

A Heteroleptic Palladium(II) Complex Containing a Bidentate Carbene/ Amido Ligand and 3-(Trifluoromethyl)-5-(2-pyridyl)pyrazolate: **Fast Catalyst Activation in the Heck Coupling Reaction**

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A multicomponent reaction between PdCl₂, fppzH, and [LH¹H²]Cl in the presence of K₂CO₃ (L = bidentate amido/carbene; fppzH = 3-(trifluoromethyl)-5-(2-pyridyl)pyrazole) allows the preparation of PdL(fppz) in good yield. The analogous platinum complex, however, needs to be prepared by a twostep procedure. The new palladium(II) and platinum(II) complexes were characterized by 1D and 2D NMR spectroscopy, X-ray crystallography, electrospray ionization mass spectrometry, and elemental analyses. X-ray photoelectron spectroscopy indicates the high electron richness of the palladium atoms in PdL(fppz). These palladium complexes are efficient in catalyzing Heck coupling reactions with challenging aryl halide substrates. The catalyst activation in PdL(fppz) is significantly faster than that in cis-PdL₂. A mere 0.5 mol % of palladium loading is enough to afford a 82% yield of coupled product from 4-chloroanisole and styrene in 24 h.

Introduction

The palladium-catalyzed Heck reaction is a powerful tool for the preparation of arylated alkenes in fine chemical synthesis.^{1–5} In comparison to aryl bromides and iodides, aryl chlorides are attractive substrates for Heck reactions in industrial applications because of their low cost and wide availability. However, these substrates, especially those deactivated aryl chlorides, are generally unreactive and typically harsh reaction conditions are required for their feasible utilization.⁶ Palladium complexes with bulky electron-rich phosphine ligands and P-containing palladacycles have demonstrated excellent Heck coupling activities with deactivated aryl chloride substrates.^{7–9} The air sensitivity and high cost of these ligands are, however, their major drawbacks. N-heterocyclic carbene (NHC) ligands have been proven to be highly versatile in a wide range of coupling reactions.^{8,10–17} However,

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Chart 1. Bidentate Palladium and Platinum Complexes



the activity of catalysts based on NHC ligands has been mostly limited to activated and nonactivated substrates.^{8,18-34} In a recent work, we demonstrated that the palladium(II) NHC complexes *cis*-1 are highly promising precatalysts for Heck

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Scheme 1. Multicomponent Synthesis of Pd(L)(fppz) Complexes



Scheme 2. Sequential Synthesis of the Pt(L)(fppz) Complex



reactions (Chart 1), capable of utilizing deactivated aryl chlorides as substrates.³⁵ In addition to the robust NHC donor, the anionic amide group of the chelate ligand can impart a high electron density on the metal center,^{36–41} thus favoring the oxidative addition of a strong C–Cl bond.^{42,43} The palladium(II) complex *cis*-1 is indeed a good precursor for active palladium(0) species. For deactivating aryl chlorides and bulky aryl bromides substrates, *cis*-1 is even more

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efficient than its palladium(0) precatalyst.³⁵ However, cis-1 needs a long catalyst activation time; in the reaction between styrene and 4-chloroacetophenone, it takes about 1 h. The formation of active species from *cis*-1 should involve ligand dissociation, allowing subsequent substrate coordination, and this process is slow due to the two strongly binding bidentate NHC/amide ligands. We envisioned that replacement of one of the bidentate carbene/amide ligands with a similar anionic but weaker binding ligand may result in a more efficient catalyst with a faster activation period. Hence, the known bidentate fppz ligand (fppz=3-(trifluoromethyl)-5-(2-pyridyl)pyrazolate) consisting of pyrazolate and pyridine functionalities was selected. Herein, we report on our successful attempt in carrying out a straightforward multicomponent reaction (MCR) to obtain pure palladium complex 3. Such a fine-tuned heteroleptic complex shows promising catalytic activity in Heck coupling reactions with a range of aryl bromides and chloride substrates.

Results and Discussion

Preparation of Palladium(II) Carbene Complexes. The new palladium complexes PdL(fppz) (3a-c) were successfully synthesized by a one-pot reaction between $PdCl_2$, $[LH^1H^2]$ - $\dot{\text{Cl}}$ (**2a**-c) (Hⁱ = NH proton; H² = NCHN proton), fppzH, and K₂CO₃ as base in DMF at 50 °C (Scheme 1). Such MCR protocol is desirable due to simplicity in operation, time savings, and reduced waste. The reaction is highly chemoselective, as the known homoleptic complex 1 or Pd(fppz)₂ was not observed in a noticeable amount. After thorough washing with methanol, pure solids of 3a-c were obtained with good yields ranging from 64 to 77%. These compounds are air-stable in the solid form and readily soluble in halogenated solvents. The three new compounds are neutral Pd(L)(fppz) complexes which have been characterized by ${}^{1}H$ and ${}^{13}C{}^{1}H$ NMR spectroscopy, elemental analyses, electrospray ionization mass spectrometry (ESI-MS), and X-ray crystallographic studies. The successful chelation of the bidentate carbene and fppz ligands are inferred by the disappearance of the original H^1 , H^2 , and NH protons on the [LH¹H²]Cl and

