DEVELOPMENT AND MECHANISTIC INVESTIGATION OF THE PALLADIUM-CATALYZED α-ARYLATION OF ALDEHYDES AND *N*-ARYLATION OF AMMONIA

BY

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DISSERTATION

Submitted in partial fulfillment of the requirements
for the degree of Doctor of Philosophy in Chemistry
in the Graduate College of the
University of Illinois at Urbana-Champaign, 2010

Urbana, Illinois

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ABSTRACT

A general method for the palladium-catalyzed α-arylation of aldehydes was developed to couple linear and branched aldehydes with electron-poor and electron-rich bromo- and chloroarenes in high yields. Catalysts generated from allylpalladium chloride (APC) and 1,1'-diphenylphosphinoferrocene (DPPF) coupled linear aldehydes with aryl bromides, and catalysts generated from APC and Q-phos coupled branched aldehydes with aryl bromides and chlorides. Arylpalladium enolate complexes of aldehydes were proposed as intermediates in this process, and these complexes were isolated and characterized. The effects of steric and electronic properties of the aryl groups on the rates of reductive elimination and yields of coupled products were evaluated. The reactivity of these complexes and an arylpalladium enolate complex of acetone was compared.

A general method for the palladium-catalyzed coupling of ammonia with aryl halides and sulfonates was also developed. The catalyst generated from $Pd[P(o\text{-tol})_3]_2$ and the alkylbisphophine CyPF-*t*-Bu is a highly active and selective catalyst for the coupling of ammonia with aryl chlorides, bromides, iodides, and sulfonates. The couplings of ammonia with this catalyst conducted with a solution of ammonia in dioxane formed primary arylamines from a variety of aryl electrophiles in high yields. Catalyst loadings as low as 0.1 mol % were sufficient for reactions of many aryl chlorides and bromides. In the presence of this catalyst, aryl sulfonates also coupled with ammonia for the first time in high yields. The utility of this method to generate amides, imides, and carbamates is illustrated by a one-pot synthesis of a small library of these carbonyl compounds from aryl bromides and chlorides, ammonia, and acid chlorides or anhydrides. Mechanistic studies showed that reactions conducted with the combination of CyPF-

t-Bu and Pd[P(*o*-tol)$_3$]$_2$ as catalyst occur with faster rates and higher yields than those conducted with CyPF-*t*-Bu and palladiun(II) as catalyst precursors.

To my parents

"*The fear of the Lord is the beginning of knowledge; fools despise wisdom and instruction.*"

Proverbs 1:7

ACKNOWLEDGMENTS

During the past five years, I have had the privilege of being mentored and working with many talented individuals. I am indebted to my advisor Professor John Hartwig for teaching me scientific writing and presentation. I thank him for giving me the opportunity to work in his labs, encouraging me, teaching me organometallic chemistry, and being so patient. I thank my thesis committee members, Prof. Scott Denmark, Prof. M. Christina White and Prof. Gregory Girolami, for their support and encouragement.

It was a pleasure to work with such a talented group of scientists in the Hartwig group. I thank the "ammonia-team" members, Prof. Qilong Shen and Jessica Klinkenberg for many hours of engaging philosophical and scientific discussions. I am especially grateful to Qilong for his help when I started research in the group, many thanks to him for sharing his vast knowledge of the literature. I thank Jessica for proofreading my research summaries and a part of my thesis. The entire Hartwig group was instrumental in my development as a scientist. They spent many hours helping me rehearse presentations, write prelim paper and learn new lab techniques. I thank Nam Holda for organizing many fun group activities.

I thank the three administrative assistants, Becky, Stacy and Susan, for their down-to-earth personalities and for feeding this hungry graduate student with Butterfingers, Starbursts, cashews and delicious chicken salads. We had so many good memories. They made me smile every time I walked into their office after an exhaustive experiment or meeting. I don't think I will ever again find administrative assistants like them.

This work would not be accomplished had my family not been so supportive and loving. I thank my brother, Kha Vo, for being a true big brother who always encourages and helps me. I

dedicate this work to my parents. I thank them for making the decision to go to America so my brother and I could get an education. They have taught me strong family values and personal integrity. They are the best parents I could ever have. I thank my mom for her wisdom and insight. She taught me how to write and how to be content in life. I thank my Dad for teaching me integrity and hard work in all areas of life. In a way, I hope to have fulfilled my parents' dream of going to America. Mom and Dad, you are the best.

Above all, I want to thank my heavenly Father who has made everything possible. This work was only possible through His unfailing love and sovereign grace. He surrounded me with a wonderful family, supportive friends and knowledgeable colleagues. Without His teaching through the Bible, I could never have looked at research as an exciting search for the truth. I thank my Lord and Savior Jesus Christ for freeing me from bondage to the pursuit of fame, money and pleasure by His blood. The joy of working in lab comes from serving others because He has served me with boundless love and sacrifice:

> "…even as the Son of Man came not to be served but to serve, and to give his life as a ransom for many." Matthew 20:28

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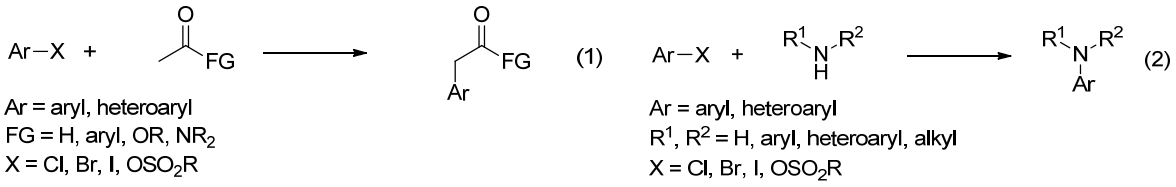
1.1. Introduction

Carbon-carbon (C-C) and carbon-heteroatom (C-X, X = N, O, S) bonds are present in molecular structures of pharmaceuticals, materials and bulk chemicals. Reactions that form these bonds are essential solutions to our energy and health challenges. During the last half of the 20th century, developments of new reactions greatly increased our living standards, and over 15 Nobel Prizes were awarded for this endeavor. Some notable reactions are olefin metatheses, Ziegler-Natta polymerizations, Diels-Alder reactions and asymmetric hydrogenations. These methods are now found in chemistry textbooks.[1] With the rising demand for energy and health care, the development of new reactions must occur at a faster pace. Thus, the first decade of this century has seen more rapid progress in the development of new reactions. Much of this effort focuses on developing transition-metal catalyzed reactions that have become essential tools for synthetic chemists.



This introductory chapter focuses on the history of the development of two key methodologies: the construction of carbon-carbon bonds by the α-arylation of carbonyl compounds with aryl halides and pseudohalides to form α-aryl carbonyl compounds (eq 1) and the construction of carbon-nitrogen bonds by the amination of aryl halides and sulfonates to form

arylamines (eq 2). The α-aryl carbonyl and *N*-aryl amine unit are found in drug candidates, natural products and polymers. For example, the α-aryl carbonyl moiety is found in a large number of analgesic and nonsteroidal anti-inflamatory drugs such as Naproxen, Ketoprofen and Diclofenac (Figure 1).[2] Numerous natural products such as lucuminic acid[3] and polimastamide A[4] also contain this moiety.

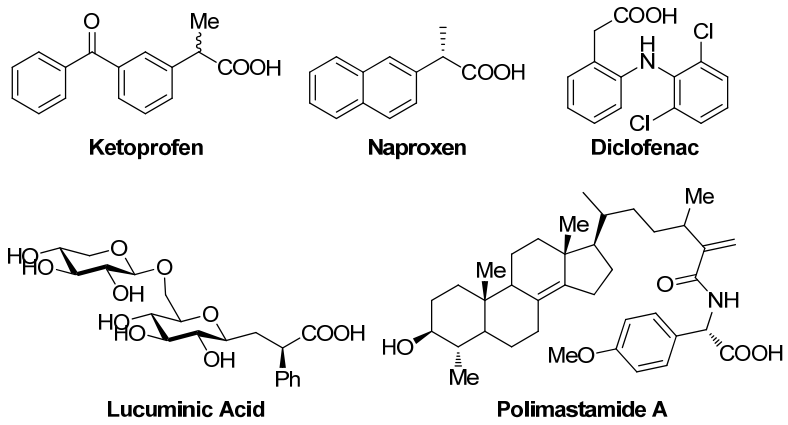


Figure 1. Examples of drugs and natural products containing the α-aryl carbonyl moiety

Arylamines are building blocks for polymers, dyes, agrochemicals and rubber,[5,6] and are found in many important drugs and drug candidates (Figure 2). For example, *N*-arylpiperazines, such as aripiprazole and (benzimidazolyl)piperazines, are candidates for anti-depressant and anti-psychotic drugs.[7-10] Torcetrapib was a high-profile drug candidate that increase HDL levels.[11] Lumiracoxib is a non-steroidal anti-inflammatory drug that contains both the arylamine and α-aryl carbonyl units. The following sections discuss the development of reactions that form these units. Discussion will focus on palladium-catalyzed methods that are central to the work described in this dissertation.

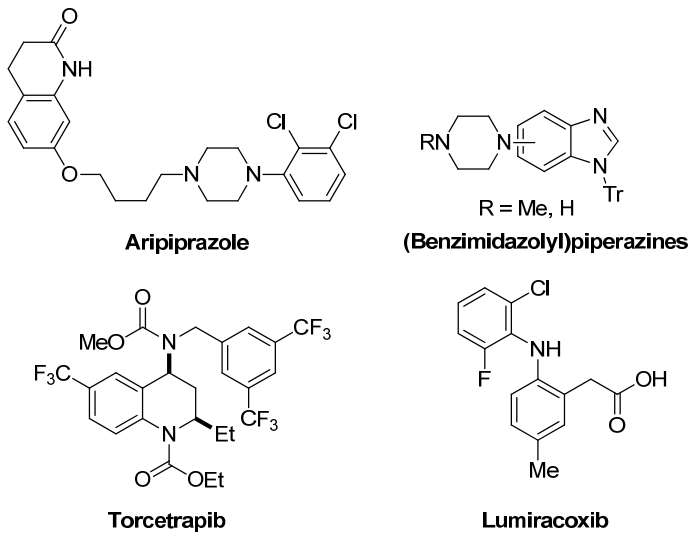


Figure 2. Examples of drugs and drug candidates containing arylamine moiety

1.2. Overview of α-Arylation of Carbonyl Compounds

1.2.1. Noncatalytic Methods

Prior to the advent of transition-metal-catalyzed reactions, the synthesis of α-aryl carbonyl compounds was achieved through nucleophilic aromatic substitution (S_NAr) of aryl halides with enolates and through nucleophilic coupling of enolates with aryl radicals ($S_{RN}1$). The S_NAr reaction occurs with only activated aryl halides, whereas the $S_{RN}1$ occurs with a broader scope of aryl halide and enolates. Thus, the $S_{RN}1$ reaction was the preferred method. The development of both methods dates back to the 1960s, but since the advent of transition-metal-catalyzed α-arylation reactions, these methods are rarely applied in contemporary synthesis.

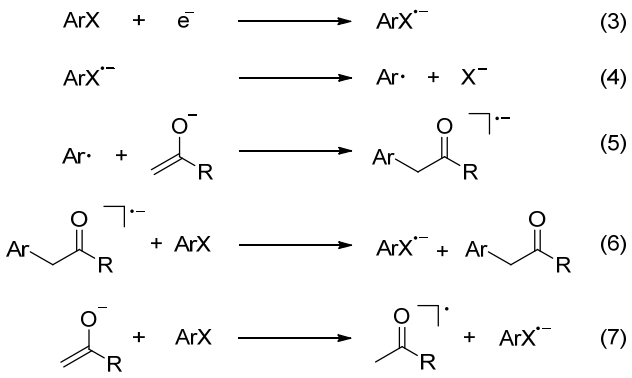
1.2.1.1. The S_NAr Reaction

The uncatalyzed nucleophilic aromatic substitution of aryl halides with enolates is known to occur through two pathways: a two-step addition-elimination pathway that is common to activated aryl halides and a two-step elimination-addition pathway via benzyne intermediates

that is common to both activated and electron-neutral aryl halides.[12] The two-step addition-elimination pathway occurs only with nitro arenes. The nucleophile scope encompasses ketones, esters and alkylnitriles.[12] The reactions occurring through benzyne intermediates encompass amides and nitriles. Benzyne intermediates are generated from reactions of aryl halides with metal amide base or from reactions of aryl diazonium compounds with alkali metal acetate.[12-14] Regioselectivity is usually low in the reactions with unsymmetrical arenes.

1.2.1.2. The $S_{RN}1$ Reaction

The $S_{RN}1$ reaction of aryl halides and carbonyl compounds dates back to the late 1960s and early 1970s. The term $S_{RN}1$ stands for substitution, radical nucleophilic, unimolecular. The reaction is initiated by a single electron transfer from an enolate to an aryl halide (eq 3) via photostimulated processes, thermal processes, added nonparticipant nucleophiles, radical anions, or dissolved alkali metals (eq 7).[12] The aryl halide radical anion dissociates to give an aryl radical species and a halide. The aryl radical species associates with the enolate nucleophile to form the α-aryl carbonyl radical anion (eq 4 and 5). Single-electron transfer from the carbonyl radical anion to an aryl halide propagates the reaction (eq 6). These reactions are usually conducted in liquid ammonia or acetonitrile to dissolve the ionic alkali metal enolate and to prevent hydrogen atom abstraction from solvent by radical intermediates.



To date, the $S_{RN}1$ reactions of carbonyl compounds with aryl halides encompass ketone, aldehyde, amide and malonate nucleophiles. Of these reactions, those of ketones occur with the broadest scope. Dialkyl ketones are more reactive than alkyl aryl ketones. Reactions of aldehydes, amides and malonates are limited to a handful of examples. The scope of electrophiles encompasses aryl iodides, aryl bromides and heteroaryl chlorides.

The limitations of the $S_{RN}1$ reaction are well understood in the context of reactions with ketones. The reactions are initiated by interactions of a ketone nucleophile with an alkali metal or by photoactivation. The yield of α-aryl ketones from reactions initiated with an alkali metal, such as potassium, is usually lower than that from reactions initiated photochemically. Both methods of activation have limitations. In the presence of potassium, alcohols are formed from the reduction of the starting ketone or product ketone. Moreover, aryl halides containing a naphthalenyl group can undergo the Birch reduction in the presence of alkali metal and ammonia solvent. Under photochemical conditions, reactions occur in the presence of an amide or *tert*-butoxide base; thus, base-sensitive functional groups are not tolerated.

Other competing reactions are common to both activation methods. Radical intermediates shown in eq 4 can undergo side reactions to terminate the chain. For example, the aryl radical can abstract a β-hydrogen on the nucleophile to form α,β-unsaturated ketone, which can further react with the ketone enolate to form a 1,5-diketone side product. Diarylation of the ketone can occur to account for up to 30% of the product composition. Low regioselectivity in reactions of dialkyl ketones is an another limitation. For example, the coupling of 2-butanone with either iodo- or bromobenzene in liquid ammonia under photostimulated conditions occurs

preferentially at the C3 position with 1.3-3.2:1 selectivity. However, arylation of 3-methyl-2-butanone is favored at the less sterically hindered position with 5-16:1 selectivity.[15]

1.2.1.3. α-Arylation of Carbonyl Compounds with Main-Group Metal Aryl Reagents

Reactions of electrophilic main-group aryl reagents with carbonyl compounds have been explored as alternatives to the S_NAr and $S_{RN}1$ reactions. Aryllead,[16] arylbismuth,[17] (π-halogenobenzene)chromium tricarbonyls,[18,19] diaryldiazonium salts,[20-25] and arylazo-*tert*-butyl sulfides[26] have been shown to react with ketones, dicarbonyl compounds or silyl enol ethers to give good yields of α-aryl carbonyl products.

Arylcopper,[27-29] arylcadmium,[30] arylboron[31] and aryl Grignards[32] have been shown to react with α-halo carbonyl compounds in an umpolung fashion. However, these methods have many drawbacks. First, α-halo carbonyl compounds are less available from commercial suppliers than the parent carbonyl compounds. Second, the scope of these reactions is limited in both the carbonyl and aryl coupling partners because the synthesis of these arylmetal reagents is difficult and the high reactivity of aryl Grignards limits functional group tolerance. Finally, stoichiometric amounts of toxic and expensive main-group reagents greatly hinder synthetic application.

1.2.2. Palladium-Catalyzed Methods

The first examples of palladium-catalyzed α-arylation of carbonyl compounds were reported in the late 1970s and early 1980s. Aryl and vinyl halides and aryl triflates were coupled with Reformatsky reagents,[33-35] silyl enol ethers[36], silyl ketene acetals[37,38] or enol acetates[39,40] in the presence of toxic additives such as thalium acetate and tributyltin methoxide. The scope of these reactions was limited to acetate esters and methyl ketones. New catalytic methods with less expensive, less toxic and more readily available alkali metal enolates were not discovered until

more than 10 years later. In 1997, the groups of Hartwig,[41] Buchwald[42] and Miura[43] reported the first examples of intermolecular[44] palladium-catalyzed coupling of aryl bromides with ketones in the presence of alkali metal bases. New developments soon followed that have transformed this methodology into a powerful tool for the synthesis of α-aryl carbonyl compounds. The following sections cover the advances in this field since 1997 and are arranged by the type of enolate nucleophile, including ketones, carboxylic acid derivatives, dicarbonyl compounds, alkylnitriles and nitroalkanes.

1.2.2.1. α-Arylation of Ketones and Derivatives with Aryl Halides and Sulfonates

Over the past decade, the scope of the direct palladium-catalyzed α-arylation of ketones has broadened to encompass dialkyl, alkyl aryl and alkyl heteroaryl ketones. In some cases, silyl enol ethers derived from ketones have been employed to overcome problems with regio- and chemoselectivity. The scope of vinyl and aryl halides encompasses vinyl bromides, aryl iodides, aryl bromides and aryl chlorides with substituents ranging from electron-rich to electron-poor. Aryl triflates, tosylates and benzenesulfonates also undergo coupling with ketones, but with narrower scope than aryl halides. Enantioselective processes have been developed to form products containing quaternary α centers with high enantiomeric purity.

1.2.2.1.1. α-Arylation of Ketones

Reactions with Aryl Halides. Several challenges are associated with the α-arylation of ketones. First, arylation of dialkyl ketones that contain α and α' C-H bonds can occur with low regioselectivity. Second, aldol additions could be major side reactions under palladium-catalyzed cross-coupling conditions. Third, diarylation of ketones containing an α-methyl or α-methylene carbon can occur because the α-aryl ketone product is more acidic than the starting ketone.

The development of new catalysts and reaction conditions provides solutions to these challenges. Generally, ketones bearing α and α' hydrogens are arylated preferentially at the less hindered position.[42,45,46] To arylate the more hindered carbon, silyl enol ethers have been used (*vide infra*). Catalysts containing hindered ligands favor monoarylation over diarylation of ketones containing an α-methyl or α-methylene carbon.

The first-generation catalysts contain bisphosphine ligands shown in Figure 3. In 1997, Hamann and Hartwig showed that palladium complexes of D*t*BPF couple ketones with aryl bromides in the presence of potassium bis(trimethylsilyl)amide (KHMDS).[41] Palucki and Buchwald showed that complexes of BINAP catalyze the same transformation in the presence of sodium *tert*-butoxide (NaO*t*Bu).[42] In the same year, Miura and coworkers reported that ligandless $PdCl_2$ catalyzes for the diarylation of 1,3-diphenyl-2-propanone in the presence of Cs_2CO_3.[43]

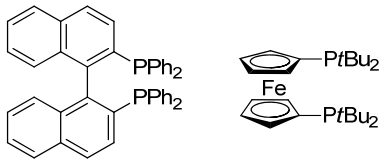


Figure 3. Bisphosphines in the first generation of catalysts for α-arylation of ketones

Reactions of aryl bromides occurred with up to 20,000 TON at 70 °C in the presence of complexes containing D*t*BPF.[45] With 2 mol % of the catalyst, phenyl bromide reacted at room temperature.[41,45] Reactions of electron-neutral and electron-rich aryl chlorides occurred at higher temperatures with yields similar to those obtained from reactions of aryl bromides. By monitoring reactions of D*t*BPF-ligated arylpalladium bromide complexes with the enolate of isobutyrophenone, Hartwig and coworkers concluded that D^{t}BPF binds to palladium through an κ^1 mode. This discovery led the researchers to test a catalyst containing the hindered and

electron-rich monophosphine P*t*Bu$_3$. Similar rates and yields were achieved with this catalyst in the α-arylation of aryl alkyl ketones with unactivated aryl bromides.[45]

Following this discovery, other research groups developed and tested other hindered alkylmonophosphines for the α-arylation of ketones (Figure 4).[46,47] Of these phosphines, Beller's di(1-adamantyl)-*n*-butylphosphine (cataCXium® A) formed catalysts that couple unactivated aryl chlorides with aryl alkyl ketones with TON up to 4100.[47] Until 2002, palladium complexes of these hindered tertiary alkylmonophosphines were the most active and selective catalysts for the coupling of ketones with aryl chlorides and bromides.

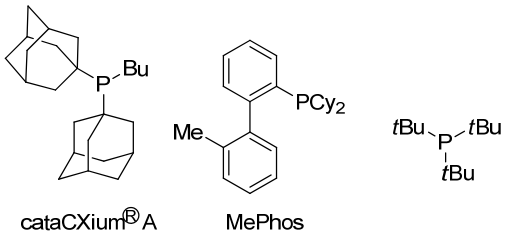


Figure 4. Electron-rich and sterically hindered monophosphines for the α-arylation of ketones

N-heterocyclic carbenes (NHCs) are more σ-donating and less π-withdrawing than phosphines and have been shown by the Nolan group to form active catalysts with palladium for the α-arylation of ketones with aryl bromides, chlorides and triflates.[48-52] With 1 mol % of the precatalysts shown in Figure 5, reactions of alkyl aryl ketones and dialkyl ketones with aryl bromides, chlorides occurred in good yield at 60-80 ^{o}C. The activity of these catalysts is similar to, but does not exceed that of catalysts containing alkylmonophosphines.

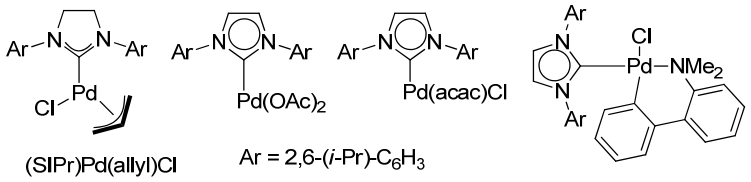


Figure 5. Nolan's precatalysts for the α-arylation of ketones

Bertrand and coworkers designed more electron rich cyclic (alkyl)(amino)carbenes (CAACs) (Figure 6) and showed that palladium complexes of CAAC couple propiophenone with sterically hindered 2-chloro-*m*-xylene at 50 ^{o}C and phenyl chloride at room temperature with up to 7200 TON.[53] Complexes containing CAAC are currently the most active catalysts for the coupling of ketones with aryl chlorides.

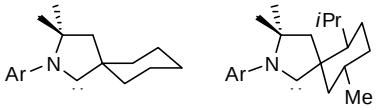
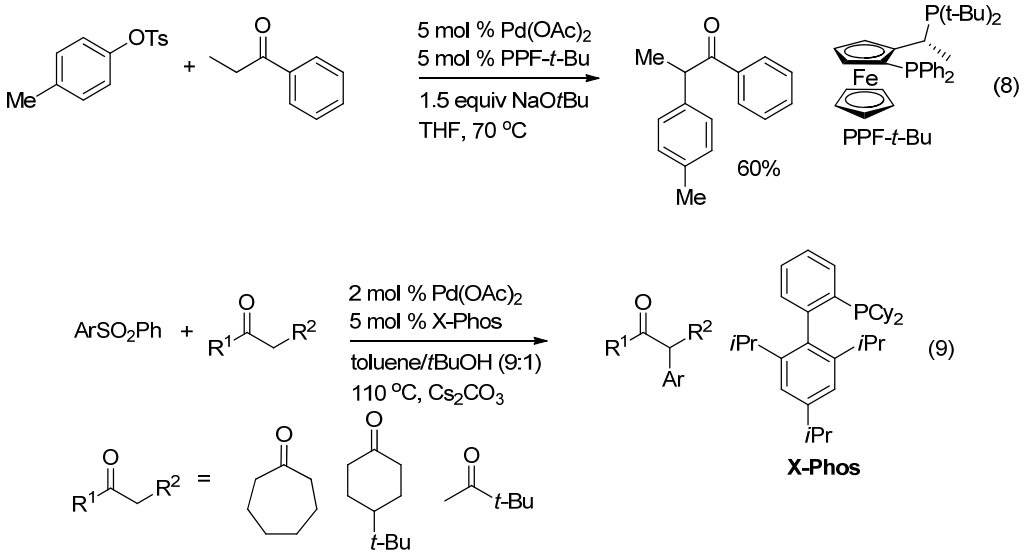


Figure 6. Bertrand's cyclic (alkyl)(amino)carbenes

Reactions with Aryl Sulfonates. The reactivity of aryl triflates toward oxidative addition to palladium is known to exceed that of aryl chlorides and to closely match that of aryl bromides. Nolan and workers reported one of the first coupling reactions of ketones with aryl triflates. The complex generated from 1 mol % of (SIPr)Pd(allyl)Cl (Figure 5) coupled dialkyl and aryl alkyl ketones with electron-neutral and electron-rich aryl triflates in good yield.[48]

Although aryl tosylates and aryl benzenesulfonates are cheaper alternatives to aryl triflates and bromides, aryl tosylates are less reactive toward oxidative addition to palladium than aryl halides and triflates. There are only two reports of α-arylation of ketones with aryl tosylates and benzenesulfonates. The first example was reported by Kawatsura and Hartwig in 1999. *p*-

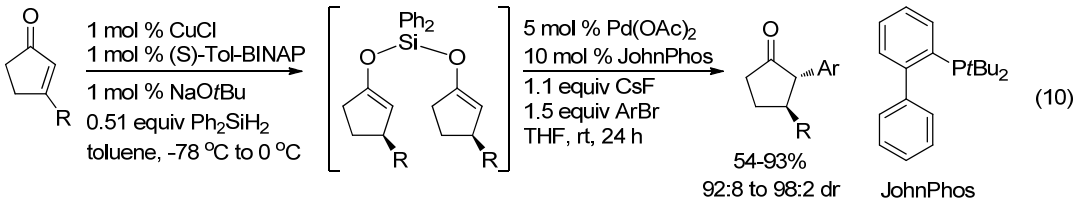
Tolyl tosylate coupled with propiophenone in the presence of the Josiphos ligand PPF-*t*-Bu in 60% yield of coupled product (eq 8).[45] In 2003, Buchwald and coworkers showed that reactions of arylbenzene sulfonate with three dialkyl ketones catalyzed by palladium complexes of X-Phos occur with remarkable selectivity for formation of the monoarylated product (eq 9).[54]

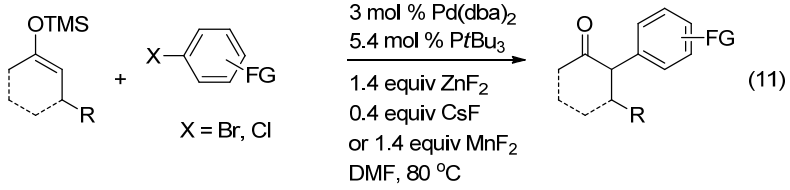


1.2.2.1.2. α-Arylation of Ketones Derived from Silyl Enol Ethers

Despite the progress toward making the α-arylation of ketones a practical synthetic method described in the previous sections, several challenges remain. First, selective arylation at the more hindered carbon of dialkyl ketones containing α-methyl and α'-methylene carbons remains a challenge. Arylation occurs at the less hindered α-methyl group. Second, the basic conditions limit control of stereochemistry. α-Aryl carbonyl products with new tertiary α-stereocenters are more acidic than the starting materials, and thus they can undergo racemization. Third, reactions conducted with a strong base, e.g. NaO*t*Bu, do not tolerate aryl halides containing ester, methyl ketone, unprotected hydroxyl and nitro groups.

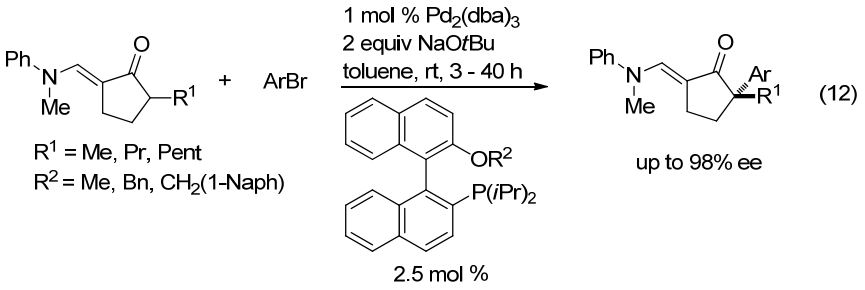
These limitations can be overcome with the reaction of a silyl enol ether with an aryl halide in the presence of a less basic additive. The Rawal and Kuwajima groups showed that ketone-derived silyl enol ethers couple with aryl halides in the presence of toxic tributyltin fluoride and palladium catalysts to form α-aryl ketones in good yield.[24,36] The Buchwald, Hartwig and Verkade groups showed that the palladium-catalyzed coupling of aryl bromides with silyl enol ethers occur in the presence of cheaper and safer fluoride additives such as MnF_2, CsF and ZnF_2.[55-57] Buchwald and coworkers described a highly diastereoselective α-arylation of enriched β-substituted pentanones from the corresponding *in situ*-generated and enantioenriched diphenylsilyl enol ethers in the presence of CsF additive (eq 10).[55] The groups of Hartwig and Verkade together reported an α-arylation of the more sterically hindered α carbon of dialkyl ketones derived from silyl enol ethers. The reactions occurred in high yield in the presence of a unique combination of ZnF_2 and CsF or MnF_2 and encompass aryl halides that contain unprotected aryl alcohol, nitro, ester, enolizable keto and cyano groups. (eq 11).[56]





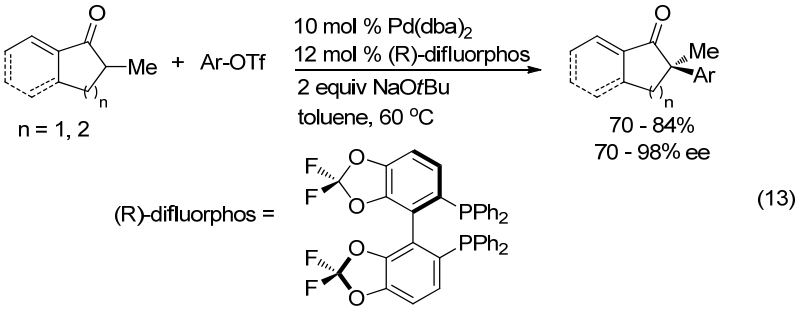
1.2.2.1.3. Enantioselective α-Arylation of Cyclic Ketones

Currently, enantioselective α-arylation of ketones occurs in high enantioselectivity with only cyclic substrates. In 1998, Buchwald and coworkers reported the first enantioselective palladium-catalyzed α-arylation of ketones using catalysts containing (*S*)-BINAP.[58] In the presence of 10 to 20 mol % of catalyst, 2-methyl-α-tetralone and 2-methyl-α-indanone coupled with aryl bromides with enantioselectivities up to 74%. α'-Blocked α-methylcycloalkanones also coupled with aryl bromides in high enantioselectivity. α'-Blocked α-methylcylcopentanone reacted with aryl bromides with much higher enantioselectivities than did the cylcohexanone analog under the same reaction conditions. Currently, no good explanation for this difference in enantioselectivity is available. In 2002, Buchwald and coworkers reported catalyst containing MOP derivatives[59] to couple α'-blocked α-substituted cyclopentanones with aryl bromides with improved enantioselectivities of up to 98% (eq 12).



In 2008, Hartwig and coworkers showed that palladium complexes of (*R*)-difluorphos couple 2-methyl-α-tetralone and 2-methyl-α-indanone with aryl triflates with 70-95% ee (eq 13).[60] The highest enantioselectivities from reactions of these cyclic ketones are currently obtained with this catalyst. Reactions with electron-poor aryl triflates occurred with much lower enantioselectivities than those with electron-rich and electron-neutral ones. The authors showed

that nickel complexes of difluorphos couple 2-methyl-α-tetralone and 2-methyl-α-indanone with electron-poor aryl triflates in higher enantioselectivity than palladium complexes of difluorphos (*vide infra*). The α-arylation of α'-blocked α-substituted cyclopentanones and cyclohexanones occurred with 77-95% ee, which are the highest enantioselectivities reported for these substrates.



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1.2.2.2. α-Arylation of Carboxylic-Acid Derivatives

Although developing the palladium-catalyzed α-arylation of esters and amides from protocols developed for the reactions of ketones appeared simple, the higher pK_a values of esters and amides[61] and the lower stability of ester-derived enolate[62] present challenges for expansion of the scope of the α-arylation pocess to the reactions of carboxylic acid derivatives. Strong bases, such as $LiNCy_2$, have been used, but they undergo rapid side reactions with electron-deficient aryl halides at the functional groups or at the acidic aromatic C-H bonds to form benzyne intermediates.[63] Weaker bases and preformed zinc and silicon enolates have been used to expand the scope of aryl halide that undergoes these coupling reactions. Catalysts that couple esters with aryl halides must react with rates that are faster than those of enolate decomposition and Claisen condensation. Catalysts containing hindered ligands must also prevent diarylation of unhindered esters and amides.

1.2.2.2.1. α-Arylation of Esters with Aryl Halides and Sulfonates

Generally, reactions of *tert*-butyl esters produced higher yield of coupled products than those of ethyl or methyl esters because *tert*-butyl esters undergo Claisen condensation more slowly methyl or ethyl esters. Only α–mono or α–disubstituted ethyl esters underwent coupling in good yield.[63] Effects of the alkali counterion of the base on the selectivity of mono- over diarylation were observed.[62,63] These effects on reactions of acetate esters were most pronounced. Reactions conducted with LiHMDS occurred with higher selectivity than those conducted with NaHMDS.[62-64] This result was explained by the greater covalency of Li-O bonds of enolates than of Na-O bonds.[65] Enolates with a more covalent metal-oxygen bond undergo slower proton transfer. The lithium enolate of the α-aryl ester product undergoes slower proton transfer with the starting ester than the sodium enolate; thus, the rates of diarylation of lithium enolate are slower. This explanation was given by Hampton and coworkers in the context of α-alkylation of sodium and potassium enolates of acetylacetone.[66]

Reactions of the more hindered *tert*-butyl propionate conducted with NaHMDS still afforded high selectivity for the monoaryl ester versus the diaryl ester.[62] Buchwald and coworkers showed that reactions catalyzed by 3 mol % of palladium complexes containing Davephos (Figure 7) occur at room temperature.[63] Aryl chlorides underwent coupling in the presence of the more electron-rich tBuDavePhos at 80 ^{o}C. Hartwig and coworkers showed that reactions of *tert*-butyl propionate catalyzed by palladium complexes of SIPr occur faster than those catalyzed by complexes of tBuDavePhos, and reactions of α-branched ethyl and methyl esters with aryl bromides and phenyl chloride occurred at room temperature with as low as 0.5 mol % of catalyst.[62]

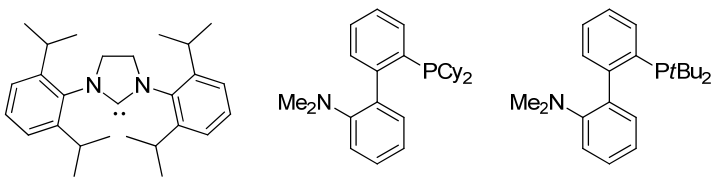


Figure 7. Ligands for the first α-arylation and α-vinylation of esters

The α-arylations of acetate esters has been more challenging than that of α-substituted esters because the enolates of acetate esters are less stable than those of propionate or α-aryl acetate esters, and diarylation is a more significant competing process. These challenges are more pronounced in reactions with aryl chlorides than in those with aryl bromides.[67,68] Biscoe and Buchwald reported that catalysts generated from the palladacycle containing the bulky *t*BuXPhos (Figure 8) couple aryl and heteroaryl chlorides with acetate esters in excellent yield. The authors proposed that the high activity of this catalyst and its bulky nature make the coupling reaction faster than decomposition of ester-derived enolate and the rates of diarylation.[68]

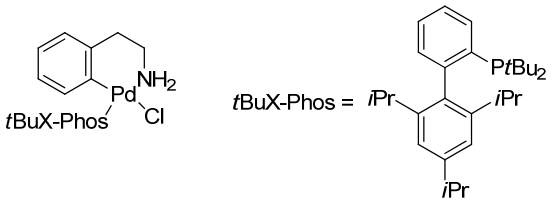
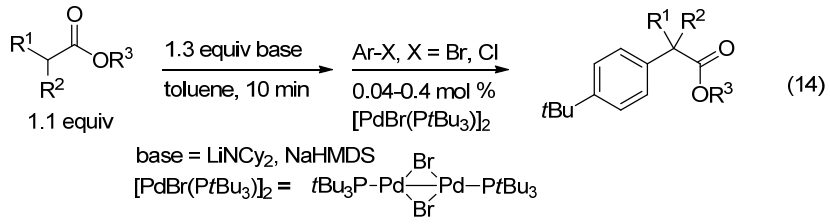


Figure 8. Buchwald's tBuX-Phos palladacycle

The α-arylation of α,α-dialkyl esters to form quarternary centers occurred with good yield in the presence of $LiNCy_2$,[64] whereas reactions in the presence of LiHMDS generated a mixture of products that include those formed from C-N coupling between the base and aryl halides. Hartwig and coworkers showed that the coupling of α,α-dialkyl esters with aryl and heteroaryl bromides occur at room temperature in the presence of $Pd(dba)_2$ and P*t*Bu_3. Before

2008, the most active catalysts for the α-arylation of esters were generated from electron-rich and sterically hindered monophosphines or *N*-heterocyclic carbenes. In 2008, Hama and Hartwig showed that the Pd(I) dimer $[PdBr(P\textit{t}Bu_3)]_2$ is the most active catalyst for the coupling of esters with aryl bromides and chlorides. Reactions of esters with aryl chlorides occurred in good yield with 0.1-0.4 mol % of the dimer. Reactions with aryl bromides occurred at room temperature in 79-87% yields with as low as 0.04 mol % of the dimer. These turnover numbers are significantly higher than those reported with catalysts containing NHCs or $P\textit{t}Bu_3$ (eq 14).[67,69] This catalyst has been used by Bercot *et al* at Amgen to perform a diastereoselective α-arylation of 4-substituted cyclohexyl esters with up to 37:1 dr.[70]



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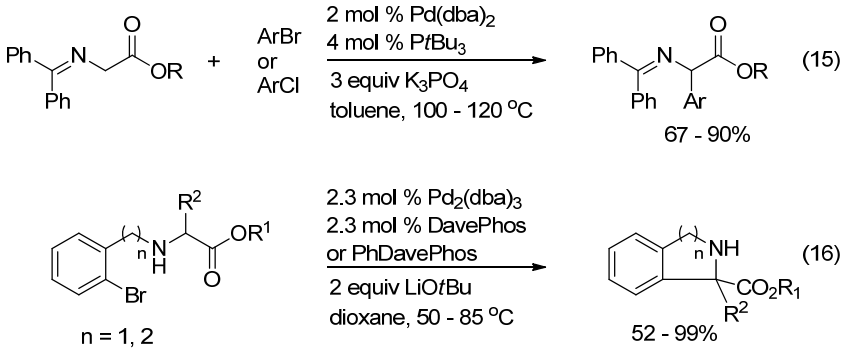
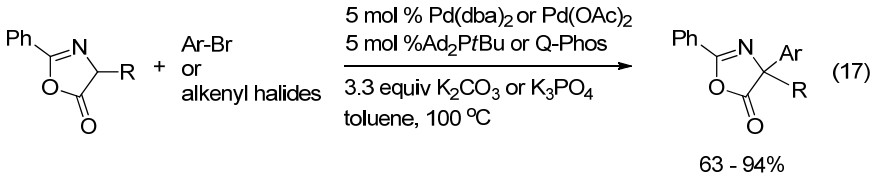
1.2.2.2.2. α-Arylation of Protected Amino Acids and Azlactones

α-Aryl amino acids are common structural motifs in many natural products and pharmaceutical compounds.[71,72] α-Aryl amino acids are usually prepared by Strecker chemistry that involves multiple functional group manipulations.[73] Thus, the palladium-catalyzed α-arylation of protected amino acids could provide a shorter route to these valuable compounds. In this vein, the catalysts for the α-arylation of esters coupled benzophenone imine-protected amino acids with aryl halides in high yield in the presence of the weak base K_3PO_4 (eq 15).[62,74] As shown in eq 16, the intramolecular α-arylation reactions of amino acid derivatives were

conducted with the stronger base LiO*t*Bu because of the higher pK_a values of the $N(sp^3)$-amino acids.[75]



Azlactones are more reactive than the benzophenone imine-protected amino acids because of their enhanced acidity and rigid cyclic structure.[76] Liu and Hartwig showed that a palladium catalyst containing sterically hindered and electron-rich bis(1-admantyl)-*tert*-butylphophine or Q-Phos couple azlactones with aryl and alkenyl halides in good yield (eq 17).[76]



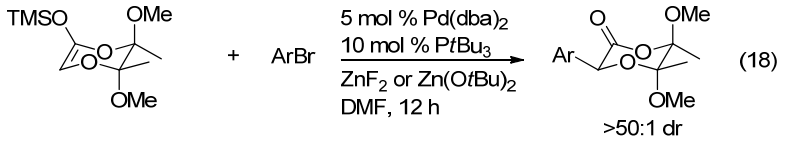
1.2.2.2.3. α-Arylation of Lactones

Because of the cyclic structure and well-defined enolate geometry of lactones, most developments in α-arylation of lactones have been focused on enantioselective reactions.[77] Spielgovel and Buchwald reported that palladium complexes of chiral, nonracemic BINAP couple α-methyl-γ-butyrolactone with aryl bromides in 60% ee.[78] They found that nickel

catalysts containing the same ligand couple α-monosubstituted lactones with aryl halides to form α-aryl lactones containing quaternary α centers in higher enantioselectivities (*vide infra*).

1.2.2.2.4. α-Arylation of Silyl Ketene Acetals and Reformatsky Reagents

The α-arylation of esters derived from silyl ketene acetals offers several advantages over the direct α-arylation of esters. For example, the substrate scope can be expanded to include base sensitive functional groups, and product containing tertiary α-stereocenters can be formed. For example, Santi and Musco showed that the reactions of the silyl ketene acetal of methyl propionate with aryl bromides occurred with 26-54% ee in the presence of TlOAc and a chiral bisphosphine such as BINAP.[38] Hartwig and coworkers showed that the reactions of silyl ketene acetals with aryl halides containing cyano, nitro, trifluoromethyl, and enolizable keto groups occur in high yield in the presence of ZnF_2 additive.[79,80] Under these conditions, added enantio-enriched imides containing a tertiary chiral α carbon did not undergo epimerization.[79,80] This observation led Liu and Hartwig to report the diastereoselective (>50:1 dr) α-arylation of the silicon enolate of Ley's dioxanone (eq 18).[80]



Reformatsky reagents are slightly more basic than silyl ketene acetals, but they are still mild enough to tolerate base-sensitive functional groups on the aryl electrophiles.[79] In addition, α-arylation reactions with Reformatsky reagents derived from acetate esters produced higher yields of coupled products than those of the corresponding lithium or sodium enolates because

zinc enolates of acetate esters are more stable than the sodium or lithium enolates.[67,79] Hartwig and coworkers showed that the Pd(I) dimer $[PdBr(PtBu_3)]_2$ or complexes containing Q-Phos are some of the most active catalysts for reactions of the Reformatsky reagent of *tert*-butyl acetate with aryl chlorides at room temperature.[67]

1.2.2.2.5. α-Arylation of Amides and Lactams

Inter- and intramolecular α-arylation of carboxamides. Like α-aryl esters, α-aryl amides are present in many natural products and have many applications in medicinal chemistry.[81] Reaction conditions for the α-arylation of amides are more basic than those for the α-arylation of esters because amides are less acidic.[61] Hartwig and coworkers reported the first examples of palladium-catalyzed inter- and intramolecular α-arylation of amides.[82] The intermolecular reactions occurred with KHMDS, whereas the intramolecular reactions that afford oxindoles were conducted with the weaker base NaO*t*Bu. Protecting groups at the nitrogen atom are usually required to conduct the α-arylation of amides because the pK_a of the N-H bond in an amide is usually lower than that of the α C-H bond.[61] Complexes generated from DPPF or BINAP coupled aryl bromides with *N*,*N*-dialkylamides in high yield. The reaction conditions developed by Hartwig and coworkers were extensively used by other research groups to synthesize a number of alkaloids shown in Figure 9.[83,84]

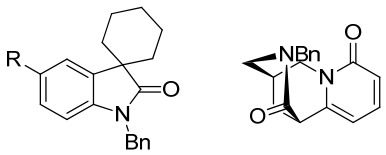


Figure 9. Alkaloids synthesized by palladium-catalyzed α-arylation of amides

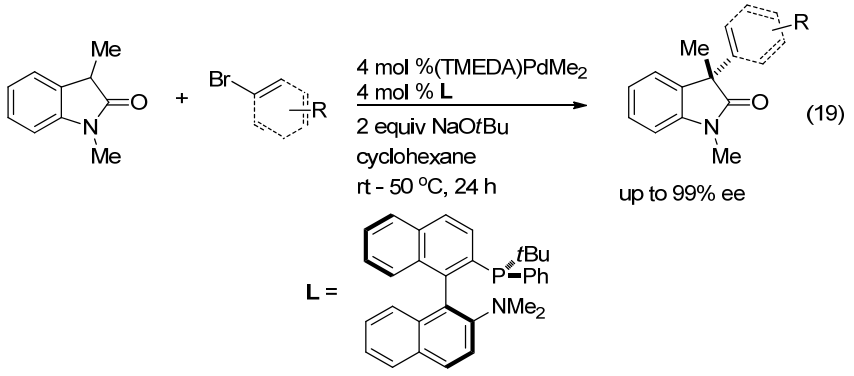
The intramolecular α-arylation that forms oxindoles occurs with faster rates than the corresponding reaction that forms δ-lactams because the 6-membered arylpalladium enolate intermediate that forms oxindole is more accessible than the 7-membered ring intermediate that forms δ-lactams (see mechanistic consideration in section 1.2.2.5). In 2001, Honda *et al* synthesized δ-lactams by the intramolecular α-arylation reactions catalyzed by palladium complexes of 1,2-diphenylphosphinoethane (dppe).[85] Complexes containing P*t*Bu$_3$ are highly active catalysts for the α-arylation of ketones and esters (*vide supra*),[86] but Lee and Hartwig observed that intramolecular reactions of 2-haloanilides catalyzed by complexes of PCy$_3$ produced higher yields of oxindoles than those catalyzed by complexes of P*t*Bu$_3$. Reactions with 2-bromoanilides occurred at room temperature and those with 2-chloroanilides occurred at 70 ^{o}C. The authors also performed a unique one-pot sequential intra- and intermolecular α-arylation of 2-bromoanilides with aryl chlorides to form 2-aryloxindoles. These methodologies were used by other research groups for the synthesis of oxindoles and γ-lactams that have significant medicinal applications.[87-90]

Like the α-arylation of esters, reactions of amides conducted with strong bases are limited in scope of aryl halide. Strong bases can racemize a tertiary α stereocenter. Additionally, highly basic conditions can lead to catalyst decomposition. To overcome these limitations, isolated zinc amides and silyl keteneimides have been studied as reagents for coupling reactions with aryl halides. For example, Hartwig and coworkers showed that the palladium-catalyzed coupling of zinc amides with aryl bromides containing unprotected hydroxyl and amino, enolizable keto, ester and nitro groups occur in good yield at room temperature. These reactions are catalyzed by the Pd(I) dimer [PdBr(P*t*Bu$_3$)]$_2$ or by a combination of Pd(dba)$_2$ and Q-Phos.[79,91] Zinc enolates of amides generated *in situ* coupled with aryl bromides in similar yield. The

Hartwig group reported a diastereoselective α-arylation of silyl keteneimides containing an Evans auxiliary. Diastereomeric ratios of up to 95:5 were obtained.[80] The auxiliary then can be cleaved readily to generate the parent amide or carboxylic acid.

Intermolecular α-arylation of lactams. The α-arylation of lactams has been achieved with oxindoles, pyrrolidinones and piperidinones. The palladium catalyst containing X-Phos has been shown to couple *N*-substituted oxindoles with aryl bromides, chlorides and triflates to form 2-aryloxindoles.[92] Buchwald and coworkers reported the first and only example of α-arylation of unprotected oxindoles with catalysts containing X-Phos. α-Arylation of unprotected oxindoles with aryl bromides, chlorides and an aryl benzenesulfonate occurred in high yield in the presence of K_2CO_3.[93] The chemoselectivity is remarkable because the pK_a values of the C3-H and N1-H hydrogens are identical (18.5 in DMSO).[94] α-Arylation of *N*-methylpyrrolidinone (NMP) has been reported with P*t*Bu$_3$ as ligand.[82] α-Arylation of *N*-substituted piperidinones were conducted with the corresponding zinc enolates that were generated *in situ*.[95-99]

Currently, there is only one report on the enantioselective α-arylation of lactams.[100] Buchwald and coworkers reported that catalysts containing the axially chiral P-stereogenic ligand shown in eq 19 couple aryl and alkenyl bromides with 1,3-dimethyloxindole in high yield and enantioselectivities.



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Enantioselective synthesis of oxindoles. The highest enantioselectivities from the intramolecular α-arylation of 2-haloanilides that forms chiral oxindoles are obtained with palladium complexes of chiral, nonracemic NHCs (Figure 10).[86,101-104] Lee and Hartwig reported the first examples with NHCs derived from (-)-isopinocampheylamine and (+)-bornylamine to form chiral, nonracemic oxindoles with up to 76% ee (eq 20).[86] In 2007, Kündig *et al.* designed and synthesized the chiral carbene **L3**. Catalysts generated from palladium and **L3** formed oxindoles with up to 94% ee (eq 21).[103] A year later, the same group reported the synthesis of 3-amino- and 3-alkoxyoxindole with up to 97% ee in the presence of complexes containing **L4** (eq 22).[104]

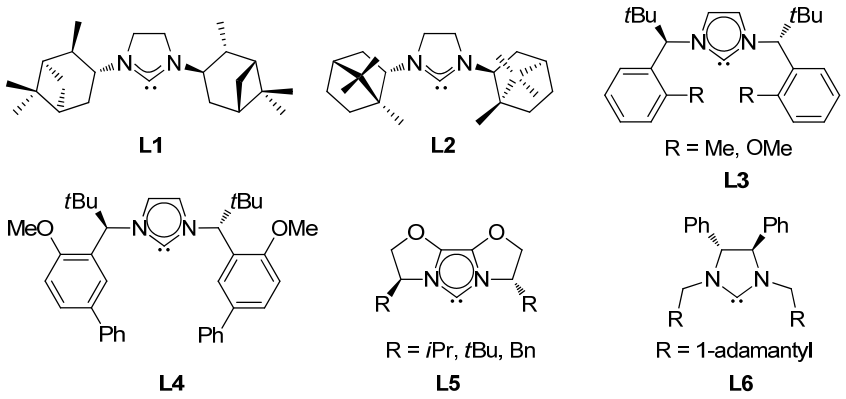
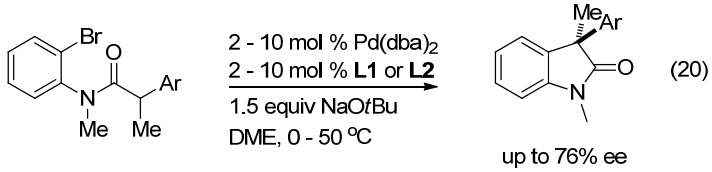
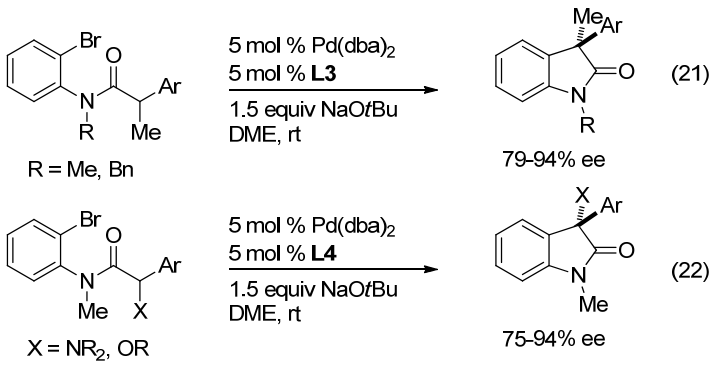


Figure 10. Chiral NHCs for the synthesis of chiral oxindoles





1.2.2.3. α-Arylation of β-Dicarbonyl Compounds

β-Dicarbonyl compounds are more acidic than ketones, esters and amides. Thus, the palladium-catalyzed α-arylation of β-dicarbonyl compounds occurs in the presence of weak bases, e.g. K_3PO_4. The palladium-catalyzed α-arylation of these types of compounds dates back to the early 1980s.[105-109] This section highlights recent advances in the α-arylation of diketones, ketoesters, cyanoesters, malononitriles malonates and their derivatives.

Hartwig and coworkers showed that a combination of D*t*BPF, P*t*Bu_3, Q-Phos, or (1-Ad)P*t*Bu_2 with palladium precatalysts form active catalysts for the coupling of dialkylmalonates and cyanoesters with aryl bromides and chlorides in high yield.[45,110] Complexes containing tBuMePhos couple diethyl malonate and 1,3-diketones with aryl bromides.[46] Verkade and coworkers showed that complexes of a proazaphosphatrane (Figure 11) couple cyanoesters with aryl chlorides and bromides in high yield.[111,112] The coupling of malononitriles with aryl chlorides and bromides are catalyzed by palladium complexes of NHC ligands,[113] PCy_3[114] and P*t*Bu_3 have also been reported.[115]

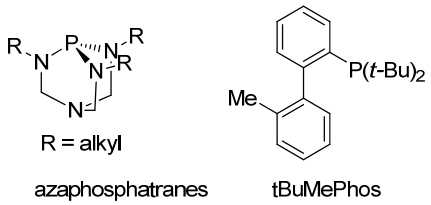


Figure 11. Verkade's proazaphosphatranes and tBuMePhos

1.2.2.4. α-Arylation of Nitriles and Nitroalkanes

Although alkyl nitriles and nitroalkanes are not carbonyl compounds, they do possess acidic α hydrogens, and the corresponding anions can undergo coupling reactions with aryl halides. A brief synopsis of the α-arylation chemistry of these nucleophiles is described in this section, though complete coverage of this field is beyond the scope of this dissertation.[116]

Several challenges are associated with the α-arylation of alkyl nitriles. The reactions of alkyl nitriles with aryl halides require strong bases, e.g. silyl amides, because the pKa values of these reagents in DMSO are 30-33.[117,118] A cyano group is more electron withdrawing than an acyl group; thus, the reactivity of nitriles could be lower than that of carbonyl compounds in palladium-catalyzed α-arylations. The Hartwig group showed that the reductive elimination of α-aryl nitriles from arylpalladium cyanoalkyls is slower than the reductive elimination of α-aryl esters, amides and ketones from aryl palladium enolates (*vide infra*).[119] The strong inductive effect of the cyano group, the binding of nitrogen to palladium and the formation of a stable dimeric palladium complex are among the reasons for the slow rates of reductive elimination. Therefore, the rates of side reactions, such as decomposition of the nitrile anion, become competitive with the catalytic reaction. Moreover, unhindered substrates such as acetonitrile undergo diarylation because the product benzyl nitrile is more acidic than acetonitrile.

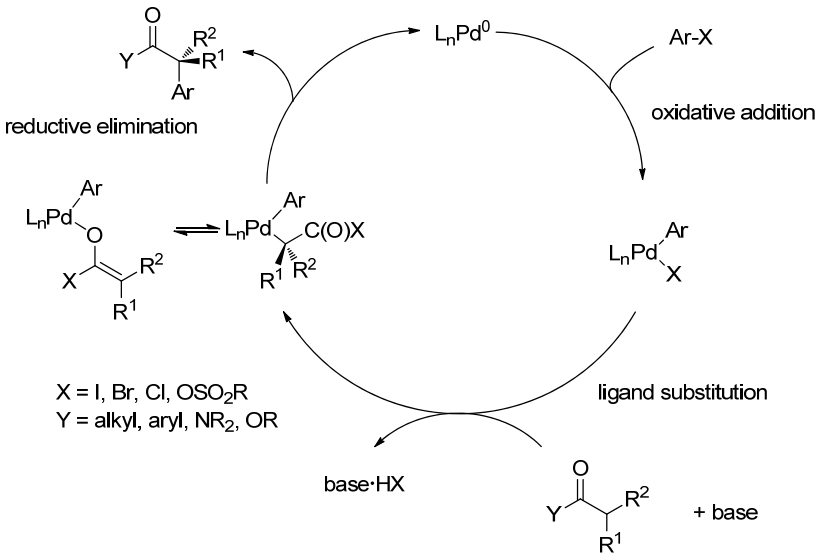
To address these challenges, silicon and zinc cyanoalkyl reagents were used. Wu and Hartwig showed that reactions of trimethylsilylacetonitrile with aryl halides in the presence of either Xantphos or P*t*Bu$_3$, palladium precursors and substoichiometric quantities of ZnF_2 form monoarylated acetonitriles in good yield.[120] However, the reactions of α-silyl secondary alkyl nitriles with aryl halides occurred in low yield. The authors showed that zinc cyanoalkyl reagents of secondary nitriles coupled with aryl bromides in good yields at room temperature. Prior to these developments, the α-arylation of secondary alkylnitriles occurred with catalysts containing either BINAP,[119] P^{t}Bu$_3$[119] or Verkade's proazaphosphatrane[112] in the presence of a strong base, e.g. NaHMDS, at 100 ^{o}C.

The pK_a values of nitroalkanes in DMSO are between 15 and 18.[61] Thus, nitroalkanes undergo α-arylation in the presence of weak bases. Vogl and Buchwald reported the first examples of coupling of nitroalkanes with aryl bromides and chlorides in the presence of *t*BuMePhos as ligand and Cs_2CO_3 as base.[121] Reactions of substrates containing both a nitroalkane and an ester occurred at the carbon α to the nitro group in high selectivities. Several intramolecular reactions that form tricyclic nitro compounds have been reported by Muratake and coworkers.[122,123] In general, the α-arylation of nitroalkanes has high functional-group tolerance because the reactions are conducted with weak bases.

