

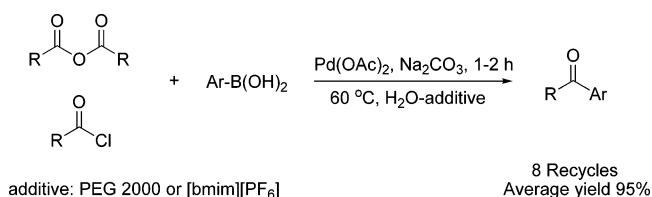
## Phosphine-Free Cross-Coupling Reaction of Arylboronic Acids with Carboxylic Anhydrides or Acyl Chlorides in Aqueous Media

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The palladium acetate-catalyzed coupling reaction of aryl boronic acid with carboxylic anhydride or acyl chloride was carried out smoothly in water in the presence of poly(ethylene glycol) (PEG) or 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF<sub>6</sub>]) to give high yields of ketones without the use of phosphine ligands. The Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-[bmim][PF<sub>6</sub>] catalytic system can be recovered and reused eight times with high efficiency for both carboxylic anhydride and acyl chloride.

### Introduction

Aryl ketones are important building blocks in the synthesis of natural products and pharmaceutical compounds, and a number of approaches for the preparation of aryl ketones have been introduced.<sup>1</sup> One general approach is the Friedel–Crafts acylation of substituted aromatic rings.<sup>2</sup> The crucial disadvantage of traditional Friedel–Crafts acylation is the use of more than a stoichiometric amount of aluminum trichloride, which is incompatible with many functional groups and generates a large amount of waste. Furthermore, the formation of ortho and para isomers with the untunable regioselectivity results in separation problems and makes the aryl ketones with meta substituent difficult to access. In contrast, the acylation of aryl metal species with functional carboxylic acid derivatives leads to single regioisomers and is extensively applied in the synthesis of aryl

ketones.<sup>3</sup> Generally, the mild organometallic compounds, such as organotin,<sup>4</sup> -zinc,<sup>5</sup> -cadmium,<sup>6</sup> or -boron reagents,<sup>7</sup> can be used for the active acid chlorides, and more aggressive carbon nucleophiles, usually Grignard or organolithium compounds, are required for the less active acid derivatives (i.e., anhydrides and amides).<sup>8</sup> The formation of tertiary alcohols, however, diminishes the yields in some cases.<sup>9</sup>

Recently, Yamamoto et al.<sup>10</sup> and Goossen et al.<sup>11</sup> reported independently a new method for obtaining aryl ketones under

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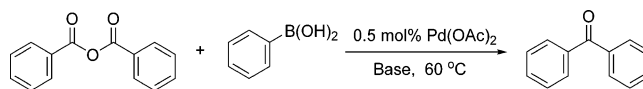
mild conditions based on the cleavage of the C–O bond of carboxylic anhydrides in the presence of palladium catalysts. This method is superior to the previous methods in terms of reaction conditions, efficiency, and functional group compatibility. However, both Yamamoto's and Goossen's studies showed that the phosphine ligands played a key role in the successful execution of the reactions, and no ketone product was obtained under the given conditions in the absence of phosphine ligands.

Concerns over hazardous waste generated during the catalytic reactions and separation of the products from the catalyst led to increasing attention on the use of less toxic and environmentally compatible materials in the design of new synthetic methods. Recently, the reaction in water has attracted much attention, and there is increasing recognition that organic reactions carried out in water may offer advantages over those in organic solvents.<sup>12</sup> We have recently described the phosphine-free palladium acetate-catalyzed Suzuki reaction in aqueous media in the presence of poly(ethylene glycol) (PEG)<sup>13a</sup> or ionic liquid.<sup>13b</sup> These catalytic systems are air-stable, insensitive to moisture, and reusable with impressive reactivity for a wide range of substrates. Herein, we report on the evaluation of palladium-catalyzed cross-coupling of aryl boronic acid with carboxylic anhydride or acyl chloride in the absence of phosphine ligands in water. The method is straightforward, and the ketones can be synthesized under mild reaction conditions in high yields in short reaction times.

