Distillable Acid–Base Conjugate Ionic Liquids for Cellulose Dissolution and Processing**

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Future biorefinery concepts are seriously entertaining the use of ionic liquids (ILs) as a platform media for the processing of woody material as a second-generation biomass feedstock. The main motivation is the demonstrated efficiency of some molten salts in the dissolution of cellulose, a major structural and solvolytically resistant component of lignocellulosic materials.

The first report of the use of molten salts for the modification of cellulose came in the form of a patent by Graenacher,[1] where alkyl pyridinium chlorides were used to dissolve cellulose, thus allowing for efficient chemical modification from those media. The melting points of most alkyl pyridinium chloride salts are above 100 °C and, as such, these species do not fall under the common definition of ionic liquids. Nevertheless, the molten compounds solvated cellulose to such a state as to allow for acylation to a high degree. The next generational advance was the discovery by Rogers and co-workers[2] that dialkyl imidazolium based ionic liquids, with melting points below 100 °C, can dissolve cellulose. The most successful of these was 1-butyl-3-methylimidazolium chloride ([bmim]Cl). This advance was further refined by Ohno et al.[3] into room-temperature ionic liquids capable of dissolving cellulose, such as 1-ethyl-3-methylimidazolium formate ([emim][CO$_2$H])[3a] or 1-ethyl-3-methylimidazolium dimethylphosphate ([emim][Me$_2$PO$_4$]).[3b] From the structures listed in the claims of the Rogers patent,[2b] BASF have also refined this list down to room-temperature ionic liquids, such as 1-ethyl-3-methylimidazolium acetate ([emim]-[OAc]). It has been reported by BASF, by oral dissemination and unofficial reports, that [emim][OAc] has higher dissolving efficiency for cellulose and has lower toxicity than structures such as [bmim]Cl. However, no detailed studies comparing chlorides with carboxylates or other such structures have been published, although certainly their undeniable high efficiency for dissolution and chemoselectivity has been demonstrated for a number of cellulose modification applications.[4]

Despite the high efficiency for the solvation of cellulose, lignin,[5] and even wood[6] in an increasing range of dialkyl imidazolium based ionic liquids, sustainability of prospective processes will depend on the chemical stability of solutes and ionic liquids under process and recycling conditions. There are already some indications that ionic liquids such as [emim][OAc] react chemically with lignocellulosic solutes.[7] This reactivity may lower the recovery of the media upon recycling, although, in the case of the reaction of C2 imidazolium positions with C1 reducing end groups of cellulose,[7a,b] it is possible that this reaction is reversible under aqueous conditions, owing to the lability of the conjugate linkage.

A bigger concern is the method of recycling to yield a pure ionic liquid. For most processes, high-purity ionic liquid will be required to maintain efficiency of dissolution and overall sustainability of the process. Decomposition of dialkyl imidazolium based ILs containing basic anions in the presence or absence of solutes proceeds according to three main pathways. From knowledge of the chemical stability of these cations, the pathways are most easily illustrated using a 1,3-diethylimidazolium cation ([eeim]$^+$) as countercation (Scheme 1).
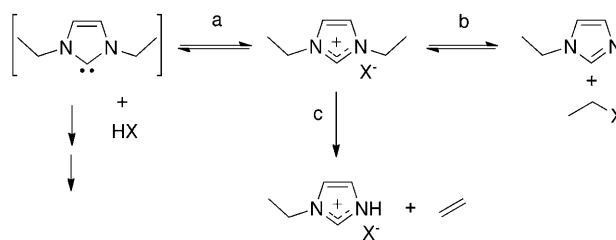
Scheme 1. The major decomposition pathways observed for dialkyl imidazolium based ionic liquids. Pathway a involves formation of a dialkyl imidazol-2-ylidene intermediate, which can react with additional solutes.

