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The highly efficient Suzuki–Miyaura cross-coupling reaction using cyclopalladated *N*-alkylferrocenylimine as a catalyst in aqueous medium at room temperature under ambient atmosphere

Bing Mu, Tiesheng Li *, Jingya Li, Yangjie Wu *

Department of Chemistry, Key Lab of Chemical Biology and Organic Chemistry of Henan Province, Key Lab of Advanced Nano-information Materials of Zhengzhou, Zhengzhou University, Zhengzhou 450052, PR China

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Abstract

A series of *N*-alkyl-substituted cyclopalladated ferrocenylimines were used in palladium-catalyzed Suzuki–Miyaura cross-coupling reactions of aryl halides in room temperature and CH_3OH/H_2O media under aerobic conditions. As for the catalysts, the length of *N*-alkyl chains has no significant effect on the catalytic activity. Using 0.01 mol% of dimer **3a** in the presence of K_2CO_3 as base offered excellent yields in the reaction of activated and non-activated aryl bromides with phenylboronic acid.

Keywords: Cyclopalladated ferrocenylimines; *N*-alkyl chains; Suzuki–Miyaura cross-coupling reactions; Room temperature; Aqueous media

1. Introduction

The Suzuki–Miyaura cross-coupling reaction has become a common transformation for the formation of carbon–carbon bonds because their products [1], in particular biaryls, are recurring functional groups in many natural products and biologically active compounds as well as useful blocks in organic synthesis [2]. This coupling is also especially useful because of the broad tolerance to different functional groups, the ability to couple sterically demanding substrates, mild reaction conditions, non-toxic and easy to handle reagents [3]. Consequently, considerable effort has been dedicated to develop efficient and active catalytic systems for Suzuki–Miyaura cross-coupling reaction in the past years [2d,2e,2f,4]. Most of these reactions were performed in traditional organic solvents and usually required elevated reaction temperatures to function efficiently. From an economic, environmental and safe standpoint, however, it is desirable to avoid any use of expensive and hazardous organic solvents, an inert atmosphere, and to proceed the reactions under mild conditions (e.g., room temperature) [5]. To satisfy these concerns, water or aqueous solution represents a very attractive medium for Suzuki couplings of aryl halides [6], especially in large-scale industrial synthesis, and the development of milder reaction conditions would also be a significant advance [7]. There has recently been considerable interest in the synthesis of new, high activity, air-stable palladium-based catalyst that can be used in room-temperature Suzuki cross-coupling reaction in aqueous solvents since such catalysts have the potential to be used in industrial systems [8]. However, the low solubility of the majority of organic compounds in water and stability of the metal catalysts in water are great problems [9]. In order to circumvent this crucial problem, the applications of water soluble ligands [10], phase-transfer catalysts [11], or the use of microwaves [12] had been described. Recently, inverse phase-transfer catalysts such as cyclodextrins or calix-arenes [13,14], and surfactants [10d,15] have also proved to be good additives for Suzuki–Miyaura reactions in aqueous media. For example, catalytic species derived from calix-arene based

* Corresponding authors. Tel./fax: +86 371 67766667.
E-mail addresses: lts34@zzu.edu.cn (T. Li), wyj@zzu.edu.cn (Y. Wu).

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imidazolium salts as ligand precursors and inverse phase-transfer catalysts showed high activity in the Suzuki–Miyaura cross-coupling of aryl chlorides at 80 °C [14]. Also, fewer catalytic systems could perform the cross-coupling reaction of aryl bromides or aryl chlorides at room temperature in aqueous solvent under air conditions [10a].

In previous studies [16], we found that cyclopalladated ferrocenylimines with long alkyl chains were highly efficient catalysts in the Suzuki–Miyaura cross-coupling reaction. Although there are high activities obtained in the amphiphilic catalysts, a high reaction temperature (110 °C) was still required to afford high yield of the product. In view of the observations that the surfactants could accelerate Suzuki–Miyaura cross-coupling reactions because the surfactants could form microemulsions and had the function as phase transfer reagent [10d], we are especially interested in the possibility of using cyclopalladated ferrocenylimines with long-chain hydrocarbon as catalysts and surfactants for Suzuki–Miyaura cross-coupling reactions in room temperature and aqueous solvents under air. Further research by using cyclopalladated ferrocenylimines with short alkyl chains was also studied.

2. Results and discussion

2.1. Synthesis and characterization of complexes *3a* and *3b*

The ferrocenylimine was synthesized by the condensation of acetylferrocene with *n*-butylamine in the presence of active Al_2O_3 at 75 °C for 1–2 days and the progress of the condensation reaction was controlled by recording the infrared spectra of the solution. The ferrocenylimine obtained without further purification was used for the cyclopalladation. Compounds **3a**, **3b** were prepared according to the general procedure [17]. They are highly soluble in most of the common solvents (chloroform, dichloromethane, benzene, toluene, ethyl acetate, etc.), slightly soluble in petroleum ether, hexane and insoluble in water.

