ORGANOMETALLICS

Article

Cite This: *Organometallics* XXXX, XXX, XXX−XXX

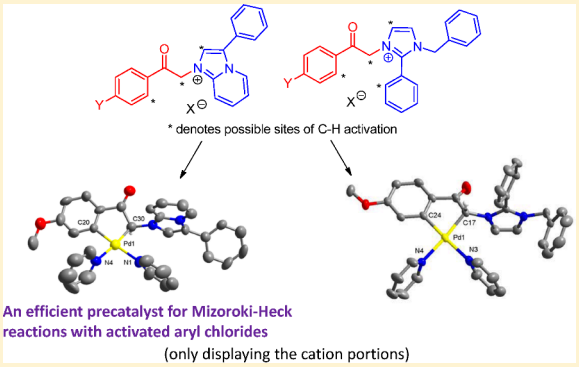
Synthesis and Characterization of *C,C*-Type Palladacycles and Their Catalytic Application in Mizoroki−Heck Coupling Reaction

Chi Hou Lo and Hon Man Lee*

Department of Chemistry, National Changhua University of Education, Changhua 50058, Taiwan

Supporting Information

ABSTRACT: Two series of ligand precursors, based on imidazo[1,2-*a*]pyridine and C2-phenyl substituted imidazole moieties, were developed and synthesized in high yields, featuring an *N*-CH_2(C═O)Ar substituent on the imidazole ring. Upon reacting with palladium acetate, both series of ligands underwent double C−H bond activations at the methylene and *o*-aryl carbon sites on the *N*-CH_2(C═O)Ar substituent, yielding *C,C*-type palladacycles bearing five-membered chelate rings. A dimeric palladium complex with bridging bromides was obtained from the ligand precursor with the bromide anion, whereas an ionic palladium complex with two "throw away" pyridine ligands was formed with the precursor of the tetrafluoroborate anion. All complexes are air-stable and were characterized by ^{1}H and ^{13}C NMR spectroscopy and elemental analysis. The structures of three of the new complexes were further established by single-crystal X-ray diffraction studies. These complexes have been screened for catalyzing Mizoroki−Heck coupling reaction using ionic salt as solvent. The complex based on imidazo[1,2-*a*]pyridine, which has an electron-donating 4-methoxyphenyl ring on the ligand scaffold, was the most efficient catalyst, capable of using activated aryl chloride and sterically hindered aryl bromide as substrates. It was also successfully applied in the green process of one-pot Mizoroki−Heck coupling/*trans*-esterification reaction in molten ionic salt.



INTRODUCTION

Palladacycles or cyclopalladated compounds have attracted much interest in the last two decades due to their wide applicability in catalysis,[1] and their bioactive, mesogenic, and photoluminescent properties.[2] Common palladacycles in the literature are *C,E*-types which contain nitrogen, oxygen, phosphorus, and sulfur donors, etc.[1a−g] For *C,C*-palladacycles, the two Pd−C bonds can be used for the development of new catalytic reactions, such as the construction of cyclic structures,[3] hence are usually implicated as important intermediates in catalytic cycles. Preformed *C,C*-type palladacycles are, however, relatively rare.[3d,4] Lautens and García-López et al. recently reported several exemplary model intermediates including spiro *C,C*-type palladacycles for the Pd-catalyzed cascade remote C−H functionalization of *N*-(2-haloaryl)acrylamides.[3d] Previously, we reported various palladium(II) complexes based on a ligand scaffold bearing an imidazolyl moiety and an *N*-CH_2(C═O)R substituent (R = NR′Ar, or Me) (Chart 1).[4a,5] The ligand scaffold contains various sites that can undergo C−H or N−H cleavage, generating different palladium complexes. These include six-membered *C,C*-type palladacycle **A**,[4a] six-membered *C,C*-type palladacycle **B**,[4a] palladalactam **C**,[4a] abnormal *N*-heterocyclic carbene (aNHC) complex **D**,[5a] and monodentate zwitterionic palladium complex **E**.[5b,c] We envision that further modification of the *N*-CH_2(C═O)R substituent in the ligand scaffold could potentially lead to different palladation behavior. In a previous work, Urriolabeitia et al. utilized a series of *N*-ylides including a derivative of imidazole, affording several orthometalated complexes via regioselective C−H bond activation.[4b] Taking all of these into consideration, we intended to further explore the possibility of obtaining novel palladium complexes based on the ligand scaffold. We choose to append an aryl group directly adjacent to the carbonyl carbon in the *N*-CH_2(C═O)R substituent (R = Ar). The target ligand precursors also possess various potential sites for C−H activation. These could possibly lead to the formation of a variety of palladium complexes, including a *C,C*-type palladacycle of five-membered chelate ring, aNHC complex, zwitterionic palladium complex, or even a tridentate *C,C,C*-type pincer complex. Herein, we report our results on the synthesis and characterization of the new ligand precursors and their successful palladation. The *C,E*-type palladacycles have been generally applied in catalyzing Mizoroki−Heck coupling reaction.[1a−g,6] In contrast, the use of a *C,C*-type palladacycle in this reaction is very rare. Hence, another objective of this work is to explore the potential catalytic applications of *C,C*-type palladacycles in Mizoroki−Heck coupling reaction.

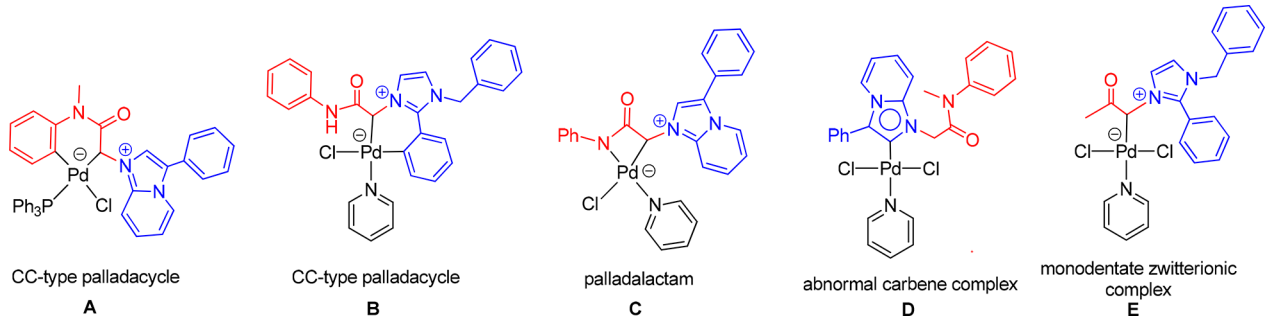
RESULTS AND DISCUSSION

Design and Synthesis of Ligand Precursors. Scheme 1 shows the synthetic pathways for the preparation of the two

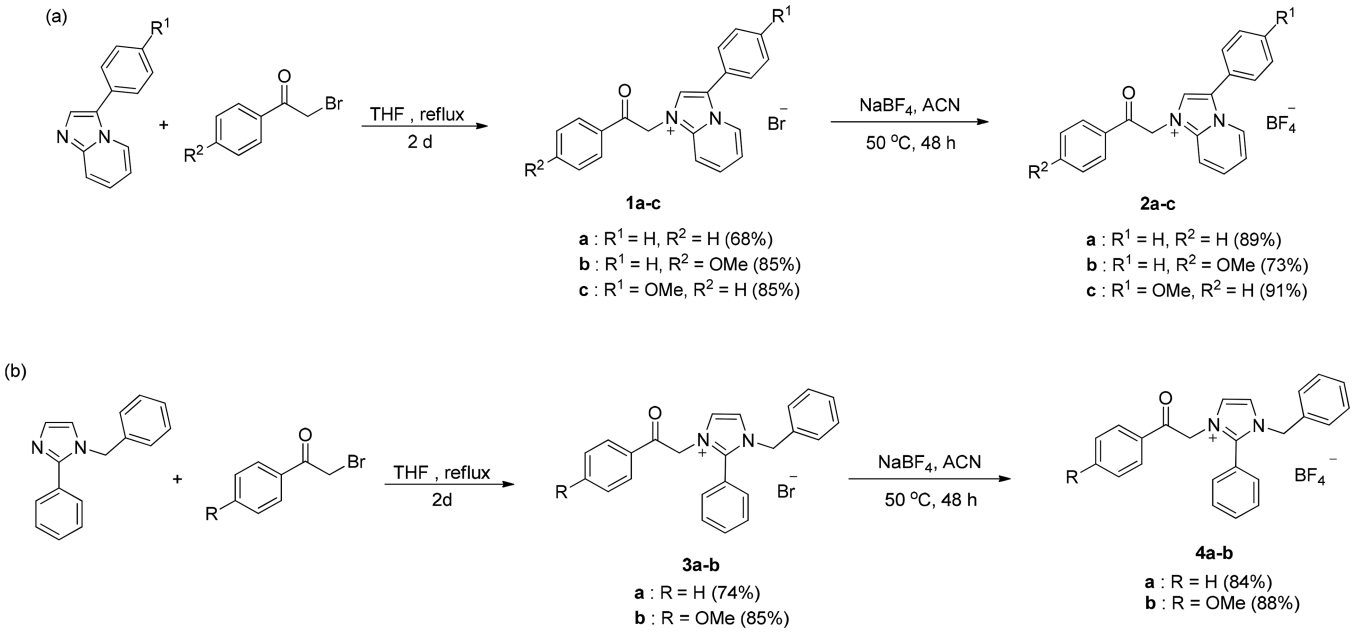
Received: January 27, 2018

DOI: 10.1021/acs.organomet.8b00054
Organometallics XXXX, XXX, XXX−XXX

Chart 1. A Range of Palladium(II) Complexes Based on a Ligand Scaffold with an Imidazolyl Moiety and an *N*-CH_2(C═O)R Substituent (R = NR′Ar or Me)[4a,5]



