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Synthesis and X-ray Structure Determination of Highly Active Pd(II), Pd(I), and Pd(0) Complexes of Di(*tert*-butyl)neopentylphosphine (DTBNpP) in the Arylation of Amines and Ketones

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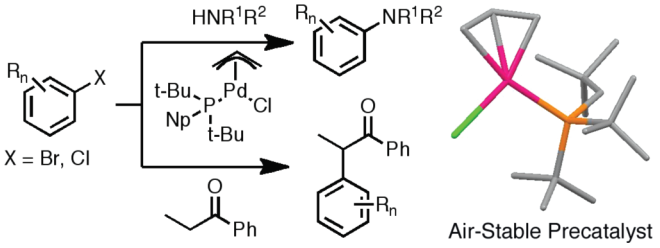
Received June 21, 2010



The air-stable complex Pd(η^3-allyl)(DTBNpP)Cl (DTBNpP = di(*tert*-butyl)neopentylphosphine) serves as a highly efficient precatalyst for the arylation of amines and enolates using aryl bromides and chlorides under mild conditions with yields ranging from 74% to 98%. Amination reactions of aryl bromides were carried out using 1−2 mol % Pd(η^3-allyl)(DTBNpP)Cl at 23−50 °C without the need to exclude oxygen or moisture. The C−N coupling of the aryl chlorides occurred at relatively lower temperature (80−100 °C) and catalyst loading (1 mol %) using the Pd(η^3-allyl)(DTBNpP)Cl precatalyst than the catalyst generated in situ from DTBNpP and $Pd_2(dba)_3$ (100−140 °C, 2−5 mol % Pd). Other Pd(DTBNpP)$_2$-based complexes, (Pd(DTBNpP)$_2$ and Pd(DTBNpP)$_2$Cl$_2$) were ineffective precatalysts under identical conditions for the amination reactions. Both Pd(DTBNpP)$_2$ and Pd(DTBNpP)$_2$Cl$_2$ precatalysts gave nearly quantitative conversions to the product in the α-arylation of propiophenone with *p*-chlorotoluene and *p*-bromoanisole at a substrate/catalyst loading of 100/1. At lower substrate/catalyst loading (1000/1), the conversions were lower but comparable to that of Pd(*t*-Bu$_3$P)$_2$. In many cases, the tri-*tert*-butylphosphine (TTBP) based Pd(I) dimer, [Pd(μ-Br)(TTBP)]$_2$, stood out to be the most reactive catalyst under identical conditions for the enolate arylation. Interestingly, the air-stable Pd(I) dimer, Pd_2(DTBNpP)$_2$(μ-Cl)(μ-allyl), was less active in comparison to [Pd(μ-Br)(TTBP)]$_2$ and Pd(η^3-allyl)(DTBNpP)Cl. The X-ray crystal structures of Pd(η^3-allyl)(DTBNpP)Cl, Pd(DTBNpP)$_2$Cl$_2$, Pd(DTBNpP)$_2$, and Pd_2(DTBNpP)$_2$-(μ-Cl)(μ-allyl) are reported in this paper along with initial studies on the catalyst activation of the Pd(η^3-allyl)(DTBNpP)Cl precatalyst.

DOI: 10.1021/jo101187q Published on Web 09/01/2010

Introduction

The use of Pd-mediated cross-coupling reactions has been increasing steadily, especially over the past two decades, in academia and industry due in part to the emergence of new ligand classes that promote cross-couplings of electrophiles with a range of leaving groups (Br, Cl, OSO_2R) and a variety of nucleophiles (Figure 1).[1] A common feature among these new ligand classes is significant steric demand and strong σ-donating ability necessary to promote the oxidative addition and reductive elimination steps. Typically such transformations are carried out using a catalyst generated in situ by combining a Pd source, such as $Pd(dba)_n$ or $Pd(dba\text{-}Z)_n$[2] ($n = 1.5-2$), $Pd(OAc)_2$, or $[Pd(\eta^3\text{-allyl})Cl]_2$, with the free ligand or its protonated form to generate the PdL active species.[3] Although these practices are quite useful in both small-scale and process chemistry operations, they suffer from many drawbacks. The free trialkylphosphine ligands are typically air-sensitive or even pyrophoric, while the air-stable phosphonium or imidazolium preligands can be hygroscopic. Generation of the catalyst in situ can also lead to reproducibility problems due to difficulty in controlling the ligand/Pd ratio and the air-sensitivity of the ligands in solution phase. Catalysts derived from these ligands in general give optimal results with 1:1 or 2:1 L/Pd ratios, while excess ligand often inhibits the activity of the catalytic system and is not cost efficient. Generation of the active species from the ligand and Pd source may also result in induction periods or undesired side products due to the formation of metal complexes with different reactivity.

Therefore, there is an increasing interest in using preformed palladium complexes of these ligands as precatalysts. Whereas some of the ligands in Figure 1 tend to be relatively air-sensitive or even pyrophoric, their preformed Pd complexes, particularly Pd(II) complexes, are often air-stable and easily handled. In addition, it is possible to precisely control the L/Pd molar ratio of the catalyst on the basis of the stoichiometry of the precatalyst species. In this way, the chemistry to form the active species may also be carefully controlled through the choice of the appropriate precatalyst.

Recent studies by Grasa and Colacot showed that the preformed catalyst, $(DtBPF)PdCl_2$ (Pd-118, **1**, Figure 2) was significantly superior in the α-arylation reactions in terms of

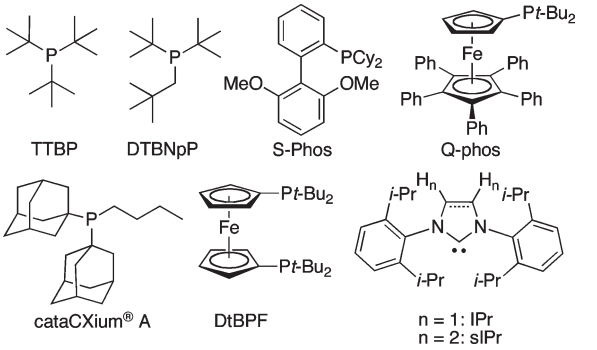


FIGURE 1. Examples of sterically demanding, electron-rich ligands used in Pd-catalyzed coupling reactions.

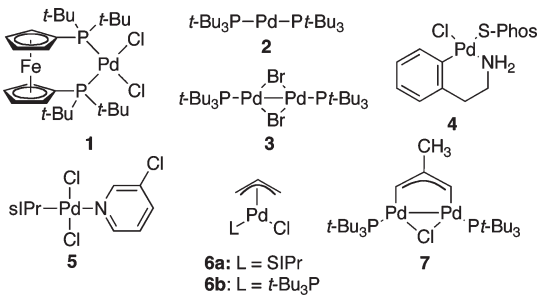


FIGURE 2. Examples of precatalysts with sterically demanding, electron-rich ligands.

selectivity and activity, in comparison to the corresponding in situ systems.[4] Preformed $Pd(0)L_2$ complexes, such as $Pd(TTBP)_2$ (**2**), are kinetically less active and therefore show modest activity at room temperature presumably because of the undesired 2:1 L/Pd ratio,[5] although **2** has been effectively used at elevated temperatures where ligand dissociation is more facile.[6] The $Pd(TTBP)_2$ complex has also been studied by Hartwig to understand the oxidative addition product in the catalytic cycle.[7] Prashad of Novartis found that the TTBP complex of a Pd(I) dimer, $[Pd(\mu\text{-Br})(TTBP)]_2$ (**3**), was an effective and superior precatalyst in the Buchwald–Hartwig (B–H) coupling reaction in comparison to the in situ system.[8] Hartwig also observed similar effects in both C–N coupling and α-arylation reactions using **3** as a precatalyst.[9] Palladacycle adducts of S-Phos (**4**) and related ligands were shown to be highly effective precatalysts for amination of aryl chlorides.[10] The PEPPSI catalyst system (**5**) developed by Organ is a stable precursor to NHC-Pd

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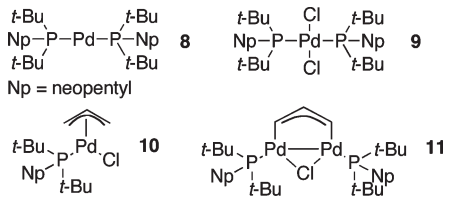

FIGURE 3. Preformed DTBNpP complexes from this study.

catalyst systems (NHC = *N*-heterocyclic carbene, i.e., sIPr).[11] Nolan has shown that Pd(η^3-allyl)(NHC)Cl complex (**6a**) provide effective catalysts for a range of Pd-catalyzed cross-coupling reactions.[12] There are only a few examples of the use of Pd-allyl complexes of electron-rich, sterically demanding ligands (**6b**) as precatalysts, however.[13] Pd(I)-μ-allyl dimers, such as **7**, can also be used as precatalysts.[14]

Shaughnessy et al. have reported recently that di(*tert*-butyl)neopentylphosphine (DTBNpP) in conjunction with $Pd_2(dba)_3$ acts as an effective catalyst system for B−H, Sonogashira, Suzuki, and Heck coupling reactions of aryl bromides and chlorides.[15] In the case of B−H amination, the DTBNpP-derived catalyst proved to be more active than that derived from TTBP. The increased activity of the DTBNpP catalyst system in C−N coupling was attributed to the larger calculated cone angle of this ligand in comparison to TTBP.

Because DTBNpP is a pyrophoric material, an air-stable precatalyst would be highly attractive for large-scale applications. We also sought to structurally characterize the palladium complexes of these ligands in order to further understand their role in creating high activity catalyst systems. Four new Pd complexes of DTBNpP, Pd(DTBNpP)$_2$ (**8**), *trans*-Pd(DTBNpP)$_2$Cl$_2$ (**9**), Pd(η^3-allyl)(DTBNpP)Cl (**10**), and Pd_2(DTBNpP)$_2$(μ-allyl)(μ-Cl) (**11**) (Figure 3), were structurally characterized during this study. Complex **10** provided a superior catalyst for the arylation of amines and ketones compared to the active catalysts derived from **8** or **9** or generated in situ ($Pd_2(dba)_3$/DTBNpP). This study also provides our preliminary mechanistic investigations supporting the formation of the active catalytic species from **10**.

