Synthesis, Purification and Characterization of Ionic Liquids

Bronya Clare, Amal Sirwardana, and Douglas R. MacFarlane

Abstract The synthesis, purification and characterization of ionic liquids is reviewed. The major synthetic routes to low melting ionic salts are described in detail. The intrinsic properties of ionic liquids make purification difficult and therefore a special emphasis is placed on currently employed purification methodologies. Synthetic methods which are designed to avoid specific impurities are also discussed. For the same reasons highlighted above characterization of ionic liquids presents unique challenges; the available methods and some of the issues of their use are also reviewed.

Keywords Ionic Liquids • Synthesis • Purification • Characterization

Contents

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1 Introduction

1.1 Overview

Ionic liquids (ILs) in principle are a diverse group of salts which are liquid at ambient temperatures. While early work in the field tended to presume that ionic liquids had very similar properties as a class, it is now widely recognized that, in fact, they offer a very wide range of properties and that one of the only properties that can be thought of as ubiquitous among ionic liquids is ion conductivity [1]. As the field has thus grown in recent years, producing a wide range of properties in an even wider range of salt structures, the synthetic methods applied to the preparation of these salts have become more sophisticated and capable of targeting more complex compounds. Our goal in this chapter is to provide a comprehensive overview of the synthetic approaches currently available, in such a way that a researcher beginning the synthesis of a new target compound can easily appreciate the synthetic methodology options that might be applied. We also discuss a number of the purification and characterization issues that arise and that are in some cases unique to the ionic liquids field, because of the very nature of the compounds involved.

We begin with a brief overview of the types of cations and anions that are known in the field, as of mid-2008. Part of our goal here is to provide a guide to some of the nomenclature that follows in the remainder of the chapter.

1.2 Cations

The ionic liquid cation is generally an organic structure of low symmetry. The cationic centre most often involves a positively charged nitrogen or phosphorus. Those described thus far are based on ammonium, sulphonium, phosphonium, imidazolium, pyridinium, picolinium, pyrrolidinium, thiazolium, oxazolium or pyrazolium cations, usually completely substituted. The more recent research has mainly focused on room temperature ionic liquids composed of asymmetric dialkylimidazolium cations associated with a variety of anions. Through modification of the cation, the properties of the liquid, notably the melting point and liquid range [2], viscosity [3] and miscibility with other solvents [4], can be altered. On the basis of the cation, ILs may be divided into six groups: (1) five-membered heterocyclic cations, (2) six-membered and benzo-fused heterocyclic cations, (3) ammonium, phosphonium and sulphonium based cations, (4) functionalized imidazolium cations and (5) chiral cations. The discussion below briefly overviews these different families of IL cations.

1.2.1 Five-Membered Heterocyclic Cations

Figure 1 shows some five-membered cations including imidazolium, pyrazolium, triazolium, thiazolium and oxazolium. While the halide salts are usually solids at room temperature there are many anions that lower the melting points of the salts
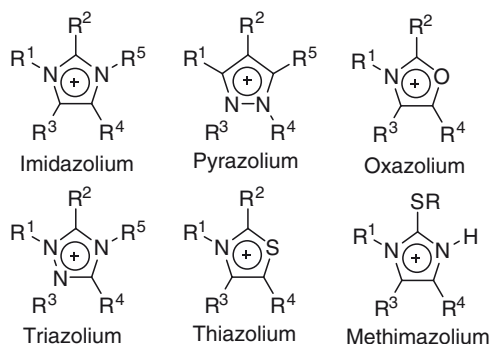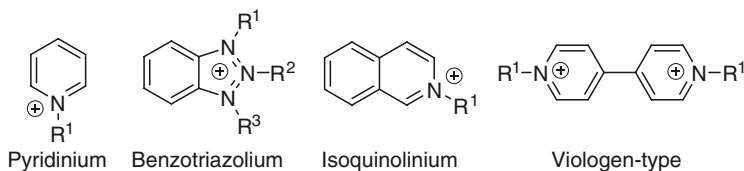
Fig. 1 Five-membered heterocyclic cations

below room temperature. It is generally assumed that non-symmetrical *N,N'*-alkylimidazolium cations yield salts having the lowest melting points; however, dibutyl, dioctyl, dinonyl and didecylimidazolium hexafluorophosphates are also liquid at room temperature [5], 1-Butyl-3-methyl and 1-ethyl-3-methylimidazolium cations are probably the most investigated structures of this class.

Similarly, the halide triazolium salts are solids at room temperature, but metathesis to salts, such as bis(trifluoromethanesulphonyl)amide, triflate or tetrafluoroborate, lowers the melting point to near or below room temperature.

1.2.2   Six-Membered and Benzo-Fused Heterocyclic Cations

Figure 2 shows some cations with aromatic character that have been investigated as ionic liquids, such as the pyridinium, viologen-type, benzotriazolium and isoquinolinium cations. Moving up one carbon from the five-membered heterocyclic cations, there is a second, though less explored, class of heterocyclic room-temperature ionic liquids – the pyridinium RTILs. These salts have been known for quite some time, but interest in them has been far less intense than that of the imidazolium family. This is likely due to their more limited stability in the presence of nucleophiles and the toxicity of pyridine. Gordon et al. [6] have reported a series of pyridinium hexafluorophosphate salts with long alkyl chains (C_{12}–C_{18}), some of which melt below 100 °C. A more recent area of focus is the viologen family of ionic liquids. While most viologens are very high melting solids, there is a handful that do exhibit much lower melting points, though not quite room temperature. Benzotriazolium based ILs are often good solvents for aromatic species [7].

Pyridinium   Benzotriazolium   Isoquinolinium   Viologen-type

Fig. 2 Six-membered and benzo-fused heterocyclic cations
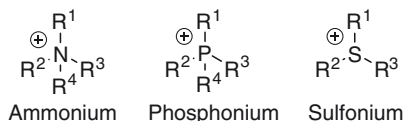
**Fig. 3** Ammonium, phosphonium and sulphonium cations

1.2.3 Ammonium, Phosphonium and Sulphonium Based Cations

Tetraalkylammonium (Fig. 3) salts have been known for centuries. In terms of their use as RTILs, earlier studies led to the conclusion that longer alkyl chains were required to obtain room temperature melting points. These are typically prepared by alkylation of the parent amine. To obtain low melting points, typically at least two or three different alkyl groups are required to create crystal packing constraints; this usually requires several steps of alkylation. Although phosphonium RTILs are certainly known and finding growing applications in organic synthesis and other areas [8], there is surprisingly little in the way of published data regarding their physical properties [9]. The hydrogen sulphate salt of the tetrabutylphosphonium cation has a melting point of 122–124 °C, while the hydrogen sulphate salt of the tributyldecylphosphonium cation is a room temperature liquid [10]. In terms of other physical properties, the viscosity of these phosphonium RTILs are generally somewhat higher than their ammonium counterparts, but decrease very rapidly with increasing temperature. Phosphonium salts are generally more stable thermally than ammonium salts [9]. Phosphonium salts are typically made by alkylation of the parent phosphine [11]. As will be discussed further below, for the larger phosphonium cations this is straightforward, however the pyrophoric nature of the lighter alkyl phosphines makes this a more difficult matter. One of the least studied types of RTILs are those based on the trialkylsulphonium cation.

As might be expected, the melting point and density typically decrease as the size of the cation increases. The viscosity, however, reaches a minimum with the triethyl compound and then often increases significantly for the tributyl compound.

1.2.4 Functionalized Imidazolium Cations

Recent advances in ionic liquids research has provided routes for achieving functionalized ionic liquids (Fig. 4) in which a functional group is covalently tethered to the cation or anion of the ionic liquid, especially to the two N atoms of the

FG = OH, NH$_2$, SH, SO$_3$OH, CONH$_2$...
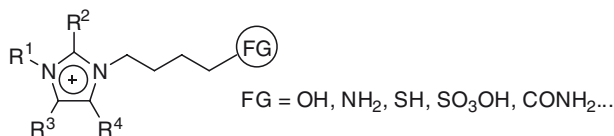
Fig. 4 Functionalized imidazolium cations

imidazole ring. It is expected that these functionalized ionic liquids may further enlarge the application scope of ionic liquids in chemistry.

1.2.5 Chiral Cations

There are growing numbers of reports indicating that chiral ionic liquids may be useful in many areas of science and technology, though synthesis and use of chiral ILs is in its infancy. For example, the use of ephedrinium-based chiral ILs (Fig. 5) as a gas chromatography stationary phase has been reported [12]. Chiral ILs can be prepared either from chiral starting materials (Scheme 1b) or using asymmetric synthesis (Scheme 1a) [13].
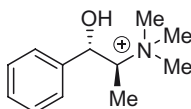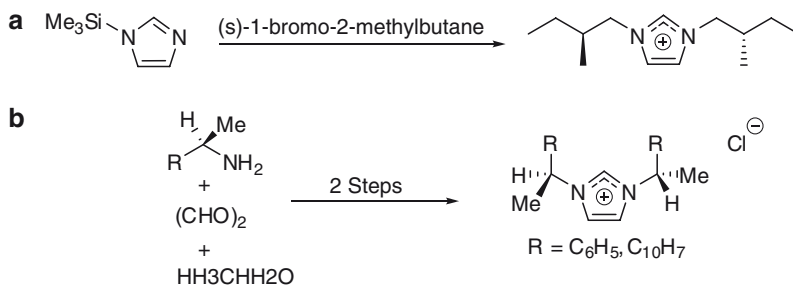

Fig. 5 (1S, 2R)-(+)-N,N-dimethylephedrinium ion

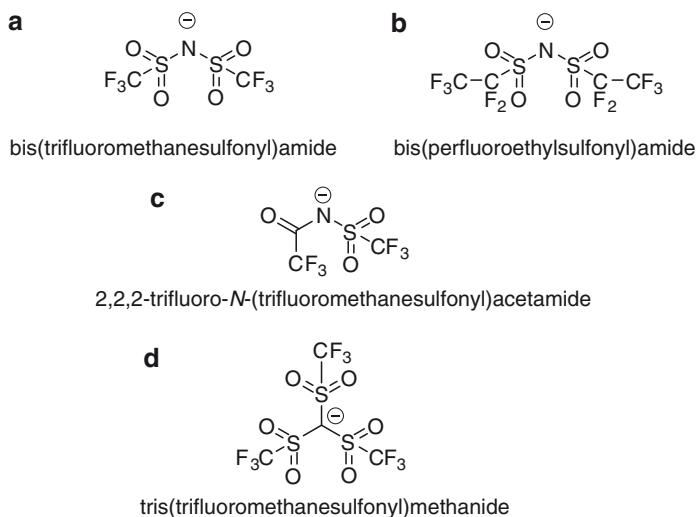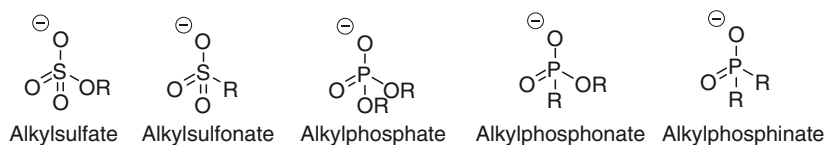**Scheme 1** Synthesis of chiral cations

1.3 Anions

Anions that form room temperature ionic liquids are usually weakly basic inorganic or organic compounds that have a diffuse or protected negative charge. On the basis of the anion, ILs may be divided into six groups: (1) ILs based on $AlCl_3$ and organic salts [14]; (2) ILs based on anions like PF_6^- [5, 15], BF_4^- [16, 17], and SbF_6^- [15];

(3) ILs based on anions like **a** [18, 19], **b** [19, 20], **c**[7] and **d**[19] in Fig. 6; (4) ILs based on anions like alkylsulphates [21], alkylsulphonates [22], alkylphosphates [9], alkylphosphinates [9] and alkylphosphonates [9] (Fig. 7); (5) ILs based on anions such as mesylate, [23, 24] tosylate ($CH_3PhSO_3^-$) [24], trifluoroacetate ($CF_3CO_2^-$) [3], acetate ($CH_3CO_2^-$) [7], SCN^- [25], triflate ($CF_3SO_3^-$) [15, 23, 26] and dicyanamide [($N(CN)_2^-$] [27, 28]; (6) ILs based on anions such as the borates [29] and carboranes (Fig. 8) [30].

bis(trifluoromethanesulfonyl)amide   bis(perfluoroethylsulfonyl)amide

2,2,2-trifluoro-*N*-(trifluoromethanesulfonyl)acetamide

tris(trifluoromethanesulfonyl)methanide

Fig. 6 Amide and methanide anions

Alkylsulfate   Alkylsulfonate   Alkylphosphate   Alkylphosphonate   Alkylphosphinate

