Azolium-based systems: application of an anion exchange resin (A^- form) method and ^1H NMR analysis of the charged-assisted $(C–H)^+\cdot$anion hydrogen bonds[†]

Immaculada Dinarès,* Neus Mesquida,* Anna Ibáñez, and Ermitas Alcalde

Laboratory of Organic Chemistry, Faculty of Pharmacy, University of Barcelona,
Joan XXIII s/n, 08028 Barcelona, Spain
E-mail: idinares@ub.edu, neusmesquida@ub.edu

Dedicated to Prof. Rosa M. Claramunt on the occasion of her 65th birthday

DOI: http://dx.doi.org/10.3998/ark.5550190.p008.203

Abstract
The counteranion exchange of quaternary 1,2,3-triazolium salts was examined using a simple method that permitted halide ions to be swap for a variety of anions using an anion exchange resin (A^{-} form). The method was applied to 1,2,3-triazolium-based ionic liquids and the iodide-to-anion exchange proceeded in excellent to quantitative yields, concomitantly removing halide impurities. Additionally, an anion exchange resin (N_3^{-} form) was used to obtain the benzyl azide from benzyl halide under mild reaction. Likewise, following a similar protocol, bis(azidomethyl)arenes were also synthesized in excellent yields. The results of a proton NMR spectroscopic study of simple azolium-based ion pairs are discussed, with attention focused on the significance of the charged-assisted $(C–H)^+\cdots$anion hydrogen bonds of simple azolium systems such as 1-butyl-3-methylimidazolium and 1-benzyl-3-methyl-1,2,3-triazolium salts.

Keywords: Imidazolium salts, 1,2,3-triazolium salts, anion exchange resin, hydrogen bonds, ionic liquids

---

Introduction

Azolium systems have gained a place among the anion-binding functional groups, ranging from anion receptors and sensors to transporters,[2-9] and as ionic liquids (ILs) their utility has expanded into domains beyond chemistry.[10-14] The greenness of the most established IL syntheses and purification procedures has been analyzed and evaluated.[13] Thus, the chemical aspects of imidazolium-based ILs, including their synthesis, counteranion exchange and purity, have been the subject of numerous studies with the aim of obtaining pure IL salts, especially halide-free ion pairs. However, little attention has been paid to the use of an anion exchange resin (AER).[1,12-14] Examples of anion exchange resin application to ILs reported in the open literature use either the AER (OH^- form) or the AER (A^- form) method.[1,14] We have recently examined the preparation of an AER (A^- form) conveniently loaded with a selected anion after treatment with either acids or ammonium salts in water, or hydroalcoholic media, or organic solvents. The halide-to-anion exchange of quaternary imidazolium salts **1·X** and their transformation to the corresponding ion pairs **1·A** was carried out in methanol or organic solvents providing a pure ionic liquid in excellent to quantitative yields (Figure 1). Moreover, the transformation of both lipophylic quaternary heteroaromatic cations and low hydrophilic anions also proceeded in excellent to quantitative yields.[1] This simple procedure offers a convenient way to replace halide anions by a broad range of anions in and also eliminates halide impurities and minimizes the formation of toxic by-products with consequential environmental benefits.

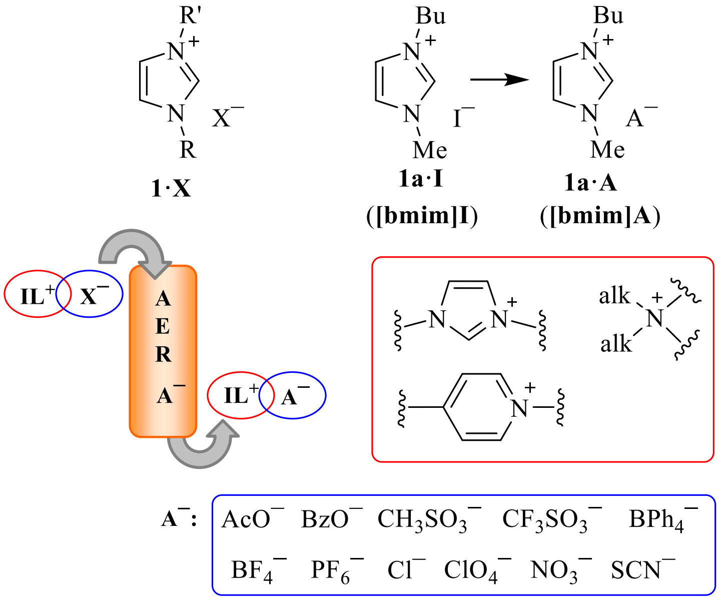
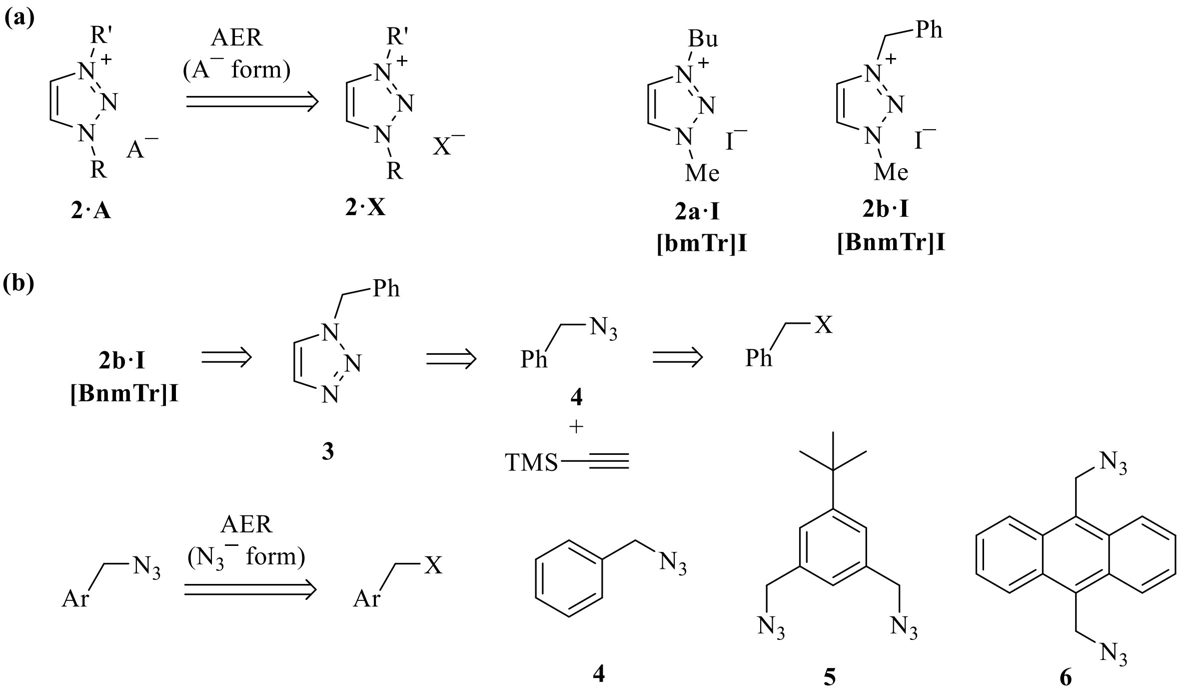


Figure 1. Application of the anion exchange resin (A^- form) method in non-aqueous media to representative imidazolium-based ionic liquids **1·X**.[1]

A logical extension of our previous studies on imidazolium-based systems was to examine 1,3-dialkyl-1,2,3-triazolium **2·X**, which have been described as stable and recyclable solvents.[15-18] The present study is focused on the application of the AER (A^- form) method for the iodide-to-anion exchange of the selected triazolium ion pairs. The reported synthesis of 1-benzyl-3-methyl-1,2,3-triazolium iodide **2b·I** (**[BnmTr]I**) requires benzyl azide **4** for the preparation of the click-derived 1,2,3-triazole **3**,[15] as shown in the retrosyntetic Scheme 1. Thus, an AER (N_3^- form) was prepared and used to obtain azide **4** and bis(azidomethyl)arenes **5** and **6**. It should be noted that in the last years theoretical calculations have confronted the question of what is responsible for the anion–cation non-covalent interactions in pure imidazolium-based ILs and have challenged the role of $(C–H)^+$ hydrogen bonds in explaining IL properties.[19,20] A relevant part of the present study is focused on the significance of the noncovalent interactions involved between the azolium motifs and a variety of anions, with special attention given to nonclassical charged-assisted $(C–H)^+\cdots$anion hydrogen bonds. Thus, the ion pairs prepared provided the opportunity to learn about the hydrogen-bonding interactions of simple azolium systems such as 1-butyl-3-methylimidazolium **1a·A** (**[bmim]A**) and 1-benzyl-1-methyl-1,2,3-triazolium **2b·A** (**[BnmTr]A**) salts in solution-phase by proton NMR spectroscopy.



