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Convenient synthesis of various ionic liquids from onium hydroxides and ammonium salts

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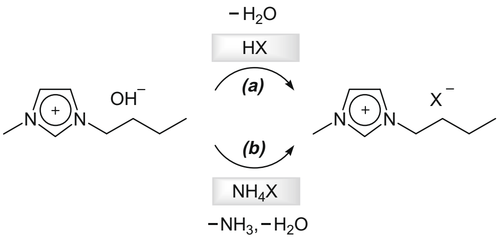
ABSTRACT

Hydroxide ionic liquids, such as 1-alkyl-3-methylimidazolium hydroxides, undergo smooth anion metathesis with ammonium salts to produce a variety of ionic liquids in excellent yields. It is a practical supplement of traditional neutralization method due to the broader range of starting materials containing desired anions.

In the past few years, the use of room temperature ionic liquids as attractive solvents has blossomed in organic transformations due to their unique properties (non-volatility, non-flammability, reasonable stability, and excellent dissolving capacity) and the potential in designing task-specific ionic liquids by the employment of functional anions or cations.[1] More recently, ionic liquids were also found to be efficient solvents in material chemistry.[2] Despite the significant developments in the utility of ionic liquids, they are still expensive solvents for many of the chemists. In order to facilitate the general acceptance of ionic liquids, cost and availability issues are necessary to be addressed. Ionic liquids are frequently prepared by ion-exchange (metathesis) method.[3] This procedure involves two steps, namely, quaternization[4] and anion metathesis. Anion metathesis is performed by treating quaternary ammonium halides with the salts containing desired anions in large amounts of organic solvents such as acetone,[5] methanol,[6] and acetonitrile.[7] Generally, however, the metathesis is exceedingly slow (e.g., 72 h[5c]). Water is an appropriate solvent in the synthesis of water-immiscible ionic liquids such as [bmim][PF_6].[8] In these cases, hydrophobic ionic liquid phase can be isolated spontaneously from aqueous solution phase.

Ionic liquids with different anions can also be obtained by the neutralization of basic hydroxide ionic liquids, such as [bmim][OH], with the corresponding acid (Scheme 1, route a).[9] It is a very practical approach to halide-free ionic liquids with advantages such as high yields and rapid reactions. Unfortunately, this method has its own limitations. Some acids, such as thiocyanic acid (HSCN), are unstable under reaction conditions. On the other hand, some of the acids are highly corrosive and toxic. For example, aqueous HBF_4 and HPF_6 are dangerous and unstable acids, both liberating HF upon decomposition, and both acids must be kept at low temperature to avoid rapid decomposition. It is difficult to find 'pure' lactic acid because concentrated aqueous solutions of lactic acid (>30 wt %) contain a distribution of oligomers that arise via intermolecular esterification.[10] Thus, the development of alternative approaches to ionic liquids starting from omium hydroxides is still in demand.

To increase the utility of onium hydroxides in the synthesis of ionic liquids, we have developed a novel 'ammonia elimination' strategy using 1-alkyl-3-methylimidazolium hydroxide as versatile intermediate, and report herein our preliminary results. The salient feature of this method is the use of ammonium salts instead of free acids (Scheme 1, route b), thus avoiding the inherent limitation of



Scheme 1.

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traditional neutralization method. Firstly, many of the ammonium salts are commercially available in high purities. Secondly, most of them are safe, stable, and non-corrosive in comparison with their parent acids. During the anion metathesis between hydroxide ionic liquids and ammonium salts, NH_4OH can be removed readily by rotary evaporation under reduced pressure, with the non-volatile residue as the component of desired ionic liquids. Undoubtedly, gaseous ammonia will not contaminate the final products.

1-Alkyl-3-methylimidazolium salts are a class of commonly used ionic liquids.[11] As a starting point for the development of our methodology, the synthesis of [bmim][OH] was initially investigated. Two processes have been reported for the synthesis of hydroxide ionic liquids. In the first process, hydroxide ionic liquids were prepared from halide ionic liquid precursors by anion exchange using hydroxide-type ion exchange resin such as Amberlite IRA-400 (OH^-).[9] The ion exchange resin method routinely affords hydroxide ionic liquids that are much pure, although large amount of ion exchange resin is necessary in order to obtain halide-free products. In the second process, hydroxide ionic liquids were synthesized by direct anion exchange between halide ionic liquids and alkali hydroxide (KOH or NaOH) in appropriate organic solvents.[12] Indeed, direct anion metathesis in organic solvents is a simple procedure; however, the ionic liquid thus obtained is often contaminated by a small quantity of halides which remains from incomplete metathesis reaction.

