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Amines as Activating Ligands for Phosphine Palladium(II) Precatalysts: Effect of Amine Ligand Identity on the Catalyst Efficiency

Jordan K. Pierce, Lindsey D. Hiatt, James R. Howard, Huaiyuan Hu, Fengrui Qu, and Kevin H. Shaughnessy*

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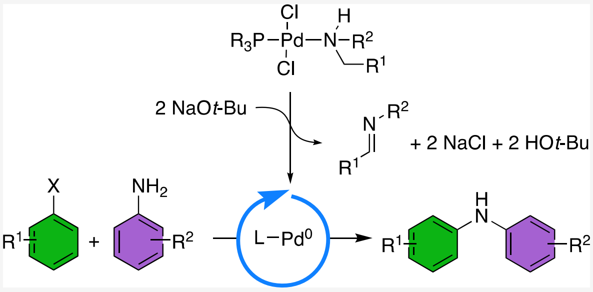

ABSTRACT: Palladium-catalyzed cross-coupling reactions between C−X/C−H bonds and nucleophilic reagents remain a staple in organic synthesis. These reactions rely on the in situ generation of an active LPd^0 species. Air-stable palladium(II) precatalysts that readily form the LPd^0 species under catalytic conditions have been identified as effective precatalysts. The alkyl amine ligand can serve as potential reducing ligands for palladium(II) complexes in the presence of a base through a sequence of β-hydrogen elimination and base-promoted reductive elimination of the resulting palladium hydride. A series of air-stable (^{t}Bu$_2$PNp)Pd(amine)Cl$_2$ (Np = neopentyl) complexes were synthesized with a range of structurally different primary and secondary amine ligands. These complexes allowed the effect of the amine ligand structure on the catalyst performance in cross-coupling of aryl halides and aniline derivatives to be analyzed. The identity of the amine ligand has a significant effect on catalyst activity and lifetime. Precatalysts with primary *n*-alkylamine ligands afford the most active catalysts. Reactions using (^{t}Bu$_2$PNp)Pd(*n*-butylamine)Cl$_2$ as the precatalyst provide excellent yields at room temperature under 1 h. Moreover, (Np$_3$P)Pd(*n*-butylamine)Cl$_2$ was synthesized and exhibited promising activity for sterically demanding aniline derivatives and aryl chlorides. Preliminary mechanistic studies show that the structure of the amine ligand has a significant effect on the selectivity for palladium(0) formation that correlates with the activity of the precatalysts.

■ INTRODUCTION

Palladium-catalyzed cross-coupling reactions between C−X/C−H bonds and nucleophilic reagents have been extensively studied due to their efficiency in forming C−C and C-heteroatom bonds.[1] The functional group tolerance and generality of these reactions allow for the synthesis of agrochemicals, pharmaceuticals, and natural products.[2] Early work focused on identifying privileged classes of ligands that provide effective cross-coupling catalysts. These privileged ligand classes include bulky trialkylphosphines,[3] 2-biarylphosphines,[4] and *N*-heterocyclic carbene (NHC) ligands.[5] The electron-donating nature of these ligands promotes oxidative addition of unreactive bonds. Additionally, the steric bulk promotes low coordination numbers, which further promotes oxidative addition.

Cross-coupling reactions with modern ligands rely on the generation of an active LPd^0 species.[6] Traditional methods involving in situ catalyst formation from the free ligand and palladium precursor provide limited control over the speciation of the active species.[7] Recent research has shown that the improved catalyst performance can be achieved by the generation of the active LPd^0 species through the use of preformed palladium−ligand complexes with the desired 1:1 L/Pd ratio.[8] Palladium(II) complexes are often preferred due to their higher stability than palladium(0) complexes. Examples of palladium(II) precatalysts include (allyl)Pd(L)Cl complexes (**1** and **2**),[9] Buchwald palladacycle precatalysts (**3** and **4**),[10] palladium aryl halide complexes (**5**),[11] and pyridine-enhanced precatalyst purification stabilization and initiation (PEPPSI) complexes (**6**).[12] A key design feature in complexes **1**−**5** is a ready path to reduction to the LPd^0 in the presence of basic and/or nucleophilic reagents typically present in cross-coupling reactions.

Nolan first reported the use of (η^3-allyl)Pd(NHC)Cl precatalysts (**1**) in cross-coupling reactions.[9a,13] Shaughnessy and Colacot later reported phosphine palladium allyl complexes.[9b,14] These complexes have been applied to a variety of C−C and C-heteroatom coupling reactions. Activation occurs by

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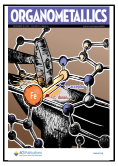

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reductive coupling of the nucleophile with the allyl ligand.[13a,15] During the activation process, the active LPd^0 species can comproportionate with the remaining palladium(II) allyl complex to form catalytically inactive μ-allyl dipalladium(I) complexes.[9c,14a] The comproportionation reaction can be inhibited by substitution on the allyl ligand.[9b,c] Hazari developed 1-(^{t}Bu)indenyl complexes (**2**) that do not undergo this comproportionation reaction, which results in higher activity catalysts.[16]

N,*C*-Palladacycle precatalysts developed by Buchwald, known as G1−G4 precatalysts (**3**,**4**), have become widely used.[10] These complexes are primed to undergo reductive elimination upon deprotonation of a coordinated amine. Of these precatalysts, the G3 complex is the most widely used, although the carbazole byproduct can act as a catalyst inhibitor in some cases.[14b,17] Arylpalladium complexes (**5**), so-called oxidative addition catalysts (OACs), have been shown to be effective precatalysts for cross-coupling reactions.[11a,b,d,18] These species can be activated by the reaction with the nucleophilic coupling partner in reactions, although this results in a small amount of byproduct derived from the original aryl group on the precatalyst.

The PEPPSI complexes (**6**) reported by Organ are convenient palladium(II) NHC precatalysts that are effective in a wide range of palladium-catalyzed reactions.[12b,19] 3-Chloropyridine serves as a weakly coordinating ligand that occupies the fourth coordination site on palladium and is also thought to stabilize the LPd^0 active species. Unlike the other precatalysts in Figure 1, the PEPPSI complexes require an external reductant to generate the LPd^0 species. These precatalysts are often employed in cross-coupling reactions between aryl halides and organometallic reagents where the organometallic reagent acts as the reducing agent.[12b]

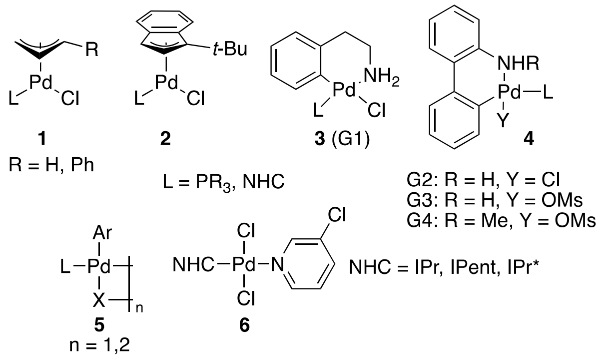
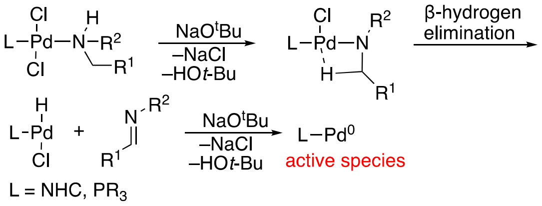


Figure 1. Examples of palladium(II) precatalysts.

