Product as reaction solvent: an unconventional approach for ionic liquid synthesis

Cinzia Chiappe,[a] *

[a]Dipartimento di Farmacia, Università di Pisa, via Bonanno 33, 56126 Pisa, Italy.

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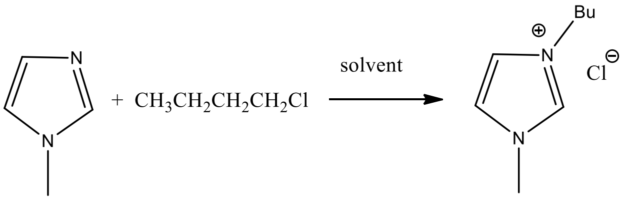
ABSTRACT.

This paper reports

INTRODUCTION

Ionic liquids (ILs) are salts with melting temperatures below 100 °C, usually constituted by a large and asymmetric organic cation associated to an organic or inorganic anion. Due to their ionic character, ILs exhibit peculiar physico-chemical properties, including a negligible vapor pressure, low flammability, high thermal and chemical stabilities, broad liquid temperature range and high solvation ability for organic, inorganic and polymeric compounds.[1-3] The ability of some specific ILs to dissolve important bio-polymers, such as cellulose, chitin and keratin, has become an area of intense activity in the last ten years.[4-6] For their unique properties, which can be moreover tailored through an appropriate cation and anion selection, ILs have been proposed as solvents, media, electrolytes or additives in the most diverse applications: organic synthesis, catalysis, extraction processes, electrochemistry, nanotechnology and so on.[2,7-11] The high potentiality shows by ILs in different strategic areas of research is expected to lead to an increasing demand. Currently, ILs are mainly produced in batch reactors and various companies already supply a portfolio of ILs; however, at relatively high prices, at least when compared with molecular solvents. The costs depend on various factors including the production scale, type of reactor and process. Production process affects actually not only the ILs prices but also their environmental impact: synthesis requires normally large amounts of organic solvents. It is indeed usually carried out through one or two-step processes: the alkylation of a N-, P- or S-containing organic compound, for example *N*-methylimidazole (MIM), giving normally a halide based IL, followed by an eventual anion exchange (metathesis reaction). Principally the alkylation step, *i.e.* the Menschutkin reaction in the case of tertiary amines, requires energy and time consuming conditions, in particular when less expensive but also less reactive chloroalkanes are used. It is moreover often complicated by the formation of two phase systems, both in organic solvents and when the process in carried without addition of a solvent.[12]

In 2007 Kralish et al., using MIM and chlorohexane as a model system, suggested the solvent-free process at 70 °C in batch-reactor as the best procedure in terms of energy demand, toxicological aspects and costs to synthesize 1-hexyl-3-methylimidazolium chloride.[13] However the solvent-free process is very slow with chloroalkanes at this temperature. For example, when MIM was reacted at 70 °C with chlorobutane (BuCl) 50 h were necessary to reach 90% conversion into the expected 1-butyl-3-methylimidazolium chloride, [bmim]Cl.



Scheme 1. [bmim]Cl synthesis *via* Menschutkin reaction

Although an increase in reaction temperature generally has positive effects in terms of energy demand and reaction times, it is generally to be avoided, owing to the formation of colored contaminants arising from *N*-methylimidazole decomposition and polymerization.

Reactions in solvent are therefore preferred at lab scale or whenever the IL purity is an important target. Although a large number of media have been employed for the alkylation reaction, including also not exactly environmental friendly solvents, Welton et al. have recently reported[14] an improved procedure to synthesize [bmim]Cl using ethyl acetate as reaction medium, which is able to guarantee the formation of a pure uncolored product, although it requires long reaction times (three days at 45 °C followed by four days at 75 °C).

