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Cyclopalladated Ferrocenylimine as Efficient Catalyst for the Syntheses of Arylboronate Esters

Lianhui Wang,[a,b] Jingya Li,[b] Xiuling Cui,[a,*] Yusheng Wu,[b] Zhiwu Zhu,[a] and Yangjie Wu[a,*]

[a] Department of Chemistry, Henan Key Laboratory of Chemical Biology and Organic Chemistry, Key Laboratory of Applied Chemistry of Henan Universities, Zhengzhou University, Zhengzhou 450052, People's Republic of China
Fax: (+86)-371-6776-7753 (X.C.), (+86)-371-6776-6667 (Y.W.); e-mail: cuixl@zzu.edu.cn or wyj@zzu.edu.cn
[b] Tetranov Biopharm, Inc.,Zhengzhou 450052, People's Republic of China

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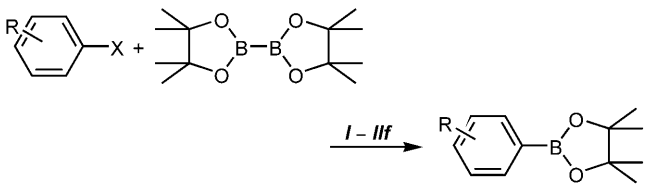
Abstract: The cyclopalladated ferrocenylimine ***I*** and its phosphine adducts ***IIa–f*** were prepared and evaluated in the borylation of aryl halides. The tricyclohexylphosphine adduct ***IIb*** exhibited highly catalytic activity for the coupling of aryl and heteroaryl bromides containing various functional groups with low catalyst loading (2 mol%). Aryl and heteroaryl chlorides were smoothly converted into the corresponding boronates in the presence of the monophosphinobiaryl ligand (XPhos) adduct ***IIf***. It was proposed that palladacycle was only a reservoir of the catalytically active species from the investigation on the reaction mechanism.

Keywords: aryl halides; boronates; borylation; cyclopalladated ferrocenylimines; mechanistic probe

Introduction

Arylboronic acids and their esters are versatile intermediates in organic synthesis to construct carbon-carbon, carbon-nitrogen and carbon-oxygen bonds due to their unique reactivity and air stability.[1] In addition, attention has recently also been paid to their applications in molecular recognition and pharmaceutical candidates owing to their high stability and low toxicity.[2] Their increasing importance has been justified in the development of new, mild and efficient methods to provide access to a large pool. Of particular interest is the synthesis of arylboronic acids and their esters substituted with a wide range of functional groups. The palladium-catalyzed cross-coupling reactions of bis(pinacolato)diboron or pinacolborane with organic electrophiles have emerged as a general and powerful tool.[3,4] This protocol offers a direct and efficient route to variously functionalized boronic esters. However, the aryl iodides or bromides are necessary to be used as the substrates. So far there are few reports for the efficient borylation of heteroaryl halides and less expensive aryl chlorides.[4c–e]

Palladacycles are one class of the most popular organopalladium reagents and efficient catalysts for constructing carbon-carbon and carbon-heteroatom bonds.[5] Moreover, they are easily synthesized, facilely modified and of comparative stability. Since Beller and Herrmann reported the application of palladacycles derived from $(o\text{-tol})_3P$ and $Pd(OAc)_2$ into the Heck reaction and Suzuki–Miyaura reaction,[6] there has been a growing interest in the utility of palladacycles as catalyst precursors.[5] In our previous work, we have focused on the cyclopalladated ferrocenylimines as efficient catalysts for organic reactions, such as Heck reaction, Suzuki reaction, amination reaction and so on.[7] Herein, we would like to disclose our work on cyclopalladated ferrocenylimine as a catalyst precursor for the borylation of aryl halides with bis-(pinacolato)diboron (Scheme 1). Yields of 46–99% were obtained for aryl bromides containing various substituents in the presence of 2 mol% complex ***IIb***. Meanwhile, this process is also suitable for cheaper, however, less reactive aryl chlorides in the presence of 5 mol% complex ***IIf***. The related reaction mechanism was investigated.



X = Cl, Br;
R = CN, NO_2, NH_2, OMe, CF_3, Me, COMe, COOMe, etc.

Scheme 1. Palladacycles-catalyzed borylation.

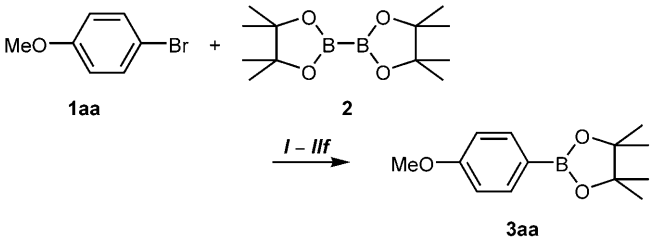
Results and Discussion

Catalytic Activity of Complexes *I*, *IIa–f* in the Borylation of Aryl Halides

To evaluate the activity of the cyclopalladated ferrocenylimine ***I*** and its adducts ***IIa–f*** (Scheme 2), the borylation of 1-bromo-4-methoxybenzene **1aa** with bis(pinacolato)diboron **2** was chosen as a model reaction in dioxane at 80 °C in the presence of 2 mol% catalyst and KOAc as base. As shown in Table 1, cyclopalladated ferrocenylimine dimer ***I*** only provided a trace amount of the desired product (Table 1, entry 1). When 2 mol% PCy_3 was added, the yield was improved to 81% (Table 1, entry 2). To explore the influence of the phosphine ligand on this reaction, various phosphine adducts of cyclopalladated ferrocenylimine ***IIa–f*** were prepared from dimer ***I*** (Scheme 2). To our delight, a 79% yield was obtained in the presence of 0.5 mol% ***IIb***. The yield was not improved significantly when more than 0.5 mol% PCy_3 was added (Table 1, entry 3 *vs.* entry 4). Complexes ***IIa***, ***IIc***, ***IId*** and ***IIe*** gave moderate yields (Table 1, entries 5, 7–9), while complexes ***IIb*** and ***IIf*** gave 93% yields (Table 1, entries 6, 10). Moreover, the homocoupling and dehalogen by-products were not observed by GC-MS in the presence of complexes ***IIb*** and ***IIf***. These results indicated that the phosphine ligand had a great influence on the borylation and highly hindered-phosphines promoted such reactions dramatically.[4e]

Complex ***IIb*** was chosen as catalyst for the following study as PCy_3 is cheap and its adduct is stable at high temperatures. The yield was not improved significantly when the catalyst loading was increased from 2 mol% to 5 mol% (Table 1, entry 6 *vs.* 12). On the other hand, the yield decreased when the loading of catalyst ***IIb*** was reduced to 0.5 mol% from 2 mol% (Table 1, entry 6 *vs.* entries 3 and 11).

