N-Heterocyclic Carbene/Pd(II)/1-Methylimidazole Complex Catalyzed Suzuki–Miyaura Coupling Reaction of Aryl Chlorides in Water

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Abstract: A well-defined N-heterocyclic carbene (NHC)/palladium chloride/imidazole complex exhibited high catalytic activity in the Suzuki–Miyaura coupling reactions of aryl or heteroaryl chlorides performed in water. Under optimal conditions, all reactions gave the desired coupling products in good to high yields.

Key words: N-heterocyclic carbenes, palladium, imidazole, Suzuki–Miyaura coupling, water

Transition-metal-catalyzed reactions between organoboranes and organic electrophiles, now named Suzuki–Miyaura coupling, have become a versatile method for carbon–carbon bond formations.[1] During the past years, much effort, mainly focused on finding supporting ligands, has been made to improve the efficiency of these reactions, especially for those involving aryl chlorides, which are low-cost and easily available.[2] Recently, great progress had been made in the chemistry of N-heterocyclic carbenes (NHCs) and their transition-metal complexes.[3] Nowadays, many NHC-palladium complexes have been shown to be good catalyst in the Suzuki–Miyaura coupling reactions of aryl chlorides.[4]

In contrast to common organic solvents, water is non-toxic, non-flammable, cheap, and easily available. A variety of organic transformations have been successfully achieved in water.[5] Yet, despite the advantageous features, only a few papers on the Suzuki–Miyaura coupling of aryl chlorides catalyzed by NHC-palladium complexes in neat water have been reported to date.[6] Recently, we have synthesized a well-defined NHC-palladium chloride-1-methylimidazole [NHC-Pd(II)-Im] complex **1** derived from $PdCl_2$, IPr·HCl, and 1-methylimidazole. It was found that the complex was an efficient catalyst in the amination reactions of aryl chlorides (Figure 1).[7] These results prompted us to further investigate other applications of this complex. In our continuing investigations on Suzuki–Miyaura coupling reactions performed in neat water,[8] we found that NHC-Pd(II)-Im complex **1** was an efficient catalyst in Suzuki–Miyaura coupling of aryl/heteroaryl chlorides performed in neat water. Herein, we wish to report these results in detail.

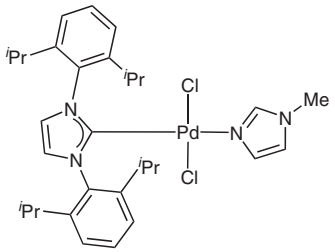
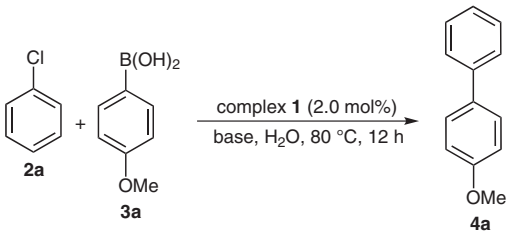


Figure 1 NHC-Pd(II)-Im complex **1**

In initial studies, a model reaction of chlorobenzene (**2a**; 0.5 mmol) with 4-methoxyphenylboronic acid (**3a**; 0.6 mmol) catalyzed by NHC-Pd(II)-Im complex **1** (2.0 mol%) was carried out in water (2.0 mL) at 80 °C for 12 hours to establish the best base. For each of the bases screened, the reactions took place smoothly to give the desired coupling product **4a** in good to high yields (Table 1), however, *t*-BuOK gave the best result (Table 1, entry 2). Therefore, the optimal reaction conditions were established as NHC-Pd(II)-Im complex **1** (2.0 mol%) as the catalyst, *t*-BuOK (2.0 equiv) as the base, and water (2.0 mL) as the solvent at 80 °C.[9,10]

Table 1 Optimization of the Complex **1** Catalyzed Reaction of **2a** with **3a** in Water



2a 3a 4a

Entry[a]	Base	Yield (%)[b]
1	NaOH	87
2	*t*-BuOK	95
3	KOH	78
4	$KHCO_3$	68
5	Na_2CO_3	80
6	K_2CO_3	79

[a] Reaction conditions: **2a** (0.5 mmol), **3a** (0.6 mmol), **1** (2.0 mol%), base (2.0 equiv), H_2O (2.0 mL), 80 °C, 12 h.
[b] Isolated yield.

