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From curiosities to commodities: ionic liquids begin the transition

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A growing variety of ionic liquids are becoming commercially available, a development that will feed the surge of research using these unorthodox liquids.

Ionic liquids (IL) are attracting the attention of a growing number of scientists and engineers, a fact manifested by the rapidly increasing rate at which papers on the topic are being published.[1] For the sake of those readers not familiar with ionic liquids, suffice it to say that they are salts that are liquid at low temperature – many at room temperature or below – and that in a molten form are composed wholly of ions. Several excellent reviews on their synthesis and uses are available.[1,2]

So why all the fuss about *salt*? First, ionic liquids have negligible vapor pressures. Since evaporative loss is a major mode of molecular solvent discharge into the environment, the use of select ionic liquids may offer environmental advantages in industrial processes to which they are suited. Second, ionic liquids can dissolve an array of substrates, and a growing number of studies report that when used in place of molecular solvents, IL can provide improvements in product yields, selectivities or ease of product recovery. Finally, there is the human factor. New opportunities to work with unorthodox substances – such as salts that are liquids at less than hellish temperatures – are rare and appealing.

The most widely used ionic liquids are probably *N*,*N*-dialkylimidazolium salts (Fig. 1). Figures from the RSC, ACS and Elsevier publications databases support this assertion. To illustrate, of eighty-three RSC publications in 2002 dealing with ionic liquids, seventy-four involved imidazolium salts. The percentages from ACS and Elsevier imprint journals for 2002 are similar.[3]

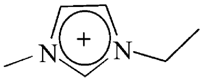

Fig. 1 The 1-ethyl-3-methyl imidazolium cation, [emim].

Much of the focus on imidazolium salts is due to the utility that early research demonstrated them to possess – a case of success begetting success. Perhaps more significantly, the use of imidazolium salts – especially the "water stable" varieties – is *easy*. These members of the ionic liquid family are readily prepared, and are now becoming commercially available.

Several start-up and established chemical manufacturers have "crossed the Rubicon" and introduced commercial IL lines.[4] Among the entries into this arena

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Fig. 2 A selection of ionic liquids available from commercial manufacturers.

are Covalent Associates, Cytec, Merck (Darmstadt), Ozark Fluorine Specialties, Sachem and Solvent Innovation (Fig. 2). Certain of these companies provide investigational samples directly to researchers, while also selling materials through retailers like Aldrich and Strem. Another large retailer, Acros, markets research sized samples obtained from Seddon's QUILL.[5]

To date, commercial offerings of salts explicitly described as ionic liquids are largely imidazolium based. Notably, BASF has recently disclosed the involvement of an imidazolium ionic liquid in a commercial process, the production of alkoxyphenyl phosphines.[6] Other processes said to be poised for licensing such as the French Petroleum Institute's butene–dimerization process, also feature imidazolium based ionic liquids. Nevertheless, there is a degree of compositional variety amongst commercial imidazolium IL offerings. This diversity arises almost wholly from the pairing of a very small number of cations, principally 1-butyl-3-methylimidazolium [bmim] or 1-ethyl-3-methylimidazolium [emim], with any of a growing number of anions.

The most commonly employed IL anions are polyatomic inorganic species. Most prominent among the these is PF_6^-, a work-horse anion that Wilkes and Zaworotko paired with imidazolium cations in preparing early water-stable, hydrophobic IL.[7] It and the related ion BF_4^- are probably the most common anions used in IL research. And, though little variation in properties might be expected between same-cation salts of these species, the actual differences can be dramatic. For example, [bmim]PF_6 is immiscible with water, where [bmim]BF_4 is water-soluble. This sort of variation arising from different ion pairings gave rise to Seddon's description of IL as "designer solvents."[8] Further, it is the impetus driving the continued search for new ionic liquids.

Despite their widespread use, IL featuring PF_6^- and BF_4^- have been reported to sometimes decompose when heated in the presence of water, giving off HF. This drawback has prompted some companies to introduce alternate anions, though many of these are still fluorous materials. In these, the fluorine of the anion is bonded to carbon, the C-F bond being inert to hydrolysis. Thus, IL based upon $CF_3SO_3^-$, $(CF_3SO_3)_2N^-$ and related anions are being marketed.

For reactions involving the use of a metal catalyst in an IL, a low capacity for coordination on the part of the anion is essential, and fluorous species like PF_6^- will probably remain the best in that regard.[2] Still, fluorinated anions tend to be expensive. Some, especially $(CF_3SO_3)_2N^-$, seem unlikely to ever be cheap enough to use in formulating ILs for use on larger scales, save for use in high-value applications.

In response to safety and cost concerns, some manufacturers – notably Solvent Innovation and Sachem – have introduced new ILs with non-fluorous anions. Among the most interesting are salts in which the anions are derived from inexpensive bulk chemicals (Fig. 3). The principal offerings by Solvent Innovation in this category are IL featuring alkylsulfate anions which are likely to be reasonably non-toxic and biodegradable.[9] One specific ionic liquid, ECOENG 500 (Peg-5 cocomonium methosulfate), is the first commercially available ionic liquid for which full toxicological data is available.[10] Sachem, an established bulk chemicals producer, has recently introduced the Terrasail line of IL based upon the docusate (dioctylsulfosuccinate) anion. Docusate is known to exhibit low mammalian toxicity, and is widely used in food, drug and cosmetic applications. In contrast to other ionic liquids, many incorporating docusate are highly lipophilic, some being fully miscible with hydrocarbons.

