Tetrahedron Letters 52 (2011) 3588–3591

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Solvent-free aza-Markovnikov and aza-Michael additions promoted by a catalytic amount of imidazolide basic ionic liquids

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A R T I C L E I N F O

Article history:
Received 3 March 2011
Revised 21 April 2011
Accepted 29 April 2011
Available online 6 May 2011

Keywords:
Ionic liquids
Imidazolide
Solvent-free reactions
Aza-Markovnikov addition
Aza-Michael addition

A B S T R A C T

A family of imidazolide ionic liquids were synthesized and characterized. These ionic liquids combined the virtues of strong basicity and relatively good thermal stability. Catalytic properties of these imidazolide ionic liquids were investigated and satisfactory yield was achieved when 2.0 mol % of [Bmim]Im was used as catalyst for aza-Markovnikov addition under solvent-free condition at room temperature in one hour. Experimental results show that a hydrogen bond is not formed between [Bmim]Im/imidazole and vinyl ester, and its existence is not necessary for the [Bmim]Im catalyzed aza-Markovnikov addition either. A possible mechanism for [Bmim]Im-catalyzed aza-Markovnikov addition was proposed. The use of imidazolide ionic liquids in aza-Michael addition was investigated as well.

The Markovnikov addition is among the most useful carbon-carbon, oxygen-carbon, or nitrogen-carbon bond-forming reactions and it is widely used in organic chemistry and pharmaceutical synthesis.[1] This reaction is traditionally performed under harsh reaction conditions.[2] The aza-Markovnikov addition of *N*-heterocycles to vinyl esters has recently received much attention with some effective approaches, for example, using acylases as biocatalysts, ionic liquid as both catalyst and reaction medium, and anhydrous K_3PO_4 as catalyst in DMF.[3–5] However, such processes still need polar solvent as reaction medium or require a large amount of ionic liquid acting as catalyst and reaction medium as well. Here, we are interested in solvent-free reactions catalyzed by task-specific ionic liquids in order to decrease the amount of organic solvent and ionic liquid consumed.

Ionic liquids have attracted extensive research interest in recent years as environmentally benign solvents and catalysts due to their favorable properties.[6] They can be designed as task-specific ionic liquids by careful development and choice of novel component ions to endow them some special physical or chemical properties.[7] A typical progress is the appearance of the air, water stable, basic ionic liquids.[8] Well known examples including lactate,[9] dicyanamide,[10] carboxylates,[11] amino acid anions,[12] and amine-functionalized cations[13] have been reported, but the basicity of these ionic liquids is far weaker from the point of view of basic catalyst. The strongly basic hydroxide ionic liquids were the most investigated basic ionic liquids.[14] However, the preparation of these hydroxide ionic liquids with good quality is difficult due to their unsatisfied stability. Therefore, development of strongly basic ionic liquids with good stability is a practical and significative issue in basic ionic liquids.

We have reported imidazolide ionic liquid by introducing the imidazolide anion into the ionic liquid for the first time,[15] superbase-based protic imidazolide ionic liquids were developed afterward and applied for the rapid and reversible capture of CO_2.[16] Herein, the synthesis and characterization of imidazolide basic ionic liquids were extended, their acid–base property and thermal stability were also discussed. Furthermore, a mild and efficient aza-Markovnikov addition of imidazole to vinyl acetate catalyzed by these imidazolide ionic liquids under solvent-free condition was reported and the possible mechanism was proposed. In addition, the applicability of imidazolide ionic liquids was also extended to aza-Michael addition.

Nitrogen-containing heterocyclic compounds, such as imidazole, triazole, and tetrazole, have been widely used to form energetic azolate anions in energy conservation studies.[17] Azole compounds are also a potential resource for the development of basic azolate anions though little attention had been paid to the acid–base property of azolate ionic liquids. The imidazolide basic ionic liquids were developed here by anion exchange of bromide ionic liquids with imidazolide salt (Scheme 1).

