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Substituted 2-(2'-pyridyl)benzimidazole palladium(II) complexes as an efficient catalytic system for Suzuki–Miyaura cross-coupling reactions

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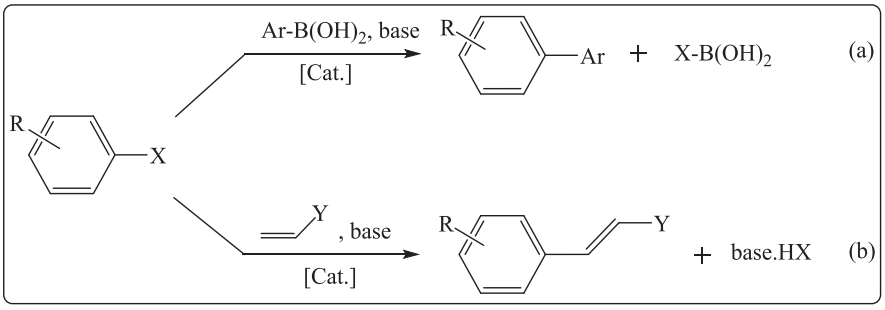
Abstract: A new series of N,N-type 2-(2'-pyridyl)benzimidazole ligands (**2A$_1$**, **2A$_2$**, **3B$_1$**, **3B$_2$**, **3B$_3$**, and **4C$_1$**) and their Pd(II) complexes (**5A$_1$**, **5A$_2$**, **6B$_1$**, **6B$_2$**, **6B$_3$**, and **7C$_1$**) were prepared and characterized by conventional spectroscopic methods and elemental analyses. The incorporation of N-coordinated benzimidazole complexes of palladium gave high catalytic activity in the Suzuki–Miyaura coupling of aryl halides substrates. After determining the best active catalyst as **5A$_1$**, bearing the mesityl substituent on the benzimidazole ring with the Pd(II) ion, optimization studies were carried out via changing the substrate, base, time, atmosphere, and the effect of water. The DMF:H_2O (4/1) and Cs_2CO_3 as base were found to be critical for the efficiency of the reaction yield (100%).

Key words: Palladium, 2-(2'-pyridyl)benzimidazole, aryl halides, phenylboronic acid, Suzuki–Miyaura

1. Introduction

There has been a long-standing interest in the properties of palladium complexes because they are widely used as catalysts for carbon–carbon bond forming reactions.[1] These reactions are key steps in many syntheses of organic chemicals and natural products, as well as in a variety of industrial processes.[2] Important examples for this type of catalysis are the Suzuki–Miyaura,[3] Negishi,[4] Kumada,[5] Hiyama,[6] and Stille[7] reactions. The palladium-catalyzed reaction of aryl chlorides with arylboronic acid (the Suzuki–Miyaura reaction, Scheme 1a) or with alkenes (the Heck reaction, Scheme 1b) is one of the most common methods for C–C bond formation and has attracted much current interest.[8–12]



Scheme 1. Cross-coupling of an aryl halide: (a) the Suzuki–Miyaura and (b) Heck–Mizoroki reaction.

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The Suzuki–Miyaura reaction is one of the most important carbon–carbon bond forming reactions and has been widely used in industrial organic synthesis.[13,14] Traditionally, this reaction is promoted by catalysts based on Pd, which is a precious metal. Due to several advantages, including relative mild reaction conditions, tolerance of a broad range of functional groups, and the compatibility towards water as solvent or cosolvent, the Suzuki–Miyaura reaction is applicable for the preparation of, for example, fine chemicals and pharmaceuticals on an industrial scale.[15−17] Hence, the Suzuki–Miyaura cross-coupling reaction is one of the most widely used methods for the construction of biaryl compounds, owing to the stability and low toxicity of the organoboranes relative to other organometallic reagents.[18−25]

The traditional Suzuki–Miyaura reaction usually proceeds using P- and N-ligand based palladium catalysts,[25] and much attention has been paid to improve the Suzuki–Miyaura reaction by designing various new ligands. Pd–N coordinated complexes also showed good catalytic performance in Suzuki–Miyaura coupling reactions.[26−29] However, most of these ligands are expensive, which has significantly limited their industrial applications. Therefore, the development of efficient catalytic systems consisting of economical catalysts is still a highly desirable goal.

We report here the synthesis and spectroscopic characterization of the Pd(II) complexes (**5A$_1$**, **5A$_2$**, **6B$_1$**, **6B$_2$**, **6B$_3$**, and **7C$_1$**) of different *N*-benzylated 2-(2'-pyridyl)benzimidazole (PBI) ligands (**2A$_1$**, **2A$_2$**, **3B$_1$**, **3B$_2$**, **3B$_3$**, and **4C$_1$**) were determined by ^{1}H and ^{13}C NMR spectra. All of the Pd(II) complexes (**5A$_1$**, **5A$_2$**, **6B$_1$**, **6B$_2$**, **6B$_3$**, and **7C$_1$**) were screened in the Suzuki–Miyaura cross-coupling reactions of aryl halides with phenylboronic acid. The optimal catalytic conditions were investigated in detail via changing the substrate, base, time, atmosphere, and the effect of water.

