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Advanced Synthesis & Catalysis

Efficient Catalyst for Both Suzuki and Heck Cross-Coupling Reactions: Synthesis and Catalytic Behaviour of Geometry-Constrained Iminopyridylpalladium Chlorides

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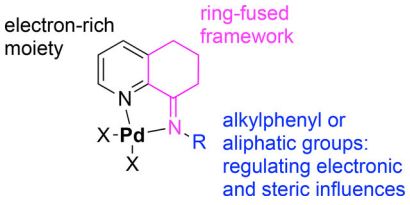
Abstract: A series of geometry-constrained iminopyridyl-palladium chlorides were synthesized and characterized. These phosphine-free palladium complexes were explored for their catalytic activities in both Suzuki and Heck cross-coupling reactions, achieving turnover numbers as high as 10^6 towards various aryl bromides, even those containing various functionalities. In addition, the influence of substituents with steric and electronic factors was reflected by the differences observed in their activities.

Keywords: Iminopyridyl complexes; Palladium; Heck reaction; Suzuki reaction

Introduction

Palladium-catalyzed coupling reactions have been regarded as one of the most powerful transformations in organic synthesis.[1–3] Despite the tremendous progress, there remains a great demand for economic and practicable coupling processes with ultra-low catalyst loadings and higher turnover numbers due to the employment of precious metal catalysts.[4–7] As described by Farina from an industrial point of view, "any Pd-based methodology with TONs of 10^5–10^6 and adequate turnover frequency (TOF) will be very practical…… Beyond this level it is rather meaningless, from a practical standpoint, to venture".[8] There thus remains a significant interest in developing efficient palladium catalyst with ultra-low loadings.

In order to develop a palladium catalyst with high TONs, researchers have direted most efforts to enhancing the stability of the active palladium species by using auxiliary ligands, which can be finely tuned with regard to their steric and electronic properties by installing various substituents.[9–13] Electron-rich ligands such as phosphorus ligands[14–25] and N-heterocyclic carbene (NHCs),[26–29] capable of providing facile coordination to palladium as well as facilitating the oxidative addition process, are mostly employed. Alternatively, the palladacycles pioneered by Herrmann and Beller in the 1990s[30–39] were considered as highly active precursors with high TONs. Hence, various palladacycles bearing phosphine-free nitrogen ligands, such as quinoline,[40] oxazolines,[41,42] pyridines,[43–45] imidazoles,[46–48] pyrazoles[49] and ureas,[50,51] were developed, ligands with bidentate or multidentate coordination were employed to elongate the lifetime of the active Pd(0) species.[52] Structure/activity correlations indicated that the pyridine-imine ligand could intervene in the catalytic cycle in two ways:[53] (i) coordination of the pyridine makes the palladium center electron-rich, increasing the ability for oxidative addition and (ii) coordination of imino group could make the palladium center more electrophilic, allowing facile transmetalation or reductive elimination. On the basis of this rationale, a series of palladium complexes bearing geometry-constrained imino-



Scheme 1. The geometry-constrained iminopyridyl palladium complexes.

pyridine derivatives (8-aryl- or 8-alkylimino-5,6,7-trihydroquinolines) were synthesized (Scheme 1). The ring-fused framework is able to establish a strained environment and maintain the planar positions of the two nitrogen atoms, allowing the palladium complex to be more tightly ligated and stable. According to their analogs in ethylene polymerization,[54–57] the ring-strain of the fused framework significantly affected the activities and the properties of the metal catalyst. In this work, the palladium complexes of the iminopyridine ligands were synthesized, their applications as catalysts in both Suzuki and Heck couplings were demonstrated, and TONs as high as 4.5×10^6 were achieved.

