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A general halide-to-anion switch for imidazolium-based ionic liquids and oligocationic systems using anion exchange resins (A^- form)†‡

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Further studies on the application of an AER (A^- form) method broadened the anion exchange scope of representative ionic liquids and bis(imidazolium) systems. Depending on the hydrophobicity nature of the targeted imidazolium species and counteranions, different organic solvents were used to swap halides for assorted anions, proceeding in excellent to quantitative yields.

The incorporation of imidazolium quaternary salts in a wide array of cationic and oligocationic systems situate them at the crossroads of multidisciplinary fields in chemistry.[2–4] The role of ionic liquids (ILs), besides their increasing importance as green solvents, has been broadened to ionic liquid salt forms of active pharmaceutical ingredients (APIs),[5] energetic ionic liquids (EILs)[6] and tuneable aryl alkyl ionic liquids (TAAILs).[7] Their industrial applications have also been reviewed.[8] Chemical aspects of imidazolium-based ILs concern their preparation, counteranion exchange and purity.[2,9–12]

The common synthetic route to imidazolium-based systems is a subclass of the Menschutkin reaction and gives the targeted imidazolium system in which the counteranions, halide ions, can be exchanged by different methods. A habitual method is to swap the halide ion for another anion using an inorganic salt (MA) that is also used to remove halide ions in ILs. The halide-containing by-product salts can then be eliminated by extraction or precipitation followed by filtration. Overcoming the purification complexity remains a challenging issue with the aim of obtaining pure IL salts, especially halide-free ion pairs.

The apparent directness of the counteranion exchange process does not imply that it is either simple or trivial since isolation and purification of pure heteroaromatic quaternary systems, *e.g.* imidazolium salts, is sometimes difficult and can be a serious problem when the solubility of the different ionic species present in the solution mixture is similar (Scheme S1, ESI‡).[4] A comparative study of the transformation of *N*-azolylpyridinium salts to the corresponding pyridinium azolate betaines showed that the method of choice makes use of a strongly basic anion exchange resin (AER) converted to the hydroxide form.[13] From 1986 onwards, this procedure was then conveniently applied to a variety of *N*-azolylimidazolium salts with several interannular linkers, including aza-analogues of sesquifulvalene with a betaine character.[14] Exploiting our standard anion exchange procedure, AER (OH^- form), the counteranions of different types of bis(imidazolium) cyclophanes, protophanes and calix[4]arenes were exchanged.[15,16] Recently, Rogers and co-workers have reported an imidazolium-based platform for ILs built up from a methyleneimidazolium tetrazolate subunit, and using an AER (OH^- form) to prepare the betaine structural motif.[17]

There are only a few reports on the application of anion exchange resins to imidazolium-based ILs using either an AER (OH^- form) or AER (A^- form) for the counteranion exchange (Scheme S1, ESI‡). Taking advantage of the anion exchange resin (OH^- form) method, Ohno and co-workers prepared Bio-ILs.[18] Likewise, several ionic liquid buffers were prepared.[19] To the best of our knowledge, there are very few examples in open chemistry literature, applying the AER (A^- form) protocol in water or aqueous methanol. Thus, non-aqueous ionic liquids (NAILs) have been prepared using an AER (PO_4^{3-} form).[20] In a likewise manner with an AER ($R/Ar–SO_3^-$ form), several *N*,*N*′-dialkylpyrrolidinium iodides have been transformed to the corresponding mesylate and tosylate salts.[21] Using an AER (CS^- form) loaded with camphorsulfonate anion, both **ILs·OTs**[22] and following a worthless protocol from **ILs·Br**[23] gave the corresponding **ILs·[CS]**. Treatment of **[bmim][Cl]** with several AER (A^- form) produced the anion exchange giving **[bmim][A]**.[24] Recently, we examined the preparation of an AER (A^- form) conveniently loaded with a variety of anions in water and hydromethanolic media. The counteranion exchange of representative ILs was carried out in aqueous methanol or methanol, providing a pure ionic liquid in quantitative yield.[1] Among different purification protocols of imidazolium ILs,[2,9–13] ion exchange resins should be a plausible method of choice although few reports have examined this.[9,12,25]

In this communication, we report our studies focused on extending the scope of the AER (A^- form) method to swap the halide ion for another anion in water or hydromethanolic media to dipolar nonhydroxylic organic solvents, *e.g.* CH_3CN and $CH_3CN : CH_2Cl_2$ (3 : 7), for halide-free synthesis of