2. Results and discussion

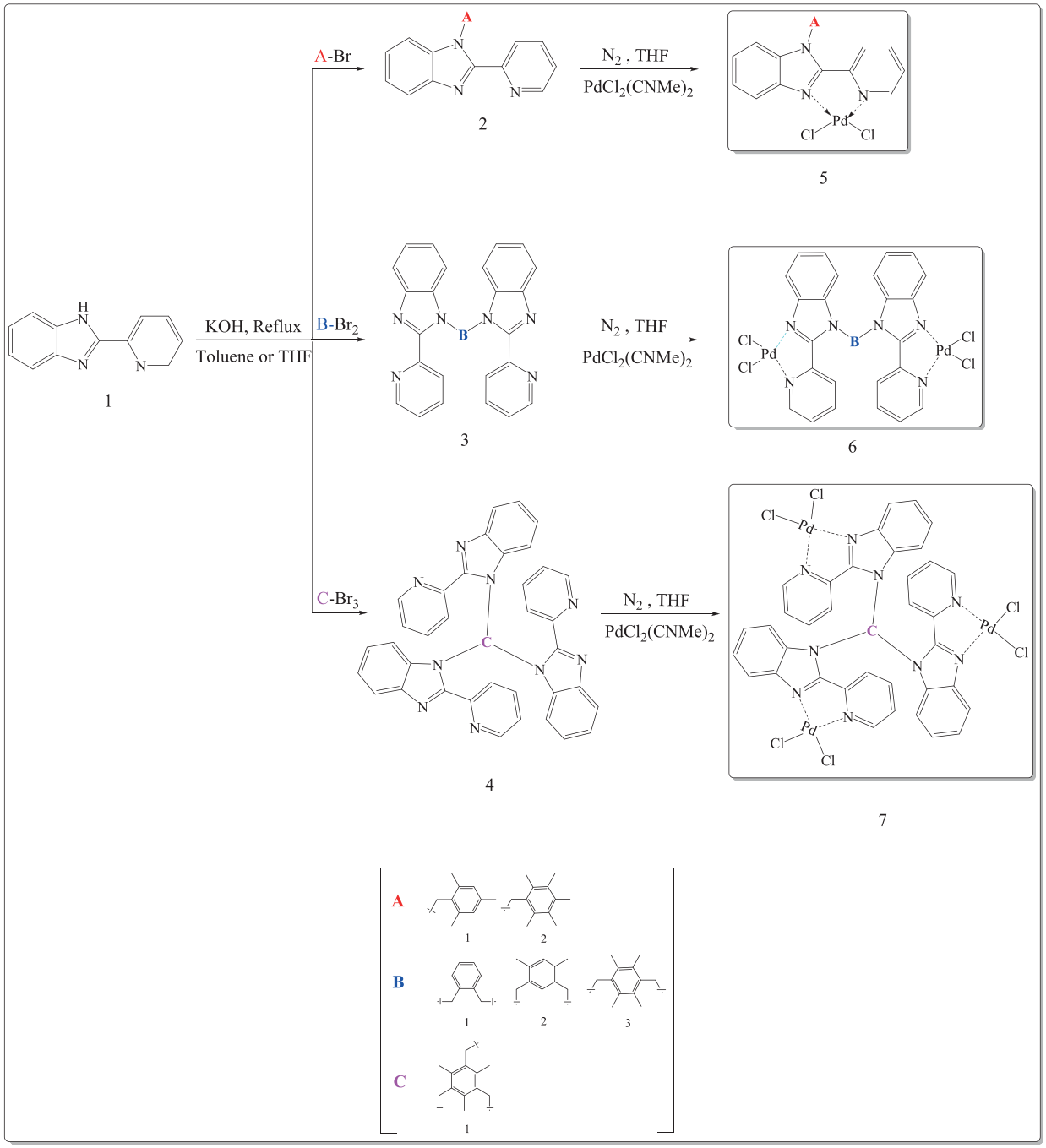
2.1. Synthesis of compounds

As summarized in Scheme 2, PBI ligands (**2A$_1$**, **2A$_2$**, **3B$_1$**, **3B$_2$**, **3B$_3$**, and **4C$_1$**) were prepared in moderate yield by one pot reaction via deprotonation of PBI using a base such as NaH or KOH, followed refluxing the 1:1 molar ratio of benzyl halides in anhydrous toluene or tetrahydrofuran (THF) (Scheme 2). Desired PBI ligands (**2A$_1$**, **2A$_2$**, **3B$_1$**, **3B$_2$**, **3B$_3$**, and **4C$_1$**) were obtained in high yields as white solids following recrystallization (70%–87%) and satisfactory spectroscopic results were acquired for all ligands. As summarized in Scheme 2, the Pd complexes (**5A$_1$**, **5A$_2$**, **6B$_1$**, **6B$_2$**, **6B$_3$**, and **7C$_1$**) were obtained by reactions of PBI (**2A$_1$**, **2A$_2$**, **3B$_1$**, **3B$_2$**, **3B$_3$**, and **4C$_1$**) with $PdCl_2(CNMe)_2$ in good yields as yellow solids following recrystallization. The ^{1}H and ^{13}C NMR spectra with elemental analysis results support the 1:1 ratio of metal/ligand, as expected. The multinuclear NMR spectra and elemental analysis showed that the ligands and their complexes supported the proposed structures.

2.2. Spectroscopic characterization

The NMR spectra of ligands (**2A$_1$**, **2A$_2$**, **3B$_1$**, **3B$_2$**, **3B$_3$**, and **4C$_1$**) and their Pd(II) complexes were recorded in DMSO-d_6 or $CDCl_3$ at room temperature and the assignments made for the observed chemical shifts are listed in the Experimental section. A comparison of the chemical shifts of the aromatic protons and carbons of the PBI ligands (**2A$_1$**, **2A$_2$**, **3B$_1$**, **3B$_2$**, **3B$_3$**, and **4C$_1$**) with their Pd(II) complexes indicated the formation of a dative M←N bond as expected and also confirmed the participation of the nitrogen atoms in coordination for metal complexes. These aromatic protons and carbons also become nonequivalent as a result of

their different exposure to the ring current effect due to the different substituent groups, which were otherwise identical. In the ^{1}H NMR spectra, the significative signal for ligands (**2A$_1$**, **2A$_2$**, **3B$_1$**, **3B$_2$**, **3B$_3$**, and **4C$_1$**) and their Pd(II) complexes were observed at 5.50–6.40 ppm for N–C$\underline{H}_2$ proton and at 45.2–68.7 ppm range for N–$\underline{C}$H$_2$ carbon. These values and the other NMR data are in good agreement with the proposed structures.



Scheme 2. The structures of the prepared compounds.

