

## Palladium-Catalyzed Cross-Coupling of $\alpha$ -Diazocarbonyl Compounds with Arylboronic Acids

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Suzuki–Miyaura reaction of aryl and vinyl halides or triflates with organoboron reagents has developed into one of the most important C–C bond-forming reactions.<sup>1,2</sup> The mild and simple reaction conditions, the availability of various boronic acids that are normally nontoxic and stable, and easy workup and separation of the products are some of the factors that are responsible for the increasing popularity of the Suzuki–Miyaura reaction. Our recent interest is focused on the development of new methodology based on palladium-catalyzed reactions of  $\alpha$ -diazocarbonyl compounds.<sup>3</sup> Although  $\alpha$ -diazocarbonyl compounds have been extensively applied as metal carbene precursors,<sup>4</sup> the palladium-catalyzed reaction has received only limited attentions.<sup>5–7</sup> We have conceived that the combination of Pd–carbene reaction with the transmetalation of boronic acids would lead to novel transformations. Herein we report a palladium-catalyzed cross-coupling reaction of arylboronic acids with  $\alpha$ -diazocarbonyl compounds. The reaction affords  $\alpha$ -aryl  $\alpha,\beta$ -unsaturated carbonyl compounds, presumably through migratory insertion reactions of palladium carbene intermediate.

On the outset of this study, we have used methyl  $\alpha$ -diazopropionate **1** and phenylboronic acid **2a** as the substrates. When **1** and **2a** were catalyzed with Pd(PPh<sub>3</sub>)<sub>4</sub> in the presence of benzoquinone (BQ) and K<sub>2</sub>CO<sub>3</sub>, methyl 2-phenylacrylate **3a** was isolated in moderate yield (Table 1, entry 1). In the absence of the oxidant BQ, the reaction gave trace 2-phenylacrylate **3a** (entry 2). We went on to screen other reaction parameters, such as temperature, solvent, and base. It was found that the reaction proceeded more efficiently at high-temperature (entry 3). The bases, such as K<sub>2</sub>CO<sub>3</sub>, Cs<sub>2</sub>CO<sub>3</sub>, and Et<sub>3</sub>N afforded similar results, while *i*-Pr<sub>2</sub>NH was found the most suitable base to promote the reaction with high yield (entries 6, 7). Polar solvent DCE could accelerate the reaction but led to slightly low yield, while MeCN was found not favorable (entries 8, 9). Several other palladium catalysts were then examined. Pd(OAc)<sub>2</sub>, PdCl<sub>2</sub>(PPh<sub>3</sub>)<sub>2</sub>, and Pd(OAc)<sub>2</sub>/phosphine ligands all led to lower yields of **3a** (entries 10–14). Finally, for comparison the reaction was carried out in the absence of Pd(PPh<sub>3</sub>)<sub>4</sub>. No product **3a** could be detected.

A series of arylboronic acids were then subjected to the optimized reaction conditions with methyl  $\alpha$ -diazopropionate **1**. The reaction finished in 15 min with high efficiency and afforded methyl  $\alpha$ -arylacrylates in moderate to good yields (Table 2). The reaction with *o*-, *m*-, and *p*-monoalkyl substituted arylboronic acids all proceeded efficiently (entries 2–5). The low yield in the reaction with 3,5-dimethylsubstituted arylboronic acid was due to its low solubility in toluene (entry 6). The reaction was found marginally affected by electronic effects of the substituents of boronic acids. The electron-donating group increased the reaction efficiency as compared with electron-withdrawing groups (entries 7, 8, 9). It is noteworthy that chloro and bromo substituents are tolerated in the reaction conditions, which is advantageous for further transformations (entries 10, 11).