In the present work, a hybrid two-step procedure modified from literature methods has been developed as shown in Figure 1.[13] Crude ionic liquid was prepared by a classic anion metathesis procedure (Fig. 1, a). In the literature procedure, solid potassium hydroxide was added to a solution of [bmim][Br] in dry methylene chloride and the mixture was stirred vigorously at room temperature for 10 h to give [bmim][OH].[12a] It was found in our investigation that, however, the use of methylene chloride often led to a brownish product. So we decided to screen a range of organic solvents for anion metathesis. Among them, THF was found to be a much appropriate solvent by which a colorless or yellowish crude ionic liquid could be obtained.

The presence of halide could be confirmed by adding aqueous silver nitrate into a sample solution pre-treated with HNO_3 (Fig. 1, b). To remove the halide impurities, the aqueous solution of crude [bmim][OH] was then passed through a column charged with anion-exchange resin to afford halide-free [bmim][OH] ionic liquid, which gives negative result in the silver nitrate test (Fig. 1, c). [C_5mim][OH] could also be prepared by a similar synthetic procedure. It has been reported that omium hydroxides are not particularly stable and cannot be used as concentrated aqueous solutions, but 40% aqueous solution of certain omium hydroxides is stable.[14] In our experiments, as-synthesized omium hydroxides were stored and used as 30–40 wt % aqueous solutions.

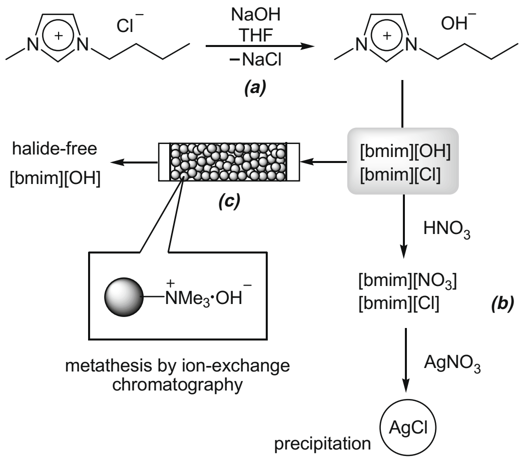
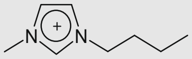
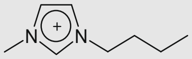
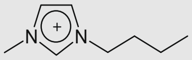
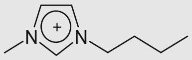
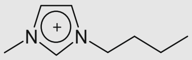
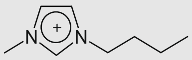
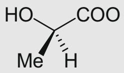
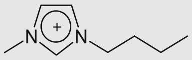
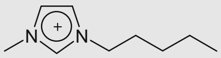


Figure 1. Synthesis of onium hydroxide.

Table 1
Synthesis of various ionic liquids from onium hydroxides and ammonium salts

Entry	Cations	Anions	Yield[a] (%)
1		BF_4	99
2		PF_6	98
3		p-TsO	99
4		MsO	99
5		PhCOO	96
6			97
7		SCN	96
8		BF_4	99

[a] Isolated yields.

