# How to separate ionic liquids: Use of Hydrophilic Interaction Liquid Chromatography and mixed mode phases

C. Lamouroux*, G. Foglia, G. Le Rouzo

*CEA Saclay DEN/DPC/SECR Laboratoire de Spéciation des Radionucléides et des Molécules, 91191 Gif-sur-Yvette, France*

## ARTICLE INFO

## ABSTRACT

This chromatographic study deals with the development of a convenient and versatile method to separate Room Temperature Ionic Liquids. Different modes of chromatography were studied. The study attempts to answer the following question: "what were the most important interactions for the separation of ionic liquids?". The results show that the essential interactions to assure a good retention of RTILs are the ionic ones and that hydrophobic interactions play a role in the selectivity of the separation. The separation of five imidazolium salt with a traditional diol columns in Hydrophilic Interaction Chromatography (HILIC) was demonstrated. It shows that neutral diol grafted column allows an important retention that we assume is due to the capability of diol to develop a thick layer of water. Furthermore, stationary phase based on mixed interaction associating ion exchange and hydrophobic properties were studied. Firstly, it will be argued that it is possible to separate RTILs with a convenient retention and resolution according to a reverse phase elution with the Primesep columns made of a brush type long alkyl chain with an embedded negatively charged functional group. Secondly, a sucessful separation of RTILs in HILIC mode with a mixed phase column containing a cationic exchanger and a hydrophobic octyl chain length will be demonstrated.

## 1. Introduction

Ionic liquids (ILs) are room temperature molten salts composed by an organic or inorganic anion (chloride, tetrafluoroborate, hexafluorophosphate, triflate, bistrifluorosulfodiimide) and a cation such as alkyl-pyridinium, alkyl-ammonium or alkyl-immidazolium. The combination of these different associations has expanded considerably the number of possible salts that differ in properties such as viscosity, melting point, density [1,2]. They constitute a new class of non-molecular solvents with some unique properties. They possess a wide range of solubilising capabilities for polar and apolar molecules as well as for ions. They have interesting electrochemical properties such as a significant dielectric constant, a high electrical conductivity, and a wide range of electroactivity. They also have good thermal and chemical stabilities. Ionic liquids are a new class of solvent with various uses.

In the nuclear fuel cycle, RTILs appear potentially attractive for future reprocessing treatments [3]. Firstly, it has recently been shown that the imidazolium RTILs possess unique solvation properties for actinide and lanthanide cations. The electrochemical properties of those imidazolium RTILs could make them potential media for lanthanides or actinides electrorefining. For the same reasons RTILs could replace conventional organic diluents for separation processes by solvent extraction. However, to use RTILs in nuclear application, understanding of their radiolytic behaviour is needed. The best technique for quantifying and determining the degradation products is liquid chromatography coupled with mass spectrometry.

Therefore, the development of a sensitive and reproducible method of separation compatible with coupling to electrospray mass spectrometry is required. Understanding of the preponderant mechanism governing the retention of ILs is then necessary.
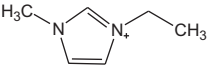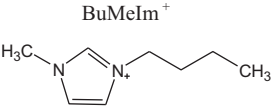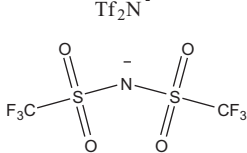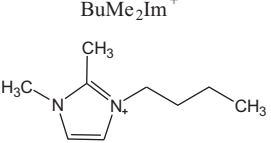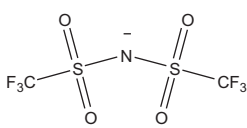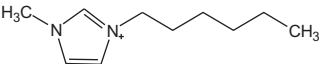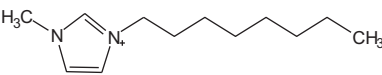
Several works reported the separation of alkylimidazolium RTILs cations with the reversed chromatography mode [4–7]. The reversed phase mode has been widely used for separation of various imidazolium cations on alkyl-bonded stationary phase, phenyl bonded [7] stationary phase, or silica packings functionalized with mixed polar and apolar functions. It is shown that retention time and selectivity is weak when the hydrocarbon chain is less than four carbon atoms.