## Results and Discussion

Our initial experiments comprised attempts to accomplish the reaction in water in the presence of 0.5 mol % Pd(OAc)<sub>2</sub>. Similar to the results of Suzuki reaction in aqueous media,<sup>13</sup> the reaction in pure water, pure PEG, or pure ionic liquid delivered poor yields (Table 1, entries 1, 2, 14). The addition of PEG led to a rapid increase of activity in the aqueous media (Table 1, entries 3–5), and the optimal ratio of water and PEG was 3:3 g (Table 1, entry 4). The catalytic system was perfectly stable to air, and the reaction could be conducted without the rigorous exclusion of oxygen. Among the PEG species tested, including

**TABLE 1.** Coupling Reaction of Phenylboronic Acid with Benzoic Anhydride in Water with Different Bases<sup>a</sup>



| entry | base                            | solvent (g) <sup>b</sup>                          | time (h) | yield <sup>b</sup> (%) |
|-------|---------------------------------|---|----------|------------------------|
| 1     | Na <sub>2</sub> CO <sub>3</sub> | H <sub>2</sub> O (6)                              | 1        | 56                     |
| 2     | Na <sub>2</sub> CO <sub>3</sub> | PEG (6)   | 1        | 20                     |
| 3     | Na <sub>2</sub> CO <sub>3</sub> | PEG/H <sub>2</sub> O (3:2.5)                      | 1        | 89                     |
| 4     | Na <sub>2</sub> CO <sub>3</sub> | PEG/H <sub>2</sub> O (3:3)                        | 1        | 94                     |
| 5     | Na <sub>2</sub> CO <sub>3</sub> | PEG/H <sub>2</sub> O (3:3.5)                      | 1        | 90                     |
| 6     | Na <sub>2</sub> CO <sub>3</sub> | PEG/H <sub>2</sub> O (3:3)                        | 1        | 97 <sup>c</sup>        |
| 7     | Na <sub>2</sub> CO <sub>3</sub> | PEG/H <sub>2</sub> O (3:3)                        | 2        | 99                     |
| 8     | K <sub>2</sub> CO <sub>3</sub>  | PEG/H <sub>2</sub> O (3:3)                        | 2        | 90                     |
| 9     | K <sub>3</sub> PO <sub>4</sub>  | PEG/H <sub>2</sub> O (3:3)                        | 2        | 78                     |
| 10    | NaOAc                           | PEG/H <sub>2</sub> O (3:3)                        | 2        | 39                     |
| 11    | KOH                             | PEG/H <sub>2</sub> O (3:3)                        | 2        | 63                     |
| 12    | KF                              | PEG/H <sub>2</sub> O (3:3)                        | 2        | 71                     |
| 13    | Et <sub>3</sub> N               | PEG/H <sub>2</sub> O (3:3)                        | 2        | 50                     |
| 14    | Na <sub>2</sub> CO <sub>3</sub> | [bmim][PF <sub>6</sub> ]                          | 2        | 9                      |
| 15    | Na <sub>2</sub> CO <sub>3</sub> | [bmim][PF <sub>6</sub> ]/H <sub>2</sub> O (3:2.5) | 2        | 82                     |
| 16    | Na <sub>2</sub> CO <sub>3</sub> | [bmim][BF <sub>4</sub> ]/H <sub>2</sub> O (3:2.5) | 2        | 20                     |
| 17    | Na <sub>2</sub> CO <sub>3</sub> | [bmim][Cl]/H <sub>2</sub> O (3:2.5)               | 2        | NR                     |
| 18    | Na <sub>2</sub> CO <sub>3</sub> | [bmim][PF <sub>6</sub> ]/H <sub>2</sub> O (3:2.5) | 2        | 98 <sup>d</sup>        |

<sup>a</sup> Reaction conditions: Benzoic anhydride (1.0 mmol), PhB(OH)<sub>2</sub> (1.2 mmol), base (1.6 mmol). <sup>b</sup> Isolated yield. <sup>c</sup> Reaction temperature was 80 °C. <sup>d</sup> Pd(OAc)<sub>2</sub> was 1.8 mol %.