Scheme 1. Synthesis of Ligand Precursors

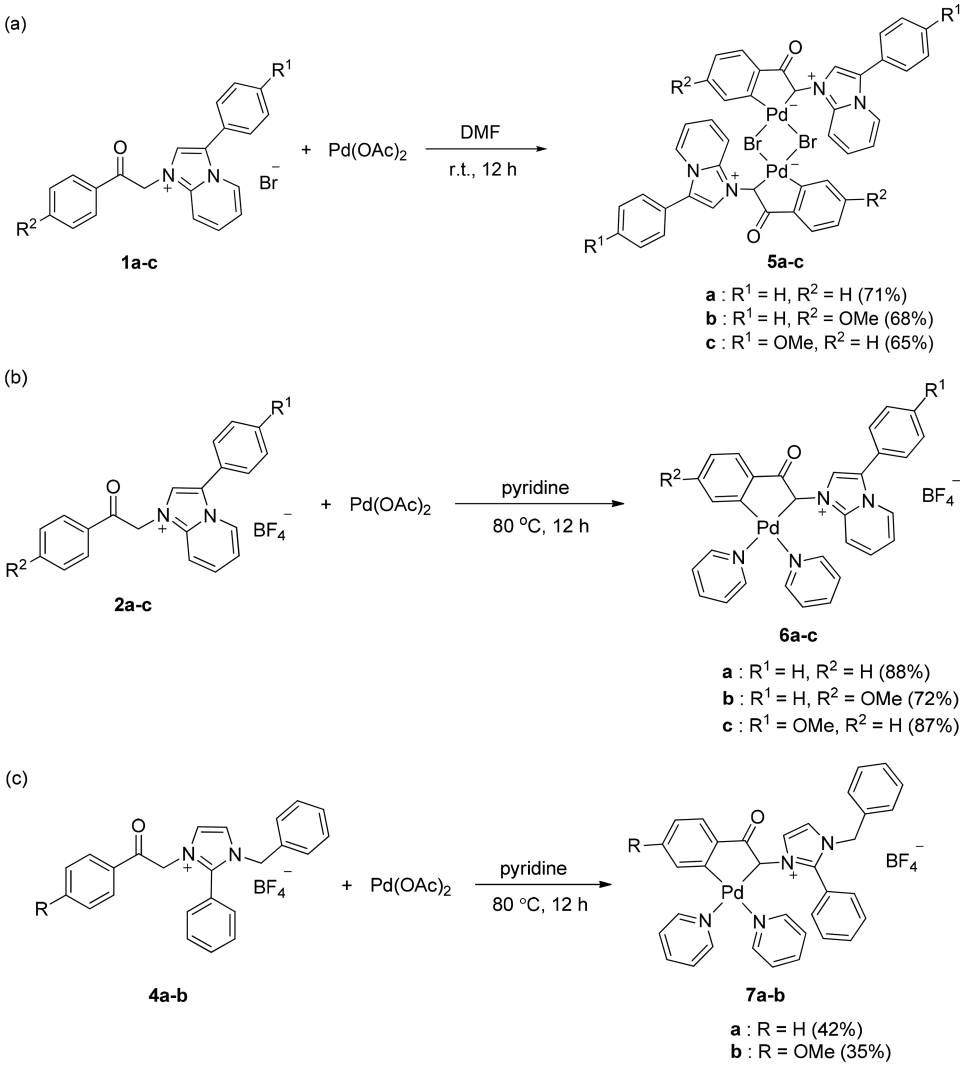


series of ligand precursors. For the first series (Scheme 1a), compounds **1a−c** and **2a−c** contain an imidazo[1,2-*a*]pyridine ring, whereas, in the second series (Scheme 1b), the imidazole rings in **3a−b** and **4a−b** contain a C2-phenyl group. The reason for such design is that the C2-phenyl group from **3a−b** and **4a−b** can potentially have an *ortho* carbon site for palladation (see complex **B** in Chart 1). This is not possible for compounds **1a−c** and **2a−c**. The key reaction for the preparation of the imidazolium bromides is the quaternization reaction between an imidazole derivative and organic bromide. To enrich the electron density of the palladium center for the oxidative addition of aryl halide substrates, the ligand scaffold was appended with electron-donating methoxy groups on phenyl rings, yielding isomers **b** and **c**. Compounds **1a−c** and **3a−b** with bromide anions were obtained as white solids with 68−85% yields. Salt metathesis reactions between these bromide salts with $NaBF_4$ in acetonitrile (ACN) allowed the formation of imidazolium salts **2a−c** and **4a−b** with non-coordinating tetrafluoroborate anions with 73−91% yields. The characteristic signal for the methylene protons next to the carbonyl group was observed at ca. 6.4 ppm in **1** and **2**, 6.0 ppm in **3**, and 5.6 ppm in **4**. Their corresponding ^{13}C NMR signals were at ca. 53.2−55.9 ppm.

Synthesis of Palladium Complexes. The palladation of these new ligand precursors was investigated (Scheme 2). Different reaction conditions have been attempted previously, and only reactions of the ligand precursors **1a−c** and palladium acetate in DMF at room temperature successfully yielded pure products of dimeric *C,C*-type palladacycles **5a−c**. The bidentate ligand carries formally a net anionic charge, and a bromide ligand is needed for the charge balance on the palladium(II) center. To attain a stable palladium(II) structure, a dimeric compound was formed by the bridging coordination of bromide ligands. Notably, these complexes were zwitterionic in nature with a positive charge on the nitrogen atom and a net anion charge at the palladium center. The successful formation of these dimeric, bromide-bridged complexes was confirmed by the diagnostic peak of the $[Pd_2L_2Br]^+$ ion at m/z = 914.8 in the ESI-MS of **5a**. Interestingly, an equally intense m/z peak at 1412.5, attributable to a trimeric $[Pd_3L_3Br_2]^+$ ion, was also observed. The presence of this signal indicates that the μ-Br coordination in the dimeric complex can dissociate facilely into the neutral unsaturated mononuclear [PdLBr] species in solution. This species reacts with the dimeric $[Pd_2L_2Br]^+$ ion to form the trimeric $[Pd_3L_3Br_2]^+$ ion. Diagnostic ^1H and ^{13}C NMR signals were also measured. The methylene signal corresponding to the two protons in **1a** appeared at 6.49

DOI: 10.1021/acs.organomet.8b00054
Organometallics XXXX, XXX, XXX−XXX

Scheme 2. Synthesis of *C,C*-Type Palladacycles



ppm. After complexation, the Pd−C*H* signal corresponding to one proton was shifted downfield to 6.84 ppm. Consistently, the coordinating methylene carbon signal appeared at 54.6 ppm. The signal was shifted downfield to 68.6 ppm upon complexation. The coordinated phenyl carbon resonances in **5a−c** were observed in the range of 153.8−156.8 ppm, which is typical for this type of carbon.[4b]

The bromide ions from the ligand precursors **1a−c** transformed into the bridging ligands in the dimeric complexes **5a−c**. We then used ligand precursors **2a−c** that contained noncoordinating tetrafluoroborate anions, which were expected to result in mononuclear complexes. As expected, the complexation reaction between **2a−c** and palladium acetate in dry pyridine resulted in ionic *C,C*-type palladium complexes **6a−c** bearing two pyridine ligands and BF_4 anions. A similar downfield shift in proton signal was observed upon complexation. The Pd−C*H* proton signal in **6a** appeared downfield at 6.72 ppm compared with that of the CH_2 proton at 6.41 ppm in the ligand precursor **2a**. The mononuclear structure and ionic nature of **6a−c** was established by single-crystal X-ray diffraction studies of **6a**,**b**.

The ligand precursors **4a−b** have a phenyl group attached to the C2 carbon of the imidazolyl ring. As such, they can react with palladium acetate to potentially form *C,C*-type palladium complexes like the aforementioned **6a−c**, bearing a five-membered chelate ring, or *C,C*-type palladacycles like **B** in Chart 1, bearing a six-membered chelate ring. The possibility of forming a tridentate pincer *C,C,C*-type complex containing both five- and six-membered chelate rings also exists. We discovered that the reaction between precursors **4a−b** with palladium complexes yielded the *C,C*-type palladacycles **7a−b**, with 42% and 35% yields, respectively. The characteristic Pd−C*H* signal appeared at 6.04 and 5.98 ppm in **7a−b**, respectively, which shifted significantly downfield relative to those of the methylene signals at ca. 5.17 ppm in precursors **4a−b**. The much lower yields of these reactions were attributable to the competitive reactions of the formation of the *trans*-$PdCl_2(pyridine)_2$ side product.[7]

It should be noted that the absence of C2 protons on the imidazole/imidazo[1,2-*a*]pyridine rings in both series of ligand precursors prevented the formation of palladium complexes with normal NHC ligands. Conversely, the formation of palladium abnormal NHC complexes[5a,8] would be possible upon the deprotonation of the C4/5 sites (see complex **D** in Chart 1). Despite this, the formation of palladium abnormal NHC complexes was not observed for both series of ligand precursors. The formation of complex **E** is not observed either,

DOI: 10.1021/acs.organomet.8b00054
Organometallics XXXX, XXX, XXX−XXX

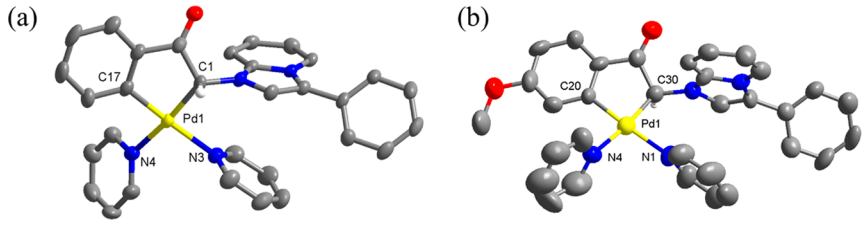


Figure 1. (a) Molecular structure of cationic portion of **6a** (left) at 50% probability level. Hydrogen atoms except that on C1 and C30 are omitted for clarity. Selected bond distances (Å) and angles (deg): Pd1−C1, 2.050(5); Pd1−C17, 1.992(5); Pd1−N3, 2.150(4); Pd1−N4, 2.123(4); C1−Pd1−C17, 80.37(19); C17−Pd1−N4, 96.25(19); N3−Pd1−N4, 90.26(16); C1−Pd1−N3, 93.66(17); C17−Pd1−N3, 172.17(18); C1−Pd1−N4, 172.50(17). (b) Molecular structure of cationic portion of **6b** (right) at 50% probability level. Hydrogen atoms except that on C1 and C30 are omitted for clarity. Selected bond distances (Å) and angles (deg): Pd1−C30, 2.022(7); Pd1−C20, 1.989(7); Pd1−N1, 2.122(6); Pd1−N4, 2.116(7); C20−Pd1−C30, 79.6(3); C20−Pd1−N4, 94.7(3); N1−Pd1−N4, 90.0(3); C30−Pd1−N1, 95.7(3); C20−Pd1−N1, 175.0(3); C30−Pd1−N4, 173.7(3).

which is also attributable to the higher stability of bidenatate vs monodentate coordination.