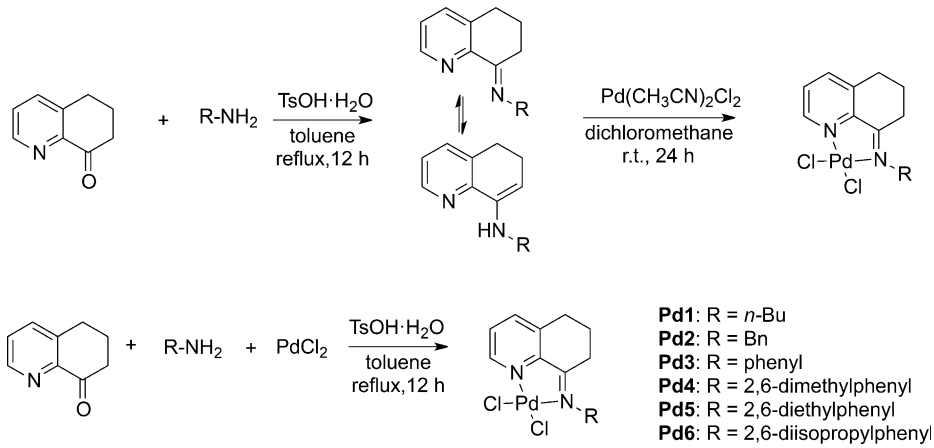
Results and Discussion

Syntheses and Characterization of Palladium Complexes

The palladium complexes could be stepwise prepared through the stoichiometric coordination of $PdCl_2(CH_3CN)_2$ with ligands, which were prepared by condensation of 5,6,7-trihydroquinolin-8-one and arylamines according to our previous report.[58] The ligand compounds were prepared as the mixture of isomeric imine and enamine due to the inherent facile tautomerization (Scheme 2).[58] Moreover, the reversible nature of the reaction between 5,6,7-trihydroquinolin-8-one and *n*-butylamine made it difficult to obtain the pure desired ligand. Gratifyingly, the one-pot condensation of 5,6,7-trihydroquinolin-8-one, amine, and $PdCl_2$ at same equivalent amounts in refluxing toluene effectively formed the palladium complexes **Pd1–Pd6** in moderate to good yields (Scheme 2). Therefore, this is a practical way to prepare these palladium complexes in a one-pot reaction procedure. Complexes **Pd1–Pd6** were stable in air in both solid and solution states; moreover, their melting points were measured to be higher than 230 °C (dec.), indicating good thermal stability. The analytical data from their NMR and IR spectra as well as elemental analyses were in good agreement at every aspect with the proposed structure.[32,59–61] To further elucidate the structures, all complexes were individually investigated by the single crystal X-ray diffraction.

Single crystals of all palladium complexes were obtained by the slow diffusion of diethyl ether into dichloromethane solutions, respectively.[62] The solid-state structures of all palladium complexes by X-ray diffraction established the square-planar coordination geometry around the palladium center with a slight distortion being attributed to the non-aromatic six-membered framework, in which each Pd atom is coordinated with two nitrogen atoms of the imino-pyridine ligand as well as two chlorides. Their molecular structures are shown in Figure 1, Figure 2, Figure 3, Figure 4, Figure 5, and Figure 6, respectively, and selected bond lengths and angles are tabulated in Table 1.

Regarding the structure of the ligands in the palladium complexes, the bond lengths of N-2–C-8 characteristically revealed the double-bonding imino group in the range of 1.275(16) Å for **Pd1** and 1.293(12) for **Pd6**, while the single-bonding characteristics were observed for N-2–C-10 with lengths between 1.419(13) Å for **Pd6** and 1.478(3) Å for **Pd2**. The bond lengths of Pd–N ranged within 2.00 Å and 2.04 Å as the typical bonds between Pd^{2+} and sp^2-hy-



Scheme 2. Two methods for the iminopyridine palladium complexes

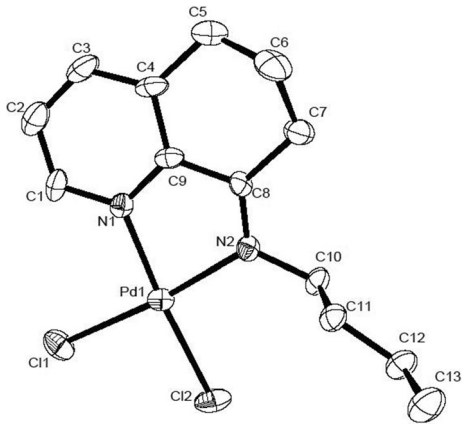


Figure 1. ORTEP drawing of **Pd1** with thermal ellipsoids at 30% probability. Hydrogen atoms have been omitted for clarity.

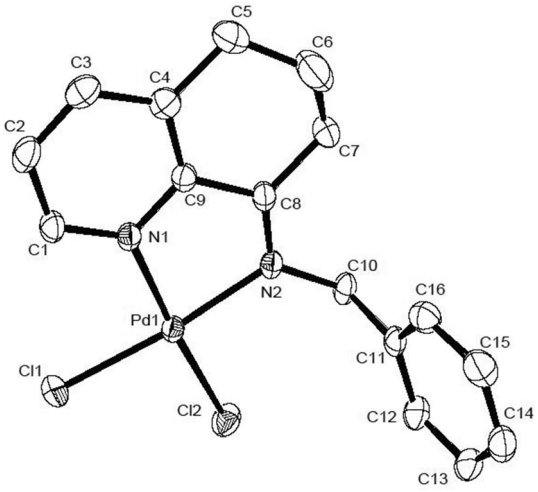


Figure 2. ORTEP drawing of **Pd2** with thermal ellipsoids at 30% probability. Hydrogen atoms have been omitted for clarity.

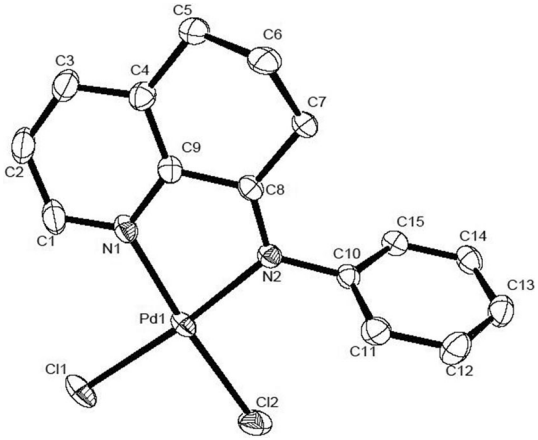


Figure 3. ORTEP drawing of **Pd3** with thermal ellipsoids at 30% probability. Hydrogen atoms have been omitted for clarity.