Fig. 7 Phosphate, phosphonate, phosphinate, sulphate and sulphonate anions

Fluoroacetoxyborate   Bis(oxalato)borate   Alkyl carborane
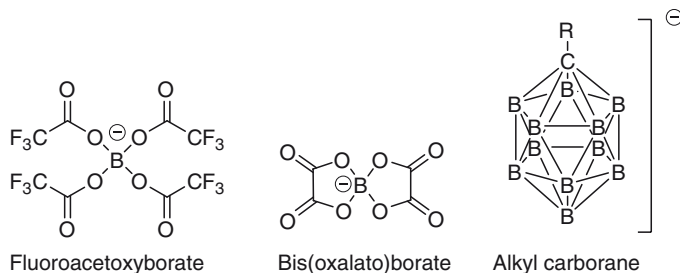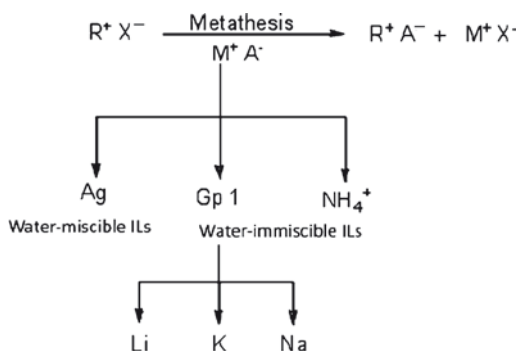
Fig. 8 Borate and borane anions

2   Synthesis

2.1   *Metathesis*

A great many ionic liquids are prepared by a metathesis reaction from a halide or similar salt of the desired cation. The general metathesis reaction can be divided into two categories (Scheme 2) depending on the water solubility of the target ionic liquid: metathesis via (1) Free acids or group 1 metals/ammonium salts, or (2) Ag salt metathesis.

$$R^+ X^- \xrightarrow[\text{M}^+ \text{A}^-]{\text{Metathesis}} R^+ A^- + M^+ X^-$$

Ag   Gp 1 NH_4^+

Water-miscible ILs   Water-immiscible ILs

Li   K   Na

Scheme 2 General metathesis routes to ionic liquids

2.1.1   Metathesis Reactions Involving Free Acids, Group 1 Metals or Ammonium Salts

The most common approach to the preparation of *water immiscible* ionic liquids is the metathesis reaction of the corresponding halide salt, either with the free acid of the anion, or its metal or ammonium salt. Among these alternatives the free acid may be the favored approach as the hydrogen halide produced can easily be removed by washing with water. Here we explain the metathesis reactions based on metal salts, including ammonium salts. In 1996, Bonhote et al. [3] reported the synthesis of dialkylimidazolium bis(triflyl)amides and dialkylimidazolium nonafluorobutanesulphonate by reacting the corresponding halide or triflate with lithium bis(triflyl)amide, $LiNTf_2$, or potassium nonafluorobutanesulphonate in aqueous solution. The resulting ionic liquids were extracted from the aqueous solution into dichloromethane. $[C_2mim]$ $[BF_4]$ can be prepared by metathesis reaction of the corresponding chloride or bromide with sodium tetrafluoroborate in propanone; however this leaves appreciable amounts of chloride or bromide ions in the ionic liquid, as sodium halides are slightly soluble in propanone [16]. Therefore, Fuller et al. [31] reported the metathesis reaction of $[C_2mim]Cl$ with ammonium tetrafluoroborate in propanone in high purity.

The water solubility of ionic liquids is very dependent on both the cation and anion. Generally, water solubility decreases with increasing the alkyl chain length on the cation. Seddon et al. [16] have discussed the metathesis reaction of the halide salt

with HBF_4 or $NaBF_4$ in water, followed by extraction into dichloromethane yielding improved purity depending on the length of the alky chain (*n*) on the imidazolium cation. For example, for *n* = 6–10 the IL separates as a dense liquid, whereas for chain length *n* > 10 a solid separates from the aqueous reaction mixture. Chains lengths *n* = 4 and 5 can be extracted and purified from aqueous solution by partitioning into an organic solvent. For shorter chains the partition coefficient water:IL:organic solvent is too close to 1, hence the separation is not efficient. In that case metathesis via the alkyl halide with a silver salts is more useful.

Alternatively, the metathesis reaction can be carried out completely in an organic solvent such as CH_2Cl_2 [32] or acetone [31]. In both solvents the starting materials are not completely soluble; however the reaction can be carried out as a suspension. For example, in the case of CH_2Cl_2, the metathesis reaction of 1-alkyl-3-methylim-idazole with metal salt can be carried out at room temperature for about 24 h and then the suspension filtered. However, the halide by-products have a limited solubility in CH_2Cl_2 and they can dissolve slightly in the IL/CH_2Cl_2 mixture. Therefore it is necessary that the organic layer be washed with water several times in order to remove the unwanted halides.

When the hydroxide salt is available (for example choline hydroxide is a readily available form of the choline cation), it is very straightforward to react the hydrox-ide with the acid of the desired anion in water. As long as the resultant ionic liquid can be separated into an organic phase, it is usually straightforward to remove the HX by-product by washing.

2.1.2   Ag Salt Metathesis

The preparation of water-miscible ionic liquids is an important but more difficult task since it requires separation of the by-products from the desired ionic liquid. This can be achieved via the simple metathesis reaction of the corresponding chloride or bromide with the silver salt of the anion. In 1992, Wilkes and Zaworotko [33] reported the first of the new generation of ionic liquids, $[C_2mim][BF_4]$, via metathesis of $[C_2mim]I$ with $AgBF_4$ in methanol. A range of other silver salts has been used for this reaction (such as $AgNO_3$, $AgNO_2$, $AgBF_4$, $Ag[CO_2CH_3]$ and Ag_2SO_4) in methanol or aqueous methanol. Additionally, we have described the use of $Ag[N(CN)_2]$ salts for metathesis reaction to produce dicyanamide ILs [27]. Ag(OH) is a useful approach to generating some of these silver salts where these are not otherwise readily available. Similarly, Reed et al. [30] obtained imidazolium carborane salts by metathesis reactions of silver carboranes with imidazolium chlorides or bromides in varying solvents.

Unfortunately, this route is expensive and forms a large amount of silver halide as by-product. Complete precipitation of silver halides from organic solvents can also be quite slow, leading to silver-contaminated products. The nature of the precipitate can also be troublesome; in some cases the silver halide forms as sub-micron particles which are difficult to filter. For these reasons, the preferred and most common metathesis approach is still to carry out the reaction in aqueous solution with either the free acid of the appropriate anion, or its ammonium or alkali metal salt as described in Sect. 2.1.1.

2.1.3 Ion Exchange Materials

Currently both natural and synthetic ion exchange materials are used extensively in industry and the laboratory for separation, purification and as convenient heterogeneous reagents for synthetic cation or anion exchange [34]. While ion exchange materials are commonly perceived to be appropriate for the industrial scale synthesis of ILs, very little information is openly available regarding their use in IL synthesis. Essentially ion exchange materials are salts where one of the ions is fixed in a stationary (solid/gel) phase and the counter ion (in solution) is exchangeable. As shown in (1) for anion exchange, when a solution is passed through a column of ion exchange material, the counter ion of the material $[A]^-$ will equilibrate with the corresponding ion of the solution $[B]^-$. Providing the column is of sufficient length and/or the equilibrium constant for (1) is sufficiently large, exchange will take place until complete exchange occurs and only species $[cation]^+ [A]^-$ is eluted as a pure solution:

$$[resin]^+[A]^- + [cation]^+[B]^- \Leftrightarrow [resin]^+[B]^- + [cation]^+[A]^-. \qquad (1)$$

Ion exchange is almost always a reversible process and ion exchange materials usually show a preference for one ion over another. The most successful synthetic ion exchange occurs when the ion exchange material shows a strong preference for the counter ion of the starting material over the corresponding ion of the product, i.e. the reaction from left to right in (1) will be most successful if the ion exchange material prefers $[B]^-$ over $[A]^-$. The factors which determine this preference are complex, but in crude, well known terms ion exchange materials tend to have a higher affinity for ions:

- With a higher valence
- With a smaller (solvated) volume
- With greater polarizability
- Which interact more strongly with the exchange material

Commonly, target IL cations and anions are available as either the alkali metal salt or the halide salt and the above principles suggest many ion exchange materials will show a preference for these counter ions and therefore IL synthesis from these starting materials will be successful. The preference principles may hinder the initial loading of an ion exchange material with an IL ion; however there are additional techniques available to load a lower affinity ion onto an ion exchange material. For example, as long as the affinity difference is not too great, a high concentration and multiple passes of the loading solution will usually be effective. Acid/base neutralization can also be used to load a low affinity ion onto the ion exchange material, e.g. for a low affinity anion the ion exchange material can be preloaded with OH^- ions and then reacted with the acid of the of the low affinity anion.

Surprisingly, literature on the use of ion exchange materials for IL synthesis is scant; however two useful examples illustrate the process. Lall et al. described the use of an anion exchange material to synthesize polyammonium phosphate ILs from their parent halides [35] and Mizuta et al. have a patent on the use of an anion exchange material to produce $[C_2mim][DCA]$ from $[C_2mim][Br]$ on an industrial scale [36].

Determining the conditions required for successful ion exchange synthesis, including the choice of an optimum ion exchange material, can be a lengthy process and must be adjusted for each target product. This is considered a major hindrance to the use of ion exchange materials for the laboratory scale synthesis of ILs; however, many IL ions have similar chemical and physical properties and should therefore behave similarly in ion exchange. It is therefore the belief of the authors that the time investment required in determining suitable ion exchange conditions for the laboratory scale synthesis of ILs is in many cases justified, especially if > 100-g quantities and/ or repeated preparations over an extended period of time are envisaged. Ion exchange also has the advantage of performing both synthesis and purification in one step.

2.2 Halogen Free Synthesis

The vast majority of ionic liquids are usually prepared by quaternisation of imidazoles, alkylamines or phosphines, often employing alkyl halides as alkylating agents, followed by anion metathesis (see Sect. 2.1 herein). Though the anion metathesis methods produce a large number of ionic liquids of good quality, production of high purity materials is a little problematic due to contamination by residual halide. The presence of halides in the resulting ionic liquids can drastically change the physical properties [37], and may result in catalyst poisoning and deactivation [38]. Therefore, various synthetic strategies have been devised to synthesize halide free ionic liquids. Dupont et al. [39] reported the direct synthesis of 1,3-disubstituted imidazolium tetrafluoroborate ionic liquids using a one step procedure (2). Reaction of formaldehyde with n-butylamine followed by addition of methylamine, aqueous HBF_4 solution and aqueous glyoxal solution affords, in 66% yield, a mixture of $[C_4mim][BF_4]$, $[BBIM][BF_4]$ and $[C_1mim][BF_4]$ in a molar ratio of 5:4:1:
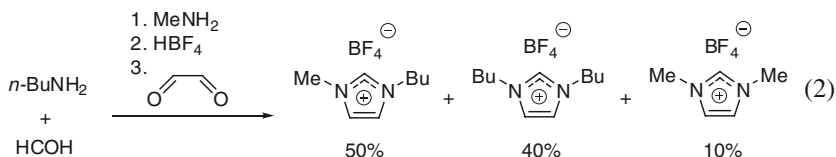
Other direct syntheses of halide free ionic liquids can be categorized into three groups: (1) synthesis via N-heterocyclic carbene intermediates, (2) phosphorus based direct reactions with imidazoles and (3) sulfur-based direct reactions with imidazoles as discussed further below.

2.2.1 Synthesis of Ionic Liquids via N-Heterocyclic Carbene (NHC) Intermediates

Carbenes are molecules which have a lone pair of electrons on a carbon atom; this in turn renders them highly reactive. As a result, carbenes are useful intermediates in the synthesis of chemical compounds. Generally they can only be isolated in
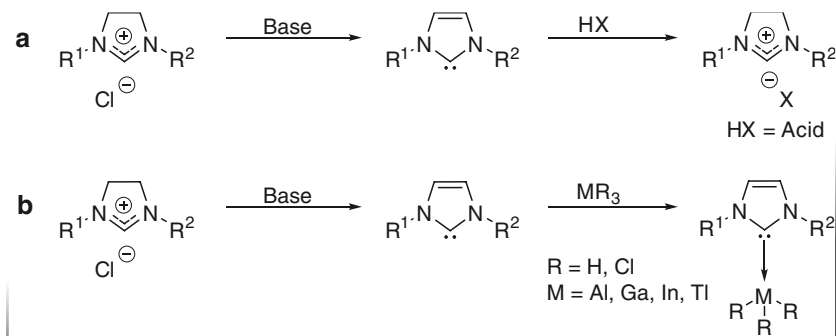
Scheme 3 Synthesis of ionic liquids via a carbene

the form of, for example, metal carbenoid species. The synthesis of ionic liquids via carbenes can be achieved either by the reaction of NHC adducts with acids (Scheme 3a), or reaction of NHC-organometallic intermediates with acids (Scheme 3b).