In relation to lignocellulose chemistry, pathway a, which involves formation of dialkyl imidazol-2-ylidene intermediates, has been demonstrated in the conjugation of cellulosic reducing end groups at C2 on the imidazolium ring. The publication by Liebert and Heinze,[7a] whereby the more basic [emim][OAc] reacts with oligocellulose reducing end groups to a much greater extent than [bmim]Cl or [emim]Cl, suggests that this reaction is likely dependent on the basicity of the anion. The initial step of this reaction is most likely deprotonation at C2, and therefore it will occur to a greater degree in the presence of more basic anions. Although dissociation of dialkyl imidazolium based ion pairs into the corresponding unconjugated acid of the anion and the dialkyl imidazol-2-ylidene (carbene) occurs in solution, these species

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have not yet been detected in the vapor phase upon thermal decomposition of the neat ionic liquids.

Pathways b and c have been observed to contribute to the thermal decomposition of a large range of basic dialkyl imidazolium salts.[8] A recent publication by Rinaldi and co-workers[8a] demonstrates that pathway b occurs even at low temperatures (100–160 °C), whereas at temperatures above 160 °C, pathway c dominates. The temperatures described for pathway b may well be within process and drying conditions for the use of these ionic liquids in bioprocessing and other applications. This mode of decomposition is not compatible with maintaining the sustainability of these processes. Although this method of decomposition has been described as 'sluggish' in the Rinaldi report, formation of volatile alkenes at these temperatures prevents equilibration and enables a gradual acidification of the dissolution media by buildup of the protonated alkyl imidazolium salt. Pathway c generates alkyl halides and pseudo-halides, which can be hydrolyzed or alcoholized, in the presence of water or lignocellulosic solutes, respectively. This process will also result in formation of acid, which would catalyze decomposition of dissolved biopolymers. From a recyclability point of view, pathway c also effectively allows for dissociation by the reverse Menshutkin reaction. This characteristic can facilitate the recovery by distillation of the starting materials required for reformation of the starting ionic liquid by the forward Menshutkin reaction. This process, however, is again likely to yield low-purity and potentially corrosive ionic liquids. Unfortunately, to date there are no reports describing the decomposition, distillation, and reformation of [emim][OAc] as a key structure, or any other basic imidazolium-based ionic liquid, for that matter. Reports do exist, however, describing the distillation of some ionic liquids through vaporization of ion pairs[9a] and dissociated neutral species.[9b] A patent by BASF[9c] details essentially the short-path distillation of ionic liquids such as [emim][OAc] and [emim][Me$_2$PO$_4$], although thorough analyses, product recoveries, and purity of fractions are not reported. In general, detailed reports into the efficient recycling of ionic liquids capable of dissolving cellulose are not forthcoming.

The concept of distillable ionic liquids for bioprocessing is not unknown in the literature, however. N,N-Dimethylammonium-N',N'-dimethylcarbamate (DIMCARB), formed from the addition of dimethylamine to carbon dioxide, has been reported by the MacFarlane group to efficiently extract tannins from certain plant species.[10] The residual ionic liquid can then be distilled, thus allowing for the recovery of the hydrolyzable polyphenolic compounds. This process represents one of the more successful direct applications of functional ionic liquids in the area of bioprocessing, beyond the imidazolium series.

Within the present research, we have developed a new generation of ionic liquid structures based upon the conjugation of the organic superbase 1,1,3,3-tetramethylguanidine (TMG) with carboxylic acids such as formic, acetic, and propionic acids. This method produces ionic liquids that both rapidly dissolve cellulose to high concentration and are recyclable by distillation with recoveries and purities over 99 %. To demonstrate this dissociation, distillation, and

reconstitution, a 1:1 mixture of TMG and propionic acid ([TMGH][CO$_2$Et] (**1**)) was distilled using a Büchi kugelrohr short-path distillation apparatus (3 g, 100–200 °C over 30 min, 1.0 mmHg). This distillation process is presented in Figure 1 along with an illustration of the temperature-dependent, conjugated–unconjugated acid–base equilibrium.
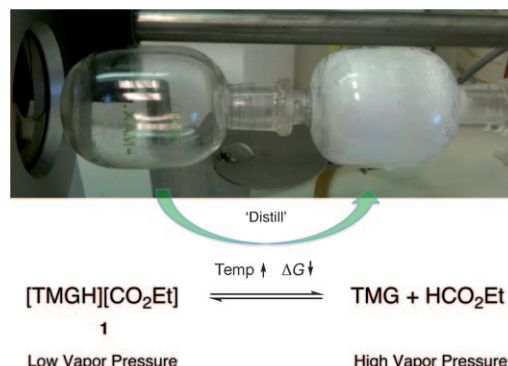

