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Palladium(II) complexes featuring bidentate pyridine–triazole ligands: Synthesis, structures, and catalytic activities for Suzuki–Miyaura coupling reactions

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ABSTRACT

Preparation of the Pd(II) complexes containing 2-(4-R-1,2,3-triazol-1-yl)pyridine [R = C_6H_5 (**1**), NC_5H_4 (**2**), *n*-C_6H_{13} (**3**)] were described. Crystal structures of **1** and **2** revealed a square planar geometry with bidentate ligand coordination to Pd using different N donor of the triazole ring. Catalytic studies indicated that **1**–**3** exhibited moderate to high activity for Suzuki–Miyaura coupling between aryl bromides and phenylboronic acid under mild and aerobic conditions.

1. Introduction

Pd-catalyzed cross coupling is considered one of the most important reactions in organic synthesis [1,2]. Among many types of C–C cross-coupling reactions, Suzuki–Miyaura coupling [3] is most widely used because of its high catalytic efficiency, commercially available starting materials, and low catalyst toxicity. Most prominent Pd catalysts for Suzuki–Miyaura coupling reaction are supported by electron-rich phosphane [4–8] or *N*-heterocyclic carbene (NHC) ligands [9–15]. Although these catalysts are highly active, their sensitivity to oxygen requires an inert atmosphere to carry out the cross-coupling reactions. More recent progress in the area of Pd-catalyzed cross-coupling has shown an increase in the use of nitrogen-based chelates such as porphyrin [16], β-diketiminate [17], and pyridine-based compounds [18–23] as catalyst supports. Rigidity and high stability towards air of the nitrogen-based ligands lead to more stabilization of the resulting catalysts. As a result, the cross-coupling reactions can usually be performed at high temperatures and sometimes under aerobic conditions [24,25]. Despite various examples of Pd catalysts for Suzuki reaction, development of such catalysts to allow reduced catalyst loading, mild reaction conditions, and wide substrate scope is still of importance.

1,2,3-Triazole compounds have emerged as promising ligands in catalysis [26–31]. The preparation involves the copper-catalyzed azide-alkyne cycloaddition (CuAAC) or "click" reaction to afford the 1,4-disubstituted-1,2,3-triazole compound in good yields [32–34]. The aromatic, thermally robust triazole product is analogous to pyridine but the substituents on the triazole ring can be more readily adjusted depending on the organic azide and terminal alkyne substrates. Based on facile synthesis and substituent modification, the triazole-based ligands appear attractive as catalyst supports. Recently, the pyridine–triazole compounds 2-((4-R-

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1,2,3-triazol-1-yl)methyl)pyridine (R = C_6H_5, *n*-C_3H_7) have been investigated as ligands for Pd-catalyzed Suzuki reactions [18,19]. However, the corresponding Pd(II) catalysts [Pd(η^3-C_3H_5)(2-((4-R-1,2,3-triazol-1-yl)methyl)pyridine)][X] (X = BF_4, ClO_4) were air-sensitive, most likely as a result of the Pd–C(allyl) bond. Along the same line, a series of mono- and multi-nuclear palladium complexes containing 2-pyridyl-1,2,3-triazole ligands have recently been investigated as catalysts for C–C cross coupling reactions [35]. We were particularly interested in exploring the bidentate pyridine–triazole ligands of the type 2-(4-R-1,2,3-triazol-1-yl)pyridine (R = C_6H_5, NC_5H_4, *n*-C_6H_{13}) for Suzuki–Miyaura cross-coupling reaction. It was expected that an increase in ligand rigidity and π conjugation combined with weaker electron-donating property would result in the corresponding Pd(II) complexes $PdCl_2$[2-(4-R-1,2,3-triazol-1-yl)pyridine] that were stable in air and more active as catalysts toward C–C cross-coupling reactions.

2. Experimental section

Ligand syntheses were carried out under Ar using standard Schlenk techniques or in a Braun drybox. Toluene (Fisher Scientific) was dried using PURE SOLV MD-5 solvent purification system from Innovative Technology Inc. All other solvents were used as received. $(CuOTf)_2\cdot C_6H_6$ (Aldrich) was used as received and stored under Ar. $Cu(OTf)_2$, ethylenediaminetetraacetic acid (EDTA), 1-octyne, phenylacetylene, 2-ethynylpyridine, phenylboronic acid, and aryl bromides were purchased from Aldrich and used without further purification. 2-Azidopyridine [36] and $Pd(cod)Cl_2$ (cod = 1,5-cyclooctadiene) [37] were prepared according to the literature.

^{1}H (500.1 MHz), $^{13}C\{^1H\}$ (124.7 MHz) NMR spectra were acquired on Bruker AV-500 spectrometer equipped with a 5 mm proton/BBI probe. All NMR spectra were recorded at room temperature and referenced to protic impurities in the deuterated solvent for ^{1}H and solvent peaks for $^{13}C\{^1H\}$. Multiplicities are reported as follows: s (singlet), d (doublet), t (triplet), p (pentet), m (multiplet), dd (doublet of doublets), or dt (doublet of triplets). Elemental analyses were conducted by Chemistry Department, Mahidol University. The solutions obtained from the catalytic experiments were analyzed by GLC on a 6850 Agilent Technologies gas chromatograph. GC–MS spectra were recorded on an HP 5890 series II gas chromatograph interfaced to an HP 5971 quadrupole mass detector.

