ORGANOMETALLICS
Article

Organometallics **2010,** *29,* 6343–6349 6343
DOI: 10.1021/om100746r

Abnormal N-Heterocyclic Carbene Promoted Suzuki−Miyaura Coupling Reaction: A Comparative Study

Xiangya Xu, Baochang Xu, Yongxin Li, and Soon Hyeok Hong*

Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore

Received July 29, 2010

A C2-protected imidazolium salt that generates an abnormal N-heterocyclic carbene (NHC) was applied for the palladium-catalyzed Suzuki−Miyaura coupling reactions. The abnormal NHC precursor promoted the reactions while suppressing homocoupling of aryl boronic acid, which was observed with the corresponding normal NHC precursor. The related well-defined abnormal NHC-based palladium complexes also showed better activity than the normal NHC-based analogues, exhibiting faster reaction rates especially at the initial stage of the reaction.

Introduction

N-Heterocyclic carbenes (NHCs) have been intensively studied in organometallic chemistry and homogeneous catalysis for the past decade.[1] The NHCs are stronger neutral electron donors and less oxidation sensitive than tertiary phosphines, so as to be excellent ligands for transition metals. Most of the NHCs are derived from imidazolium or 4,5-dihydroimidazolium salts and bind a metal at the C2 position. However, it has been reported that metalation of imidazolium salts can take place at the C4 or the C5 carbon since Crabtree and co-workers discovered it for the first time.[2] These "abnormal" N-heterocyclic carbenes (aNHCs) are reported as even stronger donors than C2-binding "normal" N-heterocyclic carbenes (nNHCs), which may provide new opportunities in catalysis.[1,3]

It has been reported that the binding mode of NHC to a metal such as Pd could have a substantial effect on the catalytic behavior.[4] When normally bound $[Pd(IMes)_2Cl_2]$ complex **1** and mixed bound complex **2** (Figure 1) were screened for the Suzuki−Miyaura and the Heck cross-coupling reactions, interestingly, complex **1** was inactive for the cross-coupling reactions, while complex **2** was active. This study suggested that a catalytically active NHC-Pd precursor

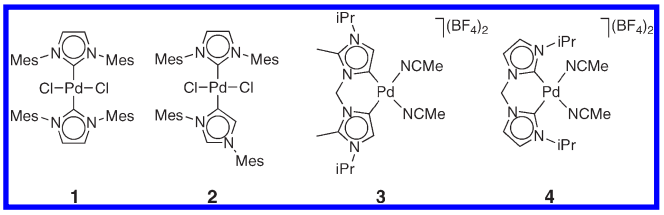

Figure 1. Normal and abnormal NHC-based Pd complexes.

cannot be complex **1** in the Suzuki and the Heck coupling reactions under in situ catalytic conditions using IMes·HCl and a Pd precursor, and abnormal binding of carbene might play a role during the catalysis. Albrecht and co-workers also reported that the catalytic activity of cationic C4-bound Pd(dicarbene) complex **3** is significantly higher in alkene hydrogenation than its C2-bound analogue **4** (Figure 1).[5]

However, most examples including ones shown above have different steric effects near the Pd center, making it difficult to conclude whether the observed activity is from steric differences or from the different electronic environment of aNHC.[6,7] In addition, in contrast to extensive use of imidazolium salt for in situ generation of NHC-based catalytic species in Pd catalysis,[8] to the best of our knowledge,

*To whom correspondence should be addressed. E-mail: hongsh@ntu.edu.sg.

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Published on Web 11/09/2010

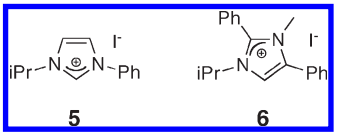


Figure 2. Normal and abnormal NHC precursors.

there is no example of using abnormal binding carbene precursors for similar in situ generation of catalyst species. During our recent research focus on the NHC-based transition metal complexes for efficient organic transformations,[9] we became interested in abnormal NHC as a new ligand scaffold in homogeneous catalysis. Herein, we report the first example of using a C2-protected imidazolium salt as an aNHC precursor in a Pd-catalyzed cross-coupling reaction. To confirm the observation from in situ catalysis, we also screened the activity of the related well-defined aNHC and nNHC Pd complexes.

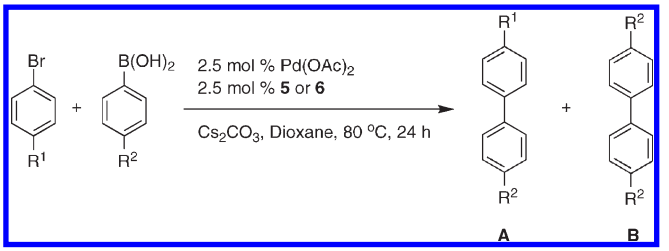
Results and Discussion

NHC Precursor. Two imidazolium salts, **5** and **6**, were chosen as NHC precursors to investigate the activity between the normal and the abnormal carbenes (Figure 2). Both precursors have isopropyl and phenyl groups as wingtip groups, providing similar steric effects of the NHC ligands. Percent buried volumes ($\%V_{bur}$) of the chosen nNHC and aNHC, calculated on the basis of X-ray crystal structures of **7** and **9** using SambVca software, are 29.5 for the nNHC of **5** and 30.0 for the aNHC of **6** (radius of the sphere, R, is 3.5 Å; M−NHC length is 2.1 Å; Bondi radii scaled by 1.17).[10] For compound **6**, the C2 and C4 carbons are functionalized by phenyl groups, leaving the C5 position available only for the binding of Pd.[11] The phenyl group was chosen to avoid possible C−C cleavage observed when a methyl or an isopropyl group was used as the C2 protecting group.[12] The precursor **5** is a stereotype of NHC precursors used in in situ-generated transition metal catalysis. While the most acidic C2 position is the most favorable binding site, there is a possibility for palladium to bind to the C4 or C5 position, as in the case of **2**.[4]

