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Novel Brønsted Acidic Ionic Liquids and Their Use as Dual Solvent−Catalysts

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From undergraduate laboratories to chemical manufacturing plants, the use of strong Brønsted acids is ubiquitous.[1] In this context, solid acids are being more widely used since, as nonvolatile materials, they are deemed less noxious than traditional liquid acids.[2] Still, solid acids have shortcomings as well. Among the more troublesome of these are restricted accessibility of the matrix-bound acidic sites, high molecular weight/active-site ratios, and rapid deactivation from coking.[3,4]

Bearing in mind both the advantages and disadvantages of solid acids, the identification of systems that are Brønsted acids with solidlike nonvolatility but that manifest the motility, greater effective surface area, and potential activity of a liquid phase continues to be useful. Combining just these characteristics, ionic liquids (IL) have been described as one of the most promising new reaction mediums.[5] Not only can these unusual materials dissolve many organic and inorganic substrates, they are also readily recycled and are tunable to specific chemical tasks.[6−11] While IL that manifest innately Lewis-acidic character are well-precedented and have been thoroughly studied (especially those based upon chloroaluminate anions[12]) we report here what we believe to be the first ionic liquids that are designed to be strong Brønsted acids. In each of the new IL, an alkane sulfonic acid group is covalently tethered to the IL cation.

The synthetic approach used to assemble the zwitterionic precursors to these acidic IL is well-precedented. Reaction of the neutral nucleophiles *N*-butyl imidazole or triphenylphosphine with 1,4-butane- or 1,3-propane sultone, respectively, produces the requisite zwitterions in excellent yields.[13] In the second step, the simultaneous realization of the latent acidity of the zwitterions and their conversion into ionic liquids is accomplished. The chemical yields for both the zwitterion formation and acidification steps are essentially quantitative. Moreover, since neither reaction produces byproducts, the IL syntheses are 100% atom efficient.

The zwitterion acidification is accomplished by combining 1:1 molar quantities of the zwitterions with an acid possessing a pK_a sufficiently low to convert the pendant sulfonate group into an alkane sulfonic acid, the pK_a of the latter being expected to be ∼−2. The result is the transformation of the zwitterion into an IL cation bearing an appended sulfonic acid group, with the conjugate base of the exogenous acid becoming the IL anion. Given that in these systems effectively two sites of formal negative charge are present per acidic proton, the systems may be regarded as internally self-buffered. For the IL syntheses reported here, the donor acids were trifluoromethane sulfonic acid and *p*-toluenesulfonic acid hydrate, pTSA•H_2O. These acids were chosen largely because of the resistance of their anions toward hydrolytic decomposition, a common problem with some strong acid anions (e.g., PF_6^-). These acids were then used to convert, respectively, zwitterions **1** and **2** to IL **1a** and **2a** (Figure 1).[14] Each acidification is accomplished by stirring together the neat reagents and warming gently for 2−24 h.

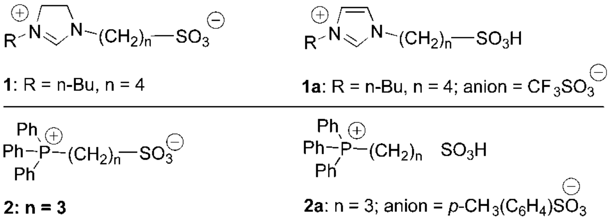
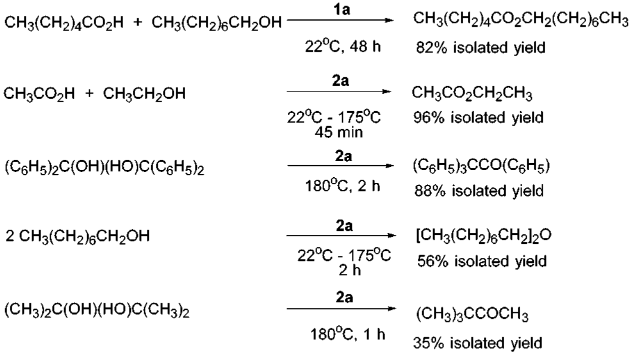


Figure 1. Brønsted acidic IL and the precursor zwitterions.

Scheme 1. Representative Reactions Using IL **1a** and **2a**



The new IL **1a** is a somewhat viscous liquid at room temperature, while **2a** is a stiff glass that liquefies around 80 °C. In keeping with the behavior of other IL, neither of the new species fumes or manifests any observable degree of vapor pressure, unlike strong acids dissolved in conventional IL, which frequently continue to emit noxious vapors. Further, treatment of **1a** under vacuum (10 Torr) at 150 °C results in no observed loss of triflic acid (CF_3SO_3H bp = 162 °C at 760 Torr) from the IL. Conversely, washing **2a** with toluene or diethyl ether results in no extraction of free pTSA (soluble in either liquid). Both of these behaviors are consistent with the donor acids being fully incorporated into their respective IL structures, rather than remaining simply mixtures of added strong acid with dissolved zwitterion, in which case some retention of premixing characteristics (e.g., triflic acid volatility) would be expected.

