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(N-Heterocyclic Carbene)$PdCl_2$(TEA) Complexes: Studies on the Effect of the "Throw-Away" Ligand in Catalytic Activity

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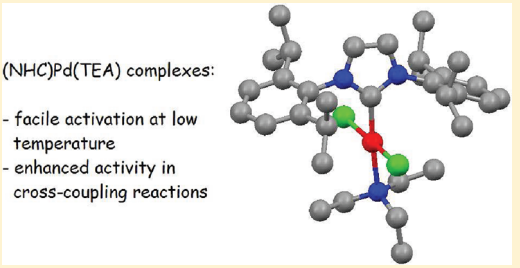
Supporting Information

ABSTRACT: The synthesis and characterization of a series of (N-heterocyclic carbene)$PdCl_2$(TEA) (TEA = triethylamine) complexes are presented. A comparison of their activity in the Suzuki–Miyaura and Buchwald–Hartwig reactions with similar (N-heterocyclic carbene)Pd(II) complexes is also presented.



INTRODUCTION

Palladium-catalyzed cross-coupling reactions are extremely useful tools in diverse areas of chemistry.[1] Initial efforts focused on the rich variety of organometallic nucleophiles that could be used for these reactions[2] and more recently interest has shifted to the activation of more challenging and varied electrophiles.[3] This approach has required the development of bulky, strongly donating, and often highly elaborated ligands for a precise electronic and steric tuning of the metal center. It has been shown that, in many cases, an equimolar ratio of the bulky ligand to metal is ideal for these cross-coupling reactions.[4] In general, the use of in situ systems for these transformations can become troublesome,[5] and therefore the design and synthesis of well-defined complexes has attracted much attention. The search for a "universal" (highly active, robust, versatile, shelf-stable, and easy to prepare) catalyst or precatalyst for cross-coupling reactions has led to the design and synthesis of a multitude of well-defined Pd(II) complexes, many of them even commercially available.[6]

A crucial piece of information for effective catalyst design is an understanding of the transition from a stable Pd(II) complex to the active Pd(0) species that enters the catalytic cycle. During this process the Pd(II) complex must lose some of the ligands attached to the metal center ("throw-away" ligands). Those that remain define the properties of the Pd(0) center that is active during the catalytic process. Ideally, the "throw-away" ligands should be inexpensive and easy to remove during the activation step.

A particularly successful family of "universal" well-defined Pd(II) complexes was recently developed by Organ and co-workers: (N-heterocyclic carbene)$PdCl_2$(3-Cl-pyridine) complexes or Pd-PEPPSI-(NHC) (PEPPSI = pyridine, enhanced, precatalyst, preparation, stabilization, and initiation) (**1**, Figure 1).[6a] Extensive studies on the structure, activation, and activity of these complexes have been published since their first appearance in 2006.[7] Recent studies suggest that the activation of these complexes starts with the reduction of Pd(II) to Pd(0) by the organometallic coupling partner, followed by chloride dissociation and ultimately departure of the pyridine, leading to the formation of the [(NHC)-Pd(0)] active species that starts the catalytic cycle.[7d] A similar and very interesting family of complexes was recently reported by Cazin and co-workers, in which the pyridine fragment was substituted by an alkyl or aryl phosphite ((NHC)$PdCl_2P(OR)_3$, **2**, Figure 1).[8] In both cases, the authors carried out NMR studies to determine that the 3-Cl-pyridine and $P(OR)_3$ ligands remain attached to the metal center after the reduction to Pd(0). A major difference between these two scaffolds is that 3-Cl-pyridine departs from the metal center to yield the active species, while $P(OR)_3$, a stronger σ-donor, might remain coordinated to Pd during the catalytic cycle.[8]

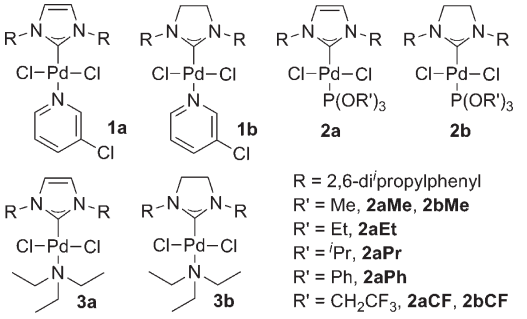


Figure 1. (NHC)$PdCl_2$ complexes with different "throw-away" ligands compared in this study.

