

## Suzuki Coupling Reaction Catalyzed by Cyclopalladated Complexes of Tertiary Arylamines in Ionic Liquid

Hua YI, Jin Biao LIU, Qiang LI, Jie TANG\*

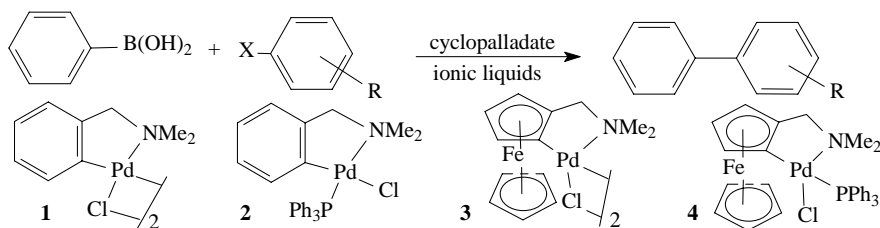
Department of Chemistry, East China Normal University, Shanghai 200062

**Abstract:** Suzuki cross-coupling reaction of phenylboronic acid with aryl halides catalyzed by cyclopalladated complexes of tertiary arylamines immobilized in ionic liquid  $[\text{Bmim}]^+\text{BF}_4^-$  was reported. The catalytic system proved to be efficient and be reused at least 3 times without significant loss of activity.

**Keywords:** Cyclopalladated complex, aryl halides, Suzuki coupling, biaryl, ionic liquid.

The Suzuki cross-coupling reaction<sup>1</sup> is one of the most powerful methodologies for the generation of new carbon-carbon bonds, particularly in the synthesis of biaryls. The traditional Suzuki cross-coupling reaction, however, suffers from a number of drawbacks such as catalyst loss into the product, catalyst decomposition and poor reagent solubility. Ionic liquids, because of their great versatility of chemical and physical properties<sup>2</sup>, have been demonstrated to be ideal immobilizing agents for various transition-metal catalyst precursors. And the organic products can be easily separated from the ionic solution. Thus, the above problems of traditional Suzuki coupling may be solved by the use of ionic liquids as reaction media<sup>3</sup>. Cyclopalladates are the most recently developed and studied homogenous palladium catalysts and represent the most promising ones in C-C bond-forming reactions because of their structural versatility and easy synthetic accessibility<sup>4</sup>. In our previous study, the thermally and air stable cyclopalladated complexes of tertiary arylamines **1**, **2**, **3** and **4** (Scheme 1) had been successfully applied in Heck coupling<sup>5</sup> and Ullmann coupling in ionic liquid<sup>6</sup>.

**Scheme 1** Suzuki-coupling catalyzed by cyclopalladates in ionic liquids



\* E-mail: jtang@chem.ecnu.edu.cn.

The cyclopalladated complexes of tertiary arylamines **1-4** could be readily prepared<sup>7</sup>. Herein we further report the application of **1-4** as catalysts for Suzuki cross coupling in ionic liquid.

The reaction of 4-bromoanisole with phenylboronic acid in [Bmim]<sup>+</sup>BF<sub>4</sub><sup>-</sup> was initially investigated using 1.0% eq. complex **4** as catalyst and 3eq. Na<sub>2</sub>CO<sub>3</sub> as base. Unfortunately, the result was disappointing with a yield less than 5% (**Table 1**, entry 1). But when some water was added to the reaction mixture, the cross-coupling product, 4-methoxybiphenyl, was produced in good yield (**Table 1**, entry 4). The dramatic effect of water on the reaction was possibly due to the solubility of Na<sub>2</sub>CO<sub>3</sub> and removal of the by-products KHCO<sub>3</sub> and K[XB(OH)<sub>3</sub>] generated in the reaction<sup>8</sup>. Triethylamine was less efficient than Na<sub>2</sub>CO<sub>3</sub> for the cross-coupling reaction (**Table 1**, entries 6 and 7). However, a poor yield was obtained when the coupling reaction was conducted in [Bmim]<sup>+</sup>Br<sup>-</sup> (**Table 1**, entry 5).