Imidazolium bromide precursors **1a**–**1d** were prepared according to standard preparative procedures.[18] And low reaction temperatures were selected as it was reported that imidazolium ionic liquids with higher qualities can be achieved under mild temperature.[19]

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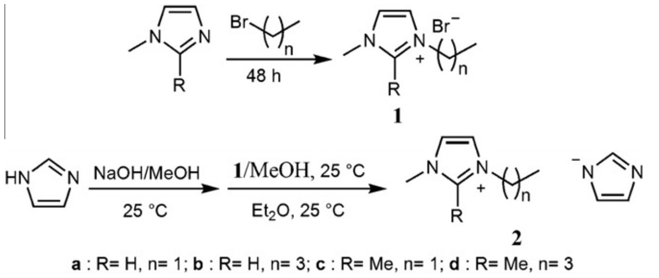
doi:10.1016/j.tetlet.2011.04.117



Scheme 1. Synthesis of imidazolide ionic liquids.

The imidazolide anion was introduced to the desired salts **2a–2d** by metathetic reaction. Equal molar of NaOH and imidazole were mixed and reacted in MeOH. Then the resulting clear, colorless mixture was added to the solution of imdazolium bromide/MeOH. Filtration followed by concentration of the filtrate provided the desired products. Tetrabutylammonium imidazolide ([TBA]Im) was also obtained by anion-exchange of tetrabutylammonium bromide with sodium imidazolide. Imidazolide ionic liquids were purified by addition of anhydrous Na_2SO_4 during the preparation and washing with Et_2O in workup to get rid of water and salts, respectively. All these imidazolide ionic liquids are pale yellow liquids at room temperature, stable in air and moisture. The lower melting points of these imidazolide ionic liquids may be explained by the charge delocalisation and the rigid, planar structure in the imidazolide anion. The structure of the products is verified with ^1H NMR, ^{13}C NMR, FT-IR, and ESI-MS. Ion-exchange chromatography[20] and ^1H NMR[21] analysis showed that purity degree of imidazolium imidazolides were no less than 95%. As to [TBA]Im, the ion-exchange was not complete (about 81% ion-exchange rate).

The basicity of imidazolide ionic liquids was preliminarily investigated. At first, we compared the pK_b values of imidazolide to those of acetate and hydroxide in aqueous solution. The pK_b value of imidazolide is −0.5,[22] which is intermediate between those of acetate (9.25) and hydroxide (−1.7). In other words, the basicity of imidazolide ionic liquids is much stronger than that of acetate ionic liquids ($\Delta pK_b = -9.8$) and weaker than that of hydroxide ionic liquids ($\Delta pK_b = 1.2$). In addition, the distribution of base strength of these imidazolide ionic liquids (H_-) was also intuitively manifested by the Hammett-Deyrup H-function method.[23] 2,4-Dinitroaniline ($H_- = 15.0$) and 4-nitroaniline ($H_- = 18.4$) were used for Hammett indicators after carefully screening procedure. These imidazolide ionic liquids together with [Bmim]OH and NaOH were able to have the color of 2,4-dinitroaniline ($H_- = 15$) changed from yellow to purple (its basic color), but unable to convert 4-nitroaniline ($H_- = 18.4$) to its basic color (orange). Thus, the basic strength of imidazolide could be denoted as strong bases with $15.0 < H_- < 18.4$ according to the reported determination method.[24]

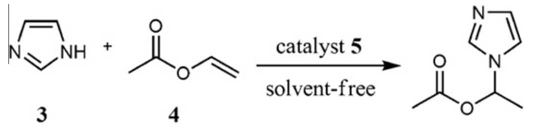
The thermal stability of [Bmim]Im was surveyed by thermogravimetric analysis and compared with other two typical basic ionic liquids 1-butyl-3-methylimidazolium acetate ([Bmim]CH_3COO) and 1-butyl-3-methylimidazolium hydroxide ([Bmim]OH), which were synthesized according to standard preparative procedures.[11,14] It has been reported that the strong Lewis basicity of the anion tends to induce thermal decomposition at lower temperature.[11,25] However, the thermal stability of [Bmim]Im is close to that of [Bmim]CH_3COO and much better than that of [Bmim]OH. Further experimental results showed that all alkylimidazolium imidazolide salts had similar thermal stability with minor distinction according to the following sequence: [Emim]Im < [Emmim]Im < [Bmim]Im < [Bmmim]Im. These imidazolide ionic liquids began to decompose at above 160 °C and decomposed completely around 300 °C. Thus, imidazolide ionic liquids not only have strong basicity comparable to hydroxide ionic liquids, but also have relatively good thermal stability with respect to acetate ionic liquids.