2.1. Synthesis and characterization

2.1.1. 2-(4-Phenyl-1,2,3-triazol-1-yl)pyridine (**L_1**)

The preparation was slightly modified from the literature [38]. Under Ar, to a foil-wrapped 100 mL Schlenk flask equipped with a stir bar, 2-azidopyridine (0.50 g, 4.16 mmol), and $(CuOTf)_2\cdot C_6H_6$ (0.21 g, 0.42 mmol) were added toluene (20 mL), followed by PhC≡CH (0.50 mL, 4.58 mmol). The reaction mixture was heated at 120 °C for 24 h. After cooling to room temperature, all volatiles were removed under reduced pressure. The remaining solid was then diluted with CH_2Cl_2 (30 mL) and filtered. The brown filtrate was stirred in a 10% v/v NH_4OH solution (30 mL) of EDTA (0.12 g, 0.42 mmol) for 2 h. The solution was extracted with CH_2Cl_2 (3 × 30 mL), washed with saturated aqueous solution of NaCl (30 mL), and dried in anhydrous Na_2SO_4. All volatiles were then removed under vacuum. Slow evaporation of the benzene solution at room temperature produced a colorless crystalline solid in 63% yield (0.58 g, 2.61 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.81 (s, 1H, N=C*H*), 8.52 (m, 1H, Ar*H*), 8.25 (d J = 8 Hz, 1H, Ar*H*), 7.94 (d J = 7 Hz, 3H, Ar*H*), 7.47 (t J = 7 Hz, 2H, Ar*H*), 7.37 (m, 2H, Ar*H*).

An alternative synthesis involved the use of $Cu(OTf)_2$ (0.15 g, 0.42 mmol) and Cu^0 (5 cm^2 sheet) as pre-catalysts under the same reaction conditions. The product **L_1** was obtained in 79% yield (0.73 g, 3.28 mmol).

2.1.2. 2-[4-(2-Pyridyl)-1,2,3-triazol-1-yl]pyridine (**L_2**)

Compound **L_2** was prepared in an identical manner to **L_1** using 2-azidopyridine (1.00 g, 8.30 mmol), $(CuOTf)_2\cdot C_6H_6$ (0.42 g, 0.83 mmol), and 2-ethynylpyridine (0.94 g, 9.10 mmol). Recrystallization by slow evaporation of the benzene solution afforded **L_2** as a crystalline brown solid in 65% yield (1.20 g, 5.40 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.17 (s, 1H, N=C*H*), 8.64 (d J = 5 Hz, 1H, py*H*), 8.53 (d J = 5 Hz, 1H, py*H*), 8.23 (m, 2H, py*H*), 7.93 (m, 1H, py*H*), 7.81 (dt J = 8 Hz, 2 Hz, 1H, py*H*), 7.36 (m, 1H, py*H*), 7.26 (m, 1H, py*H*). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 150.2, 149.8, 149.3, 148.9, 148.8, 139.1, 136.9, 123.8, 123.1, 120.6, 119.6, 114.0 (aryl *C*). MS (ESI, positive) m/z for $[C_{12}H_9N_5 + Na]^+$, found: 246.10. Anal. Calcd. for $C_{12}H_9N_5$: C, 64.56; H, 4.06; N, 31.37. Found: C, 64.42; H, 3.86; N, 31.21.

2.1.3. 2-(4-Hexyl-1,2,3-triazol-1-yl)pyridine (**L_3**)

Compound **L_3** was prepared in an identical manner to **L_1** from 2-azidopyridine (0.37 g, 3.08 mmol), $(CuOTf)_2\cdot C_6H_6$ (0.16 g, 0.31 mmol), and 1-octyne (0.50 mL, 3.36 mmol). The product was purified by column chromatography over silica gel using hexane/ethyl acetate (7:3) as eluent to afford **L_3** as yellow oil in 54% yield (0.38 g, 1.65 mmol). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.40 (dd J = 4 Hz, 1 Hz, 1H, py*H*), 8.23 (s, 1H, N=C*H*), 8.10 (dt J = 8 Hz, 1 Hz, 1H, py*H*), 7.82 (m, 1H, py*H*), 7.24 (m, 1H, py*H*), 2.73 (t J = 8 Hz, 2H, CH_2), 1.66 (p J = 8 Hz, 2H, CH_2), 1.34–1.22 (m, 6H, CH_2), 0.81 (m, 3H, CH_3). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ 149.4, 148.9, 148.4, 139.0, 123.1, 118.0, 113.7 (aryl *C*), 31.6, 29.2, 28.8, 25.6, 22.5, 14.0 (hexyl *C*). MS (ESI, positive) m/z for $[C_{13}H_{18}N_4 + Na]^+$, found: 253.15. Anal. Calcd. for $C_{13}H_{18}N_4$: C, 67.80; H, 7.88; N, 24.33. Found: C, 68.07; H, 8.06; N, 24.67.

2.1.4. $PdCl_2(L_1)$ (**1**)

To a CH_2Cl_2 solution (20 mL) of $Pd(cod)Cl_2$ (0.19 g, 0.67 mmol) was added **L_1** (0.15 g, 0.67 mmol) and the reaction mixture was stirred at room temperature. After 24 h, brown yellow precipitates were filtered and washed with 30 mL of CH_2Cl_2. The complex **1** was obtained in 66% yield (0.18 g, 0.44 mmol). ^{1}H NMR (500 MHz, CD_3CN): δ 9.19 (s, 1H, N=C*H*), 9.13 (d J = 5 Hz, 1H, Ar*H*), 8.39 (m, 1H, Ar*H*), 8.01 (d J = 8 Hz, 1H, Ar*H*), 7.94 (d J = 7 Hz, 2H, Ar*H*), 7.74 (t J = 7 Hz, 1H, Ar*H*), 7.57 (t J = 7 Hz, 2H, Ar*H*), 7.52 (t J = 7 Hz, 1H, Ar*H*). MS (ESI, positive) m/z for $[C_{13}H_{10}N_4PdCl_2 + Na]^+$, found: 422.92. Anal. Calcd. for $C_{13}H_{10}N_4PdCl_2$: C, 39.08; H, 2.52; N, 14.02. Found: C, 38.97; H, 2.48; N, 14.03.