The new compounds **3a**, **3b** were characterized by IR, ^{1}H NMR, ^{13}C NMR, ^{31}P NMR spectra, MS, and elemental analysis. For compound **3b**, the appearance of only one signal around 38 ppm in ^{31}P NMR spectra suggested the formation of a single isomer [18].

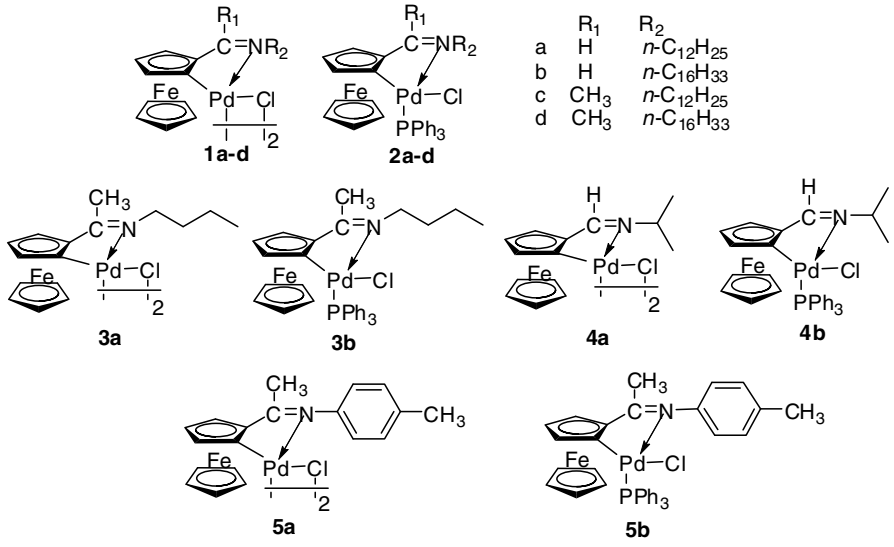
2.2. Suzuki–Miyaura cross-coupling reactions

We have previously shown that complexes **1a–d**, **2a–d** (Scheme 1) were efficient catalysts for the coupling of a range of aryl halides with phenylboronic acid in toluene at 110 °C [16]. In the present study, complexes **1a–d**, **2a–d** still showed high activity in the room-temperature Suzuki–Miyaura cross-coupling reactions in CH_3OH/H_2O media under air.

The coupling reaction of the relatively unactivated 4-bromotoluene with phenylboronic acid, catalyzed by palladacycle **2c**, was selected as a model reaction. As shown in Table 1, K_2CO_3 were found to be the most effective base although KOH, NaOH can be also used, giving slightly lower yields. Among the tested aqueous-organic solvents, CH_3OH/H_2O system afforded the highest yield (Table 1, entry 1). When the loading of H_2O was increased (Table 1, entry 13), the system also gave the desired products in high yield.

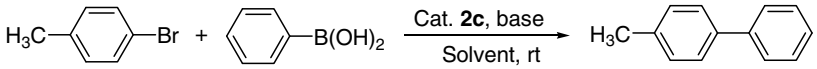
With the appropriate solvent ($CH_3OH/H_2O = 1:1$) and base (K_2CO_3) in hand, the relative activities of several palladacycles (Table 2) for the same model reaction were studied. When the reaction was carried out at room temperature, dimeric complexes exhibited higher activity than monomeric complexes.

A variety of electronically and structurally diverse aryl bromides could be coupled efficiently with phenylboronic



Scheme 1.

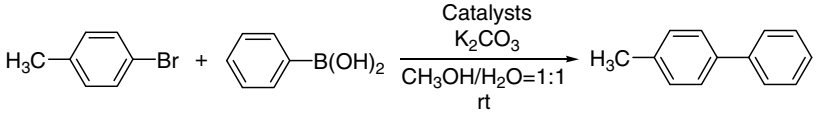
Table 1
Investigation of the Suzuki–Miyaura reaction conditions[a]



