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Synthesis, characterization, and applications of novel di-2-pyridyl imine ligands

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ABSTRACT

Two novel di-2-pyridyl imines, 2,4,6-trimethyl-(di-2-pyridylmethylene)aniline (**1**) and 2,6-di-isopropyl-(di-2-pyridylmethylene)aniline (**2**), were prepared through condensation reactions between 2,2′-dipyridyl ketone and 2,4,6-trimethylaniline and 2,6-di-isopropylaniline. They reacted readily with bis(benzonitrile)dichloropalladium(II) to afford palladium imine complexes. The crystal structure of the palladium complex (**3**) bearing the 2,4,6-trimethyl-(di-2-pyridylmethylene)aniline ligand revealed coordination of a pyridyl group and an imine group to the metal center. The novel ligands were successfully employed in the Suzuki coupling reaction of *p*-bromoanisole and phenylboronic acid.

Palladium-catalyzed Suzuki cross-coupling reaction of an aryl halide and an arylboronic acid is a powerful and versatile tool in organic synthesis [1–4]. The most commonly used ancillary ligands for the palladium catalyst are bulky tertiary phosphines. However, some phosphines are air-sensitive and require air-free handling in order to avoid ligand oxidation. Recently, alternative ligands such as *N*-heterocyclic carbenes (NHCs) [5–8], as well as ligand free systems [9–12], have been employed in the coupling reactions. Nitrogen ligands, such as amines [13], diazabutadienes [14], and salicylaldimines [15], have attracted considerable interest due to their stability and excellent activity. Unsymmetrical iminopyridine ligands containing one imino group and one pyridyl group have been extensively investigated and successfully employed recently in catalytic transformations including olefin polymerization and oligomerization [16–20], alkyne dimerization and cyclotrimerization [21–24], hydroboration and aromatic C–H borylation [25,26], hydrogenation of unsaturated hydrocarbons [27], and pyridine formation [28], and have been evaluated as potential anti-cancer agents [29]. In comparison, the chemistry of iminopyridine ligands containing two pyridyl groups is relatively unexplored [30–32]. Here we wish to report the synthesis, characterization, and catalytic application of air-stable di-2-pyridyl imine ligands, which contain two pyridyl groups and one imino (C=N) group.

Reactions of 2,2′-dipyridyl ketone and 2,6-di-isopropylaniline or 2,4,6-trimethylaniline in toluene afforded the corresponding di-2-pyridyl imines, 2,4,6-trimethyl-(di-2-pyridylmethylene)aniline (**1**) [33] and 2,6-di-isopropyl-(di-2-pyridylmethylene)aniline (**2**) [34] (Scheme 1). Both compounds could be handled and stored in air for months without decomposition. The ^{1}H NMR spectra of **1** and **2** in $CDCl_3$ showed eight distinct signals for the eight pyridyl hydrogen atoms, indicating the two pyridyl groups are non-equivalent after the introduction of the bulky trimethyl and di-isopropyl aryl imine groups. In **2**, the two methyl groups in the isopropyl moiety are also non-equivalent (1.15 and 1.97 ppm, respectively). Both compounds showed strong absorption at 1630 cm^{-1} for ν(C=N) in the FTIR spectra.

Addition of a solution of **1** in CH_2Cl_2 to a solution of $(PhCN)_2PdCl_2$ in CH_2Cl_2 afforded palladium complex 3 as an orange solid [35]. Its ^{1}H NMR spectrum showed downfield shift of up to 1.0 ppm in one pyridyl group and 0.3 ppm in the methyl groups of the mesityl moiety, while the chemical shifts of the other pyridyl group were almost unchanged. This suggested ligand coordination to Pd through the imino group and only one pyridyl group in the complex. Its IR spectrum showed red-shift of ν(C=N) from 1630 to 1608 cm^{-1} upon coordination to the metal center. Slow evaporation of a solution of **3** in acetone afforded orange crystals suitable for X-ray diffraction analysis [36]. The crystal structure confirmed the coordination mode of the ligand (Fig. 1). In the solid state, the complex exists as a monomer, with Pd(II) ion adopting a distorted square-planar geometry. The Pd–N bond distances of 2.022(2) and 2.026(2) Å are similar to the reported Pd–N values in related complexes [15,19,37]. The reaction of **2** and $(PhCN)_2PdCl_2$ in CH_2Cl_2 afforded a yellow precipitate. Its ^{1}H NMR spectrum contained multiple isopropyl signals, indicating the existence of a mixture. This suggested multiple coordination modes of the ligand, whereas it can bond through one pyridyl group and the imine group or both pyridyl groups. We were unable to grow suitable crystals for X-ray analysis from the mixture.