PEG 600, PEG 1000, PEG 2000, PEG 4000, and PEG 6000, PEG 2000 showed the best reactivity, and therefore PEG 2000 was used as the source of PEG throughout the studies. The increase of temperature from 60 to 80 °C has a positive effect on the acylation reaction (Table 1, entry 6), but more byproduct of biphenyl from the self-coupling of phenylboronic acid was observed. A prolongation of reaction time led to a profound increase in yield of benzophenone without the increase of biphenyl (Table 1, entry 7). The reaction under nitrogen presented virtually the same yields of desired product, albeit the amount of biphenyl was decreased. When the various bases were screened, Na<sub>2</sub>CO<sub>3</sub> and K<sub>2</sub>CO<sub>3</sub> resulted in a good yield (Table 1, entries 7 and 8). Moderate yields were afforded by using the bases of K<sub>3</sub>PO<sub>4</sub>, KOH, and KF (Table 1, entries 9, 11, 12). NaOAc and Et<sub>3</sub>N gave the desired product with low yields (Table 1, entries 10 and 13). It should be noted that the reaction rate in this aqueous condition was faster than that in organic solvent with the activation of phosphine ligands.<sup>10,11</sup>

As a new type of reaction media, ionic liquids have many unique properties,<sup>14</sup> and therefore we tested the palladium acetate-catalyzed acylation reaction in water using ionic liquids as the additives. It was found that hydrophobic 1-butyl-3-methylimidazolium hexafluorophosphate ([bmim][PF<sub>6</sub>]) could improve the cross-coupling reaction. Again, the ratio of water and [bmim][PF<sub>6</sub>] acted on the reactivity, and best yield was obtained when the ratio of [bmim][PF<sub>6</sub>] and water achieved 3:2.5 g (Table 1, entries 14 and 15). Compared with the Pd(OAc)<sub>2</sub>–H<sub>2</sub>O–PEG system, more Pd(OAc)<sub>2</sub> was required to complete the reaction under the reaction conditions with the Pd(OAc)<sub>2</sub>–H<sub>2</sub>O–[bmim][PF<sub>6</sub>] system (Table 1, entries 7 and 18). The efficiency of the ionic liquid was strongly influenced by the

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nature of the anions. For example, 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF<sub>4</sub>]) presented a very poor effect on the reactivity (Table 1, entry 16), and no reaction was observed in the mixture of water and hydrophilic 1-butyl-3-methylimidazolium chloride ([bmim][Cl]) under the reaction conditions (Table 1, entry 17).

The scope and limitations of the cross-coupling reaction in Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-PEG and Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-[bmim][PF<sub>6</sub>] were investigated, and the results are presented in Table 2. Either the electron-deficient or the electron-rich aryl boronic acid showed excellent reactivity and furnished the products in high yields in short reaction times in both catalytic systems (Table 2, entries 1–4). Naphthalen-2-ylboronic acid afforded the desired product in excellent yield (Table 2, entry 5). The more sterically hindered naphthalen-1-ylboronic acid also delivered the desired ketone in high yield (Table 2, entry 6). The catalytic systems were compatible with heteroarylboronic acids as exemplified in the reaction of thiophen-2-ylboronic acid and thiophen-3-ylboronic acid with benzoic anhydride to give the ketone in excellent yields (Table 2, entries 7 and 8).

The aromatic carboxylic anhydride with electron-donating substituents in benzoic anhydride could be converted into the corresponding ketones in good to excellent yields and showed little difference in the reactivity in the two systems (Table 2, entries 9–11). The reactivity of chlorobenzoic anhydride in Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-PEG was better, although all chlorobenzoic anhydrides delivered the desired ketones in good yields in the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-[bmim][PF<sub>6</sub>] system (Table 2, entries 12–14). The yields of 2-substituted chlorobenzoic anhydride were slightly decreased (Table 2, entry 14). Reactions involving the aromatic carboxylic anhydride bearing electron-withdrawing groups in benzoic anhydride delivered low yields in the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-PEG system, but moderate to good yields were obtained in the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-[bmim][PF<sub>6</sub>] system (Table 2, entries 15 and 16). The method was applicable to furan-2-carboxylic anhydride, and excellent yields were obtained in both of the systems (Table 2, entry 17). The reactions of aliphatic carboxylic anhydrides were sluggish in the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-PEG system, but the desired products were afforded in moderate yields in the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-[bmim][PF<sub>6</sub>] system under the reaction conditions (Table 2, entries 18 and 19).