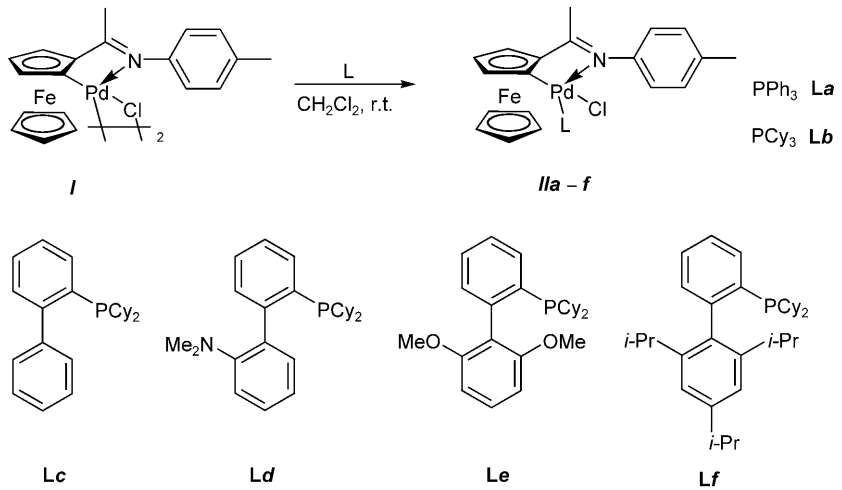
Table 1. Screening of catalysts for borylation of 1-bromo-4-methoxybenzene (**1aa**).[a]



Entry	Catalyst	Catalyst (mol%)	Yield (**3aa**) [%][b]
1	***I***	1	trace
2[c]	***I***	1	81
3	***IIb***	0.5	79
4[d]	***IIb***	0.5	82
5	***IIa***	2	50
6	***IIb***	2	93
7	***IIc***	2	73
8	***IId***	2	68
9	***IIe***	2	60
10	***IIf***	2	93
11	***IIb***	1	90
12	***IIb***	5	92

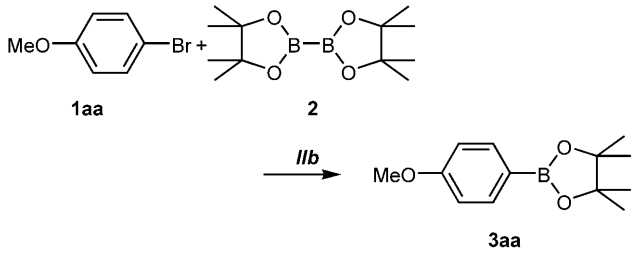
[a] *Reaction conditions:* 0.5 mmol **1aa**, 1.2 equiv. bis(pinacolato)diboron, 2 equiv. KOAc, dioxane 2 mL, 3 h, 80 °C.
[b] Isolated yields based on **1aa**.
[c] 2 mol% PCy_3 were added.
[d] 0.5 mol% PCy_3 was added.

The various reaction conditions were examined by fixing a 2 mol% loading of catalyst ***IIb***. It was found that the base played a critical role on the catalytic efficiency (Table 2). Stronger bases, such as $K_3PO_4 \cdot 7H_2O$ and Cs_2CO_3 afforded the desired product in 61% and 27% yields, respectively (Table 2, en-



Scheme 2. Synthesis of catalysts.

Table 2. Screening of bases and solvents for borylation of 1-bromo-4-methoxybenzene (**1aa**).[a]



Entry	Base	Solvent	*t* [h]	Yield (**3aa**) [%][b]
1	Na_2CO_3	dioxane	3	trace
2	K_2CO_3	dioxane	3	26
3	$K_3PO4{\cdot}7\,H_2O$	dioxane	3	61
4	Cs_2CO_3	dioxane	3	37
5	NaOAc	dioxane	3	trace
6	Et_3N	dioxane	3	0
7	KOAc	dioxane	3	93
8	KOAc	DMSO	3	22
9	KOAc	THF	3	89
10	KOAc	DMF	3	57
11	KOAc	Toluene	3	77
12	KOAc	Dioxane	1	79
13	KOAc	Dioxane	6	93
14	KOAc	Dioxane	3	92[c]

[a] *Reaction conditions:* 0.5 mmol **1aa**, 1.2 equiv. bis(pinacolato)diboron, cat. ***IIb*** 2 mol%, 2 equiv. base, solvent 2 mL, 3 h, 80 °C.
[b] Isolated yield based on **1aa**.
[c] 110 °C.

tries 3 and 4), and the homo-coupling compound was the main sub-product since stronger bases were speculated to promote the Suzuki reaction of aryl boronate **3aa** with **1aa**. No product was observed when triethylamine (TEA) was used as a base (Table 2, entry 6). NaOAc and Na_2CO_3 only gave a trace of **3aa** (Table 2, entries 1 and 5), while an excellent yield was obtained when KOAc was used as the base (Table 2, entry 7).

The desired product was obtained in 93% when dioxane was used as solvent (Table 2, entry 7). Polar solvents, that is, DMSO and DMF, did not favor this reaction (Table 2, entries 8 and 10). Moreover, the yield was not improved evidently by prolonging the reaction time from 3 h to 6 h (Table 2, entry 7 *vs.* 13) and increasing temperature from 80 °C to 110 °C (Table 2, entry 13 *vs.* 14).