Structural Description. The structures of complexes **6a**, **6b**, and **7b** were confirmed by X-ray crystallographic studies (Figures 1 and 2). The crystallographic data are tabulated in

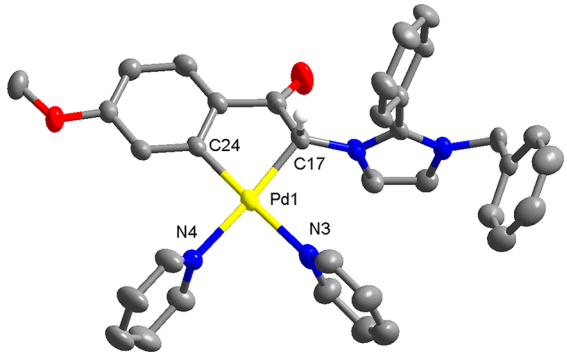


Figure 2. Molecular structure of cationic portion of **7b** at 50% probability level. Hydrogen atom except that on C17 is omitted for clarity. Selected bond distances (Å) and angles (deg): Pd1−C17, 2.044(3); Pd1−C24, 1.995(3); Pd1−N3, 2.140(3); Pd1−N4, 2.116(2); C17−Pd1−C24, 80.60(11); C24−Pd1−N4, 95.64(9); N3−Pd1−N4, 86.79(9); C17−Pd1−N3, 97.09(10); C24−Pd1−N3, 176.17(10); C17−Pd1−N4, 175.57(10).

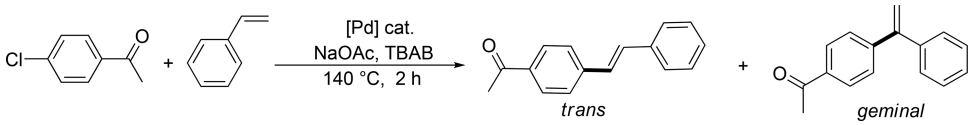
Table S1 in the Supporting Information. In general, the palladium center in each of the structures exhibits a distorted square planar coordination geometry. The bite angles of these ligands are all similar at ca. 80°. The Pd−CH distances are in the range of 2.022(7)−2.050(5) Å, which are longer than those of the Pd−C distances from the phenyl rings (1.989(7)−1.995(3) Å). This reflects the stronger coordination of the latter as a carbon donor. The Pd−CH distances are comparable to that found in a related palladacycle reported by Urriolabeitia et al. (1.964(2) Å), but the Pd−C distances from the phenyl rings were significantly longer than that of 1.964(2) Å in the reported structure.[4b] In line with the expected *trans* influence, the Pd−N bonds *trans* to the coordinated CH groups are slightly shorter than those *trans* to the phenyl groups. This is exemplified by the two Pd−N bond distances of 2.123(4) and 2.150(4) Å in **6a**.

Mizoroki−Heck Coupling Reaction. The potential applications of the new palladium complexes as catalysts in Mizoroki−Heck coupling reaction were investigated (Table 1). With reference to our previously reported conditions of 0.5 mol % palladium loading, NaOAc as base, *n*-tetrabutylammonium bromide (TBAB) as solvent, and a reaction time of 2 h at 140 °C,[9] a benchmark reaction between 4-chloroacetophenone and styrene was studied. TBAB is a solid at room temperature, but becomes liquid at elevated temperatures. As shown from entries 1−6, among the new complexes tested, dimeric **5a** and ionic **6b** and **7b** were very active precatalysts, giving quantitative yields of coupled product with high *trans*/*gem* ratios. The higher activity of **6b** vs **6a** (entries 3 vs 2) and **7b** vs **7a** (entries 6 vs 5) reflects the effectiveness of having the electron-donating 4-methoxy group on the phenyl ring. Entries 3 and 4 indicate that the position of the 4-methoxy group on the ligand scaffold is also important in defining the performance of the catalyst. A higher activity (100% vs 89%) was achieved if the electron-donating group was installed on the phenyl ring next to the carbonyl group. The dimeric complex **5a** delivered somewhat better activity than **6a**, possessing two pyridine "throw away" ligands (entries 1 vs 2). To determine the effectiveness of **5a**, **6a**, and **7b** in catalyzing the reaction, the palladium loading was reduced from 0.5 to 0.2 mol %. In all three cases, quantitative yields were still achieved (entries 7−9). Further reducing the palladium loading to 0.1 mol % revealed that complex **6b** was the most active precatalyst with 88% yield (entry 11), whereas complex **7b**, with the phenyl ring attached at the C2 position, gave only a 12% yield. The higher activity of **6b** compared to **7b** can be attributed to the planar imidazo[1,2-*a*]pyridine moiety in **6b**, which is less sterically bulky than the nonplanar C2-phenyl substituted imidazole ring in **7b** (see Figure 2). Ligand-free palladium acetate has been previously shown to exhibit good Mizoroki−Heck coupling activity. To gauge the performance of **6b**, the activity of palladium acetate was also investigated.[10] A comparison of entries 11 and 13 indicated that **6b** delivered a better yield than the ligand-free palladium acetate. Overall, the optimized reaction conditions of 0.2−0.5 mol % **6b**, NaOAc as base, TBAB as solvent, and a reaction temperature of 140 °C were established.

On the basis of the explored conditions, the substrate scope of the reaction was tested, beginning with a series of aryl chlorides (Table 2). As shown in entries 1−3, activated aryl chlorides can be effectively coupled with styrene in 2 h, producing yields in the range of 82−97%. 4-Trifluoromethylphenyl chloride can also be used as a substrate, albeit with a slightly lower yield of 66% (entry 4). The catalyst system is, however, less effective in utilizing electron-neutral and electron-rich aryl chloride substrates (entries 5−7). For example, only a 13% yield was obtained with 4-chloroanisole, even with an increase in palladium loading from 0.2 to 0.5 mol % (entry 7). The reactivity trend of these aryl chloride substrates was similar

DOI: 10.1021/acs.organomet.8b00054
Organometallics XXXX, XXX, XXX−XXX

Table 1. Catalyst Screening for Mizoroki−Heck Coupling Reaction[a]



entry	cat.	Pd mol %	yield (%)
1	**5a**	0.5	100 (92.8)
2	**6a**	0.5	85 (95:5)
3	**6b**	0.5	100 (96:4)
4	**6c**	0.5	89 (94:6)
5	**7a**	0.5	63 (94:6)
6	**7b**	0.5	100 (96:4)
7	**5a**	0.2	100 (96:4)
8	**6b**	0.2	**100 (94:6)**
9	**7b**	0.2	100 (96:4)
10	**5a**	0.1	80 (96:4)
11	**6b**	0.1	88 (96:4)
12	**7b**	0.1	12 (92:8)
13	$Pd(OAc)_2$	0.1	79 (95:5)

[a]Reaction conditions: 1.4 mmol of styrene, 1 mmol of 4-chloroacetophenone, 1.1 mmol of NaOAc, 2 g of TBAB, 0.1−0.5 mol % of [Pd] cat., 140 °C. Yield determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard.

upon replacing styrene with *n*-butyl acrylate as the coupling partner (entries 8−11). The catalyst system is, however, ineffective with unactivated *n*-hexene as alkene substrate. Using 3,4-dimethoxystyrene, prolonged reaction time (12 h) was needed to produce the same yield levels (entries 12−15). For example, the reaction between the styrene derivative and 4-nitrophenyl chloride produced a quantitative yield of product in 12 h. Similarly, prolonged heating permitted coupling between 4-chlorobenzonitrile and phenyl acrylate with 60% yield (entry 16). Overall, complex **6b** is effective in utilizing activated aryl chlorides as substrates with good to excellent yielding coupled products.

Since aryl bromides are more commonly used in organic synthesis, the substrate scope of aryl bromides was also investigated (Table 3). Because the activity of aryl bromide is generally higher than that of aryl chloride, we focused on challenging aryl bromide substrates with steric hindrance. As shown in entries 1 and 2, 2- or 3-bromoanisoles could be effectively coupled with styrene, giving good yields of coupled products in 12 h. 3,4,5-Trimethoxyphenyl bromide reacted with styrene with 42% yield (entry 3). Increasing the palladium loading to 0.5 mol % improved the yield to 63%. The highly bulky 2-bromomesitylene could couple with styrene, affording a mediocre yield of 44% (entry 4). Similar yields were obtained upon changing styrene to *n*-butyl acrylate and 3,4-dimethoxystyrene (entries 5−10). Overall, the complex **6b** can utilize sterically hindered aryl bromides as substrates with average to good yielding coupled products.

Interestingly, when methyl acrylate was employed as a coupling partner, the expected methyl ester product was not formed. Instead, *trans*-esterification occurred, producing *n*-butyl ester and *n*-pentyl ester when TBAB and tetrapentyl ammonium bromide (TPeAB) were used as solvents, respectively (Scheme 3). It is apparent that the *n*-butyl and *n*-pentyl groups are from TBAB and TPeAB, respectively. To prove this, a simple reaction between 4-chlorobenzonitrile and methyl acrylate, catalyzed by **6b**, was conducted in organic solvent. As expected, only the methyl ester, (*E*)-methyl 3-(4-cyanophenyl)acrylate, was obtained, albeit with low yield. It was reported that the *trans*-esterification involving TBAB can occur without the presence of palladium metal.[11] Further, heating of the methyl ester in TBAB for 12 h afforded the corresponding *n*-butyl ester with 90% yield. To further confirm the reaction profile of the Mizoroki−Heck coupling and *trans*-esterification, the reaction between 4-chloronitrile and methyl acrylate was allowed to react over 2 h. Only the methyl ester product was obtained with 23% yield. Prolonging the reaction time to 12 h led to the complete conversion to *n*-butyl ester. This indicates that the *trans*-esterification reaction is slow compared with the Mizoroki−Heck coupling reaction.