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Table	1.	Crystal	lographi	: Data o	f:	3a-0	e and	5
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	3a	3b	3c	5
empirical formula	C ₂₁ H ₁₇ F ₃ N ₆ OPd	C ₂₇ H ₂₁ F ₃ N ₆ OPd	$C_{31}H_{23}F_{3}N_{6}OPd \cdot 0.25CH_{2}Cl_{2}$	C ₂₁ H ₁₇ F ₃ N ₆ OPt
formula wt	532.81	608.90	680.19	621.50
cryst syst	triclinic	triclinic	triclinic	triclinic
space group	$P\overline{1}$	$P\overline{1}$	$P\overline{1}$	$P\overline{1}$
a, Å	7.7528(4)	12.7589(2)	12.526(2)	7.837(4)
b, Å	11.5739(5)	14.0925(2)	12.809(2)	11.700(6)
<i>c</i> , Å	12.4410(6)	14.1825(3)	19.525(4)	12.451(6)
α, deg	74.197(2)	92.1710(10)	99.602(4)	74.083(15)
β , deg	89.651(2)	95.8850(10)	95.938(4)	88.881(15)
γ , deg	72.023(2)	103.8680(10)	111.943(4)	71.196(14)
$V, Å^3$	1017.99(8)	2457.54(7)	2817.6(9)	1036.3(9)
T, K	150(2)	150(2)	150(2)	150(2)
Ź	2	4	4	2
no. of unique data	5222	12492	10 762	5224
no. of params refined	290	685	781	290
$R1^a (I > 2\sigma(I))$	0.0375	0.0301	0.0544	0.0450
wR2 ^{b} (all data)	0.0995	0.0822	0.1568	0.1044

$${}^{a} \mathbf{R} \mathbf{1} = \sum (||F_{o}| - |F_{c}||) / \sum |F_{o}|. {}^{b} \mathbf{w} \mathbf{R} \mathbf{2} = [\sum (|F_{o}|^{2} - |F_{c}|^{2})^{2} / \sum (F_{o}^{2})]^{1/2}.$$

fppzH ligand precursors. The diastereotopic nature of the methylene protons further confirms the bidentate chelation of the carbene ligand. The assignments of these diastereotopic signals are assisted by acquiring their HMBC spectra (see Figure 1S in the Supporting Information for the HMBC spectrum of 3c). For example, the cross-peak analyses in 3c established that the doublets at 4.40 and 5.45 ppm are attached to the same carbon adjacent to the C=O group, whereas those at 6.00 and 6.71 ppm belong to the methylene protons adjacent to the naphthyl group. The carbene signals for 3a-c are located easily at ca. 156 ppm, since in each case the quaternary carbon uniquely correlates with all the methylene protons in its HMBC spectrum. These carbene signals are shifted upfield compared with those of cis (~164 ppm) and trans (\sim 170 ppm) isomers of the bis-bidentate complex 1.³⁶ In fact, these upfield carbene resonances indicate the stereochemistry of these complexes as depicted in Scheme 1, since carbene resonances at ca. 150 ppm are characteristic for a palladium-(II) complex with carbene trans to a pyridine moiety.^{36,44–46} Such stereochemistry was eventually confirmed by an X-ray diffraction study. Thus, the MCR is highly stereoselective, producing only the isomer with the carbene moiety trans to the pyridine (A). The absence of the other isomer with the two ligands in cis positions (B) can be revealed from the computational studies with the B3LYP functional. In the gas phase, complexes 3a-c in form A are thermodynamically much more stable than the other isomeric forms by 13.9, 9.9, and 9.9 kcal/ mol, respectively. It is worth mentioning that the stereochemistry in A with a trans disposition of the two neutral atoms and the two anionic donors is relevant to that in the PEPSSI complexes reported by Organ et al.^{17,45,46}

Preparation of an Analogous Platinum(II) Complex. To investigate whether the MCR protocol is also suitable for the preparation of analogous platinum complexes, the reaction between K₂PtCl₄, ligand precursor **2a**, fppzH, and base was carried out. However, this failed to yield a desirable product. The ¹H NMR spectrum of the reaction mixture shows the formation of Pt(fppzH)Cl₂ and unreacted **2a**. Instead, the

Table 2. Selected Bond Distances (Å) and Angles (deg) of 3a-cand 5^a

	3a	3b ^b	$3c^b$	5
M1-C1	1.969(3)	1.957(2)	1.977(5)	1.968(7)
M1-N3	2.046(3)	2.0404(18)	2.058(5)	2.049(6)
M1-N4	2.122(3)	2.1303(18)	2.132(4)	2.108(5)
M1-N5	1.998(3)	2.0098(18)	2.009(4)	1.996(6)
C1-M1-N3	85.77(13)	84.82(8)	85.2(2)	85.9(3)
C1-M1-N5	97.55(12)	98.41(5)	98.2(2)	98.6(3)
N3-M1-N4	97.89(11)	97.05(7)	97.64(18)	97.1(2)
N4-M1-N5	78.84(11)	79.54(7)	78.97(18)	78.5(2)
C1-M1-N4	175.76(13)	175.93(8)	177.1(2)	176.8(3)
N3-M1-N5	176.52(11)	175.60(7)	176.38(18)	175.4(2)