Electronic properties of the corresponding carbenes of **5** and **6** were examined by Crabtree and co-workers by measuring carbonyl stretching frequencies of $Ir(CO)_2Cl(NHC)$ complexes.[13] While the nNHC from **5** showed slightly higher electron-donating property (ν(CO) 2061, 1976 cm^{-1}) than PCy_3 (ν(CO) 2072, 1984 cm^{-1}), aNHC from **6** exhibited much better electron-donating ability, as reported by a significantly decreased CO frequency (ν(CO) 2045, 1961 cm^{-1}) of $Ir(CO)_2Cl(aNHC)$. In addition, recent calculations done with an isolated crystalline aNHC showed that the aNHC is more basic than its normal NHC isomer.[14]

In summary, the NHC precursors **5** and **6** were chosen to rationally investigate the effect of abnormal NHC: (1) they have a similar steric effect near the Pd center; (2) **6** will show the effect of aNHC only in catalysis, while it is possible for **5** to bind normally or abnormally, although it is logically believed that normal NHC binding is more favored; and (3) aNHC from **6** is a better electron donor than nNHC from **5**.

Table 1. NHC-Promoted Suzuki−Miyaura Cross-Coupling Reactions (NHC:Pd = 1:1)[a]



			5		6	
entry	R^1	R^2	A	B	A	B
1	OMe	Me	58 (55)	35	67 (64)	< 0.1
2	H	Me	77 (75)	15	88 (84)	< 0.1
3	F	Me	72 (67)	19	76 (69)	< 0.1
4	Me	OMe	40 (33)	10	49 (42)	< 0.1
5	Me	H	51 (43)	5	44 (35)	2
6	Me	F	20 (16)	2	14 (9)	0.6
7	H	OMe	62 (57)	11	75 (64)	< 0.1
8	H	F	12 (10)	2	44 (38)	< 0.1

[a] GC yields using dodecane as an internal standard; isolated yields are shown in parentheses, average of at least two runs.

In Situ-Generated NHC-Promoted Pd-Catalyzed Reactions. With the chosen NHC precursors **5** and **6**, we compared the activity in the Suzuki−Miyaura coupling reactions using $Pd(OAc)_2$ (Tables 1 and 2).[15] On the basis of extensive screens, Cs_2CO_3 and dioxane were chosen as the optimal base and solvent. A mixture of $Pd(OAc)_2$, an NHC precursor, and Cs_2CO_3 in dioxane was stirred at 80 °C for 30 min to generate catalytically active NHC−Pd complexes before the addition of the substrates. The reactions were promoted by both ligands.[16] The abnormal NHC precursor **6** gave slightly better yields in most cases whether it was used as 2 equiv or 1 equiv versus Pd. Interestingly, undesirable deboronation homocoupling of aryl boronic acids was not observed with **6**, unlike with **5**. The symmetrical biaryl generated from the homocoupling of the aryl

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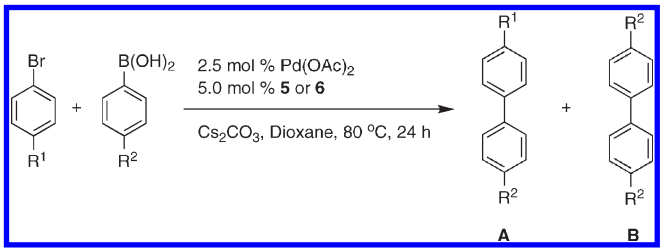
(16) 40% yield was obtained from a reaction of bromobenzene and *p*-tolylboronic acid (entry 2) under the same conditions as in Table 1 without any NHC precursor.

Table 2. NHC-Promoted Suzuki−Miyaura Cross-Coupling Reactions (NHC:Pd = 2:1)[a]



			5		6	
entry	R^1	R^2	A	B	A	B
1	OMe	Me	60 (57)	23	76 (73)	< 0.1
2	H	Me	79 (76)	14	90 (89)	< 0.1
3	F	Me	75 (72)	28	84 (76)	< 0.1
4	Me	OMe	41 (34)	10	64 (61)	< 0.1
5	Me	H	30 (25)	4	66 (62)	2
6	Me	F	6 (4)	4	29 (24)	1.3
7	H	OMe	67 (63)	7	78 (70)	< 0.1
8	H	F	30 (25)	3	50 (41)	< 0.1

