



## Pd–CNT-catalyzed ligandless and additive-free heterogeneous Suzuki–Miyaura cross-coupling of arylbromides

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### ABSTRACT

Pd–CNT efficiently catalyzed Suzuki–Miyaura coupling of arylbromides under ligandless and additive-free conditions in aqueous media. For hydrophilic substrates, the reaction could be carried out in neat water.

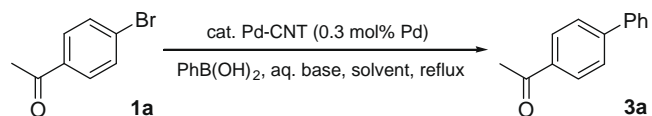
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Suzuki–Miyaura cross-coupling is one of the most powerful and versatile methods for the synthesis of biaryls.<sup>1</sup> During the last decades, numerous modifications to the standard protocol have emerged to either improve its scope<sup>2</sup> and efficiency,<sup>3</sup> or to render it more economic and environmental friendly.<sup>4</sup> Most of these approaches concentrated on two key aspects, namely, the ligand<sup>5</sup> and the additive.<sup>6</sup> Normally, Suzuki coupling requires either a ligand or an additive to stabilize the Pd species during the reaction, otherwise Pd<sup>0</sup> tends to aggregate and precipitate before completion of the reaction. To our knowledge, coupling that is both ligandless and additive-free is rare, and the type of catalyst is limited to Pd/C<sup>7</sup> and colloidal Pd nanoparticles (NPs),<sup>8</sup> including those formed by using Pd(II) salts as the pre-catalysts.<sup>9</sup>

Recently metal-decorated carbon nanotubes (CNTs) have attracted considerable interests from multiple disciplines due to their interesting catalytic, electrical, and mechanical properties as well as the significance in material sciences.<sup>10</sup> Ideally, Pd–CNT could offer conspicuous advantages of heterogeneous catalysis<sup>11</sup> while retaining high catalytic activity of NPs. Thus, such catalysts would be highly desirable from the perspectives of transition metal catalysis, green chemistry, and sustainable chemistry. Herein we describe Suzuki coupling of arylbromides catalyzed by Pd–CNT under ligandless and additive-free conditions in aqueous media.

The Pd–CNT catalysts used in this work were prepared by depositing Pd(dba)<sub>2</sub> on purified MWCNT<sup>12</sup> followed by activation under reductive atmosphere. Optimization of reaction parameters for Suzuki coupling was carried out using 4-bromoacetophenone (**1a**) and phenylboronic acid (**2a**) as the coupling partners (Table 1).

**Table 1**  
Optimization of reaction conditions<sup>a</sup>



Entry	Solvent	Base	Time (h)	Yield <sup>b</sup> (%)
1	EtOH	2 M Na <sub>2</sub> CO <sub>3</sub>	3	95
2	Acetone	2 M Na <sub>2</sub> CO <sub>3</sub>	12	85
3	MeCN	2 M Na <sub>2</sub> CO <sub>3</sub>	12	~5
4	Toluene	2 M Na <sub>2</sub> CO <sub>3</sub>	12	NR
5	Dioxane	2 M Na <sub>2</sub> CO <sub>3</sub>	12	81
6	EtOH	2 M K <sub>2</sub> CO <sub>3</sub>	3	98
7	EtOH	satd NaHCO <sub>3</sub>	3	NR
8	EtOH	2 M NaOAc	3	NR
9 <sup>c</sup>	EtOH	2 M Na <sub>2</sub> CO <sub>3</sub>	12	86
10 <sup>d</sup>	EtOH	2 M Na <sub>2</sub> CO <sub>3</sub>	3	97

<sup>a</sup> Conditions: 0.5 mmol **1a**, 0.75 mmol PhB(OH)<sub>2</sub>, 3.0 mg 5 wt % Pd–CNT (0.3 mol % Pd), 4.0 mL solvent, 2.0 mL base solution, reflux.

<sup>b</sup> Isolated yields.

<sup>c</sup> 15 mg 1.0 wt % Pd–CNT was used as the catalyst, 0.3 mol % Pd.

<sup>d</sup> 1.5 mg 10 wt % Pd–CNT was used as the catalyst, 0.3 mol % Pd.

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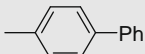
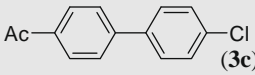
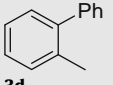
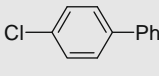
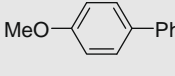
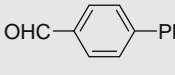
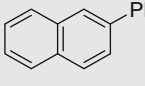




