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Well-defined NHC–Pd(II)–Im (NHC=*N*-heterocyclic carbene; Im=1-methylimidazole) complexes catalyzed amination of aryl chlorides

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ABSTRACT

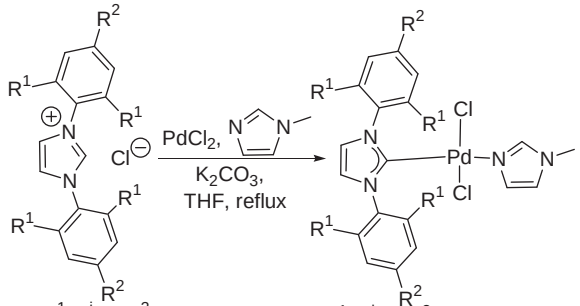
A new class of well-defined NHC–Pd(II)–Im complexes was synthesized and was found to be an efficient catalyst for the amination reactions of aryl chlorides. Under the optimal reaction conditions, a range of amines can be coupled to give the amination products in good to high yields.

1. Introduction

Palladium-catalyzed C–N cross-coupling reactions have become a versatile strategy for *N*-containing compounds with biological, pharmaceutical, and materials interest.[1] Since the initial amination reactions were reported,[2] various ligands, mainly phosphine-based ones, were reported to facilitate the cross-coupling reactions of aryl halides, especially aryl chlorides.[3] During the past years, *N*-heterocyclic carbenes (NHCs), generally with higher air-, moisture-, and thermal stability than phosphines, have drawn people's attention greatly.[4] In the area of palladium-catalyzed cross-coupling reactions, NHC–Pd complexes also have been proven to be good catalysts for the amination reactions of aryl chlorides.[5] In our continuing research for developing novel NHC-metal complexes in carbon–carbon bond formations,[6] we found that a new type of well-defined NHC–Pd(II)–Im complexes (Im=1-methylimidazole) can be synthesized from readily available starting materials as IPr·HCl, IMes·HCl with $PdCl_2$, and 1-methylimidazole under mild reaction conditions. We also found that the NHC–Pd(II)–Im complexes are efficient catalysts for the amination reactions of aryl chlorides. Herein, we wish to report these results in detail.

2. Results and discussion

First, heating the mixture of imidazolium salts **1** with $PdCl_2$, K_2CO_3, 1-methylimidazole in refluxing THF led to the corresponding NHC–Pd(II)–Im complexes **2** in moderate to high yields (Scheme 1). The structure of complex **2a** was unambiguously determined by X-ray single crystal diffraction (Fig. 1).[7] It clearly showed that the central palladium atom is C,N-coordinated by one ligand from the carbene and 1-methylimidazole nitrogen atom, which together with the two chlorine atoms gives the square planar coordination. Representative data of bond distances and angles are also shown in Fig. 1.



Scheme 1. Synthesis of NHC–Pd(II)–Im complexes.

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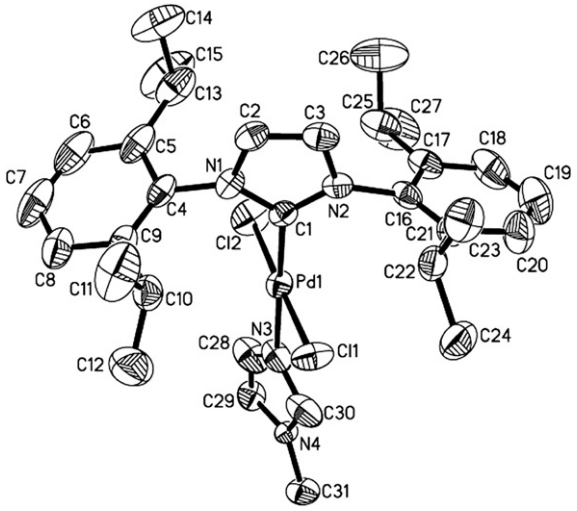
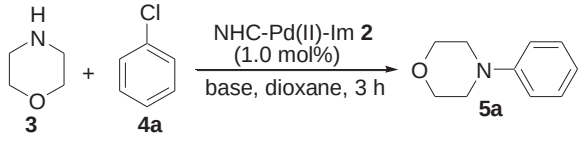


Fig. 1. ORTEP drawing of complex **2a** with thermal ellipsoids at the 30% probability level. Selected bond distances (Å) and angles (deg): Pd_1-C_1=1.954(5), Pd_1-N_3=2.088(4), Pd_1-Cl_1=2.2817(14), Pd_1-Cl_2=2.2826(14), $C_1-Pd_1-N_3$=178.15(19), $C_1-Pd_1-Cl_1$=87.61(12), $C_1-Pd_1-Cl_2$=91.96(12), $N_3-Pd_1-Cl_1$=90.54(15), $N_3-Pd_1-Cl_2$=89.89(15), $Cl_1-Pd_1-Cl_2$=179.14(7).

With the NHC–Pd(II)–Im complexes in hand, we then submitted them in the amination reactions of aryl chlorides. Initial examinations were carried out using morpholine **3** (0.8 mmol) and chlorobenzene **4a** (0.73 mmol) as the substrates, NHC–Pd(II)–Im complex **2a** (1.0 mol %) as the catalyst in dioxane (1.0 mL) at 80 °C for 3 h to find out the best base (Table 1, entries 1–12). As the different weak or strong bases were tested, the reaction could only be performed with LiO^{t}Bu or KO^{t}Bu as the base, with the latter as the best one (Table 1, entries 10 and 12). Using NHC–Pd(II)–Im complex **2b** as the catalyst, inferior result was obtained (Table 1, entry 13). The initial attempt to carry out the reaction at lower temperature with less effect on the yield was successful. For example, it was found that when the reaction was carried out at 70 °C, the target product **5a** can be obtained in similar yield (Table 1, entry 14). But when the reaction temperature was further decreased to 60 °C, the yield was somewhat lower (Table 1, entry 15). So the optimal reaction conditions were established as using NHC–Pd(II)–Im complex **2a** as the catalyst, KO^{t}Bu as the base, dioxane as the solvent with the temperature of 70 °C (Table 1, entry 14).