1.2.2.5. Mechanistic Consideration

The basic steps of the palladium-catalyzed α-arylation of carbonyl compounds have been discussed in review articles.[116,124,125] The catalytic cycle begins with the oxidative addition of the aryl halide to a Pd(0) complex to generate an arylpalladium halide species. This species undergoes a ligand substitution reaction with the carbonyl compound in the presence of a base to form enolate complexes that are either *O*-bound or *C*-bound. The *C*-bound enolate complex then

reductively eliminates the α-aryl carbonyl compounds and regenerates the active Pd(0) species (Scheme 1).



Scheme 1. Catalytic cycle of the palladium-catalyzed α-arylation of carbonyl compounds

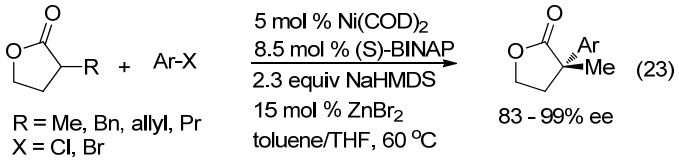
Mechanistic studies from the Hartwig group showed that the rate of reductive elimination from arylpalladium enolate complex is dependent on the steric properties, but is independent on the pK_a of the carbonyl compounds. The reductive elimination of α-carbonyl compounds from arylpalladium enolates of ketones, esters, and amides occurred with rate differences no greater than a factor of 3. The rates of reductive elimination from arylpalladium enolates are faster than those from arylpalladium cyanoalkyl complexes by a factor of 3. The rate is dependent on steric properties of the enolate ligand, but the difference in magnitudes is small. More sterically hindered enolates underwent faster reductive elimination.

1.2.3. Other Transition-Metal Catalyzed α-Arylation

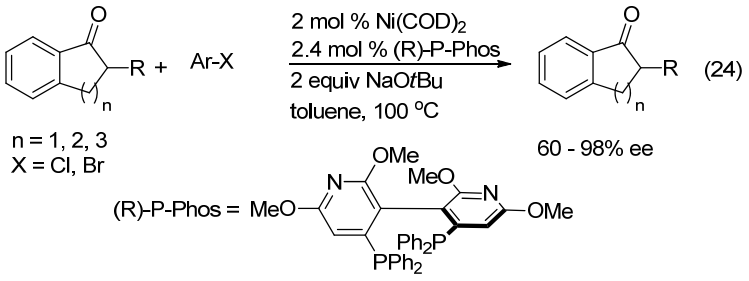
Nickel complexes have also been shown to catalyze the α-arylation of carbonyl compounds, but with much narrower scope than palladium catalysts. In 1973, Semmelhack and

coworkers reported the intramolecular α-arylation of lithium enolates of ketones in the presence of stoichiometric amounts of nickel complexes and base.[126] In 1977, Millard and Rathke discovered the first catalytic coupling of aryl iodides, aryl and vinyl bromides with isolated lithium enolates in the presence of 20 mol % of $NiBr_2$.[127] The coupling of Reformatsky reagents[33] acyclic ketones[128] and malononitrile[129] with aryl iodides, bromides and chlorides also occurred in good yields of coupled products in the presence of nickel catalysts containing an NHC or triphenylphosphine.

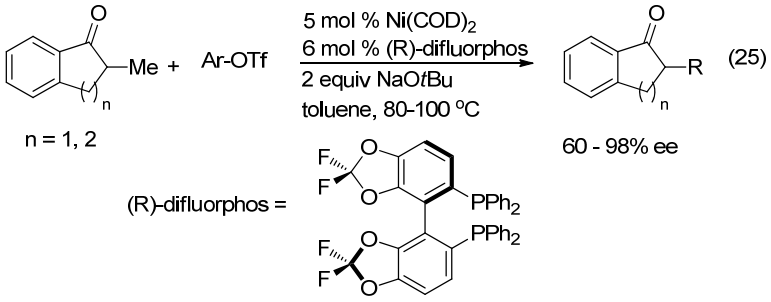
Nickel complexes have been studied as one approach to address asymmetric α-arylation of carbonyl compounds because nickel is smaller than palladium; thus, chiral ligands on nickel are closer to the metal center, potentially leading to greater chiral induction. In 2002, Spielvogel and Buchwald reported the first examples of nickel-catalyzed enantioselective α-arylation (eq 23). The enantioselectivities of these reactions were much higher than the reactions catalyzed by palladium catalysts containing (*S*)-BINAP.[78]



In 2006, Chan and coworkers reported a nickel-catalyzed enantioselective α-arylation of α-substituted 1-indanone, 1-tetralone and 1-benzosuberone (eq 24).[130] The reactions catalyzed by nickel complexes of (*R*)-P-Phos occurred with remarkable enantioselectivities of up to 98% at 100 °C. However, several researchers have not been able to reproduce these results.[60]



In 2008, Hartwig and coworkers reported the α-arylation of α-methylindanone and α-methyltetralone with electron-poor aryl triflates with 86-98% ee (eq 25).[60] The enantioselectivities obtained for reactions of α-methylindanone are the highest reported.[60] The authors also found that the stoichiometric reaction of an enantiopure arylnickel bromide complex containing (*R*)-segphos with the sodium enolate of 2-methylindanone occurred with higher enantioselectivity than the catalytic process. They attributed this result to the presence of less selective catalysts that are formed from decomposition of the catalyst. The enantioselectivity indeed improved at higher catalyst loading.[60]



Copper has also been used in α-arylation reactions, but the scope of enolate nucleophile is limited to dicarbonyl compounds. The scope of aryl electrophiles encompasses aryl iodides

and activated aryl bromides. Extensive reviews of copper-catalyzed α-arylation reactions have been published.[15,125]

1.2.4. Summary

Although far from complete, this overview of the α-arylation of carbonyl compounds covers some of the important developments over the past 3 decades and has highlighted that palladium- and nickel-catalyzed methods represent the state of the art tools for the synthesis of α-aryl carbonyl compounds. New catalysts and mild reaction conditions have been developed to improve the scope of the enolate nucleophiles and aryl electrophiles. Most importantly, breakthroughs in asymmetric α-arylation have delivered more powerful tools that are applicable to pharmaceutical and natural-product synthesis. Several complex molecules containing α-aryl carbonyl units have been synthesized on laboratory scale by palladium-catalyzed α-arylation of carbonyl compounds.[131-133]

Prior to 2007, there were 3 examples of palladium-catalyzed α-arylation of aldehydes, but the scope of aldehydes and aryl halides was limited. Not until 2007 was a general synthesis of α-aryl aldehydes from palladium-catalyzed α-arylation of aldehydes developed. Chapter 2 and 3 will describe the development and mechanistic study of this important reaction.

1.3. Overview of Amination of Aryl Halides and Sulfonates

1.3.1. Noncatalytic Methods

1.3.1.1. Nucleophilic Aromatic Substitution

Aniline and its derivatives are prepared industrially by nucleophilic attack of the amine nucleophiles on the aryl halides.[134,135] Reactions occur in good yield with aryl halides that are activated by electron-withdrawing substituents. More electron-rich haloarenes react at higher temperature with lower yield of desired products. Sterically bulky substituents near the carbon undergoing nucleophilic attack retard the reaction rate. Most reactions can be conducted in the absence of a base, but those conducted with hydroxide or carbonate bases generally occur in higher yield. The trend of reactivity of the aryl halides is ArF>ArCl>ArBr>ArI.[136] Thus, reactions of fluoro- and chloroarenes have the broadest scope. The scope of nucleophiles encompasses primary alkyl- and arylamines and ammonia.[137] Reactions of primary arylamines occur at higher temperatures than those of primary alkylamines because primary arylamines are less nucleophilic.[138] Reactions of ammonia with aryl halides have been reported, although these reactions occur at higher temperatures than those of amines.[137]

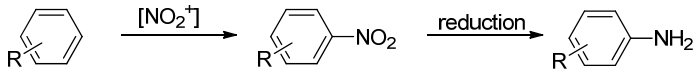
1.3.1.2. Substitution via Aryne Intermediates

In the context of industrial-scale synthesis of arylamines, reactions of alkaline metal amides are less common than those of the parent amines because reactions conducted with alkali amides and aryl halides generate benzyne intermediates that form two possible structural isomers of the arylamine product. However, these reactions can be conducted at much lower temperature than the direct nucleophilic aromatic substitution reactions.[139]

Support for the presence of aryne intermediates has been provided by reactions of an isotopically labeled aryl chloride with potassium amide in liquid ammonia.[140,141] Aryne intermediates have also been observed in flash-photolysis and mass spectrometry experiments.[142] They have been trapped by nickel carbonyl complexes and characterized by ^{1}H NMR spectroscopy.[143]

1.3.1.3. Reduction of Nitroarenes

The reduction of nitroarenes is currently the most widely used method for the industrial-scale synthesis of primary arylamines (Scheme 2).[144] Nitroarenes are usually synthesized by the nitration of arenes with electrophilic nitrating reagent such as nitric acid in the presence of sulfuric acid.[145,146] The reduction of nitroarenes to primary arylamines is well-developed. Zinc, tin and iron metal in acid are common reducing agents.[147,148] Catalytic hydrogenation of nitroaromatics is also widely used.[149] However, these methods do not tolerate functional groups that are reduced readily under acidic conditions in the presence of metals or under catalytic hydrogenation conditions.



Scheme 2. Synthesis of anilines from arenes via a nitration and reduction sequence

1.3.2. Palladium-Catalyzed Methods

The palladium-catalyzed synthesis of aniline and its derivatives dates back to the early 1980s. Early in its development, tin amides were used as the source of amine nucleophiles. Reactions of tin amides with aryl halides were catalyzed by $[P(o\text{-tol})_3]_2PdCl_2$.[150,151] Because tin amides and tin halide byproducts are toxic, a tin-free method was desired. Buchwald and

coworkers showed that aminoboranes also reacted with aryl halides in the presence of catalysts containing P(*o*-tol)$_3$.[152] Not until 1995 was the palladium-catalyzed amination of aryl halides with amines in the presence of bases developed. The following sections summarize developments that has occurred since 1995 and are arranged by amine nucleophile in the order of decreasing nucleophilicity:[153] secondary amines, primary amines, and sp^2-hybridized nitrogen nucleophiles.

1.3.2.1. Amination with Secondary Amines

1.3.2.1.1. Cyclic and Acyclic Alkylamines

Coupling with Aryl Halides. In 1995, the groups of Buchwald and Hartwig reported the first tin- and boron-free palladium-catalyzed coupling of aryl bromides with secondary amines in the presence of either NaO*t*Bu or LiHMDS as base and P(*o*-tol)$_3$ as ligand.[152,154] The scope of aryl halides was expanded with second-generation catalysts containing BINAP and DPPF to encompass aryl iodides and heteroaryl halides.[155-157] However, the turnover numbers from reactions catalyzed by second-generation catalysts were not much better than those from reactions catalyzed by the first-generation catalyst. Palladium complexes of Xantphos (Figure 12) also couple heteroaryl bromides with secondary cyclic alkylamines.[158]

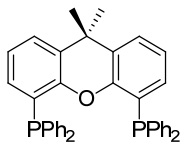


Figure 12. Xantphos

In the late 1990s, hemilabile monophosphine ligands were investigated by the groups of Buchwald (Kumada's ligand),[159] Guram at Symyx,[160,161] Singer at Pfizer,[162,163] and Uemura[164]

(Figure 13). Palladium complexes of these ligands coupled acyclic secondary amines with aryl halides in high yield, although the turnover numbers of these systems were not outstanding.

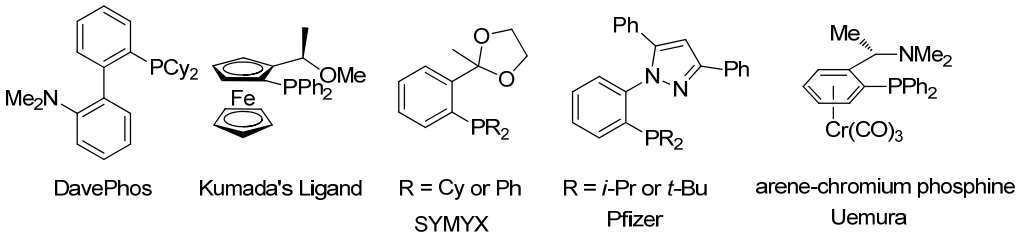


Figure 13. Hemilabile ligands for amination of aryl halides

From studies of the second-generation catalyst of BINAP and the catalyst containing Kumada's ligand, the Buchwald group designed the monophosphine DavePhos that includes elements of a hemilabile ligand and the second-generation catalysts. Palladium complexes of DavePhos coupled cyclic and acyclic secondary alkylamines with aryl bromides and chlorides in high yield at 80 ^{o}C. The Buchwald group found that the dimethylamino group in DavePhos was detrimental to catalytic activity in some cases. Thus, Cyclohexyl JohnPhos (Figure 14) was prepared and palladium complexes of this ligand were shown to couple aryl bromides and aryl chlorides with cyclic and acyclic secondary alkylamines at room temperature with 1-5 mol % loading.[165] Beller and coworkers designed structural analogs of Cyclohexyl JohnPhos that have similar structure-activity relationships and are more synthetically accessible (Figure 14). However, complexes containing Beller's ligands coupled secondary alkylamines with aryl chlorides at higher temperatures than catalysts generated from Cyclohexyl JohnPhos.[166]

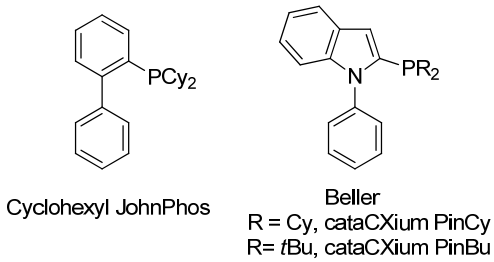


Figure 14. Beller ligands

In 1998, Nishiyama and coworkers at Tosoh Company introduced what many consider the third-generation catalyst that contains P*t*Bu$_3$.[8,167] The coupling of diarylamines and cyclic secondary alkylamines with aryl bromides in the presence of this ligand and Pd(OAc)$_2$ occurred with up to 6400 turnover numbers. Hartwig and coworkers reported that a 1:1 combination of this ligand and Pd(dba)$_2$ catalyze reactions of cyclic and acyclic secondary alkylamines with aryl chlorides in high yield.[168]

Other electron-rich and sterically bulky monophosphines were investigated (Figure 15). Q-phos, a ligand discovered in the Hartwig group, formed highly active catalysts with palladium in the coupling of secondary alkylamines with aryl chlorides with 0.5-1.0 mol % loadings.[169] Verkade and coworkers designed proazaphosphatranes (Figure 15) and proposed that the nitrogens bound to phosphorus can donate electron density to the phosphorus. Additionally, the steric bulk of proazaphosphatranes could be readily adjusted by changing the substituents on the nitrogen atoms. Palladium complexes of these ligands coupled secondary cyclic alkyl amines with aryl bromides and chlorides, although with higher loadings than catalysts generated from Q-Phos.[170,171]

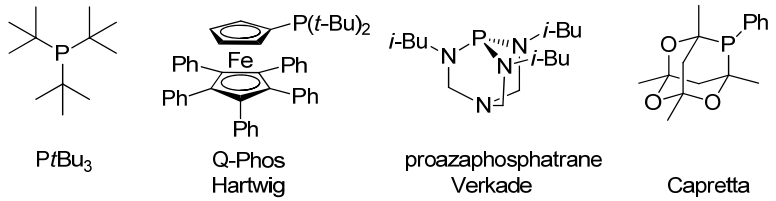


Figure 15. Electron-rich and sterically hindered monophosphines

Another class of ligands that form active palladium catalysts for the amination of aryl halides is *N*-heterocyclic carbenes (NHCs). NHCs are more σ-donating and less π-accepting than phosphines (*vide supra*).[172] In the early 2000s, Nolan and coworkers showed that the coupling of acyclic and cylic alkylamines with aryl bromides and aryl chlorides occurred at room temperature with catalysts containing NHCs at higher loadings than reactions with catalysts containing P*t*Bu$_3$.[173-175] Hartwig and coworkers achieved 5000 TON with catalysts containing SIPr in reactions of secondary alkylamines with aryl chlorides at 100 ^{o}C.[176] Similar to the observation made by the Hartwig group with P*t*Bu$_3$ (*vide supra*), the Nolan group observed that a 1:1 ratio of NHC to palladium generates catalysts that react with rates of coupling twice as fast as catalysts formed from a 2:1 ratio.[177] Thus, discrete precatalysts shown in Figure 16 generate complexes that couple aryl chlorides with secondary cyclic and acyclic alkylamines at room temperature.[173,175,178-180] (IPr)PdCl$_2$ was shown to be one of a few palladium precatalysts that form active complexes for the amination of aryl halides under air.[173]

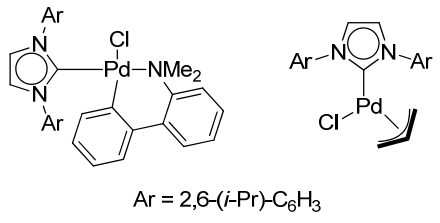
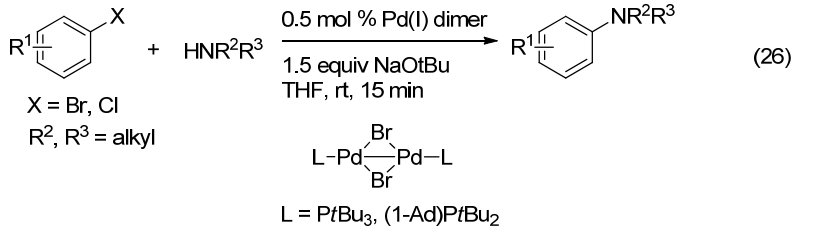
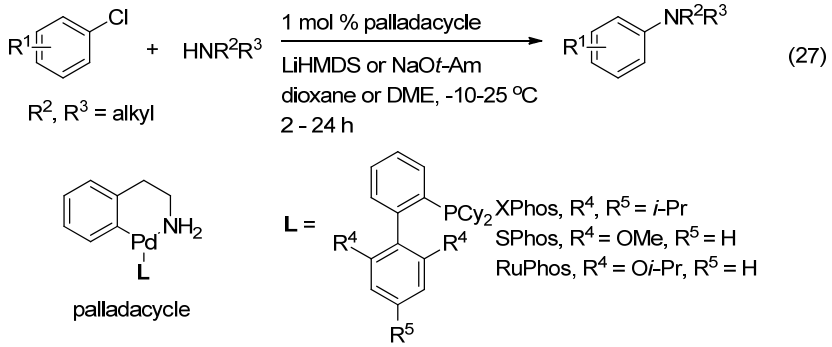


Figure 16. Nolan's NHC-Pd precatalysts

The generation of active catalysts from palladium precursors often determines the turnover numbers and frequencies. Ideal precatalysts should generate active species in 100% yield. In addition, a 1:1 combination of ligand to palladium has been shown to generate more active catalysts (*vide supra*). In light of these facts, Hartwig and coworkers tested air-stable alkyl palladium(I) dimers that are readily reduced to active Pd(0) species.[181,182] Reactions of aryl chlorides with secondary alkylamines occurred to full conversion within 15 minutes at room temperature with only 0.5 mol % of the dimer (eq 26).[181] In 2008, Biscoe and Buchwald reported that 1 mol % of palladacycles of S-Phos, X-Phos and RuPhos form highly active catalysts for the coupling of cyclic and acyclic alkylamines with aryl chlorides at 10 °C to room temperature.[183] The reaction times ranged from 2 to 24 h (eq 27). Currently, the Pd(I) dimers are the most active catalysts for the coupling of cyclic and acyclic secondary alkylamines with aryl chlorides.





Coupling of Aryl Sulfonates. The cleavage of the S-O bond in aryl sulfonates to form phenols is a major side reaction under palladium-catalyzed cross-coupling conditions. Conditions

with weak bases have been developed to give rates of amination that are much faster than rates of side reactions. For example, the amination of aryl triflates with secondary alkylamines occurred in modest yield with complexes generated from BINAP[184] and DPPF[185] in the presence of NaO*t*Bu. Higher yields of tertiary amines were obtained from reactions conducted with Cs_2CO_3.[186] Buchwald and coworkers showed that palladium complexes generated from JohnPhos catalyzed reactions of secondary alkylamines with electron-rich and electron-neutral aryl triflates in the presence of NaO*t*Bu at room temperature.[165] Reactions of electron-poor aryl triflates gave poor yield of the desired product because cleavage of the S-O bond in electron-poor aryl triflates is faster than that of the S-O bond in electron-neutral and electron-rich aryl triflates. However, the yield was improved by conducting the reactions in the presence of K_3PO_4 as base at 80 ^oC.[165] [(IPr)Pd(allyl)Cl] is the only other catalyst that has been shown to couple secondary alkylamines with aryl triflates in high yield.[187]

Aryl tosylates, as mentioned in previous sections, are less reactive than aryl halides and aryl triflates. Only palladium complexes of X-Phos have been shown to catalyze reactions of secondary alkylamines and aryl tosylates or similarly unreactive sulfonates in high yield.[188]

1.3.2.1.2. Amination with Alkyl Arylamines and Diarylamines

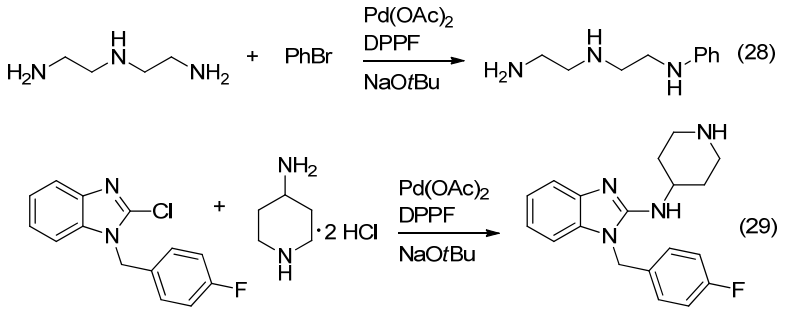
Diarylamines are less nucleophilic than dialkylamines. The reactions of diarylamines with aryl halides occur in good yield in the presence of palladium complexes of electron-rich and bulky monophosphines. For example, a 1:1 ratio of palladium to P*t*Bu_3 formed catalysts that couple diarylamines with aryl bromides and chlorides at room temperature and 70 ^oC, respectively.[168] Complexes generated from Q-Phos exhibited similar activity.[169] The most active catalyst for this type of coupling is $[PdBr(PtBu_3)]_2$.[181,185] At 0.5 mol % of this dimer, diarylamines and alkyl arylamines reacted with arylbromides to full conversion within 15

minutes at room temperature. These reactions provided high yields of triarylamines, which have been applied to the development of conducting polymers and materials.[189-191] Reactions of diarylamines and aryl triflates occurs with palladium complexes generated from bisphosphines such as DPPF and BINAP.[192] Currently, only complexes generated from X-Phos are known to couple of diarylamines with aryl tosylates in high yield.[188]

1.3.2.2. Amination with Primary Amines

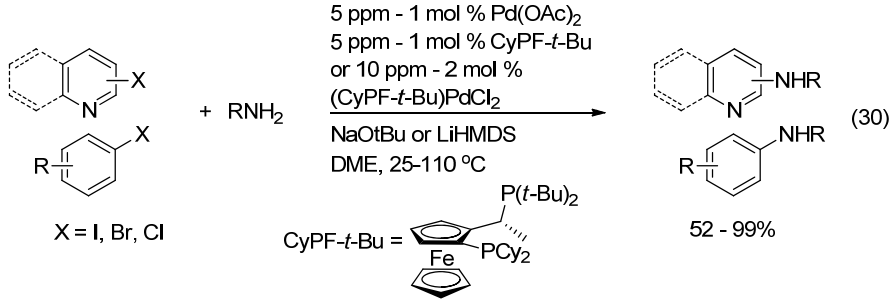
1.3.2.2.1. Primary Alkylamines

Coupling with Aryl Halides. The palladium-catalyzed amination with primary alkylamines and secondary acyclic alkylamines are challenging for similar reasons. β-Hydrogen elimination from the aryl palladium amido complex and diarylation of primary alkylamines are major side reactions. Initial reports showed that catalysts contain BINAP or DPPF, which are second-generation catalysts for the *N*-arylation of secondary amines, couple primary alkylamines with electron-poor aryl bromides in high yield.[155,156] The high selectivity of *N*-arylation of primary over secondary alkylamines with these ligands has been shown by reactions of aryl halides with substrates containing both types of amine (eq 28 and 29).[193,194]



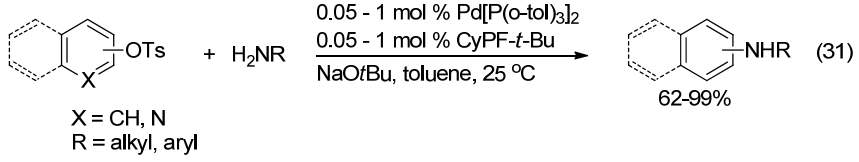
Reactions of unactivated aryl chlorides occur in low yield with the second-generation catalysts, but occur in high yield with third-generation catalysts containing electron rich alkyl monophosphines. For example, catalysts generated from Q-Phos,[169] JohnPhos,[165] or cataCXium® PinBu (Figure 14 and 15),[166] coupled aryl chlorides with primary alkylamines in good selectivity and yield at 70-120 °C. Reactions of sterically hindered aryl chlorides occurred with higher selectivity for monoarylated products than reactions of unhindered aryl chlorides. Excess starting amine was usually required to achieve selectivity greater than 20:1 in favor of the monoaryl alkylamines. Catalysts generated from the NHC palladacycle shown in Figure 16 and from a combination of $Pd(OAc)_2$ and IPr-HCl coupled primary alkylamines with aryl chlorides in excellent yield.[175,179] Improved yield was obtained from reactions in an ionic liquid.[195] Despite these results, the yield of aryl alkylamines still ranged from 50-70%. Moreover, an excess of primary alkylamines was needed for high selectivity, and catalyst loadings were in the range of 1 mol %.

In 2005, Shen and Hartwig reported the most active and selective, fourth-generation[196] catalyst for the *N*-arylation of primary alkylamines.[197] The sterically hindered and electron-rich bisphosphine, CyPF-*t*-Bu, first developed at Ciba-Geigy for asymmetric hydrogenation, formed complexes with $Pd(OAc)_2$ that couple primary alkylamines with aryl and heteroaryl halides with unprecedented turnover numbers, 20,000-100,000 (eq 30).[197-199]



Coupling with Aryl Sulfonates. Catalysts that couple secondary amines with aryl triflates in high yield also couple primary alkylamines with aryl triflates. Complexes containing BINAP coupled unhindered aryl triflates with primary alkylamines in good yield.[184] Reactions conducted with Cs_2CO_3 occurred in higher yields of aryl alkylamines than reactions conducted with NaO*t*Bu.[186] (IPr)Pd(allyl)Cl was shown to catalyze reactions of unhindered aryl triflates with primary alkylamines in high yield in the presence of NaO*t*Bu.[187] Reactions of *ortho*-substituted aryl triflates catalyzed by both catalytic systems occurred low yield.

There are only four reports of the coupling of aryl tosylates with primary alkylamines. In 1998, Hamman and Hartwig reported the first palladium-catalyzed amination of an aryl tosylate. Hexylamine coupled with *p*-tolyl tosylate in the presence of $Pd(OAc)_2$ and PPF-*t*-Bu to form *N*-hexyl toluidine in excellent yield.[200] In 2003, the Buchwald group showed that complexes containing X-Phos coupled primary alkylamines with aryl tosylates in high yield.[188] In the same year, Roy and Hartwig conducted the coupling of primary alkylamines with aryl tosylates under much milder conditions in the presence of either PPF-*t*-Bu or CyPF-*t*-Bu.[201] In 2008, Ogata and Hartwig showed that a combination of $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu forms a highly active catalyst for the coupling of aryl tosylates with primary alkylamines at room temperature with up to 2000 TON (eq 31).



(31)

1.3.2.2.2. Primary Arylamines

Coupling with Aryl Halides. The development of the palladium-catalyzed amination with primary arylamines and primary alkylamines addresses fundamentally different challenges. The arylpalladium amido complex that reductively eliminates diarylamines lacks a β-hydrogen and, therefore, cannot undergo β-hydrogen elimination. Studies by the Hartwig group revealed that reductive elimination of arylamines occurs faster with a more basic nitrogen nucleophile. Reductive elimination from an alkylamido complex is faster than reductive elimination from an arylamido complex, which is faster than reductive elimination from a diarylamido complex.[202] Thus, catalysts for the arylation of diarylamines have been shown to couple primary arylamines with aryl halides in high selectivity for the diarylamine products. For example, catalysts generated from both bisphosphines, such as BINAP,[203-205] DPPF[155] and D*t*BPF,[200] and hindered monophosphines such as P*t*Bu$_3$,[168,206,207] Q-Phos,[169] cataCXium® PinBu,[166] DavePhos,[208] X-Phos,[188] proazaphosphatranes,[170,209] and a bicyclic triaminophosphine ligand (Figure 17)[171] coupled primary arylamines with aryl bromides and chlorides in high yield and selectivity.

Several new ligands have been shown to generate more selective catalysts for this transformation. For example, palladium complexes of DPEphos, originally designed by van Leeuwen for hydroformylation, coupled primary arylamines with aryl bromides in higher selectivity and yield than complexes of BINAP or DPPF. NHC-palladium complexes developed by the Nolan group also couple primary arylamines with aryl chlorides in high yield and selectivity at room temperature.[173,175,178-180] Catalysts containing CyPF-*t*-Bu are currently one of the most active and selective catalysts for the coupling of primary arylamines with aryl halides. These catalysts coupled aryl and heteroarylamines with aryl iodides, bromides and chlorides in high yield with up to 19,000 TON.[198,200] However, reactions of electron-poor primary arylamines

occurred in low yield in the presence of complexes of CyPF-*t*-Bu. In 2008, Buchwald and coworkers reported that 1 mol % of complexes of BrettPhos (Figure 17) couple electron-rich and electron-poor arylamines with aryl chlorides at 110 ^{o}C.[210] In general, the catalyst containing BrettPhos is less active than the catalyst containing CyPF-*t*-Bu for the reactions of electron-rich and electron-neutral arylamines, but is more active for the reactions of electron-poor arylamines.

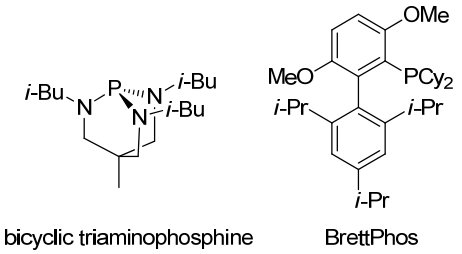


Figure 17. Bicyclic triaminophosphine

Coupling with Aryl Sulfonates. Like reactions with aryl halides, the coupling of primary arylamines with aryl triflates occurred in 50-70% yield in the presence of catalysts containing DPPF[185] and BINAP.[184,186] Again, reactions conducted with Cs_2CO_3 as base occurred in much higher yield than those conducted with NaO*t*Bu.[186] The most active catalyst for the coupling of primary arylamines with triflates contains JohnPhos. Reactions in the presence of this catalyst occurred at room temperature in good yield.[165]

Hamman and Hartwig reported the first coupling of an aryl tosylate with a primary arylamine in the presence of catalysts containing D*t*BPF.[200] Buchwald and coworkers showed that the catalyst containing X-Phos couple aniline with *p-tert*-butylphenyl benzenesulfonate in 96% yield in the presence of 5 mol % phenylboronic acid as a reducing agent for the catalyst precursor.[188] As mentioned previously, the most active catalysts for the coupling of aryl and heteroaryl tosylates with primary aryl- and heteroarylamines are generated from Pd[P(*o*-tol)$_3$]$_2$

and CyPF-*t*-Bu. These reactions occurred at room temperature in excellent yield with 0.1-1 mol % of catalyst.[211] Buchwald and coworkers reported that a palladacycle of BrettPhos formed a catalyst that couple electron-deficient primary arylamines with aryl mesylates in high yield.[210] The catalyst containing BrettPhos is currently the most active catalyst for the coupling of electron-poor primary arylamines with aryl chlorides and aryl sulfonates.

1.3.2.3. Amination with sp^2-Hybridized Nitrogen Nucleophiles

In general, the rates of palladium-catalyzed amination of aryl halides correlate with the nucleophilicity of the reacting nitrogen species.[212] Several studies have revealed that the rates of reductive elimination to form the C-N bond fit this trend.[213] Thus, sp^2-hybridized nitrogen nucleophiles, which are less nucleophilic than sp^3-hybridized nucleophiles, undergo palladium-catalyzed coupling with aryl halides and sulfonates less readily. These reactions, especially with aryl iodides and bromides have been shown to occur with higher yield with copper catalysts (*vide infra*) than with palladium catalysts, although reactions with the less reactive aryl chlorides and tosylates occur in higher yield with palladium catalysts. This section covers the state of the art of palladium-catalyzed coupling of carbazoles, indoles and pyrroles with aryl halides and sulfonates. Reactions of imines such as benzophenone imine are covered in the next section.

The first examples of palladium-catalyzed arylation of sp^2-hybridized nitrogen nucleophiles were reported by Mann and Hartwig with DPPF as ligand.[213] These reactions were conducted at higher temperatures than the reactions with amines. Because of the lower pK_a of these nucleophiles, weak bases such as Cs_2CO_3 were employed. The authors showed that the palladium catalyst is deactivated by the binding of pyrrole if used in excess.[213] The scope included pyrrole and indole, though only one example of coupling of pyrrole was reported with an electron-poor aryl bromide. Subsequently, reactions catalyzed by complexes containing P*t*Bu$_3$

occurred under milder conditions with faster rates and higher yield of coupled products.[168] Catalysts containing P*t*Bu$_3$ also coupled unactivated aryl chlorides with pyrroles and indoles in good yield. Movassaghi and Ondrus showed that the catalyst contain X-Phos couple pyrroles with vinyl triflates in good yield.[214] Nolan and coworkers showed that NHC-palladium complexes catalyze the coupling of indoles with unhindered aryl and heteroaryl bromides.[175] Surprisingly, these reactions occurred in the presence of the strong base NaOH. However, reactions with electron-rich and/or sterically hindered aryl halides occurred in low yields of coupled products because arylation occurred at the C3 position of indole.[175] In 2000, Buchwald and coworkers reported that catalysts containing DavePhos or ligands shown in Figure 18 couple hindered and electron-rich aryl bromides, aryl chlorides and aryl triflates with indoles that are unsubstituted at C3 in good yield.[215]

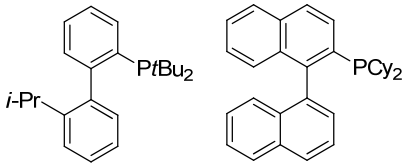


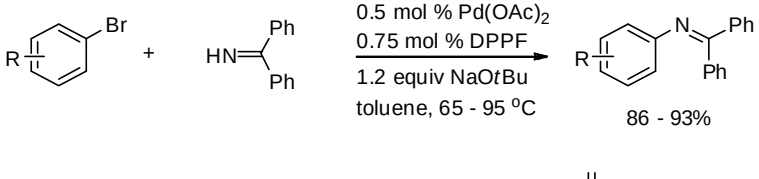
Figure 18.

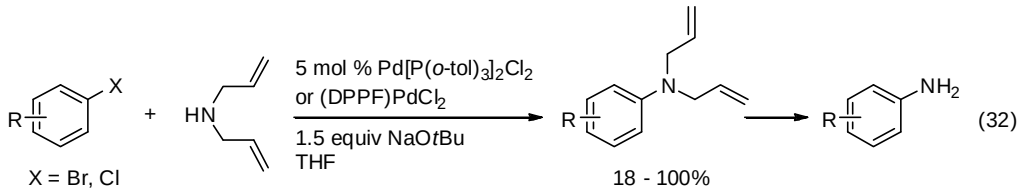
There are only two examples of the coupling of an aryl tosylate with sp^2-hybridized nitrogen nucleophiles. Buchwald and coworkers showed that catalysts containing X-Phos couple an aryl and an alkenyl benzenesulfonate with indole in high yield.[188] Ogata and Hartwig showed that the combination of Pd[P(*o*-tol)$_3$]$_2$ and CyPF-*t*-Bu forms catalysts that couple benzophenone imine with phenyl tosylate at room temperature in excellent yield.[211]

1.3.2.4. Amination with Ammonia Surrogates

As discussed above, the scope of the palladium-catalyzed amination of aryl halides and sulfonates encompasses primary and secondary alkyl- and arylamines. Reactions of other classes of nitrogen nucleophile have been developed but are not covered in this chapter. These nucleophiles are hydrazones,[216,217] carbamates,[168,218] amides[188,218-225] and sulfoximines. Until 2006, ammonia had been the most prominent nitrogen nucleophile that was not included in the substrate scope.[226]

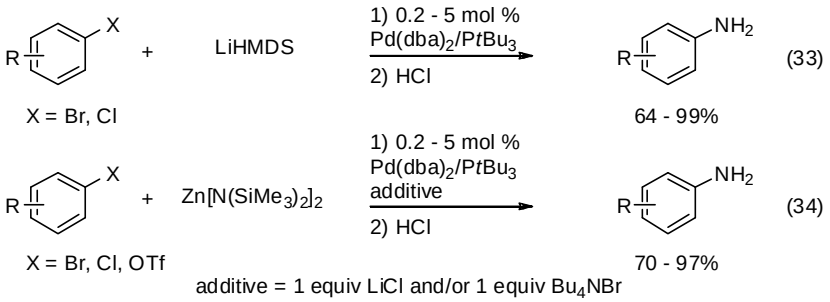
Ammonia surrogates such as benzophenone imine, aldimines, diallyl amines and silylamines had been used in place of ammonia. The Hartwig group showed that catalysts generated from $Pd(OAc)_2$ and DPPF couple benzophenone imine with aryl bromides (eq 31).[213] The *N*-aryl benzophenone imine product was then cleaved under acidic conditions to afford primary arylamines. Buchwald and coworkers employed BINAP as ligand to perform the same transformation.[227] The *N*-heterocyclic carbene IPr was shown by Nolan and coworkers to form palladium complexes that catalyze the same transformation.[175] The Putman[228] and Barluenga[229] groups used diallylamine (eq 32) and aldimines respectively as the ammonia surrogates.





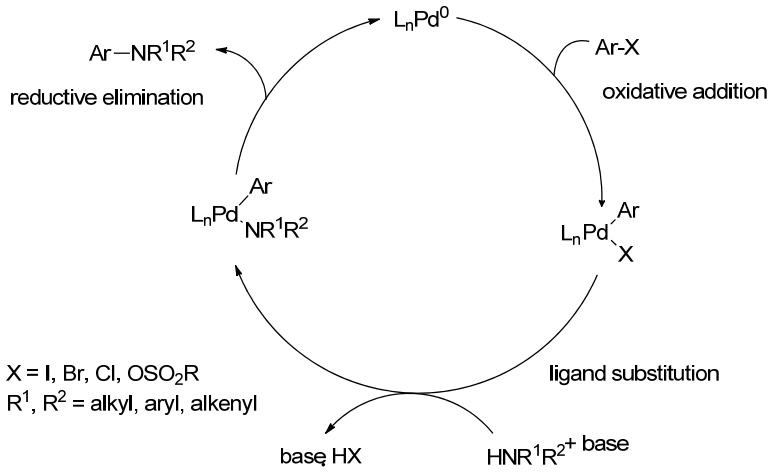
Disilylamines or their conjugate bases are less expensive ammonia surrogates. In 2001, the Hartwig group reported the coupling of unfunctionalized aryl halides with LiHMDS. Acidic hydrolysis of the resulting silyl-protected anilines afforded primary arylamines (eq 33).[230] In a

subsequent report, zinc trimethylsilylamide was found to be a milder ammonia surrogate than LiHMDS and coupled with aryl halides and triflates bearing base-sensitive functional groups (eq 34).[231] Tetrabutylammonium bromide was added to enhance the rate of oxidative addition of aryl triflates to palladium.[232] Triphenylsilylamine, Ph_3SiNH_2, is another versatile ammonia equivalent that was used by Buchwald and coworkers. Ph_3SiNH_2 is less sterically hindered than LiHMDS and can couple with *ortho*-substituted aryl halides to afford hindered primary arylamines. However, Ph_3SiNH_2 is much more expensive than LiHMDS.



1.3.2.5. Mechanistic Considerations

The catalytic cycle of the palladium-catalyzed amination of aryl halides and sulfonates is similar to that of the α-arylation of carbonyl compounds. The Pd(0) catalyst undergoes oxidative addition with an aryl halide to form an arylpalladium halide complex. This complex undergoes ligand substitution with an amine and base to form an arylpalladium amido species. This amido complex reductively eliminates the arylamine product and regenerates the catalyst (Scheme 3). The effects of the basicity and nucleophilicity of the amine nucleophile were discussed previously.[196]



Scheme 3. Catalytic cycle of the palladium-catalyzed amination of aryl halides

1.3.3. Other Transition-metal Catalysts

Copper-catalyzed aminations of aryl halides (Ullmann reaction) constitutes an alternative method for the synthesis of arylamines. An extensive review of this subject is beyond the scope of this chapter, but numerous detailed reviews on this subject have been published.[233-235] However, the advantages and disadvantages of copper-catalyzed amination versus palladium-catalyzed methods merit a brief discussion.

In general, copper catalysts are much cheaper than palladium catalysts. However, they are most reactive towards aryl iodides and bromides. Reactions with the more abundant aryl chlorides and sulfonates have been observed only in a few isolated cases. Even reactions with the more active aryl iodides and bromides usually require catalyst loadings higher than 1 mol %. In many cases, loadings up to 40 mol % required. In addition, copper catalysts bind well to nitrogen containing compounds, making the purification of products difficult in some cases. With the scope and TON achieved with palladium catalysts, it is hard for the low cost of copper to offset these limitations and replace palladium systems in the synthesis of arylamines. Nevertheless,

copper catalysts are best used with sp^2-hybridized nitrogen nucleophiles and offer an alternative to palladium systems.

1.3.4. Summary

Although far from complete, this overview of the amination of aryl halides and sulfonates covers the most important developments of the field in the past 30 years. Of all methods described in this overview, palladium-catalyzed processes have exhibited the broadest scope of both amines and aryl halides. The scope encompasses secondary and primary alkyl and arylamines. Reactions of aryl triflates and aryl tosylates can now be conducted at room temperature with low catalyst loading. Several new generations of catalysts have been developed since 1995. Up to 100,000 turnover numbers have been achieved.

These methods that form aryamines have been widely used in the synthesis of many important drugs and drug candidates. For example, *N*-arylpiperazines, such as aripiprazole and (benzimidazolyl)piperazines, are candidates for anti-depressant and anti-psychotic drugs and have been prepared by palladium-catalyzed amination of aryl halides.[7-10] Torcetrapib, a drug candidate that increased HDL levels, was prepared by palladium-catalyzed C-N coupling (Figure 2).[11]

Before 2006, the scope of palladium-catalyzed amination did not encompass ammonia. When the work described in this dissertation began, palladium-catalyzed coupling of ammonia with aryl halides to form primary arylamines occurred with limited scope and at high pressure. Chapter 4 will detail the expansion of the substrate scope through the development of low-pressure reaction conditions and a highly active catalyst.

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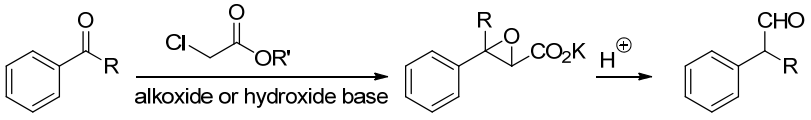
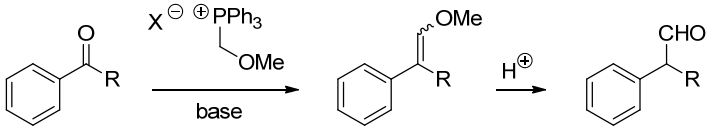
Chapter 2. α-Arylation of Aldehydes with Bromo- and Chloroarenes Catalyzed by Allylpalladium Chloride and DPPF or Q-phos

2.1. Introduction

α-Aryl aldehydes are precursors to many important synthetic intermediates containing alcohol,[1,2] carboxylic acid,[3] imine, amine,[4] olefin and nitrile functional groups. Such aldehydes have been synthesized by the hydrolysis of products generated from the Darzens reaction[3-5] (Scheme 4) or Wittig reaction[3,4,6,7] (Scheme 5) that involves alkyl aryl ketones and benzaldehydes with α-chloro acetate or (methoxymethyl)-triphenylphosphonium chloride, respectively. These methods involve alkyl aryl ketones that are not readily available from commercial sources. In addition, quaternary α centers cannot be formed by these methods. Thus, a method that forms α-aryl aldehydes containing secondary, tertiary, and quaternary α centers from simple building blocks is needed.



Scheme 4.



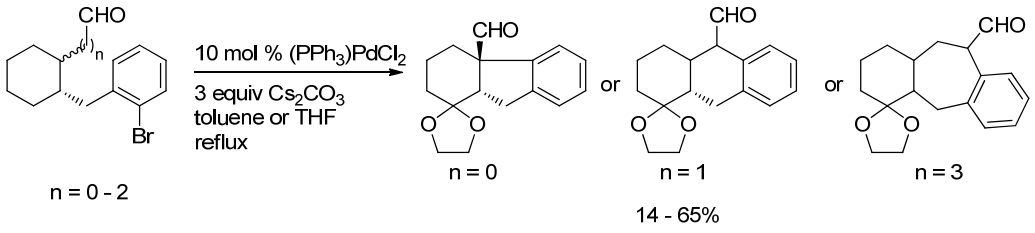
Scheme 5.

In Chapter 1, we reviewed methods that were developed for the synthesis of α-aryl carbonyl compounds. Of those methods, the palladium-catalyzed α-arylation of carbonyl compounds with

aryl halides and aryl sulfonates had the broadest scope of nucleophiles that include ketones, esters, amides, and malonates.[8-10] However, the scope of carbonyl compounds did not encompass aldehydes. The palladium-catalyzed α-arylations of aldehydes to form α-aryl aldehydes have been challenging to develop because the aldol reactions are competing processes under cross-coupling reaction conditions. Thus, efforts have focused on the development of new catalysts and reaction conditions that enhance the α-arylation process and retard aldol condensations.

2.2. Background

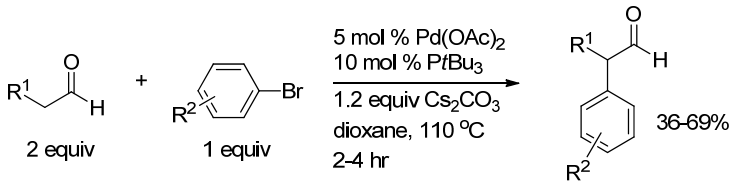
Prior to 2008, there were only four reports on the palladium-catalyzed α-arylation of aldehydes. In 1999, Muratake *et al*. reported the first palladium-catalyzed intramolecular α-arylation of aldehydes shown in Scheme 6.[11] The intramolecular reactions catalyzed by $PdCl_2(PPh_3)_2$ occurred in low yields of the fused tricyclic compounds.



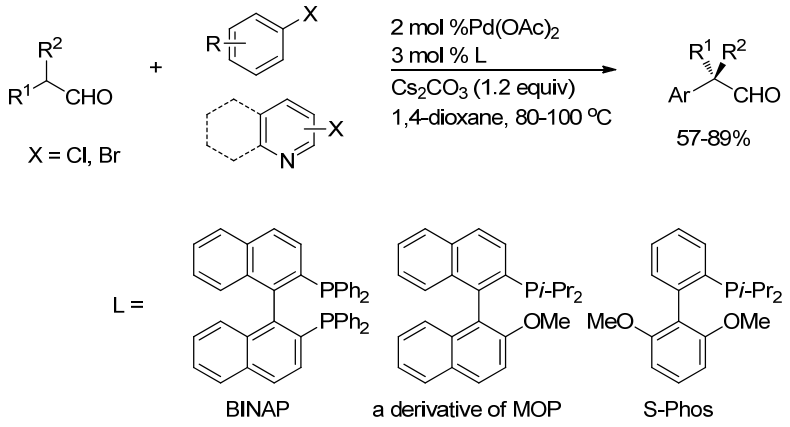
Scheme 6. First Intramolecular Palladium-Catalyzed α-arylation of Aldehydes

In 2002, Miura and coworkers described the first palladium-catalyzed intermolecular α-arylation of aldehydes (Scheme 7).[12] Complexes generated from 5 mol % of $Pd(OAc)_2$ and 10 mol % of P(*t*-Bu)$_3$ coupled linear and α-branched aldehydes with unfunctionalized aryl bromides containing only to form α-aryl aldehydes in 36-67% yield. In 2005, Bertrand and coworkers reported that a palladium catalyst containing cyclic(amino)alkyl carbenes coupled isobutanal with 2-chlorotoluene in 98% GC yield.[13] While the work of this chapter was ongoing, Martín and

Buchwald reported palladium complexes of mono- and bisphosphines catalyzed the α-arylation of linear and branched aldehydes with aryl bromides and chlorides (Scheme 8).[14] The catalyst generated from 2 mol % of $Pd(OAc)_2$ and 3 mol % of BINAP coupled linear aldehydes with aryl bromides in good yield. The catalyst containing a derivative of MOP, designed by Hayashi for the asymmetric hydrosilylation of olefins, coupled linear aldehydes with aryl chlorides. The catalyst containing S-Phos coupled aryl bromides and aryl chlorides with α-branched aldehydes in high yield. Most examples in this work involved reactions of electron-poor aryl halides; few reactions of electron-rich or electron-neutral aryl halides were reported. Only example of a reaction of an electron-rich aryl halide that was sterically biased was described. Therefore, a general protocol that couples both electron-rich and electron-deficient aryl halides with aldehydes is needed.



Scheme 7.



Scheme 8.

Herein, we report a more general protocol for the palladium-catalyzed α-arylations of aldehydes with electron-rich and electron-poor aryl bromides and aryl chlorides. Complexes of a bisphosphine ligand coupled linear aldehydes with electron-poor or electron neutral aryl bromides in good yield. The catalyst containing Q-Phos coupled branched aldehydes with bromo- and chloroarenes in high yield. These catalysts generated from a palladium(II) precursor that undergoes facile reduction to palladium(0) reacted with rates that are faster than the rates of previous catalysts.

2.3. Results and Discussion

2.3.1. Identification of Catalysts and Optimization of Reaction Conditions for the Coupling of Octanal with 1-Bromo-4-tert-butylbenzene

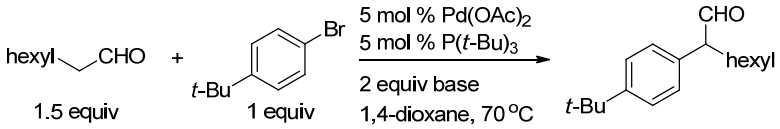
Our initial study of the palladium-catalyzed α-arylation of aldehydes focused on the identification of a catalyst that reacts with rates that are faster than those of competing aldol condensations. We evaluated various combinations of catalyst precursors and phosphine ligands for the coupling of octanal and 1-bromo-4-*tert*-butylbenzene in the presence of a base. The results of this study are shown in the following sections.

2.3.1.1. Identification of a Base for the α-Arylation of Aldehydes

We evaluated the effects of bases on the reactions catalyzed by complexes of P*t*Bu_3, which were shown by Miura and coworkers to couple 4-bromotoluene with linear octanal in 67% yield. mol% of $Pd(OAc)_2$ and 5 mol% of P(*t*-Bu)$_3$ in dioxane. The results of this study are summarized in Table 1. Reactions conducted with a silylamide and an alkoxide base in 1,4-dioxane occurred to 88% and 31% conversion, respectively, to afford trace amounts of the coupled product (entries 1 and 2). The mixture of side products included those formed from

Aldol condensations. The reaction conducted with Cs_2CO_3 occurred in 53% yield of the coupled product (entry 3). The mass balance consisted of predominantly *tert*-butylbenzene that was formed from the hydrodehalogenation of the aryl bromide. The reaction conducted with K_3PO_4 occurred to only 20% conversion after 15 h. We concluded that reactions conducted with Cs_2CO_3 as base occurred in the highest yield of coupled products.

Table 1. Evaluation of Bases in the α-Arylation of Octanal



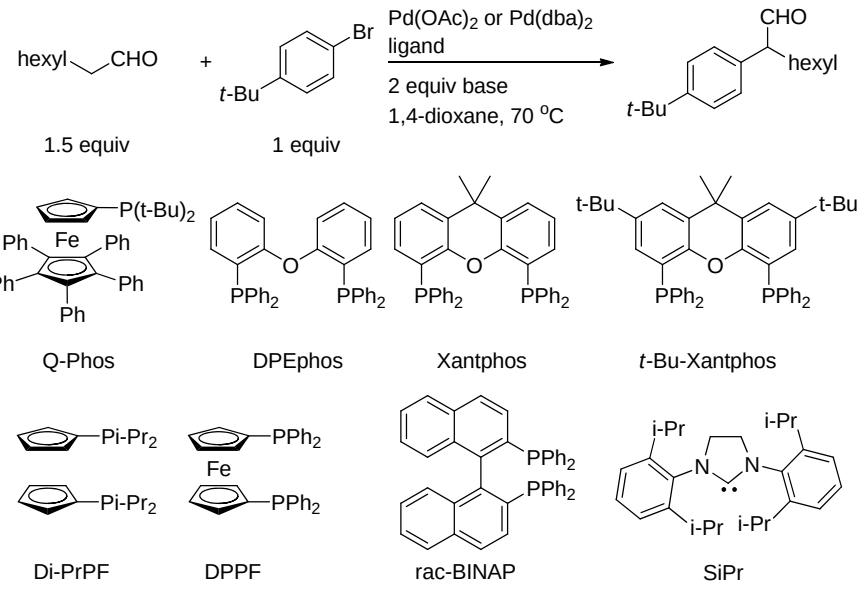
entry	base	time [h]	conversion, %[a]	yield, %[a]
1	KHMDS	15.5	88	trace
2	NaO*t*Bu	15.5	31	trace
3	Cs_2CO_3	15.5	70	53
4	K_3PO_4	15.5	20	trace

[a] Conversions and yields were determined by GC with dodecane as an internal standard.

2.3.1.2. Identification of Catalysts

We surveyed catalysts generated from various ligands and the catalyst precursors $Pd(OAc)_2$ and $Pd(dba)_2$ in reactions conducted with Cs_2CO_3 as base. The results of this study are summarized in Table 2. Of the catalysts used in this study, those generated from $Pd(dba)_2$ and monodentate P(*t*-Bu)$_3$ or bidentate dppf formed the coupled product in the highest yields (entries 1 and 8) with *tert*-butylbenzene as 20-30% side products. The combinations of $Pd(dba)_2$ with other ligands formed the α-aryl octanal in lower yields (entries 2-6 and 8-11).

Table 2. Survey of Ligands for the α-Arylation of Octanal



entry	Pd precusor	ligand	time [h]	conversion.[a]	yield, %[a]
1	5 mol% $Pd(dba)_2$	5 mol% $P(t\text{-}Bu)_3$	15	100	65
2	5 mol% $Pd(dba)_2$	5 mol% Q-Phos	15	100	60
3	5 mol% $Pd(dba)_2$	5 mol% DPEphos	36	90	40
4	5 mol% $Pd(dba)_2$	5 mol% Xantphos	25.5	92	60
5	5 mol% $Pd(dba)_2$	5 mol% *t*-Bu-Xantphos	20	100	61
6	5 mol% $Pd(dba)_2$	5 mol% Di-PrPF	24	38	20
7	5 mol% $Pd(dba)_2$	5 mol% dppf	24	92	68
8	5 mol% $Pd(dba)_2$	5 mol% rac-binap	24	70	66
9	5 mol% $Pd(OAc)_2$	5 mol% PCy_3	36	24	trace
10	5 mol% $Pd(OAc)_2$	5 mol% DPEphos	36	90	49
11	5 mol% $Pd(OAc)_2$	5 mol% SiPr	36	18	trace

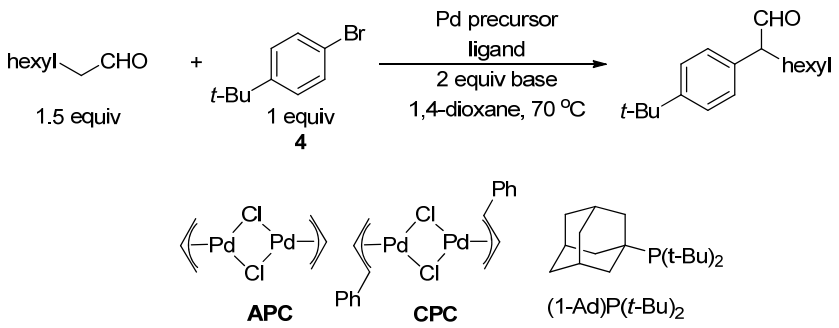
[a] Conversions and yields were determined by GC with dodecane as an internal standard.

To obtain higher yields of the coupled product, we investigated various palladium precursors that could from active catalysts in high concentrations. Thus, we studied catalyst precursors that are Pd(0) complexes or are complexes readily reduced to Pd(0) in the presence of a base and a nucleophile. Bis(tri-*tert*-butylphosphine)palladium, allylpalladium chloride (APC),

cinnamylpalladium chloride (CPC), and $[PdBr(P\textit{t}Bu_3)]_2$ dimer were tested. The results from this study are shown in Table 3.

Reactions conducted with $[PdBr(P\textit{t}\text{-}Bu_3)]_2$ (2.5 mol%) in DME or toluene occurred to full conversion after 8 h in low yields of the α-aryl aldehyde (entries 1-3) and high yield of *tert*-butylbenzene. Complexes generated from 5 mol % of bis(tri-*tert*-butylphosphine)palladium formed the coupled product in low yield (entry 4). Catalysts generated from 2.5 mol% of APC and 5 mol% of DPPF formed **8** in low yield (entry 5). The reaction conducted with 5 mol % of the more sterically hindered and more electron-deficient CPC and 5 mol % of dppf also occurred in low yield of the coupled product (entry 6). However, for reasons that we do not yet understand, the combination of 2.5 mol % of CPC and 10 mol % of dppf generated catalysts that form the α-aryl aldehyde in excellent yield (entry 7). We also evaluated complexes generated from CPC and monophosphines, and found that reactions catalyzed by these complexes occurred in lower yield (entries 8-12). We concluded that the catalyst generated from CPC and dppf couple octanal with 1-bromo-4-*tert*-butylbenzene in the highest yields.

