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Ionic liquid catalyzed Henry reactions

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Abstract—The 1,1,3,3-tetramethyl guanidine (TMG)-based ionic liquid was used as a recyclable catalyst for Henry reactions to produce 2-nitroalcohols. Good yields were obtained even after 15 reactions.

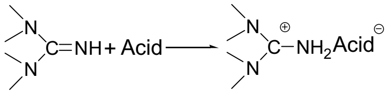
Ionic liquids (ILs) have attracted extensive interest in recent years as environmentally benign solvents due to their favorable properties, such as nonflammability, negligible vapor pressure, reusability, and high thermal stability.[1] Over the past few years, a variety of catalytic reactions have been successfully conducted using ILs as solvents. Many interesting results have been obtained, which demonstrate advantages of using ILs as alternatives for organic solvents. Especially, one of the advantage of ILs is the behavior of an acid or base catalyst. The most frequently used acidic or basic ILs are the chloroaluminates. These acidic ILs has been utilized to catalyze alkylation,[2] esterification,[3] acrylation,[4] and Diels–Alder reactions.[5] However, the sensitivity of these ILs to water limits their use. Other types of acidic ILs have also been reported to effectively catalyze esterification.[6] Recently, another family of acid–base ILs were reported by Watanabe et al.[7]

The Henry reaction is one of the most useful carbon–carbon bond forming reactions and has wide synthetic applications in organic synthesis by which 2-nitroalcohols are formed on treatment of nitroalkanes and carbonyl derivatives with a basic catalyst.[8] The products, nitroalcohols are useful intermediates in the preparation of nitroalkenes, α-nitroketones, and β–aminoalcohols derivatives, such as ephedrine and norephedrine.[9]

Henry reactions can be catalyzed by organic and inorganic bases. Several years ago, 1,1,3,3-tetramethyl guanidine (TMG) and its cyclic analogs have been utilized as efficient catalysts. The protocol was thought to have significant advantages to achieve milder reaction conditions and shorter reaction times.[10]

Recently, guanidine-based ILs were synthesized.[11] In this work, we used guanidine-based ILs, 1,1,3,3-tetramethylguanidinium (TMG) trifluoroacetate ([TMG][F_3Ac]) and TMG lactate ([TMG][Lac]), which were prepared by neutralizing TMG with trifluoroacetic acid or lactic acid (Scheme 1). The two ILs are liquids at ambient temperature. In this letter, we focus on their use as recyclable solvents and catalysts for Henry reactions of nitroalkanes and carbonyl compounds. The detailed information about the synthesis and characterization will be discussed elsewhere.[12]

The successful results of [TMG][Lac] IL catalyzed Henry reactions are given in Table 1. The catalyst can be applied to both aromatic and aliphatic aldehydes with the latter giving higher yield than the former (entries 1–3 vs 4–6). Reaction also occurred when cyclohexanone was used, but the yield was much lower (entry 7). All reactions proceeded cleanly under mild conditions. No side products were found. When nitroethane was used instead of nitromethane (entries 8–10), the yields of



Scheme 1.

Keywords: Henry reaction; Ionic liquid; Basic catalysis; 2-Nitroalcohol.

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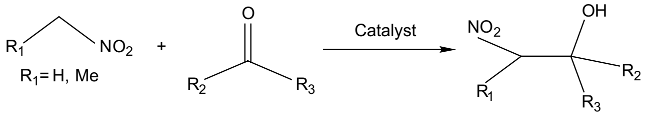
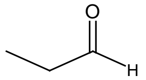
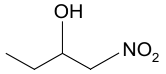
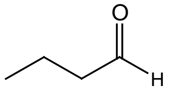
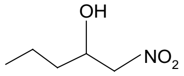
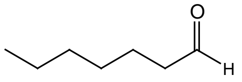
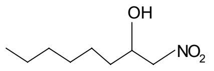
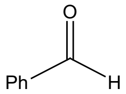
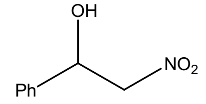
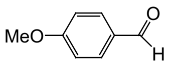
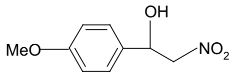
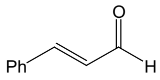
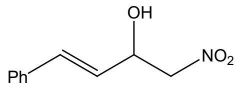
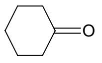
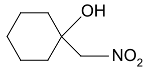
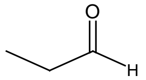
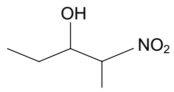
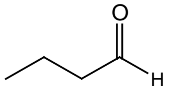
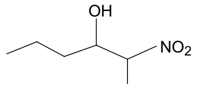
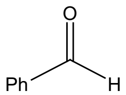
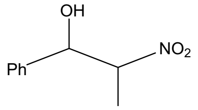
Table 1. Synthesis of 2-nitroalcohols by [TMG][Lac] catalyzed Henry reactions[a]