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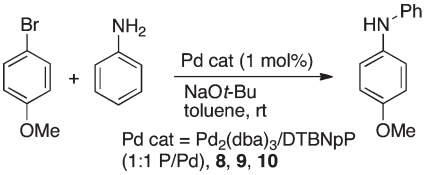
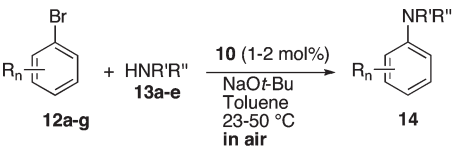
Results and Discussion

Buchwald−Hartwig Amination with Precatalysts. The Shaughnessy group has previously shown that DTBNpP in combination with $Pd_2(dba)_3$ provides a catalyst capable of coupling various amines with aryl bromides at room temperature and aryl chlorides at elevated temperatures (100−140 °C).[15a] The ability of **8**, **9**, and **10** to provide active catalytic species for the coupling of 4-bromoanisole and aniline in toluene at room temperature (eq 1) was compared to that of the in situ system derived from $Pd_2(dba)_3$/DTBNpP (1:1 Pd/DTBNpP). As has previously been shown, the in situ system gave complete conversion to *N*-phenyl-*p*-anisidine within 30 min (Table 1). Pd(DTBNpP)$_2$ (**8**) showed little activity at room temperature, however. Presumably the dissociation of DTBNpP from **8** to form the Pd(DTBNpP) active species is slow at room temperature as has previously been seen with Pd(TTBP)$_2$.[5b,c] In contrast, we had previously observed that the catalyst derived in situ from DTBNpP and $Pd_2(dba)_3$ gave complete conversion after 1 h at room temperature with DTBNpP/Pd ratios ranging from 1 to 2:1.[15a] This result may indicate that dba plays a non-innocent role in this reaction as has been observed by others.[2a] The dichloride complex (**9**) showed essentially no activity, presumably as a result of the inability to reduce the Pd(II) catalyst precursor under the conditions employed in the study. The allyl catalyst (**10**) gave a higher initial rate of conversion (82%) after 15 min compared with that of the catalyst generated in situ (40%).



(1)

On the basis of the promising results with Pd-allyl precatalyst **10**, its ability to promote amination of aryl bromides and chlorides was further explored. Because complex **10** is air-stable, the coupling of 4-bromoanisole (**12a**) and aniline (**13a**) was attempted in air (eq 2). The reaction was assembled in air using reagents stored in air, including complex **10**. The vial was then sealed under air and stirred at ambient temperature. Complete conversion to product occurred within 30 min as determined by GC analysis. The product, *N*-phenyl-*p*-anisidine, was isolated in 89% yield (Table 2). The air-stability of complex **10** is in stark contrast to free DTBNpP, which is classified as a pyrophoric liquid.[15b]



(2)

12a: R = 4-OMe **13a:** aniline
12b: R = 4-NMe$_2$ **13b:** mesityl amine
12c: R = 4-Me **13c:** 2,6-diisopropyl aniline
12d: R = 4-CN **13d:** morpholine
12e: R = 2-Me **13e:** *N*-methylaniline
12f: R = 2-OMe
12g: R = 2,6-Me

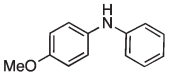
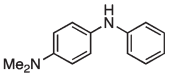
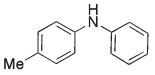
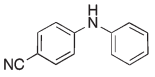
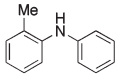
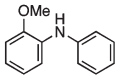
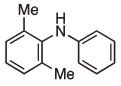
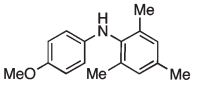
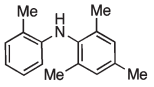
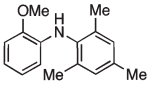
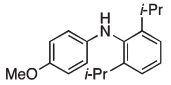
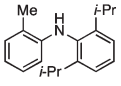
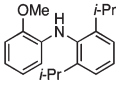
The catalyst derived from complex **10** proved to be a general catalyst for the arylation of aniline derivatives (Table 2). Excellent yields were obtained with *para*-substituted aryl

TABLE 1. Precatalyst Comparison in the Coupling of 4-Bromoanisole and Aniline

entry	precatalyst	% yield (15 min)[a]	% yield (30 min)[a]
1	$Pd_2(dba)_3$/DTBNpP (1:1)	40	100
2	**8**	3	4
3	**9**	2	3
4	**10**	82	90

[a]Yields determined by GC relative to an internal standard (mesitylene).

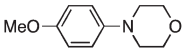
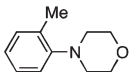
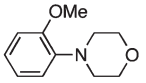
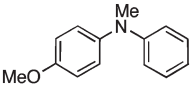
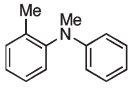
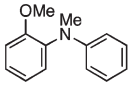
TABLE 2. Coupling of Aryl Bromides and Anilines Using Precatalyst 10

entry	12	13	14	T (°C)	Pd (%)	yield (%)[a]
1	**12a**	**13a**		23	1	89(92)
2	**12b**	**13a**		23	1	99(78)
3	**12c**	**13a**		23	1	88(86)
4	**12d**	**13a**		23	1	NR(NR)
5	**12e**	**13a**		23	2	99(79)
6	**12f**	**13a**		23	2	91
7	**12g**	**13a**		23	2	95(77)
8	**12e**	**13b**		50	2	91
9	**12e**	**13b**		50	1	85(78)
10	**12f**	**13b**		50	2	98
11	**12a**	**13c**		50	2	97
12	**12e**	**13c**		50	2	98
13	**12f**	**13c**		50	2	97

[a]Average isolated yield of product (2 trials) obtained from ArBr (0.8 mmol), amine (1.0 mmol), NaO*t*-Bu (1.2 mmol), and **10** (1 mol %) in toluene under air (eq 2). Values in parentheses are yields obtained previously using the $Pd_2(dba)_3$/DTBNpP catalyst system under identical conditions, but under a N_2 atmosphere.[15a]

bromides and aniline (entries 1−3). Yields of these reactions were comparable to those obtained under inert conditions with the in situ catalyst derived from $Pd_2(dba)_3$/DTBNpP except in the case of substrate **12b**. With this electron-rich aryl bromide, the catalyst derived from **10** gave a higher yield than obtained with the in situ catalyst. 4-Bromobenzonitrile

TABLE 3. Coupling of Aryl Bromides and Secondary Amines Using Precatalyst 10

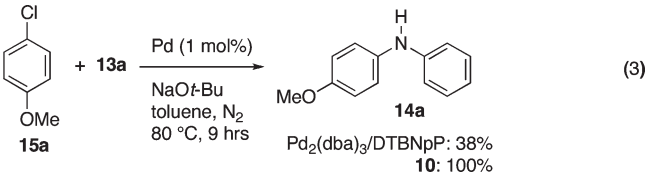
entry	12	13	14	T (ºC)	Pd (%)	yield (%)[a]
1	**12a**	**13d**		50	2	95(97)
2	**12e**	**13d**		23	2	90(93)
3	**12f**	**13d**		50	2	88
4	**12a**	**13e**		23	1	98(89)
5	**12e**	**13e**		50	1	74(90)
6	**12f**	**13e**		50	2	97

[a]Average isolated yield of product (2 trials) obtained from ArBr (0.8 mmol), amine (1.0 mmol), NaO*t*-Bu (1.2 mmol), and **10** (1 mol %) in toluene under air (eq 2). Values in parentheses are yields obtained previously using the $Pd_2(dba)_3$/DTBNpP catalyst system under identical conditions, but under an N_2 atmosphere.[15a]

failed to react using either **10** or the in situ catalyst system, possibly due to competitive binding to the Pd center. The catalyst derived from **10** also gave good results in the coupling of sterically demanding substrates. Coupling of mono- and di-*ortho*-substituted aryl bromides (entries 5−7) with aniline gave excellent yields but required a higher catalyst loading (2 mol %). The yields using **10** were approximately 20% higher than those with the in situ system in these cases. When hindered anilines **13b** and **13c** were used (entries 8−13), higher catalyst loadings (2 mol %) and higher temperatures (50 °C) were necessary for complete conversion. Even in the case of 2-substiuted aryl bromides, yields greater than 95% were obtained. In contrast, the in situ system gave only a 47% yield for the coupling of 4-bromotoluene and **13c**.[15a]

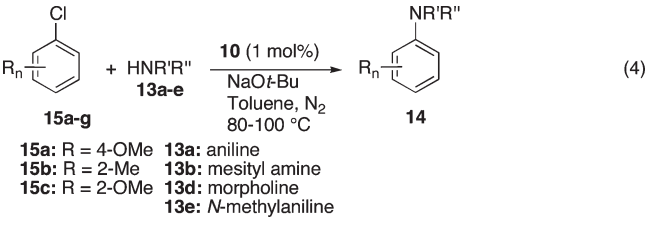
The catalyst derived from **10** also was effective for the arylation of the secondary amines such as morpholine (**13d**) and *N*-methylaniline (**13e**) in air. The arylation of morpholine required 2 mol % **10** to achieve complete conversion within a few hours at 50 °C. Excellent yields were obtained with 4-bromoanisole (**12a**) and 2-substituted aryl bromides **12e** and **12f** (Table 3). The yields obtained with **10** are comparable to those previously reported with the in situ catalyst system. Arylation of *N*-methylaniline also could be achieved in high yield. With the unhindered substrate **12a**, the reaction could be carried out at room temperature with 1 mol % **10** to give a nearly quantitative yield of product (entry 4). The 2-substituted substrates **12e** and **12f** required that the reaction to be run at 50 °C. For the deactivated substrate **12f**, 2 mol % **10** was required. The yields were comparable to those obtained with the in situ system with the exception of the coupling of **12e** and **13e**. In this case, the yield with **10** was 74% in comparison to 90% for the in situ system.