2.2.1.1 Preparation of NHCs and Reaction with Acids

Numerous methods for the generation of imidazole carbenes have been reported. For example, starting from an imidazolium halide, the use of systems such as sodium hydride in ammonia or dimethylsulphoxide (DMSO), sodium in ammonia, alkali metals in tetrahydrofuran (THF), metal *tert*-butoxides in THF or DMSO, etc. Recently, Seddon and Earle reported a simple procedure for the generation of the imidazolium carbene **2** in 90–95% yield from an imidazolium chloride **1** which does not require solvents, filtrations, or produce noxious waste products (Scheme 4) [40].

These carbenes can be used to produce the corresponding imidazolium salts by a simple reaction with the protonated form (**3–8** [41]) of the required anion (Scheme 4). The advantage of making these imidazolium salts by this process, i.e. by reaction of two neutral molecules, is that it generates ionic liquids which are not contaminated by unwanted halide ions or metal ions.

The 1,3-dialkylimidazolium-2-carboxylates **8** readily react with dry methanol, benzoylacetone and benzaldehyde in the presence of a stoichiometric amount of $NaBF_4$, KPF_6 or $NaBPh_4$ quantitatively affording the corresponding 1,3-dialkylimidazolium salt according to Scheme 5 [42].

Quite recently, Rogers et al. [43] reported the synthesis of intermediate **8a** (3) by the reaction of DMC with 1-methylimidazole **9** at 120–130 °C, in which the acidic C2-hydrogen of the resulting 1,3-dimethylimidazolium cation is abstracted by the methyl carbonate anion, leading to the heterocarbene and $HOC(O)OMe$ which is unstable and gives rise to MeOH and CO_2. Nucleophilic attack on CO_2 by the carbene is the only favored process and leads to the observed zwitterion **8a**. Then 1,3-dimethylimidazolium-2-carboxylate **8a** can be reacted with any of the acidic components in Scheme 4:
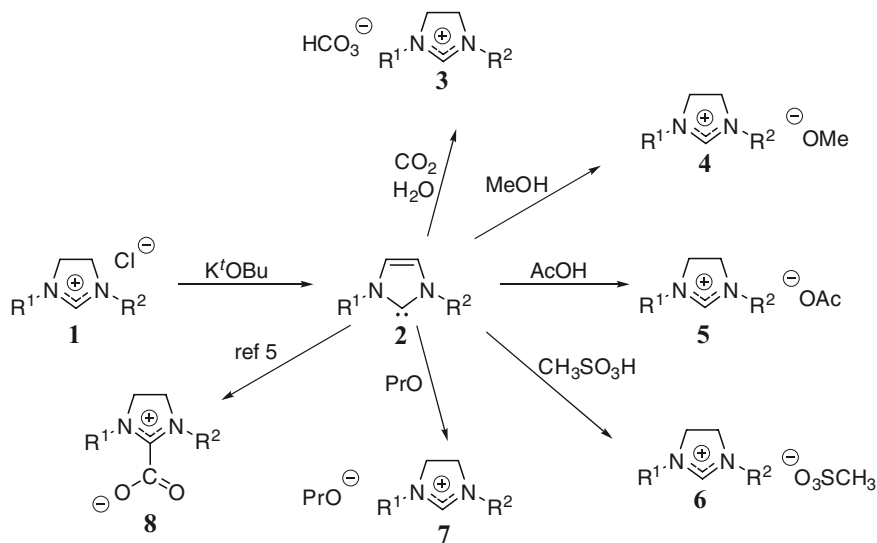
**Scheme 4** Synthesis of various ionic liquids via a carbene intermediate
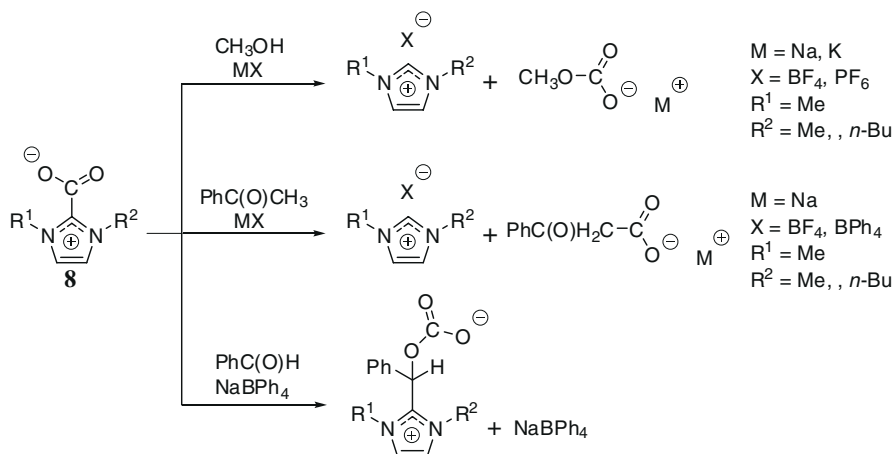
Scheme 5 Synthesis of 1,3-dialkylimidazolium salts from the dialkylimidazolium carboxylate

(3)
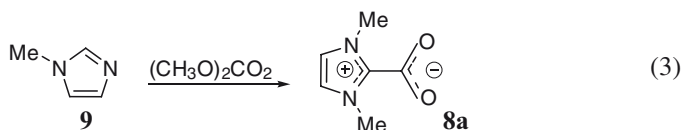
2.2.1.2 Reaction of NHC-Organometallic Intermediates with Acids

Recently, Cole et al. [44] have systematically studied the preparation, stability and synthetic utility of NHC adducted group 13 trihydrides and trihalides (Scheme 6). These

reactions suggest group-13 coordinated NHCs remain available for secondary acid–base reactions to synthesize ionic liquids. For example, the reaction of NHC stabilized aluminium trihydride species **10a** with three equivalents of phenol potentially offers a preferable path to **11** (route a). Meanwhile, the reaction of **10b** with 1,1,1,5,5,5,-hexafluoropentan-2,4-dione (F$_6$acacH) produced **12** (route b).
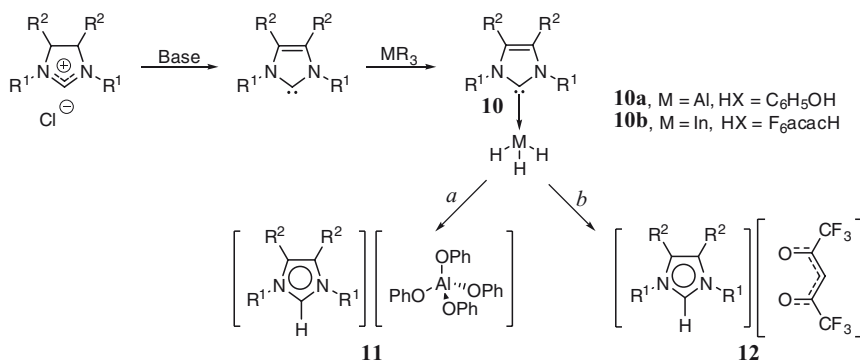
Scheme 6 Reaction of NHC-organometallic intermediates with acids

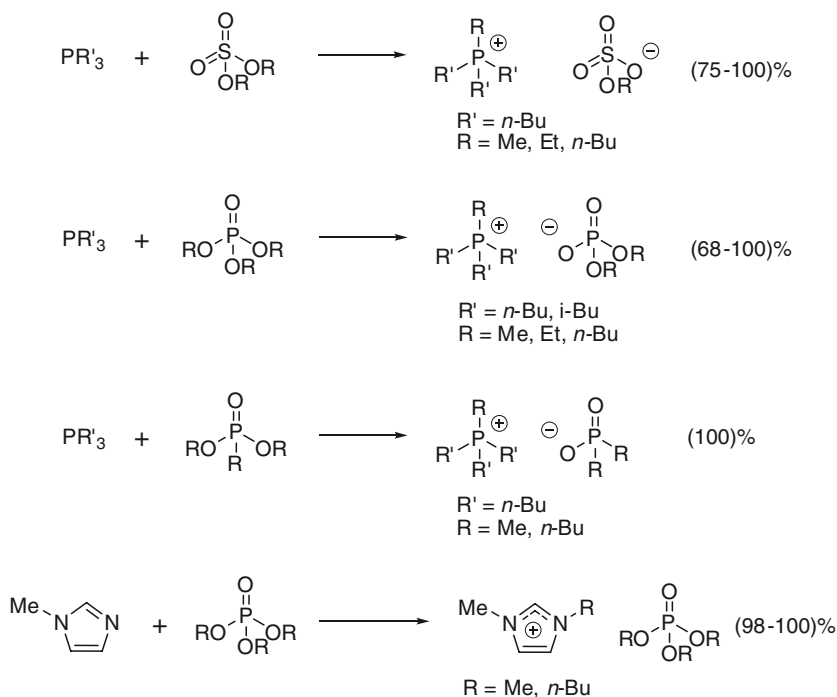### 2.2.2 Phosphorus Based Ionic Liquids

Halogen-free phosphorus based ionic liquids can be produced by direct reaction of: (1) phosphines with sulphates; (2) tertiary phosphines or imidazoles with alkylating agents such as trialkylphosphates, dialkylphosphonates and monoalkylphosphinates; or (3) phosphines with acid (Scheme 7).
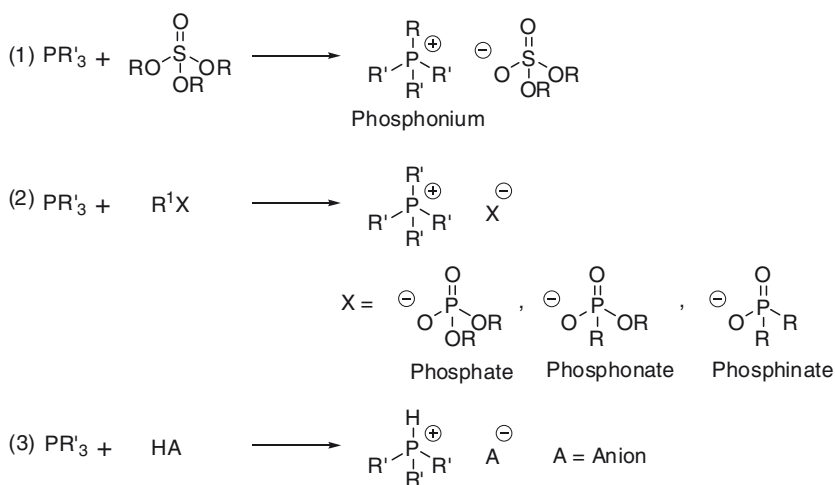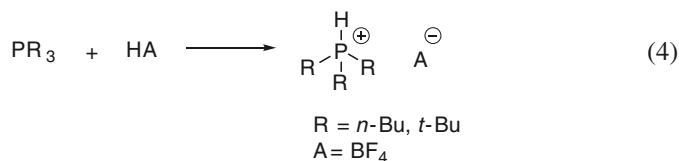

Scheme 7 Halogen free synthesis of phosphonium ionic liquids

Ammonium dialkylphosphates were first described in 1952 [45]. The alkylation products of pyridine and trialkylphosphates were described to be salts with very low melting points in 1989 [46]. Recently, Cytec filed patents on the synthesis of imidazolium based dialkylphosphate ionic liquids [9]. For example, they synthesized tetrabutylphosphonium dibutylphosphate, *N,N*-dimethylimidazolium dimethylphosphate, *N*-methyl-*N*-butylimidazolium dibutylphosphate, and *N*-methyl-*N*-ethylimidazolium ethylethanephosphonate. Downard and co-workers [9] reported synthesis of phosphonium, phosphates, phosphonates and phosphinates by direct reaction of phosphines or imidazoles with alkylating agents such as dialkylsulphate, trialkylphosphates and dialkylphosphonates and monoalkylphosphinates (Scheme 8).

