

# New, functionalised ionic liquids from Michael-type reactions—a chance for combinatorial ionic liquid development†

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We describe for the first time an alternative and far more efficient method to synthesise functionalised ionic liquids in a simple, straightforward, two-step synthesis.

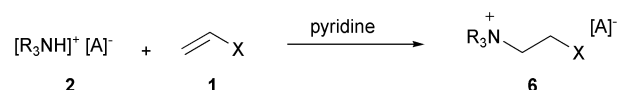
In recent years, ionic liquids have attracted a lot of interest as potential replacements for volatile organic solvents in synthetic—and especially in catalytic—applications.<sup>1</sup> While most ionic liquids investigated up to now are based on 1,3-dialkylimidazolium or 1-alkylpyridinium ions the use of cations with functionalised alkyl groups has only been described in a few papers. In their pioneering work Davis and Rogers have reported the synthesis of imidazolium salts with urea, thiourea and thioether groups in one of the *N*-alkyl substituents. These ionic liquids have been used as [PF<sub>6</sub>]<sup>−</sup> salts to extract Hg<sup>2+</sup> or Cd<sup>2+</sup> ions from aqueous solutions.<sup>2</sup> Chlorozincate and chlorostannate ionic liquids based on functionalised ammonium cations of the type [Me<sub>3</sub>NCH<sub>2</sub>CH<sub>2</sub>Y] (Y = OH, Cl, OC(O)Me or OC(O)Ph) were recently described by Abbott *et al.*<sup>3</sup>

Moreover, several research groups have described ionic liquids with imidazolium cations carrying ether, amino or alcohol functionalities.<sup>4</sup> These authors reported special solubility properties (*e.g.* improved solubility of metal halide salts) of their functionalised ionic liquids which are clearly linked to the presence of the functional group.

However, the synthesis of functionalised ionic liquids has been rather complicated so far and multi-step procedures were used in all cases mentioned above. These included the synthesis of a functionalised alkylating agent followed by the alkylation

of the amine, some further modification of the obtained salt to obtain the desired functional group and finally—in most cases—an anion exchange reaction. Obviously, the number of steps and the specific features of some of these reaction steps made it extremely difficult and expensive to obtain the functionalised ionic liquid product in high quality.

In this paper we describe an alternative synthesis that offers the chance of a much easier synthesis of functionalised ionic liquids. In a one-pot, two-step synthesis, the protonation of a tertiary amine or phosphine is followed by a Michael-type addition to an  $\alpha,\beta$ -unsaturated compound **1**, catalysed by a weak and volatile base such as *e.g.* pyridine (Scheme 1).



**Scheme 1** Synthesis of functionalised ionic liquids using a protonation–Michael reaction sequence (A = anion, X = COOR, COMe, CN).

This new pathway is based on our recently reported findings that phosphines react with acrylates in the presence of HBF<sub>4</sub> to yield the corresponding  $\gamma$ -oxophosphonium salt.<sup>5</sup> Further investigations revealed that this chemistry can be extended to amines, imidazoles and pyridines and that indeed many of the products obtained represent ionic liquids.

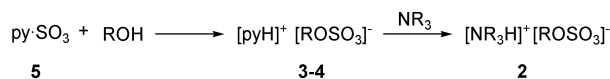
In the first step, the tertiary amine, *e.g.* *N*-methylimidazole, is protonated by a strong acid, giving the ammonium salt **2**. In this step, the anion of the final ionic liquid is introduced. Toluenesulfonic acid, MeSO<sub>3</sub>H and HBF<sub>4</sub> have been used in our studies so far. Besides these, pyridinium salts of alkylsulfates **3** and alkoxyalkylsulfates **4** have been prepared for further conversion with Michael acceptors. This was achieved by

† Electronic supplementary information (ESI) available: NMR and MS spectra consistent with the indicated structures for the compounds illustrated in Table 1. See <http://www.rsc.org/suppdata/cc/b3/b306084e/>

**Table 1** Ionic liquids synthesised *via* Michael-type addition pathway of protonated amines to methyl vinyl ketone<sup>a</sup>

No	Protonated amine	Product	Viscosity/mPa s	Yield (%)
1	[MeImH] <sup>+</sup> [OTos] <sup>−</sup>		— <sup>b</sup>	84
2	[MeImH] <sup>+</sup>		435 (1482 ppm H <sub>2</sub> O)	> 99
3	[MeImH] <sup>+</sup> [OMes] <sup>−</sup>		1255 (2900 ppm H <sub>2</sub> O)	> 99
4	[pyH] <sup>+</sup>		681 (2363 ppm H <sub>2</sub> O)	> 99
5	[pyH] <sup>+</sup>		915 (339 ppm H <sub>2</sub> O)	> 99

<sup>b</sup> Abbreviations: py = pyridine, Im = imidazole, OTos = *p*-toluenesulfonate, OMes = methanesulfonate. <sup>a</sup> Solid at room temperature, mp 62 °C.



**Scheme 2** Preparation of pyridinium alkylsulfates by direct and solvent-free reaction of the py-SO<sub>3</sub> complex with the corresponding alcohol.

solvent-free addition of stoichiometric amounts of pyridine-SO<sub>3</sub> complex **5** with the corresponding alcohols (Scheme 2).