2.1.5. $PdCl_2(L_2)$ (**2**)

To a stirring 80 mL CH_2Cl_2 solution of $Pd(cod)Cl_2$ (0.27 g, 0.90 mmol) was added a 20 mL CH_2Cl_2 solution of **L_2** (0.20 g, 0.90 mmol) at room temperature. The solution was stirred for 4 h, after which the reaction mixture was filtered and the precipitates were washed with 30 mL of CH_2Cl_2, resulting in a brown yellow solid in 87% yield (0.31 g, 0.78 mmol). ^{1}H NMR (500 MHz, DMSO-d_6): δ 10.1 (s, 1H, N=C*H*), 9.02 (d J = 6 Hz, 1H, py*H*), 8.71 (d J = 5 Hz, 1H, py*H*), 8.42 (d J = 8 Hz, 1H, py*H*), 8.35 (t J = 7 Hz, 1H, py*H*), 8.24 (dt J = 7 Hz, 2 Hz, 1H, py*H*), 8.12 (d J = 8 Hz, 1H, py*H*), 7.73 (m, 2H, py*H*). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6): δ 149.5, 149.1, 148.4, 148.0, 147.4, 141.4, 140.8, 126.0, 125.9, 122.7, 122.5, 115.9 (aryl *C*). MS (ESI, positive) m/z for $[C_{12}H_9N_5PdCl_2 + 2Na]^{2+}$, found: 446.99. Anal.

Calcd. for $C_{12}H_9N_5PdCl_2$: C, 35.98; H, 2.26; N, 17.48. Found: C, 35.78; H, 2.13; N, 17.25.

2.1.6. $PdCl_2(L_3)$ (**3**)

Synthesis of complex **3** followed that of **1**. Pd(cod)Cl_2 (0.083 mg, 0.29 mmol) and $\mathbf{L_3}$ (0.067 mg, 0.29 mmol) was stirred in 10 mL CH_2Cl_2 at room temperature for 4 d, after which the solvent was removed *in vacuo*. The resulting yellow solid was washed with diethyl ether (15 mL). Crystallization by a layer diffusion of DMF and EtOH at room temperature afforded the complex **3** in 41% yield (0.048 mg, 0.12 mmol). ^{1}H NMR (500 MHz, CD_3CN): δ 9.06 (d $J = 6$ Hz, 1H, py*H*), 8.62 (s, 1H, N=C*H*), 8.33 (t $J = 8$ Hz, 1H, py*H*), 7.93 (d $J = 8$ Hz, 1H, py*H*), 7.68 (t $J = 7$ Hz, 1H, py*H*), 2.84 (t $J = 8$ Hz, 2H, trzCH_2), 1.72 (p $J = 8$ Hz, 2H, CH_2), 1.40–1.32 (m, 6H, CH_2), 0.90 (m, 3H, CH_3). ^{13}C{^{1}H} NMR (125 MHz, CD_3CN): δ 152.0, 150.1, 147.8, 144.5, 126.6, 122.9, 114.5 (aryl *C*), 32.2, 29.4, 29.3, 26.4, 23.3, 14.4 (hexyl *C*). MS (ESI, positive) *m/z* for $[C_{13}H_{18}N_4PdCl_2 + Na]^+$, found: 430.98. Anal. Calcd. For $C_{13}H_{18}N_4PdCl_2$: C, 38.30; H, 4.45; N, 13.74. Found: C, 38.32; H, 4.52; N, 14.03.

2.2. X-ray analysis

The single crystal X-ray analyses of pyridine-tetrazole, complexes **1** and **2** were carried out at the Mahidol crystallographic facility. Diffraction measurements were made on a 4 K Bruker SMART [39] CCD area detector diffractometer using graphite-monochromated Mo $K\alpha$ radiation ($\lambda = 0.71073$ Å). Crystals were mounted in paratone oil and held at room temperature during data collection. Cell constants and an orientation matrix for data collection were obtained from a least-square refinement using the measured positions of reflections in the range $0.998° < \theta < 29.6°$ (for pyridine-tetrazole), $0.407° < \theta < 28.7°$ (for **1**), and $0.998° < \theta < 26.7°$ (for **2**). The frame data were integrated by the program SAINT [32] and corrected for Lorentz and polarization effects. The structure was solved by the maXus crystallographic software package [40], using direct methods (SIR97) [41] and refined by full-matrix least-squares method on $(F_{obs})^2$ using the SHELXL97 software package [42].

For pyridine-tetrazole. Crystals were grown from slow evaporation of the 1:1 THF:Et_2O solution of pyridine-tetrazole at room temperature.

For **1**. Orange crystals were grown by layering MeOH onto a DMF solution of **1** at room temperature.

For **2**. Orange crystals were grown by layering EtOH onto a DMF solution of **2** at room temperature.

Both complexes **1** and **2** crystallize in the $P2_1/c$ space group. All non-hydrogen atoms were refined anisotropically while the hydrogen atoms were placed in calculated positions and not refined. Crystallographic data of both **1** and **2** are listed in Table 1. Selected bond lengths and angles are shown in Table 2.

2.3. General procedures for Suzuki–Miyaura cross-coupling reactions

The Pd catalyst stock solution (2.5 mM) was freshly prepared prior to use by diluting the Pd catalyst (0.025 mmol) with DMF in a 10 mL volumetric flask. Then, the round bottom flask was successively charged with ArBr (1.00 mmol), $PhB(OH)_2$ (1.10 mmol), K_2CO_3 (1.00 mmol), H_2O (5 mL), DMF (5 mL), followed by addition of an appropriate amount of the Pd catalyst solution. The reaction mixture was stirred at room temperature for a given time, after which the product was extracted by 3 × 15 mL of CH_2Cl_2. The combined organic layers were washed with 50 mL of saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, and the solvent was removed *in vacuo*. The isolated yields were determined after purification by thin layer chromatography on silica gel using hexane/ethyl acetate (9:1) as eluent. For 4-$(NO_2)C_6H_4Ph$, hexane was used as eluent. The resulting biaryl products were characterized by ^{1}H NMR spectroscopy and GC–MS methods.