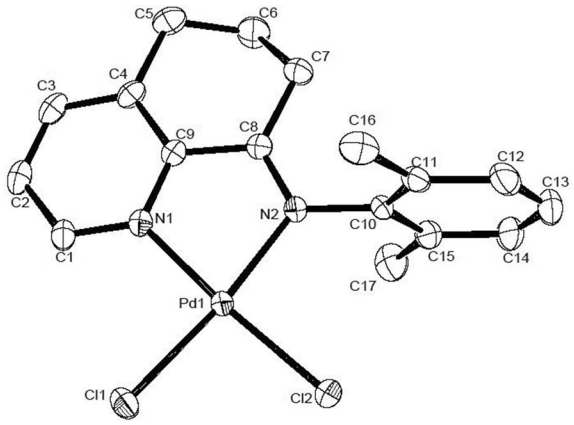


Figure 4. ORTEP drawing of **Pd4** with thermal ellipsoids at 30% probability. Hydrogen atoms have been omitted for clarity.

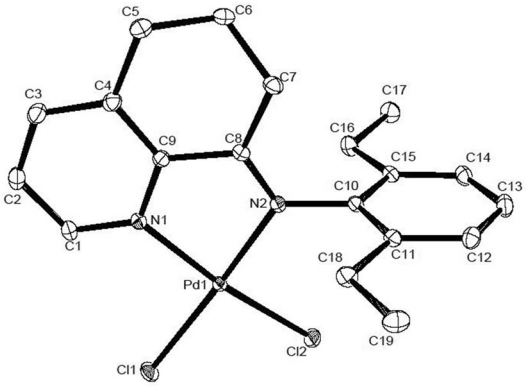


Figure 5. ORTEP drawing of **Pd5** with thermal ellipsoids at 30% probability. Hydrogen atoms have been omitted for clarity.

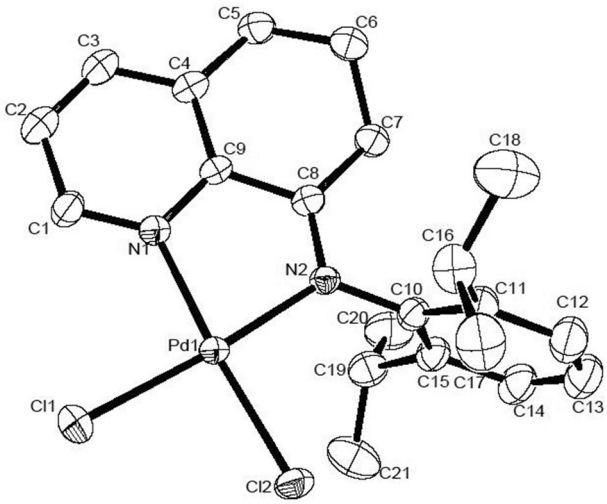


Figure 6. ORTEP drawing of **Pd6** with thermal ellipsoids at 30% probability. Hydrogen atoms have been omitted for clarity

Table 1. Selected bond lengths [Å] and angles [°] for palladium complexes.

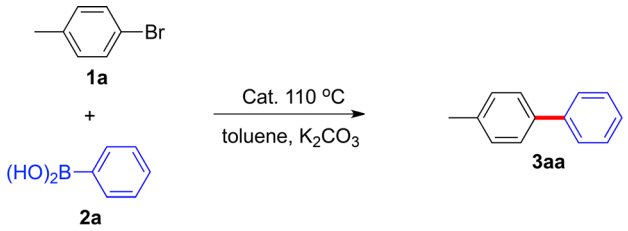
	Pd1	Pd2	Pd3	Pd4	Pd5	Pd6
			Bond lengths [Å]			
Pd(1)–N(1)	2.004(11)	2.0173(19)	2.033(2)	2.0256(15)	2.0252(18)	2.035(8)
Pd(1)–N(2)	2.021(11)	2.0285(19)	2.030(2)	2.0192(15)	2.0213(17)	2.022(8)
Pd(1)–Cl(1)	2.292(4)	2.2989(7)	2.2905(8)	2.2952(5)	2.2938(6)	2.290(3)
Pd(1)–Cl(2)	2.276(4)	2.2841(7)	2.2791(8)	2.2709(5)	2.2672(6)	2.268(3)
N(1)–C(1)	1.333(16)	1.334(3)	1.328(3)	1.333(2)	1.331(3)	1.309(13)
N(1)–C(9)	1.334(17)	1.357(3)	1.362(3)	1.360(2)	1.365(3)	1.360(13)
N(2)–C(8)	1.275(16)	1.289(3)	1.289(3)	1.291(2)	1.291(3)	1.293(12)
N(2)–C(10)	1.463(16)	1.478(3)	1.446(3)	1.444(2)	1.440(3)	1.419(13)
	Pd1	**Pd2**	**Pd3**	**Pd4**	**Pd5**	**Pd6**
			Bond angles [°]			
N(1)–Pd(1)–Cl(1)	94.2(3)	94.22(6)	94.02(6)	95.38(4)	95.23(5)	94.8(3)
N(1)–Pd(1)–Cl(2)	175.4(3)	175.68(6)	174.97(6)	171.78(4)	172.68(5)	175.4(2)
N(2)–Pd(1)–Cl(1)	174.0(3)	174.29(6)	173.84(7)	171.42(4)	172.75(5)	175.7(2)
N(2)–Pd(1)–Cl(2)	95.8(3)	95.81(6)	95.67(7)	94.40(4)	94.28(5)	94.5(2)
N(2)-Pd(1)-N(1)	79.8(4)	80.20(8)	80.18(8)	80.23(6)	80.33(7)	80.9(3)
Cl(1)–Pd(1)–Cl(2)	90.19(17)	89.73(3)	90.22(3)	90.727(19)	90.61(2)	89.78(11)

