

## Chloroferrate(III) Ionic Liquid as Recyclable Catalyst for the Acetylation of Alcohols and Phenols and for 1,1-Diacylation of Aldehydes

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A Lewis acidic ionic liquid, [bmim][FeCl<sub>4</sub>], was employed to catalyze acetylation of alcohols and phenols, and the conversion of aldehydes to corresponding 1,1-diacetates without conventional organic solvents. The catalyst is easily available, water-tolerant, recoverable and easy to handle.

**Keywords:** Functional ionic liquid; Lewis acid; Acetylation; Ester; 1,1-Diacetate.

### INTRODUCTION

Acetylation of alcohols and phenols is a fundamental reaction in organic synthesis. This reaction is generally carried out using Ac<sub>2</sub>O as the acetylating agent in the presence of bases such as triethylamine, pyridine or DMAP as catalyst.<sup>1</sup> Vedejs and co-workers<sup>2</sup> have reported tributylphosphine as a less basic catalyst to catalyze the acetylation of alcohols. A variety of new catalysts, e.g. iodine,<sup>3</sup> zeolite H-FER,<sup>4</sup> imidazole,<sup>5</sup> K<sub>5</sub>CoW<sub>12</sub>O<sub>40</sub>,<sup>6</sup> RuCl<sub>2</sub>,<sup>7</sup> NbCl<sub>5</sub>,<sup>8</sup> Al(HSO<sub>4</sub>)<sub>3</sub>,<sup>9</sup> vanadyl sulfate,<sup>10</sup> tin(IV) tetraphenylporphyrin perchlorate,<sup>11</sup> acetonyltriphenylphosphonium bromide (ATPB)<sup>12</sup> and 3*H*-benzothiazol-2-ylideneamines,<sup>13</sup> have been used for the acetylation of alcohols and phenols. Recently, recyclable catalysts such as Yb[N(SO<sub>2</sub>C<sub>8</sub>H<sub>17</sub>)<sub>2</sub>]<sub>3</sub><sup>14</sup> and dicyanamide based ionic liquid<sup>15</sup> were found to be effective catalysts for the acetylation of alcohols and carbohydrates. On the other hand, acylals (1,1-diacetates) have been introduced as a suitable protection group for this purpose because of their remarkable stability to neutral and basic conditions.<sup>16</sup> In addition, they can be converted into other useful functional groups by reaction with appropriate nucleophiles<sup>17</sup> and used as carbonyl surrogates for asymmetric synthesis.<sup>18</sup> Hence, methods for their synthesis have received considerable attention. Usually, diacetates are prepared from the reaction of aldehydes and acetic anhydride under the catalysis of a variety of protic or Lewis acids. These include strong acids like sulfuric acid,<sup>19</sup> phosphoric acid<sup>20</sup> and perchloric acid<sup>21</sup> and Lewis acids such as FeCl<sub>3</sub>,<sup>22</sup> Sc(OTf)<sub>3</sub>,<sup>23</sup> Cu(OTf)<sub>2</sub>,<sup>24</sup> Bi(OTf)<sub>3</sub>,<sup>25</sup> InBr<sub>3</sub>,<sup>26</sup>

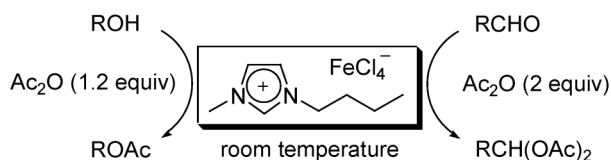
Zr(HSO<sub>4</sub>)<sub>4</sub>,<sup>27</sup> VSO<sub>4</sub><sup>28</sup> and cyanuric chloride.<sup>29</sup> However, many of these acetylation catalysts also suffer from certain drawbacks. The Brønsted acids can cause many problems such as corrosion; while the Lewis acids are often expensive, toxic and unrecoverable. Hence, there is still a great demand for the development of efficient and recoverable acid catalysts to generate esters and acylals under mild conditions.

Organic chemists from both academia and industry have started giving serious thought to the detrimental effect of non-green processes and chemicals on the environment. As green alternative solvents, metal containing Lewis acidic ionic liquids have been studied extensively for use in acid catalyzed reactions. Unfortunately, some of these ionic liquids, e.g. [bmim][AlCl<sub>4</sub>], are extremely sensitive to moisture and must be handled either *in vacuo* or under inert atmosphere at all times.<sup>30</sup> Recently, imidazolium chloroferrates have been introduced as a new series of Lewis acidic ionic liquids for Friedel-Crafts acylation<sup>31</sup> and sulfonylation<sup>32,33</sup> of aromatics, Ferrier rearrangement<sup>34</sup> and aryl Grignard cross-coupling of alkyl halides.<sup>35</sup> In comparison with [bmim][AlCl<sub>4</sub>] ionic liquid, [bmim][FeCl<sub>4</sub>] is reasonably air and moisture stable and are capable of dissolving a wide range of organic compounds. Our group has reported that [bmim][FeCl<sub>4</sub>] could be employed as an efficient and recyclable catalyst in the synthesis of 4-aryl-dihydropyrimidinones through Biginelli reactions.<sup>36</sup> As a continuation of our research program on Lewis acidic ionic liquids, we wish to report herein an efficient and general