Finally, the one-pot Mizoroki−Heck coupling/*trans*-esterification green reaction, using a range of activated chlorides with methyl acrylate, was investigated (Table 4). In general, the corresponding *n*-butyl ester coupled products were obtained in excellent yields (entries 1−5). 3-Bromoanisole was also successfully applied as a substrate, giving product with 92% yield (entry 6).

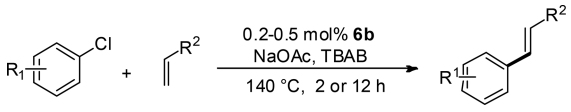
It has been shown that cross-coupling reactions catalyzed by soluble palladium precatalysts can proceed via heterogeneous mechanistic pathways.[12] To understand the possible involvement of a heterogeneous pathway, a mercury drop test[13] was performed on the benchmark reaction between 4-chloroacetophenone and styrene, catalyzed by **6b**. In the presence of mercury, the product yield was markedly reduced from quantitative to 57%. This suggested that, beside homogeneous pathways, a heterogeneous process is also likely to be involved. To further confirm the involvement of heterogeneous species in the reaction mixture, a drop of the reaction mixture was allowed to evaporate and was examined under TEM. This revealed the presence of palladium nanoparticles. The size of these particles was ca. 2−3 nm (Figure S1 in the Supporting Information).

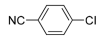
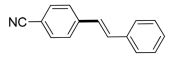
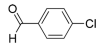
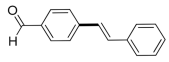
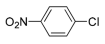
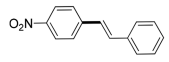
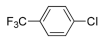
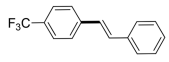
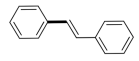
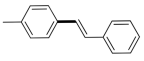
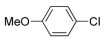
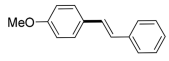
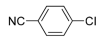
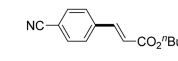
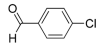
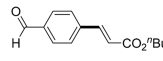
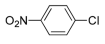
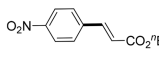
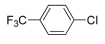
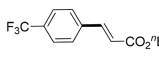
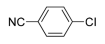
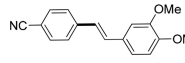
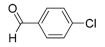
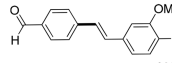
CONCLUSION

Continuing our interest in the ligand scaffold based on an imidazolyl moiety and an *N*-CH_2(C═O)R substituent, we fine-tuned our ligand scaffold by the installation of an aryl group on the carbonyl carbon (R = Ar). Two different series of ligand precursors based on imidazo[1,2-*a*]pyridine and C2-phenyl substituted imidazole moieties were developed. These ligand

DOI: 10.1021/acs.organomet.8b00054
Organometallics XXXX, XXX, XXX−XXX

Table 2. Substrate Scope of Aryl Chlorides[a]



entry	Time (h)	Ar—Cl	Alkene	Product	Yield (%)
1	2				91
2	2				82
3	2				97
4	2				66
5	2				10 (14[b])
6	2				10[b]
7	2				13[b]
8	2				80
9	2				78
10	2				96
11	2				46
12	12				86
13	12				71
14	12				> 99
15	12				30
16	12				60

[a]Reaction conditions: 1.4 mmol of alkene, 1 mmol of aryl chloride, 1.1 mmol of NaOAc, 2 g of TBAB, 0.2 mol % of **6b**, 140 °C, isolated yield. [b]0.5 mol % of **6b**.

precursors possess multiple sites for C−H activation that can give rise to a range of different palladium complexes. Both sets of ligands reacted regioselectively with palladium acetate, forming a series of *C,C*-type palladacycles featuring five-membered chelate rings via double C−H bond activation at the methylene and *o*-aryl carbons. This result highlights the strong directing effect of the carbonyl group. Among the new complexes, the mononuclear complex with the ligand scaffold bearing an imidazo[1,2-*a*]pyridine moiety and an electron-donating methoxy group, was found to be the most effective in catalyzing the Mizoroki−Heck coupling reaction. Subsequently, the screened complex was successfully applied in the one-pot Mizoroki−Heck coupling/*trans*-esterification green reaction, with activated aryl chloride substrates in ionic salt as solvent. Further investigation on the reactivity of these complexes with compounds of unsaturated bonds is ongoing in our lab in the hope of devising new catalytic transformations.

Table 3. Substrate Scope of Hindered Aryl Bromides[a]

entry	Ar X	Alkene	Product	Yield (%)
1				81
2				91
3				42(63)[b]
4				44
5				65
6				86
7				54
8				45
9				56
10				71

[a]Reaction conditions: 1.4 mmol of alkene, 1 mmol of aryl bromide, 1.1 mmol of NaOAc, 2 g of TBAB, 0.2 mol % of **6b**, 140 °C, 12 h, isolated yield. [b]0.5 mol % of **6b**.

EXPERIMENTAL SECTION

General Information. All manipulations were performed under a dry nitrogen atmosphere using standard Schlenk techniques. Solvents were dried with standard procedures. Starting chemicals were purchased from a commercial source and used as received. ^{1}H and ^{13}C{^{1}H} NMR spectra were recorded at 300.13 and 75.47 MHz, respectively, on a Bruker AV-300 spectrometer. Elemental analyses were performed on a Thermo Flash 2000 CHN-O elemental analyzer. ESI-MS was carried out on a Finnigan/Thermo Quest MAT 95XL mass spectrometer at National Chung Hsing University (Taiwan).

Synthesis of 1a. A mixture of 3-phenylimidazo[1,2-*a*]pyridine (1.60 g, 8.24 mmol) and 2-bromo-1-phenylethanone (1.65 g, 8.24 mmol) in THF (30 mL) was placed in a Schlenk flask. The mixture was heated to 80 °C for 2 days. After cooling, the white solid was collected on a frit, washed with THF three times, and dried under vacuum. Yield: 2.22 g (68%). Mp = 206.4−207.1 °C. ESI-HRMS *m/z*: $[M - Br]^+$ Calcd for $C_{21}H_{17}N_2O$ 313.1340; Found 313.1334. ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.49 (s, 2H, CH_2), 7.62−7.79 (m, 9H, Ar *H*), 8.15 (d, 3H, $^{3}J_{HH}$ = 6.0 Hz, 8.41 (d, 1H, $^{3}J_{HH}$ = 9.0 Hz, Ar *H*), 8.51 (s, 1H, imi *H*), 8.90 (d, 1H, $^{3}J_{HH}$ = 6.0 Hz, Ar *H*). ^{13}C{^{1}H} NMR (75.4 MHz, DMSO-d_6): δ 54.6 (CH_2), 112.5, 118.6, 124.8, 125.0 (quaternary *C*), 126.7 (quaternary *C*), 127.6, 129.0, 129.5, 129.7, 130.1, 130.9, 134.3 (quaternary *C*), 134.7, 135.0, 140.7 (quaternary *C*), 192.0 (*C*═O).

DOI: 10.1021/acs.organomet.8b00054
Organometallics XXXX, XXX, XXX−XXX

Scheme 3. Mizoroki−Heck Coupling Reaction and *Trans*-esterification in Ionic Salt: (a) One-Pot and (b) Stepwise Procedures

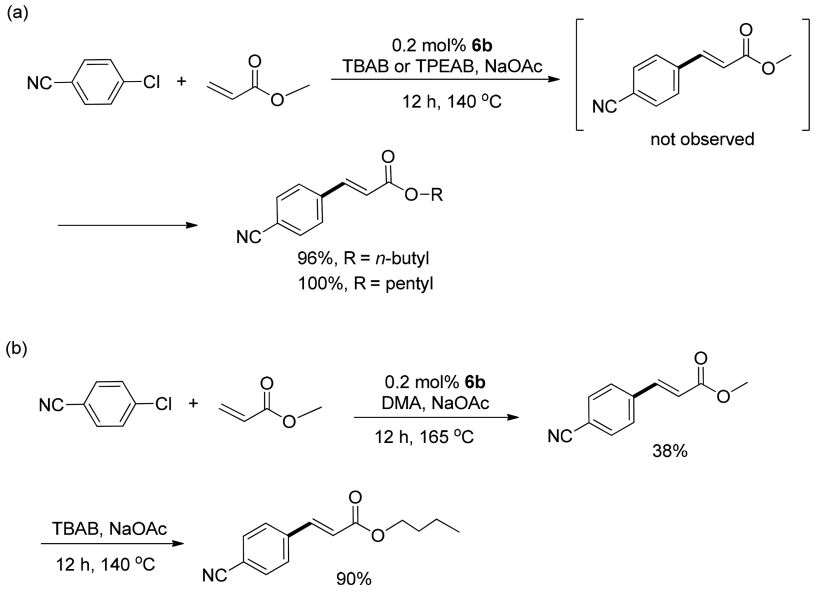
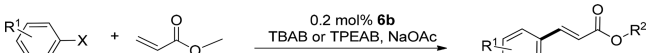
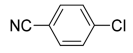
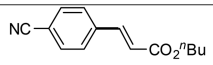
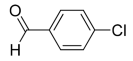
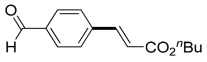
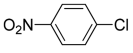
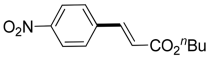
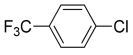
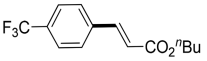
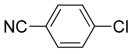
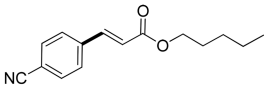
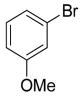
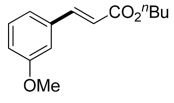


Table 4. One-Pot Mizoroki−Heck Coupling Reaction and *Trans*-esterification of Aryl Halides and Methyl Acrylate[a]



Entry	Reactant	Product	Yield (%)
1			96
2			92
3			98
4			90
5[b]			100
6			92

[a]Reaction conditions: 1.4 mmol of methyl acrylate, 1 mmol of aryl halide, 1.1 mmol of NaOAc, 2 g of TBAB, 0.2 mol % of **6b**, 140 °C, 12 h, isolated yield. [b]TPeAB instead of TBAB.