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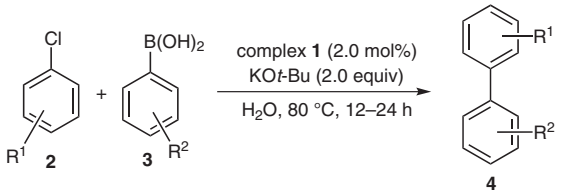
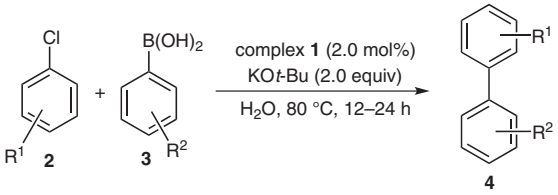
The optimized reaction conditions were then applied to a variety of arylboronic acids and aryl chlorides to investigate the generality of the method. As can be seen from Table 2, all reactions occurred smoothly to give the corresponding coupling products in moderate to excellent yields within 12–24 hours. It seems that the reactions involving 4-methoxyphenyl chloride (**2b**) gave the products in somewhat lower yields (Table 2, entries 1, 2, 6, 13, and 14), except for the reaction of **2b** with 2-methylphenylboronic acid (**3d**), which gave product **4c** in good yield (Table 2, entry 3). Sterically hindered substituents on either substrates **2** or **3** had almost no effect on the reactions. For instance, reactions involving substrates **2c**, **2e**, **2f** and **2i** with 3-methoxy, 3-methyl, 2-methyl, and 2,6-dimethyl groups on the phenyl rings, respectively, all gave the expected products in good to high yields (Table 2, entries 4, 7, 8, 11, and 12). 2-Methylphenylboronic acid (**3d**) also gave products **4c**, **4j**, **4r**, and **4s** in high yields, respectively (Table 2, entries 3, 11, 19, and 20). Reactions of heteroaryl chlorides such as 2-chloropyridine (**2j**), 3-chloropyridine (**2k**) and 2-chlorothiophene (**2l**) with 4-methoxyphenylboronic acid (**3a**), 2-methylphenylboronic acid (**3d**) and 1-naphthylboronic acid (**3f**) also gave the corresponding coupling products in good to high yields within 12–24 hours (Table 2, entries 15–17 and 19–24). 3-Chlorothiophene (**2m**) was found not to be a good partner and only 55% yield of the corresponding product **4q** was obtained (Table 2, entry 18).

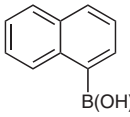
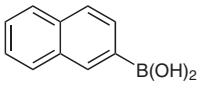
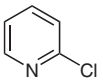
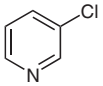
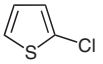
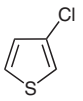
Table 2 Complex **1** Catalyzed Coupling Reactions of Aryl Chlorides **2** with Boronic Acids **3** under the Optimized Conditions



Entry[a]	**2** (R^1)	**3** (R^2)	Time (h)	Product	Yield (%)[b]
1	**2b** (4-OMe)	**3b** (H)	24	**4a**	69
2	**2b**	**3c** (4-Me)	24	**4b**	67
3	**2b**	**3d** (2-Me)	12	**4c**	86
4	**2c** (3-OMe)	**3b**	24	**4d**	86
5	**2d** (4-NO_2)	**3b**	12	**4e**	95
6	**2b**	**3e** (4-F)	12	**4f**	69
7	**2e** (3-Me)	**3a** (4-OMe)	12	**4g**	99
8	**2f** (2-Me)	**3a**	24	**4c**	99
9	**2g** (4-Ac)	**3a**	12	**4h**	99
10	**2h** (4-CHO)	**3b**	24	**4i**	93
11	**2i** (2,6-$Me_2C_6H_3$)	**3d**	24	**4j**	96

Table 2 Complex **1** Catalyzed Coupling Reactions of Aryl Chlorides **2** with Boronic Acids **3** under the Optimized Conditions (continued)