Table 1
Crystallographic data.

	1	**2**
Empirical formula	$C_{13}H_{10}Cl_2N_4Pd$	$C_{12}H_9Cl_2N_5Pd$
Formula weight	399.55	400.54
T (K)	293(2)	293(2)
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$	$P2_1/c$
a (Å)	9.3309(4)	8.0063(3)
b (Å)	14.8679(6)	18.6094(9)
c (Å)	11.9702(6)	9.3511(4)
α (°)	90.00	90.00
β (°)	122.549(2)	103.547(2)
γ (°)	90.00	90.00
V (Å^3)	1399.80(11)	1354.48(10)
Z	4	4
ρ_{calc} (mg mm^{-3})	1.906	1.964
μ (mm^{-1})	1.701	1.760
Crystal size (mm)	0.20 × 0.18 × 0.15	0.30 × 0.22 × 0.20
Color, habit	Orange, cube	Orange, cube
Reflections collected	6325	6145
Independent reflections (R_{int})	3214 (0.0481)	2668 (0.0561)
Data/restraints/parameters	3214/0/182	2668/0/181
Goodness of fit	1.13	1.04
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0595$	$R_1 = 0.0311$
	$wR_2 = 0.1590$	$wR_2 = 0.0809$
Final R indices (all data)	$R_1 = 0.0823$	$R_1 = 0.0344$
	$wR_2 = 0.1703$	$wR_2 = 0.0831$
Largest diff. peak/hole	1.056 and −1.268	0.929 and −0.614

Table 2
Selected bond lengths (Å).

	1	**2**	Pd(pytrz^{iPr})Cl_2[a]
Pd–N_{py}	2.054(5)	2.066(2)	2.055(4)
Pd–N_{trz}	2.014(5)	1.999(2)	2.007(4)
Pd–Cl1	2.271(2)	2.270(1)	2.264(1)
Pd–Cl2	2.274(2)	2.275(1)	2.285(1)
N2–N3	1.372(6)	1.308(3)	1.312(6)
N3–N4	1.274(7)	1.342(3)	1.349(5)

[a] Ref. [46].

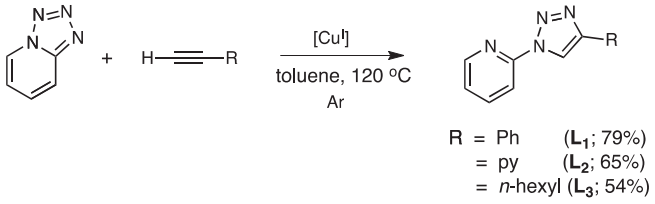
Table 3
Selected bond angles (°).

	1	**2**	Pd(pytrz^{iPr})Cl_2[a]
N_{py}–Pd–N_{trz}	79.65(19)	79.89(10)	80.60(20)
Cl1–Pd–Cl2	90.97(5)	91.19(3)	91.01(5)
N_{trz}–Pd–Cl1	95.86(14)	93.89(7)	94.0(1)
N_{py}–Pd–Cl2	93.46(14)	95.15(8)	94.4 (1)
ω[b]	11.5(9)	27.2(4)	52.3(2)

[a] Ref. [46].
[b] The dihedral angle between the triazole and aryl substituent planes.

2.4. Mercury poisoning tests

To a round bottom flask charged with Hg (0.10 g, 0.50 mmol, Hg:Pd = 500:1) was added 4-$(NO_2)C_6H_4Br$ (0.20 g, 1.00 mmol), $PhB(OH)_2$ (0.13 g, 1.10 mmol), K_2CO_3 (0.14 g, 1.00 mmol) and 10 mL of DMF:H_2O, followed by 0.0010 mmol of Pd catalyst (**1** or **2**). The reaction mixture was stirred at room temperature and, after a given



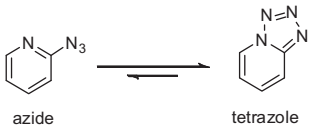
Scheme 1. Synthesis of $\mathbf{L_1}$–$\mathbf{L_3}$.

time, the coupling product was extracted by 3 × 15 mL of CH_2Cl_2. The combined organic layers were washed with 50 mL of saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, and the solvent was removed *in vacuo*. The isolated yields were determined after purification by thin layer chromatography on silica gel using hexane as eluent.

3. Results and discussion

3.1. Pyridine–triazole ligands and their Pd(II) complexes

The 2-(4-R-1,2,3-triazol-1-yl)pyridine compounds [R = C_6H_5 ($\mathbf{L_1}$), NC_5H_4 ($\mathbf{L_2}$), *n*-C_6H_{13} ($\mathbf{L_3}$)] were prepared following the literature [38]. A reaction between 2-azidopyridine and one equiv of a terminal alkyne catalyzed by $[Cu(OTf)]_2 \cdot C_6H_6$ or, alternatively, the more air stable mixture of $Cu^{II}(OTf)_2$ and Cu^0 in toluene at 120 °C afforded the corresponding pyridine–triazole products $\mathbf{L_1}$–$\mathbf{L_3}$ in moderate yields (54–79%; Scheme 1). It should be noted that the 2-azidopyridine substrate is expected to exist as an equilibrium between closed form (tetrazole) and open form (azide) in solution (Eq (1)) [43]. We found that, in solid state, only tetrazole form was obtained (Fig. 1). The presence of the tetrazole form of 2-azidopyridine may explain the harsh reaction conditions and reactive Cu^{I} catalyst generally required for formation of the pyridine–triazole products $\mathbf{L_1}$–$\mathbf{L_3}$ [36,38,44,45].



