One-pot and Solventless Synthesis of Ionic Liquids under Ultrasonic Irradiation

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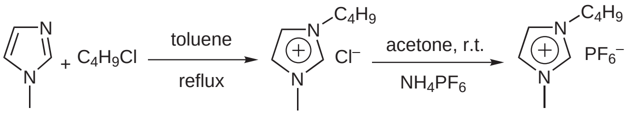
Abstract: A novel method is described for the one-pot synthesis of various ionic liquids in a competitive time. By using ultrasonic irradiation, different families of nitrogen-bearing ionic liquids can be obtained in a solvent-free or in aqueous medium, which gives a greener touch to the overall process.

Key words: ionic liquids, ultrasound, solvent-free reaction

The use of volatile organic compounds (VOCs) in synthesis is becoming more and more inconvenient in terms of ecological impact. Thus, room-temperature ionic liquids (RTILs) that have aroused a great interest because of their unusual physicochemical properties have been designed to solve this problem. Thanks to their purely ionic nature, RTILs possess a negligible vapor pressure; in addition they can be recycled by distillation, making them interesting candidates for avoiding both air pollution and waste production. Moreover, they can be used in a large variety of chemical transformations owing to their tunable polarity, high thermal stability, high liquid range and good solvating ability.[1] In this way, many applications have been described in organic chemistry,[2] catalysis,[3] inorganic chemistry[4] or electrochemistry.[5] Mainly because of the lack of thermodynamic and toxicological data,[6] the possibility to use ionic liquids on a large scale is still unexplored. Their conventional synthesis includes two steps, the quaternarization of a heteroatom by an alkyl halide followed by the metathesis of the resulting anion with its corresponding salt. An example of this synthesis for the well-known 1-butyl-3-methylimidazolium hexafluorophosphate ($BmimPF_6$) with ammonium salt is given in Scheme 1.



Scheme 1 Classical synthesis of $BmimPF_6$

The metathesis step can also be performed using toxic hexafluorophosphoric acid.[7] Furthermore, a large volume of volatile organic solvents (such as acetone, toluene, acetonitrile) is involved in both steps which is quite problematic considering that one of the main goals in green chemistry is to ban VOCs. Lastly, the time required to obtain a ready-to-use ionic liquid can last up to a few days if one considers synthesis and purification, avoiding a larger-scale production. Consequently, this reaction has already been improved by using non-conventional activation methods such as microwave in a solventless procedure.[8] Sonochemistry can also be a tool for improving this synthesis. Indeed, it is known to enhance some processes through a physical phenomenon called cavitation, which is the formation, growth and collapse of bubbles in an elastic liquid.[9] By imploding, these bubbles create local high pressure (up to 1000 bar) and high temperature (up to 5000 K) that lead to high-energy radical mechanisms[10] and also create some interesting physical effects such as micromixing, mass transport or reduction of particle size.[11] As the metathesis using ammonium salt is a heterogeneous process, the ultrasound methods could be of great benefit since they are able to reduce ammonium salt particles and, thus, increase their reactivity.[12]

In a previous paper, Xu et al. described a one-pot three-component synthesis of ionic liquids under thermal heating in heterogeneous conditions but the reaction time remained significantly long (from 15 h with 1-alkyl bromide to 35 h with 1-alkyl chloride) to obtain satisfactory yields (up to 87%).[13]

In the present article, we report the first one-pot synthesis of RTILs under ultrasonic irradiation. Our first experiment was a solvent-free one-pot synthesis of $BmimPF_6$ since it is one of the most used and known RTIL. Different acoustic powers were utilized and the reaction conditions are described in Table 1.

Even if the results were not as good as expected, an influence of the power on the product yield was observed (entries 1 and 2 in Table 1). In both sonication attempts, the reaction mixture rapidly turned brown leading to low-purity $BmimPF_6$. Usually, the quaternarization occurs with heat whereas metathesis takes place at room temperature. The degradation observed is maybe due to this antagonistic system. We then decided to check the thermal stability of our reagents. 1-Methylimidazole was considered as stable since no degradation was observed by GC–MS analysis after sonication. In our first few attempts of

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Table 1 Preliminary Results of Solvent-Free One-Pot Synthesis of $BmimPF_6$[a]

Entry	Activation method	Temp (°C)	Time (min)	Yield (%)
1	Ultrasound 20 kHz (37 W)	60	30	24
2	Ultrasound 20 kHz (50 W)	80	30	59
3	Magnetic stirring (ca 500 rpm)	140	30	29

[a] Amine–NH_4PF_6–1-chlorobutane = 1:1:1.

‘one-pot’ reaction we noticed decomposition at an early stage for ammonium hexafluorophosphate which stopped the overall reaction. So, thermogravimetric analyses were performed in the presence of air on four commercially available hexafluorophosphate salts (NH_4PF_6, $LiPF_6$, $NaPF_6$ and KPF_6) to determine their stabilities. The results of these analyses are given in Table 2.