Table 3. Study of Catalyst Precursors for the α-Arylation of Octanal



entry	Pd precatalyst	ligand	solvent	time, h	conv., %[a]	yield, %[a]
1	2.5% $\{PdBr[P(t\text{-}Bu_3)]\}_2$	–	DME	8	100	trace
2	2.5% $\{PdBr[P(t\text{-}Bu_3)]\}_2$	–	toluene	8	100	37
3	2.5% $\{PdBr[P(t\text{-}Bu_3)]\}_2$	–	1,4-dioxane	13.5	95	30
4	5.0% $Pd[P(t\text{-}Bu)_3]_2$	–	1,4-dioxane	24	100	50
5	2.5% APC	5% dppf	1,4-dioxane	24	74	24
6	2.5% CPC	5% dppf	1,4-dioxane	24	81	30
7	2.5% CPC	10% dppf	1,4-dioxane	14	100	94
8	2.5% CPC	5% xantphos	1,4-dioxane	14	100	88
9	2.5% CPC	5% rac-binap	1,4-dioxane	14	67	trace
10	2.5% CPC	10% $P(t\text{-}Bu)_3$	1,4-dioxane	14	100	66
11	2.5% CPC	10% Q-phos	1,4-dioxane	14	100	82
12	2.5% CPC	7% X-Phos	1,4-dioxane	14	100	80

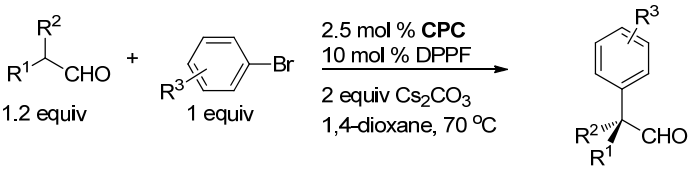
[a] Conversions and yields were determined by GC with dodecane as an internal standard.

2.3.2. Evaluation of the Substrate Scope of Reactions Catalyzed by Cinnamylpalladium Chloride and DPPF.

To study the scope of the couplings of aldehydes and aryl halides catalyzed by complexes generated from 2.5 mol% of CPC and 10 mol% of DPPF, we evaluated the couplings of the linear octanal, the β-branched isovaleraldehyde and the α-branched 2-methylbutanal with electron-neutral, electron-rich, and electron-poor aryl bromides. The results of this study are summarized in Table 4. The electron-rich 4-bromoanisole coupled with all three aldehydes in

low yields (entries 2, 5 and 8). The electron-neutral 1-bromo-4-*tert*-butylbenzene coupled with the linear aldehyde in good yield (entry 1), but this bromoarene coupled with the β-branched and α-branched aldehydes in low yields from 93% and 74% conversion of the bromoarene after 32 h (entries 4 and 7). The electron-poor 4-bromobenzotrifluoride coupled with the linear aldehyde in 66% yield and with the α-branched aldehyde in 82% yield (entries 3 and 9). The reaction of this electron-poor bromoarene with the β-branched aldehyde occurred to 72% conversion and 45% yield after 32 h. The results in this study showed that complete conversions of aryl halides occurred within 20-21 h in reactions of the linear aldehyde, whereas the complete conversion of bromoarnes occurred after 30 h in reactions of branched aldehydes. These results suggested that the catalyst generated from 2.5 mol % of CPC and 10 mol % of DPPF and CPC couple only linear aldehydes with aryl bromides in high yield. These results led us to test complexes of monophosphines in the α-arylation of branched aldehydes.

Table 4. Scope of Reactions Catalyzed by CPC and DPPF



entry	aldehyde	aryl halides	time [h]	% conversion[c]	% yield[a]
1	hexyl, CHO	Br, *t*-Bu	19	100	86
2	hexyl, CHO	Br, MeO	21	100	48
3	hexyl, CHO	Br, F_3C	21	100	66
4	Me, Me, CHO	Br, *t*-Bu	32	93	59
5	Me, Me, CHO	Br, MeO	32	85	<5
6	Me, Me, CHO	Br, F_3C	32	100	45[b]
7	Me, CHO, Me	Br, *t*-Bu	32	74	<5
8	Me, CHO, Me	Br, MeO	32	100	<5
9	Me, CHO, Me	Br, F_3C	36	100	83[b]

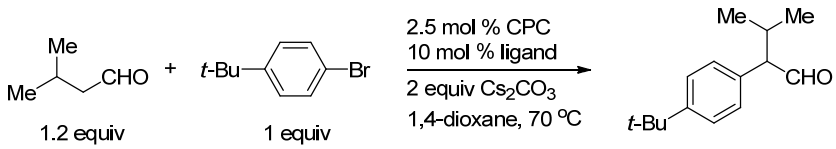
[a]Determined after purification by column chromatography. [b]Determined by ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as an internal standard. [c]Determined by GC with dodecane as an internal standard.

2.3.3. Identification of Catalysts for the α-Arylation of Branched Aldehydes

To identify catalysts for the α-arylation of branched aldehydes, we tested complexes generated from CPC and alkyl monophosphines in the reaction of 1-bromo-*t*-butylbenzene with the β-branched isovaleroaldehyde and the α-branched 2-methylbutanal in dioxane at 70 °C. We

also compared the rates and yields from reactions catalyzed by complexes of monophosphines with reactions catalyzed by complexes of bisphosphines. The results of this study are summarized in Table 5. The coupling reactions catalyzed by complexes of monophosphines occurred at a slower rate and in lower yields than those catalyzed by complexes of bisphosphines (entries 1-3 versus 4-6). This difference in rate and yield is consistent with the difference observed in the substrate scope study (Table 4). Of the catalysts we tested, the one generated from (1-Ad)P(*t*-Bu)$_2$ and CPC formed the coupled product in the highest yield.

Table 5. Survey of Ligands for the α-Arylation of Isobutyraldehyde



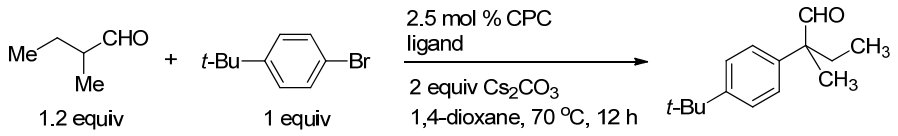
entry	ligand	time [h]	conversion, %[a]	yield, %[a]
1	P(*t*-Bu)$_3$	12 h	100	69
2	(1-Ad)P(*t*-Bu)$_2$	12 h	100	82
3	Q-Phos	12 h	100	69
4	5 mol% xantphos	24 h	89	52
5	5 mol% DPEphos	24 h	52	trace
6	5 mol% rac-BINAP	24 h	63	trace

[a]Determined by GC with dodecane as an internal standard.

We also surveyed a number of monodentate ligands for the α-arylation of the α-branched 2-methylbutanal. The results of this survey are shown in Table 6. Reactions catalyzed by complexes of P*t*Bu$_3$, (1-Ad)P(*t*Bu$_3$)$_2$, S-Phos, and Q-Phos occurred to full conversion in similarly yields. Reactions conducted with Q-phos occurred with the highest yield of coupled product.

Thus, we concluded that reactions of branched aldehydes occur in the highest yields when catalyzed by complexes of monophosphines.

Table 6. Survey of Ligands for the α-Arylation of 2-Methylbutyraldehyde



entry	ligand	conversion, %[a]	% yield[a]
1	10 mol % P(*t*-Bu)$_3$	100	70
2	7.5 mol % JohnPhos	45	6
3	5 mol % (1-Ad)P(*t*-Bu)$_2$	95	75
4	5 mol % Q-Phos	100	84
5	5 mol % S-Phos	100	74

[a] Conversions and yields were determined by GC with dodecane as an internal standard.

2.3.4. Identification of APC as the Catalyst Precursor and Optimization of Reaction Conditions

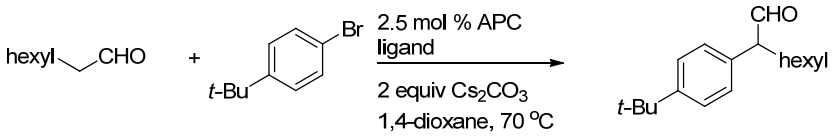
Because CPC was not commercially available, we reinvestigated allylpalladium chloride (APC) as the catalyst precursor. We previously showed that the catalyst generated from 2.5 mol % of APC and 5 mol % of DPPF coupled 1-bromo-4-*tert*-butylbenzene with octanal in 24% yield (Table 3 entry 5). Because the reactions catalyzed by CPC occurred in the highest yield with catalysts generated from a 1:4 ratio of palladium to dppf, we studied complexes generated from 2.5 mol % of APC and 10 mol % of DPPF in the coupling of 1-bromo-4-*tert*-butylbenzene with octanal. This reaction occurred in 94% yield.

We also surveyed catalysts generated from APC and various ligands to ensure that we have a catalyst that couple aldehydes with aryl halides in high yields. The results of this study are shown in Table 7. Of the catalysts generated from APC, a combination of 2.5 mol% of the APC

dimer and 10 mol% of dppf in the presence of Cs_2CO_3 formed the coupled product in highest yield (entry 1). Reactions catalyzed by complexes bearing other bisphosphines and monophosphine ligands formed the coupled product in lower yields (entries 2-4).

Thus, we optimized the conditions of reactions that are catalyzed by complexes generated from APC and found that reactions of linear aldehydes occurred in the highest yields with 1 mol % of APC, 4 mol % of DPPF, 2 equivalents of Cs_2CO_3 and 0.25 M of bromoarene and 0.30 M of aldehyde in dioxane. The reactions of branched aldehydes occurred in the highest yields when conducted with 0.5 mol % of APC, 1 mol % of Q-phos, 2 equivalents of Cs_2CO_3, 0.50 M of bromoarene and 0.60 M of aldehyde in THF. Chloroarenes also reacted with branched aldehydes under these conditions to give high yields of coupled products, albeit with higher catalyst loadings (1 mol% of APC and 2 mol% of Q-phos).

Table 7.



Entry	Ligand	Yield, %[b]
1	10 mol % DPPF	94
2	5 mol % Xantphos	88
3	10 mol % rac-BINAP	32
4	10 mol % Q-Phos	82

[a]Reaction conditions: 0.24 mmol octanal, 0.20 mmol 1-bromo-4-*tert*-butylbenzene, 0.40 mmol Cs_2CO_3, 1.0 mL 1,4-dioxane. [b] Yields were determined by GC with dodecane as an internal standard.

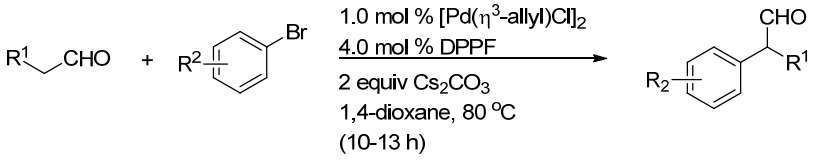
2.3.5. Scope of the α-Arylation of Linear Aldehydes

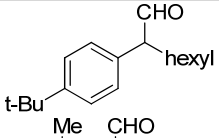
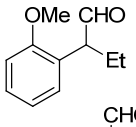
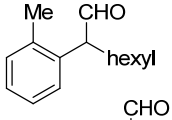
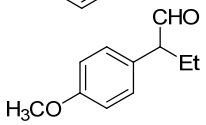
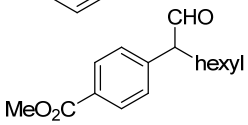
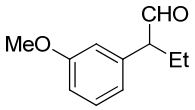
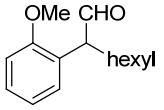
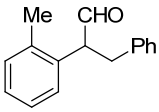
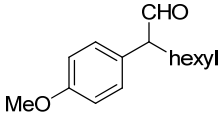
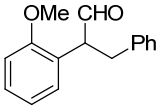
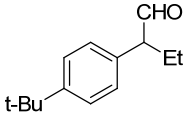
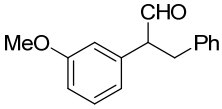
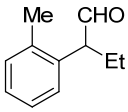
Having optimized the reaction conditions for the α-arylation of linear aldehydes, we evaluated substrate scope and the results are summarized in Table 8. The scope of this process encompassed electron-neutral and electron-poor aryl bromides. For example, octanal coupled with electron-neutral 1-bromo-4-*tert*-butylbenzene and 2-bromotoluene in excellent yields (entries 1 and 2). The reaction of octanal with the electron-poor methyl 4-bromobenzoate formed the coupled product in good yield (entry 3). The steric properties of the bromoarene favorably affected the yield of coupled product. For example, the reaction of the hindered and electron-rich 2-bromoanisole with octanal occurred in high yield (entry 4), whereas the less hindered electron-rich 4-bromoanisole formed the coupled product in 29% yield (entry 5).

Reactions of *n*-butyraldehyde also occurred in good yields, although these yields were slightly lower than those from reactions octanal. For example, reactions of 1-bromo-4-*tert*-butylbenzene with butyraldehyde and octanal occurred in 67 and 83% yield, respectively (entries 6 and 1), and reactions of 2-bromotoluene with butyraldehyde and octanal occurred in 75% and 93% yield, respectively. Although subtle, we attribute this difference in yields to the difference in steric bulk of these aldehydes. Culkin and Hartwig showed that the rates of reductive elimination from arylpalladium enolate complexes of hindered ketones are faster than those from arylpalladium enolate complexes of unhindered ketones.[15] Thus, we hypothesized that reductive elimination of coupled products from the arylpalladium enolate of octanal occurs faster than the reductive elimination from the enolate complex of the butyraldehyde, leading to faster rate of coupling and yield of coupled product. Again, more sterically hindered bromoarenes reacted in higher yield than unhindered bromoarenes. For example, butyraldehyde coupled with 2-bromoanisole and 4-bromoanisole in 70% and 33% yield, respectively (entries 8 and 9). The

reaction of *meta*-substituted 3-bromoanisole with butyraldehyde formed the coupled product in good yield (entry 8). Reactions of *ortho*- and *meta*-substituted bromoarenes with the aromatic linear hydrocinnamyl aldehyde formed the coupled products in good yields (entries 11-13). Reactions of the linear aldehydes with chloroarenes and bromopyridines resulted in low conversions and yields after 24 h at 80 °C.

Table 8. Scope of Coupling of Linear Aldehydes with Aryl Bromides.[a]



entry	product	yield, %[b]	entry	product	yield, %[b]
1		83	8		70
2		93	9		33
3		67	10		70
4		77	11		67
5		29	12		76
6		67	13		61
7		75			

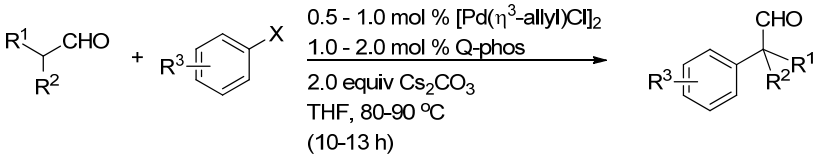
[a] Reaction conditions: 1.2 mmol aldehyde, 1.0 mmol aryl halide, 2.00 mmol Cs_2CO_3, 4 mL 1,4-dioxane. [b] Yield of isolated product (average of two runs).

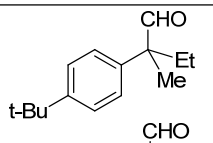
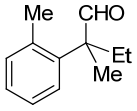
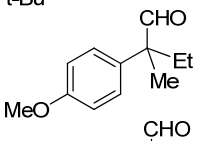
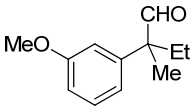
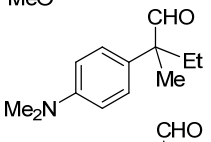
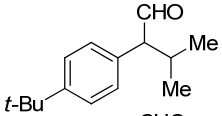
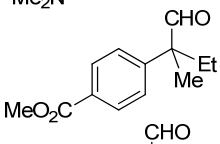
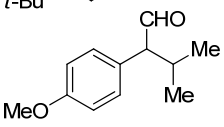
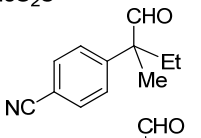
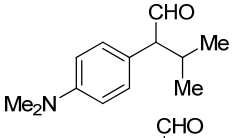
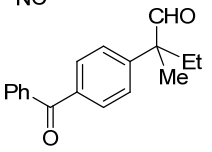
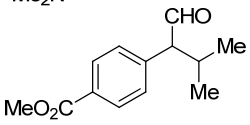
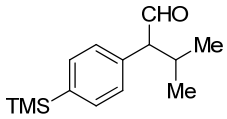
2.3.6. Scope of the α-Arylation of α- and β-branched Aldehydes

We evaluated the scope of reactions of branched aldehydes, and the results of this studyare summarized in Table 9. Electron-rich, electron-poor and electron-neutral bromoarenes reacted with α-branched 2-methylbutyraldehyde to form α-aryl aldehydes containing an α quaternary center in high yields (entries 1-4, 6 and 8). Both *ortho*- and *meta*-subtituted bromoarenes coupled with this aldehyde in high yields (entries 9 and 10). Reactions of the less reactive aryl chlorides[16] with 2-methylbutyraldehyde also occurred in high yields. For example, methyl 4-chorobenzoate, 4-chlorobenzonitrile and 3-chloroanisole reacted with 2-methylbutyraldehyde to give the corresponding α-aryl aldehydes in good yields (entries 5, 7 and 11).

Under the conditions developed for reactions of α-branched aldehydes, reactions of β-branched isovaleraldehyde occurred with aryl bromides to form coupled products in good yields. The scope of aryl bromide that undergoes this process is broad; electron neutral (entry 12), electron-rich (entries 13 and 14) and electron-poor (entry 15) bromoarenes reacted to form the β-branched, α-aryl aldehydes in good yields. In some cases, reactions of β-branched aldehydes occurred under the conditions used for reactions of linear aldehydes. For example, the reaction between 1-bromo-4-(trimethylsilyl)benzene and isovaleraldehyde formed the coupled product in good yield in the presence of catalysts generated from APC and DPPF (entry 16).

Table 9. Scope of the Coupling of Branched Aldehydes with Aryl Bromides.[a]



entry	product		yield, %[b]	entry	product		yield, %[b]
1		X = Br	91	9		X = Br	71
2		X= Br	81	10		X= Br	83
				11		X = Cl	76
3		X = Br	86	12		X = Br	80
4		X = Br	81				
5		X = Cl	77	13		X = Br	73
6		X = Br	80	14		X = Br	67
7		X = Cl	67				
8		X = Br	79	15		X = Br	67
				16[c]		X = Br	85

[a] Reaction conditions: 1.2 mmol aldehyde, 1.0 mmol aryl halide, 2.00 mmol Cs_2CO_3. For X = Br, 0.005 mmol APC, 0.01 mmol Q-phos, 2 mL THF, 80 °C; For X = Cl, 0.01 mmol APC, 0.02 mmol Q-phos, 4 mL THF, 90°C. [b] Yield of isolated product (average of two runs). [c] Reaction was conducted with 1 mol % APC and 4 mol % DPPF in 1,4-dioxane.

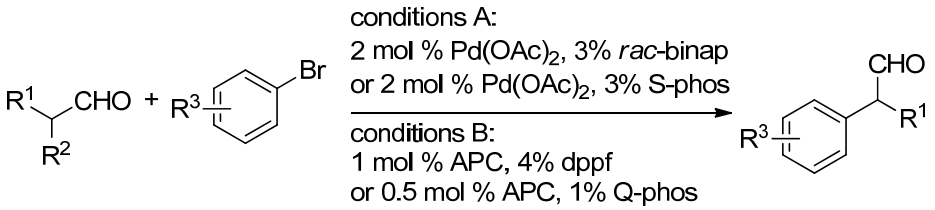
2.3.7. Comparison of Two Catalyst Systems: $Pd(OAc)_2$ and rac-BINAP versus $Pd(\eta^3\text{-allyl})Cl]_2$ and DPPF

We compared the protocols developed by Martín and Buchwald (*vide supra*) with those developed in this work. Table 10 provides a comparison of the reactions of electron-neutral with

linear aldehydes and electron-rich bromoarenes with α-branched aldehydes catalyzed under the conditions reported by Martín and Buchwald (conditions A) and under the conditions reported here (conditions B).

The coupling of both *n*-butanal and *n*-octanal with the electron-neutral 1-bromo-4-*tert*-butylbenzene occurred in substantially lower yields with 2 mol % of $Pd(OAc)_2$ and 3 mol % of *rac*-BINAP as catalyst than with 1 mol % of APC and 4 mol % of DPPF (entries 1 and 2). Likewise, the reactions of 2-methylbutyraldehyde with electron-rich 4-bromo-*N*,*N*-dimethylaniline and 4-bromoanisole formed the coupled products in much higher yields with the catalyst generated from APC and Q-phos.

Table 10. Comparison of Catalytic Systems



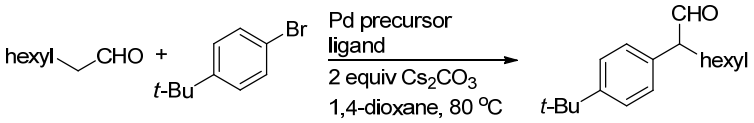
Entry		Conditions A[a]	Conditions B[b]
1	R^1 = Et, R^2 = H R^3 = *p*-*t*-Bu	10% GC	67% isolated
2	R^1 = *n*-C_6H_{13}, R^2 = H R^3 = *p*-*t*-Bu	10% GC	83% isolated
3	R^1 = Et, R^2 = Me R^3 = *p*-NMe_2	65% GC	86% isolated
4	R^1 = Et, R^2 = Me R^3 = *p*-OMe	44% GC	81% isolated

[a] Reaction conditions A for entries 1 and 2: 1.2 mmol aldehyde, 1.0 mmol bromoarene, 1.2 mmol Cs_2CO_3, 0.020 mmol $Pd(OAc)_2$, 0.030 mmol *rac*-binap, 4 mL 1,4-dioxane, 14 h. For entries 3 and 4, 0.030 mmol of S-phos was used as with reaction time of 16.5 h.

[b] Reaction conditions B for entries 1 and 2: 1.0-1.2 mmol aldehyde, 1.0 mmol bromoarene, 2.0 mmol Cs_2CO_3, 0.010 mmol APC, 0.04 mmol dppf, 4 mL 1,4-dioxane. For entries 3 and 4, 0.005 mmol APC, 0.010 mmol of Q-phos and 2 mL of THF were used instead.

We attribute this difference in yields to both the palladium precursor and ligand. The beneficial effect of precursor is shown by reactions of octanal conducted with both DPPF and *rac*-BINAP. The results of this comparison are summarized in Table 11. The catalyst generated from 4.5 mol % of $Pd(dba)_2$ and 9.0 mol % of DPPF formed the coupled product in lower yield than the catalyst generated from 1 mol % of APC and 4 mol % of DPPF, and the catalyst generated from 10 mol % of *rac*-BINAP and 2.5 mol % of APC formed the coupled product in higher yield than that generated from 2 mol % of $Pd(OAc)_2$ and 3 mol % of *rac*-BINAP. However, the yield from the reaction catalyzed by APC and *rac*-BINAP remained low, and a comparison of the reactions conducted with APC and DPPF or BINAP shows that DPPF contributes significantly to the observation of a high yield of coupled product.

Table 11. Effects of Palladium Precursor and Ligand[a]



Ligand = DPPF[b]			Ligand = rac-BINAP		
precursor	conv.	yield	precursor	conv.	yield
4.5% $Pd(dba)_2$	81%	60%	2% $Pd(OAc)_2$[d]	52%	10%
1% APC	100%	83%[c]	2.5% APC[e]	85%	32%

[a] Conversions and yields were determined by GC with dodecane as an internal standard. [b] A ratio of 2:1 of DPPF to palladium was used. [c] Isolated yield of coupled product. [d] 3 mol % of *rac*-BINAP was used. [e] 10 mol % of rac-BINAP was used.

2.4. Conclusion and Outlook

In conclusion, we have developed an improved method for the palladium-catalyzed α-arylation of aldehydes. The scope of the arylation of linear aldehydes encompasses electron-poor and electron-neutral aryl bromides, whereas the scope of the arylation of branched aldehydes encompasses electron-rich, electron-neutral and electron-poor aryl halides. α-Aryl aldehydes containing quaternary α centers can be formed in high yields. One key to observing this broad scope includes the use of a palladium precursor that can be easily reduced to active $L_nPd(0)$ species.

Future work will focus on the expansion of scope to couplings of electron-rich aryl halides, heteroaryl halides, aryl tosylates, and aryl triflates with linear aldehydes. In the reactions of these aryl halides with linear aldehydes, side products are formed from the hydrodehalogenation of the aryl halides. One possible mechanism of hydrodehalogenation is the β-hydrogen elimination from an arylpalladium enolate complex of aldehyde, and the resulting arylpalladium hydrido complex undergoes reductive elimination to form the arene. Thus, we sought to understand the effects of steric and electronic properties of ligands on the stability and reactivity of such enolate complexes. The results of this study are described in the next chapter.

2.5. Experimental Information

General Procedures. Unless otherwise noted, all manipulations were conducted under an inert nitrogen or argon atmosphere with flame-dried glassware. Rotary evaporation was done at 25-30 ^{o}C. Flash column chromatography was performed as described by Still et al on silica gel (Silicycle, 60 A pore size, 40-64 um particle size, pH Suspension 10%: 6.5-7.5).[17] Analytical thin-layer chromatography was performed on glass plates coated with silica gel (Silicycle, 60 A pore size, 40-64 um particle size) and visualized with both ultraviolet light and dinitrophenylhydrazine (DNP) solution.

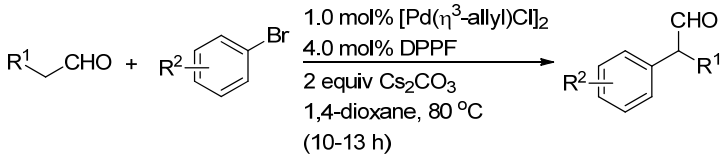
Materials. 1,1'-Bis(diphenylphosphino)ferrocene (DPPF) was purchased from Strem Chemicals and used without further purification. 1,2,3,4,5-Pentaphenyl-1'-(di-tertbutylphosphino) ferrocene (Q-phos) was obtained as a gift from Johnson-Matthey or synthesized as described by Hartwig and coworkers.[18] 1-Adamantyl-di-tert-butylphosphine (1-Ad)P*t*Bu$_2$ was synthesized as decribed by Stambuli et al.[19] Palladium(η^3-allyl)chloride dimer was purchased from Strem Chemicals or synthesis as described by Auburn et al.[20] Palladium(η^3-cinnamyl)chloride dimer was synthesized as described by Auburn et al.[20] Pd(OAc)$_2$ was obtained as a gift from Johnson-Matthey. All aldehydes were fractionally distilled, followed by sparging with nitrogen gas before use. Cesium carbonate (99.9%) was purchased from Aldrich and used without further purification. Tribasic potassium phosphate (ACS Reagent Grade, ≥98%) was purchased from Aldrich and ground using a mortar and pestle under ambient conditions and used without further drying. All aryl halides were purchased from Aldrich and used without further purification. Ethylene glycol dimethyl ether and 1,4-dioxane (ACS Reagent grade) were purchased from Aldrich and dried over sodium-benzophenone ketyls and vacuum transferred

before use. Tetrahydrofuran and toluene were dried with a solvent purification system by percolation through neutral alumina under positive pressure of argon. Solvents for filtration and chromatography were certified ACS grade.

Instruments. ^{1}H and ^{13}C NMR spectra were recorded either on Varian Unity-400 or 500 MHz (126 MHz, ^{13}C) spectrometers or a Bruker AM 400 MHz spectrometer. Spectra are referenced to residual chloroform (d = 7.26 ppm, ^{1}H; 77.0 ppm, ^{13}C) or residual benzene (d = 7.15 ppm, ^{1}H; 128.62 ppm, ^{13}C). Chemical shifts are reported in ppm, multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and b (broad). Coupling constants, *J*, are reported in hertz, and integration is provided and assignments are indicated. All ^{31}P NMR chemical shifts are reported in parts per million relative to an 85% H_3PO_4 standard. Chemical shifts downfield of the standard are reported with positive values. Analytical gas chromatography (GC) was performed using a Hewlett-Packard 5890 Gas Chromatograph fitted with a flame ionization detector. The GC method used involved injections onto a Hewlett-Packard HP5 (30m x 0.32 mm) capillary column. The injector temperature was 250 ^{o}C and the detector temperature was 300 ^{o}C with a H_2 carrier gas flow of 16 mL/min. The column temperature program was as follows: 120 ^{o}C to 250 ^{o}C at 40 ^{o}C/min, then hold for 3 min for a total run time of 6.25 min. Retention times (t_R) were obtained using Agilent Chemstation software. Response factors were generated by triplicate runs of three molar ratios of the analyte to dodecane standard dissolved in ethyl acetate. Infrared (IR) spectra were measured as thin films (neat) in NaCl cells, using a Perkin Elmer Spectrum BX spectrophotometer, and peaks are reported in cm^{-1} along with relative signal intensities: s (strong); m (medium); w (weak). Microanalysis (CHN) was performed on an Exeter CE440 analyzer at the University of Illinois Microanalysis Laboratory or at Robertson Microlit Laboratories, Edison, New Jersey.

EXPERIMENTAL PROCEDURES

General Procedures for the α-Arylation of Linear Aldehydes (Table 8)



Without use of a glove box:

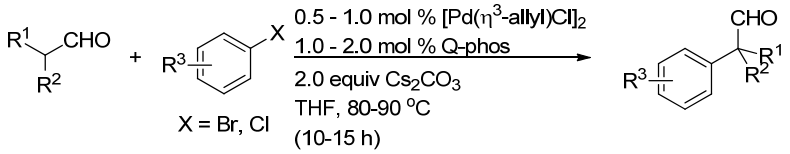
APC (3.7 mg, 0.010 mmol), DPPF (0.0222 mg, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol) and an aryl halide (if it is a solid) (1.00 mmol) were added in the described order to a 25-mL Schlenk flask that contained a magnetic stirbar. The flask was evacuated and back-filled with nitrogen three times. A solution of a linear aldehyde (1.10 mmol) and an aryl halide (if it is a liquid (1.00 mmol) in 1,4-dioxane (4 mL) was then added via a gas-tight syringe. The flask was placed in an 80 ^{o}C oilbath for 10-13 h. After complete conversion of the aryl halide was determined by GC analysis, the reaction mixture was diluted with ethyl acetate (10 mL) and filtered through a pad of Celite. The filtrate was concentrated under vacuum and the crude product was purified using flash column chromatography on silical gel (hexanes/diethyl ether) to give the α-aryl aldehyde.

With use of a glove box:

Inside a nitrogen-filled drybox, APC (3.7 mg, 0.010 mmol), DPPF (0.0222 mg, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), a linear aldehyde (1.20 mmol) and an aryl halide (1.00 mmol) were added in the described order to a 5-dram scintillation vial containing a magnetic stirbar. 1,4-Dioxane (4 mL) was then added via a gas-tight syringe. The vial was sealed with a Teflon-lined screwcap, removed from the drybox, and placed in a 80 ^{o}C oilbath for 10-13

h. After complete conversion of the aryl halide was observed by GC/MS analysis, the reaction mixture was diluted with ethyl acetate (10 mL) and filtered through a pad of Celite. The filtrate was concentrated under vacuum and the crude product was purified by flash column chromatography on silical gel using (hexanes/diethyl ether) to give the α-aryl aldehyde.

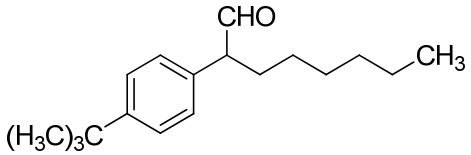
General Procedures for the α-Arylation of Branched Aldehydes (Table 9)



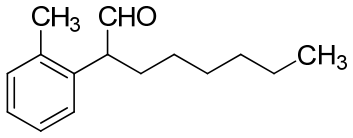
General Procedures for the α-Arylation of Branched Aldehydes with Aryl Bromides. Inside a nitrogen-filled drybox, APC (0.0018 g, 0.0050 mmol), Q-phos (0.0071 g, 0.010 mmol), cesium carbonate (0.652 g, 2.00 mmol), a branched aldehyde (1.20 mmol) and an aryl bromide (1.00 mmol) were added in the described order to a 1-dram scintillation vial containing a magnetic stir bar. THF (2 mL) was then added via a gas-tight syringe. The vial was sealed with a Teflon-lined screw cap, removed from the drybox, and placed in a 80 ^{o}C oil bath for 10-13 h. After complete conversion of the aryl halide was observed by GC/MS analysis, the reaction mixture was diluted with ethyl acetate (10 zmL) and filtered through a pad of Celite. The filtrate was concentrated under vacuum and the crude product was purified by flash column chromatography on silical gel using (hexanes/diethyl ether) to give the α-aryl aldehyde.

General Procedures for the α-Arylation of Branched Aldehydes with Aryl Chlorides. The general procedure for α-arylation of branched aldehydes with aryl bromides was followed with the following modifications: reactions were conducted with APC (0.0037 g, 0.010 mmol), Q-phos (14.2 mg, 0.0200 mmol) and THF (4 mL) in a 5-dram scintillation vial at 90 ^{o}C.

EXPERIMENTAL AND COMPOUND CHARACTERIZATION DATA

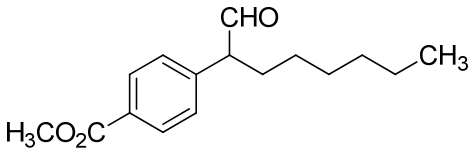


2-(4-*t*-Butylphenyl)octanal (Table 8, entry 1). Following the general procedure for α-arylation of linear aldehydes, APC (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), octyl aldehyde (0.141 g, 1.20 mmol), 1-bromo-4-*t*-butylbenzene (0.213 g, 1.00 mmol) were combined in 1,4-dioxane (4.0 mL) and stirred at 80 °C for 12 h. Following the general procedure for work up, the filtrate was purified by flash-column chromatography (silica gel, 2% ether-hexanes) to give the title compound as a clear, colorless oil (0.216 g, 83%). R_f = 0.41 (4% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (d, *J* = 2.2 Hz, 1H, C**H**O), 7.39 (d, *J* = 8.4 Hz, 2H, Ar**H**), 7.13 (d, *J* = 8.3 Hz, 2H, Ar**H**), 3.47 (dt, *J* = 2.2 Hz, 1H, C**H**CHO), 2.06 (m, 1H, C**H**$_2$CH(Ar)CHO), 1.73 (m, 1H, C**H**$_2$CH(Ar)CHO), 1.33 (s, 9H, CC**H**$_3$). 1.34-1.21 (m, 8H, CH_3(C**H**$_2$)$_4$C**H**$_2$CH(Ar)CHO), 0.87 (t, *J* = 6.9 Hz, 3H, C**H**$_3$CH$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 150.3, 133.3, 128.4, 125.9, 58.7, 34.5, 31.6, 31.3, 29.6, 29.1, 27.1, 22.6, 14.0.



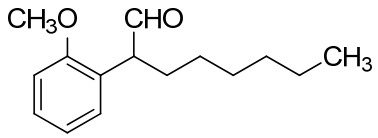
2-(2-Methylphenyl)octanal (Table 8, entry 2). Following the general procedure for α-arylation of linear aldehydes, APC (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), octyl aldehyde (0.141 g, 1.20 mmol), 1-bromo-2-methylbenzene (0.171 g, 1.00 mmol) were combined in 1,4-dioxane (4.0 mL) and stirred at 80 °C for 12 h.

Following the general procedure for work up, the filtrate was purified by flash-column chromatography (silica gel, 4% ether-hexanes) to give the title compound as a clear, colorless oil (0.205 g, 94%). R_f = 0.25 (4% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.60 (d, *J* = 2.0 Hz, 1H, C**H**O), 7.25-7.17 (m, 3H, Ar**H**), 7.11-7.08 (m, 1H, Ar**H**), 3.75 (dt, *J* = 2.0, 7.2 Hz, 1H, C**H**CHO), 2.36 (s, 3H, ArC**H**$_3$), 2.10 (m, 1H, C**H**$_2$CH(Ar)CHO), 1.71 (m, 1H, C**H**$_2$CH(Ar)CHO), 1.35-1.20 (m, 8H, CH_3(C**H**$_2$)$_4$C**H**$_2$CH(Ar)CHO), 0.87 (t, *J* = 6.8 Hz, 3H, C**H**$_3$CH$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 137.1, 134.9, 130.8, 127.8, 127.3, 126.5, 55.0, 31.6, 29.5, 29.3, 27.1, 22.5, 19.9, 14.0. IR (NaCl, thin film, neat) 3065 (w), 3020 (w), 2955 (s), 2928 (s), 2857 (s), 2811 (m), 2711 (w), 1723 (s), 1685 (m), 1685 (m), 1490 (m), 1462 (s), 1379 (m), 756 (m), 726 (m).

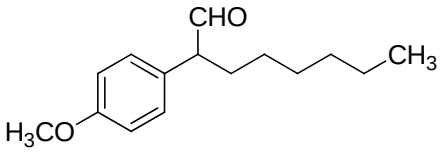


Methyl 4-(2-oxo-1-*n*-hexylethyl)benzoate (Table 8, entry 3). Following the general procedure for α-arylation of linear aldehydes, APC (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), octyl aldehyde (0.141 g, 1.10 mmol), methyl 4-bromobenzoate (0.215 g, 1.00 mmol) were combined in 1,4-dioxane (4.0 mL) and stirred at 80 ^{o}C for 12 h. Following the general procedure for work up, the filtrate was purified using flash-column chromatography (silica gel, gradient elution 4%, 8%, 12% and 16% diethyl ether-hexanes) to give the title compound as a clear, colorless oil (0.1674 g, 64%). R_f = 0.27 (16% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (d, *J* = 2.0 Hz, 1H, C**H**O), 8.03 (d, *J* = 8.4 Hz, 2H, Ar**H**), 7.26 (d, *J* = 8.3 Hz, 2H, Ar**H**), 3.90 (s, 3H, C**H**$_3$O), 3.56 (ddd, *J* = 8.4, 6.5, 1.9 Hz, 1H, C**H**CHO), 2.08 (m, 1H, C**H**$_2$CH(Ar)CHO), 1.74 (m, 1H, C**H**$_2$CH(Ar)CHO), 1.33-1.16 (m, 8H, CH_3(C**H**$_2$)$_4$C**H**$_2$CH(Ar)CHO), 0.84 (t, *J* = 6.9 Hz, 3H, C**H**$_3$CH$_2$). ^{13}C NMR

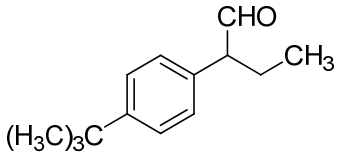
(100 MHz, $CDCl_3$) δ 200.2, 166.7, 141.7, 130.2, 129.3, 128.7, 59.1, 52.1, 31.5, 29.7, 29.0, 26.9, 22.5, 14.0. IR (NaCl, thin film, neat) 2928 (s), 2857 (s), 1727 (s), 1611 (m), 1576 (w), 1435 (s), 1417 (m), 1279 (b), 1181 (m), 1113 (s), 1019 (m). Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 72.99; H, 8.73.



2-(2-Methoxyphenyl)octanal (Table 8, entry 4). Following the general procedure for α-arylation of linear aldehydes, APC (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), octyl aldehyde (0.141 g, 1.20 mmol), 2-bromoanisole (0.187 g, 1.00 mmol) were combined in 1,4-dioxane (4.0 mL) and stirred at 80 ^oC for 12 h. Following the general procedure for work up, the filtrate was purified using flash-column chromatography (silica gel, gradient elution 1%, 2%, 3% and 4% ether-hexanes) to give the title compound as a clear, colorless oil (0.180 g, 77%). R_f = 0.28 (4% diethyl ether-hexanes; UV, DNP). ^1H NMR (400 MHz, $CDCl_3$) δ 9.66 (d, *J* = 1.0 Hz, 1H, C**H**O), 7.29 (dd, *J* = 7.9, 1.4 Hz, 1H, Ar**H**), 7.10 (dd, *J* = 7.5, 1.7 Hz, 1H, Ar**H**), 6.96 (td, *J* = 7.5, 1.0 Hz, 1H, **ArH**), 6.91 (d, *J* = 8.2 Hz, 1H, Ar**H**), 3.81 (s, 3H, OC**H**$_3$), 3.76 (dd, *J* = 7.9, 6.5 Hz, 1H, C**H**CHO), 2.08 (m, 1H, C**H**$_2$CH(Ar)CHO), 1.70 (m, 1H, C**H**$_2$CH(Ar)CHO), 1.33-1.18 (m, 8H, CH_3(C**H**$_2$)$_4$$CH_2$CH(Ar)CHO), 0.85 (t, *J* = 6.9 Hz, 3H, C**H**$_3$$CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.9, 157.4, 129.8, 128.6, 125.7, 120.8, 110.8, 55.4, 53.1, 31.6, 29.2, 28.3, 27.2, 22.6, 14.1. IR (NaCl, thin film, neat) 3002 (w), 2928 (s), 2856 (s), 2709 (m), 1725 (s), 1599 (m), 1586 (m), 1493 (s), 1465 (s), 1438 (m), 1289 (m), 1246 (s), 1051 (m), 1030 (m), 754 (s).

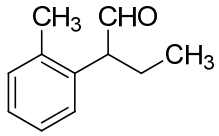


2-(4-Methoxyphenyl)octanal (Table 8, entry 5). Following the general procedure for α-arylation of linear aldehydes, APC (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), octyl aldehyde (0.141 g, 1.20 mmol), 1-bromo-4-methoxybenzene (0.187 g, 1.00 mmol) were combined in 1,4-dioxane (4.0 mL) and stirred at 80 ^{o}C for 12 h. Following the general procedure for work up, the filtrate was purified using flash-column chromatography (silica gel, 4% ether-hexanes) to give the title compound as a clear, colorless oil (0.069 g, 29%). R_f = 0.20 (4% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (d, *J* = 2.2 Hz, 1H, C**H**O), 7.11 (d, *J* = 8.7 Hz, 2H, Ar**H**), 6.91 (d, *J* = 8.7 Hz, 2H, Ar**H**), 3.81 (s, 3H, ArOC**H**$_3$), 3.43 (ddd, *J* = 2.1, 6.6, 8.5 Hz, 1H, C**H**CHO), 2.03 (m, 1H, C**H**$_2$CH(Ar)CHO), 1.69 (m, 1H, C**H**$_2$CH(Ar)CHO), 1.32-1.19 (m, 8H, CH_3(C**H**$_2$)$_4$CH$_2$CH(Ar)CHO), 0.85 (t, *J* = 6.9 Hz, 3H, C**H**$_3$CH$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 158.9, 129.8, 128.2, 114.4, 58.3, 55.2, 31.6, 29.6, 29.1, 27.0, 22.6, 14.0. IR (NaCl, thin film, neat) 2929 (s), 2856 (m), 2708 (w), 1723 (s), 1610 (m), 1583 (w), 1513 (s), 1465 (m), 1442 (w), 1303 (m), 1251 (s), 1179 (m), 1106 (w), 1036 (m), 829 (m), 809 (w). Anal. Calcd for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 77.07; H, 9.50.



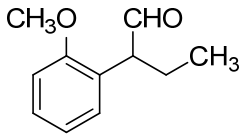
2-(4-*tert*-Butylphenyl)butyraldehyde (Table 8, entry 6). Following the general procedure for α-arylation of linear aldehydes, APC (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), butyraldehyde (0.0865 g, 1.20 mmol), 1-bromo-4-*tert*-

butylbenzene (0.213 g, 1.00 mmol) were combined in 1,4-dioxane (4.0 mL) and stirred at 80 °C for 12 h. The crude product was purified using flash-column chromatography (silica gel, gradient elution: 1% ether-hexanes, 2% ether-hexanes, 3% ether-hexanes, then 4% ether-hexanes) to give the title compound as a clear, colorless oil (0.137 g, 67%). R_f = 0.25 (4% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (d, *J* = 2.2 Hz, 1H, C**H**O), 7.39 (d, *J* = 8.4 Hz, 2H, Ar**H**), 7.13 (d, *J* = 8.2 Hz, 2H, Ar**H**), 3.39 (m, 1H, C**H**CHO), 2.10 (m, 1H, C**H**$_2$CH(Ar)CHO), 1.75 (m, 1H, C**H**$_2$CH(Ar)CHO), 1.32 (s, 9H, ArC(C**H**$_3$)$_2$), 0.91 (t, *J* = 7.4 Hz, 3H, C**H**$_3$CH$_2$CH(Ar)CHO). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 150.4, 133.1, 128.4, 125.9, 60.3, 34.5, 31.3, 22.8, 11.8. IR (NaCl, thin film, neat) 2963 (s), 2904 (m), 2873 (m), 2811 (w), 2710 (w), 1726 (s), 1685 (w), 1507 (m), 1463 (m), 1364 (m), 1269 (m), 1109 (m), 1017 (w), 829 (m). Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.44; H, 10.04.

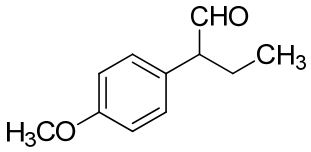


2-(2-Methylphenyl)butyraldehyde (Table 8, entry 7). Following the general procedure for α-arylation of linear aldehydes, Pd(η^3-allyl)Cl]$_2$ (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), butyraldehyde (0.0865 g, 1.20 mmol), 1-bromo-2-methylbenzene (0.171 g, 1.00 mmol) were combined in 1,4-dioxane (4.0 mL) and stirred at 80 °C for 12.5 h. Following the general procedure for work up, the filtrate was purified using flash-column chromatography (silica gel, gradient elution: 1% ether-hexanes, 2% ether-hexanes, 3% ether-hexanes, then 4% ether-hexanes) to give the title compound as a clear, colorless oil (0.122 g, 75%). R_f = 0.23 (4% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.62 (d, *J* = 2.0 Hz, 1H, C**H**O), 7.25-7.18 (m, 3H, Ar**H**), 7.09-7.07 (m, 1H, Ar**H**), 3.69 (dt, *J* = 7.2 Hz, 1H, C**H**CHO), 2.36 (s, 3H, ArC**H**$_3$), 2.14 (m, 1H, CH$_3$C**H**$_2$CH(Ar)CHO), 1.75 (m, 1H,

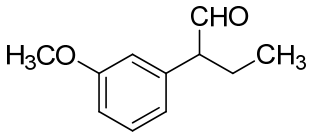
$CH_3C\mathbf{H}_2CH(Ar)CHO$), 0.93 (t, J = 7.2 Hz, 3H, $C\mathbf{H}_3CH_2CH(Ar)CHO$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 137.2, 134.7, 130.8, 127.8, 127.3, 126.5, 56.5, 22.7, 19.9, 11.8. IR (NaCl, thin film, neat) 3065 (w), 3020 (w), 2965 (s), 1934 (m), 2875 (m), 2813 (w), 2711 (w), 1718 (s), 1490 (m), 1462 (m), 1381 (m), 757 (s), 726 (m). Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.29; H, 9.00.



2-(2-Methoxyphenyl)butyraldehyde (Table 8, entry 8). Following the general procedure for α-arylation of linear aldehydes, APC (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), butyraldehyde (0.0865 g, 1.20 mmol), 1-bromo-2-methoxybenzene (0.187 g, 1.00 mmol) were combined in THF (4.0 mL) and stirred at 80 ^oC for 12 h. Following the general procedure for work up, the filtrate was purified using flash-column chromatography (silica gel, gradient elution: 2% ether-hexanes, 4% ether-hexanes, 6% ether-hexanes, then 8% ether-hexanes) to give the title compound as a clear, colorless oil (0.128 g, 71%). R_f = 0.28 (8% diethyl ether-hexanes; UV, DNP). ^1H NMR (400 MHz, $CDCl_3$) δ 9.67 (d, J = 0.8 Hz, 1H, C**H**O), 7.31-7.30 (m, 1H, Ar**H**), 7.09 (dd, J = 8.0, 1.7 Hz, 1H, Ar**H**), 6.99-6.91 (m, 2H, Ar**H**), 3.81 (s, 3H, OC$\mathbf{H}_3$), 3.69 (dt, J = 7.2, 0.8 Hz, 1H, C**H**CHO), 2.18-2.08 (m, 1H, $CH_3C\mathbf{H}_2CH(Ar)CHO$), 1.78-1.67 (m, 1H, $CH_3C\mathbf{H}_2CH(Ar)CHO$), 0.89 (t, J = 7.4 Hz, 3H, $C\mathbf{H}_3CH_2CH(Ar)CHO$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.8, 157.4, 129.9, 128.6, 125.4, 120.8, 110.7, 55.3, 54.7, 21.5, 11.8. Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.21; H, 8.15.

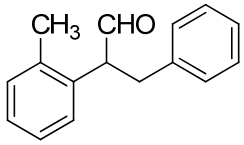


2-(4-Methoxyphenyl)butyraldehyde (Table 8, entry 9). Following the general procedure for α-arylation of linear aldehydes, APC (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), butyraldehyde (0.0865 g, 1.20 mmol), 1-bromo-4-methoxybenzene (0.187 g, 1.00 mmol) were combined in 1,4-dioxane (4.0 mL) and stirred at 80 ^{o}C for 12 h. The crude product was purified using flash-column chromatography (silica gel, gradient elution: 3% ether-hexanes, 6% ether-hexanes, 9% ether-hexanes, then 12% ether-hexanes) to give the title compound as a clear, colorless oil (0.058 g, 33%). R_f = 0.26 (12% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (d, *J* = 2.0 Hz, 1H, C**H**O), 7.11 (d, *J* = 8.8 Hz, 2H, Ar**H**), 6.91 (d, *J* = 8.8 Hz, 2H, Ar**H**), 3.80 (s, 3H, OC**H**$_3$), 3.36 (m, 1H, CH_3CH_2C**H**(Ar)CHO), 2.08 (m, 1H, CH_3C**H**$_2$CH(Ar)CHO), 1.71 (m, 1H, CH_3C**H**$_2$CH(Ar)CHO), 0.89 (t, *J* = 7.6 Hz, 3H, C**H**$_3$CH$_2$CH(Ar)CHO).^{13}C NMR (100 MHz, $CDCl_3$) δ 201.11, 158.94, 129.81, 128.02, 114.38, 59.93, 55.23, 22.83, 11.66. IR (NaCl, thin film, neat) 2963 (s), 2934 (s), 2873 (m), 2836 (m), 2710 (w), 1722 (s), 1675 (w), 1610 (s), 1582 (m), 1513 (s), 1463 (s), 1442 (m), 1379 (w), 1303 (m), 1250 (s), 1179 (s), 1129 (w), 1033 (s), 830 (s). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.31; H, 8.14.



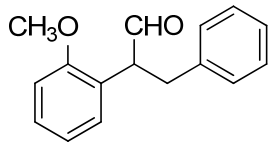
2-(3-Methoxyphenyl)butyraldehyde (Table 8, entry 10). Following the general procedure for α-arylation of linear aldehydes, APC (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), butyraldehyde (0.0865 g, 1.20 mmol), 1-bromo-3-

methoxybenzene (0.187 g, 1.00 mmol) were combined in 1,4-dioxane (4.0 mL) and stirred at 80 ^{o}C for 12 h. Following the general procedure for work up, the filtrate was purified using flash-column chromatography (silica gel, gradient elution: 2% ether-hexanes, 4% ether-hexanes, 6% ether-hexanes, then 8% ether-hexanes) to give the title compound as a clear, colorless oil (0.125 g, 70%). R_f = 0.26 (8% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.66 (d, *J* = 2.0 Hz, 1H, C**H**O), 7.29 (t, *J* = 7.9 Hz, 1H, Ar**H**), 6.84 (m, 1H, Ar**H**), 6.79 (d, *J* = 7.6 Hz, 1H, Ar**H**), 6.73 (m, 1H, Ar**H**), 3.81 (s, 3H, ArOC**H**$_3$), 3.38 (m, C**H**CHO), 2.09 (m, 1H, CH_3C**H**$_2$CH(Ar)CHO), 1.75 (m, 1H, CH_3C**H**$_2$CH(Ar)CHO), 0.90 (t, *J* = 7.4 Hz, 3H, C**H**$_3$$CH_2$CH(Ar)CHO). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 160.0, 137.7, 130.0, 121.1, 114.5, 112.7, 60.8, 55.2, 22.8, 11.7. IR (NaCl, thin film, neat) 2964 (s), 2936 (s), 2876 (m), 2836 (m), 2715 (w), 1722 (s), 1600 (s), 1584 (s), 1492 (s), 1464 (s), 1436 (s), 1380 (w), 1319 (m), 1293 (s), 1261 (s), 1157 (m), 1126 (w), 1048 (s), 996 (w), 876 (w), 780 (s), 700 (s). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.18; H, 8.01.



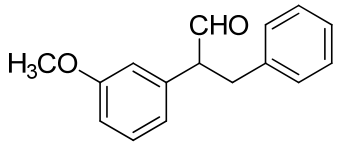
3-Phenyl-2-(2-methylphenyl)propionaldehyde (Table 8, entry 11). Following the general procedure for α-arylation of linear aldehydes, APC (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), hydrocinnamaldehyde (0.134 g, 1.00 mmol), 1-bromo-2-methylbenzene (0.171 g, 1.00 mmol) were combined in 1,4-dioxane (4.0 mL) and stirred at 80 ^{o}C for 12 h. Following the general procedure for work up, the filtrate was purified using flash-column chromatography (silica gel, gradient eluction: 1%, 2%, 3%, and then 4% diethyl ether in hexanes) to give the title compound as a clear, colorless oil (0.149 g, 67%). R_f = 0.26 (12% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (d, *J* = 1.2

Hz, 1H, C**H**O), 7.27-7.04 (m, 9H, Ar**H**), 4.09 (ddd, *J* = 1.2, 6.4, 13.6 Hz, 1H, C**H**CHO), 3.51 (dd, *J* = 6.4, 13.6 Hz, 1H, PhC**H**$_2$CH(Ar)CHO), 2.90 (dd, *J* = 8.0, 13.6 Hz, 1H, PhC**H**$_2$CH(Ar)CHO), 2.12 (s, 3H, ArC**H**$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.1, 139.3, 137.6, 134.6, 131.2, 129.3, 128.6, 128.5, 127.8, 126.9, 126.5, 57.2, 36.5, 19.9. IR (NaCl, thin film, neat) 3062 (m), 3026 (m), 2948 (m), 2927 (m), 2860 (w), 2816 (m), 2719 (m), 1722 (s), 1602 (m), 1495 (s), 1453 (s), 1383 (w), 1146 (m), 1078 (w), 1048 (w), 1030 (m), 862 (w), 757 (s), 726 (s), 670 (s).

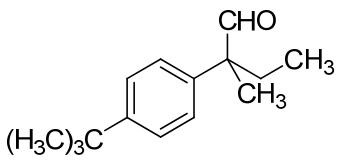


3-Phenyl-2-(2-methoxyphenyl)propionaldehyde (Table 8, entry 12). Following the general procedure for α-arylation of linear aldehydes, APC (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), hydrocinnamaldehyde (0.134 g, 1.00 mmol), 1-bromo-2-methoxybenzene (0.187 g, 1.00 mmol) were combined in 1,4-dioxane (4.0 mL) and stirred at 80 ^{o}C for 12 h. Following the general procedure for work up, the filtrate was purified using flash-column chromatography (silica gel, gradient eluction: 2.5%, 5%, 7.5%, 10% diethyl ether in hexanes) to give the title compound as a clear, colorless oil (0.182 g, 76%). R_f = 0.23 (12% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (s, 1H, C**H**O), 7.30-7.13 (m, 4H, Ar**H**), 7.07-7.05 (m, 2H, Ar**H**), 6.97-6.88 (m, 3H, Ar**H**), 4.06 (dd, *J* = 6.4, 8.0 Hz, 1H, C**H**CHO), 3.76 (s, 3H, ArOC**H**$_3$), 3.50 (dd, *J* = 6.4, 13.8 Hz, 1H, PhC**H**$_2$CH(Ar)CHO), 2.95 (dd, *J* = 8.0, 13.8 Hz, 1H, PhC**H**$_2$CH(Ar)CHO). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.8, 157.2, 139.5, 130.3, 129.1, 128.9, 128.1, 126.0, 124.9, 120.8, 110.8, 55.4, 55.3, 34.6. IR (NaCl, thin film, neat) 3062 (m), 3027 (m), 3003 (m), 2937 (m), 2836 (m), 2724 (m), 1724 (s), 1600 (s), 1586 (s), 1494 (s), 1464 (s), 1454 (s), 1438 (s), 1387 (w), 1324 (m), 1290 (m), 1247 (s), 1179

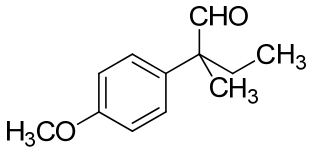
(m), 1163 (m), 1119 (m), 1080 (m), 1051 (s), 1029 (s), 864 (w), 754 (s), 700 (s). Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 80.11; H, 6.90.



3-Phenyl-2-(3-methoxyphenyl)propionaldehyde (Table 8**, entry 13).** Following the general procedure for α-arylation of linear aldehydes, APC (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), hydrocinnamaldehyde (0.134 g, 1.00 mmol), 1-bromo-3-methoxybenzene (0.187 g, 1.00 mmol) were combined in 1,4-dioxane (4.0 mL) and stirred in a 5-dram scintillation vial at 80 °C for 12 h. The crude product was purified using flash-column chromatography (silica gel, gradient elution: 2.5%, 5%, 7.5%, 10% diethyl ether in hexanes) to give the title compound as a clear, colorless oil (0.182 g, 61%). R_f = 0.23 (12% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (d, *J* = 1.5 Hz, 1H, C**H**O), 7.29-7.07 (m, 6H, Ar**H**), 6.83 (dd, *J* = 2.5, 8.3 Hz, 1H, Ar**H**), 6.74 (d, *J* = 7.6 Hz, 1H, Ar**H**), 6.67 (m, 1H, Ar**H**), 3.81 (m, 1H, C**H**CHO), 3.77 (s, 3H, ArOC**H**$_3$), 3.46 (dd, *J* = 6.8, 14.0 Hz, 1H, PhC**H**$_2$CH(Ar)CHO), 2.97 (dd, *J* = 7.8, 14.0 Hz, 1H, PhC**H**$_2$CH(Ar)CHO). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.7, 159.9, 138.7, 137.1, 129.0, 130.0, 128.3, 126.3, 121.2, 114.6, 113.0, 60.9, 55.2, 35.9. IR (NaCl, thin film, neat) 3085 (w), 3061 (m), 3027 (m), 3003 (w), 2938 (m), 2835 (m), 2719 (m), 1728 (s), 1683 (m), 1600 (s), 1584 (s), 1495 (s), 1464 (s), 1435 (s), 1387 (w), 1320 (m), 1287 (s), 1260 (s), 1151 (s), 1076 (w), 1048 (s), 873 (m), 781 (m), 752 (m), 600 (s).