In cases where the coupling partners do not provide effective reduction pathways, external reducing agents can be used to activate the catalyst. For example, Organ found that the PEPPSI catalyst system required elevated temperatures in the coupling of aryl chlorides with arylthiolates. Addition of LiO*i*-Pr or morpholine significantly improved catalyst activity.[20] A precatalyst incorporating morpholine as a ligand in place of 3-chloropyridine proved to be a superior catalyst for these reactions.[21] The role of morpholine in the activation was hypothesized to involve β-hydrogen elimination followed by base-mediated HX reductive elimination to give the LPd^0 species (Scheme 1). In the course of preparing this manuscript, Nicasio reported a (ArPR$_2$)Pd(morpholine)Cl$_2$ complex as an effective catalyst for coupling of aryl bromides and aniline derivatives, which presumably operates by a similar mechanism.[22]

Scheme 1. Proposed Amine Activation Pathway for Mixed Ligand Amine Palladium(II) Complexes



Our group has studied the use of simple, air-stable [LPdCl$_2$]$_2$ complexes (L = ^{t}Bu$_2$PNp and PNp$_3$ and Np = neopentyl) as catalyst precursors in cross-coupling reactions. These complexes are effective catalysts for Suzuki couplings, where the boronic acid coupling partner reduces the palladium(II) precatalyst to the active species.[23] The palladium(II) dimers require high temperatures to catalyze the coupling of aryl halides and aniline derivatives, however. In this case, there is no effective reduction pathway. Additives such as isopropanol and enolizable ketones serve as effective reductants and provide active catalysts under mild conditions for these reactions.[24]

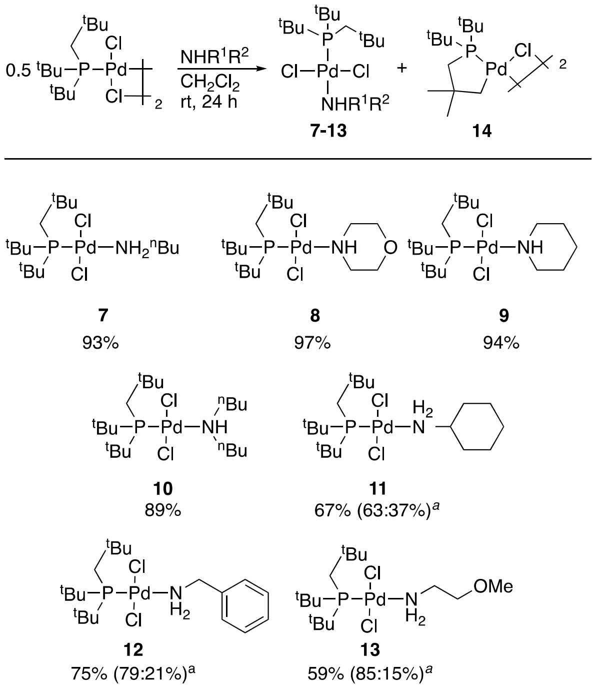
To provide more effective catalysts, we sought to prepare monophosphine complexes containing a ligand that could act as an internal reductant under cross-coupling conditions. Inspired by Organ's (NHC)Pd(morpholine)Cl$_2$ precatalyst,[20] we chose to explore amines as activating ligands. We hypothesized that these complexes would undergo base-mediated reduction to LPd^0, as shown in Scheme 1. Organ[20] and Nicasio[22] explored only morpholine complexes as precatalysts. The effect of the amine structure on catalyst activation has not been studied in these systems, however. Herein, we report the first study of a range of phosphine palladium(II) amine complexes to determine the optimal structure for the amine activator. The identity of the amine ligand was found to play a critical role in determining the catalytic activity in these systems.

■ RESULTS AND DISCUSSION

Synthesis and Characterization of Palladium Amine Complexes. (^{t}Bu$_2$PNp)Pd(amine)Cl$_2$ complexes (**7**−**13**) were synthesized by the reaction of two equivalents of amine with the previously reported [(^{t}Bu$_2$PNp)PdCl$_2$]$_2$ (Scheme 2).[23] The isolated precatalysts are indefinitely air stable at ambient temperature. Target complexes were isolated in moderate-to-high yields with varying degrees of purity. Complexes **7**−**10** were isolated as pure solids. Complexes **11**−**13** were isolated as mixtures containing 15−37% palladacycle **14** byproduct, as determined by ^{31}P NMR spectroscopy. Attempts to further purify complexes **11**−**13** by recrystallization were unsuccessful due to co-crystallization of the amine complexes and palladacycles. Our group has previously reported the base-promoted C−H activation of ^{t}Bu$_2$PNp complexes, resulting in the formation of a (κ^2-*P*,*C*-^{t}Bu$_2$PCH$_2$CMe$_2$CH$_2$) palladacycle (**14**).[23,25]

Crystals of complexes **7**−**13** suitable for X-ray crystallography were grown through slow evaporation of hexane solutions of the complexes (Figure 2). All complexes crystallized with slightly distorted *trans*-square planar geometries, in which the chloride ligands were deflected away

Scheme 2. Synthesis of (^{t}Bu$_2$PNp)Pd(amine)Cl$_2$ Complexes[a]



[a]Isolated as inseparable mixtures with **14**. Yield of complex **11−13** based on the molar ratio with **14** determined by ^{31}P NMR (value in parentheses).

from the sterically demanding phosphine ligand. Each complex contains one N−H bond that is aligned with one Pd−Cl bond with H−N−Pd−Cl dihedral angles, ranging from 8 to 15° (Table S2). The aligned H and Cl show close H···Cl contact distances of 2.54−2.67 Å (Table S1) that are significantly shorter than the sum of the van der Waals radii (2.95 Å).[26] Cyclohexylamine complex **11** and cyclic secondary amine complexes **8** and **9** have the shortest NH−Cl distances and smallest N−Pd−Cl angles (82.8−83.7°) for the chlorine involved in the intramolecular H···Cl contact. Complexes **7** and **10−13** have complementary intermolecular PdCl···HN short contact interactions in the solid state (H···Cl = 2.49−2.65 Å; Table S1; Figures S75, S79, S81, S83, S85). This intermolecular interaction is not observed in the morpholine (**8**) and piperidine (**9**) complexes.

Comparison of Precatalysts 7−13 in the Arylation of Aniline. Complexes **7−13** were applied to the Buchwald−Hartwig cross-coupling of 4-bromoanisole and aniline at room temperature to explore their potential as precatalysts (Scheme 3). This model reaction was chosen to include a deactivated aryl bromide and amine substrate that will not act as an efficient reductant of Pd(II). Therefore, the alkylamine ligand must reduce the palladium to the active species for the reaction to proceed. The reactions were followed by gas chromatography (GC) over a 1 h period to generate a reaction profile for each precatalyst (Figure 3). To account for palladacycle impurities, the catalyst loading for complexes **11−13** was adjusted to ensure that 1 mol % of the amine complex was present in each case. The *P*,*C*-palladacycle has previously been shown to be inactive in Buchwald−Hartwig amination reactions.[23] Therefore, residual palladacycle impurities in complexes **11−13** were not expected to have a positive or negative impact on the catalyst efficiency.

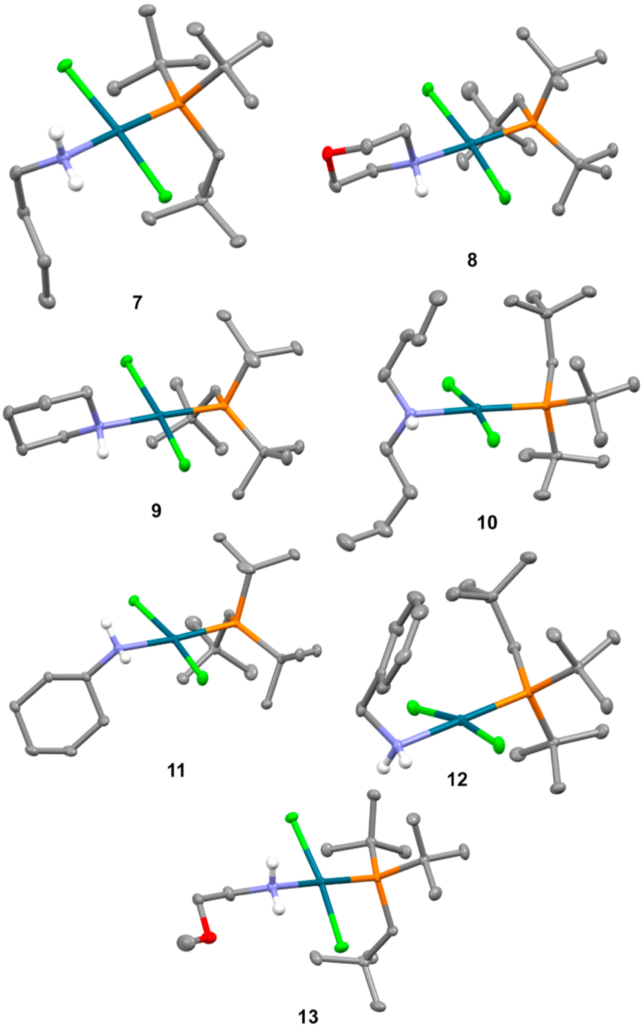
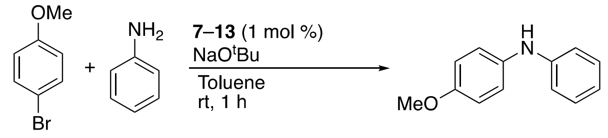


Figure 2. Thermal ellipsoid plots of complexes **7−13** determined by X-ray crystallography (50% probability). Hydrogen atoms except for those on nitrogen have been omitted for clarity.