Quite recently, to develop an optimized synthetic protocol for the alkylation of 1-alkylimidazole compounds with trimethylphosphate, the kinetics of the synthesis of 1,3-dimethylimidazolium dimethylphosphate were studied in detail [45]. The synthesis of the phosphonium salts derived from the reaction of phosphines with acids, has not been widely discussed. In 1991, Whitesides synthesized tris(2-carboxyethyl)phosphine hydrochloride [47]. Since then, air sensitive phosphonium salts have also been synthesized by the reaction of phosphine with a solution of aqueous HBF$_4$:

**Scheme 8** Direct alkylation via sulphonates, phosphonates and phosphinates

$$PR_3 \quad + \quad HA \quad \longrightarrow \quad R{-}\overset{\overset{\displaystyle H}{|} \oplus}{\underset{\underset{\displaystyle R}{|}}{P}}{-}R \quad A^{\ominus} \qquad (4)$$

$$R = n\text{-}Bu, \; t\text{-}Bu$$
$$A = BF_4$$

2.2.3 Sulfur Based Ionic Liquids

Direct synthesis of sulfur based ionic liquids has been developed as a useful synthetic method for halogen free ionic liquids. The synthesis of sulfur based ionic liquids can generally be split in to two sections: (1) sulphonate and (2) sulphate based ionic liquids (Scheme 9). The sulphate based salts are more common than the sulphonates.

a

b
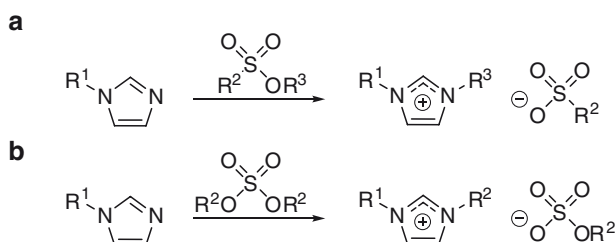
Scheme 9 Sulphate and sulphonate ionic liquids

2.2.3.1 Sulphonate Based Ionic Liquids

Direct addition of an alkylsulphonate into imidazole is useful, not only to synthesize the sulphonate anion, but also different anions via metathesis in the halogen free method. For example, the alkylation of N-alkylimidazoles such as N-methylimidazole with alkylsulphonate can be performed under solventless conditions at room temperature affording, after 48–72 h, the corresponding 1,3-dialkylimidazolium alkanesulphonate salts as crystalline solids in almost quantitative yields (5) [48]. The alkane sulphonate anions can easily be substituted by a series of other anions by metathesis:

$$(5)$$

$$R^3 = Me, \; n\text{-}Bu, \; 2\text{-}Bu, \; Et$$
$$R^2 = Me, \; n\text{-}Bu, \; (CH_2)_2OMe$$

$$X = BF_4, \; PF_6, \; PF_3(CF_2CF_3)_3, \; CF_3SO_3,$$
$$N(CF_3SO_2)_2$$

Jonathan and Mikami [49] reported a straightforward synthesis of new chiral ionic liquids bearing an imidazolium core, an easy and efficient method (6). Commercially available ethyl lactate was converted into its triflate derivative which upon reaction with 1-methylimidazole gave the triflate salt as a solid in excellent yield. Then anion metathesis was performed to obtain different anions with imidazole cation:


$$Tf = CF_3SO_2 \qquad X = PF_6, NTf_2, N(SO_2C_2F_5)_2, N(SO_2C_4F_9)_2 \qquad (6)$$
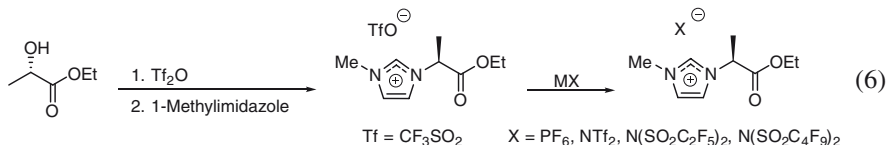
2.2.3.2 Sulphate Based Ionic Liquids

The hydrophilic ionic liquid $[C_2mim][EtSO_4]$ has received great attention, becoming one of the first ionic liquids commercially available in bulk. Ionic liquids containing methyl- and ethyl-sulphate anions can be easily and efficiently prepared under ambient conditions by the reaction of 1-alkylimidazoles with dimethyl sulphate and diethylsulphate (7) [21]:

$$R^1 = Me, Et, Pr, Bu$$
$$R^2 = Me, Et$$
$$R^3 = H, CH_3$$

$$(7)$$
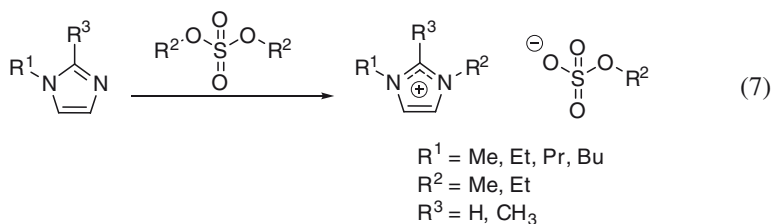
Quite recently, *trans*-esterification of 1-alkylimidazoliumsulphate was carried with functionalized and non-functionalized alcohols, to the corresponding new alkylsulphates (Scheme 10) [50].
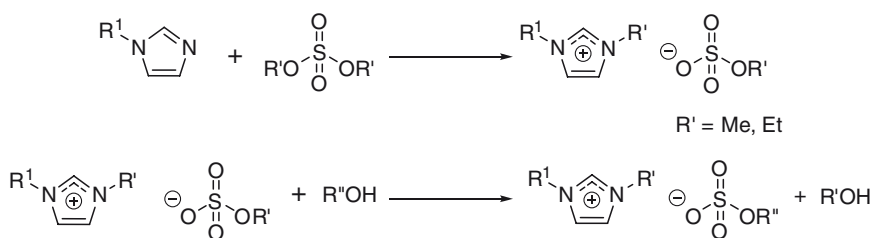
R'' OH = *n*-Butanol, *n*-Hexanol, *n*-Octanol, Diethyleneglycolmonoethylether, 2-Mehtoxyethanol, 2-Ethoxyethanol, 2-Butoxyethanol, Diethyleneglycolmonomethylether

Scheme 10 Trans-esterification routes to alkylsulphates

2.3 Protic Ionic Liquids

Protic ionic liquids (PILs) are formed by proton transfer between an equimolar mixture of a Bronsted acid and a Bronsted base. The major difference between PILs and other ILs is the presence of this exchangeable proton. Among other things, this can produce hydrogen bonding between acid and base and in some cases an H-bonded extended network. Presuming that the parent acid and base are available in a highly pure state, the acid/base neutralisation process can directly produce a highly pure ionic liquid. Angell and co-workers [51] synthesized a variety of PILs including organic and inorganic anions. Based on the Walden rule, they pointed out that systems with either associated ions or weak proton transfer form only "poor" ionic liquids [52]. Ohno et al. [53] have also described the convenient synthesis of protic ionic liquids by neutralization of organic tertiary amines with organic acids or inorganic acids (Scheme 11).

Drummond et al. [54] synthesized protic ionic liquids by combining Bronsted acid/base pairs where the primary amine cations were of the form RNH_3 and $R(OH)NH_3$ combined with organic anions of the form RCOO, R(OH)COO or with an inorganic anion. They studied physicochemical properties of synthesized PILs at nominally equimolar ratio of anion and cation (1:1 stoichiometry) and in the presence
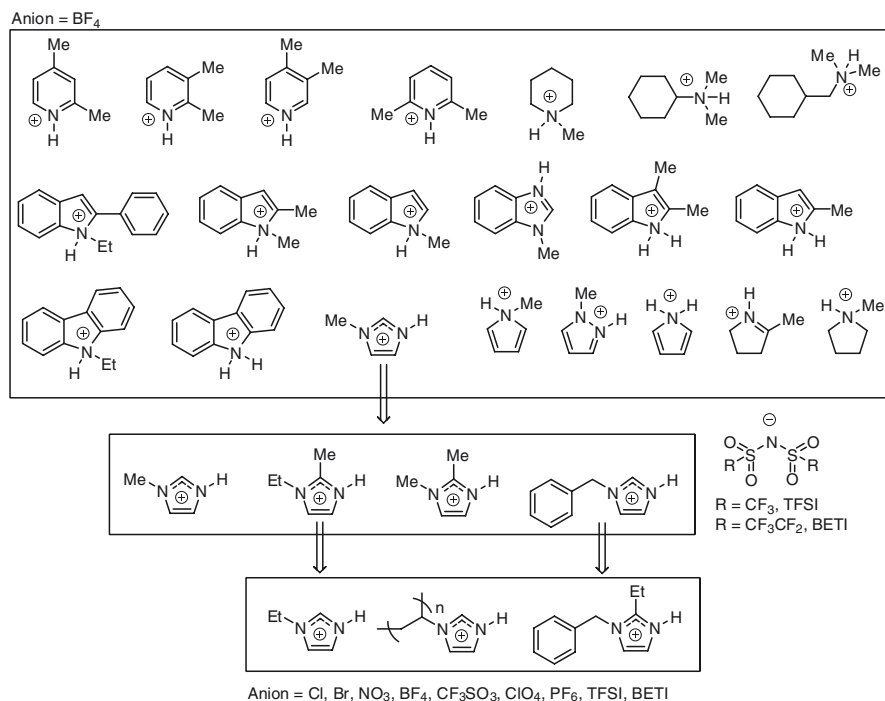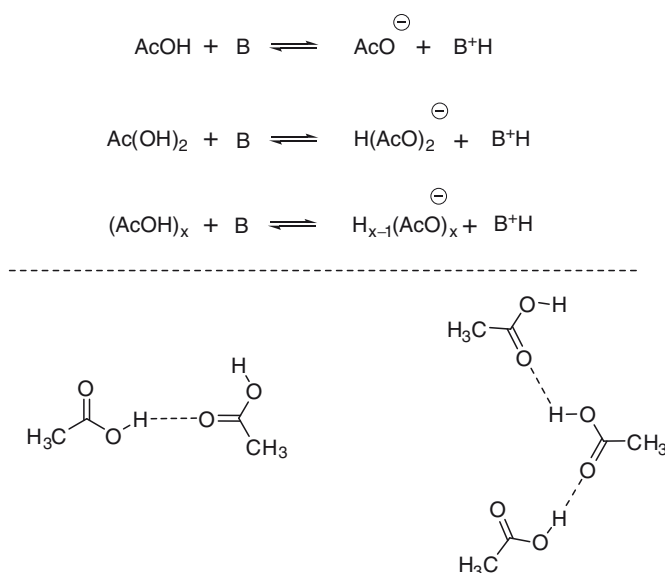

**Scheme 11** Synthesis of a variety of protic ionic liquids

of either excess acid or excess base [55]. We have prepared (Scheme 12) PILs containing the methylpyrrolidinium cation and used NMR shifts as a function of the acid strength to establish an ionization curve and suggested that the aqueous pKa values for the acid and base may be useful in obtaining an indication of how ideal, in terms of ionicity, the PIL is likely to be [56]. It appears that a difference of aqueous pKa values > 10 is required for complete proton transfer to form the salt. This is a very significant issue [1] in that for acid/base pairs where this is not true, the liquid produced is in fact a complex mixture of ions dissolved in a mixture of acid and base.

Quite recently [57], we reported the synthesis of dimeric or oligomeric mixtures of N-methylpyrrolidine and acetic acid using a simple neutralization reaction by adding the stoichiometric amount of acid dropwise to the base. It appears that the highest degree of ionicity, corresponding to the strongest degree of proton transfer, occurs at compositions much richer in acid than the equimolar composition, suggesting that the dimer and oligomeric acids are much stronger acids in neat system than monomeric acid.

Protic imidazolium and alkoxyimidazolium based ionic liquids as both solvents and Bronsted catalysts for catalytic reactions have been synthesized (Fig. 9) [58].

$$AcOH + B \rightleftharpoons AcO^{\ominus} + B^+H$$

$$Ac(OH)_2 + B \rightleftharpoons H(AcO)_2^{\ominus} + B^+H$$

$$(AcOH)_x + B \rightleftharpoons H_{x-1}(AcO)_x^{\ominus} + B^+H$$

Scheme 12 Possible formation of dimeric and higher-order oligomeric acetic acid
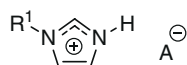
R^1 = Me, Butyl, Hexyl, Decyl, $CH_2OC_4H_9$, $CH_2OC_6H_{13}$, $CH_2OC_9H_{19}$, $CH_2OC_{10}H_{21}$
A = DL-Lactate, L-Lactate, Salicylate, BF_4, NTf_2

Fig. 9 Protoc imidazolium and alkoxyimidazolium based ionic liquids

There are two significant preparative issues that arise with protic ionic liquids:

1. As shown by Angell et al. [51] and MacFarlane et al. [59], ionic liquids can be distinctly volatile unless ΔpKa for the acid/base pair is high (>10). The volatility arises from the vapour pressure of the residual acid and base that exist in equilibrium with the ions. Since these will have different vapour pressures in principle, any evaporation from the ionic liquid will change its composition. Thus elevated temperature drying of these ILs must be treated with caution and the anion/cation stoichiometric balance proven by an appropriate method (NMR or microanalysis) after the drying is complete.
2. Primary and secondary amines can, in principle, form an amide rather than the salt when combined with certain acids. This is especially troublesome when elevated temperatures are involved in the process. Therefore, it is very important to prove the structure in those cases where amide formation is possible.