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procedure for the acylation of alcohols (or phenols) and for 1,1-diacylation of aldehydes using [bmim][FeCl<sub>4</sub>] as a recyclable catalyst (Scheme 1). After completion of the reaction, the product was extracted by ether and the ionic liquid could be reused without further purification.

Scheme 1



## RESULTS AND DISCUSSION

Initially, the chloroferrate Lewis acidic ionic liquid [bmim][FeCl<sub>4</sub>] (1-methyl-3-butyl imidazolium chloroferrate) was prepared as a viscous dark brown liquid by mixing the equimolar of the quaternary ammonium precursor, 1-butyl-3-methylimidazolium chloride [bmim]Cl, with FeCl<sub>3</sub>·6H<sub>2</sub>O.<sup>35</sup>

In order to generalize the use of [bmim][FeCl<sub>4</sub>] as an efficient catalyst for acetylation, structurally different alcohols and phenols were submitted to the action of the [bmim][FeCl<sub>4</sub>] (20 mol%) under ambient condition. The results obtained are shown in Table 1. In most cases, the esters were obtained in excellent yields. Not only primary, but also secondary alcohols and phenols underwent smooth acetylation with excellent yields. No competitive dehydration was registered in the acetylation of secondary substrates (Table 1, entries 3, 4, 6). Attempted acetylation of a tertiary alcohol (Table 1, entry 2), however, gave the acetylated product in moderate yield (71%). A minor amount (19%) of eliminated product was detected (GC) accompanied with unchanged starting material. In addition, it was worth commenting that hindered alcohols (Table 1, entries 4, 6, 7) gave good yields of product, albeit in slower reaction rate.

We next turned our attention to whether the same catalyst would be useful for the 1,1-diacetylation of aldehydes. To our delight, ionic liquid [bmim][FeCl<sub>4</sub>] was shown to be efficient and recoverable catalysts in the synthesis of *gem*-diacetates. Several structurally varied aromatic and aliphatic aldehydes reacted with two equivalent amount of acetic anhydride to afford the corresponding acylals smoothly in the presence of 20 mol% [bmim][FeCl<sub>4</sub>]


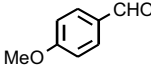
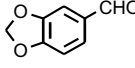
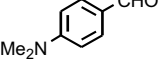
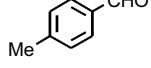
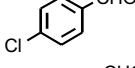
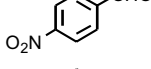
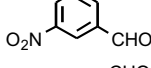
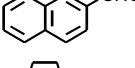
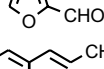
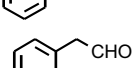
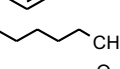
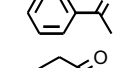
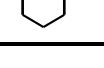

Table 1. Acetylation of alcohols and phenols catalyzed by [bmim][FeCl<sub>4</sub>]

Entry	Substrates	Time (min)	Yield (%)
1		25	89
2		120	71
3		20	90
4		70	94
5		20	91
6		90	88
7		200	92
8		20	89
9		20	93
10		30	94

at ambient temperature. In most cases, this procedure affords desired 1,1-diacetates in good to excellent yields. The results are listed in Table 2. Evidently, the present method is quite general and found to be effective for aromatic, heterocyclic, open-chain conjugated and aliphatic aldehydes although the yields for aliphatic saturated aldehyde (Table 2, entry 13) is relatively low, being associated with the formation of some of unidentified byproducts.

The reaction conditions are mild enough not to induce any damage to moieties like methoxyl and piperonyl group (Table 2, entries 2, 3) which often undergo cleavage in the presence of strong acids or certain Lewis acids. In accordance with the fact reported in a previous literature,<sup>37</sup> 4-dimethylamino benzaldehyde (Table 2, entry 4) failed to give the expected 1,1-diacetate even when the reaction mixtures were stirred at room temperature for 2 h. The starting materials were quantitatively recovered. This fact is possibly due to the strong electron-donating nature of dimethylamino group which will reduce the reactivity. Moreover, the