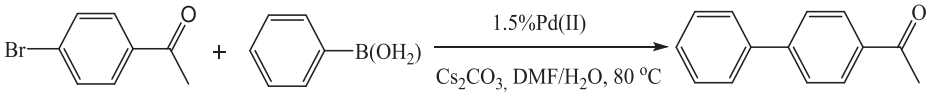
The IR spectra of the Pd(II) complexes are compared with those of the free ligand in order to determine the coordination sites that may be involved in chelation. There are some guide peaks in the spectra of the ligands, which are of good help for achieving this goal. The position and/or the intensities of these peaks are expected to change upon chelation. Coordination of the ligands to the metal through the nitrogen atom is expected to reduce the electron density in the azomethine link and lower the ν(C=N) absorption frequency. The very strong and sharp bands located at 1625–1600 cm^{-1} are assigned to the ν(C=N) stretching vibrations of the azomethine of the ligands. These bands are shifted 5–10 cm^{-1} to a lower wavenumber, which supports the participation of the azomethine group of these ligands in binding to the palladium ion.[30,31]

2.3. Catalytic studies

The palladium-catalyzed reactions of aryl halides with arylboronic acids (the Suzuki–Miyaura reaction) is the most common method for C–C bond formation.[32,33] The palladium-catalyzed reactions are usually carried out homogeneously in the presence of a base. The reactivity of the aryl halide component decreases sharply in the order X = I > Br > Cl and electron withdrawing substituents R are required for the chlorides to react.[32–38]

The palladium complexes (**5A$_1$**, **5A$_2$**, **6B$_1$**, **6B$_2$**, **6B$_3$**, and **7C$_1$**) were tested as catalysts for the Suzuki–Miyaura coupling reactions to give the biaryl compounds. We initially studied the reaction of phenylboronic acid with 4-bromoacetophenone in DMF/H_2O as a model reaction under heating to 80 °C in the presence of 1.5 mmol % of Pd(II) metal catalysts and 1.5 mmol of bases. The comparison of synthesized catalysts at the same catalytic conditions is summarized in Table 1.

Table 1. Comparison of Pd(II) complexes as catalysts in Suzuki–Miyaura coupling reactions using 4-bromoacetophenone with phenylboronic acid as substrates.

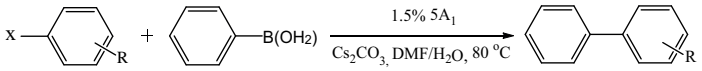


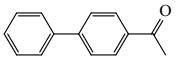
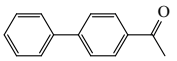
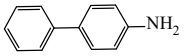
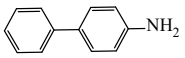
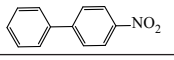
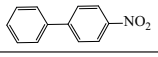
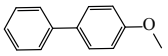
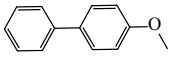
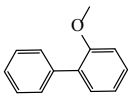
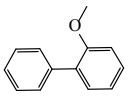
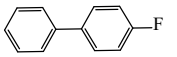
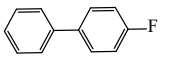
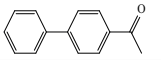
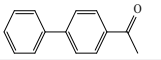
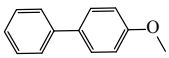
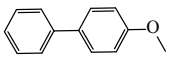
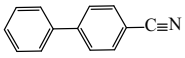
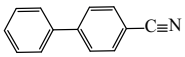
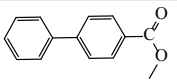
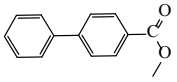
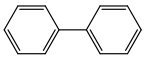
Entry	Catalysts	Solvent	Time (h)	Yield[a] (%)
1	**5A$_1$**	DMF/H_2O (4:1)	1	99.8
2	**5A$_1$**	DMF/H_2O (4:1)	2	100.0
3	**5A$_2$**	DMF/H_2O (4:1)	1	85.4
4	**5A$_2$**	DMF/H_2O (4:1)	2	90.5
5	**6B$_1$**	DMF/H_2O (4:1)	1	98.2
6	**6B$_1$**	DMF/H_2O (4:1)	2	97.7
7	**6B$_2$**	DMF/H_2O (4:1)	1	98.1
8	**6B$_2$**	DMF/H_2O (4:1)	2	99.2
9	**6B$_3$**	DMF/H_2O (4:1)	1	97.0
10	**6B$_3$**	DMF/H_2O (4:1)	2	94.7
11	**7C$_1$**	DMF/H_2O (4:1)	1	96.6
12	**7C$_1$**	DMF/H_2O (4:1)	2	96.5

Reaction conditions: 1.5 mmol % Pd, 1 mmol 4-bromoacetophenone, 1.5 mmol phenylboronic acid, 3 mL solvent (DMF(4)/H_2O(1)), heat (80 °C), base (Cs_2CO_3), [a] The yields checked by GC analysis.

The synthesized metal complexes were compared in the same catalytic conditions. From the results in Table 1, it is evident that the palladium complex that contains electron donating mesityl substituent with mono NN type **5A$_1$** complex is the most effective of the complexes examined. After determining the best active

Table 2. Suzuki–Miyaura coupling reactions of aryl halides with phenylboronic acid.



Entry	Catalysts	Arylhalide	Product	Time (h)	Yield[a] (%)
1	**5A**$_1$	4-bromoacetophenone		1	99.8
2	**5A**$_1$	4-bromoacetophenone		2	100.0
3	**5A**$_1$	4-bromoaniline		1	86.3
4	**5A**$_1$	4-bromoaniline		2	95.1
5	**5A**$_1$	1-bromo-4 nitrobenzene		1	97.9
6	**5A**$_1$	1-bromo-4-nitrobenzene		2	97.7
7	**5A**$_1$	4-bromoanisole		1	98.1
8	**5A**$_1$	4-bromoanisole		2	99.9
9	**5A**$_1$	2-bromoanisole		1	98.3
10	**5A**$_1$	2-bromoanisol		2	99.3
11	**5A**$_1$	1-bromo-4-floureben-zene		1	79.2
12	**5A**$_1$	1-bromo-4-flouroben-zene		2	62.3
13	**5A**$_1$	4-chloroacetophenone		1	60.2
14	**5A**$_1$	4-chloroacetophenone		2	74.5
15	**5A**$_1$	4-chloroanisole		1	4.2
16	**5A**$_1$	4-chloroanisole		2	3.8
17	**5A**$_1$	4-chlorobenzonitrile		1	80.3
18	**5A**$_1$	4-chlorobenzonitrile		2	85.4
19	**5A**$_1$	methyl-4-chlorobenzoate		1	73.2
20	**5A**$_1$	methyl-4-chlorobenzoate		2	78.4
21	**5A**$_1$	2-chlorobenzene		1	3.4

Reaction conditions: 1.5 mmol % **5A$_1$**, 1 mmol arylhalide, 1.5 mmol phenylboronic acid, 3 mL solvent (DMF(4)/H_2O(1)), heat (80 °C), base (Cs_2CO_3). [a] The yields checked by GC analysis

catalyst, the optimization studies were carried out by changing various parameters such as temperature, time, aryl halide, and base.

