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PALLADIUM (II) COMPLEXES CONTAINING 2-PHENYLPYRIDINE DERIVATIVES: SYNTHESIS, MOLECULAR STRUCTURES, AND CATALYTIC ACTIVITY FOR SUZUKI–MIYAURA CROSS-COUPLING REACTIONS

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The preparation and characterization of a series of new 2-phenylpyridine derivative ligands consisting of 2-(R) pyridine (R = mesityl (L1), 2,6-dimethylphenyl (L2), *o*-tolyl (L3), *m*-tolyl (L4), *p*-tolyl (L5), *o*-methoxyphenyl (L6), and *p*-methoxyphenyl (L7)) and their Pd complexes $[PdCl_2L_2]$ (L1–L7) is investigated using a combination of X-ray diffraction spectroscopy, GC-MS, and NMR. The crystal structures show that the Pd complexes adopt a square planar geometry, and the monodentate ligand is coordinated through the N donor of the pyridine ring to the Pd atom. The catalytic activities of the synthesized complexes are investigated. The square planar Pd complex *trans*-$[(2\text{-mesitylpy})_2PdCl_2)]$ shows a high efficiency in promoting Suzuki–Miyaura cross coupling in an aqueous solvent under aerobic conditions.

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INTRODUCTION

Pyridine heterocyclic compound synthesis continues to attract much attention due to its diverse applicability to various fields, including pharmaceutical and organic synthesis [1-6]. Transition metals such as Pd and copper complexes have been used successfully for the preparation of very active hypertension drugs such as Losartan and Valsartan [7-11]. The use of Pd as a catalyst for the synthesis of carbon-carbon bonds is particularly interesting due to its unique properties [12, 13]. In recent years, the use of Pd with phosphine or carbene ligands has been found to be very promising due to the high efficiency of their coupling reactions [14, 15]. Phosphorous-containing ligands are predominantly used in cross-coupling reactions; however, some drawbacks have also been recorded in their usage. Phosphine has been found to be very sensitive to both moisture and air [16]. Carbene ligands also have the disadvantage of the requirement of multiple steps in the preparation procedure, but they are more stable than phosphorus-containing ligands [17-20]. Improvements in the use of non-phosphine ligands, such as pyridine, for Pd-catalyzed cross-coupling were recently reported [21], and successes in the use of nitrogen

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chelating agents, such as porphyrin [22], diketiminate [23], and (bipyridine) pyridine compounds [24-31], have resulted in numerous advances in Pd-catalyzed cross-coupling. In the quest to synthesize a more efficient catalyst, the combination of Pd- and nitrogen-containing ligands is promising due to their stability in air, non-toxicity, and convenient handling [32].

We report herein the synthesis of a new class of Pd complexes containing 2-phenylpyridine derivatives, including 2-(R) pyridine (R = mesityl; 2,6-dimethylphenyl; *o*-tolyl; *m*-tolyl; *p*-tolyl; *o*-methoxyphenyl; *p*-methoxyphenyl) and investigate their use in a Suzuki reaction of 2-bromopyridine and 2,6-dibromopyridine with steric phenyl boronic acid in an aqueous solvent in a homogeneous catalysis system.

EXPERIMENTAL

Materials and methods. The synthesis of ligands **1**, **2**, **3**, **4**, and **6** was performed under N_2 using Schlenk techniques with $[Pd(PPh_3)_4]$ as a catalyst [33], whereas the synthesis of ligands **5** and **7** was performed under aerobic conditions, and a $[Pd(OAc)_2]$ catalyst was used [34]. Reagents for the reactions, phenylboronic acid, all solvents and pyridine halides were procured from Aldrich. $[PdCl_2(CH_3CN)_2]$, bis(acetonitrile) di-chloroPd(II), $[Pd(PPh_3)_4]$, and tetrakis (triphenylphosphine) Pd(0) were prepared according to protocols described in previous studies [35].