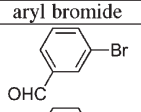
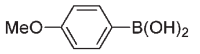
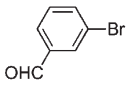
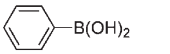
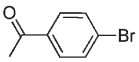
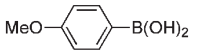
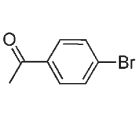
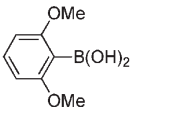
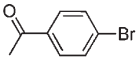
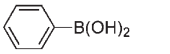
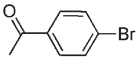
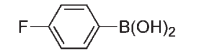
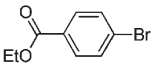
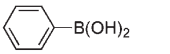
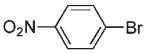
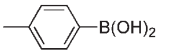
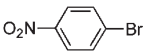
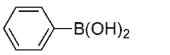
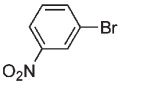
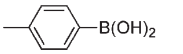
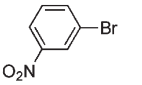
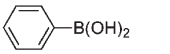
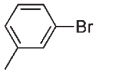
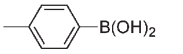
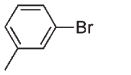
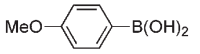
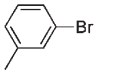
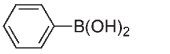
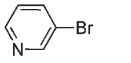
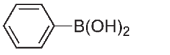
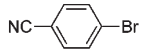
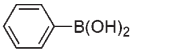
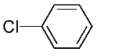
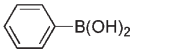
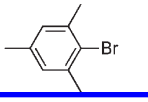
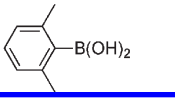
[a] GC yields using dodecane as an internal standard; isolated yields are shown in parentheses, average of at least two runs.

boronic acid has often been observed in the Suzuki−Miyaura reactions.[17]

The substrate scope of the abnormal carbene precursor **6**-promoted Suzuki−Miyaura coupling reactions was explored (Table 3). It showed excellent activity with electron-deficient aryl bromides with good functional group tolerance. However, reduced yields or no activity was observed with unactivated electron-rich aryl bromide (entries 13, 14), aryl chloride (entry 17), and sterically bulky substrates (entry 18). It has been reported that Pd complexes of sterically demanding phosphines or NHC ligands were more efficient in the Suzuki−Miyaura coupling reactions by stabilizing a putative monoligated Pd complex and facilitating the reductive elimination.[15d,18] Therefore, development of more sterically bulky abnormal carbene precursors will be required for further improvement to practically use aNHC as a supporting ligand in the Pd-catalyzed cross-coupling reactions.

A clear reaction rate difference between the nNHC and the aNHC systems was observed when the progress of the reaction of *p*-tolylboronic acid and bromobenzene was monitored by GC (Figure 3). To our surprise, the aNHC-based catalyst exhibited a much faster reaction rate than the nNHC-based system, especially at the initial stage, although we postulated that **5**, which has a more acidic C2 proton, might generate (NHC)Pd species faster, which could affect the reaction rate.[19] We think that the more electron-donating aNHC promotes oxidative addition faster, which is known as the rate-determining step in many cases of cross-coupling reactions.[20]

Table 3. Scope of aNHC-Promoted Suzuki−Miyaura Cross-Coupling Reactions (NHC:Pd = 2:1)[a]

entry	aryl bromide	boronic acid	yield (%)[b]
1			95 (84)
2			66 (59)
3			100 (93)
4			63 (55)
5			83 (71)
6			62 (52)
7			79 (70)
8			93 (87)
9			77 (63)
10			94 (82)
11			80 (71)
12			83 (67)
13			63 (55)
14			25 (9)
15			71 (67)
16			97 (92)
17			8 (4)
18			0

[a] $Pd(OAc)_2$ (2.5 mol %), **6** (5 mol %), Cs_2CO_3 (2 equiv), aryl halide (1.0 equiv), boronic acid (1.5 equiv), dioxane, 80 °C, 24 h. [b] GC yield (isolated yield), average of at least two runs.

Abnormal and Normal N-Heterocyclic Carbene-Based Pd Complexes. As different efficiencies of in situ formation of the NHC−Pd bond from **5** and **6** might affect the catalytic activity,[21] we synthesized well-defined NHC−Pd complexes **7**−**11** following the reported conditions to further investigate

(17) Adamo, C.; Amatore, C.; Ciofini, I.; Jutand, A.; Lakmini, H. *J. Am. Chem. Soc.* **2006**, *128*, 6829.

(18) (a) Snead, D. R.; Inagaki, S.; Abboud, K. A.; Hong, S. *Organometallics* **2010**, *29*, 1729. (b) Christmann, U.; Vilar, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 366. (c) Suzuki, A. *Proc. Jpn. Acad. Ser. B: Phys. Biol. Sci.* **2004**, *80*, 359. (d) Bellina, F.; Carpita, A.; Rossi, R. *Synthesis* **2004**, 2419.

(19) The aqueous pK_a of the C2-bound proton ($pK_a = 24 \pm 1$, determined experimentally as well as by calculation) of unsubstituted imidazolium cation is 9 pK_a units lower than calculated for the C4-bound proton ($pK_a = 33$) See: Magill, A. M.; Yates, B. F. *Aust. J. Chem.* **2004**, *57*, 1205, and ref 3a.