Figure 1. Distillation of compound **1** using a Büchi kugelrohr short-path distillation apparatus.

[TMGH][CO$_2$Et] (**1**) was distilled with 99.4 % recovery of the original mass. There was a clear polymeric residue amounting to 0.6 % of the original mass left in the first kugelrohr bulb. This material was insoluble in water and organic solvents, although it became swollen and opaque when treated with sulfuric acid. The purity of the distilled **1** was determined to be greater than 99 % by NMR spectroscopic analysis, which is a significant improvement on the value of greater than 95 % quoted in the BASF patent for the distillation of [emim][OAc].[9c]

To further investigate the recyclability and dissolution efficiency of these types of ionic liquids, 1:1 mixtures of TGA with formic acid ([TMGH][CO$_2$H] (**2**)), acetic acid ([TMGH]-[OAc] (**3**)), propionic acid ([TMGH][CO$_2$Et] (**1**)), butanoic acid ([TMGH][CO$_2n$Pr] (**4**)), valeric acid ([TMGH][CO$_2n$Bu] (**5**)), hexanoic acid ([TMGH][CO$_2n$Am] (**6**)), trifluoroacetic acid ([TMGH][CO$_2$CF$_3$] (**7**)), and triflic acid ([TMGH][OTf] (**8**)) were prepared. Additionally, 1,1,3,3-tetramethylguanidinium bistriflimide ([TMGH][NTf$_2$] (**9**)) was prepared by the addition of one equivalent of trimethylsilyl chloride (TMSCl) to one equivalent of TMG in ether. What was assumed to be the hydrolytically unstable [TMSTMG]Cl product was then directly treated with one equivalent of lithium bistriflimide (LiNTf$_2$) in aqueous solution, allowing for crystallization of **9** in high yield (Scheme 2). As hydrogen-bond basic media enable the breakage of intra- and intermolecular hydrogen bonds in crystalline cellulose, this selection of ionic liquids **1–9** allowed for a comparison of the properties of structures with a range of hydrogen-bond basicities; starting with the carboxylates **1–6** as the most basic followed by the trifluoroacetate **7**, then the triflate **8**, and finally the bistriflimide **9** as the least basic structures.

