



# Microwave-promoted direct amidation of unactivated esters catalyzed by heteropolyanion-based ionic liquids under solvent-free conditions



Renzhong Fu, Yang Yang\*, Yunsheng Ma, Fei Yang, Jingjing Li, Wen Chai, Quan Wang\*, Rongxin Yuan

Jiangsu Laboratory of Advanced Functional Material, School of Chemistry and Materials Engineering, Changshu Institute of Technology, Changshu 215500, PR China

## ARTICLE INFO

### Article history:

Received 20 April 2015

Revised 28 May 2015

Accepted 30 May 2015

Available online 4 June 2015

### Keywords:

Amide

Ester

Ionic liquid

Microwave-promoted

Solvent-free condition

## ABSTRACT

A simple and efficient procedure for the synthesis of amides directly from unactivated esters and amines catalyzed by heteropolyanion-based ionic liquids under microwave-promoted and solvent-free conditions has been reported. The practical protocol was found to be compatible with different structurally diverse substrates. Moderate to excellent yields, solvent-free media, and operational simplicity are the main highlights. Furthermore, the heteropolyanion-based ionic liquids were easily reusable for this amidation.

© 2015 Elsevier Ltd. All rights reserved.

The formation of amide bonds is one of the most common and important processes for both synthetic organic chemists and biologists.<sup>1</sup> Amide linkages are present in many biologically active molecules, key natural products, and synthetic polymers.<sup>2</sup> It has been noted recently that about 66% of all preliminary screening reactions in industrial medicinal chemistry laboratories involve amide formation.<sup>3</sup> Therefore, efficient synthesis of amides is an important topic of modern synthetic chemistry not only in academic research but also in industrial application.<sup>4</sup>

Traditionally, the reactions of activated carboxylic acid derivatives (such as acids, anhydrides, acyl halides, or esters) with amines are applied for the synthesis of amides, but there are limitations, such as harsh reaction conditions, poor atom efficiency, stoichiometric amount of toxic wastes, and difficulties in purification.<sup>5</sup> In addition, labile substrates and limited substrate scopes are also restricted. Thus, these drawbacks have promoted the development of a number of catalytic approaches to amide bond formation in recent years.<sup>6</sup> Among various methods, a more convenient direct amidation is catalytic coupling of esters with amines. This is a desirable approach for amide synthesis because esters are usually economical and commercially available, as well as alcohols are the sole coproducts of this transformation.<sup>7,8</sup> Unlike more reactive phenolic esters, inert alkyl esters are not

commonly used in the synthesis of amides because harsh conditions, such as high temperature, high pressure, or the use of more than stoichiometric amounts of strongly basic reagents, are required. Great efforts have recently been made to avoid this problem by using activating reagents or catalysts.<sup>9–21</sup> Efficient catalytic systems based on inorganic catalysts ( $K_3PO_4$ ,<sup>9</sup> NaOMe,<sup>10</sup>  $Mg(OCH_3)_2$  or  $CaCl_2$ ,<sup>11</sup> and  $Mg_3N_2$ ,<sup>12</sup>), organic catalysts (*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine (BEMP),<sup>13</sup> 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD),<sup>14</sup> 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU),<sup>15</sup> and *N*-heterocyclic carbene<sup>16</sup>), metallic catalysts (Ru-MACHO,<sup>17</sup>  $La(OTf)_3$ ,<sup>18</sup>  $Pd(OAc)_2$ ,<sup>19</sup> and  $DABCO(AlMe_3)_2$ ,<sup>20</sup>), and enzymatic-catalyzed transformations<sup>21</sup> have been reported. However, some of these methods still suffer from certain demerits, such as recycle of catalysts, limited substrate scopes, low selectivities, and long reaction times. Thus, the development of simple and environmentally benign but efficient catalysts which can promote direct amidation of unactivated esters under mild conditions is in high demand.

Over the past few decades, ionic liquids (ILs) have attracted more and more interests of chemists. Meanwhile, ILs have been successfully used in organic transformations as efficient and eco-friendly reaction media and/or catalysts due to their excellent properties such as negligible vapor pressure, ease of recovery, and reuse.<sup>22</sup> Recently, a series of heteropolyanion-based ILs (HPA-ILs) have been prepared as hybrid materials by combining Keggin heteropolyanions with 'taskspecific' ILs (TSILs) cations containing special functional groups.<sup>23</sup> Because of the large volume

\* Corresponding authors. Tel./fax: +86 512 52251842.