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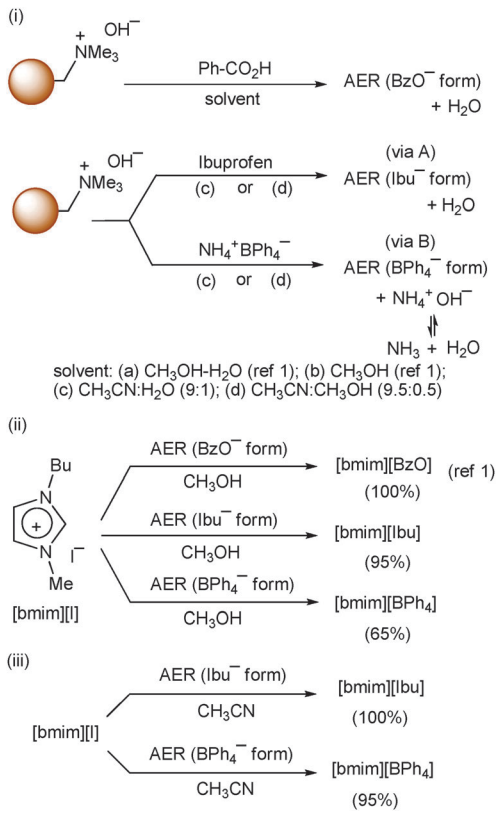
‡ Electronic supplementary information (ESI) available: Scheme S1, Tables S1–S5, Fig. S1, experimental procedures and spectral data. See DOI: 10.1039/c0cc05350c

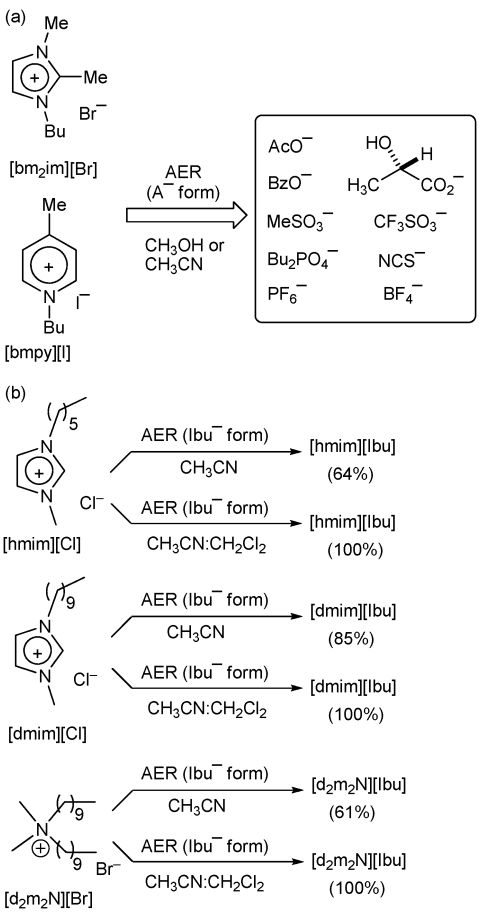
hydrophobic ILs. The usefulness of this procedure has been further developed to hydrophobic bis(imidazolium) systems.

We first examined the AER (OH^- form) loading with acids or ammonium salts using solvent mixtures with different polarities. The column was packed with resin Amberlyst A-26 (OH^- form)[26] and loaded with a 1% benzoic acid solution in different solvents, Scheme 1. The successful loading of solvent mixture CH_3CN : CH_3OH (9.5 : 0.5) afforded AER (Bz^- form) with the lowest proportion of a protic solvent, indicating that a non-aqueous solvent mixture allowed low water-soluble anions to be loaded and only a small proportion of a protic solvent was necessary for the OH^- interchange in the AER. The loading with two selected hydrophobic anions was examined: *via* A, with the anti-inflammatory acid ibuprofen and *via* B, with ammonium tetraphenylborate. The anion loading effectiveness was then checked by passing a methanolic solution of **[bmim][I]** through the AER column loaded with Bz^- anion and the iodide-to-benzoate anion switch proceeded in quantitative yield. Using AER (Ibu^- form) or (BPh_4^- form), the anion exchange in methanol proceeded in 95% and 65% yields, respectively. The test to check anion exchange in acetonitrile for the lipophilic Ibu^- or BPh_4^- anions improved the yield of **[bmim][Ibu]**[27] and **[bmim][BPh_4^-]**[28] to 100% and 95%, respectively (Scheme 1 and Table S1 in ESI‡). Parallel to this work, Viau *et al.*[27] have also reported the preparation of **[bmim][Ibu]** in 94% yield following the classic precipitation procedure from **[bmim][Cl]** (Table S1, ESI‡).



Scheme 1 AER (A^- form) procedure: the loading. (i) Loading the AER (resin (OH^- form) with acids or ammonium salts in different solvent mixtures. (ii) Checking the anion loading. (iii) Testing the anion exchange in CH_3CN.