Both new IL were screened as solvent/catalysts for several classical acid-promoted organic reactions, although we placed an emphasis upon probing the chemistry of **2a** (vide infra). The reaction types screened were Fischer esterification, alcohol dehydrodimerization and the pinacol/benzopinacole rearrangement. Reactions and results are outlined in Scheme 1.

Both new ionic liquids proved catalytically active in these reactions. However, we placed an emphasis at this early stage of our studies upon more fully probing the chemistry of **2a**. Our

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Table 1. Recycling of **2a** in the Synthesis of Ethyl Acetate

cycle	ethyl acetate, %[a]
1	82
2	91
3	96
4	81
5[b]	87

[a] Isolated yield. [b] Using regenerated **2a** plus water.

motivation for doing so originates in recent reports by Karodia and co-workers in which tetraorganophosphonium tosylate salts (mp > 70 °C) were used as solvents for several organic reactions.[15−17] In those reports, the cooling of the solvent upon completion of the reaction resulted in the separation of the IL as a solid. We reasoned that **2a** might behave similarly, providing direct access to a convenient mode of separation, decantation, which parallels the manner in which solid acids are removed from reaction media. As expected, this proved to be the case in most of the reactions in which **2a** was used.

The reaction of alcohols with strong acids is used both for alkene and ether synthesis, the favored product being selected by the judicious choice of acid and reaction conditions. Depending upon the substrate/**2a** stoichiometry, 1-octanol is selectively converted to octyl ether in 16−56% isolated yield with minimal byproduct formation. In a control experiment, $\text{pTSA}\cdot\text{H}_2\text{O}$ gave a better yield of octyl ether; however, more byproducts were formed, and the separation of the pTSA from the reaction milieu was considerably more difficult. Using Nafion-117 as a control, we found the catalyst/product separation to be straightforward and byproduct formation to be minimal, but the yield of octyl ether was quite poor (3%).

The rearrangement of pinacol to pinacolone is a process of considerable industrial importance. The latter provides a synthetic entrée to trimethylpyruvate and then *tert*-leucine, a building block of several peptidomimetic drugs and chiral catalysts.[18] Although existing procedures use H_2SO_4 or H_3PO_4 to catalyze the reaction, interest has been expressed in the replacement of these species by solid acids. Using various solid acid catalysts, reported yields of pinacolone range from 2 to 71%, but long reaction periods are typical, and the use of a volatile organic solvent is required, complicating isolation.[19] Using **2a** as catalyst/solvent, we obtained an unoptimized yield of pinacolone of 35% during a 1-h reaction period, and an 88% yield of benzopinacolone over a 2-h period. Moreover, the pinacolone is readily distilled as a pure compound straight from the reaction milieu, unreacted pinacol being retained by the solvent/catalyst phase.

Ultimately, the ease with which these IL are recycled is central to their utility. Consequently, we examined the formation of an important commodity ester,[20] ethyl acetate, from ethanol and acetic acid using **2a** as the solvent/catalyst in a batch-type process, recycling the **2a**. The results of a representative round of recycling experiments are summarized in Table 1.

As shown, the yield of the ester increases from cycles 1 to 3, only to drop off again in cycle 4. During these cycles, the mass of the solvent/catalyst medium also increases, consistent with the entrapment of materials by the cooled catalyst phase. Post-cycling analysis of the IL by GC and NMR was consistent with the retention by it of appreciable quantities of water and acetic acid. When heated under vacuum to remove these volatile materials, the catalytic activity of **2a** was found to increase, in line with the degree to which water is removed from the system.

For an equilibrium reaction in which water is a product, the initial increase in ester yield accompanying the retention of water in cycles 1−3 was unexpected. It appears that for reasons yet to be determined, the presence of a threshold quantity of water in the ionic liquid contributes to higher reaction yields. To test the plausibility of this theory, we charged a dried sample of **2a** with a bolus of water, estimated to be equivalent to the cumulative amount retained after cycles 1 and 2. Supporting the hypothesis, we found the yield of ethyl acetate (entry 5) to be greater than that obtained using dried **2a** (entry 1).

Overall, the new IL are versatile solvent/catalysts for the reactions examined, and provide further examples of the capacity of ionic liquids to be fashioned for specific chemical applications. They provide good product selectivities as well as a balance between the yields achievable using a homogeneous acid catalyst and the ease of catalyst/substrate separation provided by a heterogeneous catalyst. Even so, improvements in these systems would be welcome, such as developing IL that bear appended superacid functionalities. Efforts toward these ends are in progress, as are efforts to measure the pK_a of these acids and to understand their behavior at a molecular level.

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Supporting Information Available: Synthetic/experimental procedures, analytical data, and NMR spectra (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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