bridized nitrogen.[44,45,60] Although there was no significant difference or clear tendency regarding these bond lengths, slight influences of the substituents linked to N_{imino} were observed in that the bond lengths of Pd–$N_{pyridine}$ were slightly longer than that of Pd–N_{imino} with aryl groups (**Pd3**–**Pd6**) and the reverse effects were seen with aliphatic group (**Pd1** and **Pd2**); moreover, the ligands with the aryl-N_{imino} bond counterpoised the relative bonds of N-2–C-8, N-1–C-9, Pd-1–N-1 and Pd-1–N-2 due to the delocalized electrons of the conjugated aromatic system. In addition, the Pd–N-2 bond lengths were slightly elongated from **Pd4** to **Pd6** along with the reverse effects to N-2–C-10 bonds due to the increasing bulkiness and electron-donating influences from methyl to isopropyl substituents.

Catalytic Application of Pd Complexes for Suzuki Coupling

Typical reaction conditions for the Suzuki coupling at 0.01 mol% palladium loading are as follows:[37,48] a mixture of 20 mmol of 4-bromotoluene, 22 mmol of phenylboronic acid, and 40 mmol of K_2CO_3 in 25 mL toluene was heated at reflux for 18 h (Method **A**). In all cases high conversions were observed and are collected in entry 1 of Table 2. A higher efficiency was achieved by using a Young tube under a sealed environment;[63] the above reactions were conducted in parallel employing the Young tube for three hours (Method **B**), indicating perfect conversion yields (entry 2, Table 2). Under the same conditions as entry 2, the reactions with $PdCl_2$, $PdCl_2(CH_3CN)_2$ and $Pd(OAc)_2$ as the precatalyst were also performed, whereby 60%, 60% and 69% conversions were observed, respectively. The reactions with the same conditions as entry 2 but with additional 0.09 mL of H_2O

Table 2. Pd-catalyzed couplings between 4-bromotoluene and phenylboronic acid by using different catalyst precursors.[a]



Entry	Cat [mol%]	Time [h]	Method	Conv. [%][b] Pd1	Pd2	Pd3	Pd4	Pd5	Pd6
1	0.01	18	**A**	92	93	97	93	92	92
2	0.01	3	**B**	99	>99	>99	>99	>99	>99
3	0.01	3	**C**	98	96	>99	100	99	>99
4	0.002	6	**B**	97	>99	>99	>99	>99	>99
5	0.001	12	**B**	96	98	99	99	>99	>99
6	0.0001	48	**B**	66	95	96	96	98	>99
7	0.00001	48	**B**	-	25	29	29	47	45

[a] *Reaction conditions:* 4-bromotoluene (20 mmol), phenylboronic acid (22 mmol), K_2CO_3 (40 mmol), toluene (25 mL), Pd (10^{-4}M in toluene). Method **A**: reflux; Method **B**: in a Young tube, 110 °C in oil bath; Method **C**: 110 °C in oil bath, H_2O (0.09 mL) was added, in a Young tube.

[b] Conversions and yields were determined by GC.

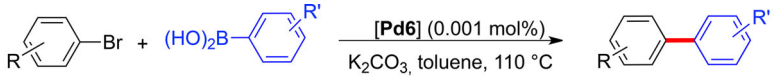
(Method **C**, entry 3) were conducted and still showed high activities. Subsequently, a higher molar ratio of substrates to the palladium adapted from 10^4 to 10^6 along with gradiently extending the reaction time were probed, the results are tabulated in Table 2 as entries 4 to 6. In general, high conversions were observed even with molar ratios of substrate to palladium of up to a million (entries 4 to 6). However, the significantly lower yield by **Pd1** was observed in entry 6 due to the aliphatic substituent of the imino group.[53] Further evaluation of the catalyst activity by increasing the molar ratio of substrates to the palladium up to 10^7 differentiated **Pd5** or **Pd6** from **Pd2** to **Pd4** as the preferential catalysts for further examination.

Beside the above results, the compound **Pd6** is easily prepared through either two-step synthesis or one-pot synthesis (described in the Experimental Section) because of the easier condensation of ketone with aniline bearing electron-donating substituents. Subsequently **Pd6** was chosen as the precursor in exploring the scope of substances for the Suzuki cross-coupling with a lower loading of 0.001 mol% of Pd. The results are collected in Table 3. In general, high conversions were achieved in all cases. Electron-withdrawing aryl bromide **1b** reacted smoothly with **2a** to yield the coupling product in high yield (entry 2) due to the active substrate in the oxidative addition step;[8] meanwhile, 4-bromoaniline **1d** coupled with **2a** to also form its product in high isolated yield (95%) (entry 4). Although electron-donating aryl bromides are sometimes deactivated in Suzuki cross-couplings,[64] 4-bromoanisole **1e** reacted with **2a** affording the corresponding product in a good yield. Noteworthy, the addition of H_2O was necessary to promote the transformation for **1e**.[65] The coupling of **1a** with electron-rich arylboronic acids, such as **2b**, **2e**, **2f** and electron-deficient **2c** and **2d** led to the desired biaryl products in good to high yields (86–100%, entries 9–13). Moreover, sterically hindered 2-bromotoluene **1f** underwent coupling with **2a** to produce the target product in 90% yield (entry 6). 1,3-Dibromobenzene **1h** was also efficiently converted to the double coupling product terphenyl **3ha** with **2a** in a facile process (entry 8). In addition, this coupling could be extended to benzyl bromide (entry 15), in which the diphenylmethane was obtained in 94% yield. More interestingly the couplings with heteroaryl bromides and heteroarylboronic acids were also achieved albeit with low conversions. On further increasing the catalyst loading to 0.02 mol% and 0.01 mol% for 2-bromothiophene **1j** (entry 16) and 3-bromopyridene **1k** (entry 17), the expected products were isolated in excellent yields of 97% and 93%, respectively. 2-Bromopyridene reacted with **2a** to form the product in a lower conversion due to the possible competitive coordination effect to palladium. The results demonstrated the high efficiency for Suzuki cross-coupling, being interpreted as the positive influence of the constrained iminopyridine palladium complex.