Actually, the Menschutkin reaction can be carried out also in ILs and, although with reactive alkylating agents (bromides and iodides) the ionic environment has only a moderate kinetic effect, significant increases in reaction rate with respect the classical molecular polar aprotic solvents have been observed when chloroalkanes have been used as alkylating agents.[15]

Therefore, to evaluate the possibility to identify new conditions able to guarantee a higher reaction rate, contemporaneously assuring a high product purity degree, the unusual approach to synthesize [bmim]Cl, using the same product as solvent in a range of temperature ranging from 100 to 120 °C was investigated. The comparison with three sustainable molecular solvents, having a sufficiently high boiling point, 1-butanol (117,7 °C), methylisobutylketone (MIBK, 117-118 °C) and water (100 °C), was also performed.

EXPERIMENTAL SECTION

All chemicals (1-methyl-imidazole, 99 %, 1-chlorobutane, 99+ %, 1-butanol 99 %, 4-methyl-2-pentanone, 99 %) were purchased from Alpha Aesar . NMR spectra were recorded on a Bruker Avance III 300 spectrometer (250 MHz).

Reaction between 1-methylimidazole and chlorobutane

Lab-scale synthesis: 1-methylimidazole (MIM, 27 g) and of 1-chlorobutane (40 g, ratio 1:1,3) were added to the selected solvent (1-butanol, 4-methyl-2-pentanone, water or [bmim] Cl, 15g) in a 250 mL round-bottomed flask equipped with a reflux condenser and magnetic stirrer of with or without solvent. The reaction mixture was heated up to reaction temperature (100 or 120 °C) under magnetic stirring. During the course of the reaction samples were collected and analysed by ^{1}H NMR.

Batch reactor synthesis: the batch synthesis of [bmim]Cl was carried in 2 L batch jacketed reactor was composed of a reflux condenser, mechanical stirrer, dropping funnel, thermocouple and heating thermostats. 1-Methyl-imidazole (120g) and 1-chlorobutane (190 g) were to the selected solvent (4-methyl-2-pentanone, water or [bmim]Cl, 250 g) and heated up to reaction temperature under stirring. During the course of the reaction samples were collected and analysed by ^{1}H NMR.

Autoclave reactor synthesis: 1-methyl-imidazole (7 g) and 1-chlorobutane (8,8 g) were added to [bmim]Cl (15 g) in a 150 mL stainless steel autoclave equipped with magnetic stirrer. The reactor was pressurized to 5 bar using an inert gas (nitrogen) and heated up to the reaction temperature (100 or 120°C) under stirring. The reaction was stopped at different times and the mixture was analysed by ^{1}H NMR.

RESULTS AND DISCUSSION

The reaction of MIM with BuCl was carried out in three organic solvents (1-butanol, MIBK and water) and in [bmim]Cl, *i.e.* in the same reaction product, using a batchwise-operating stirred lab-scale glass reactor or a close apparatus. The two reagents were mixed together with the selected solvent obtaining a single or two phase system. In 1-butanol, reagents and product are soluble in the reaction medium and the process occurs practically in a single phase. On the other hand, in MIBK the second phase is formed with the progress of the reaction, being the product insoluble in the reaction medium. Different is the situation in water and [bmim]Cl, where the reaction product and MIM are practically completely soluble and BuCl forms the second phase. In all cases, conversion was monitored at constant temperature. BuCl was generally used in excess, typically 1.3-1.5 mol per mol of MIM, due to its low solubility in the reaction mixture and its relatively low boiling point (b.p. 79 °C at 1 bar). Only when the reaction was carried out in a close apparatus (under nitrogen, 4 bar) the excess was reduced to 1.1 mol per mol of MIM. Syntheses were conducted at temperatures ranging from 100 to 118 °C.

Preliminary experiments with [bmim]Cl, butanol and MIBK were carried out at 118 °C (practically, at reflux temperature of the two molecular solvents) under comparable conditions: adding 0.44 mol of BuCl to 0.33 mol of MIM in 60 ml of solvent. Experiments with water were carried out at 100 °C.