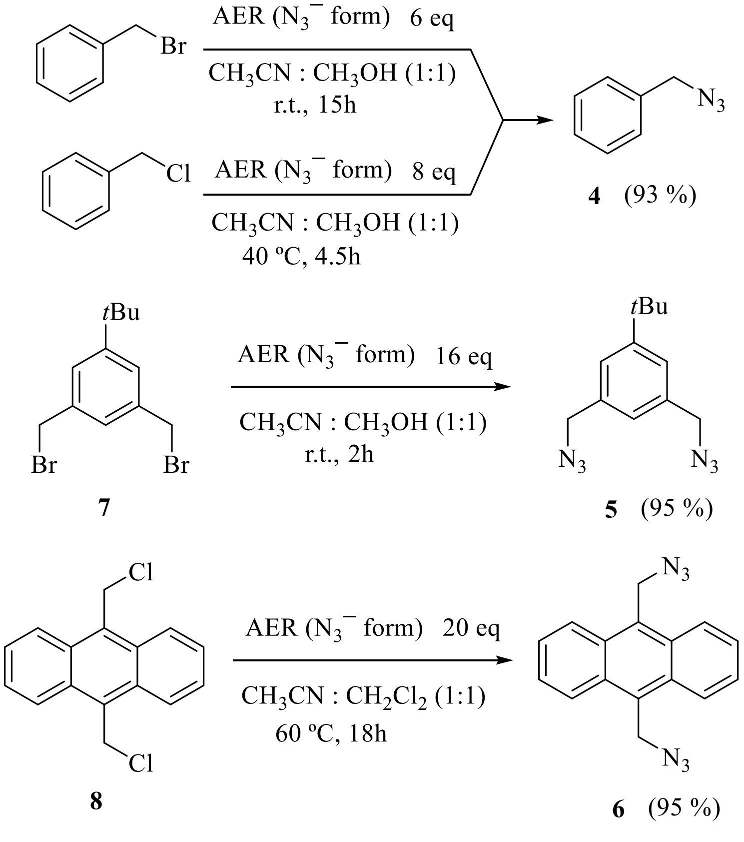
Scheme 1. 1,2,3-Triazolium-based ionic liquids **2·X**. **(a)** Halide-to-anion exchange: the anion exchange resin (A^- form) method. **(b)** Retrosynthetic pathway to the ion pair **2b·I** and to benzylic azides **4**, **5** and **6**.

Results and Discussion

Preparation of benzylic azides using an anion exchange resin (N_3^- form)

Applications of ion-exchange resins to a variety of chemical reactions have proven to be extremely useful in different chemical fields such as organic synthesis, catalysis and industrial applications[21,22] as well as chemistry in flow systems.[23] The anion exchange resin (N_3^- form) can be used both for the halide exchange like for nucleophilic substitution reactions.[24,25] Thus, the benzyl azide component **4** was prepared in excellent yield using a polymeric azide reagent protocol that consists of mixing benzyl bromide or chloride with 12 equivalents of the AER Amberlite IRA-400 (N_3^- form) at room temperature in dichloromethane,[24] and also under standard reaction conditions between sodium azide and benzyl iodide or bromide at room temperature in a dipolar aprotic solvent, e.g. dimethyl sulfoxide or dimethylformamide, in ≥ 91% yield,[26,27] since benzylic halides readily undergo nucleophilic substitution reactions.[28]

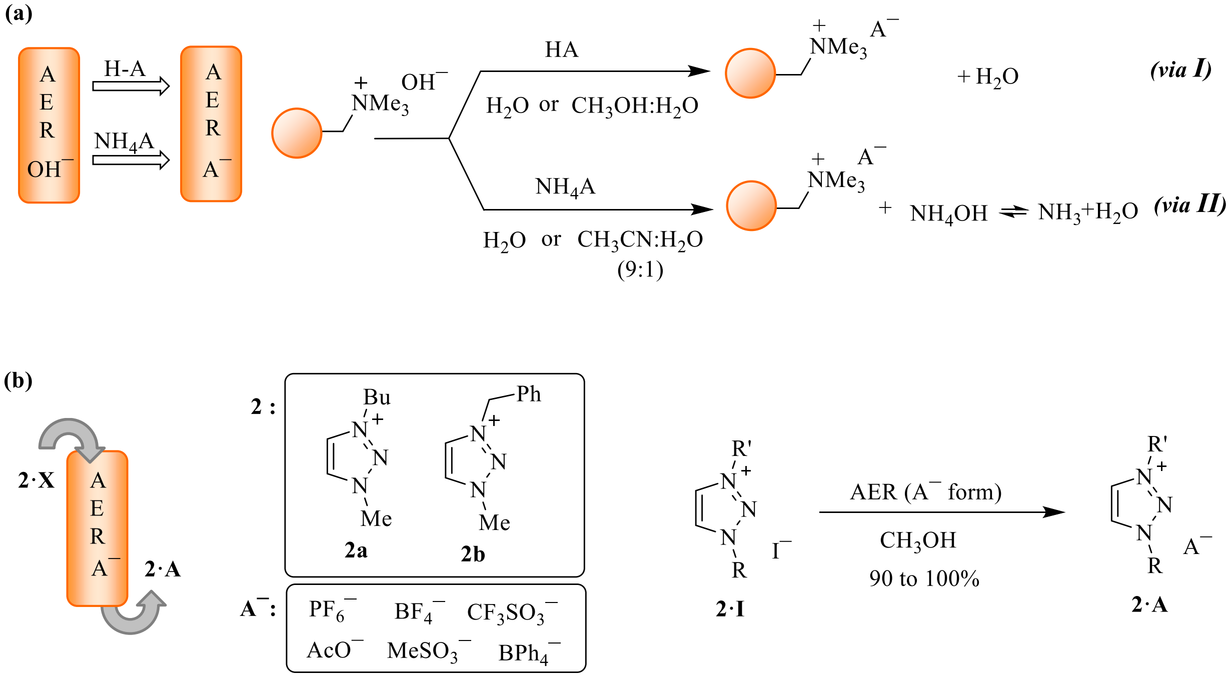
Following a modified experimental procedure previously reported by Hassner et al.,[21] benzyl azide **4** was obtained in 93% yield from both benzyl bromide and chloride using a strong basic AER (N_3^- form) in CH_3CN/CH_3OH (1:1) (Scheme 2). Applying our protocol, bis(azidomethyl)arenes **5** and **6** were prepared by stirring the reaction mixture of the corresponding benzylic halides **7** and **8** and the azide-loaded strong basic AER (N_3^- form) in organic solvents under mild and safe conditions with a direct work-up. After examining various nucleophilic substitution reaction conditions, the best results were observed when using a solvent mixture of CH_3CN/CH_3OH (1:1) or CH_3CN/CH_2Cl_2 (1:1) to give the diazides **5** and **6**, respectively, in 95% yield (Scheme 2 and *Supplementary Material*).



Scheme 2. Preparation of benzyl azide **4** and bis(azidomethyl)arenes **5**, **6** using an azide-loaded strong basic AER (N_3^- form) in organic solvents.