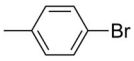
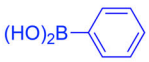
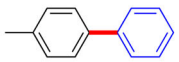
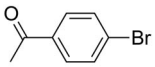
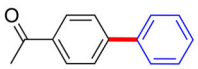
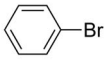
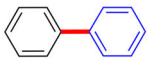
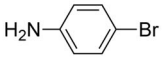
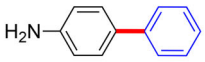
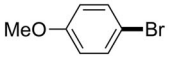
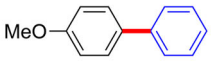
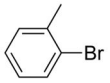
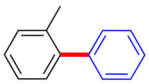
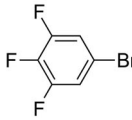
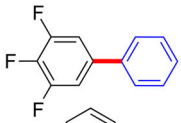
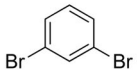
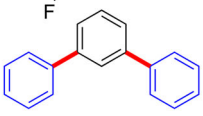
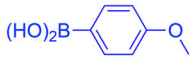
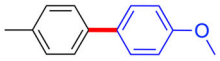
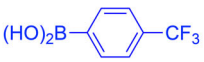
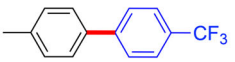
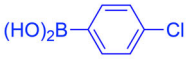
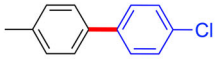
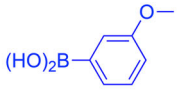
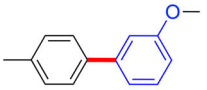
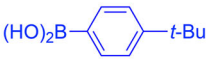
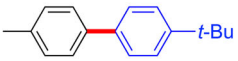
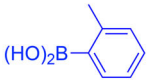
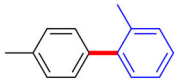
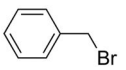
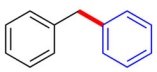
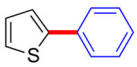
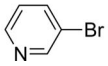
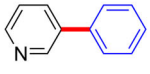
Heck Reactions by Pd6

The Heck reaction is considered to be as equally important as the Suzuki cross-coupling under palladium catalysis. After screening of the catalysts, **Pd6** was employed as the preferential choice. Simple optimization of the reaction conditions suggested that when 0.001 mol% of **Pd6** was utilized, the Pd-catalyzed Heck reaction between 4-bromotoluene **1a** and styrene occurred smoothly in DMF at 130 °C with K_2CO_3 as the base. It was reported that a cationic palladium intermediate was involved because of dissociation of one halide group and such a palladium species with a chelated ligand promoted the Heck reaction in DMF.[66] Under similar reaction conditions as for 4-bromotoluene, different aryl bromides, particularly those with electron-donating substituents, were tested. As shown in Table 4, 4-bromoaniline **1d** and 4-bromoanisole **1e** could react with styrene to deliver the Heck reaction products with high isolated yields, 94% and 96%, respectively (Table 4, entry 3 and entry 4). However, the regioselectivity for **1d** and **1e** was lower than with other substrates, which could be rationalized from the fact that geminal substitution is strongly favoured by electron-donating substituents for the cationic Heck reaction.[30,67] A more sterically hindered substrate, 2-bromotoluene (**1f**), was also tolerated at 0.001 mol% of catalyst loading. (*E*)-1-Methyl-2-styrylbenzene was isolated with 87% yield in high selectivity (Table 4, entry 5). Moreover, fluoro-substituted substrates such as 3,4,5-trifluorobromobenzene (**1g**) and 4-fluorobromobenzene **1l** were also suitable with satisfactory conversions and yields, although higher reaction temperatures and longer reaction times were necessary (Table 4, entry 6 and entry 8). Similarly, a high reaction temperature as high as 150 °C and 0.01 mol% of catalyst loading were also crucial for a high yield when 3-bromopyridine was employed (Table 4, entry 7). To our surprise, the electron-deficient 4-bromoacetophenone **1b** was less efficient. We proposed that the oxidative addition was not likely to be the rate-limiting step in the mechanistic cycle, and alkene insertion could be the slowest due to the chelation effect of the ligand.[66,68,69] This phenomenon further indicated that the palladium center was strongly stabilized by the constrained iminopyridine ligand. Furthermore, the reaction of 4-bromotoluene **1a** with ethyl acrylate could also provide the Heck coupling product selectively in 93% yield and only a 0.01 mol% amount of **Pd6** complex was required.

