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COMMUNICATION

The ligand and base-free Pd-catalyzed oxidative Heck reaction of arylboronic acids and olefins†

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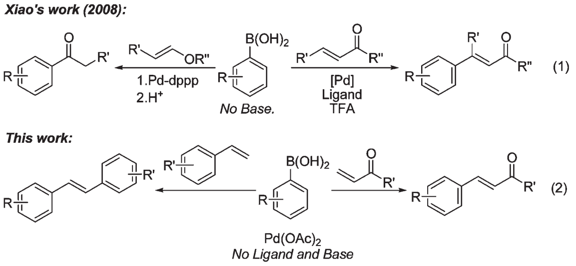
Highly effective Pd-catalyzed Heck-type oxidative couplings between arylboronic acids and terminal olefins were reported. It is noteworthy that such reactions could be carried out in the absence of the base and the ligand.

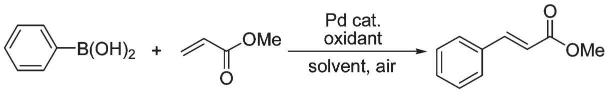
Recently the oxidative variant of the Heck reaction[1] has received considerable attention. After first reported by Dieck and Heck[2] and further development of Cho and Uemura,[3] various catalytic systems have been developed to simplify this methodology.[4] Notably Jung and co-workers, who have done a series of wonderful pioneering work in this area, firstly reported a base-free version of oxidative Heck, which has brought oxidative Heck to a new age.[5] Xiao and co-workers[6] developed an oxygen and base-free method for the olefination of arylboronic acids. However, the reported methods required Pd complex, ligands as well as oxygen.[7] Therefore, based on our interest in coupling reactions,[8] we aim to develop an oxygen, ligand and base-free catalytic system for the oxidative coupling of olefins and phenylboronic acids (Scheme 1).[9]

It was suggested that Pd(II)-catalysed oxidative Heck reactions require a regeneration of the Pd(II) step. We wish to get the H–Pd–X intermediate intercepted by hydrogen acceptors. We initially examined our hypothesis by treating phenylboronic acid with methyl acrylate in acetic acid at 110 °C in the presence of Ag_2O in air to obtain a 40% yield of the product after 18 hours (Table 1, entry 1). In the absence of Ag_2O, only trace amounts of the product was obtained (entry 2). Then we tested a range of hydrogen acceptors for the purpose of optimizing the reaction. Usual oxidants such like $K_2S_2O_8$ and Ag_2CO_3 provided lower yields of desired product (entries 3–4). Only when BQ (1,4-benzoquinone) and DDQ (2,3-dichloro-5,6-dicyanobenzoquinone)



Scheme 1 Pd-catalyzed oxidative coupling between arylboronic acids and olefins.

Table 1 Screening catalytic conditions in oxidative Heck coupling between phenylboronic acid and methylacrylate[a]