Halide-to-anion exchange: AER (A¯ form) method

The anion sources used to load the selected anions were mainly *via I* from acids or *via II* from the corresponding ammonium salt (Scheme 3 and Table 1). Thus, the AER (OH^- form) was packed in a column and treated with a hydromethanolic solution of the acid or ammonium salt. Following *via I*, the loading was performed with the hydromethanolic solution of AcOH or $MeSO_3H$ and the aqueous inorganic acids HPF_6 or HBF_4. In *via II*, anions such as $CF_3SO_3^-$, PF_6^- and BF_4^- were loaded in the resin using aqueous solutions of their ammonium salts, while the lipophilic BPh_4^- anion required CH_3CN/H_2O (9:1) solvent mixture. When the anions were loaded in the AER, we examined the efficiency of the counteranion exchange using 1,2,3-triazolium ionic liquids, due to their recent interest as stable and recyclable solvents.[15-18] A recent study has shown that the key physicochemical aspects of 1,2,3-triazolium-based ILs are their high electrochemical stability and ionic conductivity, which are comparable to their imidazolium counterparts, yet with the advantage that the 1,2,3-triazolium nucleus seems to be more robust under alkaline reaction conditions.[29]



Scheme 3. AER (A^- form) method applied to 1,2,3-triazolium ionic liquids **2·I**. **(a)** Anion loading and anion source. **(b)** Iodide-to-anion exchange of **2a·I** and **2b·I**.

The AER (A^- form) method was then applied to both 1,2,3-triazolium compounds, 1-buthyl-3-methyltriazolium iodide **2a·I** and 1-benzyl-3-methyltriazolium iodide **2b·I**, and the halide exchange for representative anions proceeded in 90% to quantitative yields when methanol was used (Table 1), improving the results obtained using classical methods.[15] However, when the recovery of the new ion pairs **2a·A** or **2b·A** was around 90%, further studies to increase the yield using a less polar solvent, for example acetonitrile, were not carried out.

Table 1. Iodide-to-anion exchange of 1,2,3-triazolium-based ionic liquids in methanol

		2a$^+$		**2b$^+$**	
Anion	**Loading**[a]	**Yield (%)**[b]	**I^- (ppm)**[c]	**Yield (%)**[b]	**I^-(ppm)**[c]
AcO^-	via I[d]	100	<20	100	<20
$MeSO_3^-$	via I[d]	92	<20	94	<20
PF_6^-	via I[e] or via II[e]	90	20-40	97	<20
BF_4^-	via I[e] or via II[e]	94	20-40	90	20-40
$CF_3SO_3^-$	via II[d]	93	20-40	92	<20
BPh_4^-	via II[f]	92	<20	—	

[a]Anion source: via I and/or via II (Scheme 3). [b]Isolated yield. [c]Halide contents after anion exchange determined by the silver chromate test. [d]Solvent loading: $CH_3OH:H_2O$. [e]Solvent loading: H_2O. [f]Solvent loading: $CH_3CN:H_2O$ (9:1).

The prepared ion pairs were dried in a vacuum oven at 60 ºC in the presence of desiccant agents and their characterization was confirmed by spectroscopic and spectrometric methods, especially ^{1}H NMR, and when necessary unambiguous assignments were made by NOESY experiments at 400 MHz. Moreover, the amount of halide content was determined by a silver chromate test following a similar protocol to that described by Sheldon and co-workers.[30] Additionally, it should also be considered that the AER used in the exchange can be recycled by treatment with 10% NaOH aqueous solution, and the recovered AER (OH^- form) can be re-utilized for a new anion loading. The chosen strong AER was Amberlyst® A-26 but other similar AERs such Aberlite® IRA-400, which allow the use of aqueous mixtures and non-aqueous solvents, can be used instead.

^{1}H NMR spectroscopy

Imidazolium-based systems form a bridge between the chemistry of ionic liquids (ILs) and anion recognition, notable noncovalent driving forces being a combination of electrostatics and hydrogen bond interactions.[6,31] Particularly significant is the role of the non-classical $(C–H)^+\cdots$anion hydrogen bonds in imidazolium-based anion receptors, sensors and carriers, as well as in ILs, which has sparked a flurry of interest and debate in the last few years. Evidence for hydrogen bonding in the solid phase of the simple 1-ethyl-3-methylimidazolium salt **[emim]I** was first reported by Seddon and co-workers in 1986,[32] and later in **[emim]A** using single-crystal X-ray diffraction analysis,[33-35] and confirmed in the solution-phase by multinuclear NMR spectroscopy.[36] Moreover, Ludwig and co-workers reported direct spectroscopic evidence for an enhanced cation-anion interaction driven by $(C–H)^+\cdots$anion hydrogen bonds in pure ILs, which gave a stronger the role to hydrogen bonds in imidazolium ILs.[19-20]

Depending on the structure of the imidazolium-based frameworks, other noncovalent intermolecular interactions can also take place between cations and counteranions, a case in point being the usually weaker CH/π noncovalent interactions that can be rather significant for anions bearing aromatic units, e.g. tetraphenylborate.[6] Thus, the structural study of **1a·BPh$_4$** (**[bmim][BPh$_4$]**) reported by Dupont et al. revealed the presence of $(C–H)^+\cdots\pi$ hydrogen bonds both in solution phase and solid state.[37,38] The anion effect has also been examined by Lungwitz and Spange using the representative **1a·A** (**[bmim]A**) ion pairs in dichloromethane as the solvent, which in fact should lower solvation of the ion pairing in favor of contact ion pairs. A hydrogen-bond accepting (HBA) ability scale was then established for varied anions of the **(bmim$^+$)** cation by means of ^{1}H NMR spectroscopy, at concentrations of 0.02 or 1.8 M, in CD_2Cl_2, and the HBA capacity of anions directly affected chemical shift values in the imidazolium moiety, especially the C(2)-H of the imidazolium ring.[38] As already mentioned, the use of CD_2Cl_2 as a solvent implies minimizing solute-solvent interactions.[37,40]

The ^{1}H NMR data obtained from the routine checking of the quaternary heteroaromatic salts [**ILs]A** provide useful information about the noncovalent interactions between the cations and the counteranions. Following with our work, the ^{1}H NMR spectral data of **1a·A** (**[bmim]A**) in a selected 0.02 M concentration were registered in $CDCl_3$ and CD_3CN and the chemical shift values of C(2)-H of the imidazolium ring were compared, as shown in Figure 2. Standard reference values were obtained from samples whose purity had been confirmed by other techniques. As expected, chemical shift values of C(2)-H varied according to the anion, with higher deshielding when a strong hydrogen bond anion binding interaction was established. Excluding **1a·BPh$_4$** (**[bmim][BPh$_4$]),** the proton chemical shift differences were greater in $CDCl_3$, reaching more than 2 ppm when comparing *e.g.* AcO^- and PF_6^-, while the differences decreased when using a solvent that enhances the solvation effect such as the nonhydroxylic dipolar CD_3CN (see figure 2).

In contrast, the observed proton NMR chemical shift of **1a·BPh$_4$** (**[bmim][BPh$_4$]**) showed a greater shielding in $CDCl_3$ for C(2)-H (δH = 4.54 ppm) due to the CH/π interactions with the aromatic units of the anion, while in a dipolar-aprotic solvent such as CD_3CN, this interaction was weakened by solvation (δH = 8.19 ppm). These results are in accordance with the abovementioned in-depth structural study of **1a·BPh$_4$** (**[bmim][BPh$_4$]**) reported by Dupont et al.[37]

The data obtained allowed us to establish a pattern of proton chemical shift values, which was then used to check the effectiveness of halide-for-anion exchange, especially useful for inorganic anions.

In addition, it is well established that the chemical shifts of the acidic C(2)–H protons in the imidazolium motifs are the most sensitive to the nature of the counteranion, solvent polarity and structural factors of imidazolium-based systems such as anion receptors and sensors[6] as well as ILs.[38,41] In order to compare imidazolium and triazolium cation behaviour, ionic liquids **1a·A** and **2b·A** were further examined by ^{1}H NMR in $CDCl_3$ and CD_3CN at concentrations of 0.002 and 0.02 M to ascertain the influence of the counteranion and the solvent polarity on the heteroaromatic proton chemical shifts of imidazolium and 1,2,3-triazolium cations (see Figure 3 and Table 2). As the counteranion, the basic oxoanion AcO^-, the halide Cl^- and the weaklycoordinating and charge diffuse PF_6^- anion were selected as representative examples,[42,43] the results being summarized in Table 2.

