Quality Control of 1-Alkyl-3-methylimidazolium Ionic Liquid Precursors with HPLC

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Abstract: A high performance liquid chromatography (HPLC) method was proposed to monitor the synthesis and purification of the 1-alkyl-3-methylimidazolium ionic liquid precursors from alkylation of 1-methylimidazole with alkyl halides and determine the purity of final products. The results showed that separation of 1-methylimidazole from the precursors could be obtained under the HPLC performance conditions such as cation exchange column, acetonitrile/KH_2PO_4 aqueous solution and 209 nm wavelength. The content of unreacted 1-methylimidazole in the precursors could be easily calculated from their corresponding HPLC peak areas with the calibration curve of 1-methylimidazole. The retention times of the 1-alkyl-3-methylimidazolium ionic liquid precursors decreased with their increasing alkyls, and the ionic liquids with the same cation and different anions had almost the same retention times.

Key words: 1-methylimidazole; purity; ionic liquid; precursor; HPLC

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1 INTRODUCTION

With rapid advancement in ionic liquids (ILs) studies and relevant publications[1−5], the purities of ILs have gained increasing attentions as both their physical and chemical properties, and their performance as solvents, particularly for catalytic reactions are heavily influenced by impurities which are mainly unreacted starting materials such as 1-methylimidazole, alkyl halides, etc[6−8].

1-Alkyl-3-methylimidazolium ILs investigated as air and water-stable novel media are obtained through exchanging the anions, such as hexafluorophosphate, tetrafluoroborate, etc., with 1-alkyl-3-methylimidazolium halides called the 1-alkyl-3-methylimidazolium IL precursors from the alkylation of 1-methylimidazole with alkyl halides which are variable to fine-tune the final IL properties to meet the different requirements[9,10], as shown in Fig.1.

For the 1-alkyl-3-methylimidazolium IL precursors, unreacted 1-methylimidazole and alkyl halide are the main impurities. As alkyl halide is a relatively volatile and low boiling liquid, it can be easily removed by evaporation under reduced pressure. However, 1-methylimidazole has a high boiling point (198.05℃) and is a coordinating base, which leads to removing it from the IL precursors difficultly. The unreacted 1-methylimidazole makes ILs smell terrible and causes potential downstream problems[11].

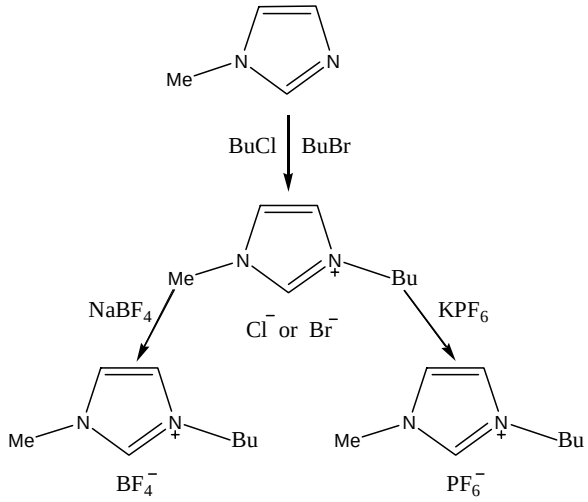

Fig.1 Synthesis procedures of 1-alkyl-3-methylimidazolium-based ILs (Me, methyl; Bu, butyl)

Commonly, there are mainly two ways to eliminate the unreacted 1-methylimidazole in 1-alkyl-3-methylimidazolium IL precursors. One is to increase the reaction conversion rate of 1-methylimidazole by prolonging reaction time, elevating reaction temperature,

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especially increasing the ratio of alkyl halides to 1-methylimidazole. Another is to purify the obtained 1-alkyl-3-methylimidazolium IL precursors by washing or extracting with ethyl acetate, toluene, etc.

How to develop a procedure to monitor the synthesis and purification processes and determine the purity of final products is the key to the quality control of 1-alkyl-3-methylimidazolium ionic liquid precursors. Holbrey et al.[12] proposed a colorimetric method to determine the content of 1-methylimidazole in 1-ethyl-3-methylimidazolium chloride ([Emim]Cl). The method was involved with the complexation of 1-methylimidazole with copper(II) chloride in ethanol to form the $[Cu(mim)_4]^{2+}$ ion, which gives a yellow solution in the absence of 1-methylimidazole and provides the necessary spectral shift to allow a colorimetric determination based on the position of the electronic maximum absorbance wavelength (λ_{max}). Though the colorimetric method is effective, it is still necessary to explore other direct approaches to meet the developments of ILs research.