Synthesis of 1b. The compound was prepared with a similar procedure to that of **1a**. A mixture of 3-phenylimidazo[1,2-*a*]pyridine (1.60 g, 8.24 mmol) and 2-bromo-1-(4-methoxyphenyl)ethanone (1.64 g, 8.24 mmol) was used. A white solid was obtained. Yield: 2.96 g (85%). Mp = 213.8−214.7 °C. ESI-HRMS *m*/*z*: $[M - Br]^+$ Calcd for $C_{22}H_{19}N_2O_2$ 343.1446; Found 343.1439. ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.91 (s, 3H, CH_3), 6.39 (s, 2H, CH_2), 7.2 (d, 2H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 7.60−7.78 (m, 6H, Ar *H*), 8.12 (br s, 3H, Ar *H*), 8.35 (d, 1H, $^3J_{HH}$ = 6.0 Hz, Ar *H*), 8.47 (s, 1H, imi *H*), 8.90 (d, 1H, $^3J_{HH}$ = 3.0 Hz, Ar *H*). ^{13}C{^{1}H} NMR (75.4 MHz, DMSO-d_6): δ 54.1 (CH_2), 56.3 (CH_3), 112.5, 114.7, 118.5, 124.9, 125.1 (quaternary *C*), 126.7 (quaternary *C*), 127.1 (quaternary *C*), 127.6, 129.7, 130.1, 130.9, 131.4, 134.6, 140.7 (quaternary *C*), 164.6 (quaternary *C*), 190.1 (*C*═O).

Synthesis of 1c. The compound was prepared with a similar procedure to that of **1a**. A mixture of 3-(4-methoxyphenyl)imidazo-[1,2-*a*]pyridine (1.87 g, 8.33 mmol) and 2-bromo-1-phenylethanone (1.66 g, 8.33 mmol) was used. A white solid was obtained. Yield: 2.99 g (85%). Mp = 253.3−253.9 °C. ESI-HRMS *m*/*z*: $[M - Br]^+$ Calcd for $C_{22}H_{19}N_2O_2$ 343.1446; Found 343.1443. ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.88 (s, 3H, CH_3), 6.42 (s, 2H, CH_2), 7.24 (d, 2H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 7.59 (t, 1H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 7.65−7.73 (m, 4H, Ar *H*), 7.81 (t, 1H, $^3J_{HH}$ = 6.0 Hz, Ar *H*), 8.08−8.16 (m, 3H, Ar *H*), 8.34−8.36 (m, 2H, imi *H*, Ar *H*), 8.82 (d, 1H, $^3J_{HH}$ = 6.0 Hz, Ar *H*). ^{13}C{^{1}H} NMR (75.4 MHz, DMSO-d_6): δ 54.4 (CH_2), 56.0 (CH_3), 112.4, 115.6, 116.9 (quaternary *C*), 118.4, 124.3, 126.7 (quaternary *C*), 127.5, 128.9, 129.5, 131.5, 134.3 (quaternary *C*), 134.5, 135.0, 140.5 (quaternary *C*), 161.2 (quaternary *C*), 192.0 (*C*═O).

Synthesis of 2a. A mixture of **1a** (2.0 g, 8.92 mmol) and $NaBF_4$ (5 g, 46 mmol) in acetonitrile (30 mL) was placed in a Schlenk flask. The mixture was heated to 80 °C for 48 h. After, the reaction was cooled, extracted with DCM (3 × 10 mL), and dried with anhydrous $MgSO_4$. The solvent was removed completely under high vacuum, and the white solid was collected on a frit, washed with ether, and dried under vacuum. Yield: 1.36 g (89%). Mp = 196.8−197.5 °C, ESI-HRMS *m*/*z*: $[M - BF_4]^+$ Calcd for $C_{21}H_{17}N_2O$ 313.1340; Found 313.1333. ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.41 (s, 2H CH_2), 7.59−7.72 (m, 6H, Ar *H*), 7.79−7.81 (m, 3H, Ar *H*), 8.11−8.17 (m, 3H, Ar *H*), 8.38 (d, 1H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 8.42 (s, 1H, imi *H*), 8.9 (d, 1H, $^3J_{HH}$ = 9.0 Hz, Ar *H*). ^{13}C{^{1}H} NMR (75.4 MHz, DMSO-d_6): δ 54.2 (CH_2), 112.3, 118.5, 124.8, 125.0 (quaternary *C*), 126.8 (quaternary *C*), 127.7, 128.9, 129.5, 129.7, 130.2, 131.0, 134.3 (quaternary *C*), 134.7, 135.1, 140.7 (quaternary *C*), 192.0 (*C*═O).

Synthesis of 2b. The compound was prepared with a similar procedure to that of **2a**. A mixture of **1b** (2.0 g, 8.9 mmol) and $NaBF_4$ (5 g, 46 mmol) was used. A white solid was obtained. Yield: 1.1 g (73%). Mp = 163.1−163.7 °C. ESI-HRMS *m*/*z*: $[M - BF_4]^+$ Calcd for $C_{22}H_{19}N_2O_2$ 343.1446; Found 343.1437. ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.91 (s, 3H, CH_3), 6.33 (s, 2H, CH_2), 7.21 (d, 2H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 7.60 (t, 1H, $^3J_{HH}$ = 6.0 Hz, Ar *H*), 7.67−7.71 (m, 3H, Ar *H*), 7.78−7.81 (m, 2H, Ar *H*), 8.09−8.13 (m, 3H, Ar *H*), 8.33 (d, 1H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 8.41 (s, 1H, imi *H*), 8.89 (d, 1H, $^3J_{HH}$ = 6.0 Hz, Ar *H*). ^{13}C{^{1}H} NMR (75.4 MHz, $CDCl_3$): δ 53.2 (CH_2), 55.6 (CH_3), 112.2, 114.4, 118.1, 123.9 (quaternary *C*), 124.5, 125.7, 126.3 (quaternary *C*), 127.0 (quaternary *C*), 129.2, 129.9, 130.9, 131.1, 134.0, 140.3 (quaternary *C*), 164.8 (quaternary *C*), 189.0 (*C*═O).

Synthesis of 2c. The compound was prepared with a similar procedure to that of **2a**. A mixture of **1c** (2.0 g, 8.9 mmol) and $NaBF_4$ (5.0 g, 46.0 mmol) was used. A white solid was obtained. Yield: 1.38 g

DOI: 10.1021/acs.organomet.8b00054
Organometallics XXXX, XXX, XXX−XXX

(91%). Mp = 159.7−160.2 °C. ESI-HRMS *m/z*: $[M - BF_4]^+$ Calcd for $C_{22}H_{19}N_2O_2$ 343.1446; Found 343.1437. ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.88 (s, 3H, CH_3), 6.38 (s, 2H, CH_2), 7.24 (d, 2H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 7.59 (t, 1H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 7.66−7.73 (m, 4H, Ar *H*), 7.81 (t, 1H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 8.08−8.16 (m, 3H, Ar *H*), 8.32−8.36 (m, 2H, Ar *H*, imi *H*), 8.82 (d, 1H, $^3J_{HH}$ = 6.0 Hz, Ar *H*). ^{13}C{^{1}H} NMR (75.4 MHz, DMSO-d_6): δ 54.1 (CH_2), 56.0 (CH_3), 112.2, 115.6, 116.9 (quaternary C), 118.4, 124.3, 126.8 (quaternary *C*), 127.6, 128.9, 129.5, 131.5, 134.3 (quaternary *C*), 134.5, 135.0, 140.5 (quaternary *C*), 161.3 (quaternary *C*), 191.8 (C═O).

Synthesis of 3a. A mixture of 1-benzyl-2-phenyl-1*H*-imidazole (2.71 g, 11.6 mmol) and 2-bromo-1-phenylethanone (2.3 g, 11.6 mmol) in THF (30 mL) was placed in a Schlenk flask. The mixture was heated to 80 °C for 2 days. After cooling, the white solid was collected on a frit, washed with THF for three times, and dried under vacuum. Yield: 3.65 g (74%). Mp = 204.7−205.2 °C. ESI-HRMS *m/z*: $[M - Br]^+$ Calcd for $C_{24}H_{21}N_2O$ 353.1653; Found 353.1651. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.24 (s, 2H, NCH_2), 5.99 (s, 2H, O═CCH_2), 7.01 (t, 2H, $^3J_{HH}$ = 3.0 Hz, Ar *H*), 7.15−7.17 (m, 3H, Ar *H*), 7.27 (t, 2H, $^3J_{HH}$ = 6.0 Hz, Ar *H*), 7.33−7.47 (m, 6H, Ar *H*), 7.78 (s, 1H, imi *H*), 7.83 (d, 2H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 8.0 (s, 1H, imi *H*). ^{13}C{^{1}H} NMR (75.4 MHz, $CDCl_3$): δ 52.6 (NCH_2), 55.9 (O═CCH_2), 125.0 (quaternary *C*), 122.4, 124.3, 127.9, 128.5, 128.9, 129.0, 129.2, 129.8, 130.3, 132.9, 133.1 (quaternary *C*), 133.4 (quaternary *C*), 134.6, 145.8 (quaternary *C*), 191.0 (*C*═O).