Table 2 Thermogravimetric Data of Commercially Available Hexafluorophosphate Salts

Entry	Salt	Temp (°C) of decomposition
1	$LiPF_6$	97
2	$NaPF_6$	128
3	NH_4PF_6	183
4	KPF_6	460

Thus, the potassium salt was chosen for the synthesis of hexafluorophosphate RTILs. Lastly, the alkyl halide was changed in order to improve the overall reactivity. As the first step involves a SN_2 mechanism, the nature of the halide is of great importance as already observed for conventional ionic liquids synthesis.[13] Since a too high temperature resulted in the degradation of some reactants, more reactive compounds were chosen to make the experimental conditions milder. Some experiments were tried with 1-octyl-3-methylimidazolium hexafluorophosphate ($OmimPF_6$) as model reactant since it is, like $BmimPF_6$, one of the most common ionic liquids, and its hydrophobic nature makes the workup easier. The results are given in Table 3.

These results tend to prove that a rapid one-pot synthesis of ionic liquids is possible as soon as starting materials are designed for this objective. As expected, high thermally stable salts are necessary to resist the harsh conditions implied by sonication. Thus, only potassium hexafluorophosphate seemed well suited for this synthesis.

However, the reaction conditions (temperature, time, etc.) were not adequate when 1-chlorooctane was used; a much longer reaction time would probably be required in that case. In addition, 1-bromooctane would have to be used for a swift synthesis even if the chloride compounds are less expensive. Some tests concerning the level of purities were performed on the obtained ionic liquid and 0.48% w/w of bromide (ion-exchange chromatography) was obtained and 0.26% w/w of water was observed with Karl-Fischer titration. Moreover, no organic impurity was observed in the ^1H and ^{13}C NMR data. These results tend to prove that the purity of ionic liquids is acceptable, at least for synthesis.

Different combinations of cations and alkyl halides were then examined to generalize this procedure to different families of hexafluorophosphate ionic liquids. The results are given in Table 4.

Average to good results were obtained for various combinations of nitrogen-bearing heterocycles and alky halides. When 1-bromobutane was used, water had to be added to solubilize the solid bromide intermediate resulting from quaternarization and to avoid precipitation. Indeed, this precipitation could be very problematic since a solid medium is able to reflect the ultrasonic waves, as it is well known, for example in medical diagnostic,[14] leading to a possible damage to the ultrasonic probe by reflecting too much energy on the ultrasound source. As our objective was to develop an ‘as green as possible process’, water was chosen. Unfortunately, results were poorer when 1-bromobutane was used probably because of the dilution of the medium by the additional water. Also, when 1-methylpyrrolidine was used, a natural precipitation of the final product was observed. As the yield was high enough for *N*-octyl-*N*-methylpyrrolidinium hexafluorophosphate, no

Table 3 One-Pot Synthesis of $OMImPF_6$ under Ultrasonic Irradiation[a]

Entry	Amine	PF_6 salt	Alkyl halide	Temp (°C)[b]	Time (min)	Yield (%)[c]
1	1-methylimidazole	$LiPF_6$	1-bromooctane	85	120	0
2	1-methylimidazole	$NaPF_6$	1-bromooctane	85	120	0
3	1-methylimidazole	NH_4PF_6	1-bromooctane	80	120	trace
4	1-methylimidazole	KPF_6	1-chlorooctane	80	120	trace
5	1-methylimidazole	KPF_6	1-bromooctane	85	120	85

[a] Amine–PF_6 salt–alkyl halide = 1:1:1’, ultrasonic irradiation: 30 kHz, acoustic power of 0.86 W/mL.

[b] Temperature increased because of ultrasound; a cryostat was used to control this heating phenomenon.

[c] Isolated yield.

Table 4 Ultrasound-Assisted Syntheses of PF_6 Ionic Liquids[a]

Entry	Amine	Alkyl halide	Temp (°C)[d]	Time (min)	Yield (%)[e]
1	1-methylimidazole	1-bromohexane	88	180	96
2	1-methylimidazole	1-bromopentane	87	180	87
3	1-methylimidazole	1-bromobutane[b]	84	180	61
4	pyridine	1-bromooctane	81	180	86
5	pyridine	1-bromohexane[c]	90	80	70
6	pyridine	1-bromopentane[c]	80	75	75
7	pyridine	1-bromobutane[b]	80	180	55
8	1-methylpyrrolidine	1-bromooctane	80	40	86
9	1-methylpyrrolidine	1-bromobutane[b]	80	120	68

[a] Amine–PF_6 salts–alkyl halide = 1:1:1; ultrasonic irradiation: 20 kHz, acoustic power of 0.99 W/mL.
[b] Water was added to avoid precipitation.
[c] Reaction stopped because of precipitation of the medium.
[d] Temperature naturally increased because of ultrasound. Cryostat was used to control this heating phenomenon.
[e] Isolated yield.

additional water was introduced and the reaction was stopped as soon as the precipitation occurred. However, the necessity of water with 1-bromobutane led once again to a decrease of the yield to 68%. Thus, this ultrasound-assisted method has proved its efficiency for the synthesis of hexafluorophosphate ionic liquids for different cations and lateral alkyl chains. However, several physicochemical key properties of ionic liquids depend on the nature of their anions. Our methodology was consequently applied to other potassium salts to achieve tetrafluoroborate and trifluoromethanesulfonate ionic liquids. The results are given in Table 5.