Moreover, these separations always need a high percentage of water in mobile phase, or the addition of non volatile buffer or ion-pairing agent, which does not constitute good conditions for the coupling to mass spectrometry. In addition, high level of water can lead to some problems of solubility for certain RTILs, such as for the association with the bis(trifluoromethylsulfonyl)imide anion.

* Corresponding author at: Department of Physico-chemistry, bât 391, 91191 Gif sur Yvette, France. Tel.: +33 1 69 08 21 70; fax: +33 1 69 08 54 11.

*E-mail addresses:* tine.lamouroux@cea.fr, christine.lamouroux@cea.fr, cedchrislucas@free.fr (C. Lamouroux).

**Table 1**
Structure of the different compounds.

| Compound | Structure | Anion | $N°$ |
|---|---|---|---|
| Imidazole | EtMeIm$^+$ | – | 0 |
| [EtMeIm]Cl | | Cl$^-$ | 1 |
| [BuMeIm][Tf$_2$N] | BuMeIm$^+$ | Tf$_2$N$^-$ | 2 |
| [BuMe$_2$Im][Tf$_2$N] | BuMe$_2$Im$^+$ | Tf$_2$N$^-$ | 3 |
| [HexMeIm]Cl | HexMeIm$^+$ | Cl$^-$ | 4 |
| [OctMeIm]Cl | OctMeIm$^+$ | Cl$^-$ | 5 |

However, the retention mechanism combining hydrophobic and ionic interactions often produces dissymmetric peaks and is not suitable for studying some complex mixtures such as radiolysis bulk. Ion chromatography [5,8–10] was also investigated with a strong cation exchange adsorbant but with this type of chromatography, mobile phase also contains non volatile salt like hydrogeno phosphate, carbonate, etc. which are not convenient for further coupling.

Thus, all these studies show clear limitations for the separation of short alkyl chains compounds in terms of retention and selectivity without addition of ion-pairing agents or non-volatile salts. In our last study, we showed the potentiality of the Hydrophilic Interaction Chromatography (HILIC) [11] mode for the separation of five BuMim, with normal phase diol. HILIC mode provides an efficient separation even for less hydrophobic cation. Another concept that may also show an extended application range is mixed-mode chromatography. Mixed-mode columns [12] may appear in a variety of facets as accomplished through distinct combinations of interactive principles and altered geometrical and spatial arrangements of functional groups.

However, the most effective seems to be the combination of orthogonal hydrophobic and ionic exchange interaction such as mixed-mode RP/ion exchanger [13]. These phases containing hydrophobic alkyl chains with embedded acidic groups in H+ form have already been used to separate cations, zwitterions and neutral compounds The objective of this work is to describe the interactions which drive the chromatographic retention and behaviour of ionic liquid in order to optimise the separation of a mixture of ionic liquids. The separation of five butyl imidazolium ionic cations, and the neutral imidazole compound was evaluated by using mixed mode column in HILIC mode, or in RP mode.

## 2. Experimental part

### 2.1. Chemicals

Ionic liquids were purchased from Aldrich and Fluka, or were synthesized according to classical metathesis protocol previously described. They were purified with activated carbon (12 h) and separated on a column with small amount of acidic alumina. Solutions obtained were dried in vacuum (5 mBar) at 80 °C for 6 h.

### 2.2. Samples preparation

Ionic liquids used in these studies are listed in Table 1. Stock solutions at $10 \, g \, L^{-1}$ of each IL in H$_2$O/ACN were prepared. The solution of the mixture is concentrated at $1 \, g \, L^{-1}$ in H$_2$O/ACN.
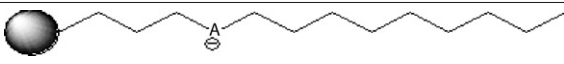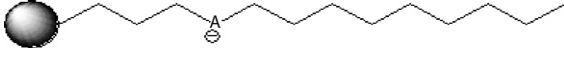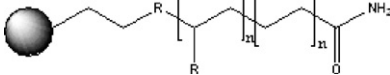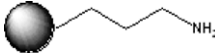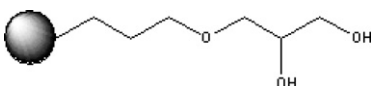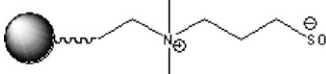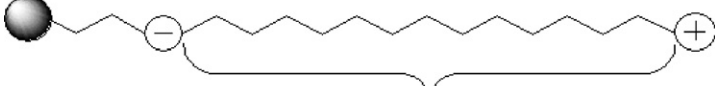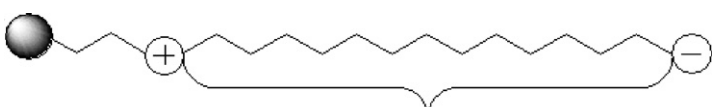
### 2.3. Chromatographic system

UV–vis analyses were performed with a Shimadzu UV-3150 PC. Samples were diluted at 1/100 in acetonitrile/water mixture (1:1 v/v). The maximum absorption wavelength was determined at 210 nm and then applied for the chromatography detection.