Entry[a]	**2** (R^1)	**3** (R^2)	Time (h)	Product	Yield (%)[b]
12	**2i**	 **3f**	24	**4k**	96
13	**2b**	 **3g**	12	**4l**	51
14	**2b**	**3f**	12	**4m**	65
15	 **2j**	**3a**	12	**4n**	99
16	 **2k**	**3a**	12	**4o**	99
17	 **2l**	**3a**	24	**4p**	87
18	 **2m**	**3a**	12	**4q**	55
19	**2j**	**3d**	12	**4r**	99
20	**2k**	**3d**	12	**4s**	99
21	**2j**	**3f**	12	**4t**	93
22	**2k**	**3f**	12	**4u**	99
23	**2k**	**3b**	12	**4v**	96
24	**2j**	**3b**	24	**4w**	81

[a] Reaction conditions: **2** (0.5 mmol), **3** (0.6 mmol), **1** (2.0 mol%), *t*-BuOK (2.0 equiv), H_2O (2.0 mL), 80 °C for the listed time.
[b] Isolated yield.

In summary, the well-defined NHC-Pd(II)-Im complex **1**, derived from readily available starting materials IPr·HCl, $PdCl_2$, and 1-methylimidazole, showed high catalytic activity in the Suzuki–Miyaura coupling reactions of aryl chlorides in water under mild conditions. Under the optimal conditions, the corresponding coupling products can be achieved in good to high yields. It is worth noting that the NHC-Pd complex catalyzed Suzuki–Miyaura cou-

pling reactions of aryl chlorides performed in water were significantly improved with respect to the previous report,[6] and similar yields were achieved compared with the best systems known in the literature under non-aqueous conditions.[4]

^{1}H and ^{13}C NMR spectra were recorded with Bruker AV-II 300 MHz or Bruker AV-III 500 MHz spectrometers; samples were analyzed as solutions in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard; coupling constants (*J* values) are given in Hz. Commercially obtained reagents were used without further purification. Flash column chromatography was carried out using Huanghai 300–400 mesh silica gel under increased pressure.

Complex 1 Catalyzed Suzuki–Miyaura Coupling Reaction; General Procedure

When aryl chloride is liquid: Under an N_2 atmosphere, arylboronic acid **3** (0.6 mmol), NHC-Pd(II)-Im **1** (2.0 mol%), *t*-BuOK (2.0 equiv), and H_2O (2.0 mL) were added to a Schlenk reaction tube, then aryl chloride **2** (0.5 mmol) was added. The mixture was stirred at 80 °C for 12–24 h (Table 2) then extracted with EtOAc, dried over anhydrous Na_2SO_4, filtered, and purified by flash column chromatography to give the pure products.

When aryl chloride is solid: Under an N_2 atmosphere, aryl chloride **2** (0.5 mmol), arylboronic acid **3** (0.6 mmol), NHC-Pd(II)-Im **1** (2.0 mol%), *t*-BuOK (2.0 equiv), and H_2O (2.0 mL) were added to a Schlenk reaction tube. The mixture was stirred at 80 °C for 12–24 h (Table 2) then extracted with EtOAc, dried over anhydrous Na_2SO_4, filtered, and purified by flash column chromatography to give the pure products.

Compound 4a[11]

White solid; yield: 87.4 mg (95%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, OCH_3), 6.96 (dd, *J* = 6.9, 2.4 Hz, 2 H, Ar), 7.28–7.33 (m, 1 H, Ar), 7.39–7.44 (m, 2 H, Ar), 7.51–7.57 (m, 4 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.3, 114.2, 126.6, 126.7, 128.1, 128.7, 133.8, 140.8, 159.1.

Compound 4b[12]

White solid; yield: 66.5 mg (67%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 6.96 (dd, *J* = 6.6, 2.1 Hz, 2 H, Ar), 7.22 (d, *J* = 8.1 Hz, 2 H, Ar), 7.45 (d, *J* = 8.1 Hz, 2 H, Ar), 7.51 (dd, *J* = 6.6, 2.1 Hz, 2 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0, 55.2, 114.1, 126.5, 127.9, 129.4, 133.7, 136.3, 137.9, 158.9.