Thin layer chromatography (TLC) was performed on silica gel GF254. Additionally, 1H (600 MHz) and ^{13}C (151 MHz) NMR spectra were acquired on a Bruker AV-600 spectrometer equipped with a 5 mm H, broadband inverse (BBI) probe to observe 1H and a cryo dual probe optimized for ^{13}C detection. All NMR spectra were recorded at room temperature. NMR peaks were assigned by a MestreNova 9.1 NMR processing program (see http://mestrelab.com/) and ACD/NMR Processor Academic Edition (see http://acdlabs.com/). GC-MS analyses were performed on a Shimadzu Series II gas chromatograph equipped with a 5971 mass selective detector. A fused silica capillary column (10 m or 12 m cross-linked 5% phenylmethylsilicone) was used, and the oven temperature was ramped from 50 °C to 280 °C at a rate of 20 °C/min. Ultrahigh purity grade helium was used as the carrier gas.

Synthesis of 2-mesitylpyridine (L1). 2-Bromopyridine (1 g, 1 equiv, 6.33 mmol), mesitylboronic acid (1.29 g, 1.2 equiv, 7.86 mmol), K_2CO_3 (1.75 g, 2 equiv, 12.66 mmol), and $Pd(PPh_3)_4$ (0.22 g, 5 mol%) were added to a round bottom flask containing toluene/ethanol/water (120 mL/15 mL/10 mL) under an N_2 atmosphere using Schlenk techniques. The reaction lasted for 48 h at 120 °C. The mixture was then cooled and diluted with ethylacetate and H_2O. Magnesium sulphate ($MgSO_4$) was used to remove any water present. After filtration, the mixture was concentrated using a rotary evaporator. Column chromatography was used for purification of the product. All volatiles were removed, and a yellow oily product with a yield of 85% was obtained (1.06 g, 5.37 mmol) with the following properties: ^1H NMR (600 MHz, $CDCl_3$) δ 8.69 (ddt, J = 5.0, 1.9, 1.0 Hz, 1H), 7.73 (td, J = 7.6, 1.8 Hz, 1H), 7.23 (ddd, J = 7.7, 4.9, 1.2 Hz, 1H), 7.21 (dt, J = 7.7, 1.1 Hz, 1H), 6.92 (d, J = 1.2 Hz, 2H), 2.31 (s, 3H), 2.00 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$), δ 160.10, 149.70, 137.81, 137.52, 136.36, 135.77, 128.34, 124.06, 121.59, 21.20, 18.3; MS (EI): *m*/*z* 196.2 $[M]^+$, 181.2 $[M–Me]^+$.

Synthesis of 2-(2,6-dimethylphenyl)pyridine (L2). 2-Bromopyridine (1 g, 1 equiv, 6.33 mmol), 2,6-dimethyl-phenylboronic acid (1.14 g, 1.2 equiv, 7.60 mmol), K_2CO_3 (1.75 g, 2 equiv, 12.66 mmol), and $Pd(PPh_3)_4$ (0.370 g, 5 mol%) were added to a round bottom flask containing toluene/ethanol/water (120 mL/15 mL/10 mL), and similar procedures as in **L1** were performed. A liquid product was obtained with a yield of 44% (0.51 g, 2.78 mmol) with the following properties: ^1H NMR (600 MHz, $CDCl_3$) δ 8.78 (ddd, J = 4.9, 1.9, 1.0 Hz, 1H), 7.81 (td, J = 7.7, 1.9 Hz, 1H), 7.31 (ddd, J = 7.6, 4.9, 1.1 Hz, 1H), 7.29 (dt, J = 7.7, 1.1 Hz, 1H), 7.25 (d, J = 1.0 Hz, 1H), 7.18-7.16 (m, 1H), 7.15 (q, J = 0.7 Hz, 1H), 2.10 (d, J = 0.8 Hz, 6H).^{13}C NMR (151 MHz, $CDCl_3$), δ 160.02, 149.77, 140.56, 136.36, 135.85, 127.94, 127.60, 124.54, 121.74, 20.29; MS (EI): *m*/*z* 182.2 $[M]^+$, 167.2 $[M–Me]^+$.