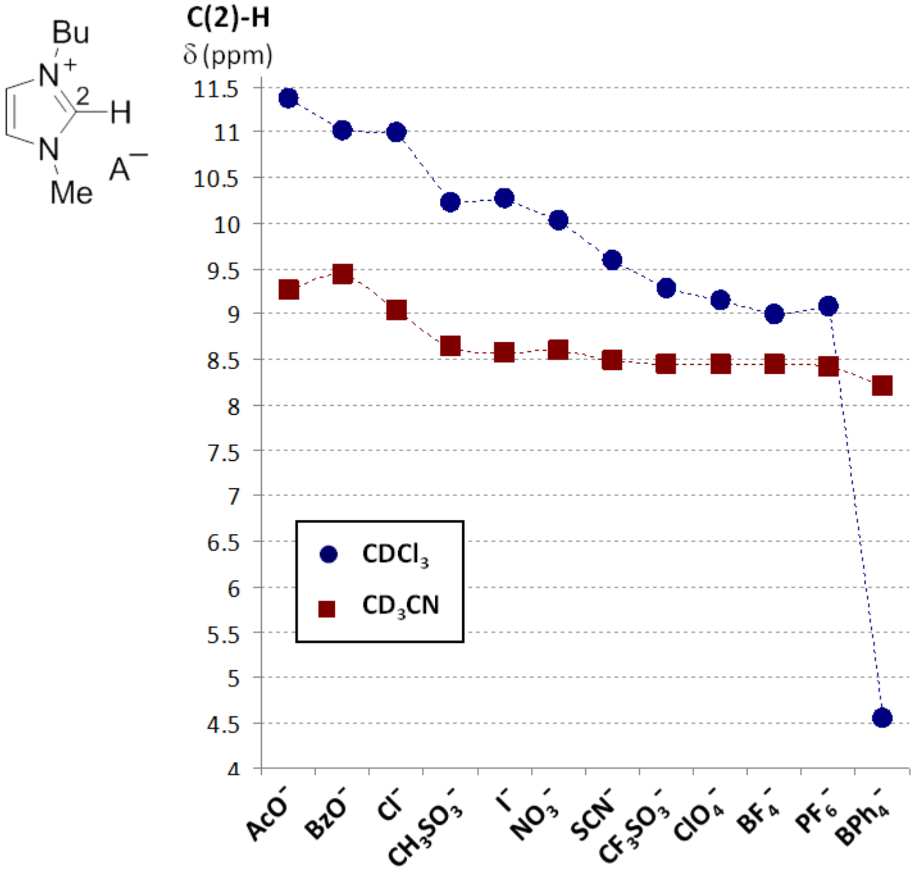


Figure 2. 1-butyl-1-methylimidazolium salts **1a·A ([bmim]A)**: ^1H NMR C(2)-H chemical shift at 300MHz of a 0.02 M solution in $CDCl_3$ (●) or CD_3CN (■).

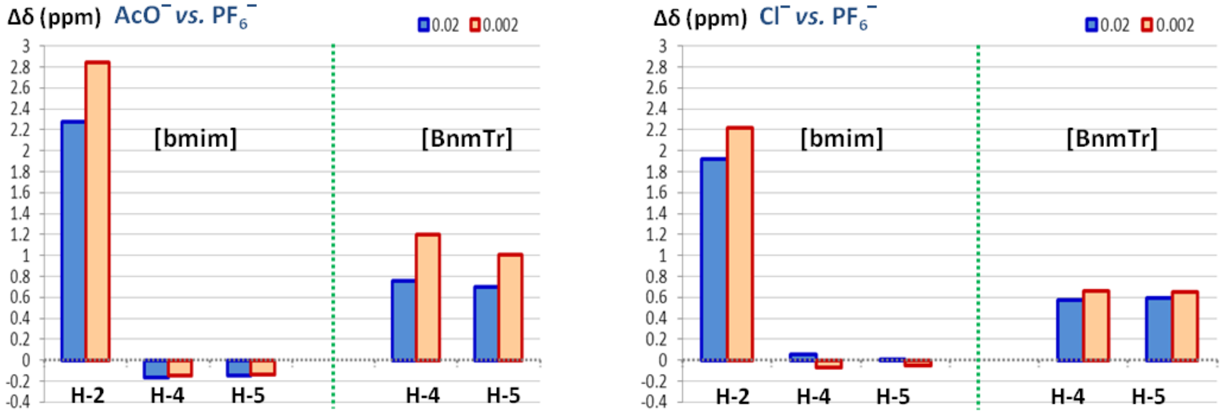
Table 2. Selected ^1H NMR (300 MHz) chemical shift values of **1a·A** (**[bmim]A**) and **2b·A** (**[BnmTr]A**) in $CDCl_3$ and CD_3CN at concentrations of 0.02 M and 0.002 M

[bmim]$^+$		**0.002 M**			**0.02 M**			**[BnmTr]$^+$**		**0.002 M**		**0.02 M**	
A^-	**Solvent**	**H-2**	**H-4**	**H-5**	**H-2**	**H-4**	**H-5**	**A^-**	**Solvent**	**H-4**	**H-5**	**H-4**	**H-5**
AcO^-	$CDCl_3$	11.81	7.08	7.07	11.35	7.09	7.08	AcO^-	$CDCl_3$	9.91	9.60	9.60[a]	9.44[a]
	CD_3CN	8.93	7.34	7.31	9.25	7.35	7.32		CD_3CN	8.61	8.43	8.89	8.61
Cl^-	$CDCl_3$	11.19	7.16	7.16	10.99	7.31	7.24	Cl^-	$CDCl_3$	9.37	9.24	9.41	9.33
	CD_3CN	8.70	7.36	7.33	9.04	7.39	7.36		CD_3CN	8.33	8.28	8.40	8.32
PF_6^-	$CDCl_3$	8.97	7.23	7.21	9.07	7.26	7.23	PF_6^-	$CDCl_3$	8.71	8.59	8.84	8.74
	CD_3CN	8.38	7.34	7.31	8.42	7.35	7.31		CD_3CN	8.31	8.26	8.32	8.27

[a] Unambiguous assignments were made by NOESY-1D (400 MHz).

The tendency of the imidazolium molecular motif in current **1a·A** (**[bmim]A**) ion pairs to form non-classical $(C–H)^{+}\cdots$anion hydrogen bonds was then qualitatively examined by ^{1}H NMR and the greatest deshielding effect corresponded to the acidic C(2)-H when comparing **1a·AcO** or **1a·Cl** with **1a·PF₆**, in both $CDCl_3$ ($\Delta\delta \geq 2$ ppm) and CD_3CN ($\Delta\delta \geq 0.3$ ppm), while differences in proton chemical shifts of C(4)-H and C(5)-H were negligible. In contrast, in quaternary 1,2,3-triazolium salts **2b·A** (**[BnmTr]A**) a significant deshielding of C(4)-H and C(5)-H was observed, although the Δδ (H-4 or H-5) was lower than Δδ (H-2) in the imidazolium cation (see Figure 3 and Table 2).