Entry	Carbonyl compound	Nitroalkane	Reaction time	Product	Yield (%)
1		CH_3NO_2	20		73
2		CH_3NO_2	6		51
			17		61
			24		72
3		CH_3NO_2	20		44
4		CH_3NO_2	20		47
5		CH_3NO_2	20		51
6		CH_3NO_2	20		61
7		CH_3NO_2	20		20
8		$C_2H_5NO_2$	20		57
9		$C_2H_5NO_2$	20		41
10		$C_2H_5NO_2$	20		14

[a] Reaction conditions: 20 °C; IL 1 g; CH_3NO_2 or $C_2H_5NO_2$ 100 mmol; carbonyl compound 5 mmol.

products were much lower. No diastereoselectivity was observed, and was in agreement with the results reported by Simoni et al.[10b] [TMG][F_3Ac] proved to be an effective catalyst as well in the reaction of nitromethane and aldehydes. Similar yields were obtained, as shown in Table 2.

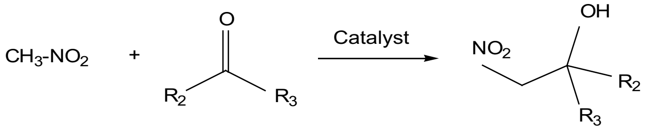
Experiments were conducted to study the reaction of nitromethane and propionaldehyde at 20 °C without guanidine-based IL. The molar ratios of propionaldehyde to nitromethane were 1:1 and 20:1, respectively. No product was detected after 20 h in both cases. Therefore, guanidine-based ILs were shown to be catalysts.

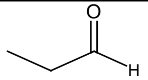
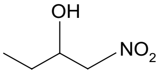
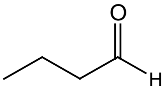
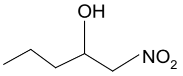
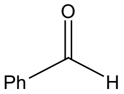
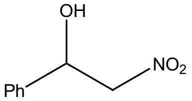
The reuse of [TMG][Lac] was studied, and the results are given in Figure 1. It is shown that the IL remained catalytic active for 15 runs when propionaldehyde was used. When cyclohexanone was used, no reduction of the activity was detected after four runs.

In summary, the TMG-based IL is shown to catalyze the Henry reactions of nitroalkanes and carbonyl compounds including aliphatic and aromatic aldehydes and cycloalkanones effectively. The reactions proceeded smoothly at room temperature to produce 2-nitroalcohols with good yields. The catalyst can be reused repeatedly.

Experiments: Typical experimental procedures: the reactions were carried out at 20 °C. The nitroalkane (100 mmol) and the carbonyl compound (5 mmol) were mixed together and then desired amount of IL was added to the mixture. The reaction mixture was stirred for a certain time. At the end of the reaction, water (3 mL) and ethyl acetate (5 mL) were added and the

Table 2. Synthesis of 2-nitroalcohols by [TMG][F_3Ac] catalyzed Henry reactions[a]



Entry	Carbonyl compound	Nitroalkane	IL (g)	Product	Yield (%)
1		CH_3NO_2	1		72
2		CH_3NO_2	1		77
			2		77
3		CH_3NO_2	1		55

[a] Reaction conditions: 20 °C; 20 h; CH_3NO_2 100 mmol; carbonyl compound 5 mmol.

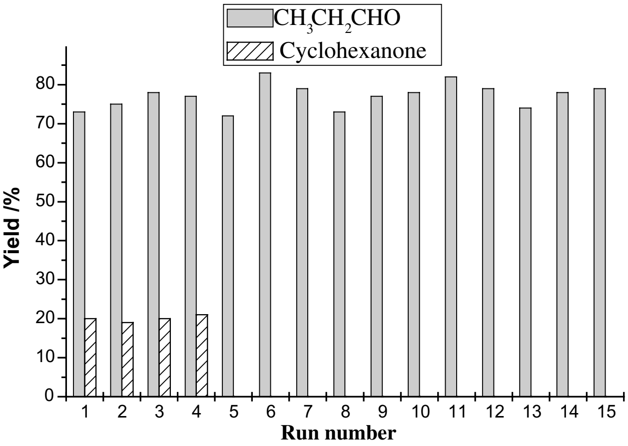


Figure 1. Reuse of the [TMG][Lac] IL in catalyzing reactions of nitromethane with propionaldehyde or cyclohexanone. Conditions: 20 °C; nitromethane 100 mmol; propionaldehyde or cyclohexanone 5 mmol; [TMG][Lac] IL 1 g; 20 h each time.

reaction mixture was separated into two layers. As TMG-based IL was soluble in water, pure IL was obtained after drying the water–IL layer, which could be reused. Pure 2-nitroalcohol was obtained from the upper ethyl acetate layer after distillation or column chromatography.

Acknowledgements

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