In order to find the optimum conditions, a series of experiments was performed with 4-bromoacetophenone and phenylboronic acid, which were to be model compounds (Table 2, entries 1 and 2). The yield was increased with increasing time from 1 to 2 h as reaction time. When we used the 4-chloroacetophenone as substrate, moderate yields (Table 2, entries 13 and 14) were achieved, but coupling of electron-neutral 4-chlorobenzene electron-rich 4-chloroanisole (Table 2, entries 15 and 16) was unsuccessful.[39]

According to Figure 1, water positively affected the reaction yield. The effect of the catalyst was examined for the Suzuki–Miyaura cross-coupling reactions (Figure 2). It can be seen that the reaction yield is strongly affected by the catalyst. The effect on the reactions of the bases was also investigated. As a base, Cs_2CO_3 was the best choice in water–DMF (1/4) systems (Figure 3). All catalytic reactions were carried out in inert atmosphere. Even in this atmosphere the catalyst was still effective (Figure 4).

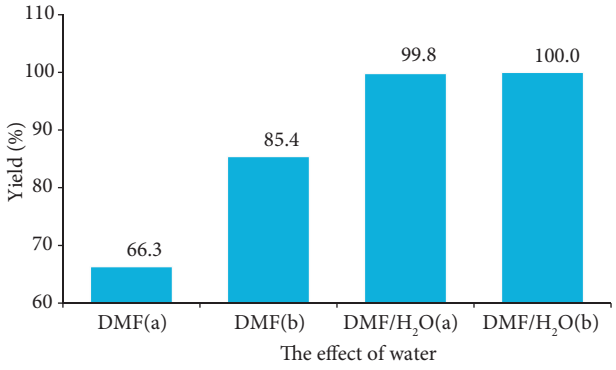


Figure 1. The effect of water.
Reaction conditions: 1.5 mmol % Pd, 1 mmol 4-bromoacetophenone, 1.5 mmol phenylboronic acid, heat (80 °C), base (Cs_2CO_3). Reaction time (a) 1 h, (b) 2 h.

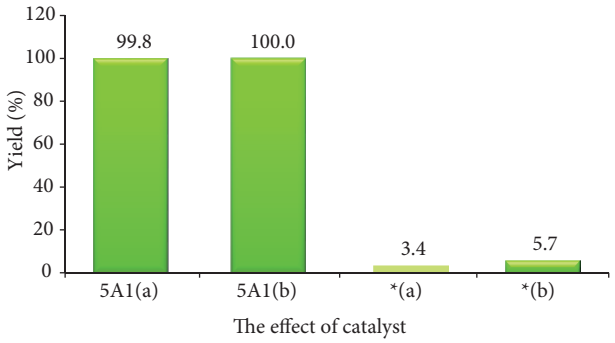


Figure 2. The effect of catalyst.
Reaction conditions: 1.5 mmol % Pd, 1 mmol 4-bromoacetophenone, 1.5 mmol phenylboronic acid, 3 mL solvent (DMF, DMF/H_2O), heat (80 °C), base (Cs_2CO_3), **5A1** (catalyst), *(without catalyst). Reaction time (a) 1 h, (b) 2 h.

3. Experimental

3.1. Materials and measurements

All reagents and solvents were of reagent-grade quality and obtained from commercial suppliers (Merck, Sigma-Aldrich, Acros Organics, and Alfa-Aesar). ^{1}H NMR spectra were recorded at 25 °C using an Agilent-VNMRS-400 spectrometer at 400 MHz or a Bruker Avance DRX spectrometer at 300 MHz. ^{13}C NMR spectra were recorded at 25 °C on a Bruker operating at 100.56 MHz or a Bruker Avance DRX spectrometer at 75.0 MHz. TMS was used as an internal reference for recording ^{1}H and ^{13}C NMR in DMSO-d_6 or $CDCl_3$ and coupling constants (J) are reported in hertz. Elemental analyses were performed by using a LECO CHNS model 932 elemental analyzer. Melting points were measured in open capillary tubes with an Electrothermal 9100 melting point apparatus and are uncorrected. FT-IR spectra were obtained from KBr pellets (3-mg sample in 300 mg of KBr) on a PerkinElmer Spectrum RXI FT-IR Fourier transform spectrometer (4000–400 cm^{-1}). All reactions were performed using a Schlenk-type flask under nitrogen and standard high vacuum-line techniques. The

mixture was separated by centrifugation, and the liquid phase was subjected to GC (Agilent 7820A) analysis with ethylene glycol dibutyl ether as internal standard and hydrogen as the carrier gas.

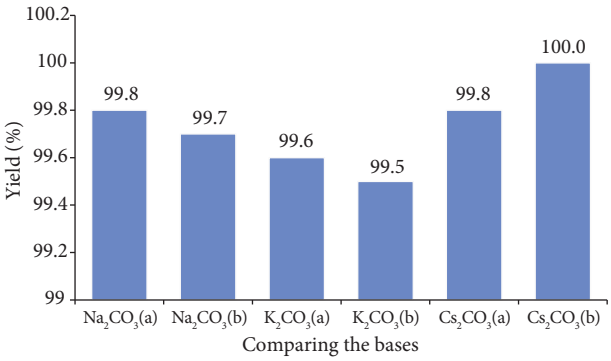


Figure 3. The effect of bases.
Reaction conditions: 1.5 mmol % Pd, 1 mmol 4-bromoacetophenone, 1.5 mmol phenylboronic acid, 3 mL solvent (DMF(4)/H_2O(1)), heat (80 °C). Reaction time (a) 1 h, (b) 2 h.