Table 1. Solvent dependent conversion of MIM and BuCl in [bmim]Cl

Solvent	**MIM:BuCl Ratio**	**T (°C)**	**P (bar)**	**Time (h)**	**Conversion (%)**	**IL Color**
1-butanol	1:1,3	120	1	96	99	orange
MIBK	1:1,3	120	1	49	99	dark yellow
[bmim]Cl	1:1,3	120	1	24	98,5	yellow
H_2O	1:1,3	100	1	220	81	colourless

Despite the relatively high temperature, MIM alkylation in both protic solvents (1-butanol, water) required however long reaction times: 99% conversion was achieved in 96 h in 1-butanol, whereas a conversion of only 81% was obtained after 220 h in water. Moreover, whereas the product formed in water was practically colorless an orange IL was obtained in 1-butanol. A yellow colored IL was obtained also in MIBK, although in this case 49 h were sufficient to achieve 99% conversion. On the other hand, [bmim]Cl was the sole medium able to assure a high conversion in a significantly lower time (24 h) giving a pale yellow colored compounds. Reactions carried out on larger scale in a batchwise-operating stirred lab-scale glass reactor gave comparable results. Moreover, as expected a less colored IL was obtained at 100 °C using as solvent both MIBK and [bmim]Cl (99% conversion after 45 and 40 h, respectively).

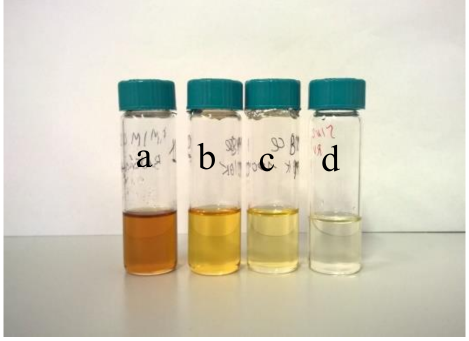


Figure 1. [bmim]Cl obtained in a) 1-butanol 118°C; b) MIBK 118°C; c) MIBK 100°C d) [bmim]Cl 100°C.

For the reaction in [bmim]Cl, an improved procedure was obtained carrying out the process in close vessel (at 100 °C under nitrogen, 4 bar). Under these conditions, despite the fact that only a small excess of BuCl was used (*ca.* 10%) a practically uncolored [bmim]Cl was obtained in few hours (>95% conversion in 8h; 99% in 14 h). (Figure 2)

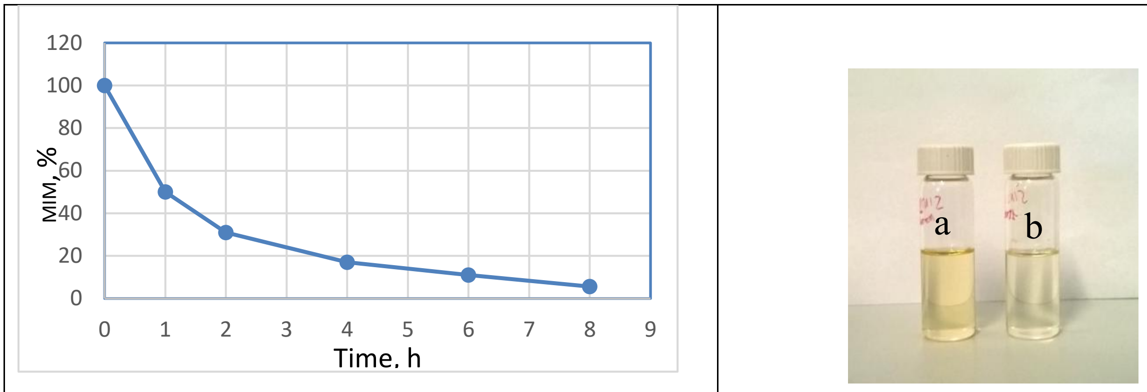


Figure 2. Left: Conversion of MIM as a function of reaction time when carried in close-apparatus using [bmim]Cl as solvent. Right: [bmim]Cl obtained: a) at 100°C in open vessel; b) at 100°C in close apparatus, under nitrogen.

After removal of the excess of BuCl at reduced pressure, the colorless liquid was cooled to room temperature and subsequently placed in a freezer overnight, during which time a white precipitate was formed.