A high performance liquid chromatography (HPLC) method is presented in this work. Based on it, obvious separation of 1-methylimidazole from the 1-alkyl-3-methlimidazolim IL precursors can be achieved, and it is convenient and effective to determine the unreacted 1-methylimidazole content in the 1-alkyl-3-methylimidazolium IL precursors quantitatively.

2 EXPERIMENTAL

2.1 Materials

Bromoethane, 1-bromobutane, dichloroethane, ethyl acetate, diethyl sulfate, toluene, trichloroethane and sodium fluoroborate (Beijing Chemical Reagents Company, China) with analytical grade were used in the experiments without further purification. 1-Bromohexane, 1-chlorohexane and 1-bromooctane (Beijing Chemical Reagents Company, China) were distilled over P_2O_5, and 1-methylimidazole was distilled from potassium hydroxide under reduced pressure. Double-distilled water was used in all experiments.

2.2 Apparatus and Methods

ILs were characterized by ^{1}H-NMR with a NMR spectrometer (ARX400, BRUKER, Switzerland). The water content of ILs was measured in a Karl Fisher titrator (Metrohm 787 KF Titrino, Switzerland). The UV–Vis spectrum was studied in a UV–Vis spectrophotometer (TU-1901, Purkinje, Beijing). The pure and mixture samples were recorded on Agilent 1100 series HPLC with the variable wavelength detector. The details of HPLC performance conditions are given as follows: column, cation exchange column (Zorbax Scx 250 mm×4.6 mm, I.D. 5 μm, Agilent)[13]; mobile phase, acetonitrile/1.36 g/L KH_2PO_4 aqueous solution (57/43, φ); flow speed, 1 mL/min; detecting wavelength, 209 nm. Rotary evaporator (RE-52A, Yarong, Shanghai, China) and vacuum oven (DZF-6020, Yiheng, Shanghai, China) were used for the purification of ILs.

2.3 Preparation and Purification of Ionic Liquids

2.3.1 [Emim]Br

1-Methylimidazole (41.0 g, 0.5 mol) was added firstly and bromoethane (54.5 g, 0.5 mol) was further added dropwise in a 500 mL three-neck round-bottom flask equipped with a reflux condenser and a magnetic stirrer, and cooled in an ice-bath, because the reaction taking place in it is highly exothermic. Having been vigorously stirred for 5 h, the mixture was refluxed in room temperature until it turned into solid completely. The solid was pounded to pieces and washed four times, each with 50 mL trichloroethane. Then the obtained [Emim]Br (87.9 g) was dried under vacuum at 70℃ for 24 h. It was characterized with ^{1}H-NMR (acetone-d_3) as follows: 8.74 (s, 1H), 7.52 (t, 1H), 7.50 (t, 1H), 4.25 (t, 2H), 3.91 (s, 3H), and 1.52 (t, 3H).

2.3.2 [Bmim]Br

1-Methylimidazole (41.0 g, 0.5 mol) and 1-bromobutane (71.9 g, 0.525 mol) were added directly to a 500 mL round-bottom flask equipped with a reflux condenser and a magnetic stirrer, and cooled in an ice-bath under vigorous stirring for 2 h. After another 72 h reaction with stirring at room temperature, two phases formed. The top phase containing residual starting materials was decanted and the bottom IL phase was extracted three times, each with 60 mL ethyl acetate. Then the product was evaporated under reduced pressure at 70℃ and dried in vacuum oven at 70℃ for 24 h. [Bmim]Br (98.5 g) was obtained. It was characterized with ^{1}H-NMR (acetone-d_3) as follows: 8.85 (s, 1H), 7.68 (t, 1H), 7.62 (t, 1H), 4.31 (t, 2H), 4.01 (s, 3H), 1.89 (m, 2H), 1.37 (m, 2H), and 0.95 (t, 3H).