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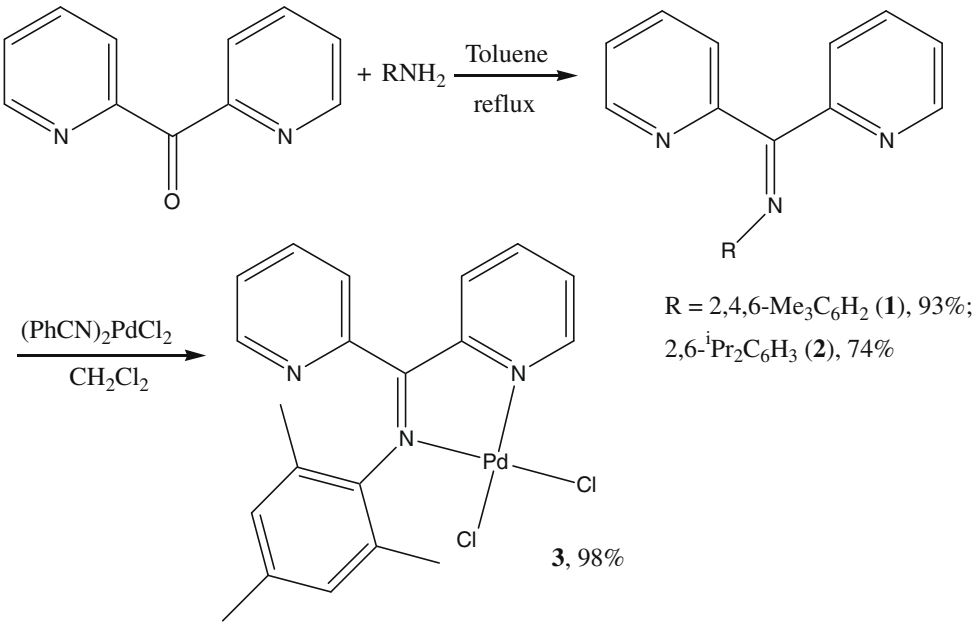


Scheme 1.

We investigated the Suzuki cross-coupling reaction between phenylboronic acid and *p*-bromoanisole, which is a deactivated and fairly inert halide [38]. Compound **2** was used for the screening of solvent and base for the reaction. The conditions and results are listed in Table 1. We examined a few common solvents and bases for the Suzuki reaction [1–3], and found that the combination of dioxane as the solvent and Cs_2CO_3 as the base afforded the best result (entry 6).

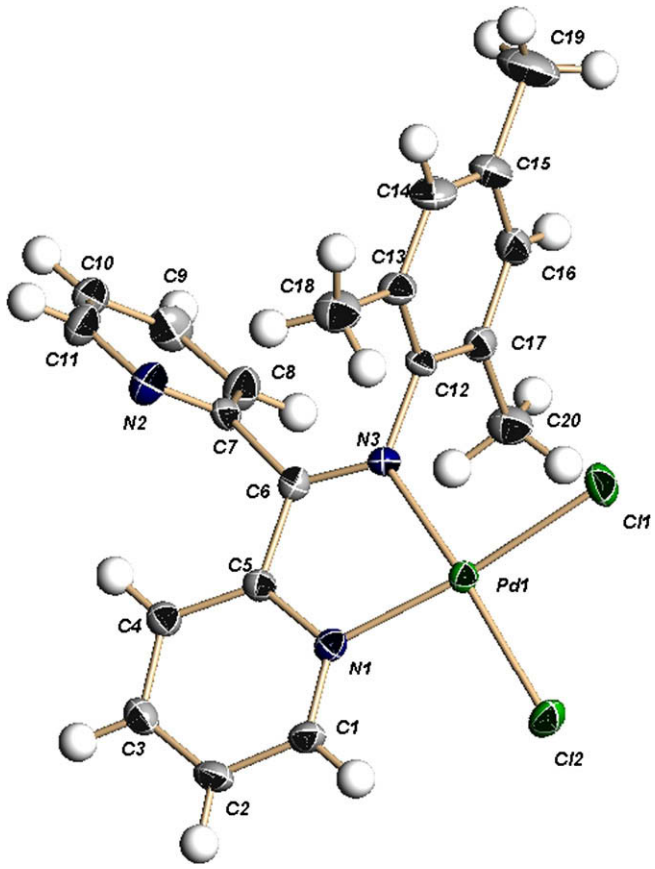


Fig. 1. Molecular Structure of **3** with ellipsoids drawn at the 30% probability level. Hydrogen atoms were omitted for clarity. Selected bond lengths (Å) and angles (°): Pd(1)–N(1) 2.022(2); Pd(1)–N(3) 2.026(2); Pd(1)–Cl(1) 2.2702(7); Pd(1)–Cl(2) 2.2931(6); N(1)–Pd(1)–N(3) 80.48(8); N(1)–Pd(1)–Cl(1) 173.22(6); N(3)–Pd(1)–Cl(1) 94.62(6); N(1)–Pd(1)–Cl(2) 94.89(6); N(3)–Pd(1)–Cl(2) 171.52(6); Cl(1)–Pd(1)–Cl(2) 90.55(3).

