often require high-pressure reactors.

Scheme 4.1 Methods for Palladium-Catalyzed Amination of Aryl Halides with Ammonia

***Previous work*:** 200 psi NH_3, 0.5 M NH_3 in 1,4-dioxane, or surrogates followed by hydrolysis



This work: $(NH_4)_2SO_4$ inexpensive, easy to handle solid, commercially available, no specialized equipment

One approach to avoid the use of gaseous ammonia and the formation of diarylamine side products is to conduct reactions with ammonia surrogates, such as benzophenone imine,[4,5] amides,[6,7] bis(trimethylsilyl)amide,[8] or carbamates.[9] However, these ammonia surrogates are much more expensive than ammonia, and these methods require a subsequent hydrolysis or hydrogenolysis step to obtain the aniline.

A few reports have been published on the amination of aryl halides with ammonia that occur with high selectivity for the primary arylamine over the diarylamine side-product. In these reactions, ammonia is either charged into the reaction vessel directly as a gas,[10] or the reaction is conducted with a commercially available solution of 0.5 M ammonia in dioxane.[11-16] Although a convenient alternative to charging reaction vessels with ammonia, the solution is costly and the concentration of the commercial ammonia solution decreases over time. Ammonium hydroxide and ammonium chloride have been used as alternatives to ammonia in copper-catalyzed coupling reactions.[17] However, the scope of electrophiles that undergo these coupling reactions is limited to aryl iodides and activated aryl bromides. The palladium-catalyzed coupling of aryl halides with ammonium hydroxide or ammonium salts has not been reported.

The combination of an inexpensive ammonium salt and base would be an attractive alternative to anhydrous, gaseous ammonia or solutions of ammonia (Scheme 4.1). Because ammonium salts are only marginally soluble in organic solvents, we considered that the concentration of ammonia could be fine-tuned by the choice of the counterion of the ammonium salt and the base.

We envisioned multiple benefits to a protocol for the amination of aryl halides involving ammonium salts. A lower concentration of ammonia could reduce catalyst poisoning, leading to lower required loadings of the catalyst. In addition, the low concentration of ammonia at any given time would minimize the safety hazard of heating a sealed vessel containing the reaction. Considering the many benefits of ammonium salts as precursors to ammonia, and to volatile amines, in palladium-catalyzed amination reactions, we sought to develop conditions to conduct palladium-catalyzed amination reactions with ammonium salts.

We report the coupling of ammonium sulfate in the presence of a base to form monoarylamines with selectivities equal or greater than those from reactions of anhydrous, gaseous ammonia or solutions of ammonia. Moreover, we show that this approach can be extended to the coupling of methyl and ethylamine, which are gases at room temperature and have rarely been used in palladium-catalyzed cross coupling.

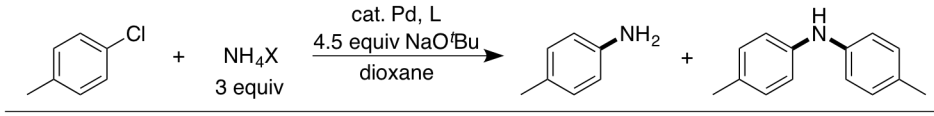
4.2 Results and Discussion

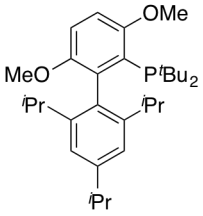
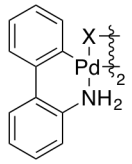
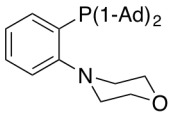
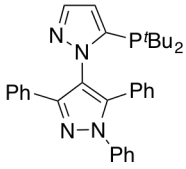
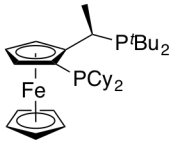
To develop the coupling of ammonium salts, we investigated the reaction of *p*-chlorotoluene with ammonium salts in the presence of several catalysts previously reported for the arylation of ammonia. Ammonia is not a good reductant of Pd(II) precursors such as $Pd(OAc)_2$ and $PdCl_2$. Therefore, palladium precursors for the coupling of ammonia are typically limited to $Pd(dba)_2$ or $Pd(P(o\text{-tol})_3)_2$, which are air-stable Pd(0) precursors,[18] palladacycles such as **Ia-b**, or allyl complexes, such as $[Pd(cinnamyl)Cl]_2$, or $[Pd(allyl)Cl]_2$, that can be activated under the reaction conditions. For each catalyst, various ammonium salts were examined. The yields of $ArNH_2$ and selectivity ($ArNH_2$:Ar_2NH) with three ammonium salts are shown in comparison to ammonia in dioxane in Table 4.1. The protocols were adapted from those previously reported.[11,13,14,16] The performance of each salt differed with each catalyst system. Ammonium acetate and ammonium sulfate were suitable salts with each catalyst system, where high yields and selectivities were obtained in reactions catalyzed by Pd and tBuBrettPhos,[13] MorDalPhos,[14] and Josiphos ligand CyPF-^{t}Bu.[11] Reactions catalyzed by Pd and BippyPhos,[16,19] either did not form any desired product or formed *p*-toluidine in low yields. Reactions with several ammonium salts, catalyzed by $Pd(P(o\text{-tol})_3)_2$ and the Josiphos ligand containing one di-cyclohexylphosphino and one di-*tert*-butylphosphino group, occurred in high yields and required the lowest catalyst loadings of the systems we studied for this transformation.[11]

These yields and selectivities demonstrate the benefit of maintaining a low effective concentration of ammonia.[20] The concentration of ammonia appears to be affected by the composition of the ammonium salt. Ammonium sulfate is crystalline.

Reactions conducted with finely ground ammonium sulfate occurred with lower selectivity (12:1) than those conducted with the salt used as received (20:1).

Table 4.1 Evaluation of Ammonium Salts and Palladium Catalysts for the Amination of Aryl Chlorides

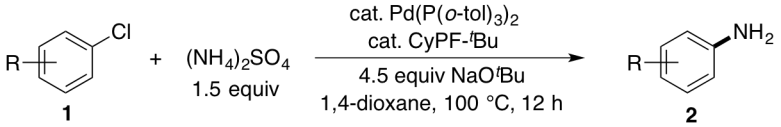


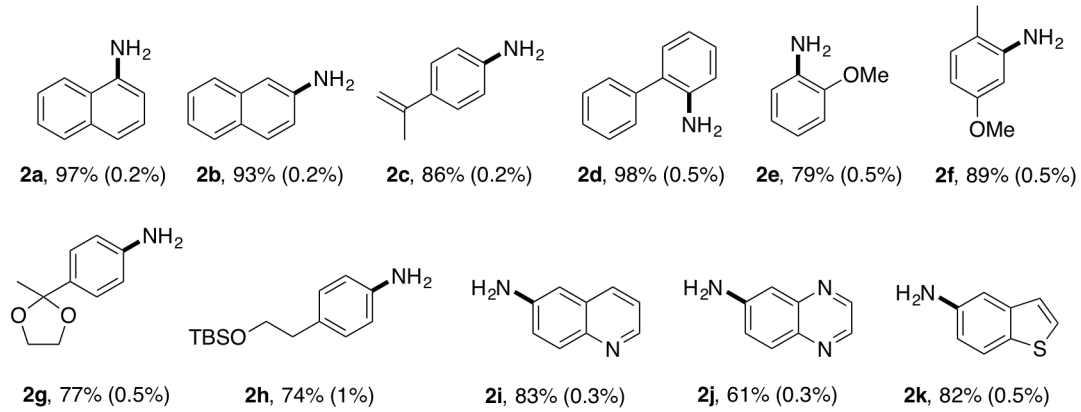
	2 mol % $Pd(dba)_2$ 5 mol % ^{t}BuBrettPhos	NH_3: 89% (22:1) NH_4Cl: 0% NH_4OAc: 81% (40:1) $(NH_4)_2SO_4$: 47% (12:1)
	1 mol % **Ia** 5 mol % ^{t}BuBrettPhos	NH_3: 85% (40:1) NH_4Cl: 0% NH_4OAc: 29% (30:1) $(NH_4)_2SO_4$: 11% (11:1)
 **Ia** X = Cl **Ib** X = OMs	1 mol % **Ib** 5 mol % ^{t}BuBrettPhos	NH_3: 81% (40:1) NH_4Cl: 0% NH_4OAc: 33% (33:1) $(NH_4)_2SO_4$: 15% (15:1)
	0.2 mol % $[Pd(cinnamyl)Cl)]_2$ 0.8 mol % MorDalPhos	NH_3: 87% (10:1) NH_4Cl: 77% (8:1) NH_4OAc: 94% (16:1) $(NH_4)_2SO_4$: 82% (10:1)
	1 mol % $Pd(dba)_2$ 1 mol % BippyPhos	NH_3: 68% (9:1) NH_4Cl: 0% NH_4OAc: 14% (2:1) $(NH_4)_2SO_4$: 33% (3:2)
	0.3 mol % $Pd(P(o\text{-tol})_3)_2$ 0.3 mol % CyPF-^{t}Bu	NH_3: 87% (12:1) NH_4Cl: 94% (16:1) NH_4OAc: 95% (19:1) $(NH_4)_2SO_4$: 95% (19:1)
		Finely ground $(NH_4)_2SO_4$: 67% (12:1)

Yields ($ArNH_2$) and selectivities ($ArNH_2$:Ar_2NH) determined by GC analysis using dodecane as an internal standard.

Results from the reaction of ammonium sulfate with a series of aryl chlorides catalyzed by $Pd(P(o\text{-tol})_3)_2$ and the Josiphos ligand are shown in Table 4.2. Primary arylamines containing *ortho* substituents of varying size, including smaller groups, such as methyl (**2f**) and methoxy (**2e**) groups, and larger groups, such as a phenyl ring (**2d**), were isolated in high yields (79-98%). Styrenyl functionality (**2c**), ketals[21] (**2g**), and silyl-protected alcohols (**2h**) were tolerated by the reaction. Benzo-fused heterocycles containing nitrogen (**2i-j**) and sulfur (**2k**) reacted with the ammonium salt in good yields. The scope of the reaction under these conditions is similar to that of the reaction with the solution of ammonia.[10,11]

Table 4.2 Scope of Palladium-Catalyzed Amination of Aryl Chlorides with Ammonium Sulfate[a]





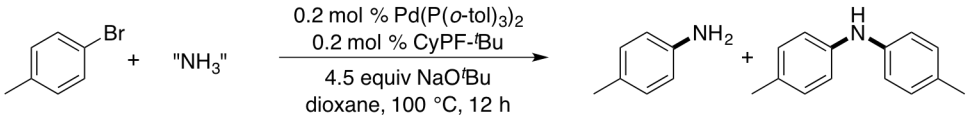
2a, 97% (0.2%) **2b**, 93% (0.2%) **2c**, 86% (0.2%) **2d**, 98% (0.5%) **2e**, 79% (0.5%) **2f**, 89% (0.5%)

2g, 77% (0.5%) **2h**, 74% (1%) **2i**, 83% (0.3%) **2j**, 61% (0.3%) **2k**, 82% (0.5%)

[a]Conditions: ArCl (0.600 mmol), ammonium sulfate (0.900 mmol), Pd(P(*o*-tol)$_3$)$_2$ (1.2-6.0 μmol, 0.2-1.0 mol %), CyPF-*t*Bu (1.2-6.0 μmol, 0.2-1.0 mol %), NaO*t*Bu (2.70 mmol), 1,4-dioxane (6 mL); 100 °C, 12 h. Isolated yields (catalyst loading in parentheses).

The coupling of ammonia with aryl bromides occurs faster and with higher selectivity for the formation of the primary arylamine than does the coupling aryl chlorides.[11] However, we observed that reactions of aryl bromides with ammonium chloride, sulfate, or acetate occurred with lower selectivity (2:1) for the primary arylamine versus the diarylamine than did the reactions of aryl chlorides (Scheme 4.2)

Scheme 4.2 Pd-Catalyzed Amination of 4-Bromotoluene with Ammonium Salts



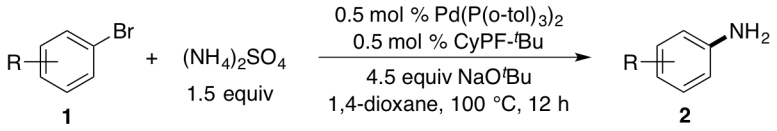
NH_3: 80% (19:1)
NH_4Cl: 60% (< 1:20)
NH_4OAc: 80% (1.7:1)
$(NH_4)_2SO_4$: 63% (1.6:1)

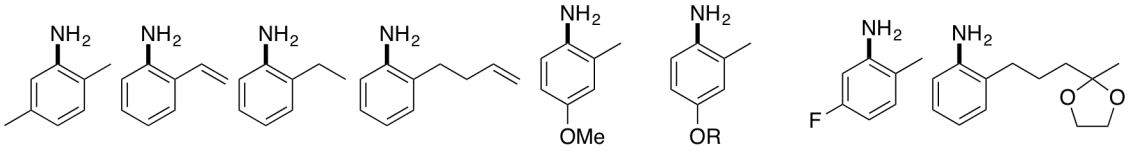
Ortho-substituted aryl bromides reacted to provide the primary arylamine in high yields without competing diarylation, presumably due to the large steric difference between the ammonia reagent and an *ortho*-substituted aniline (Table 4.3).

To understand the effect of the inorganic salts formed in the reaction, we allowed *p*-chlorotoluene to react with ammonium sulfate in the presence of the palladium catalyst with 1 equiv of added NaBr. A lower selectivity (9:1) was observed for the reaction with the added bromide salt than was observed for the analogous reaction conducted without the bromide salt (20:1) (Scheme 4.3).

To understand the difference in selectivity between the reactions of aryl chlorides and aryl bromides lacking an *ortho* substituent and to understand the impact of using the ammonium salts on the rates of different steps in the catalytic cycle, we studied the

Table 4.3 Scope of Palladium-Catalyzed Amination of *Ortho*-Substituted Aryl Bromides with Ammonium Sulfate[a]



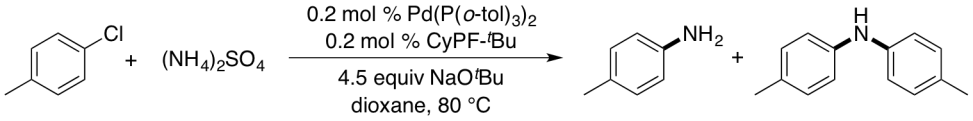


2l, 90% **2m**, 60% **2n**, 76% **2o**, 75% **2p**, 80% **2q**, R = TBS 64% **2r**, R = Bn 85% **2s**, 76% **2t**, 85%

[a] Conditions: ArBr (0.600 mmol), $(NH_4)_2SO_4$ (0.900 mmol), $Pd(P(o\text{-tol})_3)_2$ (3.0 μmol, 0.5 mol %), CyPF-^{t}Bu (3.0 μmol, 0.5 mol %), NaO^{t}Bu (2.70 mmol), 1,4-dioxane (6 mL); 100 °C, 12 h.

mechanism of these amination reactions. The mechanism of the amination of aryl halides with ammonia catalyzed by palladium-Josiphos complexes has been studied.[22] Spectroscopic studies showed that $L_2Pd(Ar)(NH_2)$ is the resting state of the catalyst, and kinetic experiments indicated that reductive elimination is the turnover-limiting step.[22]

Scheme 4.3 Spiking Experiment to Assess the Influence of the Anion on the Selectivity of the Amination of 4-Clorotoluene with Ammonium Sulfate



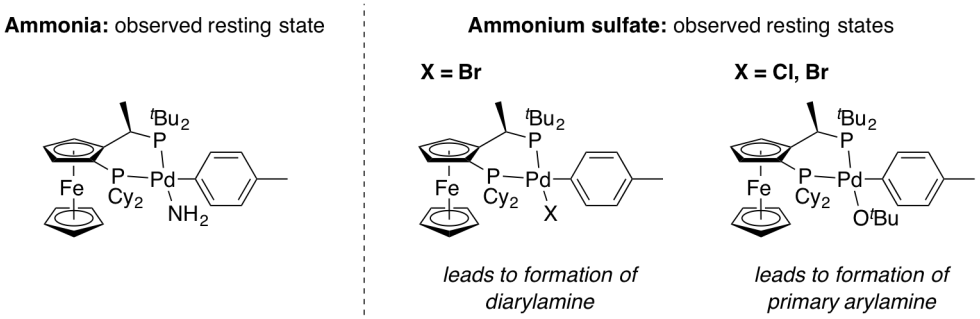
95% (19:1)

+ 1 equiv NaBr 59% (9:1)

Because the selectivity varies with the identity of the aryl halide, we considered that the catalyst resting state for the reactions of ammonium salts is not the arylpalladium-amido complex. We monitored the reaction of *p*-chlorotoluene with ammonium sulfate at 80 °C catalyzed by 10 mol % of (CyPF-^{t}Bu)Pd(P(o-tol)$_3$), formed *in situ*, in dioxane. One ligated palladium species was observed by ^{31}P NMR spectroscopy. The chemical shifts and coupling constants of the new complex were different from the reported values for the CyPF-^{t}Bu-ligated arylpalladium chloride[23] or amido[22] complexes. Instead, they were consistent with reported values for the CyPF-^{t}Bu-ligated arylpalladium *tert*-butoxide complex.[23] In contrast, a combination of the arylpalladium *tert*-butoxide complex and the arylpalladium-bromide complex in an 3:4 ratio were observed in solution during the reaction of *p*-bromotoluene with ammonium sulfate (Scheme 4.4).

Stoichiometric reactions with isolated complexes suggest that $L_2Pd(Ar)(O^tBu)$ reacts selectively with ammonia to form the primary arylamine, while $L_2Pd(Ar)(Br)$ selectively reacts with aniline to form diarylamine.[20,24]

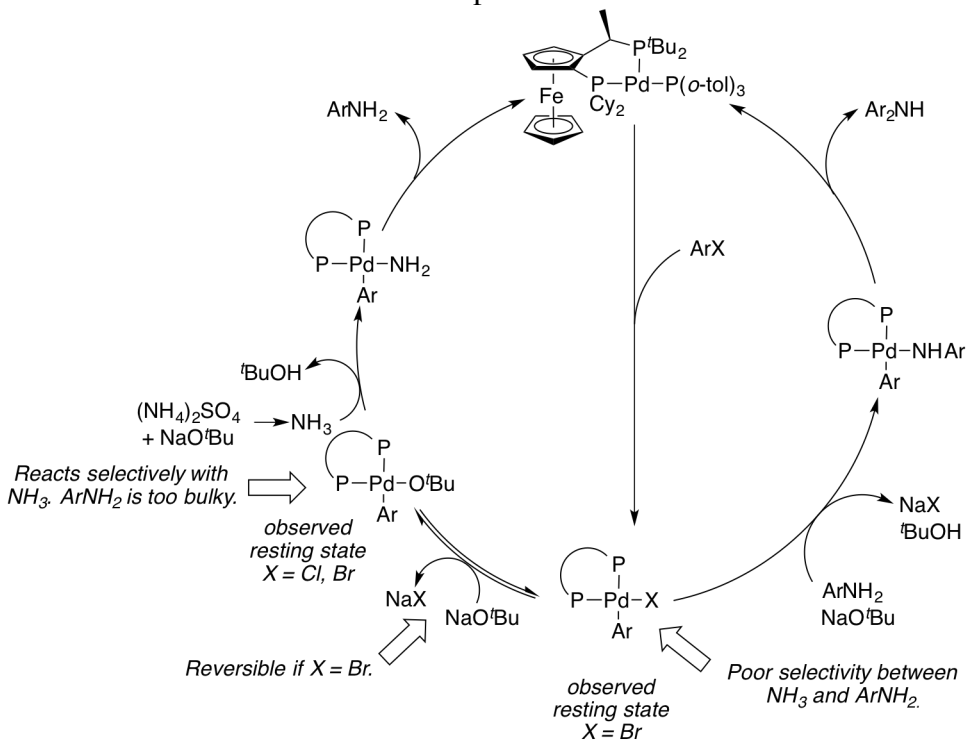
Scheme 4.4 Comparison of the Resting States for Reactions with Ammonia and Ammonium Sulfate



[a] Conditions: ArBr (0.600 mmol), $(NH_4)_2SO_4$ (0.900 mmol), $Pd(P(o\text{-tol})_3)_2$ (3.0 μmol, 0.5 mol %), CyPF-^{t}Bu (3.0 μmol, 0.5 mol %), NaO^{t}Bu (2.70 mmol), 1,4-dioxane (6 mL); 100 °C, 12 h.

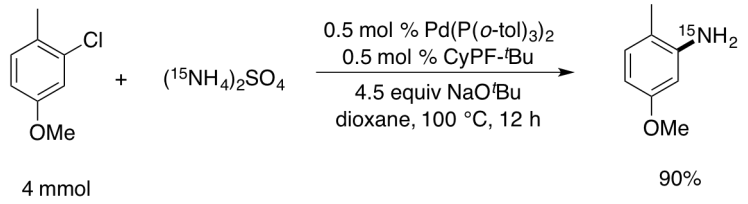
We propose that $L_2Pd(Ar)(X)$ can reacts with NaO^{t}Bu to form $L_2Pd(Ar)(O^tBu)$, which is too sterically bulky to react with aniline and therefore selectively reacts with ammonia to form $L_2Pd(Ar)(NH_2)$ that undergoes reductive elimination to form product. The reaction between $L_2Pd(Ar)(X)$ and NaO^{t}Bu is reversible when X = Br, which is consistent with Pd-Br bonds being stronger than Pd-Cl bonds and the poorer solubility and stronger ionic bond of NaCl compared to NaBr. The $L_2Pd(Ar)(Br)$ complex therefore is not bulky enough to selectively react with ammonia, in lieu of aniline, and therefore reacts with aniline, since the concentration of ammonia in solution is low. The proposed catalytic cycle is shown in Scheme 4.5.

Scheme 4.5 Proposed Mechanism



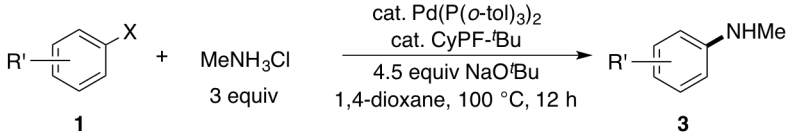
This coupling process provides a convenient method to incorporate ^{15}N into aromatic compounds. The ^{15}N label in anilines is typically installed by nitration, followed by reduction. Such a process is expensive to conduct because it requires solvent quantities of ^{15}N-labeled nitric acid. Ammonium salts are a less expensive and more conveniently handled source of ^{15}N than nitric acid or ^{15}N-labeled ammonia gas, and our coupling of ammonium salts requires only 3 equiv of solid ^{15}N per mole of substrate. To illustrate this potential application of the coupling of ammonium salts, we prepared ^{15}N-labeled 5-methoxy-2-methylaniline on 4 mmol scale. This product formed in high yield (Scheme 4.6), and the conversion of such products to a range of quinolines[25,26] and indoles[26-28] is well established.

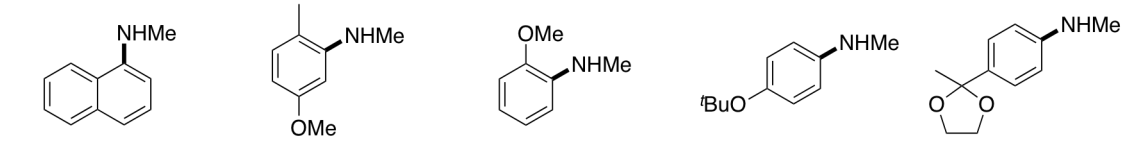
Scheme 4.6 Application to the Synthesis of ^{15}N-labelled aniline



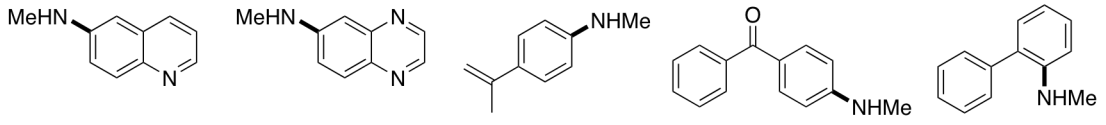
The coupling of aryl halides with ammonium salts was expanded to include the coupling of aryl halides with the ammonium salts of methylamine (bp=-6.3 °C) and ethylamine (bp=17 °C) to form the corresponding *N*-methyl and *N*-ethylanilines. There are few reports of the coupling of aryl halides with methylamine, and the source of amine is a commercially available 2.0 M solution in THF.[16,29-34] The reaction of aryl chlorides and bromides with methylamine and ethylamine hydrochloride yielded the corresponding

Table 4.4 Palladium-Catalyzed Amination of Aryl Chlorides and Bromides with Methylamine Hydrochloride





3a, X = Cl 97% (0.2%) X = Br 90% (0.2%) **3b**, X = Cl 99% (0.5%) **3c**, X = Cl 79% (0.5%) X = Br 82% (0.2%) **3d**, X = Cl 86% (0.5%) **3e**, X = Cl 91% (0.5%) X = Br 75% (0.5%)



3f, X = Cl 96% (0.3%) X = Br 91% (0.2%) **3g**, X = Cl 94% (0.3%) **3h**, X = Cl 97% (0.2%) **3i**, X = Cl 77% (0.5%) X = Br 78% (0.2%) **3j**, X = Cl 99% (0.5%) X = Br 99% (0.2%)

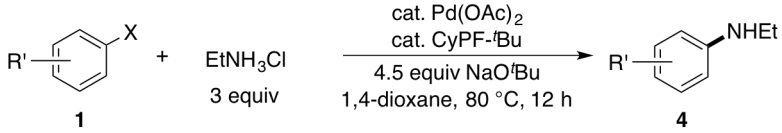
[a] Conditions: ArX (0.600 mmol), $MeNH_3Cl$ (1.80 mmol), [Pd] (1.2-3.0 μmol, 0.2-0.5 mol %), CyPF-^{t}Bu (1.2-3.0 μmol, 0.2-0.5 mol %), NaO^{t}Bu (2.70 mmol), 1,4-dioxane (6 mL); 12 h.

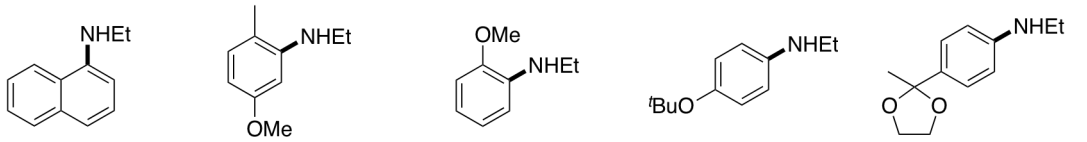
N-alkylaniline products in moderate to high yields (59-99%), as shown in Schemes 4.4 and 4.5.

Because the product of the reaction of methylamine and ethylamine are secondary amines, and the Pd-Josiphos system is selective for reaction of primary amines over secondary amines,[35] diarylamines are not observed in these reactions. *N*-alkylanilines are less volatile than the corresponding primary arylamines. Therefore, isolated yields from reactions with methyl and ethylamine hydrochloride are slightly higher than those for reactions with ammonium sulfate.

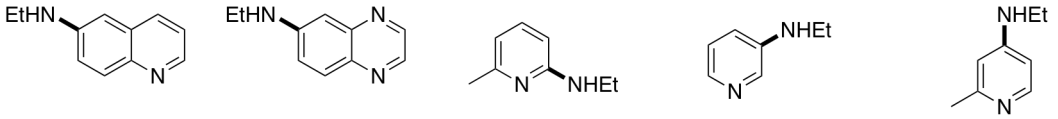
Reactions of ethylamine hydrochloride with aryl halides occur under conditions similar to those previously reported for the coupling of primary alkylamines. In this case, $Pd(OAc)_2$ is a suitable precursor, presumably because of the more facile reduction of the Pd(II) by ethylamine than by methylamine or ammonia.[35] Similarly, aryl halides, including bromopyridines (**4l-m**), coupled with ethylamine hydrochloride to form the corresponding *N*-ethylanilines (Scheme 4.5).

Table 4.5 Palladium-Catalyzed Amination of Aryl Chlorides and Bromides with Ethylamine Hydrochloride





4a, X = Cl 95% (0.2%) X = Br 94% (0.05%) **4b**, X = Cl 77% (0.2%) **4c**, X = Cl 88% (0.2%) X = Br 82% (0.05%) **4d**, X = Cl 98% (0.2%) **4e**, X = Cl 92% (0.5%) X = Br 97% (0.05%)



4f, X = Cl 98% (0.2%) X = Br 94% (0.05%) **4g**, X = Cl 95% (0.2%) **4l**, X = Br 59% (0.2%) **4m**, X = Br 90% (0.2%) **4n**, X = Br 95% (0.2%)

[a] Conditions: ArX (0.600 mmol), $MeNH_3Cl$ (1.80 mmol), [Pd] (0.30-3.0 μmol, 0.05-0.5 mol %), CyPF-^{t}Bu (0.30-3.0 μmol, 0.05-0.5 mol %), NaO^{t}Bu (2.70 mmol), 1,4-dioxane (6 mL); 12 h.

4.3 Conclusion

In summary, we have shown that ammonium salts are practical alternatives to gaseous amines for the aminations of aryl halides and can occur with distinct selectivities, distinct effects of concentration on selectivities, and via distinct resting states of the catalyst. We observed a high selectivity for the formation of primary arylamine over diarylamine in reactions of aryl chlorides with ammonium sulfate, but we observed a

mixture of mono and diarylamine in the reactions of aryl bromides with ammonium sulfate. We attribute the difference in selectivity to the difference in resting states in the amination reaction of ammonium sulfate with aryl chlorides and bromides. $L_2Pd(Ar)(O^tBu)$ was observed as the major ligated palladium species during the reaction of aryl chlorides with ammonium sulfate. However, both $L_2Pd(Ar)(O^tBu)$ and $L_2Pd(Ar)(Br)$ were observed in reactions of aryl bromides with ammonium sulfate. The $L_2Pd(Ar)(Br)$ reacts selectively with primary arylamines to afford the diarylamine side-product. This method was extended to include other gaseous amines, such as methylamine and ethylamine, to afford *N*-methyl- and *N*-ethyl-anilines.

4.4 Experimental

General Remarks.

All the manipulations were performed in a nitrogen-filled glovebox, unless mentioned otherwise. THF, pentane, and Et_2O were purified by passing the degassed solvents (N_2) through a column of activated alumina (solvent purification system purchased from Innovative Technologies, Newburyport, MA). 1,4-Dioxane (99%, extra dry) was purchased from Acros and used without further purification. Reactions were conducted in 20 mL vials fitted with a Teflon-lined screw cap under an atmosphere of nitrogen unless otherwise noted.

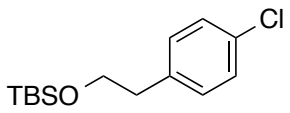
$Pd(P(o\text{-tol})_3)_2$ was prepare according to literature procedure,[36-7] and $PdCl_2$ was received as a gift from Johnson Matthey. The Josiphos ligand CyPF-^{t}Bu was either purchased or prepared according to literature procedure.[38-40] The following substrates were prepared according to literature procedures: 1g[41] (Table 2, X = Cl: CAS: 36881-02-04, X = Br: CAS: 4360-68-3), 1h[41] (Table 2), 1q[41] (Table 3, CAS: 169315-83-7), 1r[41] (CAS: 17671-75-9, Table 3), 1o[42] (Table 3, CAS: 71813-50-8), 1t[41,43] (Table 3, ketone CAS: 590400-92-3). Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification.

^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectra were recorded using a Varian 400 MHz, 500 MHz, or 600 MHz NMR spectrometer. ^1H NMR spectra were referenced to resonances of the residual protons in the deuterated solvents; and $^{31}P\{^1H\}$ NMR shifts were reported in parts per million relative to an 85% H_3PO_4 external standard. NMR spectra were processed with iNMR(4.2.0, Mestrelab). Coupling constants are reported in hertz.

Silica gel chromatography was performed using 230-400 Mesh (Grade 60) silica gel and visualized using UV light. HR-MS analyses were performed at QB3/Chemistry Mass Spectrometry Facility in the University of California, Berkeley.

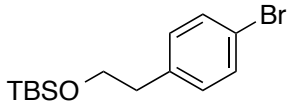
Starting Materials

(4-chlorophenethoxy)(*tert*-butyl)dimethylsilane



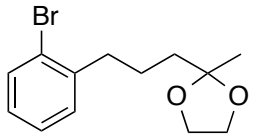
^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.19-7.16 (m, 2H), 7.08-7.05 (m, 2H), 3.70 (t, *J* = 6.8 Hz, 2H), 2.71 (t, *J* = 6.8 Hz, 2H), 0.79 (d, *J* = 5.8 Hz, 9H), -0.10 (d, *J* = 6.2 Hz, 6H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 137.92, 131.98, 130.66, 128.39, 64.31, 39.00, 18.45, -5.29.