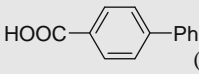
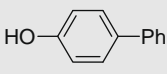
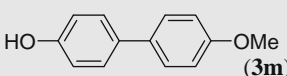
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The catalyst loading was fixed at 0.3 mol % of Pd with regard to the substrate. It was found that ethanol–H<sub>2</sub>O (2:1) constituted the best solvent system, affording excellent yield in a short time, while combinations of other common solvents for Suzuki coupling with water gave inferior results (entries 2–5). As a trend, water-miscible solvents such as acetone and dioxane fared much better than hydrophobic hydrocarbon solvents (toluene and benzene). The effect of base was also investigated. Generally, 2 M aq Na<sub>2</sub>CO<sub>3</sub> was satisfactory for most cases, and 2 M K<sub>2</sub>CO<sub>3</sub> gave slightly higher

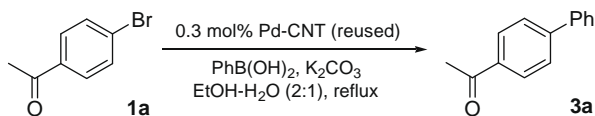
yields. Weaker bases such as NaHCO<sub>3</sub> and NaOAc were not effective. The metal loading on CNT exhibited pronounced effects on the reaction rate and yield. Albeit the total amount of Pd remained the same, using catalyst of lower Pd content (1 wt % on CNT) decelerated the reaction, and lower yield was obtained after an extended reaction time. On the other hand, the performance of 5% and 10% Pd–CNTs was comparable, and the yield obtained by the latter was only marginally higher. Thus throughout our subsequent study, 5 wt % Pd–CNT was used as the standard catalyst.

**Table 2**  
Pd–CNT-catalyzed Suzuki coupling

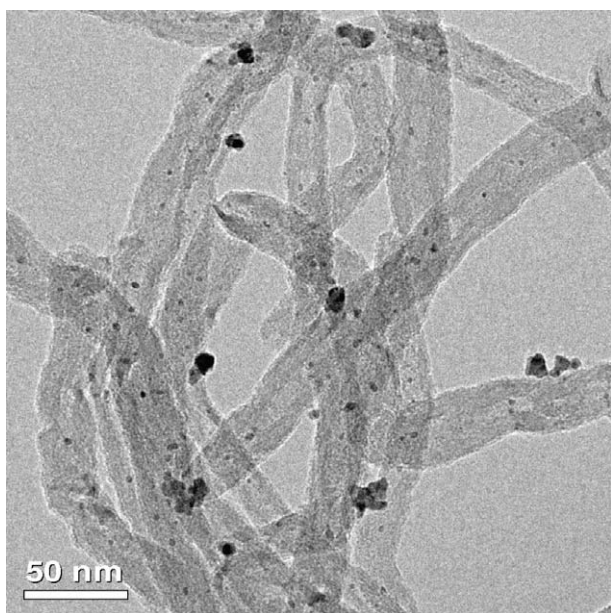
Entry	Ar–Br ( <b>1</b> )	Ar'–B(OH) <sub>2</sub> ( <b>2</b> )	Solvent	Base	Time (h)	Product ( <b>3</b> )	Yield <sup>a</sup> (%)
1	4-MeC <sub>6</sub> H <sub>4</sub> Br ( <b>1b</b> )	PhB(OH) <sub>2</sub> ( <b>2a</b> )	EtOH	2 M Na <sub>2</sub> CO <sub>3</sub>	6	 ( <b>3b</b> )	75
2	<b>1b</b>	<b>2a</b>	EtOH	2 M K <sub>2</sub> CO <sub>3</sub>	7	<b>3b</b>	99
3	<b>1a</b>	4-ClC <sub>6</sub> H <sub>4</sub> B(OH) <sub>2</sub> ( <b>2b</b> )	EtOH	2 M K <sub>2</sub> CO <sub>3</sub>	8	 ( <b>3c</b> )	90
4	2-MeC <sub>6</sub> H <sub>4</sub> Br ( <b>1c</b> )	<b>2a</b>	EtOH	2 M Na <sub>2</sub> CO <sub>3</sub>	8	 ( <b>3d</b> )	67
5	<b>1c</b>	<b>2a</b>	EtOH	2 M K <sub>2</sub> CO <sub>3</sub>	8	<b>3d</b>	70
6	4-ClC <sub>6</sub> H <sub>4</sub> Br ( <b>1d</b> )	<b>2a</b>	EtOH	2 M Na <sub>2</sub> CO <sub>3</sub>	6	 ( <b>3e</b> )	80
7	<b>1d</b>	<b>2a</b>	EtOH	2 M K <sub>2</sub> CO <sub>3</sub>	8	<b>3e</b>	96
8	4-MeOC <sub>6</sub> H <sub>4</sub> Br ( <b>1e</b> )	<b>2a</b>		2 M Na <sub>2</sub> CO <sub>3</sub>	8	 ( <b>3f</b> )	99
9	4-OHCC <sub>6</sub> H <sub>4</sub> Br ( <b>1f</b> )	<b>2a</b>	EtOH	2 M Na <sub>2</sub> CO <sub>3</sub>	6	 ( <b>3g</b> )	93
10	2-C <sub>10</sub> H <sub>7</sub> Br ( <b>1g</b> )	<b>2a</b>	EtOH	2 M Na <sub>2</sub> CO <sub>3</sub>	16	 ( <b>3h</b> )	92
11	 ( <b>1h</b> )	<b>2a</b>	EtOH	2 M Na <sub>2</sub> CO <sub>3</sub>	8	 ( <b>3i</b> )	85
12	 ( <b>1i</b> )	<b>2a</b>	EtOH	2 M Na <sub>2</sub> CO <sub>3</sub>	7	 ( <b>3j</b> )	97
13	4-HO <sub>2</sub> CC <sub>6</sub> H <sub>4</sub> Br ( <b>1j</b> )	<b>2a</b>	EtOH	2 M Na <sub>2</sub> CO <sub>3</sub>	10	 ( <b>3k</b> )	90
14	<b>1j</b>	<b>2a</b>	H <sub>2</sub> O	2 M Na <sub>2</sub> CO <sub>3</sub>	10	<b>3k</b>	96
15	4-HOC <sub>6</sub> H <sub>4</sub> Br ( <b>1k</b> )	<b>2a</b>	H <sub>2</sub> O	2 M Na <sub>2</sub> CO <sub>3</sub>	10	 ( <b>3l</b> )	99
16	<b>1k</b>	4-MeOC <sub>6</sub> H <sub>4</sub> B(OH) <sub>2</sub> ( <b>2c</b> )	H <sub>2</sub> O	2 M Na <sub>2</sub> CO <sub>3</sub>	12	 ( <b>3m</b> )	94
17 <sup>b</sup>	4-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> Cl ( <b>1l</b> )	<b>2a</b>	EtOH	2 M K <sub>2</sub> CO <sub>3</sub>	12	–	NR