Synthesis of 3b. The compound was prepared with a similar procedure to that of **3a**. A mixture of 1-benzyl-2-phenyl-1*H*-imidazole (2.7 g, 11.8 mmol) and 2-bromo-1-(4-methoxyphenyl)ethanone (2.65 g, 11.8 mmol) was used. A white solid was obtained. Yield: 4.43 g (85%). Mp = 208.1−208.4 °C. ESI-HRMS *m/z*: $[M - Br]^+$ Calcd for $C_{25}H_{23}N_2O_2$ 383.1759; Found 383.1752. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.77 (s, 3H, CH_3), 5.30 (s, 2H, NCH_2), 6.07 (s, 2H, O═CCH_2), 6.86 (d, 2H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 7.09−7.12 (m, 2H, Ar *H*), 7.26−7.29 (m, 3H, Ar *H*), 7.44−7.56 (m, 5H, Ar *H*), 7.77 (d, 1H, $^3J_{HH}$ = 3.0 Hz, imi *H*), 7.93 (d, 2H, $^3J_{HH}$ = 12.0 Hz, Ar *H*), 8.09 (d, 1H, $^3J_{HH}$ = 3.0 Hz, imi *H*). ^{13}C{^{1}H} NMR (75.4 MHz, $CDCl_3$): δ 52.7 (NCH_2), 55.6 (CH_3), 55.7 (O═CCH_2), 114.3, 120.7 (quaternary *C*), 122.0, 124.6, 126.2 (quaternary *C*), 127.9, 129.1, 129.3, 129.8, 130.5, 131.2, 132.9, 133.1 (quaternary *C*), 146.1 (quaternary *C*), 164.8 (quaternary *C*), 189.1 (*C*═O).

Synthesis of 4a. A mixture **3a** (2.0 g, 4.32 mmol) and $NaBF_4$ (2.48 g, 22.6 mmol) in acetonitrile (30 mL) was placed in a Schlenk flask. The mixture was heated to 80 °C for 48 h. After, the reaction was cooled, extracted with DCM (3 × 10 mL), and dried with anhydrous $MgSO_4$. The solvent was removed completely under high vacuum, and the white solid was collected on a frit, washed with ether, and dried under vacuum. Yield: 1.7 g (84%). Mp = 204.0−204.6 °C. ESI-HRMS *m/z*: $[M - BF_4]^+$ Calcd for $C_{24}H_{21}N_2O$ 353.1653; Found 353.1651. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.17 (s, 2H, NCH_2), 5.65 (s, 2H, O═CCH_2), 7.09 (t, 2H, $^3J_{HH}$ = 3.0 Hz, Ar *H*), 7.30−7.31 (m, 3H, imi *H*, Ar *H*), 7.40 (t, 2H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 7.45−7.49 (m, 5H, imi *H*, Ar *H*), 7.52−7.58 (m, 3H, imi *H*, Ar *H*), 7.85 (d, 2H, $^3J_{HH}$ = 6.0 Hz, Ar *H*). ^{13}C{^{1}H} NMR (75.4 MHz, $CDCl_3$): δ 52.5 (NCH_2), 55.1 (O═CCH_2), 120.5 (quaternary *C*), 122.1, 124.1, 127.8, 128.3, 129.1, 129.3, 129.8, 130.3, 132.9 (quaternary *C*), 133.0 (quaternary *C*), 133.1, 134.8, 146.1 (quaternary *C*), 190.8 (*C*═O).

Synthesis of 4b. The compound was prepared with a similar procedure to that of **4a**. A mixture of **3b** (2.05 g, 4.32 mmol) and $NaBF_4$ (2.5 g, 22.6 mmol) was used. A white, moisture-sensitive solid was obtained. Yield: 1.79 g (88%). ESI-HRMS *m/z*: $[M - BF_4]^+$ Calcd for $C_{25}H_{23}N_2O_2$ 383.1759; Found 383.1748. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.79 (s, 3H, CH_3), 5.16 (s, 2H, NCH_2), 5.58 (s, 2H, O═CCH_2), 6.85 (d, 2H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 7.06−7.09 (m, 2H, Ar *H*), 7.27−7.32 (m, 3H, imi *H*, Ar *H*), 7.44−7.51 (m, 6H, Ar *H*), 7.54−7.58 (m, 1H, Ar *H*), 7.83 (d, 2H, $^3J_{HH}$ = 9.0 Hz, Ar *H*). ^{13}C{^{1}H} NMR (75.4 MHz, $CDCl_3$): δ 52.5 (NCH_2), 54.8 (O═CCH_2), 55.6 (CH_3), 114.3, 120.6 (quaternary *C*), 122.0, 124.1, 126.0 (quaternary *C*), 127.8, 129.1, 129.4, 130.0, 130.8, 132.9, 133.2 (quaternary *C*), 146.2 (quaternary *C*), 164.8 (quaternary *C*), 188.9 (*C*═O).

Synthesis of 5a. To a 20 mL Schlenk flask containing $Pd(OAc)_2$ (0.047 g, 0.21 mmol), **1a** (0.1 g, 0.25 mmol) was added dry DMF (8 mL). The mixture was allowed to stir at room temperature for overnight. 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 with diethyl ether and filtered on a frit and dried under vacuum. An air-stable, yellow solid was obtained. Yield: 0.15 g (71%); Mp = 214.3-215.2 °C. Anal. Calcd for $C_{42}H_{30}Br_2N_4O_2Pd_2$: C, 50.81; H, 3.04; N, 5.64. Found: C, 50.73; H, 3.07; N, 5.33%. ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.84 (s, 2H, Pd−C*H*), 7.15 (br s, 4H, Ar *H*), 7.42−7.47 (m, 4H, Ar *H*), 7.61−7.68 (m, 6H, Ar *H*), 7.72−7.74 (m, 4H, Ar *H*), 7.93 (t, 2H, Ar *H*, $^3J_{HH}$ = 9.0 Hz), 8.17−8.27 (m, 4H, Ar *H*), 8.41 (s, 2H, imi *H*), 8.78 (d, 2H, $^3J_{HH}$ = 6.0 Hz, Ar *H*). ^{13}C{^{1}H} NMR (75.4 MHz, DMSO-d_6): δ 68.6 (Pd−*C*H), 112.8, 114.3, 117.5, 124.5 (quaternary *C*), 125.1, 125.7, 126.6, 128.9 (quaternary *C*), 129.4, 129.8, 130.1, 130.5, 132.3, 134.5, 139.7 (quaternary *C*), 141.4 (quaternary *C*), 153.8 (Pd−*C*), 199.1 (*C*═O).

Synthesis of 5b. The compound was prepared with a similar procedure to that of **5a**. A mixture of $Pd(OAc)_2$ (0.044 g, 0.20 mmol), **1b** (0.1 g, 0.24 mmol), was added in dry DMF (8 mL). An air-stable, yellow solid was obtained. Yield: 0.14 g (68%). Mp = 228.6−229.4 °C. Anal. Calcd for $C_{44}H_{34}Br_2N_4O_4Pd_2$: C, 50.19; H, 3.25; N, 5.32. Found: C, 50.16; H, 3.12; N, 5.48%. ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.76 (s, 6H, CH_3), 6.71−6.79 (m, 3H, Pd−C*H*, Ar *H*), 7.37−7.46 (m, 4H, Ar *H*), 7.60−7.67 (m, 6H, Ar *H*), 7.71−7.73 (m, 4H, Ar *H*), 7.89−7.94 (m, 4H, Ar *H*), 8.08−8.17 (m, 3H, Ar *H*), 8.40 (s, 2H, imi *H*), 8.78 (d, 2H, $^3J_{HH}$ = 6.0 Hz, Ar *H*). ^{13}C{^{1}H} NMR (75.4 MHz, DMSO-d_6): δ 55.5 (CH_3), 68.0 (Pd−*C*H), 112.3, 117.4, 125.0 (quaternary *C*), 125.7, 125.9, 126.3 (quaternary *C*), 126.6, 129.3, 129.7, 130.1, 130.2 (quaternary *C*), 130.5, 132.3, 134.5, 139.6 (quaternary *C*), 156.8 (Pd−*C*), 160.1 (quaternary *C*), 199.3 (C═O).

Synthesis of 5c. The compound was prepared with a similar procedure to that of **5a**. A mixture of $Pd(OAc)_2$ (0.044 g, 0.20 mmol), **1c** (0.1 g, 0.24 mmol), was added in dry DMF (8 mL). An air-stable, yellow solid was obtained. Yield: 0.13 g (65%). Mp = 203.3−203.5 °C. Anal. Calcd for $C_{44}H_{34}Br_2N_4O_4Pd_2$: C, 50.19; H, 3.25; N, 5.32. Found: C, 49.71; H, 3.34; N, 5.39%. ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.86 (s, 6H, CH_3), 6.82 (s, 2H, Pd−C*H*), 7.15−7.25 (m 7H, Ar *H*), 7.40−7.44 (m, 4H, Ar *H*), 7.62−7.74 (m, 5H, Ar *H*), 7.91 (t, 2H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 8.14−8.30 (m, 6H, imi *H*, Ar *H*), 8.69 (d, 2H, $^3J_{HH}$ = 6.0 Hz, Ar *H*). ^{13}C{^{1}H} NMR (75.4 MHz, DMSO-d_6): δ 55.9 (CH_3), 68.5 (Pd−*C*H), 115.5, 117.3, 117.6, 124.5 (quaternary *C*), 125.0, 125.2, 126.5, 128.9 (quaternary *C*), 129.5, 129.8, 131.1, 131.9, 134.6, 139.4 (quaternary *C*), 141.5 (quaternary *C*), 153.8 (Pd−*C*), 160.9 (quaternary *C*), 199.2 (*C*═O).

