This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. This Accepted Manuscript will be replaced by the edited, formatted and paginated article as soon as this is available.

You can find more information about Accepted Manuscripts in the Information for Authors.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal’s standard Terms & Conditions and the Ethical guidelines still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.
Facile, High-Yielding Preparation of Pyrrolidinium, Piperidinium, Morpholinium and 2,3-Dihydro-1H-isoinodolinium Salts and Ionic Liquids from Secondary Amines

Antony J. Ward, Anthony F. Masters and Thomas Maschmeyer

Received (in XXX, XXX) Xth XXXXXXXXXX 20XX, Accepted Xth XXXXXXXXXX 20XX
DOI: 10.1039/b000000x

High yield and purity heterocyclic ionic liquids can be obtained via the microwave irradiation of equimolar amounts of a secondary amine and of an α,ω-dibromoalkane (i.e., 1,4-dibromobutane, 1,5-dibromopentane, bis(2-bromoethyl)ether, or α,ω-dibromo-ω-xylene) in water, in the presence of potassium carbonate, followed by anion exchange with lithium bis(trifluoromethanesulfonyl)imide, affording pyrrolidinium, piperidinium and morpholinium ionic liquids, respectively. Using this methodology, a large number of homologous ionic liquids can be prepared from a small number of readily available and relatively cheap starting materials, including a new class of ionic liquids based on the 2,3-dihydro-1H-isoinodolinium ring system. Analysis (using SWOT and the GSK “greenness” assessments) of this synthetic method and comparison with current literature preparations reveals that this new method delivers significant benefits across a range of relevant parameters.

Introduction

Generally, ionic liquids (ILs), i.e. molten salts with low melting points, consist of unsymmetrical organic cations (e.g., N,N-dialkylimidazolium, N,N-dialkylpyrrolidinium, N-alkylpyridinium, N,N-dialkylpiperidinium, tetraalkylammonium) paired with charge diffuse organic or inorganic anions (such as Cl-, Br-, PF6-, BF4-,(CF3SO2)2N+, CF3SO2-). ILs are characterized by negligible vapour pressure, non-flammability, high ionic conductivity, excellent solvating properties for a wide range of materials, high thermal and electrochemical stability, and a large liquidus range.

In addition to their frequent use as solvents for synthesis and catalysis,3-7 there has been growing interest in ILs as components within a diverse range of applications. Examples of such applications include: electrolytes for use in electrochemistry,8 electrochemical devices (including batteries),9-14 double-layer capacitors,15,16 fuel cells,17,18 and photo-electrochemical cells;20,24 as media for the electrodeposition of metals and semiconductors;25 as heat stabilizers26 and anti-oxidants for lubricating oils;27-29 in gas storage30,31 and separations;32-35 and in separation science.36-38 One of the most established (albeit, until recently, unrecognised) industrial uses of ionic liquids has been in the production of α-caprolactam.39

Of great value to the field of ionic liquids is the development of generic synthetic methods that are capable of producing a wide range of ILs from only a small pool of readily available, inexpensive and easily purified precursors. An increasingly common example of such a generic method is the preparation of chiral ionic liquids from the chiral pool, using readily accessible acid-base chemistry.40,41 To date, most frequently used ILs are prepared by quaternisation of the parent ring system. However, such simple heterocyclic systems are often expensive and difficult to purify due to their high boiling points. Additionally, significant time and effort must be expended purifying the quaternised intermediate prior to anion exchange.42 As a contribution towards the goal of devising a set of generic, straightforward and rapid methods for facile IL synthesis, we describe the high yielding preparations of a range of ionic liquids based on pyrrolidinium, piperidinium, oxazolium, and 2,3-dihydro-1H-isooindolinium that uses readily available and cheap secondary amines and α,ω-dibromoalkanes significantly extending the method described earlier by Ju and Varma.43