 ${}^{a}M = Pd$ for **3a-c** and M = Pt for **5**. b Only data from one of the two independent molecules are given.

target analogous Pt complex was successfully prepared in sequential steps. The fppzH ligand is introduced to the platinum metal first by preparing the known complex Pt(fppzH)Cl₂ (Scheme 2). A subsequent carbene transfer reaction between Ag(LH¹)Cl (4) and Pt(fppzH)Cl₂ in the presence of K₂CO₃ affords Pt(L)(fppz) complex 5 in 44% yield (Scheme 2). The silver complex 4 was straightforwardly prepared by the reaction of Ag₂O and 2a in DMF. Similar silver carbene complexes bearing the carbene/amide ligands have been reported previously.^{47,48} Complex 5 is air-stable with average solubility in halogenated solvents. The spectroscopic data of 5 are essentially similar to those of its palladium analogue 3a. The carbene signal is observed at 156.3 ppm, comparing favorably with that of 155.5 ppm in 3a.

Crystallographic Studies. The structures of Pd complexes 3a-c and the Pt complex 5 have been successfully determined by X-ray diffraction studies. Crystallographic data and their selected bond distances and angles are given in Table 1 and 2, respectively. Figures 1 and 2 give their thermal ellipsoid plots, confirming the trans disposition of the carbene and pyridine moieties. The geometric parameters of the Pd complex 3a and its analogous Pt complex 5 are highly comparable to each other. All these complexes adopt a distorted-square-planar coordination geometry. The bite angle of the carbene is greater than that of fppz ligand (ca. 85° vs 79°). In each complex, the three M–N distances are significantly different in length. In

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Figure 1. Molecular structures of 3a (left) and 5 (right) with 50% probability ellipsoids. Hydrogen atoms have been omitted for clarity.



Figure 2. Molecular structures of 3b (left) and 3c (right) with 50% probability ellipsoids. Only one of their independent molecules in an asymmetric unit is shown. Hydrogen atoms have been omitted for clarity.

Table 3. Mizoroki-Heck Reaction^a



entry	cat.	time	temp, °C	heating	yield, %	6:6′
1	3b	2 h	120	conventional	0	
2	3b	2 h	130	conventional	90	92:8
3	cis-1b	2 h	140	conventional	96	93:7
4	3a	2 h	140	conventional	98	94:6
5	3b	2 h	140	conventional	96	93:7
6	3c	2 h	140	conventional	89	94:6
7	3b	2 h	160	conventional	97	94:6
8	3b	15 min	140	MW	98	91:9
9	cis-1b	15 min	140	MW	15	100:0

^{*a*} Conditions: 1 mmol of aryl halide, 1.4 mmol of alkene, 1.1 mmol of NaOAc, 2 g of TBAB, 0.5 mol % of [Pd] cat., 15 min-2 h, 120-160 °C. Yields and selectivity were determined by NMR using 1,3,5-trimethoxybenzene as internal standard.

general, the metal-pyridine bond trans to the carbene moiety is the longest (M1-N4 distance ~2.12 Å), followed by the metal-amido bond (M1-N3 distance ~2.05 Å). The metalpyrazole bond is the shortest (M1-N5 distance ~2.00 Å). The Pd-C distances in **3a**-c are ca. 1.97 Å: that is, shorter than that in *trans*-**1b** (2.020(4) Å) but comparable to that in *cis*-**1b** (1.966(2) Å).³⁶ The Pd1-N3 distances, in contrast, are shorter than that of 2.081(1) Å in *cis*-**1b** but similar to that of 2.051(4) Å in *trans*-**1b**.³⁶

X-ray Photoelectron Spectroscopy (XPS). The electronic properties of $3\mathbf{a}-\mathbf{c}$ were investigated by XPS. The binding energies of Pd electrons in the core $3d_{3/2}$ and the $3d_{5/2}$ orbitals in $3\mathbf{a}-\mathbf{c}$ are essentially identical at about 342.6 and 337.4 eV, respectively. These values are somewhat higher than those of

341.7 and 336.6 eV in *cis*-**1b**, in support of our prediction that the fppz ligand is less basic than the carbene ligand. Intriguingly, these binding energies in **3a**-**c** and *cis*-**1b** are comparable to those in elemental Pd(0) (340.5 and 335.1 eV)⁴⁹ and Pd⁰(LH¹)₂(MA) (LH¹ derived from **2** with R = Ph) (MA = maleic anhydride) (340.7 and 335.4 eV) and thus are very low for the Pd(II) atoms,⁵⁰ reflecting the strong electrondonating effect of the bidentate ligands. For comparison, the corresponding binding energies in a Pd(II) complex with a

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Figure 3. The time-yield curves of **3b** vs *cis*-**1b** in the Heck coupling reaction of 4-chloroacetophone and styrene.

bidentate carbene ligand with abnormal binding are much higher at ca. 348.0 and 342.6 eV.⁵¹

Catalytic Studies. The catalytic performance of complexes 3a-c in Heck coupling reactions of aryl halides with alkenes was studied. The reaction between 4-chloroacetophenone and styrene was chosen as the benchmark reaction for initial investigation. We employed our previous conditions of light palladium loading of 0.5 mol % and the cheap ionic liquid tetran-butylammonium bromide (TBAB) as solvent (Table 3).35 Entry 1 shows that no coupling activity was observed at 120 °C. An increment of just 10 °C results in a surge of coupled product. The phenomenon, also demonstrated in cis-1b previously, can be explained by the feasible formation of an active Pd⁰ species, such as [Pd⁰L]⁻, only above a critical temperature. As shown by entries 2, 5, and 7, the best temperature for the catalytic reaction is at 140 °C, producing an excellent yield of 96% coupled product in 2 h. Complexes 3a,b and cis-1b essentially produced the same overall yields, reflected by entries 3-5. Complex 3c with N-naphthylmethyl substitutions, in contrast, gave poorer vields (entry 6).