Acyl chlorides are widely available acid derivatives and more active than carboxylic anhydride in the cross-coupling reaction with boronic acid, but sensitive to moisture.<sup>15</sup> We applied the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-PEG and Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-[bmim][PF<sub>6</sub>] systems to the cross-coupling of acyl chloride with aryl boronic acid, and we were pleased to find that the coupling reaction was quite general and efficient under our mild reaction conditions. After the optimization of reaction conditions, various ketones were prepared in good to excellent yield as shown in Table 3 in both systems, and the competitive hydrolysis for most of the acyl chlorides appears to be minimized. Except for 4-nitrobenzoyl chloride (Table 3, entry 15), all of the aryl acyl chlorides with both electron-releasing and electron-withdrawing substituents showed excellent reactivity in both systems (Table 3, entries 9–14). The aliphatic chlorides were more sensitive to water, and the related carboxylic acid from the hydrolysis

was isolated after the reaction. However, the coupling yields of aliphatic acyl chloride in the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-[bmim][PF<sub>6</sub>] system were superior to those in the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-PEG system (Table 3, entries 17 and 18), analogous to results with aliphatic carboxylic anhydrides (Table 2, entries 18 and 19). The hydrolysis of the aliphatic carboxylic anhydride and aliphatic acyl chloride appeared to be inhibited partially, and the coupling reaction rate was enhanced when [bmim][PF<sub>6</sub>] was used as the additive, showing a special effect on the cross-coupling reaction.<sup>16</sup> PEGs are miscible with water, and PEG 2000 has a solubility of about 60% in water at 20 °C.<sup>17</sup> Thus, the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-PEG system is a homogeneous aqueous catalytic system, which possibly facilitates the hydrolysis of more sensitive alkyl chlorides or alkyl carboxylic hydrides and leads to the low yields. In contrast, [bmim][PF<sub>6</sub>] is immiscible with water, and the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-[bmim][PF<sub>6</sub>] system is two phase with the catalyst in [bmim][PF<sub>6</sub>]. In this two-phase system, the hydrolysis reactions might be retarded since the aliphatic acyl chlorides or aliphatic carboxylic anhydrides are more isolated from water, which should be beneficial to the cross-coupling reaction.

The reusability and efficiency of Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-PEG catalytic systems were investigated on the model coupling reactions of benzoic anhydride with phenylboronic acid and benzoyl chloride with phenylboronic acid. Since PEG 2000 was insoluble in diethyl ether, the product was easily isolated by extraction with diethyl ether. The residue was recycled, and the efficiency of the recyclability was shown in Figure 1. It was seen that the efficiency of reusability of the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-PEG system for both coupling reactions was rapidly decreased, although benzoyl chloride was more active than benzoic anhydride.

The Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-[bmim][PF<sub>6</sub>] system was superior to the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-PEG system as the recyclable catalytic system (Figure 2). We found that washing the residue in every cycle with water was important to the efficiency of recyclability. For example, the reactivity of the catalyst in the cycles was reduced significantly when the residue was not washed with water after the reaction. A possible reason for this was that the salt byproducts generated in the coupling reaction retarded the proceeding of the coupling reaction.<sup>18</sup> Since [bmim][PF<sub>6</sub>] was immiscible with water, and after washing in every cycle with water, the high efficiency in the recyclable experiment was obtained (Figure 2). Unfortunately, PEGs were soluble in water, and it was difficult to improve the reactivity of the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-PEG system in the recycle experiments (Figure 1). High recyclable efficiency (the average isolated yield of 95% for eight consecutive runs) using the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-[bmim][PF<sub>6</sub>] system was obtained for both benzoic anhydride and benzoyl chloride, which demonstrates the practical recyclable property of this catalyst.