With the desired precursors in hand, several anions were then introduced by ammonia elimination strategy.[15] In this study, eight ionic liquids were selected as examples to demonstrate the utility of our synthetic route (Table 1). Treatment of various ammonium salts with equimolar amount of omium hydroxides immediately resulted in ammonia evolution. The mixture was degassed and dehydrated under reduced pressure to afford desired ionic liquids. Due to the facts mentioned above, it is difficult to find ‘pure’ lactic acid in laboratories because of the presence of oligomers. However, pure ammonium lactate could be obtained readily by fed-batch fermentation of *Rhizopus oryzae* from corncob hydrolysate.[16] Seddon and co-workers have introduced the synthesis of [bmim][lactate] ionic liquid by the metathesis between sodium lactate and [bmim][Cl] in acetone.[17] In our procedure, [bmim][lactate] was obtained in 97% yield by the reaction of aqueous [bmim][OH] with ammonium L-(+)-lactate (Table 1, entry 6). Other ionic liquids (e.g., [bmim][benzoate][18] and [bmim][SCN][19]), which had been synthesized previously through traditional anion metathesis, were also prepared successfully by our method. To broaden the scope of substrates, [C_5mim][OH] has also been tested as a starting material. Aqueous solution of [C_5mim][OH] was treated with NH_4BF_4 to give ionic liquid [C_5mim][BF_4] in excellent yields (Table 1, entry 8).

Anion metathesis is an equilibrium reaction. In the cases using onium halides as starting materials, the equilibrium could be broken by the precipitation of insoluble silver halides with soluble silver salts (e.g., $AgBF_4$),[20] or by using a suitable organic co-solvent from which the formed alkali halides can be precipitated.[5] In the present method, metathesis occurred irreversibly due to the elimination of gaseous ammonia. In contrast to traditional anion metathesis, this procedure yields ionic liquids without any non-volatile impurities after the removal of ammonia and water under reduced pressure.[21]

Hydroxide ionic liquid, such as tetrabutyl phosphonium hydroxide, is now commercially available as a concentrated aqueous solution.[14] Recently, Wasserscheid’s group has revealed the production of 5% aqueous solutions of [emim]OH at the kilogram scale by electrodialysis from the non-toxic bulk ionic liquid [emim][$EtOSO_3$].[22] This environmentally benign process could be modified for the efficient and economical synthesis of various onium hydroxide intermediates. This fact implies that hydroxide ionic liquids might be a new series of readily available reagents on the catalog of chemical suppliers in the near future. Hence, ammonia elimination method described in this Letter provides an attractive and practical route to access various ionic liquids in chemical laboratories.

In summary, we have demonstrated that ammonium salts are practical alternatives to the corresponding acids for the synthesis of ionic liquids when onium hydroxides are employed as precursors. In comparison with direct neutralization method, the present approach is less eco-friendly because of the release of ammonia gas, which should be treated before final disposal. However, it is very suitable when the parent acids are unstable, dangerous, or could not be obtained in pure form. In other words, it is a valuable supplement of direct neutralization method due to the broader range of anion sources.