**Table 1.** Conditions on Pd-Catalyzed Reaction of **1** and **2a**<sup>a</sup>

entry	catalyst (mol %)	solvent	base	T(°C)	time	yield (%) <sup>b</sup>
1	Pd(PPh <sub>3</sub> ) <sub>4</sub> (5)	PhMe	K <sub>2</sub> CO <sub>3</sub>	60	30 min	53
2 <sup>c</sup>	Pd(PPh <sub>3</sub> ) <sub>4</sub> (5)	PhMe	K <sub>2</sub> CO <sub>3</sub>	60	3 h	trace
3	Pd(PPh <sub>3</sub> ) <sub>4</sub> (5)	PhMe	K <sub>2</sub> CO <sub>3</sub>	80	30 min	64
4	Pd(PPh <sub>3</sub> ) <sub>4</sub> (5)	PhMe	Cs <sub>2</sub> CO <sub>3</sub>	80	30 min	45
5	Pd(PPh <sub>3</sub> ) <sub>4</sub> (5)	PhMe	Et <sub>3</sub> N	60	30 min	50
6	Pd(PPh <sub>3</sub> ) <sub>4</sub> (2.5)	PhMe	<sup>t</sup> Pr <sub>2</sub> NH	80	15 min	74
7 <sup>d</sup>	<b>Pd(PPh<sub>3</sub>)<sub>4</sub>(2.5)</b>	<b>PhMe</b>	<b><sup>t</sup>Pr<sub>2</sub>NH</b>	<b>80</b>	<b>15 min</b>	<b>82<sup>e,f</sup></b>
8 <sup>d</sup>	Pd(PPh <sub>3</sub> ) <sub>4</sub> (2.5)	DCE	<sup>t</sup> Pr <sub>2</sub> NH	80	5 min	68
9	Pd(PPh <sub>3</sub> ) <sub>4</sub> (5)	MeCN	K <sub>2</sub> CO <sub>3</sub>	60	12 h	8
10 <sup>d</sup>	Pd(OAc) <sub>2</sub> (2.5)	PhMe	<sup>t</sup> Pr <sub>2</sub> NH	80	2 h	19
11 <sup>d</sup>	PdCl <sub>2</sub> (PPh <sub>3</sub> ) <sub>2</sub> (2.5)	PhMe	<sup>t</sup> Pr <sub>2</sub> NH	80	30 min	27
12 <sup>d</sup>	Pd <sub>2</sub> (dba) <sub>3</sub> (2.5)/PPh <sub>3</sub> (10)	PhMe	<sup>t</sup> Pr <sub>2</sub> NH	80	15 min	41
13 <sup>d</sup>	Pd(OAc) <sub>2</sub> (2.5)/dppf(2.5)	PhMe	<sup>t</sup> Pr <sub>2</sub> NH	80	1 h	34
14	Pd(OAc) <sub>2</sub> (5)/PPh <sub>3</sub> (20)	PhMe	K <sub>2</sub> CO <sub>3</sub>	60	3.5 h	51
15 <sup>d</sup>	none	PhMe	<sup>t</sup> Pr <sub>2</sub> NH	80	15 h	0

<sup>a</sup> The reaction was carried out with 1.0 equiv of **1** and 3.0 equiv of **2a**.

<sup>b</sup> Isolated yield. <sup>c</sup> The reaction was carried out in the absence of BQ.

<sup>d</sup> Reaction run using 5 equiv of <sup>t</sup>Pr<sub>2</sub>NH. <sup>e</sup> Biphenyl was isolated in 6% yield based on **1**. <sup>f</sup> When 2.0 equiv of **2a** was used, **3a** was isolated in 76% yield.

**Table 2.** Pd(PPh<sub>3</sub>)<sub>4</sub>-Catalyzed Reaction of **2a**–**l** with **1**<sup>a</sup>

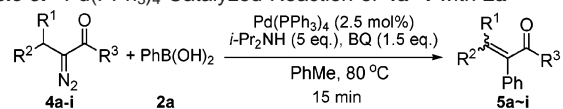
entry	2, Ar	3, yield (%) <sup>b</sup>	entry	2, Ar	3, yield (%) <sup>b</sup>
1	<b>2a</b> , C <sub>6</sub> H <sub>5</sub>	<b>3a</b> , 82	7	<b>2g</b> , <i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	<b>3g</b> , 86
2	<b>2b</b> , <i>o</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	<b>3b</b> , 88	8	<b>2h</b> , <i>m</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	<b>3h</b> , 58
3	<b>2c</b> , <i>m</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	<b>3c</b> , 83	9	<b>2i</b> , <i>p</i> -CHOC <sub>6</sub> H <sub>4</sub>	<b>3i</b> , 44
4	<b>2d</b> , <i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	<b>3d</b> , 83	10	<b>2j</b> , <i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	<b>3j</b> , 77
5	<b>2e</b> , <i>p</i> - <sup>t</sup> BuC <sub>6</sub> H <sub>4</sub>	<b>3e</b> , 83	11	<b>2k</b> , <i>p</i> -BrC <sub>6</sub> H <sub>4</sub>	<b>3k</b> , 77
6	<b>2f</b> , 3,5-Me <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	<b>3f</b> , 49	12	<b>2l</b> , 1-naphthyl	<b>3l</b> , 83

<sup>a</sup> The reaction was carried out with 1.0 equiv of **1** and 3.0 equiv of **2a**–**l**.