Results and discussion

The creation of a generic method for the preparation of a large range of new and existing ionic liquids from a small pool of cheap and readily available chemicals, using energy efficient methods and minimal purification is an area of increasing importance given the great interest in the applications of ILs. Since the most widely used ionic liquids (with the exception of imidazolium ILs) consist of a quaternised nitrogenous ring systems, the most logical starting point is the derivatisation of secondary amines. Using K2CO3 in water to deprotonate the amine in the presence of an α,ω-dibromoalkane at 120 °C results in the formation of the desired quaternised ring system. The ILs can be isolated easily in high yield through judicious choice of a suitable anion. Throughout this paper the bis(trifluoromethanesulfonyl)imide anion has been used, as its
presence results in hydrophobic ILs, which can be readily separated from water and washed to remove any inorganic contaminants. Thus, using this method we have prepared 36 ILs or salts (of a total possible 44) in four homologous series using 15 different starting materials.

It should be noted that we have found this reaction to only be significantly accelerated when using a focused or monomodal microwave system (with microwave power up to 850 W). Attempts to perform this reaction in a standard multimodal laboratory microwave system (with microwave power up to 1000 W) did not result in the isolation of any of the desired products after irradiation times of up to 60 min., indicating that substantially longer reaction times are necessary to achieve the desired products. In both cases, the microwave reactors were operated in a manner whereby only the temperature of the reaction mixture was set (i.e., the microwave power was not fixed for a continuous irradiation experiment). Consequently, it is not believed that the power of the irradiation is a critical parameter. In focused microwave systems the radiation is directed through an accurately designed wave guide into the reaction vessel mounted at a fixed distance from the radiation source, thereby creating a standing wave or single mode. The greater reaction rates in the monomodal microwave presumably arise as a result of the more uniform heating pattern and the higher microwave field strengths that can be obtained.

Once the set irradiation time was completed (and in those cases where the bromide salt was water-soluble), the homogeneous aqueous solution was extracted with diethyl ether to remove any unreacted organic precursors. Anion exchange was then performed by addition of one equivalent of lithium bis(trifluoromethanesulfonyl)imide, which resulted in the desired salt separating from the aqueous phase. Subsequently, additional salt was extracted from the aqueous phase using CH₂Cl₂ and the combined organic phases washed with water to remove excess NTf₂⁻ anion and other salt contaminants present. Removal of the solvent and drying at 60 °C in vacuo afforded the desired products with no further purification necessary.

Irradiation of the equimolar mixture of secondary amine and either 1,4-dibromobutane or 1,5-dibromopentane in the presence of aqueous K₂CO₃ at 120 °C followed by anion exchange resulted in the isolation of the desired pyrrolidinium and piperidinium salts (Scheme 1) with yields usually greater than 80% (Table 1). In general, 20 min. and 40 min. irradiation times, respectively, were required when 1,4-dibromobutane and 1,5-dibromopentane were used. The longer reaction time when using the 1,5-dibromopentane was required due to its lower reactivity as a consequence of the longer alkyl chain length. When sterically hindered secondary amines were used, such as di-sec-butylamine (Entries 5 and 6) or di-isoproppylamine (Entries 9 and 10), the yields drop dramatically to 10–24%, even after prolonged irradiation times. When dioctylamine was used, the resultant bromide salt was immiscible in water and consequently no effective anion exchange was possible (Entries 20 and 21) using the standard anion metathesis protocol. Attempts to use 1,6-dibromohexane to form the corresponding N,N-dialkylhexahydroazepinium salts were not successful, despite the formation of the 7-membered ring being favourable (by the 7-exo-tet mechanism) according to Baldwin’s rules and the fact that such rings were formed when using primary amines under the same methodology.

### Table 1. Syntheses and properties of pyrrolidinium and piperidinium NTf₂ salts prepared from secondary amines and α,ω-dihaloalkanes at 120 °C.