The time—yield relationship of *cis*-**1b** vs **3b** in the initial 2 h was studied. Figure 3 clearly illustrates the success of our design principle by using a weaker binding ligand of the fppz ligand in **3b**, as *cis*-**1b** needs about 1 h of catalyst activation, whereas the process takes just ca. 30 min for **3b**.

Microwave-assisted synthesis is a valuable technique for organic chemists because the radiation can enhance the reaction rate and in many cases improve product yields as well.^{52,53} Entry 8 in Table 3 shows that **3b** affords an excellent yield of 98% coupled product in just 15 min with microwave heating. In sharp contrast, *cis*-**1b** affords a much lower yield of 15% under identical conditions (entry 9), confirming once again that catalyst activation of **3b** is much faster.

Next, we tested the activity of 3b in utilizing hindered aryl bromide substrates (Table 4). A general condition was established involving 0.5 mol % of 3b at 140 °C in 12 h. Indeed, the catalyst system is capable of delivering good trans product yields with a range of challenging aryl bromide substrates. Generally, good yields of coupled products can be obtained from the reactions between deactivated aryl bromides bearing methoxyl groups and styrene (entries 1, 4, and 5). In particular, the highly deactivating substrate 5-bromo-1,2,3-trimethoxybenzene can be utilized to generate the coupled product in 72% yield (entry 5). Changing styrene to *n*-butyl acrylate as a coupling partner results in, however, a lower yield of coupled products (entries 13-15). (E)-3,4,5,4'-Tetramethoxystilbene (12), designated as DMU-212, is a strong candidate for antitumor applications.⁵⁴ Entry 12 shows that it can be prepared in 59% yield with only a 0.5 mol % Pd precatalyst loading. Our protocol is much more cost-effective than the reported procedure requiring 40 mol % of Pd loading.⁵⁴ Hindered aryl bromides with two ortho substituents can also be coupled effectively (entries 7, 10 and 16, 17). For example, decent 53 and 55% yields of 11 and 17, respectively, can be achieved from the very bulky 1-bromo-2,4,6-triisopropylbenzene (entries 10 and 17). Complex 3b delivers somewhat better yields of coupled products than cis-1b, as indicated by entry 5 vs 6 and 10 vs 11. Lowering the precatalyst loading below 0.5 mol % led to inferior yields of products, as indicated in entries 1-3 and 7-9.

The catalyst system of **3b** is also effective for a range of aryl chlorides (Table 5). Excellent yields of coupled products can be achieved within 2 h with activated aryl chlorides (entries 1, 2, 5, 6, 19, 20, and 22–25). A longer reaction time of 12 h is needed for the nonactivated substrate chlorobenzene, generating coupled products with styrene and n-butyl acrylate in 87 and 68% yields, respectively (entries 12 and 26). Different isomers of chlorotoluene can also be coupled with styrene (entries 13, 15, and 16). A 60% yield of coupled product can be achieved from 4-chlorotoluene, whereas in contrast the yield drops to 37% with 2-chlorotoluene, indicating the significance of steric hindrance for aryl chloride substrates. The catalyst system is also capable of employing deactivated aryl chlorides as coupling partners (entries 17, 18 and 29, 30). A reasonable 66% of coupled product can be obtained from 4-chloroanisole and styrene (entry 17). Further prolonging the reaction time to 24 h affords a good yield of 82% (entry 18). Entry 9 vs entry 11 again illustrates the faster activation of 3b such that a 94% yield of coupled product can already be obtained already from 4-chlorobenzonitrile in 1 h, whereas catalyst activation of cis-1b was not yet completed. Nevertheless, a similar level of yields was achieved from cis-1b and **3b** in the long run (entries 13 vs 14 and 20 vs 21). The catalytic data suggest that **3b** and *cis*-**1b** share a similar catalytic pathway via the plausible 14-electron active species $[Pd^0L]^-$. However, replacement with the weaker binding fppz ligand in **3b** leads to a faster catalyst activation because of the more facile ligand dissociation. The optimal precatalyst loading is again 0.5 mol %, as reduction of the palladium amount to 0.1 or 0.2 mol % led to greatly inferior yields (entries 2-4 and 6-8).