<sup>b</sup> Isolated yield.

Next we studied the scope of the reaction with various  $\alpha$ -diazocarbonyl compounds (Table 3). A series of  $\alpha$ -alkyl substituted diazocarbonyl compounds were examined and all gave the cross-coupling products in good yields. In the cases where trisubstituted olefins were formed, the *E* and *Z* selectivity were low (entries 2, 3, 4). Notably, tetra-substituted olefin, which is difficult to access, can be obtained in moderate yield (entry 5). The reaction also worked well with  $\alpha$ -diazoketones, including cyclic substrate (entries 6–9).

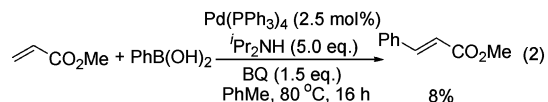
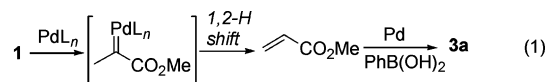
To elucidate the reaction mechanism of this novel palladium-catalyzed cross-coupling reaction, we examined the possibility of a process of 1,2-H shift of Pd–carbene intermediate,<sup>8</sup> followed by a Heck–Mizoroki-type reaction (eq 1).<sup>9</sup> When methyl acrylate and

**Table 3.** Pd(PPh<sub>3</sub>)<sub>4</sub>-Catalyzed Reaction of **4a–i** with **2a**<sup>a</sup>

entry	diazo <b>4a–i</b>	product	yield (%) <sup>b</sup>
1			84
2			92 (Z:E = 1:2.5)
3			80 (Z:E = 1:1.5) <sup>c</sup>
4			97 (Z:E = 1:2.3)
5			65
6			90
7			87
8			93
9			75

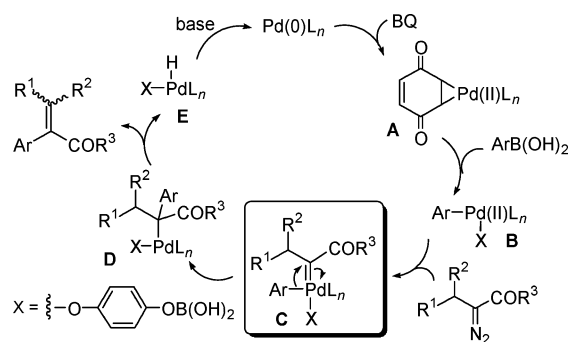
<sup>a</sup> Reaction conditions: **4a–i** (1 equiv), **2a** (3 equiv). <sup>b</sup> Isolated yield. <sup>c</sup> Ratio determined by <sup>1</sup>H NMR of the crude product.

phenylboronic acid were subjected to the identical reaction conditions, methyl cinnamate was isolated in low yield, and no **3a** could be detected (eq 2). Therefore, this pathway can be ruled out.



Very recently, Van Vranken and co-workers have reported palladium-catalyzed three-component coupling of vinyl halides, trimethylsilyldiazomethane, and amines to generate allylamines.<sup>6</sup> Barluenga and co-workers have reported a palladium-catalyzed cross-coupling reaction of *N*-tosylhydrazones and aryl halides, in which diazo compounds are generated in situ.<sup>7a</sup> In both reactions, palladium carbene species are suggested as the key intermediates, from which migratory insertion reactions occur.

On the basis of these results, we propose a possible mechanism as shown in Scheme 1. The reaction is initiated by the oxidation of Pd(0)L<sub>n</sub> by BQ to generate Pd(II) intermediate **A**. Then transmetalation with arylboronic acid takes place to give intermediate **B**. The reaction of  $\alpha$ -diazocarbonyl compound with palladium complex **B** would produce Pd complex **C**. Migratory insertion of

**Scheme 1.** Mechanistic Rationale

the aryl group to the carbenic carbon of the Pd–carbene gives intermediate **D**. Finally,  $\beta$ -hydride elimination of **D** affords the product and regenerates the Pd(0) species with the aid of base.

In summary, we have reported the first palladium-catalyzed cross-coupling reaction of  $\alpha$ -diazocarbonyl compounds with arylboronic acids. It provides a novel access to  $\alpha$ -aryl substituted  $\alpha,\beta$ -unsaturated carbonyl compounds. The reaction most likely proceeds through a migratory insertion of the Pd–carbene species, a process that has attracted attention only very recently.<sup>5c,e,6,7a,10</sup>

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**Supporting Information Available:** Experiment procedure and characterization data for all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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