**Table 1** Cross-coupling of 4-bromoanisole with phenylboronic acid catalyzed by cyclopalladate **4**<sup>a</sup>

Entry	Ionic liquid	Water/mL	Base	Time/h	Yield <sup>b</sup>
1	[Bmim] <sup>+</sup> BF <sub>4</sub> <sup>-</sup>	0	Na <sub>2</sub> CO <sub>3</sub>	4	<5
2	[Bmim] <sup>+</sup> BF <sub>4</sub> <sup>-</sup>	0.8	Na <sub>2</sub> CO <sub>3</sub>	1	8
3	[Bmim] <sup>+</sup> BF <sub>4</sub> <sup>-</sup>	0.8	Na <sub>2</sub> CO <sub>3</sub>	2	50
4	[Bmim] <sup>+</sup> BF <sub>4</sub> <sup>-</sup>	0.8	Na <sub>2</sub> CO <sub>3</sub>	3	79(0:100) <sup>c</sup>
5	[Bmim] <sup>+</sup> Br <sup>-</sup>	0.8	Na <sub>2</sub> CO <sub>3</sub>	4	<5
6	[Bmim] <sup>+</sup> BF <sub>4</sub> <sup>-</sup>	0	Et <sub>3</sub> N	4	18 <sup>d</sup> (42:58) <sup>c</sup>
7	[Bmim] <sup>+</sup> BF <sub>4</sub> <sup>-</sup>	0.8	Et <sub>3</sub> N	4	55 <sup>d</sup> (7:93) <sup>c</sup>

<sup>a</sup> Reaction Condition: 4-Bromoanisole 0.5 mmol, phenylboronic acid 0.6 mmol, base 1.5 mmol, PPh<sub>3</sub> 0.02 mmol and complex **4** (1.0 mol% Pd) was heated 105-110°C in 2 mL ionic liquid.

<sup>b</sup> Isolated yield. <sup>c</sup> Homo-coupling (mol) /cross-coupling (mol). <sup>d</sup> The two products were difficult to separate.

**Table 2** Palladium catalyzed 4-bromoanisole with phenylboronic acid<sup>a</sup>

Entry	Catalyst	Time(h)	Yield <sup>b</sup>
1	PdCl <sub>2</sub>	8	66
2	<b>1</b>	5	53
3	<b>2</b>	5	38
4	<b>3</b>	5	84
5	<b>4</b>	5	81

<sup>a</sup> Reaction condition: 4-Bromoanisole 0.5 mmol, phenylboronic acid 0.6 mmol, base 1.5 mmol, PPh<sub>3</sub> 0.02 mmol, water 0.8 mL and catalyst (1.0 mol%Pd) was heated 105-110°C in 2 mL ionic liquid [Bmim]<sup>+</sup>BF<sub>4</sub><sup>-</sup>. <sup>b</sup> Isolated yield.

The catalysts including complexes **1-4** and PdCl<sub>2</sub> for Suzuki cross-coupling reaction were investigated using the model reaction of 4-bromoanisole with phenylboronic acid in ionic liquid [Bmim]<sup>+</sup>BF<sub>4</sub><sup>-</sup> and the results are summarized in **Table 2**.

From **Table 2**, it could be seen that complex **3** and **4** showed higher catalytic activity than **1** and **2** for Suzuki cross-coupling reaction in ionic liquid (**Table 2**, entries

2–5), which was different from Ullmann coupling reaction<sup>6</sup>. Palladium chloride PdCl<sub>2</sub> could also catalyze the Suzuki coupling reaction (Table 2, entry 1) with a catalytic activity higher than **1** and **2**, but lower than **3** and **4**. The activity of PdCl<sub>2</sub> should be attributed to the *in situ* formation of palladium N-heterocarbene complex<sup>9</sup>.

The reaction activity of aryl halides decreased from iodides, bromides to chlorides. In order to investigate the electronic and steric effects of aryl halides on Suzuki coupling reaction in ionic liquid, the reaction of various substituted aryl halides with phenylboronic acid was conducted under the optimized reaction condition (Table 3). Both electro-donating and withdrawing groups on the aryl halides, such as MeO or COOH showed few effects on the cross-coupling products (Table 3, entries 1, 3 and 5). However, 1-bromo-4-nitrobenzene, looked like to destroy the catalyst thus no coupling product was detected under identical conditions. Steric factors affected the reaction significantly. For example, *para*-methyl iodobenzene, gave higher yield than the *ortho* one (Table 3, entries 6 and 7).