Aryl chlorides are more challenging substrates than aryl bromides because of their larger bond dissociation energies.[16] The $Pd_2(dba)_3$/DTBNpP in situ catalyst system was previously shown to be moderately active toward the coupling of aryl chlorides and amines.[15a] Good yields could be obtained, but the reactions typically required higher temperatures (80−140 °C) and/or higher catalyst loadings (1−5 mol %). Initial attempts to carry out the amination of aryl chlorides in air with catalyst **10** gave low conversions presumably as a result of the faster rate of catalyst decomposition at higher temperature. Therefore, all reactions with aryl chlorides were carried out under nitrogen. A direct comparison of the catalyst derived from **10** and the in situ system was carried out in the coupling of 4-chloroanisole (**15a**) and aniline (**13a**) at 80 °C using 1 mol % Pd (eq 3). Precatalyst **10** gave 43% conversion (GC) after 4 h, while the in situ system had only reached 28% conversion. After 9 h, the catalyst derived from **10** had completely converted the aryl chloride to the product. In contrast, only 38% conversion was obtained with the in situ catalyst after 9 h. Thus, it appears that the catalytic species derived from **10** is more suitable for the coupling of aryl chlorides than the catalyst generated in situ from $Pd_2(dba)_3$ and DTBNpP.



(3)

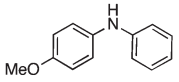
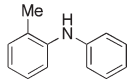
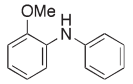
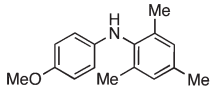
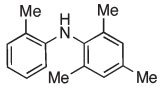
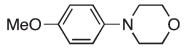
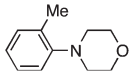
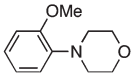
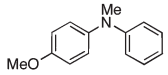
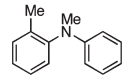
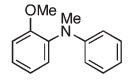
Since complex **10** showed good activity for the coupling of aryl chlorides, it was applied to the coupling of 4-chloroanisole (**15a**), 2-chlorotoluene (**15b**), and 2-chloroanisole (**15c**) with a range of amines (eq 4, Table 4). All reactions were carried out using 1 mol % **10** under nitrogen at 80 to 100 °C. Coupling of **15a** with aniline gave an excellent yield (97%) at 80 °C. The more hindered substrates **15b** and **15c** required higher temperature (100 °C) but also gave excellent yields for the arylation of aniline (entries 2−3). Sterically hindered mesityl amine (**13b**) was coupled with 4-chloroanisole in 95% yield at 100 °C. With the more hindered aryl chloride **15b**, only a 54% yield was obtained with **13b**. In contrast, the in situ system required temperatures of 120−140 °C to couple aryl chlorides with aniline at 1 mol % loading.[15a]



(4)

With morpholine, a trend similar to that observed for aniline was seen. With the unhindered **15a** substrate, the reaction could be carried out efficiently at 80 °C using 1 mol % catalyst. With more hindered substrates (**15b** and **15c**), the reaction had to be performed at 100 °C to achieve complete conversion when the catalyst loading is 1 mol % **10**. Using the in situ catalyst system, **15a** could be coupled with morpholine at 80 °C but required 5 mol % Pd. *N*-Methylaniline was arylated in excellent yield at 100 °C using all three aryl chlorides with the precatalyst, **10**. Under similar conditions, the in situ catalyst system required 5 mol % Pd to achieve similar conversion at 100 °C.

TABLE 4. Coupling of Aryl Chlorides and Amines Using Precatalyst 10

entry	15	13	14	T (°C)	yield (%)[a]
1	**15a**	**13a**		80	97
2	**15b**	**13a**		100	95
3	**15c**	**13a**		100	96
4	**15a**	**13b**		100	95
5	**15b**	**13b**		100	54
6	**15a**	**13d**		80	91
7	**15b**	**13d**		100	91
8	**15c**	**13d**		100	84
9	**15a**	**13e**		100	95
10	**15b**	**13e**		100	98
11	**15c**	**13e**		100	97

[a]Average isolated yields obtained from the reaction of ArCl (0.8 mmol), amine (1.0 mmol), NaO*t*-Bu (1.2 mmol), **10** (1 mol %) in toluene under nitrogen (eq 4).

Preliminary Studies of Pd-DTBNpP-Based Catalysts in the α-Arylation of Aryl Halides. We were also interested in the structure−activity relationship of the Pd/DTBNpP-based catalysts in the α-arylation of ketones. As a model reaction, α-arylation of propiophenone with an electron-neutral substrate, 4-chlorotoluene, was performed in the presence of NaO*t*-Bu base under 1 M substrate concentration, at two different temperatures (60 and 100 °C) and catalyst loadings (1 and 0.1 mol %) (eq 5). Table 5 summarizes the relative activities of both isolated as well as in situ catalysts. When the reactions were run at 60 °C, Pd(η^3-allyl)(DTBNpP)Cl (**10**) and Pd_2(DTBNpP)$_2$(μ-Cl)(μ-allyl) (**11**) led to moderate-high conversions (Table 5, entries 11 and 14), whereas catalysts **8** and **9** showed no conversion (Table 5, entries 5 and 8).

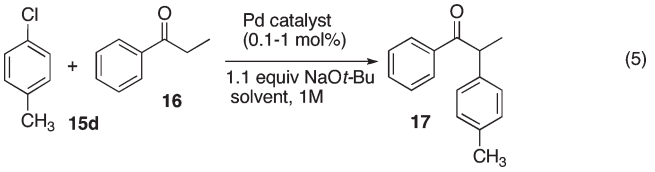
(16) Oxidative addition rate has been correlated to the C−X (X = I, Br, Cl, F) bond dissociation energy (kcal/mol: Ph−I = 67; Ph−Br = 84; Ph−Cl = 97.1; Ph−F = 126), a deciding factor in the oxidative addition step of the Pd-catalyzed coupling: (a) Blanksby, S. J.; Ellison, G. B. *Acc. Chem. Res.* **2003**, *36*, 255–263. (b) Grushin, V. V.; Alper, H. *Chem. Rev.* **1994**, *94*, 1047–1062. (c) McMillen, I. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493. (d) Cox, J. D.; Pilcher, G. *Thermochemistry of Organic and Orgonometallic Compounds*; Academic Press: London, 1970.

TABLE 5. Catalyst Effect in the α-Arylation of Propiophenone with 4-Chlorotoluene[a]

entry	precatalyst	solvent/T (°C)	catalyst loading (mol %)	conv (%)[b]
1	$Pd_2(dba)_3$/DTBNpP (1/1)	THF/60	1	52
2		Dioxane/100	1	42
3	$Pd_2(dba)_3$/DTBNpP (1/2)	THF/60	1	8
4		Dioxane/100	1	83
5	$Pd(DTBNpP)_2$ (**8**)	THF/60	1	NR
6		Dioxane/100	1	>99
7		Dioxane/100	0.1	55[d]
8	$Pd(DTBNpP)_2Cl_2$ (**9**)	THF/60	1	NR
9		Dioxane/100	1	>99[c]
10		Dioxane/100	0.1	66[d]
11	Pd(DTBNpP)(η^3-allyl)Cl (**10**)	THF/60	1	78
12		Dioxane/100	1	79
13		Dioxane/100	0.1	20
14	$Pd_2(DTBNpP)_2$(μ-Cl)-	THF/60	1	78
15	(μ-allyl) (**11**)	Dioxane/100	1	68
16		Dioxane/100	0.1	18

[a]Reaction conditions: 2 mmol of 4-chlorotoluene, 2.2 mmol of propiophenone, 2.2 mmol of NaO*t*-Bu, 0.02 mmol of catalyst, 2 mL of solvent, 60 °C, 20 h unoptimized reaction time (eq 5). [b]GC conversion. [c]85% isolated yield. [d]Reaction conditions: 5 mmol of 4-chlorotoluene, 5.5 mmol of propiophenone, 5.5 mmol of NaO*t*-Bu, 0.005 mmol of catalyst (*S*/*C* 1000), 5 mL dioxane, 100 °C, 20 h.

Notably, at this lower temperature, the catalytic systems with a Pd/ligand molar ratio of 1:1 performed better than the systems with a 1:2 Pd/L molar ratio (Table 5, entries 1 and 11 vs entries 3, 5, and 8). However, at higher temperatures (100 °C), the reactivity trend was reversed. The catalysts with a Pd/DTBNpP ratio of 1:2 gave quantitative conversions (Table 5, entries 6 and 9 vs entry 12). A more pronounced difference in reactivity was observed between PdL_2 (**8** and **9**) and PdL (**10**) DTBNpP-based catalysts at lower catalyst loadings (entries 7 and 10 vs entry 13).



(5)

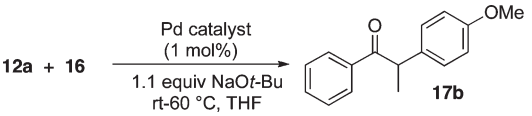
These results could be explained on the basis that generally the 12-electron Pd(0)L species is kinetically more active than the coordinatively saturated 14-electron $Pd(0)L_2$ counterpart at lower temperatures.[5a,c] Grasa and Colacot have reported that the bulky electron-rich bidentate 1,1′-bis(di-*tert*-butylphosphino)ferrocene ligand (DtBPF) remains coordinated during catalysis based on the NMR spectroscopic evidence. These results indicate the presence of Pd(0)-(DtBPF) species at the ground state, which suggests that the 14-electron Pd(DTBNpP) complex could directly undergo oxidative addition at elevated temperature.[4a] Alternatively, if the PdL species were required, as is generally hypothesized for sterically demanding monodentate ligands,[3] higher temperature would promote ligand dissociation from PdL_2 species to form the active PdL species. At higher temperature, the PdL_2 species would presumably be more stable than low-coordination PdL species, however. Thus at higher temperature, a higher L/Pd ratio could lead to catalysts with longer lifetimes than those derived from the optimal 1:1 ratio. Notably, at 100 °C, precatalysts **8** and **9** gave much better activity in comparison to the in situ system: $Pd_2(dba)_3$/DTBNpP (Pd/DTBNpP = 1/2) (Table 5, entries 6 and 9 vs entry 4). The Pd(I) dimer **11** behaved somewhat similar to **10**, with slightly lower conversions (Table 5, entry 14−16).