Scheme 3. Cross-Coupling of 4-Bromoanisole and Aniline Using Precatalysts 7−13



Initially, the precatalyst efficiency was compared for complexes **7−9** (Figure 3). The reactions catalyzed by butylamine complex **7** exhibited a significantly higher initial rate and overall conversion to product than complexes **8** or **9**. Within 15 min at ambient temperature, 98% conversion was observed. Morpholine precatalyst **8** was also effective; however, the reaction required 60 min to reach completion and resulted in slightly lower yield. The reactions employing piperidine complex **9** exhibited poor catalyst activity and minimal conversion. Using [(^{t}Bu$_2$PNp)PdCl$_2$]$_2$ with no amine ligand under the same reaction conditions afforded only 5% conversion after 24 h, which matched previous reports from our group.[24] These results suggest that the identity of the amine ligand has a significant impact on the catalyst performance.

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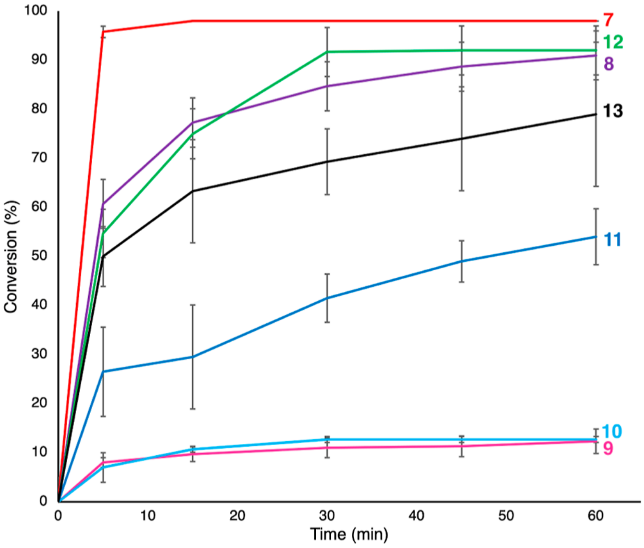


Figure 3. Reaction profiles for the coupling of 4-bromoanisole and aniline using precatalysts **7**−**13** under conditions in Scheme 3. Reactions with **11**−**13** were run with 1 mol % of the amine complex, taking into account the presence of palladacycle **14**. Data points are the average of three independent trials.

The initial results indicated that primary alkyl amines are effective activating ligands. Interestingly, morpholine gave significantly better results than the structurally similar piperidine ligand. The higher activity with the morpholine ligand could potentially be due to the inductive electron-withdrawing effect of the oxygen. Based on these initial results, additional palladium amine complexes were studied in this reaction. Complex **10** containing an acyclic secondary amine gave similarly low activity to that seen with piperidine complex **9**.

The efficiency of additional primary amine ligands was then explored. Reactions using cyclohexylamine precatalyst **11** exhibited moderate activity giving 54% yield after 60 min. The more sterically hindered β-carbon may inhibit the β-hydrogen elimination process with this complex. To confirm that the palladacycle impurity does not decrease the catalyst performance with these complexes, the reaction using complex **7** was performed with addition of **14** (**7**/**14** = 5:1, 1 mol % **7**). No change to the reaction profile was observed for catalyst **7** with the added **14**.

Reactions employing benzylamine precatalyst **12** gave a reactivity profile comparable to that of morpholine complex **8** but less active than butylamine complex **7**. We hypothesized that β-hydrogen elimination might be faster for this amine since it would result in a more stable conjugated imine product. The slower initial rate would suggest that this is not the case, however. Benzylamine and benzaldehyde imines are known to be prone to the formation of *N*,*C*-palladacycles,[27] which could serve as a potential catalyst deactivation pathway in this system.

Morpholine complex **8** performed well despite bearing a secondary amine ligand, whereas piperidine complex **9** was much less active. The catalyst efficiency could be a result of the inductive electron-withdrawing effect of the oxygen. This observation motivated us to synthesize complex **13** with a 2-methoxyethylamine ligand. The 2-methoxyethylamine ligand appeared promising as a linear primary alkyl amine bearing an electron-withdrawing methoxy substituent. Precatalyst **13** provided moderate activity but was less effective than butylamine complex **7**, morpholine complex **8**, and benzylamine complex **12**.

Based on these results, $(^t\mathrm{Bu}_2\mathrm{PNp})\mathrm{Pd}(n\text{-butylamine})\mathrm{Cl}_2$ (**7**) was identified as the optimal amine precatalyst for Buchwald−Hartwig amination reactions. The morpholine (**8**) and benzylamine (**12**) were also effective precatalysts but gave lower activity compared to complex **7**. The results suggest that primary amines with sterically unhindered β-carbons provide superior results. The lone exception to this trend is morpholine.

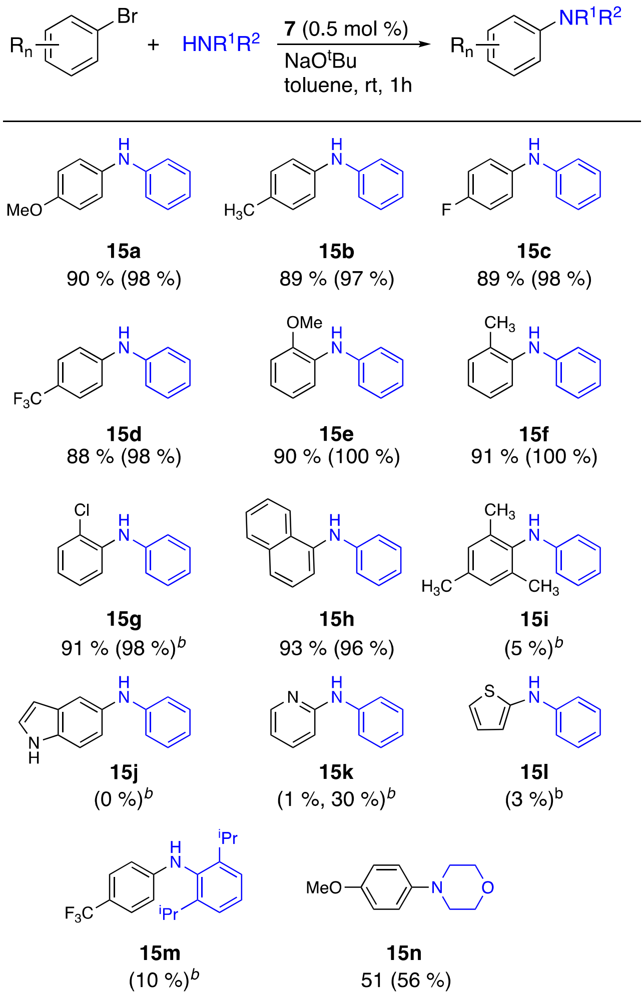
Precatalyst **7** was also compared to the other known catalyst systems. A direct comparison was made between complex **7** and the previously reported in situ $^t\mathrm{Bu}_2\mathrm{PNp}/\mathrm{Pd}_2(\mathrm{dba})_3$ system[28] using the model reaction with 0.5 mol % Pd loading (Scheme 3). The reactions using complex **7** reached completion within 15 min and resulted in 98% conversion (Figure S66). Reactions catalyzed by $^t\mathrm{Bu}_2\mathrm{PNp}/\mathrm{Pd}_2(\mathrm{dba})_3$ exhibited a slower initial rate and required 60 min to reach 90% conversion. At 0.25 mol % Pd loading, precatalyst **7** gave slow conversion with 77% yield achieved after 24 h (Figure S67). Reactions catalyzed by $^t\mathrm{Bu}_2\mathrm{PNp}/\mathrm{Pd}_2(\mathrm{dba})_3$ with 0.25 mol % Pd loading exhibited significantly lower activity with 37% conversion observed after 24 h. Complex **7** is also more active than $(\eta^3\text{-allyl})\mathrm{Pd}((t\text{-Bu})_2\mathrm{PNp})\mathrm{Cl}$ (**1**, L = $^t\mathrm{Bu}_2\mathrm{PNp}$). The $(\eta^3\text{-allyl})\mathrm{Pd}((^t\mathrm{Bu}_2\mathrm{PNp})\mathrm{Cl}$ precatalyst gave 82% conversion after 15 min and 90% after 30 min,[14a] in comparison to 96% after 5 min and 98% at 15 min for complex **7** under the same conditions.

