Cite this: Chem. Commun., 2011, 47, 3222-3224

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## COMMUNICATION

## Reaction of elemental chalcogens with imidazolium acetates to yield imidazole-2-chalcogenones: direct evidence for ionic liquids as proto-carbenes<sup>†</sup>

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Received 26th November 2010, Accepted 20th January 2011 DOI: 10.1039/c0cc05223j

Mechanistic analysis of the reaction between elemental sulfur or selenium and 1,3-dialkylimidazolium acetate ionic liquids, in the absence of an external base or solvent, affords evidence for the equilibrium presence of carbene species in these ionic liquids. It demonstrates the potential to control, through anion selection, the concentration of carbene in stable ionic liquids.

Ionic liquids (ILs) have come under increasing scrutiny over the last decade for, among many reasons, the ability to tailor and introduce unique property sets into liquid systems, including, for example, the ability to react and solubilize numerous (traditionally hard to dissolve) substances.<sup>1</sup> The solvating powers of ILs are often considered to be a property of one or another of their constitutive ions; not necessarily the combination of a particular cation–anion pair. For example, the enhanced solubility and possibly reactivity of chitin *vs.* cellulose in 1-ethyl-3-methylimidazolium acetate ([C<sub>2</sub>mim][OAc]) compared to 1-ethyl-3-methylimidazolium chloride ([C<sub>2</sub>mim]Cl) has been credited to the increased basicity of the acetate compared to the chloride anion.<sup>2</sup> However, introduction of increasingly basic anions can also lead to increasingly stronger interactions with the acidic protons in the imidazolium ring of the IL cation.<sup>3</sup>

If the putative 1,3-dialkylimidazolium hydroxide ILs are considered (and they have been erroneously reported as pure materials on a number of occasions<sup>4</sup>), in the absence of other proton sources, the hydroxide anion will readily abstract a proton from the C(2) ring position of the cation. Thus, imidazolium hydroxide 'ionic liquids' are unstable with respect to spontaneous base-induced decomposition (Scheme 1) unless stabilized by the presence of a proton donor such as a protic solvent, *e.g.*, water, methanol, *etc.*, which will protonate the *N*-heterocyclic carbene (NHC) formed and drive the equilibrium back to the left hand side. In contrast,  $[C_2mim][OAc]$  is a relatively stable IL,<sup>5</sup>



**Scheme 1** Possible acid–base equilibrium between the constitutive ions of a 1,3-dialkylimidazolium IL.

suggesting that the equilibrium proposed in Scheme 1 can be effectively tuned by appropriate choice of ions.<sup>6</sup>

We have an interest in understanding how solubility and reactivity in/of ILs can be controlled through the specific combination of particular cations and anions.<sup>7</sup> One aspect of these ongoing investigations is the potential for nominally stable ionic liquids, such as [C<sub>2</sub>mim][OAc], to be activated *via* direct *'in situ'* NHC formation to uniquely combine favorable IL properties (thermal/chemical stability, *etc.*) with NHC reactivity.

NHCs are versatile compounds with use as ligands in organometallic chemistry, as catalysts, and as nucleophilic reagents.<sup>8</sup> Among the many materials that can be accessed through carbene chemistry, imidazole-2-chalcogenones in general, and thiones in particular, are of interest. Tao et al. have reviewed the major applications of imidazole-2-thiones,9 which, besides their pharmaceutical and clinical uses,10 include examples of industrial application as antioxidants for rubber, as vulcanization accelerators, and their utilization in light-sensitive photographic and photothermographic materials. In addition, 1,3-disubstituted imidazole-2-thiones are versatile catalysts for initiating crosslinking of epoxy and isocyanate resins.<sup>11</sup> Imidazole-2-selones have been identified as potential anti-hyperthyroid drugs,<sup>12</sup> and also as catalysts for carbonylation reactions of amines.<sup>13</sup> Similarly, (benz)imidazole-2-tellones have been shown to have antimicrobial activity against Gram-positive bacteria.<sup>14</sup>

The most common approach to imidazole-2-thione preparation consists of the reaction of an imidazolium salt with a base and elemental sulfur, either sequentially (through the initial formation of the carbene intermediate), or in a single step (*via* transient carbene generation).<sup>15</sup> The bases used include, for instance, potassium *tert*-butoxide (in sequential reactions), or potassium carbonate and sodium methoxide (in single step reactions), yielding salt by-products which must be separated from the imidazole-2-thione produced. In addition, the reaction is conducted in the presence of an organic, typically flammable, solvent, such as pentane, tetrahydrofuran, or methanol.