Under the optimized reaction conditions (1 equiv. of aryl halide, 1.2 equiv. of bis(pinacolato)diboron, 2 equiv. of KOAc, 2 mol% complex ***IIb***, dioxane as solvent, 80 °C), the scope of the substrates for this reaction was investigated. As shown in Table 3, the catalyst ***IIb*** exhibited high catalytic activity in the borylation of a range of aryl and heteroaryl bromides and afforded arylboronate esters **3a** in up to 99% yields. Moreover, a wide variety of functional groups including nitro, cyano, ester, acetyl, and dimethylamino groups were tolerated under the reaction conditions. Aryl bromides with both electron-donating and electron-withdrawing substituents were compatible with this reaction system, providing the corresponding coupling products in good to excellent yields (72–99%, Table 3, entries 1–10). Direct borylation of **1al** also afforded naphthylboronate in moderate yield (Table 3, entry 11). Heteroaryl bromides were also applied to the borylation with **2** successfully. For benzyl bromide, 5-bromo-*N,N*-dimethyl-2-pyridinamine and 4-bromo-2-methoxypyridine, good to excellent yields were obtained (Table 3, entries 12, 15 and 16). 3-Bromothiophene and 2-bromothiophene were also smoothly transformed to the desired products. However, the yields are lower than other cases (Table 3, entries 13 and 14).

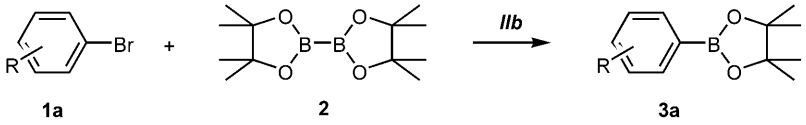
An aryl chloride is one kind of interesting substrate due to its being cheaper and commercially available. However, to the best of our knowledge, there are only two reports of the successful combination of aryl chlorides with bis(pinacolato)diboron.[4c,e] Thus, we turned our attention to the aryl chlorides **1b** for the palladium-catalyzed borylation with bis(pinacolato)diboron **2** (shown in Table 4). Catalyst ***IIf*** was chosen as catalyst since it exhibited more efficiency than catalyst ***IIb*** (Table 4, entry 1 *vs.* entry 2). Under optimized reaction conditions (1 equiv. of aryl chlorides, 1.5 equiv. of bis(pinacolato)diboron, 5 mol% catalyst ***IIf***, 3 equiv. of KOAc, in dioxane at 110 °C), aryl chlorides with both electron-donating and electron-withdrawing substituents at *para*- and *meta*-positions were successfully converted into the corresponding boronate esters in 83–93% yields (Table 4, entries 2–5 and 8). This catalytic system was also applied for heteroaryl chlorides. The borylation of 4-chloro-2-pyridinecarbonitrile **1bh** and 4-chloro-2-methoxypyridine **1bi** resulted in good conversion (Table 4, entries 9 and 10) even with 2 mol% catalyst loading. However, *ortho*-substituted aryl chlorides are still challenging substrates. 1-Chloro-2-nitrobenzene **1be** and 2-chlorobenzenamine **1bf** only gave 39% and 58% yield, respectively.

Mechanistic Probes

For exploring the mechanism of the borylation reaction promoted by cyclopalladated ferrocenylimine, we performed the following experiments.[8]

The parallel experiments were performed using **1aa** (1.0 mmol), **2** (1.2 mmol), KOAc (2.0 mmol), and complex ***IIa*** or ***IIb*** (0.005 mmol) in 1, 4-dioxane (4 mL). Figure 1 revealed that complex ***IIb*** showed higher activity than complex ***IIa*** and both complexes ***IIa*** and ***IIb*** exhibited an induction period (20 min).

Table 3. Palladium-catalyzed borylation of aryl bromides **1a** with **2**.[a]



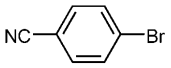
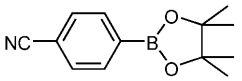
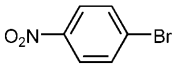
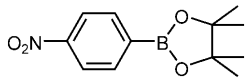
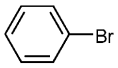
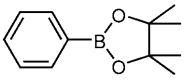
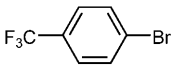
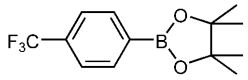
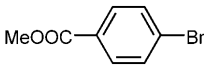
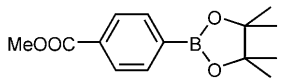
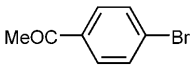
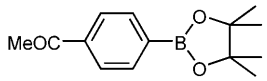
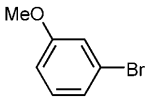
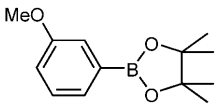
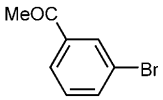
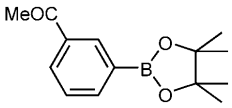
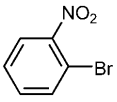
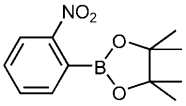
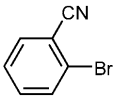
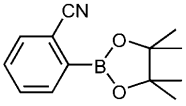
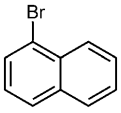
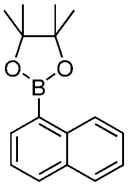
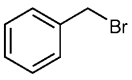
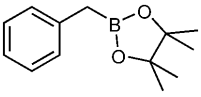
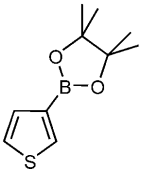
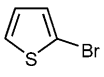
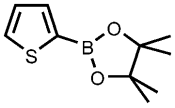
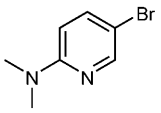
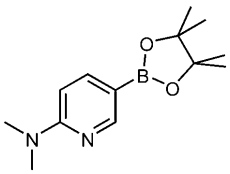
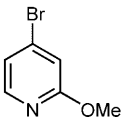
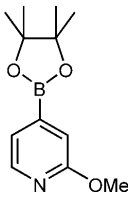
Entry		1		3	Yield of **3** [%][b]
1	(**1ab**)		(**3ab**)		98
2	(**1ac**)		(**3ac**)		86
3	(**1ad**)		(**3ad**)		93
4	(**1ae**)		(**3ae**)		76
5	(**1af**)		(**3af**)		85
6	(**1ag**)		(**3ag**)		>99
7	(**1ah**)		(**3ah**)		90
8	(**1ai**)		(**3ai**)		94
9	(**1aj**)		(**3aj**)		72
10	(**1ak**)		(**3ak**)		78
11	(**1al**)		(**3al**)		66
12	(**1am**)		(**3am**)		85
13	(**1an**)		(**3an**)		54
14	(**1ao**)		(**3ao**)		46

Table 3. (Continued)

Entry	1		3		Yield of **3** [%][b]
15	(**1ap**)		(**3ap**)		74
16	(**1aq**)		(**3aq**)		91

[a] *Reaction conditions:* 0.5 mmol aryl bromides **1a**, 1.2 equiv. bis(pinacolato)diboron, 2 mol% Cat. ***IIb***, 2 equiv. KOAc, dioxane 2 mL, 3 h, 80 °C.
[b] Isolated yields based on **1a**.