TABLE 6. Catalyst Effect in the α-Arylation of Propiophenone with 4-Bromoanisole[a]

entry	precatalyst	*T* (°C)	conv (%)[b]
1	$Pd_2(dba)_3$/DTBNpP (1/1)	60	39
2	$Pd_2(dba)_3$/DTBNpP (1/2)	60	49
3	$Pd(DTBNpP)_2$ (**8**)	rt	NR
4		60	95
5	$Pd(DTBNpP)_2Cl_2$ (**9**)	rt	73
6		60	85
7	Pd(DTBNpP)(η^3-allyl)Cl (**10**)	rt	61
8		60	97
9	$Pd_2(DTBNpP)_2$(μ-Cl)(μ-allyl) (**11**)	rt	44
10		60	76
11	[Pd(μ-Br)(TTBP)]$_2$ (**3**)	rt	95[c]
12		60	99

[a]Reaction conditions: 2 mmol of 4-bromoanisole, 2.2 mmol of propiophenone, 2.2 mmol of NaO*t*-Bu, 0.02 mmol of catalyst, 2 mL THF, 20 h unoptimized reaction time. [b]GC conversion. [c]89% isolated yield.

A similar study was carried out for a challenging aryl bromide substrate (4-bromoanisole), but under milder conditions (room temperature and 60 °C, Table 6). At room temperature, the isolated catalyst $Pd(DTBNpP)_2Cl_2$ was the most reactive catalytic system in the DTBNpP series (73% conversion, entry 5), while [Pd(μ-Br)(TTBP)]$_2$ led to 95% conversion at room temperature. Interestingly both the PdL based neopentyl catalysts (**10** and **11**) were slightly inferior under identical conditions. When the temperature was increased to 60 °C, $Pd(DTBNpP)_2$ (**8**) gave nearly quantitative conversion to the desired product (entry 4). Similarly to the amination reactions and to the α-arylation of 4-chlorotoluene, the isolated catalysts were found to perform better compared to their in situ systems (entries 4 and 6 vs entries 1 and 2). The substrate scope of these catalysts in the α-arylation of various carbonyl compounds is currently under investigation and will be addressed in a separate paper.



(6)

Structural Characterization of Palladium Complexes. Complexes **8**−**11** gave X-ray quality crystals upon recrystallization from cold hexane (Figures 4−7). The complexes had structural characteristics similar to those of previously reported structures of PdL_2,[17] *trans*-PdL_2Cl_2,[18] Pd(η^3-allyl)-(L)Cl,[19] and $Pd_2(DTBNpP)_2$(μ-allyl)(μ-Cl)[14d] (L = sterically demanding alkylphosphine). One feature of note is the response of the neopentyl substituent to changes in the coordination environment at the metal center. In the case

(17) Tanaka, M. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1992**, *C48*, 739–740.
(18) DiMeglio, C. M.; Ahmed, K. J.; Luck, L. A.; Weltin, E. E.; Rheingold, A. L.; Bushweller, C. H. *J. Phys. Chem.* **1992**, *96*, 8765–8777.
(19) (a) Viciu, M. S.; Navarro, O.; Germaneau, R. F.; Kelly, R. A., III; Sommer, W.; Marion, N.; Stevens, E. D.; Cavallo, L.; Nolan, S. P. *Organometallics* **2004**, *23*, 1629–1635. (b) Albert, J.; Bosque, R.; Cadena, J. M.; Delgado, S.; Granell, J.; Muller, G.; Ordinas, J. I.; Bardia, M. F.; Solans, X. *Chem.—Eur. J.* **2002**, *8*, 2279–2287. (c) Alberti, D.; Goddard, R.; Pörschke, K.-R. *Organometallics* **2005**, *24*, 3907–3915.

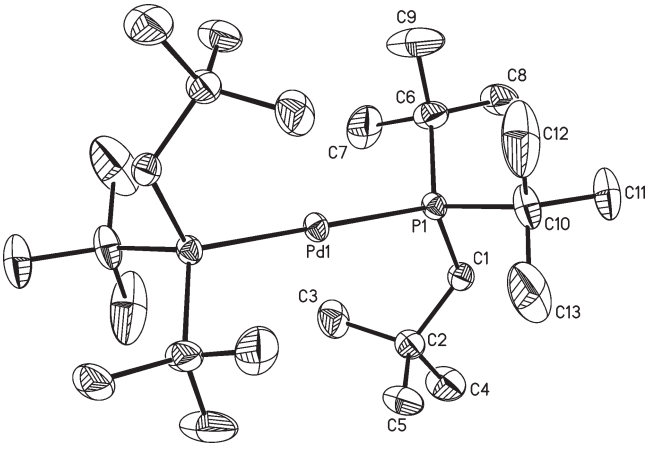


FIGURE 4. Thermal ellipsoid plot (50% level) of the molecular structure of $Pd(DTBNpP)_2$ (**8**). Ellipsoids are drawn at the 50% level. Hydrogen atoms on the DTBNpP ligand have been removed for clarity. Selected bond lengths (Å) and angles (deg): Pd1−P1, 2.2961(4); P1−C1, 1.869(1); P1−C6, 1.893(2); P1−C10, 1.894(2); P1−Pd1−P1, 180.0; C1−P1−C6, 101.55(7); C1−P1−C10, 102.17(7); C1−P1−Pd1, 118.14(5); C6−P1−C10, 110.58(7); C6−P1−Pd1 112.12(5); C10−P1−Pd1, 111.48(5); C2−C1−P1, 119.62(9).

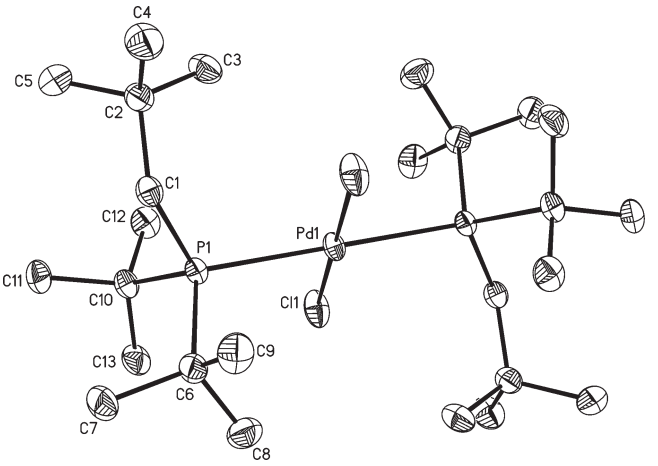


FIGURE 5. Thermal ellipsoid plot (50% level) of one of the two molecules of *trans*-$Pd(DTBNpP)_2Cl_2$ (**9**) in the asymmetric unit. Hydrogen atoms have been removed for clarity. Selected bond lengths (Å) and angles (deg) for both unique molecules: Pd−P, 2.4148(4), 2.4082(4); Pd−Cl, 2.3036(4), 2.3096(4); P−C1, 1.8522(14), 1.8518(13); P−C6/10, 1.9031(14), 1.9079(14), 1.9017(13), 1.9027(14); Cl−Pd−P, 90.78(1), 89.22(1), 91.79(1), 88.21(1); C1−P−C6/10, 100.92(6), 106.85(6), 106.65(6), 101.70(6); C6−P−C10, 109.04(6), 108.85(6); C1−P−Pd, 112.60(5), 113.45(5); C10−P−Pd 120.16(4), 119.66(4); C6−P−Pd 105.53(4), 104.99(4); C2−C1−P, 126.24(9), 126.52(9).

of **8**, the neopentyl arms are essentially *syn* coplanar with the Pd−P bond (Pd1−P1−C1−C2 = 0.3(1)°) resulting in the neopentyl group exerting maximal steric demand. This conformation is similar to the calculated structure of Pd(DTBNpP).[15a] In contrast, complexes **9** and **10** have large Pd−P−C−$C(Me)_3$ dihedral angles (**9**, 64.5(1)° and 64.3(1)°; **10**, −59.8(3)°) to allow space for the other substituents at the Pd center. The Pd(I) μ-allyl complex (**11**) has small Pd−P−C−$C(Me)_3$ dihedral angles of 0.5(3)° and 3.2(3)° similar to that of **8**. The steric strain in these systems can also be seen in

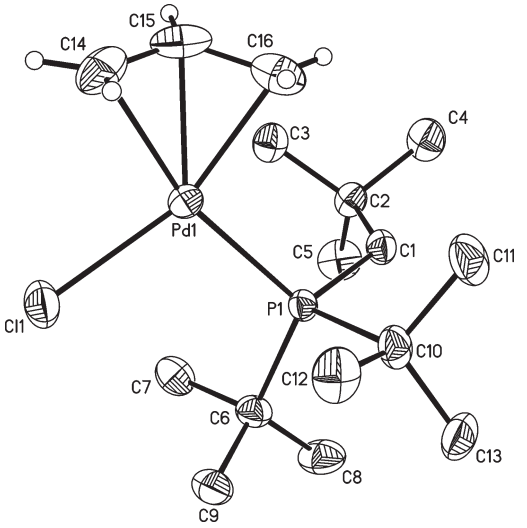


FIGURE 6. Thermal ellipsoid plot (50% level) of the molecular structure of Pd(η^3-allyl)(DTBNpP)Cl (**10**). Hydrogen atoms on the DTBNpP ligand have been removed for clarity. Selected bond lengths (Å) and angles (deg): Pd1−P1, 2.3439(6); Pd1−Cl1, 2.3781(7); Pd1−C14, 2.198(3); Pd1−C15, 2.145(3); Pd1−C16, 2.121(4); P1−C1, 1.862(3); P1−C10, 1.900(2); P1−C6, 1.893(3); P1−Pd1−Cl1, 103.98(2); C16−Pd1−P1, 97.9(1); C14−Pd1−Cl1, 90.5(1); C6−P1−Pd1, 114.93(8); C10−P1−Pd1, 107.90(9); C1−P1−Pd1, 114.76(9); C2−C1−P1, 126.3(2).

the P−C−$C(Me)_3$ angle. For less-hindered complexes **8** and **11**, which are able to adopt Pd−P−C−$C(Me)_3$ dihedral angles near zero, the P−C−$C(Me)_3$ angles are 119.62(9)° and 122.1(3)°, respectively. Complexes **9** and **10**, with more hindered Pd centers, have larger P−C−$C(Me)_3$ angles of 126.52(9)° and 126.3(2)°, respectively, which reflects the additional steric strain of these systems. These results suggest that the neopentyl substituent has a certain degree of conformational flexibility to allow coordination of additional ligands at Pd.