The acylation in the absence of phosphine ligands in water was thought to proceed through the mechanism previously described by Yamamoto et al.<sup>10b</sup> and Goossen and Ghosh.<sup>11b</sup> The oxidative addition of carboxylic anhydride onto palladium(0) gives the (acyl)(carboxylato)palladium(II) intermediate,

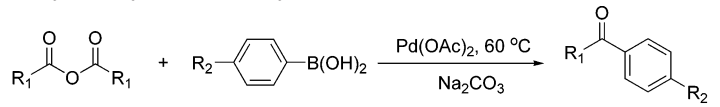
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
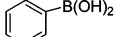
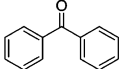

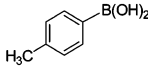
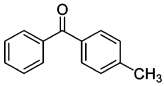

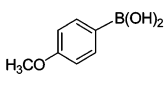
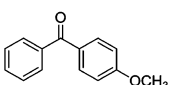

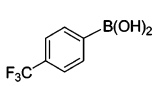
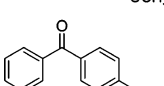


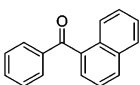

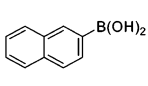
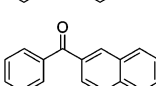

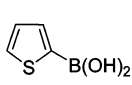
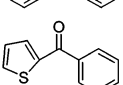

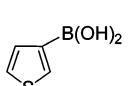
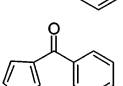
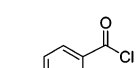
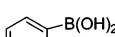
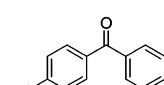
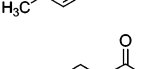

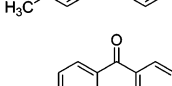
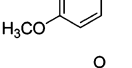

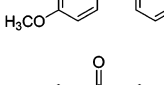
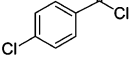

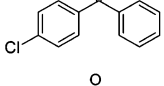
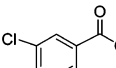
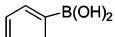
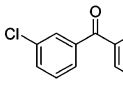
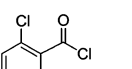
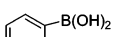
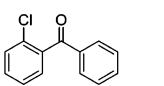
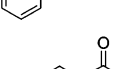

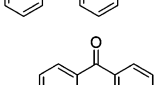
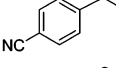

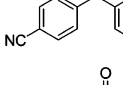
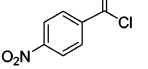

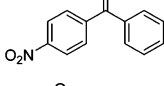
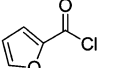
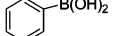
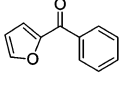
TABLE 2. Cross-Coupling of Carboxylic Anhydrides with Aryl Boronic Acids<sup>a</sup>