Table 3. Pd-catalyzed Suzuki cross-coupling of aryl bromides and arylboronic acid derivatives.[a]



1 2 3

Entry	ArBr		Ar'B(OH)$_2$		Time [h]	Ar-Ar'		Yield [%][b]
1		(**1a**)		(**2a**)	18		(**3aa**)	95
2		(**1b**)	**2a**		18		(**3ba**)	100
3		(**1c**)	**2a**		18		(**3ca**)	95
4		(**1d**)	**2a**		18		(**3da**)	93
5		(**1e**)	**2a**		18		(**3ea**)	89[c]
6		(**1f**)	**2a**		36		(**3fa**)	90
7		(**1g**)	**2a**		18		(**3ga**)	99
8		(**1h**)	**2a**		18		(**3ha**)	94
9	**1a**			(**2b**)	18		(**3ab**)	100
10	**1a**			(**2c**)	18		(**3ac**)	96
11	**1a**			(**2d**)	18		(**3ad**)	97
12	**1a**			(**2e**)	36		(**3ae**)	86
13	**1a**			(**2f**)	18		(**3af**)	100
14	**1a**			(**2g**)	18		(**3ag**)	98
15		(**1i**)	**2a**		18		(**3ia**)	94
16		(**1j**)	**2a**		36		(**3ja**)	97[d]
17		(**1k**)	**2a**		36		(**3ka**)	93[e]

[a] *Reaction conditions:* ArBr **1** (10 mmol), ArB(OH)$_2$ (11 mmol), K_2CO_3 (20 mmol), catalyst (10^{-4} mmol, 0.001 mol%), toluene (10 mL), Young tube, 110 °C, purge with N_2 for 3 min, 18 (36) h.

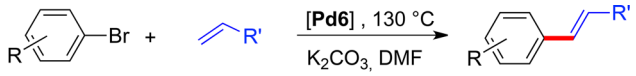
[b] Isolated yields.

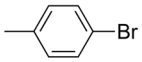
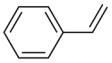
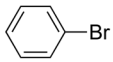
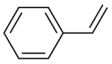
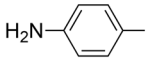
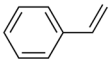
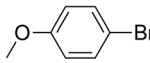
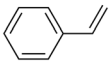
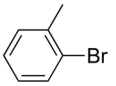
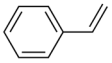
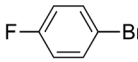
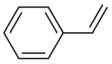
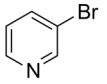
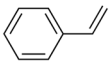
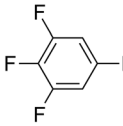
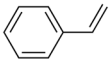
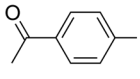
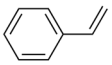
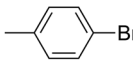
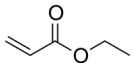
[c] 0.1 mL H_2O was added.

[d] **1j** (5 mmol), **2a** (6 mmol), K_2CO_3(10 mmol), catalyst (10^{-4} mmol, 0.002 mol%), toluene (5 mL), H_2O (0.1 mL) Young tube.

[e] ArBr **1** (10 mmol), ArB(OH)$_2$ (11 mmol), K_2CO_3 (20 mmol), catalyst (10^{-3} mmol, 0.01 mol%), toluene (10 mL).

Table 4. Heck reactions between aryl bromides and alkenes by **Pd6**.[a]



Entry	ArBr	Alkene	Catalyst [mol%]	Temp. [°C]	Time [h]	Yield[b] [%]	Selectivity[c] [%]
1	 (**1a**)		0.001	130	24	93	93
2	 (**1c**)		0.001	130	24	95	>99
3	 (**1d**)		0.001	130	24	94	81
4	 (**1e**)		0.001	130	24	96	89
5	 (**1f**)		0.001	130	24	87	97
6	 (**1l**)		0.001	130	36	82	94
7	 (**1k**)		0.01	150	24	95	93
8	 (**1g**)		0.01	130	36	81	97
9	 (**1b**)		0.01	130	36	91	91[d]
10	 (**1a**)		0.01	130	24	93	100

[a] *Reaction conditions:* ArBr (10 mmol), alkene (12 mmol), K_2CO_3 (12 mmol), catalyst (10^{-4} mmol, 0.001 mol%), DMF (10 mL), Young tube, 130 °C, purge with N_2 for 3 min.
[b] Isolated yields including 1,1-disubstituted ethylene.
[c] The selectivity was determined by ^{1}H NMR spectrometry.
[d] The isomers are 4-acetyl-*trans*-stilbene and 4-acetyl-*cis*-stilbene, respectively.

Conclusions

In summary, a series of the geometry-constrained iminopyridylpalladium complexes were synthesized and characterized. These phosphine-free palladium complexes have provided excellent reactivities in both Suzuki and Heck cross-couplings for most common substrates with extremely high turnover numbers (> 10^6). The successful development of these iminopyridine ligands for cross-coupling reactions should be helpful for the design of more efficient and robust palladium catalyst with even higher TONs.

Experimental Section

General Procedures

All reactions were carried out under an air atmosphere unless otherwise noted. All ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ADVANCE III 500 MHz spectrometer in deuteriated solvents with tetramethylsilane (TMS) as internal standard. NMR multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, m = multiplet, br = broad signal. Chemical shifts are given in ppm and are referenced to TMS (^{1}H, ^{13}C). All spectra were obtained at 25 °C in the solvent indicated. Coupling constants *J* are given in Hz. GC analyses were performed on an Agilent 6890 instrument with FID detector using an HP-5 capillary column [30 m × 0.32 mm (i.d.), 0.25 μ]. High-resolution mass spectra were recorded in the EI mode on a Waters Synapt-G2 HDMS. Flash column chromatography was performed on neutral silica gel (200–300 mesh) with ethyl acetate/petroleum ether as eluent. Melting points were determined on Buchi M-565 apparatus. X-ray crystallography was performed on an Oxford Xcalibur Eos Gemini Ultra with MoKα radiation. Details of the X-ray structure determinations and refinements are provided in Table 1. IR spectra were recorded on a Thermo Nicolet AVATAR 370 FT-IR. Elemental analysis was carried out using a Flash EA 1112 microanalyzer. All solvents and reagents were used directly from commercial sources without further purification.