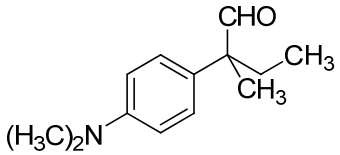


2-Methyl-2-(4-tert-butylphenyl)butyraldehyde (Table 9, entry 1). Following the general procedure for α-arylation of branched aldehydes, APC (0.0018 g, 0.005 mmol), Q-phos (0.0071 g, 0.010 mmol), cesium carbonate (0.652 g, 2.00 mmol), 2-methylbutyraldehyde (0.103 g, 1.20 mmol), 1-bromo-4-*tert*-butylbenzene (0.213 g, 1.00 mmol) were combined in THF (2.0 mL) and stirred in at at 80 ^{o}C for 13 h. The crude product was purified using flash-column chromatography (silica gel, 2% diethyl ether-hexanes) to give the title compound as a clear, colorless oil (0.200 g, 91%). R_f = 0.26 (2% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (s, 1H, C**H**O), 7.39 (d, *J* = 8.4 Hz, 2H, Ar**H**), 7.18 (d, *J* = 8.4 Hz, 2H, Ar**H**), 2.02-1.86 (m, 2H, $CH_3C\mathbf{H}_2$), 1.42 (s, 3H, $CH_3CH_2C(C\mathbf{H}_3)(Ar)(CHO)$), 1.32 (s, 9H, $ArC(C\mathbf{H}_3)_3$), 0.81 (t, *J* = 7.6 Hz, 3H, $C\mathbf{H}_3CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.91, 149.96, 136.75, 126.84, 125.67, 53.85, 34.40, 31.26, 28.36, 18.19, 8.45. IR (NaCl, thin film, neat) 3031 (w), 2964 (s), 2871 (m), 2802 (w), 2706 (w), 1725 (s), 1509 (m), 1462 (m), 1394 (m), 1363 (m), 1271 (m), 1119 (m), 1015 (m), 907 (w), 827 (m). Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.86; H, 10.45.

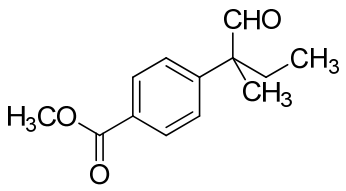


2-Methyl-2-(4-methoxyphenyl)butyraldehyde (Table 9, entry 2). Following the general procedure for α-arylation of branched aldehydes, APC (0.0018 g, 0.0050 mmol), Q-phos (0.0071 g, 0.010 mmol), cesium carbonate (0.652 g, 2.00 mmol), 2-methylbutyraldehyde (0.103 g, 1.20 mmol), 1-bromo-4-methoxybutylbenzene (0.187 g, 1.00 mmol) were combined in THF (2.0 mL) and stirred at 80 ^{o}C for 13 h. The crude product was purified using flash-column chromatography (silica gel, 4% diethyl ether-hexanes) to give the title compound as a clear, colorless oil (0.156 g, 81%). R_f = 0.21 (4% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.45 (s,

1H, C**H**O), 7.16 (d, *J* = 8.8 Hz, 2H, Ar**H**), 6.91 (d, *J* = 8.8 Hz, 2H, Ar**H**), 3.79 (s, 3H, OC**H**$_3$), 2.02-1.82 (m, 2H, $CH_3C\mathbf{H}_2$), 1.40 (s, 3H, $CH_3CH_2C(C\mathbf{H}_3)$(Ar)CHO), 0.78 (t, *J* = 7.6 Hz, 3H, $C\mathbf{H}_3CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.9, 158.8, 131.8, 128.6, 114.4, 55.5, 53.8, 28.7, 18.5, 8.6. IR (NaCl, thin film, neat) 2968 (s), 2936 (s), 2879 (m), 2836 (m), 2707 (m), 2706 (m), 1718 (s), 1609 (s), 1580 (m), 1513 (s), 1458 (s), 1443 (m), 1388 (w), 1370 (w), 1299 (m), 1253 (s), 1116 (w), 1035 (s), 1010 (w), 907 (m), 828 (s), 791 (m), 776 (m). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.85; H, 8.25.

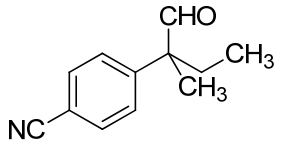


2-Methyl-2-(4-*N*,*N*-dimethylaminophenyl)butyraldehyde (Table 9, entry 3). Following the general procedure for α-arylation of branched aldehydes, APC (0.0018 g, 0.0050 mmol), Q-phos (0.0071 g, 0.010 mmol), cesium carbonate (0.652 g, 2.00 mmol), 2-methylbutyraldehyde (0.103 g, 1.20 mmol), 4-bromo-*N*,*N*-dimethylaniline (0.200 g, 1.00 mmol) were combined in THF (2.0 mL) and stirred at 80 ^{o}C for 13 h. The crude product was purified using flash-column chromatography (silica gel, gradient elution: 4%, 5%, 6%, then 8% ether-hexanes) to give the title compound as a clear, colorless oil (0.176 g, 86%). R_f = 0.26 (8% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.44 (s, 1H, C**H**O), 7.14 (d, *J* = 8.4 Hz, 2H, Ar**H**), 6.76 (d, *J* = 8.8 Hz, 2H, Ar**H**), 2.96 (s, 6H, $N(C\mathbf{H}_3)_2$), 1.97-1.84 (m, 2H, $CH_3C\mathbf{H}_2$), 1.41 (s, 3H, $CH_3CH_2C(C\mathbf{H}_3)$(Ar)CHO), 0.82 (t, *J* = 7.6 Hz, 3H, $C\mathbf{H}_3CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.7, 149.4, 127.9, 126.7, 112.6, 53.2, 40.4, 28.1, 17.9, 8.3. Anal. Calcd for $C_{13}H_{19}NO$: C, 76.06; H, 9.33; N, 6.82. Found: C, 75.88; H, 9.56; N, 6.80.



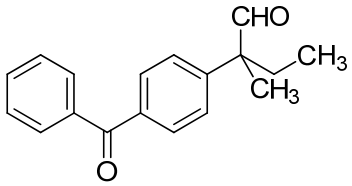
2-Methyl-2-(4-methylbenzoate)butyraldehyde (Table 9, entry 4). Following the general procedure for α-arylation of branched aldehydes, APC (0.0018 g, 0.0050 mmol), Q-phos (0.0071 g, 0.010 mmol), cesium carbonate (0.652 g, 2.00 mmol), 2-methylbutyraldehyde (0.103 g, 1.20 mmol), methyl 4-bromobenzoate (0.200 g, 1.00 mmol) were combined in THF (2.0 mL) and stirred at 80 °C for 13 h. The crude product was purified using flash-column chromatography (silica gel, 8% diethyl ether-hexanes) to give the title compound as a clear, colorless oil (0.179 g, 81%). R_f = 0.21 (8% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (s, 1H, C**H**O), 8.00 (d, *J* = 8.8 Hz, 2H, Ar**H**), 7.30 (d, *J* = 8.8 Hz, 2H, Ar**H**), 3.88 (s, 3H, $CO_2C\mathbf{H}_3$), 2.02-1.82 (m, 2H, $CH_3C\mathbf{H}_2$), 1.42 (s, 3H, $CH_3CH_2C(C\mathbf{H}_3)(Ar)(CHO)$), 0.75 (t, *J* = 7.2 Hz, 3H, $C\mathbf{H}_3CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.9, 166.6, 145.1, 129.8, 128.9, 127.1, 54.4, 52.0, 28.6, 18.1, 8.2. IR (NaCl, thin film, neat) 2971 (s), 2880 (m), 2843 (m), 2809 (m), 2710 (w), 1736 (s), 1731 (s), 1716 (s), 1609 (s), 1572 (w), 1508 (w), 1460 (m), 1435 (s), 1410 (m), 1383 (w), 1372 (w), 1316 (s), 1278 (br), 1191 (s), 1117 (s), 1018 (s), 966 (w), 909 (w), 856 (w), 822 (w), 771 (s), 707 (s). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.58; H, 7.29.

2-Methyl-2-(4-methylbenzoate)butyraldehyde (Table 9, entry 5). Following the general procedure for α-arylation of branched aldehydes, APC (0.0037 g, 0.010 mmol), Q-phos (0.0142 g, 0.0200 mmol), cesium carbonate (0.652 g, 2.00 mmol), 2-methylbutyraldehyde (0.103 g, 1.20 mmol), methyl 4-chlorobenzoate (0.171 g, 1.00 mmol) were combined in THF (4.0 mL) and stirred in a 5-dram scintillation vial at 90 °C for 15 h. The crude product was purified to give the title compound as a clear, colorless oil (0.170 g, 77%).

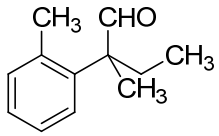


2-Methyl-2-(4-cyanophenyl)butyraldehyde (Table 9, entry 6). Following the general procedure for α-arylation of branched aldehydes, APC (0.0018 g, 0.0050 mmol), Q-phos (0.0071 g, 0.010 mmol), cesium carbonate (0.652 g, 2.00 mmol), 2-methylbutyraldehyde (0.103 g, 1.20 mmol), 4-bromobenzonitrile (0.182 g, 1.00 mmol) were combined in THF (2.0 mL) and stirred at 80 ^{o}C for 13 h. The crude product was purified using flash-column chromatography (silica gel, 16% diethyl ether-hexanes) to give the title compound as a clear, colorless oil (0.150 g, 80%). R_f = 0.20 (8% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.51 (s, 1H, C**H**O), 7.65 (d, *J* = 8.4 Hz, 2H, Ar**H**), 7.36 (d, *J* = 7.7 Hz, 2H, Ar**H**), 1.99-1.85 (m, 2H, $CH_3C\mathbf{H}_2$), 1.45 (s, 3H, $CH_3CH_2C(C\mathbf{H}_3)(Ar)(CHO)$), 0.77 (t, *J* = 7.2 Hz, 3H, $C\mathbf{H}_3CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.4, 145.5, 132.4, 128.0, 118.5, 111.1, 54.6, 28.7, 18.2, 8.2. IR (NaCl, thin film, neat) 2972 (s), 2939 (m), 2881 (m), 2813 (w), 2714 (w), 2229 (s), 1725 (s), 1607 (s), 1505 (m), 1460 (m), 1403 (m), 1018 (m), 1005 (w), 908 (m), 833 (m), 785 (w), 734 (w). Anal. Calcd for $C_{12}H_{13}NO$: C, 76.98; H, 7.00. Found: C, 76.90; H, 7.60.

2-Methyl-2-(4-cyanophenyl)butyraldehyde (Table 9, entry 7). Following the general procedure for α-arylation of branched aldehydes, APC (0.0037 g, 0.010 mmol), Q-phos (0.0142 g, 0.0200 mmol), cesium carbonate (0.652 g, 2.00 mmol), 2-methylbutyraldehyde (0.103 g, 1.20 mmol), 4-chlorobenzonitrile (0.138 g, 1.00 mmol) were combined in THF (4.0 mL) and stirred at 90 ^{o}C for 15 h. The crude product was purified to give the title compound as a clear, colorless oil (0.126 g, 67%).

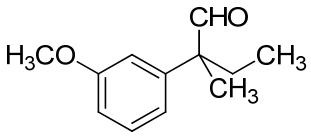


2-Methyl-2-(4-benzoylphenyl)butyraldehyde (Table 9, entry 8). Following the general procedure for α-arylation of branched aldehydes, APC (0.0018 g, 0.0050 mmol), Q-phos (0.0071 g, 0.010 mmol), cesium carbonate (0.652 g, 2.00 mmol), 2-methylbutyraldehyde (0.103 g, 1.20 mmol), 4-bromobenzophenone (0.261 g, 1.00 mmol) were combined in THF (2.0 mL) and stirred in a 1-dram scintillation vial at 80 °C for 12 h. The crude product was purified using flash-column chromatography (silica gel, 16% diethyl ether-hexanes) to give the title compound as a clear, colorless oil (0.194 g, 73%). R_f = 0.23 (16% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.56 (s, 1H, C**H**O), 7.84-7.79 (m, 4H, Ar**H**), 7.59 (m, Ar**H**), 7.48 (m, 2H, Ar**H**), 7.38 (m, 2H, Ar**H**), 1.99 (m, 2H, $CH_3C\mathbf{H}_2$), 1.48 (s, 3H, $CH_3CH_2C(C\mathbf{H}_3)(Ar)(CHO)$), 0.82 (t, J = 7.5 Hz, 3H, $C\mathbf{H}_3CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.0, 196.1, 144.7, 137.3, 136.3, 132.5, 130.4, 130.0, 128.3, 127.1, 54.6, 28.7, 18.3, 8.3. IR (NaCl, thin film, neat) 3059 (w), 2970 (s), 2879 (m), 2808 (w), 2710 (w), 1724 (s), 1659 (s), 1605 (s), 1579 (s), 1565 (w), 1447 (m), 1406 (m), 1317 (s), 1278 (s), 1196 (w), 1179 (m), 1152 (w), 1090 (w), 1027 (w), 1017 (w), 1001 (w), 939 (s), 926 (s), 849 (m), 794 (m), 751 (m), 702 (s), 647 (m). Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 80.89; H, 6.49.



2-Methyl-2-(2-methylphenyl)butyraldehyde (Table 9, entry 9). Following the general procedure for α-arylation of branched aldehydes, APC (0.0018 g, 0.0050 mmol), Q-phos (0.0071 g, 0.010 mmol), cesium carbonate (0.652 g, 2.00 mmol), 2-methylbutyraldehyde (0.103 g, 1.20

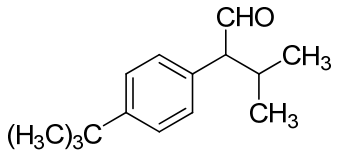
mmol), 2-bromotoluene (0.171 g, 1.00 mmol) were combined in THF (2.0 mL) and stirred at 80 ^{o}C for 12 h. The crude product was purified using flash-column chromatography (silica gel, 2% diethyl ether-hexanes) to give the title compound as a clear, colorless oil (0.125 g, 71%). R_f = 0.21 (2% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H, C**H**O), 7.34-7.16 (m, 4H, Ar**H**), 2.23 (s, 3H, ArC**H**$_3$), 2.10-1.91 (m, 2H, CH_3C**H**$_2$), 1.41 (s, 3H, CH_3CH_2C(C**H**$_3$)(Ar)CHO), 0.76 (t, J = 7.6 Hz, 3H, C**H**$_3CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.4, 138.4, 136.6, 132.2, 127.6, 127.4, 126.1, 54.7, 26.8, 21.1, 19.7, 8.3. IR (NaCl, thin film, neat) 3060 (w), 3017 (w), 2969 (s), 2938 (m), 2879 (m), 2798 (m), 2701 (m), 1724 (s), 1488 (m), 1459 (m), 1386 (m), 905 (m), 758 (s), 726 (s). Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.58; H, 9.43.



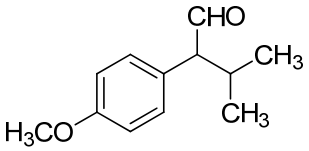
2-Methyl-2-(3-methoxyphenyl)butyraldehyde (Table 9, entry 10). Following the general procedure for α-arylation of branched aldehydes, APC (0.0018 g, 0.0050 mmol), Q-phos (0.0071 g, 0.010 mmol), cesium carbonate (0.652 g, 2.00 mmol), 2-methylbutyraldehyde (0.103 g, 1.20 mmol), 3-bromoanisole (0.187 g, 1.00 mmol) were combined in THF (2.0 mL) and stirred at 80 ^{o}C for 12 h. The crude product was purified using flash-column chromatography (silica gel, 2% diethyl ether-hexanes) to give the title compound as a clear, colorless oil (0.160 g, 83%). R_f = 0.22 (2% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.49 (s, 1H, C**H**O), 7.29 (t, J = 8.00 Hz, 1H, Ar**H**), 6.84-6.78 (m, 3H, Ar**H**), 3.80 (s, 3H, OC**H**$_3$), 2.02-1.83 (m, 2H, CH_3C**H**$_2$), 1.41 (s, 3H, CH_3CH_2C(C**H**$_3$)(Ar)CHO), 0.79 (t, J = 7.6 Hz, 3H, C**H**$_3CH_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.5, 159.8, 141.5, 129.7, 119.5, 113.5, 111.8, 55.1, 54.2, 28.4, 18.1, 8.3. IR (NaCl, thin film, neat) 2969 (s), 2938 (s), 2879 (m), 2835 (m), 2805 (w), 2707 (w), 1725 (s)

1600 (s), 1582 (s), 1492 (s), 1463 (s), 1433 (s), 1388 (w), 1371 (w), 1317 (m), 1292 (s), 1256 (s), 1206 (m), 1174 (m), 1045 (s), 1004 (w), 911 (m), 778 (s), 701 (s). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.21; H, 8.61.

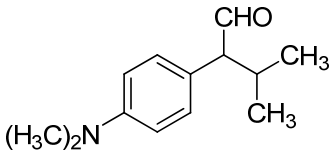
2-Methyl-2-(3-methoxyphenyl)butyraldehyde (Table 9**, entry 11).** Following the general procedure for α-arylation of branched aldehydes, APC (0.0037 g, 0.010 mmol), Q-phos (0.0142 g, 0.0200 mmol), cesium carbonate (0.652 g, 2.00 mmol), 2-methylbutyraldehyde (0.103 g, 1.20 mmol), 3-chloroanisole (0.138 g, 1.00 mmol) were combined in THF (4.0 mL) and stirred in a 5-dram scintillation vial at 90 °C for 15 h. The crude product was purified to give the title compound as a clear, colorless oil (0.146 g, 76%).



3-Methyl-2-(4-*tert*-butylphenyl)butyraldehyde (Table 9, entry 12). Following the general procedure for α-arylation of branched aldehydes, APC (0.0018 g, 0.0050 mmol), Q-phos (0.0071 g, 0.010 mmol), cesium carbonate (0.652 g, 2.00 mmol), 3-methylbutyraldehyde (0.103 g, 1.20 mmol), 1-bromo-4-*t*-butylbenzene (0.213 g, 1.00 mmol) were combined in THF (2.0 mL) and stirred at 80 °C for 12 h. The crude product was purified using flash-column chromatography (silica gel, 4% diethyl ether-hexanes) to give the title compound as a clear, colorless oil (0.174 g, 80%). R_f = 0.25 (2% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (d, *J* = 3.2 Hz, 1H, C**H**O), 7.37 (d, *J* = 8.4 Hz, 2H, Ar**H**), 7.11 (d, *J* = 8.4 Hz, 2H, Ar**H**), 3.15 (dd, *J* = 3.2 Hz, 9.4 Hz, 1H, C**H**CHO), 2.45-2.35 (m, 1H, $(CH_3)_2C\mathbf{H}$), 1.31 (s, 9H, $ArC(C\mathbf{H}_3)_3$), 1.03 (d, *J* = 6.4 Hz, 3H, $(C\mathbf{H}_3)_2CHCH(Ar)CHO$), 0.77 (d, *J* = 6.8 Hz, 3H, $(C\mathbf{H}_3)_2CHCH(Ar)CHO$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.3, 150.3, 132.2, 128.9, 125.8, 66.3, 34.5, 31.3, 28.6, 21.2, 20.1. Anal. Calcd for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.19; H, 10.01.

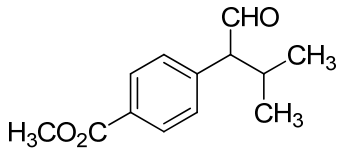


2-(4-Methoxyphenyl)-3-methylbutyraldehyde (Table 9, entry 13). Following the general procedure for α-arylation of branched aldehydes, APC (0.0018 g, 0.005 mmol), Q-phos (0.0071 g, 0.010 mmol), cesium carbonate (0.652 g, 2.00 mmol), 3-methylbutyraldehyde (0.103 g, 1.20 mmol), 1-bromo-4-methoxybenzene (0.187 g, 1.00 mmol) were combined in THF (2.0 mL) and stirred at 80 ^{o}C for 12 h. The crude product was purified using flash-column chromatography (silica gel, 8% diethyl ether-hexanes) to give the title compound as a clear, colorless oil (0.140 g, 73%). R_f = 0.28 (8% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.65 (d, *J* = 3.2 Hz, 1H, C**H**O), 7.09 (d, *J* = 8.8 Hz, 2H, Ar**H**), 6.89 (d, *J* = 8.8 Hz, 2H, Ar**H**), 3.79 (s, 3H, OC**H**$_3$), 3.12 (dd, *J* = 9.6, 3.2 Hz, 1H, C**H**CHO), 2.37 (m, 1H, $(CH_3)_2$C**H**CH(Ar)CHO), 1.02 (d, *J* = 6.4 Hz, 3H, (C**H**$_3$)$_2$CH), 0.75 (d, *J* = 6.4 Hz, 3H, (C**H**$_3$)$_2$CH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 158.9, 130.2, 127.2, 114.2, 65.9, 55.1, 28.5, 21.1, 19.9. IR (NaCl, thin film, neat) 2959 (s), 2909 (m), 2871 (m), 2836 (m), 2709 (w), 1723 (s), 1610 (s), 1582 (w), 1511 (s), 1466 (m), 1442 (w), 1387 (w), 1368 (w), 1319 (w), 1303 (m), 1251 (s), 1180 (s), 1140 (w), 1121 (w), 1035 (s), 829 (m). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.67; H, 8.49.



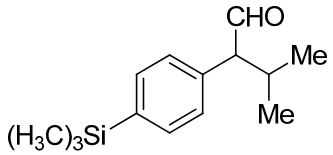
2-(4-*N*,*N*'-Dimethylaminophenyl)-3-methylbutyraldehyde (Table 9, entry 14). Following the general procedure for α-arylation of branched aldehydes, APC (0.0018 g, 0.0050 mmol), Q-phos (0.0071 g, 0.010 mmol), cesium carbonate (0.652 g, 2.00 mmol), 3-methylbutyraldehyde (0.103 g, 1.20 mmol), 4-bromo-*N*,*N*-dimethylaniline (0.200 g, 1.00 mmol) were combined in THF (2.0

mL) and stirred at 80 °C for 12 h. The crude product was purified using flash-column chromatography (silica gel, 10% diethyl ether-hexanes) to give the title compound as a clear, colorless oil (0.138 g, 67%). R_f = 0.26 (10% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (d, *J* = 3.2 Hz, 1H, C**H**O), 7.04 (d, *J* = 8.8 Hz, 2H, Ar**H**), 6.72 (d, *J* = 8.8 Hz, 2H, Ar**H**), 3.07 (dd, *J* = 9.4, 3.2 Hz, 1H, C**H**CHO), 2.95 (s, 6H, N(C**H**$_3$)$_2$), 2.36 (m, 1H, $(CH_3)_2$C**H**CH(Ar)CHO), 1.02 (d, *J* = 6.4 Hz, 3H, (C**H**$_3$)$_2$CH), 0.78 (d, *J* = 6.4 Hz, 3H, (C**H**$_3$)$_2$CH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.2, 149.8, 130.0, 122.5, 112.8, 65.9, 40.5, 28.3, 21.2, 20.0. IR (NaCl, thin film, neat) 3075 (w), 2957 (s), 2928 (s), 2908 (s), 2869 (s), 2805 (s), 2707 (m), 1721 (s), 1613 (s), 1564 (w), 1519 (s), 1481 (m), 1467 (m), 1445 (m), 1387 (m), 1352 (s), 1223 (m), 1205 (m), 1189 (w), 1165 (m), 1142 (m), 1128 (m), 1061 (m), 947 (m), 815 (s). Anal. Calcd for $C_{13}H_{19}NO$: C, 76.06; H, 9.33; N, 6.82. Found: C, 76.21; H, 9.51; N, 6.84.



Methyl 4-(2-oxy-1-isopropylethyl)benzoate (Table 9, entry 15). Following the general procedure for α-arylation of branched aldehydes, APC (0.0018 g, 0.0050 mmol), Q-phos (0.0071 g, 0.010 mmol), cesium carbonate (0.652 g, 2.00 mmol), 3-methylbutyraldehyde (0.103 g, 1.20 mmol), methyl 4-bromobenzoate (0.215 g, 1.00 mmol) were combined in THF (2.0 mL) and stirred at 80 °C for 12 h. The crude product was purified using flash-column chromatography (silica gel, 12% diethyl ether-hexanes) to give the title compound as a clear, colorless oil (0.148 g, 67%). R_f = 0.21 (10% diethyl ether-hexanes; UV, DNP). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.71 (d, *J* = 3.2 Hz, 1H, C**H**O), 8.02 (d, *J* = 8.1 Hz, 2H, Ar**H**), 7.26 (d, *J* = 8.1 Hz, 2H, Ar**H**), 3.90 (s, 3H, $ArCO_2C$**H**$_3$), 3.26 (dd, *J* = 3.2, 9.5 Hz, 1H, C**H**CHO), 2.44 (m, 1H, $(CH_3)_2$C**H**CH(Ar)CHO), 1.04 (d, *J* = 6.6 Hz, 3H, (C**H**$_3$)$_2$CH), 0.75 (d, *J* = 6.7 Hz, 3H, (C**H**$_3$)$_2$CH). ^{13}C NMR (100 MHz,

$CDCl_3$) δ 200.4, 166.7, 140.7, 130.0, 129.3 (overlap of two peaks), 66.6, 52.1, 29.1, 21.1, 20.0. IR (NaCl, thin film, neat) 2960 (s), 2873 (m), 2843 (m), 2715 (w), 1722 (s), 1609 (s), 1574 (w), 1467 (m), 1436 (s), 1418 (m), 1389 (w), 1370 (w), 1282 (br), 1182 (s), 1140 (w), 1113 (s), 1045 (w), 1020 (m), 966 (w), 857 (w), 770 (s), 708 (s). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.96; H, 7.59.



2-(4-Trimethylsilylphenyl)-3-methylbutyraldehyde (Table 9, entry 16). Following the general procedure for α-arylation of linear aldehydes, APC (0.0037 g, 0.010 mmol), DPPF (0.0222 g, 0.0400 mmol), cesium carbonate (0.652 g, 2.00 mmol), isovaleraldehyde (0.103 g, 1.20 mmol), 1-bromo-4-(trimethylsilyl)benzene (0.229 g, 1.00 mmol) were combined in 1,4-dioxane (4.0 mL) and stirred at 80 ^oC for 12 h. The crude product was purified using flash-column chromatography (silica gel, 2% diethyl ether in hexanes) to give the title compound as a clear, colorless oil (0.199 g, 85%). R_f = 0.28 (2% diethyl ether-hexanes; UV, DNP). ^1H NMR (400 MHz, $CDCl_3$) δ 9.69 (d, *J* = 3.3 Hz, 2H, Ar**H**), 7.51 (d, *J* = 8.1 Hz, 2H, Ar**H**), 7.18 (d, *J* = 7.9 Hz, 2H, Ar**H**), 3.17 (dd, *J* = 3.3 Hz, 9.5 Hz, 1H, C**H**CHO), 2.43 (m, 1H, $(CH_3)_2C$**H**), 1.04 (d, *J* = 6.6 Hz, 3H, $(C\mathbf{H}_3)_2CH$), 0.78 (d, *J* = 6.7 Hz, 3H, $(C\mathbf{H}_3)_2CH$), 0.27 (s, 9H, $ArSi(C\mathbf{H}_3)_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1, 139.6, 135.9, 133.9, 128.7, 66.8, 28.7, 21.2, 20.1, -1.2. Anal. Calcd. for $C_{14}H_{22}OSi$: C, 71.73; H, 9.46. Found: C, 71.74; H, 9.74.

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Chapter 3. Synthesis, Characterization and Reactivity of Arylpalladium Enolate Complexes of Aldehydes

3.1. Introduction

Transition-metal enolate complexes play an important role in fundamental organometallic reactions.[1] Late transition-metal enolate complexes have been proposed as intermediates in catalytic transformations,[2-6] and studies on the structure and reactivity of such complexes have revealed important information for the development of new catalysts and reaction conditions.[3,7-10] During the past decade, Hartwig and coworkers have isolated, characterized and studied palladium and nickel enolate complexes that are intermediates in catalytic α-arylation of carbonyl compounds.[2,11,12] These complexes undergo reductive elimination to form α-aryl carbonyl products and regenerate active catalysts. Studies of the structure and reactivity of these complexes have revealed factors that influence the rate and selectivity of the catalytic reactions.[3,7,8,13]

In chapter 2, we described an α-arylation of aldehydes that is catalyzed by complexes containing two different classes of phosphines. Reactions of electron-neutral aryl bromides with linear aldehydes containing chain lengths that are longer than 3 carbons occurred in good yield in the presence of palladium complexes of DPPF. Reactions of branched aldehydes with aryl bromides and chlorides occurred in good yield in the presence of complexes of Q-Phos.[14] Reactions of branched aldehydes encompass a broader scope of aryl halide than those of linear aldehydes. In 2007, Martin and Buchwald reported that complexes of BINAP catalyze reactions of linear aldehydes with aryl bromides and complexes of S-Phos catalyze reactions of branched aldehydes with aryl bromides and chlorides.[15,16] In both our and Buchwald's examples, reactions of linear aldehydes were catalyzed by complexes of bisphosphines, and reactions of branched

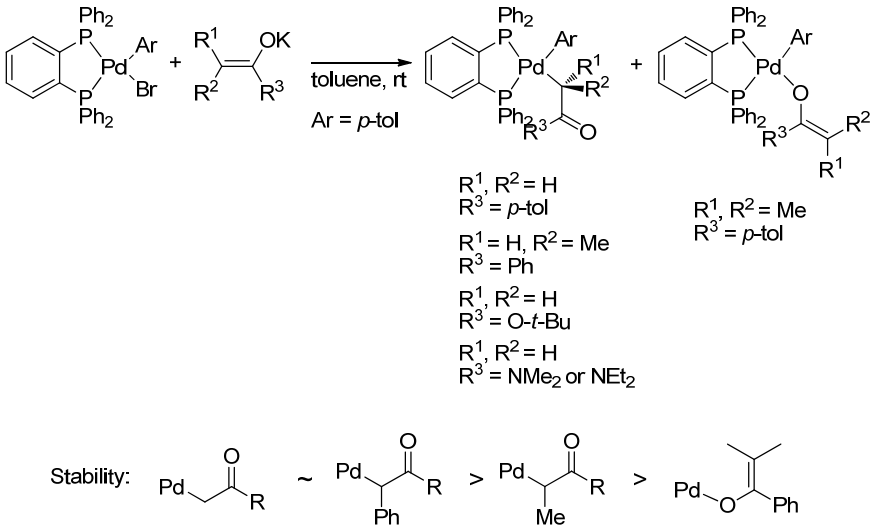
aldehydes were catalyzed by complexes of monophosphines. We observed that reactions of linear aldehydes with electron-rich and electron-poor aryl bromides occurred in lower yield than those of linear aldehydes with electron-neutral aryl bromides. Although in 2008 Martin and Buchwald reported that complexes of Xantphos couple electron-rich aryl bromides with linear aldehydes in higher yield than complexes of BINAP or DPPF,[16] the yields of coupled products formed from these substrates are still lower than 70%.

We sought to understand the factors that influence the rates and yields in palladium-catatalyzed α-arylation of aldehydes. From previous studies of arylpalladium enolate complexes of ketones, esters and amides, we hypothesized that the key bond-forming step of the catalytic α-arylation of aldehydes is the reductive elimination from an arylpalladium enolate of aldehyde. However, this reaction is not understood because no isolated arylmetal enolate of aldehyde is known.

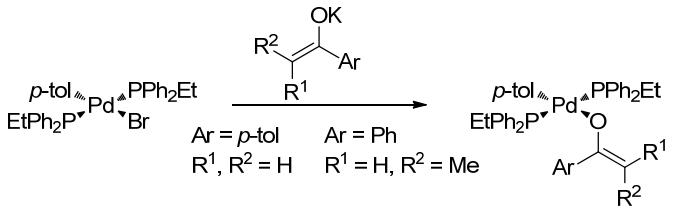
3.2. Background

Although arylpalladium enolate complexes of aldehydes unknown, the analogous complexes of ketones, esters and amides have been isolated and characterized. The effects of steric and electronic properties of ancillary ligands on the structure and reactivity of arylpalladium enolate complexes of ketones, esters and amides have been evaluated. In 2001, Culkin and Hartwig reported the first examples of isolated arylpalladium enolate complexes of ketones, amides and esters.[3] Ligand-substitution reactions of arylpalladium bromide complexes of 1,2-bis(diphenylphosphino)benzene (DPPBz) (Scheme 9) or ethyldiphenylphosphine ($EtPh_2P$) (Scheme 10) with potassium enolates of ketones, esters and amides afforded the corresponding palladium enolates in high yields.

The enolate connectivity (*O*- vs *C*-bound form), stability and rates of reductive elimination are influenced by the steric and electronic properties of the enolate carbon bound to palladium. In general, enolates of monocarbonyl compounds bound to transition-metal centers can adopt *C*-bound,[17-25] *O*-bound[26-29] or η^3-oxaallyl binding modes.[30-33] DPPBz-ligated arylpalladium enolate complexes of ketones that have α-methyl and methylene carbons contain a *C*-bound enolate, except for that from benzyl phenyl ketone. Complexes containing enolates of ketones that have α-methine carbons are *O*-bound enolates. The rates of reductive elimination from arylpalladium complexes containing enolates of ketones decrease with increasing steric bulk at the α carbon (Scheme 9). The influence of electronic properties of the enolates on the rates of reductive elimination is smaller than that of steric properties of the enolates. Differences in rates between reactions of complexes of ketones, esters and amides were not greater than a factor of 3. Thus, the rates of reductive elimination have no correlation with the pK_a values of the corresponding carbonyl compounds.[3]



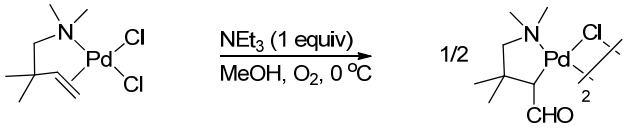
Scheme 9. Synthesis of DPPBz-ligated Arylpalladium Enolate Complexes of Ketones, Esters and Amides



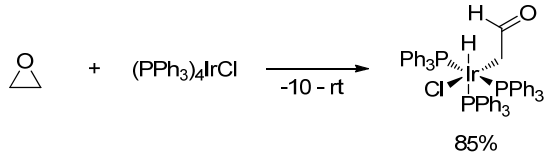
Scheme 10. Synthesis of $EtPh_2P$-ligated Arylpalladium Enolate Complexes of Ketones

There are far fewer examples of transition-metal enolate complexes of aldehydes than of ketones, esters and amides. All early transition-metal enolate complexes of aldehydes are *O*-bound enolates because early transition metals are hard and can participate in dπ-pπ bonding. Aldehyde enolate complexes of scandium,[34], zirconium,[35,36] thallium,[37] yttrium,[38,39] and osmium have been isolated and characterized,[40,41] but only six examples of discrete late-transition metal aldehyde-enolate complexes have been reported. In 1977, Alyea *et al* reported a Wacker oxidation of an amino-alkene palladium(II) complex to form a *C*-bound palladium enolate shown in Scheme 11.[42] Milstein and Calabrese reported an iridium(III) enolate of acetaldehyde that is formed from the oxidative addition of ethylene oxide to tetrakis(triphenylphosphine)iridium chloride (Scheme 12).[43] In the early 1980s, Sugimoto and coworkers synthesized porphyrinatocobalt enolate complexes of acetaldehyde from the hydrolysis of the acetal of the product that is generated from the reaction of the perchlorate salt of (tpp)Co(III) with ethylvinylether (Scheme 13).[44,45] Wu and Bergman reported a hydridorhodium enolate complex of acetaldehyde formed by oxidative addition of the C-H bond of ethylene oxide to $Cp^*(PMe_3)RhH_2$, followed by rearrangement. A stable complex was then formed by reaction of the hydridorhodium enolate complex with methyl iodide (Scheme 14).[46] In 1993, Jennings and coworkers isolated and characterized a strained platinum(II) enolate of an aldehyde as shown in Scheme 15.[47] Finally, Montgomery and coworkers showed that a nickel(0) species undergoes

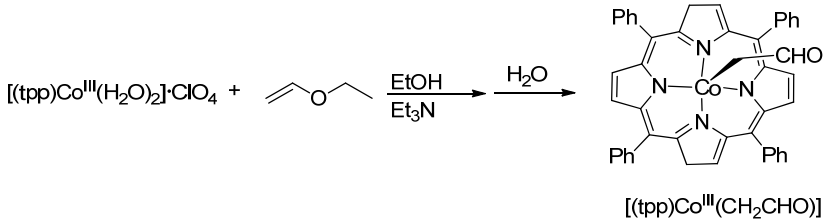
oxidative cyclization of an enyne to form an *O*-bound nickel enolate of aldehyde (Scheme 16).[13] These late transition-metal enolate complexes of aldehydes either have aldehydes that are chelating ligands, or lacks a metal-bound carbon group that can couple with the aldehyde enolate through a reductive elimination process.



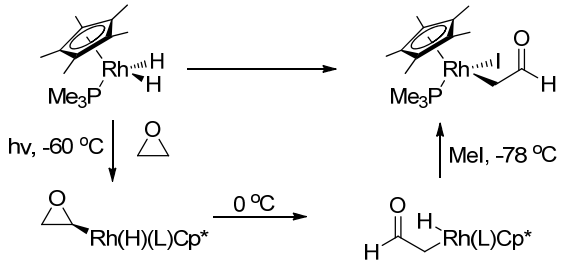
Scheme 11. Wacker Oxidation of Amino-alkenylpalladium Dichloride



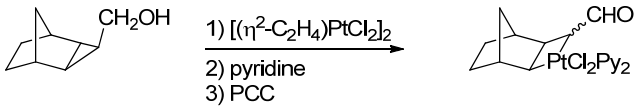
Scheme 12. Iridium(III) Enolate of Acetaldehyde



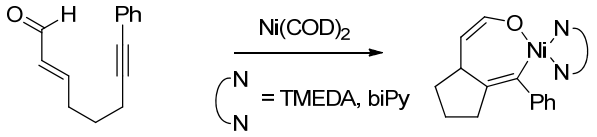
Scheme 13. (Tetraphenylporphyrinato)Co^{III} Enolate of Acetaldehyde



Scheme 14. Rhodium Enolate of Acetaldehyde



Scheme 15. Platinum(II) Enolate



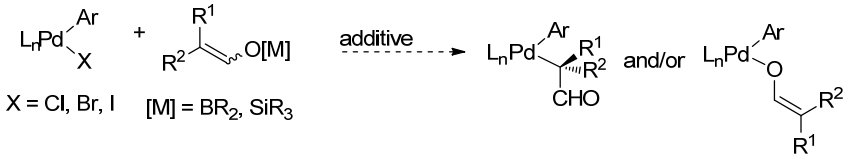
Scheme 16. Synthesis of *O*-Bound Nickel Enolate of Aldehyde

Herein, we report the synthesis, isolation and characterization of arylpalladium enolate complexes of aldehydes that are sufficiently stable to be isolated, but sufficiently reactive to undergo reductive elimination of α-aryl aldehydes in good yields. These complexes are less stable toward reductive elimination than those of ketones. The relative rates of reductive elimination of arylacetaldehydes fit from established trends. Complexes containing electron-withdrawing aryl groups underwent reductive elimination with rates that are faster than those of complexes containing more electron-rich aryl groups. The magnitude of difference in rates of reactions of enolate complexes of aldehydes is similar to that previously observed with related enolate complexes of ketones. Complexes containing hindered aryl groups reacted with faster rates and in higher yields of arylacetaldehydes than complexes bearing unhindered aryl groups. The magnitude of this difference is similar to that observed with related complexes of ketones.

3.3. Results and Discussion

3.3.1. Identification of Ancillary Ligands and Aldehydes that Lead to Stable Arylpalladium Enolate Complexes of Aldehydes

We considered two possible factors that could influence the rate of formation and the stability of arylpalladium enolate complexes of aldehydes and, therefore, affect the ability to isolate these complexes. First, the synthesis of arylpalladium complexes of aldehyde enolates from an alkali metal enolate of an aldehyde is more challenging than that of analogous complexes of ketones because alkali metal enolates of aldehydes are less stable than those of ketones. Thus, we envisioned the formation of palladium enolate complexes of aldehydes from reactions of boron or silicon enolates of aldehydes with arylpalladium bromide complexes in the presence of a fluoride additive (Scheme 17). Second, the steric and electronic effects of the ancillary ligands and of the aldehydes on the stability of the desired complexes are unknown. Thus, our initial studies focused on forming complexes with ancillary ligands, such as DPPBz and $EtPh_2P$, which led to stable arylpalladium enolate complexes of ketones (*vide supra*).

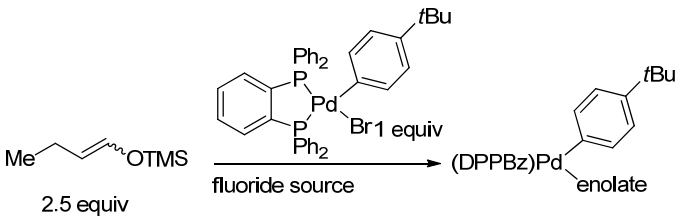


Scheme 17. Proposed Synthesis of Arylpalladium Enolate Complexes of Aldehydes

We investigated the formation of aldehyde enolate complexes containing DPPBz by the reaction of an arylpalladium bromide complex containing an electron-neutral aryl group with a silicon enolate of butanal in the presence of fluoride additives. The results of this study are

shown in Table 12. Reactions conducted with CsF, TBAF and TASF occurred to low conversion over 6 hours. The reaction in the presence of TBAT occurred to full conversion within 15 minutes, but separation of the desired complex from the byproducts that are generated from TBAT by precipitation with pentane did not give analytically pure materials.

Table 12. Survey of Fluoride Source in the Synthesis of Palladium Enolate of Butanal

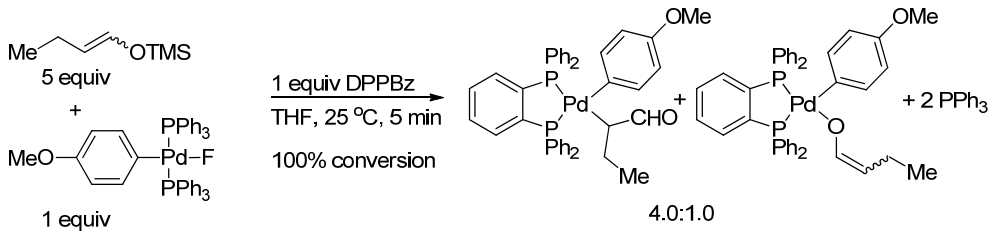


entry	fluoride source	solvent	*t* [h]	conversion (%)[a]
1	CsF	CH_3CN	6	N.R.[b]
2	TBAF[c]	THF	6	N.R.[b]
3	TASF[d]	THF	6	<20
4	TBAT[e]	THF	0.25	80

[a] Determined by ^{1}H NMR spectroscopy. [b] N.R. = no reaction.
[c] TBAF = tetrabutylammonium fluoride. [d] TASF = Tris(dimethylamino)sulfonium difluorotrimethylsilicate.
[e] TBAT = Tetrabutylammonium difluorotriphenylsilicate.

To simplify the purification procedure, we envisioned that the reaction of an arylpalladium fluoride with a silyl enol ether would generate the enolate complex and TMSF as byproduct, the latter of which can be evaporated readily in vacuum. Thus, the known PPh_3-ligated (*p*-anisyl)palladium fluoride was synthesized according to procedures developed by Pilon and Grushin,[48] and the reaction of this complex with (1-butenyloxy)trimethylsilane in the presence of DPPBz occurred to full conversion within 1 minute to yield the mixture of *C*- and *O*-bound enolate complexes in Scheme 18. The structures of the enolate complexes were elucidated

by ^{1}H NMR spectroscopy. These complexes underwent complete decay at room temperature within 30 minutes to form about 40% yield of the α-anisyl butyraldehyde product and (DPPBz)Pd(0)$(PPh_3)_n$ species. Thus, we concluded that DPPBz-ligated enolate complexes of butanal are too unstable at room temperature to isolate.

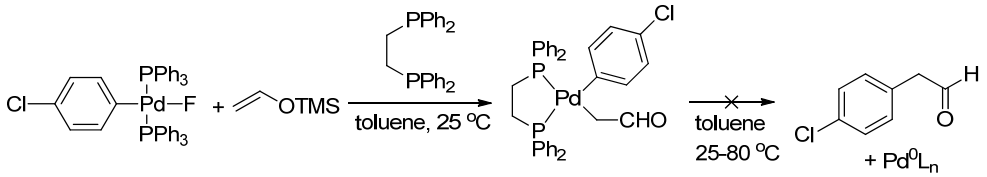


Scheme 18. Reaction of an Arylpalladium Fluoride with a Silyl Enol Ether

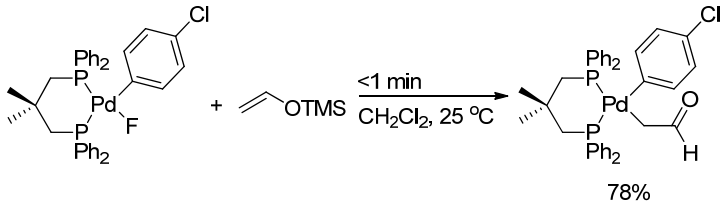
Because the reductive elimination of a DPPBz-ligated arylpalladium enolate of butyraldehyde occurred at room temperature, we evaluated combinations of steric and electronic properties of ancillary ligands and aldehydes that lead to a complex that is sufficiently stable for isolation and sufficiently reactive to undergo reductive elimination of an α-aryl aldehyde. First, we investigated the electronic effect of the ancillary ligand on the stability of a butanal-derived enolate complex. Because 1,2-bis(diphenylphosphino)ethane (DPPE) is more electron donating than DPPBZ and both ligands have similar bite angle,[49] we envisioned that the DPPE-ligated enolate of butanal could be more stable than the corresponding DPPBz-ligated complex. Indeed, the complex containing DPPE is stable at room temperature for more than 24 h. However, the complex did not undergo reductive elimination to give α-aryl butanal product in good yield. Thus, we evaluated complexes of a ligand that has similar electronic properties to and larger bite angle than DPPE. Bis(diphenylphosphino)-2,2-dimethylpropane (dppdmp) has been used as a

ligand in ruthenium-catalyzed allylation of phenol.[50] The bite angle of dppdmp is similar to 1,2-bis(diphenylphosphino)propane (dppp) (91°), which has a larger bite angle than DPPE (85°) and DPPBz (83°).[49] The reaction of (dppdmp)palladium(*p*-anisyl)fluoride with (1-butenyloxy)trimethylsilane occurred to full conversion within 1 minute to form the enolate complex, but this complex decomposed at room temperature after 2 hours.

We then evaluated the steric effects of the aldehyde on the stability of enolate complexes. Because known transition-metal enolate complexes of aldehyde are mostly derived from acetaldehyde (*vide supra*) and acetaldehyde lacks a β-C(sp^3)-H bond that allows β-hydrogen elimination to occur, we hypothesized that enolate complexes of acetaldehyde are more stable than those of more hindered aldehydes. Thus, we evaluated acetaldehyde-derived enolates that contain DPPE and dppdmp. The results of this study are shown in Scheme 19 and Scheme 20. The reaction of a PPh_3-ligated *p*-chlorophenylpalladium fluoride with vinyloxytrimethylsilane in the presence of DPPE occurred to full conversion within 10 minutes to form the desired enolate complex. However, the enolate complex underwent complete decay to form chlorobenzene at 80 °C (Scheme 19). The reaction of a dppdmp-ligated arylpalladium fluoride with vinyloxytrimethylsilane gave a *C*-bound enolate complex (Scheme 20). This complex underwent reductive elimination at 80 °C to form *p*-chlorophenyl acetaldehyde in 57% yield.



Scheme 19.



Scheme 20.

3.3.2. Synthesis and Characterization of Arylpalladium Enolate Complexes of Acetaldehyde

The aldehyde complex shown in Scheme 20 was characterized by X-ray diffraction and ^{1}H NMR spectroscopy (Figure 19). Selected bond distances and bond angles are provided in Table 13 and Table 14. The plane containing palladium center and the four atoms bound to it is only slightly distorted, demonstrated by the 360.4^o sum of the angles around Pd. The C2-O bond distance of 1.19 Å is consistent with a C-O double bond,[51] and a carbonyl stretching band was observed at 1703 cm^{-1} in the IR spectrum. In addition, the bond angles around C2 (130^o, 115^o and 115^o) are consistent with *sp*^{2} hybridization. The C1-C2 bond distance of 1.40 Å is consistent with a C-C single bond.[51] The Pd-C1 bond distance of 2.16 Å is similar to the corresponding bond distances of *C*-bound palladium enolate complexes of ketones.[3,20]

^{1}H and ^{13}C NMR spectroscopic data were consistent with the structure determined by X-ray diffraction. For example, the ^{13}C-NMR spectrum displayed a doublet of doublets for the palladium-bound methylene carbon and a multiplet at δ 200.9 for the carbonyl carbon. The ^{1}H-NMR spectrum obtained in $CDCl_3$ displayed a triplet at δ 8.86 for the aldehyde hydrogen and a multiplet at δ 2.38 for the palladium-bound methylene. The ^{1}H-NMR spectrum obtained in C_6D_6 displayed a triplet at δ 9.80 for the aldehyde hydrogen and triplet of doublets at δ 2.77 for the palladium-bound methylene.

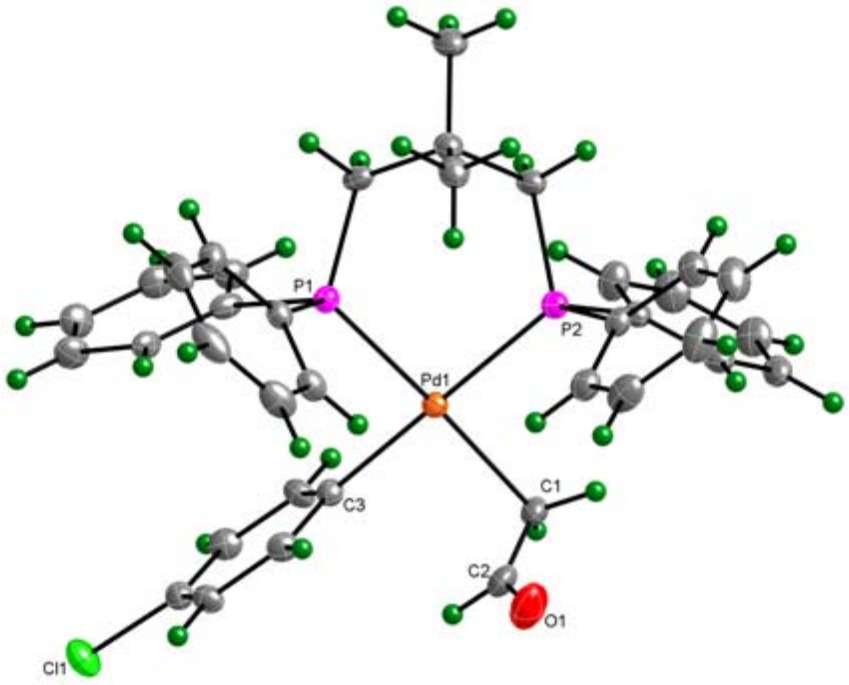


Figure 19. ORTEP diagram of (dppdmp)Pd(C_6H_4-4-Cl)(CH_2CHO)·CH_2Cl_2. Thermal ellipsoids are shown at 30% probability.

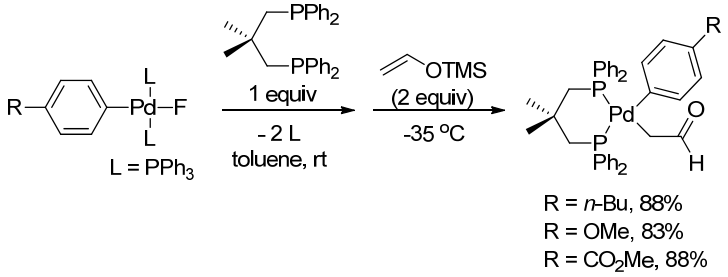
Table 13. Selected Intramolecular Bond Distances of (dppdmp)Pd(C_6H_4-4-Cl)(CH_2CHO)·CH_2Cl_2

Atom	Atom	Distance [Å]	Atom	Atom	Distance [Å]
Pd(1)	C(1)	2.165(7)	Pd(1)	P(2)	2.3130(9)
Pd(1)	C(3)	2.060(3)	C(1)	C(2)	1.395(9)
Pd(1)	P(1)	2.2841(9)	C(2)	O(1)	1.19(3)

Table 14. Selected Intramolecular Bond Angles of (dppdmp)Pd(C_6H_4-4-Cl)(CH_2CHO)·CH_2Cl_2

Atom	Atom	Atom	Angle [°]	Atom	Atom	Atom	Angle [°]
P(1)	Pd(1)	P(2)	94.50(3)	C(1)	Pd(1)	C(3)	91.3(10)
P(1)	Pd(1)	C(3)	86.83(9)	Pd(1)	C(1)	C(2)	103(2)
P(2)	Pd(1)	C(1)	87.8(10)	C(1)	C(2)	O(1)	130(3)

To evaluate the electronic effects of the aryl groups on the rates of reductive elimination from arylpalladium enolate complexes of acetaldehyde and yields of coupled products, we synthesized a series of arylpalladium acetaldehyde complexes containing *para*-substituted aryl groups, and the results are shown in Scheme 21. Complexes containing electron-neutral, electron-rich and electron-poor aryl groups were formed in high yields from reactions of vinyloxytrimethylsilane with *in-situ* generated (dppdmp)Pd(aryl)fluoride complexes toluene at -35 °C.



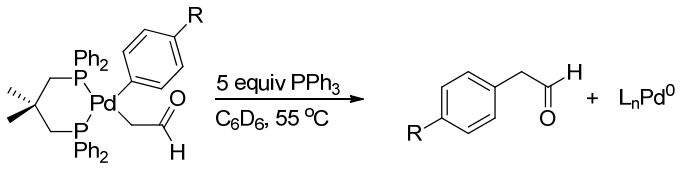
Scheme 21. Synthesis of dppdmp-Ligated Arylpalladium Enolate Complexes of Acetaldehyde

3.3.3. Reductive Elimination from Arylpalladium Enolate Complexes of Aldehydes

The rate of reductive elimination and yields of arylacetaldehydes are shown in Table 15. The reductive elimination from these complexes occurred to full conversion, but in low yield of the coupled products. Analysis of the product mixtures revealed that the major side products are

arenes that originate from the aryl group bound to palladium. Previous studies of the reductive elimination of C-N and C-C bonds from arylpalladium amido and enolate complexes showed that the formation of arenes is common. The origin of hydrogens that are not from ligands containing β-hydrogens has been investigated, but no clear origin for this hydrogen has been reported.

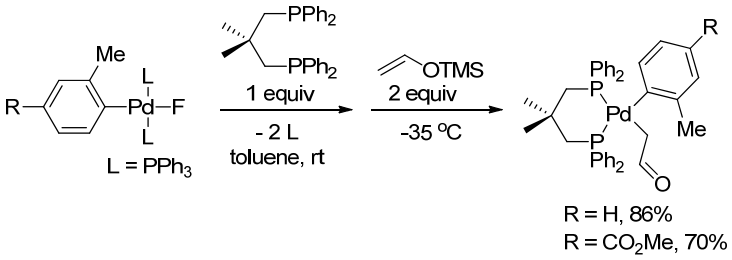
Table 15. Reductive Elimination from Palladium Enolate Complexes Containing Unhindered Aryl Groups



entry	R	$t_{1/2}$, (min)[a]	Yield, %[a]
1	-OMe	–	37
2	-n-Bu	23	51
3	-CO_2Me	–	15

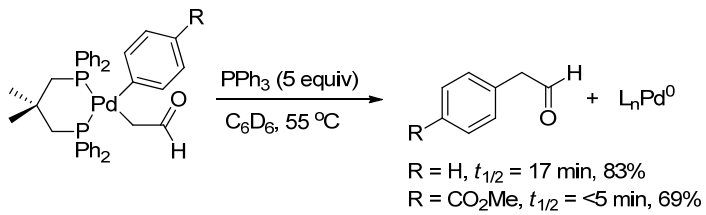
[a]Half-lives were determined from k_{obs} values that were obtained by kinetic measurements over 3 half-lives. [b]Determined by ^{1}H NMR spectroscopy with 1,3,5-trimethoxybenzene as an internal standard.

During our preliminary study of the reductive elimination from dmppdmp-ligated enolate complexes, we observed that complexes containing *ortho*-substituted aryl groups undergo reductive elimination of arylacetaldehydes in higher yield than complexes containing *para*-substituted aryl groups. Thus, we prepared complexes containing *ortho*-substituted aryl groups, and the results are shown in Scheme 22. Each complex contains an *ortho*-methyl substituent on the palladium-bound aryl group. The electronic properties of the palladium-bound aryl groups were varied by preparing complexes containing different substituents at the para position.



Scheme 22. Synthesis of Hindered Enolate Complexes of Acetaldehyde

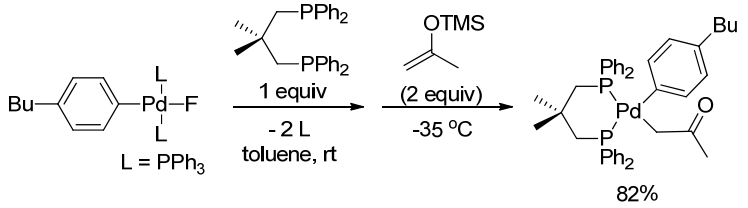
The relative rates of reductive elimination are shown in Scheme 23. The half-life for the reaction of the complex containing the *para*-benzoate group was less than 5 min at 55 °C. The reaction of the complex containing an electron-neutral aryl group was 3.4 times slower than than that of the complex containing the benzoate group. These data showed that the reactions of complexes of aldehyde enolates and those of complexes of ketone enolates[8] have similar sensitivity to the electronic properties of the para substituent. These data also showed that the rates of reductive elimination from these hindered complexes were faster than the rates of reductive elimination from the corresponding unhindered complexes by a factor of about 1.3 (Table 15, entry 2). The magnitude of this difference is similar to the difference in rates of reductive elimination from DPPBz-ligated arylpalladium ketone-enolate complexes containg aryl groups with and without ortho substituents.[3]



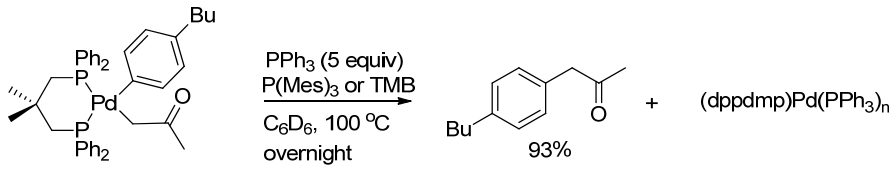
Scheme 23. Reductive Elimination from Hindered Arylpalladium Enolate Complexes of Acetaldehyde

3.3.4. Comparison of the Relative Rates of Reductive Elimination from Arylpalladium Enolate Complexes of Acetaldehyde and Acetone

We sought to compare the rates of reductive elimination from arylpalladium enolate complexes of acetaldehyde versus those of related complexes of acetone. An acetone-derived enolate complex containing the *p*-butylphenyl group was prepared by the protocols developed for the synthesis of aldehyde-derived enolate complexes as shown in Scheme 24. This complex underwent reductive elimination at 55 °C with a half-life over 12 h, but at 100 °C, this complex reductively eliminated the α-aryl ketone in 93% yield after 12 h (Scheme 25). The complex of acetaldehyde, however, underwent reductive elimination at 55 °C with a half-life of 23 min (Table 15). These data suggest that enolate complexes of acetone undergo reductive elimination much more slowly than do those of acetaldehyde.