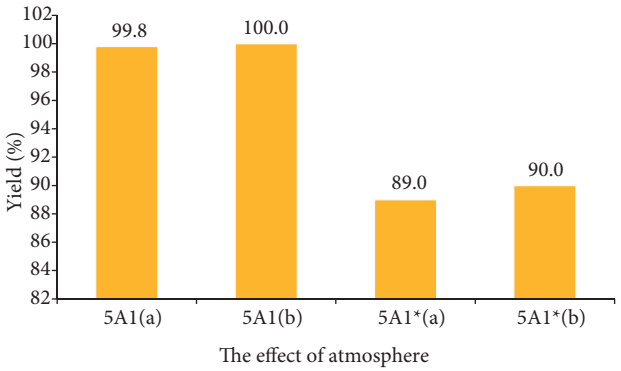


Figure 4. The effect of atmosphere.
Reaction conditions: 1.5 mmol % Pd, 1 mmol 4-bromoacetophenone, 1.5 mmol phenylboronic acid, 3 mL solvent (DMF(4)/H_2O(1)), heat (80 °C), base (Cs_2CO_3), **5A$_1$** (The reaction was carried out in inert atmosphere), **5A$_1$** *(The reaction was carried out in air). Reaction time (a) 1 h, (b) 2 h.

3.2. General procedure for the Suzuki–Miyaura coupling reactions

Pd(II) complex (1.5% mmol), phenylboronic acid (1.5 mmol), aryl halides (1 mmol), base (1.5 mmol), and solvent (3 mL) were added to a Schlenk tube under nitrogen atmosphere. The Schlenk tube was stirred at 80 °C for the desired hours. The reaction mixture was then cooled to room temperature, diluted with CH_2Cl_2, and filtered through Celite. The yield of the reaction was determined by GC (Agilent 7820A).

3.3. General procedure for synthesis of the ligands

The ligands **2A$_1$**[40] and **2A$_2$**[41] were synthesized by modification of the method in the published procedure.

The remaining ligands were synthesized as follows:

In a two-necked, 100-mL round-bottom flask equipped with a blanket of nitrogen (N_2) was placed 30 mL of anhydrous toluene or tetrahydrofuran (THF) at room temperature for each ligand. KOH (0.56 g, 10.0 mmol) was added to these solutions, then a solution of 2-pyridylbenzimidazole (1.95 g, 10.0 mmol) in anhydrous toluene (10 mL) was slowly added and stirred at reflux for 6 h. To these solutions, benzyl halides were added such as 2,4,6-trimethylbenzyl bromide (2.13 g, 10.0 mmol) for ligand **2A$_1$**, 2,3,4,5,6-pentamethylbenzylbromide (2.45 g, 10.0 mmol) for ligand **2A$_2$**, 1,2-bis(bromomethyl)benzene (1.32 g, 5.0 mmol) for ligand **3B$_1$**, 2,4-bis(bromomethyl)-1,3,5-trimethylbenzene (1.53 g, 5.0 mmol) for ligand **3B$_2$**, 1,4-bis(bromomethyl)-2,3,5,6-tetramethylbenzene (1.60 g, 5.0 mmol) for ligand **3B$_3$**, and 1,3,5-tris(bromomethyl)-2,4,6-trimethylbenzene (1.33 g, 3.3 mmol) for ligand **4C$_1$**, respectively, and then heated under reflux for 24 h. The volatiles were evaporated in vacuum to dryness. The residue was dissolved in CH_2Cl_2 and filtered via cannula on Celite. The solution was concentrated to 15 mL and then the desired product was precipitated in 30 mL of n-hexane.

For 2A$_1$: Color: white, yield: 85%, mp: 169–172 °C. Anal. Calc. for [$C_{22}H_{21}N_3$] (M.W: 327.17

g/mol): C, 80.70; H, 6.47; N, 12.83; found: C, 80.73; H, 6.37; N, 12.84. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm); 2.15 (s, 6H, mes-($C\underline{H}_3$)$_2$); 2.26 (s, 3H, mes-$C\underline{H}_3$); 6.22 (s, 2H, N-$C\underline{H}_2$); 6.76 (d, J = 8.0 Hz, 1H, Ar-C$\underline{H}$); 6.83 (s, 2H, mes($C\underline{H}$)$_2$); 7.03–7.07 (m, 1H, Ar-C$\underline{H}$); 7.20–7.35 (m, 2H, Ar-C$\underline{H}$); 7.85–7.89 (m, 2H, Ar-C$\underline{H}$); 8.44–8.46 (dd, J = 8.0, 8.4 Hz, 1H, Ar-C$\underline{H}$); 8.70–8.72 (m, 1H, Ar-C$\underline{H}$). ^{13}C NMR (75.48 MHz, $CDCl_3$, δ ppm): 20.4 and 21.1 (mes-($\underline{C}H_3$); 46.1 (N-$\underline{C}H_2$); 112.0; 120.1; 122.8; 123.6; 124.1; 125.7; 129.6; 129.9; 136.4; 137.3; 137.5; 137.7; 142.4; 148.6; 150.7; 151.0 (Ar-$\underline{C}$H)

For 2A$_2$: Color: white, yield: 82%, mp: 143–145 °C. Anal. Calc. for [$C_{24}H_{25}N_3$] (MW: 355.20 g/mol): C, 81.09; H, 7.09; N, 11.82; found: C, 80.56; H, 7.91; N, 11.53. ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm); 1.26 (s, 6H, o-($C\underline{H}_3$)$_2$); 1.36 (s, 6H, m-($C\underline{H}_3$)$_2$); 2.13–2.20 (s, 3H, $p-C\underline{H}_3$); 5.50 (s, 2H, N-$C\underline{H}_2$); 6.86 (s, 1H, Ar-C$\underline{H}$); 7.11 (s, 1H, Ar-C$\underline{H}$); 7.26 (s, 1H, Ar-C$\underline{H}$); 7.35 (s, 1H, Ar-C$\underline{H}$); 7.49 (s, 1H, Ar-C$\underline{H}$); 8.46 (s, 1H, Ar-C$\underline{H}$); 10.19 (s, 2H, Ar-C$\underline{H}$). ^{13}C NMR (100.56 MHz, $CDCl_3$, δ ppm): 17.0; 17.4; 29.6; 31.7; 34.4 and 35.2 ($\underline{C}H_3$); 49.3 (N-$\underline{C}H_2$); 117.9; 121.2; 122.4; 125.5; 126.5; 133.8; 134.0; 137.5; 140.7; 158.0; 167.9 (Ar-$\underline{C}$H).

