

Brønsted acidic ionic liquids: the dependence on water of the Fischer esterification of acetic acid and ethanol

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Abstract

Initial studies involving the Fischer esterification of acetic acid utilizing task specific ionic liquid (TSIL) **1** and ethanol revealed an interesting trend when comparing overall conversions with the level of reuse. A rise in product yield was observed up to the third recycling of the ionic liquid (IL) medium. Post-run analyses revealed that the TSIL remained unchanged and the by-products of the reaction, acetic acid and water, were being retained. Use of TSILs in the Fischer esterification reaction was both high yielding and programmable if the proper ratio of both water and reagents to immobilized medium was observed.

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1. Introduction

Ionic liquid (IL) technology when used in place of classical organic solvents, offers a new and environmentally benign approach toward modern synthetic chemistry [1–4]. IL technology has been successfully applied in several classical organic processes [5,6]. The implementation of task specific ionic liquids (TSILs) further enhances the versatility of classical ionic liquids where both reagent and medium are coupled [7–15]. The union of reagent with medium has been found to be a viable alternative approach toward modern synthetic chemistry especially when considering the growing environmental demands being placed on chemical processes.

Previous reports from these laboratories have documented the feasibility of the application and reuse of TSILs in classical organic processes [5,6]. One study focused on the use of Brønsted acid TSILs in modern synthetic chemistry. The functionalized ionic liquids were prepared by reaction of triphenylphosphine with cyclic sultones. The resulting zwitterions were then converted into ionic liquids upon reaction with *p*-toluenesulfonic acid [5]. Three different Brønsted acid TSILs were prepared and found to be low melting salts

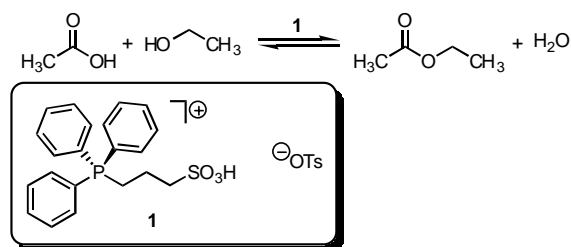
comprised of cationic moieties which are covalently tethered to alkane sulfonic acid groups. Each Brønsted acid TSIL was found to be a useful medium catalyzing processes such as the Fischer esterification (Scheme 1), alcohol dehydrodimerization, aldol condensation [16], and pinacol rearrangement. Yields varied from moderate to high for each series. The ionic liquid medium combines the low volatility and ease of separation from product normally associated with solid acid catalysts.

Our initial studies involving the Fischer esterification of acetic acid utilizing TSIL **1** and ethanol revealed an interesting trend when comparing overall conversions with the level of reuse. A rise in product yield was observed up to the third recycling of the ionic liquid medium (Table 1). Upon performing additional runs with TSIL **1**, overall conversion of acetic acid to ethyl acetate repeatedly resulted in a systematic drop in isolated yield after the third cycle. Post-run analyses concluded that the TSIL remained unchanged and the by-products of the reaction, acetic acid and water, were being retained.

These results were of particular interest considering recent reports documenting the stability of IL media under various reaction conditions. Aggarwal and co-workers have reported on the stability and inert nature of the ionic liquid medium in base-catalyzed processes [17–19]. A drop in overall conversion was observed due to the unsuspected reaction of deprotonated imidazolium salt with aldehyde. An

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Scheme 1.

Table 1
Reuse of ionic liquid medium

Cycle	Ethyl acetate yield (%) ^a
1	82
2	91
3	96
4	81

^a Isolated yield. Ratio of reactants to TSIL is 1:1 (total volume reactants:mass TSIL).

extension of this work was recently reported by Nair et al. [20]. Central to our understanding of alternative viable protocols using IL technology was the role of the medium in organic processes. Accordingly, we wish to report our continued studies of the Fischer esterification reaction using task-specific ionic liquid technologies.