Table 1
Optimization for the NHC–Pd(II)–Im complexes **2** catalyzed coupling of morphline **3** with chlorobenzene **4a**

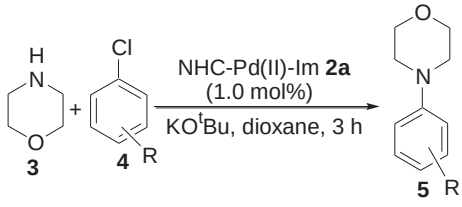


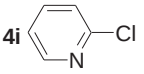
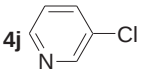
Entry[a]	Base	Temp	Yield (%)[b]
1	NaO^{t}Bu	80 °C	Trace
2	NaOH	80 °C	Trace
3	$NaHCO_3$	80 °C	—
4	Na_2CO_3	80 °C	—
5	K_2CO_3	80 °C	—
6	$KHCO_3$	80 °C	—
7	KOH	80 °C	—
8	$K_3PO_4.3H_2O$	80 °C	—
9	Li_2CO_3	80 °C	—
10	LiO^{t}Bu	80 °C	11
11	Cs_2CO_3	80 °C	—
12	KO^{t}Bu	80 °C	96
13[c]	KO^{t}Bu	80 °C	13
14	KO^{t}Bu	70 °C	94
15	KO^{t}Bu	60 °C	76

[a] Otherwise specified, all reactions were carried out with **3** (0.8 mmol), **4a** (0.73 mmol), base (1.0 mmol), **2a** (1.0 mol %), dioxane (1.0 mL) at the listed temperature for 3 h.
[b] Isolated yields.
[c] Complex **2b** as the catalyst.

With the optimal reaction conditions in hand, we then first investigated the reactions of morpholine **3** with a variety of aryl chlorides **4** (Table 2). As can be seen from Table 2, with electron-donating groups substituted aryl chlorides **4b**–**f** as the substrates, all reactions proceeded smoothly to give the coupling products **5** in good to high yields with 3 h (Table 2, entries 1–5). With 4-cyanophenyl chloride **4g** as the substrate, only 52% yield of product **5g** was obtained, which can be further increased to 71% with the temperature of 50 °C (Table 2, entry 6). With other electron-deficient aryl chlorides, such as 4-chlorobenzaldehyde, 4′-chloroacetophenone, and 4-chloronitrobenzene as the substrates, the reactions became disordered and no desired products were obtained under the identical conditions. Sterically hindered substrate, such as 2,6-dimethylchlorobenzene **4h** was also found to be a suitable substrate and moderate yield of product **5h** was obtained (Table 2, entry 7). Heteroaryl chloride as 2-pyridinyl chloride **4i**, as well as 3-pyridinyl chloride **4j**, was also found to be good substrate to give products **5i** and **5j** in high yields, respectively (Table 2, entries 8 and 9).

Table 2
NHC–Pd(II)–Im complex **2a** catalyzed coupling of morphline **3** with aryl chlorides **4**

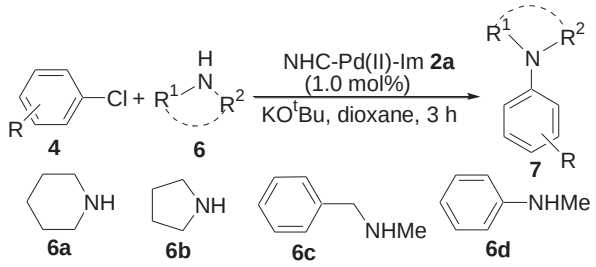


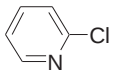
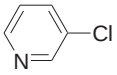
Entry[a]	**4** (R)	Yield (%)[b]
1	**4b** (4-Me)	5b, 86
2	**4c** (3-Me)	5c, 75
3	**4d** (2-Me)	5d, 86
4	**4e** (4-OMe)	5e, 90
5	**4f** (3-OMe)	5f, 99
6	**4g** (4-CN)	5g, 52, 71[c]
7	**4h** (2,6-Me2)	5h, 70
8	**4i** 	5i, 92
9	**4j** 	5j, 95

[a] Otherwise specified, all reactions were carried out with **3** (0.8 mmol), **4** (0.73 mmol), KO^{t}Bu (1.0 mmol), **2a** (1.0 mol %), dioxane (1.0 mL) at 70 °C for 3 h.
[b] Isolated yields.
[c] The reaction was carried out at 50 °C.