Entry	Pd cat. (mol%)	Oxidant	Solvent	T (°C)	Yield[b] (%)
1	$Pd(OAc)_2$ (2)	Ag_2O	AcOH	110	40
2	$Pd(OAc)_2$ (2)	—	AcOH	110	Trace
3	$Pd(OAc)_2$ (2)	$K_2S_2O_8$	AcOH	110	<5
4	$Pd(OAc)_2$ (2)	Ag_2CO_3	AcOH	110	<5
5	$Pd(OAc)_2$ (2)	BQ	AcOH	110	54
6	$Pd(OAc)_2$ (2)	DDQ	AcOH	110	84
7	$Pd(OAc)_2$ (2)	TBHP	AcOH	110	NR
8	$Pd(OAc)_2$ (2)	DDQ	AcOH	90	82
9	$Pd(OAc)_2$ (2)	DDQ	AcOH	70	73
10	$PdCl_2$ (2)	DDQ	AcOH	90	62
11	$Pd(PPh_3)_2Cl_2$ (2)	DDQ	AcOH	90	NR
12	$Pd(dba)_2$ (2)	DDQ	AcOH	90	69
13	Pd/C (2)	DDQ	AcOH	90	47
14[c]	$Pd(OAc)_2$ (2)	—	AcOH	90	Trace
15	$Pd(OAc)_2$ (2)	DDQ	DMSO	90	Trace
16	$Pd(OAc)_2$ (2)	DDQ	DMF	90	Trace
17	$Pd(OAc)_2$ (2)	DDQ	PEG-400	90	Trace
18	$Pd(OAc)_2$ (2)	DDQ	Dioxane	90	16
19[d]	$Pd(OAc)_2$ (2)	DDQ	AcOH	90	89
20[e,f]	$Pd(OAc)_2$ (2)	DDQ	AcOH	90	99
21[e,g]	$Pd(OAc)_2$ (2)	DDQ	AcOH	90	92
22[e,h]	$Pd(OAc)_2$ (2)	DDQ	AcOH	90	99
23[e,h,i]	$Pd(OAc)_2$ (2)	DDQ	AcOH	90	62
24[e,h,j]	$Pd(OAc)_2$ (2)	DDQ	AcOH	90	96
25[e,h,j,k]	$Pd(OAc)_2$ (2)	DDQ	AcOH	90	46

[a] Catalytic conditions: Phenylboronic acid (0.5 mmol), methylacrylate (3.0 mmol), oxidant (1.0 equiv), additive, solvent (3 mL), 70–110 °C, 18–30 h, air. [b] Isolated yield based on phenylboronic acid. [c] In oxygen atmosphere. [d] 4 equiv of Ac_2O as the additive. [e] 5 equiv of Ac_2O as the additive. [f] 30 h. [g] 24 h. [h] 27 h. [i] 0.5 equiv DDQ. [j] In Ar. [k] 4 equiv DDQ.

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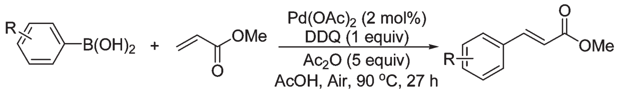
† Electronic supplementary information (ESI) available: Experimental details and copies of HRMS and NMR spectra of product. See DOI: 10.1039/c2ob25462j

Table 2 Pd-catalyzed Heck coupling between methylacrylate and various arylboronic acids[a]



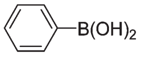
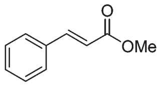
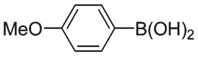
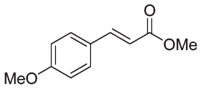
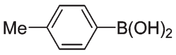
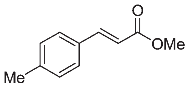
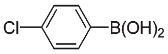
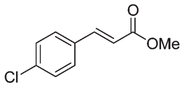
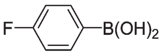
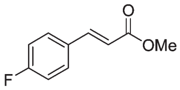
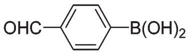
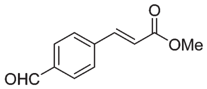
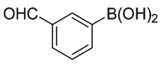
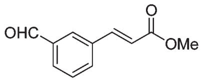
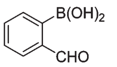
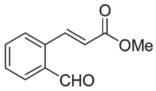
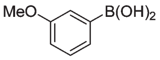
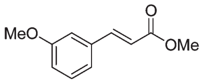
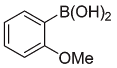
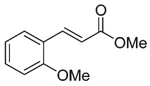
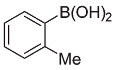
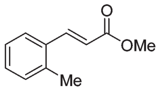
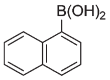
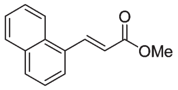
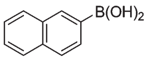
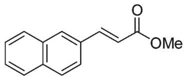
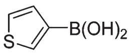
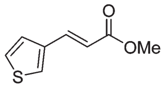
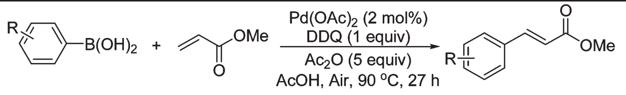
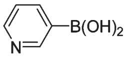
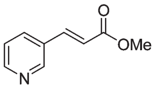
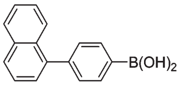
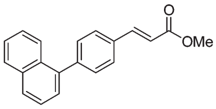
Entry	$ArB(OH)_2$	Product	Yield[b] (%)
1			99
2			42
3			56
4			92
5			60
6			38
7			51
8			Trace
9			84
10			75
11			25
12			45
13			77
14			49