Synthesis of 2-*o*-tolylpyridine (L3). 2-Bromopyridine (1 g, 1 equiv, 6.33 mmol), *o*-tolylboronic acid (1.03 g, 1.2 equiv, 7.58 mmol), K_2CO_3 (1.75 g, 2 equiv, 12.66 mmol), and $Pd(PPh_3)_4$ (0.37 g, 5 mol%) were added to a round bottom flask containing toluene/ethanol/water (120 mL/15 mL/10 mL), and similar procedures as in **L1** were performed. A yellow oily product was obtained with a yield of 78% (0.84 g, 4.96 mmol) with the following properties: ^1H NMR (600 MHz,

$CDCl_3$) δ 8.70 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 1H), 7.80 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.76 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.69 (ddd, *J* = 8.0, 7.5, 1.9 Hz, 1H), 7.37 (ddd, *J* = 8.3, 7.4, 1.8 Hz, 1H), 7.20 (ddd, *J* = 7.4, 4.9, 1.2 Hz, 1H), 7.08 (td, *J* = 7.5, 1.1 Hz, 1H), 7.00 (dd, *J* = 8.3, 1.0 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$), δ 157.05, 156.22, 149.51, 135.75, 131.25, 129.97, 129.26, 125.22, 121.75, 121.17, 111.45, 55.98; MS (EI): *m*/*z* 168.2 $[M]^+$, 167.1 $[M–H]^+$.

Synthesis of 2-*m*-tolylpyridine (L4). 2-Bromopyridine (1 g, 1 equiv, 6.33 mmol), *m*-tolylboronic acid (1.03 g, 1.2 equiv, 7.58 mmol), K_2CO_3 (1.75 g, 2 equiv, 12.66 mmol), and $Pd(PPh_3)_4$ (0.37 g, 5 mol%) were added to a round bottom flask containing toluene/ethanol/water (120 mL/15 mL/10 mL), and similar procedures as in **L1** were performed. A yellow oily product was obtained with a yield of 83% (0.97 g, 5.73 mmol) with the following properties: ^{1}H NMR (600 MHz, $CDCl_3$) δ ^{13}C NMR (151 MHz, $CDCl_3$), δ 157.54, 149.43, 139.16, 138.29, 136.71, 129.64, 128.54, 127.59, 123.95, 121.94, 120.67, 21.40; MS (EI): *m*/*z* 169.2 $[M]^+$, 168.2 $[M–H]^+$.

Synthesis of 2-(*p*-tolyl)pyridine (L5). 2-Bromopyridine (0.5 g, 1 equiv, 3.16 mmol), *p*-tolylpboronic acid (0.52 g, 1.2 equiv, 3.82 mmol), $K_3PO_4{\cdot}3H_2O$ (1.69 g, 2 equiv, 6.35 mmol), and Pd(II) acetate (0.02 g, 3 mol%), which was used as a catalyst, were mixed in a round bottom flask containing isopropanol:water (40:30 mL). The reaction lasted for 48 h at 120 °C. The mixture was stirred continuously using a magnetic stirrer, and both TLC and GC were performed. The mixture was cooled and diluted with ethylacetate and H_2O. Magnesium sulphate ($MgSO_4$) was used to remove any water present. After filtration, the mixture was concentrated using a rotary evaporator. Column chromatography was performed to purify the product. All volatiles were removed, and a yellow oily product with a yield of 55% was obtained (0.30 g, 1.77 mmol) with the following properties: ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.67 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H), 7.9-7.88 (m, 2H), 7.74-7.68 (m, 2H), 7.29-7.27 (m, 2H), 7.19 (ddd, *J* = 7.0, 4.8, 1.6 Hz, 1H), 2.41 (s. 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.58, 149.67, 139.02, 136.80, 136.69, 129.50, 126.90, 121.94, 120.44, 21.33; MS (EI): *m*/*z* 169.2 $[M]^+$, 168.2 $[M–H]^+$.

Synthesis of 2-(2-methoxyphenyl)pyridine (L6). 2-Bromopyridine (1 g, 1 equiv, 6.33 mmol), 2-(2-methoxyphenyl) boronic acid (1.20 g, 1.2 equiv, 7.90 mmol), K_2CO_3 (1.75 g, 2 equiv, 12.66 mmol), and $Pd(PPh_3)_4$ (0.370 g, 5 mol%) were added into a round bottom flask containing toluene/ethanol/water (120 mL/15 mL/10 mL), and similar procedures as in **L1** were performed. A yellow oily product was obtained with a yield of 46% (0.49 g, 2.64 mmol) and the following properties: ^{1}H NMR (600 MHz, $CDCl_3$ δ 8.69 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H), 7.74 (td, *J* = 7.7, 1.8 Hz, 1H), 7.42-7.37 (m, 2H), 7.32-7.23 (m, 4H), 2.36 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$), δ 160.12, 149.30, 140.56, 136.26, 135.91, 130.80, 129.74, 128.35, 126.03, 124.16, 121.70, 20.43; MS (EI): *m*/*z* 184.2 $[M]^+$, 154.1 $[M–OMe]^+$.

