Metallic Lewis acids-catalyzed acetylation of alcohols with acetic anhydride and acetic acid in ionic liquids: study on reactivity and reusability of the catalysts

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Abstract

The catalytic activity and reusability of the metallic Lewis acids, $Cu(OTf)_2$, $Yb(OTf)_3$, $Sc(OTf)_3$, $In(OTf)_3$, $HfCl_4 \cdot (THF)_2$ and $InCl_3$, for acetylation of alcohols with acetic anhydride and acetic acid has been examined in environmentally benign room temperature ionic liquids, [bmim][X] (bmim = 1-*n*-butyl-3-methylimidazolium, $X = PF_6$, BF_4, SbF_6). All of the catalysts effectively catalyzed the acetylation with acetic anhydride in an ionic liquid, [bmim][PF_6]. In direct acetylation with acetic acid, $Yb(OTf)_3$, $Sc(OTf)_3$ and $InCl_3$ showed excellent catalytic activity in the [bmim][PF_6] ionic liquid and were reasonably recycled.
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1. Introduction

The acylation of alcohols is one of the most frequently used processes in organic synthesis [1]. In its long history, numerous methods have been devised. Acylation of alcohols is typically performed with acid anhydrides in the presence of basic catalysts such as 4-(dimethylamino)pyridine (DMAP) or 4-pyrrolidinopyridine (PPY) [2]. More recently, various metallic triflates including $Cu(OTf)_2$ [3], $Sc(OTf)_3$ [4], $Yb(OTf)_3$ [4c], $In(OTf)_3$ [5], $Bi(OTf)_3$ [6] and $HfCl_4 \cdot (THF)_2$ [7], etc. have been reported to be effective catalysts for acylation with acetic anhydride or acetic acid. These catalysts are very useful,

but also suffer from some drawbacks. Metal triflates are rather expensive and some of them are liable to air and moisture. Moreover, although some of the reactions are conducted without solvent, these metallic Lewis acid catalysts are frequently used for acylation in environmentally harmful organic solvents such as CH_2Cl_2. In viewpoint of today's environmental consciousness, the use of environmentally benign reaction mediums is very important. In this connection, room temperature ionic liquids that are air and moisture stable have received in recent years a good deal of attention as potential cleaner solvents [8]. Deng et al. reported for the first time an application of an ionic liquid, 1-butylpyridinium chloride-aluminum(III) chloride, as a catalyst and reaction medium for acylation of alcohol with acetic acid [9]. Quite recently, Imrie et al. carried out DCC/DMAP promoted esterifications of ferrocenemonocarboxylic acid in ionic

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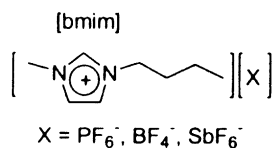
[bmim]

$$X = PF_6^-, BF_4^-, SbF_6^-$$

Fig. 1.

liquids [10]. Utilization of the ionic liquids particularly in metal-catalyzed reactions allowed easy recovery and reuse of the catalysts. During our ongoing study on catalyst recycling, we have found $Sc(OTf)_3$, $La(OTf)_3$ and $InCl_3$ are effectively immobilized in room temperature ionic liquids, especially, consisting of 1-n-butyl-3-methylimidazolium cations [bmim][X] (Fig. 1) [11]. Prompted by these results, we decided to examine the catalytic activity and reusability of the well-known metallic Lewis acids, $Cu(OTf)_2$, $Yb(OTf)_3$, $Sc(OTf)_3$, $In(OTf)_3$, $HfCl_4 \cdot (THF)_2$ and $InCl_3$ in ionic liquids for acetylation of alcohols with acetic anhydride and acetic acid. Here we wish to report the results.
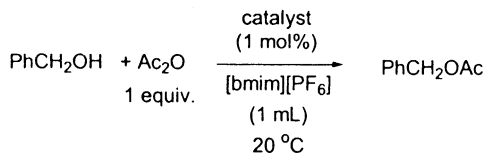
2. Results and discussion

To examine the catalytic activity of the Lewis acids in ionic liquids, acetylation of benzyl alcohol with acetic anhydride was chosen as a model reaction. In the presence of 1 mol.% of catalyst, an equimolar mixture of benzyl alcohol and acetic anhydride in [bmim][PF$_6$] was stirred at 20 °C, and followed by TLC until all starting benzyl alcohol was consumed (Table 1).