Table 2 *(Contd.)*



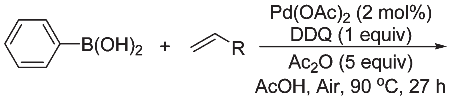
Entry	$ArB(OH)_2$	Product	Yield[b] (%)
15			35
16			62

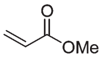
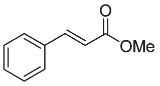
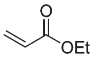
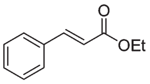
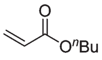
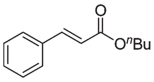
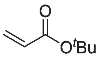
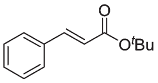
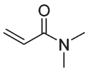
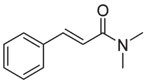
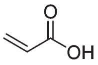
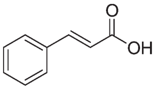
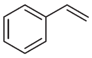
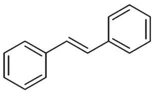
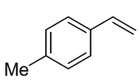
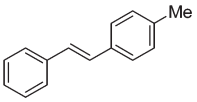
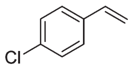
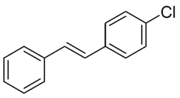
[a] Reaction conditions: Aryl boronic acid (0.5 mmol), methylacrylate (3.0 mmol), DDQ (1.0 equiv), Ac_2O (5 equiv), AcOH (3 mL), 27 h, 90 °C, air. [b] Isolated yield based on arylboronic acid (average of two runs).

were used as oxidants, the reactions were performed smoothly (54% yield for BQ and 84% yield for DDQ, respectively) (entries 5–6). When TBHP (*tert*-butyl hydroperoxide) was employed as the oxidant, no formation of the product was observed (entry 7). Decrease of the temperature to 90 °C led to slightly lower yield of 82% (entry 8) and at 70 °C the yield dropped to 73% (entry 9). We next tested a series of palladium catalysts (entries 10–13). The use of other Pd sources gave lower yields or even led to no formation of the expected product. Therefore we believe that DDQ plays a quite vital role in our catalytic system. The control reaction indicated that only a trace of product could be obtained in the absence of DDQ even in an oxygen atmosphere (entry 14). It was supposed that the H–Pd–OAc intermediate might react with acetic acid and DDQ to better release $Pd(OAc)_2$. Then, several commonly-used solvents, including DMF, DMSO, PEG-400 and dioxane were investigated in the study, but the reactions performed poorly on those (entries 15–18). Acetic anhydride was used as the additive in order to trap the hydrogen atom from the H–Pd–OAc intermediate. 4 equiv of acetic anhydride affords the desired product with a yield of 89% (entry 19), 5 equiv of Ac_2O would achieve almost quantitative transformation when the reaction time was increased to 30 hours (entry 20). A slightly decreased yield of 92% was obtained when the reaction time was reduced to 24 hours (entry 21). An excellent yield of 99% was obtained when the reaction was conducted for 27 hours (entry 22). Under the same conditions, only 0.5 equiv of DDQ afforded a decreased yield (62%, entry 23). The reaction performed in argon atmosphere also acquired a good result (96%, entry 24). In addition, excessive DDQ without air gave a much lower yield (46%, entry 25).