2.3.3 [Hmim]Br

1-Methylimidazole (16.4 g, 0.2 mol) and 50 mL anhydrous toluene were added into a 250 mL three-neck round-bottom flask equipped with a reflux condenser and a magnetic stirrer, and cooled in an ice-bath. Then 1-bromohexane (39.6 g, 0.24 mol) was further added dropwise to the vigorously stirred mixture. The reaction mixture was protected from light by wrapping the flask in aluminum foil. Having been stirred for 24 h, the mixture was heated to the final reaction temperature of 50℃ and reacted for 48 h. A slightly viscous, colorless product was separated from the toluene phase and

washed two times, each with 25 mL toluene and then two times, each with 25 mL ethyl acetate. The obtained [Hmim]Br (41.1 g) was vaporized under reduced pressure to remove residual organic components and dried under vacuum at 70 ℃ for 24 h. It was characterized with ^{1}H-NMR (acetone-d_3) as follows: 8.87 (s, 1H), 7.69 (t, 1H), 7.65 (t, 1H), 4.35 (t, 2H), 4.00 (s, 3H), 1.92 (m, 2H), 1.40 (m, 4H), 1.37 (m, 2H), and 0.94 (t, 3H).

2.3.4 [Hmim]Cl

[Hmim]Cl was synthesized as that of [Hmim]Br. The reactants were also stirred under ice cooling for 24 h. Due to the lower reactivity of 1-chlorohexane, the reaction mixture was heated to a final reaction temperature of 60 ℃ over a period of 8 h and stirred vigorously for 72 h. The characterization of [Hmim]Cl with ^{1}H-NMR was similar to that of [Hmim]Br.

2.3.5 [Omim]Br

The procedure of [Omim]Br synthesis was like that of [Hmim][Br], just replacing 1-bromohexane with 1-bromooctane. The reactants were allowed to react at a final reaction temperature of 60 ℃ for 72 h. It was characterized with ^{1}H-NMR (acetone-d_3) as follows: 8.94 (s, 1H), 7.74 (t, 1H), 7.67 (t, 1H), 4.33 (t, 2H), 4.01 (s, 3H), 1.94 (m, 2H), 1.35 (m, 5H), 1.30 (m, 5H), and 0.87 (t, 3H).

2.3.6 [Emim]$C_2H_5SO_4$

A solution of 1-methylimidazole (41.0 g, 0.5 mol) and 100 mL toluene was added in a 500 mL three-neck round-bottom flask equipped with reflux condenser and magnetic stirrer, and cooled in an ice-bath. Diethyl sulfate (77 g, 0.5 mol) was added dropwise so as to maintain the reaction temperature below 40 ℃ because the reaction was highly exothermic. After 3 h reaction, the mixture was stirred at room temperature for 6 h. It was clearly seen that the IL phase was separated from the toluene phase. The upper toluene phase was decanted and the lower IL phase was washed three times, each with 50 mL toluene. The obtained [Emim]$C_2H_5SO_4$ (109.1 g) was vaporized under reduced pressure to remove residual organic components and dried under vacuum at 70 ℃ for 24 h. The characterization result of [Emim]$C_2H_5SO_4$ with ^{1}H-NMR (acetone-d_3) was obtained as follows: 8.86 (s, 1H), 7.66 (t, 1H), 7.60 (t, 1H), 4.33 (t, 2H), 4.067 (2H, q,), 4.02 (s, 3H), 1.55 (t ,3H), and 1.26 (t, 3H).

2.3.7 [Bmim]BF_4

[Bmim]Br (109.5 g, 0.5 mol) was transferred into a 1 L container, followed by addition of $NaBF_4$ aqueous solution (60.5 g, 0.55 mol). After 24 h reaction with vigorous stirring, [Bmim]BF_4 was extracted three times, each with 60 mL dichloroethane. The total dichloroethane solution containing the product was washed with water several times until bromine free as determined by silver nitrate test. The [Bmim]BF_4–dichloroethane mixture was added into a round-bottomed flask and vaporized under reduced pressure to remove residual dichloroethane. The final product (96.1 g) was dried under vacuum at 70 ℃ for 24 h. The characterization of [Bmim]BF_4 with ^{1}H-NMR was almost the same as that of [Bmim]Br.

Water content in the ILs mentioned above was less than 200×10^{-6} after they were dried under vacuum at 70 ℃ for 24 h.

3 RESULTS AND DISCUSSION

UV–Vis absorption spectrum of 1-methylimidazole shown in Fig.2 indicates that 1-methylimidazole has the maximum absorbance peak at 209 nm[14]. According to experimental result, 1-alkyl-3-methylimidazolium IL precursors also have UV absorbance in different degrees at the wavelength. So 209 nm was chosen as the detecting wavelength of HPLC to obtain a highly intense absorbance of 1-methylimidazole so as to improve the precision of following measurements.