Experiments were performed on a Shimadzu HPLC system equipped with a binary pump (LC-10ADVP), an autosapler (SIL-10AF) and a UV detector. The column was thermostated at 25 °C and the detection wavelength was set to 210 nm corresponding to the maximum absorption of the ILs. Samples volume injected were 10 μL and the elution was carried out under isocratic conditions.

The columns and their characteristics used in the experiments are described in Table 2. The flow rate was 0.2 mL min$^{-1}$ adjusted with the internal diameter of the column.

**Table 2**
Nature of the different chromatographic stationary phases.

| Column name | Dimensions (mm) | Stationnary phase |
|---|---|---|
| Primesep 100 (Sielc Technologies) | 150 × 2.1 | |
| Primesep 200 (Sielc Technologies) | 150 × 2.1 | |
| TSKGelAmide (Tosoh Bioscience) | 150 × 2.1 | |
| Supelcosil LC-CN (Discovery) | 250 × 2.1 | |
| (1) - Uptisphere NH2 (Interchrom) | 250 × 2.1 | |
| (2) - YMCPack NH2 (Waters) | 250 × 2.1 | |
| 1 - Uptisphere OH (Interchrom) | 250 × 2.1 | |
| 2 - YMCPack OH (Waters) | 250 × 2.1 | |
| ZIC-HILIC (Sequant) | 150 × 2.1 | |
| Obelisc R (Sielc Technologies) | 150 × 2.1 | |
| Obelisc N (Sielc Technologies) | 150 × 2.1 | |
| Uptisphere MM1 (Interchrom) | 250 × 2.1 | Hydrophobic/strong cation exchanger (SCX) |
| Uptisphere MM3 (Interchrom) | 250 × 2.1 | Hydrophobic/strong anion exchanger (SAX) |

Four different types of phase were used to study the separation of RTILs:

(i) Classical reversed phase such as the metasil basic
(ii) Some acidic mixed-mode phases working in RP mode but with additional ion-exchange properties. Primesep 100 is a reverse-phase analytical column with embedded acidic ion-pairing groups and Primesep 200 is a reverse-phase analytical column with embedded weak acidic ion-pairing groups. The acidic groups of Primesep 100 are stronger than those of Primesep 200. The mobile phase was composed of acetonitrile/water (60/40) with 0.1% TFA
(iii) Several classical normal phases such as diol, cyano, $NH_2$. TSKGel Amide 80 (Tosoh Bioscience) is a spherical silica-based stationary phase with covalently bonded carbamoyl groups. Zic-HILIC (Sequant) is a silica based sulfobetaine type bonded phase. These phases were tested in HILIC mode with a mobile phase composed of acetonitrile/water (90/10) with 5 mM ammonium acetate
(iv) Some mixed-mode phase such as Uptisphere MM1, obelisk N, Obelisc R

## 3. Results and discussion

To understand the phenomena that control the retention of RTILs and to propose some explanations and chromatographic conditions to separate some RTILs differing by the number of carbon, different chromatographic modes were tested (reversed phase, mixed-mode column and HILIC mode).