Encouraged by these results, we also carried out the amination reactions of aryl chlorides with other amines as piperidine **6a**, pyrrolidine **6b**, *N*-methylbenzylamine **6c**, and *N*-methylaniline **6d** at the temperature of 70–90 °C. For the reactions of piperidine **6a** with aryl chlorides **4a**, **4b**, **4e**, and **4f**, good to high yields of products **7a**–**d** were achieved under the optimal reaction conditions (Table 3, entries 1–4). 2-Pyridinyl chloride **4i**, as well as its analogue, 3-pyridinyl chloride **4j**, was found to be a good substrate for the corresponding amination reaction (Table 3, entries 5 and 6). Extending the scope to pyrrolidine **6b** as a partner instead of the highly active morpholine **3** and piperidine **6a** only gave moderate

Table 3
NHC–Pd(II)–Im complex **2a** catalyzed coupling of a variety of amines **6** with aryl chlorides **4**



Entry[a]	**4** (R)	**6**	Temp	Yield (%)[b]
1	**4a** (H)	**6a**	90 °C	**7a**, 82
2	**4b** (4-Me)	**6a**	90 °C	**7b**, 88
3	**4e** (4-OMe)	**6a**	90 °C	**7c**, 85
4	**4f** (3-OMe)	**6a**	90 °C	**7d**, 94
5	**4i** 	**6a**	90 °C	**7e**, 89
6	**4j** 	**6a**	90 °C	**7f**, 85
7	**4a**	**6b**	90 °C	**7g**, 65
8	**4b**	**6b**	80 °C	**7h**, 64
9	**4f**	**6b**	80 °C	**7i**, 65
10	**4i**	**6b**	80 °C	**7j**, 92
11	**4a**	**6c**	70 °C	**7k**, 88
12	**4b**	**6c**	70 °C	**7l**, 86
13	**4c** (3-Me)	**6c**	70 °C	**7m**, 80
14	**4d** (2-Me)	**6c**	70 °C	**7n**, 60
15	**4e**	**6c**	70 °C	**7o**, 68
16	**4f**	**6c**	70 °C	**7p**, 88
17	**4i**	**6c**	70 °C	**7q**, 99
18	**4j**	**6c**	70 °C	**7r**, 90
19	**4a**	**6d**	80 °C	**7s**, 86
20	**4e**	**6d**	80 °C	**7t**, 92
21	**4f**	**6d**	80 °C	**7u**, 99
22	**4i**	**6d**	80 °C	**7v**, 86
23	**4j**	**6d**	80 °C	**7w**, 81

[a] All reactions were carried out with **4** (0.73 mmol), **6** (0.8 mmol), KO^{t}Bu (1.0 mmol), **2a** (1.0 mol %), dioxane (1.0 mL) at the listed temperature for 3 h.
[b] Isolated yields.

yields at 80 or 90 °C (Table 3, entries 7–9), except for the reaction between **6b** and 2-pyridinyl chloride **4i**, which gave product **7j** in high yield (Table 3, entry 10). *N*-Methylbenzylamine **6c** was also tested as a partner and the reactions proceeded smoothly to give products **7k**–**r** in moderate to high yields (Table 3, entries 11–18). It seems that substituents on aryl chlorides **4** have some effect on the reactions. For instance, for the reaction involving hindered 2-methylphenyl chloride **4d**, product **7n** was obtained only in 60% yield (Table 3, entry 14). For the reaction involving **4e**, with an electron-donating *para*-methoxy group on the phenyl ring, the yield was also not good enough (Table 3, entry 15). With *N*-methylaniline **6d** as the substrate, all reactions took place smoothly under the similar conditions at 80 °C to give products **7s**–**w** in good to high yields, regardless of aryl or heteroaryl chlorides (Table 3, entries 19–23).

3. Conclusion

In conclusion, we have synthesized a new type of well-defined NHC–Pd(II)–Im complexes and systematically investigated their applications in amination reactions of aryl chlorides. A range of amines as morpholine **3**, piperidine **6a**, pyrrolidine **6b**, *N*-methylbenzylamine **6c**, and *N*-methylaniline **6d** can be used as the substrates in the coupling reactions with aryl and heteroaryl chlorides. Both electron-neutral and electron-rich aryl- and heteroaryl chlorides showed good to high yields. The NHC–Pd(II)–Im complexes are air- and moisture-stable.

4. Experimental section

4.1. General methods

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance-500 MHz spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard; *J*-values are in hertz. Dioxane was treated with standard method. Commercially obtained reagents were used without further purification. Flash column chromatography was carried out using Huanghai 300–400 mesh silica gel at increased pressure.

4.2. Experimental procedures

*4.2.1. Synthesis of complex **2a**.* Under N_2 atmosphere, a mixture of compound **1a** (3.18 mmol), $PdCl_2$ (3.02 mmol), K_2CO_3 (3.16 mmol), and 1-methylimidazole (12.0 mmol) was stirred in anhydrous THF (15 mL) under reflux for 20 h. The solvent was removed under reduced pressure, and the residue was purified by a flash chromatography on silica gel (CH_2Cl_2) to give NHC–Pd(II)–Im complex **2a** (93%) as a yellow solid. The single crystal for X-ray diffraction was obtained by recrystallization from CH_2Cl_2 and ethyl acetate.

*4.2.2. Synthesis of complex **2b**.* Under N_2 atmosphere, a mixture of compound **1b** (1.05 mmol) and $PdCl_2$ (1.0 mmol), K_2CO_3 (1.0 mmol), and 1-methylimidazole (4.0 mmol) was stirred in anhydrous THF (5 mL) under reflux for 20 h. The solvent was removed under reduced pressure, and the residue was purified by a flash chromatography on silica gel (CH_2Cl_2) to give NHC–Pd(II)–Im complex **2b** (65%) as a yellow solid.