<table>
<thead>
<tr>
<th>R⁻¹, R⁻²</th>
<th>DIHALO COMPOUND</th>
<th>REACTION TIME (min)</th>
<th>YIELD (%)</th>
<th>m.p. (°C)</th>
<th>T⁺ (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>R⁻¹ = R⁻² = CH₂C₂H₅</td>
<td>Br(CH₃)₂Br</td>
<td>20</td>
<td>84</td>
<td>69–71</td>
</tr>
<tr>
<td>2</td>
<td>R⁻¹ = R⁻² = CH₂C₂H₅</td>
<td>Br(CH₃)₂Br</td>
<td>40</td>
<td>81</td>
<td>107–109</td>
</tr>
<tr>
<td>3</td>
<td>R⁻¹ = R⁻² = CH₂C₂H₅</td>
<td>Br(CH₃)₂Br</td>
<td>20</td>
<td>88</td>
<td>38–40</td>
</tr>
<tr>
<td>4</td>
<td>R⁻¹ = R⁻² = CH₂C₂H₅</td>
<td>Br(CH₃)₂Br</td>
<td>40</td>
<td>88</td>
<td>57–59</td>
</tr>
<tr>
<td>5</td>
<td>R⁻¹ = R⁻² = CH(CH₂)₂CH₂Br</td>
<td>Br(CH₃)₂Br</td>
<td>60</td>
<td>24</td>
<td>-72°</td>
</tr>
<tr>
<td>6</td>
<td>R⁻¹ = R⁻² = CH(CH₂)₂CH₂Br</td>
<td>Br(CH₃)₂Br</td>
<td>80</td>
<td>10</td>
<td>-73°</td>
</tr>
<tr>
<td>7</td>
<td>R⁻¹ = R⁻² = CH₂C₂H₅</td>
<td>Br(CH₃)₂Br</td>
<td>20</td>
<td>83</td>
<td>50–52</td>
</tr>
<tr>
<td>8</td>
<td>R⁻¹ = R⁻² = CH₂C₂H₅</td>
<td>Br(CH₃)₂Br</td>
<td>40</td>
<td>82</td>
<td>65–67</td>
</tr>
<tr>
<td>9</td>
<td>R⁻¹ = R⁻² = CH(CH₂)₂CH₂Br</td>
<td>Br(CH₃)₂Br</td>
<td>40</td>
<td>23</td>
<td>58–60</td>
</tr>
<tr>
<td>10</td>
<td>R⁻¹ = R⁻² = CH(CH₂)₂CH₂Br</td>
<td>Br(CH₃)₂Br</td>
<td>60</td>
<td>23</td>
<td>90–92</td>
</tr>
<tr>
<td>11</td>
<td>R⁻¹ = R⁻² = CH₂C₂H₅</td>
<td>Br(CH₃)₂Br</td>
<td>20</td>
<td>85</td>
<td>92–94</td>
</tr>
<tr>
<td>12</td>
<td>R⁻¹ = R⁻² = CH₂C₂H₅</td>
<td>Br(CH₃)₂Br</td>
<td>40</td>
<td>88</td>
<td>92–94</td>
</tr>
<tr>
<td>13</td>
<td>R⁻¹ = C₆H₄Br⁻² = C₆H₅Br⁻</td>
<td>Br(CH₃)₂Br</td>
<td>20</td>
<td>86</td>
<td>-87°</td>
</tr>
<tr>
<td>14</td>
<td>R⁻¹ = C₆H₄Br⁻² = C₆H₅Br⁻</td>
<td>Br(CH₃)₂Br</td>
<td>40</td>
<td>86</td>
<td>-75°</td>
</tr>
<tr>
<td>15</td>
<td>R⁻¹ = C₆H₄Br⁻² = CH₂Br⁻²</td>
<td>Br(CH₃)₂Br</td>
<td>20</td>
<td>83</td>
<td>-15 (-83°)</td>
</tr>
<tr>
<td>16</td>
<td>R⁻¹ = C₆H₄Br⁻² = CH₂Br⁻²</td>
<td>Br(CH₃)₂Br</td>
<td>40</td>
<td>87</td>
<td>-72°</td>
</tr>
<tr>
<td>17</td>
<td>R⁻¹ = CH₂Br⁻² = CH₂Br⁻²</td>
<td>Br(CH₃)₂Br</td>
<td>20</td>
<td>90</td>
<td>113–115</td>
</tr>
<tr>
<td>18</td>
<td>R⁻¹ = CH₂Br⁻² = CH₂Br⁻²</td>
<td>Br(CH₃)₂Br</td>
<td>20</td>
<td>88</td>
<td>110–112</td>
</tr>
<tr>
<td>19</td>
<td>R⁻¹ = CH₂Br⁻² = CH₂Br⁻²</td>
<td>Br(CH₃)₂Br</td>
<td>40</td>
<td>89</td>
<td>127–129</td>
</tr>
<tr>
<td>20</td>
<td>R⁻¹ = R⁻² = CH₂Br⁻²</td>
<td>Br(CH₃)₂Br</td>
<td>20</td>
<td>94</td>
<td>126–127</td>
</tr>
<tr>
<td>21</td>
<td>R⁻¹ = R⁻² = CH₂Br⁻²</td>
<td>Br(CH₃)₂Br</td>
<td>40</td>
<td>94</td>
<td>149–151</td>
</tr>
</tbody>
</table>