Compound 4c[13]

Colorless oil; yield: 84.9 mg (86%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 6.94 (dd, *J* = 6.9, 1.8 Hz, 2 H, Ar), 7.21–7.26 (m, 6 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5, 55.2, 113.5, 125.7, 126.9, 129.9, 130.2, 130.3, 134.3, 135.4, 141.5, 158.5.

Compound 4d[14]

Colorless oil; yield: 79.2 mg (86%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, OCH_3), 6.87–6.91 (m, 1 H, Ar), 7.12–7.20 (m, 2 H, Ar), 7.31–7.38 (m, 2 H, Ar), 7.40–7.45 (m, 2 H, Ar), 7.57–7.60 (m, 2 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.2, 112.6, 112.8, 119.6, 127.1, 127.4, 128.7, 129.7, 141.0, 142.7, 159.9.

Compound 4e[14]

Pale-yellow solid; yield: 94.8 mg (95%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45 (t, *J* = 7.5 Hz, 1 H, Ar), 7.50 (dd, $^1J = {}^2J$ = 7.5 Hz, 2 H, Ar), 7.62 (d, *J* = 7.5 Hz, 2 H, Ar), 7.68 (d, *J* = 8.5 Hz, 2 H, Ar), 7.95 (d, *J* = 8.5 Hz, 2 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 124.1, 127.4, 127.8, 128.9, 129.1, 138.8, 147.1, 147.6.

Compound 4f[13]

White solid; yield: 69.5 mg (69%).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, OCH_3), 6.97 (dd, *J* = 6.6, 2.1 Hz, 2 H, Ar), 7.06–7.12 (m, 2 H, Ar), 7.45–7.51 (m, 4 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.3, 114.2, 115.5 (d, J_{C-F} = 21.0 Hz), 128.0, 128.1 (d, J_{C-F} = 8.3 Hz), 132.8, 136.9 (d, J_{C-F} = 3.0 Hz), 159.1, 162.1 (d, J_{C-F} = 243.8 Hz).

Compound 4g[15]

Pale-yellow solid; yield: 98.1 mg (99%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.41 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 6.96 (d, *J* = 7.0 Hz, 2 H, Ar), 7.12 (d, *J* = 7.0 Hz, 1 H, Ar), 7.29–7.36 (m, 3 H, Ar), 7.52 (d, *J* = 7.0 Hz, 2 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.5, 55.3, 114.1, 123.8, 127.4, 127.5, 128.1, 128.6, 133.9, 138.3, 140.8, 159.1.

Compound 4h[16]

White solid; yield: 111.9 mg (99%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.63 (s, 3 H, CH_3), 3.87 (s, 3 H, OCH_3), 7.00 (d, *J* = 9.0 Hz, 2 H, Ar), 7.58 (d, *J* = 9.0 Hz, 2 H, Ar), 7.65 (d, *J* = 8.5 Hz, 2 H, Ar), 8.01 (d, *J* = 8.5 Hz, 2 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 26.6, 55.4, 114.4, 126.6, 128.4, 128.9, 132.3, 135.3, 145.4, 159.9, 197.7.

Compound 4i[17]

Colorless oil; yield: 84.8 mg (93%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.40 (t, *J* = 7.5 Hz, 1 H, Ar), 7.48 (dd, $^1J = {}^2J$ = 7.5 Hz, 2 H, Ar), 7.63 (d, *J* = 7.5 Hz, 2 H, Ar), 7.75 (d, *J* = 8.0 Hz, 2 H, Ar), 7.95 (d, *J* = 8.0 Hz, 2 H, Ar), 10.05 (s, 1 H, CHO).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 127.3, 127.7, 128.4, 129.0, 130.2, 135.2, 139.7, 147.2, 191.9.

Compound 4j[18]

Colorless oil; yield: 94.1 mg (96%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.94 (s, 6 H, $2 \times CH_3$), 1.97 (s, 3 H, CH_3), 7.00–7.28 (m, 7 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 19.4, 20.3, 126.0, 126.9, 127.0, 127.2, 128.8, 129.9, 135.6, 135.8, 140.5, 141.1.