4.3. General procedure for the NHC–Pd(II)–Im catalyzed amination reactions of morpholine with aryl chlorides

Under N_2 atmosphere, KO^{t}Bu (1.0 mmol), NHC–Pd(II)–Im **2a** (1.0 mol %), dry dioxane (1.0 mL), morpholine **3** (0.8 mmol), and aryl chloride **4** (0.7 mmol) were successively added into a Schlenk reaction tube. The mixture was stirred at 70 °C for 3 h. The solvent was removed under reduced pressure and the residue was purified by a flash chromatograph on silica gel to give the pure products **5**.

*4.3.1. Compound **2a**.* A yellow solid. Mp: 230 °C (decomposed). ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 1.10 (d, J=6.5 Hz, 12H), 1.46 (d, J=7.0 Hz, 12H), 3.15–3.20 (m, 4H), 3.42 (s, 3H), 6.51 (s, 1H), 7.09 (s, 2H), 7.16 (s, 1H), 7.32 (d, J=7.5 Hz, 4H, Ar), 7.46 (t, J=7.5 Hz, 2H, Ar), 7.61 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 23.2, 26.2, 28.6, 33.9, 119.0, 123.9, 124.8, 128.5, 130.0, 135.2, 138.3, 146.7, 156.5. IR (neat) ν 3137, 2969, 2953, 2927, 2864, 1736, 1587, 1536, 1481, 1455, 1444, 1417, 1328, 1270, 1109, 1089, 1046, 840, 800, 754, 738, 730 cm^{-1}. MS (ESI) m/z 613 $[M-Cl]^+$; Anal. Calcd for $C_{31}H_{42}Cl_2N_4Pd$ requires C, 57.46%; H, 6.53%; N, 8.65%. Found: C, 57.34%; H, 6.49%; N, 8.60%.

*4.3.2. Compound **2b**.* A yellow solid. Mp: 214 °C (decomposed). ^{1}H NMR ($CDCl_3$, 500 MHz, TMS) δ 2.347 (s, 6H), 2.354 (s, 12H), 3.46 (s, 3H), 6.55 (s, 1H), 7.02 (s, 4H, Ar), 7.03 (s, 2H), 7.21 (s, 1H), 7.76 (s, 1H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ 19.1, 21.1, 33.9, 118.9, 124.0, 128.5, 129.2, 135.3, 136.3, 138.5, 138.9, 154.0. IR (neat) ν 3130, 2956, 2915, 2856, 1735, 1608, 1537, 1486, 1409, 1232, 1112, 1093, 964, 928, 839, 731,

706 cm^{-1}. Anal. Calcd for $C_{25}H_{30}Cl_2N_4Pd \cdot EtOAc$ requires C, 53.42%; H, 5.87%; N, 8.59%. Found: C, 53.13%; H, 5.82%; N, 8.61%.

4.3.3. Compound ***5a***[8]. A pale yellow solid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.26–7.31 (m, 2H, Ar), 6.88–6.94 (m, 3H, Ar), 3.87 (t, J=5.0 Hz, 4H), 3.17 (t, J=5.0 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.3, 129.2, 120.0, 115.7, 66.9, 49.4.

4.3.4. Compound ***5b***[9]. A pale yellow solid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.10 (d, J=8.0 Hz, 2H, Ar), 6.84 (d, J=8.0 Hz, 2H, Ar), 3.87 (t, J=5.0 Hz, 4H), 3.11 (t, J=5.0 Hz, 4H), 2.28 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.2, 129.7, 129.6, 116.0, 67.0, 49.9, 20.4.

4.3.5. Compound ***5c***[8]. A pale yellow solid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.18 (t, J=8.0 Hz, 1H, Ar), 6.75–6.72 (m, 3H, Ar), 3.87 (t, J=5.0 Hz, 4H), 3.16 (t, J=5.0 Hz, 4H), 2.34 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.3, 138.9, 129.0, 120.9, 116.5, 112.8, 66.9, 49.5, 21.7.

4.3.6. Compound ***5d***[9]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.18–7.21 (m, 2H, Ar), 7.00–7.04 (m, 2H, Ar), 3.86 (t, J=4.5 Hz, 4H), 2.92 (t, J=4.5 Hz, 4H), 2.33 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 151.2, 132.6, 131.2, 126.6, 123.4, 118.9, 67.4, 52.2, 17.8.

4.3.7. Compound ***5e***[9]. A white solid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 6.89 (d, J=9.0 Hz, 2H, Ar), 6.85 (d, J=9.0 Hz, 2H, Ar), 3.86 (t, J=4.5 Hz, 4H), 3.77 (s, 3H, OMe), 3.06 (t, J=4.5 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.0, 145.6, 117.8, 114.5, 67.0, 55.6, 50.8.

4.3.8. Compound ***5f***[8]. A pale yellow solid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.19 (t, J=8.0 Hz, 1H, Ar), 6.53–6.55 (m, 1H, Ar), 6.44–6.46 (m, 2H, Ar), 3.86 (t, J=5.0 Hz, 4H), 3.80 (s, 3H, OMe), 3.15 (t, J=5.0 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.6, 152.7, 129.8, 108.5, 104.7, 102.2, 66.9, 55.2, 49.3.

4.3.9. Compound ***5g***[3h]. A pale yellow solid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.51 (d, J=9.0 Hz, 2H, Ar), 6.86 (d, J=9.0 Hz, 2H, Ar), 3.85 (t, J=5.0 Hz, 4H), 3.27 (t, J=5.0 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.5, 133.5, 119.8, 114.0, 100.9, 66.4, 47.3.

4.3.10. Compound ***5h***[9]. A white solid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 6.96–7.02 (m, 3H, Ar), 3.81 (t, J=4.5 Hz, 4H), 3.10 (t, J=4.5 Hz, 4H), 2.35 (s, 6H, 2Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9, 137.0, 129.0, 125.3, 68.2, 50.0, 19.6.