2.4 Special Cases

2.4.1 Metal Based Ionic Liquids

Ionic liquids with anions containing transition metal complexes were among the earliest developed room temperature ionic liquids [60]. Transition metal based ionic liquids have been synthesized either by reaction of phosphonium or imidazolium halides with the corresponding metal halides, or by metathesis with alkali salts of the metal-based anions. Among the metal containing ionic liquids, ionic liquid-crystals are excluded in this section as they were reviewed thoroughly in 2005 [61]. Synthesis of metal based salts can be divided in to three groups: (1) transition metal salts, (2) *p*-block metal salts and (3) *f*-block metal salts.

Co and Ni based ionic liquids [62] can be synthesized directly by mixing the corresponding metal chloride with [C$_2$mim]Cl under an inert atmosphere. The metal chloride anions interact with the imidazolium ring hydrogens to form a hydrogen bonded network (Fig. 10).
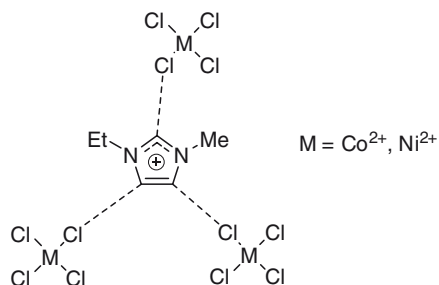

Fig. 10 Co- and Ni based ionic liquids

Vanadium-based salts [63] such as $[C_2mim]_2[VOCl_4]$ can be obtained from the reaction of $[C_2mim]Cl$ with $VOCl_2(CH_3CN)_x$. Addition of thionyl chloride to $[C_2mim]_2[VOCl_4]$ produces $[C_2mim]_2[VCl]_6$. Ferrocene containing room temperature ionic liquids [64] can be synthesized by the reaction of mono- or di-substituted (trimethylammonium) ferrocene iodide with imidazole or triazole (Scheme 13). These initially produce the ferrocene linked imidazole or triazole. Then quaternisation with methyliodide followed by metathesis with lithium bis(trifluoromethanesulphonyl) amide, $LiNTf_2$, produces the imidazolium or triazolium ionic liquids.

Several groups [65] have studied Fe^{2+} and Fe^{3+} based ionic liquids; $[C_4mim]$ $[FeCl]_4/[Fe_2Cl_7]$, $[C_4mim][FeCl_4]$, $[BDmim][Fe^{2+}Cl_4][Fe^{3+}Cl_4]_2$ have been reported. The formation of a Cu^+-based room temperature ionic liquid $[C_2mim]Cl$–$CuCl$ was reported in 1986. Very recently Sundermeyer's group [66] reported the Cu^{2+} containing ionic liquid $[C_4mim]_2[Cu_3Cl_8]$. The $[C_Rmim][ZnX_2Y_2]$ ionic liquid system (R = Me, Et, n-Bu, Benzyl; X = Y = Cl or Br or X = Cl, Y = Br) was synthesized by reacting ZnX_2 with (1-R-3-methylimidazolium)Y [67]. The single crystal X-ray structural analysis and elemental analysis of $[C_Rmim][ZnX_2Y_2]$ revealed that two imidazolium cations were paired with a dibromodichloro zincate dianion.

In 1998, Dupont et al. [68] reported the synthesis of $[C_4mim]_2[PdCl_4]$ (Fig. 11). Solid IL-coordinated Pd^{2+} complex **13** was synthesized by the reaction of a nitrile functionalized ionic liquid with $PdCl_2$ at room temperature. [69] Shreeve and co-workers [70] synthesized the IL-coordinated compound **14** (Fig. 11).

$[C_nmim][PtCl_n]$ (C_n = Et, Bu, n = 4, 6) was synthesized by the reaction of Pt^{2+} or Pt^{4+} chlorides with $[C_nmim]Cl/[AlCl_3]$ or $[C_nmim]Cl$ [71]. Several Pt metal based ionic liquids (**15**, **16** and **17**) have been reported (Fig. 12) [72].
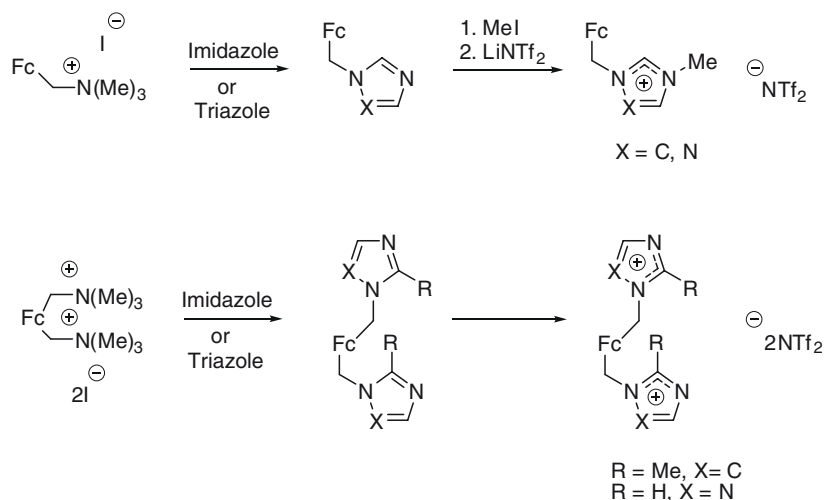
Scheme 13 Formation of imidazolium-based ionic liquids containing feurocenium
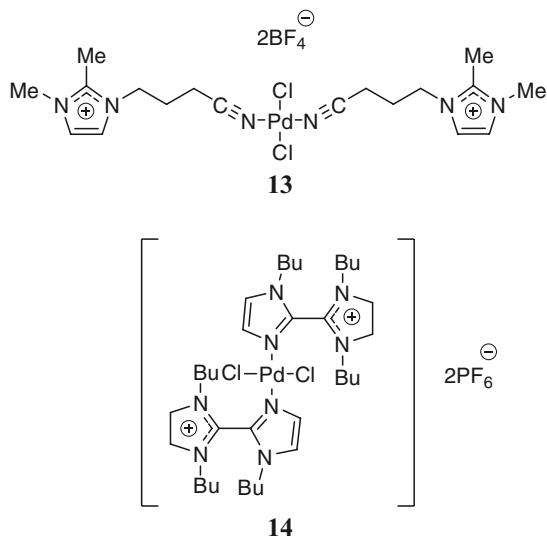
Fig. 11 Formation of imidazolium-based ionic liquids containing palladium
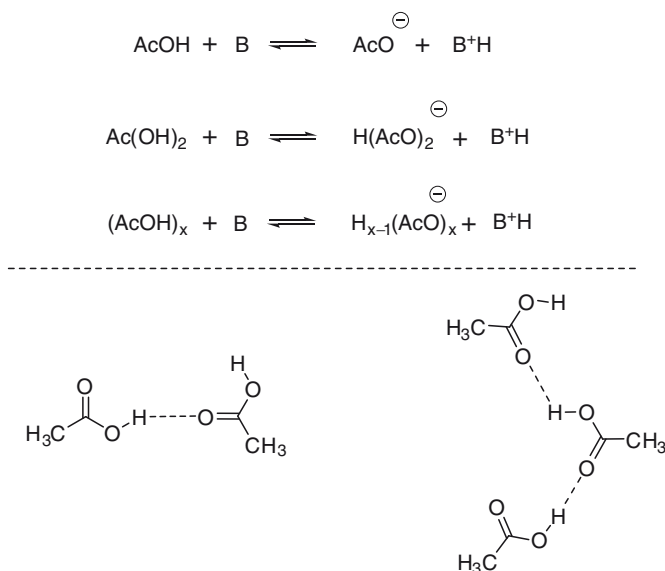
Fig. 12 Pt containing ionic liquids

Several transition metal based ionic liquids based on Nb [73], Ta [73], Ag [74], Au [75], Mn and Co [76], Rh [76] have been prepared by similar methods.

Other metal based ionic liquids have included *p*-block metal based ionic liquid systems based on Sn [77], In [78], Bi [76], Pb [79] have been prepared. In 1986,

Uranium-based salt of the type $[C_2mim]_2[UCl_6]$ was obtained from the reaction of $[C_2mim]Cl$ with UCl_4 [80]. Recently, synthesis of low-melting lanthanide-containing ionic liquids of the type $[C_4mim]_{x-3}[Ln(NCS)_x(H_2O)_y]$ ($x = 6–8$, $y = 0–2$, Ln = Y, La, Pr, Nd, Sm, Eu, Gd, Tb, Ho, Er, and Yb) have been reported [81].

2.4.2 Functionalized Ionic Liquids

During the last 8 years [82, 83], various types of functionalized ionic liquids (Fig. 13) expressly categorized as being "task-specific" ionic liquids have been designed and synthesized for specific purposes such as catalysis, organic synthesis, separation of specific materials, as well as for the construction of nanostructure materials and ion conductive materials, etc. The salts are defined as functionalized ionic liquids when they are ionic liquids in which a functional group is covalently tethered to (1) the cation, (2) the anion, or (3) a zwitterionic form of the salt. It is typically the cation that bears the reactive moiety. In fact, instances in which the anion comprises the active constituent are few.

Until recently, the method used to incorporate the functionality into the ionic liquid was almost always displacement of the halide from an organic halide containing the functional group by a parent imidazole, phosphine, etc.:

$$\tag{8}$$
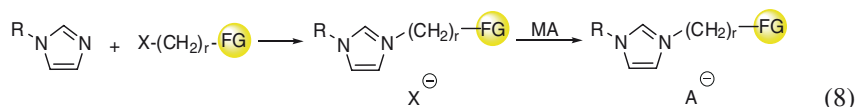
In their pioneering work Davis and Rogers [84, 85] have reported the synthesis of imidazolium salts with urea, thiourea and thioether groups in one of the *N*-alkyl substituents (Fig. 14).

Recently, novel sulphonyl-functionalized ionic liquids with SO_3H and SO_2Cl groups have been designed, synthesized and characterized. First reported were Bronsted-acidic functionalized ionic liquids bearing an alkane sulphonic acid group in an imidazole or triphenylphosphine cation (Fig. 15a) [86] or in a pyridinium cation (Fig. 15b) [87].
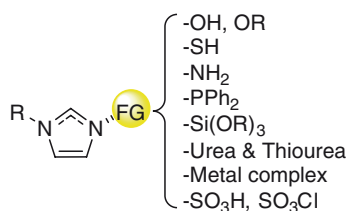
Fig. 13 Types of functionalised ionic liquids
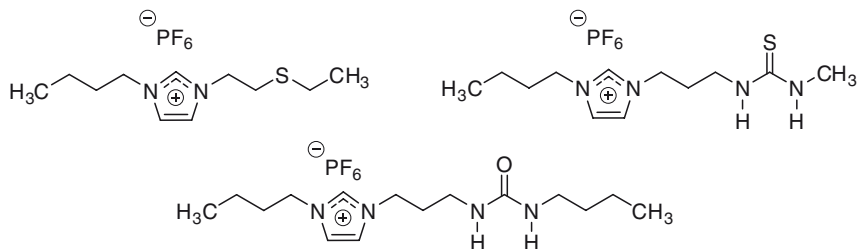
Fig. 14 Imidazolium salts with urea, thiourea and thioether groups
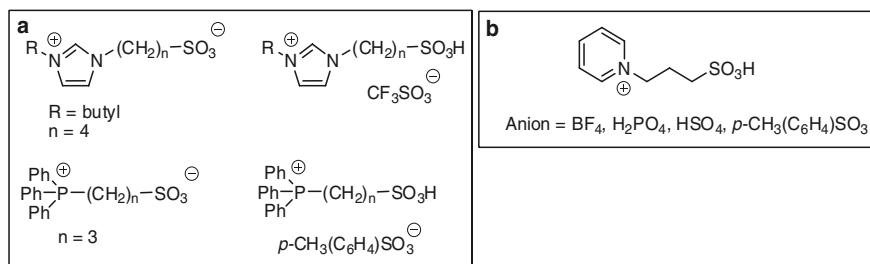
Fig. 15 Synthesis of sulphonate functionalized ionic liquids

Functionalized ionic liquids possessing two Bronsted acid sites with COOH, HSO_4 or H_2PO_4 groups were reported by Dan [40] in 2007:

$$(9)$$
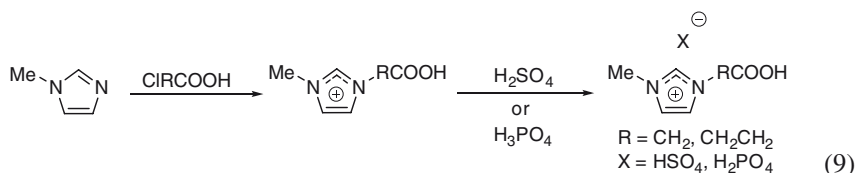
Recently, ionic liquids with amino acids as anions were synthesized by neutralization between $[C_2mim][OH]$ and amino acids [88]. Tetrabutylphosphonium amino acids $[P(C_4)_4][AA]$ were synthesized by the reaction of tetrabutylphosphonium hydroxide $[P(C_4)_4][OH]$ with amino acids, including glycine, L-alanine, L-β-alanine, L-serine and L-lysine [89]. The esters or amide derivatives of bromoacetic acid were either commercially available or formed in one step via the reaction of bromoacetyl bromide with the appropriate alcohol or amine [90–92]. An advantage of this route is that a wide range of ester and amide side chains can be prepared easily. For ionic liquids with anions other than bromide, a metathesis reaction was employed to introduce the counter ion of choice. Additionally, functionalized ionic liquids with electrophilic alkene-type appendages were synthesized.