(a) $CDCl_3$ (300 MHz)



(b) CD_3CN (300 MHz)

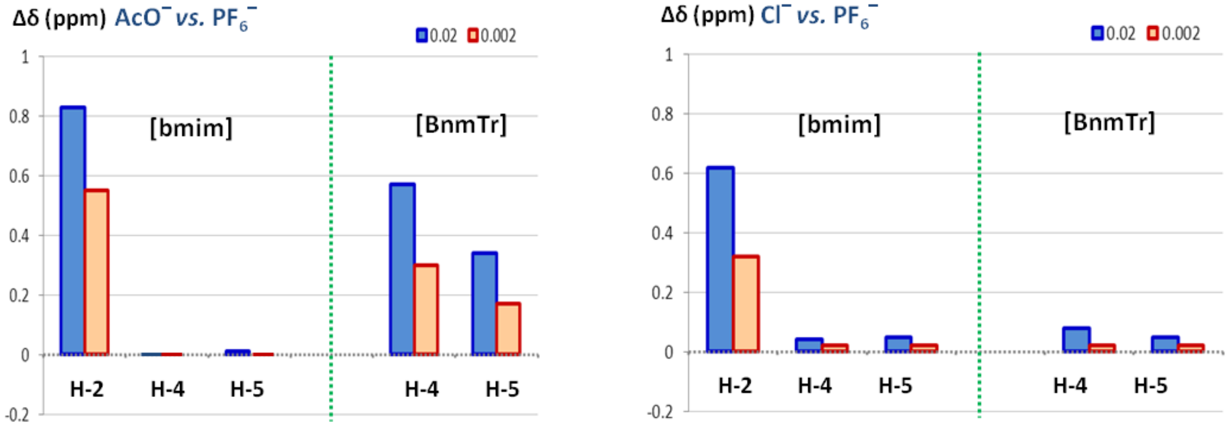


Figure 3. Differences in heterocyclic proton chemical shifts between AcO^{-} or Cl^{-} and PF_6^{-} salts at concentrations of 0.02 and 0.002 M in **(a)** $CDCl_3$ or **(b)** CD_3CN.

In relation to the solvent and concentration, in $CDCl_3$ we verified that by increasing the dilution the cation-anion interaction was enhanced and consequently higher chemical shift values were obtained at 0.002M than 0.02M, whereas the contrary was observed in CD_3CN due to the competitive solvating effect (see Figure 3 and Table 2).

Regarding the anion, both quaternary azolium salts displayed hydrogen-bonding interaction with AcO^{-}, but in CD_3CN the triazolium cation showed poor Cl^{-} binding affinity (see Figure 3). It should be noted that the basicity of the AcO^{-} anion could result in the formation of carbene species,[44,45] although this was not observed in the experiments carried out.

The results of the present work are in concordance with the anion affinity profile of the azolium units as recognition moieties in abiotic anion receptors. They also confirm that the hydrogen bonding ability and acidity of azolium based ILs should be considered when they are used as solvents, since the interactions with reactants and intermediates could affect the course of the reaction.

Conclusions

Against a pool of quaternary heteroaromatic ionic liquids, the azolium salts **2a·I** and **2b·I** were chosen to validate the utility of the AER (A^{-} form) method in non-aqueous media for a halide exchanged by assorted anions. It was then confirmed that this simple method is efficient with 1,2,3-triazolium-based ionic liquids **2·X**, improving the currently operative procedures of classical counteranion exchange, *e.g.* **2a·BF_4**, **2a·PF_6** and **2a·CF_3SO_3** prepared from **2a·I**. Recapping the results, the anion loading of the AER (OH^{-} form) with acids, ammonium salts and sodium azide was carried out in water or a hydromethanolic or CH_3CN/H_2O (9:1) solvent mixture according to the lipophilic nature of the anion source. Then, the anion exchange using the AER (A^{-} form) method in organic solvents was easily applied to the1,2,3-triazolium salts and the halide-to-anion exchange progressed in excellent to quantitative yields.

On the whole, the AER (A^{-} form) method in organic solvents is a method of choice for exchanging halide anions for a variety of anions in quaternary heteroaromatic salts, simultaneously removing halide impurities, which is often a troublesome task, and minimizing the formation of toxic by-products. In addition, the preparation of a few benzylic azides and diazides was carried out using an AER (N_3^{-} form) in organic solvent mixtures such as CH_3CN/CH_3OH (1:1) and CH_3CN/CH_2Cl_2 (1:1), resulting in a clean and mild protocol with easy work-up. The results of the ^1H NMR spectroscopic analysis focus attention on the significance of the charged-assisted $(C–H)^{+}\cdots$anion hydrogen bonds. Thus, a qualitative ^1H NMR comparison between 1-butyl-3-methylimidazolium salts and 1-benzyl-3-methyl-1,2,3-triazolium salts has shown that the nature of the azolium motifs modulated their ^1H NMR response.

Experimental Section

General. Ion exchanger resin Amberlyst A-26 (Aldrich, OH^{-} form), benzylbromide and benzylchloride together with all acids, ammonium salts, reagents and solvents were purchased from commercial suppliers, unless mentioned otherwise, and used without further purification.

All solvents were reagent grade and methanol and THF were distilled prior to use. 1-buthyl-3-methylimidazolium salts **1a·A**,[1] 1-buthyl-3-methyltriazolium iodide **2a·I**,[15] 1-benzyl-3-methyltriazolium iodide **2b·I**,[15] 1,3-bis(bromomethyl)-4-*tert*-butylbenzene **7**,[46] and 9,10-bis(chloromethyl)antracene **8**[47] were prepared according with the literature. ^{1}H NMR spectra were recorded on a Varian Gemini 300 (300 MHz) or Mercury 400 (400 MHz) spectrometers at 298 K. Chemical shifts were referenced and expressed in ppm (δ) relative to the central peak of DMSO-d_6 (2.49 ppm), CD_3CN (1.94 ppm) and TMS for $CDCl_3$. ^{13}C NMR spectra were recorded on a Varian Gemini 300 (75.4 MHz) or Mercury 400 (100.6 MHz) spectrometer at 298 K. IR spectra were recorded on a Thermo Nicolet Avatar 320 FTIR apparatus. Mass spectrometric analyses were performed by using EI at 70 eV in a Hewlett-Packard spectrometer (HP-5989A model) or by using CI at 120 eV in a Thermo Finnigan TRACE DSQ spectrometer. ESI(+)-MS and ESI(-)-MS mass spectra were obtained on a LC/MSD-TOF (2006) mass spectrometer with a pumping system HPLC Agilent 1100 from Agilent Technologies at Serveis Científico-Tècnics of universitat de Barcelona. Melting points was measured in a Gallenkamp Melting Point Apparatus MPD350.BM2.5 with digital thermoter and are uncorrected. The pH was measured with benchmeter pH1100 (Eutech Instrunments), using Hamilton Flushtrode pH electrode for hydroalcoholic solutions.

The amount of halide contents was determined by a silver chromate test following a similar protocol to that described by Sheldon and co-workers.[30] An aqueous solution (5 mL) of potassium chromate (5 % p/v in Milli-Q water, 0.257 M) was added to the sample (5-10 mg). To 1 mL of the resulting dark yellow solution was added a minimum amount of silver nitrate aqueous solution (0.24 % p/v in Milli-Q water, 0.014 M). A persistent red suspension of silver chromate would be observed if the sample was free of halide. The minimum measurable amount of silver nitrate aqueous solution was 0.011 mL; consequently, the detection limit is approx. 6 ppm for Cl^-, 13 ppm for Br^- or 20 ppm for I^-. The halide content was determined at least twice for each sample.

Additionally, the use of alumina and silica columns can leave a low level of residual particulate contamination in ILs[1,14] and then, nano-particulates may also be an issue when using strongly basic anion exchange resins (A^- form). However, the analysis of possible particulate contamination was beyond the scope of the present study.

Preparation of the AER (N3$^-$ form). 12 g of wet Amberlyst® A-26 (OH^- form) were packed in a glass column and washed with H_2O (100 mL). A 10% NaN_3 aqueous solution (160 mL, 246 mmol) was passed slowly through the AER (OH^- form) until the pH of eluates reached the same value than the original solution (pH~10.25). Then, AER (N_3^- form) was washed with H_2O (50 mL), H_2O:CH_3OH progressive mixtures (9:1, 7:3, 5:5, 3:7, 1:9; 50 mL of each mixture) and CH_3OH:CH_3CN progressive mixtures (9:1, 7:3, 5:5; 50 mL of each mixture). The calculated amount of N_3^- loaded in the resin is 5.8 mmol/g.[1]

Benzylazide (4). *(a) From benzylchloride*. The AER (N_3^- form) (12 g , 69.4 mmol of N_3^-) was added to a solution of benzylchloride (1.099 g, 1 mL, 8.68 mmol) in 30 mL of CH_3CN: CH_3OH

(1:1) solvent mixture, and the suspension was heated under stirring at 40 ºC for 2.5 h. The AER was filtered and the solvent was eliminated under vacuum providing the oily pure benzylazide **4** (1.069 g, 93% yield). As a caution the product was stored in the freezer until further use.