Scheme 24. Synthesis of Arylpalladium Enolate Complex of Acetone



Scheme 25. Reductive Elimination from Complex of Acetone

3.4. Conclusion and Outlook

A series of arylpalladium enolate complexes of acetaldehyde were synthesized and characterized. Their reactivity and stability were evaluated and compared to those of an analogous enolate complex derived from acetone. Relative rates of reductive elimination of arylacetaldehydes fit established trends. Complexes containing electron-withdrawing aryl groups underwent reductive elimination with rates that are faster than those of complexes containing more electron-rich aryl groups. The magnitude of difference in rates is similar to that observed with DPPBz-ligated arylpalladium enolate complexes of ketones. Complexes containing hindered aryl groups reacted with faster rates and in higher yields of arylacetaldehydes than complexes bearing unhindered aryl groups. The magnitude of this difference is similar to that observed with DPPBz-ligated complexes of ketones. The effect of steric properties of the aryl group on the yield of coupled products is consistent with that observed in the α-arylation of linear aldehydes that are catalyzed by palladium complexes of DPPF (see Chapter 2).

More information on factors that influence the stability and reactivity of arylpalladium enolate complexes of aldehydes is needed. The evaluation of steric and electronic properties of ancillary ligands on the stability, rates of reductive elimination and yield of arylacetaldehyde products would provide important information for the design of the next generation of catalyst in the α-arylation of aldehydes. The effects of steric properties of the aldehyde on the rates of reductive elimination and yields of α-aryl aldehydes are still ambiguous. Thus, future research includes the synthesis and characterization of complexes containing the enolate of propionaldehyde and isobutyraldehyde. If such complexes are isolated, then the evaluation of the stability, rates of reductive elimination and yield of the corresponding α-aryl aldehyde products is needed. Finally, the synthesis of arylpalladium enolate complexes containing monophosphines

would enable a study on the effect of denticity of ancillary ligand on the rates, selectivity and yields in reductive elimination reactions of arylpalladium aldehyde enolates.

3.5. Experimental Information

General Procedures. Unless otherwise noted, all manipulations were conducted under an inert nitrogen atmosphere. All reactions were conducted in flame-dried glassware. A N_2-filled glovebox was used as indicated and had O_2 level below 10 ppm.

Materials. CH_2Cl_2, toluene, benzene and pentane were dried with a solvent purification system by percolation through neutral alumina under positive pressure of argon. Vinyloxytrimethylsilane (97%) was purchased from Alfa Aesar. (Isopropenyloxy)trimethylsilane (IPOTMS) was prepared according to the procedure reported by Cazeau *et al*.[52] Triphenylphosphine was purchased from Aldrich. 1,2-bis(diphenylphosphino)benzene (DPPBz) and 1,2-bis(diphenylphosphino)ethane (DPPE) were purchased from Strem Chemicals. Benzene-d_6 and toluene-d_8 were purchased from Cambridge Isotopes Laboratories, Inc., dried over a sodium-benzophenone ketyl and vacuum transferred before use. All aryl halides were purchased from Sigma-Aldrich® or Alfa Aesar®. Aryl bromides and liquid aryl iodides were used without further purification. Solid aryl iodides were recrystallized in hot methanol. Silver(I) fluoride (99.9%, metals basis) was purchased from Sigma-Aldrich® and stored in a glovebox. Triphenylphosphine (*Reagent Plus*®, 99%) was purchased from Sigma-Aldrich®. Tetrakis(triphenylphosphine)palladium was prepared according to procedures reported by Coulson.[53] The complexes $[Pd(PPh_3)_2(Ar)(I)]$ where Ar = *p*-anisyl,[54] *o*-tol,[54] were synthesized according to the general procedure for the preparation of PPh3-ligated arylpalladium iodide complexes described below, characterized and confirmed with the cited references. $[Pd(PPh_3)_2(C_6H_4\text{-}4\text{-}OCH_3)(F)]$ and $[Pd(PPh_3)_2(C_6H_4\text{-}4\text{-}Cl)(F)]$ were prepared according to procedures reported by Pilon and Grushin.[48]

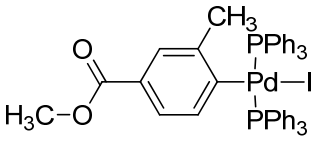
Instruments. ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra were recorded on Varian Unity-400 or 500 MHz (126 MHz, ^{13}C) spectrometers. Spectra are referenced either to residual chloroform (d = 7.26 ppm, ^{1}H; 77.0 ppm, ^{13}C), residual benzene (d = 7.15 ppm, ^{1}H; 128.62 ppm, ^{13}C), external standard reference $CFCl_3$ (d = 0 ppm, ^{19}F), or H_3PO_4 (d = 0 ppm, ^{31}P). Chemical shifts are reported in ppm. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and b (broad). Coupling constants, *J*, are reported in hertz, and integration is provided and assignments are indicated. Chemical shifts downfield of the standard are reported as positive values. Analytical gas chromatography (GC) was performed using a Hewlett-Packard 5890 Gas Chromatograph fitted with a flame ionization detector and a Hewlett-Packard HP5 (30m x 0.32 mm) capillary column. The injector temperature was 250 ^{o}C, and the detector temperature was 300 ^{o}C with a helium carrier gas flow of 16 mL/min. The column temperature program was as follows: 120 ^{o}C to 250 ^{o}C at 40 ^{o}C/min, then hold for 3 min for a total run time of 6.25 min. Retention times (t_R) were obtained using Agilent Chemstation software. Response factors were generated by triplicate runs of three molar ratios of the analyte to dodecane standard dissolved in ethyl acetate. Elemental analyses were performed at the University of Illinois at Urbana-Champaign Microanalysis Laboratory.

EXPERIMENTAL PROCEDURES

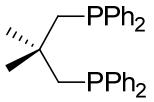
General Procedure for the Preparation of [Pd(PPh$_3$)$_2$(Ar)(I)]. Inside a glovebox, $(PPh_3)_4Pd$ (0.600 mmol) and an aryl iodide (0.660 mmol) were weighed into a 50-mL round-bottom flask. Benzene (20 mL) was added. The reaction mixture was stirred at 25 ^{o}C overnight. The solvent was removed under vacuum, and diethyl ether (5 mL) was added. The mixture was stirred for 5 min to dissolve PPh_3. The mixture was filtered through a medium-frit sintered glass funnel, and the product was washed with diethyl ether (2 mL) and dried under vacuum.

General procedure for the synthesis of dppdmp-ligated arylpalladium enolate complexes of aldehydes. Inside a drybox, [$Pd(PPh_3)_2$(aryl)(F)] (0.100 mmol) and dppdmp (0.100 mmol) were weighed into a 20-mL scintillation vial, and toluene (2.5 mL) was added via a syringe. The mixture was stirred at room temperature for 30 min. The mixture was then placed in a -35 ^oC freezer for 10 min. Vinyloxytrimethylsilane (20 μL, 0.13 mmol) was added via a syringe to the mixture at -35 ^oC. The mixture was swirled for 1 min and placed in the refrigerator for 1 h at -35 °C. Pentane, ca. 10 mL, was then added to precipitate the product. The mixture was placed in the refrigerator for 8 h. The product was then filtered, washed with cold pentane (ca. 2 mL) and dried under vacuum.

Representative Procedure for Determination of Half-lives and Yields from Reductive-Elimination Reactions. Inside a drybox, an enolate complex (0.010 g), PPh_3 (5 equiv) were weighed into a 4-mL vial, and 0.4 mL of C_6D_6 was added via a syringe. The resulting solution was transferred to a J. Young NMR tube. A solution of 1,3,5-trimethoxybenzene (10-μL, 0.5 M, 0.005 mmol) was then added via and 10-μL syringe. The tube was tightly sealed. A ^{1}H-NMR spectrum was obtained of this initial mixture. After the NMR spectrometer was calibrated and set to 55 ^oC, an array was collected until the complex was consumed after 3 half-lives. After completion of the array, the integrated data were plotted against time and fit to a first-order decay using KaleidaGraph from which the k_{obs} values were calculated. The yield of the coupled product was determined by integrating the aldehyde hydrogen resonances of the enolate complex and the aryl acetaldehyde product with respect to the internal standard.

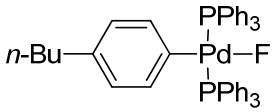


[Pd(PPh$_3$)$_2$(C$_6$H$_4$-4-(CO$_2$CH$_3$)-2-(CH$_3$)]. Inside a glovebox, (PPh$_3$)$_4$Pd (0.250 g, 0.216 mmol) and methyl 4-iodo-3-methylbenzoate (0.0657 g, 0.238 mmol) were weighed into a 25-mL scintillation vial. Benzene (5.0 mL) was added. The reaction mixture was stirred at 25 ^{o}C for 12 h. The solvent was removed under vacuum, and diethyl ether (5 mL) was added. The mixture was stirred for 5 min to dissolve PPh$_3$. The mixture was filtered through a medium-frit sintered glass funnel, and the product was washed with diethyl ether (2 mL) and dried under vacuum to give a white powder (0.180 g, 91%). ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.46 (m, 12H, Ar**H**), 7.31 (m, 6H, Ar**H**), 7.21 (m, 12H, Ar**H**), 6.96 (m, 1H, Ar**H**), 6.88 (m, 1H, Ar**H**), 6.71 (b, 1H, Ar**H**), 3.75 (s, 3H, **C**O$_2$C**H**$_3$), 1.90 (s, 3H, ArC**H**$_3$). ^{13}C NMR (125 MHz, CDCl$_3$) δ 168.11 (s, **C**O$_2$CH$_3$), 134.87 (t, J = 6.1 Hz), 131.9 (s), 131.7 (s), 131.6 (s), 131.5 (s), 130.2 (s), 130.0 (s), 127.74 (t, J = 5.1 Hz), 127.6 (s), 124.6 (s), 51.5 (s), 25.5 (t, J = 2.5 Hz). ^{31}P{^{1}H} NMR (202 MHz, CDCl$_3$) δ 22.6 (s). Anal. Calcd. C$_{45}$H$_{39}$IO$_2$P$_2$Pd: C, 59.59; H, 4.33. Found: C, 59.74; H, 4.59.



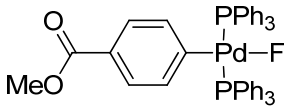
1,3-Bis(diphenylphosphino)-2,2-dimethylpropane (dppdmp).[55] Into a flame-dried, 300-mL three-necked, round-bottom flask fitted with a condenser and a gas inlet and contained a magnetic stir bar, finely cut sodium (1.44 g, 62.8 mmol) was added followed by Bu$_2$O (48 mL). The reaction mixture was heated gradually to 130 ^{o}C and stirred for 4 h. Then a 10 mL of a 2.8 M solution of Ph$_2$PCl in Bu$_2$O (28 mmol) was added dropwise via a gas-tight syringe. The resulting mixture was stirred at 130 ^{o}C for 2 h. Then 1,3-dichloro-2,2-dimethylpropane (2.04 g, 14.2 mmol) was added dropwise via a gas tight syringe. The temperature was then lowered to 90

^{o}C and the reaction stirred overnight. Then the reaction was cooled to room temperature and a 10% (w/w) aqueous NaOH solution was added slowly. The mixture was extracted with pentane (3 x 50 mL). The organic layer was then washed with brine, dried with $MgSO_4$ and evaporated under vacuum to give a white solid. Recrystallization from methanol afforded the titled compound as a crystalline solid (2.92 g, 47%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47-7.42 (8H, Ar**H**), 7.34-7.30 (12H, Ar**H**), 2.35 (d, $J_{H\text{-}P}$ = 3.3 Hz, 4H, 2xC**H**$_2$), 1.05 (s, 6H, $(CH_3)_2$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.0 (d, $J_{C\text{-}P}$ = 12.2 Hz), 133.0 (d, $J_{C\text{-}P}$ = 12.4 Hz) , 132.8 (d, $J_{C\text{-}P}$ = 11.7 Hz), 128.3, 44.1 (dd, $J_{C\text{-}P}$ = 16.6, 9.1 Hz), 35.1 (t, $J_{C\text{-}P}$ = 14.2 Hz), 30.4 (m). ^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$) δ –23.8. Anal. Calcd. $C_{29}H_{30}P_2$: C, 79.07; H, 6.86. Found: C, 78.74; H, 6.86.

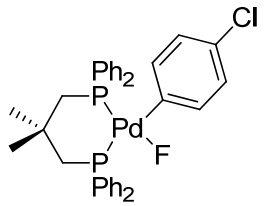


[Pd(PPh$_3$)$_2$(C$_6$H$_4$-4-(CH$_2$)$_3$CH$_3$)(F)]. Inside a drybox, [Pd(PPh$_3$)$_2$(C$_6$H$_4$-4-(CH$_2$)$_3$CH$_3$)(I)] (0.311 g, 0.349 mmol) and AgF (0.084 g, 0.65 mmol) were weighed into a 20-mL scintillation vial. Benzene (10 mL) was then added. The vial was capped with a Teflon-lined cap and brought out of the drybox. The reaction mixture was sonicated at 10-20 ^{o}C for 1.5 h. The reaction mixture was then brought back into the drybox, diluted with CH_2Cl_2 (2 mL) and filtered through Celite. The filtrate was concentrated under vacuum to ca 5 mL. Pentane was then added to precipitate the product, and the resulting gray solid was filtered and washed with cold pentane (0.185 g, 68%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (m, 12H, Ar**H**), 7.34-7.31 (m, 6H, Ar**H**), 7.26-7.23 (m, 12H, Ar**H**), 6.43 (d, *J* = 7.4 Hz, 2H, Ar**H**), 6.06 (d, *J* = 7.6 Hz, 2H, Ar**H**), 2.17 (t, *J* = 7.5 Hz, 2H, C**H**$_2$CH$_2$CH$_2$CH$_3$), 1.33 (m, 2H, CH$_2$C**H**$_2$CH$_2$CH$_3$), 1.23 (m, 2H, CH$_2$CH$_2$C**H**$_2$CH$_3$), 0.89 (t, *J* = 7.2 Hz, 3H, CH$_2$CH$_2$CH$_2$C**H**$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.0 (m), 134.5 (t, *J* = 6.5 Hz), 131.5 (s), 131.3 (s), 129.7 9 (s), 128.0 (t, *J* = 5.09 Hz), 127.5 (s), 125.2 (s), 34.7 (s), 34.4

(s), 22.3 (s), 14.0 (s). $^{31}P\{^{1}H\}$ NMR (202 MHz, $CDCl_3$) δ 18.61 (s). Anal. Calcd. $C_{46}H_{43}FP_2Pd$: C, 70.54; H, 5.53. Found: C, 70.15; H, 5.45.

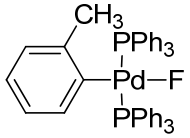


[Pd(PPh$_3$)$_2$(C$_6$H$_4$-4-(CO$_2$CH$_3$))(F)]. Inside a drybox, [Pd(PPh$_3$)$_2$(C$_6$H$_4$-4-(CO$_2$CH$_3$))(I)] (0.311 g, 0.348 mmol) and AgF (0.0886 g, 0.698 mmol) were weighed into a 20-mL scintillation vial. Benzene (10 mL) was then added. The vial was capped with a Teflon-lined cap and brought out of the drybox. The reaction mixture was sonicated at 10-20 ^{o}C for 1.25 h. The vial was then brought back into the drybox, diluted with CH_2Cl_2 (2 mL) and filtered through Celite. The filtrate was concentrated under vacuum to ca 5 mL. Pentane was then added to precipitate the product, and the resulting gray solid was filtered and washed with cold pentane (0.211 g, 77%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (m, 12H, Ar**H**), 7.34 (t, *J* = 7.4 Hz, 6H, Ar**H**), 7.26 (d, *J* = 6.2 Hz, 12H, Ar**H**), 6.82 (d, *J* = 8.1 Hz, 2H, Ar**H**), 6.73 (d, *J* = 8.1 Hz, 2H, Ar**H**), 3.76 (s, 3H, OC**H**$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.2 (s), 136.4 (t, *J* = 4.4 Hz), 134.4 (t, *J* = 6.5 Hz), 130.6 (t, *J* = 22.6 Hz), 130.0 (s), 128.2 (t, *J* = 5.1 Hz), 127.0 (s), 123.2 (s), 123.2 (s), 51.5 (s). $^{31}P\{^{1}H\}$ NMR (202 MHz, $CDCl_3$) δ 18.82 (s). ^{19}F ($CDCl_3$) δ -14.14. Anal. Calcd. $C_{44}H_{37}FO_2P_2Pd$: C, 67.31; H, 4.75. Found: C, 61.06; H, 4.43.

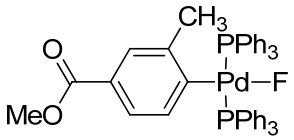


[Pd(Ph$_2$PCH$_2$C(CH$_3$)$_2$CH$_2$PPh$_2$)(C$_6$H$_4$-4-Cl)(F)]. Inside a drybox, dppdmp (0.101 g, 0.230 mmol) was combined with [Pd(PPh$_3$)$_2$(C$_6$H$_4$-4-Cl)(F)] (0.175 g, 0.230 mmol) in a 20-mL scintillation vial. Toluene (5 mL) was added and the cloudy reaction mixture was stirred for 1 h.

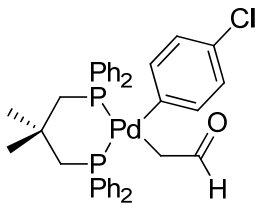
The reaction mixture was then filtered through a medium-fritted glass filter and the off-white solid was washed with toluene and dried under vacuum to afford the titled compound as an off-white solid (0.139 g, 89%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.12-8.08 (4H, Ar**H**), 7.59 (dd, *J* = 7.5, 11.6 Hz, 4H, Ar**H**), 7.45-7.37 (8H, Ar**H**), 7.32-7.29 (4H, Ar**H**), 6.94 (dd, *J* = 5.9, 8.0 Hz, 2H, Ar**H**), 6.65 (dd, *J* = 1.9, 8.3 Hz, 2H, Ar**H**), 2.35-2.32 (4H, 2 x C**H**$_2$), 0.83 (s, 6H, $(CH_3)_2$. ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.0, . ^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$) δ 24.9 (dd, $J_{P\text{-}P}$ = 45.6 Hz, $J_{P\text{-}F}$ = 167.6 Hz, 1P (trans to F)), -7.99 (dd, $J_{P\text{-}P}$ = 45.6 Hz, $J_{P\text{-}F}$ = 17.6 Hz, 1P (cis to F)). Anal. Calcd. $C_{35}H_{34}ClFP_2Pd$: C, 62.05; H, 5.06. Found: C, 62.09; H, 5.09.



[Pd(PPh$_3$)$_2$(C$_6$H$_4$-2-CH$_3$)(F)]. Inside a drybox, [Pd(PPh$_3$)$_2$(C$_6$H$_4$-2-CH$_3$)(I)] (0.173 g, 0.233 mmol) and AgF (0.0400 g, 0.315 mmol) were weighed into a 20-mL scintillation vial. Benzene (6 mL) was then added. The vial was capped with a Teflon-lined cap and brought out of the drybox. The reaction mixture was sonicated at 10-20 ^{o}C for 1.25 h. The vial was then brought back into the drybox, diluted with CH_2Cl_2 (2 mL) and filtered through Celite. The filtrate was concentrated under vacuum to ca 5 mL. Pentane was then added to precipitate the product, and the resulting gray solid was filtered and washed with cold pentane (0.153 g, 100%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (m, 12H, Ar**H**), 7.34 (m, 6H, Ar**H**), 7.27 (m, 12H, Ar**H**), 6.76 (d, *J* = 7.2 Hz, 1H, Ar**H**), 6.42 (t, *J* = 7.2 Hz, 1H, Ar**H**), 6.20 (t, *J* = 7.2 Hz, 1H, Ar**H**), 6.14 (d, *J* = 7.2 Hz, 1H, Ar**H**), 1.85 (s, 3H, ArC**H**$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.4 (s), 135.7 (m), 135.6 (m), 134.4 (t, *J* = 6.5 Hz), 131.2 (dt, *J* = 2.3, 21.5 Hz), 129.8 (s), 128.7 (s), 127.0 (t, *J* = 5.0 Hz), 123.6 (s), 122.1 (s), 26.0 (s). ^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$) δ 20.1 (s). ^{19}F ($CDCl_3$) δ -5.73. Anal. Calcd. $C_{43}H_{37}FP_2Pd$: C, 67.69; H, 5.03. Found: C, 69.15; H, 5.06.

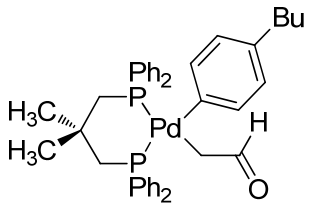


[Pd(PPh$_3$)$_2$(C$_6$H$_4$-4-(CO$_2$CH$_3$)-2- CH$_3$)(F)]. Inside a drybox, [Pd(PPh$_3$)$_2$(C$_6$H$_4$-4-(CO$_2$CH$_3$))(I)] (0.180 g, 0.198 mmol) and AgF (0.0500 g, 0.394 mmol) were weighed into a 20-mL scintillation vial. Benzene (5 mL) was then added. The vial was capped with a Teflon-lined cap and brought out of the drybox. The reaction mixture was sonicated at 10-20 ^{o}C for 1.25 h. The vial was then brought back into the drybox, diluted with CH_2Cl_2 (2 mL) and filtered through Celite. The filtrate was concentrated under vacuum to ca 3 mL. Pentane was then added to precipitate the product, and the resulting gray solid was filtered and washed with cold pentane (0.100 g, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (m, 12H, Ar**H**), 7.35 (t, *J* = 7.3 Hz, 6H, Ar**H**), 7.27 (m, 12H, Ar**H**), 6.94 (m, 1H, Ar**H**), 6.86 (m, 1H, Ar**H**), 6.79 (b, 1H, Ar**H**), 3.80 (s, 3H, OC**H**$_3$), 1.95 (s, 3H, ArC**H**$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3 (s), 145.3 (s), 141.6 (s), 135.5 (t, *J* = 4.3 Hz), 134.6 (t, *J* = 6.5 Hz), 130.6 (t, *J* = 22.6 Hz), 130.0 (s), 129.0 (s), 128.6 (s), 128.1 (t, *J* = 5.1 Hz), 124.1 (m), 51.4 (s), 25.9 (m). ^{31}P{^{1}H} NMR (161.9 MHz, $CDCl_3$) δ 19.95 (s). ^{19}F ($CDCl_3$) δ -9.45 (s).



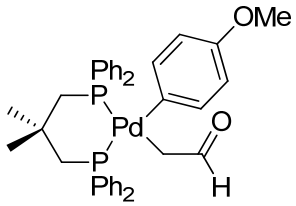
[Pd(Ph$_2$PCH$_2$C(CH$_3$)$_2$CH$_2$PPh$_2$)(C$_6$H$_4$-4-Cl)(CH$_2$CHO)] (Figure 19). Inside a drybox, [(dppdmp)Pd(C$_6$H$_4$-4-Cl)(F)] (0.0800 g, 0.118 mmol) was dissolved in CH_2Cl_2 (2 mL) and vinyloxytrimethylsilane (40 μL, 0.26 mmol) was added via a syringe. The reaction was stirred at room temperature for 5 min, and then concentrated under reduced pressure to ca 1 mL. Pentane was added to precipitate the product. The mixture was place in a -35 ^{o}C refrigerator for 1 day.

The product was filtered and washed with cold pentane to give an off-white powder (0.064 g, 78%). Recrystallization by dissolving the solid in CH_2Cl_2, layering with pentane and storing the mixture at -35 ^oC for 3 days afforded crystals that were suitable for an X-ray structural analysis. ^1H NMR (500 MHz, C_6D_6) δ 9.67 (t, *J* = 5.1 Hz, 1H, C**H**O), 7.81-7.78 (4H, Ar**H**), 7.26-7.20 (8H, Ar**H**), 7.13-7.08 (4H, Ar**H**), 6.95-6.89 (6H, Ar**H**), 6.78 (dd, *J* = 1.4, 8.0 Hz, 2H, Ar**H**), 2.77 (td, *J* = 5.2, 9.5 Hz, 2H, Pd(C**H**$_2$CHO)), 1.96 (dd, $J_{C\text{-}P}$ = 9.4, 11.8 Hz, 4H, PC**H**$_2$C(CH$_3$)$_2$C**H**$_2$P), 0.38 (s, 6H, PCH$_2$C(C**H**$_3$)$_2$CH$_2$P). $^{31}P\{^1H\}$ NMR (202 MHz, $CDCl_3$) δ 9.2 (d, $J_{P\text{-}P}$ = 38.9 Hz), 6.8 (d, $J_{P\text{-}P}$ = 45.6 Hz).

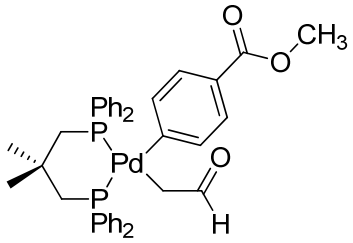


[Pd(Ph$_2$PCH$_2$C(CH$_3$)$_2$CH$_2$PPh$_2$)(C$_6$H$_4$-4-(CH$_2$)$_3$CH$_3$)(CH$_2$CHO)] (Scheme 21). The general procedure for the synthesis of complexes of aldehyde enoalates was followed with [Pd(PPh$_3$)$_2$(C$_6$H$_4$-4-(CH$_2$)$_3$CH$_3$)(F)] (0.0800 g, 0.102 mmol), dppdmp (0.045 g, 0.102 mmol), vinyloxytrimethylsilane (20 μL, 0.13 mmol), and toluene (2.5 mL). The product was an off-white solid (0.065 g, 88%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.86 (t, *J* = 5.4 Hz, 1H, C**H**O), 7.76 (m, 4H, Ar**H**), 7.50-7.43 (6H, Ar**H**), 7.37 (m, 4H, Ar**H**), 7.29 (m, 2H, Ar**H**), 7.22 (m, 4H, Ar**H**), 6.84 (t, *J* = 7.5 Hz, 2H, Ar**H**), 6.42 (d, *J* = 6.1 Hz, 2H, Ar**H**), 2.38 (m, 2H, Pd(C**H**$_2$CHO)), 2.33 (m, 4H, PC**H**$_2$C(CH$_3$)$_2$C**H**$_2$P), 2.26 (t, *J* = 7.7 Hz, 2H, C**H**$_2$CH$_2$CH$_2$CH$_3$), 1.37 (m, 2H, CH$_2$C**H**$_2$CH$_2$CH$_3$), 1.23 (m, 2H, CH$_2$CH$_2$C**H**$_2$CH$_3$), 0.87 (t, *J* = 7.3 Hz, 3H, CH$_2$CH$_2$CH$_2$C**H**$_3$), 0.66 (s, 6H, PCH$_2$C(C**H**$_3$)$_2$CH$_2$P). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.9 (m, **C**HO), 136.7 (t, *J* = 3.0 Hz), 135.3 (s), 133.8 (d, *J* = 12.4 Hz), 133.4 (d, *J* = 11.3 Hz), 133.1 (s), 132.8 (s), 132.6 (s), 130.3 (d, *J* = 1.8 Hz), 129.7 (d, *J* = 2.0 Hz), 128.7 (d, *J* = 9.6 Hz), 128.1 (d, *J* = 9.9 Hz), 127.1 (d,

J = 8.3 Hz), 42.0 (dd, $J_{C\text{-}Pcis}$ = 5.8, $J_{C\text{-}Ptrans}$ = 58.4 Hz, Pd(**C**H_2CHO)), 40.71 (dd, J = 6.1, 17.1 Hz), 39.70 (dd, J = 5.4, 16.4 Hz), 35.2 (dd, J = 2.7, 3.9 Hz), 35.0 (s), 34.1 (s), 33.2 (t, J = 6.8 Hz), 22.4 (s), 14.0 (s). $^{31}P\{^1H\}$ NMR (202 MHz, $CDCl_3$) δ 9.33 (d, $J_{P\text{-}P}$ = 37.6 Hz), 5.99 (d, $J_{P\text{-}P}$ = 37.6 Hz). Anal. Calcd. $C_{41}H_{46}OP_2Pd$: C, 68.09; H, 6.41. Found: C, 68.09; H, 6.54.

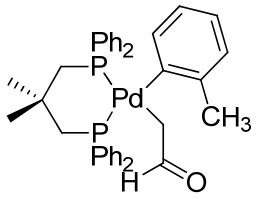


[Pd(Ph$_2$PCH$_2$C(CH$_3$)$_2$CH$_2$PPh$_2$)(C$_6$H$_4$-4-OCH$_3$)(CH$_2$CHO)] (Scheme 21). The general procedure for the synthesis of complexes of aldehyde enoalates was followed with [Pd(PPh$_3$)$_2$(C$_6$H$_4$-4-OCH$_3$)(F)] (0.0600 g, 0.0792 mmol), dppdmp (0.0350 g, 0.0795 mmol), vinyloxytrimethylsilane (20 μL, 0.13 mmol), and toluene (2.5 mL). The product was an off-white solid (0.046 g, 83%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.84 (t, J = 5.4 Hz, 1H, C**H**O), 7.77 (m, 4H, Ar**H**), 7.52-7.45 (m, 8H), 7.39-7.24 (m, 8H), 6.81 (t, J = 7.64 Hz, 2H, Ar**H**), 6.28 (t, J = 7.1 Hz, 2H, Ar**H**), 3.58 (s, 3H, OC**H**$_3$), 2.40 (m, 2H, Pd(C**H**$_2$CHO)), 2.34 (m, 4H, PC**H**$_2$C(CH$_3$)$_2$C**H**$_2$P), 0.67 (s, 6H, PCH$_2$C(C**H**$_3$)$_2$CH$_2$P). $^{31}P\{^1H\}$ NMR (202 MHz, $CDCl_3$) δ 9.15 (d, $J_{P\text{-}P}$ = 36.6 Hz), 6.28 (d, $J_{P\text{-}P}$ = 37.7 Hz).



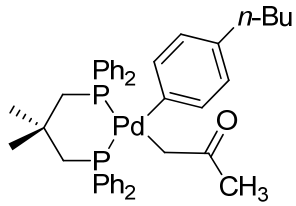
[Pd(Ph$_2$PCH$_2$C(CH$_3$)$_2$CH$_2$PPh$_2$)(C$_6$H$_4$-4-CO$_2$CH$_3$)(CH$_2$CHO)] (Scheme 21). The general procedure for the synthesis of complexes of aldehyde enolates was followed with [Pd(PPh$_3$)$_2$(C$_6$H$_4$-4-CO$_2$CH$_3$)(F)] (0.0600 g, 0.0792 mmol), dppdmp (0.0296 g, 0.0672 mmol),

vinyloxytrimethylsilane (20 μL, 0.33 mmol), and toluene (2.5 mL). The product was an off-white solid (0.043 g, 88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (t, *J* = 5.4 Hz, 1H, C**H**O), 7.77-7.73 (m, 4H, Ar**H**), 7.52-7.47 (m, 8H, Ar**H**), 7.37-7.31 (m, 6H, Ar**H**), 7.26-7.17 (m, 4H, Ar**H**), 7.11 (t, *J* = 7.3 Hz, 2H, Ar**H**), 3.77 (s, 3H, OC**H**$_3$), 2.39 (m, 4H, PC**H**$_2$C(CH$_3$)$_2$C**H**$_2$P), 2.31 (m, 2H, Pd(C**H**$_2$CHO)), 0.66 (s, 6H, PCH$_2$C(C**H**$_3$)$_2$CH$_2$P). ^{13}C NMR (125 MHz, $CDCl_3$) δ 200.6 (m), 168.7 (s), 137.0 (s), 133.7 (d, *J* = 12.3 Hz), 133.3 (d, *J* = 11.4 Hz), 130.5 (s), 130.1(s), 129.0 (s), 128.8 (d, *J* = 9.7 Hz), 128.3 (d, *J* = 10.1 Hz), 128.2 (s), 126.5 (d, *J* = 7.5 Hz), 125.3 (s), 67.9 (s), 51.4 (s), 35.2 (d, *J* = 2.6 Hz), 33.1 (d, *J* = 7.4 Hz), 25.6 (s), 21.4 (s). ^{31}P{^{1}H} NMR (202 MHz, $CDCl_3$) δ 9.16 (d, $J_{P\text{-}P}$ = 39.2 Hz), 6.50 (d, $J_{P\text{-}P}$ = 39.2 Hz).



[Pd(Ph$_2$PCH$_2$C(CH$_3$)$_2$CH$_2$PPh$_2$)(C$_6$H$_4$-2-CH$_3$)(CH$_2$CHO)] (Scheme 23). The general procedure for the synthesis of complexes of aldehyde enolates was followed with [Pd(PPh$_3$)$_2$(C$_6$H$_4$-2-CH$_3$)(F)] (0.0800 g, 0.126 mmol), dppdmp (0.0556 g, 0.126 mmol), vinyloxytrimethylsilane (20 μL, 0.33 mmol), and toluene (5 mL). The product was an off-white solid (0.074 g, 86%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.90 (dd, *J* = 4.1, 6.8 Hz, 1H, C**H**O), 7.96 (m, 2H, Ar**H**), 7.85 (m, 2H, Ar**H**), 7.56-7.34 (m, 11H, Ar**H**), 7.29 (m, 1H, Ar**H**), 7.15 (t, *J* = 6.9 Hz, 1H, Ar**H**), 6.97 (t, *J* = 6.6 Hz, 2H, Ar**H**), 6.75 (m, 2H, Ar**H**), 6.60 (t, *J* = 7.3 Hz, 1H, Ar**H**), 6.54 (t, *J* = 7.1 Hz, 1H, Ar**H**), 6.40 (m, 1H, Ar**H**), 2.47 (m, 2H, Pd(C**H**$_2$CHO)), 2.30 (m, 4H, PC**H**$_2$C(CH$_3$)$_2$C**H**$_2$P), 1.92 (s, 3H, ArC**H**$_3$), 1.09 (s, 3H, PCH$_2$C(C**H**$_3$)(CH$_3$)CH$_2$P), 0.31 (s, 3H, PCH$_2$C(CH$_3$)(C**H**$_3$)CH$_2$P). ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.6 (m), 137 (s), 135 (d, *J* = 13.4 Hz), 134.8 (d, *J* = 13.3 Hz), 132.8 (d, *J* = 11.0 Hz), 131.2 (dd, *J* = 2.5, 9.7 Hz), 130.9 (s), 129.7

(s), 128.9 (d, J = 9.5 Hz), 128.8 (s), 128.6 (d, J = 9.6 Hz), 128.4 (s), 127.1 (d, J = 9.3 Hz), 123.4 (d, J = 7.8 Hz), 122.2 (s), 38.6 (m), 36.3 (m), 35.2 (m), 30.1 (m), 26.3 (s), 11.5 (s). $^{31}P\{^{1}H\}$ NMR (202 MHz, $CDCl_3$) δ 8.36 (d, J = 39.4 Hz), 4.91 (d, J = 39.4 Hz). Anal. Calcd. $C_{38}H_{40}O_2P_2Pd$: C, 67.01; H, 5.92. Found: C, 66.97; H, 6.00.



[Pd(Ph$_2$PCH$_2$C(CH$_3$)$_2$CH$_2$PPh$_2$)(C$_6$H$_4$-4-(CH$_2$)$_3$CH$_3$)(CH$_2$C(O)CH$_3$)] (Scheme 24). The general procedure for the synthesis of complexes of aldehydes was followed with [Pd(PPh$_3$)$_2$(C$_6$H$_4$-4-(CH$_2$)$_3$CH$_3$)(F)] (0.0800 g, 0.102 mmol), dppdmp (0.045 g, 0.102 mmol), IPOTMS (37 μL, 0.21 mmol), and toluene (2 mL). The product was an off-white solid (0.062 g, 82%). ^{1}H NMR δ 7.82 (t, J = 8.6 Hz, 4H, Ar**H**), 7.46 (m, 8H, Ar**H**), 7.39-7.35 (m, 6H, Ar**H**), 7.22 (m, 2H, Ar**H**), 6.78 (t, J = 7.3 Hz, 2H, Ar**H**), 6.40 (d, J = 7.0 Hz, 2H, Ar**H**), 2.33 (m, 4H, PC**H**$_2$C(CH$_3$)$_2$C**H**$_2$P), 2.24 (t, J = 7.5 Hz, 2H, Pd(C**H**$_2$C(O)CH$_3$)), 2.16 (t, J = 9.5 Hz, 2H, C**H**$_2$CH$_2$CH$_2$CH$_3$), 1.35 (m, 2H, CH$_2$C**H**$_2$CH$_2$CH$_3$), 1.20 (m, 2H, CH$_2$CH$_2$C**H**$_2$CH$_3$), 1.02 (s, 3H, Pd(CH$_2$C(O)C**H**$_3$)), 0.85 (t, J = 7.3 Hz, CH$_2$CH$_2$CH$_2$C**H**$_3$), 0.64 (s, 3H, PCH$_2$C(C**H**$_3$)$_2$CH$_2$P). $^{31}P\{^{1}H\}$ NMR (202 MHz, $CDCl_3$) δ 9.74 (d, $J_{P\text{-}P}$ = 38.5 Hz), 6.47 (d, $J_{P\text{-}P}$ = 38.5 Hz). Anal. Calcd. $C_{42}H_{48}OP_2Pd$: C, 68.43; H, 6.56. Found: C, 68.11; H, 6.47.

The Procedure for Reductive Elimination from the Palladium Enolate Complex of Acetone (Scheme 25**).** Inside a drybox, the enolate complex of acetone (0.010 g, 0.014 mmol), PPh_3 (0.018 g, 0.068 mmol) were weighed into a 4-mL vial, and 0.4 mL of C_6D_6 was added via a syringe. The resulting solution was transferred to a J. Young NMR tube. A solution of 1,3,5-trimethoxybenzene (10-μL, 0.5 M, 0.005 mmol) was then added via and 10-μL syringe. The tube

was tightly sealed. A ^{1}H-NMR spectrum was obtained of this initial mixture. The tube was then placed in an oil bath at 100 ^{o}C for 12 h, after which time the reaction occurred to full conversion. The yield of coupled product was determined to be 93% by integrating the methylene resonances of the palladium enolate complex and the methylene protons of 4'-butylacetophenone with respect to the internal standard.

Table 16. Crystal data and structure refinement for [(dppdmp)Pd(C_6H_4-4-Cl)(CH_2CHO)].

Empirical formula	C38 H39 Cl3 O P2 Pd	
Formula weight	786.38	
Temperature	193(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 10.0140(7) Å	α= 90°.
	b = 18.2018(13) Å	β= 92.180(4)°.
	c = 20.0480(14) Å	γ = 90°.
Volume	3651.6(4) $Å^3$	
Z	4	
Density (calculated)	1.430 Mg/m^3	
Absorption coefficient	0.844 mm^{-1}	
F(000)	1608	
Crystal size	0.241 x 0.143 x 0.138 mm^3	
Theta range for data collection	1.51 to 25.60°.	
Index ranges	-12<=h<=12, -21<=k<=21, -24<=l<=24	
Reflections collected	60712	
Independent reflections	6745 [R(int) = 0.0918]	
Completeness to theta = 25.60°	98.1 %	
Absorption correction	Integration	
Max. and min. transmission	0.9431 and 0.9004	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6745 / 431 / 525	
Goodness-of-fit on F^2	1.030	
Final R indices [I>2sigma(I)]	R1 = 0.0362, wR2 = 0.0742	
R indices (all data)	R1 = 0.0638, wR2 = 0.0835	
Largest diff. peak and hole	0.495 and -0.351 $e.Å^{-3}$	

Table 17. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for [(dppdmp)Pd(C_6H_4-4-Cl)(CH_2CHO)]. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	4643(1)	2790(1)	8017(1)	23(1)
Cl(1)	611(1)	355(1)	9317(1)	41(1)
P(1)	4914(1)	3182(1)	9096(1)	23(1)
P(2)	5783(1)	3772(1)	7577(1)	24(1)
O(1)	5890(30)	1307(16)	7010(19)	64(4)
C(1)	4490(40)	2337(17)	7018(8)	34(3)
C(2)	4860(20)	1610(20)	7120(20)	43(3)
O(1B)	5953(18)	1445(13)	6804(12)	67(3)
C(1B)	4290(20)	2324(10)	7033(5)	33(2)
C(2B)	4852(14)	1626(13)	7026(12)	44(2)
C(3)	3463(3)	1964(2)	8377(2)	25(1)
C(4)	3898(3)	1289(2)	8634(2)	30(1)
C(5)	3025(3)	791(2)	8912(2)	30(1)
C(6)	1695(3)	970(2)	8942(2)	29(1)
C(7)	1217(3)	1624(2)	8680(2)	31(1)
C(8)	2101(3)	2110(2)	8404(2)	29(1)
C(9)	6173(3)	2656(2)	9564(2)	24(1)
C(10)	6838(3)	2088(2)	9247(2)	29(1)
C(11)	7796(3)	1676(2)	9587(2)	38(1)
C(12)	8108(4)	1823(2)	10246(2)	44(1)
C(13)	7468(4)	2383(2)	10566(2)	43(1)
C(14)	6502(3)	2799(2)	10233(2)	32(1)
C(15)	3413(9)	3068(8)	9585(6)	28(2)
C(16)	3340(9)	2496(8)	10042(6)	29(2)
C(17)	2187(10)	2397(7)	10396(4)	37(2)
C(18)	1108(9)	2869(7)	10293(6)	35(2)
C(19)	1181(9)	3440(6)	9836(7)	34(2)
C(20)	2334(11)	3540(7)	9482(6)	34(2)

Table 17 (continued)

C(15B)	3422(12)	3143(11)	9578(8)	27(2)
C(16B)	3201(12)	2652(10)	10094(8)	32(2)
C(17B)	1950(14)	2613(9)	10370(6)	36(2)
C(18B)	920(11)	3064(9)	10130(8)	36(2)
C(19B)	1141(13)	3554(8)	9614(9)	37(2)
C(20B)	2392(16)	3594(10)	9339(8)	33(2)
C(21)	5373(3)	4152(2)	9240(2)	28(1)
C(22)	6487(3)	4502(2)	8834(2)	29(1)
C(23)	6718(4)	5276(2)	9120(2)	42(1)
C(24)	7795(3)	4069(2)	8911(2)	33(1)
C(25)	6039(4)	4598(2)	8093(2)	29(1)
C(26)	4905(3)	4158(2)	6845(2)	26(1)
C(27)	3739(4)	4559(2)	6936(2)	40(1)
C(28)	2991(4)	4821(2)	6389(2)	43(1)
C(29)	3380(4)	4681(2)	5748(2)	41(1)
C(30)	4525(4)	4277(2)	5653(2)	36(1)
C(31)	5282(3)	4023(2)	6203(2)	31(1)
C(32)	7453(3)	3541(2)	7315(2)	26(1)
C(33)	8292(4)	4053(2)	7030(2)	36(1)
C(34)	9597(4)	3865(2)	6895(2)	47(1)
C(35)	10078(4)	3180(3)	7051(2)	46(1)
C(36)	9259(4)	2663(2)	7327(2)	41(1)
C(37)	7941(3)	2840(2)	7453(2)	32(1)
C(38)	1161(8)	5958(3)	8487(3)	54(2)
Cl(2)	498(6)	5418(3)	7829(2)	106(2)
Cl(3)	1506(9)	5427(5)	9194(3)	102(2)
C(38B)	1443(19)	5670(20)	8350(9)	74(4)
Cl(2B)	-100(20)	5661(10)	7912(8)	100(5)
Cl(3B)	1320(20)	5469(14)	9197(6)	60(4)
C(38D)	1300(90)	5130(20)	8283(16)	69(4)
Cl(2D)	1010(40)	5671(18)	7572(13)	98(6)
Cl(3D)	920(40)	5618(19)	9004(14)	82(5)

Table 18. Bond lengths [Å] and angles [°] for [(dppdmp)Pd(C_6H_4-4-Cl)(CH_2CHO)].

Pd(1)-C(3)	2.060(3)
Pd(1)-C(1B)	2.164(5)
Pd(1)-C(1)	2.165(7)
Pd(1)-P(1)	2.2841(9)
Pd(1)-P(2)	2.3130(9)
Cl(1)-C(6)	1.749(3)
P(1)-C(15B)	1.812(8)
P(1)-C(9)	1.815(3)
P(1)-C(15)	1.837(6)
P(1)-C(21)	1.845(3)
P(2)-C(32)	1.821(3)
P(2)-C(26)	1.821(3)
P(2)-C(25)	1.838(3)
O(1)-C(2)	1.19(3)
C(1)-C(2)	1.395(9)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
C(2)-H(2)	0.9500
O(1B)-C(2B)	1.247(19)
C(1B)-C(2B)	1.392(7)
C(1B)-H(1C)	0.9900
C(1B)-H(1D)	0.9900
C(2B)-H(2B)	0.9500
C(3)-C(8)	1.392(4)
C(3)-C(4)	1.397(4)
C(4)-C(5)	1.390(5)
C(4)-H(4)	0.9500
C(5)-C(6)	1.375(5)
C(5)-H(5)	0.9500
C(6)-C(7)	1.379(5)
C(7)-C(8)	1.382(5)
C(7)-H(7)	0.9500

Table 18 (continued)

C(8)-H(8)	0.9500
C(9)-C(14)	1.393(4)
C(9)-C(10)	1.396(4)
C(10)-C(11)	1.377(5)
C(10)-H(10)	0.9500
C(11)-C(12)	1.373(5)
C(11)-H(11)	0.9500
C(12)-C(13)	1.376(6)
C(12)-H(12)	0.9500
C(13)-C(14)	1.380(5)
C(13)-H(13)	0.9500
C(14)-H(14)	0.9500
C(15)-C(16)	1.3900
C(15)-C(20)	1.3900
C(16)-C(17)	1.3900
C(16)-H(16)	0.9500
C(17)-C(18)	1.3900
C(17)-H(17)	0.9500
C(18)-C(19)	1.3900
C(18)-H(18)	0.9500
C(19)-C(20)	1.3900
C(19)-H(19)	0.9500
C(20)-H(20)	0.9500
C(15B)-C(16B)	1.3900
C(15B)-C(20B)	1.3900
C(16B)-C(17B)	1.3900
C(16B)-H(16B)	0.9500
C(17B)-C(18B)	1.3900
C(17B)-H(17B)	0.9500
C(18B)-C(19B)	1.3900
C(18B)-H(18B)	0.9500
C(19B)-C(20B)	1.3900
C(19B)-H(19B)	0.9500
C(20B)-H(20B)	0.9500
C(21)-C(22)	1.543(5)

Table 18 (continued)

C(21)-H(21A)	0.9900
C(21)-H(21B)	0.9900
C(22)-C(24)	1.530(5)
C(22)-C(23)	1.536(5)
C(22)-C(25)	1.546(4)
C(23)-H(23A)	0.9800
C(23)-H(23B)	0.9800
C(23)-H(23C)	0.9800
C(24)-H(24A)	0.9800
C(24)-H(24B)	0.9800
C(24)-H(24C)	0.9800
C(25)-H(25A)	0.9900
C(25)-H(25B)	0.9900
C(26)-C(31)	1.378(4)
C(26)-C(27)	1.395(5)
C(27)-C(28)	1.389(5)
C(27)-H(27)	0.9500
C(28)-C(29)	1.380(5)
C(28)-H(28)	0.9500
C(29)-C(30)	1.381(5)
C(29)-H(29)	0.9500
C(30)-C(31)	1.393(5)
C(30)-H(30)	0.9500
C(31)-H(31)	0.9500
C(32)-C(37)	1.390(5)
C(32)-C(33)	1.392(5)
C(33)-C(34)	1.386(5)
C(33)-H(33)	0.9500
C(34)-C(35)	1.369(6)
C(34)-H(34)	0.9500
C(35)-C(36)	1.378(5)
C(35)-H(35)	0.9500
C(36)-C(37)	1.391(5)
C(36)-H(36)	0.9500
C(37)-H(37)	0.9500

Table 18 (continued)

C(38)-Cl(3)	1.738(6)
C(38)-Cl(2)	1.755(5)
C(38)-H(38A)	0.9900
C(38)-H(38B)	0.9900
C(38B)-Cl(3B)	1.747(9)
C(38B)-Cl(2B)	1.747(9)
C(38B)-H(38C)	0.9900
C(38B)-H(38D)	0.9900
C(38D)-Cl(2D)	1.746(9)
C(38D)-Cl(3D)	1.747(9)
C(38D)-H(38G)	0.9900
C(38D)-H(38H)	0.9900

C(3)-Pd(1)-C(1B)	87.5(6)
C(3)-Pd(1)-C(1)	91.3(10)
C(1B)-Pd(1)-C(1)	5.4(14)
C(3)-Pd(1)-P(1)	86.83(9)
C(1B)-Pd(1)-P(1)	174.3(6)
C(1)-Pd(1)-P(1)	175.1(8)
C(3)-Pd(1)-P(2)	174.58(9)
C(1B)-Pd(1)-P(2)	91.2(6)
C(1)-Pd(1)-P(2)	87.8(10)
P(1)-Pd(1)-P(2)	94.50(3)
C(15B)-P(1)-C(9)	105.9(6)
C(9)-P(1)-C(15)	103.4(4)
C(15B)-P(1)-C(21)	99.2(6)
C(9)-P(1)-C(21)	105.06(15)
C(15)-P(1)-C(21)	103.2(5)
C(15B)-P(1)-Pd(1)	115.0(6)
C(9)-P(1)-Pd(1)	112.39(11)
C(15)-P(1)-Pd(1)	113.6(4)
C(21)-P(1)-Pd(1)	117.76(11)
C(32)-P(2)-C(26)	106.12(15)
C(32)-P(2)-C(25)	103.97(16)
C(26)-P(2)-C(25)	100.97(15)

Table 18 (continued)

C(32)-P(2)-Pd(1)	113.84(11)
C(26)-P(2)-Pd(1)	112.00(11)
C(25)-P(2)-Pd(1)	118.48(12)
C(2)-C(1)-Pd(1)	103(2)
C(2)-C(1)-H(1A)	111.2
Pd(1)-C(1)-H(1A)	111.2
C(2)-C(1)-H(1B)	111.2
Pd(1)-C(1)-H(1B)	111.2
H(1A)-C(1)-H(1B)	109.1
O(1)-C(2)-C(1)	130(3)
O(1)-C(2)-H(2)	115.0
C(1)-C(2)-H(2)	115.0
C(2B)-C(1B)-Pd(1)	108.4(13)
C(2B)-C(1B)-H(1C)	110.0
Pd(1)-C(1B)-H(1C)	110.0
C(2B)-C(1B)-H(1D)	110.0
Pd(1)-C(1B)-H(1D)	110.0
H(1C)-C(1B)-H(1D)	108.4
O(1B)-C(2B)-C(1B)	127.5(19)
O(1B)-C(2B)-H(2B)	116.2
C(1B)-C(2B)-H(2B)	116.2
C(8)-C(3)-C(4)	116.5(3)
C(8)-C(3)-Pd(1)	116.7(2)
C(4)-C(3)-Pd(1)	126.7(2)
C(5)-C(4)-C(3)	122.0(3)
C(5)-C(4)-H(4)	119.0
C(3)-C(4)-H(4)	119.0
C(6)-C(5)-C(4)	119.2(3)
C(6)-C(5)-H(5)	120.4
C(4)-C(5)-H(5)	120.4
C(5)-C(6)-C(7)	120.7(3)
C(5)-C(6)-Cl(1)	119.0(3)
C(7)-C(6)-Cl(1)	120.3(3)
C(6)-C(7)-C(8)	119.1(3)
C(6)-C(7)-H(7)	120.4

Table 18 (continued)

C(8)-C(7)-H(7)	120.4
C(7)-C(8)-C(3)	122.4(3)
C(7)-C(8)-H(8)	118.8
C(3)-C(8)-H(8)	118.8
C(14)-C(9)-C(10)	118.5(3)
C(14)-C(9)-P(1)	122.2(3)
C(10)-C(9)-P(1)	119.3(2)
C(11)-C(10)-C(9)	120.9(3)
C(11)-C(10)-H(10)	119.5
C(9)-C(10)-H(10)	119.5
C(12)-C(11)-C(10)	119.9(4)
C(12)-C(11)-H(11)	120.1
C(10)-C(11)-H(11)	120.1
C(11)-C(12)-C(13)	120.0(3)
C(11)-C(12)-H(12)	120.0
C(13)-C(12)-H(12)	120.0
C(12)-C(13)-C(14)	120.7(4)
C(12)-C(13)-H(13)	119.6
C(14)-C(13)-H(13)	119.6
C(13)-C(14)-C(9)	119.9(3)
C(13)-C(14)-H(14)	120.0
C(9)-C(14)-H(14)	120.0
C(16)-C(15)-C(20)	120.0
C(16)-C(15)-P(1)	120.1(6)
C(20)-C(15)-P(1)	119.9(6)
C(15)-C(16)-C(17)	120.0
C(15)-C(16)-H(16)	120.0
C(17)-C(16)-H(16)	120.0
C(16)-C(17)-C(18)	120.0
C(16)-C(17)-H(17)	120.0
C(18)-C(17)-H(17)	120.0
C(17)-C(18)-C(19)	120.0
C(17)-C(18)-H(18)	120.0
C(19)-C(18)-H(18)	120.0
C(20)-C(19)-C(18)	120.0

Table 18 (continued)

C(20)-C(19)-H(19)	120.0
C(18)-C(19)-H(19)	120.0
C(19)-C(20)-C(15)	120.0
C(19)-C(20)-H(20)	120.0
C(15)-C(20)-H(20)	120.0
C(16B)-C(15B)-C(20B)	120.0
C(16B)-C(15B)-P(1)	125.4(9)
C(20B)-C(15B)-P(1)	114.1(9)
C(15B)-C(16B)-C(17B)	120.0
C(15B)-C(16B)-H(16B)	120.0
C(17B)-C(16B)-H(16B)	120.0
C(16B)-C(17B)-C(18B)	120.0
C(16B)-C(17B)-H(17B)	120.0
C(18B)-C(17B)-H(17B)	120.0
C(19B)-C(18B)-C(17B)	120.0
C(19B)-C(18B)-H(18B)	120.0
C(17B)-C(18B)-H(18B)	120.0
C(18B)-C(19B)-C(20B)	120.0
C(18B)-C(19B)-H(19B)	120.0
C(20B)-C(19B)-H(19B)	120.0
C(19B)-C(20B)-C(15B)	120.0
C(19B)-C(20B)-H(20B)	120.0
C(15B)-C(20B)-H(20B)	120.0
C(22)-C(21)-P(1)	119.6(2)
C(22)-C(21)-H(21A)	107.4
P(1)-C(21)-H(21A)	107.4
C(22)-C(21)-H(21B)	107.4
P(1)-C(21)-H(21B)	107.4
H(21A)-C(21)-H(21B)	106.9
C(24)-C(22)-C(23)	108.6(3)
C(24)-C(22)-C(21)	111.5(3)
C(23)-C(22)-C(21)	106.5(3)
C(24)-C(22)-C(25)	111.8(3)
C(23)-C(22)-C(25)	106.8(3)
C(21)-C(22)-C(25)	111.3(3)

Table 18 (continued)

C(22)-C(23)-H(23A)	109.5
C(22)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5
C(22)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
C(22)-C(24)-H(24A)	109.5
C(22)-C(24)-H(24B)	109.5
H(24A)-C(24)-H(24B)	109.5
C(22)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5
C(22)-C(25)-P(2)	118.6(2)
C(22)-C(25)-H(25A)	107.7
P(2)-C(25)-H(25A)	107.7
C(22)-C(25)-H(25B)	107.7
P(2)-C(25)-H(25B)	107.7
H(25A)-C(25)-H(25B)	107.1
C(31)-C(26)-C(27)	118.4(3)
C(31)-C(26)-P(2)	122.9(3)
C(27)-C(26)-P(2)	118.6(3)
C(28)-C(27)-C(26)	120.4(3)
C(28)-C(27)-H(27)	119.8
C(26)-C(27)-H(27)	119.8
C(29)-C(28)-C(27)	120.5(4)
C(29)-C(28)-H(28)	119.7
C(27)-C(28)-H(28)	119.7
C(28)-C(29)-C(30)	119.5(3)
C(28)-C(29)-H(29)	120.2
C(30)-C(29)-H(29)	120.2
C(29)-C(30)-C(31)	119.8(3)
C(29)-C(30)-H(30)	120.1
C(31)-C(30)-H(30)	120.1
C(26)-C(31)-C(30)	121.4(3)
C(26)-C(31)-H(31)	119.3

Table 18 (continued)

C(30)-C(31)-H(31)	119.3
C(37)-C(32)-C(33)	118.9(3)
C(37)-C(32)-P(2)	118.3(3)
C(33)-C(32)-P(2)	122.7(3)
C(34)-C(33)-C(32)	120.2(4)
C(34)-C(33)-H(33)	119.9
C(32)-C(33)-H(33)	119.9
C(35)-C(34)-C(33)	120.4(4)
C(35)-C(34)-H(34)	119.8
C(33)-C(34)-H(34)	119.8
C(34)-C(35)-C(36)	120.2(4)
C(34)-C(35)-H(35)	119.9
C(36)-C(35)-H(35)	119.9
C(35)-C(36)-C(37)	119.9(4)
C(35)-C(36)-H(36)	120.1
C(37)-C(36)-H(36)	120.1
C(32)-C(37)-C(36)	120.4(3)
C(32)-C(37)-H(37)	119.8
C(36)-C(37)-H(37)	119.8
Cl(3)-C(38)-Cl(2)	111.0(5)
Cl(3)-C(38)-H(38A)	109.4
Cl(2)-C(38)-H(38A)	109.4
Cl(3)-C(38)-H(38B)	109.4
Cl(2)-C(38)-H(38B)	109.4
H(38A)-C(38)-H(38B)	108.0
Cl(3B)-C(38B)-Cl(2B)	112.9(11)
Cl(3B)-C(38B)-H(38C)	109.0
Cl(2B)-C(38B)-H(38C)	109.0
Cl(3B)-C(38B)-H(38D)	109.0
Cl(2B)-C(38B)-H(38D)	109.0
H(38C)-C(38B)-H(38D)	107.8
Cl(2D)-C(38D)-Cl(3D)	111.0(12)
Cl(2D)-C(38D)-H(38G)	109.4
Cl(3D)-C(38D)-H(38G)	109.4
Cl(2D)-C(38D)-H(38H)	109.4