Cations bearing nitrile functional groups which were used as ligands for organometallic chemistry, have been synthesized by several groups (Scheme 14) [90].

Phosphines bearing imidazolyl moieties have attracted substantial interest because of their potential to bind soft and hard transition metals via phosphorus or nitrogen. There are only a very few reports on phosphine functionalized ionic liquids (Fig. 16) – (1) Type 1: 2-imidazolium phosphines (D$^+$X$^-$) [91], (2) Type 2: guanidininium phosphines (C$^+$X$^-$) [92], and (3) Type 3: 3-imidazolium phosphines (B$^+$X$^-$) [91].

Afonso et al. [93] reported the synthesis of functionalized ionic liquids, based on imidazolium cations that contains ether or alcohol as functional groups. Alkylation of methylimidazole with the appropriate alkyl halide is followed by halogen exchange with slight excess KPF$_6$, NaBF$_4$ or NaCF$_3$CO$_2$ in order to reduce the amount of remaining halogen content.

n = 1; R^1 = Me; R^2 = H; A = PF$_6$, BF$_4$
n = 2; R^1 = Me; R^2 = H; A = PF$_6$, BF$_4$
n = 3; R^1 = Me; R^2 = H; A = PF$_6$, BF$_4$, NTf$_2$, N(CN)$_2$
n = 3; R^1 = C$_3$H$_8$CN; A = NTf$_2$, N(CN)$_2$
n = 3; R^1 = Me, R^2 = Me; BF$_4$, PF$_6$
n = 4; R^1 = C$_4$H$_8$CN; A = PF$_6$, BF$_4$, NTf$_2$, N(CN)$_2$

X = BF$_4$, PF$_6$, NTf$_2$
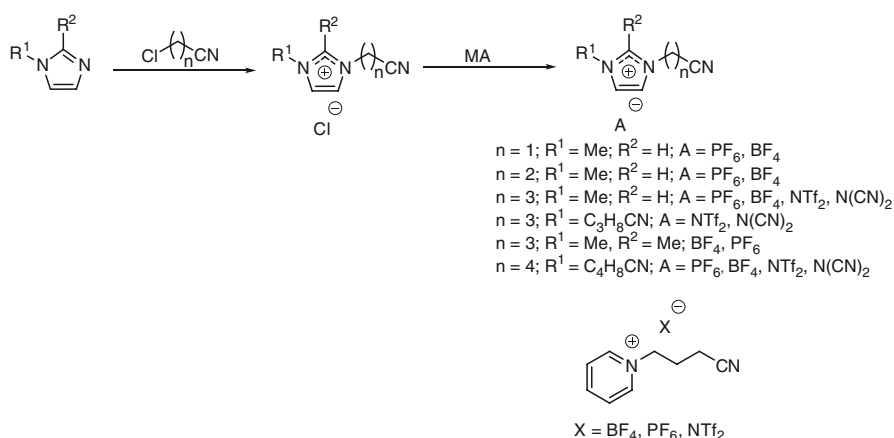
Scheme 14 Nitrile functionalized ionic liquids

R^1, R^2 = H, alkyl
X = Cl, BF$_4$, PF$_6$

R = Ph; R^2 = H, alkyl
X = BF$_4$, Cl, PF$_6$, R$_2$PO$_2$

D$^+$X$^-$ B$^+$X$^-$ C$^+$X$^-$
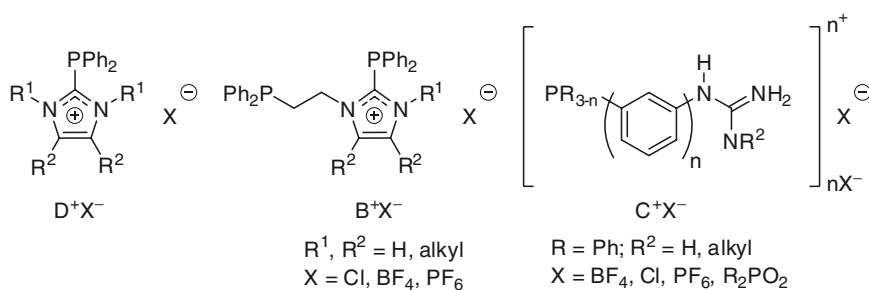
Fig. 16 Phosphine functionalized ionic liquids

2.4.2.1   Miscellaneous

Synthesis of functionalized hydrophobic ionic liquids bearing the 2-hydroxyben-zylamine substructure, and their application in partitioning of metal ions from water have been described (Scheme 15) [94].

(S)-Proline-modified functionalized chiral ionic liquid is useful as a recoverable catalyst for direct asymmetric reactions [95]:

$$(10)$$
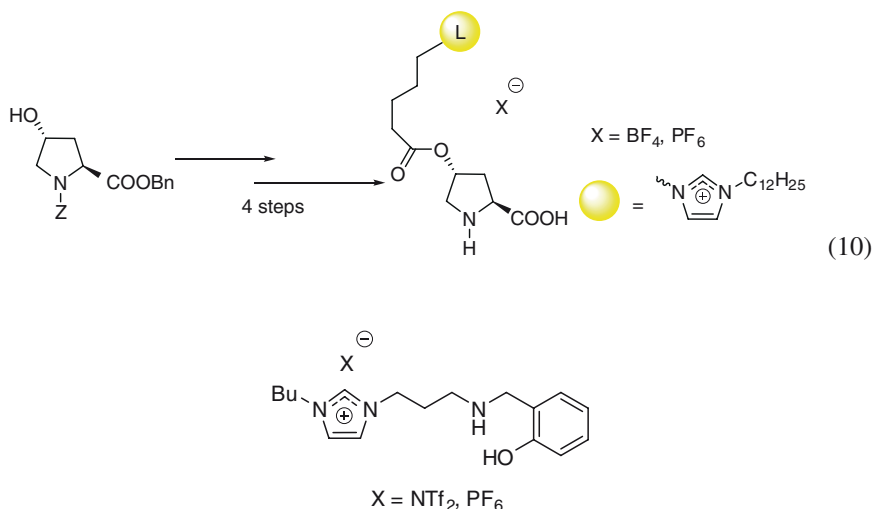
Scheme 15 Functionalized hydrophobic ionic liquids

Bazureau et al. reported the synthesis of novel ester and carbonyl groups appended functionalized grafted ionic liquid phases. Two synthetic strategies were developed for the preparation of the ionic liquid phases (Scheme 16) [96].
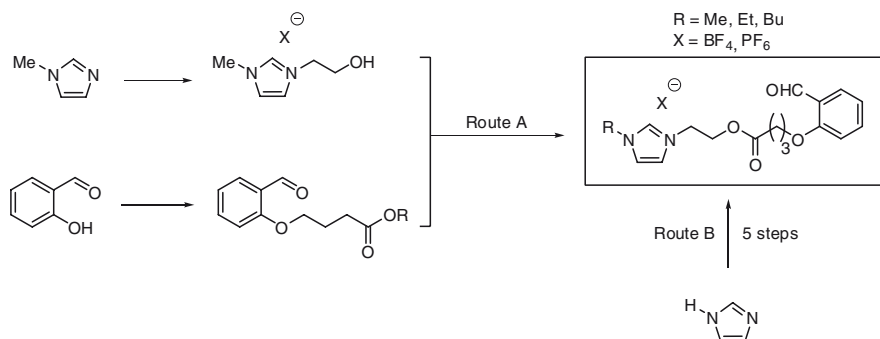
Scheme 16 Ester and carbonyl groups appended functionalized ionic liquid phases

Bazureau et al. reported the synthesis of poly(ethyleneglycol) functionalized -ionic liquid phases as functionalized ionic liquids which are promising tools for synthetic applications in ionic-phase combinatorial chemistry [97]. Moreover, several research groups have described ionic liquids with imidazolium cations carrying amino functionality. Davis et al. [98] reported for the first time a functionalized ionic liquid with NH_2 group, *n*-propylamine-3-butylimidazolium tetrafluoroborate **18**, for capturing CO_2 (Scheme 17).

2.4.2.2 Functional Group Covalently Tethered to the Anion

Electroactive, functionalized ionic liquid, tetraalkylphosphonium polyoxometalates were synthesized by the substitution of sodium tungstate with tetaralkylphosphoni-umbromide $[(C_6H_{13})_3P(C_{14}H_{29})]_2W_6O_{19}$ [99].

2.4.2.3 Zwitterionic-Type

Ohno et al. [100] reported that the synthesis of zwitterionic-type molten salts and their polymers (Scheme 18). Since zwitterionic-type salts have both cation and anion in intramolecular form, these ions cannot migrate with the potential gradient.
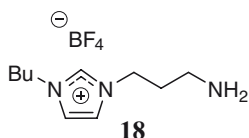
Scheme 17 Functionalized ionic liquids with NH_2 group
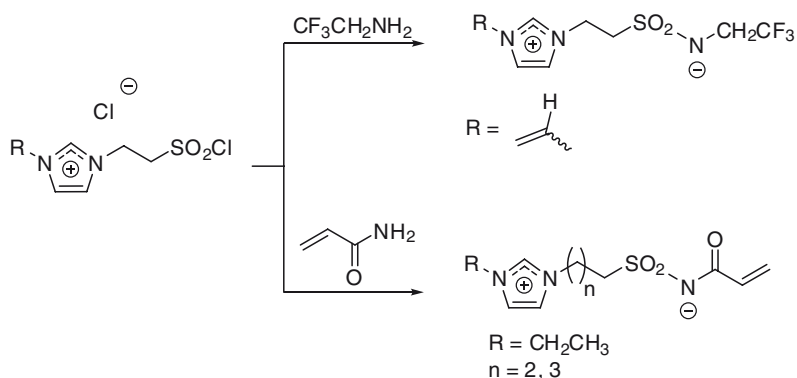
Scheme 18 Zwitterionic-type malten salts and their polymers
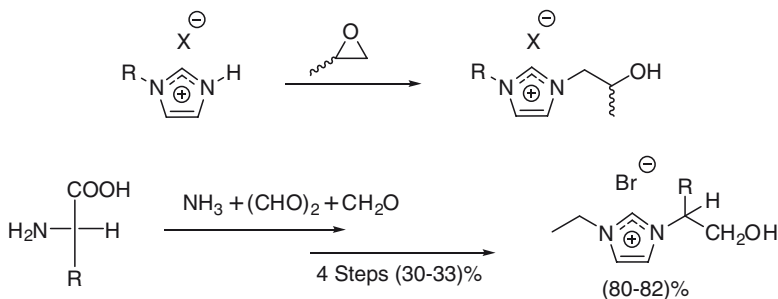
Scheme 19 Alcohol substituted ionic liquids

At least two alcohol-group specific synthetic approaches have recently been disclosed (Scheme 19). In the first, Holbrey and Rogers [101] describe a simple, high-yielding one pot method for the synthesis of alcohol-appended imidazolium functionalized ionic liquid. In the reaction, a pre-formed imidazolium-H salt of the functionalized ionic liquid anion is reacted with an epoxide, the latter ring opening to the alcohol without further alcohol-epoxide oligomerization. The second method built up the imidazolium ring up from a four-component condensation of amino acids, ammonia, formaldehyde and glyoxal [102]. The latter approach, while multi-step and lower yielding, produced functionalized ionic liquids that were also optically active.

Recently, Wasserscheid and co-workers [103] introduced a complementary method for functionalized ionic liquid synthesis (11). In a one-pot, two step synthesis, the protonation of an imidazolium or pyridinium cation followed by a Michael-type addition to methyl vinyl ketone was reported. The only drawback is the limited thermal stability of the cations, which at moderately elevated temperatures undergo a retro-Michael reaction:

$X = OTos, OMes, MeSO_3, BF_4$

○ = Imidazole, Pyridine, etc.