For 3B$_1$: Color: white, yield: 84%, mp: 183–190 °C. Anal. Calc. for [$C_{32}H_{24}N_6$] (M.W: 492.21 g/mol): C, 78.03; H, 4.91; N, 17.06; found: C, 78.01; H, 4.89; N, 17.09. ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm); 6.40 (s, 4H, N-$C\underline{H}_2$); 6.69–6.67 (m, 2H, Ar-C$\underline{H}$); 7.00-7.03 (m, 2H, Ar-C$\underline{H}$); 7.21–7.37 (m, 8H, Ar-C$\underline{H}$); 7.79–7.84(m, 2H, Ar-C$\underline{H}$); 7.91 (d, J = 7.6 Hz, 2H, Ar-C$\underline{H}$); 8.47–8.50 (t, J = 6.2 Hz, 4H, Ar-C$\underline{H}$). ^{13}C NMR (100.56 MHz, $CDCl_3$, δ ppm): 47.1 (N-$\underline{C}H_2$); 111.0; 120,5; 123,3; 124.0; 124.2; 125.0; 126.5; 127.8; 134.5; 137.1; 137.2; 142.9; 148.7; 150.1; 150.6 (Ar-$\underline{C}$H).

For 3B$_2$: Color: white, yield: 87%, mp: 214–220 °C. Anal. Calc. for [$C_{35}H_{30}N_6$] (MW: 534.25 g/mol): C, 78.63; H, 5.66; N, 15.72; found: C, 77.05; H, 5.93; N, 15.01. ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm); 2.02 (s, 3H, $C\underline{H}_3$); 2.60 (s, 6H, $C\underline{H}_3$); 6.22 (s, 4H, N-$C\underline{H}_2$); 6.55 (d, J= 5.2 Hz, 2H, Ar-C$\underline{H}$); 6.87–6.93 (m, *3*H, Ar-C$\underline{H}$); 7.16–7.20 (t, J= 8.2 Hz, 2H, Ar-C$\underline{H}$); 7.31–7.35 (m, 2H, Ar-C$\underline{H}$); 7.74–7.75 (m, 2H, Ar-C$\underline{H}$); 7.82–7.86 (m, 2H, Ar-C$\underline{H}$); 8.36–8.39 (m, 2H, Ar-C$\underline{H}$); 8.65–8.67 (m, *2*H, Ar-C$\underline{H}$). ^{13}C NMR (100.56 MHz, $CDCl_3$, δ ppm): 16.1 and 20.8 ($\underline{C}H_3$); 46.5 (N-$\underline{C}H_2$); 111.9; 120,5; 122,5; 123.6; 124.0; 125.6; 128.4; 129.2; 131.6; 131.7; 136.7; 137.2; 137.4; 137.7; 138.0; 143.0; 148.6; 150.7; 151.0 (Ar-$\underline{C}$H).

For 3B$_3$: Color: white, yield: 70%, mp: 185–200 °C. Anal. Calc. for [$C_{36}H_{32}N_6$] (MW: 548.27 g/mol): C, 78.80; H, 5.88; N, 15.32; found: C, 78.97; H, 5.76; N, 15.27. ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm); 2.18 (s, 12H, ($C\underline{H}_3$)$_4$); 6.33 (s, 4H, N-$C\underline{H}_2$); 6.58 (d, J= 8.4 Hz, 2H, Ar-C$\underline{H}$); 6.95–6.99 (m, 2H, Ar-C$\underline{H}$); 7.20–7.26 (m, 4H, Ar-C$\underline{H}$); 7.81 (d, J= 8.0 Hz, 2H, Ar-C$\underline{H}$); 7.87–7.91 (t, J= 7.8 Hz, 2H, Ar-C$\underline{H}$); 8.41–8.44 (t, J= 8.8 Hz, 2H, Ar-C$\underline{H}$); 8.74 (d, J= 4.0 Hz, 2H, Ar-C$\underline{H}$). ^{13}C NMR (100.56 MHz, $CDCl_3$, δ ppm): 16.1; 17.2 and 20.8 ($\underline{C}H_3$); 47.6 and 49.3 (N-$\underline{C}H_2$); 112.3; 120.0; 122.7; 123.8; 125.0; 125.7; 132.0; 134.2; 135.8; 138.2; 143.1; 144.6; 149.2; 150.1; 151.2 (Ar-$\underline{C}$H).

For 4C$_1$: Color: white, yield: 84%, mp: 242–245 °C. Anal. Calc. for [$C_{48}H_{39}N_9$] (MW: 741.33 g/mol): C, 77.71; H, 5.30; N, 16.99; found: C, 77.69; H, 5.36; N, 16.95. ^{1}H NMR (400 MHz, $CDCl_3$, δ ppm); 2.26 (s, 9H, ($C\underline{H}_3$)$_3$); 6.31 (s, 6H, N-$C\underline{H}_2$); 6.45 (d, J = 8.4 Hz, 2H, Ar-C$\underline{H}$); 6.77 (d, J = 7.6 Hz, 2H, Ar-C$\underline{H}$); 7.17–7.36 (m, 7H, Ar-C$\underline{H}$); 7.46–7.52 (m, 1H, Ar-C$\underline{H}$); 8.37–8.44 (m, 6H, Ar-C$\underline{H}$); 8.63 (d, J = 4.4 Hz, 3H, Ar-C$\underline{H}$); 8.69 (d, J = 4.8 Hz, 3H, Ar-C$\underline{H}$). ^{13}C NMR (100.56, MHz, $CDCl_3$, δ ppm): 17.3 ($\underline{C}H_3$); 47.1 (N-$\underline{C}H_2$); 111.9; 120.4; 122.5; 123.8; 124.0; 125.6; 132.7; 137.3; 138.5; 143.1; 148.6 (Ar-$\underline{C}$H).