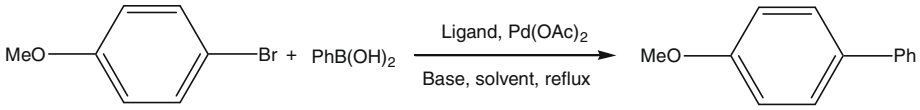
Next we evaluated the efficiency of the novel di-2-pyridyl imines and related bidentate nitrogen ligands under similar conditions. Palladium acetate and imine **1**, as well as palladium complex **3** bearing the imine, gave excellent yields (entries 7 and 8). Compound **2** was found to be more efficient than **1** as a ligand. This may be attributed to more steric hindrance and better donating ability in **2** which are beneficial factors in the catalytic systems [1–4]. We compared the efficiency of related iminopyridines containing only one pyridyl group, 2,4,6-trimethyl-(2-pyridylmethylene)aniline (**4**) and 2,6-di-isopropyl-(2-pyridylmethylene)aniline (**5**) [37]. In our studies, the monopyridyl imines gave good but lower yields than the novel dipyridyl imines (entries 9 and 10). The improved efficiency of the dipyridyl imines over the monopyridyl imines is likely due to the extra basic pyridyl group which provides additional nitrogen functionality that is beneficial to catalytic properties [39,40]. Furthermore, good yields (entries 11 and 12) were obtained when the reactions were carried out in air using palladium acetate and the dipyridyl imine ligands, suggesting the ligand systems are rather robust in air.

In conclusion, we have prepared and characterized two novel di-2-pyridyl imines and a palladium complex bearing one of the imines. They were successfully employed in the Suzuki reaction of *p*-bromoanisole and phenylboronic acid. They demonstrated better catalytic efficiency than related monopyridyl imines. Both imines were easy to prepare and stable in air, making them potential alternative ligands to the commonly used yet air-sensitive phosphine ligands.

Appendix A. Supplementary material

CCDC 736562 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via http://www.ccdc.cam.ac.uk/data_request/cif.

Table 1
Suzuki reactions using imine ligands.[a]



Entry	Solvent	Base	Ligand	Yield (%)[b]
1	Toluene	K_3PO_4	**2**	70
2	Toluene	K_2CO_3	**2**	67
3	Toluene	Cs_2CO_3	**2**	76
4	Dioxane	K_3PO_4	**2**	82
5	Dioxane	K_2CO_3	**2**	84
6	Dioxane	Cs_2CO_3	**2**	99
7	Dioxane	Cs_2CO_3	**1**	88
8	Dioxane	Cs_2CO_3	**3**	88[c]
9	Dioxane	Cs_2CO_3	**4**	78
10	Dioxane	Cs_2CO_3	**5**	81
11	Dioxane	Cs_2CO_3	**1**	77[d]
12	Dioxane	Cs_2CO_3	**2**	89[d]

[a] 1 mmol, *p*-bromoanisole; 1.5 mmol, phenylboronic acid; 2 mol%, $Pd(OAc)_2$ and 2 mol%, ligand or 2 mol%, palladium imine complex **3**; 1.5 mmol, Cs_2CO_3; 10 mL, dioxane, reflux.
[b] GC yield based on *p*-bromoanisole.
[c] Palladium complex **3** was used instead of palladium acetate and a ligand.
[d] Experiments carried out in air.