(20) (a) Matos, K.; Soderquist, J. A. *J. Org. Chem.* **1998**, *63*, 461. (b) Stille, J. K.; Lau, K. S. Y. *Acc. Chem. Res.* **1977**, *10*, 434. (c) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (d) Iglesias, M.; Albrecht, M. *Dalton Trans.* **2010**, *39*, 5213.

(21) The C2 (**5**) or C5 (**6**) proton was monitored by ^1H NMR spectroscopy in a mixture of **5** or **6** (0.025 mmol), $Pd(OAc)_2$ (0.025 mmol), and Cs_2CO_3 (1 mmol) in THF-d_6 (1 mL) at 80 °C. The results indicated that **5** reacts faster with $Pd(OAc)_2$ (100% of the C2 proton of **5** disappeared, vs 82% of the C5 proton of **6**, after 30 min).

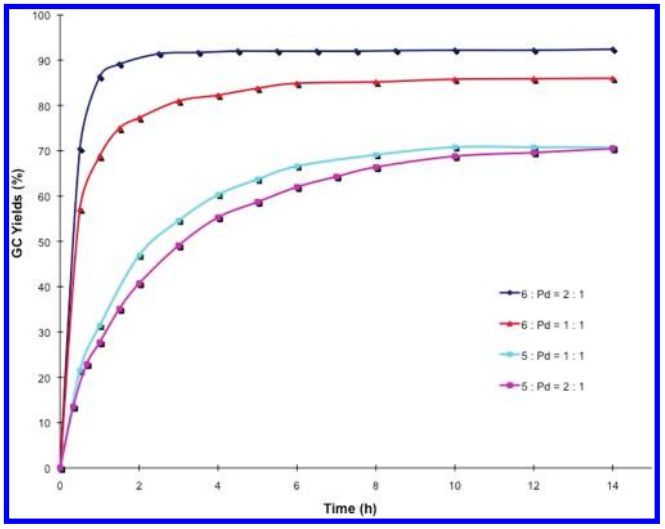
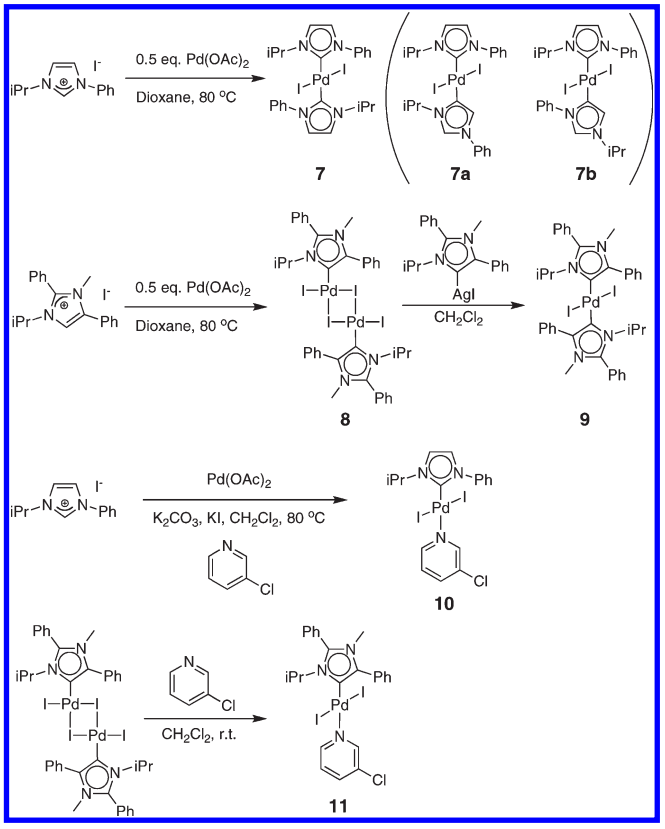


Figure 3. Comparison of reaction progress in in situ catalytic systems.

Scheme 1. Syntheses of NHC−Pd Complexes



the effect of nNHC and aNHC on the Pd-catalyzed reaction (Scheme 1).[4,22] Interestingly, we could not observe any mixed (NHC)(aNHC)PdI_2 complex **7a** or **7b** under the same conditions as generation of **2** formed from $Pd(OAc)_2$ and an imidazolium salt without Cs_2CO_3.[4] Even in the presence of Cs_2CO_3, only **7** was obtained. With aNHC precursor **6**, dimer complex **8** was obtained even though we used 2 equiv of **6**. Complex **9** was synthesized from **8** by the addition of an aNHC−Ag complex. Pd-PEPPSI-NHC (PEPPSI = pyridine-enhanced precatalyst preparation, stabilization, and initiation) complexes **10** and **11** have been prepared to compare the reactivity and structural difference between aNHC and nNHC.[22] The structures of complexes **7**−**11** were all characterized by X-ray crystallography (Figure 4).[23] The bond lengths between Pd−C(carbene) were 2.017(5) Å in **7** and 2.021(5) Å in **9**, indicating similar bond lengths, in contrast to our expectation of a shorter bond length in **9** reflecting the more electron-donating property of aNHC. Similar bond lengths between Pd and carbene carbons of aNHC and nNHC were also reported in complex **2**.[4] It has been reported that $M-C_{carbene}$ bond distances are not very sensitive to small changes in bond order.[3a] Similarly, the $Pd-N_{pyridine}$ distances in **10** and **11** were also comparable, as observed with other PEPPSI-type NHC-based Pd precatalysts.[22]