2. Experimental section

2.1. General remarks

Gas chromatographic analyses were performed using an Agilent 6850 system (FID). ¹H NMR (300 MHz) and ¹³C NMR (75 MHz) spectra were obtained as solutions in either CDCl₃ or D₂O. Chemical shifts were reported in parts per million (ppm, δ) and referenced to CHCl₃ (δ 7.27) or D₂O (δ 4.88). Acetic acid and ethanol were not purified prior to use. All the reaction setups employed a 5 ml reaction conical vial equipped with a magnetic spin vane. Attached to the conical vial was a Hickman–Hinkle still head which itself was equipped with a Claisen adapter and reflux condenser. Proper alignment of one of the two inlet ports of the Claisen adapter is essential for the addition of reagents via a syringe pump. The setup was equipped with a drying tube packed with CaCl₂ and heated externally via a sand bath.

2.2. Representative procedure

To the 5 ml reaction conical vial charged with 2.1 g IL (4.0 mmol) was added via syringe acetic acid (1.0 ml, 17.5 mmol) and ethanol (1.0 ml, 17.5 mmol). The reaction mixture was allowed to warm to a maximum temperature of 175 °C (external temperature) over a period of 45 min. Although completion of reaction was observed prior to

reaching the maximum temperature, reuse of the reaction setup/IL made it necessary to remove all volatile components via distillation prior to the next cycle. With each cycle, reaction completion was identified by NMR analysis, confirmed by GC analysis [GC ((HP-1 methyl siloxane; $f = 1.0$ ml/min) 50 °C (2 min), 10 °C/min, 275 °C (10 min)) 3.21 min (EtOH), 3.37 min (EtOAc), 3.42 min (AcOH)] and documented via the mass of distillate obtained. Each cycle afforded pure ethyl acetate without any appreciable amounts of starting material (<7% assuming loss of EtOH due to an EtOH/EtOAc azeotrope (31 wt.% and bp of 78 °C)). Biphasic mixtures were separated and factored into product formation was maximum water content of 3.3%.

2.3. Control reaction

A 5 ml reaction conical vial was charged with acetic acid (1.0 ml, 17.5 mmol) and ethanol (1.0 ml, 17.5 mmol). The reaction mixture was allowed to warm to a maximum temperature of 175 °C (external temperature) over a period of 45 min. Observed were no appreciable amounts of distillate even after continuous heating 30 min after the 45 min window. The distillate that was collected consisted of EtOH (97%) and EtOAc (7%). Remaining in the reaction conical vial was AcOH.

2.4. Regeneration and subsequent reuse of ionic liquid medium

The mass of the reaction vial rose after each reaction of ethanol with acetic acid in the presence of Brønsted acid TSIL **1**. Since the equilibrium shifts to the right and ethyl acetate is removed via distillation, retained in the reaction vial was primarily water. This is based upon the mass balance of reaction cycles and product yields in addition to using NMR analysis to confirm the presence of acetic acid. An increase of over 151% (w/w) was documented after multiple runs. Removal of the VOCs using heat (<175 °C) at atmospheric pressure was unsuccessful. However, when the setup was evacuated (10 Torr) and warmed to 65 °C over a period of no less than 5 h, a drop in mass was documented. As confirmed by ¹H NMR analysis, the resulting ionic liquid contained residual quantities of AcOH.

3. Results and discussion

As documented in Table 1, a drop in isolated yield was observed after the third iterative use of the sulfonic acid tethered ionic liquid medium. This trend was observed not only in this study but in all parallel studies. Careful post-run analyses all concluded that the TSIL was inert to the reaction parameters, and thus, subsequent recycling events were only modified by the retention of by-products. That is, upon analysis of both mass balance and NMR post-run analyses, residual quantities of acetic acid and water were found to

Table 2
Dependence of water

Entry	Water content ^a	Ethyl acetate yield (%) ^b
1	0	62
2	10	71
3	30	84
4	60	80
5	90	78

^a Based upon volume of water added when compared to initial weight of TSIL ($\mu\text{l}/\text{mg}$).

^b Isolated yield. Ratio of reactants to TSIL is $\sim 3:1$ (total volume reactants:mass TSIL).

be part of the zwitterionic melt, thus, accounting for the increase of material in the reaction vial. The retention of materials also lowered the viscosity of the medium (*vide infra*). Because these reactions were high yielding, the amount of acetic acid was found to be secondary, and thus, the bulk of material retained was water.