Conclusions. The multicomponent reaction between the imidazolium ligand precursor fppzH and $PdCl_2$ is highly chemo- and regioselective, affording pure Pd(L)(fppz) in good yield. The geometrical isomer with carbene and pyridine groups trans to each other was thermodynamically much more stable. For the preparation of the analogous platinum(II) complex, however, a two-step reaction consisting of a carbene transfer step has to be employed. We demonstrated that fine tuning of palladium precatalyst with a slightly weaker binding fppz ligand replacing one of the two

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		Ar—Br +	R 0.1-0.5 mol% NaOAc, TBA 12 h, 140 °C	B Ar	
entry	cat.	Ar–Br	alkene	product	yield, %
1 2 3	3b	Br		OMe 7	$89\\81b\\68c$
4	3b	Br OMe		Me 8	91
5 6	3b cis-1b	MeO MeO OMe		MeO MeO OMe	72 68
7 8 9	3b	Br			$87 \\ 52b \\ 44c$
10 11	3b cis-1b	Br			53 40
12	3b	MeO MeO OMe	OMe	MeO MeO MeO MeO MeO DMU-212	59
13	3b	Br		OMe 13	50
14	3b	Br OMe		CO ₂ ⁿ Bu OMe 14	82
15	3b	MeO MeO OMe		MeO MeO OMe 15	61
16	3b	Br		CO2"Bu	83
17	3b	Br		CO ₂ ⁿ Bu	55

^{*a*} Conditions: 1 mmol of aryl halide, 1.4 mmol of alkene, 1.1 mmol of NaOAc, 2 g of TBAB, 0.50 mol % of [Pd] cat. unless stated otherwise, 140 °C, 12 h, isolated yields. ^{*b*} 0.20 mol % of [Pd] cat. ^{*c*} 0.10 mol % of [Pd] cat.

bidentate carbene/amido ligands in *cis*-1 is feasible, leading to faster catalyst activation. The new catalyst is a highly effective precatalyst for Heck coupling reactions with a wide range of aryl halides, including deactivated aryl chloride substrates.

Experimental Section

General Procedure. All manipulations were performed under a dry nitrogen atmosphere using standard Schlenk techniques. Solvents were dried with standard procedures. Starting chemicals were purchased from commercial source and used as received.

Table 5. Heck Reactions of Aryl Chlorides^a

	R ¹	CI +	² 0.1-0.5 m NaOAc 1-24 h, ⁻	ol% [Pd] cat. , TBAB 140 °C	→ R ² + R ^{1.} rans	R ² gem	
entry	cat.	Ar–Cl	alkene	product	time, h	yield, %	trans, %
1 2 3 4	3b	°		°	1 2 2 2	91 93 78^{b} 67^{c}	98 96 98 100
5 6 7 8	3b	o ⊢ CI		0	1 2 2 2	90 >99 61^{b} 54^{c}	100 90 100 100
9 10 11	3b 3b cis-1b	NC-CI		NC	1 2 1	94 >99 0	100 80 0
12	3 b	С		20	12	87	96
13 14	3b cis-1b	Me		Me	12 12	60 54	94 94
15	3b	Me		Me 22	12	37	100
16	3b	MeCI		Me 23	12	54	100
17 18	3b	MeO-CI		MeO-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C-C	12 24	66 82	90 90
19 20 21	3b 3b cis-1b	°	∕CO2″Bu	о со ₂ "Ви 25	1 2 2	80 98 94	100 100 100
22 23	3b	O H −CI		о Н — СО ₂ ^л Ви 26	1 2	87 94	100 100
24 25	3b	NC-CI		NC-CO2 ⁿ Bu 27	1 2	85 88	100 100
26	3b	Сі		28 CO ₂ "Bu	12	68	100
27 28	3b	Me		Me-CO ₂ "Bu 29	12 24	59 67	100 100
29 30	3b	MeO-CI		MeO-CO2"Bu	12 24	48 54	100 100

^{*a*} Conditions: 1 mmol of aryl halide, 1.4 mmol of alkene, 1.1 mmol of NaOAc, 2 g of TBAB, 0.50 mol % of [Pd] cat. unless stated otherwise, 1–24 h, 140 °C, isolated yields. ^{*b*} 0.20 mol % [Pd] cat. ^{*c*} 0.10 mol % [Pd] cat.

cis-1b, ³⁶ 2, ³⁶ fppzH, ⁵⁵ and Pt(fppzH)Cl₂⁵⁶ were prepared according to the literature procedure. ¹H, and ¹³C{¹H} NMR spectra were recorded at 300.13 and 75.48 MHz, respectively, on a Bruker AV-300 spectrometer. The chemical shifts for ¹H and ¹³C spectra were referenced by the residual solvent signals relative to tetramethylsilane at 0 ppm. Elemental analysis was performed on a Thermo Flash 2000 CHN-O elemental analyzer. Microwave irradiation experiments were conducted in a Milestone Start S microwave system. Reaction times refer to hold times at the temperature indicated in Table 5. The temperature was measured with an IR sensor on the outside of the reaction vessel. ESI-MS was carried out on a Finnigan/Thermo Quest MAT 95XL mass spectrometer at National Chung Hsing University (Taiwan). X-ray photoelectron spectroscopy was performed on a ESCA PHI 1600 system using Mg K α radiation ($h\nu = 1253.6 \text{ eV}$) at National Tsing Hua University (Taiwan).