As shown in the ^1H NMR spectra of [Emim]Im and [Bmim]Im, the peaks of imidazolium C(2)-protons disappeared, which probably resulted from the hydrogen deuterium (H/D) exchange[26] owing to the interaction between the stronger acidity ($pK_a \sim 21–23$) of imidazolium C(2)-protons[27] and the strong Lewis basicity of the imidazolide anion. Further investigation about the ^1H NMR spectrum of equal molar of [Bmim]Im and ethanol mixture showed that proton peaks of the hydroxyl and imidazolium C(2)-proton also disappeared as expected, which verifies the above interpretation about the H/D exchange. In addition, the notable H/D exchange of imidazolium C(4)-proton and C(5)-proton had not been seen under our condition.

We employed the imidazolide ionic liquids in the Markovnikov addition of imidazole to vinyl acetate. The progress of the reaction was monitored by thin-layer chromatography (TLC) and the product yield was obtained after flash chromatography. Firstly, the feasibility of aza-Markovnikov addition of imidazole (10 mmol) to vinyl acetate (60 mmol) in the presence of [Bmim]Im (0.02 mmol) under solvent-free condition at 50 °C for 4 h was evaluated and the expected product was formed with 92% yield (Table 1, entry 1). Then, aza-Markovnikov addition of imidazole and vinyl acetate was carried out and the effect of reaction parameters to the yield of products were all investigated in detail.

At first, it was observed that the decrease in reaction temperature had no obvious effect on the reaction yield and Markovnikov addition could proceed smoothly both at room temperature in 1 h and at 50 °C (Table 1, entries 2 and 3). Then, the influence of feed molar ratio of vinyl acetate to imidazole was investigated. Systematically reducing the number of equivalents of vinyl acetate led to somewhat higher yield, and the highest yield was obtained when a 1.2:1 equiv of vinyl acetate to imidazole was used (Table 1, entries 2 and 4 vs. entry 5). As for the influence of the amount of [Bmim]Im on the reaction, it was found that 2 mol % [Bmim]Im was sufficient to promote the reaction extensively, insufficient amount of [Bmim]Im led to dramatical dropping of the yield (Table 1, entries 6 and 7). Additional amount of [Bmim]Im (3 mol %) provided limited

Table 1
Markovnikov addition of imidazole to vinyl acetate



Entry	Catalyst **5**	Ratio **4**:**3**	Ratio **5**:**3**	*T* (°C)	*t* (h)	Yield[a] %
1	[Bmim]Im	6.0	0.02	50	4	92
2	[Bmim]Im	6.0	0.02	rt	1	90
3	[Bmim]Im	6.0	0.02	50	1	89
4	[Bmim]Im	4.0	0.02	rt	1	91
5	[Bmim]Im	1.2	0.02	rt	1	92
6	[Bmim]Im	1.2	0.01	rt	1	59
7	[Bmim]Im	1.2	0.01	rt	2	71
8	[Bmim]Im	1.2	0.03	rt	1	93
9	[Bmim]Im	1.2	0.03	rt	0.5	81
10	None	1.2	0	rt	1	21
11	None	6.0	0	rt	7	21
12	NaOH	1.2	0.02	rt	1	62
13	[Bmim]CH_3COO	1.2	0.02	rt	1	57
14	[Bmim]CH_3COO	1.2	0.02	rt	2	79
15	[Bmim]Br	1.2	0.02	rt	1	28
16	[Bmim]Br	1.2	0.02	rt	2	49
17	[Bmmim]Im	1.2	0.02	rt	1	93
18	[TBA]Im	1.2	0.02	rt	1	91

[a] Isolated yields.