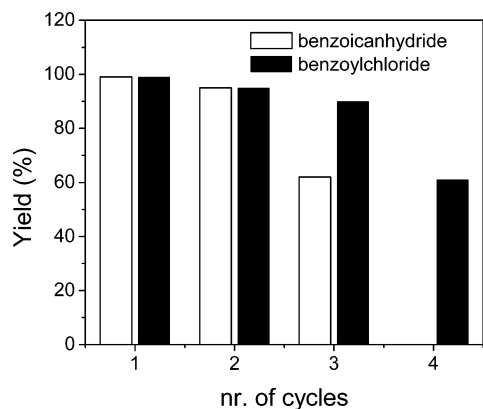
| Entry | R <sub>1</sub> | R <sub>2</sub>   | Product | Time (h) | Yield (%) <sup>b</sup> | Yield (%) <sup>c</sup> |
|-------|----------------|------------------|---------|----------|------------------------|------------------------|
| 1     |                | H                |         | 2        | 98                     | 97                     |
| 2     |                | CH <sub>3</sub>  |         | 2        | 97                     | 97                     |
| 3     |                | OCH <sub>3</sub> |         | 2        | 97                     | 94                     |
| 4     |                | CF <sub>3</sub>  |         | 3        | 90                     | 87                     |
| 5     |                |                  |         | 2        | 96                     | 95                     |
| 6     |                |                  |         | 2        | 90                     | 71                     |
| 7     |                |                  |         | 2        | 94                     | 88                     |
| 8     |                |                  |         | 2        | 96                     | 91                     |
| 9     |                | H                |         | 2        | 89                     | 91                     |
| 10    |                | H                |         | 2        | 96                     | 78                     |
| 11    |                | H                |         | 2        | 76                     | 41                     |
| 12    |                | H                |         | 2        | 91                     | 89                     |
| 13    |                | H                |         | 2        | 95                     | 83                     |
| 14    |                | H                |         | 3        | 82                     | 76                     |
| 15    |                | H                |         | 2        | 30                     | 75                     |
| 16    |                | H                |         | 2        | 66                     | 91                     |
| 17    |                | H                |         | 2        | 97                     | 96                     |
| 18    |                | H                |         | 12       | 9                      | 30                     |
| 19    |                | H                |         | 2        | 20                     | 73                     |

<sup>a</sup> Reaction conditions: Carboxylic anhydride (1.0 mmol), aryl boronic acid (1.2 mmol), Na<sub>2</sub>CO<sub>3</sub> (1.6 mmol). <sup>b</sup> Isolated yield in a mixture of H<sub>2</sub>O and PEG 2000 (3:3 g), 0.5 mol % Pd(OAc)<sub>2</sub>. <sup>c</sup> Isolated yield in a mixture of H<sub>2</sub>O and [bmim][PF<sub>6</sub>] (2.5:3 g), 1.8 mol % Pd(OAc)<sub>2</sub>.

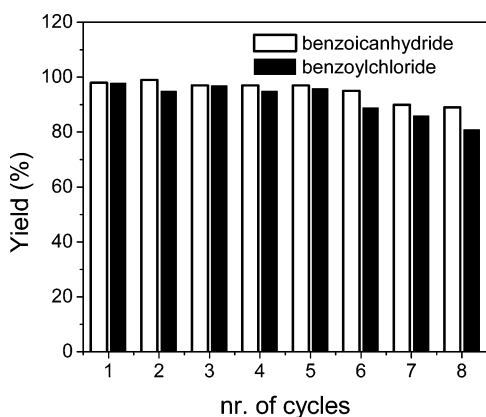
TABLE 3. Cross-Coupling Reactions of Acyl Chlorides with Aryl Boronic Acids<sup>a</sup>

| Entry | Acid Chloride   | Boronic Acid  | Product   | Yield (%) <sup>b</sup> | Yield (%) <sup>c</sup> |
|-------|---|---|---|------------------------|------------------------|
| 1     |    |    |    | 99                     | 97                     |
| 2     |    |    |    | 93                     | 95                     |
| 3     |    |    |    | 99                     | 99                     |
| 4     |    |    |    | 93 <sup>d</sup>        | 89 <sup>d</sup>        |
| 5     |    |    |    | 91                     | 80                     |
| 6     |    |    |    | 97                     | 96                     |
| 7     |    |    |    | 97                     | 89                     |
| 8     |    |    |    | 92                     | 90                     |
| 9     |    |    |    | 92                     | 95                     |
| 10    |   |   |   | 96                     | 88                     |
| 11    |  |  |  | 92                     | 99                     |
| 12    |  |  |  | 91                     | 94                     |
| 13    |  |  |  | 78                     | 80                     |
| 14    |  |  |  | 77                     | 98                     |
| 15    |  |  |  | 35                     | 52                     |
| 16    |  |  |  | 99                     | 99                     |
| 17    |  |  |  | no                     | 54                     |
| 18    |  |  |  | 15                     | 78                     |

<sup>a</sup> Reaction conditions: Acyl chloride (1.0 mmol), aryl boronic acid (1.2 mmol), Na<sub>2</sub>CO<sub>3</sub> (1.6 mmol). <sup>b</sup> Isolated yield in a mixture of H<sub>2</sub>O and PEG 2000 (3:3 g), 0.2 mol % Pd(OAc)<sub>2</sub>, 1 h. <sup>c</sup> Isolated yield in a mixture of H<sub>2</sub>O and [bmim][PF<sub>6</sub>] (2.5:3 g), 0.9 mol % Pd(OAc)<sub>2</sub>, 2 h. <sup>d</sup> Reaction time was 3 h.