Application of $(^t\mathrm{Bu}_2\mathrm{PNp})\mathrm{Pd}(n\text{-butylamine})\mathrm{Cl}_2$ in Buchwald−Hartwig Amination Reactions. Complex **7** was applied to the coupling of a range of aryl halides and amines (Scheme 4). The reactions proceeded efficiently at ambient temperature with 0.5 mol % catalyst. Excellent yields were obtained for para- and ortho-substituted aryl bromides. Aryl bromides bearing an electron-rich or neutral para-substituent (**15a**−**15b**) provided comparable yields to previously reported $^t\mathrm{Bu}_2\mathrm{PNp}/\mathrm{Pd}_2(\mathrm{dba})_3$ systems.[28]

A similar trend was observed for aryl bromides bearing an electron-withdrawing *para*-substituent (**15c**−**15d**). Electron-rich and neutral *ortho*-substituents were also well tolerated (**15e**−**15f**). Product **15f** was isolated in a higher yield using complex **7** (91%) than that with the $^t\mathrm{Bu}_2\mathrm{PNp}/\mathrm{Pd}_2(\mathrm{dba})_3$ system (79%).[28] An *ortho*-chloride substituent was tolerated (**15g**); however, the reaction required 24 h to reach completion. No competition between the activation of Br and Cl was observed, as determined by GC−MS analysis of the reaction mixture. The reason for the slower reaction for this substrate is unclear. Since chloride and methyl substituents have similar steric parameters, the slower conversion of **15g** is presumably not purely a steric effect.[29] Possible chelation with the proximal chloride could play a role, although this is not seen with the methoxy group in **15e**. 1-Bromonaphthalene efficiently coupled with aniline to afford product **15h** in an excellent yield.

The $^t\mathrm{Bu}_2\mathrm{PNp}/\mathrm{Pd}_2(\mathrm{dba})_3$ system requires elevated temperatures (50−140 °C) to couple aryl halides with two ortho-substituents.[28] Complex **7** gave a trace amount of product using 2-bromomesitylene at room temperature. Heating the reaction did not improve the yield likely due to competitive catalyst deactivation by palladacycle formation. Precatalyst **7** also failed to couple heterocyclic aryl bromides (**15j**−**15l**) and

Scheme 4. Coupling of Aryl Halides and Amines Using Precatalyst 7[a]



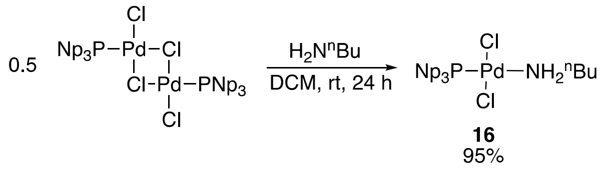
[a] Reactions performed under conditions illustrated unless otherwise noted. Equivalent yields were obtained with 0.5 mol % catalyst loading compared to 1 mol %. Isolated yields reported as the average of two independent trials. GC yields reported in parentheses. [b] Reaction time extended to 24 h.

bulky amines (**15m**). ^{t}Bu$_2$PNp/Pd$_2$(dba)$_3$ systems also exhibit poor reactivity for bulky aniline derivatives.[30]

Complex 7 successfully coupled 4-bromoansiole and morpholine to afford product **15n** in a moderate yield at room temperature. Precatalyst 7 failed to couple 4-bromoanisole with bulkier secondary amines, such as dibutylamine and dicyclohexylamine. The in situ ^{t}Bu$_2$PNp/Pd(OAc)$_2$ system affords significantly better yields at 80 °C for the coupling of 4-bromoanisole with morpholine (79%) and dibutylamine (86%).[28]

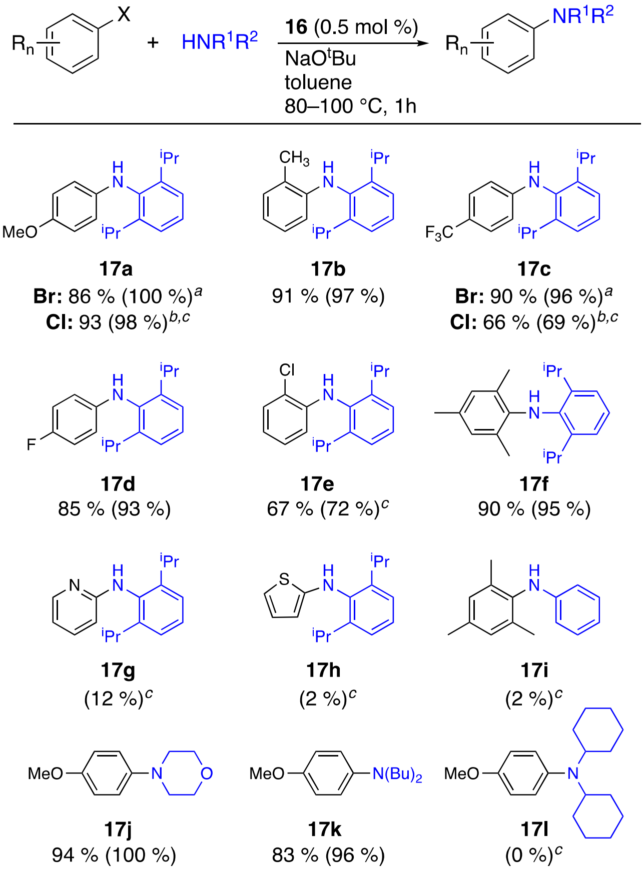
Synthesis and Application of (PNp$_3$)Pd(*n*-butylamine)Cl$_2$ in Buchwald–Hartwig Amination Reactions. The sterically demanding and relatively rigid ^{t}Bu$_2$PNp ligand provides ineffective catalysts for coupling of sterically demanding substrates. In contrast, the more flexible PNp$_3$ ligand provides catalysts that efficiently catalyze cross-coupling reactions across a range of sterically demanding aryl halides and amines.[11a,30] To see if the use of butyl amine could be translated to other catalyst systems, (PNp$_3$)Pd(*n*-butylamine)Cl$_2$ (**16**) was synthesized (Scheme 5).

Scheme 5. Synthesis of (PNp$_3$)Pd(*n*-butylamine)Cl$_2$



Precatalyst **16** was applied to the coupling of a range of aryl halides and amines (Scheme 6). The PNp$_3$ ligand is less prone to cyclometallation, which allows catalytic reactions to be performed at higher temperatures than was possible with the ^{t}Bu$_2$PNp system. Coupling of aryl bromides with 2,6-diisopropylaniline occurs efficiently at 80 °C with 0.5 mol % **16**. Good yields were obtained for para- and ortho-substituted aryl bromides. Substantially, lower yields were observed in reactions performed at ambient temperature and 40 °C. Aryl bromides bearing an electron-rich or neutral substituent (**17a–17b**) provided comparable yields to the PNp$_3$/Pd$_2$(dba)$_3$ systems.[30] Aryl bromides containing electron-withdrawing para-substituents were well tolerated (**17c–17d**). The coupling of 1-bromo-2-chlorobenzene and 2,6-diisopropylaniline proceeded slowly, as seen with 7, and resulted in a moderate yield of product **17e**. There was no competition

Scheme 6. Coupling of Aryl Halides and Amines Using Precatalyst 16[a]



[a] Reactions performed with aryl bromides at 80 °C unless noted. Isolated yields reported as the average of two independent trials. GC yields reported in parentheses. [b] Reactions performed using the aryl chloride at 100 °C. [c] Reaction time extended to 24 h.