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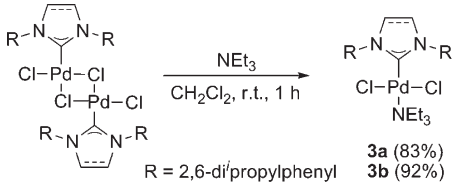
Organ later showed that an (NHC)$PdCl_2$(pyridine) complex is more active than the 3-chloropyridine analogue, suggesting that this improved activity could be due either to a higher dissociation rate of the pyridine (making more active species available to the substrate, which would explain the observed higher yields in shorter reaction times) or to a higher tendency to recoordinate to the [(NHC)-Pd(0)] species,[7d] trapping and conserving the active species in solution when inactive and slowing the death of the catalyst.

In order to obtain more information on this process, we prepared a new family of complexes using triethylamine (TEA) as the "throw-away" ligand, (NHC)$PdCl_2$(TEA) (**3**, Figure 1). The "throw-away" ligand of choice, TEA, was selected due to the intermediate σ-donor capabilities, between 3-Cl-pyridine and $P(OR)_3$, and the low steric demand.[9]

RESULTS AND DISCUSSION

Scheme 1. Synthesis of (NHC)$PdCl_2$(TEA) Complexes



The synthesis of complexes **3a** and **3b** was very straightforward and was achieved by combining the corresponding [(NHC)-$PdCl_2$]$_2$ dimer with an excess of TEA in CH_2Cl_2 at room temperature. After 1 h, the desired complexes could be isolated in very good yields by evaporating the solvent and washing the pale yellow solids with cold pentane (Scheme 1). Both complexes were fully characterized by means of elemental analysis and ^1H and ^{13}C NMR spectroscopy. The solid-state structures were unambiguously determined by X-ray diffraction. Both complexes show a slightly distorted square-planar geometry with the chloride ligands perpendicular to the plane of the NHC and TEA trans to it. As usual in NHC-bearing complexes, the Pd−$C_{carbene}$ distance is in the range of a single bond (1.968(4) Å for **3a** and 1.970(3) for **3b**), longer than that of the corresponding parent dimers.[8] This value is actually one of the most valuable pieces of data in these complexes, since it should have a clear correlation with the trans influence imparted by the "throw-away" ligand. Interestingly, while an obvious and expected downfield shift in the $^{13}C\{^1H\}$ NMR of the carbene carbon signal for the more σ-donating "throw-away" ligands is observed (Table 1), this trend is not followed by the Pd−$C_{carbene}$ distances for complexes **1a**−**3a**. These distances are nearly identical for **1a** and **3a**, while **2a** has an expected much longer bond distance due to a higher trans influence. A similar disparity can be observed when the SIPr-bearing complexes are compared.

A comparison of the activity of IPr-bearing complexes for the Suzuki−Miyaura coupling[1] of 2,6-dimethylphenyl chloride and phenylboronic acid is shown in Table 2.[10] A significant difference in performance between **1a** and **3a** could be observed at 40 °C, and this difference increased notably when the reaction temperature was decreased to 25 °C.[11] As a comparison, the parent dimer [(IPr)$PdCl_2$]$_2$ (**4a**) was also tested (Table 2, entries 3 and 6). Since all these complexes are presumed to deliver the same active species [(IPr)-Pd(0)], this difference in performance can only be attributed to the "throw-away" ligands attached to the Pd center. With everything else being equal, one would expect that TEA, being a stronger σ-donor, would have less tendency to