While IL derived from polyatomic anions still dominate commercial offerings, this is beginning to change. Cytec has awakened to the fact that many phosphonium halides that it has offered for years for phase-transfer applications are ionic liquids in their own rights, and has recently reported on their industrial preparation.[11] Sachem also produces salts that were developed as phase transfer catalysts, but that are functionally ionic liquids.

The promotion of halide IL is well-timed. It coincides with recent findings by Rogers and others that hard, coordinating

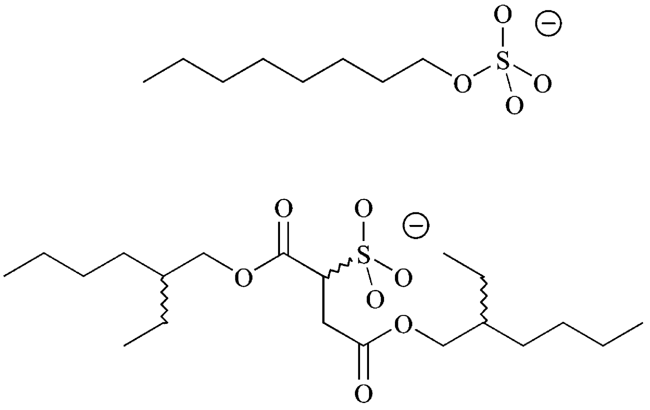

Fig. 3 n-Octyl sulfate (top); docusate (bottom).

anions like chloride can be critical in facilitating the dissolution by IL of biomolecules like cellulose and other oligosaccharides.[12] These findings also reemphasize that IL are not, as is sometimes asserted, simply a dispersive matrix. Rather, they can and do interact with dissolved molecules.

Increasing the capacity of IL to interact with dissolved molecules in specific ways is the focus of several research programs. New IL are being introduced in which a functional group is incorporated as a part of the cation or anion structure. These functional groups can impart a particular reactivity pattern to the IL, enhancing its capacity for interaction with specific solute types. For example, safe-to-handle Brönsted acidic IL with appended sulfonic acid groups were recently reported, as was their use as solvent-catalysts for esterification and other organic reactions.[13] Others, bearing appended amines, can separate CO_2 from gas streams, while IL with large aromatic head groups show enhanced activity for the extraction of aromatics in aqueous biphasic systems.[14] IL with tethered carboxylate groups have been used as supports for "IL-phase synthesis," a versatile extension of the solid-phase synthesis concept.[15]

While the development of such "task-specific"[13] IL has been largely a process of design, there is a huge role for discovery to play as well, a role that numerous chemical manufacturers are well-positioned to exploit. A recent, cursory survey of chemical catalogs by the authors uncovered over one hundred commercially available salts that melt below 150 °C.[16] Many others were just above this melting point, suggesting that many new IL might be readily created by matching a desired cation from such a salt with a different anion, or vice-versa. These compounds constitute "incognito" IL, begging to be used.

Of course, the availability of incognito IL is due to their *existing* use in some other type of application. For example, 1,8-diazabicyclo[5.4.0]undec-7-ene hydrotribromide (DBU-HBr_3, mp 119–122 °C) is a superb reagent for high-yield aromatic brominations.[17] Naturally, such pre-existing applications point to potential uses as IL for the compounds themselves or salts related to or derived from them.

An example of a readily available, incognito IL that has already been creatively exploited is acetylcholine chloride. This salt, a non-toxic natural product, melts between 147°–149 °C, making it (by our criteria) an ionic liquid. Davies has recently demonstrated that it, when combined with select inorganic salts, forms eutectics with even lower melting points.[18] These eutectics, themselves composed wholly of ions, are interesting new ionic liquids with built-in, water-stable Lewis acidic character.

Other low-melting biomolecular salts, many of them amino acid derivatives, can be obtained commercially as well. Examples include L-alanine ethyl ester hydrochloride (mp 78 °C) and L-serine methyl ester hydrochloride (106 °C). Like many other lower-melting salts, these may not be ionic liquids in a strict sense. Melts likely manifest equilibrium concentrations of neutral species, meaning that they are not composed only of ions. However, as melts in contact with a secondary, low-polarity organic phase, it is doubtful that any neutral melt component would partition into the latter, allowing the melt to *function* in a fashion similar to a "true" ionic liquid.

At a minimum, many of the ions in these low-melting, commercially available salts are potentially versatile skeletons that suggest themselves as starting points for modification into IL with built-in functional groups. Wasserscheid has recently reported just this sort of process, using the alkaloid ephedrine (available as ephedrine hydrochloride) as the framework for building-up a chiral IL.[19]

The current trend towards the commercialization of IL creates opportunities for new researchers to participate, while working with materials of known purities (this being a key concern).[20] Coincident with this development, there is a growing realization that there exists a plethora of available low-melting salts never before exploited in a molten form, offering new opportunities for exploration and discovery. There is then no doubt that research into the use of ionic liquids as solvents, reagents, catalysts and materials will continue to grow. Indeed, for these remarkable salts, the future looks bright.

Fig. 4 Not all ionic liquids are actually "liquid" at room temperature. Left is methyltri-n-butylammonium docusate, with a mp around 40 °C. Right is an RTIL (room temperature ionic liquid) 1-butyl-3-methyl imidazolium diethyleneglycolmonomethylethersulfate. Note that some ionic liquids are colorless, while others are pale yellow to orange in colour.

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SOME SOURCES OF INFORMATION ON IONIC LIQUIDS

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