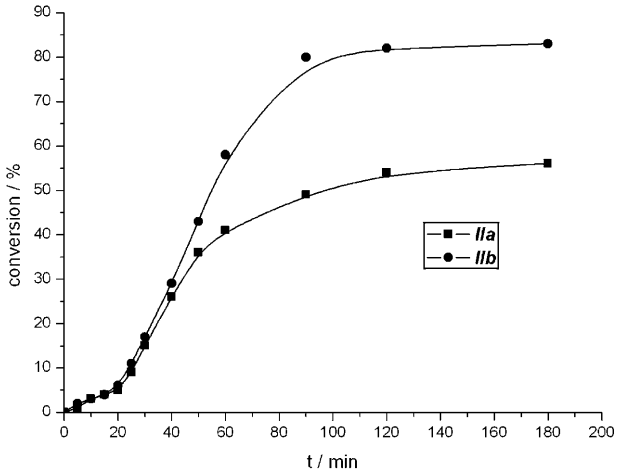


Figure 1. Conversion *vs* reaction time in the borylation of 1-bromo-4-methoxybenzene **1aa** with bis(pinacolato)diboron **2** using ***IIa*** or ***IIb*** as catalyst. *Reaction conditions:* 1.0 mmol **1aa**, 1.2 mmol bis(pinacolato)diboron, 0.5% mmol complex ***IIa*** or ***IIb***, 2 mmol KOAc, dioxane 4 mL, 80 °C. The reactions were monitored by GC.

The results indicated that complexes ***II*** were catalyst precursors rather than real catalysts. The phosphine ligand may promote the release of the 'real catalyst' species from palladacycle, and stabilize the active species under the reaction conditions to suppress the formation of Pd black.

Conclusions

In conclusion, a series of cyclopalladated ferrocenylimine complexes ***I***, ***IIa–f*** were prepared. Complexes ***IIb*** and ***IIf*** exhibited high catalytic activity for preparation of arylboronic esters from aryl bromides, aryl chlorides and heteroaryl halides and tolerated various functional groups. A wide range of aryl and heteroaryl boronates were efficiently obtained under mild reaction conditions. The kinetic studies suggested that the adduct of cyclopalladated ferrocenylimine was a precatalyst and the catalytically active species are formed *in situ* from palladacycle ***II***. The investigations of their application for borylation/Suzuki–Miyaura coupling reactions are currently underway in our laboratory.

Experimental Section

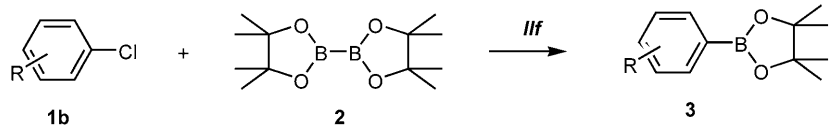
General

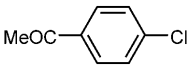
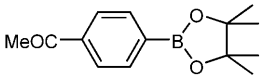
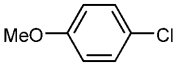
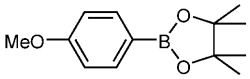
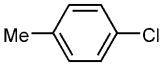
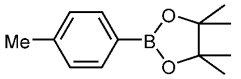
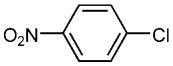
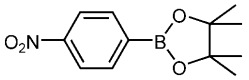
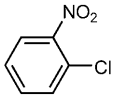
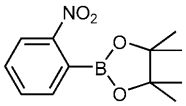
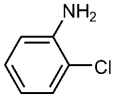
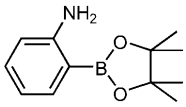
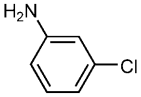
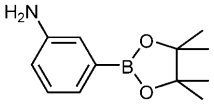
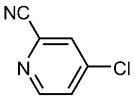
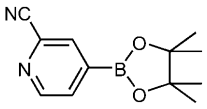
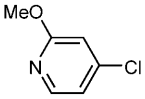
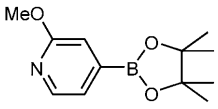
^{1}H NMR and ^{13}C NMR were recorded on a Bruker DPX 400 instrument using $CDCl_3$ as the solvent and tetramethylsilane (TMS) as the internal standard. $^{31}P\{^{1}H\}$ NMR were recorded on a Bruker Avance 300 instrument using $CDCl_3$ as the solvent and 85% H_3PO_4 as the external standard. All coupling constants (*J* values) are reported in hertz (Hz). Melting points were measured on an XT4 A microscopic apparatus and uncorrected. High resolution mass spectra were recorded on a Waters Q-Tof micro™ spectrometer using the electrospray ionization (ESI) technique. GC analyses were performed on an Agilent 4890D gas chromatograph. Preparative TLC was performed on silica gel plates developed with acetic ether/petroleum ether. All solvents were dried according to the standard methods. The aryl halides **1** and bis(pinacolato)diboron **2** were obtained from commercial sources and were generally used without further purification. Cyclopalladated ferrocenylimine dimer ***I*** was synthesized according to the reported procedure.[9]

General Method for Preparation of the Phosphine Adducts of Cyclopalladated Ferrocenylimine *IIa–IIf* (Scheme 2)

A solution of palladacyclic dimer ***I*** (91.2 mg, 0.1 mmol) and ligand (L_a–L_f) (0.22 mmol) in CH_2Cl_2 (10 mL) was stirred at

Table 4. Palladium-catalyzed borylation of aryl chlorides **1b** with **2**.[a]



Entry	1		3		Yield of **3** [%][b]
1					46[c]
2	(**1ba**)		(**3ag**)		90
3	(**1bb**)		(**3aa**)		93
4	(**1bc**)		(**3ba**)		85
5	(**1bd**)		(**3ac**)		83
6	(**1be**)		(**3aj**)		39
7	(**1bf**)		(**3bb**)		58
8	(**1bg**)		(**3bc**)		91
9	(**1bh**)		(**3bd**)		75[d]
10	(**1bi**)		(**3aq**)		77[d]

[a] *Reaction conditions:* 0.5 mmol aryl halide, 1.5 equiv. bis(pinacolato)diboron, 5 mol% Cat., 3 equiv. KOAc, dioxane 2 mL, 3 h, 110 °C.
[b] Isolated yields based on **1b**.
[c] ***IIb*** as catalyst.
[d] 2 mol% Cat., 1.2 equiv. of bis(pinacolato)diboron, 6 h.

room temperature for 30 min. The solvent was moved and the product was purified on a silica gel column (CH_2Cl_2 as eluent). The first band was collected and afforded complexes ***IIa–IIf*** after removal of solvent. Complexes ***IIa–IIf*** were recrystallized from CH_2Cl_2-petroleum ether.