Synthesis of 2-(4-methoxyphenyl)pyridine (L7). 2-Bromopyridine (1 g, 1 equiv, 6.33 mmol), (*p*-methoxyphenyl) boronic acid (1.15 g, 1.2 equiv, 7.57 mmol), $K_3PO_4{\cdot}3H_2O$ (3.371 g, 2 equiv, 12.66 mmol) and $[Pd(OAc)_2]$ (0.04 g, 3 mol%), which was used as a catalyst, were mixed in a round bottom flask containing isopropanol:water (40:30 mL), using similar procedures as in **L1**. A white solid product was obtained upon cooling with a yield of 58% (0.37 g, 1.99 mmol) and the following properties: proton NMR (600 MHz, Chloroform-d), δ 8.65(ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H), 7.96-7.93 (m, 2H), 7.71 (ddd, *J* = 8.0, 7.3, 1.9 Hz, 1H), 7.67 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.17 (ddd, *J* = 7.3, 4.8, 1.2 Hz, 1H), 7.05-6.94 (m, 2H), 3.87 (s, 3H). ^{13}C NMR (151 MHz, Chloroform-d), δ 160.68, 157.33, 149.69, 136.85, 132.16, 128.28, 121.56, 119.95, 114.24, 55.61. MS (EI): *m*/*z* 185.1 $[M]^+$, 170.1 $[M–Me]^+$. M.P. (53.6-54.8 °C).

Synthesis of $PdCl_2(L1)_2$ (1). Sample **L1** (0.11 g, 2.2 equiv, 0.56 mmol) and $[PdCl_2(PhCN)_2]$ (1 equiv, 0.1 g, 2.60 mmol) were dissolved with CH_2Cl_2 (30 mL), stirred for 24 h, and then cooled. Then, petroleum ether was added to promote precipitation. After 15 minutes, a yellow precipitate was filtered with petroleum ether. A product consisting of a yellow complex was obtained with a 72% yield (0.11 g, 0.19 mmol) and the following properties: ^{1}H NMR (600 MHz, DMSO-d_6) δ 8.61 (ddd, *J* = 4.9, 1.9, 1.0 Hz, 2H), 7.81 (td, *J* = 7.7, 1.9 Hz, 2H), 7.30 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 4H), 7.21 (dt, *J* = 7.7, 1.2 Hz, 2H), 6.96 (s, 2H), 6.88 (s, 4H), 2.23 (s, 6H), 1.87 (s, 12H).13C NMR (151 MHz, DMSO-d_6) δ 159.09, 149.43, 139.70, 137.86, 136.52, 134.97, 128.00, 124.62, 121.91, 20.71, 19.88.

Complexes **2**-**7** were prepared in a similar way to complex **1**, and their yields and data analysis results are reported in the supporting material.

TABLE 1. Selected Bond Lengths for Complex Molecule **1**

Bond	Length, Å	Bond	Length, Å
Pd1—Cl2	2.310(4)	Pd2—Cl4	2.295(4)
Pd1—Cl1	2.305(4)	Pd2—Cl3	2.295(4)
Pd1—N2	2.034(12)	Pd2—N4	2.050(10)
Pd1—N1	2.024(11)	Pd2—N3	2.048(11)
N2—C15	1.33(2)	N4—C43	1.319(19)
N2—C19	1.36(2)	N4—C47	1.355(17)
N1—C5	1.363(19)	N3—C29	1.330(19)
N1—C1	1.34(2)	N3—C33	1.358(17)