Compound 4k[19]

White solid; yield: 111.4 mg (96%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.90 (s, 6 H, $2 \times CH_3$), 7.17–7.35 (m, 6 H, Ar), 7.45–7.56 (m, 2 H, Ar), 7.85–7.91 (m, 2 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.4, 125.4, 125.7, 125.8, 126.0, 126.4, 127.2, 127.25, 127.31, 128.3, 131.7, 133.7, 137.0, 138.7, 139.6.

Compound 4l[20]

White solid; yield: 60.0 mg (51%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, OCH_3), 7.00 (d, *J* = 8.0 Hz, 2 H, Ar), 7.43–7.49 (m, 2 H, Ar), 7.64 (d, *J* = 7.5 Hz,

2 H, Ar), 7.70 (d, *J* = 8.5 Hz, 1 H, Ar), 7.82–7.88 (m, 3 H, Ar), 7.97 (s, 1 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.3, 114.3, 125.0, 125.4, 125.6, 126.2, 127.6, 128.0, 128.3, 128.4, 132.3, 133.6, 133.7, 138.1, 159.2.

Compound 4m[12]
White solid; yield: 76.1 mg (65%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.88 (s, 3 H, OCH_3), 7.01–7.03 (m, 2 H, Ar), 7.39–7.51 (m, 6 H, Ar), 7.83 (d, *J* = 8.5 Hz, 1 H, Ar), 7.89 (d, *J* = 8.5 Hz, 1 H, Ar), 7.92 (d, *J* = 8.5 Hz, 1 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.3, 113.7, 125.4, 125.7, 125.9, 126.1, 126.9, 127.3, 128.2, 131.1, 131.8, 133.1, 133.8, 139.9, 158.9.

Compound 4n[13]
White solid; yield: 91.6 mg (99%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.86 (s, 3 H, OCH_3), 7.00 (d, *J* = 8.5 Hz, 2 H, Ar), 7.15–7.18 (m, 1 H, Ar), 7.67–7.71 (m, 2 H, Ar), 7.95 (d, *J* = 8.5 Hz, 2 H, Ar), 8.65 (d, *J* = 4.5 Hz, 1 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.3, 114.1, 119.8, 121.4, 128.1, 132.0, 136.6, 149.5, 157.1, 160.4.

Compound 4o[13]
White solid; yield: 91.3 mg (99%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.86 (s, 3 H, OCH_3), 7.01 (dd, *J* = 6.5, 2.0 Hz, 2 H, Ar), 7.33 (dd, *J* = 8.0, 5.0 Hz, 1 H, Ar), 7.52 (dd, *J* = 7.0, 2.0 Hz, 2 H, Ar), 7.83 (dt, *J* = 8.0, 2.0 Hz, 1 H, Ar), 8.54 (dd, *J* = 5.0, 1.5 Hz, 1 H, Ar), 8.81 (d, *J* = 2.0 Hz, 1 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.3, 114.5, 123.5, 128.2, 130.2, 133.8, 136.2, 147.8, 147.9, 159.8.

Compound 4p[13]
White solid; yield: 82.6 mg (87%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.83 (s, 3 H, OCH_3), 6.91 (dd, *J* = 6.5, 2.0 Hz, 2 H, Ar), 7.04 (dd, *J* = 5.0, 4.0 Hz, 1 H, Ar), 7.19–7.21 (m, 2 H, Ar), 7.53 (dd, *J* = 6.5, 2.0 Hz, 2 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.3, 114.3, 122.1, 123.8, 127.2, 127.3, 127.9, 144.3, 159.2.

Compound 4q[21]
White solid; yield: 52.4 mg (55%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, OCH_3), 6.94 (d, *J* = 9.0 Hz, 2 H, Ar), 7.34–7.38 (m, 3 H, Ar), 7.53 (d, *J* = 9.0 Hz, 2 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 55.3, 114.2, 118.9, 126.0, 126.2, 127.6, 128.8, 142.0, 158.9.