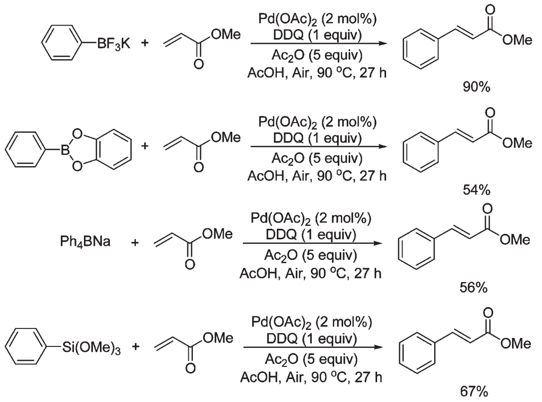
With the optimized protocol in hand, we then set out to investigate the scope and limitations of this oxidative coupling reaction. The results are shown in Table 2. Different substituents and different substituting sites on the benzene ring were tested under our standard conditions, and most of the substrates could achieve moderate to good yields. We found that electron-rich phenylboronic acids (Table 2, entries 2–3, 9–11) as well as electron-deficient phenylboronic acids (entries 4–8) all proceed smoothly. *Ortho*-substituted phenylboronic acids were also examined, and less amount of product was obtained in the view of steric hindrance effect (entries 8, 10–11). *O*-formyl phenylboronic acid could only afford only trace of product, since the formyl group may have a poisoning effect on the Pd-catalyst through coordinating to it. The two isomers of naphthylboronic acid were then investigated in the reaction (entries 12–13): 1-naphthylboronic

Table 3 Pd-catalyzed Heck coupling between phenylboronic acid and various terminal olefins[a]

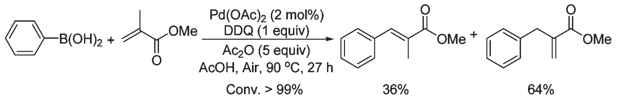


Entry	Olefin	Product	Yield[b] (%)
1			99
2			65
3			78
4			89
5			61
6			99
7			69
8			99
9			99

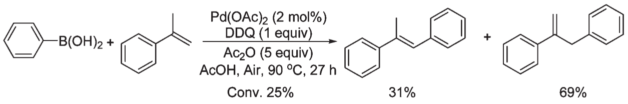
[a] Reaction conditions: Phenylboronic acid (0.5 mmol), olefin (3.0 mmol), DDQ (1.0 equiv), Ac_2O (5 equiv), AcOH (3 mL), 27 h, 90 °C, air. [b] Isolated yield based on phenylboronic acid (average of two runs).



Scheme 2 Oxidative coupling between methylacrylate and organoboron or organosilicon-based reagents.



Scheme 3 Oxidative coupling between α-methylacrylate and phenylboronic acid using $Pd(OAc)_2$/DDQ/Ac_2O/AcOH system.



Scheme 4 Oxidative coupling between α-methylstyrene and phenylboronic acid using $Pd(OAc)_2$/DDQ/Ac_2O/AcOH system.

acid afforded the desired product with 45% yield, which was lower than its isomer (77%). When heteroarylboronic acids were used, the reaction could also proceed smoothly and the desired heteroaryl olefins were acquired in moderate yields between 35% and 49% (entries 14–15). 4-(1-Naphthyl)phenylboronic acid could also participate in the coupling successfully, affording the desired product in yield of 62% (entry 16).