X-ray analysis. Suitable crystals for all compounds were selected under a microscope and mounted on an Agilent SuperNova (dual source) Agilent Technologies diffractometer equipped with graphite-monochromatic Cu/MoK_α radiation for data collection. The samples were fixed on a glass tip on a magnetic base copper rod using glue. Data collection was accomplished using the CrysAlisPro software [36] at 296 K under Mo (for compound **1**) and Cu (for compounds **2-5**) K_α radiation. The crystallographic parameters for both molecules are given in Table 1. The structure of the solution was determined using SHELXS-97 [37] and refined by full-matrix least-squares methods of F^2 using SHELXL-97 [37] with an in-built X-Seed [38]. All non-hydrogen atoms were refined anisotropically by full-matrix least squares methods [37]. The C–H hydrogen atoms were positioned geometrically and treated as riding atoms, where C–H = 0.93 Å with $U_{iso}(H) = 1.2U_{eq}(C)$ for aromatic carbon atoms and C–H = 0.96 Å with $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl carbon atoms. The figures were generated using Olex2 [39]. Crystals **1**, **2**, **3**, **4**, and **5** were grown by slow evaporation of the dichloromethane solution of the complexes at room temperature. The CCDC numbers for compounds **1-5** are 1892837-1892841, respectively.

RESULTS AND DISCUSSION

NMR spectra of the complexes tended to be invisible, except for complex **5**, when using $CDCl_3$ as a solvent due to the lack of solubility. To acquire the NMR spectra, the remaining complexes were dissolved in DMSO-d_6 using a heat gun.

X-ray crystallographic analysis successfully detected single crystals for complexes **1-5**. The crystals were obtained by slow evaporation of the CH_2Cl_2 solution from the complexes at room temperature.

Complex **1** was crystalized in a monoclinic crystal system as two independent molecules, *A* (C1–C28) and *B* (C29–C56), per unit cell. In both molecules, the Pd metal adopted a square planar geometry, and ligands were in the *trans* position. The torsion angles between pyridine and the aromatic rings in molecule A were 77.03(5)° and 37.23(6)° and 74.56(5)° and 39.93(5)° in molecule *B*. Both molecules used the intermolecular hydrogen bonding to generate inversion dimers through the C–H…Cl type interaction (Figs. 1, 2).

The torsion angles between the pyridine and rings in each molecule were 59.12(2)°, 78.42(1)°, 45.19(2)° and 39.48(3)° for molecules **2**, **3**, **4** and **5**, respectively (Fig. 3).

Catalytic testing. To test the catalytic activities of complexes **1**-**7** in the coupling reaction, 2,6-dibromopyridine (**1a**) and *o*-tolylpyridine (**2a**) were chosen as substrates for the model reaction. Complex **1** generally worked well at 0.3 mol%, although di-coupling with *o*-tolylboronic acid was steric (94.52%), and an excellent yield was obtained using a mol% greater than 1 (entry 1), as shown in Table 2. Product **3a** with a high yield (99%) was obtained with methanol (entry 1). However, for nonpolar 1,4 dioxane, a low yield (50%) was obtained (entry 2), and toluene showed poor activity (11%) (entry 3). Notably, no coupling activity was observed in water (entry 4). From the aforementioned data, we can conclude that the solvent system plays a significant role in the solubility of the reagents, aiding entry into the catalytic cycle. For the purpose of this study, methanol was used because it is inexpensive, readily available and has the highest efficiency.

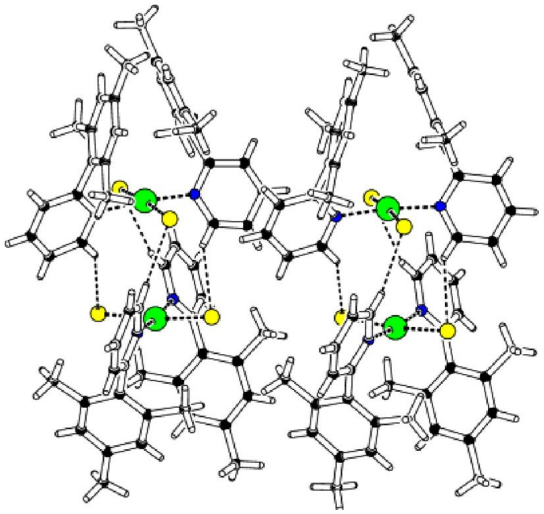


Fig. 1. View showing intermolecular hydrogen bonding (dashed lines).