* Isolated yield. † Isolated as the bromide salt. ‡ Decomposes before melting. § Determined by differential scanning calorimetry. ‡ Glass transition.
The decomposition point of the salts was determined by thermogravimetric analysis (TGA) and the data are shown in Table 1. The NTf2 salts show remarkable thermal stability, with the majority of the salts decomposing at temperatures greater than 300 °C. In general, the pyrrolidinium NTf2 salts have higher thermal stability as compared to the equivalent piperidinium salts:

an exception being found in the case of the N,N-diethyl-substituted salts and the N-butyl-N-ethyl-substituted derivatives for which the piperidinium salt has a higher decomposition point than the corresponding pyrrolidinium salt. The pyrrolidinium NTf2 salts have decomposition points ranging from 322–393 °C, whilst the piperidinium salts have decomposition points ranging from 316–370 °C. Salts containing sec-butyl and iso-propyl groups have significantly lowered decomposition points with all such compounds showing decomposition below 305 °C.

With the success of this procedure when using the α,α,β-dihaloalkanes, the method was expanded to the use of bis(2-bromoethyl)ether as the precursor for the backbone of the ring system to form the corresponding morpholinium salts (Scheme 2). As was the case with the 1,5-dibromopentane precursor, an increase in reaction time from 20 to 40 min. was required to achieve a yield of more than 75%. Nevertheless, a small decrease in the isolated yields of the products to 78–87% (Table 2) could not be avoided. As was the case with 1,5-dibromopentane, the decrease in yield appears to be due to the increase in the chain length of the dihalogenated precursor. When pyrrolidine and piperidine were used as the secondary amines, a significant decrease in yield (to ~50%) was observed as compared to the dialkyl secondary amines after 40 min. of irradiation. However, increasing the reaction time to 60 min. resulted in yields of only ~65%.