**Table 3** Suzuki coupling reaction of arylhalides with phenylboronic acid<sup>a</sup>

Entry	R	X	Time(h)	Yield
1	4-CHO	Br	3	81 <sup>b</sup>
2	4-CH <sub>3</sub>	Br	3 / 6 / 12	62 <sup>c</sup> / 76 <sup>c</sup> / 80 <sup>c</sup>
3	4-OCH <sub>3</sub>	Br	3	79 <sup>b</sup>
4	4-CH <sub>3</sub>	Cl	6	14 <sup>c</sup>
5 <sup>d</sup>	4-COOH	I	3	85 <sup>c</sup>
6	4-CH <sub>3</sub>	I	3	88 <sup>c</sup>
7	2-CH <sub>3</sub>	I	3	41 <sup>c</sup>

<sup>a</sup>Reaction Condition: aryl halide 0.5 mmol, phenylboronic acid 0.6 mmol, Na<sub>2</sub>CO<sub>3</sub> 1.5 mmol, PPh<sub>3</sub> 0.02 mmol, water 0.8 mL and catalyst (1.0 mol% Pd) was heated 105–110°C in 2 mL ionic liquid [Bmim]<sup>+</sup>BF<sub>4</sub><sup>-</sup>. <sup>b</sup>Isolated yield. <sup>c</sup>GC yield. <sup>d</sup>Na<sub>2</sub>CO<sub>3</sub> 2.0 mmol.

**Table 4** Recycling of the cyclopalladate **4** in the cross-coupling of 4-bromoanisole with phenylboronic acid<sup>a</sup>

Run	Bromide(%) <sup>b</sup>	Biphenyl (%) <sup>b</sup>	Cross-coupling(%) <sup>b</sup>	Homo-coupling(%) <sup>b</sup>
1	23	9	62	6
2	29	7	59	5
3	39	4	57	---

<sup>a</sup>Reaction Condition: 4-bromotoluene 0.5 mmol, phenylboronic acid 0.6 mmol, Na<sub>2</sub>CO<sub>3</sub> 1.5 mmol, PPh<sub>3</sub> 0.02 mmol, water 0.8 mL and **4** (1.0 mol% Pd) was heated 105–110°C in 2 mL [Bmim]<sup>+</sup>BF<sub>4</sub><sup>-</sup>.

<sup>b</sup>Detected by GC.

Recovery of the catalyst cyclopalladated complex **4** for the cross-coupling reaction of 4-bromotoluene with phenylboronic acid in ionic liquid [Bmim]<sup>+</sup>BF<sub>4</sub><sup>-</sup> was investigated. The results are listed in Table 4. It was found that complex **4** could be reused at least 3 times without losing the catalytic activity (Table 4, entries 1, 2 and 3).

In summary, we have demonstrated that the cyclopalladated complexes can be successfully applied as efficient catalysts in Suzuki coupling reaction of aryl halides with phenylboronic acid in ionic liquid [Bmim]<sup>+</sup>BF<sub>4</sub><sup>-</sup>. Compared with the traditional

reaction conditions for Suzuki coupling reaction, the advantages of cyclopalladates-ionic liquids catalytic system are obvious. The cyclopalladate **4** and the ionic liquid [Bmim]<sup>+</sup>BF<sub>4</sub><sup>-</sup> are readily accessible and air-stable. And more importantly, polar volatile organic solvents that are normally required for the Suzuki coupling reaction were successfully replaced with involatile [Bmim]<sup>+</sup>BF<sub>4</sub><sup>-</sup>, making the work-up procedure simple and environmentally friendly. The catalyst cyclopalladate **4** immobilized in ionic liquid can be easily recycled and reused 3 times without significant loss of activity, showing potentials as a practical and economical catalytic system for the preparation of widely used biaryl compounds. Work along this line is in progress in our laboratory.

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