Characterization data for *IIa*:[9] Red solid, 83% yield, mp 233–235 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.78 (m, 6H, ArH), 7.38 (m, 9H, ArH), 7.16 (d, 2H, J = 7.9 Hz, ArH), 6.93 (d, 2H, J = 7.9 Hz, ArH), 4.46 (s, 1H, C_5H_3), 4.12 (s, 1H), 3.94 (s, 5H, C_5H_5), 3.38 (s, 1H, C_5H_3), 2.33 (s, 3H, CH_3), 2.09 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 182.4, 145.1, 134.8, 134.7, 134.5, 132.1, 131.6, 130.1, 128.7, 127.8, 123.2, 101.7, 90.4, 76.8, 70.4, 69.0, 66.9, 21.0, 16.9; ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 46.7; HR-MS (ESI): m/z = 684.0735, calcd. for $C_{37}H_{33}ClFeNPPd$ ([M−Cl]$^+$): 684.0735.

Characterization data for *IIb*:[10] Red solid, 76% yield, mp 197–200 °C. ^{1}H NMR ($CDCl_3$): δ = 7.15 (d, 1H, J = 8.0 Hz, ArH), 6.83 (d, 2H, J = 7.1 Hz, ArH), 4.52 (s, 1H, C_5H_3), 4.40 (s, 1H, C_5H_3), 4.38 (s, 1H, C_5H_3), 4.22 (s, 1H, C_5H_5), 2.53 (m, 3H), 2.32 (s, 3H, CH_3), 2.12 (m, 3H, PCy_2), 2.02 (s, 3H, CH_3), 1.85 (m, 3H), 1.75 (m, 16H), 1.25 (m, 10H); ^{13}C NMR ($CDCl_3$): δ = 181.5, 145.7, 134.2, 128.7, 123.2, 90.5, 70.5, 69.2, 67.4, 34.2, 34.0, 30.3, 29.8, 27.6, 27.6, 27.5, 27.5, 26.4, 21.0, 17.1; ^{31}P{^{1}H} NMR ($CDCl_3$): δ = 37.9; HRMS (ESI): m/z = 702.2144, calcd. for $C_{37}H_{51}ClFeNPPd$ ([M−Cl]$^+$): 702.2143.

Characterization data for *IIc*: Red solid, air stable, easily soluble in methylene chloride or chloroform, and poorly soluble in methanol or DMSO, 82% yield, mp 150–152 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (m, 1H, ArH), 7.39

(m, 7H, ArH), 7.19 (d, 2H, $J=7.8$ Hz, ArH), 7.15 (m, 1H, ArH), 6.88 (d, 2H, $J=8.0$ Hz, ArH), 4.41 (s, 1H, C_5H_3), 4.14 (s, 1H, C_5H_3), 4.11 (s, 5H, C_5H_5), 3.27 (s, 1H, C_5H_3), 2.35 (s, 3H), 2.03 (s, 3H, CH_3; 1H, PCy_2), 1.98–0.88 (21H, PCy_2); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=181.7$, 145.7, 145.4, 142.1, 134.3, 131.9, 131.8, 129.3, 128.9, 128.8, 127.5, 127.2, 127.0, 126.7, 125.3, 125.2, 123.2, 90.0, 70.4, 68.6, 66.6, 53.4, 27.0, 26.9, 26.8, 26.4, 25.9, 25.8, 21.0, 16.9; $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$): $\delta=59.1$; HR-MS (ESI): $m/z=772.1989$, calcd. for $C_{43}H_{49}ClFeNPPd$ ($[M-Cl]^+$): 772.1987.

Characterization data for *IId*: Red solid, air stable, easily soluble in methylene chloride or chloroform, and poorly soluble in methanol or DMSO, 71% yield, mp 157–159 °C. ^1H NMR (400 MHz, $CDCl_3$): $\delta=8.5$–7.9 (m, 1H, ArH, *trans*:*cis* = 0.7:0.3), 7.7–7.21 (4H, ArH), 7.18–7.14 (4H, ArH), 7.10–7.06 (1H, ArH), 6.91–6.87 (2H, ArH), 4.7–4.4 (s, 1H, C_5H_3), 4.37 (s, 1H, C_5H_3), 4.13 (s, 5H, C_5H_5), 4.07 (s, 1H, C_5H_3), 2.71 (m, 1H), 2.8–0.87 (34H); $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$): $\delta=66.8$, 65.2 (*trans*:*cis* = 2.4:1); HRMS (ESI): $m/z=815.2411$, calcd. for $C_{45}H_{54}ClFeN_2PPd$ ($[M-Cl]^+$): 815.2409.

Characterization data for *IIe*: Red solid, air stable, easily soluble in methylene chloride or chloroform, and poorly soluble in methanol or DMSO, 87% yield, mp 172–175 °C. ^1H NMR (400 MHz, $CDCl_3$): $\delta=8.6$–7.9 (m, 1H, ArH, *trans*:*cis* = 0.5: 0.5), 7.53 (m, 1H, ArH), 7.52–7.33 (m, 2H, ArH), 7.18 (d, 2H, $J=7.5$ Hz, ArH), 7.17–6.90 (1H, ArH), 6.99 (d, 2H, $J=7.7$, ArH), 6.67–6.65 (m, 2H, ArH), 4.42–4.33 (s, 1H, C_5H_3), 4.14–4.11 (s, 5H, C_5H_5), 4.04–3.97 (s, 1H, C_5H_3), 3.75–3.55 (6H, NMe_2), 2.9 (1H, C_5H_3), 2.7–0.87 (28H); $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$): $\delta=64.1$, 62.6 (*trans*:*cis* = 1:0.9); HR-MS (ESI): $m/z=832.2197$, calcd. for $C_{45}H_{53}ClFeNO_2PPd$ ($[M-Cl]^+$): 832.2198.