Table 2. [bmim][FeCl<sub>4</sub>] catalyzed synthesis of *gem*-diacetates

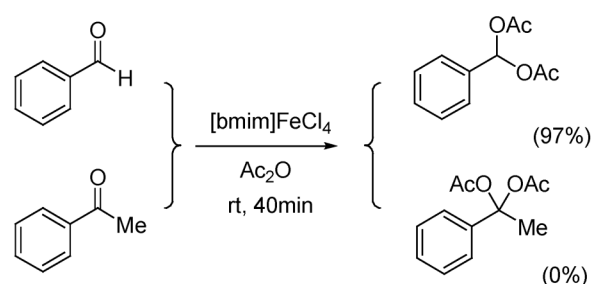
Entry	Substrates	Time (min)	Yield (%)
1		40	89
2		30	90
3		40	88
4		120	0
5		40	91
6		50	92
7		240	91
8		240	89
9		40	88
10		100	79
11		60	80
12		90	87
13		90	72
14		60	0
15		60	0

existence of the quinoid structure with an aldehyde may also decrease the reactivity of the aldehyde group.<sup>38</sup> Mention must be made here that the aldehydes bearing electron-withdrawing substituents such as nitrobenzaldehyde (Table 2, entries 7, 8) also gave good results under presented conditions, despite the fact that much longer reaction times were needed to achieve complete conversion. Polycyclic aromatic aldehyde as 2-naphthaldehyde (Table 2, entry 9) yielded corresponding diacetate in 88% yield. Acid sensitive substrates like furfural (Table 2, entry 10) was also diacetylated by this procedure, gave the corresponding 1,1-diacetates in good yield without the formation of large amount of side products, which are normally

observed under strongly acidic conditions. No isomerization for conjugated aldehydes was observed in the presence of [bmim][FeCl<sub>4</sub>]. In our experiments,  $\alpha,\beta$ -unsaturated cinnamaldehyde (Table 2, entry 11), was diacetylated smoothly without the isomerization of double bond.

It is worth noting that this method is highly selective for the preparation of the acylals from aldehydes. Ketones, e.g. cyclohexanone and acetophenone (Table 2, entry 14, 15), did not yield any acylals under the present conditions. In a competitive experiment as shown in Scheme II, equimolar mixture of benzaldehyde and acetophenone was allowed to react with acetic anhydride at room temperature in the presence of [bmim][FeCl<sub>4</sub>], gave only 1,1-diacetates of benzaldehyde (GC yield: 97%) while the ketone functionality remained unaffected. Hence, this method represents a chemoselective protection of aldehydes in the presence of ketones.

Scheme II



Besides economical considerations, a successful recycling of catalyst will also lead to a cleaner process, which will not leave any catalyst contamination in the products of the reaction. In our procedure, recycling of [bmim][FeCl<sub>4</sub>] is very simple. After the extraction of products, immiscible ionic liquid was collected by phase separation. No further purification process is needed. Recyclability of [bmim][FeCl<sub>4</sub>] was demonstrated using the synthesis of 4-chlorobenzaldehyde 1,1-diacetate as a model (Fig. 1). It is clear that the recovered ionic liquid could be reused in successive runs without remarkable diminution in the efficiency (yield: 88-93%).

In summary, the use of ionic liquid [bmim][FeCl<sub>4</sub>] as catalyst for these transformations avoids the problem in the recovery of Lewis acid catalysts. This procedure has several advantages: (1) The preparation of ionic liquid [bmim][FeCl<sub>4</sub>] was very simple from easily available reagents; (2) [bmim][FeCl<sub>4</sub>] could be directly reused after simple extrac-

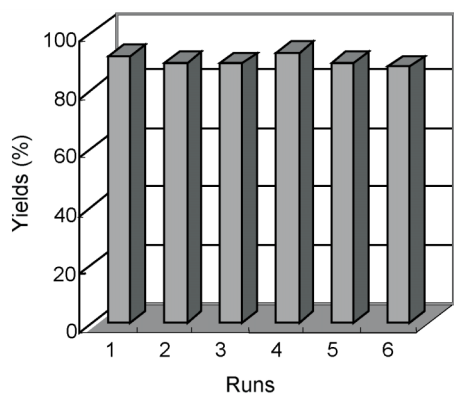


Fig. 1. Recyclability of [bmim][FeCl<sub>4</sub>].

tion; (3) [bmim][FeCl<sub>4</sub>] shows efficient catalytic activity. These significant features are expected to contribute to the development of a green strategy for the acetylation of hydroxyl compounds and 1,1-diacylation of aldehydes.