(b) From benzylbromide. The AER (N_3^- form) (8.7 g , 50.3 mmol of N_3^-) was added to a solution of benzylbromide (1.438 g, 1 mL, 8.40 mmol) in 30 mL of CH_3CN:CH_3OH (1:1) solvent mixture, and the suspension was stirred at room temperature for 1.5 h. The AER was filtered and the solvent was eliminated under vacuum, providing the oily pure benzylazide **4** (1.040 g, 93% yield). As a caution, the product was stored in the freezer until further use. IR (NaCl): 3031, 2096 (N_3), 1454, 1227, 695 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.35 (s, 2H), 7.34-7.40 (m, 5H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 54.85, 128.1, 128.2, 128.8, 135.4.

1,3-bis(Azidomethyl)-4-tert-butylbenzene (5). The AER (N_3^- form) (3.45 g , 20 mmol of N_3^-) was added to a solution of 1,3-bis(bromomethyl)-4-*tert*-butylbenzene **7** (0.400 g, 1.250 mmol) in 25 mL of CH_3CN:CH_3OH (1:1) solvent mixture and the suspension was stirred at room temperature for 2 h. Then, the AER was filtered, washed with CH_3CN:CH_3OH (1:1) (25 mL) and the solvent was removed under vacuum, to afford the pure diazide **5** (0.290 g, 95%) as orange oil. As a caution, the product was stored in the freezer until further use. IR (NaCl): 2967, 2111 (N_3), 1600, 1323, 1269, 690 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 (s, 9H), 4.37 (s, 4H), 7.10 (s, 1H), 7.30 (s, 2H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 31.2, 34.8, 54.9, 125.0, 125.1, 135.8, 152.7. CIMS *m/z* (%): 263 (75) [$M+NH_4$], 217 (100) [$M+H-N_2$]; 189 (74) [$M+H-2N_2$].

9,10-bis(Azidomethyl)antracene (6). The AER (N_3^- form) (3.14 g , 18.18 mmol of N_3^-) was added to a solution of 9,10-bis(chloromethyl)antracene **8** (0.250 g, 0.909 mmol) in 40 mL of CH_3CN:CH_2Cl_2 (1:1) solvent mixture and the suspension was heated under stirring at 40 ºC for 7.5 h. The AER was filtered, washed with CH_3CN: CH_2Cl_2 (1:1) (25 mL) and the solvent was removed under vacuum, to afford the pure diazide **6** (0.290 g, 95%) as orange solid. As a caution, the product was stored in the freezer until further use. mp 107–108 °C. IR (KBr): 3065, 2922, 2075 (N_3), 1445, 1088, 750 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.36 (s, 4H), 7.65 (m, 4H), 8.37 (m, 8H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 46.4, 124.5, 126.6, 128.1, 130.4.

Anion loading in the AER (OH^- form)

(via I) Acids as anion source. 2.5 g (~ 3 cm^3) of commercial wet strongly basic anion exchange Amberlyst A-26 (OH^- form) was packed in a glass column (1 cm diameter) and washed with water, and the column bed was equilibrated progressively with water-methanol mixtures until reaching the selected solvent media used afterwards for anion loading (~ 25 mL of each solvent mixture). A 1% acid solution in the appropriate solvent was passed slowly through the resin until the eluates had the same pH value as the original selected acid solution, and then the resin was washed with solvent until constant pH. The process was carried out at room temperature, using gravity as the driving force.

(via II) Ammonium salts as anion source. 2.5 g (~ 3 cm^3) of commercial wet strongly basic anion exchange Amberlyst A-26 (OH^- form) was packed in a glass column (1 cm diameter) and washed with water (~ 25 mL). A 1% ammonium salt aqueous solution was passed slowly through the resin until the eluates had the same pH value as the original selected acid solution,

and then the resin was washed with water until constant pH. The process was carried out at room temperature, using gravity as the driving force. In order to load BPh_4^- anion, a $CH_3CN:H_2O$ (9:1) solvent mixture was used and the process involves to wash the AER (OH^- form) with the same solvent mixture previously to pass the ammonium salt solution.

Anion exchange: general procedure. A solution of the triazolium salt (0.5-0.6 mmol) in 10 mL of methanol was passed slowly through a column packed with ~ 3 cm^3 of AER (A^- form), and then washed with 25 mL of solvent. The combined eluates were evaporated, and the residue obtained was dried in a vacuum oven at 60 ºC with P_2O_5 and KOH pellets.

1-Buthyl-3-methyltriazolium acetate (2a·AcO). Iodide exchange of **2a·I** (0.110 g, 0.412 mmol) was carried out with AER (AcO^- form) following the general procedure described above, and using CH_3OH as solvent. Brown oil (82 g, quantitative yield). ^1H NMR (300 MHz, $CDCl_3$): δ 0.96 (t, 3H), 1.38 (m, 2H), 1.94 (s, 3H, AcO), 1,98 (m, 2H), 4.42 (s, 3H), 4.64 (t, 2H), 9.66 (s, 1H), 9.92 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 13.3, 19.3, 31.1, 40.1, 53.4, 53.6, 131.0, 132.0, 133.5. Iodide content < 20 ppm according silver chromate test.

1-Buthyl-3-methyltriazolium methylsulphonate (2a·MeSO₃). Iodide exchange of **2a·I** (0.100 g, 0.374 mmol) was carried out with AER ($MeSO_3^-$ form) following the general procedure described above, and using CH_3OH as solvent. Yelow oil (0.081 g, 92% yield). ^1H NMR (300 MHz, $CDCl_3$): δ 0.97 (t, 3H), 1.40 (m, 2H), 1,99 (m, 2H), 2.76 (s, 3H, $MeSO_3$), 4.45 (s, 3H), 4.68 (t, 2H), 9.22 (s, 1H), 9.32 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 13.2, 19.3, 31.2, 39.4, 40.1, 53.5, 131.5, 132.4. Iodide content < 20 ppm according silver chromate test.

1-Buthyl-3-methyltriazolium tetrephenylborate (2a·BPh₄). Iodide exchange of **2a·I** (0.110 g, 0.412 mmol) was carried out with AER (BPh_4^- form) following the general procedure described above, and using CH_3OH as solvent. Light brown solid (0.175 g, 92% yield). mp 149-50 ºC. ^1H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, 3H), 1.13 (m, 2H), 1,50 (m, 2H), 3.00 (s, 3H), 3.49 (t, 2H), 5.48 (s, 1H), 5.50 (s, 1H), 6.78 (d, 8H), 6.95 (t, 4H), 7.51 (t, 8H). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 13.2, 19.2, 30.8, 38.9, 52.9, 122.0, 125.9, 129.3, 130.3, 135.9, 164.1 (m, C-B). Iodide content < 20 ppm according silver chromate test.

1-Buthyl-3-methyltriazolium hexafluorophosphate (2a·PF₆). Iodide exchange of **2a·I** (0.100 g, 0.374 mmol) was carried out with AER (PF_6^- form) following the general procedure described above, and using CH_3OH as solvent. Yellow oil (0.96 g, 90% yield). ^1H NMR (300 MHz, $CDCl_3$): δ 0.98 (t, 3H), 1.40 (m, 2H), 2.00 (m, 2H), 4.38 (s, 3H), 4.60 (t, 2H), 8.59 (s, 1H), 8.63 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 13.2, 19.3, 31.1, 40.0, 53.8, 130.4, 131.5. NMR spectral data were according with those reported in the literature.[15] Iodide content < 20 ppm according silver chromate test.