The activities of complexes **7**−**11** were compared in the coupling reaction of *p*-tolylboronic acid and bromobenzene (Figure 5 and Table 5). Abnormal NHC-based complexes **9** and **11** showed much better activity than **7** and **10**, indicating that aNHC better promoted the Pd coupling reaction than nNHC. Abnormal NHC-based complexes **8**, **9**, and **11** exhibited faster reaction rates, as observed in the in situ catalysts, without the induction period like **7** (Figure 5).[24] Significantly reduced activity of **7** compared with the in situ system (40% vs 76%) might indicate the possibility of C4 or C5 binding of NHC during in situ generation of a Pd catalyst using nNHC precursor **5**, as suggested by the previous report of complexes **1** and **2**.[4] However, unlike complex **1**, complex **7** showed moderate activity in the coupling reaction. We think that the reported inactivity of complex **1** is presumably due to the steric effects of the four bulky mesityl hanging groups of the two IMes, which prevent the approach of boronic acids to the Pd center, which is required for the generation of active Pd(0) species. Surprisingly, bis-aNHC Pd complex **9** exhibited a comparably fast reaction rate with the PEPPSI mono-NHC complex **11**, presumably reflecting the promoted oxidative addition step by aNHC, consistent with the in situ results, although bis-nNHC Pd complex **7** showed a much slower rate than the corresponding PEPPSI **10**, as previously reported with the similar type Pd complexes.[22]

Conclusion

In conclusion, we have shown that an abnormal NHC is a better ligand than a normal NHC in the Pd-catalyzed Suzuki−Miyaura reactions with suppressing homocouplings of arylboronic acids when sterically similar NHC precursors are used. The corresponding well-defined abnormal and normal NHC-based Pd complexes were synthesized and structurally characterized. The aNHC-based Pd precatalyst systems

(22) (a) O'Brien, C. J.; Kantchev, E. A. B.; Valente, C.; Hadei, N.; Chass, G. A.; Lough, A.; Hopkinson, A. C.; Organ, M. G. *Chem.—Eur. J.* **2006**, *12*, 4743. (b) 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. (c) Organ, M. G.; Çalimsiz, S.; Sayah, M.; Hoi, K. H.; Lough, A. J. *Angew. Chem., Int. Ed.* **2009**, *48*, 2383. (d) Çalimsiz, S.; Sayah, M.; Mallik, D.; Organ, M. G. *Angew. Chem., Int. Ed.* **2010**, *49*, 2014. (e) John, A.; Shaikh, M. M.; Ghosh, P. *Dalton Trans.* **2009**, 10581.

(23) See Supporting Information CIF file and Table S1. The data were also deposited in the Cambridge Crystallographic Centre as CCDC-753452 (**7**), CCDC-753453 (**8**), CCDC-753454 (**9**), CCDC-782053 (**10**), and CCDC-782075 (**11**).

(24) (a) Herrmann, W. A.; Böhm, V. P. W.; Gstöttmayr, C. W. K.; Grosche, M.; Reisinger, C. P.; Weskamp, T. *J. Organomet. Chem.* **2001**, *617*, 616. (b) Böhm, V. P. W.; Gstöttmayr, C. W. K.; Weskamp, T.; Herrmann, W. A. *J. Organomet. Chem.* **2000**, *595*, 186. (c) Herrmann, W. A.; Elison, M.; Fischer, J.; Köcher, C.; Artus, G. R. J. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2371.