Synthesis of 3a. To a 50 mL Schlenk flask containing a mixture of PdCl₂ (0.20 g, 1.13 mmol), 2a (0.28 g, 1.13 mmol), 2-(3-(trifluoromethyl)-1H-pyrazol-5-yl)pyridine (0.24 g, 1.13 mmol), and K₂CO₃ (0.47 g, 3.39 mmol) in DMF (20 mL) was added dry DMF (20 mL). The mixture was heated at 50 °C with stirring for 10 h. The solvent was completely removed under vacuum. The residue was dissolved in dichloromethane. The organic layer was then washed twice with water. After drying with anhydrous magnesium sulfate, the solvent was completely removed under vacuum. The residue was washed twice with a small amount of methanol. The air-stable white solid was then filtered on a frit and dried under vacuum. Yield: 0.46 g, 77%. Mp: 301.7-307.5 °C dec. Anal. Calcd for C₂₁H₁₇F₃N₆OPd: C, 47.34; H, 3.22; N, 15.77. Found: C, 47.05; H, 3.30; N, 15.71. ¹H NMR (CDCl₃): δ 4.18 (s, 3H, CH₃), 4.37 (d, ²*J*(H,H) = 14.3 Hz, 1H, CH_AH_BCO , 5.37 (d, ²J(H,H) = 14.6 Hz, 1H, CH_AH_BCO), 6.77 $(s, 1H, pyrazole H), 6.78-6.85 (m, 1H, Ph H), 6.94 (d, {}^{3}J(H,H) =$ 1.8 Hz, 1H, imi H), 6.96–7.01 (m, 1H, Py H), 7.06 (d, ${}^{3}J$ (H,H) = 1.8 Hz, 1H, imi H, 7.20 (t, ${}^{3}J(\text{H},\text{H}) = 7.7 \text{ Hz}, 2\text{H}, \text{Ph } H$), 7.38 (d, ${}^{3}J(H,H) = 5.6$ Hz, 1H, Py H), 7.49 (d, ${}^{3}J(H,H) = 7.9$ Hz, 1H, Py *H*), 7.68 (td, ${}^{3}J(H,H) = 7.7$ Hz, ${}^{4}J(H,H) = 1.3$ Hz, 1H, Py *H*), $8.02 \text{ (d, }^{3}J(\text{H},\text{H}) = 7.6 \text{ Hz}, 2\text{H}, \text{Ph} \text{H}).$ ¹³C{¹H} NMR (CDCl₃): δ 38.2 (CH₃), 58.5 (CH₂), 101.2 (pyrazole CH), 118.9, 122.0 (q, ${}^{1}J_{CF} = 268.4 \text{ Hz}, CF_{3}$, 121.7, 121.8, 122.4, 123.4, 126.2, 128.0, 139.3, 143.5 (q, ${}^{2}J_{CF}$ = 36.3 Hz, pyrazole C), 147.0, 148.6, 151.1, 153.2, 155.5 (PdC), 169.2 (CO). ESI-MS: *m*/*z* 533.0 [M + H]⁺. Crystals suitable for X-ray crystallography were obtained by vapor diffusion of hexane into a chloroform solution containing the compound.

Synthesis of 3b. The procedure was identical with that of 3a except that 2b (0.37 g, 1.13 mmol) was used instead. A pale yellow solid was obtained. Yield: 0.49 g, 72%. Mp: 278.4-282.6 °C dec. Anal. Calcd for $C_{27}H_{21}F_3N_6OPd$: C, 53.26; H, 3.48; N, 13.80. Found: C, 52.90; H, 3.71; N, 13.81. ¹H NMR $(CDCl_3)$: $\delta 4.39 (d, {}^2J(H,H) = 14.4 Hz, 1H, CH_AH_BCO), 5.40$ $(d, {}^{2}J(H,H) = 14.4 \text{ Hz}, 1H, CH_{A}H_{B}CO), 5.43 (d, {}^{2}J(H,H) =$ 15.0 Hz, 1H, CH_CH_DPh), 6.22 (d, ${}^2J(H,H) = 15.0$ Hz, 1H, CH_CH_DPh), 6.76–6.81 (m, 2H, pyrazole H and Py H), 6.90 (d, J(H,H) = 1.8 Hz, 1H, imi H), 6.93-6.95 (m, 1H, Py H), 7.05 (d, ${}^{3}J(H,H) = 1.5$ Hz, 1H, imi H), 7.10 (t, ${}^{3}J(H,H) = 7.7$ Hz, 2H, Ph *H*), 7.24–7.37 (m, 6H, Ph *H* and Py *H*), 7.47 (d, ${}^{3}J$ (H,H) = 7.8 Hz, 1H, Py H), 7.66 (td, ${}^{3}J(H,H) = 7.8$ Hz, ${}^{4}J(H,H) = 1.5$ Hz, 1H, Py H), 7.73 (d, ${}^{3}J$ (H,H) = 7.9 Hz, 2H, Ph H). ${}^{13}C{}^{1}H$ NMR (CDCl₃): δ 54.0 (CH₂Ph), 58.7 (CH₂CO), 101.3 (pyrazole CH), 118.9, 121.7 (imi-C), 122.3 (q, ${}^{1}J(C,F) = 267.8$ Hz, CF_{3}), 123.2, 126.1, 127.9, 128.2, 128.3, 128.9, 136.5, 139.3, 143.5 (q, $^{2}J(C,F) = 36.2 \text{ Hz}, \text{ pyrazole } C), 146.8, 148.5, 151.1, 153.0, 155.7$ (PdC), 169.1 (CO). ESI-MS: m/z 609.1 [M + H]⁺. Crystals suitable for X-ray crystallography were obtained by vapor diffusion of diethyl ether into a dichloromethane solution of the solid.