1-Buthyl-3-methyltriazolium triflate (2a·CF₃SO₃). Iodide exchange of **2a·I** (0.100 g, 0.374 mmol) was carried out with AER ($CF_3SO_3^-$ form) following the general procedure described above, and using CH_3OH as solvent. Yelow oil (0.100 g, 93% yield). ^1H NMR (300 MHz, $CDCl_3$): δ 0.94 (t, 3H), 1.37 (m, 2H), 1.96 (m, 2H), 4.36 (s, 3H), 4.59 (t, 2H), 8.74 (s, 1H), 8.76 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 13.2, 19.2, 31.2, 40.5, 53.9, 130.9, 131.9, 120.6 (m, C-

F). NMR spectral data were according with those reported in the literature.[15] Iodide content < 20 ppm according silver chromate test.

1-Buthyl-3-methyltriazolium tetrafluoroborate (2a·BF$_4$). Iodide exchange of **2a·I** (0.110 g, 0.412 mmol) was carried out with AER (BF$_4^-$ form) following the general procedure described above, and using CH$_3$OH as solvent. Yelow oil (0.088 g, 94% yield). ^{1}H NMR (300 MHz, CDCl$_3$): δ 0.98 (t, 3H), 1.40 (m, 2H), 2.00 (m, 2H), 4.39 (s, 3H), 4.14 (t, 2H), 8.66 (s, 1H), 8.73 (s, 1H). ^{13}C NMR (CDCl$_3$, 75.4 MHz): δ 13.2, 19.3, 31.1, 40.0, 53.7, 130.7, 131.8. NMR spectral data were according with those reported in the literature.[15] Iodide content < 20 ppm according silver chromate test.

1-Benzyl-3-methyltriazolium acetate (2b·AcO). Iodide exchange of **2b·I** (0.100 g, 0.332 mmol) was carried out with AER (AcO$^-$ form) following the general procedure described above, and using CH$_3$OH as solvent. Colorless oil (0.077 g, quantitative yield). ^{1}H NMR (300 MHz, CDCl$_3$): δ 1.98 (s, 3H, AcO), 4.40 (s, 3H), 5.82 (s, 2H), 7.42 (m, 3H), 7.47 (m, 2H), 9.44 (s, 1H), 9.60 (s, 1H). ^{13}C NMR (CDCl$_3$, 75.4 MHz): δ 39.9, 56.6, 57.3, 129.0, 129.1, 129.5, 130.9, 132.0, 132.5, 133.5. Iodide content < 20 ppm according silver chromate test.

1-Benzyl-3-methyltriazolium methylsulphonate (2b·MeSO$_3$). Iodide exchange of **2b·I** (0.100 g, 0.332 mmol) was carried out with AER (MeSO$_3^-$ form) following the general procedure described above, and using CH$_3$OH as solvent. Colorless oil (0.084 g, 94% yield). ^{1}H NMR (300 MHz, CDCl$_3$): δ 2.78 (s, 3H, MeSO$_3$), 4.43 (s, 3H), 5.87 (s, 2H), 7.40 (m, 3H), 7.52 (m, 2H), 9.25 (s, 1H), 9.29 (s, 1H). ^{13}C NMR (CDCl$_3$, 75.4 MHz): δ 39.5, 40.2, 57.1, 129.2, 129.3, 129.7, 131.4, 131.8, 132.6, Iodide content < 20 ppm according silver chromate test.

1-Benzyl-3-methyltriazolium hexafluorophosphate (2b·PF$_6$). Iodide exchange of **2b·I** (0.100 g, 0.332 mmol) was carried out with AER (PF$_6^-$ form) following the general procedure described above, and using CH$_3$OH as solvent. White solid (0.103 g, 97% yield). mp 89-90 ºC. ^{1}H NMR (300 MHz, CDCl$_3$): δ 4.37 (s, 3H), 5.75 (s, 2H), 7.44 (m, 5H), 8.74 (s, 1H), 8.84 (s, 1H). ^{13}C NMR (CDCl$_3$, 75.4 MHz): δ 40.1, 57.2, 129.3, 129.4, 129.7, 130.5, 131.4, 131.8. Iodide content < 20 ppm according silver chromate test.

1-Benzyl-3-methyltriazolium triflate (2b·CF$_3$SO$_3$). Iodide exchange of **2b·I** (0.100 g, 0.332 mmol) was carried out with AER (CF$_3$SO$_3^-$ form) following the general procedure described above, and using CH$_3$OH as solvent. Colorless oil (0.099 g, 92% yield). ^{1}H NMR (300 MHz, CDCl$_3$): δ 4.37 (s, 3H), 5.75 (s, 2H), 7.43 (m, 3H), 7.48 (m, 2H), 8.71 (s, 1H), 8.78 (s, 1H). ^{13}C NMR (CDCl$_3$, 75.4 MHz): δ 40.5, 57.5, 129.4, 129.5, 130.0, 130.8, 131.2, 132.2, 120.5 (m, C-F). NMR spectral data were according with those reported in the literature.[15] Iodide content < 20 ppm according silver chromate test.

1-Benzyl-3-methyltriazolium tetrafluoroborate (2b·BF$_4$). Iodide exchange of **2b·I** (0.100 g, 0.332 mmol) was carried out with AER (BF$_4^-$ form) following the general procedure described above, and using CH$_3$OH as solvent. White solid (0.078 g, 90% yield). mp 74-5 ºC. ^{1}H NMR (300 MHz, CDCl$_3$): δ 4.33 (s, 3H), 5.72 (s, 2H), 7.40 (m, 3H), 7.46 (m, 2H), 8.51 (s, 1H), 8.55 (s, 1H). ^{13}C NMR (CDCl$_3$, 75.4 MHz): δ 40.1, 57.3, 129.3, 129.4, 129.8, 130.7, 131.5, 132.0.

NMR spectral data were according with those reported in the literature.[15] Iodide content < 20 ppm according silver chromate test.

Acknowledgements

The authors thank to the support of the University of Barcelona, SCT-UB for the use of their instruments, and the AGAUR (Generalitat de Catalunya), *Grup de Recerca Consolidat* 2009SGR562.

References

[†] Imidazolium-based frameworks. 25. Part 24: reference 1.

1. Alcalde, E.; Dinarès, I.; Ibá-ez, A.; Mesquida, N. A *Molecules* **2012**, *17*, 4007–4027 and references cited.
2. Recent reviews on anion complexation include references 3-5 and those that provide an overview on azolium-based systems include references 6-9. Recent reviews on ionic liquids include references 10-11 and those that provide a current overview on ILs from the viewpoint of their synthesis, anion exchange (metathesis) and purification include references 12-14.
3. Hargrove, A. E.; Nieto, S.; Zhang,T.; Sessler, J. L.; Anslyn, E. V. *Chem. Rev.* **2011**, *111*, 6603–6782.
   http://dx.doi.org/10.1021/cr100242s
   PMid:21910402 PMCid:PMC3212652
4. Wenzel, M.; Hiscock, J.R.; Gale, P.A. *Chem. Soc. Rev.* **2012**, *41*, 480-520
   http://dx.doi.org/10.1039/c1cs15257b
   PMid:22080279
5. Caltagirone, C.; Gale, P.A. *Chem. Soc. Rev.* **2009**, *38*, 520–563.
   http://dx.doi.org/10.1039/b806422a
   PMid:19169465
6. Alcalde, E.; Dinarès, I.; Mesquida, N. *Top. Heterocycl. Chem.* **2010**, *24*, 267–300.
   http://dx.doi.org/10.1007/7081_2010_34
7. Xu, Z.; Kim, S.K.; Yoon, *J. Chem. Soc. Rev.* **2010**, *39*, 1457–1466.
   http://dx.doi.org/10.1039/b918937h
   PMid:20419201
8. Baker, M.V.; Brown, D.H. *Mini-Rev. Org. Chem. 2006*, *3*, 333–354.
   http://dx.doi.org/10.2174/157019306778742869
9. Lee, S.; Flood, A.H. *Top. Heterocycl. Chem.* **2012**, *28*, 85–107.
   http://dx.doi.org/10.1007/7081_2011_70