(4-bromophenethoxy)(*tert*-butyl)dimethylsilane



^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.41-7.38 (m, 2H), 7.10-7.07 (m, 2H), 3.78 (t, *J* = 6.8 Hz, 2H), 2.77 (t, *J* = 6.8 Hz, 2H), 0.87 (t, *J* = 4.1 Hz, 9H), -0.02 (t, *J* = 4.3 Hz, 6H). **^{13}C-NMR** (126 MHz, $CDCl_3$): δ 138.44, 131.34, 131.07, 120.03, 64.22, 39.06, 26.04, 18.45, -5.29.

2-(3-(2-bromophenyl)propyl)-2-methyl-1,3-dioxolane



^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 7.8 Hz, 1H), 7.23-7.21 (m, 2H), 7.04 (dt, *J* = 8.1, 4.5 Hz, 1H), 3.97-3.89 (m, 4H), 2.75 (tt, *J* = 4.9, 2.5 Hz, 2H), 1.75-1.72 (m, 4H), 1.32 (s, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 141.66, 132.78, 130.33, 127.50, 127.37, 124.51, 109.99, 64.70, 38.77, 36.18, 24.34, 23.91.

General Protocol for Amination Reaction with Ammonium Sulfate

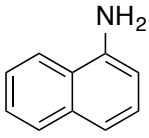
In a nitrogen-filled glovebox, $Pd(P(o\text{-tol})_3)_2$ and CyPF-P^{t}Bu (1:1 ratio) were dissolved in dioxane and mixed for 5 min. A 20 mL scintillation vial was charged with aryl halide (0.60 mmol, 1 equiv), ammonium sulfate (0.90 mmol, 1.5 equiv), and sodium *tert*-butoxide (2.7 mmol, 4.5 equiv). To this vial was added 6 mL of anhydrous dioxane and the appropriate amount of catalyst from the stock solution. The reaction vial was sealed with a Teflon-lined screw cap and removed from the glovebox. The reaction was stirred at the desired temperature for 12 h. The reaction mixture was diluted with EtOAc and filtered through a pad of Celite. The filtrate was concentrated *in vacuo*, and the crude product was purified by flash column chromatography.

General Protocol for Amination Reaction with $MeNH_3Cl$ or $EtNH_3Cl$

In a nitrogen-filled glovebox, $Pd(P(o\text{-tol})_3)_2$ or $Pd(OAc)_2$ and CyPF-P^{t}Bu (1:1 ratio) were dissolved in dioxane and mixed for 5 min. A 20 mL scintillation vial was charged with aryl halide (0.60 mmol, 1 equiv), $MeNH_3Cl$ or $EtNH_3Cl$ (1.80 mmol, 3 equiv), and sodium *tert*-butoxide (2.7 mmol, 4.5 equiv). To this vial was added 6 mL of anhydrous dioxane and the appropriate amount of catalyst from the stock solution. The reaction vial was sealed with a Teflon-lined screw cap and removed from the glovebox. The reaction was stirred at the desired temperature for 12 h. The reaction mixture was diluted with EtOAc and filtered through a pad of Celite. The filtrate was concentrated *in vacuo*, and the crude product was purified by flash column chromatography.

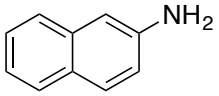
Organic Compound Characterization

Naphthalen-1-amine (**2a**) (CAS: 134-32-7)



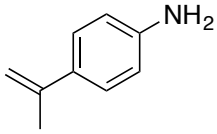
The reaction to form this product was conducted with 0.2 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.2 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (5:1 Hexanes:EtOAc). The title compound was isolated as an off-white solid in 97% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.85-7.82 (m, 2H), 7.51-7.45 (m, 2H), 7.37-7.30 (m, 2H), 6.80 (dd, *J* = 6.9, 1.6 Hz, 1H), 4.13 (s, 2H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 142.14, 134.47, 128.62, 126.41, 125.91, 124.92, 123.73, 120.87, 119.04, 109.75.

Naphthalen-2-amine (**2b**) (CAS: 91-59-8)



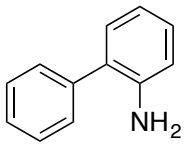
The reaction to form this product was conducted with 0.2 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.2 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (4:1 Hexanes:EtOAc). The title compound was isolated as a peach-orange solid in 93% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.2 Hz, 1H), 7.67 (d, *J* = 8.6 Hz, 1H), 7.60 (d, *J* = 8.2 Hz, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 7.24 (m, 1H), 6.99 (s, 1H), 6.96 (d, *J* = 8.7 Hz, 1H), 3.84 (s, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 144.08, 134.89, 129.19, 127.95, 127.70, 126.33, 125.78, 122.45, 118.21, 108.57.

4-(Prop-1-en-2-yl)aniline (**2c**) (CAS: 1962-08-9)



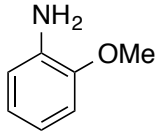
The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (3:1 Hexanes:EtOAc). The title compound was isolated as an orange-red oil in 86% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.32 (d, *J* = 8.5 Hz, 2H), 6.66 (d, *J* = 8.3 Hz, 2H), 5.27 (s, 1H), 4.94 (s, 1H), 3.69 (s, 2H), 2.12 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 145.84, 142.71, 131.54, 126.47, 114.73, 109.35, 21.85.

[1,1'-Biphenyl]-2-amine (**2d**) (CAS: 90-41-5)



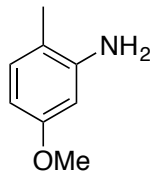
The reaction to form this product was conducted with 0.5 mol % Pd(P(o-tol)3)2 and 0.5 mol % CyPF-PtBu for 12 h. The crude product was purified by flash column chromatography (5:1 Hexanes:EtOAc). The title compound was isolated as a dark yellow solid in 98% yield. 1H-NMR (600 MHz, CDCl3): δ 7.48 (m, 4H), 7.39-7.37 (m, 1H), 7.18 (m, 2H), 6.87 (t, J = 7.3 Hz, 1H), 6.80 (d, J = 7.9 Hz, 1H), 3.78 (s, 2H). 13C-NMR (151 MHz, CDCl3): δ 143.37, 139.45, 130.36, 129.01, 128.72, 128.40, 127.55, 127.07, 118.57, 115.53.

2-Methoxyaniline (**2e**) (CAS: 90-04-0)



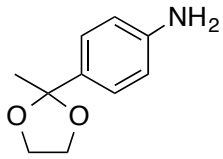
The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (5:1 Hexanes:EtOAc). The title compound was isolated as a yellow oil in 79% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 6.82-6.80 (m, 2H), 6.76-6.73 (m, 2H), 3.86 (s, 3H), 3.80 (s, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 147.32, 136.15, 121.07, 118.46, 115.02, 110.45, 55.42.

5-Methoxy-2-methylaniline (**2f**) (CAS: 50868-72-9)



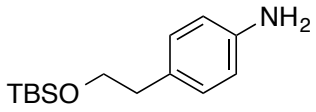
The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (4:1 Hexanes:EtOAc). The title compound was isolated as a beige solid in 89% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 6.95 (d, *J* = 8.1 Hz, 1H), 6.29 (m, 2H), 3.76 (s, 3H), 3.63 (s, 2H), 2.11 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 159.00, 145.44, 130.94, 114.80, 103.65, 100.99, 55.18, 16.49.

4-(2-Methyl-1,3-dioxolan-2-yl)aniline (**2g**) (CAS: 19073-16-6)



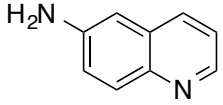
The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 14 h. The crude product was purified by flash column chromatography (1:1 Hexanes:EtOAc). The title compound was isolated as a colorless solid in 77% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.26 (d, *J* = 8.5 Hz, 2H), 6.65 (d, *J* = 8.5 Hz, 2H), 4.02-4.00 (m, 2H), 3.79-3.77 (m, 2H), 3.67 (s, 2H), 1.63 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 27.57, 64.31, 108.91, 114.59, 126.37, 133.27, 145.99.

4-(2-((*tert*-Butyldimethylsilyl)oxy)ethyl)aniline (**2h**) (CAS: 173901-21-8)



The reaction to form this product was conducted with 1.0 mol % Pd(P(*o*-tol)$_3$)$_2$ and 1.0 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (5:1 Hexanes:EtOAc). The title compound was isolated as a yellow oil in 74% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.04 (d, *J* = 8.2 Hz, 2H), 6.67 (d, *J* = 8.3 Hz, 2H), 3.79 (t, *J* = 7.3 Hz, 2H), 3.61 (s, 2H), 2.77 (t, *J* = 7.3 Hz, 2H), 0.94 (s, 9H), 0.05 (s, 6H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 144.57, 129.96, 129.12, 115.18, 65.04, 38.85, 26.03, 18.43, -5.29.

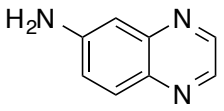
Quinolin-6-amine (**2i**) (CAS: 580-15-4)



The reaction to form this product was conducted with 0.3 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.3 mol % CyPF-P^{t}Bu for 10 h. The crude product was purified by flash column chromatography (1:1 Hexanes:EtOAc, Hexanes contain 10% NEt_3). The title compound was isolated as beige

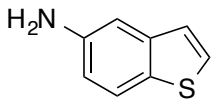
solid in 83% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.65 (dd, *J* = 4.2, 1.5 Hz, 1H), 7.90 (t, *J* = 7.6 Hz, 2H), 7.27 (m, 1H), 7.16 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.90 (d, *J* = 2.5 Hz, 1H), 3.96 (s, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 146.86, 144.55, 143.49, 133.73, 130.59, 129.75, 121.52, 121.38, 107.41.

Quinoxalin-6-amine (**2j**) (CAS: 6298-37-9)



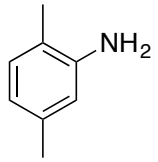
The reaction to form this product was conducted with 0.3 mol % $Pd(P(o\text{-tol})_3)_2$ and 0.3 mol % CyPF-P^{t}Bu for 10 h. The crude product was purified by flash column chromatography (100% EtOAc, followed by 20:1 EtOAc:MeOH). The title compound was isolated as a bright yellow solid in 61% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.66 (d, *J* = 1.8 Hz, 1H), 8.55 (d, *J* = 1.8 Hz, 1H), 7.88 (d, *J* = 8.9 Hz, 1H), 7.19 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.14 (d, *J* = 2.5 Hz, 1H), 4.23-4.19 (s, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 148.03, 145.08, 144.90, 141.05, 138.07, 130.47, 122.11, 108.02.

Benzo[*b*]thiophen-5-amine (**2k**) (CAS: 20532-28-9)



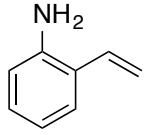
The reaction to form this product was conducted with 0.5 mol % $Pd(P(o\text{-tol})_3)_2$ and 0.5 mol % CyPF-P^{t}Bu for 14 h. The crude product was purified by flash column chromatography (3:1, followed by 1:1 Hexanes:EtOAc, Hexanes contain 10% NEt_3). The title compound was isolated as a colorless solid in 82% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.64 (d, *J* = 8.5 Hz, 1H), 7.39 (d, *J* = 5.4 Hz, 1H), 7.16 (d, *J* = 5.4 Hz, 1H), 7.10 (d, *J* = 2.2 Hz, 1H), 6.79 (dd, *J* = 8.5, 2.2 Hz, 1H), 3.69 (t, *J* = 0.6 Hz, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 143.56, 140.88, 130.43, 127.08, 123.05, 122.95, 114.86, 108.28. d

2,5-Dimethylaniline (**2l**) (CAS: 95-78-3)



The reaction to form this product was conducted with 0.5 mol % $Pd(P(o\text{-tol})_3)_2$ and 0.5 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (3:1 Hexanes:EtOAc). The title compound was isolated as an oil in 90% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 6.95 (d, *J* = 7.5 Hz, 1H), 6.55-6.52 (m, 2H), 3.55 (s, 2H), 2.26 (s, 3H), 2.14 (s, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 144.42, 136.67, 130.35, 119.43, 119.36, 115.76, 21.12, 16.96.

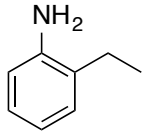
2-Vinylaniline (**2m**) (CAS: 3867-18-3)



The reaction to form this product was conducted with 0.5 mol % $Pd(P(o\text{-tol})_3)_2$ and 0.5 mol % CyPF-P^{t}Bu for 12 h. The crude product was isolated by flash column chromatography (4:1 Hexanes:EtOAc). The title compound was isolated as an oil in 60% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.31 (d,

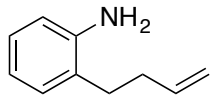
J = 7.6 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.80 (m, *J* = 10.7 Hz, 2H), 6.70 (d, *J* = 8.0 Hz, 1H), 5.65 (d, *J* = 17.4 Hz, 1H), 5.34 (d, *J* = 11.0 Hz, 1H), 3.77-3.70 (s, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 143.66, 132.72, 128.74, 127.31, 124.07, 118.91, 116.07, 115.69.

2-Ethylaniline (**2n**) (CAS: 578-54-1)



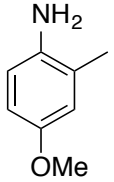
The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 8 h. The crude product was isolated by flash column chromatography (5:1 Hexanes:EtOAc). The title compound was isolated as a yellow oil in 76% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.11-7.05 (m, 1H), 6.78 (t, *J* = 7.4 Hz,), 6.70 (d, *J* = 7.8 Hz,), 3.63 (s, 1H), 2.55 (q, *J* = 7.5 Hz, 1H), 1.28 (t, *J* = 7.5 Hz, 2H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 144.04, 128.40, 128.12, 126.87, 118.86, 115.42, 24.07, 13.07.

2-(But-3-en-1-yl)aniline (**2o**) (CAS: 6992-97-8)



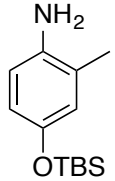
The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 12 h. The crude product was isolated by flash column chromatography (6:1 Hexanes:EtOAc). The title compound was isolated as a yellow oil in 75% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.08-7.04 (m, 2H), 6.76 (td, *J* = 7.4, 1.1 Hz, 1H), 6.70 (d, *J* = 7.6 Hz, 1H), 5.93 (ddt, *J* = 17.0, 10.3, 6.6 Hz, 1H), 5.12 (dq, *J* = 17.1, 1.7 Hz, 1H), 5.04 (m, 1H), 3.65 (s, 2H), 2.61 (m, 2H), 2.43-2.38 (m, 2H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 144.12, 138.20, 129.49, 127.12, 126.03, 118.85, 115.67, 115.16, 32.93, 30.79.

4-Methoxy-2-methylaniline (**2p**) (CAS: 102-50-1)



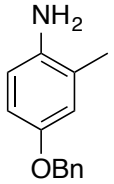
The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 6 h. The crude product was isolated by flash column chromatography (2:1 Hexanes:EtOAc). The title compound was isolated as a yellow oil in 80% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.68-6.63 (m, 3H), 3.75 (s, 3H), 2.17 (s, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 152.75, 138.24, 124.08, 116.43, 116.06, 112.14, 55.78, 17.78.

4-((*tert*-Butyldimethylsilyl)oxy)-2-methylaniline (**2q**) (CAS: 347196-56-9)



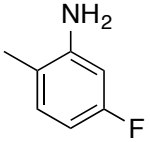
The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 6 h. The crude product was isolated by flash column chromatography (6:1 Hexanes:EtOAc). The title compound was isolated as a yellow oil in 64% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 6.56 (m, 3H), 3.34-3.33 (s, 2H), 2.13 (s, 3H), 0.97 (s, 9H), 0.16 (s, 6H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 148.46, 137.77, 124.28, 122.09, 118.12, 116.32, 25.81, 18.22, 17.66, -4.42.

4-(Benzyloxy)-2-methylaniline (**2r**) (CAS: 4792-60-3)



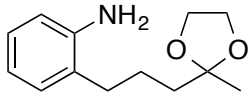
The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 12 h. The crude product was isolated by flash column chromatography (3:1 Hexanes:EtOAc). The title compound was isolated as a yellow oil in 86% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.30-7.14 (m, 5H), 6.64-6.44 (m, 3H), 4.84 (m, 2H), 3.19 (s, 2H), 2.01 (m, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 151.94, 138.43, 137.64, 128.49, 127.75, 127.48, 124.03, 117.61, 115.96, 113.28, 70.72, 17.73.

5-Fluoro-2-methylaniline (**2s**) (CAS: 367-29-3)



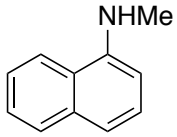
The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 8 h. The crude product was isolated by flash column chromatography (5:1 Hexanes:EtOAc). The title compound was isolated as an oil in 76% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 6.97 (t, J = 7.2 Hz, 1H), 6.40 (t, J = 9.9 Hz, 2H), 3.69 (s, 2H), 2.12 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 162.24 (d, $J_{C\text{-}F}$ = 240.9 Hz), 145.82 (d, $J_{C\text{-}F}$ = 10.6 Hz), 131.12 (d, $J_{C\text{-}F}$ = 9.6 Hz), 117.62 (d, $J_{C\text{-}F}$ = 2.6 Hz), 104.67 (d, $J_{C\text{-}F}$ = 21.0 Hz), 101.56 (d, $J_{C\text{-}F}$ = 24.6 Hz), 16.62 (s).

2-(3-(2-Methyl-1,3-dioxolan-2-yl)propyl)aniline (**2t**)



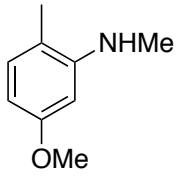
The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 6 h. The crude product was isolated by flash column chromatography (2:1 Hexanes:EtOAc). The title compound was isolated as an oil in 85% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.04 (m, 2H), 6.73 (t, J = 7.4 Hz, 1H), 6.67 (m, 1H), 3.97-3.91 (m, 4H), 3.66 (s, 2H), 2.51 (t, J = 6.5 Hz, 2H), 1.75-1.72 (m, 4H), 1.33 (s, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 144.21, 129.52, 126.99, 126.50, 118.70, 115.56, 110.11, 64.72, 38.91, 31.36, 24.03, 23.23. **HR-MS** (ESI): $[M+H]^+$ = 222.1489 (calc'd: 222.1489). **IR** (neat) ν_{max} 3462, 3371, 3879, 1624, 1062, 751 cm^{-1}.

***N*-Methylnaphthalen-1-amine** (**3a**) (CAS: 2216-68-4)



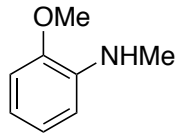
The reaction to form this product was conducted with 0.2 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.2 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (7:1 Hexanes:EtOAc). The title compound was isolated as a yellow oil in 97% (X = Cl) or 90% (X = Br) yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.84 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 8.2 Hz, 1H), 7.46 (m, J = 7.0 Hz, 3H), 7.29 (d, J = 8.1 Hz, 1H), 6.64 (d, J = 7.5 Hz, 1H), 4.44 (s, 1H), 3.04 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 144.53, 134.25, 128.67, 126.69, 125.71, 124.68, 123.47, 119.81, 117.32, 103.80, 31.03.

5-Methoxy-*N*,2-dimethylaniline (**3b**) (CAS: 156267-11-7)



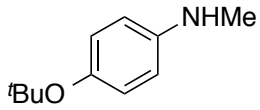
The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (5:1 Hexanes:EtOAc). The title compound was isolated as a pale yellow oil in 99% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 8.30 (s, 1H), 8.00 (d, *J* = 7.6 Hz, 1H), 7.29-7.26 (m, 1H), 4.85 (s, 3H), 4.64 (s, 1H), 3.93 (s, 3H), 3.12 (s, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 159.55, 148.31, 130.21, 114.58, 100.49, 96.69, 55.25, 30.77, 16.61.

2-Methoxy-*N*-methylaniline (**3c**) (CAS: 10541-78-3)



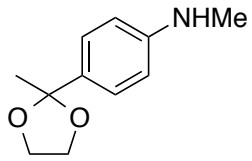
The reaction to form this product was conducted with 0.5 mol % (X = Cl) or 0.2 mol % (X = Br) Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % (X = Cl) or 0.2 mol % (X = Br) CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (10:1 Hexanes:EtOAc). The title compound was isolated as a yellow-orange oil in 79% (X = Cl) or 82% (X= Br) yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 6.92 (t, *J* = 7.6 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 6.69 (t, *J* = 7.7 Hz, 1H), 6.62 (d, *J* = 7.7 Hz, 1H), 4.25 (s, 1H), 3.86 (s, 3H), 2.88 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 146.88, 139.38, 121.34, 116.27, 109.31, 109.23, 55.39, 30.36.

4-(*tert*-Butoxy)-*N*-methylaniline (**3d**) (CAS: 1175905-77-7)



The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (3:1 Hexanes:EtOAc). The title compound was isolated as a bright yellow oil in 86% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.85 (d, *J* = 8.8 Hz, 3H), 6.52 (d, *J* = 8.8 Hz, 3H), 3.55 (s, 1H), 2.81 (s, 3H), 1.27 (s, 9H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 28.75, 31.27, 77.70, 112.52, 125.43, 145.67, 146.32.

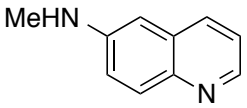
***N*-Methyl-4-(2-methyl-1,3-dioxolan-2-yl)aniline** (**3e**)



The reaction to form this product was conducted with 0.5 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.5 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (3:1 Hexanes:EtOAc). The title compound was isolated as a yellow solid in 91% (X = Cl) or 75% (X = Br) yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.30 (d, *J* = 8.2 Hz, 2H), 6.58 (d, *J* = 8.2 Hz, 2H), 4.01 (m, 2H), 3.79 (m, 2H), 2.84 (s, 3H), 1.65 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 148.95, 131.75, 126.27, 111.84, 109.00, 64.30, 30.71, 27.62. **HR-MS** (ESI): $[M+H]^+$ = 194.1176 (calc'd = 194.1176). **IR** (solution $CHCl_3$) ν_{max} 3683, 3019, 1601, 1215, 669 cm^{-1}.

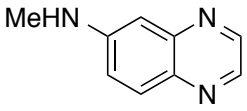
***N*-Methylquinolin-6-amine** (**3f**) (CAS: 83407-38-9)

The reaction to form this product was conducted with 0.3 mol % (X = Cl) or 0.2 mol % (X = Br) Pd(P(*o*-tol)$_3$)$_2$ and 0.3 mol % (X = Cl) or 0.2 mol % (X = Br) CyPF-P^{t}Bu for 12



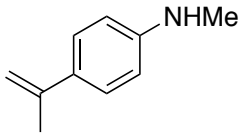
h. The crude product was purified by flash column chromatography (1:3 Hexanes:EtOAc, Hexanes contain 10% NEt_3). The title compound was isolated as a yellow-brown solid in 96% (X = Cl) or 91% (X = Br) yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.61 (m, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 9.0 Hz, 1H), 7.27-7.25 (m, 1H), 7.09 (m, 1H), 6.68 (s, 1H), 4.07 (s, 1H), 2.94 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 147.17, 146.00, 143.19, 133.78, 130.18, 130.08, 121.33, 121.28, 102.30, 30.64.

***N*-Methylquinoxalin-6-amine** (**3g**) (CAS: 1338986-47-2)



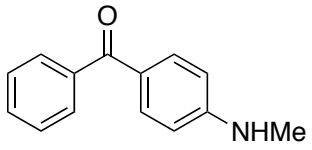
The reaction to form this product was conducted with 0.3 mol % $Pd(P(o\text{-tol})_3)_2$ and 0.3 mol % CyPF-P^{t}Bu for 13 h. The crude product was purified by flash column chromatography (100% EtOAc). The title compound was isolated as bright yellow solid in 94% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.63 (s, 1H), 8.50 (s, 1H), 7.82 (d, *J* = 9.0 Hz, 1H), 7.12 (dd, *J* = 9.1, 1.7 Hz, 1H), 6.94 (s, 1H), 4.36 (s, 1H), 2.98 (d, *J* = 4.9 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 150.16, 145.58, 144.87, 140.23, 138.00, 129.95, 122.06, 103.07, 30.43.

***N*-Methyl-4-(prop-1-en-2-yl)aniline** (**3h**) (CAS: 1629-30-7)



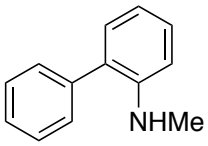
The reaction to form this product was conducted with 0.2 mol % $Pd(P(o\text{-tol})_3)_2$ and 0.2 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (7:1 Hexanes:EtOAc). The title compound was isolated as a pale yellow oil in 97% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.37 (d, *J* = 8.6 Hz, 2H), 6.59 (d, *J* = 8.6 Hz, 2H), 5.27 (s, 1H), 4.93 (s, 1H), 3.76 (s, 1H), 2.86 (s, 3H), 2.14 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 148.77, 142.79, 130.16, 126.39, 111.99, 108.77, 30.72, 21.86.

(4-(Methylamino)phenyl)(phenyl)methanone (**3i**) (CAS: 26178-74-5)



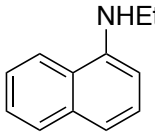
The reaction to form this product was conducted with 0.5 mol % (X = Cl) or 0.2 mol % (X = Br) $Pd(P(o\text{-tol})_3)_2$ and 0.5 mol % (X = Cl) or 0.2 mol % (X = Br) CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (3:1 Hexanes:EtOAc). The title compound was isolated a pale yellow solid in 77% (X = Cl) or 78% (X = Br) yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.76 (d, *J* = 8.6 Hz, 2H), 7.72 (d, *J* = 7.5 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 6.58 (d, *J* = 8.6 Hz, 2H), 4.34 (s, 1H), 2.91 (d, *J* = 3.3 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 195.17, 152.96, 139.18, 132.95, 131.15, 129.43, 128.00, 126.03, 110.95, 30.11.

***N*-Methyl-[1,1'-biphenyl]-2-amine** (**3j**) (CAS: 14925-09-8)



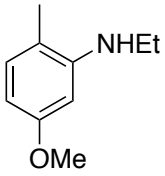
The reaction to form this product was conducted with 0.5 mol % (X = Cl) or 0.2 mol % (X = Br) $Pd(P(o\text{-tol})_3)_2$ and 0.5 mol % (X = Cl) or 0.2 mol % (X = Br) CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (15:1 Hexanes:EtOAc). The title compound was isolated as a pale yellow oil in 99% (X = Cl, Br) yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.49-7.44 (m, 4H), 7.40-7.36 (m, 1H), 7.31 (td, *J* = 7.8, 1.2 Hz, 1H), 7.13 (dd, *J* = 7.4, 1.5 Hz, 1H), 6.81 (td, *J* = 7.4, 0.9 Hz, 1H), 6.73 (d, *J* = 8.1 Hz, 1H), 4.01 (s, 1H), 2.83 (s, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 146.22, 139.57, 130.09, 129.48, 128.93, 128.84, 127.64, 127.25, 116.87, 109.86, 30.84.

***N*-Ethylnaphthalen-1-amine** (**4a**) (CAS: 118-44-5)



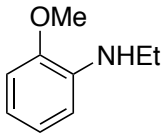
The reaction to form this product was conducted with 0.2 mol % (X = Cl) or 0.05 mol % (X = Br) $Pd(OAc)_2$ and 0.2 mol % (X = Cl) or 0.05 mol % (X = Br) CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (20:1 Hexanes:EtOAc). The title compound was isolated as a pale yellow oil in 95% (X = Cl) or 94% (X = Br) yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.64-7.61 (m, 2H), 7.29-7.23 (m, 2H), 7.18 (t, *J* = 7.9 Hz, 1H), 7.07-7.04 (m, 1H), 6.44 (d, *J* = 7.5 Hz, 1H), 4.05 (s, 1H), 3.13 (q, *J* = 7.1 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 143.70, 134.40, 128.77, 126.78, 125.76, 124.71, 123.43, 119.92, 117.29, 104.36, 38.82, 14.91.

***N*-Ethyl-5-methoxy-2-methylaniline** (**4b**) (CAS: 60111-39-9)



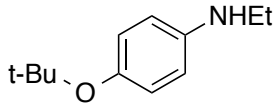
The reaction to form this product was conducted with 0.2 mol % $Pd(P(OAc)_2$ and 0.2 mol % CyPF-P^{t}Bu for 14 h. The crude product was purified by flash column chromatography (10:1 Hexanes:EtOAc). The title compound was isolated as a colorless oil in 77% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.96 (d, *J* = 8.9 Hz, 1H), 6.23-6.20 (m, 2H), 3.79 (s, 3H), 3.41 (s, 1H), 3.19 (q, *J* = 7.1 Hz, 2H), 2.08 (s, 3H), 1.31 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 159.45, 147.40, 130.29, 114.41, 100.45, 97.12, 55.23, 38.42, 16.68, 14.95.

***N*-ethyl-2-methoxyaniline** (**4c**) (CAS: 15258-43-2)



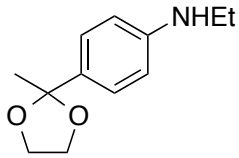
The reaction to form this product was conducted with 0.2 mol % (X = Cl) or 0.05 mol % (X = Br) $Pd(OAc)_2$ and 0.2 mol % (X = Cl) or 0.05 mol % (X = Br) CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (3:1 Hexanes:EtOAc). The title compound was isolated as a pale yellow oil in 88% (X = Cl) or 82% (X= Br) yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.92 (td, *J* = 7.6, 1.4 Hz, 1H), 6.81 (dd, *J* = 7.9, 1.3 Hz, 1H), 6.73-6.64 (m, 2H), 4.17 (s, 1H), 3.88 (s, 3H), 3.21 (q, *J* = 7.2 Hz, 2H), 1.33 (t, *J* = 7.2 Hz, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 146.81, 138.46, 121.38, 116.33, 109.90, 109.38, 55.42, 38.25, 14.95.

4-(*tert*-Butoxy)-*N*-ethylaniline (**4d**) (CAS: 1368636-78-5)



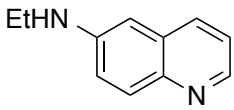
The reaction to form this product was conducted with 0.2 mol % $Pd(OAc)_2$ and 0.2 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (7:1 Hexanes:EtOAc). The title compound was isolated as a bright yellow oil in 98% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 6.84-6.82 (m, 2H), 6.53-6.50 (m, 2H), 3.37 (s, 1H), 3.11 (q, *J* = 7.1 Hz, 2H), 1.24 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 146.25, 144.75, 125.37, 112.82, 77.60, 39.00, 28.69, 14.97.

***N*-Ethyl-4-(2-methyl-1,3-dioxolan-2-yl)aniline** (**4e**)



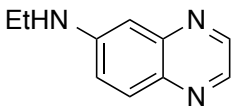
The reaction to form this product was conducted with 0.5 mol % (X = Cl) or 0.05 mol % (X = Br) $Pd(OAc)_2$ and 0.5 mol % (X = Cl) or 0.05 mol % (X = Br) CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (3:1 Hexanes:EtOAc). The title compound was isolated as a colorless solid in 92% (X = Cl) or 97% (X= Br) yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.29-7.27 (m, 2H), 6.57-6.56 (m, 2H), 4.02-4.00 (m, 2H), 3.80-3.78 (m, 2H), 3.60 (s, 1H), 3.16 (q, *J* = 7.1 Hz, 2H), 1.64 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 146.88, 130.55, 125.12, 110.95, 107.83, 63.13, 37.28, 26.41, 13.72. **HR-MS** (ESI): $[M+H]^+$ = 208.1332 (calc'd: 208.1332). **IR** (solution $CHCl_3$) ν_{max} 3623, 3019, 1600, 1216, 771, 669 cm^{-1}.

***N*-Ethylquinolin-6-amine** (**4f**) (CAS: 860199-85-5)



The reaction to form this product was conducted with 0.2 mol % (X = Cl) or 0.05 mol % (X = Br) $Pd(OAc)_2$ and 0.2 mol % (X = Cl) or 0.05 mol % (X = Br) CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (1:2 Hexanes:EtOAc, Hexanes contain 2.5% NEt_3). The title compound was isolated as a beige solid in 98% (X = Cl) or 94% (X = Br) yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.60 (dd, *J* = 4.2, 1.6 Hz, 1H), 7.91-7.89 (m, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.24 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.07 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.67 (d, *J* = 2.6 Hz, 1H), 3.91 (s, 1H), 3.25 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 146.25, 146.02, 143.20, 133.68, 130.19, 130.18, 121.33, 121.30, 102.77, 38.43, 14.60.

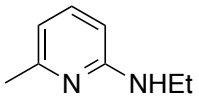
***N*-Ethylquinoxalin-6-amine** (**4g**) (CAS: 1179094-62-2)



The reaction to form this product was conducted with 0.2 mol % $Pd(OAc)_2$ and 0.2 mol % CyPF-P^{t}Bu for 13 h. The crude product was purified by flash column chromatography (100% EtOAc). The title compound was isolated as bright yellow solid in 95% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.60 (d, *J* = 1.8 Hz, 1H), 8.47 (d, *J* = 1.8 Hz, 1H), 7.79 (d, *J* = 9.1 Hz, 1H), 7.08 (dd, *J* = 9.1, 2.5 Hz, 1H), 6.92 (d, *J* = 2.5 Hz, 1H), 4.29 (s, 1H), 3.27 (q, *J* = 7.2 Hz,

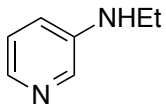
2H), 1.30 (t, *J* = 7.2 Hz, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 149.30, 145.61, 144.89, 140.19, 137.98, 130.02, 122.27, 103.37, 38.28, 14.44.