4.3.11. Compound ***5i***[8]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 8.19–8.20 (m, 1H, Ar), 7.48–7.51 (m, 1H, Ar), 6.62–6.67 (m, 2H, Ar), 3.82 (t, J=5.0 Hz, 4H), 3.49 (t, J=5.0 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 147.9, 137.5, 113.8, 106.9, 66.7, 45.6.

4.3.12. Compound ***5j***[8]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 8.30 (s, 1H, Ar), 8.12 (t, J=3.0 Hz, 1H, Ar), 7.18 (t, J=3.0 Hz, 2H, Ar), 3.87 (t, J=5.0 Hz, 4H), 3.18 (t, J=5.0 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.9, 141.1, 138.3, 123.5, 122.1, 66.6, 48.6.

4.3.13. Compound ***7a***[10]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.16–7.19 (m, 2H, Ar), 6.87 (d, J=8.5 Hz, 2H, Ar), 6.75 (t, J=7.5 Hz, 1H, Ar), 3.08 (t, J=5.5 Hz, 4H), 1.61–1.66 (m, 4H), 1.48–1.52 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.3, 129.0, 119.2, 116.5, 50.7, 25.9, 24.3.

4.3.14. Compound ***7b***[11]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.07 (d, J=8.5 Hz, 2H, Ar), 6.87 (d, J=8.5 Hz, 2H, Ar), 3.10 (t, J=5.0 Hz, 4H), 2.27 (s, 3H, Me), 1.70–1.74 (m, 4H), 1.54–1.59 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.3, 129.5, 128.7, 116.9, 51.3, 25.9, 24.3, 20.4.

4.3.15. Compound ***7c***[12]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 6.92 (d, J=9.0 Hz, 2H, Ar), 6.83 (d, J=9.0 Hz, 2H, Ar), 3.77 (s, 3H, OMe), 3.03 (t, J=5.5 Hz, 4H), 1.70–1.75 (m, 4H), 1.52–1.57 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.6, 146.9, 118.7, 114.3, 55.6, 52.3, 26.1, 24.2.

4.3.16. Compound ***7d***[13]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.16 (t, J=8.5 Hz, 1H, Ar), 6.56 (dd, J=8.5, 2.5 Hz, 1H, Ar), 6.49 (t, J=2.5 Hz, 1H, Ar), 6.39 (dd, J=8.5, 2.5 Hz, 1H), 3.79 (s, 3H, OMe), 3.16 (t, J=5.5 Hz, 4H), 1.68–1.72 (m, 4H), 1.56–1.60 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 153.6, 129.6, 109.3, 104.0, 102.8, 55.1, 50.5, 25.8, 24.3.

4.3.17. Compound ***7e***[11]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 8.17 (dd, J=5.0, 1.0 Hz, 1H, Ar), 7.42–7.44 (m, 1H, Ar), 6.64 (d, J=8.5 Hz, 1H, Ar), 6.53–6.56 (m, 1H, Ar), 3.52 (d, J=5.0 Hz, 4H), 1.64 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.8, 147.9, 137.3, 112.4, 107.1, 46.3, 25.5, 24.7.

4.3.18. Compound ***7f***[11]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 8.29 (d, J=2.5 Hz, 1H, Ar), 8.04 (dd, J=4.5, 1.0 Hz, 1H, Ar), 7.16–7.19 (m, 1H, Ar), 7.12 (dd, J=8.5, 4.5 Hz, 1H, Ar), 3.18 (t, J=5.5 Hz, 4H), 1.68–1.73 (m, 4H), 1.57–1.61 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.7, 140.0, 138.9, 123.4, 122.6, 49.8, 25.5, 24.1.

4.3.19. Compound ***7g***[13]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.23 (dd, J=8.5, 7.5 Hz, 2H, Ar), 6.66 (t, J=7.5 Hz, 1H, Ar), 6.58 (d, J=7.5 Hz, 2H, Ar), 3.29 (t, J=6.5 Hz, 4H), 1.99–2.02 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 129.1, 115.4, 111.7, 47.6, 25.4.

4.3.20. Compound ***7h***[11]. A pale yellow solid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.04 (d, J=8.0 Hz, 2H, Ar), 6.51 (d, J=8.0 Hz, 2H, Ar), 3.26 (t, J=6.0 Hz, 4H), 2.26 (s, 3H, Me), 1.99 (t, J=6.0 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.2, 129.6, 124.3, 111.8, 47.8, 25.4, 20.3.

4.3.21. Compound ***7i***[13]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.14 (t, J=8.0 Hz, 1H, Ar), 6.25 (d, J=8.0 Hz, 1H, Ar), 6.21 (d, J=8.0 Hz, 1H, Ar), 6.12 (s, 1H, Ar), 3.80 (s, 3H, OMe), 3.28 (t, J=6.5 Hz, 4H), 1.98–2.01 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 149.3, 129.8, 104.9, 100.5, 97.9, 55.1, 47.6, 25.4.

4.3.22. Compound ***7j***[11]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 8.14–8.15 (m, 1H, Ar), 7.39–7.43 (m, 1H, Ar), 6.48–6.51 (m, 1H, Ar), 6.34 (d, J=8.5 Hz, 1H, Ar), 3.44 (t, J=6.5 Hz, 4H), 1.98–2.01 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 148.1, 136.9, 111.0, 106.5, 46.6, 25.5.