Table 18 (continued)

Cl(3D)-C(38D)-H(38H)	109.4
H(38G)-C(38D)-H(38H)	108.0

Table 19. Anisotropic displacement parameters ($Å^2x\ 10^3$) for [(dppdmp)Pd(C_6H_4-4-Cl)(CH_2CHO)]. 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}
Pd(1)	25(1)	22(1)	21(1)	0(1)	-2(1)	-1(1)
Cl(1)	34(1)	38(1)	53(1)	10(1)	7(1)	-7(1)
P(1)	22(1)	25(1)	21(1)	-1(1)	-1(1)	2(1)
P(2)	26(1)	24(1)	22(1)	2(1)	-2(1)	0(1)
O(1)	86(7)	61(8)	46(10)	-4(7)	23(8)	17(6)
C(1)	45(6)	36(4)	22(5)	-4(4)	3(4)	-11(4)
C(2)	58(5)	46(4)	24(6)	-10(5)	9(4)	-8(4)
O(1B)	76(4)	84(7)	43(7)	-17(5)	16(5)	14(5)
C(1B)	46(5)	33(3)	18(3)	-1(3)	-9(3)	-13(3)
C(2B)	59(4)	50(4)	24(6)	-13(4)	10(3)	-12(3)
C(3)	24(2)	27(2)	23(2)	-2(1)	0(1)	-3(1)
C(4)	30(2)	27(2)	33(2)	-4(2)	1(2)	3(2)
C(5)	32(2)	24(2)	32(2)	2(2)	-3(2)	1(2)
C(6)	31(2)	30(2)	24(2)	-1(2)	-1(2)	-6(2)
C(7)	23(2)	35(2)	36(2)	-2(2)	-5(2)	3(2)
C(8)	29(2)	24(2)	35(2)	5(2)	-4(2)	-2(2)
C(9)	20(2)	26(2)	26(2)	5(1)	-1(1)	-2(1)
C(10)	25(2)	28(2)	35(2)	6(2)	3(2)	-1(2)
C(11)	21(2)	34(2)	59(3)	10(2)	4(2)	6(2)
C(12)	24(2)	44(3)	63(3)	23(2)	-12(2)	-3(2)
C(13)	43(2)	51(3)	32(2)	18(2)	-14(2)	-18(2)
C(14)	31(2)	37(2)	27(2)	2(2)	0(2)	-5(2)
C(15)	23(3)	29(4)	33(3)	-14(3)	2(3)	3(3)
C(16)	26(3)	30(4)	32(3)	-9(3)	12(3)	1(3)
C(17)	33(4)	34(5)	44(3)	-5(3)	9(3)	5(3)
C(18)	22(3)	40(5)	44(4)	-2(4)	8(3)	2(3)
C(19)	23(3)	37(4)	42(5)	-6(4)	1(3)	8(3)
C(20)	30(3)	32(3)	41(4)	-8(3)	5(3)	2(3)

Table 19 (continued)

C(15B)	23(3)	26(4)	33(4)	-11(3)	4(3)	-3(3)
C(16B)	27(3)	31(5)	40(4)	-3(4)	11(3)	6(3)
C(17B)	29(4)	34(5)	46(4)	3(4)	15(4)	6(4)
C(18B)	24(4)	37(5)	48(5)	2(4)	12(4)	5(4)
C(19B)	28(3)	39(4)	44(6)	0(4)	-3(4)	4(3)
C(20B)	25(3)	35(4)	40(4)	-6(4)	4(3)	1(3)
C(21)	33(2)	25(2)	24(2)	-5(1)	-5(2)	3(2)
C(22)	33(2)	26(2)	27(2)	0(2)	-2(2)	-5(2)
C(23)	57(3)	34(2)	35(2)	-4(2)	-6(2)	-13(2)
C(24)	29(2)	38(2)	32(2)	2(2)	-4(2)	-6(2)
C(25)	37(2)	24(2)	27(2)	0(2)	-3(2)	-4(2)
C(26)	29(2)	24(2)	25(2)	0(1)	-2(1)	-6(2)
C(27)	35(2)	53(3)	31(2)	5(2)	2(2)	7(2)
C(28)	28(2)	53(3)	48(3)	9(2)	-5(2)	10(2)
C(29)	39(2)	47(3)	36(2)	10(2)	-14(2)	-3(2)
C(30)	48(2)	38(2)	23(2)	1(2)	-5(2)	-12(2)
C(31)	35(2)	27(2)	30(2)	-1(2)	-2(2)	-3(2)
C(32)	25(2)	33(2)	19(2)	-1(2)	-2(1)	0(2)
C(33)	35(2)	41(2)	31(2)	8(2)	-3(2)	-4(2)
C(34)	31(2)	70(3)	42(2)	9(2)	1(2)	-12(2)
C(35)	27(2)	76(3)	35(2)	2(2)	-1(2)	9(2)
C(36)	40(2)	51(3)	33(2)	-2(2)	-8(2)	15(2)
C(37)	32(2)	38(2)	25(2)	-1(2)	-3(2)	0(2)
C(38)	72(4)	41(4)	49(4)	-5(3)	4(3)	1(3)
Cl(2)	105(3)	146(4)	68(2)	-48(2)	17(2)	-46(2)
Cl(3)	153(5)	70(3)	83(3)	19(2)	-15(3)	24(3)
C(38B)	90(7)	71(8)	60(7)	-4(7)	9(7)	-5(7)
Cl(2B)	132(10)	92(8)	76(7)	5(6)	-3(7)	-68(7)
Cl(3B)	90(7)	53(7)	37(6)	-1(6)	21(6)	26(6)
C(38D)	83(8)	68(8)	56(8)	-7(8)	7(8)	-7(8)
Cl(2D)	122(12)	98(11)	76(10)	-23(10)	23(10)	-16(10)
Cl(3D)	106(10)	67(10)	73(10)	5(9)	0(9)	11(9)

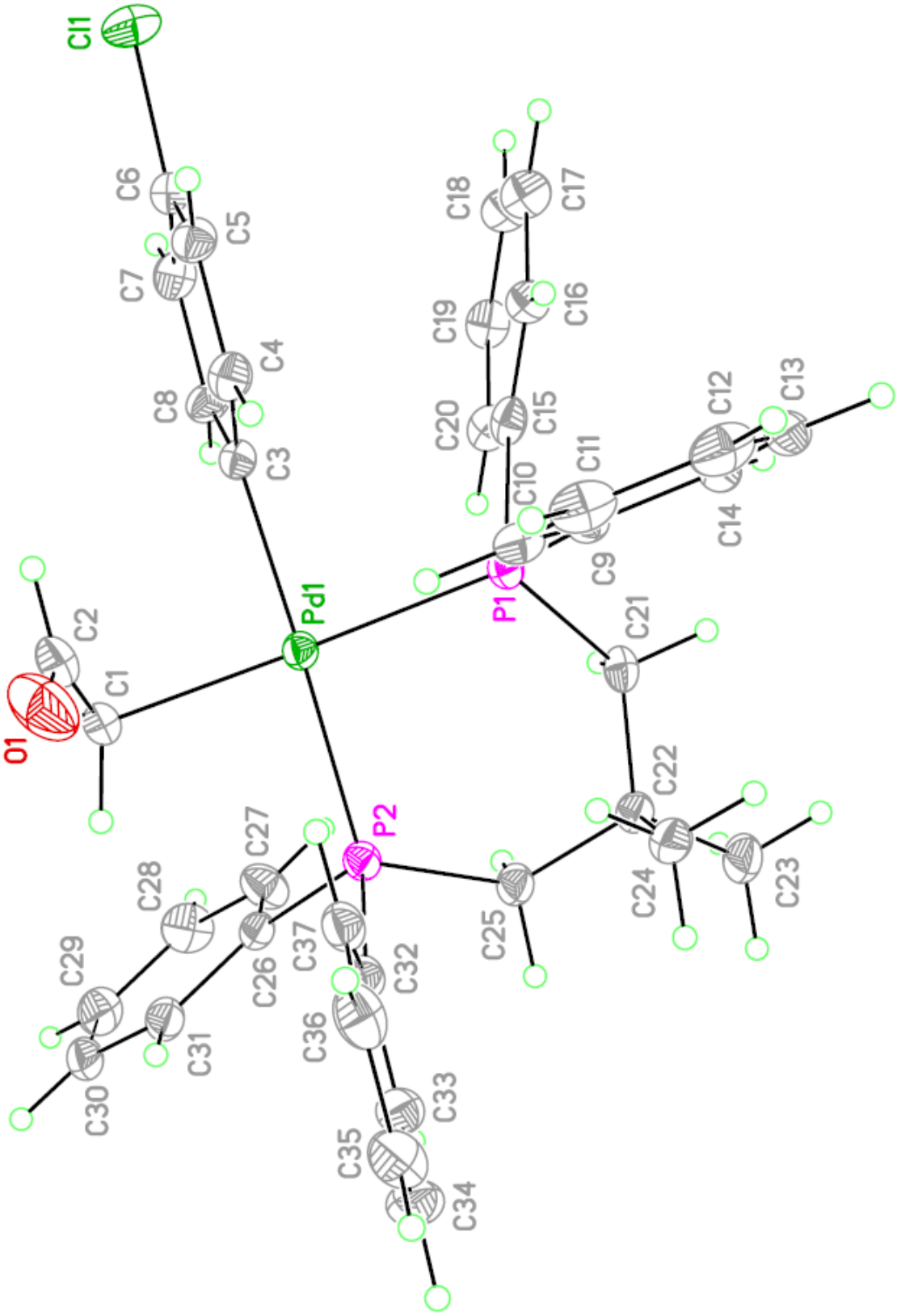
Table 20. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10 ^{3}) for [(dppdmp)Pd(C_6H_4-4-Cl)(CH_2CHO)].

	x	y	z	U(eq)
H(1A)	3560	2373	6830	41
H(1B)	5096	2591	6717	41
H(2)	4200	1301	7298	51
H(1C)	3316	2293	6928	39
H(1D)	4697	2639	6694	39
H(2B)	4341	1242	7211	53
H(4)	4819	1166	8620	36
H(5)	3343	332	9079	35
H(7)	293	1739	8689	38
H(8)	1767	2561	8226	35
H(10)	6627	1984	8791	35
H(11)	8240	1291	9365	46
H(12)	8765	1538	10481	53
H(13)	7693	2485	11021	51
H(14)	6062	3182	10460	38
H(16)	4078	2174	10113	35
H(17)	2137	2006	10709	44
H(18)	320	2801	10535	42
H(19)	443	3763	9766	40
H(20)	2384	3930	9170	41
H(16B)	3905	2344	10258	39
H(17B)	1799	2277	10722	43
H(18B)	65	3037	10318	43
H(19B)	437	3863	9450	44
H(20B)	2543	3929	8986	40
H(21A)	4555	4450	9160	33
H(21B)	5636	4205	9718	33

Table 20 (continued)

H(23A)	7439	5517	8885	63
H(23B)	6967	5242	9596	63
H(23C)	5896	5565	9061	63
H(24A)	8494	4322	8671	50
H(24B)	7664	3575	8728	50
H(24C)	8063	4035	9386	50
H(25A)	6713	4907	7878	35
H(25B)	5190	4877	8078	35
H(27)	3454	4653	7374	48
H(28)	2205	5099	6456	52
H(29)	2864	4860	5376	49
H(30)	4796	4173	5214	44
H(31)	6074	3751	6134	37
H(33)	7971	4532	6927	43
H(34)	10160	4214	6693	57
H(35)	10980	3060	6968	55
H(36)	9593	2186	7430	50
H(37)	7372	2481	7635	38
H(38A)	1993	6198	8348	65
H(38B)	514	6348	8595	65
H(38C)	2044	5310	8148	89
H(38D)	1851	6164	8305	89
H(38G)	2246	4977	8312	82
H(38H)	738	4684	8250	82

ORTEP diagram of [(dppdmp)Pd(C_6H_4-4-Cl)(CH_2CHO)] 35% probability ellipsoids.



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Chapter 4. Palladium-Catalyzed Coupling of Ammonia with Aryl Chlorides, Bromides, Iodides and Sulfonates: A General Method for the Preparation of Primary Arylamines

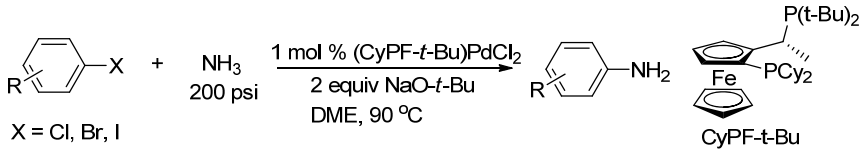
4.1. Introduction

Although ammonia is among the least expensive bulk chemicals, its application in transition-metal catalysis is rare. Because of ammonia's high basicity, small size and strong N-H bond (107 kcal/mol),[1] most of its reactions with transition metal complexes yield Lewis acid-base adducts[2] that are often highly stable. Thus, catalyst turnover in the presence of ammonia has been difficult to achieve. There are only a few transition-metal-catalyzed processes that incorporate ammonia into more complex molecules, and most of these reactions were published recently. These reactions include rhodium-catalyzed reductive amination of aldehydes,[3] iridium-catalyzed reductive amination of α-keto acids,[4] rhodium- and iridium-catalyzed hydroaminomethylation of olefins,[5] ruthenium-catalyzed synthesis of primary amines from primary alcohols and ammonia,[6] gold-catalyzed hydroamination of alkynes and allenes,[7] palladium- and iridium-catalyzed allylic amination,[8-10] and copper-[11-13] and palladium-catalyzed[14-16] coupling of ammonia with aryl halides.

The copper- and palladium-catalyzed coupling of ammonia with aryl halides has attracted attention recently because of the value of primary arylamines in the preparation of agrochemicals, dyes and pharmaceuticals.[17,18] The copper-catalyzed method has been known since the 1960s,[19] but significant progress has only been made recently.[11-13] In spite of the recent advances, copper-catalyzed coupling with ammonia is limited in scope and requires high loadings of copper and ligand. The copper-catalyzed coupling does not occur in high yield with

electron-rich aryl bromides or *ortho*-substituted aryl bromides or iodides. The copper-catalyzed reactions also do not occur in substantial yield with aryl chlorides or sulfonates, which are less expensive and more accessible than aryl iodides and bromides or aryl triflates, respectively.[11] Finally, catalyst loadings of greater than 10 mol % is usually required. This high loading can complicate isolation of basic products from the copper catalyst.

The palladium-catalyzed coupling of ammonia with aryl halides was first achieved in our laboratory in 2006 (Scheme 26).[14] This process occurred with complexes generated from a Pd(II) precursor ligated by the electron-rich and sterically bulky Josiphos ligand (CyPF-*t*-Bu). The reactivity of the catalyst containing this ligand for the arylation of ammonia has been attributed to two factors.[20] First, the rigid backbone that arises from the orientation of the methyl and ferrocenyl group directs the phosphorus atoms and their electron pairs toward the metal center, creating tight chelation and resulting stability toward displacement by strong Lewis bases, such as ammonia. Second, the strong electron-donation and steric bulk of the ligand make palladium(0) complexes of it highly reactive toward oxidative addition of aryl chlorides and tosylates.[21] This work and subsequent reports by Buchwald[15] in 2007 and Beller[16] in 2009 constitute the only reported palladium-catalyzed couplings of ammonia with aryl halides.[15] After this work was reported, Stradiotto and coworkers reported a highly active P,N-ligand for the coupling of ammonia with aryl halides and sulfonates in excellent yields.[22,23]



Scheme 26.

Although palladium-catalysts have the potential to create a process that occurs with broader scope than the copper-catalyzed reactions, a detailed evaluation of the reaction scope was not included in the first reports of palladium-catalyzed coupling of ammonia. Only one example of the reaction of an aryl chloride was reported in our preliminary communication.[14] No reactions to form isolated primary arylamines from chloroarenes were included in Buchwald's report although sequences that form four mixed di- and triarylamines were initiated with chloroarenes. The reactions reported by Beller require temperatures of 120 °C, and were conducted under 10 bar of N_2 to obtain good yield of primary arylmines.[16] Moreover, the coupling of aryl sulfonates with ammonia was not reported; cleavage of the S-O bond of the sulfonyl group was reported to occur in the presence of ammonia and the strong base NaO-*t*-Bu faster than C-N coupling.[14] For similar reasons, aryl halides containing base-sensitive functional groups such as esters, nitriles, and ketones containing enolizable protons underwent reactions at the functional group faster than they underwent C-N coupling. Finally, our studies in 2006 were conducted with a high pressure of ammonia in order to achieve good selectivity for formation of the monoarylamine over the corresponding diarylamine.

To address these limitations, we studied reactions in the presence of a catalyst that would react under milder conditions than the one we used for our initial studies. We recently reported a combination of Pd(0) precursor and the Josiphos ligand that circumvents the difficulties with generation of the active catalyst from the typical Pd(0) source $Pd_2(dba)_3$ or the typical Pd(II) source $Pd(OAc)_2$.[24] With the strongly electron-donating Josiphos ligand, back-donation into the remaining dba ligand of the (CyPF-*t*-Bu)Pd(dba) leads to slow dissociation of dba to generate the catalytically active (CyPF-*t*-Bu)Pd(0). With a reagent lacking β-hydrogens, a clear pathway to generate the Pd(0) species from $Pd(OAc)_2$ and the Josiphos ligand does not exist. A catalyst

precursor, in combination with CyPF-*t*-Bu, that generates a higher concentration of active catalyst could allow the coupling of ammonia to occur with less reactive aryl chlorides and tosylates. Identification of such a catalyst catalyst could also allow the reactions to be conducted under conditions that are mild enough to be compatible with base-sensitive functional groups and under conditions involving a lower pressure of ammonia.

Herein, we report a general method for the coupling of ammonia with aryl chlorides, bromides, iodides and tosylates catalyzed by a combination of $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu. The coupling occurs in high yield and with high selectivity for formation of the primary arylamines in the presence of catalyst loadings as low as 0.1 mol %. The substrate scope now includes a wide range of aryl bromides and chlorides, including those containing base-sensitive functional groups. For the first time, the coupling of aryl tosylates and ammonia is also shown to occur in good yield. The utility of this catalyst for sequential, one-pot arylations of ammonia to prepare unsymmetrical diarylamines and for the arylation of ammonia to form *N*-aryl imides, amides, and carbamates by a one-pot two-step sequence is demonstrated. Preliminary mechanistic studies reveal the origins of the greater reactivity of this catalyst system, relative to that of the CyPF-*t*-Bu systems reported previously.

4.2. Results and Discussion

4.2.1. Identification of Conditions for the Amination of 1-Bromo-4-tert-butylbenzene in a 0.5 M Solution of Ammonia.

To identify the conditions for coupling of aryl halides with ammonia at ambient pressure, we examined reactions of the electronically neutral and sterically unhindered 1-bromo-4-*tert*-butylbenzene in 0.5 M solutions of ammonia in either 1,2-dimethoxyethane (DME) or 1,4-dioxane. These two solvents were chosen because previous studies of the coupling of aryl halides

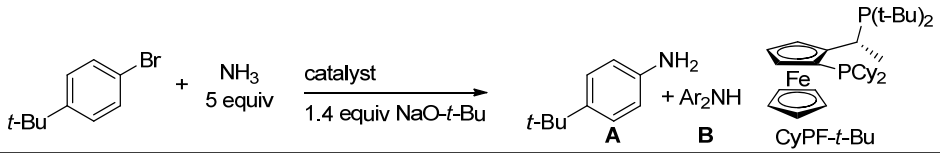
with ammonia in our laboratory showed that reactions in ethereal solvents occurred to better conversions than those in hydrocarbon solvents, such as toluene. Catalysts generated from either one-component precatalysts or combinations of a precatalyst and the CyPF-*t*-Bu ligand were tested. NaO-*t*-Bu was used as the base. The conversion of the aryl halide and the selectivity for formation of monoarylamines versus diarylamines were measured by GC and ^{1}H NMR analysis respectively.

We compared reactions initiated with CyPF-*t*-Bu as ligand and the commercially available $Pd(OAc)_2$ or $Pd_2(dba)_3$ as palladium source with reactions initiated with the one-component catalyst (CyPF-*t*-Bu)$PdCl_2$ that we used in our initial work on the coupling of ammonia.[14] Catalysts generated from $Pd(OAc)_2$ exhibited much lower reactivity than those generated from $Pd(dba)_2$ or (CyPF-*t*-Bu)$PdCl_2$. The test reaction catalyzed by the complex generated from equimolar amounts of $Pd(OAc)_2$ and CyPF-*t*-Bu occurred to only 50% conversion after 12 h (Table 21, entry 1), whereas reactions catalyzed by complexes generated from $Pd(dba)_2$, (CyPF-*t*-Bu)$PdCl_2$ or $Pd[P(o\text{-tol})_3]_2$ as palladium sources occurred to full conversion after 12 h (Table 1, entries 2-6). This difference in reactivity contrasts results recently reported by our group on the coupling of heteroaryl chloride with primary alkylamines[20] in which complexes generated from $Pd(OAc)_2$ were much more reactive than those generated from $Pd(dba)_2$.

Of the reactions that occurred to full conversion, those conducted in 1,4-dioxane occurred with much greater selectivity for formation of monoarylamine versus diarylamine than did reactions conducted in DME (entries 3 and 5 vs. 4 and 6). In 1,4-dioxane, high selectivity for formation of the primary arylamine was observed from reactions catalyzed by complexes generated from $Pd_2(dba)_3$ or $Pd[P(o\text{-tol})_3]_2$ (entries 2 and 5). To determine the method that

generates the most active catalyst, we studied reactions conducted with $Pd_2(dba)_3$ or $Pd[P(o\text{-}tol)_3]_2$ as precatalyst under the conditions of entries 2 and 5 of Table 21 for the coupling of 4-chlorotoluene with ammonia. Although both systems led to reactions of aryl bromides to high conversions, the system comprising the combination of $Pd[P(o\text{-}tol)_3]_2$ and CyPF-*t*-Bu was substantially more active than that comprising $Pd_2(dba)_3$ and CyPF-*t*-Bu for the coupling of ammonia with aryl chlorides. More specifically, the reaction of 4-bromo-*tert*-butylbenzene with ammonia catalyzed by the catalyst generated from $Pd[P(o\text{-}tol)_3]_2$ and CyPF-*t*-Bu occurred with conversion and selectivity that was similar to that of the reaction catalyzed by complexes generated from $Pd_2(dba)_3$ and CyPF-*t*-Bu. However, the reaction of 4-chlorotoluene with ammonia in the presence of 0.5 mol % of $Pd[P(o\text{-}tol)_3]_2$ and CyPF-*t*-Bu occurred to full conversion after 12 h, whereas the reaction catalyzed by 0.5 mol % of the combination of $Pd_2(dba)_3$ and CyPF-*t*-Bu occurred to less than 10% conversion of 4-chlorotoluene after 24 h.

Table 21. Effects of Precatalysts and Solvents on the Coupling of 4-Bromo-*tert*-butylbenzene with Ammonia in 0.5 M Solutions[a]



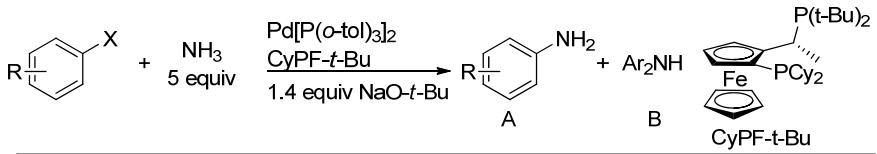
entry	catalyst	loading (%)	solvent	conc. [M][b]	conversion (%)[c]	A:B[d]
1	$Pd(OAc)_2$/CyPF-*t*-Bu	0.5	1,4-dioxane	0.038	50	–
2	$Pd_2(dba)_3$ / CyPF-*t*-Bu	0.25[e]	1,4-dioxane	0.038	100	17:1
3	(CyPF-*t*-Bu)$PdCl_2$	0.5	1,4-dioxane	0.038	100	7:1
4	(CyPF-*t*-Bu)$PdCl_2$	2.0	DME	0.038	100	0.7:1.0
5	$Pd[P(o\text{-}tol)_3]_2$/CyPF-*t*-Bu	0.5	1,4-dioxane	0.038	100	>30:1
6	$Pd[P(o\text{-}tol)_3]_2$/CyPF-*t*-Bu	0.5	DME	0.038	100	0.7:1.0

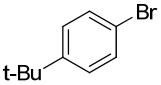
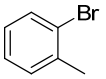
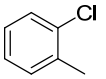
[a]Reactions conducted with 1:1 ratio of metal to ligand, 0.5 mmol aryl bromide, 5 mL of 0.5 M ammonia solution, 1.4 equiv NaOtBu in 1,4-dioxane. [b]Temperature of bath. [c]Determined by GC analysis. [d]Determined by ^{1}H NMR spectroscopy.

Having established that the combination of $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu provides the more active catalyst system and that a 0.5 M solution of ammonia in dioxane is a suitable reaction medium for the coupling of ammonia with aryl chlorides and bromides, we sought reaction conditions for a general coupling of aryl halides with ammonia at low catalyst loading. We identified two general sets of conditions. The first set of reaction conditions was identified for reactions of *meta*- and *para*-substituted aryl halides. A substrate concentration of 0.038-0.05 M was used to ensure an excess of ammonia is present and a catalyst loading of 0.5 mol % was used to ensure suitable rates. At this concentration and catalyst loading, the reaction of 4-*tert*-butylbenzene occurred to full conversion and high selectivity (Table 22, entry 1). Reactions of these classes of aryl bromides conducted with catalyst loadings below 0.5 mol % occurred to low conversion (Table 22, entry 2). Reactions conducted with higher concentrations of the bromoarene (0.1 M) occurred to completion with only 0.25 mol % of catalyst, but the selectivity for the monoarylation product was lower (Table 22, entry 3). Thus, we found the optimal concentration and catalyst loading for reactions of *meta*- and *para*-substituted aryl halides to be 0.038-0.05 M and 0.5 mol % respectively.

For reactions of *ortho*-substituted aryl halides, a second set of conditions was identified. Reactions of 2-bromotoluene and 2-chlorotoluene with ammonia at 0.1 M of the haloarene occurred with similar selectivities to the same reactions at 0.05 M concentration (Table 22, entries 4 and 5). At the 0.1 M concentration, these reactions occurred to full conversion of the aryl halides in the presence of only 0.1 mol % catalyst.

Table 22. Determination of the Catalyst Loading Required for the Coupling of Ammonia with *ortho*-substituted Aryl Halides[a]



entry	aryl halide	loading (%)	concentration [M]	T [°C][b]	*t* [h]	conv. (%)[c]	A:B[d]
1		0.5	0.04	80	24	100	>30:1
2		0.25	0.04	80	24	<10	–
3		0.1	0.1	100	24	100	2:1
4		0.1	0.1	100	24	100	17:1
5		0.1	0.1	100	24	100	17:1

[a]Reactions conducted with 1:1 ratio of metal to ligand, 0.5 mmol aryl bromide, 5 mL of 0.5 M ammonia solution, 1.4 equiv NaOtBu in 1,4-dioxane. [b]Temperature of bath. cDetermined by GC analysis. dDetermined by 1H NMR spectroscopic analysis.

4.2.2. Scope of the Coupling of Aryl Bromides with Ammonia.

Using the reaction conditions identified in section 2.1, we evaluated the scope of the coupling of aryl bromides with ammonia as a 0.5 M solution in dioxane. The results of this study are summarized in Table 23 and 4. The scope of these reactions encompasses those of aryl bromides that are electron-rich, electron-neutral and electron-poor and those of aryl bromides that have a range of substitution patterns.

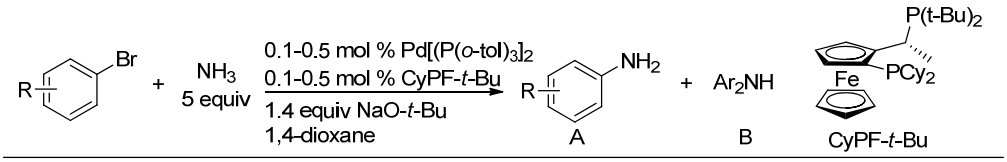
4.2.2.1. Ortho-Substituted Aryl Bromides

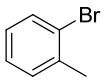
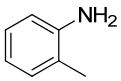
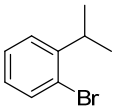
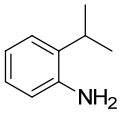
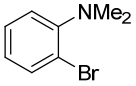
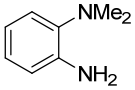
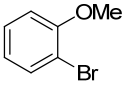
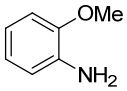
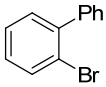
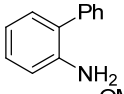
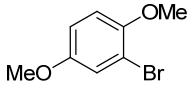
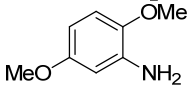
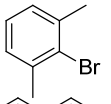
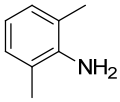
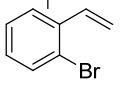
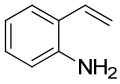
The reactions of ortho-substituted aryl bromides with ammonia encompass those of substrates containing a wide range of functional groups. For example, ammonia coupled with electron-neutral and sterically hindered bromoarenes (Table 23, entries 1 and 3), as well as ortho-substituted aryl bromides containing aromatic and vinylic substituents (Table 23, entries 9 and

13) in excellent yield to form the primary arylamine products in the presence of 0.5 mol % of the catalyst. It is notable that the reaction of 2-bromostyrene occurred without substantial polymerization. Electron-rich, ortho-substituted aryl halides also coupled with ammonia in high yield to form the primary arylamine. For example, the reactions of ammonia with 2-bromo-*N*,*N*-dimethylaniline and 2-bromoanisole occurred with 0.5 mol % of the catalyst at 80 °C for only 4 h to afford excellent yield of the coupled product (Table 23, entries 5 and 7). 2-Bromo-*m*-xylene is a challenging substrate for both palladium- and copper-catalyzed amination chemistry because of its steric bulk.[13] Nevertheless, the reaction of this substrate with ammonia occurred with 0.5 mol % of the catalyst at 100 ^{o}C for 15 h to afford excellent yield of the primary arylamine product (Table 23, entry 12).

Reactions of ammonia with a 0.1 M concentration of ortho-substituted aryl halides even occurred with catalyst loadings down to 0.1 mol %. Reactions conducted with 0.1 mol % catalyst required a longer reaction time (12 h) and a higher temperature (100 ^{o}C) for complete conversion of ortho-substituted aryl bromides than those conducted with 0.5 mol % of catalyst. However, yields and selectivities of the primary arylamines remained high for substrates containing alkyl, aryl, amino, and methoxyl substituents (Table 23, entries 2, 4, 6, 8, 10 and 11). These reactions were conducted with the lowest loadings of any copper or palladium catalyst for the coupling of aryl halides with ammonia.

Table 23. Coupling of ortho-Substituted Aryl Bromides with Ammonia.[a]



entry	aryl bromide	loading (%)	concentration [M]	T [°C][b]	*t* [h]	product	yield (%)[c]	A:B[d]
1		0.5	0.038	80	4		83	>50:1
2		0.1	0.1	100	12		71	17:1
3		0.5	0.07	80	4		93	>50:1
4		0.1	0.1	100	12		84	>50:1
5		0.5	0.07	80	4		89	>50:1
6		0.1	0.1	100	12		82	>50:1
7		0.5	0.038	80	4		85	>50:1
8		0.1	0.1	100	12		95	>50:1
9		0.5	0.038	80	12		96	>50:1
10		0.1	0.1	100	24		99	>50:1
11		0.1	0.1	100	12		95	>50:1
12		0.5	0.1	80	15		88	>50:1
13		0.5	0.038	80	5		66	--

[a]Reactions conducted with 1:1 ratio of metal to ligand, 0.5 mmol aryl bromide, 5 mL of 0.5 M ammonia solution, 1.4 equiv NaOtBu in 1,4-dioxane. [b]Temperature of bath. cIsolated yield after purification by flash column chromatography. dDetermined by 1H NMR spectroscopic analysis.

4.2.2.2. Meta- and para-Substituted Aryl Bromides

In our prior work, the reactions of sterically unhindered aryl bromides occurred with lower selectivity for formation of monarylamine versus diarylamines, especially when a low pressure of ammonia was used.[14,15] Under our new conditions, however, high selectivity was observed for the formation of primary arylamines from reactions of *para*-, as well as *meta*-substituted aryl bromides, with ammonia as a 0.5 M solution in dioxane. These results are

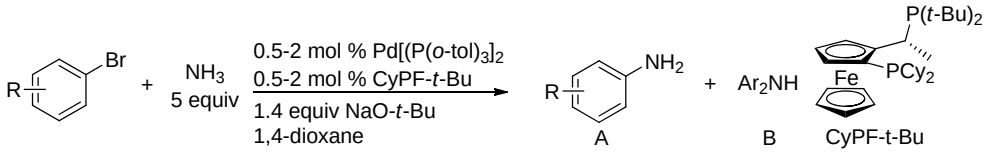
summarized in Table 24. Electron-neutral 1-bromo-4-*t*-butylbenzene and 1-bromo-3,5-di-*t*-butylbenzene (0.134 g, 0.500 mmol) coupled with ammonia to afford primary arylamine products in 88% and 78% yield respectively (entries 1 and 2). 4-Bromobiphenyl also coupled with ammonia in excellent yield (entry 3).

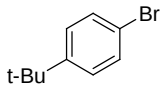
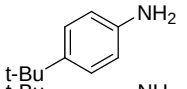
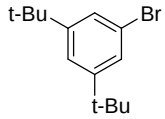
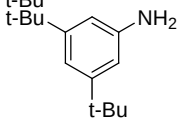
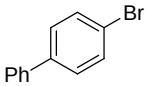
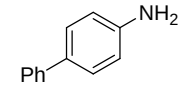
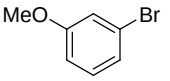
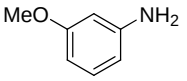
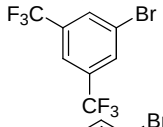
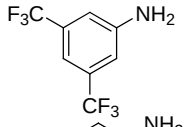
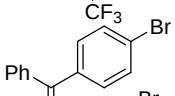
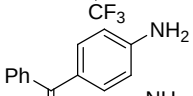
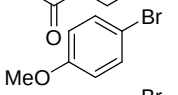
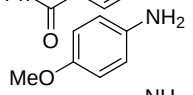
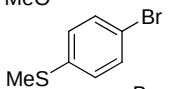
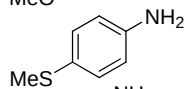
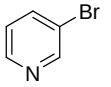
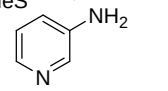
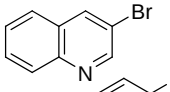
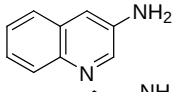
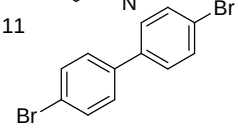
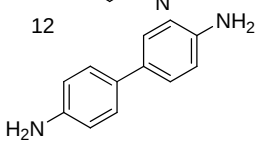
The scope of this process encompasses aryl bromides with a wide range of electronic properties. For example, reactions of electron-deficient 3-bromoanisole and 3,5-bis(trifluoromethyl)bromobenzene with ammonia occurred with 0.5 mol % catalyst loading at substrate concentration of 0.038 M to give the primary arylamine products in excellent yield and selectivity (entries 4 and 5). An aryl bromide containing keto functionality also coupled with ammonia in high yield (entry 6). Reactions of electron-rich aryl bromides with ammonia occurred to give good yield of aniline product, but required somewhat higher temperatures and catalyst loadings (*vide infra*). However, 4-bromoanisole and 4-bromothioanisole still coupled with ammonia in the presence of 1 mol % of the catalyst at 90 – 100 ^{o}C to give 53% and 91% yield respectively (entries 7 and 8).

Heteroaryl bromides also reacted with ammonia in the presence of Pd[P(*o*-tol)$_3$]$_2$ and CyPF-*t*-Bu to give valuable heteroaryl amines in good yields. For example, reactions of 3-bromopyridine and 3-bromoquinoline with ammonia in the presence of 0.5 mol % of the catalyst occurred to full conversion after 12 h at 80 °C to give the primary arylamine products in good yields (entries 9 and 10). 4,4'-Benzidine is the core motif of *N*,*N*'-bis(3-methylphenyl)-*N*,*N*'-diphenylbenzidine (TPD), which is used in hole-transport layer in electroluminescent devices.[25] The coupling of 4,4'-dibromobiphenyl with ammonia to form 4,4'-benzidine by formation of two C-N bonds occurred with 2.0 mol % of the catalyst at 100 ^{o}C in good yield. Overall, the results

presented in Table 24 demonstrate the broadest substrate scope under the mildest conditions for the coupling of ammonia with aryl bromides with any current catalyst.

Table 24. Coupling of *meta*- and *para*-Substituted Aryl Bromides with Ammonia.[a]



entry	aryl bromide	loading (%)	concentration [M]	T [°C][b]	*t* [h]	product	yield (%)[c]	A:B[d]
1		0.5	0.038	80	6		88	19:1
2		0.5	0.038	80	5		78	--
3		0.5	0.038	80	5		98	--
4		0.5	0.038	80	5		99	>50:1
5		0.5	0.038	80	5		61	12:1
6		0.5	0.038	80	12		77	--
7		1.0	0.05	100	15		53	9:1
8		1.0	0.05	90	15		91	>50:1
9		0.5	0.038	80	12		60	--
10		0.5	0.05	80	12		64	--
11		2.0	0.05	100	12		79	>50:1

[a]Reactions conducted with 1:1 ratio of metal to ligand, 0.5 mmol aryl bromide, 5 mL of 0.5 M ammonia solution, 1.4 equiv NaOtBu in 1,4-dioxane. [b]Temperature of bath. cIsolated yield after purification by flash column chromatography. [d]Determined by ^{1}H NMR spectroscopic analysis.

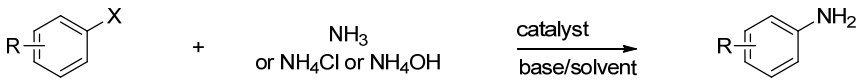
4.2.2.3. Comparison to the Reactions Catalyzed by Copper Catalysts

Chang,[12] Taillefer[11] and Thadani[13] recently reported copper-catalyzed coupling of aryl halides with ammonia. Chang showed that complexes generated from 20 mol % CuI and 40 mol % of L-proline catalyze the coupling of aryl iodides and electron-poor aryl bromides with NH_4Cl or NH_4OH. Taillefer reported the coupling of aryl iodides and aryl bromides with NH_4OH in the presence of 10 mol % $Cu(acac)_2$ and 40 mol % 2,4-pentadione. Although the reactions conducted with 2,4-pentadione as the ligand precursor occur with broader scope than those with proline, both papers reported that aryl iodides and bromides containing ortho-substituents coupled with ammonia in low yields. In contrast to these two reports, Thadani and coworkers recently reported that the copper-carbene complex **3** catalyzes the coupling of *ortho*-substituted as well as electron-rich aryl bromides.

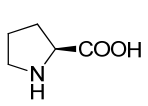
Table 25 provides a comparison of the activity of the palladium catalyst generated from $Pd[P(o\text{-}tol)_3]_2$ and CyPF-*t*-Bu (condition D) to the copper catalysts generated *in situ* from CuI and L-proline **1** (condition A) or 2,4-pentadione **2** (condition B) or the discrete complex **3** containing an *N*-heterocyclic carbene ligand (condition C) for the reactions of ammonia with ortho-substituted 2-iodotoluene and 2-bromoanisole and electron-neutral 4-bromo-*tert*-butylbenzene. The data in this table were obtained from reactions conducted under the reported optimal conditions for each of the catalyst systems.[11-13] The reaction of 2-iodotoluene with ammonia in dioxane in the presence of 0.5 mol % of an equimolar amount of $Pd[P(o\text{-}tol)_3]_2$ and CyPF-*t*-Bu gave 73% of o-toluidine. The reaction of 2-iodotoluene with ammonia in water catalyzed by copper complexes containing L-proline **1** and 2,4-pentadione **2** gave substantially lower yields. The reaction conducted with complex **3** did not occur to form any coupled product that could be observed by GC/MS.[26] Likewise, the coupling of the *ortho*-substituted 2-

bromoanisole with ammonia in the presence of the copper catalysts occurred with yields that are substantially lower than those of the reaction catalyzed by 0.1 mol% of an equimolar amount of $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu (Table 25, entry 2).

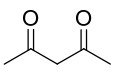
Table 25. Comparison of the Activity of Copper Catalysts versus $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu in the Coupling of Ammonia with Aryl Halides



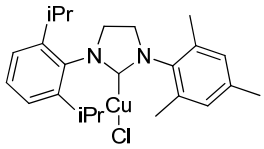
entry	aryl halide	conditions A[a]	conditions B[b]	conditions C[c]	conditions D[d]
1	X = I, R = 2-Me	17%	30%	--[e]	73%
2	X = Br, R = 2-OMe	trace	--[e]	--[e]	95%
3	X = Br, R = 4-*t*Bu	84%	55%	--[e]	88%



1, L-proline



2, 2,4-pentadione



3

[a]Reaction conditions A: 0.5 mmol aryl halide, 0.65 mmol NH_4OH, 0.1 mmol CuI, 0.2 mmol L-proline, 1.5 mmol K_2CO_3 , 1 mL DMSO, 0.05 mL H_2O, 80 °C, 24 h. [b]Reaction conditions B: 1 mmol aryl halide, 300 mL NH_4OH, 0.1 mmol $Cu(acac)_2$, 0.4 mmol 2,4-pentadione, 2 mmol Cs_2CO_3, 2 mL DMF, 90 °C, 24 h. [c]Reaction conditions C: 1 mmol aryl halide, 0.05 mmol 3, 2 mmol K_2CO_3, 5 mL (1:1, MeOH/NMP), 90 °C, 24 h. [d]Reaction conditions D: 0.5 mmol aryl halide, 5 mL of 0.5 M ammonia in dioxane, 0.7 mmol NaO*t*Bu; entry 1: 0.0025 mmol $Pd[P(o\text{-tol})_3]_2$/CyPF-*t*-Bu, 5 ml of 0.5 M ammonia in dioxane, 80 °C; entry 2: 0.0005 mmol $Pd[P(o\text{-tol})_3]_2$/CyPF-*t*-Bu, 5 ml of 0.5 M ammonia in dioxane, 100 °C; entry 3: 0.0025 mmol $Pd[P(o\text{-tol})_3]_2$/CyPF-*t*-Bu, 5 ml of 0.5 M ammonia in dioxane, 5 mL dioxane, 80 °C. [e]No product observed by GC/MS.

The differences in yields from the reactions of sterically unhindered substrates with the different catalysts were less dramatic, but the reaction catalyzed by 0.5 mol% of $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu still formed the primary arylamine in the highest yield. The coupling of 4-bromo-*tert*-butylbenzene with ammonia in the presence of copper complexes containing 40 mol % **1** and 40 mol % **2** gave 84% and 55% yield of 4-*tert*-butylaniline, respectively. Again, the reaction catalyzed by complex **3** afforded no coupled product that could be observed by GC/MS. In

contrast, the reaction catalyzed by 0.5 mol% of $Pd[P(o\text{-}tol)_3]_2$ and CyPF-*t*-Bu formed the primary arylamine in 88% yield.

4.2.3. Scope of the Coupling of Ammonia with Aryl Chlorides and Aryl Iodides.

Because aryl chlorides are more accessible and less expensive than aryl bromides and iodides, the synthesis of primary arylamines from aryl chlorides would be particularly valuable. However, the strong C-Cl bond makes these aryl halides less reactive than their bromide and iodide counterparts, and prior to our current work, only one example of the coupling of ammonia with an aryl chloride had been reported to give high yield of the primary arylamine product, and this example was conducted with a catalyst generated from CyPF-*t*-Bu.[14] We show here that the reactions of a series of aryl chlorides with ammonia catalyzed by the combination of $Pd[P(o\text{-}tol)_3]_2$ and CyPF-*t*-Bu leads to high yields of primary arylamine with relatively low catalyst loadings for a range of aryl chlorides.

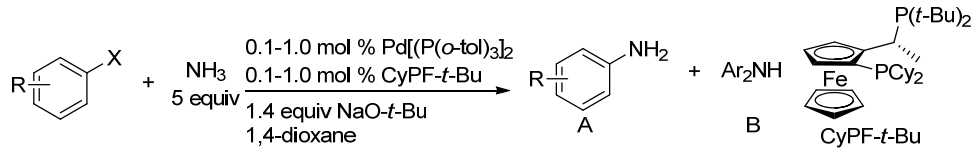
The scope of the coupling of ammonia with aryl chlorides and iodides is summarized in Table 26. The catalyst generated from $Pd[P(o\text{-}tol)_3]_2$ and CyPF-*t*-Bu catalyzed the coupling of ammonia with aryl chlorides in high yields under the same reaction conditions described for the coupling of aryl bromides. The reactions of ortho-subsituted aryl chlorides occurred in particularly high yields and selectivities for the primary arylamine. For example, reactions of 2-chlorotoluene and 2,5-dimethylchlorobenzene with ammonia occurred with 0.5 mol % of the catalyst at 80 °C for 24 h to afford the aniline products in 64% and 85% yield respectively (entries 1 and 3). Like the couplings of *ortho*-substituted aryl bromides, these aryl chlorides coupled with ammonia in the presence of only 0.1 mol % of catalyst at substrate concentration of 0.1 M without significant reduction in yield (entries 2 and 4). The electron-rich 2-chloroanisole also reacted under this low catalyst loading to give high yield of the coupled product (entry 5).

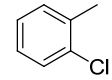
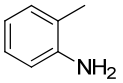
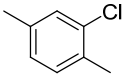
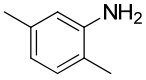
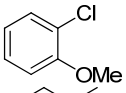
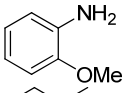
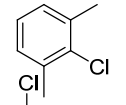
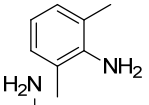
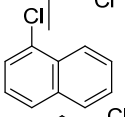
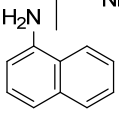
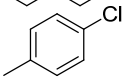
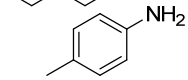
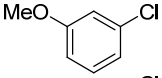
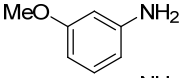
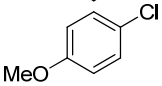
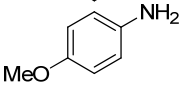
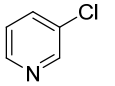
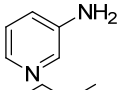
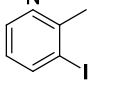
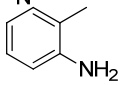
Even the coupling of the 2,6-disubstituted 2-chloro-*m*-xylene with ammonia in the presence of 1 mol % catalyst occurred to full conversion of the aryl chloride to afford high yield of the primary arylamine product (entry 6). The reaction of ammonia with the pseudo ortho-substituted, fused polyarene 1-chloronaphthalene also occurred in high yield (entry 7).

Sterically unhindered aryl chlorides and heteroaryl chlorides ranging from electron-deficient to electron-rich also coupled with ammonia in high yield and selectivity. For example, reactions of 4-chlorotoluene and 3-chloroanisole with ammonia occurred at 0.038 M concentration of the substrate to afford good yields of coupled products (entries 8 and 9). The coupling of electron-rich substrates with ammonia is challenging for reasons that are discussed later in this paper. Nevertheless, the reaction of electron-rich 4-chloroanisole with ammonia occurred with 1 mol % of the catalyst at 100 ^{o}C for 12 h to give 69% yield of *p*-anisidine. The conditions for reactions of aryl chlorides proved to be suitable for the reactions of heteroaryl chlorides. The reaction of 3-chloropyridine with ammonia occurred in 64% isolated yield (entry 11).

The generality of this method is further demonstrated by the high yields of primary arylamines derived from aryl iodides. Aryl iodides are known to react with nitrogen nucleophiles in yields and selectivities that are often lower than those of reactions of aryl bromides.[27-40] Nevertheless, the reaction of 2-iodotoluene with ammonia in the presence of 0.5 mol % of catalyst occurred to full conversion and formed the coupled product in good yield (entry 12).

Table 26. Coupling of Aryl Chlorides and Iodides with Ammonia.[a]



entry	aryl bromide	loading (%)	concentration [M]	T [°C][b]	*t* [h]	product	yield (%)[c]	A:B[d]
1		0.5	0.07	100	24		64	17:1
2		0.1	0.1	100	24		63	--
3		0.07	0.07	100	24		85	>50:1
4		0.1	0.1	100	24		63	--
5		0.1	0.1	100	24		84	--
6		1	0.1	100	24		89	>50:1
7		0.5	0.038	100	12		89	--
8		1	0.038	100	10		55	12:1
9		0.5	0.038	100	12		99	--
10		1	0.05	100	12		69	--
11		1	0.038	100	12		64	--
12		0.5	0.1	80	12		73	--

[a]Reactions conducted with 1:1 ratio of metal to ligand, 0.5 mmol aryl chloride, 5 mL of 0.5 M ammonia solution, 1.4 equiv NaO*t*Bu in 1,4-dioxane. [b]Temperature of bath. cIsolated yield after purification by flash column chromatography. [c]Determined by ^{1}H NMR spectroscopy.

4.2.4. Scope of the Coupling of Aryl Sulfonates with Ammonia.

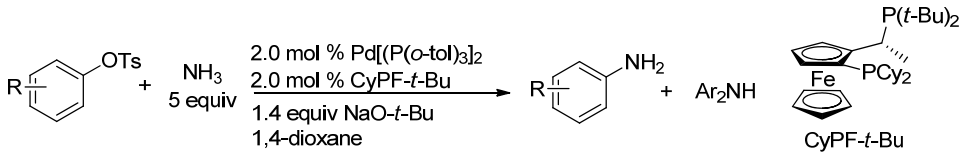
Prior to this work, the coupling of ammonia with aryl sulfonates formed the primary arylamine in low yields with all catalysts reported.[14] The yields were low because the C-N coupling process competes with uncatalyzed cleavage of the S-O bond of the sulfonyl group by

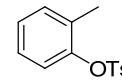
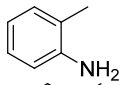
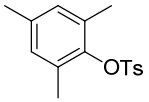
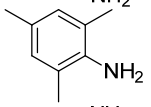
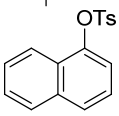
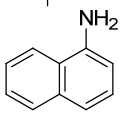
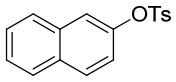
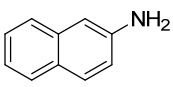
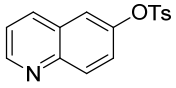
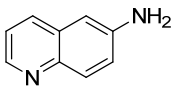
ammonia in the presence of the strong base NaO-*t*-Bu to form aryl alcohols as the major product. In 2003, we showed that the complex generated from Pd[P(*o*-tol)$_3$]$_2$ and CyPF-*t*-Bu undergoes the oxidative addition of aryl tosylates rapidly at room temperature.[21] More recently, the authors' laboratory showed that the coupling of aryl tosylates with alkyl- and arylamines occurs at room temperature in the presence of the catalyst generated from Pd[P(*o*-tol)$_3$]$_2$ and CyPF-*t*-Bu.[24] The low temperatures of the coupling of primary amines suggested that the coupling of ammonia could occur faster than cleavage of an aryl sulfonates. Indeed, we found that reactions conducted with 2 mol % catalyst, a temperature of 50 ^{o}C, and tosylate as the specific type of sulfonate group led to reactions with ammonia that are sufficiently faster than S-O bond cleavage to obtain the primary amine in substantial yields. Reactions of aryl triflates led to the phenol as the major product from S-O bond cleavage.

The results of our study on the scope of the coupling of aryl tosylates with ammonia under these conditions are shown in Table 27. Reactions of sterically hindered aryl tosylates with ammonia produced primary arylamines in good to excellent yield. For example, 2-methylphenyl *p*-toluenesulfonate and 2,4,6-trimethylphenyl *p*-toluenesulfonate coupled with ammonia in the presence of 2 mol % of the catalyst at 50 ^{o}C for 24 h to give primary arylamines in 65% and 86% yield respectively (entries 1 and 2). Less sterically hindered aryl tosylates reacted with ammonia to give slightly lower yields of the arylamine than did *ortho*-substituted aryl tosylates. We attributed this result to the faster rates of formation of aryl alcohol from less sterically hindered tosylates. For example, the reactions of 1-naphthyl *p*-toluenesulfonate and 2-naphthyl *p*-toluenesulfonate with ammonia occurred with 2 mol % of the catalyst to afford the coupled products in 67% yield in both cases (entries 3 and 4). Heteroaryl tosylates also coupled with ammonia to form synthetically useful, albeit lower, yields of the primary heteroarylamines. For

example, the reaction of 6-quinolinyl *p*-toluenesulfonate with ammonia afforded 55% yield of the coupled product (entry 5). Improvements in the reactions of sterically unhindered aryl tosylates will be the focus of future work, but these results represent the first coupling of aryl sulfonates with ammonia and demonstrate that a method to attractive way to prepare primary arylamines from aryl alcohols by this approach is feasible.

Table 27. Coupling of Ammonia with Aryl Tosylates.[a]



entry	aryl bromide	loading (%)	concentration [M]	T [°C][b]	*t* [h]	product	yield (%)[c]	A:B[d]
1		2	0.1	50	24		65	17:1
2		2	0.1	50	24		86	>50:1
3		2	0.05	50	24		67	>50:1
4		2	0.05	50	24		67	--[e]
5		2	0.05	50	24		55	--[e]

[a]Reactions conducted with 1:1 ratio of metal to ligand, 0.5 mmol aryl chloride, 5 mL of 0.5 M ammonia solution, 1.4 equiv NaO-*t*-Bu in 1,4-dioxane. [b]Temperature of bath. [c]Isolated yield after purification by flash column chromatography. [d]Determined by 1H NMR spectroscopic analysis. eUndeterminable by ^{1}H NMR spectroscopy.

4.2.5. Coupling of Ammonia with Aryl Halides Containing Base-sensitive Functional Groups

4.2.5.1. Identification of Reaction Conditions

The scope of the palladium-catalyzed coupling of ammonia with aryl halides that contain base-sensitive functional groups, such as ketones with enolizable protons, esters and nitriles, has been limited. The limitation on scope arises from the use of the strong base NaO-*t*-Bu.

Our initial attempt to expand the scope of the coupling of ammonia to encompass base-sensitive functional groups focused on conducting reactions with weak bases, such as Cs_2CO_3 and K_3PO_4 that have helped to address issues of functional group compatibility in the coupling of amines.[41,42] We studied reactions of ammonia with ethyl 4-bromobenzoate to evaluate conditions required to obtain high yield and selectivity of the primary arylamine from base-sensitive haloarenes.

The reaction of ammonia with methyl 4-bromobenzoate conducted in 0.5 M solutions of dioxane in the presence of 0.5 mol % of equimolar amounts of $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu and 5 equiv of K_3PO_4 occurred to full conversion, but only the diarylamine product was observed. Apparently the more acidic arylamine product reacts faster than ammonia in reactions conducted with the weaker base. However, reactions conducted with higher concentration of ammonia occurred with higher selectivity for formation of the primary arylamine. For example, the reaction of ethyl 4-bromobenzoate with 200 psi of ammonia in the presence of 0.5 mol % of equimolar amounts of $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu and 5 equiv of K_3PO_4 occurred to full conversion and gave a 30:1 ratio of the primary arylamine to the diarylamine.

4.2.5.2. Scope of the Coupling of Ammonia with Aryl Halides and Sulfonates Containing Base-Sensitive Functional Groups

Using the conditions descrived in section 2.5.1, we studied the scope of the coupling of ammonia with aryl halides that contain base-sensitive functional groups in the presence of $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu as catalyst. The results of this study are summarized in Table 28. Aryl halides and tosylates containing base-sensitive, electron-withdrawing functional groups at the *para*-position coupled with ammonia in high yield. For example, reactions of ethyl 4-bromobenzoate and methyl 4-bromobenzoate with ammonia occurred with only 0.5 mol % of the catalyst to give 94% and 83% yield of primary arylamines respectively (entries 1 and 3). Aryl halides containing ketones with enolizable protons such as 4'-bromoacetophenone and 4'-bromopropiophenone coupled with ammonia to give high yield of coupled products (entries 5 and 7).

Cyano functionality is typically stable toward reactions in the presence of NaO-*t*-Bu and either alkyl- or arylamine nucleophiles,[27,43] but 4-halobenzonitriles reacted with ammonia in the presence of NaO-*t*-Bu with and without the palladium catalyst to form multiple products. In contrast to the reactions of ammonia in the presence of strong base, the reaction of 4-bromobenzonitrile with ammonia and K_3PO_4 as base catalyzed by $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu occurred to give 71% yield of the coupled product (entry 8).

The ability of the catalyst generated from $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu to add aryl halides under mild conditions and the apparent stability of this catalyst toward iodide byproduct also led to increases in reaction scope. For example, reactions of ammonia with 4-chloro methylbenzoate and 4-chlorobenzonitrile occurred to give high yields of primary arylamines without formation of amide or amidine side products (entries 4 and 9). Moreover, the reaction of

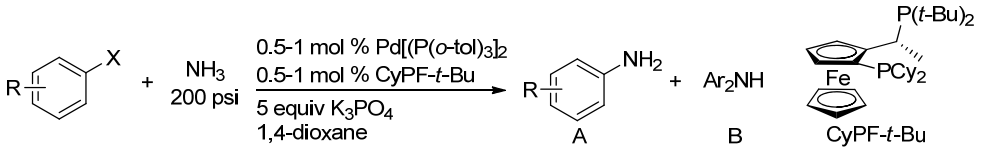
the electron-poor 4'-iodoacetophenone with ammonia in the presence of 1 mol % of Pd[P(*o*-tol)$_3$]$_2$ and CyPF-*t*-Bu afforded good yield of the aniline product (entry 6).

