Pergamon

Tetrahedron Letters 44 (2003) 5037–5039

TETRAHEDRON LETTERS

Ionic liquid-regulated sulfamic acid: chemoselective catalyst for the transesterification of β-ketoesters

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Received 10 April 2003; revised 30 April 2003; accepted 7 May 2003

Abstract—1-Propyl-3-methylimidazolium chloride ([C_3MIm]Cl) ionic liquid and sulfamic acid (NH_2SO_3H), as a synergetic catalytic medium, were used for the transesterification of acetoacetate with alcohols of different structures. It shows the good ability for the chemoselective transesterificatin of β-ketoesters and maintains its catalytic activity in the reuse. © 2003 Elsevier Science Ltd. All rights reserved.

1. Introduction

Ionic liquids (ILs) consisting of 1,3-dialkylimidazolium cations and their counter ions have attracted growing interest in the last few years,[1] and particularly in the last two years, much efforts have paved the way for alternative and new synthetic strategies in the realm of synthetic organic chemistry, due to their advantages of negligible vapor pressure and wide liquid range, etc.[2] In general, the thermodynamics and kinetics of the reactions in ILs are very different from those in conventional molecular solvents. Furthermore, ILs could even control some reaction processes to selectively obtain specific products, which was usually impossible in conventional molecular solvents. ILs could provide some reactions with particular controllability. In this paper, we report an ionic liquid regulated catalyst, sulfamic acid, which displays the ability to selectively catalyze transesterification of β-ketoesters in an ionic liquid medium, instead of ketalization.

β-Ketoesters are employed widely as chemical intermediates in the pharmaceutical, agrichemical, chemical and polymer industries.[3] A lot of useful catalysts, including homogeneous ones of sulfated tin oxide,[4] yttria-zirconia based strong Lewis acid,[5] *p*-TSA,[6] zinc,[7] basic 4-DMAP[8] and heterogeneous ones of zeolites,[9] kaolinitic clay,[10] montmorillomite K-10[11] and so on, have been efficiently employed in transesterification of β-ketoesters. A type of distannoxanes could catalyze this process even in neutral conditions.[12] Although these methods are suitable for certain synthetic conditions, sometimes, there exist some drawbacks such as expensive reagents, long reaction time, tedious workup, low selectivity, and large amounts of solid supports which would eventually result in the generation of a large amount of toxic waste.[13] Biocatalytic transesterification of β-ketoesters in ILs had been reported, but the sensitivity and unstability of the catalysts were still serious problems.[14]

The development of the mild, low-cost and high performance acid catalysts for green chemistry have attracted much interest.[15] Sulfamic acid (NH_2SO_3H), with mild acidity, involatility and incorrosivity, is insoluble in

Table 1. Comparison of transesterification in the NH_2SO_3H/[C_3MIm]Cl system within different medium[a]

Entry	Solvent	Homo/ hetero[b]	Conversion (%)[c]	Selectivity (%)[c]
1	–	Hetero	95	79
2	Hexane	Hetero	93	80
3	CH_2Cl_2	Hetero	92	75
4	[C_3MIm]Cl	Homo	96	98
5	[C_5MIm]Cl[d]	Homo	94	99

[a] Reaction conditions: 10 g [C_3MIm]Cl or 10 ml organic solvents, 1.0 g sulfamic acid, 0.10 mol methyl acetoacetate, 0.12 mol butanol, 3.0 h, 80°C.

[b] Homo is the homogenous system, and hetero is the heterogenous system.

[c] Detected by GC.

[d] 1-Pentyl-3-methylimidazolium chloride.

Keywords: ionic liquid; sulfamic acid; chemoselective; transesterification; β-ketoesters.

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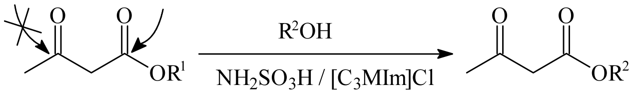
doi:10.1016/S0040-4039(03)01187-0

common organic solvents. It is very stable[16] and has been used as an efficient heterogeneous acid catalyst for ketalization.[17] The intrinsic ability of ILs to dissolve substrates of wide diversity, from organics to organometallics to inorganics, and its facility of recycling add itself to the chemists' arsenal for the execution of diverse processes. During the course of our studies on ILs, we found 1-propyl-3-methylimidazole chloride ([C_3MIm]Cl) has the excellent solubility for sulfamic acid, and its solubility in [C_3MIm]Cl even exceeded 80 g/100 ml at 80°C. This prompted us to systematacially investigate the transesterification of β-ketoesters using this homogeneous NH_2SO_3H/[C_3MIm]Cl system.