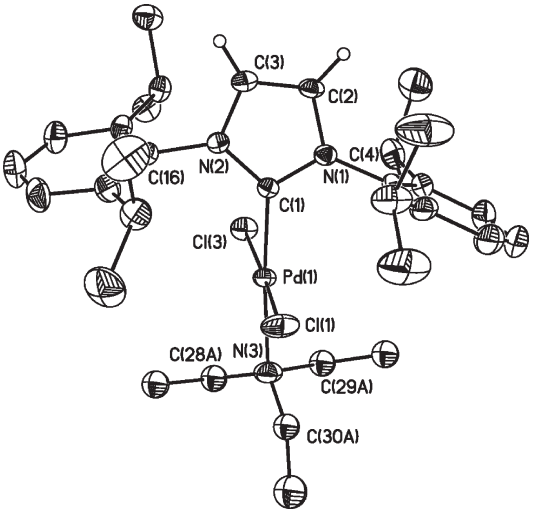


Figure 2. Crystal structure of (IPr)$PdCl_2$(TEA) (**3a**) with thermal ellipsoids drawn at the 50% probability level. Hydrogen atoms are omitted for clarity except those in the backbone of the NHC.

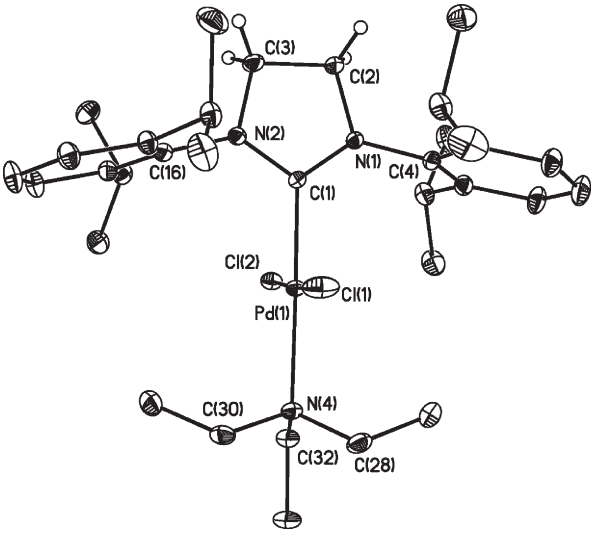


Figure 3. Crystal structure of (SIPr)$PdCl_2$(TEA) (**3b**) with thermal ellipsoids drawn at the 50% probability level. Hydrogen atoms are omitted for clarity except those in the backbone of the NHC.

Table 1. Comparison of Pd−$C_{carbene}$ Bond Distances and $\delta C_{carbene}$

	1a[b]	3a	2aPh[c]	2aMe[c]	2aPr[c]	1b[d]	3b	2bMe[c]
Pd−$C_{carbene}$ (Å)	1.969(3)	1.968(4)	2.0357(19)	2.056(4)	2.0482(11)	1.990(3)	1.970(3)	2.051(2)
$\delta C_{carbene}$ (ppm)[a]	153.5	154.2	167.8	171.1	172.6	150.3	185.9	198.1

[a] Spectra recorded in $CDCl_3$. [b] Ref 7d. [c] Ref 8. [d] See Supporting Information for X-ray diffraction data.

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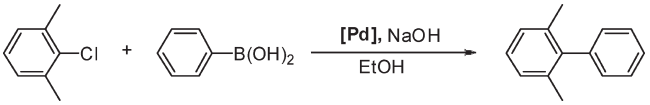
Table 2. Activity Comparison for the Suzuki−Miyaura Coupling of 2,6-Dimethylphenyl Chloride and Phenylboronic Acid at Mild Temperatures



entry	[Pd]	temperature (°C)	time	yield (%)[a,b]
1	**1a**	40	2 h	98
2	**3a**	40	20 min	98
3	**4a**	40	20 min	58[c]
4	**1a**	25	3 h	37[d]
5	**3a**	25	1.5 h	96
6	**4a**[e]	25	1.5 h	30[f]

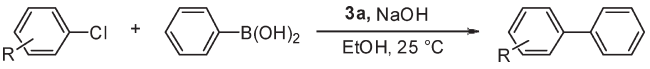
[a] Reaction conditions: aryl halide (0.50 mmol), phenylboronic acid (0.55 mmol), NaOH (0.6 mmol), 1 mL; [Pd], 1 mol %; ethanol, 1 mL. [b] Conversion to coupling product, based on aryl halide, determined by GC using hexamethylbenzene as internal standard, average of 2 runs. [c] After 3 h, the yield of the reaction was 95%. [d] After 5 h, the yield of the reaction was 85%. [e] 0.5 mol % of dimer. [f] After 3 h, the yield of the reaction was 90%.