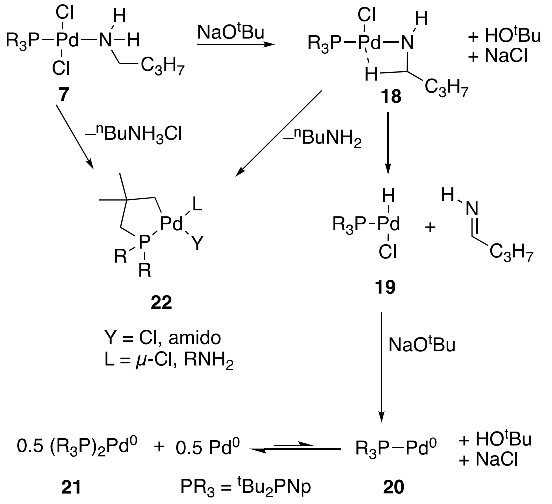
between the activation of Br and Cl. Complex **16** successfully coupled 2-bromomesitylene with 2,6-diisopropylaniline to afford **17f**. However, the bulky aryl bromide could not be coupled with less sterically demanding amines, such as aniline (**17i**). This matches previous results with the PNp_3/Pd catalyst system.[11a] Presumably, the aniline coordinates to the active species and accelerates palladacycle formation. Complex **16** was unable to couple heterocycles (**17g**–**17h**).

Notably, para-substituted aryl chlorides were successfully coupled with 2,6-diisopropylaniline when reacted at 100 °C. The corresponding products **17a** and **17c** were isolated in moderate-to-good yields. Product **17a** was isolated in a significantly higher yield using complex **16** (93%) in comparison to the $PNp_3/Pd_2(dba)_3$ system (83%).[30]

The tolerance of the amine coupling partner was briefly investigated. Reactions with 2,6-diisopropylaniline provided moderate-to-good yields across a range of aryl bromides (**17a**–**17f**). Morpholine and dibutylamine gave good yields of arylated products (**17j**–**17k**). However, complex **16** failed to couple more sterically demanding secondary amines, such as dicyclohexylamine (**17l**).

Precatalyst Activation Studies. As seen in Figure 3, the identity of the amine ligand significantly impacts the catalyst efficiency. Primary amines with sterically accessible β-carbons provide the most active catalysts. We hypothesize that the amine adduct is deprotonated to give palladium amido intermediate **18** with loss of chloride to open a site for the β-hydrogen on the amine ligand to coordinate. β-Hydrogen elimination would produce palladium hydride **19** and the corresponding imine (Scheme 7). Intermediate **19** is expected to undergo base-promoted reductive elimination to produce the (^{t}Bu$_2$PNp)Pd^0 active species (**20**). In the absence of aryl halide, complex **20** would undergo disproportionation to (^{t}Bu$_2$PNp)$_2$Pd^0 (**21**) and unligated Pd^0. Alternatively, metalation of the ^{t}Bu$_2$PNp ligand potentially promoted by the amine ligand of **7** or the amido ligand in **18** to generate palladacycle **22** can occur. Palladacycle formation would represent a catalyst deactivation pathway. Once generated, the active species (**20**) should have the same activity independent of the identity of the precatalyst. Therefore, differences in the effectiveness of these precatalysts are likely due to the rate or selectivity of generating the (^{t}Bu$_2$PNp)Pd^0 active species.

Scheme 7. Plausible Activation Mechanism for Complex 7



In order to determine the effect of the amine ligand on catalyst activation, we studied the activation process of complexes **7**–**9** under catalytic conditions (Scheme 3) by ^{31}P NMR spectroscopy. Reactions were performed with 5 mol % precatalyst to provide sufficient sensitivity in the ^{31}P NMR spectrum. Kinetic profiles of the activation process could not be determined due to the fast rate of consumption of **7**–**9**, which was largely complete within 5 min at room temperature. However, some mechanistic insights were obtained through observation of the phosphorus-containing species formed during the cross-coupling of 4-bromoanisole and aniline using precatalysts **7**–**9** (Figure 4). Peaks of interest included palladacycle complexes (**14**, 83 ppm), unreacted amine precatalysts (**7**–**9**, 59 ppm), L$_2$Pd^0 species (**21**, 44 ppm), uncoordinated ^{t}Bu$_2$PNp ligands (19 ppm), and [(^{t}Bu$_2$PNp)Pd(Ar)Br]$_2$ (52 ppm).[23]

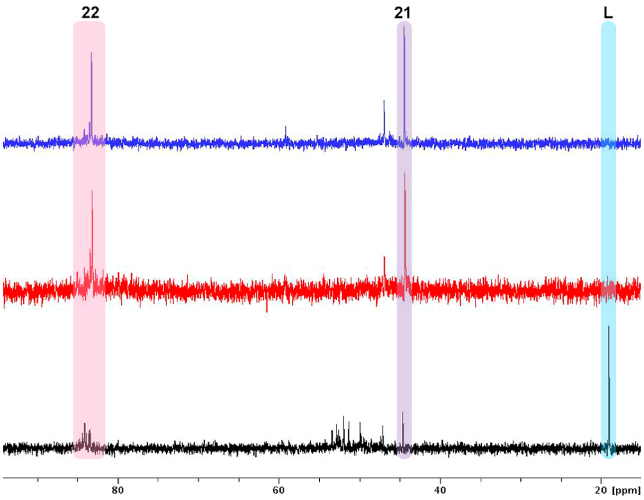


Figure 4. ^{31}P NMR analysis of the catalytic reaction using precatalysts **7**–**9** (5 mol %) after 5 min at room temperature. Complex **7** (blue), complex **8** (red), and complex **9** (black). Integrated spectra provided in the Supporting Information (Figures S68–S73).

Analysis of the reaction mixture catalyzed by complex **7** after 5 min showed nearly complete consumption of the starting complex (Figure 4). The major species present were (^{t}Bu$_2$PNp)$_2$Pd^0 (**21**, 44%) and a palladacycle species (**22**, 32%), plus an unidentified peak at 47 ppm that is in the region of palladium(II) complexes of ^{t}Bu$_2$PNp (Table 1). Analysis of this system after 20 min showed a decrease in (^{t}Bu$_2$PNp)$_2$Pd^0

Table 1. Product Distributions from Complexes 7–9 under Catalytic Conditions[a]

complex	time (min)	integrated ratio[b] 22	7/8/9	21	L[c]	other[d]
7	5	32	2	44	0	22
7	20	47	4	27	5	17
8	5	41	8	37	0	14
8	20	34	5	25	8	28
9	5	27	0	5	27	41
9	20	19	0	2	22	57

[a] Complex **7**–**9** (0.025 mmol), 4-bromoanisole (0.5 mmol), NaO^{t}Bu (0.75 mmol), aniline (0.6 mmol), toluene (1.5 mL), rt. [b] Integration ratio from ^{31}P{^{1}H} NMR spectrum. [c] Free ^{t}Bu$_2$PNp. [d] Total relative integrated area of unidentified species in the 47–55 ppm region.

(**21**, 27%) and a corresponding increase in the palladacycle (47%) (Figure S69). A small amount of free ligand was also present, presumably from decomposition of complex **21**.

The activation of complex **8** was analyzed in the same way as complex **7**. At 5 min, the amount of $(^t\mathrm{Bu_2PNp})_2\mathrm{Pd}^0$ was lower (37%) than that for complex **7**, and there was a larger amount of palladacycle **22** (Table 1). At 20 min, the spectrum appeared similar but with a larger percentage of species in the 47−55 ppm range (Figure S71). In contrast to the results with complex **7** and **8**, complex **9** gave only a small amount of palladium(0) complex **21** (5%) after 5 min. A large number of phosphorus-containing species were observed from 47 to 55 ppm, which comprised the majority of the phosphorus present. The other species present were with several resonances in the palladacycle region and significant amount (27%) of free $^t\mathrm{Bu_2PNp}$ that was not seen with complexes **7** or **8**. No major change was noted after 20 min (Figure S73), although the signal for the palladium(0) species (**21**) had decreased slightly (2%).

