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Functionalized ionic liquids with highly polar polyhydroxylated appendages and their rapid synthesis via thiol-ene click chemistry

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ABSTRACT

The thiol-ene 'click' reaction of 1-thioglycerol with ionic liquids incorporating cations bearing appended vinyl- and/or allyl groups is a versatile, single-step means for their conversion into derivatives bearing up to eight hydroxyl groups per cation.

Functionalized or 'task-specific' ionic liquids (TSILs) have been subjects of considerable scrutiny for the past decade.[1] Distinguished from more conventional ILs by way of incorporating ion-tethered functional groups, these salts have proven useful in applications ranging from separations to catalysis. However, since the functional groups in TSILs are generally heteroatom based, their syntheses routinely demand careful planning to minimize the formation of undesired byproducts from competing side reactions.[2] Consequently, approaches which stress the assembly of molecular targets by way of reactions orthogonal to those undergone by the targeted functional group ought to be of great interest to those working in the area. In this context, we recently reported[3] the first express application of the Sharpless et al.[4] 'click' concept to the preparation of TSILs, specifically new amine-functionalized ILs for CO_2-capture.[5] While the latter can be vexing to prepare by other means, our two-step click approach involving sequential ring-opening and neutralization reactions enabled us to prepare cleanly and in very high yields a library of 70+ TSILs in a remarkably short period of time.[3]

Impressed by the power of the click paradigm, we have become attentive to new developments in the area. One we find to be of particular note is the radical-based thiol-ene reaction, which has recently been used to superb effect in the preparation of highly functionalized dendrimers and related macromolecules.[6] Because of the possibility for rearrangement of these reactive intermediates, radical-based reactions can be problematic; however, the thiol-ene reaction is reputed to be well-behaved and to consistently produce high yields of targeted products. Accordingly, we decided to attempt thiol-ene reactions on a handful of *ene*-functionalized ILs to assess its potential utility in TSIL synthesis. Here we report our results.

Four ILs (**1**–**4**, Fig. 1) were selected as *ene* substrates for the study. In each case, the IL cation was imidazolium-based and bore an appended *N*-vinyl or *N*-allyl group. These were chosen to assess the effect, if any, of having the alkene connected directly to the center of cationic charge versus being separated from it. Likewise, a variety of anions were used as elements of the substrate salts, providing us an opportunity to observe any noticeable control exerted by them over the course of the reaction. Finally, in this initial screening we used a single thiol, 1-thioglycerol, for the photoaddition reactions. The latter has been shown by others to reliably photoadd to alkenes, and its use in the present case allowed us to demonstrate the incorporation of a targeted group (—OH) into an IL by way of the orthogonal reaction of *ene*-bearing IL ions and a building block bearing both the functional group of interest and the requisite thiol moiety. Equally important, it would provide (if successful) very direct, simple access to imidazolium ILs with glyceryl-like *vic*-diol moieties. We note that such ILs have been shown by Chiappe et al. to be "more favourable in comparison with the "classical" ionic liquids such as BMIM-based ones" in the Heck reaction, and that they "evidenc[e] good catalyst stability and a high recyclability".[7]

The coupling reaction of thioglycerol to **1**–**4** was carried out using an approach modeled on that used by Hawker et al. for the thiol-ene based assembly of functionalized dendrimers.[8] We found methanol to be well-suited as the reaction solvent, but there was no conspicuous improvement in outcomes when the reactions were conducted under nitrogen. Also, in our hands the use of small quantities of DMPA (2,2-dimethoxy-2-phenyl) acetophenone) relative to alkene (mol/mol) gave erratic results under air or N_2, prompting us to significantly increase the amount of this photoinitiator used in each reaction. While the mechanistic basis for this apparent diminution in catalyst efficiency from that normally observed is unclear, our use of larger quantities did not