Initial Studies of the Generation of the Active Species from 10. The improved performance of precatalyst **10** for the arylation of amines compared to the in situ catalyst system raises the question of how the active species generated from **10** differs from that obtained from $Pd_2(dba)_3$ and DTBNpP. Combinations of $Pd_2(dba)_3$ and DTBNpP give exclusively $Pd(DTBNpP)_2$ (**8**) as the P/Pd ratio is varied from 1 to 3 as determined by ^{31}P NMR spectroscopy. This result is similar to what has previously been reported for the TTBP/$Pd_2(dba)_3$ system.[5c] Complex **8** acts as a precursor to the 12-electron Pd(DTBNpP) active species (**18**),[3] which cannot be observed by ^{31}P NMR spectroscopy. In the case of **10**, we presumed that a nucleophilic species (i.e., *tert*-butoxide) would displace the allyl ligand to generate the Pd(DTBNpP) active species in solution. The Pd(DTBNpP) complex would be expected to disproportionate into $Pd(DTBNpP)_2$ and uncoordinated Pd^0 in the absence of other trapping ligands. Nolan has proposed a similar activation mechanism for Pd(allyl)NHC precatalysts and has trapped the transient Pd(NHC) complex with phosphine ligands.[19a,20]

To test this hypothesis, a solution of **10** was treated with 1.3 equiv of NaO*t*-Bu in C_6D_6. A $^{31}P\{^1H\}$ NMR spectrum

(20) Fantasia, S.; Nolan, S. P. *Chem.—Eur. J.* **2008**, *14*, 6987–6993.

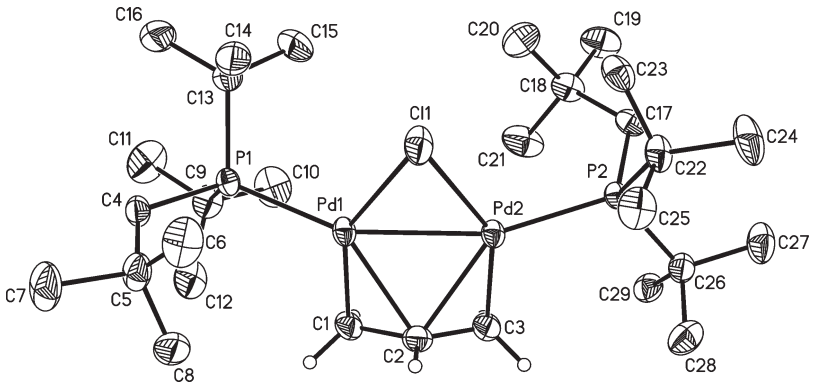
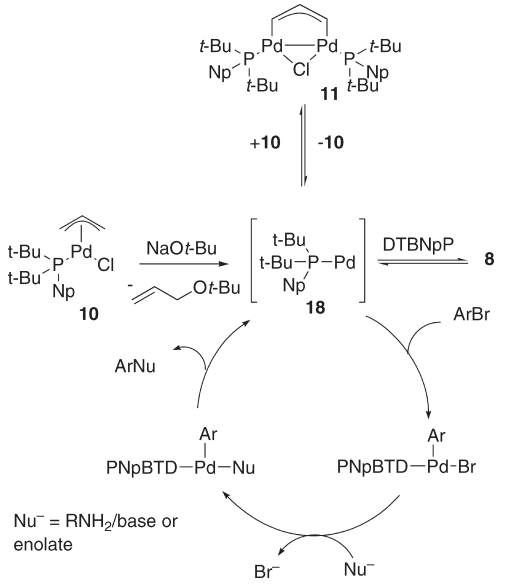


FIGURE 7. Thermal ellipsoid plot (50% level) of the molecular structure of $[Pd(\mu\text{-}\eta^3\text{-allyl})(DTBNpP)(\mu\text{-Cl})]_2$ (**11**). Hydrogen atoms on the DTBNpP ligand have been removed for clarity. Selected bond lengths (Å) and angles (deg): Pd1−Pd2, 2.6561(5); Pd1−P1, 2.336(1); Pd1−Cl1, 2.430(1); Pd1−C1, 2.063(4); Pd1−C2, 2.388(4); Pd2−P2, 2.3219(9); Pd2−Cl1, 2.426(1); Pd2−C3, 2.044(4); Pd2−C2, 2.389(4); P1−C9, 1.899(4); P1−C4, 1.870(4); P1−C13, 1.909(4); P1−Pd1−Cl1, 111.13(4); P1−Pd1−C1, 104.45(11). Pd1−P1−C9, 111.18(13); Pd1−P1−C4, 120.3(1); P1−C4−C5, 120.8(3), P2−Pd2−Cl1, 111.63(3); P2−Pd2−C3, 104.7(1); Pd2−P2−C22, 108.6(1); Pd2−P2−C17, 117.5(1); P2−C17−C18, 122.1(3).

taken after 10 min (see Supporting Information) showed complete loss of **10** and formation of **11** (79%) along with small amounts of **8** (6%), and free DTBNpP (15%). These results are consistent with previous reports of the synthesis of $[Pd(\mu\text{-allyl})(L)Cl]_2$ complexes by treatment of $Pd(\eta^3\text{-allyl})(L)Cl$ with hydroxide or alkoxide bases.[14d,21] The Pd(DTBNpP) complex appears to form, but rapidly reacts with **10** to form **11**. Under the catalytic conditions, the aryl halide would presumably compete with **10** for the Pd(DTBNpP) intermediate. To determine whether **11** is formed under the catalytic reaction conditions, the coupling of 4-bromotoluene and aniline was carried out under our normal conditions, but with a higher loading of **10** (7.5 mol %). The reaction mixture was then analyzed by $^{31}P\{^1H\}$ NMR spectroscopy (see Supporting Information). A complex spectrum was obtained with major peaks at 59 (**10**, 4%), 53 (26%), 51.5 (8%), 49.8 (**11**, 34%), 46.7 (6%), 44.2 (**8**, 10%), and 18.5 (DTBNpP, 12%) ppm. The species responsible for the peaks at 53, 51.5, and 46.7 ppm have not been identified, although these may be oxidative addition products as they were observed only in the presence of aryl bromide.

These results show that in the presence of an alkoxide nucleophile, **10** is rapidly converted to the Pd(I) dimer **11**. Presumably, the reaction of *tert*-butoxide with **10** results in the generation of Pd(DTBNpP) (**18**), which is then trapped by unreacted **10** to give **11** (Scheme 1). Complex **11** is also observed as a major phosphorus-containing species under the catalytic reaction conditions. We hypothesize that the Pd(DTBNpP) species generated from **10** can be competitively trapped by the aryl halide (catalytic cycle) or by remaining **10** to produce **11**. The role of complex **11** in the catalytic reaction is not yet known. Complex **11** could serve as a source of **18** if its formation is reversible, alternatively it could be a catalyst deactivation pathway if its formation is not reversible. Initial studies show that complex **11** is a competent precatalyst in the enolate arylation reactions, although it was somewhat less active for the coupling of 4-bromoanisole and propiophenone than **10**. In the coupling of 4-chlorotoluene with propiophenone, **10** and **11** gave

SCHEME 1. Proposed Mechanism for the Generation of the Active Species from 10 in the Presence of NaO*t*-Bu



identical results. In contrast, complex **11** was a significantly less effective precatalyst in the coupling of 4-bromoanisole and *N*-methylaniline. In this reaction, complex **10** gave 93% conversion after 1 h, while the catalyst derived from complex **11** gave only 9% conversion. The reaction with complex **11** did reach 91% conversion after 24 h, however. Further studies on the role of **11** in these catalyst systems are ongoing.

Conclusions

In conclusion, complex **10** serves as an air-stable precatalyst that is highly effective for the coupling of aryl halides and amines. The catalyst derived from **10** is sufficiently air-stable to allow amination of aryl bromides in air under mild conditions. Significantly, this catalyst system is highly effective with electronically and sterically challenging aryl bromide and aniline substrates. Higher yields are obtained in these cases (Table 2) than with the catalyst generated in situ from $Pd_2(dba)_3$ and DTBNpP. Complex **10** also provides a

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more active catalyst for the amination of aryl chlorides than the catalyst generated in situ, allowing the reactions to be carried out at moderate temperatures with low catalyst loadings. Complex **10** gave a more active catalyst for the coupling of 4-bromoanisole with propiophenone than the in situ catalyst system. Precatalysts **8** and **9** gave results comparable to those using **10**, in contrast to the amination reaction where these precatalysts were completely ineffective. The catalyst derived from **10** also gave good yields in the coupling of 4-chlorotoluene with propiophenone, but the catalysts derived from **8**, **9**, and DTBNpP/$Pd_2(dba)_3$ (2:1 L/Pd) gave higher yields. Complexes **8**, **9**, **10**, and **11** were structurally characterized. Complex **10** reacts with NaO*t*-Bu to generate the μ-allyl Pd(I)-dimer **11** even in the presence of aryl halides. Complex **11** is an air-stable Pd(I) species that is catalytically competent in the coupling of aryl halides with propiophenone, which suggests that it may serve as a stable resting state under the catalytic conditions. Although we are reporting the C−N coupling of aryl bromides using **10** at room temperature in air to prove the concept, we recommend large-scale operations be carried under inert conditions as organic solvents need to be handled under nitrogen for safety reasons.