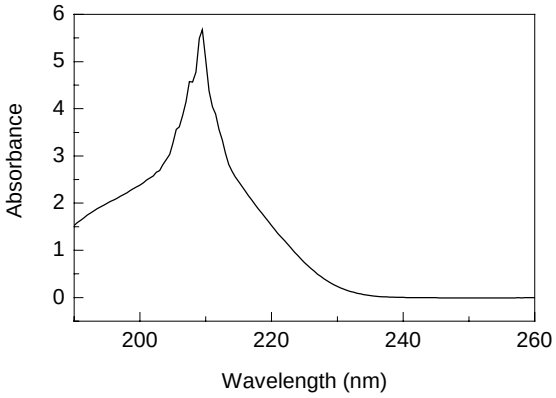


Fig.2 UV–Vis spectrum of 1-methylimidazole

In HPLC, it is found that 1-methylimdazole can be separated from the 1-alkyl-3-methylimidazolium IL precursors under the performance conditions as follows: cation exchange column, acetonitrile/KH_2PO_4 aqueous solution as mobile phase, and 209 nm detecting wavelength. Moreover, the separation of 1-methylimidazole from 1-alkyl-3-methylimidazolium IL precursors can be optimized by regulating mobile phase because the retention time of 1-methylimidazole decreases less than those of the precursors with increasing the ratio of acetonitrile to H_2PO_4 aqueous solution and the concentration of KH_2PO_4 aqueous solution. For example, a separation pattern of the

mixture sample (1-methylimidazole, [Emim]Br, [Bmim]Br, [Hmim]Br and [Omim]Br) was obtained under the conditions mentioned in the section of apparatus and methods, as shown in Fig.3. It is obviously demonstrated that five components identified with the corresponding pure substances were separated well.

For the above 1-alkyl-3-methylimidazolium IL precursors (Fig.4), their retention times follow the order of [Emim]Br>[Bmim]Br>[Hmim]Br>[Omim]Br, also seen from Fig.3, as increasing alkyl of the cations decreases the interaction between the cations and the cation exchange column of HPLC.

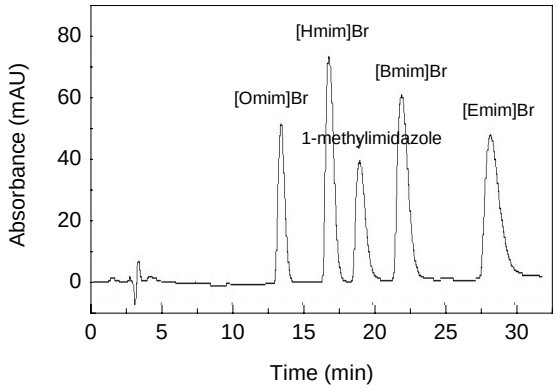
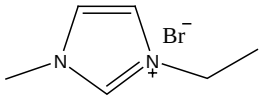
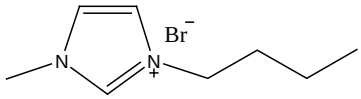


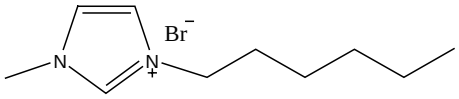
Fig.3 HPLC spectrum of the mixture of 1-methylimidazole