Synthesis of 6a. To a 20 mL Schlenk flask containing $Pd(OAc)_2$ (0.047 g, 0.21 mmol), **2a** (0.1 g, 0.25 mmol) was added dry pyridine (8 mL). The mixture was allowed to stir at room temperature for overnight. 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. Diethyl ether and THF was added and the solid formed was filtered on a frit and dried under vacuum. An air-stable yellow solid was obtained. Yield: 0.11 g (88%); Mp = 212.3-213.1 °C. Anal. Calcd for $C_{31}H_{25}BF_4N_4OPd$: C, 56.18; H, 3.80; N, 8.45. Found: C, 56.03; H, 3.81; N, 8.37%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.62 (d, 1H, $^3J_{HH}$ = 3.0 Hz, Ar *H*), 6.72 (s, 1H, Pd−C*H*), 6.96−7.02 (m, 2H, Ar *H*), 7.09 (t, 1H, *J* = 9.0 Hz, Ar *H*), 7.38−7.58 (m, 10H, Py *H*, Ar *H*), 7.77−7.88 (m, 3H, imi *H*, Py *H*), 8.17 (d, 2H, $^3J_{HH}$ = 6.0 Hz, Ar *H*), 8.25 (d, 2H, $^3J_{HH}$ = 3.0 Hz, Py *H*), 8.75 (d, 2H, $^3J_{HH}$ = 6.0 Hz, Py *H*). ^{13}C{^{1}H} NMR (75.4 MHz, $CDCl_3$): δ 35.2 (Pd−*C*H), 113.4, 117.6, 124.1 (quaternary *C*), 125.0, 125.8, 127.6, 128.5, 128.7, 128.9 (Py *C*), 129.2, 129.4, 130.0 (Py *C*), 130.6, 130.7, 132.9, 134.3, 138.0 (quaternary *C*), 138.3 (Py *C*), 138.4 (Py *C*), 142.3 (quaternary *C*), 150.0 (Py *C*), 151.3 (Pd−*C*), 151.7 (Py *C*), 200.4 (*C*═O).

DOI: 10.1021/acs.organomet.8b00054
Organometallics XXXX, XXX, XXX−XXX

Synthesis of 6b. The compound was prepared with a similar procedure to that of **6a**. A mixture of $Pd(OAc)_2$ (0.044 g, 0.20 mmol), **2b** (0.1 g, 0.25 mmol), was added in dry pyridine (8 mL). An air-stable, yellow solid was obtained. Yield: 0.10 g (72%). Mp = 263.1−263.4 °C. Anal. Calcd for $C_{32}H_{27}BF_4N_4O_2Pd$: C, 55.48; H, 3.93; N, 8.09. Found: C, 55.49; H, 3.94; N, 8.19%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.58 (s, 3H, CH_3), 6.64−6.67 (m, 2H, Ar *H*, Pd−C*H*), 6.99 (t, 2H, $^3J_{HH}$ = 6.0 Hz, Ar *H*), 7.21−7.25 (m, 1H, Ar *H*), 7.37−7.42 (m, 5H, Py *H*, Ar *H*), 7.47−7.56 (m, 4H, Py *H*, Ar *H*), 7.76−7.91 (m, 3H, imi *H*, Py *H*), 8.06−8.09 (m, 3H, Ar *H*), 8.24 (d, 2H, $^3J_{HH}$ = 6.0 Hz, Py *H*), 8.77 (d, 2H, $^3J_{HH}$ = 6.0 Hz, Py *H*). $^{13}C\{^1H\}$ NMR (75.4 MHz, 75.4 MHz, $CDCl_3$): δ 31.0 (Pd−CH), 55.0 (CH_3), 111.6, 113.3, 114.4, 117.6, 118.7, 124.1, 125.0, 125.5 (quaternary *C*), 125.8, 127.0 (quaternary *C*), 128.9 (Py *C*), 129.9 (Py *C*), 130.6, 131.2 (quaternary *C*), 132.8, 135.6, 138.0 (Py *C*), 138.4 (Py *C*), 138.5 (quaternary *C*), 150.0 (Py *C*), 151.6 (Py *C*), 154.9 (Pd−*C*), 160.7, 200.3 (*C*═O).

Synthesis of 6c. The compound was prepared with a similar procedure to that of **6a**. A mixture of $Pd(OAc)_2$ (0.044 g, 0.20 mmol), **2c** (0.1 g, 0.25 mmol), was added in dry pyridine (8 mL). An air-stable, yellow solid was obtained. Yield: 0.12 g (87%). Mp = 218.6−219.6 °C. Anal. Calcd for $C_{32}H_{27}BF_4N_4O_2Pd$: C, 55.48; H, 3.93; N, 8.09. Found: C, 55.32; H, 3.78; N, 8.27%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.83 (s, 3H, CH_3), 6.63 (d, 1H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 6.69 (s, 1H, Pd−C*H*), 6.92−7.13 (m, 7H, Py *H*, Ar *H*), 7.19−7.24 (m, 1H, Ar *H*), 7.30−7.33 (m, 1H, Ar *H*), 7.38−7.46 (m, 3H, Py *H*, Ar *H*), 7.57 (d, 1H, $^3J_{HH}$ = 6.0 Hz, Ar *H*), 7.69 (s, 1H, imi *H*), 7.78−7.85 (m, 2H, Py *H*), 8.12−8.15 (m, 2H, Ar *H*), 8.22 (d, 2H, $^3J_{HH}$ = 6.0 Hz, Py *H*), 8.75 (d, 2H, $^3J_{HH}$ = 3.0 Hz, Py *H*). $^{13}C\{^1H\}$ NMR (75.4 MHz, DMSO-d_6): δ 39.1−40.8 (Pd−CH, overlapping with residual DMSO signals), 56.0 (CH_3), 115.6, 116.9, 117.6, 124.3 (quaternary *C*), 124.7, 125.0, 126.5, 129.6 (quaternary *C*), 130.3, 130.5 (Py *C*), 131.1, 132.8, 134.5, 138.4 (Py *C*), 139.3 (quaternary *C*), 142.8 (quaternary *C*), 150.3 (Py *C*), 152.0 (Pd−*C*), 161.1 (quaternary *C*), 199.6 (C═O).

Synthesis of 7a. To a 20 mL Schlenk flask containing $Pd(OAc)_2$ (0.05 g, 0.23 mmol), **4a** (0.1 g, 0.23 mmol), NaOAc (0.018 g, 0.23 mmol) was added in dry pyridine (8 mL). The mixture was allowed to stir at room temperature for overnight. 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. Diethyl ether and THF were added, and the solid formed was filtered on a frit and dried under vacuum. An air-stable yellow solid was obtained. Yield: 0.06 g (42%); Mp = 231.2−231.4 °C. Anal. Calcd for $C_{34}H_{29}BF_4N_4OPd$: C, 58.10; H, 4.16; N, 7.97. Found: C, 58.52; H, 4.41; N, 7.72%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.03 (AB q, 2H, Δ_{AB} = 18.7 Hz, J_{AB} = 15.0 Hz, CH_2), 6.04 (s, 1H, Pd−C*H*), 6.51 (d, 1H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 6.88−7.03 (m, 4H, imi *H*, Ar *H*), 7.10 (t, 1H, $^3J_{HH}$ = 9.0 Hz, Ar *H*), 7.25−7.26 (m, 2H, Ar *H*), 7.29 (m, 1H, Ar *H*), 7.36−7.43 (m, 7H, Py *H*, Ar *H*), 7.54−7.60 (m, 4H, Ar *H*), 7.78−7.87 (m, 2H, Py *H*), 8.24 (d, 2H, $^3J_{HH}$ = 6.0 Hz, Py *H*), 8.63 (d, 2H, $^3J_{HH}$ = 6.0 Hz, Py *H*). $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$): δ 30.5 (Pd−CH), 52.3 (CH_2), 121.5, 121.7 (quaternary *C*), 125.0, 125.3, 125.5, 126.1, 126.5, 128.0 (Py *C*), 129.1, 129.3 (Py *C*), 130.2, 130.5, 130.9, 132.8 (quaternary *C*), 133.7, 134.4, 138.7 (Py *C*), 139.4 (Py *C*), 142.8 (quaternary *C*), 143.5 (quaternary *C*), 150.1 (Py *C*), 151.7 (Py *C*), 152.9 (Pd−*C*), 202.5 (*C*═O).

Synthesis of 7b. The compound was prepared with a similar procedure to that of **7a**. A mixture of $Pd(OAc)_2$ (0.04 g, 0.23 mmol), **4b** (0.1 g, 0.23 mmol), was added in dry pyridine (8 mL). An air-stable, yellow solid was obtained. Yield: 0.04 g (35%). Mp = 235.8−236.4 °C. Anal. Calcd for $C_{35}H_{31}BF_4N_4O_2Pd$: C, 57.36; H, 4.26; N, 7.65. Found: C, 57.34; H, 4.26; N, 7.59%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.57 (s, 3H, CH_3), 5.03 (AB q, 2H, Δ_{AB} = 19.5 Hz, $^2J_{AB}$ = 16.5 Hz, CH_2), 5.98 (s, 1H, Pd−C*H*), 6.66 (dd, 1H, $^3J_{HH}$ = 9.0 Hz, $^4J_{HH}$ = 3.0 Hz, Ar *H*), 6.88−6.91 (m, 2H, Ar *H*), 7.05 (d, 1H, $^3J_{HH}$ = 3.0 Hz, imi *H*), 7.25−7.26 (m, 2H, Ar *H*), 7.32−7.43 (m, 8H, imi *H*, Py *H*, Ar *H*), 7.52−7.59 (m, 5H, Ar *H*), 7.79−7.87 (m, 2H, Py *H*), 8.23 (d, 2H, $^3J_{HH}$ = 6.0 Hz, Py *H*), 8.66 (d, 2H, $^3J_{HH}$ = 3.0 Hz, Py *H*). $^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$): δ 30.3 (Pd−CH), 52.2 (CH_2), 55.0 (CH_3), 111.4, 118.8, 121.3, 121.5 (quaternary *C*), 124.7, 125.8, 126.3, 127.3, 127.8 (Py *C*), 128.9, 129.2 (Py *C*), 130.4, 132.6, 133.5 (quaternary *C*), 135.9 (quaternary *C*), 138.5 (Py *C*), 139.3 (Py *C*), 143.6 (quaternary *C*), 149.9 (Py *C*), 151.5 (Py *C*), 156.1 (Pd−*C*), 160.9 (quaternary *C*), 202.0 (C═O).

General Procedure for Mizoroki−Heck Reaction. In a typical reaction, a mixture of aryl halide (1 mmol), styrene (1.4 mmol), base (1.1 equiv), and palladium catalyst (0.2 mol %) in TBAB (2 g) was stirred at 140 °C for an appropriate period of time (2−12 h). After, the reaction was cooled, extracted with ethyl ether (3 × 10 mL), and dried with anhydrous $MgSO_4$. The solvent was removed completely under high vacuum. Crude products were purified through flash column chromatography on 230−400 mesh silica gel using hexane or hexane/ethyl acetate as eluent with a suitable ratio according to the TLC experiments. Yield was determined by using 1,3,5-trimethoxybenzene as internal standard.