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[33] *Preparation of* **1**: A 40 mL solution of di-2-pyridyl ketone (3.68 g, 20.0 mmol) and trimethylanaline (2.70 g, 20.0 mmol) in toluene was refluxed in the presence of Amberlyst-15 (0.020 g) in a 100 mL Schlenk flask. The flask was equipped with a Dean-Stark trap to remove water. After three days the mixture was cooled to room temperature and filtered. The volatiles were removed under a reduced pressure to afford orange solids. Recrystallization from ethanol afforded yellow crystalline solids (5.59 g, 93%). M.p. 121–123 °C. Anal. Calc. for $C_{20}H_{19}N_3$: C, 79.70; H, 6.35; N, 13.94. Found: C, 79.99; H, 6.59; N, 13.97. 1H ($CDCl_3$, 250.14 MHz, ppm): δ 8.61 (m, 2H, overlapping Hpyridine), 8.29 (d, 1H, J = 7.5 Hz, Hpyridine), 7.85 (dt, 1H, J = 7.5, 2.5 Hz, Hpyridine), 7.52 (dt, 1H, J = 7.5, 2.5 Hz, Hpyridine), 7.37 (ddd, 1H, J = 7.5, 5.0, 2.5 Hz, Hpyridine), 7.17 (ddd, 1H, J = 7.5, 5.0, 2.5 Hz, Hpyridine), 7.02 (t, 1H, J = 7.5 Hz, Hpyridine), 6.70 (s, 2H, C_6H_2), 2.19 (s, 3H, CH_3), 2.05 (s, 6H, CH_3). GC/MS (EI): 301 (M+). IR (KBr, cm^{-1}): 2963 (s), 2923 (s), 2865 (s), 1630 (s), 1582 (s), 1568 (m), 1478 (s), 1469 (s), 1321 (s), 1138 (s), 934 (s), 854 (m), 804 (m), 748 (s), 661 (s).
[34] *Preparation of* **2**: In a manner similar to the preparation of **1**, di-isopropylaniline and di-2-pyridyl ketone were condensed to afford **2** as yellow solids (5.05 g, 74%). M.p. 143–145 °C. Anal. Calc. for $C_{23}H_{25}N_3$: C, 80.43; H, 7.34; N, 12.23. Found: C, 80.22; H, 7.63; N, 12.35. 1H ($CDCl_3$, 250.14 MHz, ppm): δ 8.62 (t, 2H, J = 7.5 Hz, Hpyridine), 8.31 (d, 1H, J = 7.5 Hz, Hpyridine), 7.87 (t, 1H, J = 7.5 Hz, Hpyridine), 7.48 (t, 1H, J = 7.5 Hz, Hpyridine), 7.38 (t, 1H, J = 7.5 Hz, Hpyridine), 7.15 (t, 1H, J = 7.5 Hz, Hpyridine), 7.00 (m, 4H, overlapping Hpyridine and C_6H_3), 2.97 (sept, 2H, J = 7.5 Hz, $CH(CH_3)_2$), 1.15 (d, 6H, J = 7.5 Hz, $CH(CH_3)_2$), 0.97 (d, 6H, J = 7.5 Hz, $CH(CH_3)_2$). GC/MS (EI): 343 (M+). IR (KBr, cm^{-1}): 3047 (m), 2999 (m), 2964 (s), 2958 (m), 2915 (m), 1630 (s), 151 (s), 1567 (s), 1463 (s), 1433 (s), 1360 (m), 1320 (s), 994 (s), 971 (m), 783 (s), 760 (m), 745 (s), 735 (s), 685 (m).
[35] *Preparation of* **3**: Compound **1** (0.602 g, 2.00 mmol) was dissolved in 5 mL CH_2Cl_2 and added to a solution of $(PhCN)_2PdCl_2$ (0.767 g, 2.00 mmol) in 5 mL CH_2Cl_2. The mixture was stirred overnight and filtered to afford orange solids (0.940 g, 98%). M.p. 354 °C (dec.). Anal. Calc. for $C_{20}H_{19}C_{12}N_3Pd$: C, 50.18; H, 4.00; N, 8.78. Found: C, 49.96; H, 4.03; N, 8.70. 1H ($CDCl_3$, 250.14 MHz, ppm): δ 9.62 (d, 1H, J = 7.5 Hz, Hpyridine), 8.69 (d, 1H, J = 7.5 Hz, Hpyridine), 8.05 (dt, 1H, J = 7.5, 2.5 Hz, Hpyridine), 7.76 (dt, 1H, J = 7.5, 2.5 Hz, Hpyridine), 7.63 (dt, 1H, J = 7.5, 2.5 Hz, Hpyridine), 7.47 (d, 1H, J = 7.5 Hz, Hpyridine), 7.38 (t, 1H, J = 7.5 Hz, Hpyridine), 7.06 (d, 1H, J = 7.5 Hz, Hpyridine), 6.71 (s, 2H, C_6H_2), 2.33 (s, 6H, CH_3), 2.16 (s, 3H, CH_3). IR (KBr, cm^{-1}): 3070 (m), 2970 (m), 2914 (m), 1608 (w), 1588 (s), 1578 (s), 1474 (s), 1462 (m), 1374 (w), 1345 (m), 1143 (m), 996 (m), 855 (m), 750 (s), 633 (m), 612 (m).
[36] The crystal data for **3** were collected on a Simens SMART diffractometer with graphite monochromated Mo Kα radiation (λ = 0.71073 Å). Crystal data: $C_{20}H_{19}C_{12}N_3Pd$, M = 478.68, monoclinic, $P2(1)/c$, Z = 4, T = 198 K, a = 15.566(3) Å, b = 7.177(1) Å, c = 18.225(3) Å, $\alpha = \gamma = 90°$, β = 105.353(2)°. V = 1963.4(6) $Å^3$, D_{calc} = 1.619 Mg/m^3, μ = 1.226 mm^{-1}, $F(0\,0\,0)$ = 960. Refinement method was full-matrix least squares on F^2 using SHELXTL-97 program, 6928

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