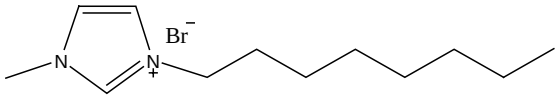
(a) [Emim]Br



(b) [Bmim]Br



(c) [Hmim]Br



(d) [Omim]Br

Fig.4 Structures of [Emim]Br, [Bmim]Br, [Hmim]Br and [Omim]Br

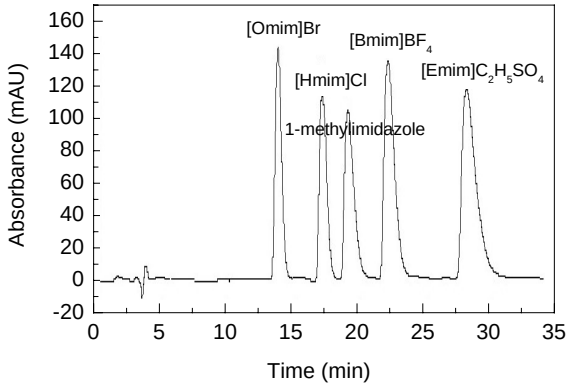


Fig.5 HPLC spectrum of the mixture of 1-methylimidazole

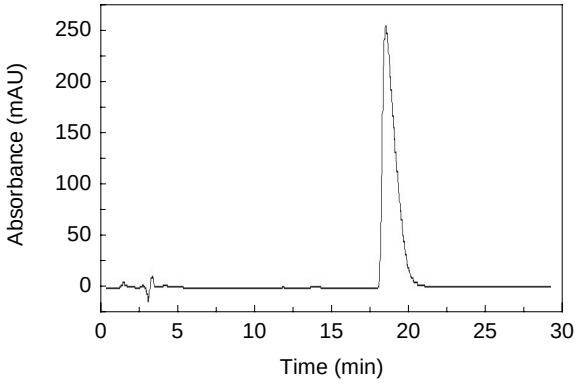


Fig.6 HPLC spectrum of 1-methylimidazole aqueous solution

The proposed HPLC method can be applied for 1-alkyl-3-methylimidazolium IL precursors with different cations and same anion as mentioned above. It can be also applied for ILs with different cations and anions, as shown in Fig.5, which is a HPLC spectrum of mixture of 1-methylimidazole, [Emim]$C_2H_5SO_4$, [Bmim]BF_4, [Hmim]Cl and [Omim]Br under the same experimental conditions as Fig.3. It can be seen from Figs.3 and 5 that there are almost the same retention times for the same cations, because the cation exchange column of HPLC has stronger interactions with cations, while little interactions with anions.

For determination of the content of unreacted 1-methylimidazole in 1-alkyl-3-methylimidazolium IL precursors quantitatively with HPLC, the calibration curve of 1-methylimidazole was needed. A series of contents of 1-methylimidazole aqueous solutions (5, 10, 25, 50, 75, 100 mg/L) were set up and measured with HPLC under the experimental conditions mentioned above. Fig. 6 is one of the HPLC spectra of the 1-methylimidazole aqueous solutions.

Based on the peak areas of 1-methylimidazole and its corresponding contents, the calibration curve of 1-methylimidazole can be obtained, as shown in Fig.7.

With the calibration curve, the contents of unreacted 1-methylimidazole in the 1-alkyl-3-methylimidazolium IL precursors can be calculated from its corresponding HPLC peak areas.

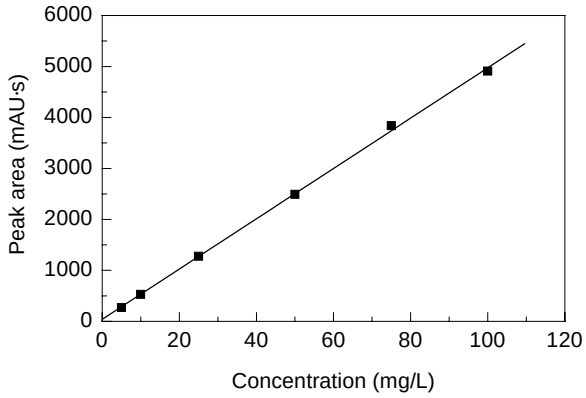


Fig.7 Calibration curve of 1-methylimidazole

4 CONCLUSIONS

The HPLC method is presented to monitor the synthesis and purification, and determine the purity of final products for the quality control of the 1-alkyl-3-methylimidazolium ionic liquid precursors. Some conclusions are drawn as follows:

(1) The separation of 1-methylimidazole from the precursors can be obtained with HPLC under the following performance conditions: cation exchange column, acetonitrile/KH_2PO_4 aqueous solution as mobile phase, and 209 nm detecting wavelength.

(2) By regulating the ratio of acetonitrile to KH_2PO_4 aqueous solution, the concentration of KH_2PO_4 aqueous solution and flow rate of the mobile phase, the separation of 1-methylimidazole from the precursors can be optimized.

(3) The retention times of the precursors decrease with the increasing alkyl of the cations, and the ILs with the same cation and different anions have almost same retention times.

(4) The contents of unreacted 1-methylimidazole in the precursors can be easily calculated from its corresponding HPLC peak areas with the calibration curve of 1-methylimidazole.

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