X-ray crystal structures were obtained for compounds **1** and **9** (Figure 2). The crystal structure for **1** shows a repeating dimeric ion-pair conformation in the crystal lattice, with
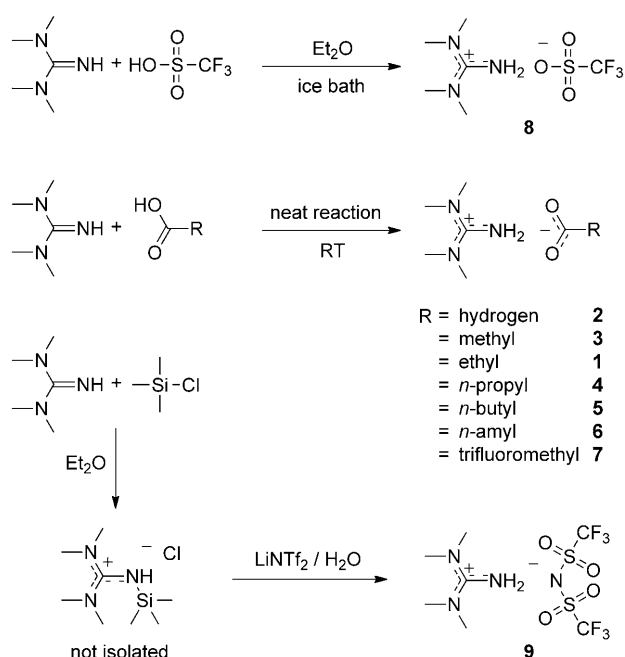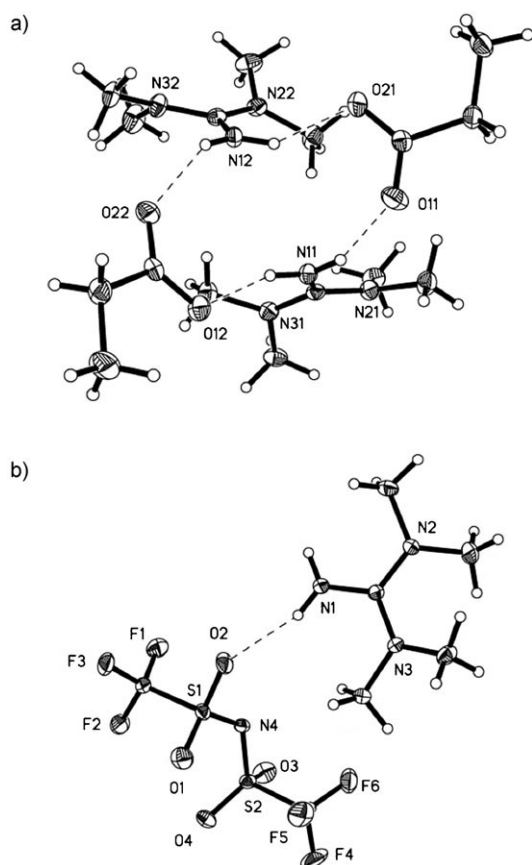
Scheme 2. Synthesis of compounds **1–9**.

Figure 2. X-ray structures of compounds **1** (a) and **9** (b).

strong internal hydrogen bonds running between O21···H12A-N12-H12B···O22 and O12···H11A-N11-H11B···O11 on adjacent propionate counterions. This strong

NH···O hydrogen bonding, with donor–acceptor separations of 2.755(2) to 2.828(2) Å, is not surprising, as carboxylates are among the most basic of anions observed in stable ionic liquids. The crystal structure for **9** shows hydrogen bonds between O2···H1B-N1-H1A···O4 bridging ion pairs in a continuous chainlike pattern. Bond lengths are 2.970(2) (N1···O4) and 2.940(2) Å (N1···O2). Unusually, the hydrogen bonds present in this structure do not involve N4, where the formal negative charge is located. This finding, however, is not unexpected owing to the electron-withdrawing nature of its adjacent functionalities. In both structures **1** and **9**, extensive close-contact networks involving electronegative atoms exist to bind the hydrogen-bonded motifs together.

To demonstrate the recyclability of these types of ionic liquids, compounds **1–9** were analyzed using thermogravimetric analysis (TGA) at atmospheric pressure (Figure 3). As
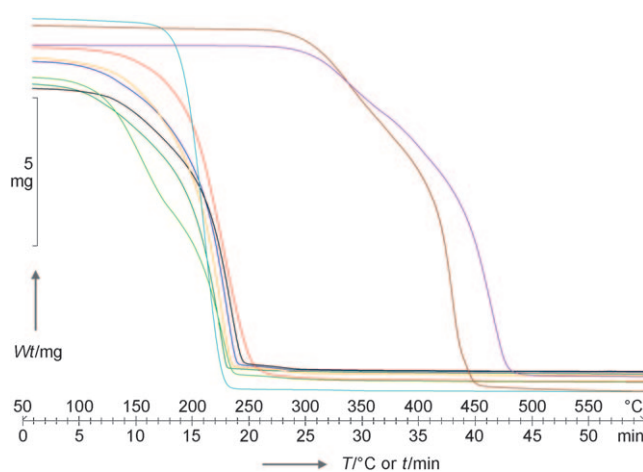