Further confirmation of the proposed activation pathway (Scheme 7) could be achieved by observation of the imine byproduct through ^{1}H NMR analysis. The HC═N proton should be readily observed as it would appear in a region with no competing resonances from the starting materials and products. Evidence for the imine byproduct was not observed, however. It is possible that the imine undergoes further reactions under the strongly basic reaction conditions preventing it from being observed.

The selectivity with which the palladium(0) species is generated from these complexes correlates with their effectiveness as precatalysts in the *N*-arylation reaction. Complex **7**, which provides the most active catalyst, shows the highest selectivity for the generation of palladium(0) complex **21**. The major competing reaction is the known cyclometallation of the $^t\mathrm{Bu_2PNp}$ ligand. Complex **8**, which also provides an effective catalyst, also generates the palladium(0) complex, although less efficiently than complex **7**. In contrast, complex **9**, which does not generate an effective catalyst, primarily appears to undergo decomposition under the reaction conditions to give a large number of other products, including free ligand. Only trace amounts of LPd^0 are formed with this system. The inability to generate the palladium(0) active species accounts for the poor activity seen using precatalyst **9**.

CONCLUSIONS

Air stable mixed palladium(II) complexes bearing an amine ligand and neopentyl-substituted phosphine ligand have been shown to efficiently catalyze the Buchwald−Hartwig amination reactions. The identity of the amine ligand significantly impacts catalyst efficiency and lifetime. Precatalysts derived from linear primary alkyl amines exhibit superior activity with fast initial rates. In contrast, piperidine or di(*n*-butyl)amine were ineffective activating ligands. $(^t\mathrm{Bu_2PNp})\mathrm{Pd}(n\text{-butylamine})\mathrm{Cl_2}$ (**7**) was identified as the optimal amine precatalyst. Complex **7** shows an increased coupling rate for aryl bromides with aniline at ambient temperature in comparison to the catalyst generated in situ from $^t\mathrm{Bu_2PNp}$ and $\mathrm{Pd_2(dba)_3}$. $(\mathrm{PNp_3})\mathrm{Pd}(n\text{-butylamine})\mathrm{Cl_2}$ (**16**) efficiently catalyzed cross-coupling reactions across a range of sterically demanding aryl halides and amines. Notably, complex **16** provided satisfactory yields when coupling electron-rich and electron-deficient aryl chlorides.

^{31}P NMR analysis of reaction mixtures demonstrates that the catalyst efficiency is correlated to the propensity of the precatalysts to undergo side reactions during the catalyst activation process. Butylamine complex **7** most efficiently generates the active LPd^0 species and undergoes minimal side reactions when compared to less effective precatalysts **8** and **9**. In particular, the piperidine complex (**9**) provides little LPd^0 species according to ^{31}P NMR analysis of catalytic reaction mixtures.

These results suggest that *n*-butylamine is particularly effective as an activating ligand. This may be due to a more efficient β-hydrogen elimination pathway on the sterically accessible alkyl chain. The major catalyst deactivation pathway in these systems is cyclometallation of the neopentyl ligand, which we have previously observed.[11a,23,31] The amine ligand appears to promote cyclopalladation in the $^t\mathrm{Bu_2PNp}$ system (**7**) at elevated temperatures, which limits the ability to use this precatalyst at higher temperature. In contrast, cyclometallation of $\mathrm{PNp_3}$ occurs less readily allowing complex **16** to be used at higher temperature. It is possible that the poor performance of secondary amine complexes (**9** and **10**) is due to the increased basicity of the secondary nitrogen, which would be expected to accelerate ligand cyclometallation. The morpholine complex (**8**) is an exception to this trend, which may be due to the lower basicity of morpholine compared to piperidine or dibutylamine.

The cyclometallation deactivation pathway occurs readily in neopentyl ligands and may not be observed with other ligands that are less prone to metalation. Efforts are currently underway to study other $\mathrm{LPdCl_2(amine)}$ precatalyst systems to determine whether similar structural effects on the ability of the amine to act as an activating ligand will be seen.

EXPERIMENTAL SECTION

General Procedures and Materials. Reagents were purchased from commercial suppliers and used as received, except when noted. Toluene was refluxed over sodium and freshly distilled prior to use. Di-*tert*-butylneopentylphosphine was donated by FMC Lithium. Trineopentylphosphine, bis(acetonitrile)dichloropalladium(II), $[(^t\mathrm{Bu_2PNp})\mathrm{PdCl_2}]_2$, $[(\mathrm{TNpP})\mathrm{PdCl_2}]_2$, and palladacycle **14** were synthesized following reported methods.[23] Air sensitive reactions were performed under nitrogen using double-manifold inert-atmosphere techniques. GC samples were measured using a Shimadzu GC-2014 Gas Chromatograph using a 10 °C/min increasing rate from 100 to 250 °C. NMR spectra were acquired on a Brüker 500 MHz spectrometer. $\mathrm{C_6D_6}$ was used as the solvent for NMR characterization of complexes **7**−**13**. Dissolving these complexes in more polar solvents, such as $\mathrm{CDCl_3}$, results in dissociation of the amine ligand to give an equilibrium mixture of **7**−**13**, the free amine, and $[(^t\mathrm{Bu_2PNp})\mathrm{PdCl_2}]_2$.

General Procedure for Synthesis of Mixed Palladium(II) Precatalysts. In a 3 dram vial in air, $[(^t\mathrm{Bu_2PNp})\mathrm{PdCl_2}]_2$ (0.15 mmol) was dissolved in 3 mL of dichloromethane prior to the dropwise addition of the amine (0.30 mmol). The mixture was stirred at 22 °C for 24 h and concentrated to remove dichloromethane. The resulting solid was washed with 3 × 5 mL of hexane and dried under vacuum to give spectroscopically pure material. X-ray quality crystals were obtained by slow evaporation of methylene chloride/hexane solutions.

$[(^t\mathrm{Bu_2PNp})\mathrm{Pd}(\mathrm{CH_3(CH_2)_3NH_2})\mathrm{Cl_2}]$ (7). Using the general procedure, $[(^t\mathrm{Bu_2PNp})\mathrm{PdCl_2}]_2$ (118.4 mg, 0.1504 mmol) and *n*-butylamine (32 μL, 0.32 mmol) were reacted to produce the target complex as an air-stable orange solid (130.2 mg, 93%). ^{1}H NMR (500 MHz, $\mathrm{C_6D_6}$): δ 2.58 (ttd, J = 7.2, 3.4 Hz, 2H), 2.16 (d, J = 13.4 Hz, 2H), 1.96 (br s, 2H), 1.52 (d, J = 14.2 Hz, 18H), 1.46 (d, J = 1.1 Hz, 9H), 1.11 (pent, J = 7.4 Hz, 2H), 0.94 (sext, J = 7.4 Hz, 2H), 0.69 (t, J = 7.3 Hz, 3H).

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^{13}C NMR (125 MHz, C$_6$D$_6$): δ 43.3 (d, $J_{C\text{-}P}$ = 2.6 Hz), 37.1 (d, $J_{C\text{-}P}$ = 17.9 Hz), 34.1 (d, $J_{C\text{-}P}$ = 2.5 Hz), 34.0 (d, $J_{C\text{-}P}$ = 14.3 Hz), 33.9 (d, $J_{C\text{-}P}$ = 6.1 Hz), 31.5 (d, $J_{C\text{-}P}$ = 3.3 Hz), 31.1 (d, $J_{C\text{-}P}$ = 2.9 Hz), 20.1, 14.0. ^{31}P{^{1}H} NMR (202.5 MHz, C$_6$D$_6$): δ 57.5.