***N*-ethyl-6-methylpyridin-2-amine** (**4l**) (CAS: 39179-00-5)



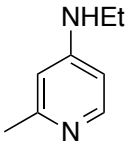
The reaction to form this product was conducted with 0.2 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.2 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (5% MeOH in DCM). The title compound was isolated as a dark yellow oil in 59% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.32 (t, *J* = 7.7 Hz, 1H), 6.42 (d, *J* = 7.2 Hz, 1H), 6.16 (d, *J* = 8.2 Hz, 1H), 4.47 (d, *J* = 0.6 Hz, 1H), 3.22 (quintet, *J* = 6.4 Hz, 2H), 2.34 (s, 3H), 1.22 (t, *J* = 7.2 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 158.65, 157.02, 18.01, 112.17, 102.39, 37.19, 24.37, 14.89.

N-ethylpyridin-3-amine (Table 4, **4m**) (CAS: 32405-70-2)



The reaction to form this product was conducted with 0.2 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.2 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (5% MeOH in DCM). N-Ethylacetamide was observed by ^{1}H NMR spectroscopy. The compound was dissolved in Et_2O and washed with brine. The title compound was isolated as a dark yellow oil in 90% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.99 (d, *J* = 2.5 Hz, 1H), 7.92 (d, *J* = 4.5 Hz, 1H), 7.04 (dd, *J* = 8.3, 4.7 Hz, 1H), 6.83 (ddd, *J* = 8.3, 2.7, 1.1 Hz, 1H), 3.72 (s, 1H), 3.13 (q, *J* = 7.1 Hz, 2H), 1.24 (td, *J* = 7.1, 0.5 Hz, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 144.37, 138.52, 136.00, 123.72, 118.34, 38.12, 14.72.

N-ethyl-2-methylpyridin-4-amine (Table 4, **4n**) (CAS: 1536965-39-5)



The reaction to form this product was conducted with 0.2 mol % Pd(P(*o*-tol)$_3$)$_2$ and 0.2 mol % CyPF-P^{t}Bu for 12 h. The crude product was purified by flash column chromatography (5% MeOH in DCM). N-Ethylacetamide was observed by ^{1}H NMR spectroscopy. The compound was dissolved in Et_2O and washed with brine. The title compound was isolated as a dark yellow oil in 96% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.75 (d, *J* = 5.9 Hz, 1H), 6.10 (dd, *J* = 5.9, 2.1 Hz, 1H), 5.81 (d, *J* = 2.0 Hz, 1H), 4.12 (s, 1H), 3.86 (s, 3H), 3.15-3.10 (m, 2H), 1.21 (t, *J* = 7.2 Hz, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 165.72, 155.84, 146.59, 104.43, 90.55, 53.23, 37.42, 14.44.

Preparation of ^{15}N-labeled 5-methoxy-2-methylaniline on 4 mmol scale

In a nitrogen-filled glovebox, Pd(P(*o*-tol)$_3$)$_2$ (0.012 mmol, 0.3 mol %) and CyPF-P^{t}Bu (0.012 mmol, 0.3 mol %) were dissolved in dioxane and mixed for 5 min. A 100 mL round bottom flask was charged with aryl halide (4.0 mmol, 1 equiv), ammonium salt (6.0 mmol, 1.5 equiv), and sodium *tert*-butoxide (18 mmol, 4.5 equiv). To this vial was added 40 mL of anhydrous dioxane. The reaction vial was sealed with a rubber septum

and removed from the glovebox. The reaction was stirred 100 °C for 12 h. The reaction mixture was then diluted with EtOAc and filtered through a pad of Celite. The filtrate was concentrated *in vacuo*, and the crude product was purified by flash column chromatography (4:1 Hexanes : EtOAc) to afford the title compound as a beige solid in 90% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.96 (d, J = 8.0 Hz, 1H), 6.29 (m, 2H), 3.76 (s, 3H), 3.64 (s, 2H), 2.11 (s, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 159.04 , 145.52 (d, $J_{C\text{-}N}$ = 10.9 Hz), 131.00, 114.85 (d, $J_{C\text{-}N}$ = 2.1 Hz), 103.68 , 101.02 (d, $J_{C\text{-}N}$ = 2.9 Hz), 55.24, 16.56. **HR-MS** (ESI): $[M+H]^+$ = 139.0883 (calc'd: 139.0884).

Determination of Concentration of Ammonia under Reaction Conditions

In a nitrogen-filled glovebox, $(NH_4)_2SO_4$ (0.104 mmol, 1.4 equiv) was added to a J-Young NMR tube. NaO^{t}Bu (0.312, 4.5 equiv) and 1,5-cyclooctadiene (internal standard, 0.070 mmol, 1 equiv), dissolved in 0.7 mL THF-d_8, were added to the J-Young NMR tube, which was sealed in the glovebox. ^{1}H NMR spectra were acquired at various temperatures. The concentration of ammonia in solution was calculated at each temperature and is reported below:

Table 4.6 Concentration of Ammonia in Solution under Reaction Conditions

Entry	Temperature (K)	$[NH_3]$ (M)
1	308	0.160
2	318	0.154
3	328	0.128
4	338	0.114
5	348	0.090
6	353	0.075
7[a]	297	0.250

[a] Spectrum acquired to cooled sample after heating

The decreasing concentration of ammonia with an increase in temperature suggests that the ammonia is in the headspace of the NMR tube, and not dissolved. However, after the heating, a spectrum was acquired at ambient temperature (the last entry in the table), indicating that heating does promote the formation of ammonia, by dissolution of the salt by the NaO^{t}Bu.

Determination of Resting State of the Catalytic Reaction

In a nitrogen-filled glovebox, $Pd(P(o\text{-tol})_3)_2$ (0.0070 mmol, 10 mol %), CyPF-P^{t}Bu (0.0070 mmol, 10 mol %), aryl halide (0.070 mmol, 1 equiv), and sodium *tert*-butoxide (0.315 mmol, 4.5 equiv) were dissolved in 0.7 mL of dioxane. The ammonium salt (0.105 mmol, 1.5 equiv) was weighed directly into a J-Young NMR tube. The solution of reagents was added to the J-Young NMR tube and sealed in the glovebox. The NMR tube was removed from the glovebox. The J-Young NMR tube was placed in a spectrometer pre-heated to 80 °C. Spectra were acquired during the course of the reaction. A fine powder of NaCl or NaBr formed, and the color of the reaction was dark orange. This color

was the same as that of the reactions run for isolation of the products. In addition, spectra acquired at ambient temperature on a sample heated for 10 min at 80 °C were identical to those obtained while heating in the spectrometer probe.

Figure 4.1 Observation of Resting State X = Cl

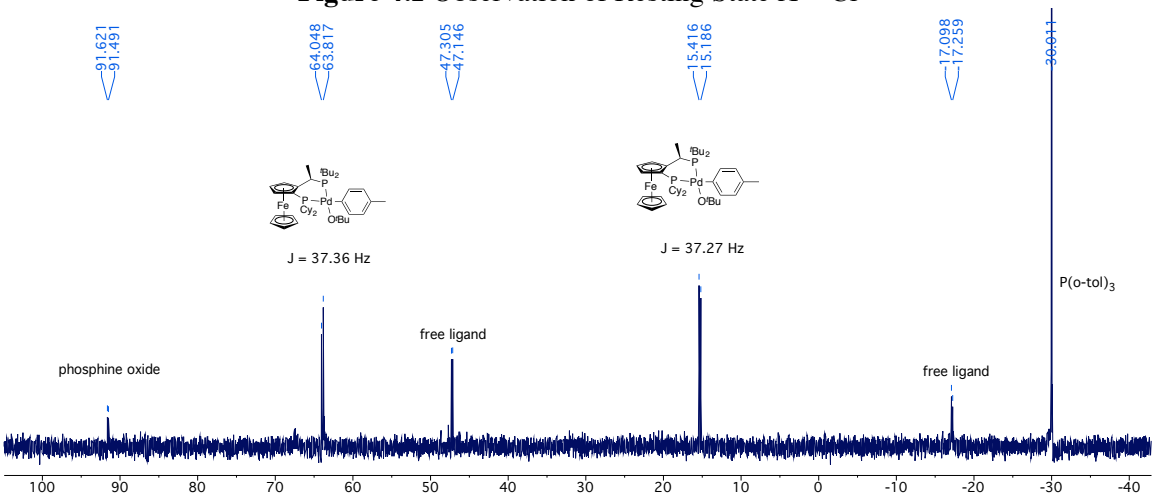
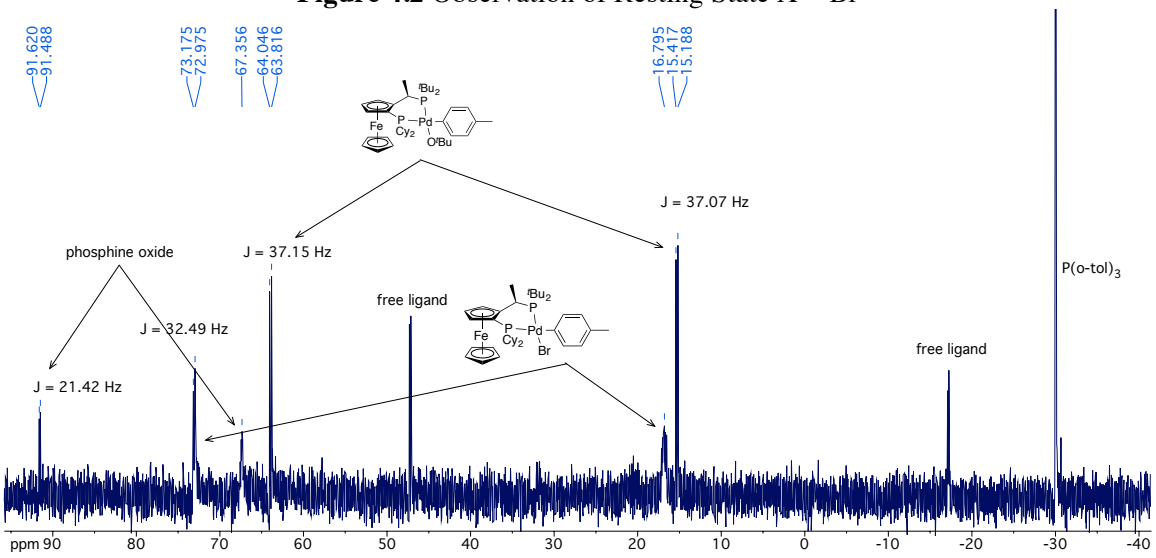


Figure 4.2 Observation of Resting State X = Br



Independent Synthesis of (CyPF-^{t}Bu)Pd(p-tolyl)(O^{t}Bu)

(CyPF-^{t}Bu)Pd(*p*-tolyl)(Cl)[23] (1 equiv) and NaO^{t}Bu (3 equiv) were dissolved in THF (0.060M) and heated to 100 °C for 5 min, as the solution turned from bright orange to dark red. The solution was cooled and brought back into a glovebox, where it was filtered through a syringe filter to remove the NaCl. The solvent was removed *in vacuo*. The addition of ether to the residue caused precipitation of a bright orange solid, which

was collected by filtration as the title compound (10%-40% yield). The compound is best stored at -30 °C under inert atmosphere. **^{31}P-NMR** (162 MHz, THF): δ 63.28 (d, *J* = 37.3 Hz), 14.64 (d, *J* = 36.7 Hz). See spectra for **^{1}H NMR** in THF-d_8 (better resolution of aromatic and Cp region) and C_6D_6 (better resolution of aliphatic region).

Figure 4.3 ^{31}P NMR (THF)

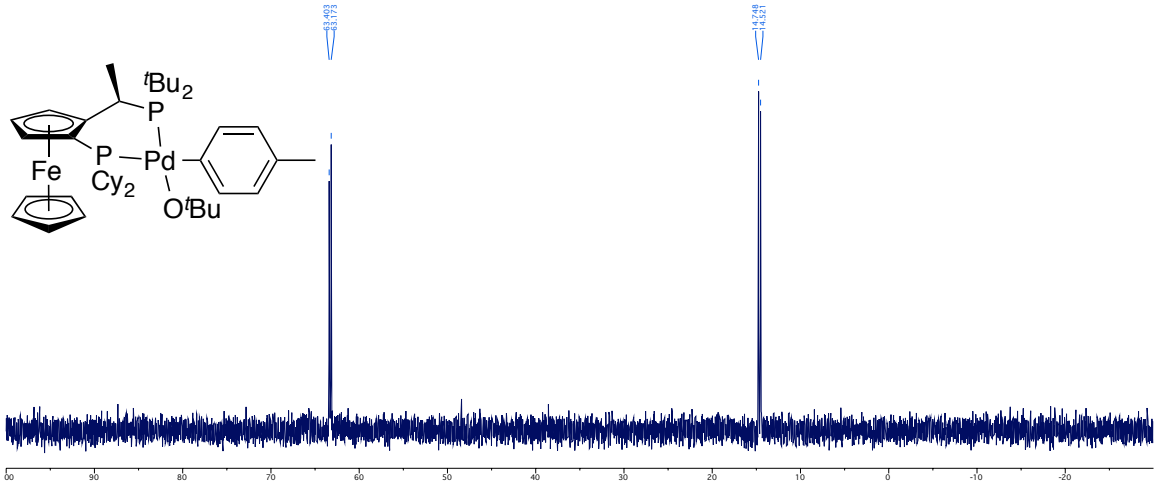


Figure 4.4 ^{1}H NMR (THF-d_8)

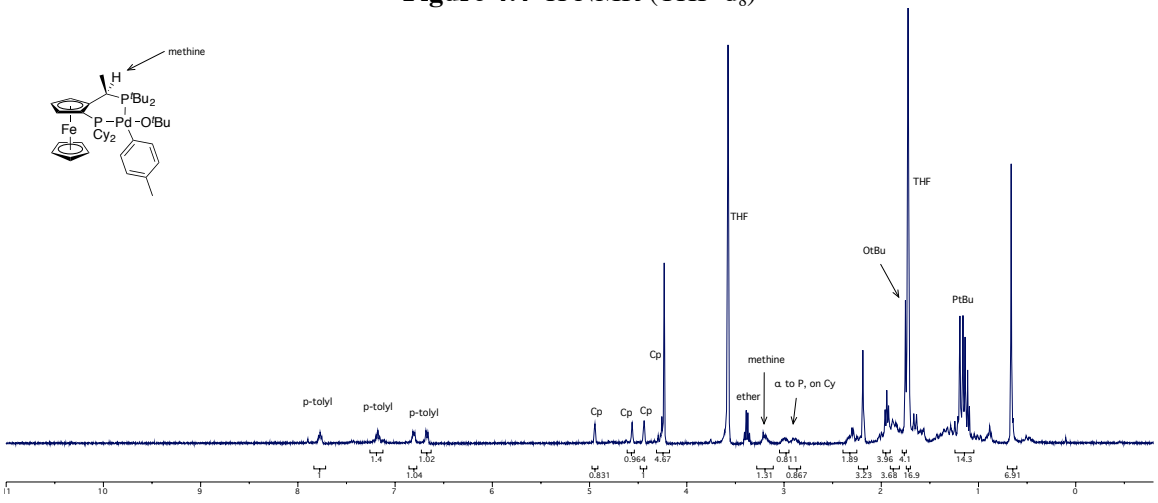
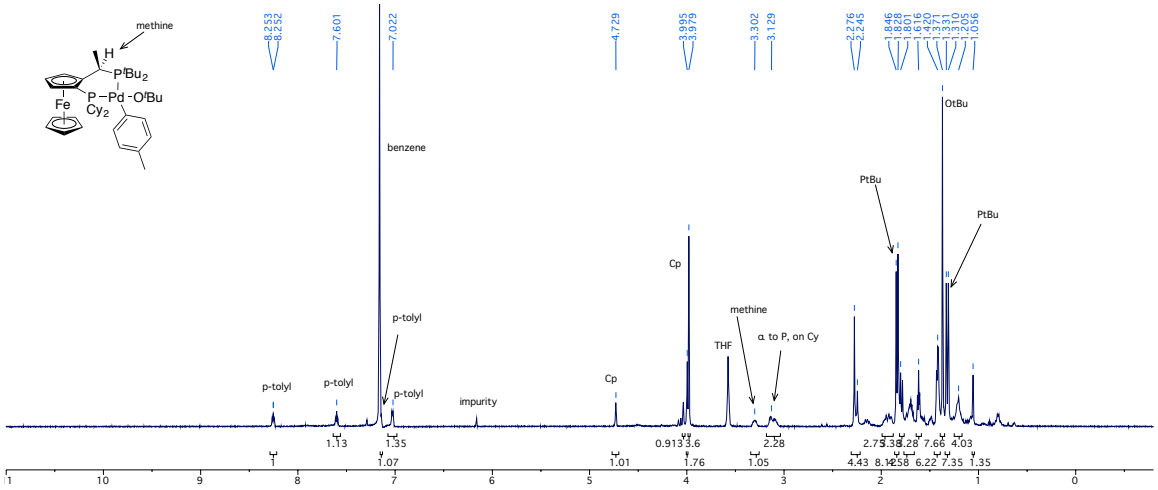


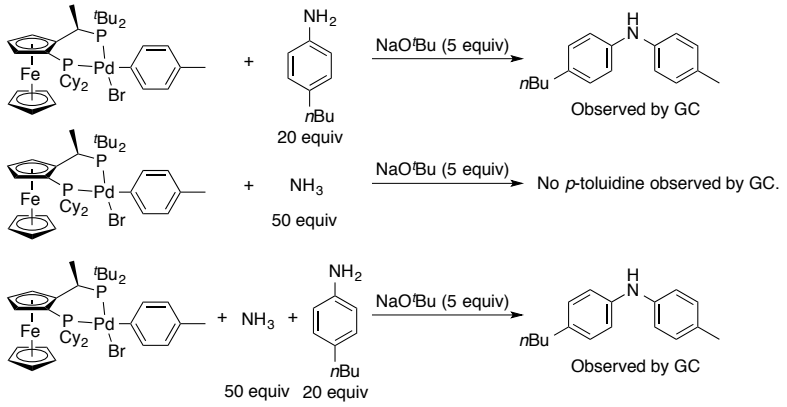
Figure 4.5 ^{1}H NMR (C_6D_6)



Stoichiometric Reactions with (CyPF-^{t}Bu)Pd(p-tolyl)(Br)

(CyPF-^{t}Bu)Pd(*p*-tolyl)(Br)[9] (0.0070 mmol, 1 equiv) was mixed with NaO^{t}Bu (0.035 mmol, 5 equiv) and either 4-*n*-butylaniline (0.14 mmol, 20 equiv) or NH_3 solution (0.35 mmol, 50 equiv), or a combination of both. The reaction solutions were analyzed by GC.

Scheme 4.7 Stoichiometric Reactions with $L_2Pd(Ar)(Br)$



4.5 References

Reproduced in part with permission from Organic Letters.
Copyright 2014 American Chemical Society. "Palladium-Catalyzed Amination of Aryl Chlorides and Bromides with Ammonium Salts"
Green, R.A.; Hartwig, J.F. *Org. Lett.* **2014**, *16*, 4388.

(1) Klinkenberg, J. L.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2010**, *50*, 86.
(2) Aubin, Y.; Fischmeister, C.; Thomas, C. M.; Renaud, J.-L. *Chem. Soc. Rev.* **2010**, *39*, 4130.

(3) Enthaler, S. *ChemSusChem* **2010**, *3*, 1024.
(4) Grasa, G. A.; Viciu, M. S.; Huang, J.; Nolan, S. P. *J. Org. Chem.* **2001**, *66*, 7729.
(5) Wolfe, J. P.; Ahman, J.; Sadighi, J. P.; Singer, R. A.; Buchwald, S. L. *Tetrahedron Lett.* **1997**, *38*, 6367.
(6) Ikawa, T.; Barder, T. E.; Biscoe, M. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 13001.
(7) Huang, X.; Buchwald, S. L. *Org. Lett.* **2001**, *3*, 3417.
(8) Lee, D.-Y.; Hartwig, J. F. *Org. Lett.* **2005**, *7*, 1169.
(9) Bhagwanth, S.; Waterson, A. G.; Adjabeng, G. M.; Hornberger, K. R. *J. Org. Chem.* **2009**, *74*, 4634.
(10) Shen, Q.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 10028.
(11) Vo, G. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 11049.
(12) Surry, D. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 10354.
(13) Cheung, C. W.; Surry, D. S.; Buchwald, S. L. *Org. Lett.* **2013**, *15*, 3734.
(14) Lundgren, R. J.; Peters, B. D.; Alsabeh, P. G.; Stradiotto, M. *Angew. Chem. Int. Ed.* **2010**, *49*, 4071.
(15) Alsabeh, P. G.; Lundgren, R. J.; McDonald, R.; Johansson Seechurn, C. C. C.; Colacot, T. J.; Stradiotto, M. *Chem. Eur. J.* **2013**, *19*, 2131.
(16) Crawford, S. M.; Lavery, C. B.; Stradiotto, M. *Chem. Eur. J.* **2013**, *19*, 16760.
(17) Kim, J.; Chang, S. *Chem. Commun.* **2008**, 3052.
(18) $Pd(P(o\text{-}tol)_3)_2$ is stable as a solid in air, but must be handled under inert atmosphere in solution.
(19) Singer, R. A.; Doré, M.; Sieser, J. E.; Berliner, M. A. *Tetrahedron Lett.* **2006**, *47*, 3727.
(20) See experimental section.
(21) Unprotected enolizable ketones underwent aldol condensation reactions under the basic conditions.
(22) Klinkenberg, J. L.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 11830.
(23) Alvaro, E.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 7858.
(24) A survey of alkoxide and phenoxide bases with various counterions did not improve the selectivity of the reaction.
(25) Clarke, H. T.; Davis, A. W. *Organic Syntheses* **1922**, 79.
(26) Alvarez-Builla, J.; Vaquero, J. J.; Barluenga, J. *Modern Heterocyclic Chemistry*; 4 ed.; John Wiley & Sons: Weinheim, 2011.
(27) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*, 2875.
(28) Gribble, G. W. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1045.
(29) Fors, B. P.; Watson, D. A.; Biscoe, M. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2008**, *130*, 13552.
(30) Lundgren, R. J.; Sappong-Kumankumah, A.; Stradiotto, M. *Chem. Eur. J.* **2010**, *16*, 1983.
(31) Fors, B. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 15914.
(32) Li, J. J.; Wang, Z.; Mitchell, L. H. *J. Org. Chem.* **2007**, *72*, 3606.
(33) Alsabeh, P. G.; Lundgren, R. J.; Longobardi, L. E.; Stradiotto, M. *Chem. Commun.* **2011**, *47*, 6936.

(34) Tardiff, B. J.; McDonald, R.; Ferguson, M. J.; Stradiotto, M. *J. Org. Chem.* **2012**, *77*, 1056.
(35) Shen, Q.; Shekhar, S.; Stambuli, J. P.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2005**, *44*, 1371.
(36) Drew, D.; Doyle, J. R.; Shaver, A. G. *Inorganic Syntheses, Volume 13* **1990**, 47.
(37) Li, H.; Grasa, G. A.; Colacot, T. J. *Org. Lett.* **2010**, *12*, 3332.
(38) Togni, A.; Breutel, C.; Schnyder, A.; Spindler, F.; Landert, H.; Tijani, A. *J. Am. Chem. Soc.* **1994**, *116*, 4062.
(39) Gischig, S.; Togni, A. *Organometallics* **2004**, *23*, 2479.
(40) Yucel, B.; Sanli, B.; Soylemez, H.; Akbulut, H. *J. Organomet. Chem.* **2012**, *704*, 49.
(41) Wuts, P. G. M.; Greene, T. W. *Greene's Protective Groups in Organic Synthesis*; 4 ed.; John Wiley & Sons, Inc.: Hoboken, NJ, 2007; pp. 1–1111.
(42) Cho, S. H.; Hartwig, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 8157.
(43) Qadir, M.; Priestley, R. E.; Rising, T. W. D. F.; Gelbrich, T.; Coles, S. J.; Hursthouse, M. B.; Sheldrake, P. W.; Whittall, N.; Hii, K. K. M. *Tetrahedron Lett.* **2003**, *44*, 3675.

CHAPTER 5

Nickel-Catalyzed Amination of Aryl Chlorides with Ammonia or Ammonium Salts

5.1 Introduction

The amination of aryl halides catalyzed by transition metals is a valuable tool for the construction of arylamines.[1] Many palladium catalysts have been developed for the amination of aryl electrophiles with a wide variety of amines. However, there are few catalysts based on cost-effective and earth-abundant metals for the amination of aryl electrophiles, and little mechanistic information has been gained about the coupling reactions catalyzed by first-row metals. Copper-catalyzed aminations of aryl halides are typically limited to sterically unhindered aryl iodides and activated aryl bromides.[2] Nickel catalysts for amination reactions have been reported, but the scope of the reaction, until recently,[3,4] was limited to secondary alkyl[2,5-19] and aryl[5,8,9,11,13-20] amines.

The development of a nickel catalyst for the coupling of aryl electrophiles with primary amines and ammonia is a long-standing challenge. Nickel-catalyzed coupling reactions of aryl chlorides with primary alkylamines occurred, until recently, in low yields with unactivated substrates.[5,18] Our report of a catalyst for the coupling of unactivated aryl chlorides with primary alkylamines demonstrated the value of single-component catalysts to achieve high reactivity and selectivity.[2,3] Despite the progress on the development of first-row transition-metal catalysts for C-N coupling reactions, few studies have been published on the amination of aryl electrophiles with ammonia catalyzed by nickel. Concurrent with the work we report here,[21] Stradiotto and co-workers reported a Josiphos-ligated nickel catalyst for the coupling of aryl chlorides with ammonia.[4]

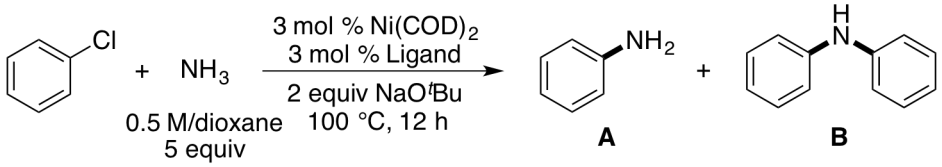
The development of the nickel-catalyzed coupling of ammonia poses several challenges. First, ammonia binds tightly to transition metals,[5-19,22,23] and causes catalyst deactivation. Ammonia is neither strongly basic nor acidic, disfavoring proton exchanges to and from the reagent, and the strong N-H bond disfavors oxidative addition of the N-H bond of ammonia. In addition, the physical properties of ammonia create challenges for conducting coupling reactions conveniently. Because it is a corrosive gas, specialized equipment is required to run reactions at high pressures. Finally, the aniline formed during the reaction can act as a nucleophile for subsequent amination reactions. Therefore, the catalyst must overcome these challenges to couple selectively ammonia over the aniline formed during the course of the reaction. Herein, we report a series of Ni-catalyzed monoarylations of ammonia with aryl electrophiles. These studies show the value of using a single component catalyst for high activity and for generating clear mechanistic information. Our mechanistic studies strongly imply that the process occurs by shuttling between Ni(0) and arylnickel(II) halide intermediates.

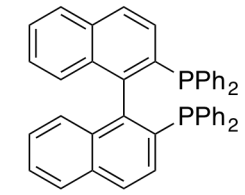
5.2 Results and Discussion

The palladium-catalyzed amination of aryl electrophiles with ammonia has been reported,[5,8,9,11,13-20,24-32] and the mechanism has been studied.[33] These studies showed that the steric bulk of the ligand is crucial to favor the binding of ammonia over the binding of aniline. Nickel complexes of bidentate ligands are known to add aryl chlorides.[3,34] Based on this information, we investigated the coupling of chlorobenzene with ammonia, added to the reaction as a solution in dioxane, catalyzed by $Ni(COD)_2$ and a variety of bidentate

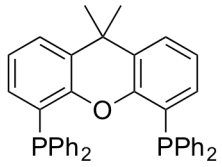
phosphine ligands (Figure 5.1). We began our evaluation of ligands by studying catalysts containing common chelating bisphosphines, such as BINAP, Xantphos, and dppf. Because BINAP-ligated nickel complexes catalyzed the amination of aryl chlorides with primary alkylamines,[3] the primary arylamines formed from the coupling of ammonia might be expected to react competitively with ammonia. Indeed, the reaction of chlorobenzene with ammonia, catalyzed by a BINAP-ligated nickel complex, occurred in low yield with low selectivity for the primary amine over the diarylamine.

Table 5.1 Evaluation of Nickel Precursors and Ligands for the Amination of Chlorobenzene with Ammonia[a]

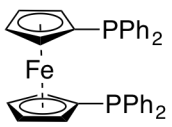




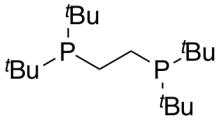
BINAP
78% conv.
39% yield
5:1



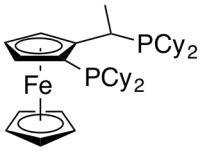
Xantphos
0% conv.



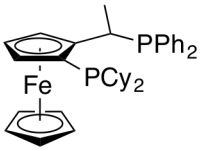
dppf
0% conv



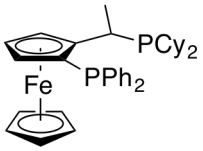
dtbpe
71% conv.
46% yield
4:1



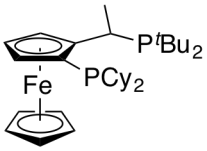
L1, CyPF-Cy
100% conv.
67% yield
32:1



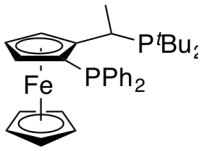
L2, CyPF-Ph
100% conv.
43% yield
2:1



L3, PPF-Cy
100% conv.
41% yield
2:1



L4, CyPF-*t*Bu
28% conv.
11% yield
>50:1



L5, PPF-*t*Bu
82% conv.
67% yield
>50:1

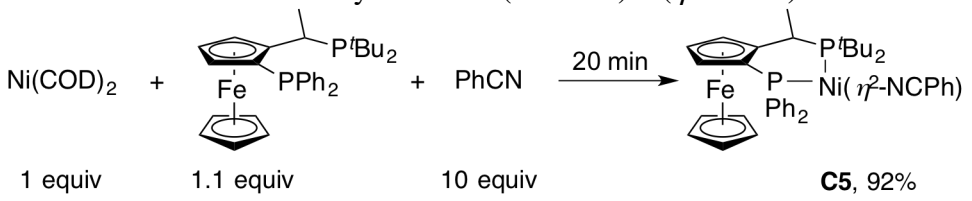
[a] Reactions performed with 0.10 mmol of chlorobenzene. Conversion, yield, and selectivity determined by GC analysis using dodecane as an internal standard.

However, reactions catalyzed by nickel complexes bound by ligands of the Josiphos family occurred to high conversions of the aryl chloride, high yields of anilines, and varying selectivities. The nickel catalyst ligated by the same Josiphos ligand as in the Pd-catalyst for the coupling of aryl halides with ammonia[24,27] gave high selectivity for the primary amine. However, the conversion and yield were low. Fortunately, reactions conducted with the smaller Josiphos ligand **L5** occurred with both high yields and high selectivity.

We have previously shown that benzonitrile stabilizes the Ni(0) intermediate in the catalytic system, and the benzonitrile-ligated nickel complex readily undergoes

oxidative addition of aryl chlorides.[3] To avoid the presence of cyclooctadiene in the reaction mixture, we prepared a single-component nickel(0) precursor containing **L5** and benzonitrile. The substitution of **L5** for cyclooctadiene in $Ni(COD)_2$ requires heating, but this ligand substitution occurs quickly at ambient temperature in the presence of benzonitrile. The combination of $Ni(COD)_2$, PPF-^{t}Bu and excess benzonitrile generated complex **C5**, containing the Josiphos ligand and a side-bound benzonitrile (Scheme 5.1).

Scheme 5.1 Synthesis of (PPF-^{t}Bu)Ni(η^2-NCPh)



The structure of this complex is shown in Figure 5.1. The η^2-bound benzonitrile ligand stabilizes Ni(0) through back-bonding into the C≡N π^* orbital. The C≡N bond in **2** is longer than a typical C≡N bond of a nitrile, (1.225(2) Å, average C≡N bond length[35]: 1.136 Å), and the C–C≡N bond axis is bent (136.4(2)°). These properties are indicative of strong π-backbonding from the nickel into the nitrile π-bond (Figure 5.1). A reaction conducted with **C5** occurred to full conversion in 3 h and afforded aniline in 80% yield with excellent (<50:1) selectivity for the primary arylamine.

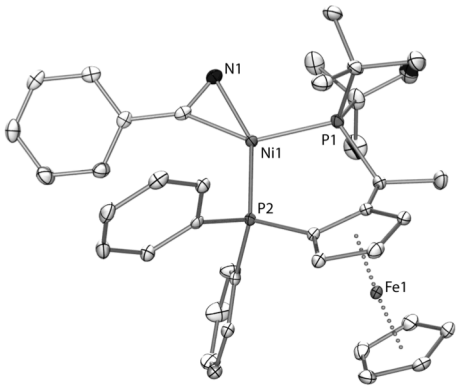
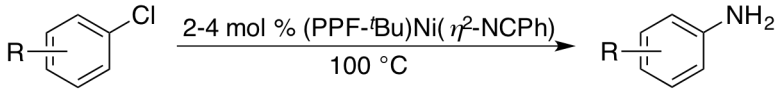


Figure 5.1 ORTEP Structure of (PPF-^{t}Bu)Ni(η^2-NCPh).
Ellipsoids shown at 50% probability, hydrogen atoms omitted for clarity.