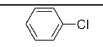
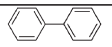
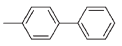
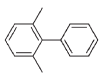
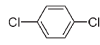
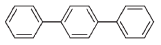
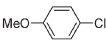
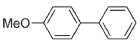
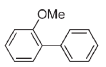
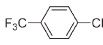
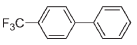
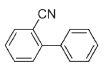
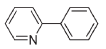
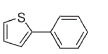
leave the [(NHC)-Pd] center, especially at a low reaction temperature, and it was expected that **3a** should be less active than **1a**. In fact the exact opposite effect was observed with complex **3a**, being significantly more active than **1a**. The solid-state structure of these complexes provides some insight into the reasons for this improved activity. The Pd−N bond distance is significantly longer for **3a** than **1a** (2.205 and 2.137 Å, respectively).[7d] This is an indication of a stronger Pd−N bond in the latter case due to the π-acceptor character of 3-Cl-pyridine.[12] In addition, we expect that TEA should have a much higher tendency to recoordinate to the [(NHC)-Pd(0)] species and conserve the catalytically active Pd(0) species, elongating its life in solution. Either of these two reasons (or a combination or both: fast TEA release and fast TEA recoordination trapping the active species in solution when inactive) could account for the difference in activity between complexes.

Following this preliminary screening, a variety of aryl chlorides were coupled with phenylboronic (Table 3) and other functionalized boronic acids (Table 4) at room temperature, using complex **3a** as precatalyst. These conditions allowed for the coupling of unactivated (Table 3, entries 2, 3, 5, 6; Table 4, entries 1, 2, 7, 8, 9, 10), activated (Table 3, entries 7, 8; Table 4, entry 5), heterocyclic (Table 3, entries 9, 10; Table 4, entries 3, 4), and mono- and diortho-substituted (Table 3, entries 3, 6, 8; Table 4, entries 1, 2, 7) aryl chlorides in short reaction times.

A similar approach was carried out for the SIPr-bearing complexes **1b**, **3b**, and the parent dimer [(SIPr)$PdCl_2$]$_2$ (**4b**).[10] Table 5 shows a comparison in performance for the Buchwald−Hartwig[1] coupling of 2,6-dimethylphenyl chloride and 2,6-diisopropylaniline at mild temperatures. When the reactions were performed at room temperature, the difference in activity is significant after 1 h, indicating that a larger amount of active species is available in solution in the case of **3b**. When the temperature was raised to 50 °C, there is a much smaller difference in activity between **1b** and **3b**, suggesting that at this temperature TEA and 3-Cl-pyridine depart from [(NHC)-Pd(0)] at a similar rate. At this temperature, the use of **3b** allowed for the coupling of a variety of aryl chlorides, including heterocyclic chlorides, with primary

Table 3. Suzuki−Miyaura Cross-Coupling of Aryl Chlorides with Phenylboronic Acid



entry	aryl chloride	product	time (min)	yield (%)[a,b]
1			45	96
2			60	96
3			90	96
4			150	93[c]
5			60	95
6			60	96
7			90	94
8			180	76[d]
9			90	82
10			90	88

[a] Reaction conditions: aryl chloride, 0.50 mmol; phenylboronic acid, 0.55 mmol; NaOH, 0.6 mmol; **3a**, 1 mol %; ethanol, 1 mL. [b] Average of 2 runs. [c] All amounts were doubled except that of the aryl chloride. [d] T = 40 °C.

(Table 6, entries 1, 2, 3, 4, 8) and secondary amines (Table 5, entries 5, 6, 7, 9, 10) and both aryl and alkyl amines, in very good yields.