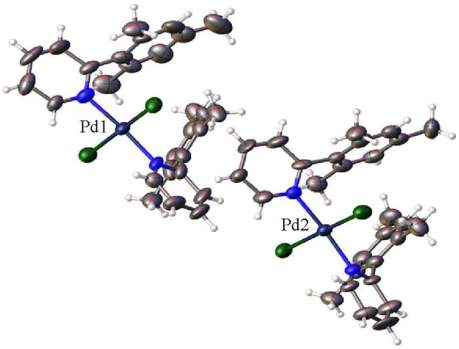


Fig. 2. ORTEP diagram for complex **1**.

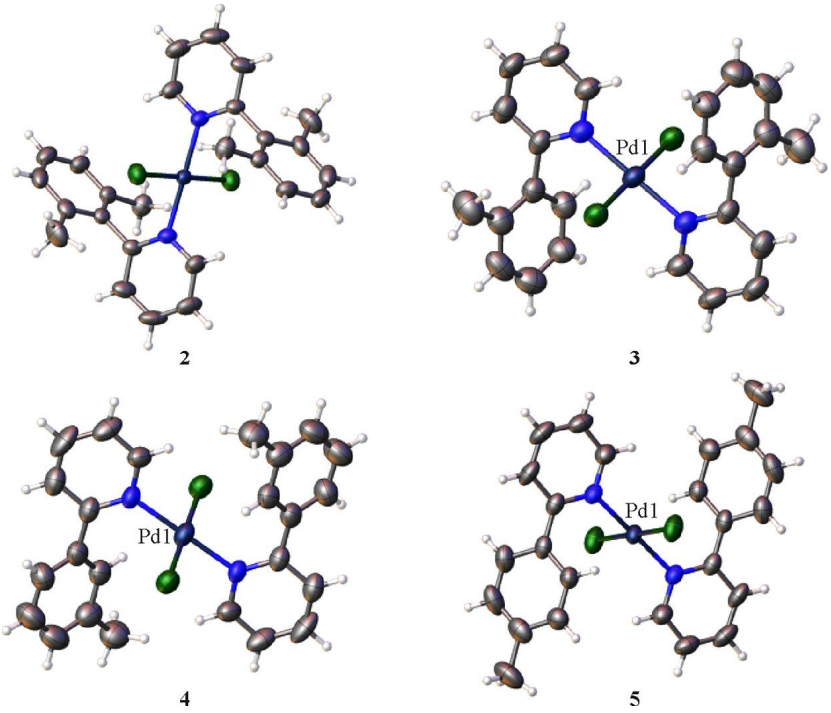
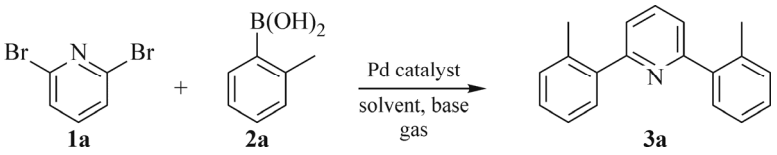


Fig. 3. ORTEP diagram of complexes **2**, **3**, **4**, and **5**.

TABLE 2. Suzuki–Miyaura Coupling of 2,6-Dibromopyridine[a]