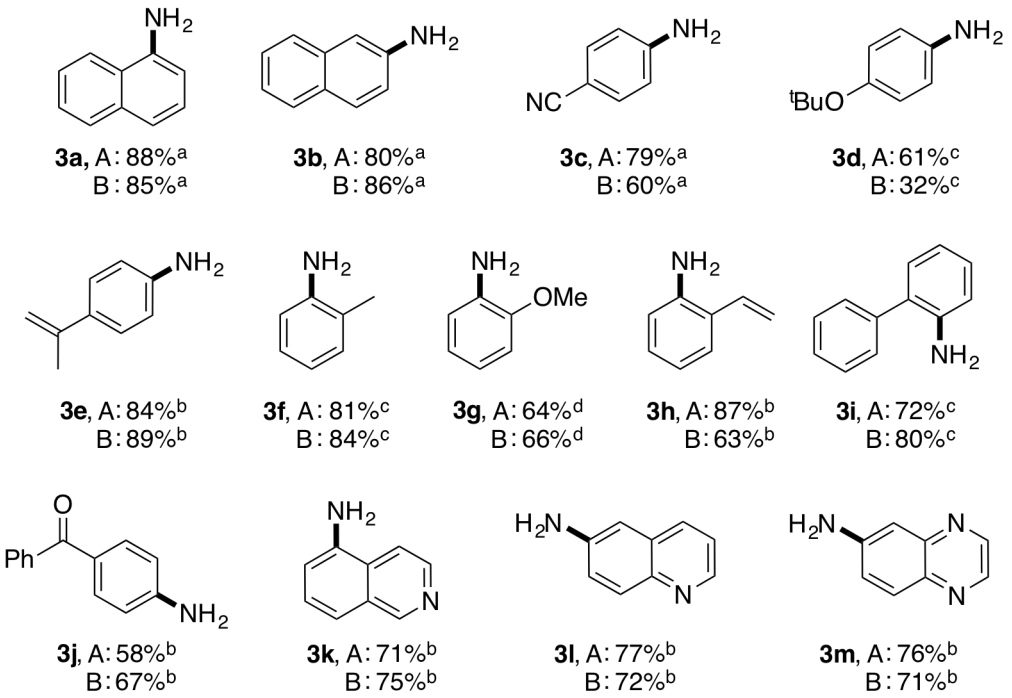
The source of ammonia for the reactions summarized in Table 5.1 is a commercially available solution of NH_3 in dioxane. Inexpensive ammonium salts are also potential sources of NH_3 for the coupling process. We recently reported palladium-catalyzed reactions of aryl halides with ammonium salts as precursors to ammonia.[36] Due to the practical advantages of assembling C-N coupling reactions with ammonium salts in place of ammonia solutions, we investigated the potential to use ammonium salts in the Ni-catalyzed amination. We investigated ammonium chloride, acetate, and sulfate as sources of ammonia. For reactions catalyzed by **C5**, only reactions conducted with ammonium sulfate gave comparable yields and selectivities to reactions conducted with

ammonia in dioxane. Furthermore, because the solvent is not limited to the commercially available solution of ammonia in dioxane when conducting reactions with ammonium salts, a range of solvents were explored. Reactions conducted in ethereal solvents occurred in the highest yields, and 2-Me-THF was selected for both its green chemistry properties and elevated boiling point compared to other ethers.[37,38]

Table 5.2 Nickel-Catalyzed Amination of Aryl Chlorides with Ammonia and Ammonium Sulfate.



Conditions A: 5 equiv NH_3, 1.5 equiv NaO^{t}Bu, 1,4-dioxane, 3 h
Conditions B: 1.5 equiv $(NH_4)_2SO_4$, 4.5 equiv NaO^{t}Bu, 2-Me-THF, 7 h



3a, A: 88%[a] B: 85%[a] | **3b**, A: 80%[a] B: 86%[a] | **3c**, A: 79%[a] B: 60%[a] | **3d**, A: 61%[c] B: 32%[c]

3e, A: 84%[b] B: 89%[b] | **3f**, A: 81%[c] B: 84%[c] | **3g**, A: 64%[d] B: 66%[d] | **3h**, A: 87%[b] B: 63%[b] | **3i**, A: 72%[c] B: 80%[c]

3j, A: 58%[b] B: 67%[b] | **3k**, A: 71%[b] B: 75%[b] | **3l**, A: 77%[b] B: 72%[b] | **3m**, A: 76%[b] B: 71%[b]

Isolated yields. Reactions were performed with 0.60 mmol of the aryl chloride.
[a] 2 mol % **C5**, [b] 3 mol % **C5**, [c] 4 mol % **C5**.

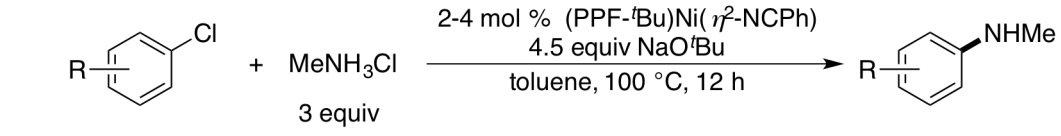
The scope of aryl chlorides that undergo the amination of aryl chlorides with ammonia or ammonium sulfate is shown in Table 5.2. Aryl chlorides containing *ortho* substituents (**2f**, **2g**, **2h**, **2i**), electron-withdrawing groups (**2c**, **2j**) and electron-donating groups (**2d**, **2g**) underwent the transformation in moderate to high yields. Heteroaryl chlorides (**2k**, **2l**, **2m**) also underwent this transformation in high yields. Nitriles (**2c**), styrenes (**2e, 2h**), and non-enolizable ketones (**2j**) were tolerated under the reaction conditions. In general, the yields of reactions conducted with ammonia are similar to the yields of reactions conducted with ammonium sulfate.

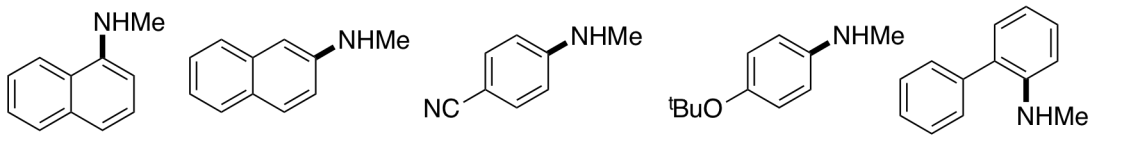
Based on the finding that $(NH_4)_2SO_4$ is a practical source of ammonia in transition-metal catalyzed coupling reactions, we investigated the reaction of aryl chlorides with ammonium salts of gaseous amines. Although methylamine is a primary

aliphatic amine, the coupling of methylamine hydrochloride with aryl chlorides catalyzed by (BINAP)Ni(η^2-NCPh), our previously reported catalyst for the coupling of aryl chlorides with primary aliphatic amines,[3] occurred in low yields.

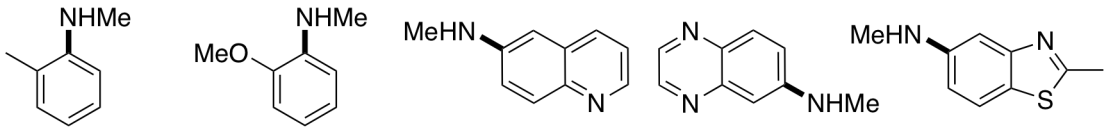
However, reactions of aryl chlorides with methylamine hydrochloride catalyzed by (PPF-^{t}Bu)Ni(η^2-NCPh) in toluene occurred in high yields (Table 5.3). The scope of aryl chlorides that undergo this transformation is similar to that for the coupling reactions with ammonia or ammonium sulfate. In addition, the catalyst loadings for reactions of aryl chlorides with ammonia or ammonium sulfate are similar to those for reactions of aryl chlorides with methylamine hydrochloride.

Table 5.3 Nickel-Catalyzed Amination of Aryl Chlorides with Methylamine Hydrochloride.





4a, 93%[a] **4b**, 97%[a] **4c**, 79%[a] **4d**, 99%[c] **4i**, 83%[c]



4f, 99%[a] **4g**, 84%[c] **4l**, 99%[b] **4m**, 86%[b] **4n**, 52%[b]

Isolated yields. Reactions were performed with 0.60 mmol of the aryl chloride.
[a] 2 mol % **C5**, [b] 3 mol % **C5**, [c] 4 mol % **C5**.

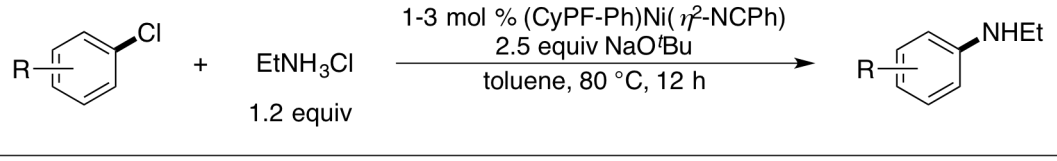
In addition to methylamine hydrochloride, ethylamine hydrochloride couples with aryl chlorides to form the corresponding *N*-ethylanilines. However, neither the reactions catalyzed by (PPF-^{t}Bu)Ni(η^2-NCPh) nor those catalyzed by (BINAP)Ni(η^2-NCPh) occurred to full conversion of *p*-chlorotoluene to *N*-ethyl-*p*-toluidine (up to 70%) under conditions with various solvents, temperatures, and reagent stoichiometries.

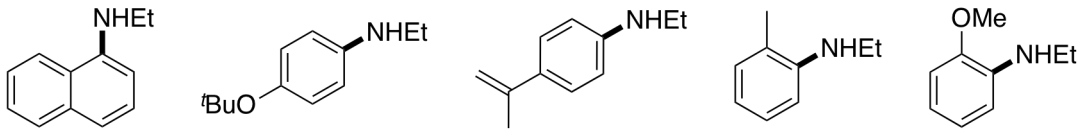
Therefore, we re-examined ligands for this reaction in which the nucleophile is larger than ammonia but is smaller than most primary alkylamines. We investigated ligands that we anticipated would promote the oxidative addition of aryl chlorides but would be less sterically bulky than those that promote the selective coupling of ammonia and methylamine. The results summarized in Table 5.1 include two examples (**L2** and **L3**) in which the reactions proceeded to full conversion, but occurred with poor selectivity. These results suggest that the catalyst in these examples would add the aryl chlorides in the presence of amines, and would be less sterically bulky than (PPF-^{t}Bu)Ni(η^2-NCPh). Indeed, nickel bound by the Josiphos ligands **L2** and **L3** containing one cyclohexyl group and one phenyl group catalyzed the amination of aryl chlorides with ethylamine hydrochloride with full conversion of the aryl chloride. We prepared

single component catalysts from both these ligands, $Ni(COD)_2$, and benzonitrile. Both complexes catalyzed the amination reaction in high yields, but the reactions catalyzed by (CyPF-Ph)Ni(η^2-NCPh) (**C2**) formed higher yields of the secondary amine product than the reactions catalyzed by (PPF-Cy)Ni(η^2-NCPh).

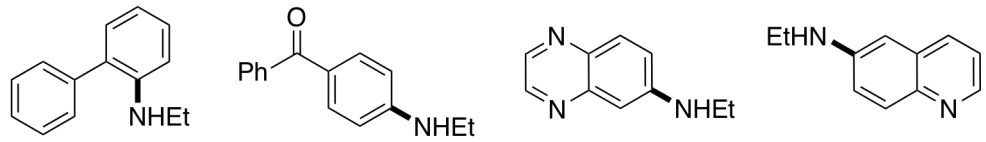
Examples of the coupling of $EtNH_3Cl$ with chloroarenes are summarized in Table 5.4. The reactions of aryl chlorides with $EtNH_3Cl$ catalyzed by **5** occurred to full conversion with lower catalyst loadings (1-3 mol %) and temperature (80 °C) than the analogous coupling reactions with ammonia, ammonium sulfate, or methylamine hydrochloride (2-4 mol %, 100 °C). The scope of the couplings of $EtNH_3Cl$ is similar to that of ammonia and $MeNH_3Cl$.

Table 5.4 Nickel-Catalyzed Amination of Aryl Chlorides with Ethylamine Hydrochloride.





4a, 99%[a] **4d**, 92%[c] **4e**, 84%[b] **4f**, 87%[c] **4g**, 85%[c]

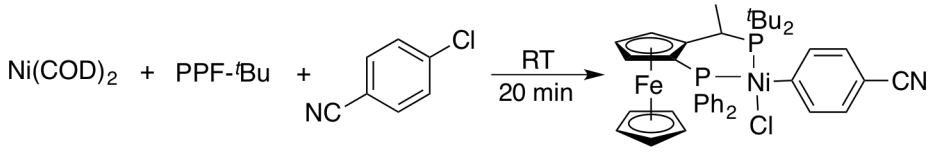


4i, 98%[b] **4j**, 96%[b] **4l**, 84%[b] **4m**, 71%[b]

Isolated yields. Reactions were performed with 0.60 mmol of the aryl chloride.
[a] 1 mol % **C2**, [b] 2 mol % **C2**, [c] 3 mol % **C2**.

Reactions catalyzed by nickel complexes have been proposed to occur via one- or two-electron pathways.[39,40] To investigate the mechanism of these coupling reactions, we conducted stoichiometric experiments with our new nickel complexes. First, we conducted the oxidative addition of aryl chlorides to nickel complex **C5**. Oxidative addition of the activated aryl chloride occurred in high yields (Scheme 5.2), while

Scheme 5.2 Oxidative Addition of 4-Chlorobenzonitrile to (PPF-^{t}Bu)Ni(η^2-NCPh)

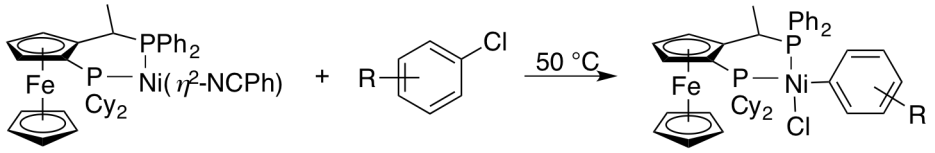


C5A, 92%

oxidative addition of electron-neutral and electron-rich aryl chlorides were slow and occurred in low yields.

Although the oxidative addition of electron-neutral and electron-rich haloarenes to the Ni(0) species containing the *t*-butyl Josiphos ligand was slow, the oxidative addition of electron-neutral, electron-rich, and ortho-substituted aryl chlorides occurred cleanly to (CyPF-Ph)Ni(η^2-NCPh), to yield the corresponding bisphosphine-ligated arylnickel chloride complexes (Scheme 5.3).

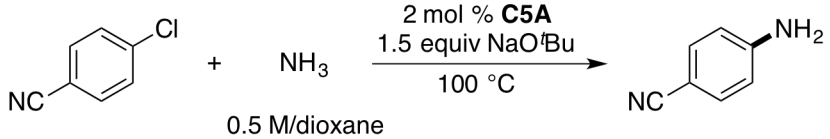
Scheme 5.3 Oxidative Addition of Aryl Chlorides to (CyPF-Ph)Ni(η^2-NCPh)



C2A, R = 4-Me 67%
C2B, R = 4-O^{t}Bu 65%
C2C, R = 2-OEt 66%

The catalytic activity of the bisphosphine-ligated arylnickel chloride complexes was evaluated by conducting the coupling reaction of chlorobenzonitrile with ammonia under the standard conditions with 2 mol % of **C2A** as catalyst.[41] The arylnickel(II) chloride complex **C2A** was found to be an equally active catalyst for the amination of 4-chlorobenzonitrile with ammonia as is **C2** (Scheme 5.4).

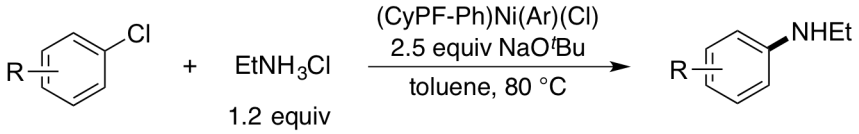
Scheme 5.4 Catalytic Competence of **C5A**

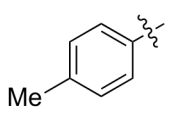


2c, 93%

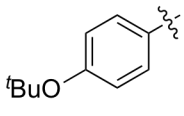
However, complexes **C2A-C** do not contain a benzonitrile moiety, and not all reactions catalyzed by these complexes occurred to full conversion. Yet, reactions catalyzed by **C2B** and **C2C** occurred to full conversion in the presence of 8 mol % of

Table 5.5 Catalytic Competences of **C2A**, **C2B**, and **C2C**

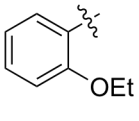




catalyst: 2 mol % **C2A**
yield: 82%
additive: none



catalyst: 2 mol % **C2B**
yield: 95%
additive: 8 mol % PhCN

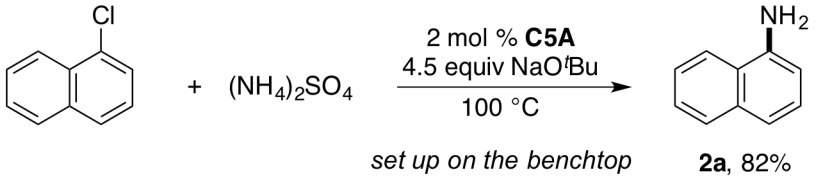


catalyst: 2 mol % **C2C**
yield: 84%
additive: 8 mol % PhCN

added benzonitrile (Table 5.5). These results imply that the Ni(II) complexes are catalytically active for the amination reaction and that benzonitrile acts as a ligand for the Ni(0) species to improve activity or stability of this intermediate.[3]

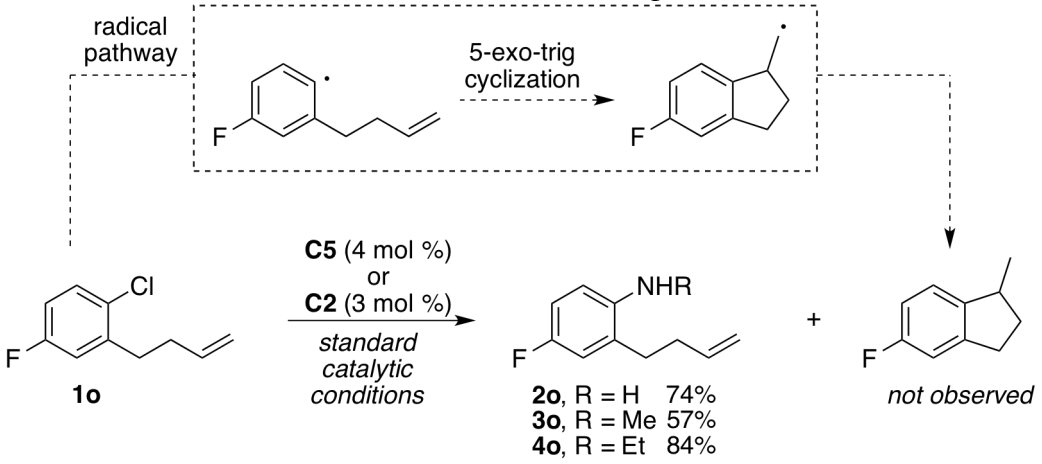
Ni(II) complexes are stable in air. We conducted a coupling reaction of 1-chloronaphthalene with ammonium sulfate catalyzed by **7**, an air-stable precursor that contains a benzonitrile functional group to stabilize Ni(0) intermediates, on the benchtop to yield 2-aminonaphthalene in 82% isolated yield (Scheme 5.5).

Scheme 5.5 Synthesis of 1-aminonaphthalene on the benchtop



To probe for the potential intermediacy of aryl radicals in the catalytic process, we conducted the coupling of a substrate (**1o**) which would rapidly undergo cyclization of an aryl radical were generated (Scheme 5.6). The coupling of this substrate with ammonium sulfate, methylamine hydrochloride and ethylamine hydrochloride was conducted under standard catalytic conditions. In all cases, no cyclized product was observed by GC-MS analysis of the crude reaction mixture. Thus, it is unlikely that free aryl radicals are formed during the catalytic reaction. Together with the kinetic competence of the arylnickel(II) halide intermediates these data imply that the reaction occurs by a catalytic cycle involving Ni(0) and arylNi(II) halide intermediates.

Scheme 5.6 Radical Clock Experiments



5.3 Conclusion

In conclusion, we report new Ni(0) complexes containing a bisphosphine ligand and a side-bound benzonitrile ligand that catalyze the coupling of aryl electrophiles with ammonia with moderate catalyst loadings at short reaction times. We also demonstrated that ammonium sulfate can be used in place of ammonia to effect the same

transformation, as can ammonium salts of the gaseous amines methylamine and ethylamine in the form of their easily handled hydrochloride salts. Preliminary mechanistic studies suggest that bisphosphine-ligated aryl nickel(II) chloride complexes are intermediates in this transformation, and the lack of cyclization with a substrate that probes for aryl intermediates suggests that free aryl radicals are not formed during the course of the reaction. Further mechanistic analysis of these reactions will be the subject of future work.

5.4 Experimental

General Remarks

All the manipulations were performed in a nitrogen-filled glovebox, unless mentioned otherwise. THF, toluene, pentane, and Et_2O were purified by passing the degassed solvents (N_2) through a column of activated alumina (solvent purification system purchased from Innovative Technologies, Newburyport, MA). Ammonia in dioxane (0.5 M) was purchased from Sigma-Aldrich and used as received. No-D NMR experiments using 1,5-cyclooctadiene as an internal standard revealed the solution of ammonia to be 0.45 M. 1,4-Dioxane (99%, extra dry) was purchased from Acros and used without further purification. 2-Me-THF was degassed and dried over 3Å molecular sieves. Reactions with ammonium salts were conducted in 20 mL vials fitted with a Teflon-lined screw cap under an atmosphere of nitrogen unless otherwise noted.

^1H, $^{13}C\{^1H\}$, and $^{31}P\{^1H\}$ NMR spectra were recorded using a Bruker 400 MHz, 500 MHz, or 600 MHz NMR spectrometer. ^1H NMR spectra were referenced to resonances of the residual protons in the deuterated solvents; and $^{31}P\{^1H\}$ NMR shifts were reported in parts per million relative to an 85% H_3PO_4 external standard. NMR spectra were processed with iNMR(4.2.0, Mestrelab). Coupling constants are reported in hertz.

Silica gel chromatography was performed using 230-400 Mesh (Grade 60) silica gel and visualized using UV light.

Dr. Antonio DiPasquale obtained the x-ray crystallographic data and solved the structures of compounds **C2**, **C5**, and **C5A**.

Safety note: reactions conducted with 2-Me-THF should be conducted in vessels that seal with a Teflon-line screw cap or in Schlenk flasks. The boiling point of 2-Me-THF (80 °C) for a reaction conducted at 100 °C and generation of gas can cause a septum to pop off. This is not an issue if the reaction is conducted in 1,4-dioxane (b.p.: 101 °C). For this concern, reactions should be conducted behind a blast shield.

Synthesis of C5

In a nitrogen-filled glovebox, a 20 mL vial was charged with $Ni(COD)_2$ (111 mg), ligand **L5** (234 mg), and 3 mL toluene. Benzonitrile (400 μL) was added, and the mixture

stirred at RT for 20 min, at which point an orange precipitate formed. Pentane (5 mL) was added to help precipitate the product. The product was collected by filtration, rinsed with pentane, and dried under high vacuum to yield **C5** in 92% yield. A single crystal suitable for X-ray diffraction was prepared by slow diffusion of pentane into a solution in toluene at RT.

^{1}H-NMR (500 MHz, THF-d_8): δ 8.25 (t, *J* = 8.7 Hz, 2H), 7.51-7.45 (m, 3H), 7.33 (t, *J* = 8.5 Hz, 2H), 7.14-7.03 (m, 7H), 6.99-6.96 (m, 2H), 4.61 (s, 1H), 4.19 (s, 1H), 3.88 (s, 1H), 3.83 (s, 5H), 3.31 (t, *J* = 6.4 Hz, 1H), 2.01 (t, *J* = 7.3 Hz, 3H), 1.52 (d, *J* = 11.7 Hz, 9H), 1.24 (d, *J* = 12.1 Hz, 9H).
^{31}P-NMR (162 MHz, THF): δ 72.77 (d, *J* = 30.3 Hz), 32.11 (d, *J* = 30.3 Hz).
Elemental analysis: Calc'd: C, 66.51; H, 6.44; N, 1.99. Found: C, 66.31; H, 6.37; N 2.24.
CCDC: 1043706

Synthesis of C2

In a nitrogen-filled glovebox, a 20 mL vial was charged with $Ni(COD)_2$ (183 mg), ligand **L2** (400 mg), and 4 mL toluene. Benzonitrile (687 μL) was added, and the mixture stirred at RT for 1 h. The toluene was removed *in vacuo*. Ether (1 mL) was added to partially solubilize the residue. Pentane (5 mL) was added to fully precipitate the compound. The product was collected by filtration, rinsed with pentane, and then dried under high vacuum to yield **C2** in 86% yield. A single crystal suitable for X-ray diffraction was prepared by layering pentane over a solution of cold toluene at -30 °C.

^{1}H-NMR (600 MHz, THF): δ 7.70-7.66 (m, 2H), 7.60 (t, *J* = 8.0 Hz, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.31-7.27 (m, 3H), 7.21-7.13 (m, 5H), 7.07 (t, *J* = 7.1 Hz, 1H), 6.96 (t, *J* = 7.0 Hz, 1H), 4.37-4.36 (m, 2H), 4.27-4.23 (m, 2H), 4.11 (s, 4H), 3.45-3.41 (m, 1H), 2.50 (d, *J* = 10.8 Hz, 1H), 2.45-2.41 (m, 1H), 2.36-2.32 (m, 1H), 2.18-2.15 (m, 1H), 2.08-1.89 (m, 6H), 1.58-1.47 (m, 3H), 1.43-1.34 (m, 6H), 1.32-1.23 (m, 2H), 1.18-1.05 (m, 4H), 0.88 (t, *J* = 7.4 Hz, 1H).
^{31}P-NMR (162 MHz, THF): δ 52.14 (d, *J* = 31.3 Hz), 20.66 (d, *J* = 31.4 Hz).
CCDC: 1043704

General Protocol for the Coupling of Aryl Halides with Ammonia in Dioxane (Conditions A)

In a nitrogen-filled glovebox, an oven-dried 25 mL round-bottom flask was charged with **2** (0.012-0.024 mmol, 2-4 mol %), aryl halide (0.60 mmol, 1 equiv), and sodium *tert*-butoxide (0.9 mmol, 1.5 equiv). The flask was sealed with a rubber septum and removed from the glovebox. To this flask was added 6 mL of a solution of ammonia in dioxane (0.5 M, 5 equiv). The reaction was stirred at 100 °C for 3 h as a closed system. The reaction was quenched by addition of EtOAc (3 mL).

Purification by extraction: The volatile materials were evaporated *in vacuo*. The residue was dissolved in EtOAc. The product was extracted with aqueous HCl. The pH of the aqueous layer was adjusted to 10 with $KOH_{(aq)}$. The product was extracted with EtOAc (3 x 10 mL). The organic layer was washed with brine, then dried over Mg_2SO_4. The volatile materials were evaporated *in vacuo*. The residue was dissolved in $CHCl_3$ (1 mL) and passed through a short pipette containing a silica plug. The volatile materials were evaporated *in vacuo* to yield the purified product.

Purification by column chromatography: The reaction mixture was filtered through Celite, and the volatile materials were evaporated *in vacuo*. The crude product was purified by flash-column chromatography to afford the purified product.

General Protocol for the Coupling of Aryl Halides with Ammonium Sulfate (Conditions B)

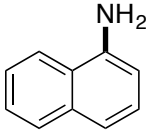
In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with **2** (0.012-0.024 mmol, 2-4 mol %), aryl halide (0.60 mmol, 1 equiv), ammonium sulfate (0.90 mmol, 1.5 equiv), sodium *tert*-butoxide (2.7 mmol, 4.5 equiv), and 2-Me-THF (3 mL). The flask was sealed with a Teflon-lined screw cap and removed from the glovebox. The reaction was stirred at 100 °C for 7 h. The reaction was quenched by addition of EtOAc (3 mL).

Purification by extraction: The volatile materials were evaporated *in vacuo*. The residue was dissolved in EtOAc. The product was extracted with aqueous HCl. The pH of the aqueous layer was adjusted to 10 with $KOH_{(aq)}$. The product was extracted with EtOAc (3 x 10 mL). The organic layer was washed with brine, then dried over Mg_2SO_4. The volatile materials were evaporated *in vacuo*. The residue was dissolved in $CHCl_3$ (1 mL) and passed through a short pipette containing a silica plug. The volatile materials were evaporated *in vacuo* to yield the purified product.

Purification by column chromatography: The reaction mixture was filtered through Celite, and the volatile materials were evaporated *in vacuo*. The crude product was purified by flash-column chromatography to afford the purified product.

Characterization of Organic Products from Reaction with Ammonia and Ammonium Sulfate

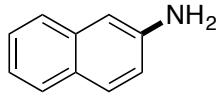
Naphthalen-1-amine (**2a**) (CAS: 134-32-7)



The reactions to form this product were conducted with 2 mol % **2**. The crude product was purified by extraction with 0.5 M $HCl_{(aq)}$. The title compound was isolated as a solid in 88% yield (conditions A) or 85% yield (conditions B). **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.86-7.83 (m, 2H), 7.50-

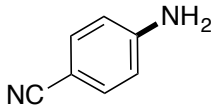
7.48 (m, 2H), 7.35 (s, 2H), 6.82 (dd, *J* = 7.0, 1.4 Hz, 1H), 4.18 (s, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 142.07, 134.40, 128.55, 126.34, 125.84, 124.85, 123.67, 120.79, 118.98, 109.69.

Naphthalen-2-amine (**2b**) (CAS: 91-59-8)



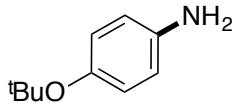
The reactions to form this product were conducted with 2 mol % **2**. The crude product was purified by extraction with 0.5 M $HCl_{(aq)}$. The title compound was isolated as a solid in 80% yield (conditions A) or 86% yield (conditions B). **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.70 (d, *J* = 8.2 Hz, 1H), 7.67 (d, *J* = 8.6 Hz, 1H), 7.60 (d, *J* = 8.3 Hz, 1H), 7.37 (ddd, *J* = 8.2, 6.9, 1.3 Hz, 1H), 7.23 (ddd, *J* = 8.1, 6.9, 1.2 Hz, 1H), 6.99 (d, *J* = 2.3 Hz, 1H), 6.95 (dd, *J* = 8.6, 2.3 Hz, 1H), 3.84 (s, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 144.09, 134.91, 129.19, 127.96, 127.70, 126.33, 125.78, 122.45, 118.21, 108.57.

4-Aminobenzonitrile (**2c**) (CAS: 873-74-5)



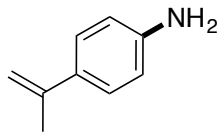
The reactions to form this product were conducted with 2 mol % **2**. The crude product was purified by extraction with 2.0 M $HCl_{(aq)}$. The title compound was isolated as a solid in 79% yield (conditions A) or 60% yield (conditions B). **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.41 (d, *J* = 8.7 Hz, 2H), 6.64 (d, *J* = 8.7 Hz, 2H), 4.15 (s, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 150.29, 133.79, 120.03, 114.42, 100.35.

4-(*tert*-Butoxy)aniline (**2d**) (CAS: 57120-36-2)



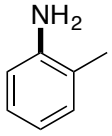
The reactions to form this product were conducted with 4 mol % **2**. The crude product was purified by extraction with 0.5 M $HCl_{(aq)}$. The title compound was isolated as an oil in 61% yield (conditions A) or 32% yield (conditions B). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.78 (d, *J* = 8.8 Hz, 2H), 6.57 (d, *J* = 8.8 Hz, 2H), 3.46 (s, 2H), 1.27 (s, 9H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 147.21, 142.39, 125.45, 115.49, 77.81, 28.76.

4-(Prop-1-en-2-yl)aniline (**2e**) (CAS: 1962-08-9)



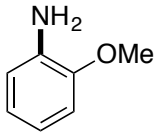
The reactions to form this product were conducted with 2 mol % **2**. The crude product was purified by extraction with 0.5 M $HCl_{(aq)}$. The title compound was isolated as an oil in 84% yield (conditions A) or 89% yield (conditions B). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.34 (d, *J* = 8.5 Hz, 2H), 6.66 (d, *J* = 8.4 Hz, 2H), 5.31 (d, *J* = 1 Hz, 1H), 4.99-4.98 (m, 1H), 3.69 (s, 2H), 2.14 (d, *J* = 0.7 Hz, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 145.91, 142.76, 131.57, 126.53, 114.79, 109.41, 21.92.