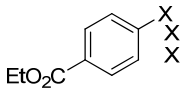
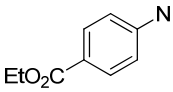
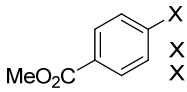
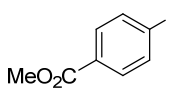
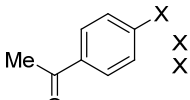
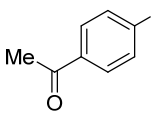
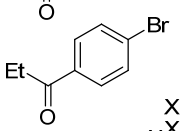
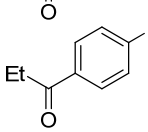
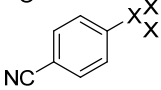
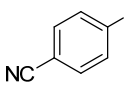
The ability of these couplings to occur with K_3PO_4 as base also allowed us to develop the coupling of aryl tosylates containing base-sensitive functionality. The rate of formation of aryl alcohol side products should be slower in the presence of ammonia and K_3PO_4 than in the presence of ammonia and NaO-*t*-Bu, while the catalyst should add the electron-poor aryl tosylate with a rate that is faster than it adds electron-neutral and electron-rich aryl tosylates. Consistent with these expectations, reactions of ammonia with 4-cyanophenyl *p*-toluenesulfonate and ethyl 4-{[(4-methylphenyl)sulfonyl]oxy}benzoate occurred with only 0.5 mol % of the catalyst to afford 73% and 79% yield of coupled products, respectively (entries 2 and 10). Because the aryl halides shown in Table 28 are electron-poor, control reactions were conducted without the palladium catalyst to determine if the reactions were truly metal catalyzed. No measurable quantity of primary arylamine product was observed in the absence of palladium for reactions of any of the aryl halides we described in Table 8. Some conversion was observed during reactions of aryl tosylates with ammonia and K_3PO_4 in the absence of catalyst at 80 ^oC, but these reactions formed the corresponding aryl alcohols by S-O bond cleavage, not the desired arylamine.

The reactions of ammonia with more electron-rich aryl halides and sulfonates that contain base-sensitive functional groups gave low yield of aniline products in the presence of Pd[P(*o*-tol)$_3$]$_2$ and CyPF-*t*-Bu as catalyst. A rationalization for this result will be provided later in this paper. Despite this limitation, our method allows for the coupling of ammonia with a set of aryl iodides, bromides, chlorides and sulfonates that contain base-sensitive functional group. The ability to conduct these reactions with this range of halide and with sulfonates constitutes a

significant expansion of the scope of related reactions described previously with other palladium or copper catalysts.[11-15]

Table 28. Coupling of Ammonia with Aryl Halides and Sulfonates Containing Base-sensitive Functional Groups.[a]



entry	aryl halide	loading (%)	con. [M]	T [°C][b]	*t* [h]	product	yield (%)[c]	A:B[d]
1		X = Br 0.5	0.1	70	12		94	30:1
2		X = OTs 0.5	0.1	70	12		73	6:1
3		X = Br 0.5	0.1	70	12		83	>30:1
4		X = Cl 0.5	0.1	70	12		79	>30:1
5		X = Br 0.5	0.1	70	12		76	--
6		X = I 1	0.1	70	12		78	--
7		0.5	0.1	70	12		85	--
8		X = Br 0.5	0.1	70	12		71	--
9		X = Cl 0.5	0.1	70	12		44	
10		X = OTs 0.5	0.1	70	12		77	

[a]Reactions conducted with 1:1 ratio of metal to ligand, 0.5 mmol aryl chloride, 5 mL of 0.5 M ammonia solution, 1.4 equiv NaO*t*Bu in 1,4-dioxane. [b]Temperature of bath. [c]Isolated yield after purification by flash column chromatography. [d]Determined by 1H NMR spectroscopy.

4.2.6. Sequential Reactions Initiated by the Coupling of Ammonia with Aryl Halides.

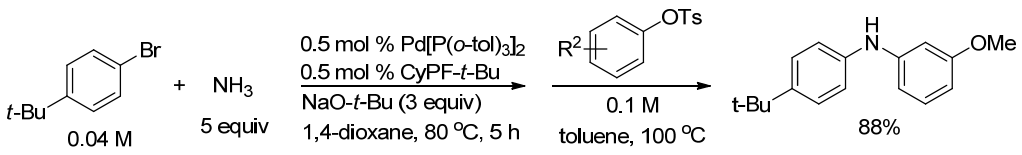
Although primary arylamines are often the desired end product, in many instances the primary arylamine would be used to generate diarylamines, amides, sulfonamides, imides or other products containing an aromatic C-N bond. In some cases, the reagents one would used for the direct coupling have not been shown to undergo C-N coupling in a reliable fashion, whereas, in other cases, one might wish to generate the arylamine as a means to generate a library of

products derived from the initial arylamine product. Having developed an efficient synthesis of arylamines, we sought to demonstrate the utility of the arylation of ammonia as a means to generate arylamine derivatives. Two examples of such sequential reaction chemistry are shown here.

4.2.6.1. Sequential Arylation of Ammonia by a Single Catalyst in One-Pot

Unsymmetrical diarylamines are intermediates to unsymmetrical triarylamines, which have numerous applications in photonic, organic polymers.[44] The work described here has demonstrated that the combination of $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu is a highly active catalyst for the coupling of aryl halides and tosylates with ammonia to form primary arylamines, and the authors' group has recently shown that this same combination of metal and ligand catalyzes the coupling of aryl and heteroaryl tosylates with arylamines at room temperature to form mixed diarylamines.[24] Thus, we sought to develop a sequential coupling of ammonia with aryl halides and sulfonates in the presence of a single catalyst to form mixed diarylamines.

The catalyst generated from $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu does allow the sequential coupling of ammonia with two different aryl electrophiles to occur in one pot. As shown in eq 2, the arylation of ammonia with 4-bromo-*tert*-butylbenzene occurs in the presence of 0.5 mol % of $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu and 3 equiv of NaO-*t*-Bu. After full conversion of the aryl bromide, evaporation of the dioxane, followed by addition of the aryl tosylate and toluene and heating led to the formation of the unsymmetrical diarylamine in high yield (Scheme 27). Sequential coupling of two different aryl halides with ammonia can also be conducted on one pot and will be reported in due course.



Scheme 27. Sequential Arylation of Ammonia

4.2.6.2. One-pot Synthesis of Amides and Imides from Aryl Halides

The coupling of ammonia with aryl halides creates the ability to conduct a one-pot synthesis of aniline derivatives that are challenging to obtain directly by C-N coupling. These derivatives include amides, imides and carbamates. The amide moiety is present in many biologically active compounds, and there has been an intense development of methods to access libraries of amides for studies on structure-reactivity relationships.[45-48] *N*-Aryl imides, in particular phthalimides, have been used extensively as intermediates in the manufacture of dyes,[49] polymers,[50,51] and pesticides,[52] and this class of compound has also been shown to be biologically active.[53,54] Amides and imides are widely prepared by reactions between amines and acid chlorides or anhydrides, but this procedure requires an arylamine reagent. Palladium-[55,56] and copper-catalyzed[57,58] amidation have limitations in substrate scope, require high catalyst loadings, and are sufficiently challenging that parallel synthesis would require attention to the development of conditions for individual substrate combinations. The *N*-arylation of imides has not been reported with palladium catalysts and has not been reported with modern copper catalysts.

The preparation of *N*-Boc-aryl amines via palladium or copper-catalyzed coupling of aryl halides with *tert*-butyl carbamate is limited to a few examples conducted with palladium catalysts generated from either xantphos or P(*t*-Bu)$_3$ as ligands.[43,59,60] No reactions of aryl chlorides or sulfonates have been reported, and the reactions of *ortho*-substituted aryl halides were limited to one electron-poor example.

Thus, the coupling of an aryl halide with ammonia, followed by addition of an acid chloride, cyclic anhydide, or Boc anhydride could provide a convenient route to a family of *N*-aryl amides, -imides and -carbamates from a single aryl halide. Our demonstration of this sequence focused on reactions of ortho-substituted aryl halides because of the particular value of the coupling of aryl halides with this class of electrophile. Yet, a sequence initiated with *meta* or *para*-substituted aryl halides would lead to analogous products.

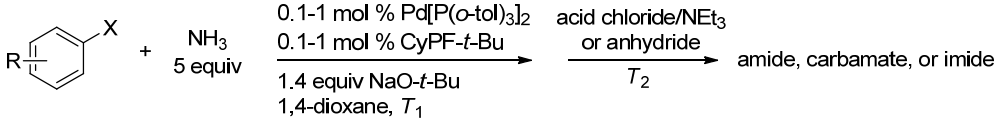
Our data illustrating the two-step, one-pot synthesis of a family of *N*-aryl amides, imides and carbamate from a single aryl halide are summarized in Table 29. *Ortho*-substituted aryl halides, such as 2-bromo-*N*,*N*-dimethylaniline and 2-chloroanisole, reacted with ammonia in the presence of only 0.1 mol % of the palladium catalysts. After evaporation of excess ammonia under reduced pressure for 5 min, the addition of acid chlorides that range from electron-rich to electron-poor into the reaction mixtures afforded the *N*-aryl amides with 68-99% yields (entries 1, 3, 5 and 6).

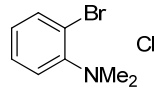
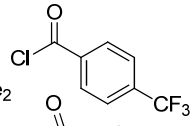
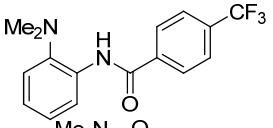
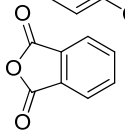
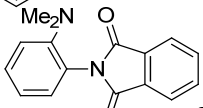
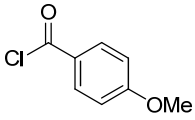
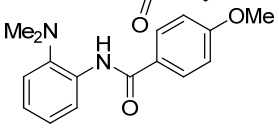
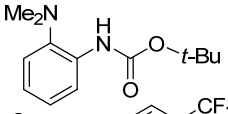
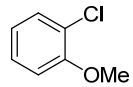
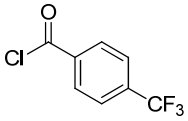
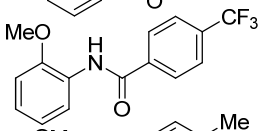
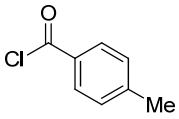
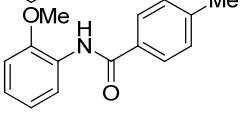
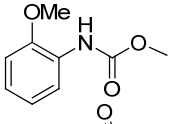
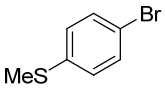
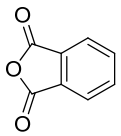
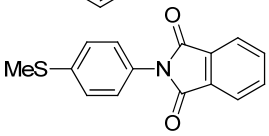
This one-pot method also formed *N*-aryl carbamates in good yield. The conversion of 2-bromo-*N*,*N*-dimethylaniline and 2-chloroanisole with low loading of the palladium catalyst (0.1 mol %) followed by addition of Boc-anhydride formed the corresponding *N*-Boc protected anilines in 75% and 68% yields, respectively (entries 4 and 7).

Finally, this sequence conducted with phthalic anhydride in the second step occurred to form *N*-aryl imides. The reactions of phthalic anhydride with sterically hindered arylamines formed by the C-N coupling gave lower yields of *N*-aryl phthalimide than those of sterically unhindered arylamines, although the imide derived from 2-bromo-*N*,*N*-dimethylaniline and 2-chloroanisole were formed by the two-step, one-pot protocol in 51% and 68% yields. The

coupling of ammonia with the less hindered 4-bromothioanisole, followed by addition of phthalic anhydride, gave 75% yield of the corresponding *N*-aryl imide.

Table 29. Synthesis of Amides and Imides from Aryl Bromides and Chlorides[a]



entry	aryl halide	electrophile	loading (%)	T_1 (°C)[b]	T_2 (°C)[b]	product	yield (%)[c]
1[d]			0.1	100	25		89
2			0.1	100	25		51
3[d]			0.1	100	50		74
4		Boc_2O	0.1	100	80		75
5[d]			0.1	100	50		82
6[d]			0.1	100	50		94
7		Boc_2O	0.1	100	80		68
8			0.1	90	25		75

[a]Reactions conducted with 1:1 ratio of metal to ligand. [b]Temperature of bath. cIsolated yield after purification by flash column chromatography.

4.2.7. Mechanistic Studies

Although a full study of the mechanism of the coupling of ammonia with aryl halides awaits further study, several initial mechanistic experiments provide insight into the factors that differentiate the current catalyst from those used previously containing the CyPF-*t*-Bu ligand and

that differentiate the reactivity of aryl halides containing electron-withdrawing groups in the para and meta positions. These experiments evaluated the efficiency of the generation of the active palladium(0) catalyst from the palladium(II) precursors and identified the turnover-liminting steps of the reactions of electron-poor aryl halides.

4.2.7.1. Studies on the Reactions of Palladium(II) Precursors with Ammonia and Base

To address the origin of the higher reactivity of complexes generated from $Pd[P(o\text{-tol})_3]_2$ than those generated from $Pd(OAc)_2$ or (CyPF-t-Bu)$PdCl_2$, we studied the catalytic reactions of 4-bromo-*tert*-butylbenzene with ammonia catalyzed by (CyPF-t-Bu)$PdCl_2$ or the combination of CyPF-*t*-Bu and $Pd(OAc)_2$. ^{31}P NMR spectra of reactions conducted with (CyPF-*t*-Bu)$PdCl_2$ or the combination of CyPF-*t*-Bu and $Pd(OAc)_2$ produced complex mixtures of palladium species, whereas the reaction catalyzed by the combination of $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu and $Pd(OAc)_2$ generated a single major species. From this observation, we concluded that the combination of $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu generates a higher concentration of active catalyst than other catalyst precursors.

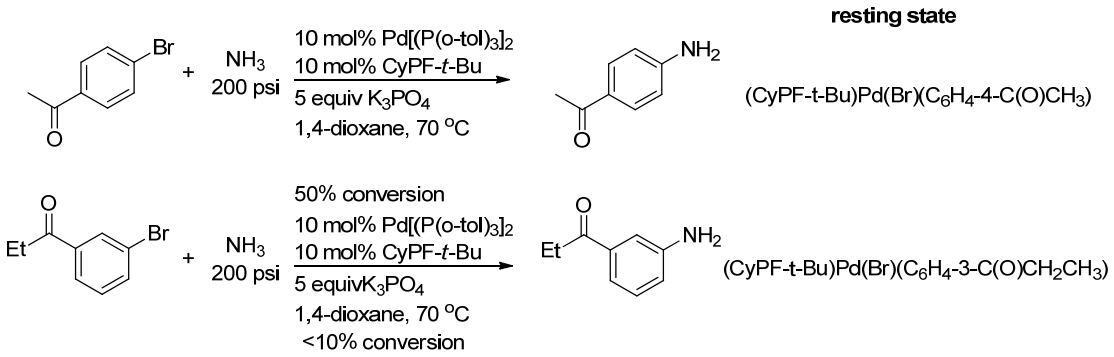
To address the fate of the Pd(II) species in the presence of ammonia and base in more detail, we determined the amount of (CyPF-*t*-Bu)Pd(0) species generated from the reaction of (CyPF-*t*-Bu)$PdCl_2$ with ammonia and base. (CyPF-*t*-Bu)$PdCl_2$ was treated with NaO-*t*-Bu and ammonia in the presence of $P(o\text{-tol})_3$ to trap any Pd(0) complex formed. This reaction generated a complex mixture of products that contained less than 10% of the Pd(0) species. Because the alkoxide base and ammonia both lack hydrogens α to the heteroatom, the Pd(II) species cannot be reduced to palladium(0) by the combination of β-hydrogen elimination from an alkoxo or amido intermediate and reductive elimination of amine or alcohol. Because the aryl group serves as the electrophilic component, rather than the nucleophilic component, formation of a bis-aryl

complex and reductive elimination of an organic biaryl product also cannot lead to formation of palladium(0) in high yield.

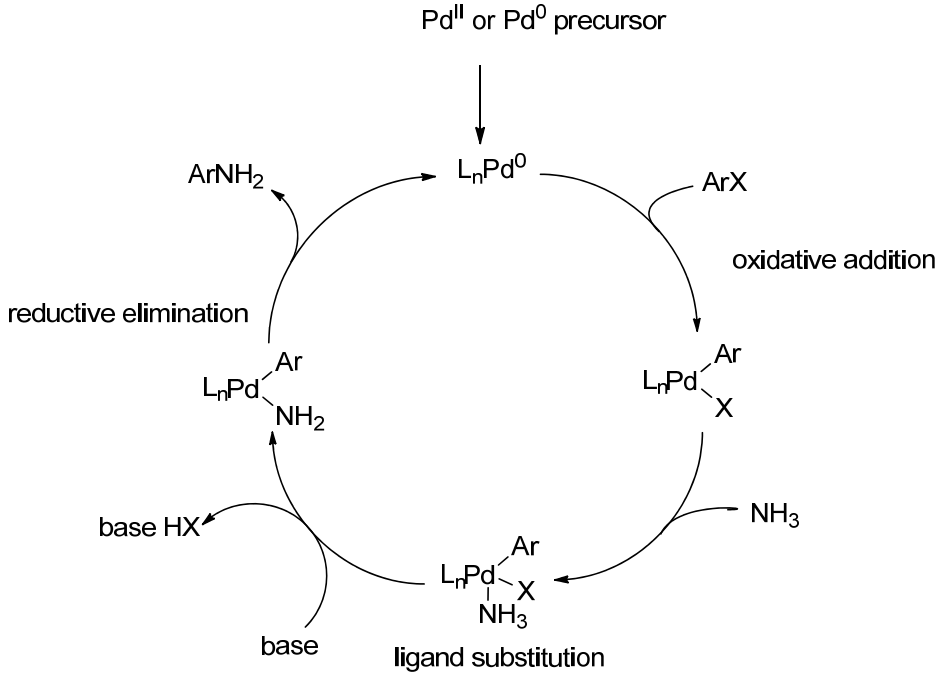
4.2.7.2. Studies on the Turnover-Limiting Step of Reactions with Weak Base

We also conducted studies to determine whether the use of a weak base would lead to turnover-limiting transmetalation. The reaction of 4'-bromoacetophenone with ammonia at 200 psi in the presence of 5 equiv of K_3PO_4 was monitored by ^{31}P NMR spectroscopy after approximately 50% conversion of the aryl bromide (Scheme 28). The resting state of the catalyst was identified to be the arylpalladium bromide complex by comparison of the ^{31}P NMR chemical shifts of the species in the catalytic reaction to those of the species formed from the reaction of $Pd[P(o\text{-tol})_3]_2$ and CyPF-*t*-Bu with 4'-bromoacetophenone. This result indicates that transmetalation is the turnover-limiting step in the reactions of aryl bromides with ammonia in the presence of the weak base K_3PO_4.

The same experiment was conducted on reactions of aryl halides containing electron-withdrawing groups in the *meta* position, such as 3'-bromopropiophenone. Again, the arylpalladium halide complex was observed. Because catalytic reactions of the meta-substituted, electron-poor aryl halides occur in low yields, it appears that the rates of the transmetalation and reductive elimination portion of the catalytic cycle are affected strongly by the relative electron-withdrawing ability of the aryl group in the *meta* or *para* position. Because the pK_a value of ammonia and monohydrogen phosphate is 40 (DMSO) and 7.0 respectively, we assume that the formation of the amido complex is facilitated by coordination of ammonia to palladium to increase the acidity of the ammonia, and the aryl group bound to palladium affects the Lewis acidity of the metal center (Scheme 29).



Scheme 28.



Scheme 29.

4.3. Conclusions

We have shown that the catalyst generated from the combination of $Pd[P(o\text{-}tol)_3]_2$ and the Josiphos ligand CyPF-*t*-Bu is highly active and selective for the coupling of ammonia with aryl halides and sulfonates to form primary arylamine products. For example, reactions of *ortho*-

substituted aryl bromides and chlorides occurred with only 0.1 mol % of catalyst loading. This catalyst leads to a reaction scope that is expanded over that with previous catalyst. This scope now encompasses aryl chlorides, bromides and iodides that possess or lack an ortho-substituent and for the first time encompasses aryl sulfonates. Moreover, this scope now includes reactions of certain aryl halides containing base-sensitive functional groups such as ketones, esters, and nitriles. The utility of this coupling process to form not only primary arylamines, but mixed secondary arylamines, *N*-aryl amides, *N*-aryl imides. and *N*-aryl carbamates by a one-pot procedure has also been demonstrated.

The efficiency of the catalyst arises from the high yield of a reactive (CyPF-*t*-Bu)Pd fragment from equimolar amounts of $Pd[P(o\text{-}tol)_3]_2$ and CyPF-*t*-Bu. Preliminary studies on the generation of the active catalyst suggest that low yields of the active palladium(0) species are generated from palladium(II) precursors, ammonia and sodium *tert*-butoxide base. Additional studies imply that the reactions with weak base occur by turnover-limiting transmetalation and that the rate of this step depends on the position of the electron-withdrawing group on the aryl ligand.

4.4. Experimental Information

General Procedures. Unless otherwise noted, all manipulations were conducted under an inert nitrogen atmosphere, using flame-dried glassware. A N_2-filled glovebox was used as indicated and had O_2 level below 10 ppm. Rotary evaporation was done at 25-30 ^oC. Flash column chromatography was performed as described by Still et al[61] on silica gel (Silicycle, 60 A pore size, 40-64 mm particle size, pH suspension 10%: 6.5-7.5). Analytical thin-layer chromatography was performed on glass plates coated with silica gel (Silicycle, 60 A pore size, 40-64 mm particle size) and visualized with both ultraviolet light and ninhydrin stain.

Materials. 1,4-Dioxane (anhydrous, 99.9%) was purchased from Aldrich and used without further purification. Ammonia in 1,4-dioxane solution (0.5 M) was either purchased from Aldrich and used without further purification or prepared according the procedure described below.[62] Ammonia (anhydrous, 99.99%) was purchased from Matheson Tri-Gas and used without further purification. Palladium bis(tri-*o*-tolylphosphine), $Pd[P(o\text{-tol})_3]_2$, was prepared according to procedures reported by Tokutaro and Hartwig,[24] or was obtained as a gift from Johnson-Matthey. This complex is now commercially available from Johnson-Matthey and Aldrich. (*R*)-(-)-1-[(*S*)-2-(Dicyclohexylphosphino)ferrocenyl]ethyl-di-*tert*-butylphosphine (CyPF-*t*-Bu) was obtained as a gift from Solvias or can be purchased from Strem Chemicals. Sodium *tert*-butoxide was purchased from Sigma-Aldrich and used without further purification. All aryl halides and acyl chlorides were purchased from Aldrich and used without further purification. Analytically pure aryl tosylates were prepared by the procedure reported by Kubota and Nakada.[63] Solvents for filtration and chromatography were certified ACS grade.

Instruments. ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra were recorded on Varian Unity-400 or 500 MHz (126 MHz, ^{13}C) spectrometers. Spectra are referenced either to residual chloroform (d = 7.26 ppm, ^{1}H; 77.0 ppm, ^{13}C), residual benzene (d = 7.15 ppm, ^{1}H; 128.62 ppm, ^{13}C), external standard reference $CFCl_3$ (d = 0 ppm, ^{19}F), or H_3PO_4 (d = 0 ppm, ^{31}P). Chemical shifts are reported in ppm. Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (hextet), m (multiplet) and b (broad). Coupling constants, *J*, are reported in hertz, and integration is provided and assignments are indicated. Chemical shifts downfield of the standard are reported as positive values. Analytical gas chromatography (GC) was performed using a Hewlett-Packard 5890 Gas Chromatograph fitted with a flame ionization detector and a Hewlett-Packard HP5 (30m x 0.32 mm) capillary column. The injector temperature was 250 ^{o}C, and the detector temperature was 300 ^{o}C with a helium carrier gas flow of 16 mL/min. The column temperature program was as follows: 120 ^{o}C to 250 ^{o}C at 40 ^{o}C/min, then hold for 3 min for a total run time of 6.25 min. Retention times (t_R) were obtained using Agilent Chemstation software. Response factors were generated by triplicate runs of three molar ratios of the analyte to dodecane standard dissolved in ethyl acetate.

EXPERIMENTAL PROCEDURES

Procedure for the Preparation of 0.5 M Ammonia Solution in 1,4-Dioxane. Into an oven-dried 100-mL, Kjeldahl-shaped Schlenk flask (14/20, glass stopcock), contained a magnetic stir bar and fitted with a vacuum valve adapter (14/20 joints), was added 1,4-dioxane (50 mL). The entire assembly was sealed and fitted onto one end of a 250-mL gas bulb, and the other end of the gas bulb was connected to a vacuum manifold. 1,4-Dioxane was frozen, and the entire assembly was evacuated to a reduced pressure, ca 50 mTorr. Ammonia (250 mL at 37.2

cmHg) was condensed into the flask 5 times. The solution was warmed to room temperature before use.

Preparation of 2.5 x 10^{-3} M M Stock Solution of Catalysts. $Pd[P(o\text{-tol})_3]_2$ (0.0018 g, 0.0025 mmol) and CyPF-*t*-Bu (0.0014 g, 0.0025 mmol) were dissolved in 1,4-dioxane (1.0 mL). The resulting orange solution was stirred at room temperature for 5 minutes before immediate use.

General Procedure A: The Coupling of Ammonia with *o*-Substituted Aryl Bromides at 0.1 mol % Catalytic Loading (Table 2). Inside a N_2-filled glovebox, the 2.5 x 10^{-3} M stock solution of the catalyst (0.20 mL) containing $Pd[P(o\text{-tol})_3]_2$ (0.00050 mmol) and CyPF-*t*-Bu (0.00050 mmol) was added to a mixture of NaO-*t*-Bu (1.4 equiv) and aryl halide (0.50 mmol) in a 20-mL scintillation vial. Ammonia (5 mL of a 0.5 M solution in dioxane) was added via a gas-tight syringe. The vial was sealed with a Teflon-lined cap and removed from the glovebox and placed in an oil bath at 100 ^{o}C for 12 h. After GC analysis indicated full conversion of the aryl halide, the reaction mixture was diluted with ethyl acetate (10 mL) and filtered through a plug of Celite. The product was purified by flash column chromatography.

General Procedure B: The Coupling of Ammonia with Aryl Halides Lacking Base-sensitive Functional Groups (Table 4 and 6). Into an oven-dried 25-mL round-bottomed flask containing a magnetic stir bar, $Pd[P(o\text{-tol})_3]_2$ (0.5-2.0 mol %), CyPF-*t*-Bu (0.5-2 mol %), NaO-*t*-Bu (1.4 equiv) and the aryl halide (0.50 mmol) (if solid) were added. The flask was sealed with a rubber septum, evacuated and refilled with nitrogen three times. 1,4-Dioxane (5 - 8 mL) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) were added via a gas-tight syringe. The aryl halide (0.50 mmol), if liquid, was added via a gas-tight syringe. The flask was then placed in an oil bath at 80-100 ^{o}C for 4-12 h. After GC analysis indicated full conversion of the aryl halide,

the reaction mixture was then diluted with ethyl acetate (10 mL) and filtered through a plug of Celite. The product was purified by flash column chromatography.

General Procedure C: The Coupling of Ammonia with Aryl Tosylates (Table 7). Into an oven-dried 25-mL round-bottomed flask containing a magnetic stir bar, $Pd[P(o\text{-tol})_3]_2$ (2.0 mol %), CyPF-*t*-Bu (2.0 mol %) and NaO-*t*-Bu (1.4 equiv) and the aryl tosylate (0.50 mmol) were added. The flask was sealed with a rubber septum, evacuated, and refilled with nitrogen three times. 1,4-Dioxane (0-5 mL) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) were added by gas-tight syringe. The flask was then placed in an oil bath at 50 ^{o}C for 12-24 h. After GC analysis indicated full conversion of the aryl halide, the reaction mixture was diluted with ethyl acetate (10 mL) and filtered through a plug of Celite. The product was purified by flash column chromatography.

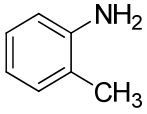
General Procedure D: The Coupling of Ammonia with Aryl Halides and Tosylates Bearing Base-sensitive Functional Groups (Table 8). Inside a glovebox, $Pd[P(o\text{-tol})_3]_2$ (0.50 mol %), CyPF-*t*-Bu (0.50 mol %), K_3PO_4 (1.4 equiv), aryl halide or tosylate (0.50 mmol), and 1,4-dioxane (5 mL) were added to a 50 mL Parr bomb that contains a magnetic stir bar. The Parr bomb was sealed, brought out of the glovebox, and connected to an ammonia cylinder. The bomb was pressurized to 80 psi, and the mixture was stirred at room temperature for 30 min. The bomb was then sealed and disconnected from the ammonia cylinder and placed in an oil bath at 70 ^{o}C for 12 h. The reaction mixture was then diluted with ethyl acetate (10 mL) and filtered through a plug of Celite. The product was purified by flash column chromatography.

General Procedure E: One-pot Synthesis of Amides and Imides (Table 9). Inside a glovebox, $Pd[P(o\text{-tol})_3]_2$ (0.10-1.0 mol %) and CyPF-*t*-Bu (0.10-1.0 mol %) were added to a mixture of NaO-*t*-Bu (1.4 equiv) and the aryl halide (1-2 mmol) contained in a 20-mL

scintillation vial equipped with a magnetic stir bar. 1,4-Dioxane (0-5 mL) and ammonia (5-20 mL of a 0.5 M solution in dioxane) were added via a gas-tight syringe. The vial was sealed with a Teflon-lined cap and removed from the glovebox and placed in an oil bath at 90-100 ^{o}C for 12 h. Then the excess ammonia was removed under reduced pressure for 5 min. The reaction mixture was then divided into equal portions using a syringe, and the electrophiles were added. Triethylamine (1 equiv) was added if the electrophiles are acid chlorides. After GC analysis showed complete conversion of the aniline, the reaction mixtures were diluted with ethyl acetate and filtered through a plug of Celite. The products were purified by flash column chromatography.

General Procedure F: The One-pot Synthesis of N-Boc Protected Anilines (Table 9). The general procedure E was followed except for the work up procedure. After filtration of the reaction mixture through Celite, the solvent was removed under reduced pressure. Ethanol (ACS reagent, >99.5%, 2 mL) was added, followed by imidazole (0.5 equiv) (ACS reagent, >99%).[64] The resulting solution was stirred at room temperature for 1 h. The solvent was then removed under reduced pressure. The product was purified by flash column chromatography.

EXPERIMENTAL DETAILS AND COMPOUND CHARACTERIZATION



***o*-Toluidine[14] (Table 23, entry 1).** The general procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol) and CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-bromotoluene (0.086 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography (silica gel, 3:1 hexanes:ethyl acetate) to give *o*-toluidine as a pale yellow liquid (0.044 g, 83%). R_f = 0.27 (3:1

hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (t, *J* = 7.9 Hz, 2H, ArH), 6.77 (t, *J* = 7.4Hz, 1H, ArH), 6.72 (d, *J* = 7.7 Hz, 1H, ArH), 3.62 (s, br, 2H, NH_2), 2.22 (s, 3H, CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.5, 130.3, 126.8, 122.2, 118.5, 114.8, 17.3.

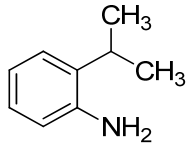
***o*-Toluidine (Table 23, entry 2).** General procedure A was followed with a 2.5 x 10^{-3} M stock solution of catalysts (0.20 mL, 0.00050 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-bromotoluene (0.086 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography to give *o*-toluidine as a pale yellow liquid (0.038 g, 71%).

***o*-Toluidine (Table 26, entry 1).** General procedure B was followed with $Pd[P(o\text{-tol})_3]_2$ (0.0018 g, 0.0025 mmol) and CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-chlorotoluene (0.063 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography to give *o*-toluidine as a pale yellow liquid (0.034 g, 64%).

***o*-Toluidine (Table 26, entry 2).** General procedure A was followed with a 2.5 x 10^{-3} M stock solution of catalysts (0.20 mL, 0.00050 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-chlorotoluene (0.063 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography to give *o*-toluidine as a pale yellow liquid (0.033 g, 63%).

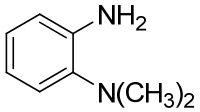
***o*-Toluidine (Table 27, entry 1).** General procedure C was followed with $Pd[P(o\text{-tol})_3]_2$ (0.0072 g, 0.010 mmol), CyPF-*t*-Bu (0.0055 g, 0.010 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-methylphenyl *p*-toluenesulfonate (0.131 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The crude product was purified by flash-column chromatography to give *o*-toluidine as a pale yellow liquid (0.035 g, 65%).

***o*-Toluidine (Table 26, entry 12).** General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol) and CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-iodotoluene (0.109 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) at 90 ^{o}C. The product was purified by flash-column chromatography to give *o*-toluidine as a pale yellow liquid (0.078 g, 73%).



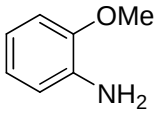
2-Isopropylaniline[14] (Table 23, entry 3). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-isopropylbromobenzene (0.100 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography (silica gel, 7:1 hexanes:ethyl acetate) to give 2-isopropylaniline as a pale yellow liquid (0.063 g, 93%). R_f = 0.30 (7:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (dd, *J* = 1.1, 7.7 Hz, 1H, ArH), 7.10 (td, *J* = 1.5, 7.7 Hz, 1H, ArH), 6.87 (t, *J* = 7.5 Hz, 1H, ArH), 6.74 (dd, *J* = 0.9, 7.9 Hz, 1H, ArH), 3.70 (s, br, 2H, NH_2), 2.97 (m, 1H, $CH(CH_3)_2$), 1.34 (d, *J* = 6.8 Hz, 6H, $CH(CH_3)_2$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.2, 132.5, 126.4, 125.3, 118.9, 115.7, 27.5, 22.2.

2-Isopropylaniline (Table 23, entry 4). General procedure A was followed with the 2.5 x 10^{-3} M stock solution of the catalyst (0.20 mL, 0.00050 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-isopropylbromobenzene (0.100 g, 0.500 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography to give 2-isopropylaniline as a pale yellow liquid (0.057 g, 84%).



***N,N*-Dimethyl-1,2-benzenediamine[65] (Table 23, entry 5).** General procedure A was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-bromo-*N,N*-dimethylaniline (0.100 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography (silica gel, 6:1 hexanes:ethyl acetate) to give *N,N*-dimethyl-1,2-benzenediamine as a pale yellow liquid (0.061 g, 89%). R_f = 0.30 (6:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.08 (dd, *J* = 1.27, 7.82 Hz, 1H, ArH), 6.98 (td, *J* = 1.37, 7.61 Hz, 1H, ArH), 6.80 (m, 2H, ArH), 4.03 (s, br, 2H, NH_2), 2.73 (s, 6H, $N(CH_3)_2$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.3, 140.5, 124.0, 119.2, 118.3, 115.0, 43.5.

***N,N*-Dimethyl-1,2-benzenediamine (Table 23, entry 6).** General procedure B was followed with the 2.5 x 10^{-3} M stock solution of the catalyst (0.20 mL, 0.00050 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-bromo-*N,N*-dimethylaniline (0.100 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography to give *N,N*-dimethyl-1,2-benzenediamine as a pale yellow liquid (0.056 g, 82%).

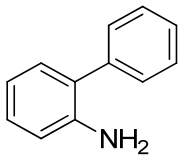


***o*-Anisidine[66] (Table 23, entry 7).** General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-bromoanisole (0.094 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography (silica gel, 6:1 hexanes:ethyl acetate) to give *o*-anisidine as a pale yellow liquid (0.052 g, 85%). R_f = 0.19 (6:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.85 (m, 2H, ArH), 6.78 (m, 2H, ArH), 3.88 (s,

3H, OCH_3), 3.81 (s, br, NH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.1, 136.0, 120.9, 118.3, 114.8, 110.3, 55.2.

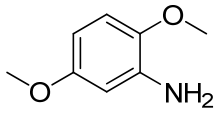
***o*-Anisidine (Table 23, entry 8).** General procedure B was followed with the 2.5 x 10^{-3}M stock solution of the catalyst (0.20 mL, 0.00050 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-bromoanisole (0.094g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography to give *o*-anisidine as a pale yellow liquid (0.059 g, 95%).

***o*-Anisidine (Table 26, entry 5).** General procedure B was followed with the 2.5 x 10^{-3} M stock solution of the catalyst (0.20 mL, 0.00050 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-chloroanisole (0.071 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography to give *o*-anisidine as a pale yellow liquid (0.051 g, 84%).

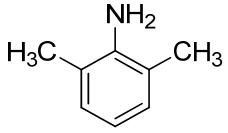


2-**Aminobiphenyl**[14] **(Table 23, entry 9).** General procedure A was followed with $Pd[P(o\text{-tol})_3]_2$ (0.0018 g, 0.50 mmol), CyPF-*t*-Bu (0.0014 g, 0.50 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-bromobiphenyl (0.117 g, 0.500 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography (silica gel, 9:1 hexanes:ethyl acetate) to give 2-aminobiphenyl as a pale yellow liquid (0.081 g, 96%). R_f = 0.25 (9:1 hexanes:ethyl acetate; UV, ninhydrin). ^1H NMR (500 MHz, $CDCl_3$) δ 7.47-7.44 (m, 4H, ArH), 7.36-7.37 (m, 1H, ArH), 7.19-7.14 (m, 2H, ArH), 6.84 (m, 1H, ArH), 6.78 (m, 1H, ArH), 3.77 (s, 1H, NH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.5, 139.5, 130.4, 129.1, 128.8, 128.5, 127.6, 127.1, 118.6, 115.6.

2-Aminobiphenyl (Table 23, entry 10). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-bromobiphenyl (0.117 g, 0.500 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography (silica gel, 9:1 hexanes:ethyl acetate) to give 2-aminobiphenyl as a pale yellow liquid (0.081 g, 99%).



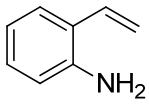
2,5-Dimethoxyaniline[67] (Table 23, entry 11). General procedure B was followed with the 2.5 x 10^{-3} M stock solution of the catalyst (0.20 mL, 0.00050 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 1-bromo-2,5-dimethoxybenzene (0.109 g, 0.500 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography (silica gel, 3:1 hexanes:ethyl acetate) to give 2,5-dimethoxyaniline as a white, crystalline solid (0.073 g, 95%). R_f = 0.20 (3:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.70 (d, *J* = 8.7 Hz, 1H, ArH), 6.34 (d, *J* = 2.8 Hz, 1H, ArH), 6.25 (dd, *J* = 2.8, 8.7 Hz, 1H, ArH), 3.82 (s, br, 2H, NH_2), 3.81 (s, 3H, *o*-OCH_3), 3.73 (s, 3H, *m*-OCH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.2, 141.7, 137.1, 111.2, 101.9, 101.7, 56.0, 55.4.



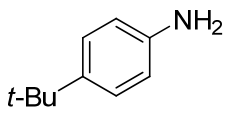
2,6-Dimethylaniline[68] (Table 23, entry 12). General procedure A was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-bromo-*m*-xylene (0.093 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography (silica gel, 6:1 hexanes:ethyl acetate) to give 2,6-dimethylaniline as a pale yellow liquid (0.053 g, 88%). R_f =

0.34 (5:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.05 (d, *J* = 7.4 Hz, 2H, ArH), 6.75 (t, *J* = 7.4, 7.4 Hz, 1H, ArH), 3.64 (s, br, 2H, NH_2), 2.27 (s, 6H, CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 128.1, 121.5, 17.8, 17.5.

2,6-Dimethylaniline (Table 26, entry 6). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-chloro-*m*-xylene (0.070 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography to give 2,6-dimethylaniline as a pale yellow liquid (0.054 g, 89%).

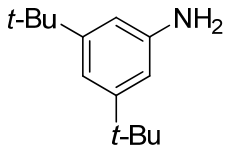


2-Aminostyrene[69] (Table 23, entry 13). General procedure A was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-bromostyrene (0.093 g, 1.0 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography (silica gel, 9:1 hexanes:ethyl acetate) to give 2-aminostyrene as colorless oil (0.0391 g, 66%). R_f = 0.25 (9:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.6 Hz, 1H, ArH), 7.12 (m, 1H, ArH), 6.80 (m, 2H, ArH), 6.70 (d, *J* = 7.9 Hz, 1H, $ArCHCH_2$), 5.66 (dd, *J* = 1.2, 17.4 Hz, 1H, ArCHCH(trans)H(cis)), 5.35 (dd, *J* = 1.3, 11.1 Hz, 1H, ArCHCH(trans)H(cis)), 3.8 (s, br, NH_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 132.6, 128.7, 127.2, 124.0, 118.8, 116.0, 115.6.

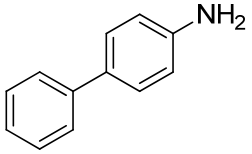


4-*t*-Butylaniline[14] (Table 24, entry 1). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol),

1-bromo-4-*t*-butylbenzene (0.107 g, 0.500 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) and 1,4-dioxane (8 mL). The product was purified by flash-column chromatography (silica gel, 6:1 hexanes:ethyl acetate) to give 4-*t*-butylaniline as a clear, pale yellow liquid (0.0659 g, 88%). R_f = 0.30 (6:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.6 Hz, 2H, ArH), 6.68 (d, *J* = 8.6 Hz, 2H, ArH), 3.52 (s, br, 2H, NH_2), 1.33 (s, 9H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 141.3, 126.0, 114.9, 33.8, 31.4.

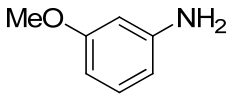


3,5-Di-*t*-butylaniline[15] (Table 24, entry 2). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 1-bromo-3,5-di-*t*-butylbenzene (0.134 g, 0.500 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) and and 1,4-dioxane (8 mL). The product was purified by flash-column chromatography (silica gel, 9:1 hexanes:ethyl acetate) to give 3,5-di-*t*-butylaniline as a white solid (0.080 g, 78%). R_f = 0.25 (9:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.86 (d, *J* = 6.9 Hz, 1H, ArH), 6.57 (d, *J* = 6.6 Hz, 2H, ArH), 3.59 (s, br, 2H, NH_2), 1.30 (s, 18H, CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.9, 145.5, 113.1, 109.8, 34.7, 31.4.



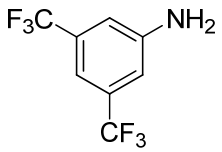
4-Aminobiphenyl[70] (Table 24, entry 3). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 4-bromobiphenyl (0.117 g, 0.500 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) and 1,4-dioxane (8 mL). The product was purified by flash-column chromatography (silica gel,

3:1 hexanes:ethyl acetate) to give 4-aminobiphenyl as a white solid (0.083 g, 98%). R_f = 0.27 (3:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.2 Hz, 2H, ArH), 7.42 (m, 4H, ArH), 7.28 (m, 1H, ArH), 6.77 (m, 2H, ArH), 3.73 (s, br, NH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.8, 141.1, 131.5, 128.6, 128.0, 126.4, 126.2, 115.3.

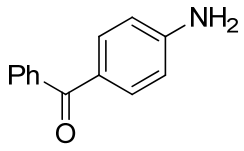


***m*-Anisidine[70] (Table 24, entry 4).** General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 3-bromoanisole (0.094 g, 0.50 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane), and 1,4-dioxane (8 mL). The product was purified by flash-column chromatography (silica gel, 3:1 hexanes:ethyl acetate) to give *m*-anisidine as a pale yellow liquid (0.061 g, 99%). R_f = 0.23 (3:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (t, *J* = 8.0, 8.0 Hz, 1H, ArH), 6.36 (dd, *J* = 2.4, 8.2 Hz, 1H, ArH), 6.31 (dd, *J* = 1.4, 7.9 Hz, 1H, ArH), 6.26 (t, *J* = 2.2, 2.2 Hz, 1H, ArH), 3.78 (s, 3H, OCH_3), 3.71 (s, br, NH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.6, 147.7, 130.0, 107.8, 103.7, 100.9, 54.9.

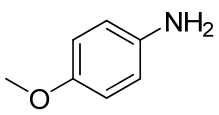
***m*-Anisidine (Table 26, entry 9).** General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 3-chloroanisole (0.071 g, 0.50 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) and 1,4-dioxane (8 mL). The product was purified by flash-column chromatography to give *m*-anisidine as a pale yellow liquid (0.061 g, 99%).



3,5-Bis(trifluoromethyl)aniline[67] (Table 24, entry 5). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 3,5-bis(trifluoromethyl)bromobenzene (0.146 g, 0.50 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) and 1,4-dioxane (8 mL). The product was purified by flash-column chromatography (silica gel, 6:1 hexanes:ethyl acetate) to give 3,5-bis(trifluoromethyl)aniline as a pale yellow oil (0.0897 g, 61%). R_f = 0.27 (6:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (s, 1H, ArH), 7.03 (s, 2H, ArH), 4.07 (s, br, NH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.3 (s), 132.5 (q, J = 32.9 Hz), 123.4 (q, J = 272.6 Hz), 114.1 (d, J = 2.95 Hz), 111.5 (dt, J = 3.9Hz). ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$ standard) δ -66.2.

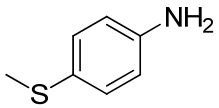


4-Aminobenzophenone[70] (Table 24, entry 6). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 4-bromobenzophenone (0.131 g, 0.50 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) and 1,4-dioxane (8 mL). The product was purified by flash-column chromatography (silica gel, 2:1 hexanes:ethyl acetate) to give 4-aminobenzophenone as an orange solid (0.076 g, 77%). R_f = 0.27 (2:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73-7.71 (m, 4H, ArH), 7.53 (t, J = 7.4 Hz, 1H, ArH), 7.45 (t, J = 7.4 Hz, 2H, ArH), 6.67 (m, 2H, ArH), 4.17 (s, br, NH_2) ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.3, 150.9, 138.8, 132.9, 131.4, 129.5, 128.0, 127.3, 113.6.

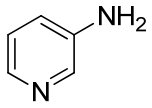


***p*-Anisidine[70] (Table 24, entry 7).** General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0036 g, 0.0050 mmol), CyPF-*t*-Bu (0.0028 g, 0.0050 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 4-bromoanisole (0.094 g, 0.50 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane), and 1,4-dioxane (5 mL) at 100 ^{o}C. The product was purified by flash-column chromatography (silica gel, 1:1 hexanes:ethyl acetate) to give *p*-anisidine as dark brown needles (0.033 g, 53%). R_f = 0.27 (1:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.75 (d, *J* = 8.8 Hz, 2H, ArH), 6.65 (d, *J* = 8.8 Hz, 2H, ArH), 3.75 (s, 3H, OCH_3), 3.43 (s, br, NH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.7, 139.9, 116.3, 114.7, 55.6.

***p*-Anisidine (Table 26, entry 10).** General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0036 g, 0.0050 mmol), CyPF-*t*-Bu (0.0028 g, 0.0050 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 4-chloroanisole (0.071 g, 0.50 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane), and 1,4-dioxane (5 mL) at 100 ^{o}C. The product was purified by flash-column chromatography (silica gel, 1:1 hexanes:ethyl acetate) to give *p*-anisidine as a pale yellow liquid (0.085 g, 69%).

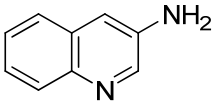


4-Aminothioanisole[71] (Table 24, entry 8). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 4-bromothioanisole (0.102 g, 0.500 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) and 1,4-dioxane (5 mL) 90 ^{o}C. The product was purified by flash-column chromatography (silica gel, 2:1 hexanes:ethyl acetate) to give 4-aminothioanisole as a dark orange liquid (0.064 g, 91%). R_f = 0.27 (2:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.18 (d, *J* = 8.6 Hz, 2H, ArH), 6.62 (d, *J* = 8.6 Hz, 2H, ArH), 3.66 (s, br, NH_2), 2.42 (s, 3H, SCH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.0, 130.9, 125.5, 115.6, 18.6.

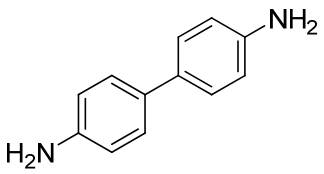


3-Aminopyridine[72] (Table 24, entry 9). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), and 3-bromopyridine (0.0790 g, 0.500 mmol). The product was purified by flash-column chromatography (silica gel, ethyl acetate) to give 3-aminopyridine as a colorless solid (0.0281 g, 60%). R_f = 0.20 (ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, *J* = 2.7 Hz, 1H, ArH), 7.96 (d, *J* = 4.6 Hz, 1H, ArH), 7.02 (dd, *J* = 4.7, 8.1 Hz, 1H, ArH), 6.92 (m, 1H, ArH), 3.80 (s, br, 2H, NH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.6, 139.7, 137.3, 123.6, 121.3.

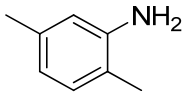
3-Aminopyridine (Table 26, entry 11). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), and 3-chloropyridine (0.057 g, 0.50 mmol). The product was purified by flash-column chromatography to give 3-aminopyridine as a colorless solid (0.030 g, 64%).



3-Aminoquinoline[67] (Table 24, entry 10). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 3-bromoquinoline (0.104 g, 0.50 mmol). The product was purified by flash-column chromatography (silica gel, ethyl acetate) to give 3-aminopyridine as a colorless solid (0.046 g, 64%). R_f = 0.26 (ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48 (d, *J* = 2.7 Hz, 1H, ArH), 7.96 (m, 1H, ArH), 7.55 (m, 1H, ArH), 7.48-7.35 (m, 2H, ArH), 7.16 (d, *J* = 2.7 Hz, 1H, ArH), 4.05 (s, br, 2H, NH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.0, 142.5, 139.8, 129.0, 128.8, 126.8, 125.7, 125.4, 114.7.



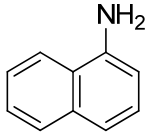
4,4'-Diaminobiphenyl[67] (Table 24, entry 11). The procedure for the preparation of 4,4'-diaminobiphenyl is modified from general procedure B, Pd[P(*o*-tol)$_3$]$_2$ (0.0072 g, 0.010 mmol), CyPF-*t*-Bu (0.0055 g, 0.0010 mmol), NaO-*t*-Bu (0.135 g, 1.40 mmol), and 4,4'-dibromobiphenyl (0.156 g, 0.500 mmol). The product was purified by flash-column chromatography (silica gel, 1:1 hexanes:ethyl acetate) to give 4,4'-diaminobiphenyl as a colorless solid (0.072 g, 79%). R_f = 0.26 (silica gel, 1:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.9 Hz, 4H, ArH), 6.68 (d, *J* = 7.9 Hz, 4H, ArH), 3.68 (s, br, 4H, NH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.9, 131.6, 127.2, 115.3.



2,5-Dimethylaniline[67] (Table 26, entry 3). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), and 2,5-dimethylchlorobenzene (0.070 g, 0.50 mmol). The product was purified by flash-column chromatography (silica gel, 6:1 hexanes:ethyl acetate) to give 2,5-dimethylaniline as a pale yellow liquid (0.051 g, 85%). R_f = 0.27 (6:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (d, *J* = 7.5 Hz, 1H, ArH), 6.59 (d, *J* = 7.5 Hz, 1H, ArH), 6.55 (s, 1H, ArH), 3.56 (s, 2H, NH_2), 2.31 (s, 3H, *m*-CH_3), 2.28 (s, 3H, *o*-CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.3, 136.5, 130.2, 119.3, 119.2, 115.6, 21.0, 16.8.

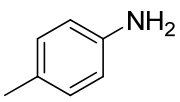
2,5-Dimethylaniline (Table 26, entry 4). General procedure A was followed with the 2.5 x 10^{-3} M stock solution of the catalyst (0.25 mL, 0.00050 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2,5-

dimethylchlorobenzene (0.070 g, 0.50 mmol). The product was purified by flash-column chromatography to give 2,5-dimethylaniline as a pale yellow liquid (0.038 g, 63%).



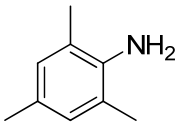
1-Aminonaphthalene[14] (Table 26, entry 7). General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 1-chloronaphthalene (0.081 g, 0.50 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) and 1,4-dioxane (8 mL) . The product was purified by flash-column chromatography (silica gel, 3:1 hexanes:ethyl acetate) to give the title compound as a colorless solid (0.064 g, 89%). R_f = 0.23 (3:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88-7.83 (m, 2H, ArH), 7.51-7.48 (m, 2H, ArH), 7.40-7.34 (m, 2H, ArH), 6.81 (dd, *J* = 1.3, 7.1 Hz, 1H ArH), 4.15 (s, br, 2H, NH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 142.0, 134.3, 128.5, 126.3, 125.8, 124.8, 123.6, 120.7, 118.9, 109.6.

1-Aminonaphthalene (Table 27, entry 3). General procedure C was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0072 g, 0.010 mmol), CyPF-*t*-Bu (0.0055 g, 0.010 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 1-naphthyl *p*-toluenesulfonate (0.149 g, 0.500 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) and 1,4-dioxane (5 mL). The product was purified by flash-column chromatography to give 1-aminonaphthalene as a colorless solid (0.048 g, 67%).

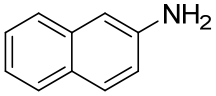


***p*-Toluidine[67] (Table 26, entry 8).** General procedure B was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0036 g, 0. 0.0050 mmol), CyPF-*t*-Bu (0.0028 g, 0.0050 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), and 4-chlorotoluene (0.063 g, 0.50 mmol). The product was purified by flash-column

chromatography (silica gel, 6:1 hexanes:ethyl acetate) to give 4-methylaniline as a clear colorless liquid (0.054 g, 55%). R_f = 0.25 (6:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00 (d, *J* = 8.0 Hz, 2H, ArH), 6.64 (d, *J* = 8.3 Hz, 2H, ArH), 3.65 (s, br, 2H, NH_2), 2.28 (s, 3H, $ArCH_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.7, 129.7, 127.7, 115.2, 20.4.

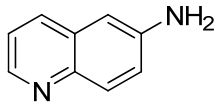


2,4,6-Trimethylaniline[67] (Table 27, entry 2). General procedure C was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0072 g, 0.010 mmol), CyPF-*t*-Bu (0.0055 g, 0.010 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2,4,6-trimethylphenyl *p*-toluenesulfonate (0.145 g, 0.50 mmol) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane). The product was purified by flash-column chromatography (silica gel, 6:1 hexanes:ethyl acetate) to give the title compound as a clear colorless liquid (0.058 g, 86%). R_f = 0.27 (6:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.86 (s, 2H, ArH), 3.50 (s, br, 2H, NH_2), 2.29 (s, 3H, *p*-CH_3), 2.24 (s, 6H, *o*-$(CH_3)_2$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 140.1, 128.7, 127.0, 121.7, 20.3, 17.5.

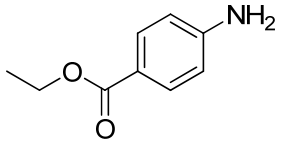


2-Aminonaphthalene[67] (Table 27, entry 4). General procedure C was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0072 g, 0.010 mmol), CyPF-*t*-Bu (0.0055 g, 0.010 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 2-naphthyl *p*-toluenesulfonate (0.149 g, 0.500 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) and 1,4-dioxane (5 mL). The product was purified by flash-column chromatography (silica gel, 6:1 hexanes:ethyl acetate) to give the title compound as a colorless solid (0.048 g, 67%). R_f = 0.23 (3:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.1 Hz, 1H, ArH), 7.70 (d, *J* = 8.6 Hz, 1H, ArH), 7.63 (d, *J* = 8.3 Hz, 1H,

ArH), 7.42 (t, J = 7.4 Hz, 1H, ArH), 7.20 (t, J = 7.4 Hz, 1H, ArH), 7.00 (s, 1H, ArH), 6.96 (d, J = 8.6 Hz, 1H, ArH), 3.81 (s, br, 2H, NH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.0, 134.8, 129.1, 127.9, 127.7, 126.3, 125.7, 122.4, 118.2, 108.5.



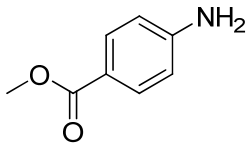
6-Aminoquinoline[67] (Table 27, entry 5). General procedure C was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0072 g, 0.010 mmol), CyPF-*t*-Bu (0.0055 g, 0.010 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 6-quinolinyl *p*-toluenesulfonate (0.150 g, 0.50 mmol), ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) and 1,4-dioxane (5 mL). The product was purified flash-column chromatography (silica gel, ethyl acetate) to give the title compound as a gray solid (0.040 g, 55%). R_f = 0.27 (ethyl acetate; UV, ninhydrin). ^1H NMR (500 MHz, $CDCl_3$) δ 8.63 (dd, J = 1.6, 4.2 Hz, 1H, ArH), 7.88 (d, J = 8.9 Hz, 1H, ArH), 7.83 (dd, J = 0.5, 8.3 Hz, 1H, ArH), 7.21 (dd, J = 4.2, 7.2 Hz, 1H, ArH), 7.11 (dd, J = 2.6, 8.9 Hz, 1H, ArH), 6.83 (d, J = 2.5 Hz,1H, ArH), 4.03 (s, br, 2H, NH_2). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.6, 144.6, 143.26, 133.6, 130.3, 129.7, 121.5, 121.2, 107.2.



Ethyl 4-aminobenzoate[67] (Table 28, entry 1). General procedure D was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), K_3PO_4 (0.530 g, 2.50 mmol), and ethyl 4-bromobenzoate (0.115 g, 0.500 mmol). The product was purified by flash-column chromatography (silica gel, gradient elution 5%, 10%, 15%, 20% and then 25% ethyl acetate in hexanes) to give ethyl 4-aminobenzoate as a colorless solid (0.070 g, 84%). R_f = 0.30 (3:1 hexanes:ethyl acetate; UV, ninhydrin). ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, J = 8.8 Hz, 2H, ArH), 6.63 (d, J = 8.8 Hz, 2H, ArH), 4.31 (q, J = 7.0 Hz, 2H, CH_3CH_2), 4.05 (br, 2H, NH_2),

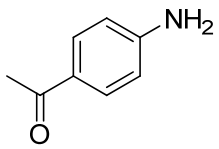
1.35 (t, J = 7.0 Hz, 3H, CH_3CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 151.1, 131.8, 120.1, 114.0, 60.6, 14.7.

Ethyl 4-aminobenzoate (Table 28, entry 2). General procedure D was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0036 g, 0.0050 mmol), CyPF-*t*-Bu (0.0028 g, 0.0050 mmol), K_3PO_4 (0.530 g, 2.50 mmol), and ethyl 4-{[(4-methylphenyl)sulfonyl]oxy}benzoate (0.160 g, 0.50 mmol). The product was purified by flash-column chromatography to give ethyl 4-aminobenzoate as a colorless solid (0.053 g, 65%).



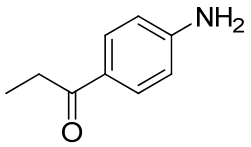
Methyl 4-aminobenzoate[70] (Table 28, entry 3). General procedure D was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), K_3PO_4 (0.530 g, 2.50 mmol), and methyl 4-bromobenzoate (0.108 g, 0.500 mmol). The product was purified by flash-column chromatography (silica gel, 3:1 hexanes:ethyl acetate) to give methyl 4-aminobenzoate as a colorless solid (0.063 g, 83%). R_f = 0.22 (3:1 hexanes:ethyl acetate; UV, ninhydrin). ^1H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.8 Hz, 2H, ArH), 6.63 (d, J = 8.8 Hz, 2H, ArH), 4.08 (br, 2H, NH_2), 3.84 (s, 3H, OCH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 151.1, 131.8, 119.9, 114.0, 51.9.