Figure 3. TGA traces for ionic liquids **1–9**. Red **2**, light green **3**, yellow **1**, dark green **4**, blue **5**, black **6**, turquoise **7**, brown **8**, purple **9**.

a measure of relative basicity of ionic liquids of the same cation, Kamlet–Taft β values for the corresponding [bmim]-based ionic liquids were taken from publications by Crowhurst et al.[11a] and Doherty et al.[11b] These values were compared to the approximate temperature ranges required for vaporization of the TMG-based ionic liquids. It is observed that the more basic carboxylates **1–7**, using the β value for 1-butyl-3-methylimidazolium acetate ([bmim]-[OAc], 1.18) for comparison, vaporize between 100 and 250 °C at atmospheric pressure. Whereas the triflate **8**, using the β value of 1-butyl-3-methylimidazolium triflate ([bmim]-[OTf], 0.46) for comparison, vaporizes between 300 and 450 °C at atmospheric pressure. Furthermore, the least basic ionic liquid in the series, the bistriflimide **9** (using the β value of 1-butyl-3-methylimidazolium bistriflimide ([bmim][NTf$_2$], 0.28) for comparison), vaporizes at the highest temperature range of 300–500 °C, at atmospheric pressure. This analysis is a very simple demonstration that the basicity of the anion dictates the volatility of the ionic liquid. It is also fortunate that a significant hydrogen-bond basicity is also required for the dissolution of cellulose, as is the case with [emim][OAc] and [bmim][OAc]. Overall, this method has afforded a new

generation of ionic liquids that are both capable of dissolving cellulose and recyclable by distillation. It is important to note that TMG-based ionic liquids themselves are not new to the scientific literature. TMG-based salts are dotted through the literature over a long period of time. In relation to ionic liquids research, TMG-based ionic liquids, including some of the compounds described in this report, have been used in organic synthesis.[12] It is clear that even these applications would benefit from the recyclability of these types of ionic liquids. One recent theoretical publication even predicted the distillability of some TMG carboxylates using a combination of molecular dynamics and ab initio approaches.[12d]

The microcrystalline cellulose (MCC) dissolution capability of each ionic liquid was tested and the data is presented in Table 1, along with the melting points for each structure. In

Figure 4. Normalized GPC traces for dissolved, regenerated, and benzoylated MCC samples. Red MCC control, green 1:1 (TMG/acetic acid), purple 2:1 (TMG/acetic acid), blue [emim][OAc].

Table 1: MCC dissolution speed[a] and melting points for ionic liquids **1–9**.

Ionic liquid	**2**	**3**	**1**	**4**	**5**	**6**	**7**	**8**	**9**
M.p. [°C] (Ref. [12a])	77–83 (67)	90–97	62	67	60	43	40 (42)	46 (41)	42
Dissolution[b]	++	+++	+++	+	−	−	−	−	−

[a] 5% w/w, 100°C, 18 h limit, magnetic stirring. [b] "+" symbols indicate complete dissolution to give clear solutions by visual inspection and optical microscopy. The number of "+" symbols refers to the speed of dissolution, and "+++" indicates dissolution within 10 min. "−" Symbols indicate no dissolution or fine dispersion.

general, the carboxylates dissolve MCC until the carbon atom count of the carboxylate anion is greater than C_4. The trifluoroacetate **7** also does not dissolve cellulose. The most rapid dissolution is for the acetate **3** and propionate **1**, with which clear solutions obtained after 10 min, with stirring at 100°C. Interestingly, a 2:1 (TMG:acetic acid) molar equivalence mixture could also dissolve cellulose under these mild conditions.