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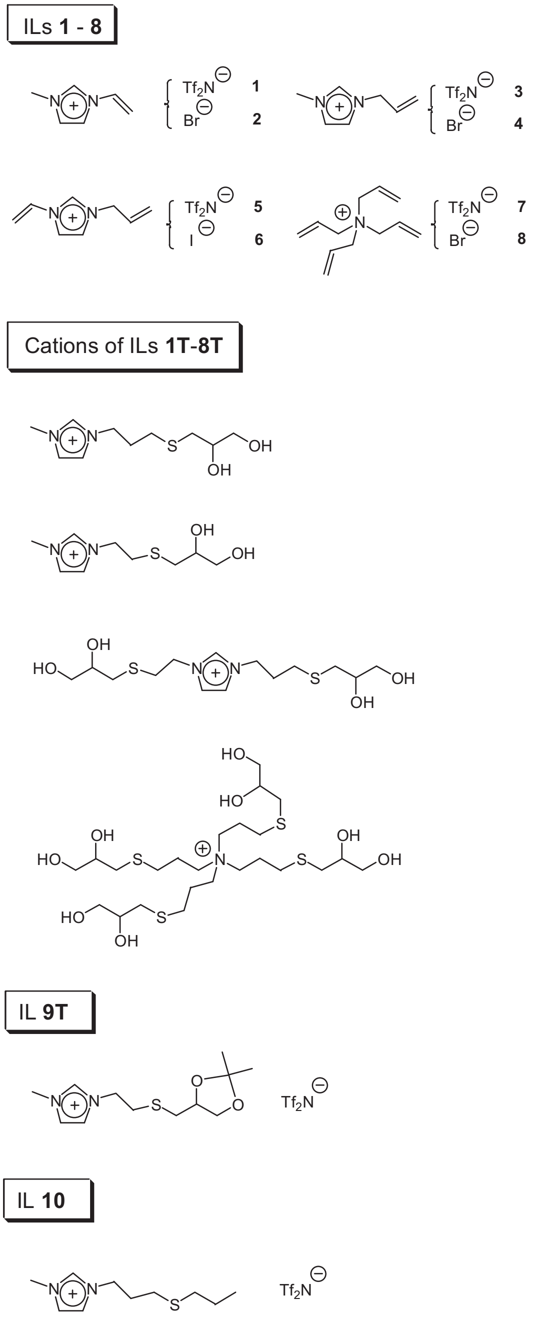

Figure 1. Structures of the *ene*-functionalized IL starting materials (*upper left*) and the ions resulting from their photoinduced thiol-ene reaction with 1-thioglycerol (*right*). The structures of the acetal derivative of IL **3T** and the nonhydroxylated IL **10** are also depicted (*lower left*).

complicate the workup and isolation of the products. Indeed, the photoiniator is readily removed by washing the reaction residue (after methanol removal) with hexane, in which none of the starting or product ILs is soluble. Likewise, in the case of the Tf_2N^- salts, any residual/excess thioglycerol was easily removed by washing with water, with which those ILs were immiscible. The new ILs were isolated as yellow oils which do not appear to undergo any visible phase transitions when cooled (**3T** and **10**, for example, undergo no transitions down to −50 °C [DSC]). The ^1H and ^{13}C NMR spectra of each new IL fully comport with its proposed structure and formulation, as does its ESI-mass spectrum.

The reactivity of the vicinal diol groups in the new ILs does not appear to deviate from established norms as a consequence of their proximity to cationic centers. For example, **3T** readily forms the new acetal-containing IL **9T** when combined with 2-propanone and an acid catalyst (pTSA). However, as might be expected, the new ILs are visibly more viscous than ILs that are thioether-containing structural counterparts which lack the highly polar —OH groups. Having shown in earlier work[9] that cation-tethered functional groups can profoundly affect the solvent characteristics (Abraham parameters) of ILs, we thought it useful to determine the temperature-dependent viscosity of a representative IL from the present work, and to likewise determine the same property for an (otherwise) exact analog devoid of the *vic*-OH groups (IL **10**, Fig. 1). As anticipated, the viscosity of **3T** proved to be significantly higher than that of **10**, almost an order of magnitude so near ambient conditions, although the density of the former is only marginally greater (Fig. 2; Table 1 [Supplementary data]). Both of these trends are consistent with increased inter-particle interaction brought upon by the inclusion of strongly associating hydroxyl groups, behavior anticipated by Chiappe et al.[7]

Given the ease with which **1**–**4** were functionalized, we expanded the scope of the study to ILs with ions bearing more than one *ene* group (Fig. 1). We did so using salts **5**–**8**, all of which were prepared using standard approaches. When combined with thioglycerol and irradiated under the same conditions as **1**–**4**, the anticipated polyaddition products were formed quantitatively (NMR) and isolated in good yields. The structures of the four cation types incorporated in ILs **1T**–**8T** (T, thioglycerol addition product) are shown in Figure 1.