(11)
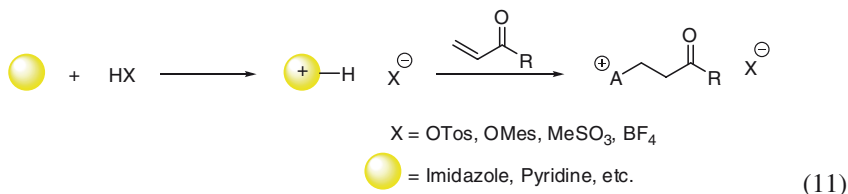
2.4.3 Microwave Synthesis

The preparation of 1,3-dialkylimidazolium halides via the classical heating method in refluxing solvents requires several hours to afford reasonable yields and also uses a large excess of alkylhalides/organic solvents as the reaction medium. The shortened reaction time, cleaner work-up procedure and unique transformations achieved

by microwave synthesis of ionic liquids can be impressive. Microwave synthesis can be classified into three groups: (1) the quaternisation step; (2) combined quaternisation and metathesis steps; (3) other routes.

2.4.3.1   The Quaternisation Step

The first report on the microwave-assisted synthesis of imidazolium-based ionic liquids appeared in 2000 [104]. Westman described a process of reacting *N*-methyl imidazole with an alkyl halide in ethyl acetate. Later Varma et al. [105, 106] reported a microwave assisted preparation of series of ambient temperature [C$_n$mim]-type ionic liquids by the reaction of 1-methylimidazole with alkyl halides/terminal dihalides under solvent-free conditions using a microwave oven as an irradiating source. The equipment used was a common household microwave oven equipped with inverter technology. The preparation of ionic liquids has also been carried out by irradiating equimolar amounts of *N*-methyl imidazole and an alkylating agent in open containers. In some cases the amount of alkylating agent had to be increased to two equivalents:

$$\text{Yield\% = 50-97\%}$$

R = Butyl-Octyl
X = Cl, Br, I   (12)
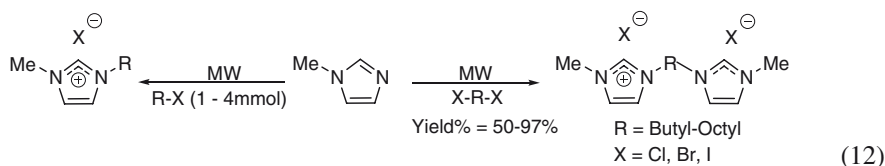
Thanh et al. [107] reported the synthesis of the chiral ionic liquids based on ephedrinium cation under solvent-free conditions and microwave activation (13). A series of different alkyl chain lengths was tested:

R = C$_4$H$_9$, C$_8$H$_{17}$, C$_{10}$H$_{21}$, C$_{16}$H$_{33}$ (13)
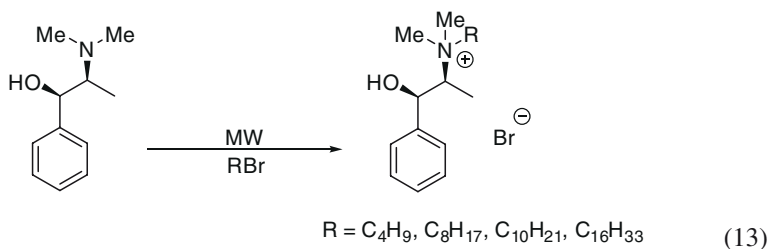
In an attempt to achieve solvent free preparation of ionic liquids, others have reported an improved approach whereby the reaction temperature was moderated by placement of the reaction vessel in a water bath. For example, Chan et al. [108] attempted to moderate the heat of the quaternisation reaction and thereby large scale preparation of imidazolium and pyridinium-based ionic liquids. Water moderation was successfully applied to avoid runaway reactions in the large-scale preparation of a number of ionic liquid precursors under solventless conditions using microwave irradiation:

$$\text{Me}-\text{N}\overset{\frown}{\underset{\smile}{}}\text{N} \xrightarrow[\text{R-X}]{\text{MW}} \text{Me}-\text{N}\overset{\oplus}{\underset{\smile}{}}\text{N}-\text{R} \quad X^{\ominus}$$

R = propyl, butyl, hexyl, octyl (82-100)%

$$\text{Pyridine} \xrightarrow[\text{R-X}]{\text{MW}} X^{\ominus}$$

R = butyl, hexyl, octyl (93-100)% (14)
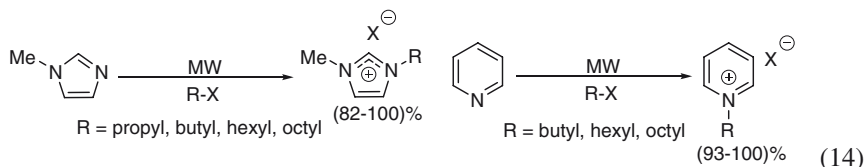
Rebeiro and later Seddon described an improved methodology to synthesize ionic liquids in an efficient way by carrying out the alkylation reaction in sealed vessels. Rebeiro et al. [109] reported a simple and quick method of preparation of alkyl pyridinium and 1-alkyl-3-methyl imidazolium salts on a large scale in a closed vessel under microwave irradiation in a microwave digestor:

$$\text{Me}-\text{N}\overset{\frown}{\underset{\smile}{}}\text{N} \xrightarrow[\text{R-X}]{\text{MW}} \text{Me}-\text{N}\overset{\oplus}{\underset{\smile}{}}\text{N}-\text{R} \quad X^{\ominus}$$

R = propyl, butyl
Temp: (85-150) °C
X = Cl, Br
(40-99)%

$$R^1 \xrightarrow[\substack{\text{R-X} \\ X = \text{Cl, Br}}]{\text{MW}} R^1 \quad X^{\ominus}$$

Pyridine (86-98)%
Temp: (120-200) °C
R = propyl-hexyl

Lutidine (10-83)%
Temp: (200-230) °C
R = propyl,butyl (15)
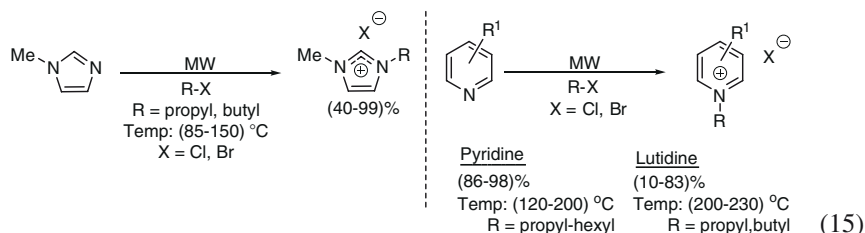
Seddon [110] described a process using a commercial multimode microwave reactor and apart from the classical [$C_n$mim]-derivatives his report also describes the preparation of *N*-alkylpyridinium-, *N*-alkyl-3-methylthiazolium- and *N*-alkyl-2-methyl-pyrazolium-based ionic liquids (Scheme 19).

2.4.3.2 Combined Quaternisation and Metathesis Steps

Recently, Cravotto and co-workers [111] demonstrated an efficient one-pot synthesis of second-generation ionic liquids, combining in one step the Menshutkin reaction and anion metathesis:

$$\text{Me}-\text{N}\overset{\frown}{\underset{\smile}{}}\text{N} \quad Cl^{\ominus} \xrightarrow[\substack{\text{CH}_2(\text{CH}_2)_6\text{CH}_2\text{Br} \\ \text{KPF}_6}]{\text{MW}} \text{Me}-\text{N}\overset{\oplus}{\underset{\smile}{}}\text{N}-\text{R} \quad PF_6^{\ominus} + \text{KBr}$$

(89-94)%

R = C_8H_{17} (16)
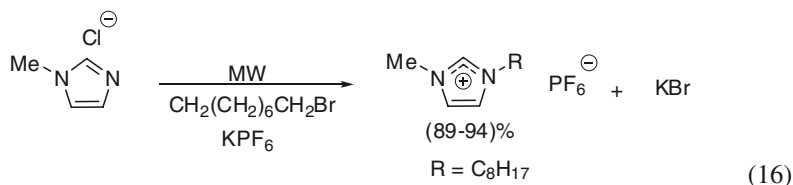
2.4.3.3 Other Routes

Microwave irradiation has also been used to speed up the synthesis of imidazolium-based ionic liquids bearing the tetrachloroaluminate counter ion [112]:

$$(17)$$
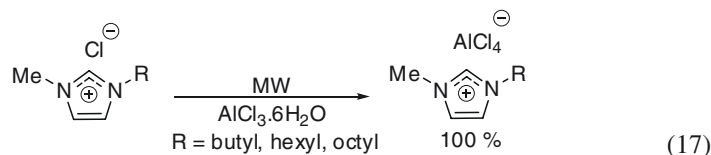
Equimolar amounts of GaCl$_3$ or InCl$_3$ were mixed with 1-butyl-3-methylimidazolium chloride, followed by MW irradiation for 30 s affording pure ionic liquid [113]:

$$(18)$$
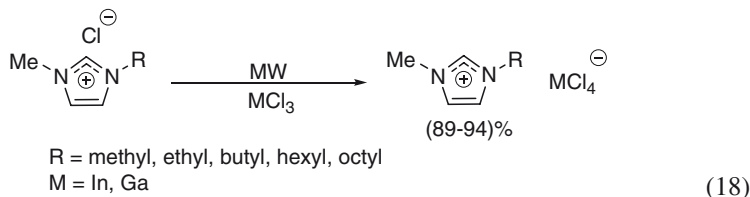
Quite recently [114], the amino acid ionic liquids were synthesized using the one-step microwave synthesis method by using 1-Glu (>99%), 42% HBF$_4$, 95–98% H$_2$SO$_4$, 65–68% HNO$_3$ acid and 37% HCl:

$$(19)$$
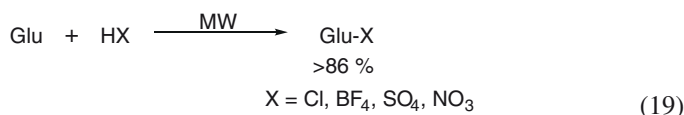
3 Purification

3.1 Common IL Impurities

The most abundant impurity found in ILs is water. Many IL applications are not affected (in fact they are sometimes enhanced) by the presence of water and so excessive drying is not always necessary. However, testing in water sensitive applications and fundamental characterization of new ILs should only be performed on very dry samples. The low volatility of most ILs allows for the removal of water by placing the wet IL under vacuum for several hours. Note however that this procedure is not appropriate for many protic ionic liquids since in those cases the conjugate acid and base species may also be volatile and loss of one of the species may occur. There can also be an issue with rigorous vacuum drying in those cases where the anion is a moderately strong base species (e.g. acetate) since small amounts of the conjugate acid can form from water and then be evaporated, leaving a hydroxide impurity. It is important to realize that vacuum drying involves mass transport of the water through the bulk of the material to the surface before it can be evaporated. Sample mass and surface area are therefore significant parameters; stirring may

also be required. It is strongly recommended that reporting of procedural details include information of sample volume and surface area in order that ensure reproducibility. It is also important to understand that during the process of evaporation of the water, or any other volatile material, the manifold pressure is often lower than the pressure at the material surface. In order to determine whether the sample has fully equilibrated with the applied vacuum one common technique involves isolating the manifold from the pump and monitoring the pressure in the manifold for approximately 20 min. When the sample is opened to the vacuum any pressure rise greater than the leak rate of the manifold indicates continued volatilisation from the sample. A typical procedure involves stirring the IL under vacuum on a standard Schlenk-line until a vacuum of approximately 0.4 mbar is maintained for 3 h. The time required for this process can be very short (a few hours) or very long (several weeks).

ILs can incorporate water very strongly and in some cases vacuum conditions alone do not reduce water to a suitable level within a suitable time-frame. The sample can be heated while under vacuum, but caution should be used as heat can accelerate IL decomposition. Alternatives include vacuum azeotropic distillation with solvents such as toluene or dissolving the IL in a low boiling solvent and placing over dry molecular sieves. Chemical drying agents (e.g. potassium metal, magnesium chloride, magnesium sulphate) can be very effective for the removal of water. However, consideration should be given to the impurities these additives will likely leave behind in the IL. If none of the above methods for drying ILs are appropriate, water should be avoided altogether, i.e. the IL can be synthesized in a dry atmosphere using dried reagents and reaction solvents.

Other common IL impurities are unreacted organic starting materials and residual organic reaction solvents. As with the removal of water, vacuum induced evaporation is usually very effective. If not, the IL can be washed with a low boiling, immiscible organic solvent such as diethyl ether, which can subsequently be removed under vacuum.

Suspended particles are a commonly overlooked impurity in ILs. They originate from many sources including:

- Metathesis byproducts (especially silver halide salts which often precipitate as very small particles)
- Sorbents
- Molecular sieves
- Chemical drying agents

Particles have been shown to affect several fundamental IL properties [115] and therefore their presence should be carefully considered. To the knowledge of these authors no methods have been shown to completely remove particulate contamination from ILs, but filtration through a 200 nm PTFE syringe filter can reduce their levels to <10 ppm [115].