Compound 4r[13]
Colorless liquid; yield: 83.9 mg (99%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.36 (s, 3 H, CH_3), 7.23–7.30 (m, 4 H, Ar), 7.40 (d, *J* = 5.0 Hz, 2 H, Ar), 7.72–7.75 (m, 1 H, Ar), 8.70 (d, *J* = 5.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.2, 121.6, 124.1, 125.8, 128.2, 129.6, 130.7, 135.7, 136.1, 140.4, 149.2, 160.1.

Compound 4s[13]
Pale-yellow liquid; yield: 84.0 mg (99%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, CH_3), 7.22 (d, *J* = 7.0 Hz, 1 H, Ar), 7.26–7.36 (m, 4 H, Ar), 7.64–7.66 (m, 1 H, Ar), 8.58–8.60 (m, 2 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.3, 123.0, 126.1, 128.1, 129.8, 130.5, 135.6, 136.4, 137.5, 138.1, 148.1, 149.9.

Compound 4t[22]
Pale-yellow liquid; yield: 95.4 mg (93%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.31–7.33 (m, 1 H, Ar), 7.47–7.63 (m, 5 H, Ar), 7.79–7.82 (m, 1 H, Ar), 7.93 (d, *J* = 8.5 Hz, 2 H, Ar), 8.12 (d, *J* = 8.0 Hz, 1 H, Ar), 8.81 (d, *J* = 5.0 Hz, 1 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 121.9, 125.0, 125.2, 125.5, 125.8, 126.4, 127.4, 128.3, 128.8, 131.1, 133.9, 136.3, 138.4, 149.4, 159.2.

Compound 4u[23]
Pale-yellow liquid; yield: 101.3 mg (99%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41–7.57 (m, 5 H, Ar), 7.80–7.83 (m, 2 H, Ar), 7.92 (t, *J* = 8.5 Hz, 2 H, Ar), 8.69 (dd, *J* = 5.0, 1.5 Hz, 1 H, Ar), 8.77 (d, *J* = 2.0 Hz, 1 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 123.1, 125.25, 125.34, 126.1, 126.5, 127.4, 128.4, 128.5, 131.5, 133.8, 136.3, 136.4, 137.3, 148.5, 150.6.

Compound 4v[23]
Colorless liquid; yield: 74.3 mg (96%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.50 (m, 4 H, Ar), 7.57–7.60 (m, 2 H, Ar), 7.87–7.89 (m, 1 H, Ar), 8.59 (dd, *J* = 4.5, 1.5 Hz, 1 H, Ar), 8.85 (d, *J* = 2.0 Hz, 1 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 123.5, 127.1, 128.1, 129.1, 134.4, 136.7, 137.8, 148.3, 148.4.

Compound 4w[22]
Colorless liquid; yield: 62.9 mg (81%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.20–7.23 (m, 1 H, Ar), 7.40–7.49 (m, 3 H, Ar), 7.71–7.74 (m, 2 H, Ar), 7.99–8.01 (m, 2 H, Ar), 8.69–8.70 (m, 1 H, Ar).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 120.5, 122.0, 126.9, 128.7, 128.9, 136.7, 139.4, 149.6, 157.4.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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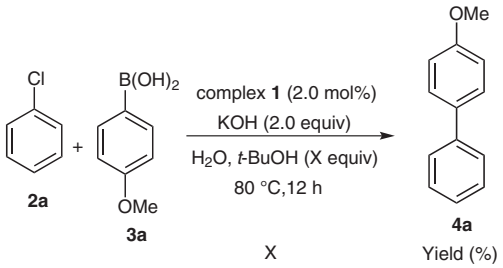
(9) Although NaOH is a suitable base for the coupling of chlorobenzene (**2a**) with 4-methoxyphenylboronic acid (**3a**), the generality using NaOH as the base is not as good as that using *t*-BuOK, which is consistent with our previously reported results (ref. 8). See the Supporting Information for the details.

(10) Further studies showed that *t*-BuOH derived from the reaction of *t*-BuOK with H_2O may be important in the reactions using *t*-BuOK as the base. Using KOH as the base, the yield can also be increased to 93% in the presence of 1.0 equivalent *t*-BuOH (Scheme 1).



X	Yield (%)
0	78
1	93

Scheme 1

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