As shown in Table 1, all catalysts examined are very effective in acetylation of benzyl alcohol in the ionic liquid [bmim][PF$_6$]. Among the catalysts, $Cu(OTf)_2$ showed the highest catalytic activity, the reaction being completed in 5 min (entry 1). Notable is that $InCl_3$ also can be an effective catalyst for acylation (entry 6). Because of its stability in water and unique capability to impart high selectivity in various chemical transformations, $InCl_3$ has recently received attention [12]. However, to date, acylation of alcohol using $InCl_3$ as a catalyst has not been reported in literature yet. (Recently, InI_3 has been used as a catalyst for transesterification. See [13].)

One of the primary aims of our study was to investigate the recycling of the metallic Lewis acid

Table 1
Acetylation of benzyl alcohol with acetic anhydride using Lewis acids in [bmim][PF$_6$][a]

$$PhCH_2OH + Ac_2O \xrightarrow[\substack{[bmim][PF_6] \\ (1\ mL) \\ 20\ ^\circ C}]{\substack{catalyst \\ (1\ mol\%)}} PhCH_2OAc$$
1 equiv.

Entry	Catalyst	Time	Yield (%)[b]		
			First	Second	Third
1	Cu(Otf)$_2$	5 min	>99	16	–
2	Yb(Otf)$_3$	1 h	>99	94	50
3	Sc(Otf)$_3$	1 h	>99	96	75
4	In(OTf)$_3$	1 h	>99	61	25
5	HfCl$_4$·(THF)$_2$	4 h	>99	65	17
6	InCl$_3$	4 h	>99	33	16

[a] Reactions were run with 1.93 mmol of benzyl alcohol.
[b] Isolated yield.

catalysts. Clearly this is important in the context of economic feasibility and sustainable development. Thus, the recovered catalysts, which were immobilized in [bmim][PF$_6$], were reused in the second run. The catalytic activities of $Cu(OTf)_2$ and $InCl_3$ were dramatically decreased to give the desired ester in only 16% (entry 1) and 33% (entry 6) yield, respectively. Similarly, the catalytic activities of the $In(OTf)_3$ and $HfCl_4 \cdot (THF)_2$ also decreased in the second and third cycles (entries 4 and 5). In contrast, $Yb(OTf)_3$ (entry 2) and $Sc(OTf)_3$ (entry 3) almost retained their catalytic activities in the second cycle, but their activities decreased drastically in the third cycle.

We next examined the catalytic activity of these catalysts for direct acetylation of benzyl alcohol with equimolar amount of acetic acid in ionic liquids (Table 2). Initially, the reaction was carried out in [bmim][PF$_6$] at 20 °C for 12 h in the presence of 1 mol.% of $Sc(OTf)_3$, but the reaction was not completed, and afforded the product ester in only 64% yield (entry 1 in Table 2). The yield was not increased at all in other ionic liquids, such as [bmim][BF$_4$] (21%, entry 2) and [bmim][SbF$_6$] (46%, entry 3). Fortunately, when the reaction time was prolonged to 48 h, the product was formed in 98% yield (entry 4). It has also been found that $Yb(OTf)_3$ (95%, entry 5 in Table 2) and $InCl_3$ (95%, entry 6 in Table 2) also effectively catalyzed the acetylation with acetic acid. However, when the solvent/catalyst system recovered

Table 2

Acetylation of benzyl alcohol with acetic acid in ionic liquids[a]

$$PhCH_2OH + AcOH \xrightarrow[\substack{[bmim][X] \\ (1\,mL) \\ 20\,^\circ C}]{\substack{catalyst \\ (1\,mol\%)}} PhCH_2OAc$$

1 equiv.

Entry	Catalyst	X	Time (h)	Yield (%)[b]		
				First	Second	Third
1	$Sc(OTf)_3$	PF_6	12	64	–	–
2	$Sc(OTf)_3$	BF_4	12	21	–	–
3	$Sc(OTf)_3$	SbF_6	12	46	–	–
4	$Sc(OTf)_3$	PF_6	48	98	87	79
5	$Yb(OTf)_3$	PF_6	48	95	85	80
6	$InCl_3$	PF_6	48	95	86	79
7	$HfCl_4 \cdot (THF)_2$	PF_6	48	86	65	56

[a] Reactions were run with 1.93 mmol of benzyl alcohol.
[b] Isolated yield.

from the First cycle were re-used, the catalytic activities were slightly decreased (entries 4–7). Unfortunately, at the present time it is not easy to explain the reason for the decreased catalytic activity of the recovered catalysts.