Halide and alkali metal salts originating as metathesis by products can remain dissolved in ILs. For hydrophobic ILs simply washing with water until no salt is detected in the washings is very effective. With hydrophilic ILs removal of these salts can be more complex. The IL can be dissolved in a water immiscible solvent

such as dichloromethane and washed as above. However, this usually leads to a significant loss in IL yield (the loss in yield can be reduced by using very cold water). Passing the IL through silica gel has also been recommended as a method to reduce alkali metal halide salts [116]. If an IL is synthesized by precipitating an alkali metal halide salt from an organic solvent such as acetone, acetonitrile, methanol, etc. these solvents should be extensively dried. Even small traces of water can greatly increase the solubility of these salts in the IL.

3.2 Sorbents

The most common method for purifying ILs involves the use of sorbents such as activated carbon, silica and alumina. These sorbents are especially useful for the removal of coloured impurities. Many different methods for the use of sorbents have appeared in the literature, below are three popular examples:

- Passerini and co-workers purified $[C_4mpyr][NTF_2]$ by stirring over carbon at 70 °C, then stirring over alumna [117]
- Seddon and co-workers used a column filled with carbon and silica to remove coloured impurities from a range of ILs with $[NTf_2]^-$, $[BF_4]^-$, $[PF_6]^-$ and $[OTf]^-$ anions [118]
- Davis et al. recommend stirring over carbon then passing down a short alumina column [119]

To reduce viscosity, most ILs are diluted with an organic solvent before sorbent exposure.

It has always been assumed that sorbents are easily removed from the ILs after exposure. However recently evidence has arisen that these sorbents remain in the "purified" IL as nanoparticulate contamination [115, 120, 121]. Microfiltration (200 nm) can reduce the contamination to very low levels (<10 ppm) although even at this low level there is still an impact on the physicochemical properties of the IL. The crystallization kinetics [115], spectroscopic [115] and electrochemical [120] properties of the ILs have all shown changes after exposure to sorbents. There are many IL applications where sorbent contamination is not likely to be of concern. However, their presence or absence will affect how an IL behaves. It is therefore essential that all data presented on sorbent-exposed ILs is accompanied by a thorough explanation on the use and subsequent removal of the sorbents.

3.3 Distillation

Distillation is one of the most popular techniques employed for the purification and separation of molecular liquids. It had always been assumed that this technique was not available for the purification of ILs due to their apparent non-volatility. In 2005,

Kreher et al. drew attention to the potential of *N,N*-dialkyl-ammonium *N',N'*-dialkylcarbamates for use as distillable ionic media [122]. However, this class of ILs is generally considered to be a special case since the IL dissociates during distillation to give the respective amine and carbon dioxide. It is also widely recognized that many *protic* ionic liquids are distillable under easily accessible conditions [123].

Rebelo et al. reported on a method to predict the normal boiling points of ILs [124] and the results of these predictions suggested that many *aprotic* ILs may be distillable and attempts were made to distill $[C_{10}mim][NTf_2]$ and $[C_{12}mim][NTf_2]$. Small droplets of undecomposed IL formed on the upper walls of the distillation flask and were subsequently characterized as pure IL. More recently [125] many ILs have been distilled without significant decomposition of the residue or distillate. The range of successfully distilled ILs included salts of the $[C_nmim]^+$, $[C_nmpyr]^+$, $[C_ndbu]^+$, $[NTf_2]^-$, $[OTf]^-$ and $[PF_6]^-$ ions. It should be noted that many ILs decomposed under the distillation conditions used including salts of tetraalkylammonium, tetraalkylphosphonium, cholinium, halide, sulphate, carboxylate and triflate ions.

The ILs were typically distilled at pressures of 0.001–5.0 mbar and temperatures of 200–300 °C. Reduced pressure was found to be essential since distillations performed close to ambient pressure led to IL decomposition. Importantly, this work also showed the possibility for separation of ILs by distillation. Distillate from IL mixtures showed a higher concentration of one IL over the other.

The nature of the vaporized ILs was a topic of some controversy until a follow up study was published [126]. Fourier transform ion cyclotron resonance mass spectrometry (FTICR-MS) was used at distillation conditions (4.0×10^{-6}–1.3×10^{-5} mbar, > 200 °C). Aprotic IL vapors were found to be made up of neutral ion pairs, not free ions or clusters (neutral or ionic). It was also confirmed that protic IL vapors consisted of neutral molecules resulting from cation to anion proton transfer. Several studies have suggested that IL volatility is likely related to the extent of ion pairing present in the liquid phase [123, 127].

The studies described here show that distillation is a viable option for the ultrapurification of many ILs. However, this technique can be very time consuming and is not yet practical for the large-scale purification of ILs.

3.4   Zone Melting

Zone melting is a technique that has been used for the purification of many materials including metals [128], molecular liquids [129] and gases [130]. In 2005 Winterton and co-workers [131] reported the first use of this technique for the purification of ILs. Zone melting separates IL components from impurities by exploiting the differences in their molecular shape. The IL is cooled inside a sealed vessel to form a long column of frozen IL. A mobile energy source (e.g. an IR Laser) is then used to melt a small region of the solid and moved so that the liquid zone travels slowly along the frozen column. Because most impurities have a different molecular shape to the IL

they do not fit neatly into the crystal lattice of the solid IL (do not form solid solutions with the IL) and therefore tend to remain within the liquid zone. As the liquid zone is moved through the crystalline salt it picks up more impurities and leaves a wake of purified crystalline material. Usually several melting/crystallization scans are used to produce high purity ILs. Zone melting has been used within capillary tubes to grow good quality single crystals for diffraction, e.g.

- $[C_2mim][BF_4]$, $[C_4mim][PF_6]$, $[C_4mim][OTf]$, $[C_4mim][NTf_2]$, $[C_6mpyr][NTf_2]$ [131]
- $[C_2mim][OTf]$, $[C_2mim][NTf_2]$ [132]

  or on larger scales for bulk IL purification achieving purities of ≥ 99.9%, e.g.
- $[C_2mim][Cl]$, $[C_2mim][Br]$ [133]

Special techniques must be used to avoid glass formation [131] and zone melting usually results in a sizable drop in yield. If reliable methods can be developed to produce a small, completely melted zone within the frozen IL, zone melting represents one of the most promising techniques being developed for the purification of ILs.

3.5   Clean Synthesis

The inherent properties of ILs can make their post-synthetic purification very difficult. For this reason many researchers [134] have adopted an approach whereby the ILs are synthesized as cleanly as possible, in order to minimise impurities from either starting materials or unwanted side reactions. For ILs containing a quaternary nitrogen many (especially coloured) impurities are thought to arise from by-products of the quaternisation process. Several simple precautions can be taken to minimize these impurities:

- Exposure to oxygen should be minimized and therefore it is often recommended [119] that starting materials are degassed and quaternisation is performed in a sealed vessel or under an inert atmosphere.
- The presence of trace acetone has been shown [119] to lead to more highly coloured quaternisation products and should therefore be completely excluded.
- The quaternisation reaction temperature should be kept at a minimum to reduce unwanted side reactions. For reactions using halide-based reagents the following temperatures are a general guide, chloride salts <80 °C, bromide salts <40 °C, and iodide salts <0 °C. It should be noted that these temperatures will not be appropriate for all reactions. It is the recommendation of these authors that novel quaternisation reactions are carried out in an ice bath and allowed to slowly warm while monitoring the reaction progress in order to determine the minimum temperature required. While reactions carried out at lower temperatures will require longer reaction times the products obtained should be of better quality.
- Quaternisation reactions are usually exothermic and it is therefore difficult to avoid local hotspots within the reaction mixture. For this reason if highly transparent/pure ILs are required, small scale (<0.3 mol) reactions are recommended [121].

If the above precautions are insufficient to produce the purity required, the starting materials required for the quaternisation reaction should be purified by distillation and/or the methods of purification outlined in "Purification of Laboratory Chemicals" by Armarego and Chai [135]. It should be noted that the starting materials often degrade over time and therefore these purification techniques should be employed immediately before the quaternisation reaction is undertaken.

For quaternisation products that are IL starting materials rather than ILs themselves, traditional purification techniques such as, distillation, recrystallisation, immiscible solvent washing and stirring over activated carbon can be used. These traditional techniques are often so effective that the previously mentioned precautions are not necessary.

While this section has focussed on quaternisation reactions, the basic principles of starting material purification and mild reaction conditions are applicable to all IL synthesis.

3.6 Phosphonium ILs

Phosphonium ILs are considered separately here as they often contain impurities not found in other ILs. These impurities are usually contained within the commercially available phosphonium chlorides which are used as ILs in their own right or as starting materials to produce subsequent ILs. Ramnial et al. [136] presented a study whereby these impurities were identified and a method for their removal was developed. Commercially available phosphonium chlorides were found to contain traces of:

- Phosphines
- Hydrochloric acid
- Water
- Phosphine oxides
- Isobutylnitrile

To remove these impurities the phosphonium chlorides were washed with aqueous sodium bicarbonate; care should be taken during this step as the sodium bicarbonate often caused excessive foaming. Next the ILs were thoroughly washed with water and extracted using hexanes. The hexanes solution was passed down a short silica column and dried by azeotropic distillation with toluene followed by treatment under vacuum.

3.7 Characterization

Because impurities can have a profound impact on subsequent IL applications [37], all data reported involving ILs should be accompanied by an analysis report on the presence (or absence) of common IL impurities. At least one technique should be used to

confirm the structure of the IL. Mass spectrometry, nuclear magnetic resonance (NMR) spectrometry, elemental analysis and X-ray crystallography can all be useful techniques for this purpose. However, many IL impurities cannot be directly quantified using these techniques and so it should be remembered that these techniques can only be used to confirm IL structure and should not be used as evidence of IL purity.

For example, in an IL contaminated with significant quantities of lithium chloride, neither lithium or chloride ions will appear in standard mass spectrometry because of their small masses, they may not significantly alter the C, H and N percentages in elemental analysis, and they are not detectable in standard ^1H and ^{13}C NMR. The presence of lithium chloride will likely prevent the growth of suitable crystals for diffraction; nonetheless, obtaining a single IL crystal suitable for analysis does not rule out the presence of lithium chloride in the bulk IL. Therefore a crystal structure should not be considered evidence of bulk purity. Thus the researcher must consider all possible sources of contamination and systematically determine specific impurities using techniques appropriate to the trace level involved.

There are four main categories of common IL impurities; water, organics (from unreacted starting materials or residual reaction solvents), halides and metals.

Water content can be crudely assessed using ^1H NMR or infra-red spectroscopy but at low levels (<1,000 ppm) must be accurately quantified using a Karl–Fischer titration.

Organic reaction solvents or unreacted starting materials can be detected by ^1H NMR for quantities greater than 1 mol%. Smaller quantities can be assessed by specific detection as described in texts such as "Vogel's textbook of quantitative chemical analysis" [137]. A useful example of specific detection involves detecting unreacted 1-methylimidazole (a common IL starting material that is difficult to remove by evaporation) [138]. Copper(II) chloride is added to the IL to form a coloured complex with 1-methylimidazole, which can be detected at high levels visually, or more accurately quantified using atomic absorption spectroscopy.

Halide impurities can be assessed using many techniques with varying degrees of accuracy. Techniques include:

- ^{19}F, ^{35}Cl NMR (>1 mol%)
- Titration with silver nitrate; monitored visually for qualitative analysis or using the Volhard procedure (>10 ppm)
- Ion selective electrodes (>100 ppm)
- Ion chromatography (>10 ppm)
- Inductively coupled plasma-mass spectrometry (>10 ppb)

In our own laboratories ion selective electrodes and ion chromatography are routinely used for halide analysis.

Metallic impurities are usually present as one of two forms; unreacted metallic starting material salts or as halide salts from metathesis by-products. Direct metal analysis is not always performed; instead the counterions from metathesis by-products or halide salts are analysed and if their levels are sufficiently low it is assumed the metal content is also sufficiently low. For metals present in other forms or where the counter ion is difficult to analyse, metal content can be assessed

directly using atomic absorption spectroscopy (available for most metals) or ion selective electrodes (available for Na^+, K^+, Ag^+, Ca^{2+}, Mg^{2+}, Cd^{2+}, Cu^{2+}, and Pb^{2+}).

It was not intended that this section exhaustively cover all possible IL impurities, instead methods for analysis of common IL impurities were suggested. As mentioned previously individual ILs should be assessed for all possible sources of contamination and texts such as "Vogel's Textbook of Quantitative Chemical Analysis" by Mendham et al. [137] should be consulted for methods to quantify impurities not covered here.

4 Conclusions

As has been stated by a number of workers the family of ionic liquids probably includes more than 10^6 compounds. The synthetic strategies available developed to prepare these compounds will continue to expand as long as there are applications demanding greater structural variety.

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