4.3.23. Compound ***7k***[10]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.31 (t, J=7.0 Hz, 2H, Ar), 7.20–7.25 (m, 5H, Ar), 6.75 (d, J=8.0 Hz, 2H, Ar), 6.71 (t, J=7.5 Hz, 1H, Ar), 4.53 (s, 2H), 3.02 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.7, 139.0, 129.2, 128.5, 126.8, 126.7, 116.5, 112.3, 56.6, 38.5.

4.3.24. Compound ***7l***[9]. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.28–7.31 (m, 2H, Ar), 7.20–7.23 (m, 3H, Ar), 7.02 (d, J=8.5 Hz, 2H, Ar), 6.67 (d, J=8.5 Hz, 2H, Ar), 4.47 (s, 2H), 2.95 (s, 3H, Me), 2.24 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.0, 139.3, 129.7, 128.5, 127.0, 126.8, 126.0, 113.0, 57.2, 38.6, 20.2.

4.3.25. Compound ***7m***. A pale yellow liquid. ^1H NMR (500 MHz, $CDCl_3$, TMS) δ 7.35–7.38 (m, 2H, Ar), 7.28–7.30 (m, 3H, Ar), 7.16 (t, J=7.5 Hz, 1H, Ar), 6.60–6.64 (m, 3H, Ar), 4.57 (s, 2H), 3.04 (s, 3H,

Me), 2.35 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.9, 139.1, 138.8, 129.0, 128.5, 126.8, 126.7, 117.5, 113.0, 109.6, 56.6, 38.4, 21.9. MS (%) (EI) (*m*/*z*) 211 (M^+, 60), 134 (62), 91 (100); HRMS (EI) calcd for $C_{15}H_{17}N$: 211.1361; found: 211.1360. IR (neat) ν 3025, 2914, 2854, 2813, 1601, 1580, 1451, 1353, 1180, 1203, 952, 764, 731, 713, 691 cm^{-1}.

4.3.26. Compound ***7n***. A pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.38 (d, *J*=7.0 Hz, 2H, Ar), 7.32 (t, *J*=7.5 Hz, 2H, Ar), 7.25 (t, *J*=7.5 Hz, 1H, Ar), 7.14–7.21 (m, 2H, Ar), 7.07 (d, *J*=8.0 Hz, 1H, Ar), 6.98 (t, *J*=7.5 Hz, 1H, Ar), 4.03 (s, 2H), 2.58 (s, 3H, Me), 2.40 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.4, 139.1, 132.8, 131.1, 128.3, 128.2, 126.9, 126.4, 123.0, 120.0, 60.7, 40.8, 18.4. MS (%) (EI) (*m*/*z*): 211 (M^+, 41), 134 (38), 120 (53), 91 (100); HRMS (EI) calcd for $C_{15}H_{17}N$: 211.1361; found: 211.1357. IR (neat) ν 3061, 3026, 2947, 2841, 2786, 1598, 1493, 1452, 1360, 1329, 1221, 1171, 1091, 1051, 1029, 943, 763, 721, 696 cm^{-1}.

4.3.27. Compound ***7o***[14]. A pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.22 (t, *J*=7.5 Hz, 2H, Ar), 7.15 (t, *J*=7.5 Hz, 3H, Ar), 6.74 (d, *J*=7.5 Hz, 2H, Ar), 6.66 (d, *J*=7.5 Hz, 2H, Ar), 4.34 (s, 2H), 3.67 (s, 3H, OMe), 2.83 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.1, 145.0, 139.3, 128.5, 127.2, 126.9, 114.9, 114.8, 58.1, 55.8, 39.1.

4.3.28. Compound ***7p***. A pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.28–7.31 (m, 2H, Ar), 7.21–7.24 (m, 3H, Ar), 7.10–7.13 (m, 1H, Ar), 6.36–6.38 (m, 1H, Ar), 6.27–6.29 (m, 2H, Ar), 4.51 (s, 2H), 3.75 (s, 3H, OMe), 3.00 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 151.1, 138.9, 129.8, 128.5, 126.8, 126.7, 105.5, 101.3, 98.9, 56.5, 55.0, 38.5. MS (%) (EI) (*m*/*z*): 227 (M^+, 87), 150 (69), 91 (100); HRMS (EI) calcd for $C_{15}H_{17}NO$: 227.1310; found: 227.1307. IR (neat) ν 2930, 2831, 1610, 1574, 1499, 1451, 1370, 1353, 1245, 1202, 1166, 1116, 1053, 956, 821, 749, 732, 711, 686 cm^{-1}.

4.3.29. Compound ***7q***[15]. A pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 8.18 (dd, *J*=4.5, 1.0 Hz, 1H, Ar), 7.21–7.30 (m, 6H, Ar), 6.56 (dd, *J*=6.5, 5.0 Hz, 1H, Ar), 6.50 (d, *J*=8.5 Hz, 1H, Ar), 4.80 (s, 2H), 3.07 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.9, 148.0, 138.7, 137.3, 128.5, 127.0, 126.9, 111.8, 105.7, 53.2, 36.1.

4.3.30. Compound ***7r***. A pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 8.16 (d, *J*=3.0 Hz, 1H, Ar), 7.96 (dd, *J*=5.0, 1.0 Hz, 1H, Ar), 7.32 (t, *J*=7.5 Hz, 2H, Ar), 7.26 (t, *J*=4.0 Hz, 1H, Ar), 7.19–7.21 (m, 2H, Ar), 7.08–7.10 (m, 1H, Ar), 6.98 (dd, *J*=8.0, 1.0 Hz, 1H, Ar), 4.54 (s, 2H), 3.06 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.3, 137.9, 137.8, 134.9, 128.7, 127.1, 126.6, 123.4, 118.6, 56.1, 38.3. MS (%) (EI) (*m*/*z*): 198 (M^+, 51), 91 (100); HRMS (EI) calcd for $C_{13}H_{14}N_2$: 198.1157; found: 198.1158. IR (neat) ν 3023, 2898, 1585, 1493, 1452, 1376, 1348, 1233, 1052, 1004, 946, 933, 726, 708, 694 cm^{-1}.