2-Toluidine (**2f**) (CAS: 95-53-4)



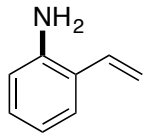
The reactions to form this product were conducted with 3 mol % **2**. The crude product was purified by extraction with 0.5 M $HCl_{(aq)}$. The title compound was isolated as an oil in 81% yield (conditions A) or 84% yield (conditions B). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.10 (t, *J* = 7.6 Hz, 2H), 6.79-6.72 (m, 2H), 3.63 (s, 2H), 2.22 (s, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 144.63, 130.52, 127.04, 122.40, 118.70, 115.01, 17.45.

2-Methoxyaniline (2g) (CAS: 90-04-0)



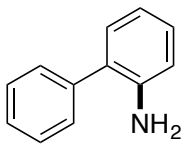
The reactions to form this product were conducted with 4 mol % **2**. The crude product was purified by extraction with 2.0 M $HCl_{(aq)}$. The title compound was isolated as an oil in 64% yield (conditions A) or 66% yield (conditions B). **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 6.83 (ddd, *J* = 7.9, 6.3, 1.4 Hz, 2H), 6.78-6.73 (m, 2H), 3.87 (s, 3H), 3.81 (s, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 147.32, 136.15, 121.07, 118.47, 115.03, 110.42, 55.42.

2-Vinylaniline (**2h**) (CAS: 3867-18-3)



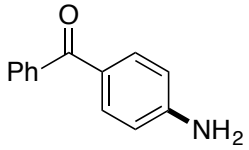
The reactions to form this product were conducted with 3 mol % **2**. The crude product was purified by extraction with 2.0 M $HCl_{(aq)}$. The title compound was isolated as an oil in 87% yield (conditions A) or 63% yield (conditions B). **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.30 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.11 (td, *J* = 7.6, 1.4 Hz, 1H), 6.81-6.76 (m, 2H), 6.69 (dd, *J* = 8.0, 1.1 Hz, 1H), 5.65 (dd, *J* = 17.4, 1.5 Hz, 1H), 5.33 (dd, *J* = 11.0, 1.5 Hz, 1H), 3.76 (s, 2H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 143.65, 132.76, 128.77, 127.36, 124.14, 118.99, 116.13, 115.75.

[1,1'-Biphenyl]-2-amine (**2i**) (CAS: 90-41-5)



The reactions to form this product were conducted with 4 mol % **2**. The crude product was purified by extraction with 2.0 M $HCl_{(aq)}$. The title compound was isolated as a solid in 72% yield (conditions A) or 80% yield (conditions B). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.47-7.46 (m, 4H), 7.38-7.34 (m, 1H), 7.19-7.14 (m, 2H), 6.84 (td, *J* = 7.4, 0.9 Hz, 1H), 6.78 (d, *J* = 7.9 Hz, 1H), 3.76 (s, 2H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 143.53, 139.55, 130.50, 129.14, 128.86, 128.54, 127.67, 127.21, 118.69, 115.64.

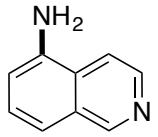
(4-Aminophenyl)(phenyl)methanone (**2j**) (CAS: 1137-41-3)



The reactions to form this product were conducted with 4 mol % **2**. The crude product was purified by extraction with 2.0 M $HCl_{(aq)}$. The title compound was isolated as a solid in 72% yield (conditions A) or 80% yield (conditions B). **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.73-7.71 (m, 4H), 7.54 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 2H),

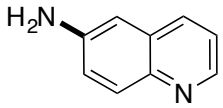
6.67 (d, *J* = 8.6 Hz, 2H), 4.15 (s, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 195.35, 151.08, 138.87, 132.94, 131.40, 129.50, 128.07, 127.26, 113.61.

5-Aminoisoquinoline (**2k**) (CAS: 1125-60-6)



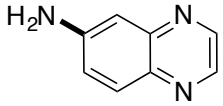
The reactions to form this product were conducted with 3 mol % **2**. The crude product was purified by extraction with 2.0 M $HCl_{(aq)}$, or by column chromatography (5% MeOH in EtOAc). The title compound was isolated as a solid in 71% yield (conditions A) or 75% yield (conditions B). **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 9.24 (d, *J* = 0.7 Hz, 1H), 8.53 (s, 1H), 7.59 (d, *J* = 5.9 Hz, 1H), 7.41 (d, *J* = 4.8 Hz, 2H), 6.97-6.94 (m, 1H), 4.22 (s, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 113.62, 114.58, 118.56, 126.55, 128.31, 129.98, 141.84, 142.65, 153.56.

6-Aminoquinoline (**2l**) (CAS: 580-15-4)



The reactions to form this product were conducted with 3 mol % **2**. The crude product was purified by extraction with 2.0 M $HCl_{(aq)}$, or by column chromatography (5% MeOH in EtOAc). The title compound was isolated as a solid in 77% yield (conditions A) or 72% yield (conditions B). **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 8.65 (dd, *J* = 4.2, 1.6 Hz, 1H), 7.91-7.88 (m, 2H), 7.28-7.25 (m, 1H), 7.16 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.90 (d, *J* = 2.6 Hz, 1H), 3.97 (s, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 107.41, 121.43, 121.64, 129.84, 130.54, 133.80, 143.46, 144.77, 146.81.

6-Aminoquinoxaline (**2m**) (CAS: 6298-37-9)



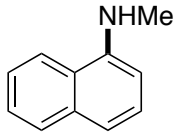
The reactions to form this product were conducted with 3 mol % **2**. The crude product was purified by extraction with 2.0 M $HCl_{(aq)}$, or by column chromatography (100% EtOAc, followed by 20:1 EtOAc:MeOH). The title compound was isolated as a solid in 76% yield (conditions A) or 71% yield (conditions B). **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 8.66 (d, *J* = 1.9 Hz, 1H), 8.55 (d, *J* = 1.9 Hz, 1H), 7.88 (d, *J* = 8.9 Hz, 1H), 7.19 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.14 (d, *J* = 2.5 Hz, 1H), 4.22 (s, 2H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 148.17, 145.21, 145.06, 141.18, 138.22, 130.60, 122.23, 108.16.

General Protocol for Amination Reaction with Methylamine Hydrochloride

In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with **2** (0.012-0.024 mmol, 2-4 mol %), aryl halide (0.60 mmol, 1 equiv), methylamine hydrochloride (1.80 mmol, 3 equiv), sodium *tert*-butoxide (2.7 mmol, 4.5 equiv), and toluene (6 mL). The flask was sealed with a Teflon-lined screw cap and removed from the glovebox. The reaction was stirred at 100 °C for 12 h. The reaction was quenched by addition of EtOAc (5 mL). The reaction mixture was filtered through Celite, and the volatile materials were evaporated *in vacuo*. The crude product was purified by flash column chromatography to afford the purified product.

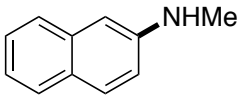
Characterization of Organic Products from Reaction with Methylamine Hydrochloride

***N*-Methylnaphthalen-1-amine** (**3a**) (CAS: 2216-68-4)



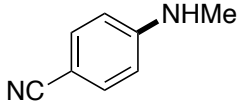
The reaction to form this product was conducted with 2 mol % **2**. The crude product was purified by column chromatography (10:1 Hexanes:EtOAc). The title compound was isolated as an oil in 93% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.85 (d, *J* = 7.9 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.51-7.42 (m, 3H), 7.30 (d, *J* = 8.1 Hz, 1H), 6.65 (d, *J* = 7.5 Hz, 1H), 4.53 (s, 1H), 3.04 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 31.66, 104.47, 117.96, 120.42, 124.05, 125.30, 126.32, 127.28, 129.26, 134.82, 145.07.

***N*-Methylnaphthalen-2-amine** (**3b**) (CAS: 2216-67-3)



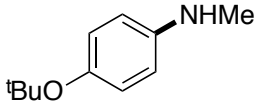
The reaction to form this product was conducted with 2 mol % **2**. The crude product was purified by column chromatography (10:1 Hexanes:EtOAc). The title compound was isolated as an oil in 97% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.75-7.68 (m, 3H), 7.44 (t, *J* = 7.5 Hz, 1H), 7.28-7.26 (m, 1H), 6.92 (d, *J* = 8.8 Hz, 1H), 6.86 (s, 1H), 3.91 (s, 1H), 2.97 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 31.21, 104.20, 118.36, 122.35, 126.40, 126.76, 127.93, 128.11, 129.26, 135.74, 147.41.

4-(Methylamino)benzonitrile (**3c**) (CAS: 4714-62-9)



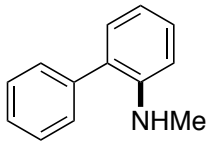
The reaction to form this product was conducted with 2 mol % **2**. The crude product was purified by column chromatography (2:1 Hexanes:EtOAc). The title compound was isolated as a white solid in 79% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.43 (d, *J* = 8.8 Hz, 2H), 6.55 (d, *J* = 8.8 Hz, 2H), 4.27 (s, 1H), 2.88 (d, *J* = 5.0 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 152.26, 133.81, 120.62, 112.05, 98.86, 30.16.

4-(*tert*-butoxy)-*N*-methylaniline (**3d**) (CAS: 1175905-77-7)



The reaction to form this product was conducted with 4 mol % **2**. The crude product was purified by column chromatography (5:1 Hexanes:EtOAc). The title compound was isolated as an oil in 99% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.85 (d, *J* = 8.8 Hz, 2H), 6.52 (d, *J* = 8.8 Hz, 2H), 3.53 (s, 1H), 2.81 (s, 3H), 1.29 (s, 9H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 146.38, 145.74, 125.50, 112.59, 77.77, 31.34, 28.82.

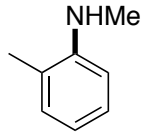
***N*-Methyl-[1,1'-biphenyl]-2-amine** (**3i**) (CAS: 14925-09-8)



The reaction to form this product was conducted with 4 mol % **2**. The crude product was purified by column chromatography (10:1 Hex-

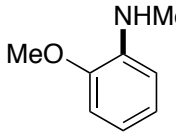
anes:EtOAc). The title compound was isolated as an oil in 83% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.47-7.43 (m, 4H), 7.37 (t, *J* = 6.4 Hz, 1H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.12 (d, *J* = 7.1 Hz, 1H), 6.81-6.79 (m, 1H), 6.72 (d, *J* = 7.9 Hz, 1H), 3.99 (s, 1H), 2.82 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 146.28, 139.63, 130.15, 129.54, 128.99, 128.89, 127.70, 127.30, 116.92, 109.91, 30.90.

***N*-Methyl-2-toluidine** (**3f**) (CAS: 611-21-2)



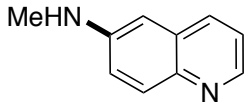
The reaction to form this product was conducted with 2 mol % **2**. The crude product was purified by column chromatography (6:1 Hexanes:EtOAc). The title compound was isolated as an oil in 99% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.19 (t, *J* = 7.7 Hz, 1H), 7.09 (d, *J* = 7.3 Hz, 1H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 3.59 (s, 1H), 2.92 (s, 3H), 2.16 (s, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 147.34, 130.01, 127.30, 122.00, 116.95, 109.22, 30.90, 17.52.

2-Methoxy-*N*-methylaniline (**3g**) (CAS: 10541-78-3)



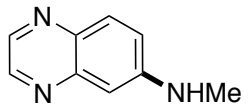
The reaction to form this product was conducted with 4 mol % **2**. The crude product was purified by column chromatography (10:1 Hexanes:EtOAc). The title compound was isolated as an oil in 84% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 6.93 (t, *J* = 7.6 Hz, 1H), 6.79 (d, *J* = 7.9 Hz, 1H), 6.70 (t, *J* = 7.7 Hz, 1H), 6.63 (d, *J* = 7.8 Hz, 1H), 4.26 (s, 1H), 3.86 (s, 3H), 2.89 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 146.99, 139.49, 121.45, 116.38, 109.42, 109.34, 55.50, 30.48.

***N*-Methylquinolin-6-amine** (**3l**) (CAS: 83407-38-9)



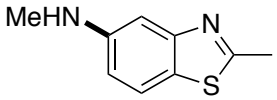
The reaction to form this product was conducted with 3 mol % **2**. The crude product was purified by column chromatography (1:3 Hexanes(containing 2.5% NEt_3):EtOAc). The title compound was isolated as an oil in 99% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.61-8.61 (m, 1H), 7.93 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 9.0 Hz, 1H), 7.27-7.25 (m, 1H), 7.08 (dd, *J* = 9.0, 2.0 Hz, 1H), 6.67 (s, 1H), 4.11 (s, 1H), 2.93 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 147.31, 146.12, 143.31, 133.92, 130.32, 130.21, 121.46, 121.42, 102.42, 30.78.

***N*-Methylquinoxalin-6-amine** (**3m**) (CAS: 1338986-47-2)



The reaction to form this product was conducted with 3 mol % **2**. The crude product was purified by column chromatography (100% EtOAc). The title compound was isolated as an oil in 86% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.64 (s, 1H), 8.50 (s, 1H), 7.82 (d, *J* = 9.0 Hz, 1H), 7.12 (dd, *J* = 9.0, 1.5 Hz, 1H), 6.94 (s, 1H), 4.36 (s, 1H), 2.98 (d, *J* = 4.4 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 150.31, 145.73, 145.02, 140.38, 138.15, 130.10, 122.21, 103.22, 30.59.

***N*,2-Dimethylbenzo[*d*]thiazol-5-amine** (**3n**) (CAS: 90558-52-4)



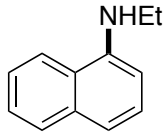
The reaction to form this product was conducted with 3 mol % **2**. The crude product was purified by column chromatography (1:2 Hexanes:EtOAc). The title compound was isolated as an oil in 52% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.53 (d, *J* = 8.6 Hz, 1H), 7.14 (s, 1H), 6.69 (d, *J* = 8.5 Hz, 1H), 3.87 (s, 1H), 2.88 (s, 3H), 2.78 (s, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 167.45, 155.07, 148.49, 123.95, 121.35, 113.15, 103.67, 30.98, 20.10.

General Protocol for Amination Reaction with Ethylamine Hydrochloride

In a nitrogen-filled glovebox, a 20 mL scintillation vial was charged with **5** (0.0060-0.018 mmol, 1-3 mol %), aryl halide (0.60 mmol, 1 equiv), ethylamine hydrochloride (0.72 mmol, 1.2 equiv), sodium *tert*-butoxide (1.50 mmol, 2.5 equiv), and toluene (3 mL). The flask was sealed with a Teflon-lined screw cap and removed from the glovebox. The reaction was stirred at 80 °C for 12 h. The reaction was quenched by addition of EtOAc (5 mL). The reaction mixture was filtered through Celite, and the volatile materials were evaporated *in vacuo*. The crude product was purified by flash column chromatography to afford the purified product.

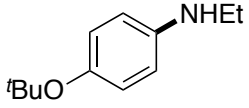
Characterization of Organic Products from Reaction with Ethylamine Hydrochloride

***N*-Ethylnaphthalen-1-amine** (**4a**) (CAS: 118-44-5)



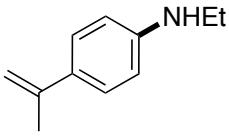
The reaction to form this product was conducted with 1 mol % **5**. The crude product was purified by column chromatography (20:1 Hexanes:EtOAc). The title compound was isolated as an oil in 99% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.83 (dd, *J* = 9.9, 8.3 Hz, 2H), 7.49-7.45 (m, 2H), 7.39 (t, *J* = 7.9 Hz, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 6.66 (d, *J* = 7.5 Hz, 1H), 4.42 (s, 1H), 3.35 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 143.56, 134.40, 128.77, 126.77, 125.78, 124.75, 123.46, 119.94, 117.43, 104.56, 38.92, 14.87.

4-(*tert*-Butoxy)-*N*-ethylaniline (**4d**) (CAS: 1368636-78-5)



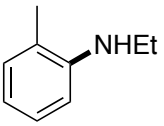
The reaction to form this product was conducted with 3 mol % **5**. The crude product was purified by column chromatography (7:1 Hexanes:EtOAc). The title compound was isolated as an oil in 92% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 6.84-6.82 (m, 2H), 6.53-6.50 (m, 2H), 3.38 (s, 1H), 3.12 (q, *J* = 7.1 Hz, 2H), 1.29 (s, 9H), 1.24 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 146.41, 144.89, 125.51, 112.97, 77.74, 39.15, 28.84, 15.11.

4-(prop-1-en-2-yl)aniline (**4e**)



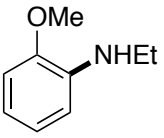
The reaction to form this product was conducted with 2 mol % **5**. The crude product was purified by column chromatography (8:1 Hexanes:EtOAc). The title compound was isolated as an oil in 84% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.39-7.36 (m, 2H), 6.62-6.58 (m, 2H), 5.29 (t, *J* = 0.7 Hz, 1H), 4.94 (t, *J* = 1.5 Hz, 1H), 3.62 (s, 1H), 3.20 (q, *J* = 7.1 Hz, 2H), 2.15 (t, *J* = 0.6 Hz, 3H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 147.98, 142.86, 130.13, 126.50, 112.40, 108.78, 38.55, 21.95, 14.97.

***N*-Ethyl-2-toluidine** (**4f**) (CAS: 94-68-8)



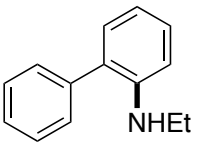
The reaction to form this product was conducted with 3 mol % **5**. The crude product was purified by column chromatography (15:1 Hexanes:EtOAc). The title compound was isolated as an oil in 87% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.17 (td, *J* = 7.7, 1.1 Hz, 1H), 7.09 (d, *J* = 7.3 Hz, 1H), 6.69 (td, *J* = 7.4, 1.0 Hz, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 3.41 (s, 1H), 3.24 (q, *J* = 7.1 Hz, 2H), 2.17 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 146.38, 130.01, 127.14, 121.70, 116.75, 109.66, 38.43, 17.45, 15.02.

***N*-Ethyl-2-methoxyaniline** (**4g**) (CAS: 15258-43-2)



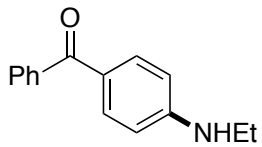
The reaction to form this product was conducted with 3 mol % **5**. The crude product was purified by column chromatography (15:1 Hexanes:EtOAc). The title compound was isolated as an oil in 85% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 6.90 (td, *J* = 7.6, 1.4 Hz, 1H), 6.79 (dd, *J* = 7.9, 1.3 Hz, 1H), 6.69 (td, *J* = 7.7, 1.5 Hz, 1H), 6.64 (dd, *J* = 7.8, 1.5 Hz, 1H), 4.13 (s, 1H), 3.87 (s, 3H), 3.19 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 146.73, 138.44, 121.31, 116.22, 109.80, 109.34, 55.36, 38.16, 14.88.

***N*-Ethyl-[1,1'-biphenyl]-2-amine** (**4i**) (CAS: 77989-56-1)



The reaction to form this product was conducted with 2 mol % **5**. The crude product was purified by column chromatography (15:1 Hexanes:EtOAc). The title compound was isolated as an oil in 98% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 7.49-7.45 (m, 4H), 7.40-7.37 (m, *J* = 1.9 Hz, 1H), 7.29-7.26 (m, 1H), 7.12 (dt, *J* = 7.4, 1.9 Hz, 1H), 6.80 (tdd, *J* = 7.4, 2.1, 1.1 Hz, 1H), 6.74 (d, *J* = 8.2 Hz, 1H), 3.88 (s, 1H), 3.18 (qd, *J* = 7.1, 1.6 Hz, 2H), 1.20 (td, *J* = 7.1, 1.8 Hz, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 145.29, 139.66, 130.28, 129.44, 128.94, 128.79, 127.55, 127.21, 116.79, 110.46, 38.56, 14.85.

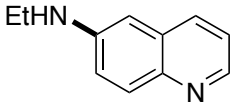
(4-aminophenyl)(phenyl)methanone (**4j**)



The reaction to form this product was conducted with 2 mol % **5**. The crude product was purified by column chromatography (4:1 Hexanes:EtOAc). The title compound was isolated as a solid in 96% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.76-7.70 (m, 4H), 7.52

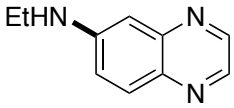
(t, *J* = 7.3 Hz, 1H), 7.45 (t, *J* = 7.3 Hz, 2H), 6.57 (d, *J* = 8.8 Hz, 2H), 4.22 (s, 1H), 3.24 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 195.26, 152.25, 139.33, 133.14, 131.27, 129.55, 128.13, 126.02, 111.31, 38.02, 14.74.

***N*-ethylquinolin-6-amine** (**4l**) (CAS: 860199-85-5)



The reaction to form this product was conducted with 2 mol % **5**. The crude product was purified by column chromatography (1:2 Hexanes(containing 2.5% NEt_3):EtOAc). The title compound was isolated as an oil in 84% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.60 (dd, *J* = 4.2, 1.6 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.86 (d, *J* = 9.0 Hz, 1H), 7.25 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.07 (dd, *J* = 9.0, 2.6 Hz, 1H), 6.68 (d, *J* = 2.6 Hz, 1H), 3.92 (s, 1H), 3.26 (q, *J* = 7.2 Hz, 2H), 1.32 (t, *J* = 7.2 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 146.24, 146.02, 143.19, 133.70, 130.19, 130.18, 121.34, 121.30, 102.78, 38.44, 14.61.

***N*-ethylquinoxalin-6-amine** (**4m**) (CAS: 1179094-62-2)



The reaction to form this product was conducted with 2 mol % **5**. The crude product was purified by column chromatography (100% EtOAc). The title compound was isolated as an oil in 71% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 8.62 (d, *J* = 1.9 Hz, 1H), 8.48 (d, *J* = 1.9 Hz, 1H), 7.81 (d, *J* = 9.1 Hz, 1H), 7.09 (dd, *J* = 9.1, 2.6 Hz, 1H), 6.94 (d, *J* = 2.6 Hz, 1H), 4.21 (s, 1H), 3.32-3.27 (m, 2H), 1.33 (t, *J* = 7.2 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 149.24, 145.57, 144.84, 140.15, 137.93, 129.97, 122.18, 103.35, 38.22, 14.37.

Synthesis of C5A

In a nitrogen-filled glovebox, a 20 mL vial was charged with $Ni(COD)_2$ (88 mg), **L5** (220 mg), and 2 mL toluene. 4-Chlorobenzonitrile (165 mg) was added, and the mixture was stirred at RT for 30 min at which point a red precipitate was formed. Pentane (2 mL) was added to aid precipitation of the compound, which was collected by filtration, rinsed with pentane, and dried on high vacuum to yield the title compound in 86-92% yield. A single crystal suitable for X-ray analysis was prepared by slow diffusion of hexanes into a saturated solution of the compound in toluene at RT.

^{31}P-NMR (162 MHz, THF): δ 67.05 (d, *J* = 39.0 Hz), 14.81 (d, *J* = 39.0 Hz).
^{1}H-NMR (500 MHz, THF): δ 7.96 (t, *J* = 8.6 Hz, 2H), 7.69 (t, *J* = 8.8 Hz, 2H), 7.50-7.42 (m, 6H), 6.51 (d, *J* = 7.7 Hz, 2H), 4.62 (s, 1H), 4.28 (s, 1H), 3.80 (d, *J* = 16.7 Hz, 5H), 3.47 (s, 1H), 2.07 (s, 3H), 1.80 (d, *J* = 11.4 Hz, 9H), 1.29 (d, *J* = 12.6 Hz, 9H).
Elemental Analysis: Calc'd: C, 63.41; H, 6.00; N, 1.90. Found: C, 63.06; H, 5.92; N, 1.82.
CCDC: 1043705

Synthesis of C2A

In a nitrogen-filled glovebox, a 4 mL vial was charged with **C2** (50 mg), 4-chlorotoluene (39 μL) and 2 mL THF. The solution was stirred at RT for 30 min and at 50 °C for 1 h (full conversion of **2** by ^{31}P NMR spectroscopy). The volatiles were removed in vacuo. The product was partially solubilized with ether (0.2 mL) and the compound was precipitated with pentane (1mL). The precipitate was collected by filtration, rinsed with pentane, and dried under high vacuum to yield the title compound in 67% yield as a red solid.

^{31}P-NMR (162 MHz, THF): δ 49.99 (d, *J* = 39.0 Hz), 13.19 (d, *J* = 38.8 Hz).
^{1}H-NMR (500 MHz, THF): δ 7.32-7.26 (m, 9H), 7.16 (t, *J* = 7.0 Hz, 2H), 6.37 (t, *J* = 6.2 Hz, 2H), 6.09 (d, *J* = 7.5 Hz, 2H), 4.70 (s, 1H), 4.23 (s, 6H), 4.01 (s, 1H), 3.24 (t, *J* = 6.1 Hz, 1H), 2.81 (q, *J* = 11.5 Hz, 1H), 2.57 (q, *J* = 11.3 Hz, 1H), 2.38-2.33 (m, 2H), 2.28-2.22 (m, 3H), 2.13-2.05 (m, 3H), 1.98 (d, *J* = 11.3 Hz, 1H), 1.92 (s, 3H), 1.89-1.75 (m, 5H), 1.55-1.48 (m, 3H), 1.36 (d, *J* = 7.7 Hz, 3H), 1.24 (dd, *J* = 10.9, 6.9 Hz, 3H).
Elemental Analysis: Calc'd: C, 66.23; H, 6.59. Found: C, 65.90; H, 6.45.

Synthesis of C2B

In a nitrogen-filled glovebox, a 4 mL vial was charged with **C2** (50 mg), 4-*tert*-butoxychlorobenzene (61 mg) and 2 mL THF. The solution was stirred at RT for 30 min and at 50 °C for 1 h (full conversion of **2** by ^{31}P NMR spectroscopy). The volatiles were removed in vacuo. The product was partially solubilized with ether (0.2 mL) and the compound was precipitated with pentane (1mL). The precipitate was collected by filtration, rinsed with pentane, and dried under high vacuum to yield the title compound in 65% yield as a red solid.

^{31}P-NMR (162 MHz, $CDCl_3$): δ 50.29 (d, *J* = 39.4 Hz), 13.34 (d, *J* = 39.3 Hz,).
^{1}H-NMR (600 MHz, THF): δ 7.39-7.32 (m, 6H), 7.29 (t, *J* = 7.1 Hz, 2H), 7.18 (td, *J* = 7.7, 1.5 Hz, 2H), 6.37 (t, *J* = 6.1 Hz, 2H), 5.97 (d, *J* = 7.3 Hz, 2H), 4.69 (s, 1H), 4.23 (s, 6H), 3.99 (s, 1H), 3.25 (quintet, *J* = 6.2 Hz, 1H), 2.81 (q, *J* = 11.2 Hz, 1H), 2.58 (q, *J* = 11.0 Hz, 1H), 2.41-2.31 (m, 2H), 2.31-2.18 (m, 3H), 2.16-2.05 (m, 3H), 1.99 (d, *J* = 12.2 Hz, 1H), 1.91-1.81 (m, 4H), 1.60-1.49 (m, 3H), 1.37 (q, *J* = 9.0 Hz, 3H), 1.23 (dd, *J* = 10.9, 6.9 Hz, 3H), 1.10-1.04 (m, 9H).
Elemental Analysis: Calc'd: C, 65.94; H, 6.86. Found: C, 65.69; H, 6.91.

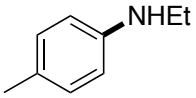
Synthesis of C2C

In a nitrogen-filled glovebox, a 4 mL vial was charged with **C2** (50 mg), 2-ethoxychlorobenzene (52 mg) and 2 mL THF. The solution was stirred at RT for 30 min and at 50 °C for 1 h (full conversion of **2** by ^{31}P NMR spectroscopy). The volatiles were removed in vacuo. The product was partially solubilized with ether (0.2 mL) and the compound was precipitated with pentane (1mL). The precipitate was collected by filtration, rinsed with pentane, and dried under high vacuum to yield the title compound in 62% yield as a red solid as a 4:1 mixture of isomers, as determined by ^{31}P NMR spectroscopy.

^{31}P-NMR (162 MHz, THF): δ 51.12 (d, *J* = 41.9 Hz, major), 48.61 (d, *J* = 43.1 Hz, minor), 12.05 (d, *J* = 42.5 Hz, major), 11.02 (d, *J* = 42.9 Hz, minor).
^{1}H-NMR (500 MHz, THF): δ 7.86-7.83 (m, 2H), 7.49 (s, 1H), 7.36 (t, *J* = 7.2 Hz, 1H), 7.25 (t, *J* = 7.1 Hz, 2H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.03-6.94 (m, 2H), 6.78 (t, *J* = 8.7 Hz, 1H), 6.35 (q, *J* = 7.0 Hz, 1H), 6.30 (t, *J* = 7.5 Hz, 1H), 6.06-6.03 (m, 1H), 5.63-5.54 (m, 1H), 4.76 (s, 1H), 4.44 (d, *J* = 19.3 Hz,), 4.21 (d, *J* = 8.4 Hz, 6H), 4.06 (t, *J* = 2.2 Hz, 1H), 3.74 (s, 1H), 2.91 (t, *J* = 7.6 Hz, 1H), 2.69-2.62 (m, 2H), 2.56-2.51 (m, 1H), 2.43-2.34 (m, 2H), 2.26-2.14 (m, 2H), 2.07-2.03 (m, 2H), 2.03-1.95 (m, 2H), 1.94-1.76 (m, 7H), 1.46 (t, *J* = 6.9 Hz, 5H), 1.42-1.35 (m, 3H), 1.30-1.26 (m, 1H), 1.21 (dd, *J* = 10.7, 6.9 Hz, 3H), 0.91 (dt, *J* = 32.1, 7.0 Hz, 1H).
Elemental Analysis: Calc'd: C, 65.26; H, 6.60. Found: C, 64.95; H, 6.80.

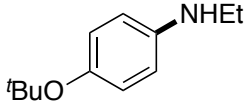
*Characterization of Organic Products from Reaction with Ethylamine Hydrochloride Catalyzed by Compounds **C2A**, **C2B**, **C2C**.*

***N*-ethyl-4-toluidine** (CAS: 622-57-1)



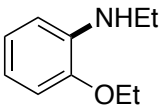
The reaction to form this product was conducted with 2 mol % **8a**. The crude product was purified by column chromatography (7:1 Hexanes:EtOAc). The title compound was isolated as an oil in 82% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 7.02-7.00 (m, 2H), 6.56 (d, *J* = 8.4 Hz, 2H), 3.38 (s, 1H), 3.15 (q, *J* = 7.1 Hz, 2H), 2.26 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 146.34, 129.82, 126.54, 113.08, 38.95, 20.51, 15.08.

***N*-ethyl-4-*tert*-butoxyaniline** (CAS: 1368636-78-5)



The reaction to form this product was conducted with 3 mol % **3b** and 8 mol % benzonitrile as an additive. The crude product was purified by column chromatography (7:1 Hexanes:EtOAc). The title compound was isolated as an oil in 95% yield. **^{1}H-NMR** (600 MHz, $CDCl_3$): δ 6.83 (d, *J* = 8.8 Hz, 2H), 6.51 (d, *J* = 8.8 Hz, 2H), 3.35 (s, 1H), 3.11 (q, *J* = 7.1 Hz, 2H), 1.29 (s, 9H), 1.24 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (151 MHz, $CDCl_3$): δ 146.37, 144.87, 125.49, 112.95, 77.73, 39.12, 28.81, 15.09.

2-ethoxy-*N*-ethylaniline (CAS: 13519-73-8)



The reaction to form this product was conducted with 2 mol % **3c** and 8 mol % benzonitrile as an additive. The crude product was purified by column chromatography (3:1 Hexanes:EtOAc). The title compound was isolated as an oil in 84% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.89-6.85 (m, 1H), 6.76 (dd, *J* = 7.9, 1.3 Hz, 1H), 6.67-6.61 (m, 2H), 4.14 (s, 1H), 4.07 (q, *J* = 7.0 Hz, 2H), 3.19 (q, *J* = 7.1 Hz, 2H), 1.45 (t, *J* = 7.0 Hz, 3H), 1.30 (t, *J* = 7.2 Hz, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 146.04, 138.54, 121.23, 116.24, 110.38, 109.89, 63.73, 38.22, 15.06, 14.96.

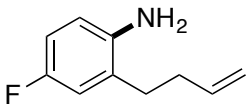
Protocol to Set Up Amination Reaction in Air

In air, a 25 mL Schlenk bomb was charged with **7** (0.012-0.024 mmol, 2-4 mol %), ammonium sulfate (0.90 mmol, 1.5 equiv), sodium *tert*-butoxide (2.7 mmol, 4.5 equiv), and aryl halide (if solid) (0.60 mmol, 1 equiv). The flask was purged with N_2 on the Schlenk line. The flask was then charged with 2-Me-THF (3 mL), and aryl halide (if liquid) (0.60 mmol, 1 equiv) via syringe. The flask was sealed and stirred at 100 °C for 7 h.