The corresponding Pd(II) complexes **1**–**3** were prepared in moderate to high yields (41–87%) as brown yellow solids from reactions between an equimolar ratio of $Pd(cod)Cl_2$ and the respective ligands $\mathbf{L_1}$–$\mathbf{L_3}$ in CH_2Cl_2 at room temperature (Scheme 2). Due to relatively low solubility of **1**–**3** in CH_2Cl_2 and $CHCl_3$, their NMR spectra were acquired in either CD_3CN or DMSO-d_6 solution.

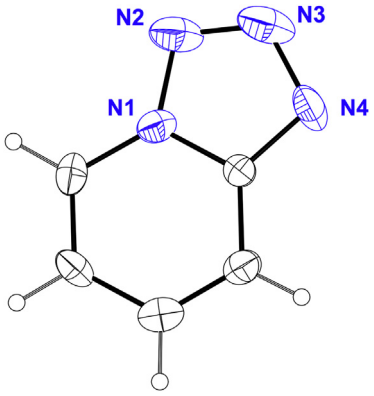
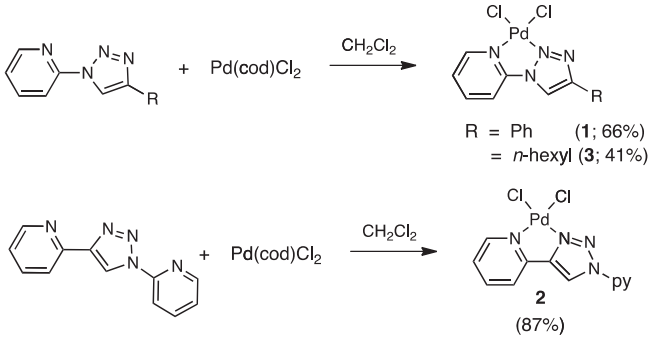


Fig. 1. Thermal ellipsoid diagram of pyridine-tetrazole at the 30% probability level.



Scheme 2. Synthesis of **1**–**3**.

Interestingly, only the pyridyl-substituted Pd(II) complex **2** was stable in DMSO-d_6, as the ^{1}H NMR spectra of **1** and **3** in DMSO-d_6 revealed the presence of free ligands as a major species, suggesting ligand displacement possibly by DMSO molecules.

Single crystals of complexes **1** and **2** suitable for X-ray crystallographic analyses were grown at room temperature from a solution mixture of DMF/MeOH and DMF/EtOH, respectively. For both complexes, the Pd(II) centers possess a square planar geometry as evidenced by the angle sum about Pd of 359.9° (**1**) and 360.1° (**2**). For **1**, Pd coordination to the pyridyl nitrogen *N*1 and the medial nitrogen *N*3 of the triazole ring was observed (Fig. 2). On contrary, according to the X-ray crystallographic analyses, ligand $\mathbf{L_2}$ favors Pd binding at the pyridyl nitrogen *N*1 and the proximal nitrogen *N*2 or the 2-(1*H*-1,2,3-triazol-4-yl)pyridine chelate pocket as shown in Fig. 3. Although crystal structures of the related Pd(II) complexes

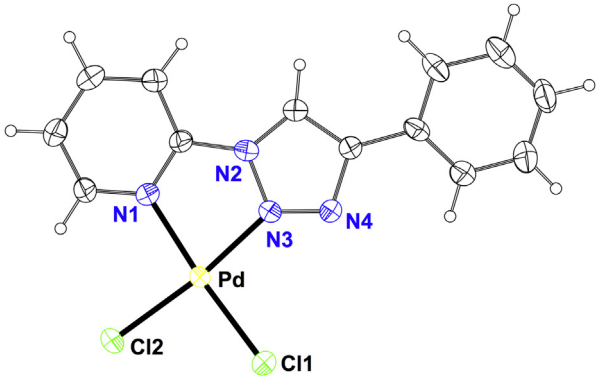


Fig. 2. Thermal ellipsoid diagram of **1** at the 30% probability level.

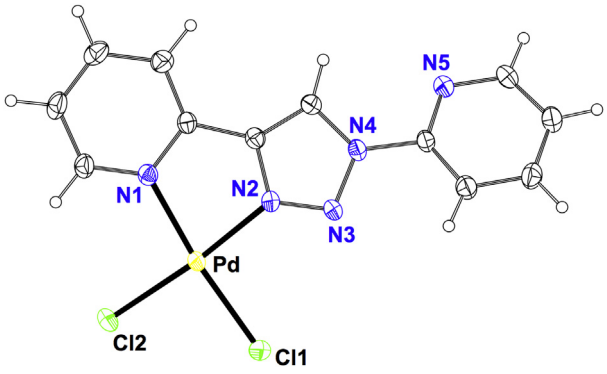


Fig. 3. Thermal ellipsoid diagram of **2** at the 30% probability level.

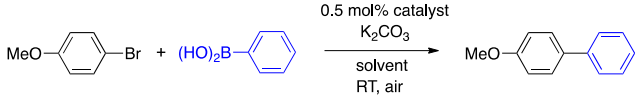
supported by bidentate pyridine–triazole ligands have been previously reported [18,19,46,47], to the best of our knowledge, **1** represents the first crystal structure of the five-membered palladacylic ring with 2-(4-phenyl-1,2,3-triazol-1-yl)pyridine binding.