4.3.31. Compound ***7s***[16]. A pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.27–7.30 (m, 4H, Ar), 7.03–7.05 (m, 4H, Ar), 6.95–6.99 (m, 2H, Ar), 3.33 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.0, 129.2, 121.2, 120.4, 40.2.

4.3.32. Compound ***7t***[3h]. A pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.17–7.21 (m, 2H, Ar), 7.09 (dd, *J*=6.5, 2.0 Hz, 2H, Ar), 6.88 (dd, *J*=6.5, 2.0 Hz, 2H, Ar), 6.78–6.79 (m, 3H, Ar), 3.80 (s, 3H, OMe), 3.25 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.2, 149.7, 142.2, 128.9, 126.2, 118.3, 115.7, 114.7, 55.5, 40.4.

4.3.33. Compound ***7u***[3h]. A pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 7.29 (t, *J*=8.0 Hz, 2H, Ar), 7.16 (t, *J*=8.0 Hz, 1H, Ar), 7.06–7.07 (m, 2H, Ar), 6.99 (t, *J*=7.5 Hz, 1H, Ar), 6.57–6.59 (m, 1H, Ar), 6.53–6.54 (m, 1H, Ar), 6.47–6.50 (m, 1H, Ar), 3.75 (s, 3H, OMe), 3.30 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 150.4, 148.8, 129.7, 129.2, 121.9, 121.6, 112.2, 105.8, 105.2, 55.2, 40.3.

4.3.34. Compound ***7v***[3h]. A pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 8.23 (dd, *J*=5.0, 1.0 Hz, 1H, Ar), 7.40 (t, *J*=8.0 Hz, 2H, Ar), 7.21–7.27 (m, 4H, Ar), 6.61 (dd, *J*=6.5, 5.0 Hz, 1H, Ar), 6.53 (d, *J*=8.5 Hz, 1H, Ar), 3.48 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.8, 147.8, 146.8, 136.5, 129.7, 126.3, 125.4, 113.1, 109.2, 38.4.

4.3.35. Compound ***7w***[3h]. A pale yellow liquid. ^{1}H NMR (500 MHz, $CDCl_3$, TMS) δ 8.30 (d, *J*=3.0 Hz, 1H, Ar), 8.12 (d, *J*=4.5 Hz, 1H, Ar), 7.33 (t, *J*=8.0 Hz, 2H, Ar), 7.21–7.23 (m, 1H, Ar), 7.13 (dd, *J*=8.5, 4.5 Hz, 1H, Ar), 7.06–7.10 (m, 3H, Ar), 3.33 (s, 3H, Me). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.9, 145.1, 141.0, 140.5, 129.6, 124.7, 123.4, 123.2, 122.4, 40.0.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2011.05.057. These data include MOL files and InChiKeys of the most important compounds described in this article.