1a **2a** **3a**

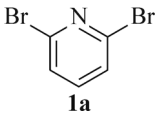
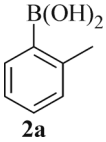
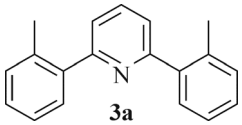
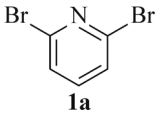
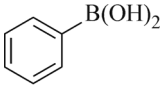
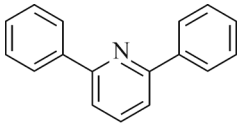
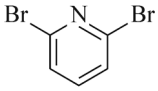
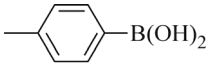
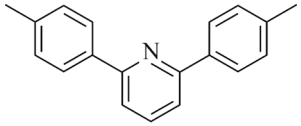
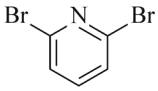
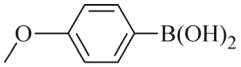
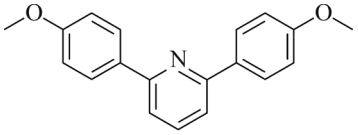
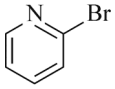
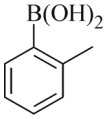
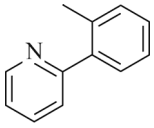
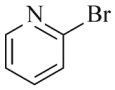
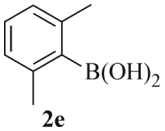
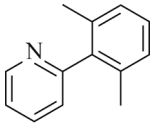
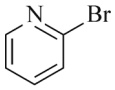
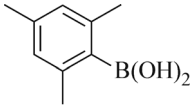
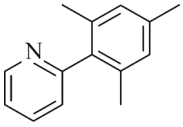
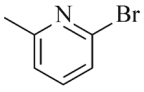
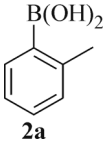
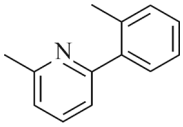
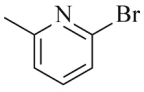
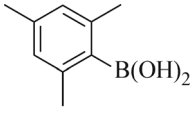
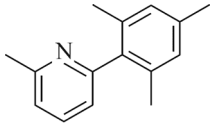
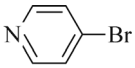
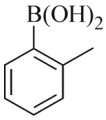
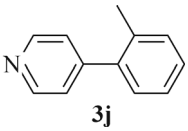
Entry	Catalyst	Solvent [b]	Time, h	Yield, % [c]
1	**1**	MeOH : H_2O	1	99
1	**1**	MeOH : H_2O	1	99 (1 mol % of Pd catalyst)
1	**1**	MeOH : H_2O	1	95 (0.3 mol % of Pd catalyst)
2	**1**	1,4-dioxane : H_2O	16	50
3	**1**	Toluene : H_2O	16	11
4	**1**	H_2O	16	0
5	**2**	MeOH : H_2O	1	98
6	**3**	MeOH : H_2O	16	63
7	**4**	MeOH : H_2O	16	46
8	**5**	MeOH : H_2O	16	53
9	**6**	MeOH : H_2O	16	97
10	**7**	MeOH : H_2O	16	51
11	**1**	MeOH : H_2O	16	97 (Using K_2CO_3)
12	**1**	MeOH : H_2O	16	87 (Using NaOH)
13	**1**	MeOH : H_2O	1	86 (Using Cs_2CO_3)
14	**1**	MeOH : H_2O	16	85 (Under argon)
15	**1**	MeOH : H_2O	16	76 (Under N_2)

[a] General conditions: 3 mol % Pd catalyst, 1.00 mmol of **1a**, 2.20 mmol of **2b**, 2.00 mmol of $K_3PO_43H_2O$, aerobic conditions.
[b] The ratio of solvent to water = 5:1.
[c] Yield isolated after TLC.

Under optimized conditions and using methanol as a solvent, the best result for the reaction was obtained when complex **1** was used. A yield of 99% of **3a** was recovered (entry 1). Complex **2**, which contains **L2** as a ligand, gave a high yield of 98% (entry 5). However, a decrease in the coupling product to 63% was observed when complex **3** was used (entry 6). Complex **4** having **L4** as a ligand, showed the lowest yield of the coupling product: only 46% (entry 7). Complex **5** was also found to be not suitable for this reaction; a yield of only 53% was obtained (entry 8). Interestingly, complex **6** containing **L6** as a ligand gave a very good isolated yield of 97% but after 16 h (entry 9). The trends of the reactions examined above supported the theory that hindrance of electron-rich ligands is more favorable for oxidative addition of Pd(0) with aryl halides [40].

The presence of a base is important for the *trans*-metalation stage to occur between Ar–Pd–*X* and incoming acids [41]. Of the bases tested, only $K_3PO_4{\cdot}3H_2O$ produced a high yield of 99% (entry 1), and K_2CO_3 gave a less yield of 97% (entry 11). NaOH, a good base for Suzuki cross-coupling, gave a yield of 87% (Table 2, entry 12). Another base Cs_2CO_3 gave the lowest yield but was considered to be relatively effective (Table 2, entry 13). Interestingly, the presence of gas influenced the coupling reaction. A large amount of the coupling product (99%) was obtained when the reaction ran under aerobic