When considering the four principle synthetic routes in ester functionality formation (esterification, alcoholysis using acid halides, reaction of carboxylate salts, and transesterification) the esterification protocol is perhaps the most versatile and practical [21,22]. As illustrated in Scheme 1, an equilibrium exists with all Fischer esterification processes, and thus, they are dependent upon either the removal (azeotrope) or sequestering of water (dehydrating agent). As described in Section 2, our apparatus is not designed to remove water while the reaction proceeds. One can conclude that water plays an important role in terms of sequestering or facilitating formation of ethyl acetate using TSIL **1** given the rise and fall of product conversion upon reuse of the same reaction medium.

Because of the need to explore the role of water in this process, we conducted a study which focused on the addition of water to TSIL **1** and its effect on the overall efficiency in the esterification of acetic acid with ethanol. Shown in Table 2 is a summary of our results. Prior to the addition of water, the TSIL was rigorously dried so that the results could be used comparatively.

Beginning with the addition of no water (entry 1), a 62% yield of ethyl acetate was observed. Although initially surprising when compared with the first entry of Table 1 where an 82% isolated yield was observed, a difference in isolated yields can be rationalized if one considers water uptake and self-diffusion coefficients normally associated with sulfonic acid resins¹ [23]. Sulfonic acids are known to be extremely hygroscopic. The data listed in Table 1 was collected using a medium which was not rigorously dried prior to use. Although heavily dependent upon the amount of exposure,

¹ Many resins consisting of sulfonic acids are extremely hygroscopic and known to have self-diffusion water uptake coefficients. Rates of water uptake is dependent upon both the extent of pretreatment and exposure to aqueous media. Water uptake, depending upon resin backbone and reaction parameters, can be as much as 50 percent or more of the initial resins dry weight.

a baseline value ranging between 10 and 30% (w/w) water content was found to exist with TSIL **1** if no effort toward maintaining an anhydrous medium was taken.

Not surprising, a rise of 9% in isolated yield was observed upon the addition of 10% (w/w) of water (71%, entry 2)². When 30% of the TSIL mass consisted of water, maximum yield of 84% was observed. This gradually dropped beginning with the addition of 60% water (80%, entry 4) and finally when 90% of the mass of TSIL consisted of water, an isolated yield of 78% was observed (entry 5).

The values presented in Table 2 were found to be programmable regardless of the level of recycling incurred. That is, the TSIL used in our initial study was recycled three times. Upon the removal of all volatile materials and reintroduction of 30% water (w/w), an 87% yield of ethyl acetate was observed. This single experiment documented not only the dependence upon water of this process but more importantly assured us that the residual amounts of acetic acid observed in the NMR were secondary and not contributing to the rise in isolated yield upon iterative use of the material.

The ratio of water to TSIL was, however, not the only factor in optimization of product conversion. The ratio of reagents to medium employed was as well found to be crucial. That is, using a volume to mass ratio of approximately 3:1 (total volume (ml) of ethanol and acetic acid to mass (mg) of TSIL **1**), a maximum yield of 84% was observed. Having the ratio approach 1:1, a higher overall yield was observed which eventually maximized to the quantitative conversion of acetic acid to ethyl acetate. Upon raising the reactant term, or more specifically, when employing a $\geq 5:1$ ratio of reactants to TSIL, a significant drop in overall conversion was observed (62%).

4. Conclusions

The data presented clearly illustrate a dependence of water of overall conversion of acetic acid to ethyl acetate using TSIL **1** the Fischer esterification reaction. Quantitative conversion was observed when (1) the ratio of reactants to TSIL approached 1:1, and (2) present in the reaction medium was a ratio of water molecules to sulfonic acid of approximately 7:1 [24]. Control studies confirmed the need to balance both water and reagent ratios in the Fischer esterification of acetic acid using TSIL **1** and ethanol for optimal conversion. Exploring the role of water in these processes using computational methods is warranted. As previously mentioned, upon each reuse of the ionic liquid medium, the viscosity of the medium dropped. While neat, the TSIL **1** is low melting. With each cycle the drop in viscosity was attributed to the retention of by-products, and thus, a liquid medium at room

² Percentages are reported using the following format: the addition of a set amount of water based upon the initial massing of TSIL. For example a water content of 10% consisted the addition of 100 μl water to an initial massing of 1.0 g TSIL.

temperature would be ideal. Efforts toward the development of a next generation TSIL of lower viscosity as well as computational studies are currently active and will be presented in due course.

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