Experimental Section

General Experimental Details. Complexes **8**−**11** are available in gram to multikilograms through JMCCT. DTBNpP was obtained from FMC, Lithium Division as a 10 weight% solution in toluene. Toluene was distilled from sodium under nitrogen. All other reagents were obtained from commercial sources and used as received. Reactions carried out in air were assembled on the benchtop using reagents that had not been degassed in glass vials that were sealed under air with rubber septa. Reactions carried out under inert conditions were assembled in a nitrogen-filled glovebox using deoxygenated reagents and solvents and carried out in septum-sealed vials under nitrogen. ^{1}H and ^{13}C NMR spectra are referenced to the NMR solvent peaks or internal TMS. $^{31}P\{^1H\}$ NMR spectra were externally referenced to 85% H_3PO_4. HRMS were obtained on a magnetic sector mass spectrometer operating in the EI mode.

Procedure for the Preparation of Pd(η^3-allyl)(DTBNpP)Cl (10). In a glovebox, a vial was charged with $[Pd(allyl)Cl]_2$ (200 mg, 0.546 mmol), 2 equiv of DTBNpP (2.43 mL, 1.10 mmol), and toluene (10 mL). The reaction mixture was stirred for 3 h and then gravity filtered to remove any residual palladium black. The remaining phosphine and solvent were removed under vacuum (0.1 Torr), leaving behind the desired palladium complex as a yellow solid (350 mg, 80%). ^{1}H NMR (500 MHz, C_6D_6): δ 4.80−4.72 (m, 1H), 4.56 (t, J = 6.84 Hz, 1H), 3.44 (dd, J = 8.97, 13.27 Hz, 1H), 3.47 (bs, 1H), 2.21 (d, J = 11.55 Hz, 1H), 2.14 (d, J = 11.71 Hz, 1H), 2.01 (t, J = 11.64, 1H), 1.29 (s, 9H), 1.22 (d, J = 12.91 Hz, 9H), 1.14 (d, J = 12.66 Hz, 9H). ^{13}C NMR (90.6 MHz, C_6D_6): δ 113.8 (d, J_{C-P} = 4.42 Hz), 80.3 (d, J_{C-P} = 19.88 Hz), 54.0, 34.7 (d, J_{C-P} = 7.24 Hz), 33.2 (d, J_{C-P} = 6.20 Hz), 31.3, 30.6. $^{31}P\{^1H\}$ NMR (C_6D_6): δ 59.0 (s). Calculated for $C_{16}H_{34}ClPPd$: C, 48.13; H, 8.58. Found: C, 47.99; H, 8.63.

General Procedure for Hartwig−Buchwald Amination of Aryl Bromides with Primary and Secondary Amines. A vial was charged with **10** (1−2 mol %), sodium *tert*-butoxide (96.1 mg, 1.20 mmol), aryl bromide (0.8 mmol), amine (1.0 mmol), and toluene (2 mL) in the presence of air and sealed under air. Reactions were allowed to stir at room temperature unless otherwise noted. All reactions were monitored by GC to ensure completion, which typically took 3−6 h. Products were purified by column chromatography through SiO_2 using a mixture of hexanes and ethyl acetate as the eluent.

***N*-Phenyl-*p*-anisidine (Table 2, entry 1).**[22] Using the general procedure, 4-bromoanisole (100 μL, 0.799 mmol) and aniline (91 μL, 1.0 mmol) were coupled using 1 mol % **10** at room temperature. Purification by flash chromatography yielded a tan solid (141 mg, 89%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.22 (t, J = 7.57 Hz, 2H), 7.08 (d, J = 7.25 Hz, 2H), 6.91 (d, J = 7.57, 2H), 6.86 (m, 3H), 5.49 (bs, 1H), 3.81 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 155.0, 144.9, 135.5, 129.0, 121.9, 119.3, 115.4, 114.4, 55.3. Mp: 102−103 °C, lit. mp 104−105.

***N*,*N*-Dimethyl-*N*′-phenylbenzene-1,4-diamine (Table 2, entry 2).**[23] Using the general procedure, aniline (91 μL, 1.0 mmol), and 4-bromo-*N*,*N*-dimethylaniline (156.9 mg, 0.7845 mmol) were coupled using 1 mol % **10** at room temperature to give the product as a gray solid (161.0 mg, 99%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19 (t, J = 7.25 Hz, 2H), 7.07 (d, J = 8.83 Hz, 2H), 6.86 (d, J = 7.57 Hz, 2H), 6.80−6.74 (m, 3H), 5.42 (bs, 1H), 2.93 (s, 6H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 147.3, 146.1, 132.4, 129.2, 123.3, 118.8, 115.0, 114.0, 41.2. Mp: 123−125 °C, lit. mp[24] 126−128 °C.

***N*-Phenyl-*p*-toluidine (Table 2, entry 3).**[25] Using the general procedure, 4-bromotoluene (102 μL, 0.829 mmol) and aniline (91 μL, 1.0 mmol) were coupled using 1 mol % **10** at room temperature to give the product as a tan solid (146 mg, 88%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.28−7.22 (m, 2H), 7.10 (d, J = 8.17 Hz, 2H), 7.04−6.99 (m, 4H), 6.89 (t, J = 7.50 Hz, 1H), 5.63 (bs, 1H), 2.32 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 144.2, 140.6, 131.2, 130.1, 129.5, 120.5, 119.2, 117.1, 20.9. Mp: 86−87 °C, lit. mp[26] 87−88

***N*-Phenyl-*o*-toluidine (Table 2, entry 5).**[6e] Using the general procedure, aniline (91 μL, 1.0 mmol) and 2-bromotoluene (94 μL, 0.78 mmol) were coupled using 2 mol % **10** at room temperature to give the product as a brown oil (146.0 mg, 99%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.19 (d, J = 7.25 Hz, 1H), 7.13 (t, J = 7.25 Hz, 1H), 6.94 (t, J = 5.99 Hz, 3H), 6.89 (t, J = 6.31 Hz, 1H), 5.36 (s, 1H), 2.25 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 143.7, 140.9, 130.7, 129.0, 128.1, 126.5, 121.7, 120.2, 118.6, 117.2, 17.6.

***N*-Phenyl-*o*-anisidine (Table 2, entry 6).**[27] Using the general procedure, 2-bromoanisole (99 μL, 0.79 mmol) and aniline (91 μL, 1.0 mmol) were coupled using 2 mol % **10** at 50 °C. The product (145 mg, 91%) was obtained as a brown oil after purification by flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27,(m, 3H), 7.14 (d, J = 8.51 Hz, 2H), 6.93 (t, J = 7.57, 1H), 6.88 (m, 3H), 6.14 (s, 1H), 3.88 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 148.5, 143.0, 133.3, 129.5, 121.4, 121.0, 120.1, 118.8, 114.9, 110.8, 55.8.

2,6-Dimethyl-*N*-phenylaniline (Table 2, entry 7).[28] Using the general procedure, 2-bromo-*m*-xylene (147.9 mg, 0.7990 mmol) and aniline (91 μL, 1.0 mmol) were coupled using 2 mol % **10** at 50 °C. The product (147 mg, 95%) was obtained as an off-white solid after purification by flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.12 (m, 5H), 6.76 (t, J = 7.25 Hz, 1H), 6.51 (d, J = 7.88 Hz, 2H), 5.18 (s, 1H), 2.22 (s, 6H). ^{13}C NMR (90.6 MHz, DMSO): δ 146.3, 138.3, 135.9, 129.2, 128.5, 125.7, 118.2, 113.5, 18.3. Mp: 50−52 °C, lit. mp 52−53 °C.

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***N*-(4-Methoxyphenyl)-2,4,6-trimethylaniline (Table 2, entry 8).**[29] Using the general procedure, 2,4,6-trimethylaniline (140 μL, 0.994 mmol) and 4-bromoanisole (100 μL, 0.799 mmol) were coupled using 2 mol % **10** at 50 °C. The product (175.0 mg, 91%) was obtained as a tan solid after purification by flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.95 (s, 2H), 6.76 (d, J = 9.14 Hz, 2H), 6.49 (d, J = 8.83 Hz, 2H), 4.96 (bs, 1H), 3.77 (s, 3H), 2.33 (s, 3H), 2.19 (s, 6H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 152.5, 140.6, 136.6, 135.1, 134.7, 129.2, 114.8, 107.7, 55.7, 20.9, 18.2. Mp: 98−99 °C, lit. mp 100.5−101.5 °C.

***N*-(2-Methylphenyl)-2,4,6-trimethylaniline (Table 2, entry 9).**[30] Using the general procedure, 2,4,6-trimethylaniline (140 μL, 0.994 mmol) and 2-bromotoluene (96 μL, 0.80 mmol) were coupled using 1 mol % **10** at 50 °C. The product (153.6 mg, 85%) was obtained as a peach solid after purification by flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.14 (d, J = 7.25 Hz, 1H), 6.98 (m, 3H), 6.71 (t, J = 7.25 Hz, 1H), 6.15 (d, J = 7.88 Hz, 1H), 4.89 (bs, 1H), 2.34 (d, J = 5.26 Hz, 6H), 2.17 (s, 6H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 144.5, 136.0, 135.6, 135.2, 130.2, 129.2, 126.9, 122.1, 117.8, 111.5, 20.9, 18.1, 17.6. Mp: 75−77 °C, lit. mp 78.5−79.5

***N*-(2-Methoxyphenyl)-2,4,6-trimethylaniline (Table 2, entry 10).**[31] Using the general procedure, 2,4,6-trimethylaniline (140 μL, 0.994 mmol) and 2-bromoanisole (99 μL, 0.79 mmol) were coupled using 2 mol % **10** at 50 °C. The product (188.0 mg, 98%) was obtained as a peach solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.11 (d, J = 7.25 Hz, 1H), 6.94 (s, 3H), 6.68 (t, J = 7.25 Hz, 1H), 6.14 (d, J = 7.88, 1H), 4.85 (s, 1H), 2.30 (9s, 6H), 2.14 (s, 6H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 144.7, 136.2, 135.8, 135.4, 130.4, 129.4, 127.1,, 122.3, 118.0, 111.7, 21.1, 18.3, 17.8. Mp: 96−98 °C, lit. mp 100−100.5 °C.