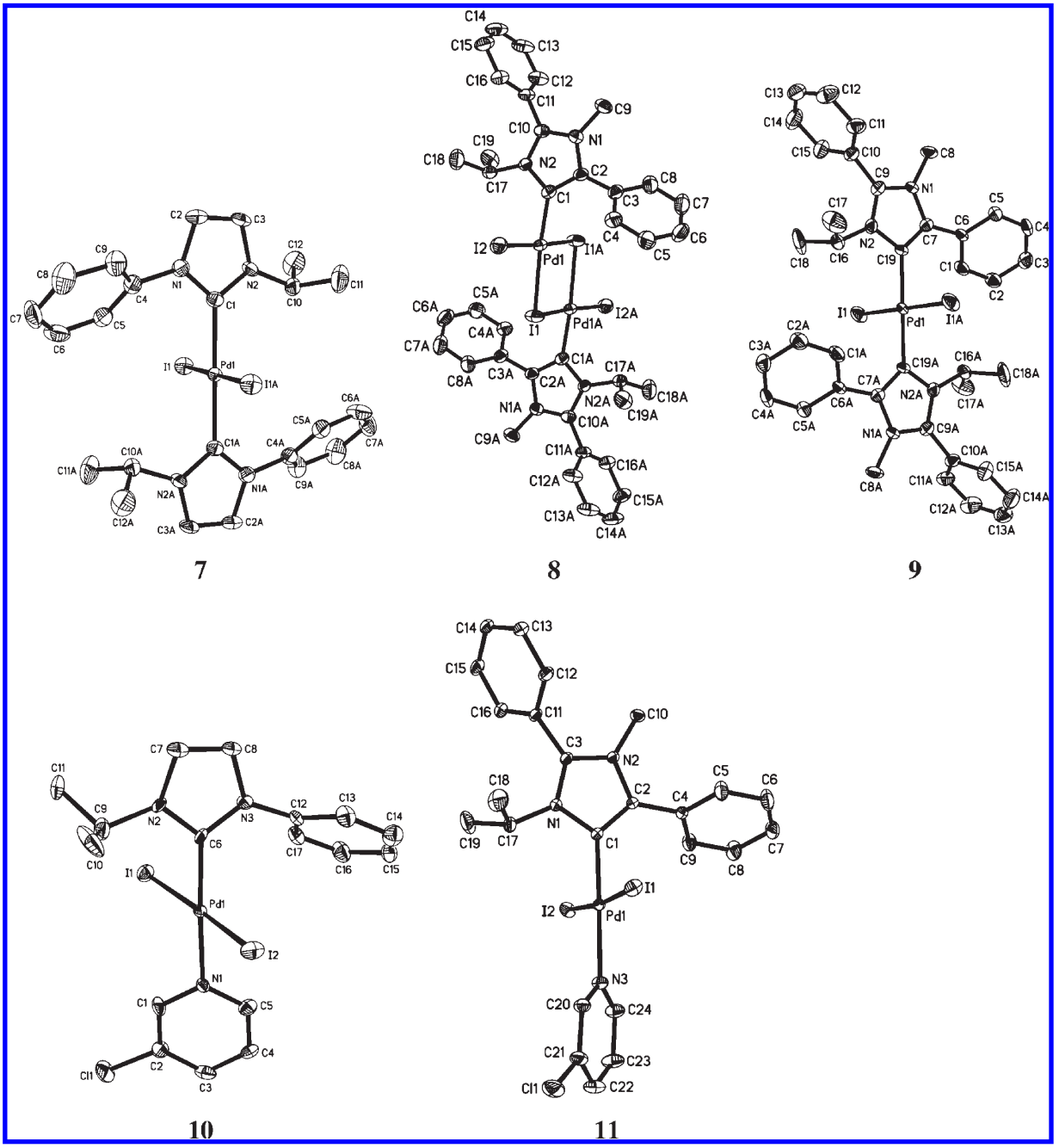


Figure 4. Crystal structures of **7**−**11** with thermal ellipsoids drawn at the 50% probability level.

exhibit consistently faster reaction progress. Further ligand design by adjusting steric bulkiness of the aNHC precursor will be necessary for improved and practical usage of aNHCs in cross-coupling reactions.

Experimental Section

General Information. All reactions were carried out with oven-dried glassware under an inert atmosphere of dry argon. All palladium compounds, boronic acid, and aryl halide were obtained from Strem, Aldrich, or Alfa Aesar and used as received. Anhydrous dioxane was purchased from Sigma-Aldrich and used as received. 1-Phenyl-3-isopropylimidazolium iodide (**5**)[13,25] and 1-isopropyl-3-methyl-2,4-diphenylimidazolium iodide (**6**)[13,26] were synthesized following literature procedures. Analytical TLC was performed on a Merck 60 F254 silica gel plate (0.25 mm thickness). Column chromatography was performed on Merck 60 silica gel (230−400 mesh). NMR spectra were recorded on a JEOL ECA400 (^{1}H NMR at 400 MHz; ^{13}C NMR at 100 MHz) spectrometer. All chemical shifts were reported in ppm using tetramethylsilane as a reference. GC yields were obtained on an Agilent 7890A instrument equipped with a HP-5 column using dodecane as an internal standard reflecting detector response factors. Mass spectrometry

Table 4. Selected Bond Lengths and Angles

	7	9	10	11	8
Pd−$C_{(carbene)}$	2.017(5)	2.021(5)	1.965(11)	1.9680(12)	1.971(5)
Pd−$N_{(pyridine)}$			2.121(9)	2.1376(11)	
Pd−I(1)	2.6189(4)	2.6244(4)	2.6021(10)	2.60993(16)	2.6672(5)
Pd−I(2)	2.6189(4)	2.6244(4)	2.6053(10)	2.60175(16)	2.6055(5)
C−Pd−C/N/I	180.00(1)	180.0(3)	176.8(4)	179.06(5)	174.66(13)

(25) Chu, Y.; Deng, H.; Cheng, J. P. *J. Org. Chem.* **2007**, *72*, 7790.
(26) Li, B.; Chiu, C. K. F.; Hank, R. F.; Murry, J.; Roth, J.; Tobiassen, H. *Org. Process Res. Dev.* **2002**, *6*, 682.

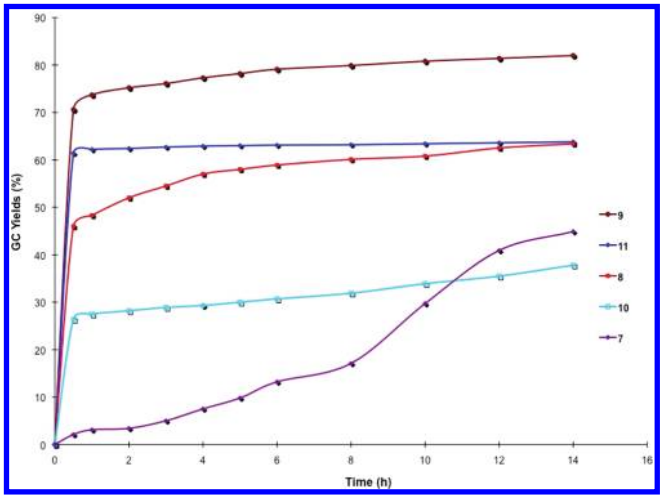
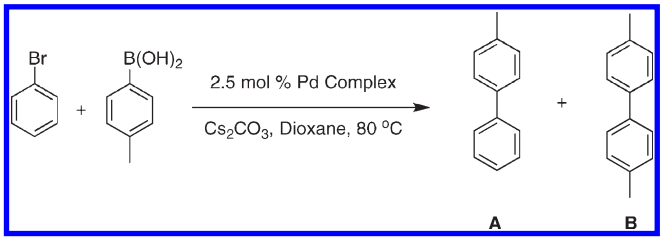