3.4. General procedure for the synthesis of the Pd(II) complexes

The complexes were synthesized as follows:

In a two-necked, 50-mL round-bottom flask equipped with a blanket of nitrogen (N_2) was placed 15 mL of anhydrous tetrahydrofuran (THF) at room temperature for each metal complex synthesis. The solution of 1.0 mmol of each ligand in 7 mL of anhydrous tetrahydrofuran (THF) was stirred for 20 min. Then $PdCl_2(CNMe)_2$ (1.0 mmol for complex **5A$_1$**, 1.0 mmol for complex **5A$_2$**, 2.0 mmol for complex **6B$_1$**, 2.0 mmol for complex **6B$_2$**, 2.0 mmol for complex **6B$_3$**, and 3.0 mmol for complex **7C$_1$**) was added to the ligand solution. Once the metal salt was added, the color of reaction mixtures immediately turned to yellowish. The reaction mixtures were stirred at 60 °C for 2 h. Then 25 mL of n-hexane was added to mixtures for precipitation and the crude product was filtered off, washed with THF, and filtered off again to remove unreacted ligands. The resulting solids were redissolved in CH_2Cl_2 (5 mL) and then precipitated with diethyl ether (10 mL) to give the clear crystal solid.

For 5A$_1$: Color: orange, yield: 79%, mp: 288–289 °C. Anal. Calc. for [$C_{22}H_{21}Cl_2N_3Pd$] (MW: 505.02 g/mol): C, 52.35; H, 4.19; N, 8.32; found: C = 52.01; H = 4.57; N = 7.83. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.07 (s, 6H, *o*-(C$\underline{H}_3$)$_2$); 2.25 (s,3H, *p*-C$\underline{H}_3$); 6.04 (s, 2H, N-C$\underline{H}_2$); 6.67 (d, J= 8 Hz; 1H, Ar-C$\underline{H}$); 6.94 (s, 2H, Ar-C$\underline{H}$); 7.20–7.17 (t, J = 7.4 Hz; 1H, Ar-C$\underline{H}$); 7.30–7.26 (t, J= 7.8 Hz, 1H, Ar-C$\underline{H}$); 7.83–7.80 (t,J = 6.6 Hz, 1H, Ar-C$\underline{H}$); 8.35–8.30 (m, 1H, Ar-C$\underline{H}$); 8.58 (d, J =8.4 Hz, 1H, Ar-C$\underline{H}$); 8.87 (d,J = 8.0 Hz, 1H, Ar-C$\underline{H}$); 9.26 (d,J = 5.2 Hz, 1H, Ar-C$\underline{H}$); ^{13}C NMR (100.56 MHz, DMSO-d_6, δ ppm): 17.8 and 21.3 (C$\underline{H}_3$); 56.6 (N-C$\underline{H}_2$); 106.5; 112.0; 119.1; 122.5; 124.2; 124.6; 128.5; 132.7; 134.8; 135.9 and 137.6 (Ar-C$\underline{H}$).

For 5A$_2$: Color: yellow, yield: 82%, mp: 268–270 °C. Anal. Calc. for [$C_{24}H_{25}Cl_2N_3Pd$] (MW: 533.05 g/mol): C, 54.10; H, 4.73; N, 7.89; found: C, 54.29; H, 5.14; N, 7.01. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm): 2.09 (s, 6H, *o*-(C$\underline{H}_3$)$_2$); 2.18 (s,6H, *m*-(C$\underline{H}_3$)$_2$); 2.25 (s, 3H,*p*-C$\underline{H}_3$); 6.05 (s, 2H, N-C$\underline{H}_2$); 6.35 (d, J = 8 Hz, 1H, Ar-C$\underline{H}$); 7.06–7.10 (t, J = 8.0 Hz, 1H, Ar-C$\underline{H}$); 7.23–7.27 (t, J = 7.8 Hz, 1H, Ar-C$\underline{H}$); 7.82–7.86 (t,J= 6.6 Hz, 1H, Ar-C$\underline{H}$); 8.34–8.38 (m, 1H, Ar-C$\underline{H}$); 8.73 (d, J = 8.8 Hz, 1H, Ar-C$\underline{H}$); 8.90 (d, J = 8.8 Hz, 1H, Ar-C$\underline{H}$); 9.31 (d, J = 5.6 Hz, 1H, Ar-C$\underline{H}$); ^{13}C NMR (100.56 MHz, DMSO-d_6, δ ppm): 17.6; 17.7 and 17.9 (C$\underline{H}_3$); 55.8 (N-C$\underline{H}_2$); 100.27; 102.23; 105.35; 109.40; 119.43; 127.55; 133.56; 134.47; 144.53; 148.58; 152.37 and 155.20 (Ar-C$\underline{H}$).

For 6B$_1$: Color: yellow, yield: 86%, mp: >300 °C. Anal. Calc. for [$C_{32}H_{24}Cl_4N_6Pd_2$] (MW: 844.89 g/mol): C, 45.36; H, 2.86; N, 9.92; found: C, 45.88; H, 2.45; N, 9.07. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm); 5.72 (s, 4H, N-C$\underline{H}_2$); 6.59 (s, 2H, Ar-C$\underline{H}$); 7.08–7.10 (m, 2H, Ar-C$\underline{H}$); 7.36–7.61 (m, 4H, Ar-C$\underline{H}$); 7.71–7.84 (m, 4H, Ar-C$\underline{H}$); 8.04–7.96 (m, 2H, Ar-C$\underline{H}$); 8.40–8.32 (m, 2H, Ar-C$\underline{H}$); 8.65 (d, J = 8.8 Hz, 1H, Ar-C$\underline{H}$); 8.99 (d, J = 8.0 Hz, 1H, Ar-C$\underline{H}$); 9.06 (d, J =5.2 Hz, 1H, Ar-C$\underline{H}$); 9.28 (d, J = 5.2 Hz, 1H, Ar-C$\underline{H}$). ^{13}C NMR (100.56 MHz, DMSO-d_6, δ ppm): 45.2 and 45.6 (N-C$\underline{H}_2$); 110.8; 120.1; 122,5; 123.8; 124.0; 124.9; 125.7; 126.2; 134.8; 136.3; 137.8; 142.7; 149.5; 151.2 (Ar-C$\underline{H}$).