E-mail addresses: [yangyangirisjs@126.com](mailto:yangyangirisjs@126.com) (Y. Yang), [wangquanzu@163.com](mailto:wangquanzu@163.com) (Q. Wang).

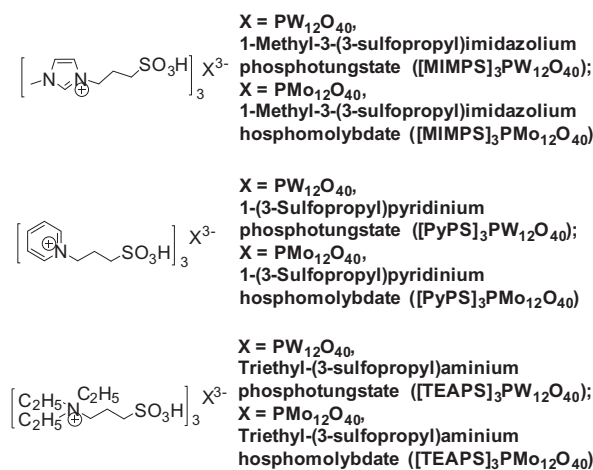
and high valence of heteropolyanions and hydrogen bonding networks, HPAILs usually have high melting points, thermal stability and chemical stability. These specialties are consistent with the requirements of a solid acid catalyst in organic reactions resulting in their advantages, such as operational simplicity, no toxicity, easily isolation, and reusability. So far, HPAILs have turned out to be an eco-benign, high-efficient, and recyclable catalyst for acid-catalyzed<sup>24</sup> or oxidative organic reactions.<sup>25</sup>

On the other hand, a large number of publications have clearly shown that many types of chemical transformations can be carried out successfully under microwave (MW) conditions during the last years.<sup>26</sup> Most importantly, MW processing frequently leads to the significant rate enhancements, yield and selectivity improvements, very simplified ease of manipulation and work-up, less environmental polluting processes as well as solvent-free organic transformations matching with the goal of green chemistry.<sup>26</sup>

Recently, our group has introduced HPAILs as eco-benign and highly efficient catalysts for amidations under MW-promoted and solvent-free conditions.<sup>27</sup> As a part of our continuing interest in developing efficient and green protocols for catalytic methods for amide bond formation, we wish to describe herein the preliminary results on MW-promoted amidation of unactivated esters catalyzed by HPAILs under solvent-free conditions (Scheme 1).

Based upon previous results of HPAIL catalyzed organic transformations reported by our group,<sup>27,28</sup> *N*-substituted imidazole, pyridine, and triethylamine based HPAILs were chosen as potential catalysts for this amidation of unactivated esters (Fig. 1). Thus, according to the procedure described in the literature<sup>24a,27,28</sup> six structurally related HPAILs were prepared.

Initially, some attempts to synthesize amides from esters and amines were conducted using ethyl formate and aniline as model reaction (Table 1). Firstly, a control experiment was performed using 1.5 equiv of ethyl formate in the absence of any catalyst and additional solvent at room temperature. After a prolonged reaction time of 24 h *N*-phenylformamide was achieved in 33% yield (Table 1, entry 1) whereas addition of 2 mol % amount of [MIMPS]<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> to the reaction mixture resulted in the desired amide product within 6 h in 63% yield (Table 1, entry 2). The results revealed that the catalyzed amidation could be promoted by HPAILs. Then it was shown that the rate and yield of the reaction both increased when the reaction mixture was conventionally heated at 50 °C for 5 h (Table 1, entry 3, 68% yield) or 70 °C for 3 h (Table 1, entry 4, 90% yield). But higher temperature (100 °C) was not beneficial to the *N*-formyl product (Table 1, entry 5, 88% yield). To our delight, when MW-assisted heating was introduced, more efficient results were observed (Table 1, entries 3–5). Then, it was observed that there is no need to use more excess of ethyl formate, as a 1.5:1 molar ratio of ethyl formate to aniline was sufficient to yield the desired product (Table 1, entry 6). Moreover little lower yields were obtained in the presence of more or less amount of catalyst (Table 1, entries 7 and 8). Afterward catalytic activities of other related catalysts prepared before were screened under the same reaction condition (Table 1, entry 4). It was shown that the catalytic activities of [MIMPS]<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> and [TEAPS]<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> were slightly lower than that of



**Figure 1.** *N*-Substituted imidazole, pyridine, and triethylamine based HPAILs.

**Table 1**

Optimization of the reaction conditions for amidation of ethyl formate with aniline catalyzed by HPAILs<sup>a</sup>