Figure 5. Comparison of reaction progress with complexes **7**−**11**.

Table 5. Suzuki−Miyaura Coupling with NHC−Pd Complexes[a,b]



entry	precatalyst	A	B
1	**7**	40	13
2	**8**	52	< 0.1
3	**9**	84	< 0.1
4	**10**	35	7
5	**11**	62	< 0.1

[a] Pd complex (2.5 mol %), Cs_2CO_3 (2 equiv), aryl halide (1.0 equiv), boronic acid (1.5 equiv), dioxane, 80 °C, 24 h. [b] Isolated yield, average of at least two runs.

was performed by a Waters Q-Tof Premier Micromass instrument, using electrospray ionization (ESI) mode.

General Procedure for the in Situ NHC−Pd-Catalyzed Suzuki−Miyaura Coupling Reactions (2.5 mol % catalyst loading). $Pd(OAc)_2$ (2.8 mg, 0.0125 mmol), NHC precursor (0.025 mmol), Cs_2CO_3 (326 mg, 1 mmol), and dioxane (2 mL) were placed in an oven-dried Schlenk flask under an argon atmosphere. The Schlenk tube was heated to 80 °C in an oil bath. After 30 min of heating, boronic acid (0.75 mmol) and aryl halide (0.5 mmol) in 2 mL of dioxane were added into the flask at room temperature. The reaction mixture was heated to 80 °C under an argon atmosphere for 24 h. After cooling to room temperature, volatiles were removed in vacuo. The residue was purified by silica gel flash column chromatography. All the products were identified by spectral comparison with literature data or with analogous literature data.

Complex 7. Under an Ar atmosphere, a Schlenk flask was charged with $Pd(OAc)_2$ (22.5 mg, 0.1 mmol), **5** (62.8 mg, 0.2 mmol), and dioxane (3 mL). The reaction mixture was heated to 80 °C for 6 h. After cooling to room temperature, the product was purified by column chromatography with CH_2Cl_2 as an eluent. Complex **7** (light yellow powder, 51.2 mg, 0.070 mmol, 70.1%) was obtained by recrystallization with CH_2Cl_2/Et_2O. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (m, 4H, CH_{arom}), 7.50 (m, 4H, CH_{arom}), 7.41(m, 2H, CH_{arom}), 7.15 (d, J = 1.8 Hz, 2H, CH_{imid}), 7.02 (d, J = 1.8 Hz, 2H, CH_{imid}), 5.18 (m, 2H, CH_{-iPr}), 1.40 (d, J = 6.8 Hz, 12H, $CH_{3\text{-}iPr}$). ^{13}C NMR ($CDCl_3$): δ 166.7, 140.5, 128.4, 127.8, 126.5, 122.5, 117.1, 52.6, 22.4. HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{24}H_{28}N_4I_2PdNa$, 754.9336; found, 754.9329. Anal. Calcd for $C_{24}H_{28}N_4I_2Pd$: C, 39.34; H, 3.85; N, 7.65. Found: C, 39.28; H, 3.56; N, 7.92.

Complex 8. Under an Ar atmosphere, a Schlenk flask was charged with $Pd(OAc)_2$ (22.5 mg, 0.1 mmol), **6** (80.8 mg, 0.2 mmol), and dioxane (3 mL). The reaction mixture was heated to 80 °C for 7 h. After cooling to room temperature, all volatiles were removed. The product was isolated by column chromatography using CH_2Cl_2 as an eluent. Complex **8** (orange powder, 59.7 mg, 0.047 mmol, 46.9%) was obtained by recrystallization from CH_2Cl_2/Et_2O. ^{1}H NMR (400 MHz, DMSO): δ 7.90 (d, J = 7.36 Hz, 4H, CH_{arom}), 7.67 (m, 10H, CH_{arom}), 7.50 (m, 4H, CH_{imid}), 7.41 (m, 2H, CH_{arom}), 5.58 (m, 2H, CH_{iPr}), 3.24 (s, 6H, NCH_3), 1.35 (d, J = 6.8 Hz, 12H, $CH_{3\text{-}iPr}$). ^{13}C NMR (DMSO): δ 143.4, 131.7, 131.3, 130.4, 129.1, 127.9, 124.9, 57.2, 54.9, 33.3, 21.8. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{38}H_{41}N_4Pd_2I_4$, 1272.7584; found, 1272.7588. Anal. Calcd for $C_{38}H_{40}N_4I_4Pd_2$: C, 35.85; H, 3.17; N, 4.40. Found: C, 35.89; H, 2.95; N, 4.56.