Entry	Base	Solvent	Yield[b] (%)
1	K_2CO_3	CH_3OH/H_2O	94
2	NaOH	CH_3OH/H_2O	87
3	$KF \cdot 2H_2O$	CH_3OH/H_2O	Trace
4	$K_3PO_4 \cdot 7H_2O$	CH_3OH/H_2O	77
5	Na_2CO_3	CH_3OH/H_2O	26
6	KOH	CH_3OH/H_2O	83
7	K_2CO_3	DMF/H_2O	37
8	K_2CO_3	THF/H_2O	8
9	K_2CO_3	1,4-Dioxane/H_2O	87
10	K_2CO_3	CH_3CN/H_2O	Trace
11[c]	K_2CO_3	Toluene/ethanol/H_2O	43
12[d]	K_2CO_3	CH_3OH	94
13[e]	K_2CO_3	CH_3OH/H_2O	98

[a] Reaction condition: 4-Bromotoluene 0.5 mmol, $PhB(OH)_2$ 0.6 mmol, base 1.0 mmol, *n*-Bu_4NBr 0.5 mmol, solvent 3 mL (v/v = 2:1), 0.5% mol of catalyst **2c**, at room temperature under air for 7 h.
[b] Isolated yields based on 4-bromotoluene in two runs.
[c] Toluene/ethanol/H_2O 3 mL (v/v/v = 1:1:1).
[d] CH_3OH 3 mL.
[e] CH_3OH/H_2O 3 mL (v/v = 1:1).

Table 2
Suzuki–Miyaura reaction: catalyst study[a]



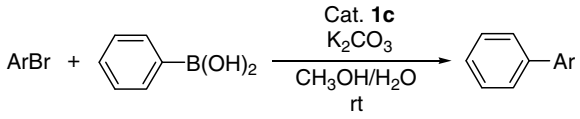
Entry	Catalyst	Yield[b] (%)
1	**1a**	99
2	**1b**	81
3	**1c**	99
4	**1d**	99
5	**2a**	38
6	**2b**	89
7	**2c**	98
8	**2d**	88

[a] Reaction condition: 4-bromotoluene 0.5 mmol, $PhB(OH)_2$ 0.6 mmol, K_2CO_3 1.0 mmol, *n*-Bu_4NBr 0.5 mmol, CH_3OH/H_2O 3 mL (v/v = 1:1), 0.5 mol% of catalyst, at room temperature under air for 7 h.
[b] Isolated yields based on 4-bromotoluene in two runs.

acid by using 0.1 mol% of complex **1c** under the optimized reaction conditions (K_2CO_3, $CH_3OH/H_2O = 1:1$, rt) (Table 3). However, using sterically hindered aryl bromides, such as 2-bromonitrobenzene, 2-bromo-*m*-xylene as substrates, the cross-coupled products were obtained in modest yields even by increasing catalyst loading and prolonging the reaction time (Table 3, entries 14, 16). Furthermore, 2-bromofluorene and 4-bromoaniline also only gave the cross-coupled products in modest yields (Table 3, entries 15, 17). When the reaction temperature was increased from room temperature to 60 °C, for 3-bromopyridine and 4-chloronitrobenzene, the coupling reactions proceeded well. When the catalyst loading of **1c** was lowered to 0.01 mol% for 4-bromotoluene reacted with phenylboronic acid, 70% isolated yield could be obtained (Table 3, entry 7). As for non-activated chlorobenzene, complex **1c** was nearly inactive under the similar reaction conditions. Moreover, the coupling reaction of 4-bromotoluene with phenylboronic acid carried out in the absence of *n*-Bu_4NBr is in a very low yield (Table 3, entry 8). This could be accredited with two reasons: one was that *n*-Bu_4NBr probably stabilized colloidal palladium nanoparticles that act as catalysts in the Suzuki coupling [19], the other was that the ammonium salts may accelerate the coupling reaction in virtue of activating the arylboronic acid to react by the formation of $[ArB(OH)_3]^-[R_4N]^+$ [11a].

We thought that it was interesting to study whether the high activity of palladacycles required long *N*-alkyl chains

Table 3
Suzuki coupling of aryl halides with phenylboronic acid[a]