Similar to previous findings, the Pd–N_{trz}(triazole) bond distances are, in general, slightly shorter than those of the Pd–N_{py}(pyridine) bonds [18,19], suggesting stronger coordinating ability of the triazole nitrogen. The bite angles are relatively small but comparable to the related known structure of $PdCl_2$[2-(1-(4-isopropylphenyl)-1,2,3-triazol-4-yl)pyridine] (Pd(pytrz^{iPr})Cl_2) [46], as shown in Table 3. Furthermore, the dihedral angles between the triazole ring and aryl substituent planes appear much smaller for **1** and **2** (11.5(9)° and 27.2(4)°, respectively) compared to that of Pd(pytrz^{iPr})Cl_2 (52.3(2)°). Based on the observed bond distances, the Pd–N_{trz} bond distance of **1**, of which N_{trz} is the medial nitrogen, is the longest compared to the other two structures, where the Pd center binds to the proximal nitrogen of the triazole ring. We reason that the medial nitrogen surrounded by two electron-withdrawing nitrogen atoms experiences stronger inductive effect and, as a result, is a weaker donor compared to the proximal nitrogen, which connects to nitrogen and a carbon atom. This hypothesis is in agreement with our experimental observations. For example, compared to preparations of the Pd(II) complex **2**, formation of **1** is much slower, requiring 24 h at room temperature whereas, for **2**, only 4 h is needed to reach 87% product yield under the same reaction conditions. In addition, unlike complex **1**, the Pd(II) complex **2** with proximal triazole nitrogen coordination were stable in DMSO, showing no ligand-DMSO displacement. Another evidence of stronger binding of the proximal triazole nitrogen to Pd(II) is based on the crystal structure of **2**. Of two possible chelating sites, Pd(II) exclusively binds at the 2-(1*H*-1,2,3-triazol-4-yl)pyridine pocket. Attempts to add another equivalent of Pd(cod)Cl_2 to the DMF solution of **2** resulted in no further palladium coordination.

3.2. Catalytic tests for Suzuki–Miyaura cross-coupling reactions

To evaluate the catalytic activities of **1**–**3** toward Suzuki–Miyaura cross-coupling reactions, 4-(MeO)C_6H_4Br and $PhB(OH)_2$ in the presence of K_2CO_3 base were used as model substrates. The effect of solvent was first investigated with the phenyl-substituted catalyst **1** (entries 1–4, Table 4). With 0.5 mol% of **1**, the best catalytic activity was obtained from using a 1:1 ratio of DMF:H_2O, which gave the coupling product in 95% yield. This is likely due to better solubility of **1** in DMF compared to other solvents studied. Under the same conditions, complexes **2** and **3** exhibited only moderate catalytic efficiency (entries 7 and 10). Lowering the catalyst loadings to 0.01 mol% resulted in significant reduction in product yields for catalysts **1** and **2** (entries 5, 6, 8, and 9).

Table 4
Suzuki–Miyaura coupling of 4-(MeO)C_6H_4Br and $PhB(OH)_2$.



Entry	Catalyst	Solvent[a]	Time (h)	Yield (%)[b]	TON
1	**1**	$CH_3CN:H_2O$	2	10	20
2	**1**	MeOH:H_2O	2	52	104
3	**1**	EtOH:H_2O	2	66	132
4	**1**	DMF:H_2O	2	95	190
5	**1**[c]	DMF:H_2O	2	85	850
6	**1**[d]	DMF:H_2O	2	8	80
7	**2**	DMF:H_2O	4	65	130
8	**2**[c]	DMF:H_2O	12	59	590
9	**2**[d]	DMF:H_2O	24	18	1800
10	**3**	DMF:H_2O	4	78	156

[a] The ratio of solvent:H_2O = 1:1.
[b] Isolated yield after thin layer chromatography.
[c] 0.1 mol% Pd catalyst.
[d] 0.01 mol% Pd catalyst.

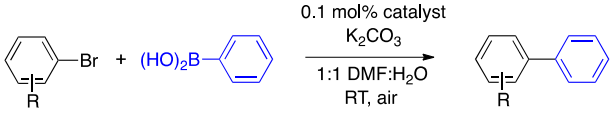
3.3. Substrate scope

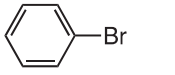
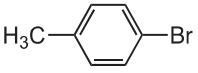
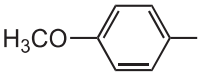
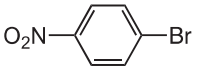
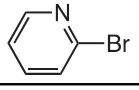
On the basis of different catalyst structures and efficiencies, complexes **1** and **2** were chosen for further studies. A coupling between $PhB(OH)_2$ and different *para*-substituted aryl bromides, using 0.1 mol% of **1** or **2** in 1:1 DMF:H_2O at room temperature afforded the corresponding biaryl products in moderate to high yields (entries 1–4, Table 5.)

Consistent with the activities observed with the model reaction, catalyst **1** is more efficient than **2** and gave higher product yields under similar reaction conditions (Table 5). Additionally, for catalyst **1**, higher product yields were obtained with the activated aryl bromides containing electron-withdrawing groups such as OMe and NO_2 (*i.e.*, inductive effect), whereas the catalyst **2** was only moderately active with no apparent trend with various *para*-substituted aryl bromide substrates. We also found that, the more sterically hindered *ortho*-substituted aryl bromides including 2-(Me)C_6H_4Br and 2,4,6-$(Me)_3C_6H_2$Br yielded no coupling product from both catalysts **1** and **2** even at 100 °C after 24 h. When the heteroaryl bromide such as 2-bromopyridine was used, low product yields of 21% and 4% were obtained in the presence of 1 mol% of **1** and **2** at 100 °C after 24 h, respectively (entry 5).

It should be mentioned that, over the course of the reactions, formation of palladium black was observed with catalysts **1** and **3** while, with **2**, the reaction remained homogeneous. This result indicates better ligand-stabilized Pd(0) species of **2**. Noted that previous work involving other triazole-containing Pd(II) catalysts

Table 5
Substrate scope for Pd-catalyzed Suzuki–Miyaura coupling reactions.