Characterization data for *IIf*: Red solid, air stable, easily soluble in methylene chloride or chloroform, and poorly soluble in methanol or DMSO, 62% yield, mp 229 °C (decomposed). ^1H NMR (400 MHz, $CDCl_3$): $\delta=8.44$ (m, 1H, ArH), 7.50 (m, 2H, ArH), 7.19–7.14 (3H, ArH), 7.06 (s, 1H, ArH), 6.97 (s, 1H, ArH), 6.86 (d, 2H, $J=7.0$, ArH), 4.39 (s, 1H, C_5H_3), 4.20 (s, 1H, C_5H_5), 4.09 (s, 1H, C_5H_3), 3.19 (s, 1H, C_5H_3), 2.92 (m, 1H), 2.81–2.68 (2H), 2.33 (s, 3H, CH_3), 2.01 (s, 3H, CH_3), 1.92–1.82 (5H), 1.60 (s, 6H), 1.45–1.42 (4H), 1.28–1.17 (15H), 1.07 (d, 4H, $J=6.5$), 0.94 (d, 4H, $J=6.3$), 0.80 (d, 3H, $J=6.4$); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta=183.0$, 150.1, 148.1, 146.8, 144.4, 138.0, 136.1, 135.7, 132.7, 132.4, 130.3, 129.9, 126.7, 126.5, 124.8, 122.8, 122.4, 99.4, 91.9, 76.6, 71.8, 69.7, 68.9, 38.6, 36.6, 35.7, 33.2, 31.9, 31.7, 30.5, 29.2, 28.7, 28.2, 28.0, 27.4, 26.8, 26.7, 25.5, 25.4, 24.7, 23.1, 22.6, 18.3; $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$): $\delta=63.1$; HR-MS (ESI): $m/z=898.3394$, calcd. for $C_{52}H_{67}ClFeNPPd$ ($[M-Cl]^+$): 898.3395.

General Procedure for Palladium-Catalyzed Borylation of 4-Bromoanisole (Table 1 and Table 2)

Table 1, entry 3, for example: A 10-mL Schlenk tube was charged with cyclopalladated ferrocenylimine ***IIb*** (7.4 mg, 0.01 mmol) in 1,4-dioxane (2.0 mL), followed by the addition of 1-bromo-4-methoxybenzene **1aa** (93.5 mg, 0.50 mmol), KOAc (98 mg, 1.0 mmol) and bis(pinacolato)diboron (153 mg, 0.60 mmol). The reaction was carried out at 80 °C for 3 h under the nitrogen. Then, the reaction mixture was diluted with diethyl ether and washed once with water. The organic layer was dried with Na_2SO_4 and the solvent was removed under reduced pressure. The crude material was purified by flash chromatography on silica gel (ethyl acetate:petroleum ether = 1:20).

General Procedure for the Palladium-Catalyzed Borylation of Aryl Bromides (Table 3)

A 10-mL Schlenk tube was charged with cyclopalladated ferrocenylimine ***IIb*** (7.4 mg, 0.01 mmol) in 1,4-dioxane (2.0 mL), followed by the addition of aryl bromide **1a** (0.50 mmol), KOAc (98 mg, 1.0 mmol) and bis(pinacolato)-diboron (153 mg, 0.60 mmol). The reaction was carried out at 80 °C for 3 h under the nitrogen. The mixture was diluted with diethyl ether and washed once with water. The organic layer was dried with Na_2SO_4 and the solvent removed under reduced pressure. The crude material was purified by flash chromatography on silica gel (ethyl acetate:petroleum ether = 1:5–1:20).

General Procedure for the Palladium-Catalyzed Borylation of Aryl Chlorides (Table 4)

A 10-mL Schlenk tube was charged with cyclopalladated ferrocenylimine ***IIf*** (21.2 mg, 0.025 mmol) in 1,4-dioxane (2.0 mL), followed by the addition of aryl chlorides **1b** (0.50 mmol), KOAc (147 mg, 1.5 mmol) and bis(pinacolato)-diboron (191 mg, 0.75 mmol). The reaction was carried out at 110 °C for 3 h under the nitrogen. The mixture was diluted with diethyl ether and washed once with water. The organic layer was dried with Na_2SO_4 and the solvent removed under reduced pressure. The crude material was purified by flash chromatography on silica gel (ethyl acetate:petroleum ether = 1:5–1:20).

Procedure of Mechanistic Probes

The parallel experiments were performed using **1aa** (1.0 mmol), **2** (1.2 mmol), KOAc (2.0 mmol), and complex ***IIa*** or ***IIb*** (0.5% mmol) in 1, 4-dioxane (4 mL). The reactions were monitored by GC.

Selected Characterization of Boronates

2-(4-Methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 1, entry 6) (3aa):[11] Yellow oil; 93% yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta=1.35$ (s, 12H), 3.82 (s, 3H), 6.91 (d, 2H, $J=8.8$ Hz), 7.79 (d, 2H, $J=8.8$ Hz).

4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-benzonitrile (Table 3, entry 1) (3ab):[12] White solid; mp 93–94 °C; 98% yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta=1.30$ (s, 12H), 7.59 (d, 1H, $J=7.9$ Hz), 7.83 (d, 1H, $J=7.9$ Hz).

4,4,5,5-Tetramethyl-2-(4-nitrophenyl)-1,3,2-dioxaborolane (Table 3, entry 2) (3ac):[13] Yellow solid; mp 107–108 °C; 86% yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta=1.36$ (s, 12H), 7.96 (d, 1H, $J=8.6$ Hz), 8.19 (d, 1H, $J=8.6$ Hz).

4,4,5,5-Tetramethyl-2-phenyl-1,3,2-dioxaborolane (Table 3, entry 3) (3ad):[11] Yellow oil; 93% yield. ^1H NMR (400 MHz, $CDCl_3$): $\delta=1.34$ (s, 12H), 7.36 (t, 2H, $J=14.6$ Hz), 7.45 (m, 1H, $J=14.6$ Hz), 7.80 (t, 2H, $J=7.9$ Hz).