Acknowledgments

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13. *Preparation of aqueous [bmim]OH*: To a 500-mL Erlenmeyer flask equipped with drying tube ($CaCl_2$) were added commercially available [bmim][Cl] (white crystalline solid, 17.45 g, 100 mol), KOH (5.60 g, 100 mol), and dry THF (100 mL). The mixture was then sonicated in an ultrasonic clean bath for 2 h. On completion of the reaction, the reaction mixture was allowed to stand overnight and was filtered through a sintered funnel. The filtrate was concentrated under vacuum for 0.5 h to afford 15.85 g of crude [bmim]OH as a viscous liquid. The crude product was then diluted with 25 mL of deionized water, and was treated by passing through a column charged with Amberlite IRA-400 (OH) (type 717) anion exchange resin in order to remove residual halide (confirmed by $AgNO_3$ test after HNO_3 neutralization). The concentration of [bmim]OH was determined to be 38 wt % via acid-base titration. It is better to store this intermediate solution in a PTFE (polytetrafluoroethylene) bottle. The resin material could be recycled by washing with concentrated base.
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15. *Representative procedure for the synthesis of [bmim][lactate]*: At room temperature, 1.07 g (10 mol) of ammonium L-lactate was added slowly into an aqueous solution containing equimolar amount of [bmim]OH (4.11 g of 38 wt % solution) under vigorous stirring. Ammonia thus formed was gradually removed at room temperature using a rotary evaporator (water-circulating pump) until no ammonia evolution could be observed. The degassed solution was then dried under vacuum at 60–70 °C for 24 h to eliminate the residual water, leaving a clear, viscous ionic liquid (2.21 g, 97% yield). Structures of the resulting ionic liquids were confirmed by proton NMR and FTIR spectroscopy. *[bmim][lactate]*: FTIR (KBr): ν_{max} 3410 (OH), 1726, 1728, 1597, 1599 cm^{-1}; ^1H NMR (CD_3OD, 400 MHz): δ_H 1.01 (t, $J = 7.5$ Hz, 3H, CH_3), 1.35 (d, $J = 7.1$ Hz, 3H, Lac-β-CH_3), 1.43–1.47 (m, 2H, CH_2), 1.91–1.98 (m, 2H, CH_2), 4.01 (s, 3H, NCH_3), 4.17 (t, $J = 7.3$ Hz, 2H, NCH_2), 4.26 (q, $J = 7.1$ Hz, 1H, Lac-α-CH), 7.39 (s, 1H, imid-H), 7.48 (s, 1H, imid-H), 9.72 (s, 1H, imid-H) ppm. *[bmim][PF_6]*: FTIR (KBr): ν_{max} 3168, 3121, 2967, 2875, 1576, 1478, 851 (PF_6), 744 cm^{-1}; ^1H NMR (CD_3OD, 400 MHz): δ_H 0.91 (t, $J = 7.4$ Hz, 3H, CH_3), 1.35–1.39 (m, 2H, CH_2), 1.91–1.96 (m, 2H, CH_2), 4.10 (s, 3H, NCH_3), 4.45 (t, $J = 7.3$ Hz, 2H, NCH_2), 7.91 (s, 1H, imid-H), 8.00 (s, 1H, imid-H), 9.25 (s, 1H, imid-H) ppm. *[bmim][benzoate]*: FTIR (KBr): ν_{max} 3166, 3121, 2967, 2859, 1599, 1575, 1472 cm^{-1}; ^1H NMR (CD_3OD, 400 MHz): δ_H 0.90 (t, $J = 7.8$ Hz, 3H, CH_3), 1.01–1.16 (m, 2H, CH_2), 1.59–1.71 (m, 2H, CH_2), 3.72 (s, 3H, CH_3), 4.05 (t, $J = 8.0$ Hz, 2H, CH_2), 7.35–7.44 (m, 2H, Ph), 7.55–7.62 (m, 1H, Ph), 7.70 (s, 1H, imid-H), 7.75 (s, 1H, imid-H), 7.92-7.96 (m, 2H, Ph), 9.20 (s, 1H, imid-H) ppm. *[bmim][SCN]*: FTIR (KBr): ν_{max} 3163, 2964, 2870, 2075 (SCN), 1575, 1477 cm^{-1}; ^1H NMR (400 MHz, CD_3OD): δ_H 0.96 (t, 3H, $J = 7.4$ Hz, CH_3), 1.29–1.47 (m, 2H, CH_2), 1.76–1.95 (m, 2H, CH_2), 3.96 (s, 3H, NCH_3), 4.22 (t, 2H, $J = 7.5$ Hz, NCH_2), 7.30 (s, 1H, imid-H), 7.35 (s, 1H, imid-H), 9.23 (s, 1 H, imid-H) ppm. *[C_5mim][BF_4]*: FTIR (KBr): ν_{max} 3162, 2965, 2871, 1574, 1467, 1061 (BF_4) cm^{-1}; ^1H NMR (CD_3OD, 400 MHz): δ_H 0.92 (t, $J = 7.0$Hz, CH_2CH_3), 1.38 (4H, m, CH_2CH_2), 1.97 (m, 2H, NCH_2CH_2), 4.06 (s, 3H, NCH_3), 4.37 (t, $J = 7.5$ Hz, 2H, NCH_2CH_2), 7.73 (s, 1H, imid-H), 7.80 (s, 1H, imid-H), 9.35 (s, 1H, imid-H) ppm.
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21. Precaution should be addressed while handling ammonia or aqueous ammonia. Ammonia is a toxic gas although its aqueous solution had been employed as a fertilizer in farms many years ago. The toxicity of ammonia solutions does not usually cause problems for humans and other mammals. However, ammonia even at dilute concentrations is highly toxic to aquatic animals. More details on the toxicity of ammonia could be obtained from the Internet: http://en.wikipedia.org. In our laboratory, the anion metathesis process was carried out in a fume hood, and the waste water containing ammonia was neutralized by diluted acetic acid before final disposal.
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