A new class of ionic liquids based on the 2,3-dihydro-1H-isoindolinium ring system could also be readily prepared in high yields using this method. Substitution of the α,ω-dibromoalkane with α,α'-dibromo-o-xylene resulted in the formation of the diydro-1H-isoindolinium ring system in yields ranging from 78–96% (Scheme 3, Table 3). In the case of the dibenzyl analogue (29) the irradiation time had to be increased to 60 min. in order to achieve a 75% yield of the bromide salt. The longer reaction time needed and lower yield obtained when compared to the equivalent piperidinium and pyrrolidinium salts may be attributed to the steric bulk of the amine and the α,α'-dibromo-o-xylene. In this case, the N,N-dibenzyl-2,3-dihydro-1H-isoindolinium bromide obtained was insoluble in water, hence, no anion exchange with LiNTf2 was possible using the standard anion metathesis protocol outlined (Experimental Section), and thus was not attempted. The products obtained after anion exchange were liquids at room temperature (with the exception of the diethyl and the spiro salts) with melting points in the range from ~43 to ~54 °C and decomposition temperatures >340 °C. In the case of the N,N-diethyl-2,3-dihydro-1H-isoindolinium bis(trifluoro-methanesulfonyl)imide IL, crystallisation occurred only after a prolonged period at room temperature. N,N-Dibenzyl-2,3-dihydro-1H-isoindolinium bromide had a decomposition point of 175 °C.
desired IL.\(^2\) The removal of coloured impurities can be achieved by heating an aqueous solution of the intermediate bromide salt at 65 °C for 24 h in the presence of activated charcoal.\(^2\) Ultimately, after the 3 steps the final yield of the desired IL is in the range of 73–87% (c.f. this work achieves yields of 82–92% for the

<table>
<thead>
<tr>
<th>R(^1), R(^2)</th>
<th>DIHALO COMPOUND</th>
<th>REACTION TIME (min)</th>
<th>YIELD (%)</th>
<th>m.p. (°C)</th>
<th>T(_{\text{dec}}) (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>22 R(^1) = R(^2) = CH(_2)C(_6)H(_5)</td>
<td>Br(CH(_2))(_2)O</td>
<td>40</td>
<td>78</td>
<td>149–151</td>
<td>265</td>
</tr>
<tr>
<td>23 R(^1) = R(^2) = C(_6)H(_5)</td>
<td>Br(CH(_2))(_2)O</td>
<td>40</td>
<td>87</td>
<td>48</td>
<td>327</td>
</tr>
<tr>
<td>24 R(^1) = R(^2) = CH(_2)</td>
<td>Br(CH(_2))(_2)O</td>
<td>40</td>
<td>87</td>
<td>50–52</td>
<td>301</td>
</tr>
<tr>
<td>25 R(^1) = CH(_2)H(_2), R(^2) = CH(_2)</td>
<td>Br(CH(_2))(_2)O</td>
<td>40</td>
<td>85</td>
<td>39–41</td>
<td>322</td>
</tr>
<tr>
<td>26 R(^1) = CH(_2)H(_2), R(^2) = CH(_2)</td>
<td>Br(CH(_2))(_2)O</td>
<td>40</td>
<td>82</td>
<td>29–31</td>
<td>294</td>
</tr>
<tr>
<td>27 R (= -(CH(_2))(_n)</td>
<td>Br(CH(_2))(_2)O</td>
<td>60</td>
<td>66</td>
<td>73–75</td>
<td>369</td>
</tr>
<tr>
<td>28 R (= -(CH(_2))(_n)</td>
<td>Br(CH(_2))(_2)O</td>
<td>60</td>
<td>64</td>
<td>119–121</td>
<td>359</td>
</tr>
</tbody>
</table>

* Isolated yield. \(^a\) Glass transition point.

Table 2 Synthesises and properties of N,N-dialkylmorpheolium N\(_2\)I: ILs prepared from secondary amines and bis(2-bromoethyl)ether at 120 °C.