TABLE 3. Coupling of Pyridyl Halides

Entry	Pyridylbromide	Boronic acid	Product	Time, h	Yield,% [b]
1	 **1a**	 **2a**	 **3a**	1	99
2	 **1a**	 **2b**	 **3b**	1	99
3	 **1a**	 **2c**	 **3c**	1	99
4	 **1a**	 **2d**	 **3d**	1	85
5	 **1b**	 **2a**	 **3e**	2	63
6	 **1b**	 **2e**	 **3f**	16	43
7	 **1b**	 **2f**	 **3g**	16	49
8	 **1c**	 **2a**	 **3h**	2	85
9	 **1c**	 **2f**	 **3i**	2	22
10	 **1d**	 **2a**	 **3j**	2	64

[a] Conditions: 2.2 mmol boronic acid coupling with 1 mmol of 2,6-dibromopyridine and 1.2 mmol boronic acid coupling with the derivatives of 1 mmol monobromopyridine; 2 equiv of $K_3PO_4 \cdot 3H_2O$, 3 mol% of catalyst 1, in MeOH:H_2O (6:1, 36 mL), 80 °C.
[b] Isolated yield.

conditions after 1 h (entry 1). However, a low yield was obtained when the reaction was conducted under argon (85%) (entry 14) and nitrogen (76%) (entry 15) 6%.

Scope of the catalytic activity of complex 1 in Suzuki coupling. Based on the catalytic efficiency of each complex in the reaction and analysis of their structure, complex **1** was chosen for the further study. Complex **1** generally worked well for di-coupling, such as when using simple substrates **1a** and **2b** to produce **3b** (99%) (Table 3, entry 2). An excellent yield of **3a** was obtained (99%) even though di-coupling substrate **2a** was more steric than **2b** (Table 3, entry 1). Substrates **1a** and **2c** produced an excellent yield of di-coupling product **3c** (99%) (Table 3, entry 3), and this reaction was more effective than electronically activated aryl heterocyclics such as **2d**, which produced an 85% yield of di-coupling product **3d** (Table 3, entry 4).

Substrate **2a** coupled with **1b** to produce a moderate yield of **3e** (63%) (Table 3, entry 5), but steric hindered substrates such as **2e** and **2f** coupled with **1b** and produced coupling products of **3f** and **3g** (43% and 49%) (Table 3, entries 6 and 7). Consistent with the previously described example regarding the effect of steric substrates, coupling of **1c** and **2a** produced a high yield of product **3h** (85% (Table 3, entry 8) but hindered substrates such as **2f** in performing coupling reactions with **1c**, resulting in a low yield of product **3i** (22%) (Table 3, entry 9). These findings imply that a steric hindrance affects the yield of coupling reactions. In addition, coupling product **3j** produced a moderate yield (64%) in coupling with substrates **1d** and **2a** (Table 3, entry 10). Interestingly, after comparing the di- and mono-coupling reactions according to the obtained yield, di-coupling of substrate **1a** with **2a** (Table 3, entry 1) showed a very high yield of **3a** (99%), and the mono-coupling of **1b** gave similar results to boronic acid and **2a** when coupling with product **3e** (63%) (Table 3, entry 5). This is not unusual because a greater electron withdrawal of halide, i.e., Br on pyridyl makes oxidative addition easier [42]. As a result, 2,6-dibromopyridine is more favorable for oxidative addition than 2-bromopyridine in the catalytic cyclic process.

CONCLUSIONS

Stable and efficient complexes were prepared, characterized, and applied for the Suzuki coupling reaction of both di- and monobromo pyridine with various types of phenylboronic acid to obtain a high product yield. Crystal structures of the catalysts show a square planar geometry around Pd atoms with monodentate ligand coordination to Pd using a nitrogen donor atom of the pyridine ring. The square planar Pd complex *trans*-$[(2\text{-MesPy})_2 \cdot Pd]Cl_2$ is highly efficient at promoting the Suzuki–Miyaura cross-coupling reaction in an aqueous solvent under oxygen, and the complex is stable in the air. Therefore, 2-mesitylpyridine, as a result of its effectiveness in the coupling reaction, can serve as alternative to phosphine ligands.

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CONFLICT OF INTERESTS

The authors declare that they have no conflict of interests.

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