***N*-(2,6-Diisopropylphenyl)-*p*-anisidine (Table 2, entry 11).** Using the general procedure, 2,6-diisopropylaniline (188 μL, 0.997 mmol) and 4-bromanisole (100 μL, 0.799 mmol) were coupled using 2 mol % **10** at 50 °C. The product (218.0 mg, 97%) was obtained as a brown oil after purification by flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.24−7.17 (m, 3H), 6.78 (d, J = 9.14, 2H), 6.49 (bd, 2H), 5.00 (bs, 1H), 3.78 (s, 3H), 3.24 (t, J = 6.94 Hz, 2H), 1.19 (d, J = 6.94, 12H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 152.3, 147.1, 142.3, 136.1, 126.7, 123.8, 114.8, 114.3, 55.7, 28.2, 23.9. HRMS-EI (m/z): $[M]^+$ calcd for $C_{19}H_{25}NO$ 283.1936, found 283.1931.

***N*-(2,6-Diisopropylphenyl)-*o*-toluidine (Table 2, entry 12).**[32] Using the general procedure, 2,6-diisopropylaniline (188 μL, 0.997 mmol) and 2-bromtoluene (96 μL, 0.80 mmol) were coupled using 2 mol % **10** at 50 °C. The product (182 mg, 86%) was obtained as an oil after purification by flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34−7.30 (m, 1H), 7.24 (d, J = 2.27, 1H), 7.14 (d, J = 7.04, 1H), 6.97 (t, J = 6.81 Hz, 1H), 6.69 (t, J = 6.56 Hz, 1H), 6.13 (d, J = 7.04 Hz, 1H) 4.93 (bs, 1H), 3.13 (sept, J = 7.04, 2H), 2.36 (s, 3H), 1.16 (dd, J = 19.3 Hz, 12H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 147.3, 146.0, 135.8, 130.2, 127.1, 123.8, 121.3, 117.5, 111.5, 28.3, 24.8, 23.0, 17.7.

***N*-(2,6-Diisopropylphenyl)-*o*-anisidine (Table 2, entry 13).**[33] Using the general procedure, 2,6-diisopropylaniline (188 μL, 0.997 mmol) and 2-bromanisole (0.8 mmol, 98.0 μL) were coupled using 2 mol % **10** at 50 °C. The product (217.0 mg, 97%) was obtained as a tan oil after purification by flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (t, J = 8.51 Hz, 2H), 7.26 (t, J = 8.51 Hz, 1H), 6.89 (d, J = 9.14, 1H), 6.71 (m, 2H), 6.14 (d, J = 7.57 Hz, 1H), 5.66 (s, 1H), 3.99 (s, 3H), 3.19 (sept, J = 6.94 Hz, 2H), 1.17 (d, J = 6.62, 12H). ^{13}C NMR (90.6 MHz, $CDCl_3$):δ 147.7, 146.3, 137.9, 135.5, 127.1, 123.7, 121.2, 116.7, 111.0, 109.8, 55.7, 28.1, 23.9.

***N*-(4-Methoxyphenyl)morpholine (Table 3, entry 1).**[34] Using the general procedure, morpholine (70 μL, 0.80 mmol) and 4-bromoanisole (100 μL, 0.799 mmol) were coupled using 2 mol % **10** at 50 °C to yield the product (147.0 mg, 95%) as a light brown solid after purification by flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.88 (q, J = 9.62 Hz, 4H), 3.86 (t, J = 4.73 Hz, 4H), 3.77 (s, 3H), 3.06 (t, J = 4.88 Hz, 4H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 154.0, 146.6, 117.8, 114.5, 67.0, 55.5, 50.8. Mp: 69−70 °C, lit. mp 71 °C.

***N*-(2-Methylphenyl)morpholine (Table 3, entry 2).**[32] Using the general procedure, morpholine (70 μL, 0.80 mmol) and 2-bromotoluene (96 μL, 0.80 mmol) were coupled using 2 mol % **10** at room temperature to give the product (128.0 mg, 90%) as an orange oil after purification by flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.18 (q, J = 7.57 Hz, 2H), 7.00 (q, J = 7.25 Hz, 2H), 3.85 (m, 4H), 2.91 (m, 4H), 2.31 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 151.0, 132.3, 130.9, 126.3, 123.1, 118.7, 67.1, 52.0, 17.5.

***N*-(2-Methoxyphenyl)morpholine (Table 3, entry 3).**[32] Using the general procedure, morpholine (70 μL, 0.80 mmol), 2-bromoanisole (99 μL, 0.79 mmol) were coupled using 2 mol % **10** at 50 °C. The product (136.3 mg, 88%) was obtained as an orange oil after purification by flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.01 (m, 1H), 6.93 (d, J = 4.10 Hz, 2H), 6.87 (d, J = 7.88 Hz, 1H), 3.89 (t, J = 4.73 Hz, 4H), 3.87 (s, 3H), 3.08 (t, J = 4.41 Hz, 4H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 151.3, 132.7, 131.2, 126.7, 123.4, 119.0, 67.5, 52.3, 17.9.

***N*-Methyl-*N*-phenyl-*p*-anisidine (Table 3, entry 4).**[6e] Using the general procedure, 4-bromoanisole (100 μL, 0.799 mmol) and *N*-methylaniline (108 μL, 1.00 mmol) were coupled using 1 mol % **10** at room temperature to yield the product (166.0 mg, 98%) as an orange oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.25 (m, 2H), 7.15 (d, J = 8.83 Hz, 2H), 6.95 (d, J = 8.83 Hz, 2H), 6.84 (m, 3H), 3.86 (s, 3H), 3.31 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 156.3, 149.8, 142.3, 128.9, 126.2, 118.4, 115.9, 114.8, 55.5, 40.5.

***N*-Methyl-*N*-phenyl-*o*-toluidine (Table 3, entry 5).**[35] Using the general procedure, 2-bromotoluene (96 μL, 0.80 mmol) and *N*-methylaniline (108 μL, 1.00 mmol) were coupled using 1 mol % at 50 °C. The product (140.0 mg, 74%) was obtained as an orange oil after purification by flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$):δ 7.17 (m, 6H), 6.70 (t, J = 8.20 Hz, 1H), 6.53 (d, J = 8.83 Hz, 2H), 3.22 (s, 3H), 2.14 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 148.9, 146.5, 136.6, 131.1, 128.7, 128.1, 127.2, 126.1, 116.5, 112.6, 38.7, 17.6.

***N*-Methyl-*N*-phenyl-*o*-anisidine (Table 3, entry 6).**[28] Using the general procedure, 2-bromoanisole (99 μL, 0.79 mmol) and *N*-methylaniline (108 μL, 1.00 mmol) were coupled using 2 mol % **10** at 50 °C. The product (166.0 mg, 97%) was obtained as a brown oil after purification by flash chromatography. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.30−7.21 (m, 4H), 7.05−7.01 (m, 2H) 6.78 (t, J = 7.25 Hz, 1H), 3.83 (s, 3H), 3.28 (s, 3H). ^{13}C NMR (90.6 MHz, $CDCl_3$): δ 156.1, 149.6, 136.9, 129.2, 128.8, 127.0, 121.4, 117.2, 113.5, 112.8, 55.7, 39.0.

General Procedure for Amination of Aryl Chlorides with Primary and Secondary Amines. Under an inert atmosphere of nitrogen gas in a glovebox, a vial was charged with **10** (1−2 mol %), sodium *tert*-butoxide (96.1 mg, 1.2 mmol), and dry toluene (2 mL). The vial was then removed from the glovebox, and the amine (1.0 mmol) and aryl bromide substrates (0.8 mmol) were

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added via glass microsyringe. Reactions were allowed to stir under nitrogen at 80−100 °C for 3−6 h. All reactions were monitored by GC to ensure completion, which typically required 4−6 h. Products were purified by column chromatography through SiO_2 using a mixture of hexanes and ethyl acetate as the eluent.

***N*-Phenyl-*p*-anisidine (Table 4, entry 1).**[22] Using the general procedure, 4-chloroanisole (98 μL, 0.80 mmol) and aniline (91 μL, 1.0 mmol) were coupled using 1 mol % **10** at 80 °C. The crude product was purified by flash chromatography to yield an off-white solid (154 mg, 97%). ^{1}H and ^{13}C NMR data were identical to the product produced from 4-bromoanisole (Table 2, entry 1). Mp: 100−102 °C, lit. mp 104−105.

***N*-Phenyl-*o*-toluidine (Table 4, entry 2).**[6e] Using the general procedure, aniline (91 μL, 1.0 mmol) and 2-chlorotoluene (96 μL, 0.82 mmol) were coupled using 1 mol % **10** at 100 °C to give the product as a brown oil (138 mg, 95%). ^{1}H and ^{13}C NMR data were identical to the product produced from 2-bromotoluene (Table 2, entry 5).

***N*-Phenyl-*o*-anisidine (Table 4, entry 3).**[27] Using the general procedure, 2-chloroanisole (102 μL, 0.801 mmol) and aniline (91 μL, 1.0 mmol) were coupled using 1 mol % **10** at 100 °C. The product (152 mg, 96%) as obtained as a brown oil after purification by flash chromatography.

***N*-(4-Methoxyphenyl)-2,4,6-trimethylaniline (Table 4, entry 4).**[29] Using the general procedure, 2,4,6-trimethylaniline (140 μL, 0.994 mmol) and 4-chloroanisole (98 μL, 0.80 mmol) were coupled using 1 mol % **10** at 100 °C. *N*-(4-Methoxyphenyl)-2,4,6-trimethylaniline (183.0 mg, 95%) was obtained as a brown solid after purification by flash chromatography. ^{1}H and ^{13}C NMR data were identical to the product produced from 4-bromoanisole (Table 2, entry 8). Mp: 97−98 °C, lit. mp 100.5−101.5 °C.