<table>
<thead>
<tr>
<th>R(^1), R(^2)</th>
<th>DIHALO COMPOUND</th>
<th>REACTION TIME (min)</th>
<th>YIELD (%)</th>
<th>m.p. (°C)</th>
<th>T(_{\text{dec}}) (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>29 R(^1) = R(^2) = CH(_2)C(_6)H(_5)</td>
<td>Br(CH(_2))(_2)C(_6)H(_5)</td>
<td>60</td>
<td>75</td>
<td>175</td>
<td></td>
</tr>
<tr>
<td>30 R(^1) = R(^2) = C(_6)H(_5)</td>
<td>Br(CH(_2))(_2)C(_6)H(_5)</td>
<td>60</td>
<td>84</td>
<td>340</td>
<td></td>
</tr>
<tr>
<td>31 R(^1) = R(^2) = CH(_2)</td>
<td>Br(CH(_2))(_2)C(_6)H(_5)</td>
<td>60</td>
<td>92</td>
<td>365</td>
<td></td>
</tr>
<tr>
<td>32 R(^1) = R(^2) = CH(_2)</td>
<td>Br(CH(_2))(_2)C(_6)H(_5)</td>
<td>60</td>
<td>92</td>
<td>363</td>
<td></td>
</tr>
<tr>
<td>33 R(^1) = CH(_2)H(_2), R(^2) = CH(_2)</td>
<td>Br(CH(_2))(_2)C(_6)H(_5)</td>
<td>60</td>
<td>83</td>
<td>347</td>
<td></td>
</tr>
<tr>
<td>34 R(^1) = CH(_2)H(_2), R(^2) = CH(_2)</td>
<td>Br(CH(_2))(_2)C(_6)H(_5)</td>
<td>60</td>
<td>91</td>
<td>391</td>
<td></td>
</tr>
</tbody>
</table>

* Isolated yield. \(^b\) Isolated as the bromide salt. \(^c\) Decomposes before melting. \(^d\) Determined by differential scanning calorimetry. \(^e\) Glass transition.

Scheme 4

![Scheme 4](image)

identical ILs). However, significantly greater molar amounts of starting materials were required, substantially longer heating times needed, and a greater number of purification steps required, as compared to our method described here.

A metric to test the sustainability and “greenness” of the current process to that shown in Scheme 4 was recently published by GSK.\(^2\) The method of determining the overall “greenness” of a process involves a standardized assessment of each reagent used within a chemical process: the calculation of an EHS (Environmental, Health, Safety) score is done by considering the presence or absence of certain risk phrases associated with each chemical followed by the geometric mean of the three scores allocated; the calculation of an Overall Clean Chemistry score by taking the geometric mean of scores allocated to assessing aspects of the process such as ease of work-up, use of co-reagents, stoichiometry, atom efficiency and other issues (such as decomposition, the need for low temperatures, the use of inert atmospheres, etc.). Finally, the Overall “Greenness” score is determined by taking the geometric mean of the EHS and Overall Clean Chemistry scores: thus, for the synthesis of 1-butyl-1-methylpyrrolidinium bis(trifluoromethanesulfon)imide (15), the Overall “Greenness” score for the method described herein is 7.5 whilst when using the methodology outlined in Scheme 4 the score is 4.2 or 4.5 (for both methods in step 1). Note that these scores have been calculated without including the reaction or extraction solvents as this method only takes into account the reagents used. The use of different substrates to make the different ring systems has little effect on the overall “greenness” of either process (see Supplementary Information for the calculations).

In attempting to increase the “greenness” of ionic liquid syntheses many variables need to be considered in order to improve the process. Analysis of the synthesis of 1-alkyl-3-methylimidazolium ionic liquids suggests the use of the strategic planning SWOT analysis to assess the greenness of any synthesis method.\(^5\) Utilising such an analysis for the syntheses outlined herein (Scheme 1) reveals that the process employed has a low E-factor, high atom economy (as only equimolar amounts of the starting materials are used) and upholds seven of the twelve Principles of Green Chemistry\(^4\) (prevention of waste; high atom economy; the elimination of the use of unnecessary auxiliary substances; low energy requirements; elimination of unnecessary derivatisation; the use of analytical methodologies to prevent formation of hazardous substances; and, the use of a chemical process to minimize the potential for chemical accidents). It should be noted that the E-factor could be lowered even further in those cases where room temperature ionic liquids are formed, as these could be effectively washed with water to remove the salt by-products without the use of CH\(_2\)Cl\(_2\). Further benefits are also derived by the use of water as the solvent as this overcomes many of the issues associated with the use of microwave heating (i.e. mass transport issues of starting materials due to viscosity of the ionic liquid as the intermediate halide salts are highly soluble; and, there is no IL decomposition due to the presence of hot-
spots). In all of the cases mentioned here, the final products were obtained as colourless to pale yellow products that were judged to be pure according to NMR spectroscopy (and melting points/glass transition points/decomposition points of the known ILS prepared were very close to the reported literature values) and hence required no additional purification steps.