Average to good yields were obtained but a drawback still remained for the synthesis of very hydrophilic ionic liquids such as 1-butyl-3-methylimidazolium tetrafluoroborate. In fact, after the completion of the reaction, the hydrophilic ionic liquids were first dissolved in water and then extracted from aqueous phase with dichloromethane to remove this ionic liquid as well as the intermediate 1-butyl-3-methylimidazolium bromide which was water-soluble.[13] There was, therefore, a necessity for the expected ionic liquid to be more soluble in dichloromethane than in water. If not, the extraction failed, leading to yields that were usually poorer for hydrophilic ionic liquid. Furthermore, the use of dichloromethane is not eco-friendly. However, the one-pot synthesis remains interesting in term of a green protocol since it removes the additional purification of the quaternary nitrogen-bearing heterocycle halide intermediate. The reduction of reaction time won by the use of ultrasound is also of great benefit in terms of economy and eco-chemistry. Moreover, no organic solvents were required during the process.

In this present work, we have developed a green protocol to synthesize easily and directly non-halide room-temperature ionic liquids. Different families of RTILs have been obtained containing various cations, anions and lateral alkyl chain length. This synthesis is in accordance with many principles of green chemistry.[16] It was done under a non-conventional activation method, it reduces the number of steps usually required for this kind of reaction, and it is done without or with an environmentally benign solvent. Lastly, it enables a quick synthesis of room-temperature ionic liquids which are generally considered as green solvents. Our team is presently focusing its efforts on generalizing this method to starting material with lower reactivity such as alkyl chloride or unreactive salts such as lithium bis(trifluoromethanesulfonimide) in order to synthesize ionic liquids with high hydrophobic character.

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Table 5 One-Pot Syntheses for Various Families of Ionic Liquids[a,15]

Entry	Amine	Salt	Alkyl halide	Temp (°C)	Time (min)	Yield (%)[d]
1	1-methylimidazole	KOTf	1-bromooctane	83	180	90
2	1-methylimidazole	KOTf	1-bromohexane	80	180	72
3	1-methylimidazole	KOTf	1-bromopentane	80	180	72
4	1-methylimidazole	KOTf	1-bromobutane[b]	80	180	70
5	pyridine	KOTf	1-bromooctane	85	180	75
6	pyridine	KOTf	1-bromohexane	90	180	75
7	pyridine	KOTf	1-bromobutane[b]	90	180	60
8	1-methylpyrrolidine	KOTf	1-bromooctane[c]	85	50	73
9	1-methylpyrrolidine	KOTf	1-bromobutane[b]	80	180	89
10	1-methylimidazole	KBF_4	1-bromooctane	80	180	78
11	1-methylimidazole	KBF_4	1-bromobutane[b]	80	180	21
12	pyridine	KBF_4	1-bromooctane	105	180	72
13	pyridine	KBF_4	1-bromobutane[b]	80	180	61
14	1-methylpyrrolidine	KBF_4	1-bromooctane	80	180	68
15	1-methylpyrrolidine	KBF_4	1-bromobutane[b]	85	180	65

[a] Amine–PF_6 salt–alkyl halide = 1:1:1; ultrasonic irradiation: 20 kHz, acoustic power of 0.99 W/mL.
[b] Water was added to avoid precipitation.
[c] Natural precipitation of product was observed after 50 min.
[d] Isolated yield.

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(15) The used ultrasonic probe was a Branson 20 kHz digital sonifer or a Ultrasons Annemasse S.A. 30 kHz probe. Acoustic powers were determined by calorimetry.[17] ^1H and ^{13}C NMR spectra were recorded on a Bruker AMX 200 MHz spectrometer. IR analyses were performed on an ATI Mattson Genesis Series FTIR instrument. All precursor products are commercially available and were used without further purification. Potassium salts (1 equiv), alkyl bromide (1 equiv) and nitrogen-bearing heterocycles were introduced in a 25-mL cooling-jacket glass reactor. H_2O was added when 1-bromobutane was used as alkyl bromide. The medium was sonicated at 20 kHz or 30 kHz for the times and at the temperatures and acoustic powers listed in Tables 1 and 3–5. A heat-conducting fluid was used in the cooling jacket to maintain the overall temperature at about 80 °C during the experiments. The final mixture was then poured into acetone and filtered through Celite. Acetone was removed under vacuum. Hydrophobic ILs were washed with H_2O (4×20 mL) and Et_2O (4×20 mL), to be finally dried at 90 °C under vacuum (3 h). Hydrophilic ILs were dissolved in H_2O (50 mL) and extracted with CH_2Cl_2 (4×25 mL); solvents were removed under vacuum and RTILs are washed with Et_2O (4×20 mL) to be finally dried at 90 °C under vacuum (3 h). All products were checked by ^1H and ^{13}C NMR spectroscopy and no organic impurity was observed. No significant trace of H_2O was observed in the IR spectra.

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