[(^{t}Bu$_2$PNp)Pd(O(CH$_2$CH$_2$)$_2$NH)Cl$_2$] (8). Using the general procedure, [(^{t}Bu$_2$PNp)PdCl$_2$]$_2$ (111.0 mg, 0.1410 mmol) and morpholine (26 μL, 0.30 mmol) were reacted to produce the target complex as an air-stable yellow solid (131.2 mg, 97%). ^{1}H NMR (500 MHz, C$_6$D$_6$): δ 3.43 (dddd, J = 3.6, 12.6, 12.6, 12.6 Hz, 2H), 3.21 (d, J = 12.0 Hz, 2H), 3.16 (br s, 1H), 2.68 (m, 2H), 2.42 (d, J = 13.3 Hz, 2H), 2.16 (d, J = 13.4 Hz, 2H), 1.51 (d, J = 13.4 Hz, 18H), 1.46 (d, J = 1.0 Hz, 9H). ^{13}C NMR (125 MHz, C$_6$D$_6$): δ 66.5 (d, $J_{C\text{-}P}$ = 3.0 Hz), 46.3 (d, $J_{C\text{-}P}$ = 2.9 Hz), 35.8 (d, $J_{C\text{-}P}$ = 17.8 Hz), 32.9 (d, $J_{C\text{-}P}$ = 14.1 Hz), 32.5 (d, $J_{C\text{-}P}$ = 6.2 Hz), 30.3 (d, $J_{C\text{-}P}$ = 3.4 Hz), 29.7 (d, $J_{C\text{-}P}$ = 2.8 Hz). ^{31}P{^{1}H} NMR (202.5 MHz, C$_6$D$_6$): δ 60.6.

[(^{t}Bu$_2$PNp)Pd((CH$_2$)$_5$NH)Cl$_2$] (9). Using the general procedure, [(^{t}Bu$_2$PNp)PdCl$_2$]$_2$ (116.8 mg, 0.1484 mmol) and piperidine (32 μL, 0.32 mmol) were reacted to produce the target complex as an air-stable yellow solid (133.9 mg, 94%). ^{1}H NMR (500 MHz, C$_6$D$_6$): δ 3.12 (m, 3H), 2.98 (m, 2H), 2.17 (d, J = 13.4 Hz, 2H), 1.53 (d, J = 13.3 Hz, 18H), 1.47 (s, 9H), 1.06 (m, 3H), 0.90 (m, 1H), 0.79 (m, 2H). ^{13}C NMR (125 MHz, C$_6$D$_6$): δ 48.7 (d, $J_{C\text{-}P}$ = 3.0 Hz), 37.0 (d, $J_{C\text{-}P}$ = 17.5 Hz), 34.1 (d, $J_{C\text{-}P}$ = 13.8 Hz), 33.9 (d, $J_{C\text{-}P}$ = 6.2 Hz), 31.4 (d, $J_{C\text{-}P}$ = 3.2 Hz), 31.2 (d, $J_{C\text{-}P}$ = 2.9 Hz), 27.8 (d, $J_{C\text{-}P}$ = 3.2 Hz), 24.0. ^{31}P{^{1}H} NMR (202.5 MHz, C$_6$D$_6$): δ 57.7. Elemental analysis: calcd for C$_{18}$H$_{40}$Cl$_2$NPPd: C, 45.15; H, 8.42; N, 2.93. Found: C, 45.08; H, 8.54; N, 3.30.

[(^{t}Bu$_2$PNp)Pd([(CH$_3$(CH$_2$)$_3$)$_2$]NH)Cl$_2$] (10). Using the general procedure, [(^{t}Bu$_2$PNp)PdCl$_2$]$_2$ (127.0 mg, 0.1613 mmol) and dibutylamine (55 μL, 0.33 mmol) were reacted to produce the target complex as an air-stable orange solid. The crude product was recrystallized from slow evaporation of hexane to afford the pure product (149.5 mg, 89%). ^{1}H NMR (500 MHz, C$_6$D$_6$): δ 3.27 (m, 3H), 2.37 (m, 2H), 2.28 (d, J = 13.4 Hz, 2H), 2.05 (m, 2H), 1.93 (m, 2H), 1.62 (d, J = 13.6 Hz, 18H), 1.56 (d, J = 1.0 Hz, 9H), 1.48 (m, 2H), 1.33 (m, 2H), 1.05 (t, J = 7.4 Hz, 6H). ^{13}C NMR (125 MHz, C$_6$D$_6$): δ 51.6 (d, $J_{C\text{-}P}$ = 2.5 Hz), 36.8 (d, $J_{C\text{-}P}$ = 17.3 Hz), 33.7 (d, $J_{C\text{-}P}$ = 13.8 Hz), 33.5 (d, $J_{C\text{-}P}$ = 6.0 Hz), 31.7, 31.2 (d, $J_{C\text{-}P}$ = 3.3 Hz), 30.7 (d, $J_{C\text{-}P}$ = 2.9 Hz), 20.5, 13.9. ^{31}P{^{1}H} NMR (202.5 MHz, C$_6$D$_6$): δ 58.2. Elemental analysis: calcd for C$_{21}$H$_{48}$Cl$_2$NPPd: C, 48.24; H, 9.25; N, 2.68. Found: C, 48.37; H, 9.34; N, 2.66.

[(^{t}Bu$_2$PNp)Pd(C$_6$H$_{11}$NH$_2$)Cl$_2$] (11). Using the general procedure, [(^{t}Bu$_2$PNp)PdCl$_2$]$_2$ (118.1 mg, 0.1500 mmol) and cyclohexylamine (34 μL, 0.30 mmol) were reacted to produce the target complex as an air-stable yellow solid (138.4 mg). Analysis by ^{31}P NMR spectroscopy showed this material to be a 63:37 mol/mol ratio of **11**/**14**. Further attempts to purify this material by recrystallization were unsuccessful. Based on this ratio, the yield of **11** was 99 mg (67%). X-ray quality crystals were obtained by slow evaporation from a saturated hexane solution. ^{1}H NMR (500 MHz, C$_6$D$_6$): δ 3.01 (m, 1H), 2.18 (d, J = 14.3 Hz, 2H), 2.08 (br s, 2H), 1.94 (m, 2H), 1.54 (d, J = 13.3 Hz, 18H), 1.47 (d, J = 1.0 Hz), 1.43 (m, 2H), 1.16 (br s, 1H), 1.00 (m, 2H), 0.81 (m, 3H). ^{13}C NMR (125 MHz, C$_6$D$_6$): δ 51.8 (d, $J_{C\text{-}P}$ = 2.0 Hz), 36.7 (d, $J_{C\text{-}P}$ = 17.9 Hz), 35.1 (d, $J_{C\text{-}P}$ = 2.3 Hz), 33.6, 33.5 (d, $J_{C\text{-}P}$ = 6.2 Hz), 31.1 (d, $J_{C\text{-}P}$ = 3.3 Hz), 30.7 (d, $J_{C\text{-}P}$ = 2.8 Hz), 25.2, 24.8. ^{31}P{^{1}H} NMR (202.5 MHz, C$_6$D$_6$): δ 57.6.

[(^{t}Bu$_2$PNp)Pd(C$_6$H$_5$CH$_2$NH$_2$)Cl$_2$] (12). Using the general procedure, [(^{t}Bu$_2$PNp)PdCl$_2$]$_2$ (122.1 mg, 0.1551 mmol) and benzylamine (35 μL, 0.32 mmol) were reacted to produce the target complex as an air-stable orange solid (138.2 mg). Analysis by ^{31}P NMR spectroscopy showed this material to be a 79:21 mol/mol ratio of **12**/**14**. Further attempts to purify this material by recrystallization were unsuccessful. Based on this ratio, the yield of **12** was 116 mg (75%). X-ray quality crystals were obtained by slow evaporation from a saturated hexane solution. Some aromatic peaks were obscured by C$_6$D$_6$. ^{1}H NMR (500 MHz, C$_6$D$_6$): δ 6.97 (m, 3H), 6.81 (m, 2H), 3.83 (m, 2H), 2.83 (br s, 2H), 2.16 (d, J = 13.4 Hz, 2H), 1.52 (d, J = 15.8 Hz, 18H), 1.46 (d, J = 1.0 Hz, 9H). ^{13}C NMR (125 MHz, C$_6$D$_6$): δ 138.9 (d, $J_{C\text{-}P}$ = 3.2 Hz), 128.6, 47.1 (d, $J_{C\text{-}P}$ = 2.6 Hz), 37.7 (d, $J_{C\text{-}P}$ = 18.1 Hz), 33.7 (d, $J_{C\text{-}P}$ = 14.3 Hz), 33.4 (d, $J_{C\text{-}P}$ = 6.1 Hz), 31.0 (d, $J_{C\text{-}P}$ = 3.4 Hz), 30.7 (d, $J_{C\text{-}P}$ = 2.8 Hz). ^{31}P{^{1}H} NMR (202.5 MHz, C$_6$D$_6$): δ 58.9.