### 3.1. Separation in reversed phase chromatography mode

The chromatogram on Fig. 1 shows the separation obtained in isocratic mode inspired by the conditions described by Stepnovski [4]. It is interesting to note that the gradient proposed by Stepnowski is not a classical reverses phase mode gradient. In fact, it begins with a higher percentage of organic solvent to a lower one. Under these conditions, contrary to what is described by Stepnowski, we note a co-elution of Ethyl and Methyl explained by the fact that the amount injected is larger than those of Stepnovski.
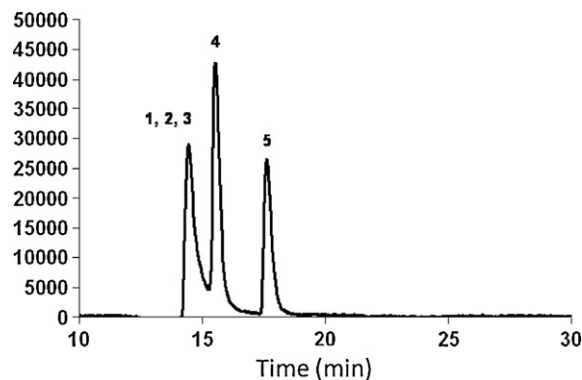
**Fig. 1.** Chromatogram in reversed phase mode of the separation of the RTILs mixture. (Metasil Basic C8, isocratic, $H_2O$/ACN 60/40 -10 mM $NH_4CH_3COOH$, 1%$CH_3COOH$).
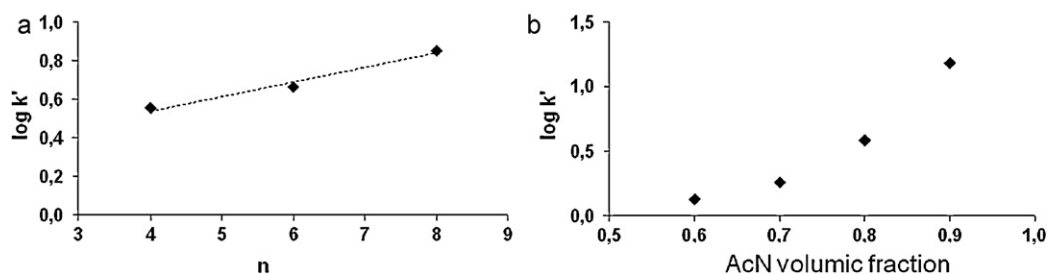
**Fig. 2.** (a) Variation of log $k'$ in function of the number of carbon on RTILs; (b)Variation of log $k'$ in function of the volumic fraction of ACN in mobile phase.

Fig. 2a represents the evolution of the retention factor (log $k$) as a function of the number of carbon in the alkyl chain. The retention increases with the hydrophobic character of the ILs, which is in agreement with a classical reversed phase mechanism. However, Fig. 2b shows the evolution of the retention factor with the percentage of acetonitrile in the mobile phase for the Bumin. It is shown that the retention factor increases with the increase of the ACN percentage, which is in contradiction with the classical behaviour observed in reversed phase chromatography. It suggests that there is another mechanism that governs the retention. The electrostatic (ionic) interactions between ILs and residual silanols can explain these observations. We underline the prominent role of the electrostatic interaction for the retention of ILs. The use of the reversed phase chromatography is known to be limited for ILs with less than four carbons. For these reasons, Stepnovski et al. have developed the separation of imidazolium cations with ion exchange chromatography (strong cation exchange based on sulfonate groups) with a mobile phase composed of a mixture of ACN/water containing phosphate salt. The problem is that phosphate salts are not volatile and not compatible with the coupling to mass spectrometry. So, to improve the separation of RTILs with a short chain length, while allowing the use of non volatile salts, we have decided to test two approaches: (i) the first is based on the use of recently developed mixed mode phases, and (ii) the second based on the use of HILIC chromatography with different types of functionality (neutral, ion exchange or zwitterionic groups).

The first approach involves the use of Primesep 100 and 200 columns developed by SIELC technologies. These phases are made with a brush type long alkyl chain with an embedded negatively charged functional group in the middle of the alkyl chain. These columns have demonstrated successful capacity for retaining quaternary amine compounds [13]. Fig. 3 shows the chromatograms obtained respectively with P100 and P200 with a mobile phase consisting of 60/40 ACN/water and 0.1% TFA. The imidazole, the only neutral compound without carbon chain, is the first eluted compound that is expected. On these two columns, the RTILs are retained according to their hydrophobic character. These results show that the mechanism is closed to that observed in reversed phase with ion pairing agent. The difference lies in the fact that it is not a dynamic exchange but a static ion exchanger incorporating into the stationary phase.