Characterization of Organic Products from Reaction with Radical Probe Substrates

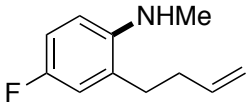
Substrate **1o** was prepared by addition of allyl Grignard reagent to 2-(bromomethyl)-1-chloro-4-fluorobenzene at -78 °C in THF.[42]

2-(but-3-en-1-yl)-4-fluoroaniline (2o)



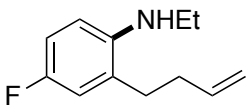
The reaction to form this product was conducted with 4 mol % **2** following protocol B. The crude product was purified by column chromatography (5:1 Hexanes:EtOAc). The title compound was isolated as an oil in 74% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.80-6.72 (m, 2H), 6.61 (dd, J = 8.6, 5.0 Hz, 1H), 5.89 (ddt, J = 17.0, 10.3, 6.6 Hz, 1H), 5.10 (dq, J = 17.1, 1.7 Hz, 1H), 5.03 (dq, J = 10.2, 1.5 Hz, 1H), 3.49 (s, 2H), 2.56 (m, 2H), 2.40-2.35 (m, 2H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 156.48 (d, $J_{C\text{-}F}$ = 235.6 Hz), 140.08 (d, $J_{C\text{-}F}$ = 2.0 Hz), 137.65, 127.74 (d, $J_{C\text{-}F}$ = 7.0 Hz), 116.37 (d, $J_{C\text{-}F}$ = 7.8 Hz), 115.74 (d, $J_{C\text{-}F}$ = 22.5 Hz), 115.50, 113.24 (d, $J_{C\text{-}F}$ = 22.2 Hz), 32.60, 30.70.

2-(but-3-en-1-yl)-4-fluoro-*N*-methylaniline (3o)



The reaction to form this product was conducted with 4 mol % **2**. The crude product was purified by column chromatography (10:1 Hexanes:EtOAc). The title compound was isolated as an oil in 57% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.89-6.81 (m, 2H), 6.89-6.81 (m, 2H), 6.55 (dd, J = 8.7, 4.8 Hz, 1H), 6.55 (dd, J = 8.7, 4.8 Hz, 1H), 5.90 (ddt, J = 17.0, 10.3, 6.6 Hz, 1H), 5.90 (ddt, J = 17.0, 10.3, 6.6 Hz, 1H), 5.11 (dd, J = 17.1, 1.5 Hz, 1H), 5.11 (dd, J = 17.1, 1.5 Hz, 1H), 5.05 (d, J = 10.2 Hz, 1H), 5.05 (d, J = 10.2 Hz, 1H), 3.63-3.39 (m, 1H), 3.52-3.48 (m, 1H), 2.87 (s, 3H), 2.87 (s, 3H), 2.54 (dd, J = 9.2, 6.4 Hz, 2H), 2.54 (m, 2H), 2.38 (q, J = 7.4 Hz, 2H), 2.38 (q, J = 7.4 Hz, 2H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 155.64 (d, $J_{C\text{-}F}$ = 234.3 Hz), 143.11 (d, $J_{C\text{-}F}$ = 1.8 Hz), 137.73, 127.24 (d, $J_{C\text{-}F}$ = 6.5 Hz), 115.58 (d, $J_{C\text{-}F}$ = 22.4 Hz), 115.40, 112.95 (d, $J_{C\text{-}F}$ = 21.7 Hz), 110.34 (d, $J_{C\text{-}F}$ = 7.6 Hz), 32.35, 31.40, 30.36.

2-(but-3-en-1-yl)-*N*-ethyl-4-fluoroaniline (4o)



The reaction to form this product was conducted with 3 mol % **5**. The crude product was purified by column chromatography (20:1

Hexanes:EtOAc). The title compound was isolated as an oil in 84% yield. **^{1}H-NMR** (400 MHz, $CDCl_3$): δ 6.83 (tdd, *J* = 7.7, 4.6, 3.3 Hz, 2H), 6.56 (dd, *J* = 8.6, 4.9 Hz, 1H), 5.91 (dd, *J* = 17.0, 10.3 Hz, 1H), 5.12 (dq, *J* = 17.1, 1.6 Hz, 1H), 5.05 (dq, *J* = 10.2, 1.4 Hz, 1H), 3.30 (s, 1H), 3.17 (q, *J* = 7.1 Hz, 2H), 2.55 (dd, *J* = 9.1, 6.3 Hz, 2H), 2.40 (q, *J* = 7.2 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (101 MHz, $CDCl_3$): δ 155.54 (d, $J_{C\text{-}F}$ = 234.3 Hz), 142.27 (d, $J_{C\text{-}F}$ = 1.9 Hz), 137.77, 127.11 (d, $J_{C\text{-}F}$ = 6.5 Hz), 115.58 (d, $J_{C\text{-}F}$ = 22.6 Hz), 115.43, 112.96 (d, $J_{C\text{-}F}$ = 21.7 Hz), 111.00 (d, $J_{C\text{-}F}$ = 7.7 Hz), 39.13, 32.41, 30.41, 15.02.

X-ray crystal structures

X-ray Crystallographic Analysis of (PPF-tBu)Ni(η^2-NCPh) (C5)

An orange rod 0.070 x 0.060 x 0.020 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using and scans. Crystal-to-detector distance was 40 mm and exposure time was 10 seconds per frame using a scan width of 0.5°. Data collection was 100.0% complete to 25.000° in θ. A total of 78606 reflections were collected covering the indices, -50<=*h*<=50, -50<=*k*<=50, -14<=*l*<=13. 7360 reflections were found to be symmetry independent, with an R_{int} of 0.0396. Indexing and unit cell refinement indicated a reverse, trigonal lattice. The space group was found to be R -3 :H (No. 148). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by direct methods (SIR-97) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2012). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2012. SQUEEZE was used to treat the disordered pentane solvent that cocrystallized with the target molecule and its use has been noted in the CIF file

Crystal data and structure refinement

Empirical formula C39 H45 Fe N Ni P2
Formula weight 704.26
Temperature 100(2) K
Wavelength 0.71073 Å
Crystal system Trigonal
Space group R -3 :H
Unit cell dimensions a = 41.8743(18) Å α= 90°.
b = 41.8743(18) Å β= 90°.
c = 11.8311(5) Å γ = 120°.
Volume 17966.0(17) Å^3
Z 18
Density (calculated) 1.172 Mg/m^3
Absorption coefficient 0.939 mm^{-1}
F(000) 6660

Crystal size	0.070 x 0.060 x 0.020 mm^3
Crystal color/habit	orange rod
Theta range for data collection	1.685 to 25.389°.
Index ranges	-50<=h<=50, -50<=k<=50, -14<=l<=13
Reflections collected	78606
Independent reflections	7360 [R(int) = 0.0396]
Completeness to theta = 25.000°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.862 and 0.800
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	7360 / 0 / 404
Goodness-of-fit on F^2	1.062
Final R indices [I>2sigma(I)]	R1 = 0.0270, wR2 = 0.0677
R indices (all data)	R1 = 0.0317, wR2 = 0.0695
Extinction coefficient	n/a
Largest diff. peak and hole	0.381 and -0.253 $e.Å^{-3}$

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	4299(1)	909(1)	9084(2)	14(1)
C(2)	3915(1)	796(1)	8806(2)	14(1)
C(3)	3658(1)	710(1)	9676(2)	17(1)
C(4)	3298(1)	612(1)	9430(2)	19(1)
C(5)	3185(1)	590(1)	8315(2)	22(1)
C(6)	3437(1)	675(1)	7451(2)	24(1)
C(7)	3801(1)	780(1)	7692(2)	19(1)
C(8)	5282(1)	805(1)	10361(2)	19(1)
C(9)	5630(1)	785(1)	10607(2)	29(1)
C(10)	5135(1)	879(1)	11458(2)	25(1)
C(11)	4982(1)	427(1)	9931(2)	22(1)
C(12)	5571(1)	1638(1)	9846(2)	25(1)
C(13)	5913(1)	1738(1)	10564(2)	34(1)
C(14)	5304(1)	1708(1)	10552(2)	30(1)
C(15)	5681(1)	1896(1)	8818(2)	35(1)
C(16)	5613(1)	1153(1)	8074(2)	16(1)
C(17)	6028(1)	1298(1)	8263(2)	24(1)
C(18)	5431(1)	783(1)	7487(1)	14(1)
C(19)	5572(1)	538(1)	7401(2)	16(1)
C(20)	5329(1)	231(1)	6729(2)	18(1)
C(21)	5031(1)	280(1)	6394(2)	15(1)
C(22)	5086(1)	619(1)	6870(1)	13(1)
C(23)	5589(1)	1064(1)	4530(2)	24(1)
C(24)	5910(1)	1213(1)	5214(2)	22(1)
C(25)	6046(1)	964(1)	5203(2)	22(1)
C(26)	5807(1)	660(1)	4515(2)	23(1)
C(27)	5525(1)	722(1)	4101(2)	24(1)
C(28)	4312(1)	315(1)	6862(1)	13(1)
C(29)	4027(1)	259(1)	6134(2)	17(1)

C(30)	3691(1)	-69(1)	6153(2)	21(1)
C(31)	3637(1)	-347(1)	6895(2)	21(1)
C(32)	3918(1)	-296(1)	7630(2)	20(1)
C(33)	4251(1)	32(1)	7614(2)	16(1)
C(34)	4757(1)	1006(1)	5726(2)	14(1)
C(35)	4817(1)	1362(1)	5815(2)	23(1)
C(36)	4824(1)	1557(1)	4856(2)	33(1)
C(37)	4763(1)	1395(1)	3802(2)	29(1)
C(38)	4703(1)	1041(1)	3700(2)	22(1)
C(39)	4705(1)	850(1)	4652(2)	17(1)
N(1)	4493(1)	1014(1)	9930(1)	19(1)
P(1)	5316(1)	1150(1)	9268(1)	14(1)
P(2)	4741(1)	760(1)	7018(1)	11(1)
Fe(1)	5520(1)	710(1)	5834(1)	13(1)
Ni(1)	4759(1)	984(1)	8649(1)	12(1)

Bond lengths [Å] and angles [°]

C(1)-N(1)	1.225(2)	C(8)-P(1)	1.8895(19)
C(1)-C(2)	1.469(3)	C(9)-H(9A)	0.9800
C(1)-Ni(1)	1.8636(18)	C(9)-H(9B)	0.9800
C(2)-C(7)	1.391(3)	C(9)-H(9C)	0.9800
C(2)-C(3)	1.399(3)	C(10)-H(10A)	0.9800
C(3)-C(4)	1.382(3)	C(10)-H(10B)	0.9800
C(3)-H(3)	0.9500	C(10)-H(10C)	0.9800
C(4)-C(5)	1.388(3)	C(11)-H(11A)	0.9800
C(4)-H(4)	0.9500	C(11)-H(11B)	0.9800
C(5)-C(6)	1.381(3)	C(11)-H(11C)	0.9800
C(5)-H(5)	0.9500	C(12)-C(13)	1.534(3)
C(6)-C(7)	1.389(3)	C(12)-C(15)	1.537(3)
C(6)-H(6)	0.9500	C(12)-C(14)	1.537(3)
C(7)-H(7)	0.9500	C(12)-P(1)	1.897(2)
C(8)-C(9)	1.532(3)	C(13)-H(13A)	0.9800
C(8)-C(10)	1.533(3)	C(13)-H(13B)	0.9800
C(8)-C(11)	1.535(3)	C(13)-H(13C)	0.9800

C(14)-H(14A)	0.9800	C(25)-Fe(1)	2.0489(18)
C(14)-H(14B)	0.9800	C(25)-H(25)	0.9500
C(14)-H(14C)	0.9800	C(26)-C(27)	1.418(3)
C(15)-H(15A)	0.9800	C(26)-Fe(1)	2.0435(19)
C(15)-H(15B)	0.9800	C(26)-H(26)	0.9500
C(15)-H(15C)	0.9800	C(27)-Fe(1)	2.0510(19)
C(16)-C(18)	1.511(3)	C(27)-H(27)	0.9500
C(16)-C(17)	1.541(2)	C(28)-C(29)	1.394(3)
C(16)-P(1)	1.8786(18)	C(28)-C(33)	1.399(3)
C(16)-H(16)	1.0000	C(28)-P(2)	1.8403(18)
C(17)-H(17A)	0.9800	C(29)-C(30)	1.390(3)
C(17)-H(17B)	0.9800	C(29)-H(29)	0.9500
C(17)-H(17C)	0.9800	C(30)-C(31)	1.382(3)
C(18)-C(19)	1.423(3)	C(30)-H(30)	0.9500
C(18)-C(22)	1.447(2)	C(31)-C(32)	1.391(3)
C(18)-Fe(1)	2.0427(17)	C(31)-H(31)	0.9500
C(19)-C(20)	1.418(3)	C(32)-C(33)	1.386(3)
C(19)-Fe(1)	2.0403(18)	C(32)-H(32)	0.9500
C(19)-H(19)	0.9500	C(33)-H(33)	0.9500
C(20)-C(21)	1.417(3)	C(34)-C(35)	1.387(3)
C(20)-Fe(1)	2.0428(19)	C(34)-C(39)	1.395(3)
C(20)-H(20)	0.9500	C(34)-P(2)	1.8262(18)
C(21)-C(22)	1.434(2)	C(35)-C(36)	1.389(3)
C(21)-Fe(1)	2.0464(18)	C(35)-H(35)	0.9500
C(21)-H(21)	0.9500	C(36)-C(37)	1.382(3)
C(22)-P(2)	1.8220(17)	C(36)-H(36)	0.9500
C(22)-Fe(1)	2.0632(17)	C(37)-C(38)	1.378(3)
C(23)-C(27)	1.414(3)	C(37)-H(37)	0.9500
C(23)-C(24)	1.418(3)	C(38)-C(39)	1.384(3)
C(23)-Fe(1)	2.0585(19)	C(38)-H(38)	0.9500
C(23)-H(23)	0.9500	C(39)-H(39)	0.9500
C(24)-C(25)	1.417(3)	N(1)-Ni(1)	1.9199(15)
C(24)-Fe(1)	2.0511(19)	P(1)-Ni(1)	2.2012(5)
C(24)-H(24)	0.9500	P(2)-Ni(1)	2.1304(5)
C(25)-C(26)	1.419(3)		

N(1)-C(1)-C(2)	136.38(17)	C(8)-C(10)-H(10C)	109.5
N(1)-C(1)-Ni(1)	73.62(11)	H(10A)-C(10)-H(10C)	109.5
C(2)-C(1)-Ni(1)	149.99(14)	H(10B)-C(10)-H(10C)	109.5
C(7)-C(2)-C(3)	119.07(17)	C(8)-C(11)-H(11A)	109.5
C(7)-C(2)-C(1)	121.34(16)	C(8)-C(11)-H(11B)	109.5
C(3)-C(2)-C(1)	119.57(16)	H(11A)-C(11)-H(11B)	109.5
C(4)-C(3)-C(2)	120.28(18)	C(8)-C(11)-H(11C)	109.5
C(4)-C(3)-H(3)	119.9	H(11A)-C(11)-H(11C)	109.5
C(2)-C(3)-H(3)	119.9	H(11B)-C(11)-H(11C)	109.5
C(3)-C(4)-C(5)	120.30(18)	C(13)-C(12)-C(15)	109.65(18)
C(3)-C(4)-H(4)	119.8	C(13)-C(12)-C(14)	108.47(17)
C(5)-C(4)-H(4)	119.8	C(15)-C(12)-C(14)	106.69(18)
C(6)-C(5)-C(4)	119.76(18)	C(13)-C(12)-P(1)	116.04(15)
C(6)-C(5)-H(5)	120.1	C(15)-C(12)-P(1)	106.36(14)
C(4)-C(5)-H(5)	120.1	C(14)-C(12)-P(1)	109.24(14)
C(5)-C(6)-C(7)	120.34(19)	C(12)-C(13)-H(13A)	109.5
C(5)-C(6)-H(6)	119.8	C(12)-C(13)-H(13B)	109.5
C(7)-C(6)-H(6)	119.8	H(13A)-C(13)-H(13B)	109.5
C(6)-C(7)-C(2)	120.23(18)	C(12)-C(13)-H(13C)	109.5
C(6)-C(7)-H(7)	119.9	H(13A)-C(13)-H(13C)	109.5
C(2)-C(7)-H(7)	119.9	H(13B)-C(13)-H(13C)	109.5
C(9)-C(8)-C(10)	109.92(16)	C(12)-C(14)-H(14A)	109.5
C(9)-C(8)-C(11)	108.38(16)	C(12)-C(14)-H(14B)	109.5
C(10)-C(8)-C(11)	106.56(16)	H(14A)-C(14)-H(14B)	109.5
C(9)-C(8)-P(1)	117.56(14)	C(12)-C(14)-H(14C)	109.5
C(10)-C(8)-P(1)	108.04(13)	H(14A)-C(14)-H(14C)	109.5
C(11)-C(8)-P(1)	105.79(12)	H(14B)-C(14)-H(14C)	109.5
C(8)-C(9)-H(9A)	109.5	C(12)-C(15)-H(15A)	109.5
C(8)-C(9)-H(9B)	109.5	C(12)-C(15)-H(15B)	109.5
H(9A)-C(9)-H(9B)	109.5	H(15A)-C(15)-H(15B)	109.5
C(8)-C(9)-H(9C)	109.5	C(12)-C(15)-H(15C)	109.5
H(9A)-C(9)-H(9C)	109.5	H(15A)-C(15)-H(15C)	109.5
H(9B)-C(9)-H(9C)	109.5	H(15B)-C(15)-H(15C)	109.5
C(8)-C(10)-H(10A)	109.5	C(18)-C(16)-C(17)	111.26(15)
C(8)-C(10)-H(10B)	109.5	C(18)-C(16)-P(1)	110.21(12)
H(10A)-C(10)-H(10B)	109.5	C(17)-C(16)-P(1)	120.32(13)

C(18)-C(16)-H(16)	104.5	C(21)-C(22)-Fe(1)	68.95(10)
C(17)-C(16)-H(16)	104.5	C(18)-C(22)-Fe(1)	68.60(10)
P(1)-C(16)-H(16)	104.5	P(2)-C(22)-Fe(1)	139.93(10)
C(16)-C(17)-H(17A)	109.5	C(27)-C(23)-C(24)	108.01(18)
C(16)-C(17)-H(17B)	109.5	C(27)-C(23)-Fe(1)	69.59(11)
H(17A)-C(17)-H(17B)	109.5	C(24)-C(23)-Fe(1)	69.54(11)
C(16)-C(17)-H(17C)	109.5	C(27)-C(23)-H(23)	126.0
H(17A)-C(17)-H(17C)	109.5	C(24)-C(23)-H(23)	126.0
H(17B)-C(17)-H(17C)	109.5	Fe(1)-C(23)-H(23)	126.5
C(19)-C(18)-C(22)	107.36(15)	C(25)-C(24)-C(23)	108.22(18)
C(19)-C(18)-C(16)	126.35(16)	C(25)-C(24)-Fe(1)	69.70(11)
C(22)-C(18)-C(16)	126.25(16)	C(23)-C(24)-Fe(1)	70.10(11)
C(19)-C(18)-Fe(1)	69.52(10)	C(25)-C(24)-H(24)	125.9
C(22)-C(18)-Fe(1)	70.12(10)	C(23)-C(24)-H(24)	125.9
C(16)-C(18)-Fe(1)	123.85(13)	Fe(1)-C(24)-H(24)	125.9
C(20)-C(19)-C(18)	108.80(16)	C(24)-C(25)-C(26)	107.65(17)
C(20)-C(19)-Fe(1)	69.77(10)	C(24)-C(25)-Fe(1)	69.87(11)
C(18)-C(19)-Fe(1)	69.70(10)	C(26)-C(25)-Fe(1)	69.50(11)
C(20)-C(19)-H(19)	125.6	C(24)-C(25)-H(25)	126.2
C(18)-C(19)-H(19)	125.6	C(26)-C(25)-H(25)	126.2
Fe(1)-C(19)-H(19)	126.5	Fe(1)-C(25)-H(25)	126.0
C(21)-C(20)-C(19)	108.23(16)	C(27)-C(26)-C(25)	108.18(18)
C(21)-C(20)-Fe(1)	69.86(10)	C(27)-C(26)-Fe(1)	70.02(11)
C(19)-C(20)-Fe(1)	69.59(11)	C(25)-C(26)-Fe(1)	69.91(11)
C(21)-C(20)-H(20)	125.9	C(27)-C(26)-H(26)	125.9
C(19)-C(20)-H(20)	125.9	C(25)-C(26)-H(26)	125.9
Fe(1)-C(20)-H(20)	126.2	Fe(1)-C(26)-H(26)	125.7
C(20)-C(21)-C(22)	108.34(16)	C(23)-C(27)-C(26)	107.93(18)
C(20)-C(21)-Fe(1)	69.58(10)	C(23)-C(27)-Fe(1)	70.16(11)
C(22)-C(21)-Fe(1)	70.20(10)	C(26)-C(27)-Fe(1)	69.45(11)
C(20)-C(21)-H(21)	125.8	C(23)-C(27)-H(27)	126.0
C(22)-C(21)-H(21)	125.8	C(26)-C(27)-H(27)	126.0
Fe(1)-C(21)-H(21)	126.0	Fe(1)-C(27)-H(27)	125.9
C(21)-C(22)-C(18)	107.24(15)	C(29)-C(28)-C(33)	118.18(17)
C(21)-C(22)-P(2)	126.66(13)	C(29)-C(28)-P(2)	123.52(14)
C(18)-C(22)-P(2)	124.16(13)	C(33)-C(28)-P(2)	117.83(13)

C(30)-C(29)-C(28)	120.97(18)	C(8)-P(1)-C(12)	111.31(9)
C(30)-C(29)-H(29)	119.5	C(16)-P(1)-Ni(1)	110.23(6)
C(28)-C(29)-H(29)	119.5	C(8)-P(1)-Ni(1)	108.82(6)
C(31)-C(30)-C(29)	120.12(18)	C(12)-P(1)-Ni(1)	113.36(6)
C(31)-C(30)-H(30)	119.9	C(22)-P(2)-C(34)	106.99(8)
C(29)-C(30)-H(30)	119.9	C(22)-P(2)-C(28)	101.07(8)
C(30)-C(31)-C(32)	119.76(18)	C(34)-P(2)-C(28)	103.23(8)
C(30)-C(31)-H(31)	120.1	C(22)-P(2)-Ni(1)	111.79(6)
C(32)-C(31)-H(31)	120.1	C(34)-P(2)-Ni(1)	121.77(6)
C(33)-C(32)-C(31)	120.05(18)	C(28)-P(2)-Ni(1)	109.74(6)
C(33)-C(32)-H(32)	120.0	C(19)-Fe(1)-C(18)	40.78(7)
C(31)-C(32)-H(32)	120.0	C(19)-Fe(1)-C(20)	40.64(8)
C(32)-C(33)-C(28)	120.92(17)	C(18)-Fe(1)-C(20)	68.85(7)
C(32)-C(33)-H(33)	119.5	C(19)-Fe(1)-C(26)	119.05(8)
C(28)-C(33)-H(33)	119.5	C(18)-Fe(1)-C(26)	155.19(7)
C(35)-C(34)-C(39)	118.34(17)	C(20)-Fe(1)-C(26)	104.93(8)
C(35)-C(34)-P(2)	118.61(14)	C(19)-Fe(1)-C(21)	68.40(7)
C(39)-C(34)-P(2)	123.04(14)	C(18)-Fe(1)-C(21)	69.13(7)
C(34)-C(35)-C(36)	120.57(19)	C(20)-Fe(1)-C(21)	40.56(7)
C(34)-C(35)-H(35)	119.7	C(26)-Fe(1)-C(21)	122.60(8)
C(36)-C(35)-H(35)	119.7	C(19)-Fe(1)-C(25)	103.71(7)
C(37)-C(36)-C(35)	120.3(2)	C(18)-Fe(1)-C(25)	120.04(7)
C(37)-C(36)-H(36)	119.9	C(20)-Fe(1)-C(25)	119.39(8)
C(35)-C(36)-H(36)	119.9	C(26)-Fe(1)-C(25)	40.59(8)
C(38)-C(37)-C(36)	119.80(19)	C(21)-Fe(1)-C(25)	156.69(8)
C(38)-C(37)-H(37)	120.1	C(19)-Fe(1)-C(27)	156.34(8)
C(36)-C(37)-H(37)	120.1	C(18)-Fe(1)-C(27)	162.50(8)
C(37)-C(38)-C(39)	119.94(18)	C(20)-Fe(1)-C(27)	122.47(8)
C(37)-C(38)-H(38)	120.0	C(26)-Fe(1)-C(27)	40.53(8)
C(39)-C(38)-H(38)	120.0	C(21)-Fe(1)-C(27)	109.81(8)
C(38)-C(39)-C(34)	121.04(18)	C(25)-Fe(1)-C(27)	68.19(8)
C(38)-C(39)-H(39)	119.5	C(19)-Fe(1)-C(24)	121.13(8)
C(34)-C(39)-H(39)	119.5	C(18)-Fe(1)-C(24)	107.45(8)
C(1)-N(1)-Ni(1)	68.64(11)	C(20)-Fe(1)-C(24)	156.02(8)
C(16)-P(1)-C(8)	108.45(8)	C(26)-Fe(1)-C(24)	67.99(8)
C(16)-P(1)-C(12)	104.51(9)	C(21)-Fe(1)-C(24)	162.24(8)

C(25)-Fe(1)-C(24)	40.43(8)	C(26)-Fe(1)-C(22)	160.68(8)
C(27)-Fe(1)-C(24)	67.92(8)	C(21)-Fe(1)-C(22)	40.85(7)
C(19)-Fe(1)-C(23)	159.12(8)	C(25)-Fe(1)-C(22)	158.58(8)
C(18)-Fe(1)-C(23)	125.43(8)	C(27)-Fe(1)-C(22)	126.54(7)
C(20)-Fe(1)-C(23)	160.18(8)	C(24)-Fe(1)-C(22)	125.25(8)
C(26)-Fe(1)-C(23)	67.89(8)	C(23)-Fe(1)-C(22)	111.81(7)
C(21)-Fe(1)-C(23)	126.53(7)	C(1)-Ni(1)-N(1)	37.75(7)
C(25)-Fe(1)-C(23)	67.99(8)	C(1)-Ni(1)-P(2)	111.76(6)
C(27)-Fe(1)-C(23)	40.26(8)	N(1)-Ni(1)-P(2)	148.18(5)
C(24)-Fe(1)-C(23)	40.36(8)	C(1)-Ni(1)-P(1)	143.64(6)
C(19)-Fe(1)-C(22)	68.60(7)	N(1)-Ni(1)-P(1)	105.90(5)
C(18)-Fe(1)-C(22)	41.28(7)	P(2)-Ni(1)-P(1)	103.789(19)
C(20)-Fe(1)-C(22)	68.54(7)		

Anisotropic displacement parameters ($Å^2 x\ 10^3$) for hartwig25. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	19(1)	12(1)	15(1)	0(1)	4(1)	10(1)
C(2)	16(1)	10(1)	19(1)	-1(1)	2(1)	9(1)
C(3)	22(1)	11(1)	17(1)	1(1)	2(1)	9(1)
C(4)	18(1)	11(1)	28(1)	3(1)	9(1)	7(1)
C(5)	16(1)	20(1)	35(1)	0(1)	-1(1)	12(1)
C(6)	26(1)	32(1)	22(1)	0(1)	-4(1)	20(1)
C(7)	23(1)	25(1)	17(1)	1(1)	3(1)	17(1)
C(8)	23(1)	29(1)	13(1)	-1(1)	-2(1)	19(1)
C(9)	32(1)	46(1)	23(1)	0(1)	-3(1)	30(1)
C(10)	30(1)	38(1)	14(1)	-2(1)	-2(1)	22(1)
C(11)	29(1)	24(1)	18(1)	3(1)	3(1)	17(1)
C(12)	21(1)	21(1)	31(1)	-13(1)	-7(1)	9(1)
C(13)	24(1)	38(1)	36(1)	-21(1)	-11(1)	13(1)
C(14)	31(1)	26(1)	38(1)	-17(1)	-10(1)	17(1)
C(15)	36(1)	19(1)	44(1)	-7(1)	-5(1)	9(1)
C(16)	12(1)	22(1)	14(1)	-3(1)	-1(1)	7(1)

C(17)	12(1)	33(1)	24(1)	-8(1)	-2(1)	8(1)
C(18)	12(1)	22(1)	10(1)	0(1)	1(1)	9(1)
C(19)	15(1)	26(1)	12(1)	2(1)	1(1)	14(1)
C(20)	20(1)	20(1)	18(1)	2(1)	4(1)	14(1)
C(21)	12(1)	17(1)	15(1)	-1(1)	1(1)	7(1)
C(22)	11(1)	17(1)	11(1)	1(1)	1(1)	8(1)
C(23)	17(1)	34(1)	22(1)	12(1)	6(1)	13(1)
C(24)	15(1)	25(1)	19(1)	4(1)	5(1)	5(1)
C(25)	13(1)	33(1)	18(1)	3(1)	4(1)	10(1)
C(26)	21(1)	35(1)	14(1)	-2(1)	5(1)	15(1)
C(27)	18(1)	35(1)	12(1)	1(1)	0(1)	9(1)
C(28)	11(1)	18(1)	12(1)	-5(1)	1(1)	8(1)
C(29)	14(1)	21(1)	17(1)	-1(1)	0(1)	10(1)
C(30)	12(1)	27(1)	22(1)	-5(1)	-3(1)	9(1)
C(31)	12(1)	21(1)	26(1)	-4(1)	4(1)	4(1)
C(32)	20(1)	19(1)	19(1)	1(1)	6(1)	10(1)
C(33)	13(1)	21(1)	15(1)	-3(1)	0(1)	10(1)
C(34)	10(1)	19(1)	14(1)	0(1)	0(1)	9(1)
C(35)	34(1)	26(1)	17(1)	-2(1)	1(1)	21(1)
C(36)	54(2)	31(1)	30(1)	6(1)	7(1)	33(1)
C(37)	33(1)	45(1)	19(1)	11(1)	5(1)	27(1)
C(38)	16(1)	36(1)	15(1)	-1(1)	1(1)	12(1)
C(39)	12(1)	23(1)	16(1)	-2(1)	1(1)	9(1)
N(1)	20(1)	25(1)	16(1)	-4(1)	2(1)	14(1)
P(1)	14(1)	18(1)	13(1)	-5(1)	-3(1)	9(1)
P(2)	10(1)	15(1)	11(1)	-2(1)	-1(1)	7(1)
Fe(1)	11(1)	20(1)	11(1)	-1(1)	1(1)	9(1)
Ni(1)	12(1)	16(1)	10(1)	-2(1)	-1(1)	9(1)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3)

	x	y	z	U(eq)

H(3)	3732	720	10441	20
H(4)	3126	558	10026	23
H(5)	2936	518	8148	27
H(6)	3360	661	6688	29
H(7)	3974	842	7093	23
H(9A)	5832	1030	10816	44
H(9B)	5700	698	9932	44
H(9C)	5582	613	11232	44
H(10A)	5045	664	11957	38
H(10B)	4932	925	11282	38
H(10C)	5333	1096	11837	38
H(11A)	4938	238	10497	34
H(11B)	5063	369	9223	34
H(11C)	4754	432	9798	34
H(13A)	6032	1999	10781	51
H(13B)	6087	1695	10125	51
H(13C)	5840	1584	11245	51
H(14A)	5235	1556	11238	45
H(14B)	5082	1642	10107	45
H(14C)	5424	1969	10762	45
H(15A)	5772	2150	9076	53
H(15B)	5465	1820	8331	53
H(15C)	5875	1884	8392	53
H(16)	5606	1326	7505	20
H(17A)	6059	1159	8877	37
H(17B)	6151	1560	8463	37
H(17C)	6136	1266	7568	37
H(19)	5794	574	7739	20
H(20)	5360	28	6536	21
H(21)	4829	116	5934	18
H(23)	5443	1175	4386	29
H(24)	6016	1441	5610	26
H(25)	6259	995	5588	26
H(26)	5832	451	4358	27
H(27)	5327	562	3620	28

H(29)	4063	448	5617	20
H(30)	3499	-102	5654	25
H(31)	3408	-571	6904	26
H(32)	3881	-486	8142	24
H(33)	4442	65	8121	19
H(35)	4853	1474	6538	28
H(36)	4871	1803	4925	40
H(37)	4763	1527	3149	35
H(38)	4661	929	2977	27
H(39)	4670	609	4573	20

X-ray Crystallographic Analysis of (PPF-^{t}Bu)Ni(4-CN-C_6H_4)(Cl) (C5A)

A red prism 0.060 x 0.050 x 0.030 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using phi and omega scans. Crystal-to-detector distance was 40 mm and exposure time was 10 seconds per frame using a scan width of 0.5°. Data collection was 99.3% complete to 25.000° in θ. A total of 29128 reflections were collected covering the indices, -10<=*h*<=11, -30<=*k*<=31, -16<=*l*<=16. 6357 reflections were found to be symmetry independent, with an R_{int} of 0.0488. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P 21/n (No. 14). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2013). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2013.