Next, in order to extend the protocol to less hydrophilic cationic systems, a random of recently reported ILs allowed us to evaluate if the anion exchange was equally successful. Thus, a methanolic solution of **[bm_2im][Br]** or **[bmpy][I]** was passed through a column packed with the convenient AER (A^- form), affording the corresponding pure **[bm_2im][A]** or **[bmpy][A]**, characterized by ^1H NMR and ESI(−)-MS. The anion exchange was effective in all cases although in a few assays the yield of the new quaternary salts was only 88%, which was then improved to 100% when the anion exchange was performed in CH_3CN (Scheme 2 and Table S2 in ESI‡). The AER (A^- form) procedure was then applied to representative hydrophobic ILs such as **[hmim][Cl]** and **[dmim][Cl]** together with the quaternary ammonium salt **[d_2m_2N][Br]** to swap the halide for the ibuprofenate anion (Scheme 2 and Table S3 in ESI‡). A solution of the corresponding quaternary salt in CH_3CN was used to perform the anion exchange but the yields were fairly moderate, 64%, 85% and 61% respectively. A more lipophilic solvent mixture of CH_3CN : CH_2Cl_2 (3 : 7) permitted the halide-to-ibuprofenate switch quantitatively, giving the targeted hydrophobic new ibuprofenate imidazolium salts **[hmim][Ibu]** and **[dmim][Ibu]**, and the



Scheme 2 AER (A^- form) procedure in organic solvents: the anion exchange. (a) In CH_3OH or CH_3CN, imidazolium and pyridinium salts: **[bm_2im][Br]**, **[bmpy][I]**. (b) In CH_3CN or CH_3CN : CH_2Cl_2 (3 : 7), imidazolium and quaternary ammonium salts: **[hmim][Cl]**, **[dmim][BrCl]**, **[d_2m_2N][Br]**.

antibacterial–anti-inflammatory salt **[d_2m_2N][Ibu]**, an example of APIs reported by Rogers and co-workers.[5]

Application of our simple halide-to-anion exchange procedure with both lipophilic cations and low hydrophilic anions confirmed its efficiency. Hence, further studies were centered on four examples of less polar imidazolium-based systems (see Fig. S1, ESI‡): the (anthrylmethyl)imidazolium fluorescent chloride **1·Cl**;[29] the known dicationic fluorescent protophane anion receptor **2·2Cl**;[4,30] the bis(imidazolium) cyclophane prototype **3·2Cl**,[4,16] and the new calix[4]arene **4·2Br** (Table S1, ESI‡).

The (anthrylmethyl)imidazolium chloride **1·Cl** was transformed to several fluorescent salts **1·A**, *e.g.* **1·PF_6^-**, **1·BF_4^-**, **1·$CF_3SO_3^-$**, in yields from 70% to 89%, following the classic counteranion exchange with inorganic salts (MA). Accordingly, the ion pair **1·Cl** recently reported by Dyson and co-workers,[29] could be an illustrative example of a less polar simple imidazolium salt to test the efficiency of the AER (A^- form) procedure in organic solvents. When the AER conveniently loaded with PF_6^-, BF_4^- or $CF_3SO_3^-$ anions was used, the anion swap in CH_3OH proceeded in yields from 73% to 93%, whereas a less polar solvent mixture, CH_3CN : CH_3OH (9 : 1) gave nearly quantitative yields of **1·PF_6^-**, **1·BF_4^-** and **1·$CF_3SO_3^-$** (Table S4, ESI‡). Using the same solvent mixture, CH_3CN : CH_3OH (9 : 1), excellent results were obtained for the chloride-to-anion switch of bis(imidazolium) protophane **2·2Cl** and cyclophane **3·2Cl** with a variety of anions to afford **2·2A** and **3·2A**, respectively. The less polar example, the new bis(imidazolium) calix[4]arene **4·2Br** was directly examined in CH_3CN solution and the exchange with representative anions such as AcO^-, BzO^- $MeSO_3^-$, $Bu_2PO_4^-$and PF_6^- proceeded in nearly quantitative yields (Table S5, ESI‡).

In summary, the reported anion exchange resin (A^- form) procedure in non-aqueous media is a simple method of choice to swap the halide ions for a broad range of anions in ionic liquids, concomitantly removing halide impurities. Depending on the hydrophobic nature of the imidazolium salt, different solvents were used, such as CH_3CN and the mixture CH_3CN : CH_2Cl_2 (3 : 7). The halide ion swap procedure progressed in excellent to quantitative yields with both lipophilic imidazolium species and low hydrophilic anions. This anion exchange procedure could be adapted to a diversity of charged molecules such as oligocationic imidazolium systems, along with quaternary heteroaromatic and ammonium salts, thereby developing its performance in fields with still broad scope and unexplored applications such as ionic liquids and anion recognition chemistry.

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