Synthesis of 3c. The procedure was similar to that of 3a. Complex 2c (0.06 g, 0.17 mmol), 2-(3-(trifluoromethyl)-1Hpyrazol-5-yl)pyridine (0.04 g, 0.17 mmol), and K₂CO₃ (0.07 g, 0.51 mmol) were used. An off-white solid was obtained. Yield: 0.07 g, 64%. Mp: 270.7-275.0 °C dec. Anal. Calcd for C₃₁H₂₃F₃N₆OPd: C, 56.50; H, 3.52; N, 12.75. Found: C, 56.19; H,3.69; N, 12.63. ¹H NMR (CDCl₃): δ 4.40 (d, ²*J*(H,H) = 14.4 Hz, 1H, CH_AH_BCO), 5.45 (d, ${}^2J(H,H) = 14.4$ Hz, 1H, CH_A - H_B CO), 6.00 (d, ²J(H,H) = 15.9 Hz, 1H, CH_C H_DNp), 6.71 (d, ²J(H,H) = 15.9 Hz, 1H, CH_C H_DNp), 6.76 (d, ³J(H,H) = 1.8 Hz, 1H, imi H), 6.79-6.81 (m, 2H, pyrazole H and Py H), 6.95 (t, ${}^{3}J(H,H) = 7.2 \text{ Hz}, 1H, \text{Ph } H), 7.00 (d, {}^{3}J(H,H) = 1.8 \text{ Hz}, \text{imi } H),$ $7.13 (t, {}^{3}J(H,H) = 8.1 Hz, 2H, Ph H), 7.24 (d, {}^{3}J(H,H) = 7.8 Hz,$ 1H, Np H), 7.37–7.48 (m, 5H, Py H and Np H), 7.65 (td, ³J(H, H) = 7.8 Hz, ${}^{4}J(H,H) = 1.2$ Hz, 1H, Py H), 7.85 (t, ${}^{3}J(H,H) =$ 7.2 Hz, 2H, Np H), 7.91 (d, ${}^{3}J(H,H) = 7.8$ Hz, 2H, Ph H), 8.09 $(d, {}^{3}J(H,H) = 7.8 \text{ Hz}, 1H, \text{Np } H). {}^{13}C{}^{1}H} \text{NMR (CDCl_3):}$ δ 50.1 (CH₂Np), 58.7 (CH₂CO), 101.4 (pyrazole CH), 119.0, 121.6, 121.7, 122.1 (q, ${}^{1}J(C,F) = 268.3$ Hz, CF_3), 123.0, 123.3, 125.5, 126.1, 126.2, 126.8, 127.1, 128.0, 128.7, 129.1, 131.1, 131.7, 133.7, 139.3, 143.6 (q, ${}^{2}J(C,F) = 36.4$ Hz, pyrazole C), 146.9, 148.6, 151.2, 153.2, 155.9 (PdC), 169.2 (CO). ESI-MS: m/z 659.0 [M + H]⁺. Crystals suitable for X-ray crystallography were obtained by vapor diffusion of diethyl ether into a dichloromethane solution of the solid.

Synthesis of 4. A mixture of **2a** (0.15 g, 0.60 mmol) and Ag₂O (0.069 g, 0.30 mmol) in DMF (30 mL) was stirred at room temperature for 8 h. Light was excluded by covering the flask with aluminum foil. The mixture was filtered through a plug of Celite. The solvent was removed completely under vacuum. The residual white solid was washed with diethyl ether (2 × 15 mL), filtered on a frit under N₂, and dried under vacuum. Yield: 0.11 g, 49%. Mp: 135.8–149.5 °C. Anal. Calcd for C₁₂H₁₃N₃OAgCl: C, 40.20; H, 3.65; N, 11.72. Found: C, 40.11; H, 3.71; N, 11.39. ¹H NMR (CDCl₃): δ 3.78 (s, 3H, CH₃), 5.03 (s, 2H, CH₂), 7.20 (t, ³*J*(H,H) = 7.7 Hz, 1H, Ph *H*), 7.31 (t, ³*J*(H,H) = 7.7 Hz, 2H, Ph *H*), 7.43 (s, 1H, imi *H*), 7.46 (s, 1H, imi *H*), 7.57 (d, ³*J*(H,H) = 7.9 Hz, 1H, Ph *H*). 10.40 (s, 1H, NH). ¹³C{¹H} NMR (CDCl₃): δ 3.8.5 (CH₃), 53.9 (CH₂), 119.7, 122.9, 123.9, 124.1, 129.3, 138.9, 165.8 (CO), 180.5 (AgC).

