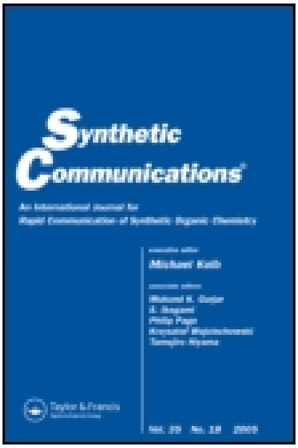

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Brønsted Acidic Ionic Liquids as Efficient and Recyclable Catalysts for Protection of Carbonyls to Acetals and Ketals Under Mild Conditions

Yuying Du [a] & Fuli Tian [a]
[a] Department of Chemistry, College of Chemistry and Chemical Engineering, Inner Mongolia University, Hohhot, China

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Brønsted Acidic Ionic Liquids as Efficient and Recyclable Catalysts for Protection of Carbonyls to Acetals and Ketals Under Mild Conditions

Yuying Du and Fuli Tian
Department of Chemistry, College of Chemistry and Chemical
Engineering, Inner Mongolia University, Hohhot, China

Abstract: A series of acidic ionic liquids have been used as efficient catalysts for the protection of various carbonyl compounds at room temperature. The features of mild conditions, satisfactory isolated yield, simple workup, and the recyclability of the catalyst were present in this process.

Keywords: Acetals, ionic liquid, ketals, protection of carbonyls

INTRODUCTION

Protection of carbonyls as acetals (or ketals) is one of the most important reactions in organic chemistry and many methods have been developed for these reactions.[1] Although a lot of conventional catalysts including acidic catalysts,[2,3] $Sc(NTf)_3$,[4] and decaborane[5] have been reported for the protection of carbonyls as dimethyl acetals, many of these procedures are associated with one or more disadvantages such as toxic and expensive catalysts, poor chemoselectivity and yield, limited examples, and nonrecovery of the catalyst.[3] Therefore, the search for a new catalyst is still actively pursued.

Ionic liquids (ILs) are a new class of solvents entirely composed of ions. Their use as an environmentally friendly alternative to conventional solvents

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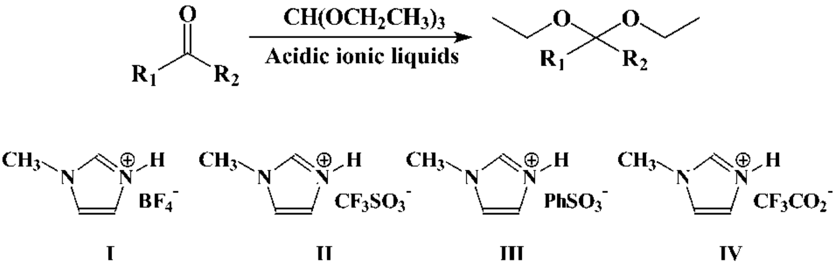
Address correspondence to Fuli Tian, Department of Chemistry, College of Chemistry and Chemical Engineering, Inner Mongolia University, Hohhot 010021, China. Tel.: +86-471-4993443; E-mail: ceac@imu.edu.cn

has gained much attention recently.[6–9] We are specifically interested in the designability of ILs because it gives us the ability to manipulate IL structure (with respect to the organic cation, inorganic anion, and the length of the side chain attached to the organic cation) as well as their properties. When an alkane sulfonic acid group is covalently attached to the imidazolium cation, the IL would be a strong Brønsted acidic material.[10] These SO_3H-functionalized ILs have exhibited great potential as replacements for conventional homogenous and heterogeneous acidic catalysts because they are flexible, nonvolatile, noncorrosive, and immiscible with many organic solvents.[11–13] However, these ILs are very expensive and have a tedious preparation procedure. To extend the scope and decrease the cost of ILs, a new and inexpensive class of acidic ILs was synthesized by simple protonation of 1-alkylimidazoles with protic acids. From the recent reports, these ILs could be applied in esterification, Mannich reaction, Biginelli condensation, Pechmann reaction, and protection of carbonyl compounds using alcohols as protection reagents.[14–18] Herein, we describe the protection of carbonyls as acetals (or ketals) using orthoformate as a protection reagent over a catalytic amount of acidic ILs (Scheme 1).