The above reported data clearly show that [bmim]Cl is an appropriate medium for its synthesis, increasing reaction rate with respect molecular solvents and assuring a high product purity. The higher reactivity observed in [bmim]Cl and MIBK, with respect BuOH and water, shows moreover that this reaction, characterized by charge increase on going from reagents to the transition state (TS), is positively affected by solvent dipolarity/polarizability although its eventual hydrogen bond ability plays an opposite role. This behavior is in agreement with a substitution reaction occurring through *early* TS, in which solvent hydrogen bonding to leaving group (chloride ion) is not important whereas the solvent-reagent interaction (in particular, with MIM) decreases reactivity(Figure 3). In the Menschutkin reaction, only when the C-leaving group bond breaking in the related TS is advanced (*late* TS), both solvent dipolarity and hydrogen bond donor ability contribute to increase reaction rate.

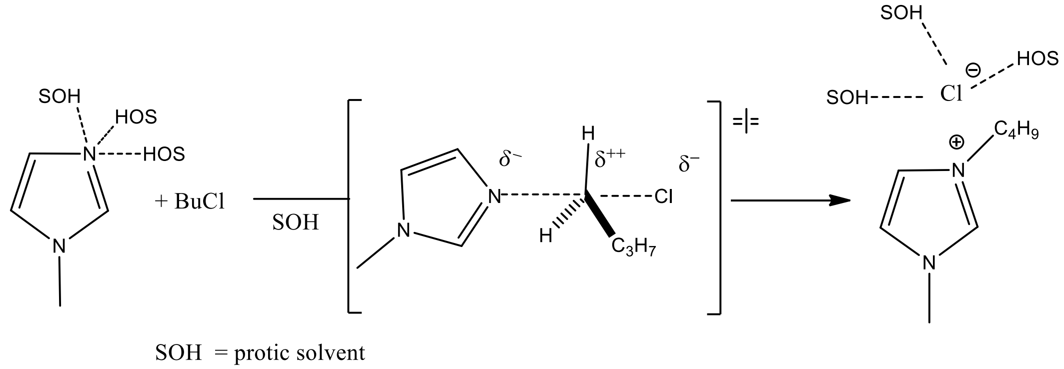


Figure 3. Reagent and TS solvation by protic solvents

It is also to note that although it has been more times evidenced the ability of $[\text{bmim}]^+$ cation to act as hydrogen bond donor, [16,17] data here reported confirm that this feature strongly depends on counteranion and decreases on increasing anion hydrogen bond acceptor ability.[18] The well-known strong cation-anion interactions, characterizing $[\text{bmim}]^+$ cation and chloride anion, evidently disfavors the ability of both the coupled ions to interact with added compounds, in particular with neutral species such as MIM, and makes [bmim]Cl a proper solvent for its self-synthesis.[18]

Finally, it must be remarked that after 20-25% conversion the reaction of MIM and BuCl under solvent free conditions should be practically in the same conditions of our process. However, the relatively long times necessary to have a high conversion and the low quality of the product obtained in the absence of solvent, in particular at high temperature, show the important role exerted by the "solvent" in first part of the reaction. Under solvent-free conditions, indeed, the moderate polarity of the reagents is probably unable to stabilize efficiently the TS and the solvent-less system, having also a reduced ability to dissipate heat, favors side-reactions giving colored by-products.

Comparison of single-phase or two-phase stirred synthesis of [bmim]Cl in molecular solvents or in [bmim]Cl

The comparison of the synthesis of [bmim]Cl in molecular solvents and in [bmim]Cl at 118 °C, under identical conditions, indicates that the time needed for a given conversion decreases drastically on going from BuOH to [bmim]Cl.

Si può fare una valutazione di quanto si risparmia in termini di energia? Passando da 96 h/118 a 48 ed infine a 24? In più nelle reazioni nei solventi molecolare c'è da aggiungere e rimuovere il solvente che ha anche un suo impatto ambientale.

Infine è possibile valutare la reazione in apparecchio chiuso, che si fa a 100 °C (temperatura inferiore) con un minor eccesso di BuCl (quindi meno reagente da allontanare) ma in 14 h si ha il 99% di conversione. Qui c'è però da considerare il sistema chiuso e la sovrappressione in azoto…???

CONCLUSIONS

ACKNOWLEDGMENT

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Synopsis

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