**FIGURE 1.** Recycling experiments for the acylation reaction using the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-PEG system. A mixture of H<sub>2</sub>O and PEG 2000 (3:3 g) was used as solvent. 0.5 mol % Pd(OAc)<sub>2</sub> for benzoic anhydride and 0.2 mol % for benzoyl chloride were used. Reaction conditions: benzoic anhydride or benzoyl chloride (1.0 mmol), PhB(OH)<sub>2</sub> (1.2 mmol), Na<sub>2</sub>CO<sub>3</sub> (1.6 mmol), 60 °C, isolated yield. Reaction time: 2 h for benzoic anhydride and 1 h for benzoyl chloride.



**FIGURE 2.** Recycling experiments for the acylation reaction using the Pd(OAc)<sub>2</sub>-H<sub>2</sub>O-[bmim][PF<sub>6</sub>] system. A mixture of H<sub>2</sub>O and [bmim][PF<sub>6</sub>] (2.5:3 g) was used as solvent. 1.8 mol % Pd(OAc)<sub>2</sub> for benzoic anhydride and 0.9 mol % for benzoyl chloride were used. Reaction conditions: benzoic anhydride or benzoyl chloride (1.0 mmol), PhB(OH)<sub>2</sub> (1.2 mmol), Na<sub>2</sub>CO<sub>3</sub> (1.6 mmol), 60 °C, isolated yield. Reaction time: 2 h for benzoic anhydride and 1 h for benzoyl chloride.

which then forms the (acyl)(aryl)palladium(II) species with an arylboronic acid. The reductive elimination liberates the coupling product with the regeneration of the active Pd(0) species to complete the catalytic cycle. Yamamoto and Goossen reported that the successful oxidative addition of anhydride onto palladium required the activation of phosphine ligands in organic solvent. In the aqueous media, the presence of additives (PEG or [bmim][PF<sub>6</sub>]) clearly enhanced the coupling reaction rate, and the reaction rate was even faster when compared with those in organic solvent in the presence of phosphine ligands. On one hand, the solubility of the organic substrates in water was greatly promoted by the addition of PEG and ionic liquid,<sup>17,19</sup> which should lead to the enhancement of the reaction rate. On the other hand, any colloidal palladium interfaces that formed during the

reaction<sup>20</sup> in pure water should have properties different from those in the presence of additives.<sup>21</sup> It was possible that the addition of PEG or [bmim][PF<sub>6</sub>] might lead to competition between water and the additives that opened the active sites on the catalyst surface. At the same time, the ionic liquid or PEG might be acting as ligand and/or stability reagent of palladium in the reaction process.<sup>22</sup>

## Conclusions

In conclusion, we have developed an environmentally benign and recyclable process for the preparation of aryl ketones, whose significant features are as follows: (i) use of expensive and environmentally unfavorable phosphine ligand is avoided, (ii) high efficiency under mild conditions in aqueous media in air, (iii) easy isolation of the product, and (iv) catalyst recycling. Further research is in progress in our laboratory to utilize these catalytic systems in wide synthetic applications.