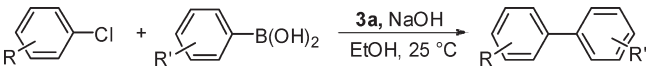
CONCLUSION

In summary, we report the synthesis and full characterization of two new NHC-palladium complexes, (IPr)$PdCl_2$(TEA) and (SIPr)$PdCl_2$(TEA). We have applied these complexes as precatalysts for Suzuki−Miyaura and Buchwald−Hartwig cross-coupling reactions. These complexes exhibit higher activity at lower temperatures than the corresponding 3-Cl-pyridine counterparts. The improved performance is either due to an easier departure of the "throw-away" ligand TEA or a higher tendency for the TEA to recoordinate to the [(NHC)-Pd(0)] and conserve the active species in solution (or a combination of both). The synthesis of other (NHC)$PdCl_2$(TEA) complexes and their application as catalysts in a variety of synthetic transformations is currently ongoing in our laboratories.

EXPERIMENTAL SECTION

General Considerations. All aryl halides and boronic acids were used as received. Technical grade ethyl alcohol was used to carry out Suzuki−Miyaura reactions. Potassium *tert*-butoxide, sodium *tert*-butoxide, and sodium hydroxide were stored under nitrogen in a glovebox. All reactions were carried out under an atmosphere of nitrogen in screw cap vials. Flash chromatography was performed on silica gel 60 (230−400 mesh) using mixtures of hexanes/ethyl acetate (10:1), unless otherwise noted. ^{1}H and ^{13}C NMR were recorded on a 300 or 500 MHz spectrometer at ambient temperature in

Table 4. Suzuki−Miyaura Cross-Coupling of Aryl Chlorides with Boronic Acids



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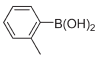
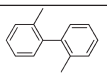
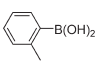
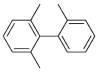
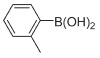
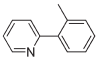
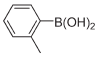
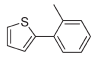
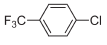
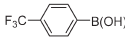
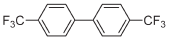
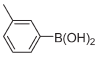
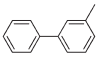
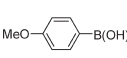
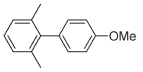
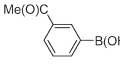
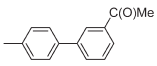
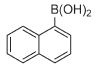
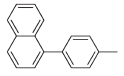
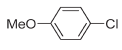
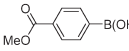
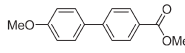
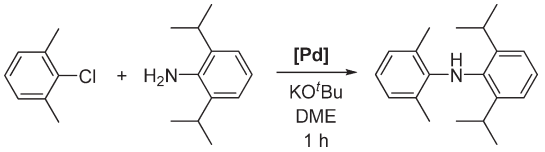
1				45	95
2				45	94
3				50	95
4				45	95
5				60	96
6				60	94
7				90	93
8				30	95
9				15	94
10				60	90

[a] Reaction conditions: aryl chloride, 0.50 mmol; boronic acid, 0.55 mmol; NaOH, 0.6 mmol; **3a**, 1 mol %; ethanol, 1 mL. [b] Average of 2 runs.

Table 5. Activity Comparison for the Buchwald−Hartwig Coupling of 2,6-Dimethylphenyl Chloride and 2,6-Diisopropylaniline at Mild Temperatures

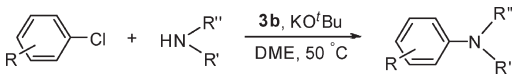


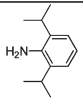
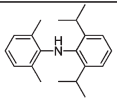
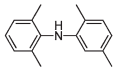
entry	[Pd] (mol %)	temperature (°C)	yield (%)[a,b]
1	**1b** (1.0)	25	<5[c]
2	**3b** (1.0)	25	44[d]
3	**1b** (1.0)	50	83
4	**3b** (1.0)	50	94
5	**4b** (1.0)[e]	50	48

[a] Reaction conditions: aryl halide, 1 mmol; amine, 1.1 mmol; KO^{t}Bu, 1.1 mmol; DME, 1 mL. [b] Conversion to coupling product based on 2,6-dimethylchlorobenzene, determined by GC using hexamethylbenzene as internal standard; average of two runs. [c] 58% after 21 h. [d] 74% after 21 h. [e] 0.5 mol % of dimer.