[(^{t}Bu$_2$PNp)Pd(CH$_3$OCH$_2$CH$_2$NH$_2$)Cl$_2$] (13). Using the general procedure, [(^{t}Bu$_2$PNp)PdCl$_2$]$_2$ (124.3 mg, 0.1579 mmol) and 2-methoxyethylamine (28 μL, 0.32 mmol) were reacted to produce the target complex as an air-stable orange solid (99.4 mg). Analysis by ^{31}P NMR spectroscopy showed this material to be an 85:15 mol/mol ratio of **13**/**14**. Further attempts to purify this material by recrystallization were unsuccessful. Based on this ratio, the yield of **13** was 87 mg (59%). A small amount of X-ray quality crystals was obtained by slow evaporation from a saturated hexane solution. Crystals from this process gave suitable elemental analysis. ^{1}H NMR (500 MHz, C$_6$D$_6$): δ 2.94 (s, 3H), 2.90 (t, J = 5.0 Hz, 2H), 2.76 (m, 2H), 2.23 (br s, 2H), 2.16 (d, J = 13.5 Hz, 2H), 1.52 (d, J = 13.4 Hz, 18H), 1.46 (d, J = 1.1 Hz, 9H). ^{13}C NMR (125 MHz, C$_6$D$_6$): δ 71.2 (d, $J_{C\text{-}P}$ = 2.4 Hz), 57.8, 42.5 (d, $J_{C\text{-}P}$ = 2.6 Hz), 36.5 (d, $J_{C\text{-}P}$ = 18.0 Hz), 33.5 (d, $J_{C\text{-}P}$ = 14.3 Hz), 33.4 (d, $J_{C\text{-}P}$ = 6.1 Hz), 30.9 (d, $J_{C\text{-}P}$ = 3.4 Hz), 30.6 (d, $J_{C\text{-}P}$ = 2.8 Hz). ^{31}P{^{1}H} NMR (202.5 MHz, C$_6$D$_6$): δ 57.8. Elemental analysis: calcd for C$_{16}$H$_{38}$Cl$_2$NOPPd: C, 40.99; H, 8.17; N, 2.99. Found: C, 41.03; H, 8.09; N, 2.98.

Synthesis of [(TNpP)Pd(CH$_3$(CH$_2$)$_3$NH$_2$)Cl$_2$]$_2$ (16). In a 3 dram vial in air, [(TNpP)PdCl$_2$]$_2$ (68.2 mg, 0.0809 mmol) was dissolved in 3 mL of dichloromethane prior to the dropwise addition of *n*-butylamine (17.5 μL, 0.177 mmol). The mixture was stirred at 22 °C for 24 h and concentrated to remove dichloromethane. The target complex was obtained as a spectroscopically pure yellow oil (75.9 mg, 95%). ^{1}H NMR (500 MHz, C$_6$D$_6$): δ 2.82 (ttd, J = 3.2, 7.2, 7.2 Hz, 2H), 2.35 (m, 2H), 2.09 (d, J = 12.7 Hz, 6H), 1.53 (pentet, J = 7.5 Hz, 2H), 1.28 (sext, J = 7.5 Hz, 2H) 1.27 (s, 27H), 0.85 (t, J = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, C$_6$D$_6$): δ 42.5 (d, $J_{C\text{-}P}$ = 2.6 Hz), 36.9 (d, $J_{C\text{-}P}$ = 24.9 Hz), 33.2 (d, $J_{C\text{-}P}$ = 2.7 Hz), 32.2 (d, $J_{C\text{-}P}$ = 6.3 Hz), 31.4 (d, $J_{C\text{-}P}$ = 4.2 Hz), 18.8, 12.7. ^{31}P{^{1}H} NMR (202.5 MHz, C$_6$D$_6$): δ 13.1.

General Procedure for Buchwald−Hartwig Amination Reaction Profiles. The palladium precatalyst (5.0 μmol, 1 mol % Pd−amine complex) was measured into a 1 dram vial in air. For complexes **11**−**13**, which contained palladacycle impurities, the amount of complex was adjusted to ensure that 1 mol % of complex **11**−**13** was present. The vial was placed into a nitrogen-filled glovebox where sodium *tert*-butoxide (0.75 mmol) was added. The vial was sealed with a Teflon septum. Upon removal, 4-bromoanisole (0.50 mmol), 1.5 mL of toluene, and aniline (0.60 mmol) were added. The reaction was stirred at 22 °C for 1 h. Conversion was monitored by GC.

General Procedure for Buchwald−Hartwig Amination Using Precatalyst 7. Precatalyst **7** (2.5 μmol, 0.5 mol %) was measured into a 1 dram vial in air. The vial was placed into a nitrogen-filled glovebox where sodium *tert*-butoxide (0.75 mmol) was added. The vial was sealed with a Teflon septum. Upon removal, the aryl halide (0.50 mmol), 1.5 mL of toluene, and arylamine (0.60 mmol) were added. The reaction was stirred at 22 °C for 1 h, except when noted. Upon completion as judged by GC, the reaction mixture was filtered through a plug of celite and rinsed with dichloromethane. The filtrate was concentrated and purified through silica gel column chromatography (5−10% ethyl acetate/hexane).

General Procedure for Buchwald−Hartwig Amination Using Precatalyst 16. A 1 dram vial was placed into a nitrogen-filled glovebox where sodium *tert*-butoxide (0.75 mmol) was added. The vial was sealed with a Teflon septum. Upon removal, the aryl halide (0.50 mmol), 0.25 mL of precatalyst **16** (2.5 μmol in 0.01 M solution with toluene), 1.25 mL of toluene, and arylamine (0.50−0.60 mmol) were added. The reaction was stirred in a pre-heated oil bath set to 80 °C for 1 h, except when noted. Upon completion as judged by GC, the reaction mixture was filtered through a plug of celite and rinsed with dichloromethane. The filtrate was concentrated and purified through silica gel column chromatography (5−10% ethyl acetate/hexane).

Analysis of Catalyst Activation under Catalytic Conditions. The precatalyst (5 mol %) was measured into a 1 dram vial in air. The vial was placed into a nitrogen-filled glovebox where sodium *tert*-

butoxide (0.75 mmol) was added. The vial was sealed with a Teflon septum. Upon removal, 4-bromoanisole (0.50 mmol), 1.5 mL of toluene, and aniline (0.60 mmol) were added. The reaction was stirred at 22 °C and analyzed by ^{31}P NMR spectroscopy.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.organomet.2c00518.

> NMR spectra (^{1}H, ^{13}C{^{1}H}, ^{31}P{^{1}H}) for complexes **7**−**13**, characterization data and NMR spectra (^{1}H, ^{13}C{^{1}H}) for compounds, reaction profiles for complex **7** and $Pd_2(dba)_3$/^{t}Bu$_2$PNp, NMR spectra from the catalyst activation studies, and X-ray crystal data for complexes **7**−**13** (PDF)

Accession Codes

CCDC 2213818−2213824 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

Kevin H. Shaughnessy − *Department of Chemistry and Biochemistry, The University of Alabama, Tuscaloosa, Alabama 35487-0336, United States*; orcid.org/0000-0002-1375-5563; Email: kshaughn@ua.edu

Authors

Jordan K. Pierce − *Department of Chemistry and Biochemistry, The University of Alabama, Tuscaloosa, Alabama 35487-0336, United States*

Lindsey D. Hiatt − *Department of Chemistry and Biochemistry, The University of Alabama, Tuscaloosa, Alabama 35487-0336, United States*

James R. Howard − *Department of Chemistry and Biochemistry, The University of Alabama, Tuscaloosa, Alabama 35487-0336, United States*

Huaiyuan Hu − *Department of Chemistry and Biochemistry, The University of Alabama, Tuscaloosa, Alabama 35487-0336, United States*

Fengrui Qu − *Department of Chemistry and Biochemistry, The University of Alabama, Tuscaloosa, Alabama 35487-0336, United States*; orcid.org/0000-0002-9975-2573

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.organomet.2c00518

Notes

The authors declare no competing financial interest.

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