10. Dupont, J. *Acc. Chem. Res*. **2011**, *44*, 1223–1231.
    http://dx.doi.org/10.1021/ar2000937
    PMid:21770406
11. Mecerreyes, D. *Progress in Polymer Science* **2011**, *36*, 1629-1648.
    http://dx.doi.org/10.1016/j.progpolymsci.2011.05.007
12. Sowmiah, S.; Srinivasadesikan, V.; Tseng, M.-C.; Chu, Y.-H. *Molecules* **2009**, *14*, 3780–3813.
    http://dx.doi.org/10.3390/molecules14093780
    PMid:19783957
13. Deetlefs, M.; Seddon, K.R. *Green Chem*. **2010**, *12*, 17–30.
    http://dx.doi.org/10.1039/b915049h
14. Clare, B.; Sirwardana, A.; MacFarlane, D.R. *Top. Curr. Chem.* **2009**, *290*, 1–40.
    http://dx.doi.org/10.1007/128_2008_31
    PMid:21107793
15. Jeong, Y.; Ryu, J.-S. *J. Org. Chem.* **2010**, *75*, 4183–4191.
    http://dx.doi.org/10.1021/jo100618d
    PMid:20499940
16. Tseng, M.-C.; Cheng, H.-T.; Shen, M.-J.; Chu, Y.-H. *Org. Lett*. **2011**, *13*, 4434–4437.
    http://dx.doi.org/10.1021/ol201793v
    PMid:21797204
17. Yoshida, Y.; Takizawa, S.; Sasai, H. *Tetrahedron Lett.* **2011**, *52*, 6877–6879.
    http://dx.doi.org/10.1016/j.tetlet.2011.09.152
18. Yacoba, Z.; Liebschera, J. *Arkivoc* **2012**, (iii), 312–329.
    http://dx.doi.org/10.3998/ark.5550190.0013.322
19. Wulf, A.; Fumino, K.; Ludwig, R. *Angew. Chem., Int. Ed.* **2010**, *49*, 449 –453 and references cited.
20. Fumino, K.; Peppel, T.; Geppert-Rybczynska, M.; Zaitsau, D.H.; Lehmann, J.K.; Verevkin, S.P.; Köckerling, M.; Ludwig, R. *Phys. Chem. Chem. Phys.* **2011**, *13*, 14064–14075.
    http://dx.doi.org/10.1039/c1cp20732f
    PMid:21666914
21. Gelbard, G. *Ind. Eng. Chem. Res.* **2005**, *44*, 8468–8498.
    http://dx.doi.org/10.1021/ie0580405
22. Alexandratos, S.D. *Ind. Eng. Chem. Res.* **2009**, *48*, 388–398.
    http://dx.doi.org/10.1021/ie801242v
23. Baumann, M.; Baxendale, I.R.; Ley, S.V. *Mol. Divers.* **2011**, *15*, 613–630.
    http://dx.doi.org/10.1007/s11030-010-9282-1
    PMid:20960230
24. Hassner, A.; Stern, M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 478–479.
    http://dx.doi.org/10.1002/anie.198604781

25. Schneider, S.; Hawkins, T.; Rosander, M.; Mills, J.; Brand, A.; Hudgens, L.; Warmoth, G.; Vij, A. *Inorg. Chem.* **2008**, *47*, 3617–3624.
    http://dx.doi.org/10.1021/ic702068r
    PMid:18345619
26. Alvarez, S.G.; Alvarez, M.T. *Synthesis* **1997**, 413–414.
    http://dx.doi.org/10.1055/s-1997-1206
27. Stefely, J.A.; Palchaudhuri, R.; Miller, P.A.; Peterson, R.J.; Moraski, G.C.; Hergenrother, P.J.; Miller, M.J. *J. Med. Chem.* **2010**, *53*, 3389–3395.
    http://dx.doi.org/10.1021/jm1000979
    PMid:20334421 PMCid:PMC2859177
28. Thomas, J. R.; Liu, X.; Hergenrother, P. J. *J. Am. Chem. Soc.* **2005**, *127*, 12434–12435.
    http://dx.doi.org/10.1021/ja051685b
    PMid:16144359
29. Sanghi, S.; Willett, E.; Versek, C.; Tuominenb, M.; Coughlin, E.B. *RSC Adv.* **2012,** *2*, 848–853 and references cited.
    http://dx.doi.org/10.1039/c1ra00286d
30. Ruiz-Toral, A.; de los Ríos, A.P.; Hernández, F.J.; Janssen, M.H.A.; Schoevaart, R.; van Rantwijk, F.; Sheldon, R.A. *Enzyme Microb. Technol.* **2007**, *40*, 1095–1099.
    http://dx.doi.org/10.1016/j.enzmictec.2006.08.027
31. Alcalde, E.; Mesquida, N.; Vilaseca, M.; Alvarez-Rúa, C.; García-Granda, S. *Supramol. Chem.* **2007**, *19*, 501–509.
    http://dx.doi.org/10.1080/10610270601132624
32. Abdul-Sada, A.K.; Greenway, A.M.; Hitchcock, P.B.; Mohammed, T.J.; Seddon, K.R.; Zora, J.A. J. Chem. Soc., *Chem. Commun.* **1986**, 1753–1754.
33. Elaiwi, A.; Hitchcock, P.B.; Seddon, K.R.; Srinivasan, N.; Tan, Y.-M.; Welton T.; Zora, J.A. *J. Chem. Soc. Dalton Trans*. **1995**, 3467–3472.
34. Aakeröy, C.B.; Evans, T.A.; Seddon, K.R.; Pálinkó, I. *New J. Chem.* **1999**, 145–152.
    http://dx.doi.org/10.1039/a809309a
35. Gurau, G.; Rodríguez, H.; Kelley, S. P:; Janiczek, P.; Kalb, R. S.; Rogers, R. D. *Angew. Chem. Int. Ed.* **2011**, *50*, 12024 –12026.
    http://dx.doi.org/10.1002/anie.201105198
    PMid:21997796
36. Avent, A.G.; Chaloner, P.A.; Day, M.P.; Seddon, K.R.; Welton, T. *J. Chem. Soc., Dalton Trans.* **1994**, 3405–3413.
    http://dx.doi.org/10.1039/dt9940003405
37. Dupont, J.; Suarez, P.A.Z.; de Souza, R.F.; Burrow, R.A.; Kintzinger, J.-P. Chem.-Eur. J. **2000**, *6*, 2377–2381.
    http://dx.doi.org/10.1002/1521-3765(20000703)6:13<2377::AID-CHEM2377>3.3.CO;2-C
38. Dupont, J. *J. Braz. Chem. Soc.* **2004**, *15*, 341–350.
    http://dx.doi.org/10.1590/S0103-50532004000300002

39. Lungwitz, R.; Spange, S. *New J. Chem.* **2008**, *32*, 392–394.
http://dx.doi.org/10.1039/b714629a
40. Reichardt, C.; Welton, T. *Solvent and Solvent Effects in Chemistry*, 4th Ed.; Wiley-VCH: Weinheim, 2011.
41. D'Anna, F.; Cascino, M.; Lo Meo, P.; Riela, S.; Noto, R. *Arkivoc* **2009** (*viii*), 30-46.
42. MacFarlane, D.R.; Pringle, J.M.; Johansson, K.M.; Forsyth, S.A.; Forsyth, M *Chem. Commun.* **2006**, 1905–1917.
http://dx.doi.org/10.1039/b516961p
PMid:16767234
43. Ueno, K.; Tokuda, H.; Watanabe, M. *Phys. Chem. Chem. Phys*. **2010**, *12*, 1649–1658.
http://dx.doi.org/10.1039/b921462n
PMid:20145829
44. Hollóczki, O.; Gerhard, D.; Massone, K.; Szarvas, L.; Németh, B.; Veszprémi, T.; Nyulaászi, L. *New J. Chem.* **2010**, *34*, 3004–3009.
http://dx.doi.org/10.1039/c0nj00380h
45. Hollóczki, O.; Nyulaászi, L. *Org. Biomol. Chem.* **2011**, *9*, 2634–2640.
http://dx.doi.org/10.1039/c1ob00007a
PMid:21399837
46. Mesquida, N. PhD Thesis, UB, 1999. http://hdl.handle.net/10803/1650.
47. Cloninger, M.J.; Whitlock, H.W. *J. Org. Chem.* **1998**, *63*, 6153–6159.
http://dx.doi.org/10.1021/jo980193x