Empirical formula C39 H44 Cl Fe N Ni P2
Formula weight 738.70
Temperature 100(2) K
Wavelength 0.71073 Å
Crystal system Monoclinic
Space group P 21/n
Unit cell dimensions a = 9.5005(4) Å α= 90°.
b = 26.2628(10) Å β= 91.007(2)°.
c = 14.0193(5) Å γ = 90°.
Volume 3497.4(2) Å^3
Z 4
Density (calculated) 1.403 Mg/m^3
Absorption coefficient 1.150 mm^{-1}

F(000) 1544
Crystal size 0.060 x 0.050 x 0.030 mm^3
Crystal color/habit red prism
Theta range for data collection 1.647 to 25.439°.
Index ranges -10<=h<=11, -30<=k<=31, -16<=l<=16
Reflections collected 29128
Independent reflections 6357 [R(int) = 0.0488]
Completeness to theta = 25.000° 99.3 %
Absorption correction Semi-empirical from equivalents
Max. and min. transmission 0.928 and 0.804
Refinement method Full-matrix least-squares on F^2
Data / restraints / parameters 6357 / 0 / 413
Goodness-of-fit on F^2 1.150
Final R indices [I>2sigma(I)] R1 = 0.0457, wR2 = 0.0925
R indices (all data) R1 = 0.0600, wR2 = 0.0967
Extinction coefficient n/a
Largest diff. peak and hole 0.584 and -0.431 e.$Å^{-3}$

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	1916(4)	6321(1)	4227(3)	14(1)
C(2)	2871(4)	5971(1)	4619(3)	16(1)
C(3)	2914(4)	5865(1)	5583(3)	16(1)
C(4)	2027(4)	6122(2)	6197(3)	18(1)
C(5)	1065(4)	6474(2)	5831(3)	19(1)
C(6)	1000(4)	6561(2)	4858(3)	17(1)
C(7)	2126(4)	6037(2)	7213(3)	23(1)
C(8)	-1038(4)	5882(1)	3485(3)	13(1)
C(9)	-913(4)	5541(2)	4243(3)	17(1)
C(10)	-1981(4)	5491(2)	4890(3)	20(1)
C(11)	-3173(4)	5787(2)	4810(3)	20(1)
C(12)	-3305(4)	6136(2)	4071(3)	19(1)
C(13)	-2249(4)	6180(2)	3415(3)	16(1)
C(14)	1378(4)	5376(1)	2671(2)	11(1)
C(15)	2829(4)	5377(2)	2587(3)	16(1)
C(16)	3565(4)	4920(2)	2539(3)	21(1)

C(17)	2843(4)	4462(2)	2555(3)	21(1)
C(18)	1401(4)	4455(2)	2612(3)	18(1)
C(19)	662(4)	4910(1)	2666(3)	14(1)
C(20)	-188(4)	5982(1)	1437(2)	11(1)
C(21)	53(4)	5598(2)	731(3)	16(1)
C(22)	-346(4)	5794(2)	-169(3)	19(1)
C(23)	-821(4)	6300(2)	-50(3)	16(1)
C(24)	-705(4)	6423(1)	935(3)	12(1)
C(25)	-3385(4)	5469(2)	1651(3)	26(1)
C(26)	-3132(4)	5136(2)	878(3)	27(1)
C(27)	-3554(5)	5392(2)	30(3)	29(1)
C(28)	-4071(4)	5874(2)	286(3)	30(1)
C(29)	-3969(4)	5923(2)	1281(3)	28(1)
C(30)	-878(4)	6944(1)	1376(3)	13(1)
C(31)	-1860(4)	7281(1)	769(3)	16(1)
C(32)	2103(4)	7213(2)	732(3)	17(1)
C(33)	1364(4)	7400(2)	-186(3)	20(1)
C(34)	2702(4)	6677(2)	558(3)	20(1)
C(35)	3356(4)	7561(2)	959(3)	23(1)
C(36)	570(4)	7803(2)	2345(3)	17(1)
C(37)	279(4)	8227(2)	1618(3)	20(1)
C(38)	-710(4)	7739(2)	2990(3)	21(1)
C(39)	1800(4)	7970(2)	3005(3)	24(1)
N(1)	2225(4)	5977(2)	8022(3)	35(1)
P(1)	421(1)	5978(1)	2667(1)	11(1)
P(2)	931(1)	7157(1)	1797(1)	11(1)
Cl(1)	3883(1)	6943(1)	3169(1)	21(1)
Fe(1)	-2016(1)	5801(1)	731(1)	16(1)
Ni(1)	1759(1)	6610(1)	2971(1)	11(1)

Bond lengths [Å] and angles [°]

C(1)-C(2)	1.398(5)	C(2)-C(3)	1.379(5)
C(1)-C(6)	1.401(5)	C(2)-H(2)	0.9500
C(1)-Ni(1)	1.920(4)	C(3)-C(4)	1.390(6)

C(3)-H(3)	0.9500	C(21)-Fe(1)	2.037(4)
C(4)-C(5)	1.391(6)	C(21)-H(21)	0.9500
C(4)-C(7)	1.443(5)	C(22)-C(23)	1.414(5)
C(5)-C(6)	1.384(5)	C(22)-Fe(1)	2.045(4)
C(5)-H(5)	0.9500	C(22)-H(22)	0.9500
C(6)-H(6)	0.9500	C(23)-C(24)	1.421(5)
C(7)-N(1)	1.148(5)	C(23)-Fe(1)	2.060(4)
C(8)-C(9)	1.394(5)	C(23)-H(23)	0.9500
C(8)-C(13)	1.394(5)	C(24)-C(30)	1.512(5)
C(8)-P(1)	1.832(4)	C(24)-Fe(1)	2.071(4)
C(9)-C(10)	1.379(5)	C(25)-C(29)	1.410(6)
C(9)-H(9)	0.9500	C(25)-C(26)	1.418(6)
C(10)-C(11)	1.377(6)	C(25)-Fe(1)	2.043(4)
C(10)-H(10)	0.9500	C(25)-H(25)	0.9500
C(11)-C(12)	1.388(5)	C(26)-C(27)	1.417(6)
C(11)-H(11)	0.9500	C(26)-Fe(1)	2.057(4)
C(12)-C(13)	1.377(5)	C(26)-H(26)	0.9500
C(12)-H(12)	0.9500	C(27)-C(28)	1.408(6)
C(13)-H(13)	0.9500	C(27)-Fe(1)	2.051(4)
C(14)-C(15)	1.386(5)	C(27)-H(27)	0.9500
C(14)-C(19)	1.400(5)	C(28)-C(29)	1.403(6)
C(14)-P(1)	1.822(4)	C(28)-Fe(1)	2.048(4)
C(15)-C(16)	1.392(5)	C(28)-H(28)	0.9500
C(15)-H(15)	0.9500	C(29)-Fe(1)	2.046(4)
C(16)-C(17)	1.384(6)	C(29)-H(29)	0.9500
C(16)-H(16)	0.9500	C(30)-C(31)	1.533(5)
C(17)-C(18)	1.374(6)	C(30)-P(2)	1.891(4)
C(17)-H(17)	0.9500	C(30)-H(30)	1.0000
C(18)-C(19)	1.390(5)	C(31)-H(31A)	0.9800
C(18)-H(18)	0.9500	C(31)-H(31B)	0.9800
C(19)-H(19)	0.9500	C(31)-H(31C)	0.9800
C(20)-C(21)	1.433(5)	C(32)-C(35)	1.531(5)
C(20)-C(24)	1.439(5)	C(32)-C(33)	1.536(5)
C(20)-P(1)	1.809(4)	C(32)-C(34)	1.539(5)
C(20)-Fe(1)	2.040(4)	C(32)-P(2)	1.884(4)
C(21)-C(22)	1.409(5)	C(33)-H(33A)	0.9800

C(33)-H(33B)	0.9800	C(37)-H(37A)	0.9800
C(33)-H(33C)	0.9800	C(37)-H(37B)	0.9800
C(34)-H(34A)	0.9800	C(37)-H(37C)	0.9800
C(34)-H(34B)	0.9800	C(38)-H(38A)	0.9800
C(34)-H(34C)	0.9800	C(38)-H(38B)	0.9800
C(35)-H(35A)	0.9800	C(38)-H(38C)	0.9800
C(35)-H(35B)	0.9800	C(39)-H(39A)	0.9800
C(35)-H(35C)	0.9800	C(39)-H(39B)	0.9800
C(36)-C(37)	1.531(5)	C(39)-H(39C)	0.9800
C(36)-C(38)	1.537(5)	P(1)-Ni(1)	2.1292(11)
C(36)-C(39)	1.542(5)	P(2)-Ni(1)	2.3126(10)
C(36)-P(2)	1.896(4)	Cl(1)-Ni(1)	2.2127(10)

C(2)-C(1)-C(6)	116.9(3)	C(10)-C(9)-H(9)	119.7
C(2)-C(1)-Ni(1)	131.3(3)	C(8)-C(9)-H(9)	119.7
C(6)-C(1)-Ni(1)	111.3(3)	C(11)-C(10)-C(9)	120.5(4)
C(3)-C(2)-C(1)	121.7(4)	C(11)-C(10)-H(10)	119.8
C(3)-C(2)-H(2)	119.2	C(9)-C(10)-H(10)	119.8
C(1)-C(2)-H(2)	119.2	C(10)-C(11)-C(12)	119.8(4)
C(2)-C(3)-C(4)	120.1(4)	C(10)-C(11)-H(11)	120.1
C(2)-C(3)-H(3)	119.9	C(12)-C(11)-H(11)	120.1
C(4)-C(3)-H(3)	119.9	C(13)-C(12)-C(11)	119.7(4)
C(3)-C(4)-C(5)	119.7(4)	C(13)-C(12)-H(12)	120.1
C(3)-C(4)-C(7)	120.4(4)	C(11)-C(12)-H(12)	120.1
C(5)-C(4)-C(7)	119.9(4)	C(12)-C(13)-C(8)	121.1(4)
C(6)-C(5)-C(4)	119.3(4)	C(12)-C(13)-H(13)	119.4
C(6)-C(5)-H(5)	120.3	C(8)-C(13)-H(13)	119.4
C(4)-C(5)-H(5)	120.3	C(15)-C(14)-C(19)	119.0(3)
C(5)-C(6)-C(1)	122.1(4)	C(15)-C(14)-P(1)	119.7(3)
C(5)-C(6)-H(6)	118.9	C(19)-C(14)-P(1)	121.0(3)
C(1)-C(6)-H(6)	118.9	C(14)-C(15)-C(16)	120.3(4)
N(1)-C(7)-C(4)	178.6(5)	C(14)-C(15)-H(15)	119.9
C(9)-C(8)-C(13)	118.3(3)	C(16)-C(15)-H(15)	119.9
C(9)-C(8)-P(1)	120.7(3)	C(17)-C(16)-C(15)	119.9(4)
C(13)-C(8)-P(1)	120.8(3)	C(17)-C(16)-H(16)	120.0
C(10)-C(9)-C(8)	120.6(4)	C(15)-C(16)-H(16)	120.0

C(18)-C(17)-C(16)	120.5(4)	C(23)-C(24)-Fe(1)	69.5(2)
C(18)-C(17)-H(17)	119.8	C(20)-C(24)-Fe(1)	68.3(2)
C(16)-C(17)-H(17)	119.8	C(30)-C(24)-Fe(1)	134.5(3)
C(17)-C(18)-C(19)	119.8(4)	C(29)-C(25)-C(26)	108.2(4)
C(17)-C(18)-H(18)	120.1	C(29)-C(25)-Fe(1)	70.0(2)
C(19)-C(18)-H(18)	120.1	C(26)-C(25)-Fe(1)	70.3(2)
C(18)-C(19)-C(14)	120.4(4)	C(29)-C(25)-H(25)	125.9
C(18)-C(19)-H(19)	119.8	C(26)-C(25)-H(25)	125.9
C(14)-C(19)-H(19)	119.8	Fe(1)-C(25)-H(25)	125.4
C(21)-C(20)-C(24)	106.6(3)	C(27)-C(26)-C(25)	107.4(4)
C(21)-C(20)-P(1)	127.0(3)	C(27)-C(26)-Fe(1)	69.6(2)
C(24)-C(20)-P(1)	124.9(3)	C(25)-C(26)-Fe(1)	69.2(2)
C(21)-C(20)-Fe(1)	69.3(2)	C(27)-C(26)-H(26)	126.3
C(24)-C(20)-Fe(1)	70.7(2)	C(25)-C(26)-H(26)	126.3
P(1)-C(20)-Fe(1)	135.8(2)	Fe(1)-C(26)-H(26)	126.4
C(22)-C(21)-C(20)	108.6(3)	C(28)-C(27)-C(26)	108.0(4)
C(22)-C(21)-Fe(1)	70.1(2)	C(28)-C(27)-Fe(1)	69.8(2)
C(20)-C(21)-Fe(1)	69.5(2)	C(26)-C(27)-Fe(1)	70.0(2)
C(22)-C(21)-H(21)	125.7	C(28)-C(27)-H(27)	126.0
C(20)-C(21)-H(21)	125.7	C(26)-C(27)-H(27)	126.0
Fe(1)-C(21)-H(21)	126.2	Fe(1)-C(27)-H(27)	125.7
C(21)-C(22)-C(23)	108.6(3)	C(29)-C(28)-C(27)	108.5(4)
C(21)-C(22)-Fe(1)	69.5(2)	C(29)-C(28)-Fe(1)	69.9(2)
C(23)-C(22)-Fe(1)	70.4(2)	C(27)-C(28)-Fe(1)	70.0(2)
C(21)-C(22)-H(22)	125.7	C(29)-C(28)-H(28)	125.7
C(23)-C(22)-H(22)	125.7	C(27)-C(28)-H(28)	125.7
Fe(1)-C(22)-H(22)	126.0	Fe(1)-C(28)-H(28)	125.9
C(22)-C(23)-C(24)	108.1(3)	C(28)-C(29)-C(25)	108.0(4)
C(22)-C(23)-Fe(1)	69.3(2)	C(28)-C(29)-Fe(1)	70.0(3)
C(24)-C(23)-Fe(1)	70.3(2)	C(25)-C(29)-Fe(1)	69.7(2)
C(22)-C(23)-H(23)	126.0	C(28)-C(29)-H(29)	126.0
C(24)-C(23)-H(23)	126.0	C(25)-C(29)-H(29)	126.0
Fe(1)-C(23)-H(23)	126.0	Fe(1)-C(29)-H(29)	125.9
C(23)-C(24)-C(20)	108.1(3)	C(24)-C(30)-C(31)	111.4(3)
C(23)-C(24)-C(30)	126.7(3)	C(24)-C(30)-P(2)	106.9(2)
C(20)-C(24)-C(30)	124.6(3)	C(31)-C(30)-P(2)	122.9(3)

C(24)-C(30)-H(30)	104.7	C(37)-C(36)-P(2)	114.4(3)
C(31)-C(30)-H(30)	104.7	C(38)-C(36)-P(2)	106.9(3)
P(2)-C(30)-H(30)	104.7	C(39)-C(36)-P(2)	110.9(3)
C(30)-C(31)-H(31A)	109.5	C(36)-C(37)-H(37A)	109.5
C(30)-C(31)-H(31B)	109.5	C(36)-C(37)-H(37B)	109.5
H(31A)-C(31)-H(31B)	109.5	H(37A)-C(37)-H(37B)	109.5
C(30)-C(31)-H(31C)	109.5	C(36)-C(37)-H(37C)	109.5
H(31A)-C(31)-H(31C)	109.5	H(37A)-C(37)-H(37C)	109.5
H(31B)-C(31)-H(31C)	109.5	H(37B)-C(37)-H(37C)	109.5
C(35)-C(32)-C(33)	109.0(3)	C(36)-C(38)-H(38A)	109.5
C(35)-C(32)-C(34)	106.9(3)	C(36)-C(38)-H(38B)	109.5
C(33)-C(32)-C(34)	109.0(3)	H(38A)-C(38)-H(38B)	109.5
C(35)-C(32)-P(2)	110.5(3)	C(36)-C(38)-H(38C)	109.5
C(33)-C(32)-P(2)	114.9(3)	H(38A)-C(38)-H(38C)	109.5
C(34)-C(32)-P(2)	106.2(3)	H(38B)-C(38)-H(38C)	109.5
C(32)-C(33)-H(33A)	109.5	C(36)-C(39)-H(39A)	109.5
C(32)-C(33)-H(33B)	109.5	C(36)-C(39)-H(39B)	109.5
H(33A)-C(33)-H(33B)	109.5	H(39A)-C(39)-H(39B)	109.5
C(32)-C(33)-H(33C)	109.5	C(36)-C(39)-H(39C)	109.5
H(33A)-C(33)-H(33C)	109.5	H(39A)-C(39)-H(39C)	109.5
H(33B)-C(33)-H(33C)	109.5	H(39B)-C(39)-H(39C)	109.5
C(32)-C(34)-H(34A)	109.5	C(20)-P(1)-C(14)	99.20(16)
C(32)-C(34)-H(34B)	109.5	C(20)-P(1)-C(8)	111.40(17)
H(34A)-C(34)-H(34B)	109.5	C(14)-P(1)-C(8)	105.17(17)
C(32)-C(34)-H(34C)	109.5	C(20)-P(1)-Ni(1)	111.47(12)
H(34A)-C(34)-H(34C)	109.5	C(14)-P(1)-Ni(1)	112.28(12)
H(34B)-C(34)-H(34C)	109.5	C(8)-P(1)-Ni(1)	115.91(12)
C(32)-C(35)-H(35A)	109.5	C(32)-P(2)-C(30)	108.78(17)
C(32)-C(35)-H(35B)	109.5	C(32)-P(2)-C(36)	111.39(18)
H(35A)-C(35)-H(35B)	109.5	C(30)-P(2)-C(36)	102.80(17)
C(32)-C(35)-H(35C)	109.5	C(32)-P(2)-Ni(1)	114.43(12)
H(35A)-C(35)-H(35C)	109.5	C(30)-P(2)-Ni(1)	109.51(12)
H(35B)-C(35)-H(35C)	109.5	C(36)-P(2)-Ni(1)	109.28(12)
C(37)-C(36)-C(38)	109.6(3)	C(21)-Fe(1)-C(20)	41.17(15)
C(37)-C(36)-C(39)	108.6(3)	C(21)-Fe(1)-C(25)	120.87(17)
C(38)-C(36)-C(39)	106.1(3)	C(20)-Fe(1)-C(25)	109.80(15)

C(21)-Fe(1)-C(22)	40.38(15)	C(27)-Fe(1)-C(26)	40.37(17)
C(20)-Fe(1)-C(22)	68.80(15)	C(21)-Fe(1)-C(23)	68.02(15)
C(25)-Fe(1)-C(22)	153.50(17)	C(20)-Fe(1)-C(23)	68.78(15)
C(21)-Fe(1)-C(29)	157.25(16)	C(25)-Fe(1)-C(23)	165.81(17)
C(20)-Fe(1)-C(29)	123.43(16)	C(22)-Fe(1)-C(23)	40.29(15)
C(25)-Fe(1)-C(29)	40.33(18)	C(29)-Fe(1)-C(23)	127.77(17)
C(22)-Fe(1)-C(29)	162.24(17)	C(28)-Fe(1)-C(23)	108.04(17)
C(21)-Fe(1)-C(28)	159.89(17)	C(27)-Fe(1)-C(23)	118.23(16)
C(20)-Fe(1)-C(28)	157.73(17)	C(26)-Fe(1)-C(23)	151.99(17)
C(25)-Fe(1)-C(28)	67.58(18)	C(21)-Fe(1)-C(24)	68.19(15)
C(22)-Fe(1)-C(28)	123.94(17)	C(20)-Fe(1)-C(24)	40.97(14)
C(29)-Fe(1)-C(28)	40.08(18)	C(25)-Fe(1)-C(24)	129.61(16)
C(21)-Fe(1)-C(27)	122.79(18)	C(22)-Fe(1)-C(24)	67.75(15)
C(20)-Fe(1)-C(27)	161.35(17)	C(29)-Fe(1)-C(24)	111.84(17)
C(25)-Fe(1)-C(27)	67.84(17)	C(28)-Fe(1)-C(24)	122.44(17)
C(22)-Fe(1)-C(27)	104.65(17)	C(27)-Fe(1)-C(24)	154.35(16)
C(29)-Fe(1)-C(27)	67.65(18)	C(26)-Fe(1)-C(24)	165.12(16)
C(28)-Fe(1)-C(27)	40.17(18)	C(23)-Fe(1)-C(24)	40.23(14)
C(21)-Fe(1)-C(26)	106.03(17)	C(1)-Ni(1)-P(1)	84.97(11)
C(20)-Fe(1)-C(26)	125.78(16)	C(1)-Ni(1)-Cl(1)	89.14(11)
C(25)-Fe(1)-C(26)	40.47(17)	P(1)-Ni(1)-Cl(1)	150.87(4)
C(22)-Fe(1)-C(26)	117.41(17)	C(1)-Ni(1)-P(2)	156.55(12)
C(29)-Fe(1)-C(26)	67.85(19)	P(1)-Ni(1)-P(2)	98.50(4)
C(28)-Fe(1)-C(26)	67.65(18)	Cl(1)-Ni(1)-P(2)	98.15(4)

Anisotropic displacement parameters ($Å^2 x\ 10^3$). The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + \ldots + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	17(2)	11(2)	14(2)	-1(2)	-5(2)	-4(2)
C(2)	17(2)	13(2)	17(2)	0(2)	-2(2)	-1(2)
C(3)	17(2)	12(2)	20(2)	4(2)	-8(2)	-3(2)
C(4)	18(2)	18(2)	17(2)	5(2)	-3(2)	-9(2)
C(5)	22(2)	17(2)	18(2)	-3(2)	0(2)	-2(2)

C(6)	19(2)	13(2)	19(2)	0(2)	-3(2)	4(2)
C(7)	23(2)	25(2)	21(2)	6(2)	-1(2)	-7(2)
C(8)	14(2)	12(2)	14(2)	-1(2)	-2(2)	-1(2)
C(9)	15(2)	17(2)	18(2)	1(2)	-2(2)	5(2)
C(10)	23(2)	23(2)	13(2)	6(2)	0(2)	2(2)
C(11)	16(2)	24(2)	20(2)	1(2)	7(2)	-1(2)
C(12)	14(2)	19(2)	24(2)	1(2)	-1(2)	5(2)
C(13)	17(2)	12(2)	19(2)	5(2)	-1(2)	0(2)
C(14)	17(2)	9(2)	8(2)	0(2)	-1(2)	1(2)
C(15)	21(2)	12(2)	13(2)	3(2)	3(2)	-1(2)
C(16)	19(2)	23(2)	20(2)	1(2)	2(2)	8(2)
C(17)	36(3)	9(2)	19(2)	2(2)	2(2)	12(2)
C(18)	29(2)	7(2)	18(2)	2(2)	-1(2)	0(2)
C(19)	17(2)	13(2)	13(2)	0(2)	-2(2)	1(2)
C(20)	13(2)	8(2)	12(2)	1(2)	-1(2)	-2(2)
C(21)	19(2)	11(2)	19(2)	2(2)	-1(2)	-1(2)
C(22)	26(2)	15(2)	15(2)	-2(2)	0(2)	-4(2)
C(23)	19(2)	13(2)	17(2)	3(2)	-3(2)	-3(2)
C(24)	12(2)	9(2)	15(2)	1(2)	0(2)	-1(2)
C(25)	19(2)	31(3)	27(2)	5(2)	-4(2)	-16(2)
C(26)	25(2)	24(3)	33(2)	2(2)	-5(2)	-15(2)
C(27)	31(3)	33(3)	23(2)	-1(2)	-7(2)	-18(2)
C(28)	19(2)	31(3)	41(3)	4(2)	-13(2)	-9(2)
C(29)	16(2)	34(3)	34(3)	-1(2)	-3(2)	-5(2)
C(30)	11(2)	13(2)	14(2)	4(2)	-1(2)	1(2)
C(31)	16(2)	14(2)	19(2)	2(2)	-6(2)	2(2)
C(32)	15(2)	18(2)	17(2)	7(2)	3(2)	0(2)
C(33)	22(2)	22(2)	15(2)	7(2)	3(2)	-1(2)
C(34)	17(2)	25(2)	17(2)	3(2)	3(2)	4(2)
C(35)	18(2)	26(2)	25(2)	7(2)	1(2)	-4(2)
C(36)	21(2)	11(2)	19(2)	-1(2)	-5(2)	-1(2)
C(37)	22(2)	10(2)	26(2)	0(2)	-6(2)	0(2)
C(38)	29(2)	14(2)	20(2)	-3(2)	2(2)	4(2)
C(39)	33(3)	11(2)	27(2)	-2(2)	-9(2)	0(2)
N(1)	46(3)	34(2)	25(2)	10(2)	-3(2)	-9(2)

P(1)	12(1)	9(1)	12(1)	1(1)	-1(1)	1(1)
P(2)	13(1)	7(1)	13(1)	2(1)	-2(1)	0(1)
Cl(1)	16(1)	19(1)	28(1)	8(1)	-9(1)	-5(1)
Fe(1)	19(1)	13(1)	15(1)	1(1)	-5(1)	-4(1)
Ni(1)	13(1)	8(1)	13(1)	2(1)	-3(1)	-1(1)

Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 10 3)

	x	y	z	U(eq)
H(2)	3506	5801	4211	19
H(3)	3551	5617	5827	20
H(5)	459	6654	6246	23
H(6)	312	6790	4609	21
H(9)	-85	5341	4315	20
H(10)	-1893	5251	5395	24
H(11)	-3903	5753	5260	24
H(12)	-4121	6344	4017	23
H(13)	-2349	6417	2906	19
H(15)	3324	5691	2562	19
H(16)	4562	4921	2496	25
H(17)	3349	4150	2527	26
H(18)	911	4139	2614	22
H(19)	-336	4905	2700	17
H(21)	420	5267	850	20
H(22)	-302	5616	-758	22
H(23)	-1160	6518	-542	20
H(25)	-3193	5400	2306	31
H(26)	-2750	4802	920	33
H(27)	-3498	5261	-600	35
H(28)	-4428	6124	-144	36
H(29)	-4245	6211	1642	34
H(30)	-1406	6881	1976	15

H(31A)	-1383	7381	184	24
H(31B)	-2106	7586	1132	24
H(31C)	-2718	7091	605	24
H(33A)	900	7726	-63	30
H(33B)	659	7149	-393	30
H(33C)	2061	7444	-686	30
H(34A)	1928	6440	422	30
H(34B)	3225	6564	1128	30
H(34C)	3335	6687	14	30
H(35A)	4063	7524	462	34
H(35B)	3773	7467	1578	34
H(35C)	3036	7916	980	34
H(37A)	-425	8111	1148	29
H(37B)	1152	8314	1294	29
H(37C)	-77	8529	1948	29
H(38A)	-831	8048	3372	31
H(38B)	-558	7447	3414	31
H(38C)	-1556	7682	2594	31
H(39A)	1582	8301	3291	36
H(39B)	2661	7999	2634	36
H(39C)	1940	7717	3511	36

X-ray Crystallographic Analysis of (CyPF-Ph)Ni(η^2-NCPh) (C2)

An orange block 0.120 x 0.100 x 0.100 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using phi and omega scans. Crystal-to-detector distance was 40 mm and exposure time was 10 seconds per frame using a scan width of 1.0°. Data collection was 100.0% complete to 25.000° in θ. A total of 116779 reflections were collected covering the indices, -27<=*h*<=27, -11<=*k*<=11, -23<=*l*<=24. 7687 reflections were found to be symmetry independent, with an R_{int} of 0.0330. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P 21/c (No. 14). The data were integrated using the Bruker SAINT software program and scaled using the SADABS software program. Solution by iterative methods (SHELXT) produced a complete heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2014.

Empirical formula C50 H57 Fe N Ni P2
Formula weight 848.46
Temperature 100(2) K
Wavelength 0.71073 Å
Crystal system Monoclinic
Space group P 21/c
Unit cell dimensions a = 22.5202(7) Å α= 90°.
b = 9.6415(3) Å β= 107.9930(10)°.
c = 20.2812(6) Å γ = 90°.
Volume 4188.3(2) $Å^3$
Z 4
Density (calculated) 1.346 Mg/m^3
Absorption coefficient 0.908 mm^{-1}
F(000) 1792
Crystal size 0.120 x 0.100 x 0.100 mm^3
Theta range for data collection 0.951 to 25.361°.
Index ranges -27<=h<=27, -11<=k<=11, -23<=l<=24
Reflections collected 116779
Independent reflections 7687 [R(int) = 0.0330]
Completeness to theta = 25.000° 100.0 %
Absorption correction Semi-empirical from equivalents
Max. and min. transmission 0.862 and 0.816
Refinement method Full-matrix least-squares on F^2
Data / restraints / parameters 7687 / 0 / 498
Goodness-of-fit on F^2 1.057
Final R indices [I>2sigma(I)] R1 = 0.0441, wR2 = 0.1096
R indices (all data) R1 = 0.0494, wR2 = 0.1132
Extinction coefficient n/a
Largest diff. peak and hole 1.097 and -0.708 $e.Å^{-3}$

Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
C(1)	5657(1)	6298(3)	3697(1)	16(1)
C(2)	5502(1)	4898(3)	3716(2)	21(1)
C(3)	4931(2)	4401(3)	3301(2)	25(1)
C(4)	4510(1)	5286(4)	2856(2)	25(1)
C(5)	4656(1)	6669(3)	2835(2)	24(1)
C(6)	5227(1)	7177(3)	3254(2)	20(1)
C(7)	6459(1)	8711(3)	4116(1)	16(1)

C(8)	6067(1)	9633(3)	4318(2)	24(1)
C(9)	6104(2)	11043(3)	4212(2)	27(1)
C(10)	6523(2)	11564(3)	3899(2)	26(1)
C(11)	6918(2)	10674(3)	3706(2)	25(1)
C(12)	6885(1)	9253(3)	3818(2)	20(1)
C(13)	6485(1)	6428(3)	5113(1)	18(1)
C(14)	5895(1)	6705(4)	5314(2)	25(1)
C(15)	7058(1)	7129(3)	5580(1)	17(1)
C(16)	7059(1)	8265(3)	6028(2)	22(1)
C(17)	7692(1)	8647(3)	6362(2)	23(1)
C(18)	8078(1)	7778(3)	6127(2)	21(1)
C(19)	7697(1)	6820(3)	5628(1)	16(1)
C(20)	7100(2)	5115(4)	6949(2)	29(1)
C(21)	7107(2)	6374(4)	7314(2)	30(1)
C(22)	7739(2)	6759(4)	7638(2)	32(1)
C(23)	8124(2)	5737(4)	7471(2)	32(1)
C(24)	7732(2)	4729(4)	7051(2)	30(1)
C(25)	8656(1)	6770(3)	4991(2)	19(1)
C(26)	8517(1)	8267(3)	4733(2)	24(1)
C(27)	9122(2)	9038(4)	4779(2)	36(1)
C(28)	9477(2)	8301(4)	4353(2)	42(1)
C(29)	9607(2)	6793(4)	4577(2)	34(1)
C(30)	9006(1)	6016(3)	4556(2)	25(1)
C(31)	8198(1)	4103(3)	5277(2)	23(1)
C(32)	8758(1)	4009(3)	5938(2)	24(1)
C(33)	8974(2)	2486(4)	6071(2)	36(1)
C(34)	8448(2)	1556(4)	6108(2)	36(1)
C(35)	7883(2)	1672(4)	5454(2)	35(1)
C(36)	7666(2)	3187(3)	5315(2)	28(1)
C(37)	7033(1)	4971(3)	3086(2)	20(1)
C(38)	6608(1)	4681(3)	2386(2)	22(1)
C(39)	6778(2)	3733(3)	1956(2)	26(1)
C(40)	6386(2)	3468(3)	1296(2)	30(1)
C(41)	5812(2)	4144(4)	1053(2)	30(1)
C(42)	5642(2)	5090(4)	1474(2)	27(1)

C(43)	6034(1)	5353(3)	2135(2)	22(1)
C(44)	9177(3)	3226(6)	3273(2)	65(1)
C(45)	9815(3)	2807(8)	3285(3)	93(2)
C(46)	10108(3)	3658(7)	2989(3)	82(2)
C(47)	9875(3)	4899(8)	2684(3)	90(2)
C(48)	9291(3)	5332(7)	2683(3)	75(2)
C(49)	8969(3)	4401(6)	2969(2)	72(2)
C(50)	8862(3)	2298(6)	3602(3)	95(2)
N(1)	7572(1)	4669(3)	3411(1)	28(1)
P(1)	6452(1)	6816(1)	4192(1)	14(1)
P(2)	7927(1)	5862(1)	4971(1)	15(1)
Fe(1)	7551(1)	6654(1)	6590(1)	19(1)
Ni(1)	7198(1)	5758(1)	3963(1)	15(1)

Bond lengths [Å] and angles [°]