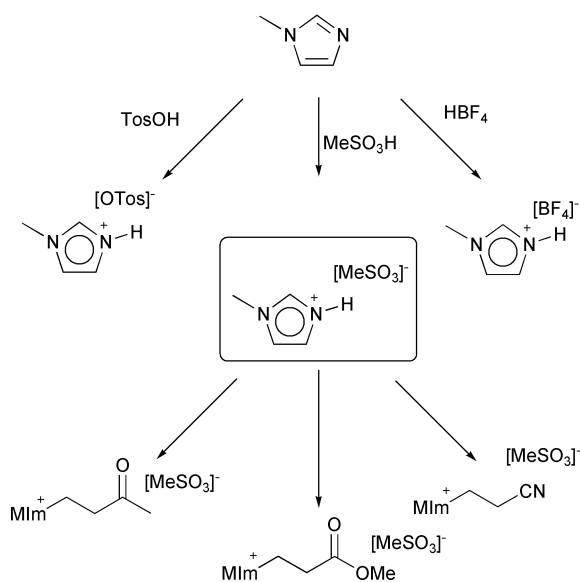
Remarkably, we found that the pyridinium salts of ethoxyethyl sulfate **4a** and methoxyethylsulfate **4b** are both room temperature liquids with low viscosity (200 mPa s at 188 ppm water for **4a**, 154 mPa s at 212 ppm water for **4b**). The pyridinium salt can directly be used in the Michael reaction or can be exchanged prior to the reaction with another amine of typically higher boiling point than pyridine.

In the second step, the protonated amine **2** is reacted with an  $\alpha,\beta$ -unsaturated compound to yield the ionic liquid **6**. The results for the addition of several imidazolium and pyridinium salts to methyl vinyl ketone are summarised in Table 1. Typically the reactions were run at 70 °C for 16 h. In cases where the protonated intermediates are liquids (e.g. pyridinium alkylsulfate salts), no solvent is necessary to facilitate the reaction.<sup>6</sup>

The materials were obtained in very high to quantitative yield in all cases described and—with entry 1 being the exception—are all room temperature liquid salts. As expected, their viscosity is somewhat higher in comparison to the viscosity of related, unfunctionalised materials. This is no surprise since the keto functionality introduces a strong hydrogen bond acceptor site into the salt. Taking this fact into account the low melting points of the obtained materials are even more remarkable.

It is also important to note that the overall reaction sequence proceeds with perfect atom efficiency since no by-product is formed. Furthermore no ion-exchange, extraction or filtration step is necessary. This allows for the first time the rapid synthesis of libraries of functionalised ionic liquids in a combinatorial fashion using the new synthetic approach.

In Scheme 3 this option is illustrated for three methylimidazolium salts in combination with three Michael acceptors.



**Scheme 3** Synthesis of libraries of functionalised ionic liquids.

As a result of our initial combinatorial experiments (3 amines, 3 acids, 5 Michael acceptors) we found that the reaction proceeds very smoothly applying acrylonitrile and unsubstituted acrylates as Michael acceptors. Substituted acrylates, such as methyl methacrylate and cinnamic acid esters, were not as successful, leading to incomplete conversion (in the case of the former) or to no reaction at all (in the case of the latter).

In all experiments described here, the reactivity did not show great dependence on the anion of the ammonium salt.

Besides the possibility to create libraries of new functionalised ionic liquids, the new synthesis offers potential for the synthesis of cheap, industrial ionic liquids since some amines, acids and Michael acceptors (such as e.g. methyl acrylate) are products of large scale industrial production processes. However, for a wider industrial application of the here described ionic liquids their limited thermal stability may be a concern, since the Michael-type addition reaction was found to be reversible at higher temperatures. An additional functional group transformation reaction could however help to solve this problem.

Finally, it should be mentioned that a highly attractive version of reaction results from the combination of an amine with a chiral acid (such as camphorsulfonic acid) and a prochiral Michael acceptor (such as cyclohexen-2-one). In this reaction a new stereocenter is created in the presence of a chiral ionic liquid. A detailed report of our ongoing work on this particular issue will be published elsewhere.

In summary, we have found a new, highly efficient way to synthesise large varieties of new, functionalised ionic liquids. Without doubt, the new method offers a powerful tool to improve our understanding of structure–property relationships with regard to functionalised ionic liquids.

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- N*-Methylimidazole (4.40 g; 53.6 mmol) is slowly added to a solution of *p*-toluenesulfonic acid monohydrate (9.51 g; 50.0 mmol) in 10 ml of ethanol. Methyl vinyl ketone (3.83 g; 54.6 mmol) is then added dropwise. The reaction vessel is sealed under argon and heated to 70 °C for 16 h. The mixture is then dissolved in methylene chloride and ethyl acetate is added. The precipitate is isolated and dried *in vacuo*, to give the product (41.9 mmol, 84%) as a white solid. <sup>1</sup>H-NMR (300 MHz, CD<sub>3</sub>CN):  $\delta$  = 8.92 (s, 1H), 7.64 (d, *J* = 7 Hz, 2H), 7.45 (s, 1H), 7.36 (s, 1H), 7.18 (d, *J* = 8 Hz, 2H), 4.33 (t, *J* = 6 Hz, 2H), 3.82 (s, 3H), 3.07 (t, *J* = 6 Hz, 2H), 2.36 (s, 3H), 2.11 (s, 3H) ppm. <sup>13</sup>C-NMR (75 MHz, CD<sub>3</sub>CN):  $\delta$  = 205.3, 146.0, 138.4, 136.8, 128.0, 125.3, 122.9, 122.4, 43.6, 41.8, 35.4, 28.7, 19.9 ppm.