To test the effect on molecular weight of dissolution and heating MCC in these ionic liquids, 10% MCC was dissolved and heated for 20 h at 105°C in 2:1 and 1:1 mixtures of TMG:acetic acid. For comparison with the dialkyl imidazolium based ionic liquids, MCC was also dissolved in [emim]-[OAc] (>95%, Iolitec-grade). The crude regenerated materials were then benzoylated using a modified literature method[13] for gel permeation chromatography (GPC) analysis in THF. Benzoic acid impurity and the degrees of substitution (DS) of benzoyl groups were also determined using a literature procedure.[14] The GPC data (Figure 4) show a slight decrease in the molecular weight of all the materials with a final degree of polymerization (DP) of 359 (DS 2.9) for the 2:1 TMG-based dissolution, a final DP of 307 (DS 2.9) for the 1:1 TMG-based dissolution, and a final DP of 292 (DS 3.0) for the [emim][OAc] dissolution in comparison to a DP of 381 (DS 3.0) for the MCC standard (undissolved) sample. It is interesting to note that the decrease in DP is actually larger for [emim][OAc] at this temperature and technical purity of ionic liquid. This decrease in molecular weight is to be expected but is rarely commented upon in publications concerning the dissolution of cellulose into ionic liquids.
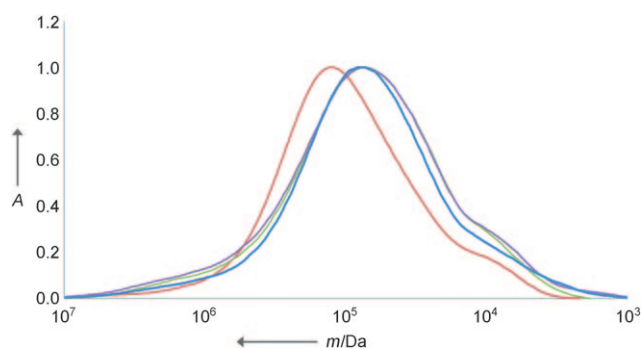
This depolymerization is undoubtedly promoted by the free acid present in the reaction mixtures. As temperature increases, the concentration of neutral species in the reaction mixture increases. This phenomenon enhances degradation as temperature increases, with the onset of rapid solution darkening at approximately 130°C. Consequently, this behavior enables the control of dissolution, with minimal degradation at temperatures below 110°C. Above 110°C, saccharification begins to occur in the absence of an additional catalyst and at relatively low temperature. This property obviously widens the application base of these types of ionic liquids to include both cellulose and potentially wood treatments, where the molecular weights or biopolymer connectivity can be either maintained or destroyed.

In conclusion, we have discovered a new generation of ionic liquids that dissolve cellulose, based upon conjugation of commercially available organic acids and TMG as a commercially available organic superbase. BASF have patented the combination of specifically 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) with organic acids for the fractionation or dissolution of a range of synthetic and biological polymers, but no mention of the quality of the recovered materials, or importantly distillation of the media has been made.[15] In our case, short-chain [TMGH]$^+$ carboxylates are both capable of rapidly dissolving cellulose (in under 10 min to 5% w/w consistency), and [TMGH][CO$_2$Et] (**1**) has been shown to be technically 'distillable' to high purity (>99% purity, >99% yield) by temperature-assisted dissociation, vaporization, and recombination of the component neutral species. This highly efficient "distillability" has not yet been observed for earlier generations of ionic liquids capable of dissolving cellulose. The dissolution capability and recyclability are dependent upon the relative basicity of the competing bases (TMG and carboxylate). This equilibrium is temperature-dependent and can be shifted favorably to give enough of the neutral components to afford a vapor pressure. Fortunately, a sufficiently basic anion, such as carboxylate, is also required to dissolve cellulose by H-bond breakage. These properties are mutually exclusive owing to the observation that when more acidic acids than carboxylates are combined with TMG, the resulting ionic liquids do not dissolve cellulose. Identification of the temperature conditions required to enable dissolution, with or without degradation of lignocellulosic

components, is also an important property to fully realize in the future application of these novel solvents. Like the ionic liquids' volatility, this property is anticipated to be partly reliant on the temperature-dependent conjugate ion-pair acid–base equilibrium.

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