Finally, acetylation of various alcohols with acetic anhydride has been carried out in [bmim][PF$_6$] in the presence of 1 mol.% of Sc(OTf)$_3$ as a catalyst at 20 °C for 1 h. As shown in Table 3, all of the primary,

Table 3

Sc(OTf)$_3$ catalyzed acetylation of alcohols in [bmim][PF$_6$][a]

Entry	Alcohol	Yield (%)[b]
1	Ph⌒⌒OH	>99
2	Ph⌒⌒⌒OH	>99
3	Ph—CH(CH₃)—OH	>99
4	1-adamantanol (OH)	>99
5	cyclohexadienol—OH	>99

[a] Reactions were run with 1.93 mmol of alcohol, 1 equivalent of acetic anhydride in 1 ml [bmim][PF$_6$] for 1 h using 1 mol.% of Sc(OTf)$_3$ at 20 °C.
[b] Isolated yield.

secondary and tertiary alcohols as well as phenol were perfectly acetylated.

3. Experimental

3.1. General remarks

All reactions were carried out in oven-dried glassware under an atmosphere of nitrogen. Column chromatography was performed using Kieselgel 60 (230–400 mesh) and TLC was carried out using glass sheets pre-coated with silica gel 60F254 purchased from Merck. The NMR spectra were recorded on a Bruker 300 spectrometer. All other chemicals were purchased from commercial suppliers and were used as received.

3.2. Synthesis of [bmim][X]

All ionic liquids were prepared from [bmim][Cl] [14]. To a solution of [bmim][Cl] (1 equivalent) in anhydrous acetone at room temperature was added 1 equivalent of sodium hexafluorophosphate for [bmim][PF$_6$], sodium tetrafluoroborate for [bmim][BF$_4$] or sodium hexafluoroantimonate for [bmim][SbF$_6$]. The reaction mixture was stirred for 24 h at 20 °C and was then filtered through a plug of Celite. The volatile was removed in vacuo, and the residue was dissolved in methylene chloride and washed with water several times. After evaporation of the methylene chloride, ionic liquid was vacuum dried for 2 days and stored under an atmosphere of dry argon. All ionic liquids contained less than 10 ppm of chlorine according to the chlorine analysis at Analysis Center in Korea Institute of Science and Technology and less than 15 ppm of water according to the Karl Fischer analysis (Metrolm model: 756KF Coulometer).

3.3. General acetylation procedure

Acetic anhydride or acetic acid (1.93 mmol) and alcohols (1.93 mmol) were added to a solution of catalyst (0.019 mmol) in 1.0 ml of ionic liquids at 20 °C under N$_2$ atmosphere. The reaction mixture was stirred at the same temperature for 1 h. Upon completion of the reaction, the organic materials were extracted with benzene (5 ml × 4). When recycling

the solvent/catalyst system, fresh alcohol and acetic anhydride (or acetic acid) were added again. After removing benzene, the product was purified by silica-gel chromatographic separation.

4. Conclusions

The catalytic activities of the metallic Lewis acids, Cu(OTf)$_2$, Sc(OTf)$_3$, Yb(OTf)$_3$, In(OTf)$_3$, HfCl$_4$· (THF)$_2$ and InCl$_3$, for acetylation of alcohols with acetic anhydride and acetic acid were examined in room temperature ionic liquids. All of these catalysts exhibited extremely high catalytic activity in acetylation with acetic anhydride in [bmim][PF$_6$]. It has also been found that Sc(OTf)$_3$, Yb(OTf)$_3$ and InCl$_3$ can be effective catalysts for acetylation of benzylalcohol with acetic acid in [bmim][PF$_6$] ionic liquid. Although the catalytic activity of the recovered catalysts was decreased upon recycling, these results may offer an opportunity to use metallic Lewis acid-catalysts for acylation of alcohols in environmentally benign ionic liquids.

Acknowledgements

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