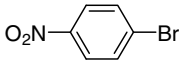
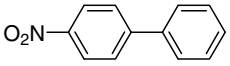
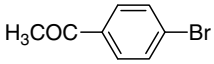
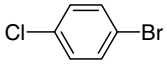
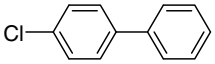
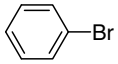
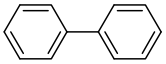
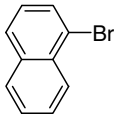
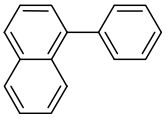
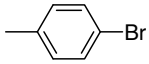
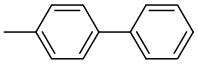
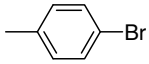
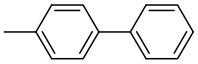
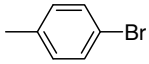
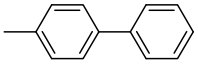
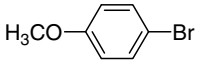
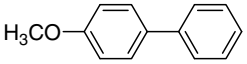
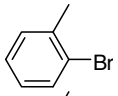
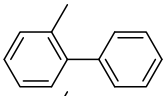
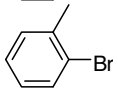
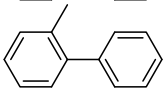
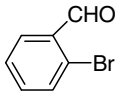
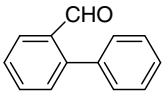
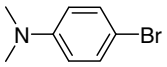
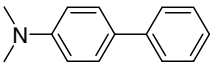
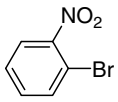
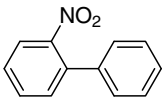
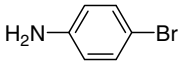
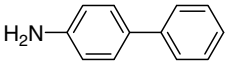
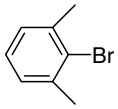
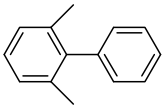
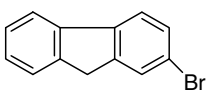
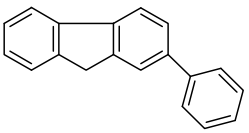
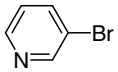
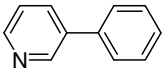
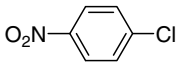
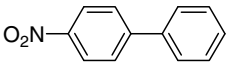
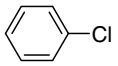
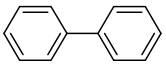
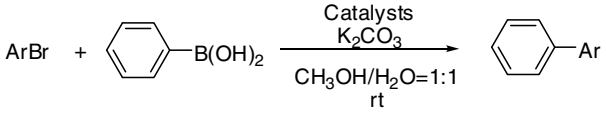
Entry	ArBr	mol%	*t* (h)	*T* (°C)	Product	Product no.	Yield[b] (%)
1		0.1	1.5	rt		**6a**	96
2		0.1	1.5	rt		**6b**	99
3		0.1	1.5	rt		**6c**	97
4		0.1	1.5	rt		**6d**	98
5		0.1	1.5	rt		**6e**	99
6		0.1	1.5	rt		**6f**	94
7		0.01	2	rt		**6f**	70
8[c]		0.1	1.5	rt		**6f**	37
9		0.1	2	rt		**6g**	97
10		0.1	2	rt		**6h**	50
11		0.1	5	rt		**6h**	99
12		0.1	5	rt		**6i**	99
13		0.1	18	rt		**6j**	99
14		0.1	18	rt		**6k**	68
15		0.1	18	rt		**6l**	56
16		0.5	12	rt		**6m**	51
17		0.5	18	rt		**6n**	49

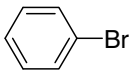
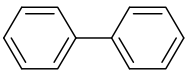
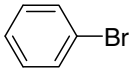
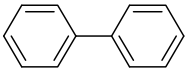
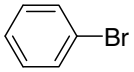
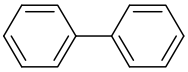
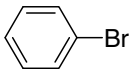
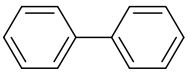
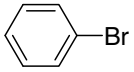
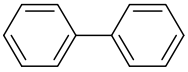
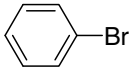
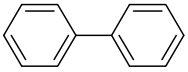
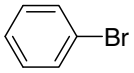
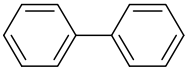
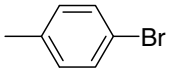
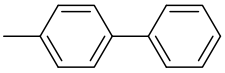
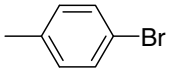
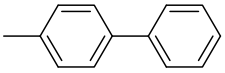
Table 3 (*continued*)

Entry	ArBr	mol%	*t* (h)	*T* (°C)	Product	Product no.	Yield[b] (%)
18		0.5	12	60		**6o**	89
19		1	12	60		**6a**	77
20		1	12	60		**6d**	Trace

[a] Reaction condition: aryl halides 0.5 mmol, $PhB(OH)_2$ 0.6 mmol, K_2CO_3 1.0 mmol, *n*-Bu_4NBr 0.5 mmol, CH_3OH/H_2O 3 mL (v/v = 1:1), 0.1 mol% of catalyst **1c**, at room temperature under air.
[b] Isolated yields based on aryl halids in two runs.
[c] *n*-Bu_4NBr was not added.