## Experimental Section

### General Procedure for the Acylation Reaction in PEG2000.

A round-bottomed flask was charged with a mixture of Na<sub>2</sub>CO<sub>3</sub> (0.170 g, 1.6 mmol), Pd(OAc)<sub>2</sub> (1 mg, 0.5 mol %), PEG2000 (3 g), and H<sub>2</sub>O (3 g). The solution was heated to 60 °C with stirring, and carboxylic anhydride (1.0 mmol) and arylboronic acid (1.2 mmol) were added. The mixture was stirred at 60 °C for the indicated time and cooled to room temperature. The resulting suspension was extracted with diethyl ether (5 mL) four times. The combined ethyl ether phase was concentrated, and the product was obtained by purification of flash chromatography on a silica gel column. In the recycle experiment, the residue was subjected to a second run of the acylation reaction by charging with the same substrates (benzoic anhydride, phenylboronic acid, and Na<sub>2</sub>CO<sub>3</sub>) without further addition of Pd(OAc)<sub>2</sub>, PEG2000, or water.

**General Procedure for the Acylation Reaction in [bmim]-[PF<sub>6</sub>].** A round-bottomed flask was charged with a mixture of Na<sub>2</sub>CO<sub>3</sub> (0.170 g, 1.6 mmol), Pd(OAc)<sub>2</sub> (4 mg, 1.8 mol %), [bmim][PF<sub>6</sub>] (3 g), and H<sub>2</sub>O (2.5 g). The solution was heated to 60 °C with stirring, and carboxylic anhydride (1.0 mmol) and arylboronic acid (1.2 mmol) were added. The mixture was stirred at 60 °C for the indicated time and cooled to room temperature. The suspension was extracted with diethyl ether (5 mL) four times. The combined ethyl ether phase was concentrated, and further purification of the product was achieved by flash chromatography on a silica gel column. In the recycle experiment, the residue after the extraction was washed with water (3 × 6 mL) and then was subjected to a second run of the acylation reaction by charging with the same substrates (benzoic anhydride, phenylboronic acid, water, and Na<sub>2</sub>CO<sub>3</sub>) without further addition of Pd(OAc)<sub>2</sub> or IL.

**T1-1 Benzophenone:** <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>, TMS): δ 7.82–7.81 (t, J = 4.1 Hz, 4 H), 7.61–7.59 (m, 2 H), 7.51–7.48 (t,

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$J = 7.7$  Hz, 4 H). MS (EI):  $m/z$  (%): 182 (75) [ $M^+$ ], 105 (100), 77 (56), 51 (15).

**T2-5 2-Benzoylnaphthene:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  8.27 (s, 1 H), 7.96 (s, 2 H), 7.94–7.92 (d,  $J = 7.6$  Hz, 2 H), 7.88–7.86 (d,  $J = 6.8$  Hz, 2 H), 7.64–7.61 (m, 2 H), 7.59–7.51 (m, 3 H). MS (EI):  $m/z$  (%): 233 ( $M + 1^+$ , 10), 232 ( $M^+$ , 60), 155 (100), 127 (80), 105 (40), 77 (75), 51 (20).

**T2-7 2-Benzoylthiophene:**  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  7.87–7.85 (m, 2 H), 7.72–7.71 (q,  $J = 2.0$  Hz, 1 H), 7.65–7.63 (q,  $J = 1.7$  Hz, 1 H), 7.61–7.57 (m, 1 H), 7.51–7.47 (m, 2 H), 7.17–7.15 (q,  $J = 2.9$  Hz, 1 H). MS (EI):  $m/z$  (%): 188 (90) [ $M^+$ ], 171 (10), 160 (10), 111 (100), 105 (40), 77 (20), 51 (12).

**T2-17 2-Benzoylfuran:**  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ , TMS):  $\delta$  7.89–7.88 (t,  $J = 4.2$  Hz, 2 H), 7.63–7.62 (d,  $J = 0.8$  Hz, 1 H), 7.53–7.49 (m, 1 H), 7.43–7.40 (t,  $J = 7.7$  Hz, 2 H), 7.16–7.15 (d,  $J = 3.5$  Hz, 1 H), 6.52–6.51 (m, 1 H). MS (EI):  $m/z$  (%): 172 ( $M^+$ , 80), 105 (100), 95 (80), 77 (60), 67 (30), 51 (10).

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**Supporting Information Available:** Experimental procedure and spectroscopic data ( $^1\text{H}$  NMR and MS) for the products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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