C(1)-C(6)	1.388(4)	C(10)-C(11)	1.376(5)
C(1)-C(2)	1.398(4)	C(10)-H(10)	0.9500
C(1)-P(1)	1.831(3)	C(11)-C(12)	1.394(4)
C(2)-C(3)	1.386(4)	C(11)-H(11)	0.9500
C(2)-H(2)	0.9500	C(12)-H(12)	0.9500
C(3)-C(4)	1.384(5)	C(13)-C(15)	1.505(4)
C(3)-H(3)	0.9500	C(13)-C(14)	1.530(4)
C(4)-C(5)	1.377(5)	C(13)-P(1)	1.883(3)
C(4)-H(4)	0.9500	C(13)-H(13)	1.0000
C(5)-C(6)	1.394(4)	C(14)-H(14A)	0.9800
C(5)-H(5)	0.9500	C(14)-H(14B)	0.9800
C(6)-H(6)	0.9500	C(14)-H(14C)	0.9800
C(7)-C(12)	1.385(4)	C(15)-C(16)	1.422(4)
C(7)-C(8)	1.401(4)	C(15)-C(19)	1.444(4)
C(7)-P(1)	1.833(3)	C(15)-Fe(1)	2.058(3)
C(8)-C(9)	1.383(5)	C(16)-C(17)	1.425(4)
C(8)-H(8)	0.9500	C(16)-Fe(1)	2.040(3)
C(9)-C(10)	1.385(5)	C(16)-H(16)	0.9500
C(9)-H(9)	0.9500	C(17)-C(18)	1.393(4)

C(17)-Fe(1)	2.025(3)	C(29)-H(29A)	0.9900
C(17)-H(17)	0.9500	C(29)-H(29B)	0.9900
C(18)-C(19)	1.441(4)	C(30)-H(30A)	0.9900
C(18)-Fe(1)	2.037(3)	C(30)-H(30B)	0.9900
C(18)-H(18)	0.9500	C(31)-C(36)	1.509(4)
C(19)-P(2)	1.823(3)	C(31)-C(32)	1.533(4)
C(19)-Fe(1)	2.084(3)	C(31)-P(2)	1.844(3)
C(20)-C(21)	1.419(5)	C(31)-H(31)	1.0000
C(20)-C(24)	1.423(5)	C(32)-C(33)	1.545(5)
C(20)-Fe(1)	2.053(3)	C(32)-H(32A)	0.9900
C(20)-H(20)	0.9500	C(32)-H(32B)	0.9900
C(21)-C(22)	1.421(5)	C(33)-C(34)	1.506(5)
C(21)-Fe(1)	2.032(3)	C(33)-H(33A)	0.9900
C(21)-H(21)	0.9500	C(33)-H(33B)	0.9900
C(22)-C(23)	1.420(5)	C(34)-C(35)	1.532(5)
C(22)-Fe(1)	2.036(3)	C(34)-H(34A)	0.9900
C(22)-H(22)	0.9500	C(34)-H(34B)	0.9900
C(23)-C(24)	1.409(5)	C(35)-C(36)	1.539(5)
C(23)-Fe(1)	2.052(3)	C(35)-H(35A)	0.9900
C(23)-H(23)	0.9500	C(35)-H(35B)	0.9900
C(24)-Fe(1)	2.061(3)	C(36)-H(36A)	0.9900
C(24)-H(24)	0.9500	C(36)-H(36B)	0.9900
C(25)-C(26)	1.534(4)	C(37)-N(1)	1.224(4)
C(25)-C(30)	1.535(4)	C(37)-C(38)	1.473(4)
C(25)-P(2)	1.849(3)	C(37)-Ni(1)	1.863(3)
C(25)-H(25)	1.0000	C(38)-C(43)	1.395(4)
C(26)-C(27)	1.529(4)	C(38)-C(39)	1.395(4)
C(26)-H(26A)	0.9900	C(39)-C(40)	1.382(5)
C(26)-H(26B)	0.9900	C(39)-H(39)	0.9500
C(27)-C(28)	1.522(6)	C(40)-C(41)	1.394(5)
C(27)-H(27A)	0.9900	C(40)-H(40)	0.9500
C(27)-H(27B)	0.9900	C(41)-C(42)	1.381(5)
C(28)-C(29)	1.525(5)	C(41)-H(41)	0.9500
C(28)-H(28A)	0.9900	C(42)-C(43)	1.383(4)
C(28)-H(28B)	0.9900	C(42)-H(42)	0.9500
C(29)-C(30)	1.536(4)	C(43)-H(43)	0.9500

C(44)-C(49)	1.305(7)	C(48)-C(49)	1.389(8)
C(44)-C(50)	1.428(8)	C(48)-H(48)	0.9500
C(44)-C(45)	1.487(9)	C(49)-H(49)	0.9500
C(45)-C(46)	1.309(9)	C(50)-H(50A)	0.9800
C(45)-H(45)	0.9500	C(50)-H(50B)	0.9800
C(46)-C(47)	1.375(9)	C(50)-H(50C)	0.9800
C(46)-H(46)	0.9500	N(1)-Ni(1)	1.911(3)
C(47)-C(48)	1.379(9)	P(1)-Ni(1)	2.1363(8)
C(47)-H(47)	0.9500	P(2)-Ni(1)	2.1918(8)

C(6)-C(1)-C(2)	118.5(3)	C(10)-C(9)-H(9)	119.7
C(6)-C(1)-P(1)	123.8(2)	C(11)-C(10)-C(9)	119.8(3)
C(2)-C(1)-P(1)	117.3(2)	C(11)-C(10)-H(10)	120.1
C(3)-C(2)-C(1)	120.7(3)	C(9)-C(10)-H(10)	120.1
C(3)-C(2)-H(2)	119.6	C(10)-C(11)-C(12)	119.7(3)
C(1)-C(2)-H(2)	119.6	C(10)-C(11)-H(11)	120.2
C(4)-C(3)-C(2)	120.2(3)	C(12)-C(11)-H(11)	120.2
C(4)-C(3)-H(3)	119.9	C(7)-C(12)-C(11)	121.4(3)
C(2)-C(3)-H(3)	119.9	C(7)-C(12)-H(12)	119.3
C(5)-C(4)-C(3)	119.7(3)	C(11)-C(12)-H(12)	119.3
C(5)-C(4)-H(4)	120.2	C(15)-C(13)-C(14)	113.5(2)
C(3)-C(4)-H(4)	120.2	C(15)-C(13)-P(1)	107.41(19)
C(4)-C(5)-C(6)	120.4(3)	C(14)-C(13)-P(1)	117.3(2)
C(4)-C(5)-H(5)	119.8	C(15)-C(13)-H(13)	105.9
C(6)-C(5)-H(5)	119.8	C(14)-C(13)-H(13)	105.9
C(1)-C(6)-C(5)	120.6(3)	P(1)-C(13)-H(13)	105.9
C(1)-C(6)-H(6)	119.7	C(13)-C(14)-H(14A)	109.5
C(5)-C(6)-H(6)	119.7	C(13)-C(14)-H(14B)	109.5
C(12)-C(7)-C(8)	118.2(3)	H(14A)-C(14)-H(14B)	109.5
C(12)-C(7)-P(1)	116.0(2)	C(13)-C(14)-H(14C)	109.5
C(8)-C(7)-P(1)	125.8(2)	H(14A)-C(14)-H(14C)	109.5
C(9)-C(8)-C(7)	120.3(3)	H(14B)-C(14)-H(14C)	109.5
C(9)-C(8)-H(8)	119.8	C(16)-C(15)-C(19)	108.1(3)
C(7)-C(8)-H(8)	119.8	C(16)-C(15)-C(13)	125.5(3)
C(8)-C(9)-C(10)	120.7(3)	C(19)-C(15)-C(13)	126.3(3)
C(8)-C(9)-H(9)	119.7	C(16)-C(15)-Fe(1)	69.01(16)

C(19)-C(15)-Fe(1)	70.56(16)	C(22)-C(21)-H(21)	125.9
C(13)-C(15)-Fe(1)	128.5(2)	Fe(1)-C(21)-H(21)	125.5
C(15)-C(16)-C(17)	107.9(3)	C(23)-C(22)-C(21)	107.8(3)
C(15)-C(16)-Fe(1)	70.37(17)	C(23)-C(22)-Fe(1)	70.27(18)
C(17)-C(16)-Fe(1)	68.91(17)	C(21)-C(22)-Fe(1)	69.42(18)
C(15)-C(16)-H(16)	126.0	C(23)-C(22)-H(22)	126.1
C(17)-C(16)-H(16)	126.0	C(21)-C(22)-H(22)	126.1
Fe(1)-C(16)-H(16)	126.2	Fe(1)-C(22)-H(22)	125.8
C(18)-C(17)-C(16)	108.6(3)	C(24)-C(23)-C(22)	108.0(3)
C(18)-C(17)-Fe(1)	70.43(18)	C(24)-C(23)-Fe(1)	70.29(18)
C(16)-C(17)-Fe(1)	70.03(17)	C(22)-C(23)-Fe(1)	69.06(18)
C(18)-C(17)-H(17)	125.7	C(24)-C(23)-H(23)	126.0
C(16)-C(17)-H(17)	125.7	C(22)-C(23)-H(23)	126.0
Fe(1)-C(17)-H(17)	125.4	Fe(1)-C(23)-H(23)	126.2
C(17)-C(18)-C(19)	109.2(3)	C(23)-C(24)-C(20)	108.6(3)
C(17)-C(18)-Fe(1)	69.47(18)	C(23)-C(24)-Fe(1)	69.64(19)
C(19)-C(18)-Fe(1)	71.27(16)	C(20)-C(24)-Fe(1)	69.49(19)
C(17)-C(18)-H(18)	125.4	C(23)-C(24)-H(24)	125.7
C(19)-C(18)-H(18)	125.4	C(20)-C(24)-H(24)	125.7
Fe(1)-C(18)-H(18)	125.4	Fe(1)-C(24)-H(24)	126.8
C(18)-C(19)-C(15)	106.2(2)	C(26)-C(25)-C(30)	109.7(3)
C(18)-C(19)-P(2)	126.7(2)	C(26)-C(25)-P(2)	110.6(2)
C(15)-C(19)-P(2)	123.9(2)	C(30)-C(25)-P(2)	111.8(2)
C(18)-C(19)-Fe(1)	67.81(16)	C(26)-C(25)-H(25)	108.2
C(15)-C(19)-Fe(1)	68.62(16)	C(30)-C(25)-H(25)	108.2
P(2)-C(19)-Fe(1)	143.94(16)	P(2)-C(25)-H(25)	108.2
C(21)-C(20)-C(24)	107.3(3)	C(27)-C(26)-C(25)	110.6(3)
C(21)-C(20)-Fe(1)	68.88(19)	C(27)-C(26)-H(26A)	109.5
C(24)-C(20)-Fe(1)	70.04(19)	C(25)-C(26)-H(26A)	109.5
C(21)-C(20)-H(20)	126.3	C(27)-C(26)-H(26B)	109.5
C(24)-C(20)-H(20)	126.3	C(25)-C(26)-H(26B)	109.5
Fe(1)-C(20)-H(20)	126.3	H(26A)-C(26)-H(26B)	108.1
C(20)-C(21)-C(22)	108.2(3)	C(28)-C(27)-C(26)	110.7(3)
C(20)-C(21)-Fe(1)	70.47(18)	C(28)-C(27)-H(27A)	109.5
C(22)-C(21)-Fe(1)	69.70(18)	C(26)-C(27)-H(27A)	109.5
C(20)-C(21)-H(21)	125.9	C(28)-C(27)-H(27B)	109.5

C(26)-C(27)-H(27B)	109.5	C(32)-C(33)-H(33B)	109.4
H(27A)-C(27)-H(27B)	108.1	H(33A)-C(33)-H(33B)	108.0
C(27)-C(28)-C(29)	111.2(3)	C(33)-C(34)-C(35)	111.6(3)
C(27)-C(28)-H(28A)	109.4	C(33)-C(34)-H(34A)	109.3
C(29)-C(28)-H(28A)	109.4	C(35)-C(34)-H(34A)	109.3
C(27)-C(28)-H(28B)	109.4	C(33)-C(34)-H(34B)	109.3
C(29)-C(28)-H(28B)	109.4	C(35)-C(34)-H(34B)	109.3
H(28A)-C(28)-H(28B)	108.0	H(34A)-C(34)-H(34B)	108.0
C(28)-C(29)-C(30)	111.8(3)	C(34)-C(35)-C(36)	111.1(3)
C(28)-C(29)-H(29A)	109.3	C(34)-C(35)-H(35A)	109.4
C(30)-C(29)-H(29A)	109.3	C(36)-C(35)-H(35A)	109.4
C(28)-C(29)-H(29B)	109.3	C(34)-C(35)-H(35B)	109.4
C(30)-C(29)-H(29B)	109.3	C(36)-C(35)-H(35B)	109.4
H(29A)-C(29)-H(29B)	107.9	H(35A)-C(35)-H(35B)	108.0
C(25)-C(30)-C(29)	110.9(3)	C(31)-C(36)-C(35)	110.7(3)
C(25)-C(30)-H(30A)	109.5	C(31)-C(36)-H(36A)	109.5
C(29)-C(30)-H(30A)	109.5	C(35)-C(36)-H(36A)	109.5
C(25)-C(30)-H(30B)	109.5	C(31)-C(36)-H(36B)	109.5
C(29)-C(30)-H(30B)	109.5	C(35)-C(36)-H(36B)	109.5
H(30A)-C(30)-H(30B)	108.1	H(36A)-C(36)-H(36B)	108.1
C(36)-C(31)-C(32)	111.9(3)	N(1)-C(37)-C(38)	135.6(3)
C(36)-C(31)-P(2)	111.7(2)	N(1)-C(37)-Ni(1)	73.19(19)
C(32)-C(31)-P(2)	116.5(2)	C(38)-C(37)-Ni(1)	151.2(2)
C(36)-C(31)-H(31)	105.2	C(43)-C(38)-C(39)	118.6(3)
C(32)-C(31)-H(31)	105.2	C(43)-C(38)-C(37)	121.1(3)
P(2)-C(31)-H(31)	105.2	C(39)-C(38)-C(37)	120.3(3)
C(31)-C(32)-C(33)	109.8(3)	C(40)-C(39)-C(38)	120.6(3)
C(31)-C(32)-H(32A)	109.7	C(40)-C(39)-H(39)	119.7
C(33)-C(32)-H(32A)	109.7	C(38)-C(39)-H(39)	119.7
C(31)-C(32)-H(32B)	109.7	C(39)-C(40)-C(41)	120.1(3)
C(33)-C(32)-H(32B)	109.7	C(39)-C(40)-H(40)	120.0
H(32A)-C(32)-H(32B)	108.2	C(41)-C(40)-H(40)	120.0
C(34)-C(33)-C(32)	111.4(3)	C(42)-C(41)-C(40)	119.7(3)
C(34)-C(33)-H(33A)	109.4	C(42)-C(41)-H(41)	120.2
C(32)-C(33)-H(33A)	109.4	C(40)-C(41)-H(41)	120.2
C(34)-C(33)-H(33B)	109.4	C(41)-C(42)-C(43)	120.3(3)

C(41)-C(42)-H(42)	119.9	C(19)-P(2)-C(31)	111.02(14)
C(43)-C(42)-H(42)	119.9	C(19)-P(2)-C(25)	101.19(13)
C(42)-C(43)-C(38)	120.7(3)	C(31)-P(2)-C(25)	103.24(14)
C(42)-C(43)-H(43)	119.6	C(19)-P(2)-Ni(1)	113.87(9)
C(38)-C(43)-H(43)	119.6	C(31)-P(2)-Ni(1)	110.28(10)
C(49)-C(44)-C(50)	127.3(6)	C(25)-P(2)-Ni(1)	116.49(10)
C(49)-C(44)-C(45)	116.6(6)	C(17)-Fe(1)-C(21)	115.95(13)
C(50)-C(44)-C(45)	116.1(6)	C(17)-Fe(1)-C(22)	101.19(14)
C(46)-C(45)-C(44)	116.4(7)	C(21)-Fe(1)-C(22)	40.88(14)
C(46)-C(45)-H(45)	121.8	C(17)-Fe(1)-C(18)	40.10(12)
C(44)-C(45)-H(45)	121.8	C(21)-Fe(1)-C(18)	152.81(13)
C(45)-C(46)-C(47)	125.1(7)	C(22)-Fe(1)-C(18)	119.43(14)
C(45)-C(46)-H(46)	117.5	C(17)-Fe(1)-C(16)	41.05(12)
C(47)-C(46)-H(46)	117.5	C(21)-Fe(1)-C(16)	101.59(13)
C(46)-C(47)-C(48)	119.8(7)	C(22)-Fe(1)-C(16)	116.56(13)
C(46)-C(47)-H(47)	120.1	C(18)-Fe(1)-C(16)	68.30(12)
C(48)-C(47)-H(47)	120.1	C(17)-Fe(1)-C(23)	120.45(14)
C(47)-C(48)-C(49)	115.1(6)	C(21)-Fe(1)-C(23)	68.41(14)
C(47)-C(48)-H(48)	122.4	C(22)-Fe(1)-C(23)	40.66(14)
C(49)-C(48)-H(48)	122.4	C(18)-Fe(1)-C(23)	109.36(14)
C(44)-C(49)-C(48)	126.9(6)	C(16)-Fe(1)-C(23)	154.35(14)
C(44)-C(49)-H(49)	116.5	C(17)-Fe(1)-C(20)	153.65(13)
C(48)-C(49)-H(49)	116.5	C(21)-Fe(1)-C(20)	40.65(14)
C(44)-C(50)-H(50A)	109.5	C(22)-Fe(1)-C(20)	68.48(14)
C(44)-C(50)-H(50B)	109.5	C(18)-Fe(1)-C(20)	165.80(13)
H(50A)-C(50)-H(50B)	109.5	C(16)-Fe(1)-C(20)	120.33(13)
C(44)-C(50)-H(50C)	109.5	C(23)-Fe(1)-C(20)	68.14(14)
H(50A)-C(50)-H(50C)	109.5	C(17)-Fe(1)-C(15)	68.66(12)
H(50B)-C(50)-H(50C)	109.5	C(21)-Fe(1)-C(15)	120.85(13)
C(37)-N(1)-Ni(1)	68.98(18)	C(22)-Fe(1)-C(15)	154.37(13)
C(1)-P(1)-C(7)	104.96(13)	C(18)-Fe(1)-C(15)	68.60(12)
C(1)-P(1)-C(13)	102.79(13)	C(16)-Fe(1)-C(15)	40.61(12)
C(7)-P(1)-C(13)	106.47(13)	C(23)-Fe(1)-C(15)	164.40(13)
C(1)-P(1)-Ni(1)	116.88(9)	C(20)-Fe(1)-C(15)	109.79(13)
C(7)-P(1)-Ni(1)	115.45(10)	C(17)-Fe(1)-C(24)	159.29(13)
C(13)-P(1)-Ni(1)	109.13(9)	C(21)-Fe(1)-C(24)	68.04(14)

C(22)-Fe(1)-C(24)	67.92(14)	C(23)-Fe(1)-C(19)	127.59(13)
C(18)-Fe(1)-C(24)	128.78(13)	C(20)-Fe(1)-C(19)	128.73(12)
C(16)-Fe(1)-C(24)	159.43(14)	C(15)-Fe(1)-C(19)	40.82(11)
C(23)-Fe(1)-C(24)	40.07(14)	C(24)-Fe(1)-C(19)	115.32(12)
C(20)-Fe(1)-C(24)	40.47(14)	C(37)-Ni(1)-N(1)	37.83(12)
C(15)-Fe(1)-C(24)	128.44(13)	C(37)-Ni(1)-P(1)	117.61(9)
C(17)-Fe(1)-C(19)	68.39(12)	N(1)-Ni(1)-P(1)	155.33(9)
C(21)-Fe(1)-C(19)	160.32(13)	C(37)-Ni(1)-P(2)	141.26(9)
C(22)-Fe(1)-C(19)	158.67(13)	N(1)-Ni(1)-P(2)	103.50(8)
C(18)-Fe(1)-C(19)	40.92(11)	P(1)-Ni(1)-P(2)	100.86(3)
C(16)-Fe(1)-C(19)	68.48(12)		

Anisotropic displacement parameters ($Å^2 x\ 10^3$). The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	13(1)	19(1)	16(1)	-3(1)	5(1)	0(1)
C(2)	20(2)	19(2)	23(2)	1(1)	5(1)	0(1)
C(3)	27(2)	20(2)	29(2)	-4(1)	9(1)	-8(1)
C(4)	14(1)	34(2)	26(2)	-11(1)	5(1)	-5(1)
C(5)	17(2)	28(2)	23(2)	-3(1)	1(1)	4(1)
C(6)	20(2)	16(1)	23(2)	-3(1)	5(1)	2(1)
C(7)	16(1)	15(1)	15(1)	-1(1)	-1(1)	-1(1)
C(8)	22(2)	23(2)	27(2)	-2(1)	9(1)	1(1)
C(9)	29(2)	18(2)	34(2)	-7(1)	8(1)	2(1)
C(10)	28(2)	17(2)	26(2)	-2(1)	-2(1)	-3(1)
C(11)	23(2)	26(2)	24(2)	4(1)	4(1)	-6(1)
C(12)	16(1)	23(2)	18(1)	1(1)	3(1)	2(1)
C(13)	16(1)	20(2)	16(1)	1(1)	4(1)	1(1)
C(14)	21(2)	37(2)	20(2)	-3(1)	8(1)	0(1)
C(15)	21(2)	16(1)	14(1)	3(1)	5(1)	2(1)
C(16)	25(2)	19(2)	20(2)	1(1)	6(1)	4(1)
C(17)	28(2)	21(2)	16(1)	-2(1)	3(1)	-4(1)

C(18)	21(2)	20(2)	19(1)	-1(1)	4(1)	-3(1)
C(19)	17(1)	15(1)	16(1)	1(1)	3(1)	-1(1)
C(20)	39(2)	27(2)	24(2)	7(1)	13(1)	-4(2)
C(21)	39(2)	34(2)	21(2)	7(1)	15(1)	6(2)
C(22)	47(2)	36(2)	13(2)	-1(1)	7(1)	1(2)
C(23)	36(2)	39(2)	17(2)	9(1)	2(1)	8(2)
C(24)	44(2)	26(2)	21(2)	7(1)	13(1)	9(2)
C(25)	13(1)	19(2)	22(2)	-1(1)	3(1)	-1(1)
C(26)	21(2)	22(2)	29(2)	5(1)	8(1)	0(1)
C(27)	30(2)	26(2)	51(2)	9(2)	11(2)	-4(2)
C(28)	26(2)	46(2)	57(2)	13(2)	16(2)	-7(2)
C(29)	16(2)	42(2)	45(2)	3(2)	12(2)	-1(2)
C(30)	15(1)	29(2)	32(2)	-2(1)	7(1)	0(1)
C(31)	21(2)	16(2)	26(2)	-1(1)	0(1)	2(1)
C(32)	18(2)	20(2)	28(2)	3(1)	-1(1)	-1(1)
C(33)	27(2)	31(2)	42(2)	9(2)	-2(2)	2(2)
C(34)	40(2)	22(2)	41(2)	7(2)	6(2)	2(2)
C(35)	34(2)	25(2)	40(2)	3(2)	2(2)	-6(2)
C(36)	26(2)	23(2)	31(2)	-1(1)	5(1)	-1(1)
C(37)	20(2)	19(2)	22(2)	-2(1)	9(1)	-1(1)
C(38)	24(2)	22(2)	20(2)	1(1)	8(1)	-4(1)
C(39)	30(2)	23(2)	26(2)	-2(1)	10(1)	-2(1)
C(40)	44(2)	23(2)	27(2)	-5(1)	16(2)	-8(2)
C(41)	34(2)	33(2)	22(2)	1(1)	6(1)	-11(2)
C(42)	20(2)	32(2)	28(2)	2(1)	6(1)	-4(1)
C(43)	21(2)	24(2)	24(2)	1(1)	9(1)	-3(1)
C(44)	90(4)	63(3)	33(2)	-10(2)	5(2)	10(3)
C(45)	82(4)	113(6)	60(4)	4(4)	-15(3)	-3(4)
C(46)	84(4)	91(5)	56(3)	-11(3)	0(3)	15(4)
C(47)	83(4)	99(5)	72(4)	-18(4)	0(3)	-5(4)
C(48)	69(4)	86(4)	59(3)	6(3)	6(3)	0(3)
C(49)	93(4)	72(4)	40(3)	-13(3)	6(3)	1(3)
C(50)	132(6)	54(3)	66(4)	4(3)	-18(4)	-23(4)
N(1)	26(2)	35(2)	25(1)	-8(1)	10(1)	5(1)
P(1)	12(1)	15(1)	15(1)	-1(1)	3(1)	2(1)

P(2)	13(1)	15(1)	16(1)	-1(1)	2(1)	1(1)
Fe(1)	22(1)	19(1)	13(1)	-1(1)	3(1)	1(1)
Ni(1)	12(1)	16(1)	15(1)	-1(1)	3(1)	2(1)

Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3).

	x	y	z	U(eq)
H(2)	5790	4282	4017	25
H(3)	4830	3449	3321	30
H(4)	4121	4941	2567	30
H(5)	4365	7280	2533	29
H(6)	5323	8133	3236	24
H(8)	5774	9287	4529	28
H(9)	5839	11660	4356	33
H(10)	6539	12531	3818	31
H(11)	7210	11027	3497	30
H(12)	7162	8645	3687	24
H(13)	6565	5409	5176	21
H(14A)	5952	6353	5783	38
H(14B)	5539	6233	4987	38
H(14C)	5814	7705	5302	38
H(16)	6702	8693	6093	26
H(17)	7829	9374	6691	27
H(18)	8521	7811	6273	25
H(20)	6740	4622	6685	35
H(21)	6751	6874	7337	36
H(22)	7880	7559	7916	39
H(23)	8568	5734	7617	38
H(24)	7867	3926	6866	35
H(25)	8933	6800	5482	22
H(26A)	8242	8262	4246	29
H(26B)	8295	8754	5017	29

H(27A)	9023	9997	4606	43
H(27B)	9386	9089	5269	43
H(28A)	9877	8787	4410	50
H(28B)	9229	8336	3856	50
H(29A)	9901	6761	5055	40
H(29B)	9807	6323	4267	40
H(30A)	8732	5944	4070	30
H(30B)	9111	5064	4737	30
H(31)	8346	3691	4903	27
H(32A)	8639	4365	6337	29
H(32B)	9104	4587	5887	29
H(33A)	9133	2165	5693	43
H(33B)	9320	2425	6512	43
H(34A)	8320	1811	6518	43
H(34B)	8595	583	6167	43
H(35A)	7537	1101	5510	43
H(35B)	7996	1308	5052	43
H(36A)	7322	3244	4873	33
H(36B)	7507	3517	5691	33
H(39)	7168	3265	2120	31
H(40)	6507	2825	1006	36
H(41)	5540	3955	601	36
H(42)	5254	5561	1307	32
H(43)	5911	5998	2422	27
H(45)	10001	1968	3496	112
H(46)	10514	3397	2983	98
H(47)	10115	5458	2476	108
H(48)	9121	6203	2499	89
H(49)	8553	4645	2940	86
H(50A)	9001	2467	4103	142
H(50B)	8957	1339	3511	142
H(50C)	8410	2452	3418	142

5.5 References

Reproduced in part with permission from Angewandte Chemie International Edition. Copyright 2015 Wiley-VCH. "Nickel-Catalyzed Amination of Aryl Chlorides with Ammonia or Ammonium Salts"
Green, R.A.; Hartwig, J.F. *Angew. Chem. Int. Ed.* **2015**, *54*, 3768.

(1) Ricci, A. *Modern Amination Methods*; Wiley-VCH Verlag GmbH: Weinheim, 2000.
(2) Kunz, K.; Scholz, U.; Ganzer, D. *Synlett* **2003**, No. 15, 2428.
(3) Ge, S.; Green, R. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 1617.
(4) Borzenko, A.; Rotta-Loria, N. L.; MacQueen, P. M.; Lavoie, C. M.; McDonald, R.; Stradiotto, M. *Angew. Chem. Int. Ed.* **2015**, *54*, 3773.
(5) Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 6054.
(6) Brenner, E.; Fort, Y. *Tetrahedron Lett.* **1998**, *39* (30), 5359.
(7) Brenner, E.; Schneider, R.; Fort, Y. *Tetrahedron* **1999**, *55*, 12829.
(8) Desmarets, C.; Schneider, R.; Fort, Y. *J. Org. Chem.* **2002**, *67*, 3029.
(9) Chen, C.; Yang, L.-M. *J. Org. Chem.* **2007**, *72*, 6324.
(10) Manolikakes, G.; Gavryushin, A.; Knochel, P. *J. Org. Chem.* **2008**, *73*, 1429.
(11) Gao, C.-Y.; Yang, L.-M. *J. Org. Chem.* **2008**, *73*, 1624.
(12) Shimasaki, T.; Tobisu, M.; Chatani, N. *Angew. Chem. Int. Ed.* **2010**, *49*, 2929.
(13) Mesganaw, T.; Silberstein, A.L; Ramgren, S.D.; Fineà Nathel, N.F.; Hong, X.; Liu, P.; Garg, N.K. *Chem. Sci.* **2011**, *2*, 1766.
(14) Ramgren, S. D.; Silberstein, A. L.; Yang, Y.; Garg, N. K. *Angew. Chem. Int. Ed.* **2011**, *50*, 2171.
(15) Hie, L.; Ramgren, S. D.; Mesganaw, T.; Garg, N. K. *Org. Lett.* **2012**, *14* , 4182.
(16) Iglesias, M. J.; Blandez, J. F.; Fructos, M. R.; Prieto, A.; Álvarez, E.; Belderrain, T. R.; Nicasio, M. C. *Organometallics* **2013**, *31*, 6312.
(17) Park, N. H.; Teverovskiy, G.; Buchwald, S. L. *Org. Lett.* **2014**, *16*, 220.
(18) Kampmann, S. S.; Sobolev, A. N.; Koutsantonis, G. A.; Stewart, S. G. *Adv. Synth. Catal.* **2014**, *356*, 1967.
(19) Fine Nathel, N. F.; Kim, J.; Hie, L.; Jiang, X.; Garg, N. K. *ACS Catal.* **2014**, *4*, 3289.
(20) Kuhl, S.; Fort, Y.; Schneider, R. *J. Organomet. Chem.* **2005**, *690*, 6169.
(21) Details of this work were described at the 248th ACS National Meeting and Exposition August 10-14, 2014, San Francisco, CA, INOR-94. CODEN: 69SZG4 AN 2014:1303205 CAPLUS.
(22) J. A. Dean, Lange's Handbook of Chemistry, McGraw-Hill, Inc., 1999.
(23) Hancock, R. D.; Bartolotti, L. J. *Chem. Commun.* **2004**, *5*, 534.
(24) Shen, Q.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 10028.
(25) Surry, D. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 10354.
(26) Schulz, T.; Torborg, C.; Enthaler, S.; Schäffner, B.; Dumrath, A.; Spannenberg, A.; Neumann, H.; Börner, A.; Beller, M. *Chem. Eur. J.* **2009**, *15*, 4528.
(27) Vo, G. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2009**, *131*, 11049.
(28) Lundgren, R. J.; Sappong-Kumankumah, A.; Stradiotto, M. *Chem. Eur. J.* **2010**, *16*, 1983.

(29) Lundgren, R. J.; Peters, B. D.; Alsabeh, P. G.; Stradiotto, M. *Angew. Chem. Int. Ed.* **2010**, *49*, 4071.
(30) Alsabeh, P. G.; Lundgren, R. J.; McDonald, R.; Johansson Seechurn, C. C. C.; Colacot, T. J.; Stradiotto, M. *Chemistry* **2013**, *19*, 2131.
(31) Cheung, C. W.; Surry, D. S.; Buchwald, S. L. *Org. Lett.* **2013**, *15*, 3734.
(32) Crawford, S. M.; Lavery, C. B.; Stradiotto, M. *Chem. Eur. J.* **2013**, *19*, 16760.
(33) Klinkenberg, J. L.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 11830.
(34) Ge, S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2011**, *133*, 16330.
(35) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, *12*, S1.
(36) Green, R. A.; Hartwig, J. F. *Org. Lett.* **2014**, *16*, 4388.
(37) Henderson, R. K.; Jiménez-González, C.; Constsable, D.J.C.; Alston, S.R.; Inglis, G.G.A.; Fisher, G.; Sherwood, J.; Binks, S.P.; Curzons, A.D. *Green Chem* **2011**, *13*, 854.
(38) Alfonsi, K.; Colberg, J.; Dunn, P. J.; Fevig, T.; Jennings, S.; Johnson, T. A.; Kleine, H. P.; Knight, C.; Nagy, M. A.; Perry, D. A.; Stefaniak, M. *Green Chem.* **2008**, *10*, 31.
(39) Schley, N. D.; Fu, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 16588.
(40) Hu, X. *Chem. Sci.* **2011**, *2*, 1867.
(41) The coupling reaction of 4-chlorobenzonitrile conducted in the absence of nickel catalyst did not yield 4-aminobenzonitrile.
(42) Wang, Y.-F.; Gao, Y.-R.; Mao, S.; Zhang, Y.-L.; Guo, D.-D.; Yan, Z.-L.; Guo, S.-H.; Wang, Y.-Q. *Org. Lett.* 2014, *16*, 1610.