$CDCl_3$. Complexes **1a** and **1b** were prepared following procedures in the literature.[6a,7d]

Table 6. Buchwald−Hartwig Coupling of Aryl Chlorides and Amines Using 3b as Precatalyst



entry	aryl chloride	amine	product	time (h)	yield (%)[a,b]
1				1	90
2				1	95
3				5.5	80
4				4.5	85
5				1	95
6				5.5	92
7				4.5	81
8				4.5	92
9				3.5	81
10				3.5	77

[a] Reaction conditions: aryl halide, 1 mmol; amine, 1.1 mmol; KO^{t}Bu, 1.1 mmol; DME, 1 mL. [b] Average of two runs.

Synthesis of (IPr)PdCl$_2$(TEA) (3a). A vial was charged with [Pd(μ-Cl)Cl(IPr)]$_2$ (210 mg, 0.19 mmol) suspended in dichloromethane (1 mL), and an excess of triethylamine (0.5 mL) was added. The solution was stirred at room temperature for 1 h. After removal of the solvent to afford a pale yellow solid, the solid was washed with cold pentane to obtain the desired compound in 83% yield (211 mg). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.83 (t, J = 7.2 Hz, N(CH_2CH_3)$_3$, 9H), 1.06 (d, J = 6.9 Hz, CHCH_3, 12H), 1.41 (d, J = 6.6 Hz, CHCH_3, 12H), 2.52 (q, J = 7.1 Hz, N(CH_2CH_3)$_3$, 6H), 3.16 (sep, J = 6.8 Hz, CHCH$_3$, 4H), 7.11 (s, CH, 2H), 7.34 (d, J = 7.8 Hz, CH, 4H), 7.48 (t, J = 7.8 Hz, CH, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 9.3 (s, N(CH_2CH_3)$_3$), 22.6 (s, iPr), 26.4 (s, iPr), 28.7 (s, CHiPr), 123.6 (s, CH aromatic), 124.8 (s, CH aromatic), 129.9 (s, C aromatic), 135.1 (s, C aromatic), 147.1 (s, C aromatic), 154.2 (s, C carbene). Anal. Calcd for $C_{33}H_{51}Cl_2N_3Pd$: C, 59.41; H, 7.71; N, 6.30. Found: C, 59.71; H, 7.95; N, 6.13.

Synthesis of (SIPr)PdCl$_2$(TEA) (3b). A vial was charged with [Pd(μ-Cl)Cl(SIPr)]$_2$ (230 mg, 0.2 mmol) suspended in dichloromethane (1 mL), and an excess of triethylamine (0.5 mL) was added. The solution was stirred at room temperature for 1 h. After removal of the solvent to afford a pale yellow solid, the solid was washed with cold pentane to obtain the desired compound in 92% yield (252 mg). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.73 (t, J = 7.1 Hz, N(CH_2CH_3)$_3$, 9H), 1.20 (d, J = 6.9 Hz, CHCH_3, 12H), 1.48 (d, J = 6.6 Hz, CHCH_3, 12H), 2.46(q, J = 7.2 Hz, N(CH_2CH_3)$_3$, 6H), 3.58 (sep, J = 6.7 Hz, CHCH$_3$, 4H), 4.08(s, CH_2, 4H), 7.29 (d, J = 7.2 Hz, CH, 4H), 7.40 (dd, J = 6.9 Hz, CH, 2H). ^{13}C{^{1}H} NMR ($CDCl_3$, 125 MHz): δ 9.2 (s, N(CH_2CH_3)$_3$),

23.6 (s, iPr), 27.2 (s, iPr), 28.7 (s, CHiPr), 46.3 (s, $N(CH_2CH_3)$), 53.3 (s, CH_2), 124.0 (s, CH aromatic), 129.2 (s, CH aromatic), 135.1 (s, C aromatic), 148.3 (s, C aromatic), 185.9 (s, C carbene). Anal. Calcd for $C_{33}H_{53}Cl_2N_3Pd$: C, 59.23; H, 7.98; N, 6.28. Found: C, 58.88; H, 8.14; N, 6.29.