Table 4
Screening of catalysts with different *N*-alkyl chains and *N*-aryl groups for Suzuki–Miyaura cross-coupling reaction[a]



Entry	ArBr	Catalysts	*t* (h)	*T* (°C)	Product	Product no.	Yield[b] (%)
1		**1c**	2	rt		**6d**	91
2		**3a**	2	rt		**6d**	95
3		**3b**	2	rt		**6d**	Trace
4		**4a**	2	rt		**6d**	95
5		**4b**	2	rt		**6d**	Trace
6		**5a**	2	rt		**6d**	66
7		**5b**	2	rt		**6d**	Trace
8		**3a**	3	rt		**6f**	77
9		**5a**	3	rt		**6f**	25

[a] Reaction condition: Aryl bromides 0.5 mmol, $PhB(OH)_2$ 0.6 mmol, K_2CO_3 1.0 mmol, *n*-Bu_4NBr 0.5 mmol, CH_3OH/H_2O 3 mL (v/v = 1:1), 0.01 mol% of catalyst, at room temperature under air.
[b] Isolated yields based on aryl halides in two runs.

for the room-temperature Suzuki–Miyaura cross-coupling reactions in aqueous media. So we synthesized cyclopalladated ferrocenylimines **3a**, **3b** and undertook a broader investigation into Suzuki–Miyaura cross-coupling reactions. Initially, the relative catalytic activity of **1c** with *n*-$C_{12}H_{25}$ group at nitrogen, **3a** and **3b** with *n*-butyl group at nitrogen, **4a** and **4b** with *i*-propyl substituent at nitrogen, **5a** and **5b** with *N*-aryl substituent (Scheme 1) was examined by the coupling reaction of aryl bromides with phenylboronic acid in the presence of K_2CO_3 as base in aqueous media ($CH_3OH/H_2O = 1:1$). Dimers **3a**, **4a** were slightly more active than **1c** (Table 4, entries 1, 2, 4, 8), while complex **5a** was low active under the same reaction conditions (Table 4, entries 6, 9). The results revealed that *N*-alkyl-substituted cyclopalladated ferrocenylimines were higher activity than those with *N*-aryl groups for the room-temperature Suzuki–Miyaura cross-coupling reactions in aqueous media, and that the length of *N*-alkyl chains has no significant influence on the catalytic activity. The possible reason for the results was that alkyl substituents at nitro-

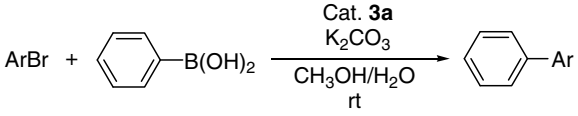
gen promoted oxidative addition of aryl halides to the Pd intermediate by making palladium more electron rich and increased the activity consequently [16], and electronic effects of *N*-alkyl chains with different length to palladium could be nearly the same. Moreover, monomers **3b**, **4b**, **5b** were almost inactive under similar reaction conditions (Table 4, entries 3, 5, 7), also suggesting that monomeric complexes containing phosphines are sensitive to moisture [20].

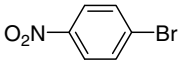
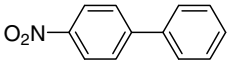
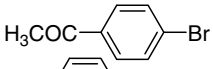
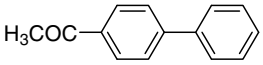
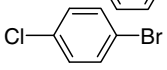
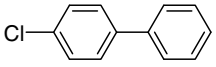
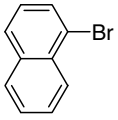
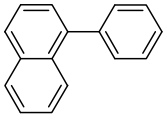
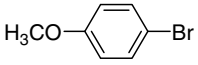
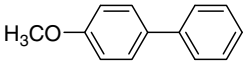
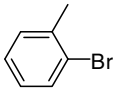
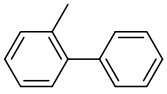
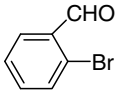
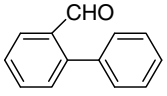
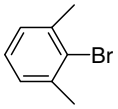
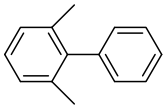
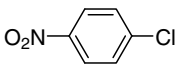
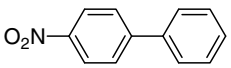
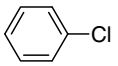
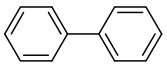
With the optimized reaction conditions above, the couplings of a number of other aryl bromides were conducted in the presence of 0.01 mol% complex **3a** (Table 5, entries 1–8). The reactions of electro-deficient aryl bromides and bromobenzene, 1-bromonaphthalene proceeded smoothly to give the coupling products with excellent yield after 2 h (Table 5, entries 1–4). Aryl bromides with electro-rich groups or containing *ortho*-substituents also provided the products in good to excellent yields by prolonging the reaction time (entries 5–7). However, 2-bromo-*m*-xylene only gave the cross-coupled product in 63% yield even by increasing catalyst loading to 0.1 mol% and prolonging the reaction time for 12 h (entry 8). For 4-chloronitrobenzene, the yield was improved to 83% in the presence of 1 mol% **3a** at 60 °C (entry 9), but chlorobenzene was found to be a poor coupling partner in the same reaction conditions, giving only 19% yield (entry 10).