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<sup>†</sup> Electronic supplementary information (ESI) available: Experimental details. See DOI: 10.1039/c0cc05223j

More recently, it has been found that microwave irradiation allows the use of softer bases such as potassium thioacetate or potassium thiocyanate,<sup>9</sup> and also a solvent-free process has been reported.<sup>16</sup> Although the latter avoids the problem of using an organic solvent, typically a solid base is still required, generating undesired inorganic by-products. The preparation of imidazole-2-tellones by the reaction of NHCs with elemental tellurium in solution has also been described,<sup>17</sup> with similar issues associated.

The solubilization of chalcogenides in a range of ILs producing radical anionic species such as  $[S_3]^{\bullet-}$  has been recently described by Boros *et al.*,<sup>1d</sup> and prompted us to investigate whether imidazolium ILs with selected suitably basic anions could be used to solubilize and then react directly with elemental sulfur in the absence of any external bases to produce imidazole-2-thiones through activated '*in situ*' NHC formation.

These first investigations were made with imidazolium acetate ILs (Scheme 2). Upon stirring stoichiometric amounts of  $S_8(s)$  and  $[C_2mim][OAc](l)$  at 25 °C for 24 h, reactive dissolution occurred, with the formation of the corresponding 1-ethyl-3-methylimidazole-2-thione in a yield near 50 mol%. Similarly, 1-ethyl-3-methylimidazole-2-selone was obtained in 90 mol% yield by directly stirring approximately stoichiometric amounts of selenium powder and  $[C_2mim][OAc]$  at 75 °C. We did not find convincing evidence for the reaction with selenium at 25 °C; however, the reactivity at 75 °C would be consistent with a shift in the equilibrium in Scheme 1 sufficiently to the right with increasing temperature to generate enough carbene concentration for the reaction to proceed.

No optimization of the reaction conditions was attempted to improve the product yields, since our focus was rather on understanding the nature of the reaction observed. Thus, the products observed and isolated here demonstrate that, in addition to the dissolution of chalcogens in ILs as previously described,<sup>1d</sup> reactive processes leading to the efficient direct synthesis of imidazole-2-chalcogenones without addition of external bases or solvents, and without generation of salt waste, can be achieved. However, the IL must be chosen such that the specific combination of a cation and anion results in a strong enough interaction to activate the C(2) proton on the heterocyclic ring,<sup>6</sup> as illustrated in Scheme 1, without leading to spontaneous decomposition of the IL as observed for the OH<sup>-</sup> salts.

For the direct reaction of  $[C_2mim][OAc]$  with the chalcogens, one of two possible mechanisms can be invoked: either the chalcogen reacts directly with the imidazolium cation, or the carbene is generated *in situ* and reacts with the chalcogen. Other 1-alkyl-3-methylimidazolium based ILs containing a range of anions (namely: Cl<sup>-</sup>, [HSO<sub>4</sub>]<sup>-</sup>, [SCN]<sup>-</sup>, [CH<sub>3</sub>SO<sub>4</sub>]<sup>-</sup>, [CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>]<sup>-</sup>, [CF<sub>3</sub>SO<sub>3</sub>]<sup>-</sup>, and [CF<sub>3</sub>COO]<sup>-</sup>) were tested,



Scheme 2 Direct reaction of chalcogens ( $E = 1/8 S_8$ , or  $Se_{(powder)}$ ) with neat IL [C<sub>2</sub>mim][OAc] (see ESI<sup>†</sup>).

and no reaction was observed with sulfur in comparative experiments. However, reaction was observed with another acetate IL: 1-butyl-3-methylimidazolium acetate.

These results imply that the first mechanism is invalid, and that the imidazolium acetate IL is acting as both the base and carbene source, with *in situ* production of the carbene which reacts with sulfur to give the thione without displacing reagents. As such, the mechanism parallels that of the typical chalcogenone synthesis from an imidazolium salt and the elemental chalcogen in the presence of an external base.

This mechanism is also supported both by the direct reaction of benzaldehyde with [C<sub>2</sub>mim][OAc] to form a carbene– benzaldehyde adduct and the formation of Pd-bis(carbene) complexes obtained by the addition of  $Pd^{2+}$  salts to this IL. The initial data for these reactions are presented in the ESI<sup>†</sup>, however more detailed studies will be forthcoming.

While the proposed mechanism might initially appear to be selfevident (the acetate anion is known to be basic), if the mechanism of formation of the carbene was just proton abstraction by the acetate anion, then loss by volatilization of the acetic acid formed would provide a continuous source of carbene. Consequently, this would also lead to intrinsic instability and decomposition of the IL in a manner comparable to that of the hydroxide case.