6,7-dihydroquinolin-8(*5H*)-one was prepared following the reported procedure.[70]

Syntheses and Characterization of the Complexes

Typical synthesis of complex Pd6 by two-step procedure: Toluene (150 mL) was added to a mixture of 6,7-dihydroquinolin-8(*5H*)-one (2.94 g, 20 mmol), 2,6-diisopropylaniline (1.77 g, 10 mmol) and $TsOH{\cdot}H_2O$ (285 mg, 1.5 mmol). The reaction mixture was stirred for 12 h under reflux temperature and then allowed to cool to room temperature. After column chromatography with petroleum ether as the eluent, *N*-(5,6,7-trihydroquinolin-8-ylidene)-2,6-diisopropylaniline was obtained as a yellow solid in quantitative yield, which was then utilized for the next step directly.

The solution of *N*-(5,6,7-trihydroquinolin-8-ylidene)-2,6-diisopropylaniline (673 mg, 2.2 mmol) in dichloromethane (25 mL) was added slowly to the mixture of $PdCl_2(CH_3CN)_2$ (519 mg, 2.0 mmol) in dichloromethane (25 mL). The resulting mixture was stirred for 24 h at room temperature. After removal of the volatiles under vacuum, the complex **Pd6** was obtained by column chromatography (dichloromethane: ethanol = 10:1) as a yellow solid; yield: 764 mg (79%).

One-pot synthesis: Toluene (30 mL) was added to a mixture of 6,7-dihydroquinolin-8(*5H*)-one (323 mg, 2.2 mmol), 2,6-diisopropylaniline (425 mg, 2.4 mmol), $PdCl_2$ (354 mg, 2.0 mmol) and $TsOH{\cdot}H_2O$ (114 mg, 0.6 mmol). The reaction mixture was stirred for 12 h at reflux temperature and then allowed to cool to room temperature. After filtration and washing by toluene and ethanol, the solid was dried under reduced pressure affording the desired complex **Pd6.** The complex was further purified after column chromatography (dichloromethane: ethanol = 10:1); yield: 550 mg (56%); mp 282 °C (dec.). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.37 (d, J = 5.6 Hz, 1H), 7.95 (d, J = 7.9 Hz, 1H), 7.69 (dd, J_1 = 7.9 Hz, J_2 = 5.6 Hz, 1H), 7.34 (t, J = 7.8 Hz, 1H), 7.22 (d, J = 7.8, 2H), 3.15 (sept, J = 6.8 Hz, 2H), 3.06 (t, J = 5.9 Hz, 2H), 2.50 (t, J = 6.6 Hz, 2H), 1.98 (m, 2H), 1.42 (d, J = 6.8 Hz, 6H), 1.15 (d, J = 6.8 Hz, 6H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 180.7, 152.1, 148.1, 144.1, 141.2, 139.9, 139.8, 129.3, 128.0, 123.4, 31.2, 27.9, 27.3, 23.6, 23.4, 21.4; HR-MS (ESI$^+$): m/z = 488.1088, calcd. for $C_{23}H_{29}ClN_3Pd$ [M−Cl+CH_3CN]$^+$: 488.1085; anal. calcd. for $C_{21}H_{26}Cl_2N_2Pd$: C 52.14, H 5.42, N, 5.79; found: C 52.14, H 5.51, N 5.80.

Complexes **Pd1**, **Pd2**, **Pd3**, and **Pd4** were prepared following the one-pot synthetic procedure as described for complex **Pd6. Pd5** was prepared following the two-step procedure as described for complex **Pd6**.

Complex Pd1: Yield: 58%; mp 233 °C (dec.); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 8.82 (d, J = 5.5 Hz, 1H), 7.82 (d, J = 7.7 Hz, 1H), 7.39 (dd, $J1$ = 7.7 Hz, $J2$ = 5.5 Hz, 1H), 3.78 (t, J = 7.9 Hz, 2H), 3.11 (t, J = 6.5 Hz, 2H), 3.06 (t, J = 6.1 Hz, 2H), 2.11 (m, 2H), 1.70 (m, 2H), 1.36 (m, 2H), 0.93 (t, J = 7.4 Hz, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 177.8, 153.6, 147.8, 142.5, 141.0, 128.1, 51.9, 30.8, 28.8, 27.1, 21.1, 19.5, 13.8; HR-MS (ESI$^+$): m/z = 384.0459, calcd. for $C_{15}H_{21}ClN_3Pd$ [M−Cl+CH_3CN]$^+$: 384.0459; anal. calcd. for $C_{13}H_{18}Cl_2N_2Pd$: C 41.13, H 4.78, N 7.38; found: C 41.26, H 4.85, N 7.48.