General Procedure for the Suzuki−Miyaura Reaction. In a glovebox, complex (1 mol %), base (0.6 mmol), and phenylboronic acid (0.55 mmol) were added in turn to a vial equipped with a magnetic bar and sealed with a screw cap fitted with a septum. Outside the glovebox, technical grade solvent (1 mL) was injected into the vial, and the mixture stirred on a stirring plate at room temperature. Aryl chloride (0.5 mmol, if liquid) was then injected (or previously charged in the glovebox if solid). The reaction was monitored by gas chromatography. When finished, the solvent was evaporated under vacuum and the product isolated by flash chromatography. The amount of product shown is the average of two runs.

General Procedure for the Buchwald−Hartwig Reaction. In a glovebox, complex (1 mol %), base (1.1 mmol), and 1,2-dimethoxyethane (DME) (1 mL) were added in turn to a vial equipped with a magnetic bar and sealed with a screw cap fitted with a septum. Outside the glovebox, the amine (1.1 mmol) and the aryl halide (1 mmol) were injected in turn through the septum. If one of the two starting materials was a solid, it was added to the vial inside the glovebox, and DME and the second starting material were added outside the glovebox under nitrogen. The reaction mixture was then stirred at 50 °C unless otherwise indicated. When the reaction reached completion, or no further conversion could be observed by gas chromatography, water was added to the reaction mixture, the organic layer was extracted with ethyl acetate and dried over magnesium sulfate, and the solvent was evaporated under vacuum. When necessary, the product was purified by flash chromatography on silica gel. The reported yields are the average of at least two runs.

■ ASSOCIATED CONTENT

Supporting Information. Characterization and crystallographic information files (CIF) of complexes **1b**, **3a**, and **3b** and characterization of coupling products. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ REFERENCES

(1) (a) Tsuji, J. *Palladium Reagents and Catalysis*, 2nd ed.; Wiley: West Sussex, England, 2004. (b) de Meijere, A., Diederich, F., Ed. *Metal-Catalyzed Cross-Coupling Reactions*, 2nd ed.; Wiley-VCH: Weinheim, Germany, 2004. (c) Negishi, E., Ed. *Handbook of Organopalladium Chemistry for Organic Synthesis*; Wiley-Interscience: New York, 2002. (d) Navarro, O.; Nolan, S. P. C-C Bond Formation by Cross-Coupling. In *Comprehensive Organometallic Chemistry III*; Crabtree, R. H., Mingos, M. P., Eds.; Elsevier: New York, 2007; Vol. 11, Chapter 1.

(2) Selected examples: (a) Miyaura, N.; Yamada, K.; Suzuki, A. *Tetrrahedron Lett.* **1979**, *36*, 3437–3439. (b) Kosugi, M.; Sasazawa, K.; Shimizu, Y.; Migita, T. *Chem. Lett.* **1977**, 301–302. (c) Milstein, D.; Stille, J. K. *J. Am. Chem. Soc.* **1978**, *100*, 3636–3638. (d) Stephen, R. D.; Castro, C. E. *J. Org. Chem.* **1963**, *28*, 3313–3315. (e) Dieck, H. A.; Heck, R. F. *J. Organomet. Chem.* **1975**, *93*, 259–263. (f) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedrom Lett.* **1975**, 4467–4470. (g) Chodkiewicz, W.; Cadiot, P. *Compt. Rend. Hebd. Seances Acad. Sci.* **1955**, *214*, 1055–1057. (h) Negishi, E. *Aspects Mech. Organomet. Chem.* **1978**, 285–317.

(3) Selected examples: (a) Littke, A. F.; Fu, G. C. *Angew. Chem., Int. Ed.* **1998**, *37*, 3387–3388. (b) Old, D. W.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722–9723. (c) Oh-e, T.; Miyaura, N.; Suzuki, A. *J. Org. Chem.* **1993**, *58*, 2201–2208. (d) Littke, A. F.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc.* **2000**, *122*, 4020–4028. (e) Grasa, G. A.; Viciu, M. S.; Huang, J.; Zhang, C.; Trudell, M. L.; Nolan, S. P. *Organometallics* **2002**, *21*, 2866–2873. (f) Brenstrum, T.; Gerristma, D. A.; Adjabeng, G. M.; Frampton, C. S.; Britten, J.; Robertson, A. J.; McNulty, J.; Capretta, A. *J. Org. Chem.* **2004**, *69*, 7635–7639. (g) Takagi, J.; Takahashi, T. I.; Miyaura, N. *J. Am. Chem. Soc.* **2002**, *124*, 8001–8006.