Single-Crystal X-ray Diffraction. Samples were collected at 150(2) K on a Bruker APEX II equipped with a CCD area detector and a graphite monochromator utilizing Mo Kα radiation (λ = 0.71073 Å). The unit cell parameters were obtained by least-squares refinement. Data collection and reduction were performed using the Bruker APEX2 and SAINT software.[14] Absorption corrections were performed using the SADABS program.[15] All the structures were solved by direct methods and refined by full-matrix least-squares methods against F^2 with the SHELXTL software package.[16] All non-H atoms were refined anisotropically. All H atoms were fixed at calculated positions and refined with the use of a riding model. A disordered DMF solvent molecule in **7b** was refined using a rigid + model. CCDC files 1816353 (**6a**), 1816354 (**6b**), and 1816355 (**7b**) contain supplementary crystallographic data for this paper.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.8b00054.

Additional drawings, crystallographic data, ^{1}H NMR assignment of coupled products, NMR spectra of ligand precursors, palladium complexes and coupled products, ESI-MS spectra of ligand precursors (PDF)

Accession Codes

CCDC 1816353−1816355 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: leehm@cc.ncue.edu.tw.

ORCID

Hon Man Lee: 0000-0002-9557-3914

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful to the Ministry of Science and Technology of Taiwan (MOST 106-2113-M-018-001) for financial support of this work.

■ REFERENCES

(1) (a) Herrmann, W. A.; Böhm, V. P. W.; Reisinger, C.-P. *J. Organomet. Chem.* **1999**, *576*, 23−41. (b) Dupont, J.; Pfeffer, M.; Spencer, J. *Eur. J. Inorg. Chem.* **2001**, *2001*, 1917−1927. (c) Bedford,

DOI: 10.1021/acs.organomet.8b00054
Organometallics XXXX, XXX, XXX−XXX

R. B. *Chem. Commun.* **2003**, 1787−1796. (d) Beletskaya, I. P.; Cheprakov, A. V. *J. Organomet. Chem.* **2004**, *689*, 4055−4082. (e) Omae, I. *Coord. Chem. Rev.* **2004**, *248*, 995−1023. (f) Dupont, J.; Pfeffer, M. *Palladacycles*; Wiley-VCH: Weinheim, Germany, 2008. (g) Albrecht, M. *Chem. Rev.* **2010**, *110*, 576−623. (h) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147−1169. (i) Alonso, D. A.; Najera, C. *Chem. Soc. Rev.* **2010**, *39*, 2891−2902.

(2) (a) Dupont, J.; Consorti, C. S.; Spencer, J. *Chem. Rev.* **2005**, *105*, 2527−2572. (b) Ghedini, M.; Aiello, I.; Crispini, A.; Golemme, A.; La Deda, M.; Pucci, D. *Coord. Chem. Rev.* **2006**, *250*, 1373−1390. (c) Caires, A. C. F. *Anti-Cancer Agents Med. Chem.* **2007**, *7*, 484−491. (d) Ryabov, A. D. In *Palladacycles*; Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, Germany, 2008; pp 307−339. (e) Juribasic, M.; Curic, M.; Molcanov, K.; Matkovic-Calogovic, D.; Babic, D. *Dalton Trans.* **2010**, *39*, 8769−8778. (f) Cutillas, N.; Yellol, G. S.; de Haro, C.; Vicente, C.; Rodríguez, V.; Ruiz, J. *Coord. Chem. Rev.* **2013**, *257*, 2784−2797. (g) Juribašić, M.; Halasz, I.; Babić, D.; Cinčić, D.; Plavec, J.; Ćurić, M. *Organometallics* **2014**, *33*, 1227−1234. (h) Kapdi, A. R.; Fairlamb, I. J. S. *Chem. Soc. Rev.* **2014**, *43*, 4751−4777. (i) Fleetham, T.; Ji, Y.; Huang, L.; Fleetham, T. S.; Li, J. *Chem. Sci.* **2017**, *8*, 7983−7990.

(3) (a) Masselot, D.; Charmant, J. P. H.; Gallagher, T. *J. Am. Chem. Soc.* **2006**, *128*, 694−695. (b) Ma, D.; Shi, G.; Wu, Z.; Ji, X.; Zhang, Y. *J. Org. Chem.* **2018**, *83*, 1065−1072. (c) Wu, Z.; Ma, D.; Zhou, B.; Ji, X.; Ma, X.; Wang, X.; Zhang, Y. *Angew. Chem., Int. Ed.* **2017**, *56*, 12288−12291. (d) Pérez-Gómez, M.; Navarro, L.; Saura-Llamas, I.; Bautista, D.; Lautens, M.; García-López, J.-A. *Organometallics* **2017**, *36*, 4465−4476.

(4) (a) Lee, J.-Y.; Huang, Y.-H.; Liu, S.-Y.; Cheng, S.-C.; Jhou, Y.-M.; Lii, J.-H.; Lee, H. M. *Chem. Commun.* **2012**, *48*, 5632−5634. (b) Grande, L.; Serrano, E.; Cuesta, L.; Urriolabeitia, E. P. *Organometallics* **2012**, *31*, 394−404.

(5) (a) Chen, S.-J.; Lin, Y.-D.; Chiang, Y.-H.; Lee, H. M. *Eur. J. Inorg. Chem.* **2014**, *2014*, 1492−1501. (b) Lee, J.-Y.; Ghosh, D.; Lee, J.-Y.; Wu, S.-S.; Hu, C.-H.; Liu, S.-D.; Lee, H. M. *Organometallics* **2014**, *33*, 6481−6492. (c) Lee, J.-Y.; Tzeng, R.-J.; Wang, M.-C.; Lee, H. M. *Inorg. Chim. Acta* **2017**, *464*, 74−80.

(6) (a) Nájera, C.; Alonso, D. A. In *Palladacycles*; Wiley-VCH Verlag GmbH & Co. KGaA: Weimheim, Germany, 2008; pp 155−207. (b) Herrmann, W. A.; Brossmer, C.; Öfele, K.; Reisinger, C.-P.; Priermeier, T.; Beller, M.; Fischer, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1844−1848. (c) Herrmann, W. A.; Öfele, K.; v. Preysing, D.; Schneider, S. K. *J. Organomet. Chem.* **2003**, *687*, 229−248. (d) Gildner, P. G.; Colacot, T. J. *Organometallics* **2015**, *34*, 5497−5508.

(7) Sureshbabu, B.; Ramkumar, V.; Sankararaman, S. *J. Organomet. Chem.* **2015**, *799*−*800*, 232−238.

(8) (a) Gründemann, S.; Kovacevic, A.; Albrecht, M.; Faller, J. W.; Crabtree, R. H. *J. Am. Chem. Soc.* **2002**, *124*, 10473−10481. (b) Grundemann, S.; Kovacevic, A.; Albrecht, M.; Robert, J. W. F.; Crabtree, R. H. *Chem. Commun.* **2001**, 2274−2275. (c) Schuster, O.; Yang, L.; Raubenheimer, H. G.; Albrecht, M. *Chem. Rev.* **2009**, *109*, 3445−3478. (d) Ke, C.-H.; Kuo, B.-C.; Nandi, D.; Lee, H. M. *Organometallics* **2013**, *32*, 4775−4784. (e) Arnold, P. L.; Pearson, S. *Coord. Chem. Rev.* **2007**, *251*, 596−609. (f) Aldeco-Perez, E.; Rosenthal, A. J.; Donnadieu, B.; Parameswaran, P.; Frenking, G.; Bertrand, G. *Science* **2009**, *326*, 556−559.

(9) (a) Lee, J.-Y.; Cheng, P.-Y.; Tsai, Y.-H.; Lin, G.-R.; Liu, S.-P.; Sie, M.-H.; Lee, H. M. *Organometallics* **2010**, *29*, 3901−3911. (b) Lee, J.-Y.; Shen, J.-S.; Tzeng, R.-J.; Lu, I. C.; Lii, J.-H.; Hu, C.-H.; Lee, H. M. *Dalton Trans.* **2016**, *45*, 10375−10388.

(10) Yao, Q.; Kinney, E. P.; Yang, Z. *J. Org. Chem.* **2003**, *68*, 7528−7531.

(11) Bencivengo, D.; San Filippo, J. *J. Org. Chem.* **1981**, *46*, 5222−5224.

(12) (a) Eberhard, M. R. *Org. Lett.* **2004**, *6*, 2125−2128. (b) Lin, Y.-C.; Hsueh, H.-H.; Kanne, S.; Chang, L.-K.; Liu, F.-C.; Lin, I. J. B.; Lee, G.-H.; Peng, S.-M. *Organometallics* **2013**, *32*, 3859−3869. (c) Keske, E. C.; Zenkina, O. V.; Wang, R.; Crudden, C. M. *Organometallics* **2012**, *31*, 6215−6221. (d) Ananikov, V. P.; Beletskaya, I. P. *Organometallics* **2012**, *31*, 1595−1604. (e) Zalesskiy, S. S.; Ananikov, V. P. *Organometallics* **2012**, *31*, 2302−2309. (f) Astakhov, A. V.; Khazipov, O. V.; Chernenko, A. Y.; Pasyukov, D. V.; Kashin, A. S.; Gordeev, E. G.; Khrustalev, V. N.; Chernyshev, V. M.; Ananikov, V. P. *Organometallics* **2017**, *36*, 1981−1992.

(13) Widegren, J. A.; Bennett, M. A.; Finke, R. G. *J. Am. Chem. Soc.* **2003**, *125*, 10301−10310.

(14) *Bruker APEX2 and SAINT*; Bruker AXS Inc.: Madison, WI, 2007.

(15) Sheldrick, G. M. *SADABS*; University of Göttingen: Göttingen, Germany, 1996.

(16) Sheldrick, G. *Acta Crystallogr., Sect. A: Found. Crystallogr.* **2008**, *A64*, 112−122.

DOI: 10.1021/acs.organomet.8b00054
Organometallics XXXX, XXX, XXX−XXX