The results show an improvement both in retention and selectivity with P100 compared with P200. According to the manufacturer, the carboxylate groups embedded into the P100 are more acidic than the P200. In fact, in P100, the embedded groups have a pKa of about 1. So, at pH 2, the carboxylate should be totally ionised, which promotes the retention of imidazolium according to an ion exchange mechanism. Conversely, the carboxylate groups on P200 have a pKa near 2, so at pH 2 only 50% of the carboxylate groups are ionised. The P100 and P200 have a similar hydrophobicity but the number of ionized

groups is higher on P100 than on P200 which explains the best retention on P100. With these two columns, the retention is governed by the ion exchange mechanism and the selectivity by the hydrophobic interactions. These observations show, as before, the importance of the electrostatic interactions in the retention of alkylimidazolium.

### 3.2. Separation in HILIC mode

As an alternative, we decided to explore the HILIC mode. The hydrophilic interaction chromatography is now well known as a method for analyzing ionic or polar compounds that are poorly resolved by reversed phase liquid chromatography. HILIC bears similarities with traditional normal phase chromatography but with the important distinction that HILIC works with semi aqueous eluents. Typical eluents consist of a mixture of water/ACN with a volatile buffer. HILIC is thus a very mass spectrometry friendly technique.

Under HILIC separation conditions [14], a water enriched layer will be established within the stationary phase and the separation is achieved by partitioning of the analytes from the eluent into this hydrophilic environment. Hydrogen bonding and dipole–dipole interactions are therefore the dominating retention mechanisms and the retention is typically an exothermic process. The charged stationary phases have a second, and very significant, dimension of selectivity due to the opportunities of electrostatic interactions with the analytes. However, the mechanism is not clear; several studies assume a mixed mechanism of partitioning and adsorption. We decided to explore the mechanisms that govern the retention of ILs in HILIC. For this, two types of phase have been tested: (i) phases grafted with neutral groups, such as cyanopropyle, aminopropyle,
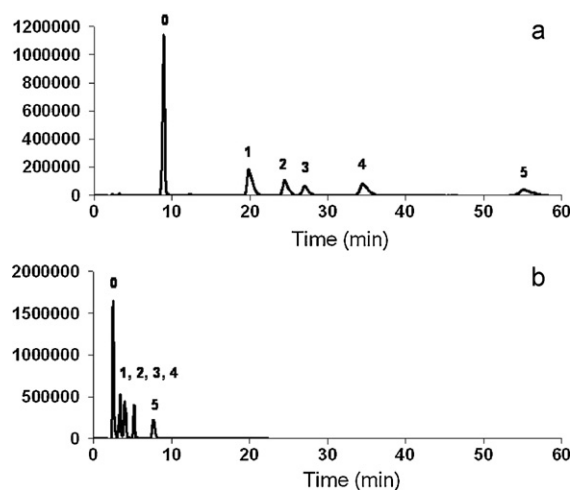


**Fig. 3.** Chromatograms of the mixture on acidic mixed mode phase on (a) Primesep 100 (b) Primesep 200. Isocratic elution ACN/H$_2$O – 0.1% TFA 60/40 v/v.
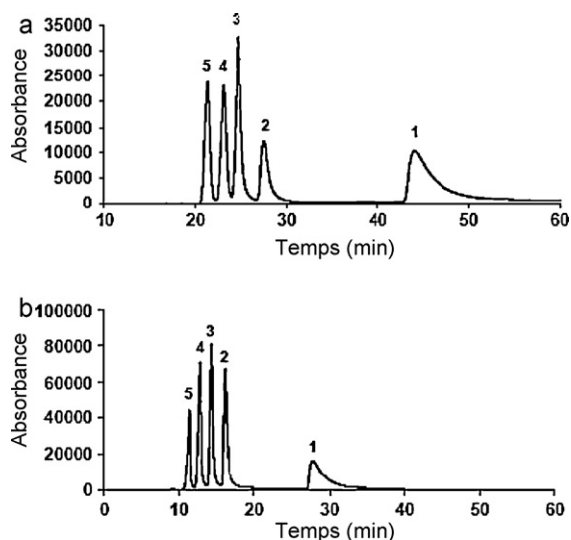
**Fig. 4.** Chromatograms of the mixture on normale phase (a) YMCPack-OH (b) Uptisphere-OH in HILIC mode (isocratic elution ACN/H$_2$O 90/10- 5 mM NH$_4$CH$_3$COOH).



