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Cyclopalladated complexes catalyzed addition of arylboronic acids to aldehydes in neat water

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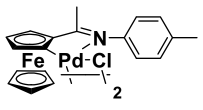
ABSTRACT

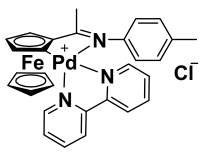
Cyclopalladated ferrocenylimine complexes gave high yields for the addition of arylboronic acids with aldehydes in neat water using a weak acid as additive.

Transition metal-catalyzed reactions have emerged as powerful tools for the carbon–carbon bond construction.[1] In the past decades, addition of carbon–metal species to carbon–heteroatom multiple bonds, such as the carbonyl, imino, and nitrile groups, is an important reaction for organic synthesis, and the addition products are important precursors for the synthesis of biologically active compounds.[2–5] Recent publications describing the rhodium-catalyzed addition of organoboron reagents to aldehydes have attracted many chemists' interest.[6–15] The extension of the scope of this reaction and the search for more efficient catalyst have been one of the most popular aims of research for organic chemists, and some recent progress of palladium catalysis has been made in this reaction under basic condition. Yamamoto and Ohta,[16] Kondo and co-workers[17] and Wu and co-workers[18] have used various tertiary phosphines as the catalyst modifier and afforded carbinol derivatives in good to excellent yields independently. Kuriyama et al.[19] has reported the use of nucleophilic N-heterocyclic carbenes (NHC) as auxiliary ligands in palladium-mediated addition of arylboronic acids and aldehydes. Lin and Lu[20] has prepared cationic Pd(II)/bipyridine complexes as very active catalysts for this reaction.

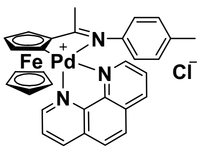
Palladacycles have been by far the most developed and extensively studied catalysts, because of their structural versatility and easily synthetic accessibility. Gibson et al.[21] initially reported phosphapalladacyclic complex-catalyzed 1,2-addition of phenylboronic acids to 4-chlorobenzaldehyde as a side reaction. Very recently, Hu and co-workers[22,23] found that palladacycles containing phosphorous donors catalyzed addition reactions efficiently to aromatic and aliphatic aldehydes at room temperature, but the one with nitrogen donor showed no catalytic activity. Among the palladacyclic complexes, we have found that cyclopalladated ferrocenylimine is an excellent catalyst for the addition of arylboronic acids to carbon–heteroatom multiple bonds.[24] However, to the best of our knowledge, there are no reports of palladacycle-catalyzed addition of organoboron reagents to aldehydes in neat water using the weak acids as additives. Herein, we would like to describe a kind of phosphine-free palladacyclic complexes (cat. **1**–**3**) containing nitrogen donors for this addition in environmentally friendly condition.



cat. 1



cat. 2



cat. 3

The palladacyclic complex **3** was prepared in good yield by simple addition of 1:5 chloroform/acetone mixture solution of bipyridine to the cyclopalladated ferrocenylimine **1** at room temperature. The compound **3** was recrystallized as a dark red

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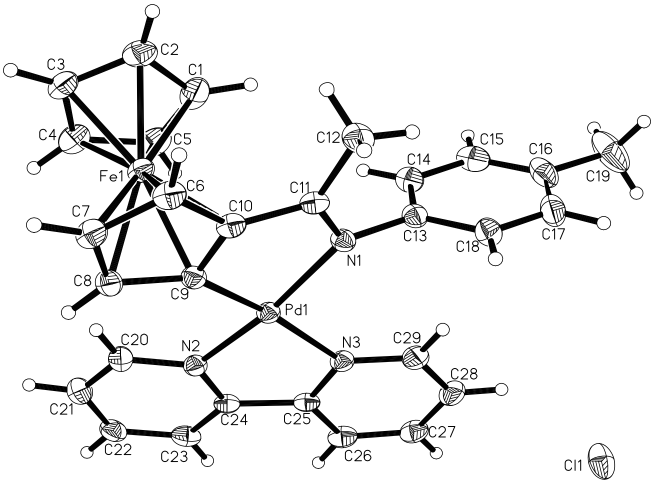


Figure 1. Molecular structure of palladacyclic complex **2**. The CCDC number is 680310. Selected bond lengths (Å) and angles (°): Pd(1)–C(9) 1.988(6), Pd(1)–N(2) 2.047(6), Pd(1)–N(1) 2.084(5), Pd(1)–N(3) 2.143(5), C(9)–Pd(1)–N(2) 99.9(2), C(9)–Pd(1)–N(1) 79.9(2), N(2)–Pd(1)–N(1) 170.9(2), C(9)–Pd(1)–N(3) 172.1(2), N(2)–Pd(1)–N(3) 78.9(2), N(1)–Pd(1)–N(3) 102.5(2).