Methyl 4-aminobenzoate (Table 28, entry 4). General procedure D was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), K_3PO_4 (0.530 g, 2.50 mmol), and methyl 4-chlorobenzoate (0.085 g, 0.50 mmol). The product was purified by flash-column chromatography to give methyl 4-aminobenzoate as a colorless solid (0.060 g, 79%).



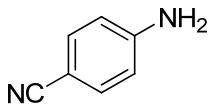
4'-Aminoacetophenone[71] (Table 28, entry 5). General procedure D was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), K_3PO_4 (0.530 g, 0.700 mmol), and 4'-bromoacetophenone (0.100 g, 0.500 mmol). The product was purified by flash-column chromatography (silica gel, 2:1 hexanes:ethyl acetate) to give methyl 4'-aminoacetophenone as a colorless solid (0.051 g, 76%). R_f = 0.22 (3:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.5 Hz, 2H, ArH), 6.64 (d, *J* = 8.5 Hz, 2H, ArH), 4.19 (s, br, 2H, NH_2), 2.50 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 151.2, 130.7, 127.6, 113.6, 26.0.

4'-Aminoacetophenone (Table 28, entry 6). General procedure D was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0036 g, 0.0050mmol), CyPF-*t*-Bu (0.0028 g, 0.0050 mmol), K_3PO_4 (0.530 g, 2.50 mmol), and 4'-iodoacetophenone (0.123 g, 0.500 mmol). The product was purified by flash-column chromatography (silica gel, 2:1 hexanes:ethyl acetate) to give methyl 4'-aminoacetophenone as a colorless solid (0.052 g, 78%).



4'-Aminopropiophenone[73] (Table 28, entry 7). General procedure D was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), K_3PO_4 (0.530 g, 2.50 mmol), and 4'-bromopropiophenone (0.107 g, 0.500 mmol). The product was purified by flash-column chromatography (silica gel, gradient elution 5%, 10%, 20% and 25% ethyl acetate in hexanes) to give 4'aminopropiophenone as a colorless solid (0.063 g, 85%). R_f = 0.30 (3:1

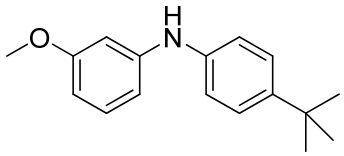
hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.8 Hz, 2H, ArH), 6.64 (d, *J* = 8.8 Hz, 2H, ArH), 4.15 (s, br, 2H, NH_2), 2.89 (q, *J* = 7.2, 7.2, 7.2 Hz, 2H, CH_3CH_2), 1.18 (t, *J* = 7.2, 7.2 Hz, 3H, CH_3CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 151.2, 130.6, 127.7, 114.0, 31.3, 8.9.



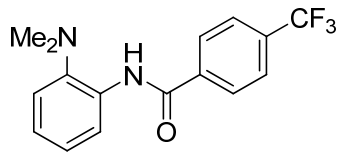
4-Aminobenzonitrile[71] (Table 28, entry 8). General procedure D was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), K_3PO_4 (0.530 g, 2.50 mmol), and 4-bromobenzonitrile (0.091 g, 0.50 mmol). The product was purified by flash-column chromatography (silica gel, gradient elution 5%, 10%, 20% and 25% ethyl acetate in hexanes) to give 4-aminobenzonitrile as a colorless solid (0.042 g, 71%). R_f = 0.26 (2:1 hexanes:ethyl acetate; UV, ninhydrin). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.7 Hz, 2H, ArH), 6.62 (d, *J* = 8.7 Hz, 2H, ArH), 4.32 (s, br, 2H, NH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 133.7, 120.2, 114.4, 100.0.

4-Aminopropiophenone (Table 28, entry 9). General procedure D was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), K_3PO_4 (0.530 g, 2.50 mmol), and 4-chlorobenzonitrile (0.069 g, 0.50 mmol). The product was purified by flash-column chromatography to give 4-aminobenzonitrile as a colorless solid (0.025 g, 44%).

4-Aminopropiophenone (Table 28, entry 10). General procedure D was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0036 g, 0.0050mmol), CyPF-*t*-Bu (0.0028 g, 0.0050 mmol), K_3PO_4 (0.530 g, 2.50 mmol), and 4-cyanophenyl *p*-toluenesulfonate (0.137 g, 0.500 mmol). The product was purified by flash-column chromatography to give 4-aminobenzonitrile as a colorless solid (0.045 g, 77%).

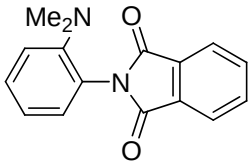


3-Methoxy-*N*-(4-*tert*-Butylphenyl)aniline (Scheme 27). Inside a drybox, Pd[P(*o*-tol)$_3$]$_2$ (0.0018 g, 0.0025 mmol), CyPF-*t*-Bu (0.0014 g, 0.0025 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol) and 4-*tert*-butylbromobenzene (0.106 g, 0.500 mmol) were added to a 20-mL scintillation vial. The vial was placed in an 80 °C oil bath for 5 hours. Then the solvent was evaporated under reduced pressure. Into this vial were added 3-methoxyphenyl *p*-toluenesulfonate (0.139 g, 0.500 mmol) and NaO-*t*-Bu (0.067 g, 0.70 mmol). The vial was then placed in a 80 °C oil bath for 8 h. The reaction mixture was filtered through a plug of Celite, concentrated, and purified by flash-column chromatography (silica gel, 4:1 hexanes:ethyl acetate) to give the title compound as a slightly yellow oil (0.112 g, 88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.6 Hz, 2H, Ar**H**), 7.21 (m, 1H, Ar**H**), 7.11 (d, *J* = 8.6 Hz, 2H, Ar**H**), 6.69 (d, *J* = 2.2 Hz, 2H, Ar**H**), 6.52 (d, *J* = 8.2 Hz, 1H, Ar**H**), 5.73 (s, 1H, N**H**), 3.82 (s, 3H, OC**H**$_3$), 1.40 (s, 9H, C(C**H**$_3$)$_3$. ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.6, 145.1, 144.3, 139.9, 130.0, 126.0, 118.5, 109.5, 105.4, 102.5, 55.0, 34.1, 31.4. Anal. Calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29; N, 5.49. Found: C, 80.05; H, 8.57; N, 5.32.

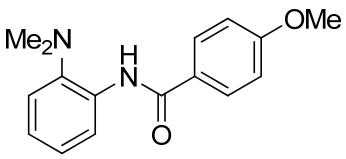


***N*-(2-Dimethylaminophenyl)-4-trifluoromethylbenzamide (Table 29, entry 1).** General procedure E was followed with Pd[P(*o*-tol)$_3$]$_2$ (0.0014 g, 0.0025 mmol), CyPF-*t*-Bu (0.0011 g, 0.0025 mmol), NaO-*t*-Bu (0.269 g, 2.80 mmol), 2-bromo-*N*,*N*-dimethylaniline (0.400 g, 2.00 mmol) and ammonia (15 mL of a 0.5 M solution in 1,4-dioxane) in a 20-mL scintillation vial. After the excess ammonia was removed, the reaction mixture was then divided into 4 equal

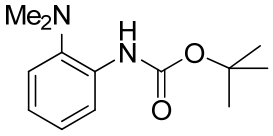
portions. 4-(Trifluoromethyl)benzoyl chloride (0.104 g, 0.500 mmol) and Et_3N (0.050 g, 0.50 mmol) was added to one portion. The resulting mixture was stirred at room temperature. The product was purified by flash-column chromatography (silica gel, 9:1 hexanes:ethyl acetate) to give *N*-(2-dimethylaminophenyl)-4-trifluoromethylbenzamide as a colorless solid (0.134 g, 87%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.48 (s, br, 1H, N**H**), 8.54 (d, *J* = 8.0 Hz, 1H, Ar**H**), 8.05 (d, *J* = 8.1 Hz, 2H, Ar**H**), 7.79 (d, *J* = 8.1 Hz, 2H, Ar**H**), 7.27 (d, *J* = 7.6 Hz, 1H, Ar**H**), 7.22 (t, *J* = 7.7 Hz, 1H, Ar**H**), 7.14 (t, *J* = 7.6 Hz, 1H, Ar**H**), 2.72 (s, 6H, N(C**H**$_3$)$_2$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.5, 143.1, 138.5, 133.2 (q, *J* = 32.7 Hz), 133.1. 127.4, 125.8 (q, *J* = 3.7 Hz), 125.3, 124.3, 123.6 (q, J = 273.5 Hz), 120.1, 119.4, 44.9. Anal. Calcd for $C_{16}H_{15}F_3N_2O$: C, 62.33; H, 4.90; N, 9.09. Found: C, 62.43; H, 5.00; N, 8.83.



2-[2-(Dimethylamino)phenyl]-1H-isoindole-1,3(2H)-dione[74] (Table 29, entry 2). Following general procedure E and the procedure described for Table 9, entry 1, phthalic anhydride (0.074 g, 0.50 mmol) was added to one of the four portions of the solution from the crude amination process. The resulting mixture was stirred at room temperature. The product was purified by flash-column chromatography (silica gel, 3:1 hexanes:ethyl acetate) to give the title compound as a colorless solid (0.068 g, 51%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 3.1, 5.4 Hz, 2H, ArH), 7.78 (dd, *J* = 3.0, 5.5 Hz, 2H, ArH), 7.40 (m, 1H, ArH), 7.19 (ddd, *J* = 1.4, 7.9, 14.3 Hz, 2H, ArH), 7.10 (td, *J* = 1.3, 7.6 Hz, 1H, ArH), 2.64 (s, 6H, N(CH_3)$_2$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.6, 151.6, 134.1, 132.1, 130.2, 130.1, 124.7, 123.6, 122.5, 120.2, 43.7.

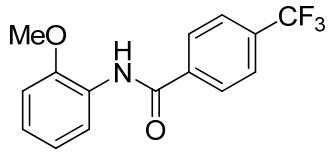


***N*-(2-Dimethylaminophenyl)-4-methoxybenzamide (Table 29, entry 3).** Following general procedure E and the procedure described for Table 9, entry 1, 4-anisolyl chloride (0.085 g, 0.50 mmol) and Et_3N (0.050 g, 0.50 mmol) were added to one of the four portions of the solution from the crude amination process. The resulting mixture was stirred at room temperature 12 h. The product was purified by flash-column chromatography (silica gel, 9:1 hexanes to ethyl acetate) to give the title compound as a colorless solid (0.100 g, 74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.31 (s, br, 1H, N**H**), 8.52 (d, *J* = 8.1 Hz, 1H, Ar**H**), 7.90 (d, *J* = 8.7 Hz, 2H, Ar**H**), 7.21 (d, *J* = 7.9 Hz, 1H, Ar**H**), 7.17 (t, *J* = 7.7 Hz, 1H, Ar**H**), 7.07 (t, *J* = 7.6, 1H, Ar**H**), 6.99 (d, *J* = 8.7 Hz, 2H, Ar**H**), 3.86 (s, 6H, N(C**H**$_3$)$_2$), 2.70 (s, 6H, OC**H**$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.4, 162.3, 142.9, 133.6, 128.7, 127.5, 125.1, 123.5, 119.8, 119.3, 113.9, 55.3, 44.8. Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.36. Found: C, 71.37; H, 6.59; N, 10.19.

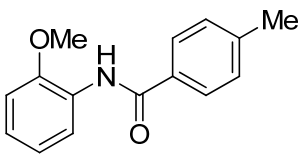


***N*-(2-*N*,*N*-Dimethylaminophenyl)-1,1-dimethylethyl ester carbamic acid[65] (Table 29, entry 4).** Following general procedure F and the procedure described for Table 9, entry 1, di-*tert*-butyl dicarbonate (0.109 g, 0.50 mmol) was added to one of the four portions of the solution from the crude amination process. The resulting mixture was stirred at 80 °C for 12 h. After evaporation of the solvent, a solution of imidazole (0.017 g, 0.025 mmol) in ethanol (2 mL) was added. The product was purified by flash-column chromatography (silica gel, 4% ethyl acetate in hexanes) to give the title compound as a colorless solid (0.089 g, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08

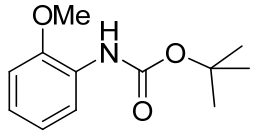
(d, J = 6.3 Hz, 1H, NH), 7.71 (s, 1H, ArH), 7.14 (d, J = 7.9 Hz, 1H, ArH), 7.09 (t, J = 7.8 Hz, 1H, ArH), 6.97 (t, J = 7.0 Hz, 1H, ArH), 2.63 (s, 6H, $N(CH_3)_2$), 1.55 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.0, 142.1, 133.9, 125.0, 122.3, 120.0, 117.7, 80.1, 44.7, 28.4.



***N*-(2-Methoxyphenyl)-4-trifluoromethylbenzamide (Table 29, entry 5).** General procedure E was followed with $Pd[P(o\text{-tol})_3]_2$ (0.0014 g, 0.0025 mmol), CyPF-*t*-Bu (0.0011 g, 0.0025 mmol), NaO-*t*-Bu (0.269 g, 2.8 mmol), 2-chloroanisole (0.285 g, 2.0 mmol) and ammonia (15 mL of a 0.5 M solution in 1,4-dioxane) in a 20-mL scintillation vial. After the excess ammonia was removed, the reaction mixture was divided into 4 equal portions. 4-(Trifluoromethyl)benzoyl chloride (0.104 g, 0.500 mmol) and Et_3N (0.050 g, 0.50 mmol) were added to one of the portions. The resulting mixture was stirred at room temperature for 12 h. The product was purified by flash-column chromatography (silica gel, 9:1 hexanes:ethyl acetate) to give the title compound as a colorless solid (0.121 g, 82%). ^1H NMR (500 MHz, $CDCl_3$) δ 8.56 (s, br, 1H, N**H**), 8.51 (d, J = 7.9 Hz, 1H, Ar**H**), 8.00 (d, J = 8.0 Hz, 2H, Ar**H**), 7.76 (d, J = 8.0 Hz, 2H, Ar**H**), 7.12 (t, J = 7.8, 7.8 Hz, 1H, Ar**H**), 7.04 (t, J = 7.7, 7.7 Hz, 1H, Ar**H**), 6.94 (d, J = 8.1 Hz, 1H, Ar**H**), 3.93 (s, 3H, O**CH**$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 163.8, 148.1, 138.6, 133.3 (q, J = 38.9, 38.9, 38.9 Hz), 133.1. 127.5, 125.8 (q, J = 3.6, 3.6, 3.6 Hz), 125.7, 124.3, 123.6 (q, J = 273.4, 273.4, 273.4 Hz), 121.2, 119.9, 55.8. Anal. Calcd for $C_{15}H_{12}F_3NO_2$: C, 61.02; H, 4.10; N, 4.74. Found: C, 61.02; H, 3.97; N, 4.71.

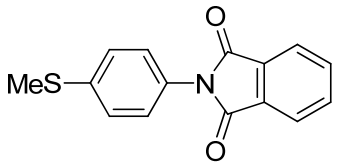


***N*-(2-Methoxyphenyl)-4-methyl-benzamide (Table 29, entry 6).** Following general procedure E and the procedure described for Table 9, entry 5, *p*-toluoyl chloride (0.077 g, 0.50 mmol) and Et_3N (0.050 g, 0.50 mmol) were added to one of the four portions of the solution from the crude amination process. The resulting mixture was stirred at room temperature. The product was purified by flash-column chromatography (silica gel, 4% ethyl acetate in hexanes) to give the title compound as a colorless solid (0.113 g, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (s, br, 1H, N**H**), 8.53 (s, 1H, Ar**H**), 7.80 (d, *J* = 8.0 Hz, 2H, Ar**H**), 7.30 (d, *J* = 7.9 Hz, 2H, Ar**H**), 7.08 (t, *J* = 7.7 Hz, 1H, Ar**H**), 7.02 (t, *J* = 7.6 Hz, 1H, Ar**H**), 6.92 (d, *J* = 8.0 Hz, 1H, Ar**H**), 3.93 (s, 3H, OC**H**$_3$), 2.43 (s, 3H, ArC**H**$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.0, 148.0, 142.0, 132.3, 129.2, 127.8, 126.9, 123.6, 121.0, 119.6, 109.8, 55.6, 21.3. Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27; N, 5.81. Found: C, 74.29; H, 6.31; N, 5.71.



***N*-(2-Methoxyphenyl)-1,1-dimethylethyl ester carbamic acid[75] (Table 29, entry 7).** Following general procedure F and the procedure described for Table 9, entry 5, di-*tert*-butyl dicarbonate (0.109 g, 0.500 mmol) was added to one of the four portions of the solution from the crude amination process. The resulting mixture was stirred at 80 °C for 12 h. After evaporation of the solvent, a solution of imidazole (0.017 g, 0.025 mmol) in ethanol (2 mL) was added. The product was purified by flash-column chromatography (silica gel, 4% ethyl acetate in hexanes) to give the title compound as a colorless solid (0.076 g, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (s, 1H, NH), 7.12 (s, 1H, ArH), 6.96 (m, 2H, ArH), 6.89 (d, *J* = 9.1 Hz, 1H, ArH), 3.85 (s, 3H,

OCH_3), 1.54 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 152.7, 147.4, 128.0, 122.2, 121.0, 118.0, 109.8, 80.1, 55.5, 28.3.



2-[4-Thioanisylphenyl]-1H-isoindole-1,3(2H)-dione (Table 29, entry 8). General procedure E was followed with $Pd[P(o\text{-tol})_3]_2$ (0.0036 g, 0.0050 mmol), CyPF-*t*-Bu (0.0028 g, 0.0050 mmol), NaO-*t*-Bu (0.067 g, 0.70 mmol), 4-bromothioanisole (0.102 g, 0.500 mmol), 1,4-dioxane (5 mL) and ammonia (5 mL of a 0.5 M solution in 1,4-dioxane) in a 20-mL scintillation vial. After the excess ammonia was removed, phthalic anhydride (0.074 g, 0.50 mmol) was added. The resulting mixture was stirred at room temperature for 12 h. The product was purified by flash-column chromatography (silica gel, 6:1 hexanes:ethyl acetate) to give the title compound as a colorless solid (0.100 g, 75%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.95 (dd, J = 3.1, 5.3 Hz, 2H, Ar**H**), 7.79 (dd, J = 3.1, 5.3 Hz, 2H, Ar**H**), 7.37 (s, 4H, Ar**H**), 2.51 (s, 3H, SC**H**$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ 167.2, 138.9, 134.4, 131.7, 128.6, 126.9, 126.8, 123.7, 15.8. Anal. Calcd for $C_{15}H_{11}NO_2S$: C, 66.89; H, 4.12; N, 5.20. Found: C, 66.89; H, 4.41; N, 4.86.

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Appendix A. Crystallographic Data for [(Q-phos)Pd(η^3-allyl)Cl]

Table 30. Crystal data and structure refinement for [(Q-Phos)Pd(allyl)(Cl)].

Empirical formula	C58 H60 Cl Fe P Pd	
Formula weight	985.73	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 12.5975(6) Å	□= 76.255(3)°.
	b = 13.4224(6) Å	□= 71.615(2)°.
	c = 15.7498(7) Å	□ = 78.485(3)°.
Volume	2432.25(19) Å^3	
Z	2	
Density (calculated)	1.346 Mg/m^3	
Absorption coefficient	0.793 mm^{-1}	
F(000)	1024	
Crystal size	0.32 x 0.207 x 0.14 mm^3	
Theta range for data collection	1.58 to 25.42°.	
Index ranges	-15<=h<=15, -16<=k<=16, -18<=l<=18	
Reflections collected	61816	
Independent reflections	8923 [R(int) = 0.0724]	
Completeness to theta = 25.42°	99.5 %	
Absorption correction	Integration	
Max. and min. transmission	0.9278 and 0.8728	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8923 / 281 / 635	
Goodness-of-fit on F^2	1.018	
Final R indices [I>2sigma(I)]	R1 = 0.0390, wR2 = 0.0857	
R indices (all data)	R1 = 0.0626, wR2 = 0.0955	
Largest diff. peak and hole	0.770 and -0.392 e.Å^{-3}	

Table 31. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for [(Q-Phos)Pd(allyl)(Cl)]. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	6003(1)	2040(1)	9770(1)	32(1)
Fe(1)	9829(1)	1189(1)	7517(1)	19(1)
Cl(1)	6716(1)	380(1)	10502(1)	49(1)
P(1)	7652(1)	2873(1)	9039(1)	24(1)
C(1)	4304(13)	1604(7)	10368(8)	54(3)
C(2)	4246(5)	2364(6)	9751(6)	54(2)
C(3)	4668(14)	3312(8)	9608(9)	54(3)
C(1B)	4340(30)	1634(13)	10621(16)	55(4)
C(2B)	4264(9)	2573(12)	10305(11)	51(3)
C(3B)	4750(30)	3200(20)	9455(19)	52(4)
C(4)	8040(3)	3227(3)	9990(2)	31(1)
C(5)	8549(3)	2224(3)	10509(2)	37(1)
C(6)	8886(3)	4005(3)	9690(3)	43(1)
C(7)	6947(3)	3655(3)	10655(2)	45(1)
C(8)	7498(3)	4060(3)	8136(2)	33(1)
C(9)	6942(3)	3745(3)	7520(2)	39(1)
C(10)	8619(3)	4427(3)	7544(2)	39(1)
C(11)	6734(4)	4971(3)	8557(3)	47(1)
C(12)	8947(2)	2056(2)	8556(2)	21(1)
C(13)	10093(3)	2271(3)	8154(2)	26(1)
C(14)	10826(3)	1333(3)	8283(2)	30(1)
C(15)	10166(3)	531(3)	8739(2)	28(1)
C(16)	9024(3)	962(2)	8895(2)	25(1)
C(17)	9413(2)	1581(2)	6271(2)	21(1)
C(18)	10613(2)	1393(2)	6125(2)	22(1)

Table 31 (continued)

C(19)	10911(2)	357(2)	6562(2)	20(1)
C(20)	9893(2)	-102(2)	6998(2)	21(1)
C(21)	8965(2)	657(2)	6834(2)	21(1)
C(22)	8810(3)	2491(2)	5789(2)	24(1)
C(23)	7943(3)	2365(3)	5462(2)	29(1)
C(24)	7430(3)	3202(3)	4954(3)	42(1)
C(25)	7763(3)	4164(3)	4759(3)	44(1)
C(26)	8621(3)	4304(3)	5074(2)	34(1)
C(27)	9141(3)	3480(2)	5581(2)	26(1)
C(28)	11447(2)	2075(2)	5489(2)	23(1)
C(29)	11451(3)	2350(2)	4575(2)	28(1)
C(30)	12243(3)	2935(3)	3950(2)	37(1)
C(31)	13036(3)	3250(3)	4228(3)	41(1)
C(32)	13041(3)	2987(3)	5125(3)	40(1)
C(33)	12248(3)	2395(3)	5757(2)	32(1)
C(34)	12080(2)	-201(2)	6466(2)	22(1)
C(35)	12783(3)	-256(3)	5591(2)	30(1)
C(36)	13841(3)	-830(3)	5463(3)	38(1)
C(37)	14220(3)	-1358(3)	6198(3)	39(1)
C(38)	13540(3)	-1297(3)	7070(3)	38(1)
C(39)	12480(3)	-727(3)	7200(2)	31(1)
C(40)	9803(2)	-1197(2)	7461(2)	23(1)
C(41)	10469(3)	-1983(3)	7010(2)	32(1)
C(42)	10367(3)	-3013(3)	7395(3)	42(1)
C(43)	9604(3)	-3271(3)	8232(3)	45(1)
C(44)	8939(3)	-2505(3)	8680(3)	41(1)
C(45)	9031(3)	-1475(3)	8302(2)	30(1)
C(46)	7782(2)	440(2)	7096(2)	23(1)
C(47)	7542(3)	-286(3)	6707(2)	31(1)
C(48)	6452(3)	-475(3)	6881(2)	36(1)
C(49)	5583(3)	41(3)	7460(3)	42(1)
C(50)	5812(3)	736(3)	7874(3)	46(1)
C(51)	6911(3)	938(3)	7696(2)	34(1)
C(52)	6211(7)	5257(6)	2898(6)	84(2)
C(53)	7148(6)	5605(7)	2225(6)	76(2)

Table 31 (continued)

C(54)	7277(7)	6648(7)	2025(6)	93(3)
C(55)	6468(9)	7342(6)	2497(7)	88(3)
C(56)	5530(7)	6993(7)	3170(6)	96(3)
C(57)	5402(6)	5951(7)	3370(5)	82(2)
C(58)	6063(9)	4211(8)	3138(8)	88(3)
C(59)	6112(7)	5720(6)	3017(5)	91(2)
C(60)	7040(8)	5175(6)	2486(6)	90(3)
C(61)	7803(6)	5707(7)	1760(5)	86(2)
C(62)	7638(7)	6783(7)	1566(5)	93(3)
C(63)	6710(8)	7327(6)	2097(6)	83(3)
C(64)	5947(6)	6795(6)	2822(6)	77(2)
C(65)	5255(9)	5151(10)	3752(7)	96(4)

Table 32. Bond lengths [Å] and angles [°] for [(Q-Phos)Pd(allyl)(Cl)].

Pd(1)-C(3B)	2.07(4)
Pd(1)-C(2B)	2.125(11)
Pd(1)-C(3)	2.174(16)
Pd(1)-C(2)	2.177(6)
Pd(1)-C(1)	2.184(15)
Pd(1)-C(1B)	2.19(3)
Pd(1)-P(1)	2.3879(9)
Pd(1)-Cl(1)	2.3942(10)
Fe(1)-C(15)	2.056(3)
Fe(1)-C(14)	2.059(3)
Fe(1)-C(20)	2.061(3)
Fe(1)-C(16)	2.063(3)
Fe(1)-C(21)	2.064(3)
Fe(1)-C(19)	2.064(3)
Fe(1)-C(18)	2.076(3)
Fe(1)-C(13)	2.080(3)
Fe(1)-C(17)	2.109(3)
Fe(1)-C(12)	2.124(3)
P(1)-C(12)	1.827(3)
P(1)-C(8)	1.891(3)
P(1)-C(4)	1.897(3)
C(1)-C(2)	1.238(8)
C(1)-H(1A)	0.9900
C(1)-H(1B)	0.9900
C(2)-C(3)	1.419(12)
C(2)-H(2A)	1.0000
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(1B)-C(2B)	1.237(11)
C(1B)-H(1C)	0.9900
C(1B)-H(1D)	0.9900
C(2B)-C(3B)	1.424(14)

Table 32 (continued)

C(2B)-H(2B)	1.0000
C(3B)-H(3C)	0.9900
C(3B)-H(3D)	0.9900
C(4)-C(6)	1.531(5)
C(4)-C(5)	1.534(5)
C(4)-C(7)	1.545(5)
C(5)-H(5A)	0.9800
C(5)-H(5B)	0.9800
C(5)-H(5C)	0.9800
C(6)-H(6A)	0.9800
C(6)-H(6B)	0.9800
C(6)-H(6C)	0.9800
C(7)-H(7A)	0.9800
C(7)-H(7B)	0.9800
C(7)-H(7C)	0.9800
C(8)-C(10)	1.528(5)
C(8)-C(9)	1.534(5)
C(8)-C(11)	1.542(5)
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(11)-H(11C)	0.9800
C(12)-C(16)	1.433(4)
C(12)-C(13)	1.440(4)
C(13)-C(14)	1.419(5)
C(13)-H(13)	1.0000
C(14)-C(15)	1.407(5)
C(14)-H(14)	1.0000
C(15)-C(16)	1.407(4)
C(15)-H(15)	1.0000

Table 32 (continued)

C(16)-H(16)	1.0000
C(17)-C(18)	1.434(4)
C(17)-C(21)	1.444(4)
C(17)-C(22)	1.483(4)
C(18)-C(19)	1.432(4)
C(18)-C(28)	1.493(4)
C(19)-C(20)	1.433(4)
C(19)-C(34)	1.492(4)
C(20)-C(21)	1.435(4)
C(20)-C(40)	1.487(4)
C(21)-C(46)	1.486(4)
C(22)-C(23)	1.399(5)
C(22)-C(27)	1.403(4)
C(23)-C(24)	1.389(5)
C(23)-H(23)	0.9500
C(24)-C(25)	1.372(5)
C(24)-H(24)	0.9500
C(25)-C(26)	1.384(5)
C(25)-H(25)	0.9500
C(26)-C(27)	1.383(5)
C(26)-H(26)	0.9500
C(27)-H(27)	0.9500
C(28)-C(33)	1.381(5)
C(28)-C(29)	1.397(5)
C(29)-C(30)	1.381(5)
C(29)-H(29)	0.9500
C(30)-C(31)	1.379(6)
C(30)-H(30)	0.9500
C(31)-C(32)	1.374(5)
C(31)-H(31)	0.9500
C(32)-C(33)	1.391(5)
C(32)-H(32)	0.9500
C(33)-H(33)	0.9500
C(34)-C(39)	1.388(5)
C(34)-C(35)	1.393(4)

Table 32 (continued)

C(35)-C(36)	1.380(5)
C(35)-H(35)	0.9500
C(36)-C(37)	1.377(5)
C(36)-H(36)	0.9500
C(37)-C(38)	1.382(5)
C(37)-H(37)	0.9500
C(38)-C(39)	1.380(5)
C(38)-H(38)	0.9500
C(39)-H(39)	0.9500
C(40)-C(45)	1.392(4)
C(40)-C(41)	1.396(4)
C(41)-C(42)	1.385(5)
C(41)-H(41)	0.9500
C(42)-C(43)	1.378(5)
C(42)-H(42)	0.9500
C(43)-C(44)	1.373(5)
C(43)-H(43)	0.9500
C(44)-C(45)	1.381(5)
C(44)-H(44)	0.9500
C(45)-H(45)	0.9500
C(46)-C(51)	1.378(4)
C(46)-C(47)	1.389(5)
C(47)-C(48)	1.377(5)
C(47)-H(47)	0.9500
C(48)-C(49)	1.371(5)
C(48)-H(48)	0.9500
C(49)-C(50)	1.376(5)
C(49)-H(49)	0.9500
C(50)-C(51)	1.392(5)
C(50)-H(50)	0.9500
C(51)-H(51)	0.9500
C(52)-C(53)	1.3900
C(52)-C(57)	1.3900
C(52)-C(58)	1.399(11)
C(53)-C(54)	1.3900

Table 32 (continued)

C(53)-H(53)	0.9500
C(54)-C(55)	1.3900
C(54)-H(54)	0.9500
C(55)-C(56)	1.3900
C(55)-H(55)	0.9500
C(56)-C(57)	1.3900
C(56)-H(56)	0.9500
C(57)-H(57)	0.9500
C(58)-H(58A)	0.9800
C(58)-H(58B)	0.9800
C(58)-H(58C)	0.9800
C(59)-C(60)	1.3900
C(59)-C(64)	1.3900
C(59)-C(65)	1.486(10)
C(60)-C(61)	1.3900
C(60)-H(60)	0.9500
C(61)-C(62)	1.3900
C(61)-H(61)	0.9500
C(62)-C(63)	1.3900
C(62)-H(62)	0.9500
C(63)-C(64)	1.3900
C(63)-H(63)	0.9500
C(64)-H(64)	0.9500
C(65)-H(65A)	0.9800
C(65)-H(65B)	0.9800
C(65)-H(65C)	0.9800

C(3B)-Pd(1)-C(2B)	39.6(4)
C(3B)-Pd(1)-C(3)	7.5(14)
C(2B)-Pd(1)-C(3)	36.2(5)
C(3B)-Pd(1)-C(2)	36.0(8)
C(2B)-Pd(1)-C(2)	26.5(4)
C(3)-Pd(1)-C(2)	38.1(4)
C(3B)-Pd(1)-C(1)	66.6(7)
C(2B)-Pd(1)-C(1)	34.3(5)

Table 32 (continued)

C(3)-Pd(1)-C(1)	66.2(4)
C(2)-Pd(1)-C(1)	33.0(3)
C(3B)-Pd(1)-C(1B)	70.4(6)
C(2B)-Pd(1)-C(1B)	33.2(4)
C(3)-Pd(1)-C(1B)	68.5(6)
C(2)-Pd(1)-C(1B)	40.3(7)
C(1)-Pd(1)-C(1B)	11.2(10)
C(3B)-Pd(1)-P(1)	101.4(6)
C(2B)-Pd(1)-P(1)	134.2(4)
C(3)-Pd(1)-P(1)	101.6(3)
C(2)-Pd(1)-P(1)	135.9(2)
C(1)-Pd(1)-P(1)	167.9(3)
C(1B)-Pd(1)-P(1)	164.6(6)
C(3B)-Pd(1)-Cl(1)	155.0(6)
C(2B)-Pd(1)-Cl(1)	116.8(4)
C(3)-Pd(1)-Cl(1)	153.0(2)
C(2)-Pd(1)-Cl(1)	120.0(2)
C(1)-Pd(1)-Cl(1)	88.4(3)
C(1B)-Pd(1)-Cl(1)	84.8(5)
P(1)-Pd(1)-Cl(1)	103.45(3)
C(15)-Fe(1)-C(14)	39.99(13)
C(15)-Fe(1)-C(20)	101.60(13)
C(14)-Fe(1)-C(20)	125.74(13)
C(15)-Fe(1)-C(16)	39.94(12)
C(14)-Fe(1)-C(16)	67.00(13)
C(20)-Fe(1)-C(16)	110.67(12)
C(15)-Fe(1)-C(21)	129.11(13)
C(14)-Fe(1)-C(21)	165.73(13)
C(20)-Fe(1)-C(21)	40.73(12)
C(16)-Fe(1)-C(21)	110.54(12)
C(15)-Fe(1)-C(19)	106.89(12)
C(14)-Fe(1)-C(19)	103.76(12)
C(20)-Fe(1)-C(19)	40.66(11)
C(16)-Fe(1)-C(19)	139.05(12)
C(21)-Fe(1)-C(19)	68.38(12)

Table 32 (continued)

C(15)-Fe(1)-C(18)	140.68(12)
C(14)-Fe(1)-C(18)	114.31(12)
C(20)-Fe(1)-C(18)	68.11(12)
C(16)-Fe(1)-C(18)	178.54(13)
C(21)-Fe(1)-C(18)	68.03(12)
C(19)-Fe(1)-C(18)	40.46(12)
C(15)-Fe(1)-C(13)	67.35(13)
C(14)-Fe(1)-C(13)	40.08(13)
C(20)-Fe(1)-C(13)	165.81(13)
C(16)-Fe(1)-C(13)	67.10(13)
C(21)-Fe(1)-C(13)	153.41(12)
C(19)-Fe(1)-C(13)	131.89(12)
C(18)-Fe(1)-C(13)	114.28(12)
C(15)-Fe(1)-C(17)	169.06(13)
C(14)-Fe(1)-C(17)	149.18(13)
C(20)-Fe(1)-C(17)	68.02(12)
C(16)-Fe(1)-C(17)	138.95(12)
C(21)-Fe(1)-C(17)	40.46(12)
C(19)-Fe(1)-C(17)	67.83(11)
C(18)-Fe(1)-C(17)	40.07(11)
C(13)-Fe(1)-C(17)	123.46(12)
C(15)-Fe(1)-C(12)	67.37(12)
C(14)-Fe(1)-C(12)	67.28(12)
C(20)-Fe(1)-C(12)	145.58(12)
C(16)-Fe(1)-C(12)	40.00(12)
C(21)-Fe(1)-C(12)	120.64(12)
C(19)-Fe(1)-C(12)	170.95(12)
C(18)-Fe(1)-C(12)	140.81(12)
C(13)-Fe(1)-C(12)	40.04(12)
C(17)-Fe(1)-C(12)	119.04(12)
C(12)-P(1)-C(8)	107.20(14)
C(12)-P(1)-C(4)	100.62(15)
C(8)-P(1)-C(4)	110.17(16)
C(12)-P(1)-Pd(1)	116.60(10)
C(8)-P(1)-Pd(1)	115.69(12)

Table 32 (continued)

C(4)-P(1)-Pd(1)	105.40(11)
C(2)-C(1)-Pd(1)	73.2(6)
C(2)-C(1)-H(1A)	116.2
Pd(1)-C(1)-H(1A)	116.2
C(2)-C(1)-H(1B)	116.2
Pd(1)-C(1)-H(1B)	116.2
H(1A)-C(1)-H(1B)	113.2
C(1)-C(2)-C(3)	127.2(12)
C(1)-C(2)-Pd(1)	73.8(8)
C(3)-C(2)-Pd(1)	70.8(8)
C(1)-C(2)-H(2A)	115.0
C(3)-C(2)-H(2A)	115.0
Pd(1)-C(2)-H(2A)	115.0
C(2)-C(3)-Pd(1)	71.1(6)
C(2)-C(3)-H(3A)	116.5
Pd(1)-C(3)-H(3A)	116.5
C(2)-C(3)-H(3B)	116.5
Pd(1)-C(3)-H(3B)	116.5
H(3A)-C(3)-H(3B)	113.5
C(2B)-C(1B)-Pd(1)	70.3(13)
C(2B)-C(1B)-H(1C)	116.6
Pd(1)-C(1B)-H(1C)	116.6
C(2B)-C(1B)-H(1D)	116.6
Pd(1)-C(1B)-H(1D)	116.6
H(1C)-C(1B)-H(1D)	113.6
C(1B)-C(2B)-C(3B)	135(2)
C(1B)-C(2B)-Pd(1)	76.5(16)
C(3B)-C(2B)-Pd(1)	68.1(16)
C(1B)-C(2B)-H(2B)	108.4
C(3B)-C(2B)-H(2B)	108.4
Pd(1)-C(2B)-H(2B)	108.4
C(2B)-C(3B)-Pd(1)	72.2(15)
C(2B)-C(3B)-H(3C)	116.4
Pd(1)-C(3B)-H(3C)	116.4
C(2B)-C(3B)-H(3D)	116.4

Table 32 (continued)

Pd(1)-C(3B)-H(3D)	116.4
H(3C)-C(3B)-H(3D)	113.3
C(6)-C(4)-C(5)	108.1(3)
C(6)-C(4)-C(7)	109.1(3)
C(5)-C(4)-C(7)	107.7(3)
C(6)-C(4)-P(1)	115.8(2)
C(5)-C(4)-P(1)	107.4(2)
C(7)-C(4)-P(1)	108.5(3)
C(4)-C(5)-H(5A)	109.5
C(4)-C(5)-H(5B)	109.5
H(5A)-C(5)-H(5B)	109.5
C(4)-C(5)-H(5C)	109.5
H(5A)-C(5)-H(5C)	109.5
H(5B)-C(5)-H(5C)	109.5
C(4)-C(6)-H(6A)	109.5
C(4)-C(6)-H(6B)	109.5
H(6A)-C(6)-H(6B)	109.5
C(4)-C(6)-H(6C)	109.5
H(6A)-C(6)-H(6C)	109.5
H(6B)-C(6)-H(6C)	109.5
C(4)-C(7)-H(7A)	109.5
C(4)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
C(4)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(10)-C(8)-C(9)	108.1(3)
C(10)-C(8)-C(11)	108.3(3)
C(9)-C(8)-C(11)	109.2(3)
C(10)-C(8)-P(1)	113.9(2)
C(9)-C(8)-P(1)	105.7(2)
C(11)-C(8)-P(1)	111.5(2)
C(8)-C(9)-H(9A)	109.5
C(8)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5

Table 32 (continued)

C(8)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(8)-C(10)-H(10A)	109.5
C(8)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
C(8)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
C(8)-C(11)-H(11A)	109.5
C(8)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(8)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
C(16)-C(12)-C(13)	105.7(3)
C(16)-C(12)-P(1)	118.3(2)
C(13)-C(12)-P(1)	131.4(2)
C(16)-C(12)-Fe(1)	67.71(16)
C(13)-C(12)-Fe(1)	68.30(17)
P(1)-C(12)-Fe(1)	146.60(17)
C(14)-C(13)-C(12)	108.4(3)
C(14)-C(13)-Fe(1)	69.19(19)
C(12)-C(13)-Fe(1)	71.65(17)
C(14)-C(13)-H(13)	125.8
C(12)-C(13)-H(13)	125.8
Fe(1)-C(13)-H(13)	125.8
C(15)-C(14)-C(13)	108.5(3)
C(15)-C(14)-Fe(1)	69.88(19)
C(13)-C(14)-Fe(1)	70.73(18)
C(15)-C(14)-H(14)	125.8
C(13)-C(14)-H(14)	125.8
Fe(1)-C(14)-H(14)	125.8
C(16)-C(15)-C(14)	107.9(3)
C(16)-C(15)-Fe(1)	70.31(18)

Table 32 (continued)

C(14)-C(15)-Fe(1)	70.13(19)
C(16)-C(15)-H(15)	126.0
C(14)-C(15)-H(15)	126.0
Fe(1)-C(15)-H(15)	126.0
C(15)-C(16)-C(12)	109.5(3)
C(15)-C(16)-Fe(1)	69.75(18)
C(12)-C(16)-Fe(1)	72.30(17)
C(15)-C(16)-H(16)	125.3
C(12)-C(16)-H(16)	125.3
Fe(1)-C(16)-H(16)	125.3
C(18)-C(17)-C(21)	107.2(3)
C(18)-C(17)-C(22)	124.5(3)
C(21)-C(17)-C(22)	127.6(3)
C(18)-C(17)-Fe(1)	68.72(17)
C(21)-C(17)-Fe(1)	68.07(17)
C(22)-C(17)-Fe(1)	136.1(2)
C(19)-C(18)-C(17)	108.7(3)
C(19)-C(18)-C(28)	124.2(3)
C(17)-C(18)-C(28)	126.3(3)
C(19)-C(18)-Fe(1)	69.33(16)
C(17)-C(18)-Fe(1)	71.20(16)
C(28)-C(18)-Fe(1)	133.7(2)
C(18)-C(19)-C(20)	107.9(3)
C(18)-C(19)-C(34)	126.0(3)
C(20)-C(19)-C(34)	125.5(3)
C(18)-C(19)-Fe(1)	70.21(16)
C(20)-C(19)-Fe(1)	69.54(16)
C(34)-C(19)-Fe(1)	132.6(2)
C(19)-C(20)-C(21)	107.9(3)
C(19)-C(20)-C(40)	126.7(3)
C(21)-C(20)-C(40)	125.1(3)
C(19)-C(20)-Fe(1)	69.80(17)
C(21)-C(20)-Fe(1)	69.74(17)
C(40)-C(20)-Fe(1)	130.5(2)
C(20)-C(21)-C(17)	108.2(3)

Table 32 (continued)

C(20)-C(21)-C(46)	123.9(3)
C(17)-C(21)-C(46)	127.2(3)
C(20)-C(21)-Fe(1)	69.53(17)
C(17)-C(21)-Fe(1)	71.46(17)
C(46)-C(21)-Fe(1)	131.5(2)
C(23)-C(22)-C(27)	117.9(3)
C(23)-C(22)-C(17)	120.1(3)
C(27)-C(22)-C(17)	121.8(3)
C(24)-C(23)-C(22)	120.2(3)
C(24)-C(23)-H(23)	119.9
C(22)-C(23)-H(23)	119.9
C(25)-C(24)-C(23)	121.0(4)
C(25)-C(24)-H(24)	119.5
C(23)-C(24)-H(24)	119.5
C(24)-C(25)-C(26)	119.6(3)
C(24)-C(25)-H(25)	120.2
C(26)-C(25)-H(25)	120.2
C(27)-C(26)-C(25)	120.2(3)
C(27)-C(26)-H(26)	119.9
C(25)-C(26)-H(26)	119.9
C(26)-C(27)-C(22)	121.0(3)
C(26)-C(27)-H(27)	119.5
C(22)-C(27)-H(27)	119.5
C(33)-C(28)-C(29)	119.0(3)
C(33)-C(28)-C(18)	122.8(3)
C(29)-C(28)-C(18)	118.1(3)
C(30)-C(29)-C(28)	120.4(3)
C(30)-C(29)-H(29)	119.8
C(28)-C(29)-H(29)	119.8
C(31)-C(30)-C(29)	119.9(4)
C(31)-C(30)-H(30)	120.0
C(29)-C(30)-H(30)	120.0
C(32)-C(31)-C(30)	120.3(3)
C(32)-C(31)-H(31)	119.8
C(30)-C(31)-H(31)	119.8

Table 32 (continued)

C(31)-C(32)-C(33)	120.0(4)
C(31)-C(32)-H(32)	120.0
C(33)-C(32)-H(32)	120.0
C(28)-C(33)-C(32)	120.3(3)
C(28)-C(33)-H(33)	119.8
C(32)-C(33)-H(33)	119.8
C(39)-C(34)-C(35)	118.2(3)
C(39)-C(34)-C(19)	123.6(3)
C(35)-C(34)-C(19)	118.1(3)
C(36)-C(35)-C(34)	120.7(3)
C(36)-C(35)-H(35)	119.7
C(34)-C(35)-H(35)	119.7
C(37)-C(36)-C(35)	120.5(3)
C(37)-C(36)-H(36)	119.8
C(35)-C(36)-H(36)	119.8
C(36)-C(37)-C(38)	119.5(3)
C(36)-C(37)-H(37)	120.2
C(38)-C(37)-H(37)	120.2
C(39)-C(38)-C(37)	120.0(3)
C(39)-C(38)-H(38)	120.0
C(37)-C(38)-H(38)	120.0
C(38)-C(39)-C(34)	121.1(3)
C(38)-C(39)-H(39)	119.4
C(34)-C(39)-H(39)	119.4
C(45)-C(40)-C(41)	118.3(3)
C(45)-C(40)-C(20)	122.8(3)
C(41)-C(40)-C(20)	118.8(3)
C(42)-C(41)-C(40)	120.7(3)
C(42)-C(41)-H(41)	119.7
C(40)-C(41)-H(41)	119.7
C(43)-C(42)-C(41)	120.1(3)
C(43)-C(42)-H(42)	120.0
C(41)-C(42)-H(42)	120.0
C(44)-C(43)-C(42)	119.9(3)
C(44)-C(43)-H(43)	120.1

Table 32 (continued)

C(42)-C(43)-H(43)	120.1
C(43)-C(44)-C(45)	120.6(3)
C(43)-C(44)-H(44)	119.7
C(45)-C(44)-H(44)	119.7
C(44)-C(45)-C(40)	120.5(3)
C(44)-C(45)-H(45)	119.7
C(40)-C(45)-H(45)	119.7
C(51)-C(46)-C(47)	118.8(3)
C(51)-C(46)-C(21)	122.7(3)
C(47)-C(46)-C(21)	118.5(3)
C(48)-C(47)-C(46)	121.2(3)
C(48)-C(47)-H(47)	119.4
C(46)-C(47)-H(47)	119.4
C(49)-C(48)-C(47)	119.9(3)
C(49)-C(48)-H(48)	120.0
C(47)-C(48)-H(48)	120.0
C(48)-C(49)-C(50)	119.5(3)
C(48)-C(49)-H(49)	120.3
C(50)-C(49)-H(49)	120.3
C(49)-C(50)-C(51)	120.9(3)
C(49)-C(50)-H(50)	119.6
C(51)-C(50)-H(50)	119.6
C(46)-C(51)-C(50)	119.7(3)
C(46)-C(51)-H(51)	120.2
C(50)-C(51)-H(51)	120.2
C(53)-C(52)-C(57)	120.0
C(53)-C(52)-C(58)	121.9(6)
C(57)-C(52)-C(58)	118.1(6)
C(54)-C(53)-C(52)	120.0
C(54)-C(53)-H(53)	120.0
C(52)-C(53)-H(53)	120.0
C(53)-C(54)-C(55)	120.0
C(53)-C(54)-H(54)	120.0
C(55)-C(54)-H(54)	120.0
C(56)-C(55)-C(54)	120.0

Table 32 (continued)

C(56)-C(55)-H(55)	120.0
C(54)-C(55)-H(55)	120.0
C(57)-C(56)-C(55)	120.0
C(57)-C(56)-H(56)	120.0
C(55)-C(56)-H(56)	120.0
C(56)-C(57)-C(52)	120.0
C(56)-C(57)-H(57)	120.0
C(52)-C(57)-H(57)	120.0
C(60)-C(59)-C(64)	120.0
C(60)-C(59)-C(65)	119.9(6)
C(64)-C(59)-C(65)	119.9(6)
C(59)-C(60)-C(61)	120.0
C(59)-C(60)-H(60)	120.0
C(61)-C(60)-H(60)	120.0
C(60)-C(61)-C(62)	120.0
C(60)-C(61)-H(61)	120.0
C(62)-C(61)-H(61)	120.0
C(61)-C(62)-C(63)	120.0
C(61)-C(62)-H(62)	120.0
C(63)-C(62)-H(62)	120.0
C(64)-C(63)-C(62)	120.0
C(64)-C(63)-H(63)	120.0
C(62)-C(63)-H(63)	120.0
C(63)-C(64)-C(59)	120.0
C(63)-C(64)-H(64)	120.0
C(59)-C(64)-H(64)	120.0
C(59)-C(65)-H(65A)	109.5
C(59)-C(65)-H(65B)	109.5
H(65A)-C(65)-H(65B)	109.5
C(59)-C(65)-H(65C)	109.5
H(65A)-C(65)-H(65C)	109.5
H(65B)-C(65)-H(65C)	109.5

Table 33. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for [(Q-Phos)Pd(allyl)(Cl)]. 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}
Pd(1)	25(1)	36(1)	31(1)	-12(1)	-2(1)	0(1)
Fe(1)	19(1)	19(1)	18(1)	-3(1)	-3(1)	-2(1)
Cl(1)	32(1)	41(1)	53(1)	5(1)	6(1)	-7(1)
P(1)	30(1)	20(1)	21(1)	-6(1)	-5(1)	1(1)
C(1)	23(3)	75(4)	64(6)	-23(3)	-2(5)	-9(3)
C(2)	25(3)	79(4)	53(4)	-25(3)	-4(3)	8(3)
C(3)	30(4)	62(4)	53(5)	-20(3)	2(3)	20(3)
C(1B)	24(5)	79(5)	54(7)	-20(5)	1(6)	1(5)
C(2B)	19(4)	72(4)	57(5)	-26(4)	0(4)	5(4)
C(3B)	27(5)	68(6)	56(6)	-21(5)	-6(5)	9(5)
C(4)	45(2)	27(2)	22(2)	-7(2)	-10(2)	-4(2)
C(5)	50(2)	37(2)	26(2)	-3(2)	-15(2)	-9(2)
C(6)	64(3)	35(2)	37(2)	-11(2)	-14(2)	-16(2)
C(7)	59(3)	46(2)	27(2)	-17(2)	-3(2)	-3(2)
C(8)	44(2)	22(2)	29(2)	-6(2)	-11(2)	6(2)
C(9)	43(2)	41(2)	27(2)	-4(2)	-11(2)	6(2)
C(10)	57(2)	25(2)	28(2)	-1(2)	-6(2)	-4(2)
C(11)	65(3)	29(2)	37(2)	-8(2)	-12(2)	15(2)
C(12)	27(2)	22(2)	16(2)	-6(1)	-6(1)	-1(1)
C(13)	29(2)	28(2)	23(2)	-7(1)	-6(1)	-10(1)
C(14)	26(2)	42(2)	24(2)	-8(2)	-9(1)	-2(2)
C(15)	33(2)	29(2)	19(2)	-4(1)	-8(1)	5(1)
C(16)	30(2)	24(2)	17(2)	-3(1)	-2(1)	-3(1)
C(17)	24(2)	22(2)	15(2)	-4(1)	-4(1)	-3(1)
C(18)	23(2)	25(2)	16(2)	-5(1)	-3(1)	-3(1)

Table 33 (continued)

C(19)	21(2)	21(2)	16(2)	-4(1)	-3(1)	-3(1)
C(20)	22(2)	20(2)	20(2)	-6(1)	-3(1)	-2(1)
C(21)	22(2)	22(2)	18(2)	-7(1)	-4(1)	-3(1)
C(22)	24(2)	26(2)	18(2)	-4(1)	-2(1)	2(1)
C(23)	29(2)	30(2)	30(2)	-7(2)	-11(2)	0(1)
C(24)	41(2)	43(2)	49(2)	-10(2)	-28(2)	7(2)
C(25)	48(2)	37(2)	42(2)	1(2)	-23(2)	10(2)
C(26)	39(2)	24(2)	32(2)	-2(2)	-7(2)	4(2)
C(27)	24(2)	28(2)	23(2)	-4(1)	-5(1)	1(1)
C(28)	24(2)	19(2)	21(2)	-3(1)	0(1)	-3(1)
C(29)	29(2)	22(2)	25(2)	-3(1)	-1(1)	1(1)
C(30)	40(2)	28(2)	27(2)	2(2)	2(2)	2(2)
C(31)	33(2)	25(2)	46(2)	3(2)	11(2)	-6(2)
C(32)	26(2)	34(2)	55(3)	-7(2)	-3(2)	-10(2)
C(33)	29(2)	34(2)	31(2)	-4(2)	-8(2)	-4(2)
C(34)	20(2)	18(2)	26(2)	-5(1)	-5(1)	-3(1)
C(35)	28(2)	32(2)	25(2)	-7(2)	-5(1)	0(1)
C(36)	28(2)	41(2)	40(2)	-16(2)	2(2)	-2(2)
C(37)	20(2)	37(2)	59(3)	-18(2)	-8(2)	4(2)
C(38)	32(2)	36(2)	44(2)	-5(2)	-17(2)	5(2)
C(39)	28(2)	32(2)	27(2)	-3(2)	-2(1)	-2(1)
C(40)	21(2)	23(2)	28(2)	-3(1)	-9(1)	-4(1)
C(41)	31(2)	27(2)	36(2)	-8(2)	-6(2)	-6(2)
C(42)	45(2)	22(2)	59(3)	-13(2)	-12(2)	1(2)
C(43)	51(2)	22(2)	58(3)	5(2)	-15(2)	-13(2)
C(44)	41(2)	35(2)	42(2)	4(2)	-8(2)	-17(2)
C(45)	30(2)	28(2)	29(2)	-1(2)	-5(2)	-5(1)
C(46)	22(2)	25(2)	22(2)	-2(1)	-8(1)	-4(1)
C(47)	27(2)	38(2)	29(2)	-15(2)	-5(1)	-4(2)
C(48)	33(2)	42(2)	38(2)	-15(2)	-10(2)	-12(2)
C(49)	24(2)	59(3)	47(2)	-18(2)	-3(2)	-16(2)
C(50)	23(2)	62(3)	52(3)	-30(2)	5(2)	-7(2)
C(51)	25(2)	40(2)	40(2)	-22(2)	-4(2)	-4(2)
C(52)	72(4)	136(5)	70(5)	-25(4)	-49(4)	-22(4)
C(53)	60(4)	122(5)	68(5)	-33(4)	-39(4)	-8(4)

Table 33 (continued)

C(54)	71(5)	133(5)	88(6)	-36(5)	-35(4)	-4(4)
C(55)	69(5)	133(5)	79(6)	-41(5)	-38(5)	0(4)
C(56)	79(6)	143(5)	80(6)	-36(5)	-40(4)	2(5)
C(57)	62(4)	139(5)	65(5)	-25(5)	-41(4)	-10(4)
C(58)	80(7)	120(7)	82(8)	14(6)	-65(6)	-22(6)
C(59)	70(4)	141(5)	79(5)	-20(4)	-43(4)	-18(4)
C(60)	74(5)	144(5)	70(5)	-43(4)	-42(4)	5(5)
C(61)	68(5)	127(5)	85(5)	-50(5)	-39(4)	4(5)
C(62)	65(5)	140(5)	90(6)	-38(5)	-31(4)	-15(5)
C(63)	68(5)	120(5)	81(6)	-45(5)	-35(4)	-5(4)
C(64)	66(5)	123(5)	71(5)	-37(4)	-43(4)	-15(4)
C(65)	84(6)	149(9)	63(6)	31(6)	-42(5)	-61(6)

Table 34. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for [(Q-Phos)Pd(allyl)(Cl)].

	x	y	z	U(eq)
H(1A)	4194	939	10262	65
H(1B)	3920	1718	10997	65
H(2A)	4103	2217	9206	65
H(3A)	4360	3713	10106	65
H(3B)	4766	3748	8993	65
H(1C)	3977	1213	10384	66
H(1D)	4243	1429	11285	66
H(2B)	4186	2951	10802	61
H(3C)	4835	3911	9474	63
H(3D)	4496	3158	8933	63
H(5A)	8631	2357	11070	55
H(5B)	9292	1981	10127	55
H(5C)	8050	1694	10663	55
H(6A)	9107	4066	10217	65
H(6B)	8537	4682	9433	65
H(6C)	9556	3766	9228	65
H(7A)	7129	3813	11165	68
H(7B)	6425	3136	10887	68
H(7C)	6592	4287	10336	68
H(9A)	6866	4325	7021	58
H(9B)	6194	3559	7876	58
H(9C)	7412	3149	7268	58
H(10A)	8476	5042	7094	58
H(10B)	9092	3875	7230	58
H(10C)	9008	4598	7930	58
H(11A)	6560	5529	8072	71
H(11B)	7125	5227	8894	71

Table 34 (continued)

H(11C)	6031	4737	8974	71
H(13)	10332	2965	7846	31
H(14)	11670	1256	8090	36
H(15)	10457	-212	8930	34
H(16)	8367	568	9207	30
H(23)	7703	1704	5588	35
H(24)	6839	3107	4739	51
H(25)	7406	4729	4410	52
H(26)	8853	4969	4942	41
H(27)	9731	3584	5792	32
H(29)	10905	2133	4383	33
H(30)	12242	3120	3330	44
H(31)	13582	3651	3797	50
H(32)	13587	3210	5313	48
H(33)	12257	2210	6375	39
H(35)	12531	104	5078	35
H(36)	14311	-860	4862	46
H(37)	14944	-1761	6107	47
H(38)	13803	-1647	7581	45
H(39)	12015	-696	7802	37
H(41)	10998	-1810	6433	38
H(42)	10823	-3542	7082	51
H(43)	9538	-3977	8499	54
H(44)	8410	-2685	9255	49
H(45)	8564	-953	8618	36
H(47)	8141	-658	6315	37
H(48)	6302	-964	6599	43
H(49)	4828	-81	7576	51
H(50)	5213	1082	8286	55
H(51)	7060	1417	7988	41
H(53)	7701	5131	1902	91
H(54)	7918	6886	1565	111
H(55)	6556	8054	2360	105
H(56)	4977	7468	3493	115
H(57)	4761	5713	3830	99

Table 34 (continued)

H(58A)	6802	3782	3050	133
H(58B)	5657	4061	2755	133
H(58C)	5626	4057	3779	133
H(60)	7152	4440	2619	108
H(61)	8437	5335	1397	104
H(62)	8159	7146	1070	112
H(63)	6597	8062	1964	100
H(64)	5313	7167	3185	92
H(65A)	5424	4412	3725	144
H(65B)	4504	5420	3672	144
H(65C)	5274	5246	4346	144

ORTEP diagram of [(Q-Phos)Pd(allyl)(Cl)]