3. Conclusion

In summary, a series of cyclopalladated ferrocenylimines with *N*-alkyl substituents were efficient catalysts for room-temperature Suzuki–Miyaura cross-coupling reaction of aryl halides with phenylboronic acid in CH_3OH/H_2O system under aerobic conditions. Results from these

Table 5
Suzuki coupling of aryl halides with phenylboronic acid[a]



Entry	ArBr	mol%	*t* (h)	*T* (°C)	Product	Product no.	Yield[b] (%)
1		0.01	2	rt		**6a**	96
2		0.01	2	rt		**6b**	99
3		0.01	2	rt		**6c**	90
4		0.01	2	rt		**6e**	99
5		0.01	3	rt		**6g**	91
6		0.01	6	rt		**6h**	76
7		0.01	6	rt		**6i**	99
8		0.1	12	rt		**6m**	63
9		1	12	60		**6a**	83
10		1	24	60		**6d**	19

[a] Reaction condition: aryl halides 0.5 mmol, $PhB(OH)_2$ 0.6 mmol, K_2CO_3 1.0 mmol, *n*-Bu_4NBr 0.5 mmol, CH_3OH/H_2O 3 mL (v/v = 1:1), 0.01 mol% of catalyst **3a**, at room temperature under air.
[b] Isolated yields based on aryl halides in two runs.

studies indicated that for *N*-alkyl substituted cyclopalladated ferrocenylimines as catalysts for room-temperature Suzuki–Miyaura cross-coupling reaction in CH_3OH/H_2O media, the long *N*-alkyl groups is not the necessary condition for the catalytic activity.

4. Experimental

4.1. General

All solvents were obtained from commercial sources and used without purification. The cyclopalladated ferrocenylimines **1a–d** and **2a–d** [16], **4a** and **4b** [21], **5a** and **5b** [17] were prepared according to the published procedures. All other chemicals were used as purchased. Melting points were measured using a WC-1 microscopic apparatus and were uncorrected. Infrared spectra were recorded on a Bruker VECTOR22 spectrophotometer in KBr pellets. ^1H, ^{13}C and ^{31}P $\{^1H\}$ NMR spectra were recorded on a Bruker DPX-400 spectrometer in $CDCl_3$ with TMS as an internal standard for ^1H NMR, ^{13}C NMR and 85% H_3PO_4 as external standard for ^{31}P {1H} NMR. Elemental analyses were determined with Elementar Analysensystem GmbH (varioEL III). Mass spectra were measured on a LC-MSD-Trap-XCT instrument. All the Suzuki reactions were accomplished without the protection of inert gas.

4.2. Preparation of complexes *3a, 3b*

A mixture of acetylferrocene (1.5 mmol) and *n*-butylamine (50 mL) was refluxed on an oil bath under nitrogen atmosphere in the presence of active Al_2O_3 at 75 °C for 1–2 days. In order to control the progress of the condensation reaction, the infrared spectra of the solution was recorded. When the infrared spectra of the samples did not exhibit the absorption band due to the asymmetrical stretching of the C=O group of the acetylferrocene [υ(C=O) 1661 cm^{-1}], the reaction mixture was carefully filtered and the filtrate was reduced to dryness. The oil obtained was used without further purification. A solution of lithium tetrachloropalladated (II) in 10 mL of methanol (Li_2PdCl_4, 1 mmol) and mole equivalents of NaOAc were added to the oil, and the resulting red solution was stirred for about 24 h. The solution was carefully filtered, and then the deep red solid obtained was purified via column chromatography (CH_2Cl_2 as eluent) to yield cyclopalladated dimer **3a**. Yield 61%, red solid, m.p. >220 °C; IR (KBr): 2956, 2862, 1105, 1001, 1581, 813 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 4.74–4.72 (1H, m, C_5H_3), 4.34–4.23 (7H, m, C_5H_5, C_5H_3), 3.45–3.36 (2H, m, CH_2), 2.13 (3H, s, CH_3–C=N), 1.82–1.63 (2H, m, CH_2), 1.45–1.41 (2H, m, CH_2), 0.99 (3H, t, $J = 7.0$ Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 180.6, 100.2, 91.3, 73.4, 73.3, 70.8, 70.7, 66.2, 65.6, 52.9, 52.0, 31.8, 20.4, 20.3, 14.2, 14.0; Anal. Calc. for $C_{32}H_{40}Cl_2Fe_2N_2Pd_2$: C, 45.32; H, 4.75; N, 3.30. Found: C, 45.69; H, 4.78; N, 3.39%.