<sup>a</sup> Isolated yields.

<sup>b</sup> Reaction attempted at 90 and 120 °C.

**Table 3**  
Catalyst recycle study

Run	Reaction time (h)	Yield <b>3a</b> <sup>a</sup> (%)
1	3	95
1st reuse	3	95
2nd reuse	3	94
3rd reuse	3.5	94

<sup>a</sup> Isolated yields.**Figure 1.** TEM image of 5 wt % Pd-CNT catalyst.

With this encouraging result in hand, the scope of the Pd-CNT-catalyzed Suzuki coupling was examined next (Table 2). Various arylbromides were subject to the optimized conditions, and excellent yields (up to quantitative) were obtained.<sup>13</sup> Both electron-deficient (entries 3 and 9) and electron-rich substrates (**1e**, **1k**) coupled efficiently. For some hydrophobic substrates (**1b**, **1d**), the difference of Na<sub>2</sub>CO<sub>3</sub> and K<sub>2</sub>CO<sub>3</sub> was significant, the use of the latter markedly increased the reaction rate and yields owing to possible template effect of the cation.<sup>14</sup> Substrate with *ortho*-substitution to the reaction site (**1c**) gave lower yield due to higher steric hindrance. Representative heteroaromatic substrates (**1h**, **1i**) also underwent smooth coupling. It is noteworthy that Suzuki coupling of hydrophilic substrates such as phenols (**1k**) and benzoic acids (**1j**) can be carried out in neat water, which afforded even better yields than the mixed solvents of aqueous ethanol (entries 13–16). In addition, the unmasked carboxylic acid and phenol group in these substrates, which often caused difficulties, were both compatible with the present protocol.<sup>15</sup> With regard to chemoselectivity, this catalytic system did not affect arylchlorides (**1d**), even that activated by a nitro group in the *para*-position at a higher reaction temperature (entry 17).

Catalyst recycling experiments were also carried out. Using the recycled Pd-CNT, the subsequent runs went to completion in comparable reaction time, and the yields obtained were as good as that

obtained for fresh catalyst, demonstrating the robustness of the Pd-CNT system (Table 3).

Our catalyst was characterized by transmission electron microscopy, and the resulting TEM image clearly showed that nano-sized Pd particles are supported on CNTs. Smaller and highly dispersed palladium NPs are much more abundant than larger aggregated ones (Fig. 1). We speculate that CNTs not only provided a high surface-to-volume ratio backbone like other nano materials did, but also possessed some unique stabilizing or accelerating factors for the active catalytic species. One of such factors could arise from the residual carboxylic acid groups formed during oxidative pre-treatment of CNTs in the preparation of the catalysts.<sup>16</sup> Mechanistic investigations along this line have been initiated.

In summary, we have shown that multi-walled carbon nanotubes (MWCNTs) are excellent support for Pd<sup>0</sup> and the resulting Pd-CNT efficiently catalyzed Suzuki-Miyaura cross-coupling of arylbromides with arylboronic acids. The reaction was carried out in aqueous solvents or neat water without the assistance of any ligands or additives, and the catalyst could be recovered by simple filtration, thus meeting the criteria of green chemistry. The low catalyst loading as well as simple reaction setup is also economically attractive. More detailed catalyst characterizations including EDX are underway. Extension of the use of Pd-CNT to other Pd-catalyzed reactions is currently pursued.

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