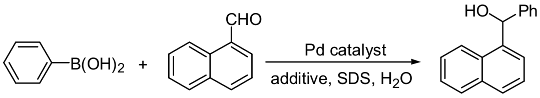
crystal. It was stable to air and moisture and very soluble in methanol. The new compound was characterized by ^{1}H NMR, ^{13}C NMR, IR, MS, and high-resolution mass spectra. These spectra were well consistent with the title compound. The structure of palladacyclic complex **2** was further confirmed by a single-crystal X-ray analysis (Fig. 1).

The addition of 1-naphthaldehyde and phenylboronic acid in water by catalyst **2** at 100 °C was chosen as the initial model for optimizing the reaction additions (Table 1). After screening a variety of acids (e.g., acetic acid, benzoic acid, phenol, NH_4Cl, and $NaH_2PO_4{\cdot}2H_2O$), $NaH_2PO_4{\cdot}2H_2O$ was found to give the best result; and the reaction is insensitive to air (Table 1, entries 1–6). A series of bases were also examined, and the results were not satisfactory (Table 1, entries 7–11). Although it was not clear what was the exact role of the weak acid, $NaH_2PO_4{\cdot}2H_2O$, it may be the protonolysis of palladium alkoxide species in hydrous conditions.[13] A ratio of dimer **1** to bpy at 1:4 afforded the diphenylmethanone in a moderate yield (Table 1, entry 13). In the absence of bpy, the reaction mixture became black and no product was obtained (Table 1, entry 14).

Using $NaH_2PO_4{\cdot}2H_2O$ as additive, the effects of changing the amount of the phenylboronic acid, catalyst loading, temperature, and reaction time were explored. A high yield of the desired product was also obtained even with the loading of **2** to 2 mol % at 100 °C (Table 1, entry 15). When shortening the reaction time or reducing the reaction temperature, the yields dropped sharply (Table 1, entries 20–23). The yields of diaryl methanol decreased with decreasing amount of phenylboronic acid (Table 1, entries 24–26), which might be prone to trimer formation of boronic acids side reaction.[7] Thus, $PhB(OH)_2$ (1.5 mmol), aldehyde (0.5 mmol), cationic Pd(II) complex 2 (2.5 mol %), $NaH_2PO_4{\cdot}2H_2O$ (1.5 mmol), and sodium dodecyl sulfonate (0.5 mmol) in water (2.0 mL) at 100 °C for 12 h were chosen as the optimized conditions (Table 1, entry 20).

We tested the optimized catalytic system in the arylation of aryl and alkyl aldehydes. As for cat. **2**, in most cases the reaction proceeded with remarkable efficiency (up to 99% yield of isolated

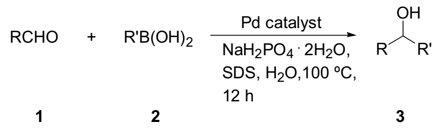
Table 1
Screening of reaction conditions[a]



Entry	Ph(OH)$_2$ (mmol)	Catalyst loading (Pd mol %)	Additive	Temperature (°C)	Time (h)	Yield[b] (%)
1	1.5	5.0	CH_3COOH	100	24	1
2	1.5	5.0	PhCOOH	100	24	0
3	1.5	5.0	PhOH	100	24	20
4	1.5	5.0	NH_4Cl	100	24	69
5[c]	1.5	5.0	$NaH_2PO_4{\cdot}2H_2O$	100	24	96
6	1.5	5.0	$NaH_2PO_4{\cdot}2H_2O$	100	24	95
7	1.5	5.0	$KF{\cdot}2H_2O$	100	24	57
8	1.5	5.0	Na_2CO_3	100	24	30
9	1.5	5.0	K_2CO_3	100	24	39
10	1.5	5.0	$K_3PO_4{\cdot}7H_2O$	100	24	25
11	1.5	5.0	*t*-BuONa	100	24	5
12[d]	1.5	5.0	—	100	24	76
13[e]	1.5	5.0	$NaH_2PO_4{\cdot}2H_2O$	100	24	75
14[f]	1.5	5.0	$NaH_2PO_4{\cdot}2H_2O$	100	24	0
15	1.5	2.0	$NaH_2PO_4{\cdot}2H_2O$	100	24	89
16	1.5	2.5	$NaH_2PO_4{\cdot}2H_2O$	100	24	95
17	1.5	3.0	$NaH_2PO_4{\cdot}2H_2O$	100	24	95
18	1.5	3.5	$NaH_2PO_4{\cdot}2H_2O$	100	24	95
19	1.5	4.0	$NaH_2PO_4{\cdot}2H_2O$	100	24	95
20	1.5	2.5	$NaH_2PO_4{\cdot}2H_2O$	100	12	92
21	1.5	2.5	$NaH_2PO_4{\cdot}2H_2O$	100	6	63
22	1.5	2.5	$NaH_2PO_4{\cdot}2H_2O$	50	12	0
23	1.5	2.5	$NaH_2PO_4{\cdot}2H_2O$	80	12	71
24	0.75	2.5	$NaH_2PO_4{\cdot}2H_2O$	100	12	74
25	1.0	2.5	$NaH_2PO_4{\cdot}2H_2O$	100	12	86
26	1.25	2.5	$NaH_2PO_4{\cdot}2H_2O$	100	12	89