***N*-(2-Methylphenyl)-2,4,6-trimethylaniline (Table 4, entry 5).**[30] Using the general procedure, 2,4,6-trimethylaniline (140 μL, 0.994 mmol) and 2-chlorotoluene (96 μL, 0.82 mmol) were coupled using 1 mol % **10** at 100 °C. *N*-(2-Methylphenyl)-2,4,6-trimethylaniline (96.0 mg, 54%) was obtained as a peach solid after purification by flash chromatography. ^{1}H and ^{13}C NMR data were identical to the product produced from 2-bromotoluene (Table 2, entry 9). Mp: 76−78 °C, lit. mp 78.5−79.5 °C.

***N*-(4-Methoxyphenyl)morpholine (Table 4, entry 6).**[34] Using the general procedure, morpholine (70 μL, 0.80 mmol) and 4-chloroanisole (98 μL, 0.80 mmol) were coupled using 1 mol % **10** at 80 °C yielded 4-(4-methoxyphenyl)morpholine as a cream-colored solid (140.0 mg, 91%). ^{1}H and ^{13}C NMR data were identical to the product produced from 4-bromoanisole (Table 3, entry 1). Mp: 68−70 °C lit. mp 71 °C.

***N*-(2-Methylphenyl)morpholine (Table 4, entry 7).**[32] Using the general procedure, morpholine (70 μL, 0.80 mmol) and 2-chlorotoluene (96 μL, 0.82 mmol) were coupled using 1 mol % **10** at 100 °C. 4-(*o*-Tolyl)morpholine (128 mg, 91%) was obtained as a yellow oil after purification by flash chromatography. ^{1}H and ^{13}C NMR data were identical to the product produced from 2-bromotoluene (Table 3, entry 2).

***N*-(2-Methoxyphenyl)morpholine (Table 4, Entry 8).**[32] Using the general procedure, morpholine (70 μL, 0.80 mmol) and 2-chloroanisole (102 μL, 0.801 mmol) were coupled using 1 mol % **10** at 100 °C. The product (129.0 mg, 84%) was obtained as an orange oil after purification by flash chromatography. ^{1}H and ^{13}C NMR data were identical to the product produced from 2-bromoanisole (Table 3, entry 3).

***N*-Methyl-*N*-phenyl-*p*-anisidine (Table 4, entry 9).**[6e] Using the general procedure, *N*-methylaniline (108 μL, 1.00 mmol) and 4-chloroanisole (98 μL, 0.80 mmol) were coupled using 1 mol % **10** at 100 °C. *N*-Methyl-*N*-phenyl-*p*-anisidine (162.0 mg, 95%) as obtained as an orange oil after purification by flash chromatography. ^{1}H and ^{13}C NMR data were identical to the product produced from 4-bromoanisole (Table 3, entry 4).

***N*-Methyl-*N*-phenyl-*o*-toluidine (Table 4, entry 10).**[35] Using the general procedure, *N*-methylaniline (108 μL, 1.00 mmol) and 2-chlorotoluene (96 μL, 0.82 mmol) were coupled using 1 mol % **10** at 100 °C. *N*-Methyl-*N*-phenyl-*o*-toluidine(153 mg, 98%) was obtained as a brown oil after purification by flash chromatography. ^{1}H and ^{13}C NMR data were identical to the product produced from 2-bromotoluene (Table 3, entry 5).

***N*-Methyl-*N*-phenyl-*o*-anisidine (Table 4, entry 11).**[28] Using the general procedure, *N*-methylaniline (108 μL, 1.00 mmol) and 4-chloroanisole (98 μL, 0.80 mmol) were coupled using 1 mol % **10** at 100 °C. *N*-Methyl-*N*-phenyl-*o*-anisidine (166.0 mg, 97%) was obtained as an orange oil after purification by flash chromatography. ^{1}H and ^{13}C NMR data were identical to the product produced from 4-bromoanisole (Table 3, entry 6).

General Procedure for α-Arylation of Propiophenone. 10 and NaO*t*-Bu were loaded in a Radley carousel tube in the air. The tube was evacuated by performing three vacuum/nitrogen refill cycles and anhydrous solvent, aryl halide and propiophenone were injected. The resulting mixture was degassed by performing three vacuum/nitrogen refill cycles and stirred at the indicated temperature, and conversion was determined by GC.

NMR Study of Precatalyst 10 Activation by NaO*t*-Bu. In a nitrogen-filled drybox, an NMR tube was charged with complex **10** (25 mg, 0.06 mmol), NaO*t*-Bu (7.0 mg, 0.07 mmol), and C_6D_6 (0.8 mL). The mixture was allowed to stand at room temperature for 10 min and then was analyzed by ^{31}P{^{1}H} NMR spectroscopy (see Supporting Information).

NMR Study of Precatalyst 10 Activation under Catalytic Conditions. In a nitrogen-filled drybox, a vial was charged with complex **10** (25 mg, 0.06 mmol), NaO*t*-Bu (96.1 mg, 1.00 mmol), aniline (93.1 μL, 1.02 mmol), 4-bromoanisole (100 μL, 0.799 mmol), and toluene (1.5 mL). The mixture was allowed to stir at room temperature for 1 h. An aliquot (0.5 mL) was removed and transferred to an NMR tube sealed under nitrogen. C_6D_6 (0.3 mL) was added as a lock solvent, and the reaction mixture was analyzed by ^{31}P{^{1}H} NMR spectroscopy (see Supporting Information). Major resonances were observed at 59 (**10**, 4%), 53 (26%), 51.5 (8%), 49.8 (**11**, 34%), 46.7 (6%), 44.2 (**8**, 10%), and 18.5 ppm (DTBNpP, 12%).

X-ray Crystallographic Data. X-ray crystallographic data collection was performed at 173(2) K using a Siemens SMART diffractometer with a CCD area detector and graphite monochromated Mo Kα radiation. The SHELXTL software, version 5, was used for solution and refinement.[36] Absorption corrections were made with SADABS.[37] ORTEP and other structural drawings were made with SHELXTL.[36]

Crystal Data for 8. $C_{26}H_{58}P_2Pd$; M = 539.06 g mol^{-1}; colorless plates, 0.48 mm × 0.32 m × 0.14 mm; orthorhombic *Pbca*, a = 8.5967(15), b = 16.076(3), c = 21.506(4) Å; α = β = γ = 90°; V = 2972.2(9) Å^3; Z = 4, D = 1.205 Mg m^{-3}; T = 173(2) K; μ (Mo Kα) = 0.742 mm^{-1}; 19172 reflections, 3578 unique reflections (R_{int} = 0.0172) which were used in all calculations. R_1 = 0.0278, wR_2 = 0.0510 (all data), R_1 = 0.0200, wR_2 = 0.0480 ($I > 2\sigma(I)$).

Crystal Data for 9. $C_{26}H_{58}Cl_2P_2Pd$; M = 609.96 g mol^{-1}, amber rectangular, 0.64 mm × 0.34 mm × 0.12 mm, monoclinic $P2_1/c$, a = 9.0627(9), b = 19.012(2), c = 18.002(2) Å; α = 90, β = 99.276(2), γ = 90°; V = 3062.4(5) Å^3; Z = 4, D = 1.323 Mg m^{-3}; T = 173(2) K; μ(Mo Kα) = 0.898 mm^{-1}; 47256 reflections, 7561 unique reflections (R_{int} = 0.0238) which were used

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in all calculations. $R_1 = 0.0274$, $wR_2 = 0.0475$ (all data), $R_1 = 0.0210$, $wR_2 = 0.0455$ ($I > 2\sigma(I)$).

Crystal Data for 10. $C_{16}H_{34}ClPPd$; $M = 399.25$ g mol^{-1}, orthorhombic $P2_12_12_1$, $a = 8.9219(5)$, $b = 13.8729(8)$, $c = 15.1814(9)$ Å; $\alpha = \beta = \gamma = 90°$; $V = 1879.04(19)$ Å^3; $Z = 4$, $D = 1.411$ Mg m^{-3}; $T = 173(2)$ K; μ(Mo Kα) = 1.203 mm^{-1}; 13195 reflections, 4441 unique reflections ($R_{int} = 0.0305$) which were used in all calculations. $R_1 = 0.0307$, $wR_2 = 0.0449$ (all data), $R_1 = 0.0242$, $wR_2 = 0.0434$ ($I > 2\sigma(I)$).

Crystal Data for 11. $C_{29}H_{63}ClP_2Pd_2$; $M = 721.98$ g mol^{-1}, yellow plate, monoclinic $C2/c$, $a = 46.091(7)$, $b = 8.9249(14)$, $c = 16.729(3)$ Å; $\alpha = 90$, $\beta = 96.884(3)$, $\gamma = 90°$; $V = 6831.8(18)$ Å^3; $Z = 8$, $D = 1.404$ Mg m^{-3}; $T = 173(2)$ K; μ(Mo Kα) = 1.240 mm^{-1}; 20461 reflections, 6976 unique reflections ($R_{int} = 0.0552$) which were used in all calculations. $R_1 = 0.0621$, $wR_2 = 0.0987$ (all data), $R_1 = 0.0419$, $wR_2 = 0.0927$ ($I > 2\sigma(I)$).

Acknowledgment. Johnson-Matthey acknowledges Fred Hancock, JMCCT Technical Director and Gerard Compagoni, JMCCT Business Director for their support on new catalyst and technology development.

Supporting Information Available: Experimental details, characterization data for compounds in Tables 2−4, X-ray crystallographic data for compounds **8**−**11**, ^{31}P NMR spectra of catalyst activation studies, and ^{1}H and ^{13}C NMR spectra of the products in Tables 2−4. This material is available free of charge via the Internet at http://pubs.acs.org.