The solution of the complex **3a** (0.1 mmol) and PPh_3 (0.3 mmol) in 10 mL of CH_2Cl_2 was stirred at room temperature for 1 h. The solution was concentrated in vacuo and was purified via column chromatography (CH_2Cl_2 as eluent). The red oil was recrystallized from CH_2Cl_2–petroleum ether to yield cyclopalladated monomer **3b**. Yield 92%, red solid, m.p. 209–211 °C; IR (KBr): 2954, 2867, 1097, 999, 1589, 816, 745, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.79–7.74 (6H, m, PPh_3), 7.43–7.37 (9H, m, PPh_3), 4.32 (1H, d, $J = 2.1$ Hz, C_5H_3), 4.06–3.98 (2H, m, C_5H_3, CH_2), 3.81 (5H, s, C_5H_5), 3.65–3.58 (1H, m, CH_2), 3.26 (1H, s, C_5H_3), 2.20 (3H, s, CH_3–C=N), 1.88–1.84 (1H, m, CH_2), 1.56–1.43 (3H, m, CH_2–CH_2), 0.98 (3H, t, $J = 7.2$ Hz, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 179.4, 135.0, 132.4, 131.9, 130.3, 128.0, 101.3, 92.0, 76.2, 70.3, 67.8, 66.2, 51.0, 32.2, 30.9, 20.4, 14.5, 14.1; ^{31}P {1H} NMR (162 MHz, $CDCl_3$): δ 37.79; Anal. Calc. for $C_{34}H_{35}ClFeNPPd$: C, 59.50; H, 5.14; N, 2.04. Found: C, 59.32; H, 5.13; N, 2.12%; MS: 650.2 $[M-Cl]^+$.

4.3. General procedure for the Suzuki–Miyaura cross-coupling reaction of aryl halide with phenylboronic acid

General procedure A: A mixture of aryl halides (0.5 mmol), phenylboronic acid (0.6 mmol), K_2CO_3 (1 mmol), TBAB (0.5 mmol), catalyst **1c** (0.1%), and CH_3OH/H_2O (1.5 mL/1.5 mL) was stirred at room temperature under air. The reaction mixture was stirred for 1.5 h, and then quenched with water. The mixture was diluted with CH_2Cl_2. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 for three times. The combined organic phase was dried with $MgSO_4$, filtrate, solvent was removed on a rotary evaporator, and the product was isolated by thin layer chromatography. The purified products were identified by ^1H NMR, ^{13}C NMR spectroscopy and melting points with the literature data.

General procedure B: Catalyst **3a** of 100 μl was introduced to a small round-bottom flask as a $CHCl_3$ solution (0.0005 mmol/mL). After $CHCl_3$ evaporated, aryl halides (0.5 mmol), phenylboronic acid (0.6 mmol), K_2CO_3 (1 mmol), TBAB (0.5 mmol), and CH_3OH/H_2O (1.5 mL/1.5 mL) were added into the small round-bottom flask. The reaction mixture was stirred at room temperature under air for 2 h and then quenched with water. The mixture was diluted with CH_2Cl_2. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 for three times. The combined organic phase was dried with $MgSO_4$, filtrate, solvent was removed on a rotary evaporator, and the product was isolated by thin layer chromatography. The purified products were identified by ^1H NMR, ^{13}C NMR spectroscopy and melting points with the literature data.

4.3.1. Compound *6a* [23]

Light yellow solid; m.p. 111–113 °C (lit. 111–112 °C). ^1H NMR (400 MHz, $CDCl_3$): δ 8.30 (2H, d, $J = 8.8$ Hz), 7.74

(2H, d, $J = 8.8$ Hz), 7.63 (2H, d, $J = 7.0$ Hz), 7.52–7.45 (3H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.6, 147.1, 138.8, 129.2, 128.9, 127.8, 127.4, 124.1.

4.3.2. Compound **6b** [24]

White solid; m.p. 117–118 °C (lit. 116–118 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (2H, d, $J = 8.3$ Hz), 7.69–7.62 (4H, m), 7.49–7.40 (3H, m), 2.64 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.8, 145.8, 139.8, 135.8, 128.9, 128.89, 128.21, 127.25, 127.20, 26.7.

4.3.3. Compound **6c** [27]

White solid; m.p. 74–76 °C (lit. 74–76 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56–7.49 (4H, m), 7.45–7.38 (4H, m), 7.37–7.33 (1H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.0, 139.7, 133.4, 128.9, 128.89, 128.4, 127.6, 127.0.