We next applied our methodology to the coupling between phenylboronic acid and various olefins (Table 3). Under the optimized conditions, various acrylates affords the desired product in yield between 65% and 99% (entries 1–4). Acryl acid and acrylamide was then studied: acryl acid could achieve almost full conversion while the yield for acrylamide decreased to 61% (entries 5–6). We then extended our protocol to the coupling of phenylboronic acid and various styrenes. Under the standard conditions, the yield of styrene was reduced to 69% (entry 7) while both the 4-methyl and 4-chloro styrenes afforded the desired product almost quantitatively (entries 8–9).

Subsequently, the scope of other boron- and silicon-based reagents was examined under the optimized conditions and most of them obtained good to excellent yields (Scheme 2). Potassium phenyltrifluoroborate gave a higher yield of 90% while for couplings of 2-phenyl-1,3,2-benzodioxaborole or sodium tetraphenylborate were 54% and 56%, respectively. To our delight, phenyltrimethoxysilane could also achieve a 67% yield, which demonstrates that our methodology was not only well-applied for organoboron reagents but also for organosilicons.

We next set out to test the regioselectivity of our methodology by treating phenylboronic acid and α-substituted olefins (Schemes 3 and 4). α-Methylacrylate and α-methylstyrene were chosen to study regioselectivity of the reaction. As shown, the hydrogen-migrating products were major in both, with the ratio of 1.78 : 1 and 2.23 : 1. In addition, the conversion of α-methylacrylate was almost quantitative despite the steric hindrance provided by the α-methyl group.[10]

We here wish to disclose a plausible mechanism (Fig. 1) which was proposed on the basis of results reported by others.[6,7a,11,12] First, Pd(II) catalyst reacts with phenylboronic acid to form an aryl-Pd(II) species **I**, which subsequently coordinates to the olefin to form a Pd(II) intermediate **II**. This intermediate will undergo an insertion to the olefin to give an intermediate **III**. After elimination of β-hydrogen, a Pd-hydride species H–Pd–OAc will be released to give the desired product, and then it would form a Pd(0)-DDQ species **IV**, which stabilizes

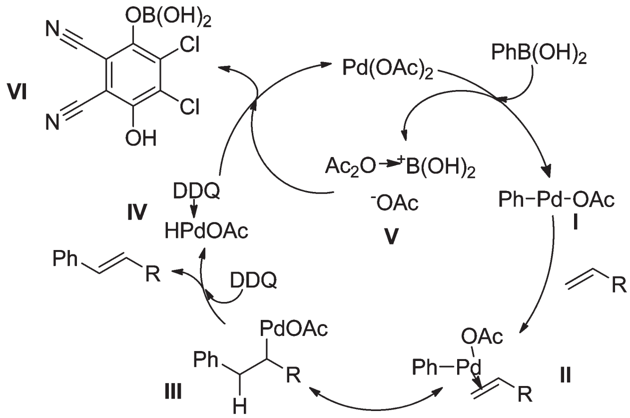


Fig. 1 Possible mechanism for the oxidative coupling of phenylboronic acids and olefins.

the Pd(0) species by preventing it from aggregating to Pd black. And then Pd(0) is oxidized to Pd(II) by DDQ, which might also stabilize the leaving group of $B(OH)_2$. **IV** will be dehydrogenated by DDQ in the presence of acetic anhydride to give Pd(II) and thus close the catalytic cycle. In this proposed mechanism, we assume that the leaving group of $B(OH)_2$ could be stabilized initially by the acetic anhydride and finally by DDQ due to its oxophility. A species **V** are supposed to be released. The **VI** species was detected by MS after reaction, which might be supportive.

In summary, we have disclosed that in the aerobic catalytic system of $Pd(OAc)_2$-DDQ-Ac_2O-AcOH, the olefination of phenylboronic acids could be well achieved. Many different types of substituted substrates are tolerated. It is noteworthy that various organoboronic reagents and an organosilicon reagent could also be used to afford the desired product. The regioselectivity of this protocol was also examined. Efforts are underway to extend this methodology to other types of olefins and aryl reagents.

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