Complex anions, formed from acid + anion pairs, have been known for some time in IL systems, and those with carboxylic acid/carboxylate conjugate systems are particularly stable.<sup>18</sup> If complex anion formation is invoked (Scheme 3), the formed acid would tie up the acetate acceptor, preventing further C(2) proton abstraction and requiring the removal of the acid to continue the reaction. The liberated acid is stabilized as a complex anion, but can still be stripped under relatively mild conditions, shown here where, by bubbling N<sub>2</sub> into the mixture of [C<sub>2</sub>mim][OAc], acetic acid, sulfur, and thione, the yields of the latter increased to 57 mol% after 24 h, and 67 mol% after 72 h.

In a further experiment,  $[C_2mim][OAc]$  was mixed with an excess of acetic acid (a 1 : 2 molar ratio), and then with elemental sulfur. No evidence for formation of the thione was observed, even after two days. This appears consistent with the postulated mechanism shown in Scheme 3, in which the proton formed through generation of the NHC intermediate is bound in an acetate–acetic acid complex anion. Thus, the presence of excess acetic acid buffers the IL, reducing the net concentration of free acetate anions present and inhibiting their interaction with the C(2) protons of the imidazolium rings.

The reaction can also be inhibited by other hydrogen bond donors such as water. In another experiment,  $[C_2mim][OAc]$ and water were mixed in a 50 : 50 wt/wt ratio, and sulfur in excess was added. After two days no trace of thione was observed, likely as a result of the disruptive action of water on the interaction between the cation and the anion of the IL (water being a better proton donor than  $[C_2mim]^+$ ).



Scheme 3 Proposed mechanism for stabilization of the volatile acetic acid generated from proton abstraction.



Scheme 4 One pot synthesis of symmetrical 1,3-dialkylimidazolium acetate (1,  $R_1 = R_2$ ) and statistical mixture of 1-alkyl-3-methyl-, 1,3-dialkyl-, 1,3-dimethylimidazolium acetates (1 + 2 + 3,  $R_1$  = methyl,  $R_1 \neq R_2$ ).

To further explore the utility of this thione synthesis, we investigated the one-pot reaction of both symmetrical 1,3-dialkylimidazolium acetate and 2:1:1 statistical mixtures of 1-alkyl-3-methyl-, 1,3-dialkyl-, and 1,3-dimethylimidazolium acetates, prepared in situ through cyclization of the corresponding amines with glyoxal, formaldehyde, and acetic acid,19 with sulfur. The mixtures of ILs over the 'pure' IL alone have potential environmental benefits and cost advantages over current technologies. Unlike the single cation hydrophilic ILs, the IL mixtures can be prepared in a one-pot, single step process, using aqueous, readily available, cheap raw materials, and therefore reducing or even eliminating the use of the organic solvents (Scheme 4). By adding sulfur to a statistical imidazolium acetate mixture, partial conversion to the corresponding mixture of thiones was achieved. Interestingly, the same ratios of the starting cations ratios were obtained in the resulting thiones mixture product. In the case of symmetric imidazole-2-thiones, only one product would be obtained, which can be easily prepared, as seen, *via* a simple one-pot strategy from cheap, commodity chemicals.

Finally, it can be noted that ILs such as 1-alkyl-3-methylimidazolium acetates are among the most widely used in the promising field of biomass treatment and processing with ILs. It is important to understand the chemistry of the IL itself in order to help explain such reports as side reactions at the C(2) position with reducing end sugars,<sup>20</sup> or other unexplained decomposition pathways or reactivity.

Overall, our work has shown that pure 1,3-dialkylimidazolium ILs can be induced to undergo reactive transformations *via* NHC carbenes as both reactant and solvent even in the absence of additional external sources of base. Here, this has been illustrated by reaction of  $[C_2mim][OAc]$  (or the corresponding statistical mixture) with sulfur or selenium to directly form the corresponding imidazole-2-chalcogenones. However, the acidity of the C(2) proton of the IL imidazolium cation and the basicity of the IL anion are in themselves not sufficient criteria to understand this chemistry, as suggested by Hollóczki *et al.*<sup>6</sup> The anion must also be capable of stabilization of the parent acid through the formation of complex anions, thus preventing the unchecked reaction and decomposition of the IL.

Considered in totality, the chemistry reported here can be regarded as an example of a 'carbene-in-a-bottle', where, through anion selection, the standing carbene concentration present in equilibrium in ILs (something we could call the effective  $pK_a$  of the C(2) hydrogen in the imidazolium IL) can be modified to provide both reactive carbene moieties and solvent for a variety of applications.

We want to thank Petroliam Nasional Berhad (PETRONAS) for financial support for this project. H.R. is also grateful to the Ministry of Science and Innovation of Spain ("Ramón y Cajal" program).

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