Complex Pd2: Yield: 44%; mp 275 °C (dec.); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.02 (d, J = 5.4 Hz, 1H), 7.80 (d, J = 7.9 Hz, 1H), 7.56 (d, J = 7.5 Hz, 2H), 7.45 (dd, J_1 = 7.9 Hz, J_2 = 5.4 Hz, 1H), 7.34 (t, J = 7.5 Hz, 2H), 7.28 (t, J = 7.5 Hz, 1H), 5.28 (s, 2H), 2.98 (m, 4H), 2.06 (m, 2H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 180.5, 153.3, 148.0, 143.0, 141.1, 136.2, 128.5, 127.6, 127.3, 54.1, 29.8, 27.0, 21.0; HR-MS (ESI$^+$): m/z = 418.0300, calcd. for $C_{18}H_{19}ClN_3Pd$ [M−Cl+CH_3CN]$^+$: 418.0302; anal. calcd. for $C_{16}H_{16}Cl_2N_2Pd$: C 46.46, H 3.90, N 6.77; found: C 46.23, H 3.90, N 6.73.

Complex Pd3: Yield: 88%; mp 270 °C (dec.); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.11 (d, J = 5.4 Hz, 1H), 7.89 (d, J = 8.0 Hz, 1H), 7.54 (dd, J_1 = 8.0 Hz, J_2 = 5.4 Hz, 1H), 7.40 (t, J = 7.4 Hz, 2H), 7.33 (t, J = 7.4 Hz, 1H), 7.20 (d, J = 7.4 Hz, 2H), 3.05 (t, J = 6.0 Hz, 2H), 2.73 (t, J = 6.3 Hz,2H), 2.00 (m, 2H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 80.0, 153.0, 148.0, 144.9, 143.5, 141.0, 128.9, 128.3, 127.1, 123.2, 31.5, 27.3, 21.2; HR-MS (ESI$^+$): m/z = 404.0155, calcd. for $C_{17}H_{17}ClN_3Pd$ [M−Cl+CH_3CN]$^+$: 404.0146; anal. calcd for $C_{15}H_{14}Cl_2N_2Pd$: C 45.08, H 3.53, N 7.01; found: C 45.39, H 3.57, N 6.83.

Complex Pd4: Yield: 57%; mp 275 °C (dec.); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.33 (d, J = 5.5 Hz, 1H), 7.94 (d, J = 7.8 Hz,1H), 7.68 (dd, J_1 = 7.8 Hz, J_2 = 5.5 Hz, 1H), 7.17 (m, 1H), 7.11 (d, J = 7.5 Hz, 2H), 3.05 (t, J = 6.0 Hz, 2H), 2.46 (d, J = 6.6 Hz, 2H), 2.29 (s, 6H), 2.01 (m, 2H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 180.2, 152.2, 148.1 143.9, 142.6, 142.1, 141.1, 129.6, 127.8, 127.0, 30.3, 27.2, 21.4, 18.0; HR-MS (ESI$^+$): m/z = 432.0463, calcd. for $C_{19}H_{21}ClN_3Pd$ [M−Cl+CH_3CN]$^+$: 432.0459; anal. calcd. for $C_{17}H_{18}Cl_2N_2Pd$: C 47.74, H 4.24, N 6.55; found: C 47.45, H 4.13, N 6.45.

Complex Pd5: Yield: 77%; mp 277 °C (dec.); ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.35 (d, J = 5.5 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.68 (dd, J_1 = 8.0 Hz, J_2 = 5.5 Hz, 1H), 7.29 (t, J = 7.7 Hz,1H), 7.17 (d, J = 7.7 Hz, 2H), 3.04 (t, J = 6.0 Hz, 2H), 2.85 (m, 2H), 2.49 (m, 4H), 1.99 (m, 2H), 1.31 (t, J = 7.6 Hz, 6H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ = 180.5, 152.1, 148.2, 144.1, 141.4, 141.2, 134.8, 129.3, 127.5, 125.4, 30.7, 27.3, 23.6, 21.4, 13.2; HR-MS (ESI$^+$): m/z = 460.0778, calcd. for $C_{20}H_{25}ClN_3Pd$ [M−Cl+CH_3CN]$^+$: 460.0772; anal. calcd. for $C_{19}H_{22}Cl_2N_2Pd$: C 50.08, H 4.87, N 6.15; found: C 50.20, H 4.97, N 6.15.

General Procedure for Pd-Catalyzed Suzuki Cross-Coupling Reactions

To a Young tube, were added aryl bromide (10 mmol), K_2CO_3 (20 mmol), and arylboronic acid (11 mmol), then complex **Pd6** (10^{-4} M in toluene, 1 mL) and toluene (9 mL) were added. The mixture was degassed with N_2 bubbling for 3 min. Then, the sealed Young tube was set into the preheated 110 °C oil bath; after stirring for 18 h, the Young tube was allowed to cool to room temperature. After filtration and extraction with toluene (50 mL), the resulting solution was concentrated under vacuum and the desired biaryl was isolated by column chromatography.

General Procedure for Pd-Catalyzed Heck Reactions

To a Young tube, aryl bromide (10 mmol), K_2CO_3 (12 mmol), alkene (12 mmol), complex **Pd6** (10^{-4} M in DMF, 1 mL) and DMF (9 mL) were added. The mixture was degassed for 3 min. After stirring for 24 h at 130 °C, the reaction temperature was allowed to cool to room temperature and water (100 mL) was added. The resulting mixture was

extract by ethyl acetate (50 mL) for 3 times. After drying and concentration, the desired product was isolated by column chromatography.

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