Synthesis of 5. A mixture of Pt(fppzH)Cl₂ (0.21 g, 0.44 mmol), 4 (0.16 g, 0.44 mmol), and K₂CO₃ (0.18 g, 0.88 mmol) in DMF (15 mL) was stirred at 80 °C for 8 h. The solvent was then removed completely under vacuum. The solvent was completely removed under vacuum. The residue was dissolved in dichloromethane. The organic layer was then washed twice with water. After it was dried with anhydrous magnesium sulfate, the solvent was completely removed under vacuum. The residue was thoroughly washed with methanol. The pale yellow solid was then filtered on a frit and dried under vacuum. Yield: 0.10 g, 44%. Mp: 338.8-340.6 °C. Anal. Calcd for C₂₁H₁₇F₃N₆OPt: C, 40.59; H, 2.76; N, 13.52. Found: C, 40.90; H, 2.57; N, 13.03. ¹H NMR $(CDCl_3)$: δ 4.14 (s, 3H, NCH₃), 4.29 (d, ²J(H,H) = 14.3 Hz, 1H, $\text{COC}H_A\text{H}_B$), 5.22 (d, ${}^2J(\text{H},\text{H}) = 14.0$ Hz, 1H, COCH_AH_B), 6.76 (s, 1H, pyrazole *H*), 6.85 (td, ${}^{3}J(H,H) = 6.6$ Hz, ${}^{4}J(H,H) =$ 1.2 Hz, 1H, Py H), 6.94 (d, ${}^{3}J$ (H,H) = 2.1 Hz, 1H, imi H), 6.97 (t, ${}^{3}J$ (H,H) = 7.2 Hz, 1H, Ph H), 7.04 (d, ${}^{3}J$ (H,H) = 2.1 Hz, 1H, imi H), 7.19 (t, ${}^{3}J(H,H) = 7.8$ Hz, 2H, Ph H), 7.53 (d, ${}^{3}J(H,H) =$ 7.8 Hz, 1H, Py H), 7.69–7.76 (m, 2H, Py H), 7.99 (d, ${}^{3}J$ (H,H) = 7.6 Hz, 2H, Ph H). ¹³C{¹H} NMR (CDCl₃): δ 37.8 (CH₃), 57.7 (CH_2) , 101.8 (pyrazole CH), 118.9, 121.1 (q, ${}^{1}J(C,F) = 179.9$ Hz, *C*F₃), 121.7, 122.4, 123.4, 126.2, 128.0, 139.4, 143.4 (q, ²*J*(C,F) = 68.6 Hz, pyrazole C), 147.2, 148.6, 151.1, 154.3, 156.3 (PdC), 169.2 (CO). ESI-MS: m/z 622.1 [M + H]⁺. Crystals suitable for X-ray crystallography were obtained by vapor diffusion of diethyl ether into a dichloromethane solution of the solid.

Catalytic Heck Reaction. In a typical run, a Schlenk tube was charged with aryl halide (1.0 mmol), alkene (1.4 mmol),

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anhydrous sodium acetate (1.1 mmol), palladium precatalyst (0.5 mol %), and 2 g of TBAB. The flask was thoroughly degassed and then placed in a preheated oil bath or under microwave irradiation at the appropriate temperature listed in Table 5. After the mixture was cooled, the mixture was diluted with water (10 mL) and extracted with diethyl ether $(3 \times 10 \text{ mL})$. The combined organic portions were then dried over anhydrous sodium sulfate. After filtration, the solvent was removed completely under vacuum. Products $6,^{57}$ 7–9,⁵⁸ 10,⁵⁹ 11,⁶⁰ 12,⁵⁴ 13,⁶¹ 14,⁶² 15,³⁵ 16,⁶¹ 17,⁶³ 18–21,⁵⁷ 22,⁶⁴ 23 and 24,⁵⁷ 25 and 26,⁶⁵ and 27–30⁶⁶ were identified by comparison of their NMR data with those in the literature; NMR yields and regioselectivity were determined by integration ratio using 1,3,5-trimethoxylbenzene as internal standard. Isolated yields were obtained after purification with column chromatography on silica gel.

X-ray Data Collection. Typically, the crystals were removed from the vial with a small amount of mother liquor and immediately coated with Paratone-N oil on a glass slide. A suitable crystal was mounted on a glass fiber with silicone grease and placed in the cold stream of a Bruker APEX II equipped with a CCD area detector and a graphite monochromator utilizing Mo

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Ka radiation ($\lambda = 0.71073$ Å) at 150(2) K. The data were corrected for Lorentz and polarization effects using the Bruker SAINT software, and an absorption correction was performed using the SADABS program.67

Computational Details. We used the three-parameter hybrid of exact exchange and Becke's exchange energy functional,⁶⁸ plus Lee, Yang, and Parr's gradient-corrected correlation energy functional (B3LYP).⁶⁹ For the optimization of molecular geometries, we used the LANL2DZ effective core potential plus basis functions.⁷⁰

Solution and Structure Refinements. All the structures were solved by direct methods and refined by full-matrix least-squares methods against F^2 with the SHELXTL software package.⁷¹ All non-H atoms were refined anisotropically. H atoms were fixed at calculated positions and refined with the use of a riding model. Crystallographic data are given in Table 1. CCDC-787474 (3a), -787475 (3b), -787476 (3c · 0.25CH₂Cl₂), and -787477 (5) contain supplementary crystallographic data for this paper. These data can obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data request/cif.

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Supporting Information Available: CIF files giving full crystallographic data for 3a-c and 5 and a figure giving the HMBC spectrum of 3c. This material is available free of charge via the Internet at http://pubs.acs.org.

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