Both the ^1H and ^{13}C NMR spectra of each IL **5T**–**8T** unambiguously shows complete thiolation, which is readily ascertained on the basis of peak integration (^1H) and the disappearance of the olefinic peaks (^1H, ^{13}C) of the starting cations. However, in neither the ESI-MS of **7T** or **8** is the expected parent ion of $m/z = 611$ observed. Instead, each produces a high-mass ion with $m/z = 394$, consistent with a structure in which two of the four thioglycerol moieties have been cleaved, leaving two intact while re-generating two of the original *N*-tethered allyl moieties. This retro-thiolation is likely promoted by severe steric crowding around the central *N* of these ions, a structural attribute that is obvious upon inspection of simple digital (ChemDraw 3D) molecular models of these entities.

Overall, the present results indicate that the construction of functionalized ILs using the thiol-ene reaction offers considerable promise as an easy means by which to create structurally elaborated IL ions. Specifically, ILs with multiple hydroxyl and thioether functional groups are readily prepared by the photoinitiated radical coupling of 1-thioglycerol and salts of imidazolium and quaternary ammonium cations bearing tethered allyl and/or vinyl groups. Neither the proximity of the unsaturated appendage to the charge locus (cf., vinylic vs allylic), the nature of the cation as aromatic (imidazolium) or nonaromatic (quaternary ammonium), or the nature of the anion appears to have a material effect on the ease with which the couplings can be accomplished. The reactions proceed quickly and cleanly, and usually give acceptable yields of products without optimization. The solubility characteristics of the ionic products makes them easy to separate from photoinitiator and excess thiol by simply washing with appropriate solvents. The incorporation of two hydroxyl groups per cation per tethered *ene* moiety gives the resulting ions richly polar appendages with multiple H-bond donor and acceptor sites, features which have a significant, temperature-dependent impact on the viscosity of these ILs.

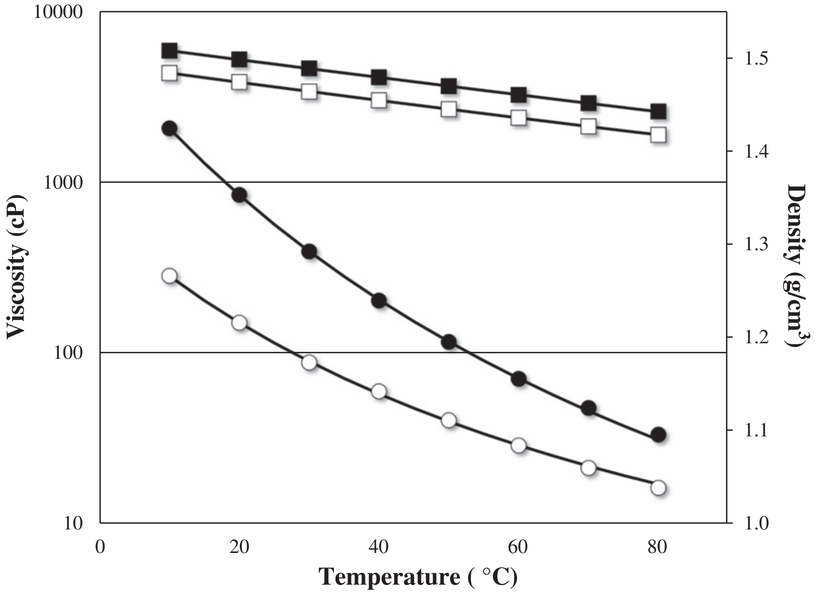

Figure 2. The viscosity (circles) and density (squares) for **10** (open markers) and **3T** (filled markers) from 10 to 80 °C. The lines are fit models for each data set.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.07.126.

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