EXPERIMENTAL

Typical Reaction Procedure

ILs were synthesized according to the literature.[14–16] A catalyst (0.5 mmol) was added to a stirred mixture of a carbonyl compounds (10 mmol) and triethyl orthoformate (15 mmol, 2.22 g) in a reaction flask. The mixture was stirred at room temperature (25°C), and the progress of the reaction was monitored using a Hewlett-Packard 6890/5793 GC/MS. After completion of the reaction, the catalyst was recovered from the mixture by filtration. The filtrate was dried over anhydrous Na_2SO_4 and then evaporated to give almost pure product. Further purification was achieved through a column of silica gel (20 cm in length, 1 cm in diameter) with petroleum ether. Purity analyses of organic products were conducted with a HP 1790 GC equipped



Scheme 1.

with a flame ionization detector (FID). The purity of product was directly given by the system of GC chemstation according to the area of each chromatograph peak. ^{1}H NMR (400-MHz) spectra were obtained as solutions in CD_3COCD_3. Chemical shifts were reported in parts per million (ppm, δ) and referenced to TMS.

RESULTS AND DISCUSSION

We initially tested the reaction of benzaldehyde with triethyl orthoformate at room temperature in the presence of IL **I**. The conversion of benzaldehyde was only 73% when using equimolar amounts of benzaldehyde and triethyl orthoformate (Table 1, entry 1). Fortunately the desired reaction was efficiently accomplished when the reaction was carried out using 1.5 equiv of triethyl orthoformate as protection reagent (entry 2). The subsequent condition-optimization experiments revealed that the 1.5 h and 5% of the catalyst was necessary to complete the reaction. When 1.0 h or 2% of the catalyst was used, the conversion only reached 84% and 70%, respectively (entries 6 and 7). ILs **II** and **III** also represent good activities for this reaction, but IL **I** seems to be slightly better compared with **II** and **III** (entries 3 and 4). When the anion of IL was changed to CF_3COO^-, only benzaldehyde was recovered at the end of the reaction (entry 5). All these results illustrate that ILs derived from strong acids have better activity than weaker ones.

Having these results in hand, we subjected other aldehydes to the these optimized conditions, and the results are listed in Table 2. Various aldehydes and ketones were efficiently converted to the corresponding diethyl acetals in the presence of triethyl orthoformate using a catalytic amount of IL **I** at room temperature. Yields of these reactions are almost quantitative in most cases. IL (5 mol%) was used in all of the cases except for acetophenone

Table 1. Scanning of catalysts and optimization of reaction conditions on the reaction of benzaldehyde with triethyl orthoformate[a]

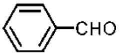
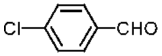
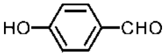
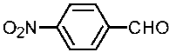
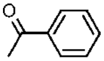
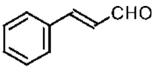
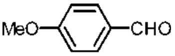
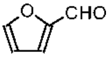
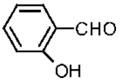
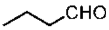
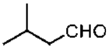
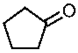
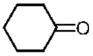
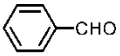
Entry	Catalysts	Amount of catalyst (%)[b]	Ratio of substrate[c]	Reaction time (h)	Conversion of benzaldehyde (%)
1	I	5	1.0	1.5	73
2	I	5	1.5	1.5	96
3	II	5	1.5	1.5	89
4	III	5	1.5	1.5	87
5	IV	5	1.5	1.5	0
6	I	2	1.5	1.5	70
7	I	5	1.5	1.0	84

[a] Reaction condition: benzaldehyde, 1.06 g.

[b] Calculated based on benzaldehyde (M/M).

[c] Ratio of triethyl orthoformate to benzaldehyde.

Table 2. Acidic IL **I**–catalyzed protection of carbonyls using triethyl orthoformate as protection reagent at room temperature

Entry	Substrates	Time (h)	Yield (%)
1		1.5	93
2		1.5	92
3		1.5	90
4		2.0	91
5		12.0	87
6		2.0	92
7		3.0	90
8		2.0	89
9		3.0	90
10		4.0	92
11		4.0	90
12		4.0	85
13		4.0	84
14[a]		1.5	90

[a]Reused three times.

(10 mol%). It was noteworthy that IL **I** was insoluable during the reaction in the reaction mixture. Thus, it could be recycled by filtration after reaction and used in the next run. In the reaction of benzaldehyde, IL **I** could be reused three times without visible loss of activity.