(4) Viciu, M. S.; Germeneau, R. F.; Navarro-Fernandez, O.; Stevens, E. D.; Nolan, S. P. *Organometallics* **2002**, *21*, 5470–5472.

(5) For an illustrative example, see: Lebel, H.; Janes, M. K.; Charette, A. B.; Nolan, S. P. *J. Am. Chem. Soc.* **2004**, *126*, 5046–5047.

(6) For instance: (a) Organ, M. G.; Avola, S.; Dubovyk, I.; Hadei, N.; Kantchev, E. A. B.; O'Brien, C. J; Valente, C. *Chem. Eur. J.* **2006**, *12*, 4749–4755. (b) Marion, N.; Navarro, O.; Mei, J.; Stevens, E. D.; Scott, N. M.; Nolan, S. P. *J. Am. Chem. Soc.* **2006**, *128*, 4101–4111. (c) 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. (d) Fraunhoffer, K. J.; White, M. C. *J. Am. Chem. Soc.* **2007**, *129*, 7274–7276. (e) Fors, B. P.; Watson, D. A.; Biscoe, M. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2008**, *130*, 13552–13554.

(7) (a) Chass, G. A.; O'Brien, C. J.; Hadei, N.; Kantchev, E. A. B.; Mu, W.-H.; Fang, D.-C.; Hopkinson, A. C.; Csizmadia, I. G.; Organ, M. G. *Chem. Eur. J.* **2009**, *15*, 4281–4288. (b) Valente, C.; Belovich, M. E.; Hadei, N.; Organ, M. G. *Eur. J. Org. Chem.* **2010**, 4343–4354. (c) Organ, M. G.; Chass, G. A.; Fang, D.-C.; Hopkinson, A. C.; Valente, C. *Synthesis* **2008**, 2776–2797. (d) Nasielski, J.; Hadei, N.; Achonduh, G.; Kantchev, E. A. B.; O'Brien, C. J.; Lough, A.; Organ, M. G. *Chem. Eur. J.* **2010**, *16*, 10844–10853. (e) Valente, C.; Baglione, S.; Candito, D.; O'Brien, C. J.; Organ, M. G. *Chem. Commun.* **2008**, 735–737. (f) Hadei, N.; Valente, C.; O'Brien, C. J.; Organ, M. G. *Angew. Chem., Int. Ed.* **2011**, *50*, 3896–3899.

(8) Diebolt, O.; Jurčik, V.; Correa da Costa, R.; Braunstein, P.; Cavallo, L.; Nolan, S. P.; Slawin, A. M. Z.; Cazin, C. S. J. *Organometallics* **2010**, *29*, 1443–1450.

(9) NHC ligands have been shown to be flexible enough to modulate their bulkiness in response to the steric requirements of the other ligands surrounding the metal center (ref 8).

(10) Only IPr-bearing complexes were tested for the Suzuki−Miyaura reaction since it has been shown that IPr-bearing complexes generally perform better in this cross-coupling reaction than SIPr-bearing complexes. On the other hand, SIPr-bearing complexes are known to generally provide the best results for Buchwald−Hartwig amination reactions. For an example, see ref 6b.

(11) The use of complexes **2** for the coupling of this specific substrate is reported only at high temperature and low catalyst loading (ref 8). Under similar reaction conditions to those in Table 2, all complexes **2** in Figure 1, with the exception of **2aPr**, afforded yields of >95% for the coupling of *p*-Cl-toluene and phenylboronic acid in 4 h. In comparison, this coupling is performed less than half that time using **3a** (Table 3, entry 1).

(12) An additional proof of a stronger Pd−N bond is that **3a** can be converted to **1a** in quantitative yield in a DCM solution with an excess of 3-Cl-pyridine, at room temperature and in less than 1 h. Attempts to achieve the opposite conversion were partially successful and only at higher temperature (55% conversion of **1a** into **3a** in refluxing TEA after 48 h).