4.3.4. Compound **6d** [22]

White solid; m.p. 69–70 °C (lit. 68–71 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60–7.58 (4H, m), 7.45–7.42 (4H, m), 7.36–7.32 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.3, 128.8, 127.3, 127.2.

4.3.5. Compound **6e** [25]

Light yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90–7.80 (3H, m), 7.50–7.36 (9H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.7, 140.2, 133.8, 131.6, 130.0, 128.2, 127.6, 127.2, 126.9, 126.0, 125.7, 125.3.

4.3.6. Compound **6f** [23]

White solid; m.p. 43–44 °C (lit. 43–44 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58–7.56 (2H, m), 7.49 (2H, d, $J = 8.1$ Hz), 7.42 (2H, t, $J = 7.5$ Hz), 7.33–7.30 (1H, m), 7.24 (2H, d, $J = 7.9$ Hz), 2.39 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.1, 138.3, 137.0, 129.4, 128.7, 126.9, 21.1.

4.3.7. Compound **6g** [27]

White solid; m.p. 86–87 °C (lit. 85–87 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56–7.52 (4H, m), 7.41 (2H, t, $J = 7.7$ Hz), 7.30–7.25 (1H, m), 6.98 (2H, d, $J = 8.8$ Hz), 3.85 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.1, 140.8, 133.8, 128.7, 128.2, 126.7, 126.65, 114.2, 55.3.

4.3.8. Compound **6h** [26]

Light yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41–7.39 (2H, m), 7.35–7.31 (3H, m), 7.26–7.23 (4H, m), 2.27 (3H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.0, 135.4, 130.3, 129.8, 129.2, 128.1, 127.3, 126.8, 125.8, 20.5.

4.3.9. Compound **6i** [28]

Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.98 (1H, s), 8.02 (1H, d, $J = 9.1$ Hz), 7.62–7.60 (1H, m), 7.48–7.35 (7H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.5, 146.0, 137.8, 133.7, 133.6, 130.8, 130.1, 128.5, 128.1, 127.8, 127.6.

4.3.10. Compound **6j** [24]

White solid; m.p. 117–119 °C (lit. 118–120 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57–7.49 (4H, m), 7.41–7.37 (2H, m), 7.27–7.23 (1H, m), 6.83 (2H, d, $J = 8.4$ Hz), 2.99 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.9, 141.2, 129.2, 128.6, 127.7, 126.3, 126.0, 113.0, 40.7.

4.3.11. Compound **6k** [28]

Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (1H, d, $J = 8.1$ Hz), 7.62 –7.58 (1H, m), 7.49–7.39 (5H, m), 7.33–7.30 (2H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.3, 137.4, 136.3, 132.3, 132.0, 128.7, 128.2, 128.18, 127.9, 124.1.

4.3.12. Compound **6l** [29]

Yellow solid; m.p. 51–52 °C (lit. 51 °C). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (2H, d, $J = 8.1$ Hz), 7.42–7.37 (4H, m), 7.26 (1H, t, $J = 8.8$ Hz), 6.74 (2H, d, $J = 8.6$ Hz), 3.70 (2H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.9, 141.2, 131.6, 128.7, 128.0, 126.4, 126.3, 115.4.

4.3.13. Compound **6m** [30]

Light-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–7.40 (2H, m), 7.35–7.31 (1H, m), 7.18–7.09 (5H, m), 2.03 (6H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.9, 141.1, 136.1, 129.0, 128.4, 127.3, 127.0, 126.6, 20.9.

4.3.14. Compound **6n** [31]

White solid; m.p. >190 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (1H, d, $J = 7.9$ Hz), 7.81 (1H, d, $J = 7.5$ Hz), 7.77 (1H, s), 7.67–7.61 (3H, m), 7.56 (1H, d, $J = 7.5$ Hz), 7.46 (2H, t, $J = 7.6$ Hz), 7.41–7.29 (3H, m), 3.96 (2H, s). ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.9, 143.5, 141.5, 141.4, 140.9, 139.9, 128.8, 127.2, 127.1, 126.8, 126.7, 126.0, 125.1, 123.8, 120.1, 120.0, 37.0.

4.3.15. Compound **6o** [30]

Light-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.85 (1H, s), 8.58 (1H, d, $J = 4.1$ Hz), 7.87 (1H, d, $J = 7.9$ Hz), 7.57 (2H, d, $J = 7.3$ Hz), 7.49–7.33 (4H, m). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.4, 148.2, 137.8, 136.7, 134.4, 129.1, 128.1, 127.1, 123.6.

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