**Fig. 5.** Evolution of log $k'$ in function of (a) the volumic fraction of ACN in mobile phase (b) the concentration of CH$_3$COONH$_4$.

diol and carbamate, and (ii) phases grafted with ionic groups. Fig. 4 shows the chromatograms obtained for the two neutral phases. As expected, imidazole is always the first eluted compound with no or weak retention.

The HILIC chromatography then was tested on classical phases (amide, amino, cyano, carbamate and diol) and on mixed-mode phases. Overall, the imidazolium cations are eluted as a function of their decreasing hydrophobic character, which is consistent with an HILIC mechanism. The retention and selectivity are very slight on amide, cyano and carbamate phases. For the cyano and amide phases, just the more polar cation is retained and all other are coeluted. The amides functions and cyanopropyle are essentially donors-acceptors of electron and are not engaged in the hydrogen interactions, which could explain the low retention observed.

Conversely, the diol stationary phases offer good retention properties. Actually, the diol stationary phases present a polarity that is comparable to bare silica and have a higher tendency to develop hydrogen bonds. The difference with the diol phase lies in its ability to capture a larger layer of water that plays an important role in the HILIC partitioning mechanism. As previously mentioned, the mechanisms involved in HILIC are based on partitioning and ion exchange mechanisms. The evolution of log $k$ as a function of the number of carbon loaded on the alkyl chain shows that log $k'$ decrease linearly with the number of CH$_2$ as expected in HILIC mode.

Based on these results obtained with ILs, we attempted to define whether the mechanism is rather an adsorption of a partitioning mechanism. We will hereafter briefly describe the basic equations governing the partitioning.

The reversed phase chromatography is considered to be (ideally) controlled by partitioning only. The linear relationship that describes the partitioning in RP mode (approximated valid over a narrow range of elution strengths) is:

$$\log k' = \log k'_A - S_1 V_B$$

where $k'_A$ is the capacity factor for the use of the stronger eluent component (acetonitrile) only as the mobile phase, $V_B$ is the volume fraction of the weaker eluent (water), and $S_1$ is the slope of log $k'$ versus $V_B$.

Fig. 5a shows the evolution of log $k'$ vs. $f(V_B)$ for the different RTILs. We can observe that the relation is not linear, so the retention mechanism is not strictly based on the partitioning. This result is
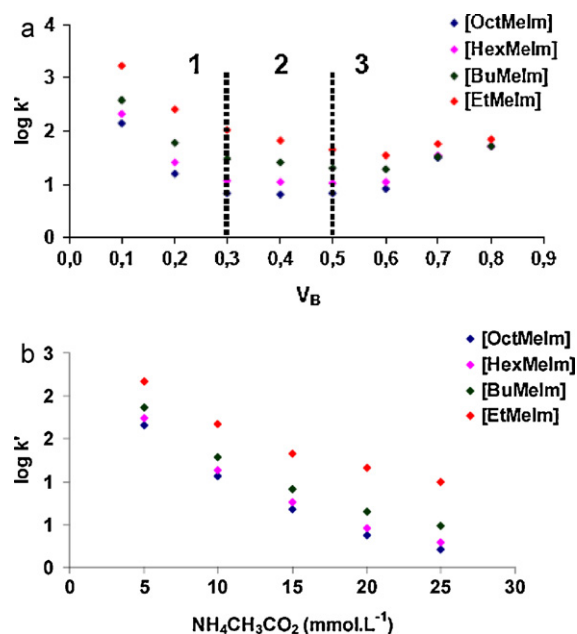
concordant with previous studies postulating that the mechanism is both controlled by adsorption by ionic interactions and partitioning. The evolution of log $k'$ vs. $f(V_B)$ can be divided in three parts: for a volume fraction of water from 5 to 30%, log $k'$ decreases with the volume fraction of water, which defines the HILIC zone. For water fraction from 30% to 60%, the retention factor is quasi constant and there is a fall of the resolution resulting from an intermediate behaviour. For water fraction up to 80%, the retention factor increases while the selectivity decreases, which corresponds to a reversed phase mechanism, not convenient for the separation of ILs.