For 6B$_2$: Color: yellow, yield: 87%, mp: >300 °C. Anal. Calc. for [$C_{35}H_{30}Cl_4N_6Pd_2$] (MW: 886.94 g/mol): C, 47.27; H, 3.40; N, 9.45; found: C, 46.98; H, 3.97; N, 9.62. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm); 1.92 (s, 3H, C$\underline{H}_3$); 2.23 (s, 6H, C$\underline{H}_3$); 6.15 (s, 4H, N-C$\underline{H}_2$); 6.72 (d,J= 8.4 Hz, 2H, Ar-C$\underline{H}$); 6.89–6.97 (m, *3*H, Ar-C$\underline{H}$); 7.14–7.20 (m, 2H, Ar-C$\underline{H}$); 7.51–7.57 (m, 2H, Ar-C$\underline{H}$); 7.72 (d, J= 8.4 Hz, 2H, Ar-C$\underline{H}$); 7.98–8.07 (m, 2H, Ar-C$\underline{H}$); 8.30 (d, J= 8.0 Hz, 2H, Ar-C$\underline{H}$); 8.78 (d,J= 4.8 Hz, *2*H, Ar-C$\underline{H}$). ^{13}C NMR

(100.56 MHz, DMSO-d_6, δ ppm): 16.8; 21.2 and 26.1 ($\underline{C}H_3$); 46.9 and 68.7 (N-$\underline{C}H_2$); 113.5; 121.3; 122.8; 124.5; 125.6; 126.7; 132.4; 133.9; 135.6; 138.2; 138.9; 139.1; 142.5; 148.7; 151.7 (Ar-$\underline{C}$H).

For 6B$_3$: Color: yellow, yield: 77%, mp: 242–247 °C. Anal. Calc. for [$C_{36}H_{32}Cl_4N_6Pd_2$] (MW: 900.95 g/mol): C, 46.92; H, 4.01; N, 9.58; found: C, 47.87; H, 3.57; N, 9.30. ^{1}H NMR (300 MHz, DMSO-d_6, δ ppm); 1.82 (s, 4H, C$\underline{H}_3$); 1.89 (s, 4H, C$\underline{H}_3$); 2.01 (s, 4H, C$\underline{H}_3$); 2.09 (s, 4H, C$\underline{H}_3$); 5.76 (s, 4H, N-C$\underline{H}_2$); 6.46 ($d, J =$ 9.0 Hz, 2H, Ar-C$\underline{H}$); 7.03–7.48 (m, 2H, Ar-C$\underline{H}$); 7.67–7.87 (m, 2H, Ar-C$\underline{H}$); 8.35–8.42 (m, 2H, Ar-C$\underline{H}$); 8.61 (s, 2H, Ar-C$\underline{H}$); 8.73 (s, 2H, Ar-C$\underline{H}$); 8.86 (s, 2H, Ar-C$\underline{H}$); 9.28 (s, 2H, Ar-C$\underline{H}$). ^{13}C NMR (75.48 MHz, $CDCl_3$, δ ppm): 18.7; 20.2 and 25.6 ($\underline{C}H_3$); 46.3 and 48.9 (N-$\underline{C}H_2$); 67.8; 113.6; 121.4; 124.2; 125.3; 133.7; 136.9; 143.6; 145.0; 150.5 (Ar-$\underline{C}$H).

For 7C$_1$: Color: yellow, yield: 83%, mp: 242–245 °C. Anal. Calc. for [$C_{48}H_{39}Cl_6N_9Pd_3$] (MW: 1268.86 g/mol): C, 45.26; H, 3.09; N, 9.90; found: C, 45.34; H, 3.17; N, 9.84. ^{1}H NMR (400 MHz, DMSO-d_6, δ ppm); 2.13 (s, 9H, (C$\underline{H}_3$)$_3$); 6.18 (s, 6H, N-C$\underline{H}_2$); 6.52 ($d, J =$ 8.0 Hz, 2H, Ar-C$\underline{H}$); 6.94–6.96 ($t, J =$ 8.0 Hz, 2H, Ar-C$\underline{H}$); 7.12–7.26 (m, 2H, Ar-C$\underline{H}$); 7.31–7.45 ($t, J =$ 8.0 Hz, 2H, Ar-$C\underline{H}$); 7.42–7.46 ($t, J =$ 7.6 Hz, 2H, Ar-C$\underline{H}$); 7.71–7.80 (m, 4H, Ar-C$\underline{H}$); 8.27–8.39 (m, 2H, Ar-C$\underline{H}$); 8.59–8.80 (m, 4H, Ar-C$\underline{H}$); 9.00 (d, $J =$ 5.6 Hz, 2H, Ar-C$\underline{H}$); 9.18 (d, $J =$ 4.0 Hz, 2H, Ar-C$\underline{H}$). ^{13}C NMR (100.56 MHz, DMSO-d_6, δ ppm): 17.5 ($\underline{C}H_3$); 125.1; 125.9; 127.6; 141.8 (Ar-$\underline{C}$H).

4. Conclusion

In the numerous catalyst optimization studies that have been published, the principal focus is often to test the robustness of the catalytic system as a function of the reaction conditions and substrate scope. Here, a simple method is given for the preparation of Pd(II) complexes that are coordinated by substituted PBI (mono-NN, di-NN, and tri-NN types) ligands. These complexes were found to be active catalysts for the Suzuki–Miyaura cross-coupling reactions using DMF/H_2O (4:1) as solvent. In order to find optimum conditions a series of experiments was performed with 4-bromoacetophenone and phenylbronic acid as model compounds. These simple reaction conditions allow for the cross-coupling of aryl halides with phenylbronic acid yielding biaryls in high yields. We also showed that temperature in this system has a minimal effect on the coupling itself. Efforts focused on identifying the effects of the base, water, time, and air in the coupling reactions.

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