[a] Unless otherwise indicated, all reactions were performed using 0.5 mmol of 1-naphthaldehyde with indicated amount of $PhB(OH)_2$, 1.5 mmol of $NaH_2PO_4{\cdot}2H_2O$, 0.5 mmol sodium dodecyl sulfonate as surfactant, catalyst **2** in 2.0 mL of water.
[b] Isolated yield.
[c] The reaction was conducted under N_2 atmosphere.
[d] No additive was used.
[e] Cat. **1**:bpy (1:4) as the catalyst.
[f] Cat. **1** as the catalyst.

Table 2
Catalysts **2** and **3** catalyzed addition of arylboronic acids to aldehydes[a]



Entry	R	R′	Product	Yield[b] (%)	
				Cat. **2**	Cat. **3**
1	1-$C_{10}H_7$	Ph	**3a**	92	32
2[c]	2-$MeOC_6H_4$	Ph	**3b**	99	85
3	Ph	Ph	**3c**	72	75
4	4-FC_6H_4	Ph	**3d**	99	53
5	4-ClC_6H_4	Ph	**3e**	84	11
6	2-ClC_6H_4	Ph	**3f**	99	95
7	2,4-$Cl_2C_6H_4$	Ph	**3g**	87	94
8	3-BrC_6H_4	Ph	**3h**	91	65
9	2-BrC_6H_4	Ph	**3i**	98	75
10	3-$NO_2C_6H_4$	Ph	**3j**	99	60
11	2-$NO_2C_6H_4$	Ph	**3k**	99	31
12	*n*-C_4H_8	Ph	—	—	—
13	2-$NO_2C_6H_4$	4-MePh	**3l**	97	72
14	2-$NO_2C_6H_4$	2-MePh	**3m**	99	41
15	2-$NO_2C_6H_4$	4-MeOPh	**3n**	99	99
16	2-$NO_2C_6H_4$	3-MeOPh	**3o**	88	56
17	2-$NO_2C_6H_4$	4-CF_3OPh	**3p**	99	38
18	2-$NO_2C_6H_4$	3-ClPh	**3q**	53	6
19	2-$NO_2C_6H_4$	2-FPh	**3r**	92	0
20	2-$NO_2C_6H_4$	2,4-F_2Ph	**3s**	53	20

[a] 0.5 mmol aldehyde, 1.5 mmol $PhB(OH)_2$, 1.5 mmol $NaH_2PO_4{\cdot}2H_2O$, 0.5 mmol sodium dodecyl sulfonate, 2.5 mol % Cat. **2** and Cat. **3**, 2.0 mL H_2O, 100 °C, 12 h.
[b] Isolated yield.
[c] $KF{\cdot}2H_2O$ as the additive.

product) under mild conditions. Benzaldehyde derivatives with electron-withdrawing groups gave good to excellent yields of benzhydrol derivatives (Table 2, entries 4–11). The efficiency of the protocol proved to have a noteworthy tolerance to functional groups. Incorporation of an *ortho*-methyl substituents on the aldehydes had no effect on the reaction yield. Interestingly, in contrast to other reaction conditions, electron-donating group at the ortho position of the aryl aldehyde gave nearly quantitative yield, using $KF\cdot 2H_2O$ as the additive (Table 2, entry 2). Pentanal and several other aliphatic aldehydes were also tested but gave no conversion (Table 2, entry 12). The lower electrophilicity of the aliphatic aldehydes likely accounted for the results.[12] A contrasting electronic effect was also observed when substituted arylboronic acids were used. Electron-rich phenylboronic acids gave excellent yields of coupling product, even though in the presence of steric hindrance (Table 2, entries 13–17). Incorporation of other catalytic systems, electron-deficient arylboronic acids, could also give moderate to good yields (Table 2, entries 18–20). In contrast cat. **2**, the methodology proved to have less efficiency for cat. **3**, and most yields obtained were not satisfactory. These results imply that the ligand 2-2′-bipyridine plays a more crucial role in this reaction.

In summary, we have developed a highly efficient and environmentally friendly procedure for aryl transfer reactions to arylaldehyde by cyclopalladated ferrocenylimine bipyridine complex **2**. Significantly most of the products were obtained with good to excellent yields which depended on the electronic effect of the substituents in the molecules of the substrates.

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