4,4,5,5-Tetramethyl-2-[4-(trifluoromethyl)phenyl]-1,3,2-dioxaborolane (Table 3, entry 4) (3ae):[11] White solid; mp 68–

69 °C; 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5 (s, 12 H), 7.61 (d, 2 H, *J* = 7.9 Hz), 7.91 (d, 2 H, *J* = 7.9 Hz).

4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-benzoic acid methyl ester (Table 3, entry 5) (3af):[12] White solid; mp 78–79 °C; 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 12 H), 3.92 (s, 3 H), 7.87 (d, 2 H, *J* = 8.1 Hz), 8.02 (d, 2 H, *J* = 8.1 Hz).

1-[4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-phenyl]-ethanone (Table 3, entry 6) (3ag):[12] White solid; mp 59–60 °C; > 99% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (s, 12 H), 2.61 (s, 3 H), 7.89 (d, 2 H, *J* = 8.2 Hz), 7.93 (d, 2 H, *J* = 8.2 Hz).

2-(3-Methoxyphenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (Table 3, entry 7) (3ah):[11] Colorless oil; 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 12 H), 3.81 (s, 3 H), 7.00 (dd, 1 H, *J* = 2.7 Hz, 8.2 Hz) 7.28 (t, 1 H, *J* = 7.8 Hz), 7.32 (s, 1 H), 7.40 (d, 1 H, *J* = 6.8 Hz).

1-[3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-phenyl]-ethanone (Table 3, entry 8) (3ai):[4b] White solid, mp 47–48 °C; 94% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (s, 12 H), 2.64 (s, 3 H), 7.47 (t, 1 H, *J* = 7.6 Hz), 7.99 (d, 1 H, *J* = 7.6 Hz), 8.06 (m, 1 H), 8.36 (s, 1 H).

4,4,5,5-Tetramethyl-2-(2-nitrophenyl)-1,3,2-dioxaborolane (Table 3, entry 9) (3aj):[14] Yellow oil; 72% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.45 (s, 12 H), 7.56 (m, 2 H), 7.66 (m, 1 H), 8.18 (d, 1 H, *J* = 7.9 Hz).

2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-benzonitrile (Table 3, entry 10) (3ak):[13] Yellow solid; mp 79–80 °C; 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.40 (s, 12 H), 7.57 (m, 2 H), 7.71 (d, 1 H, *J* = 7.6 Hz), 7.91 (d, 1 H, *J* = 7.6 Hz).

4,4,5,5-Tetramethyl-2-(1-naphthalenyl)-1,3,2-dioxaborolane (Table 3, entry 11) (3al):[11] Yellow solid; mp 54–55 °C; 66% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (s, 12 H), 7.46–7.54 (m, 3 H), 7.84 (d, 1 H, *J* = 7.7 Hz), 7.94 (d, 1 H, *J* = 8.1 Hz), 8.08 (d, 1 H, *J* = 6.8 Hz), 8.77 (d, 1 H, *J* = 8.3 Hz).

4,4,5,5-Tetramethyl-2-(phenylmethyl)-1,3,2-dioxaborolane (Table 3, entry 12) (3am):[15] Yellow oil; 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (s, 12 H), 2.31 (s, 2 H), 7.13 (m, 1 H), 7.19–7.28 (m, 4 H).

4,4,5,5-Tetramethyl-2-(3-thienyl)-1,3,2-dioxaborolane (Table 3, entry 13) (3an):[4e] Yellow solid; mp 79–80 °C; 54% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 12 H), 7.34 (dt, 1 H, *J* = 2.6, 4.8), 7.41 (dt, 1 H, *J* = 0.7 Hz, 4.8 Hz), 7.92 (dt, 1 H, *J* = 1.7 Hz, 2.5 Hz).

4,4,5,5-Tetramethyl-2-(2-thienyl)-1,3,2-dioxaborolane (Table 3, entry 14) (3ao):[11] Yellow oil; 46% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 (s, 12 H), 7.19 (dd, 1 H, *J* = 3.5 Hz, 4.2 Hz), 7.64 (m, 2 H).

***N*,*N*-Dimethyl-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridinamine (Table 3, entry 15) (3ap):** White solid; mp 89–90 °C; 74% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 12 H), 3.11 (s, 6 H), 6.46 (d, 1 H, *J* = 8.5 Hz), 7.78 (dd, *J* = 1.9 Hz, 8.6 Hz), 8.53 (d, 1 H, *J* = 1.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.7, 37.8, 83.2, 104.7, 143.0, 155.1, 160.5; HR-MS (ESI): *m/z* = 249.1773, calcd. for $C_{13}H_{21}BN_2O_2$ ($[M+H]^+$): 249.1774.

2-Methoxy-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-pyridine (Table 3, entry 16) (3aq): Yellow oil; 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.34 (s, 1 H), 3.92 (s, 3 H), 7.12 (s, 1 H), 7.18 (d, 1 H, *J* = 4.9 Hz), 8.18 (d, 1 H, *J* = 4.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.7, 53.2, 84.3, 116.4, 121.1, 146.2, 163.9; HR-MS (ESI): *m/z* = 236.1459, calcd. for $C_{12}H_{18}BNO_3$ ($[M+H]^+$): 236.1458.

4,4,5,5-Tetramethyl-2-(4-methylphenyl)-1,3,2-dioxaborolane (Table 4, entry 4) (3ba):[16] Yellow oil; 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.33 (s, 12 H), 2.36 (s, 3 H), 7.18 (d, 2 H, *J* = 7.7 Hz), 7.70 (d, 2 H, *J* = 7.7 Hz).

2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-benzenamine (Table 4, entry 7) (3bb):[13] White solid; mp 67–68 °C; 58% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 12 H), 4.72 (br s, 2 H), 6.59 (d, 1 H, *J* = 8.1 Hz), 6.66 (m, 1 H), 7.20 (m, 1 H), 7.59 (dd, 1 H, *J* = 1.4 Hz, 7.3 Hz).

3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-benzenamine (Table 4, entry 8) (3bc):[16] White solid; mp 88–89 °C; 91% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32 (s, 12 H), 3.65 (br s, 2 H), 6.78 (dd, 1 H, *J* = 1.3 Hz, 9.8 Hz), 7.12–7.21 (m, 3 H).