References and notes

1. (a) King, A. O.; Yasuda, N. In *Organometallics in Process Chemistry*; Larsen, R. D., Ed.; Springer: Berlin, 2004; pp 205–246; and references therein; (b) Lawrence, S. A. *Amines, Synthesis Properties, and Application*; Cambridge University: Cambridge, 2004; (c) Belfield, A.; Brown, G. R.; Foubister, A. J. *Tetrahedron* **1999**, *55*, 11399–11428; (d) Goodbrand, H. B.; Hu, N.-X. *J. Org. Chem.* **1999**, *64*, 670–674; (e) O'Hagan, D. *Nat. Prod. Rep.* **2000**, *17*, 435–446; (f) Craig, P. N. In *Comprehensive Medicinal Chemistry*; Drayton, C. J., Ed.; Pergamon: New York, NY, 1991; Vol. 8; (g) Kundu, N. G.; Mahanty, J. S.; Chowdhurry, C.; Dasgupta, S. K.; Das, B.; Spears, C. P.; Balzarini, J.; De Clercq, E. *Eur. J. Med. Chem.* **1999**, *34*, 389–398.
2. (a) Kosugi, M.; Kameyama, M.; Migita, T. *Chem. Lett.* **1983**, 927–928; (b) Guram, A. S.; Rennels, R. A.; Buchwald, S. L. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1348–1350; (c) Louie, J.; Hartwig, J. F. *Tetrahedron Lett.* **1995**, *36*, 3609–3612.
3. For some selected examples, please see: (a) Nishiyama, M.; Yamamoto, T.; Koie, Y. *Tetrahedron Lett.* **1998**, *39*, 617–620; (b) Netherton, M. R.; Fu, G. C. *Org. Lett.* **2001**, *3*, 4295–4298; (c) Rataboul, F.; Zapf, A.; Jackstell, R.; Harkal, S.; Riermeier, T.; Monsees, A.; Dingerdissen, U.; Beller, M. *Chem.—Eur. J.* **2004**, *10*, 2983–2990; (d) Wolfe, J. P.; Tomori, H.; Sadighi, J. P.; Yin, J.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1158–1174; (e) Kataoka, N.; Shelby, Q.; Stambuli, J. P.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 5553–5566; (f) Urgaonkar, S.; Xu, J.-H.; Verkade, J. G. *J. Org. Chem.* **2003**, *68*, 8416–8423; (g) Urganonkar, S.; Verkade, J. G. *J. Org. Chem.* **2004**, *69*, 9135–9142; (h) Reddy, C. V.; Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2008**, *73*, 3047–3062.
4. For some selected reviews on NHCs, please see: (a) Herrmann, W. A. *Angew. Chem., Int. Ed.* **2002**, *41*, 1290–1309; (b) Marion, N.; Nolan, S. P. *Acc. Chem. Res.* **2008**, *41*, 1440–1449; (c) Peris, E.; Crabtree, R. H. *Coord. Chem. Rev.* **2004**, *248*, 2239–2246; (d) Herrmann, W. A.; Öfele, K.; Preysing, D. V.; Schneider, K. S. *J. Organomet. Chem.* **2003**, *687*, 229–248; (e) Hahn, F. E.; Jahnke, M. C. *Angew. Chem., Int. Ed.* **2008**, *47*, 3122–3172; (f) Glorius, F. *N-Heterocyclic Carbenes in Transition Metal Catalysis*; Springer: Berlin, Germany, 2007; (g) Nolan, S. P. *N-Heterocyclic Carbenes in Synthesis*; Wiley-VCH: Weinheim, Germany, 2006; (h) Díez-González, S.; Nolan, S. P. *Coord. Chem. Rev.* **2007**, *251*, 874–883.
5. (a) Li, J.-Y.; Cui, M.-J.; Yu, A.-J.; Wu, Y.-J. *J. Organomet. Chem.* **2007**, *692*, 3732–3742; (b) Gooßen, L. J.; Paetzold, J.; Briel, O.; Rivas-Nass, A.; Karch, R.; Kayser, B. *Synlett* **2005**, 275–278; (c) Viciu, M. S.; Kissling, R. M.; Stevens, E. D.; Nolan, S. P. *Org. Lett.* **2002**, *4*, 2229–2231; (d) Viciu, M. S.; Kelly, R. A., III; Stevens, E. D.; Naud, F.; Studer, M.; Nolan, S. P. *Org. Lett.* **2003**, *5*, 1479–1482; (e) Jin, Z.; Guo, S.-X.; Gu, X.-P.; Qiu, L.-L.; Song, H.-B.; Fang, J.-X. *Adv. Synth. Catal.* **2009**, *351*, 1575–1585; (f) Organ, M. G.; Abdel-Hadi, M.; Avola, S.; Dubovyk, I.; Hadei, N.; Kantchev, E. A. B.; O'Brien, C. J.; Sayah, M.; Valente, C. *Chem.—Eur. J.* **2008**, *14*, 2443–2452; (g) 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; (h) Jin, Z.; Qiu, L.-L.; Li, Y.-Q.; Song, H.-B.; Fang, J.-X. *Organometallics* **2010**, *29*, 6578–6586; (i) Broggi, J.; Clavier, H.; Nolan, S. P. *Organometallics* **2008**, *27*, 5525–5531.

6. For our development in NHC-metal complexes derived from proline, please see: (a) Tang, Y.-Q.; Lu, J.-M.; Wang, X.-R.; Shao, L.-X. *Tetrahedron* **2010**, *66*, 7970–7974; (b) Tang, Y.-Q.; Lv, H.; He, X.-N.; Lu, J.-M.; Shao, L.-X. *Catal. Lett.* **2011**, , doi:10.1007/s10562-011-0563-9
7. The crystal data of **2a** has been deposited in CCDC with number 795265. Empirical formula: $C_{31}H_{42}Cl_2N_4Pd$; Formula weight: 647.99; Crystal color, habit: colorless, prismatic; Crystal system: monoclinic; Lattice type: primitive; Lattice parameters: a=9.7912(7) Å, b=22.6920(17) Å, c=14.8396(11) Å, α=90°, β=98.950(2)°, γ=90°, V=3256.9(4) Å^3; Space group: $P2(1)/c$; Z=4; D_{calcd}=1.321 g/cm^3; F_{000}=1344; Diffractometer: Bruker Smart APEX CCD; Residuals: R; Rw: 0.0426, 0.0688.
8. Guo, D.-L.; Huang, H.; Xu, J.-Y.; Jiang, H.-L.; Liu, H. *Org. Lett.* **2008**, *10*, 4513–4516.
9. Esposito, O.; Gois, P. M. P.; Lewis, A. K. de K.; Caddick, S.; Cloke, F. G. N.; Hitchcock, P. B. *Organometallics* **2008**, *27*, 6411–6418.
10. Barker, T. J.; Jarvo, E. R. *J. Am. Chem. Soc.* **2009**, *131*, 15598–15599.
11. Manolikakes, G.; Gavryushin, A.; Knochel, P. *J. Org. Chem.* **2008**, *73*, 1429–1434.
12. Hatakeyama, T.; Yoshimoto, Y.; Ghorai, S. K.; Nakamura, M. *Org. Lett.* **2010**, *12*, 1516–1519.
13. Gao, C.-Y.; Yang, L.-M. *J. Org. Chem.* **2008**, *73*, 1624–1627.
14. Kanner, C. B.; Pandit, U. K. *Tetrahedron* **1982**, *38*, 3597–3604.
15. Pasumansky, L.; Hernández, A. R.; Gamsey, S.; Goralski, C. T.; Singaram, B. *Tetrahedron Lett.* **2004**, *45*, 6417–6420.
16. Shen, Q.-L.; Ogata, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 6586–6596.