The influence of the salt concentration (CH$_3$COONH$_4$) from 5 to 25 mM was studied. When the mobile phase is salt free, an irreversible retention of RTILs is observed, probably due to the ionic interactions with the residual silanols of the stationary phase. In the same manner, the RTILs are strongly and quasi irreversibly retained on bare silica stationary phase. Notably for these reasons, use of salts are necessary in HILIC. We have chosen to use ammonium acetate, which is volatile, and suitable for further mass spectrometry coupling. Fig. 5b shows the evolution of log $k'$ with the concentration of salt in mobile phase. We observe a non-linear decrease of the retention factor with the increase of salt concentration. This behaviour is classically observed for charged compounds with HILIC and we suggest that the formation of neutral ion pairing increases with the salt concentration that contributes to a weaker retention. We conclude that only the neutral phases grafted with diol are convenient for the separation of RTILs under HILIC mode. The interactions are both partitioning and ion exchange with the silanol surface groups. Only diol grafted phases allow a good retention and selectivity that we explain by the greater capability of diol to create a thick aqueous layer.

We show that electrostatic interactions play an important role in the separation and retention of RTILs, so we decided to study the separation in HILIC mode with two distinct mixed-mode phase: (i) typical HILIC zwitterionic column such as ZIC-HILIC, but also with (ii) mixed-mode phase combining an ion exchanger (anion, cation or zwitterionic) and an hydrophobic or hydrophilic linker.
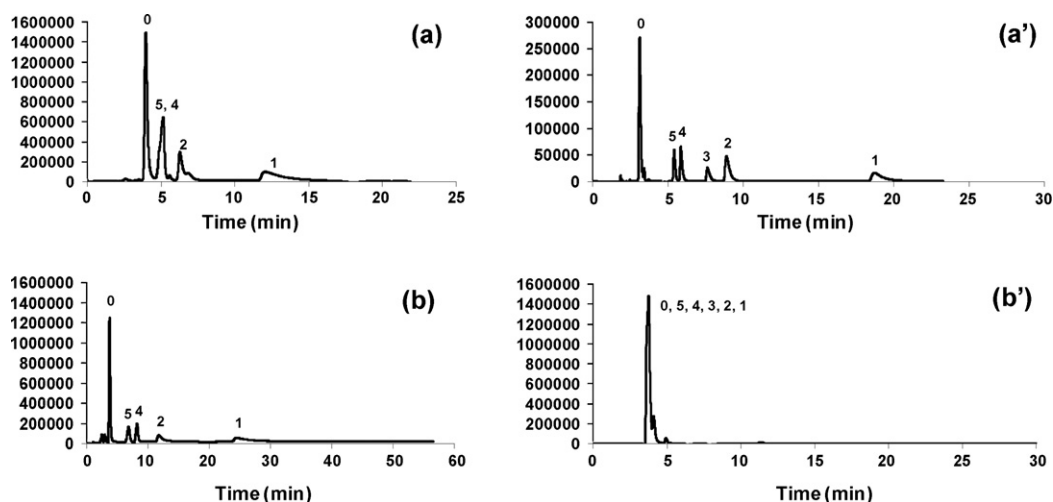
**Fig. 6.** Chromatograms of the mixture on zwitterionic phases in HILIC mode (isocratic elution ACN/$H_2O$ 90/10- 5 mM $NH_4CH_3COOH$) (a) Obelisc R (b) Obelisc N (a') Uptisphere MM1 (b') Uptisphere MM3.

(i) Zwitterionic stationary phase:These stationary phases consist in grafted silica by a highly polar zwitterionic function composed by a quaternary ammonium group and a sulfonate group. The Obelisc R and N columns are based on Liquid Separation Cell (LiSC $^{TM}$) technology and are grafted with an ionic exchanger. Obelisc R and N differ in the type and proximity of their ionised grafted groups and their hydrophobicity. Obelisc R possess the cationic groups close to the silica surface compared to and Obelisc N which has the cationic group separated by an hydrophilic chain and probably more accessible. On Zic-HILIC (a), only the EtMeIm+ is retained on the stationary phase with a weak retention time. On Obelisc columns (Fig. 6a and b), RTILs are retained in function of their polar character with retention time varying from 10 to 25 min, which is concordant with HILIC behaviour. The main distinction between Obelisc R and N lies in the co-elution of OctMeIm and HexMeIm with the R column and a better selectivity with the N column. These differences are easily explained by the nature of the stationary phase. In fact, Obelisc R has a cation exchanger at the end of the hydrophobic linker that is more accessible than Obelisc which bears a cation exchange near the silica substrate and possesses a hydrophilic linker. Due to the best accessibility of the cation exchanger, the Obelisc N is more retentive for RTILs. Based on these observations, to obtain the best separation it would be interesting to combine a hydrophobic linker with an accessible cation exchanger. So we sought the most suitable phases with these properties.