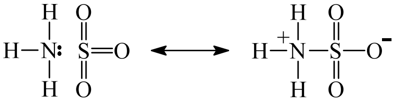
2. Results and discussion

The transesterification of methyl acetoacetate with butanol catalyzed by sulfamic acid was investigated in different medium (Table 1). Owing to the immiscibility of sulfamic acid with common organic solvents, this reaction was carried out in a heterogeneous system (entries 1–3). Lots of ketals and hemiketals derived from the ketalization of β-carbonyl of the acetoacetate with alcohols were detected, so that the selectivity to the desired product was poor. Similar results were obtained in hexane and CH_2Cl_2. In contrast, NH_2SO_3H can be dissolved in chloride-based ILs to form a homogeneous NH_2SO_3H/[C_3MIm]Cl system, and the transesterification was successfully performed in it (entries 4 and 5). It is worthy to note that the selectivity to the desired ester was significant higher in the ionic liquids than in common organic solvents and the solvent-free system, despite of the NH_2SO_3H catalyzing ketalization reported by some other researchers.[17] Therefore, it may be supposed that the [C_3MIm]Cl ionic liquid could not only act as a solvent to dissolve NH_2SO_3H, but also make it a chemoselective catalyst, and the attack of alcohols to β-site of acetoacetate would be effectively inhibited in this reaction environment (Scheme 1).

It has already been manifested that sulfamic acid was comprised not of the aminosulfonic acid form, but rather of $^+H_3NSO_3^-$ zwitterionic units by both X-ray and neutron diffraction techniques[18] (Scheme 2). Therefore, it would be supposed that both sulfamic acid and IL were in the form of inner salts to some extent. In this way, there may be a synergetic effect constituted between ionic liquid and $^+HN_3SO_3^-$ when sulfamic acid dissolved in [C_3MIm]Cl, which would account for sulfamic acid catalyzing ketalization in common organic solvents and chemoselectively catalyzing the transesterification of β-ketoesters in [C_3MIm]Cl ionic liquid. However, the detailed mechanism was not explicit.



Scheme 1.



Scheme 2.

The transesterification between some alcohols and methyl acetoacetate was conducted in the NH_2SO_3H/[C_3MIm]Cl system, and the results are listed in Table 2. This method is quite efficient for a wide range of structurally varied alcohols such as open chain, cyclic and unsaturated ones. As for *tert*-butyl alcohol (entry 3), which is often problematic in acid-catalyzed reactions, a moderate yield of product was achieved by this method. With the unsaturated alcohols of low electron-donating characteristics, the transesterification was successfully performed with satisfactory yields in this catalytic system (entries 6 and 7), which are rather difficult by common methods because of Carroll rearrangement.[8]

The reuse ability of this H_2NSO_3H/[C_3MIm]Cl system was studied in the transesterification between methyl acetoacetate and butanol. The product could be simply separated from [C_3MIm]Cl by toluene extraction and H_2NSO_3H was still left in [C_3MIm]Cl, so that the recover and reuse of the H_2NSO_3H/[C_3MIm]Cl were very convenient. As shown in entry 1, the yield of butyl acetoacetate has only a little decrease after the reuse of H_2NSO_3H/[C_3MIm]Cl system for five times.

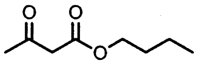
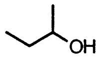
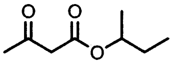
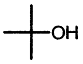
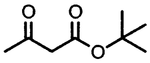
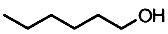
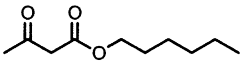
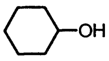
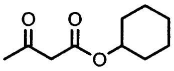
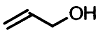
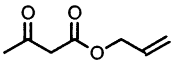
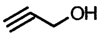
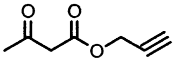
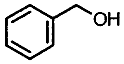
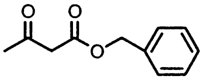
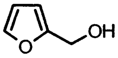
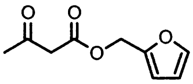
3. Conclusions

The [C_3MIm]Cl ionic liquid could not only act as a solvent to dissolve NH_2SO_3H, but also regulate it to become a chemoselective catalyst for the transesterification of β-ketoesters. Compared with common organic solvents, the undesired reactions could be effectively inhibited, and the selectivity to the desired ester was markedly improved in the H_2NSO_3H/[C_3MIm]Cl system. The separation of the product and the reuse of the catalytic system were very convenient.

4. Experimental

In a typical experiment, sulfamic acid (1.0 g) was dissolved into [C_3MIm]Cl ionic liquid (10 g) in a 100 mL round bottom flask equipped with a distillation condenser at 80°C. Then methyl acetoacetate (0.10 mol) and alcohol (0.12 mol) were introduced. The content was stirred vigorously at 80°C. After the desired reaction time, the reaction mixture was cooled to room temperature, and then was extracted with toluene (10 mL×3). The combined organic extract was analyzed by GC/MS. The pure transesterified products could be obtained by concentrating the extract and then separating it on silica gel column using light petroleum and diethyl ether as eluent.

Table 2. Transesterification of methyl acetoacetate with various alcohols in the $NH_2SO_3H/[C_3MIm]Cl$ system[a]

Entry	Alcohol	Product	Time (h)	Yield (%)[b]
1			3.0	96 (86[c])
2			3.0	95
3			4.5	75
4			3.0	95
5			3.0	94
6			3.0	93
7			4.0	92
8			4.0	93
9			4.0	93

[a]: Reaction condition: 10 g $[C_3MIm]Cl$, 1.0 g sulfamic acid, 0.10 mol methyl acetoacetate, 0.12 mol alcohols, 80°C ; [b]: GC yield; [c]: Yield of reuse five times.

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