Entry	Catalyst	Temp (°C)	Time (h)/min	Yield <sup>b</sup> (%)
1	No catalyst	rt	(24)	33
2	[MIMPS] <sub>3</sub> PW <sub>12</sub> O <sub>40</sub> , 2 mol %	rt	(6)	63
3	[MIMPS] <sub>3</sub> PW <sub>12</sub> O <sub>40</sub> , 2 mol %	50	(5) <sup>c</sup> , 25	68 <sup>c</sup> , 72
4	[MIMPS] <sub>3</sub> PW <sub>12</sub> O <sub>40</sub> , 2 mol %	70	(3) <sup>c</sup> , 10	90 <sup>c</sup> , 95
5	[MIMPS] <sub>3</sub> PW <sub>12</sub> O <sub>40</sub> , 2 mol %	100	(3) <sup>c</sup> , 10	88 <sup>c</sup> , 92
6 <sup>d</sup>	[MIMPS] <sub>3</sub> PW <sub>12</sub> O <sub>40</sub> , 2 mol %	70	10	90
7	[MIMPS] <sub>3</sub> PW <sub>12</sub> O <sub>40</sub> , 1 mol %	70	15	90
8	[MIMPS] <sub>3</sub> PW <sub>12</sub> O <sub>40</sub> , 3 mol %	70	10	92
9	[MIMPS] <sub>3</sub> PMO <sub>12</sub> O <sub>40</sub> , 2 mol %	70	15	85
10	[PyPS] <sub>3</sub> PW <sub>12</sub> O <sub>40</sub> , 2 mol %	70	10	96
11	[PyPS] <sub>3</sub> PMO <sub>12</sub> O <sub>40</sub> , 2 mol %	70	15	90
12	[TEAPS] <sub>3</sub> PW <sub>12</sub> O <sub>40</sub> , 2 mol %	70	20	85
13	[TEAPS] <sub>3</sub> PMO <sub>12</sub> O <sub>40</sub> , 2 mol %	70	25	73
14	H <sub>3</sub> PW <sub>12</sub> O <sub>40</sub> , 2 mol %	70	15	71

<sup>a</sup> Unless otherwise noted, all reactions were carried out with ethyl formate (3.0 mmol), aniline (2.0 mmol), and related catalyst under MW (700 W) and solvent-free conditions in a sealed tube.

<sup>b</sup> Isolated yields.

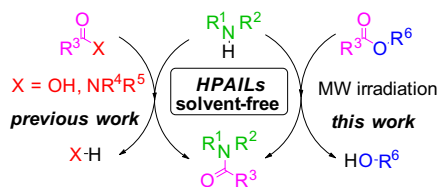
<sup>c</sup> Conventional heating.

<sup>d</sup> Ethyl formate (4.0 mmol) and aniline (2.0 mmol) were used.

[PyPS]<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> (Table 1, entries 4, 10 and 12). In the cases of catalysts combining with different heteropolyanions, the results demonstrated that PW<sub>12</sub>O<sub>40</sub> was more active than PMO<sub>12</sub>O<sub>40</sub> HPAILs (Table 1, entries 4, 9–13). When pure HPA catalyst H<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> was used for this catalyzed amidation only 71% yield was observed (Table 1, entry 14). Finally, optimum result was obtained when the reaction was performed using 2 mol % of [PyPS]<sub>3</sub>PW<sub>12</sub>O<sub>40</sub> under MW (700 W) and solvent-free condition at 70 °C for 10 min affording *N*-phenylformamide in 96% yield (Table 1, entry 10).

With these promising results in hand, we examined the substrate scope. The optimized reaction conditions were applied for formylation of various aromatic and aliphatic primary or secondary amines using formic esters as formylating agent (Table 2). Firstly, with regard to the reactivities of formic esters, *n*-butyl formate, *i*-butyl formate, benzyl formate, and more hindered *i*-propyl formate were less reactive than ethyl formate in this procedure (Table 2, 3a and 3b).

As shown in Table 2, various substituted anilines were converted to corresponding *N*-formyl amides in good to excellent yields. It was observed that aniline bearing substitution with an electron donating group (methyl) provided an excellent yield of 97% with ethyl formate (Table 2, 3b) whereas, prolonged reaction



**Scheme 1.** HPAIL catalyzed amidation reactions developed by our group.

Download English Version:

<https://daneshyari.com/en/article/5260399>

Download Persian Version:

<https://daneshyari.com/article/5260399>

[Daneshyari.com](https://daneshyari.com)