(ii) Mixed mode phase with ion-exchanger:Some more classical phases combining an octyl chain with an ionic exchanger were also tested. Then the uptisphere MM1and MM3 columns, made respectively with an octyl chain, a cation, and an anion exchanger were tested. The results are presented on Fig. 6a' and b'. As usual, the neutral compound imidazole is eluted at the dead volume due to its high polarity and the absence of ionic interactions.

For the uptisphere MM3, there is no retention and all the cations are eluted at the dead volume, which can be explained by the absence of ion exchange and a repulsion effect due to the presence of anionic exchanger on the surface. Moreover, it should be noted that the presence of a hydrophobic hydrocarbon chain is not sufficient to ensure retention of the compounds. In contrast, as expected, by combining the presence of a cationic exchanger and a hydrophobic linker (uptisphere MM1), we observe a satisfying separation of the five RTILs. Moreover, RTILs are eluted according to the increasing polarity as expected in HILIC mode.

## 4. Conclusion

Our goal was to study the retention of RTILs and to propose a versatile method to separate them. Actually, the reverse phase chromatography presents some limitations for the retention of RTILs with short alkyl chain length, and ionic chromatography is limited towards coupling with mass spectrometry. For these reasons, we have studied the preponderant interactions responsible of the retention of RTILs. The essential interactions to assure a good retention of RTILs are firstly the ionic interactions and secondly the hydrophobic ones which play a role for selectivity considerations.

Due to the polar and ionic properties of ionic liquids, HILIC based on the use of polar stationary phases and mixed mode phases with ionic exchanger, are two performant alternative methods to separate the ionic liquids. Stationary diol showed the best results in terms of retention and selectivity probably due to the capability of diol to develop a thick layer of water and, in a lesser extent, may be due to the interactions with residual silanol. Good results were also observed with mixed mode phase containing a cationic exchanger and a hydrophobic octyl chain length in HILIC mode. Moreover, the use of mixed stationary phases made of a brush type long alkyl chain with an embedded negatively charged functional group in the middle of the alkyl chain showed good retention and satisfactory selectivity for the separation of imidazolium cations.

## References

[1] H. Tokuda, S. Tsuzuki, M. Susan, K. Hayamizu, M. Watanabe, Journal of Physics. Chemistry B 110 (39) (2006) 19593–19600.
[2] W. J. Oldman, D.A. Costa, W.H. Smith, in Ionic Liquids: Industrial applications to green chemistry. ACS Symposium series 818, ed. R. D. Rogers and K. R. Seddon, American Chemical Society, Oxford, 2002.
[3] K. Binnemans, Chemical Reviews 107 (6) (2007) 2592–2614.
[4] P. Stepnowski, et al., Journal of Chromatography A 993 (1–2) (2003) 173–178.
[5] P. Stepnowski, W. Mrozik, Journal of Separation Science 28 (2) (2005) 149–154.
[6] M.J. Ruiz-Angel, A. Berthod, Journal of Chromatography A 1113 (1–2) (2006) 101–108.

[7] P. Stepnowski, et al., Analytical and Bioanalytical Chemistry 385 (8) (2006) 1483–1491.
[8] C. Villagran C, M. Deetlefs, W.R. Pitner, C. Hardacre, Analytical Chemistry 76 (2004) 2118–2123.
[9] F.P. Hao, P.R. Haddad, T. Ruther, Chromatographia 67 (2008) 495–498.
[10] S. Zhou, H. Yu, L. Yang, H.J. Ai, Journal of Chromatography A 1206 (2) (2008) 200–223.
[11] G. Le Rouzo, C. Lamouroux, et al., Journal of Chromatography A 1164 (1–2) (2006) 139–144.
[12] J. Leicunaite, I. Kiimenkovs, J. Kviesis, Compte Rendu Chimie, 2010, 13, 1335–1340.
[13] J. Li, S. Shao, M.S. Jaworsky, P.T. Kurtulik, Journal of Chromatography A 1185 (2) (2008) 185–193.
[14] P. Hemström, K. Irgum, Journal of Separation Science 29 (2006) 1784–1821.