SPECTROSCOPIC DATA FOR SELECTIVE PRODUCTS

Diethylacetal of benzaldehyde: colorless liquid; purity: 99%; bp: 222–223°C; H NMR: δ 1.25 (t, 6H, $J = 3.6$ Hz), 3.62 (m, 4H), 5.46 (s, 1H) 7.20 (d, 2H, $J = 8.4$ Hz), 7.77 (d, 2H, $J = 8.8$ Hz); MS: $m/z = 180$ (M^+), 150, 135, 122, 105, 91, 79, 77; $C_{11}H_{16}O_2$ (180.246): calcd. C, 73.30, H, 9.85; found C, 73.58; H, 9.71.

Diethylacetal of p-chlorobenzaldehyde: colorless liquid; purity: 98.5%; bp: 132–133°C/10 mmHg; H NMR: δ 1.25 (t, 6H, $J = 3.6$ Hz), 3.61 (m, 4H), 5.36 (s, 1H), 7.33 (d, 1H, $J = 8.4$ Hz), 7.50 (d, 1H, $J = 8.4$ Hz); MS: m/z = 214 (M^+), 170, 169, 141, 113, 103, 89, 77, 63; $C_{11}H_{15}O_2Cl$ (214.691): calcd. C, 61.54; H, 7.04; found C, 61.69; H, 7.18.

Diethylacetal of 2-furaldehyde: colorless liquid; purity: 98.5%; bp: 190–192°C; H NMR: δ 1.24 (t, 6H, $J = 4.0$ Hz), 3.74 (m, 4H), 5.50 (s, 1H), 6.40 (dd, 1H, $J = 8.0$ Hz), 6.47 (d, 1H, 8.4 Hz), 7.40 (m, 1H, $J = 8.4$ Hz); MS: $m/z = 170$ (M^+), 141, 125, 113, 97, 85, 69; $C_9H_{14}O_3$ (170.208): calcd. C, 63.51; H, 8.29; found C, 63.34; H, 8.11.

Diethylacetal of p-nitrobenzaldehyde: colorless liquid; purity: 98.0%; bp: 154–156°C/6 mmHg; H NMR: δ1.24 (t, 6H, $J = 4.0$ Hz), 3.63 (m, 4H), 5.47 (s, 1H), 7.63 (d, 2H, $J = 8.2$ Hz), 8.22 (d, 2H, $J = 8.2$ Hz); MS: m/z = 225 (M^+), 180, 164, 152, 136, 122, 106, 94, 77, 66, 51; $C_{11}H_{15}O_4N$ (225.244): calcd. C, 58.66; H, 6.71; N, 6.22; found C, 58.87; H, 6.50; N, 6.09.

Diethylacetal of acetophenone: colorless liquid; purity: 98.0%; bp: 110–112°C/12 mmHg; H NMR: δ1.21 (t, 6H, $J = 3.6$ Hz), 1.54 (s, 3H), 3.62 (m, 4H), 7.27 (m, 1H), 7.34 (m, 2H), 7.48 (m, 2H); MS: m/z = 194 (M^+), 179, 149, 121, 105, 91, 77, 61, 43; $C_{12}H_{18}O_2$ (194.273): calcd. C, 74.19; H, 9.34; found C, 74.33; H, 9.28.

Diethylacetal of p-methoxybenzaldehyde: colorless liquid; purity: 98.0%; bp: 169–171°C/10 mmHg; H NMR: δ 1.23 (t, 6H, $J = 3.6$ Hz), 3.62 (m, 4H), 3.82 (s, 3H), 5.41 (s, 1H), 6.72 (d, 2H, $J = 8.4$ Hz), 7.21 (d, 2H, $J = 8.8$ Hz); MS: m/z = 210 (M^+), 165, 137, 109, 94, 77, 66; $C_{12}H_{18}O_3$ (210.272): calcd. C, 68.55; H, 8.63; found C, 68.69; H, 8.51.

CONCLUSION

In summary, Brønsted acidic ILs **I**, **II**, and **III** have proved to be effective catalysts for protection of carbonyl compounds using triethyl orthoformate as protection reagent. Mild conditions, cost-efficient catalyst, simple workup, and the recyclability of the catalyst are the features obtained in these systems. Another advantage of these ILs as novel promoters for this transformation is their green property: these materials are metal-free species. This may be most attractive for the development of clean organic transformation and green chemistry, therefore, the present catalytic method is useful in organic synthesis.

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