

## Cationic Palladium(II) Catalysis: C–H Activation/Suzuki–Miyaura Couplings at Room Temperature

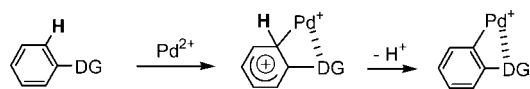
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Notwithstanding the extraordinary progress being made in Pd-catalyzed cross-couplings involving nitrogen- or oxygen-based directing groups (DG) for C–H activation chemistry, Suzuki–Miyaura couplings under very mild, room temperature conditions remain very rare.<sup>1,2</sup> Most of the highly successful approaches to date employ a combination of neutral palladium acetate as catalyst and high temperatures (>120 °C) in aromatic C–H activations.<sup>3</sup> The increased nucleophilicity of reaction partners along with acidic conditions often assist in the desired bond constructions.<sup>4</sup> Mechanistic studies indicate that aromatic C–H bonds, independent of temperature, are activated with the aid of carboxylate or carbonate anions.<sup>5,6</sup> Alternatively, electrophilic C–H activation<sup>1,5,7</sup> with cationic palladium at room temperature has been advanced (Scheme 1). While not yet of general applicability, it does raise the intriguing notion of tuning cationicity of the catalyst,<sup>8,9</sup> potentially leading to far milder conditions for C–H

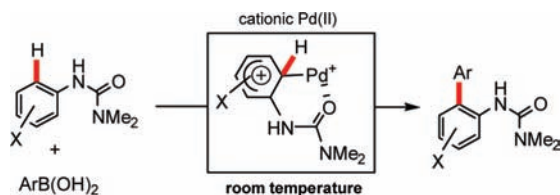
### Scheme 1. Electrophilic C–H Activation with Cationic Pd(II)



DG = directing group

activation/coupling with arylboronic acids. Herein, we report Suzuki–Miyaura couplings with aryl ureas catalyzed by a preformed cationic palladium(II) complex, which provide aniline derivatives at room temperature in the absence of metal oxidants or added acid (Scheme 2).

### Scheme 2. C–H Activation/Suzuki–Miyaura Coupling Catalyzed by Cationic Pd(II)



Initially, a study was conducted of several neutral palladium catalysts, such as Pd(OAc)<sub>2</sub>, PdCl<sub>2</sub>, and Pd<sub>2</sub>(dba)<sub>3</sub>, but none were effective (<1% biaryl). On the other hand, the combination of anilide **1a** and phenylboronic acid (**2a**, 3 equiv) in the presence of [Pd(MeCN)<sub>4</sub>](BF<sub>4</sub>)<sub>2</sub> (10 mol %) and 1,4-benzoquinone (BQ, 5 equiv) dramatically improved the extent of product formation (Table 1). While several solvents under otherwise identical conditions gave the desired biaryl in low-to-moderate yields (runs 1–6), C–H activation in EtOAc led to **3a** in 96% isolated yield (run 7). Decreased amounts of both phenylboronic acid (**2a**) and BQ could be used with equal success; lower catalyst loading, however, led to far slower reactions. Thus, this cationic palladium(II) catalyst enhances not only the rate of C–H activation<sup>10</sup> but also that for transmetalation with an arylboronic acid, which otherwise requires *ate* formation.<sup>11</sup> The BQ present is known to promote reductive elimination in metal-catalyzed couplings.<sup>12</sup>

Table 1. Solvent Effects<sup>a</sup>

run	solvent	yield (%)	run	solvent	yield (%)
1	hexane	50	5	DMF	31
2	THF	80	6	2% surfactant/water	trace
3	acetone	38	7	EtOAc	96
4	EtOH	70	8	EtOAc	94 <sup>b</sup>

<sup>a</sup> Conducted at rt for 20 h with 10 mol % [Pd(MeCN)<sub>4</sub>](BF<sub>4</sub>)<sub>2</sub>, 1,4-benzoquinone (BQ) (5 equiv), **1a** (0.25 mmol), and **2a** (3 equiv).  
<sup>b</sup> 1.5 equiv of **2a** and 3 equiv of BQ.

Under optimized conditions, various arylboronic acids having electron-donating or -withdrawing groups reacted smoothly with aromatic ureas in high yields (Table 2).<sup>13</sup> Indications that functional group tolerance appears to be good can be found from products **3d–3f** and **3k–3m**, likely reflecting the mildness of the C–H activation event. Especially noteworthy is the general trend of selective directed monoarylation (**3w–3bb**), which is typically not the case with symmetrical coupling partners.<sup>2,3</sup>

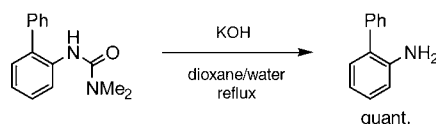
Pd(OAc)<sub>2</sub> is also reactive in this reaction but undergoes C–H Suzuki–Miyaura coupling only in the presence of an additional strong acid, HBF<sub>4</sub> (Scheme 3). Under such acidic conditions, Pd(OAc)<sub>2</sub> may release an acetate anion to generate cationic Pd(II) species.<sup>14</sup>

### Scheme 3. C–H Activation Catalyzed by Pd(OAc)<sub>2</sub>



The dimethylurea moiety was easily removed under general hydrolysis conditions to produce the corresponding amine quantitatively (Scheme 4).

### Scheme 4. Deprotection



In summary, the dramatic effect of cationic palladium in Suzuki–Miyaura reactions has been uncovered, which enables facile aromatic C–H activation and subsequent cross-couplings at room temperature. Mechanistic studies on these highly reactive cationic complexes are ongoing to further elucidate the nature of the active catalyst formed

Table 2. Representative Couplings<sup>a</sup>

products									

<sup>a</sup> Conducted at rt for 20 h with 10 mol % [Pd(MeCN)<sub>4</sub>](BF<sub>4</sub>)<sub>2</sub>, BQ (2 or 5 equiv), **1** (0.25 mmol), and **2** (1.5 or 3 equiv). The ratios of single/double arylation determined by <sup>1</sup>H NMR are shown in the parentheses. <sup>b</sup> Run for 48 h. <sup>c</sup> 2 equiv of BQ. <sup>d</sup> 1.5 equiv of **2**.

in related C–H activation reactions catalyzed by neutral Pd(OAc)<sub>2</sub> at higher temperatures or in strongly acidic media.

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**Supporting Information Available:** Experimental details. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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