Entry	Ar–Br[a]	**1**		**2**	
		Time (h)	% yield[b]	Time (h)	% yield[b]
1		2	58	12	38
2		2	62	12	36
3		2	85	12	59
4		2	99 (54)[d]	12	26 (25)[d]
5[c]		24	21[e]	24	4[e]

[a] General conditions: 0.1 mol% Pd catalyst, 1.00 mmol of ArBr, 1.10 mmol of $PhB(OH)_2$, 1.00 mmol of K_2CO_3 in DMF:H_2O (1:1, 10 mL).
[b] Isolated yield after thin layer chromatography.
[c] 1.0 mol% Pd catalyst.
[d] In the presence of excess Hg (Hg:Pd = 500:1).
[e] % yields were determined by GC with C_6Me_6 as an internal standard.

for Suzuki cross coupling also reported observation of palladium black [19]. It is possible that Pd(0) nanoparticles generated at the beginning of the reactions are responsible for catalyzing the Suzuki–Miyaura reactions [48–51]. To test whether the *in situ* generated Pd(0) aggregates are the actual catalysts for our systems, mercury poisoning experiments were carried out with catalysts **1** and **2**. A coupling between 4-$(NO_2)C_6H_4Br$ and $PhB(OH)_2$ in the presence of excess Hg (Hg:Pd = 500:1) under the same reaction conditions described for entry 4 (Table 5) revealed a reduction in biaryl product yields for catalyst **1**. On contrary, we found no change in product yields with catalyst **2**. A drop in catalytic activity of **1** suggests that the cross-coupling reactions were catalyzed, to some extent, by heterogeneous Pd(0) nanoparticles. It remains uncertain whether the observed biaryl product from the mercury poisoning reaction is the result of molecular Pd catalysts or the ligand-protected Pd(0) nanoparticles [49,51]. On the other hand, it appears that, compared to $\mathbf{L_1}$ and $\mathbf{L_3}$, ligand $\mathbf{L_2}$ stabilizes the catalytically active Pd(0) complex more efficiently and the C–C bond couplings catalyzed by **2** is most likely to proceed homogeneously.

4. Conclusion

A class of bidentate 2-(4-R-1,2,3-triazol-1-yl)pyridine ligands [R = C_6H_5 ($\mathbf{L_1}$), NC_5H_4 ($\mathbf{L_2}$), *n*-C_6H_{13} ($\mathbf{L_3}$)] was prepared *via* the CuAAC of pyridine azide and terminal alkyne substrates. X-ray crystallographic studies have shown that $\mathbf{L_1}$ and $\mathbf{L_2}$ ligands coordinated to Pd(II) center using different triazole nitrogen atoms. While the ligand $\mathbf{L_2}$ selectively bonded to Pd *via* pyridyl nitrogen and the proximal triazole nitrogen atoms, $\mathbf{L_1}$ uses the medial triazole nitrogen as a ligand donor. These differences in triazole binding may explain the more readily ligand dissociation in **1** and **3**, as evidenced by ligand displacement in DMSO. The Pd(II) complexes **1**–**3** were shown to be effective pre-catalysts for Suzuki–Miyaura coupling reaction under mild aerobic conditions. Although the nature of the real catalytic species is still inconclusive, of all three Pd(II) pre-catalysts, **1** supported by the weakest σ-donating ligand is the most active. A limitation of this catalytic system involves low solubility of **1**–**3** in most solvents studied, with the exception of DMF. Future ligand design may include incorporation of more polar functional groups into the ligand structure in order to facilitate the catalyst's solubility in alcohol and aqueous solutions. In addition, Pd coordination to the weaker σ-donor, the medial triazole nitrogen atom, appears to yield catalysts with higher activities towards Suzuki cross coupling reactions.

Acknowledgments

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Appendix A. Supplementary material

CCDC 961185, 961186, 961187 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