Complex 9. Ag_2O (3.6 mg, 0.016 mmol) and **6** (13.0 mg, 0.032 mmol) were combined in a Schlenk flask with CH_2Cl_2 (1 mL) under Ar. The mixture was stirred at room temperature for 4 h. The solution was filtrated through Celite and mixed with complex **8** (20.0 mg, 0.016 mmol). After stirring for 5 h at room temperature, the product was separated by column chromatography using CH_2Cl_2 as an eluent. Complex **9** (light yellow powder, 19.2 mg, 0.021 mmol, 65.8%) was obtained by recrystallization from CH_2Cl_2/Et_2O. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (m, 4H, CH_{arom}), 7.54 (m, 6H, CH_{arom}), 7.42 (m, 8H, CH_{arom}), 7.31 (m, 2H, CH_{arom}), 5.38 (m, 2H, CH_{iPr}), 3.19 (s, 6H, CH_3), 1.35 (d, J = 6.8 Hz, 12H, $CH_{3\text{-}iPr}$). ^{13}C NMR ($CDCl_3$): δ 145.2, 141.9, 134.2, 132.2, 131.5, 131.0, 130.9, 128.9, 127.6, 126.9, 55.8, 32.8, 23.2. HRMS-ESI (m/z): $[M + Na]^+$ calcd for $C_{38}H_{40}N_4I_2PdNa$, 935.0275; found, 935.0303. Anal. Calcd for $C_{40}H_{44}N_4Cl_4I_2Pd$ (**9**·$2CH_2Cl_2$) C, 44.37; H, 4.10; N, 5.17. Found: C, 44.29; H, 4.17; N, 5.21.

Complex 10. A Schlenk flask was charged with $Pd(OAc)_2$ (90.0 mg, 0.4 mmol), **5** (125.6 mg, 0.4 mmol), K_2CO_3 (276.0 mg, 2.0 mmol), KI (66.4 mg, 0.4 mmol), and 3-chloropyridine (2 mL) under Ar. The reaction mixture was heated to 80 °C for 16 h. After cooling to room temperature, 3-chloropyridine was evaporated under vacuum. The residue was dissolved in CH_2Cl_2 and filtered through Celite. After evaporation of all volatiles, the residue was washed with pentane and complex **10** was obtained (yellow solid, 263 mg, 0.4 mmol, 100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.80 (d, J = 1.24 Hz, 1H), 8.78 (d, J = 1.24 Hz, 1H), 8.02 (m, 2H), 7.70 (m, 1H), 7.67 (m, 2H), 7.52 (m, 1H), 7.24 (d, J = 2.0 Hz, 1H), 7.22 (m, 2H), 5.71 (m, J = 6.76 Hz, 1H), 1.64 (d, J = 6.8 Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 152.7, 151.7, 143.8, 139.9, 137.5, 132.2, 129.0, 128.8, 126.5, 124.6, 124.1, 118.1, 53.8, 22.4. HRMS-ESI (m/z): $[M + H]^+$ calcd for $C_{17}H_{19}ClI_2N_3Pd$, 659.8392; found, 659.8446. Anal. Calcd for $C_{17}H_{18}ClI_2N_3Pd$ C, 30.94; H, 2.75; N, 6.37. Found: C, 31.25; H, 2.94; N, 6.27.

Complex 11. A Schlenk flask was charged with complex **8** (95.0 mg, 0.075 mmol) in dichloromethane (2 mL) under Ar, and then 3-chloropyridine (17.0 mg, 0.15 mmol) was added. The reaction mixture was stirred at room temperature for 2 h. All volatiles were removed in vacuo. The residue was washed with pentane, and complex **11** was obtained (yellow solid, 112.2 mg, 0.15 mmol, 100%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.96 (d, J = 2.28 Hz, 1H), 8.87 (m, 1H), 7.93 (m, 2H), 7.61 (m, 4H), 7.49 (m, 5H), 7.17 (m, 1H), 5.97 (m, J = 8.24 Hz, 1H), 3.20 (s, 3H), 1.49 (d, J = 7.32 Hz, 6H). ^{13}C NMR ($CDCl_3$): δ 152.9, 151.9, 143.0, 137.2, 133.2, 132.0, 131.8, 131.5, 130.8, 129.4, 128.6, 128.5, 126.1, 124.5, 117.3, 58.2, 33.4, 22.7. HRMS-ESI (m/z): $[M + H]^+$

calcd for $C_{24}H_{25}ClI_2N_3Pd$, 753.8878; found, 753.8945. Anal. Calcd for $C_{24}H_{24}ClI_2N_3Pd$: C, 38.43; H, 3.22; N, 5.60. Found: C, 38.24; H, 3.25; N, 5.24.

Acknowledgment. The authors would like to thank Dr. Senthilkumar Muthaiah for the help of percent buried volume calculation. We thank the Singapore National Research Foundation for generous support of this research (NRF-RF2008-05). X.X. and B.X. gratefully acknowledge the Nanyang Technological University for graduate student scholarships.

Supporting Information Available: NMR spectra, X-ray crystallographic data (Table S1), and crystallographic information files (CIF) of complexes **7**−**11**. This material is available free of charge via the Internet at http://pubs.acs.org.