4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2-pyridinecarbonitrile (Table 4, entry 10) (3bd): White solid; mp 60–61 °C; 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 (s, 12 H), 7.84 (dt, 1 H, *J* = 3.8 Hz), 8.03 (s, 1 H), 8.74 (t, 1 H, *J* = 4.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.7, 85.2, 117.2, 131.8, 133.3, 133.5, 150.4; HR-MS (ESI): *m/z* = 231.1305, calcd. for $C_{12}H_{16}BN_2O_2$ ($[M+H]^+$): 231.1305.

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References

[1] For reviews on the applications of arylboronic acids and esters, see: a) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457–2483; b) N. Miyaura, *Top. Curr. Chem.* **2002**, *219*, 11–59; c) A. F. Littke, G. C. Fu, *Angew. Chem.* **2002**, *114*, 4350–4386; *Angew. Chem. Int. Ed.* **2002**, *41*, 4176–4211; d) D. G. Hall, *Boronic Acids: Preparation and Applications in Organic Synthesis and Medicine*, (Ed.: D. G. Hall), Wiley-VCH: Weinheim, **2005**; 1–99.

[2] J. Yan, H. Fang, B. H. Wang, *Med. Res. Rev.* **2005**, *25*, 490–520.

[3] For reviews on transition metal-catalyzed carbon-boron bond formation, see: a) T. Ishiyama, N. Miyaura, *J. Organomet. Chem.* **2000**, *611*, 392–402; b) T. Ishiyama, N. Miyaura, *J. Organomet. Chem.* **2003**, *680*, 3–11; c) T. Ishiyama, N. Miyaura, *Chem. Rec.* **2004**, *3*, 271–280.

[4] a) T. Ishiyama, M. Murata, N. Miyaura, *J. Org. Chem.* **1995**, *60*, 7508–7510; b) M. Murata, S. Watanabe, Y. Masuda, *J. Org. Chem.* **2000**, *65*, 164–168; c) T. Ishiyama, K. Ishida, N. Miyaura, *Tetrahedron* **2001**, *57*, 9813–9816; d) M. Murata, T. Sambommatsu, S. Watanabe, Y. Masuda, *Synlett* **2006**, *12*, 1867–1870; e) K. L. Billingsley, T. E. Barder, S. L. Buchwald, *Angew. Chem.* **2007**, *119*, 5455–5459; *Angew. Chem. Int. Ed.* **2007**, *46*, 5359–5363; f) K. L. Billingsley, S. L. Buchwald, *J. Org. Chem.* **2008**, *73*, 5589–5591; g) H. A. Duong, S. Chua, P. B.

Huleatt, C. L. L. Chai, *J. Org. Chem.* **2008**, *73*, 9177–9180; h) T. Martin, C. Laguerre, C. Hoarau, F. Marsais, *Org. Lett.* **2009**, *11*, 3690–3693.

[5] For reviews on the applications of palladacycles, see: a) R. B. Bedford, *Chem. Commun.* **2003**, 1787–1796; b) J. Dupont, C. S. Consorti, J. Spencer, *Chem. Rev.* **2005**, *105*, 2527–2572; c) J. Dupont, M. Pfeffer, in: *Palladacycles: Synthesis Characterisation and Applications*, (Ed.: J. Dupont, M. Pfeffer), Wiley-VCH: Weinheim, **2008**.

[6] a) W. A. Herrmann, C. Brossmer, K. Öfele, C. P. Reisinger, T. Priermeier, M. Beller, H. Fischer, *Angew. Chem.* **1995**, *107*, 1989–1992; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1844–1848; b) M. Beller, H. Fischer, W. A. Herrmann, K. Öfele, C. Brossmer, *Angew. Chem.* **1995**, *107*, 1992–1993; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1848–1849.

[7] a) Y. J. Wu, S. Q. Huo, J. F. Gong, X. L. Cui, L. Ding, K. L. Ding, C. X. Du, Y. H. Liu, M. P. Song, *J. Organomet. Chem.* **2001**, *637–639*, 27–46; b) C. Xu, J. F. Gong, S. F. Yue, Y. Zhu, Y. J. Wu, *Dalton Trans.* **2006**, 4730–4739; c) F. Yang, Y. J. Wu, *Eur. J. Org. Chem.* **2007**, 3476–3479; d) N. Ma, Z. W. Zhu, Y. J. Wu, *Tetrahedron* **2007**, *63*, 4625–4629; e) A. J. Yu, Y J. Wu, B. L. Cheng, K. Wei, J. Y. Li, *Adv. Synth. Catal.* **2009**, *351*, 767–771.

[8] G. R. Ren, X. L. Cui, E. B. Yang, F. Yang, Y. J. Wu, *Tetrahedron* **2010**, *66*, 4022–4028.

[9] S. Q. Huo, Y. J. Wu, C. X. Du, Y. Zhu, H. Z. Yuan, X. A. Mao, *J. Organomet. Chem.* **1994**, *483*, 139–146.

[10] J. F. Gong, G. Y. Liu, C. X. Du, Y. Zhu, Y. J. Wu, *J. Organomet. Chem.* **2005**, *690*, 3963–3969.

[11] W. Zhu, D. W. Ma, *Org. Lett.* **2006**, *8*, 261–263.

[12] S. Claudel, C. Gosmini, J. M. Paris, J. Périchon, *Chem. Commun.* **2007**, *35*, 3667–3669.

[13] M. J. Ahrens, L. E. Sinks, B. Rybtchinski, W. H. Liu, B. A. Jones, J. M. Giaimo, A. V. Gusev, A. J. Goshe, D. M. Tiede, M. R. Wasielewski, *J. Am. Chem. Soc.* **2004**, *126*, 8284–8294.

[14] O. Baudoin, D. Guénard, F. Guéritte, *J. Org. Chem.* **2000**, *65*, 9268–9271.

[15] T. Ishiyama, Z. Oohashi, T. Ahiko, N. Miyaura, *Chem. Lett.* **2002**, 8, 780–781.

[16] P. E. Broutin, I. Čerňa, M. Campaniello, F. Leroux, F. Colobert, *Org. Lett.* **2004**, *6*, 4419–4422.