References

[1] A. de Meijere, F. Diederich, Metal-catalyzed Cross-coupling Reactions, Wiley-VCH, Weinheim, 2004.
[2] K.C. Nicolaou, P.G. Bulger, D. Sarlah, Angew. Chem. Int. Ed. 44 (2005) 4442–4489.
[3] N. Miyaura, A. Suzuki, Chem. Rev. 95 (1995) 2457–2483.
[4] K.L. Billingsley, K.W. Anderson, S.L. Buchwald, Angew. Chem. Int. Ed. 45 (2006) 3484–3488.
[5] C.A. Fleckenstein, H. Plenio, Chem. Eur. J. 13 (2007) 2701–2716.
[6] C.A. Fleckenstein, H. Plenio, J. Org. Chem. 73 (2008) 3236–3244.
[7] T. Hoshi, T. Nakazawa, I. Saitoh, A. Mori, T. Suzuki, J. Sakai, H. Hagiwara, Org. Lett. 10 (2008) 2063–2066.
[8] R. Martin, S.L. Buchwald, Acc. Chem. Res. 41 (2008) 1461–1473.
[9] G. Altenhoff, R. Goddard, C.W. Lehmann, F. Glorius, Angew. Chem. Int. Ed. 42 (2003) 3690–3693.
[10] O. Diebolt, P. Braunstein, S.P. Nolan, C.S.J. Cazin, Chem. Commun. (2008) 3190–3192.
[11] E.A.B. Kantchev, C.J. O'Brien, M.G. Organ, Angew. Chem. Int. Ed. 46 (2007) 2768–2813.
[12] N. Marion, O. Navarro, J. Mei, E.D. Stevens, N.M. Scott, S.P. Nolan, J. Am. Chem. Soc. 128 (2006) 4101–4111.
[13] M. Micksch, T. Strassner, Eur. J. Inorg. Chem. (2012) 5872–5880.
[14] C.J. O'Brien, E.A.B. Kantchev, C. Valente, N. Hadei, G.A. Chass, A. Lough, A.C. Hopkinson, M.G. Organ, Chem. Eur. J. 12 (2006) 4743–4748.
[15] M.G. Organ, S. Çalimsiz, M. Sayah, K.H. Hoi, A.J. Lough, Angew. Chem. Int. Ed. 48 (2009) 2383–2387.
[16] I.D. Kostas, A.G. Coutsolelos, G. Charalambidis, A. Skondra, Tetrahedron Lett. 48 (2007) 6688–6691.
[17] D.-H. Lee, M.-J. Jin, Org. Lett. 13 (2011) 252–255.
[18] E. Amadio, M. Bertoldini, A. Scrivanti, G. Chessa, V. Beghetto, U. Matteoli, R. Bertani, A. Dolmella, Inorg. Chim. Acta 370 (2011) 388–393.
[19] E. Amadio, A. Scrivanti, G. Chessa, U. Matteoli, V. Beghetto, M. Bertoldini, M. Rancan, A. Dolmella, A. Venzo, R. Bertani, J. Organomet. Chem. 716 (2012) 193–200.
[20] P. Liu, M. Yan, R. He, Appl. Organomet. Chem. 24 (2010) 131–134.
[21] L. Shen, S. Huang, Y. Nie, F. Lei, Molecules 18 (2013) 1602–1612.
[22] V. Montoya, J. Pons, V. Branchadell, J. Garcia-Antón, X. Solans, M. Font-Bardia, J. Ros, Organometallics 27 (2008) 1084–1091.
[23] J.A. Perez, J. Pons, X. Solans, M. Font-Bardia, J. Ros, Inorg. Chim. Acta 358 (2005) 617–622.
[24] N. Shahnaz, B. Banik, P. Das, Tetrahedron Lett. 54 (2013) 2886–2889.
[25] C. Zhou, J. Wang, L. Li, R. Wang, M. Hong, Green. Chem. 13 (2011) 2100–2106.
[26] H. Duan, S. Sengupta, J.L. Petersen, N.G. Akhmedov, X. Shi, J. Am. Chem. Soc. 131 (2009) 12100–12102.
[27] E. Hao, Z. Wang, L. Jiao, S. Wang, Dalton Trans. 39 (2010) 2660–2666.
[28] C. Hua, K.Q. Vuong, M. Bhadbhade, B.A. Messerle, Organometallics 31 (2012) 1790–1800.
[29] S. Özçubukçu, E. Ozkal, C. Jimeno, M.A. Pericàs, Org. Lett. 11 (2009) 4680–4683.
[30] E. Ozkal, S. Özçubukçu, C. Jimeno, M.A. Pericàs, Catal. Sci. Technol. 2 (2012) 195–200.
[31] P. Sangtrirutnugul, P. Maisopa, L. Chaicharoenwimolkul, A. Sunsin, E. Somsook, V. Reutrakul, J. Appl. Polym. Sci. 127 (2013) 2757–2763.
[32] C.W. Tornøe, C. Christensen, M. Meldal, J. Org. Chem. 67 (2002) 3057–3064.
[33] V.V. Rostovtsev, L.G. Green, V.V. Fokin, B.K. Sharpless, Angew. Chem. Int. Ed. 41 (2002) 2596–2599.
[34] M. Meldal, C.W. Tornøe, Chem. Rev. 108 (2008) 2952–3015.
[35] D. Wang, D. Denux, J. Ruiz, D. Astruc, Adv. Synth. Catal. 355 (2013) 129–142.
[36] I. Stengel, A. Mishra, N. Pootrakulchote, S.-J. Moon, S.M. Zakeeruddin, M. Gratzel, P. Bäuerle, J. Mater. Chem. 21 (2011) 3726–3734.
[37] D. Drew, J.R. Doyle, A.G. Shaver, Inorg. Synth. 28 (1990) 346–349.
[38] B. Chattopadhyay, C.I.R. Vera, S. Chuprakov, V. Gevorgyan, Org. Lett. 12 (2010) 2166–2169.
[39] SMART v.5.6, Bruker AXS Inc., Madison, WI, USA, 2000.
[40] S. Mackay, C.J. Gilmore, C. Edwards, N. Stewart, K. Shankland, Bruker Nonius, MacScience, The Netherlands, 1999. Japan & The University of Glasgow.
[41] A. Altomare, M.C. Burla, M. Camalli, G.L. Cascarano, C. Giacovazzo, A. Gaugliardi, A.G.G. Moliterni, G. Polidori, R. Spagna, J. Appl. Cryst. 32 (1999) 115–119.
[42] G.M. Sheldrick, SHELXL97, University of Göttingen, Germany, 1997.
[43] J.H. Boyer, E.J. Miller, J. Am. Chem. Soc. 81 (1959) 4671–4673.
[44] G. Colombano, C. Travelli, U. Galli, A. Caldarelli, M.G. Chini, P.L. Canonico, G. Sorba, G. Bifulco, G.C. Tron, A.A. Genazzani, J. Med. Chem. 53 (2010) 616–623.
[45] M. Pizzotti, S. Cenini, F. Porta, W. Beck, J. Erbe, J. Chem. Soc. Dalton Trans. (1978) 1155–1160.
[46] D. Schweinfurth, R. Pattacini, S. Strobel, B. Sarkar, Dalton Trans. (2009) 9291–9297.
[47] K.J. Kilpin, E.L. Gavey, C.J. McAdam, C.B. Anderson, S.J. Lind, C.C. Keep, K.C. Gordon, J.D. Crowley, Inorg. Chem. 50 (2011) 6334–6346.
[48] G.K. Rao, A. Kumar, J. Ahmed, A.K. Singh, Chem. Commun. 46 (2010) 5954–5956.
[49] G.K. Rao, A. Kumar, B. Kumar, D. Kumar, A.K. Singh, Dalton Trans. 41 (2012) 1931–1937.
[50] G.K. Rao, A. Kumar, S. Kumar, U.B. Dupare, A.K. Singh, Organometallics 32 (2013) 2452–2458.
[51] K.N. Sharma, H. Joshi, A.K. Sharma, O. Prakash, A.K. Singh, Organometallics 32 (2013) 2443–2451.