## EXPERIMENTAL SECTION

Reagents and solvents are purchased from commercial resources. The ionic liquid [bmim][FeCl<sub>4</sub>] was synthesized according to a published procedure by mixing [bmim]Cl with FeCl<sub>3</sub>·6H<sub>2</sub>O, yielding the dark brown ionic liquid as a lower phase within several minutes.<sup>35</sup> All products are known and gave spectral (<sup>1</sup>H NMR and IR) data consistent with the assigned structures. IR spectra were recorded on a Nicolet Nexus 470 spectrophotometer in KBr pellets. <sup>1</sup>H NMR spectra were recorded on Bruker AV 400 spectrometer in CDCl<sub>3</sub> with TMS as internal standard. To solid products, melting points (uncorrected) were also recorded.

### General procedure for the acetylation of alcohols and phenols

A mixture of alcohol (or phenol) (10 mmol), acetic anhydride (freshly distilled, 1.53 g, 15 mmol) and [bmim][FeCl<sub>4</sub>] (0.67 g, 2 mmol) was added in a reaction vial, and the mixture was stirred for under room temperature. The reactions were monitored by TLC and taken to completion. After reaction, Et<sub>2</sub>O (5 mL × 3) was added into the mixture and the immiscible upper layer (organic phase) was decanted. The organic layer was washed with 5% aqueous solution of NaHCO<sub>3</sub> and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent followed by chromatography on a silica gel column affords the pure esters.

### General procedure for the synthesis of acylals

A mixture of aldehyde (10 mmol), acetic anhydride

(freshly distilled, 2.04 g, 20 mmol) and [bmim][FeCl<sub>4</sub>] (0.67 g, 2 mmol) was stirred at room temperature for a certain period of time as required to complete the reaction (TLC). Upon completion, the reaction mixture was extracted with Et<sub>2</sub>O (5 mL × 4). The combined extract after being washed with aqueous NaHCO<sub>3</sub>, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and evaporated to give the crude product. The crude product thus obtained was purified by recrystallization from cyclohexane, or by column chromatography on a silica gel column.

### Selected characterization data

Menthyl acetate (Table 1, entry 4): Colorless liquid. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ<sub>H</sub> 0.76 (d, *J* = 7.0 Hz, 3H, CH<sub>3</sub>), 0.89 (d, *J* = 7.0 Hz, 3H, CH<sub>3</sub>), 0.90 (d, *J* = 6.6 Hz, 3H, CH<sub>3</sub>), 0.84-1.14 (m, 3H, CH<sub>3</sub>), 1.30-1.60 (m, 2H, CH<sub>2</sub>), 1.79-1.93 (m, 2H, CH<sub>2</sub>), 1.93-2.04 (m, 2H, CH<sub>2</sub>), 2.03 (s, 3H, CH<sub>3</sub>CO), 4.67 (m, 1H, CH) ppm.

4-Chlorobenzaldehyde 1,1-diacetate (Table 2, entry 6): White crystalline solid. M.p. 79-80 (Lit.<sup>39</sup>: 76-78 °C). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ<sub>H</sub> 2.17 (s, 6H, 2Ac), 7.39 (d, 2H, *J* = 6.8 Hz, ArH), 7.47 (d, 2H, *J* = 6.8 Hz, ArH), 7.65 (s, 1H, CH) ppm. FTIR (KBr): ν<sub>max</sub> 3060, 2988, 1765, 1588, 1469, 1370, 1215, 968 cm<sup>-1</sup>.

Cinnamaldehyde 1,1-diacetate (Table 2, entry 11): White crystalline solid. M.p. 82-84 °C (Lit.<sup>39</sup>: 78-80 °C). <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ<sub>H</sub> 2.13 (s, 6H, 2Ac), 6.23 (dd, 1H, *J* = 16.5 Hz, *J* = 7.2 Hz, PhCH=), 6.84 (d, 1H, *J* = 16.5 Hz, CH=), 7.26-7.39 (m, 6H, ArH and CH) ppm. FTIR (KBr): ν<sub>max</sub> 3065, 3010, 1756, 1602, 1500, 1423, 1247, 1089, 998 cm<sup>-1</sup>.

Phenylacetaldehyde 1,1-diacetate (Table 2, entry 12): Colorless liquid. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ<sub>H</sub> 1.94 (s, 6H, 2Ac), 2.97 (d, 2H, *J* = 5.7 Hz, PhCH<sub>2</sub>), 6.84 (t, 1H, *J* = 5.7 Hz, CH), 7.07-7.26 (m, 5H, ArH) ppm. FTIR (KBr): ν<sub>max</sub> 3065, 3030, 1756, 1601, 1500, 1423, 1277, 1089, 998 cm<sup>-1</sup>.

## ACKNOWLEDGEMENTS

Financial support for this work from the Shanghai Commission of Science and Technology (08431901800) and the Shanghai Leading Academic Discipline Project (B507) are gratefully acknowledged.

Received April 3, 2009.

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