Conclusions

Rapid, high-yielding syntheses of a range of ionic liquids from readily available (and inexpensive) secondary amines and a variety of α,ω-dihaloalkanes have been introduced, including a route to a new class of ionic liquids based on the 2,3-dihydro-1H-isoindolinium ring system. Coupled with the easy work-up this represents an excellent generic synthetic method to four families of heterocyclic ILs. The application of different metrics (the GSK reagent guide and SWOT) indicates that the new synthetic procedure is significantly greener than the corresponding synthesis using existing procedures.

Experimental

The following chemicals were used without further purification: 1,4-dibromobutane, piperidine, lithium bis(trifluoromethanesulfonyl)imide, bis(2-bromoethyl)ether (all Aldrich), 1,5-dibromopentane (Fluka), pyrrolidine (BDH), α,α′-dibromo-o-xylene (Aldrich) and potassium carbonate (Merck). The amines N-butyl-N-ethylamine, N-butyl-N-iso-propylamine, N-dibenzylamine, di-propyl amine, dibenzylamine, 1,4-dibromobutane, piperidine, lithium bis(trifluoromethanesulfonyl)imide. The resultant reaction mixture was washed with diethyl ether (2 × 10 mL). To the aqueous phase was added lithium bis(trifluoromethanesulfonyl)imide (0.800 g, 2.79 mmol) and the resultant solution was stirred for 1 h at room temperature. The reaction mixture was extracted with dichloromethane (3 × 20 mL) and the combined organic phases were washed with water (2 × 10 mL) and separated. The solvent of the combined organic phases was removed in vacuo to afford the desired product. The product was dried at 60 °C in vacuo overnight to remove all traces of water.

Procedure for conventional heating. To a sealed stainless steel autoclave was added diethylamine (1.44 g, 11.2 mmol), 1,5-dibromopentane (2.56 g, 11.2 mmol), potassium carbonate (1.54 g, 11.2 mmol) and water (15 mL). The autoclave was sealed and heated at 120 °C in an oil bath for 16 h. Upon termination of the heating, the autoclave was cooled to room temperature and the reaction worked up according to the method described above. Yield 4.26 g (80%). See below for characterisation.

N,N-Dibenzylypyrrolidinium bis(trifluoromethanesulfonyl)imide. White powder. Yield: 4.97 g (84%). m.p. 69–71 °C. Tₘₛ 328 °C. ¹H NMR (CDCl₃): δ 7.38 (m, 10H, ArC), 4.39 (s, 4H, ArCH₂), 3.42 (m, 4H, NCH₂ ring), 1.93 (m, 4H, NCH₂CH₂ ring) ppm. ¹³C{¹H} NMR (CDCl₃): δ 133.0, 131.15, 129.71, 127.12, 120.05 (q, JCF = 321 Hz, CF₃), 64.70, 58.39, 21.41 ppm. ¹⁹F NMR (CDCl₃): δ -79.19 (s) ppm. m/z (ESI+): 252 (M⁺, 100%), 783 ([2M + NTf₂]⁺), 11. IR (thin film, NaCl): ν 3605(m), 3036(m), 3013(m), 2984(m), 1497(s), 1456(vs), 1323(vs), 1180(vs), 1168(vs), 1130(vs), 1060(vs), 910(m), 891(m), 788(s) cm⁻¹.

N,N-Dibenzyllpyrrolidinium bis(trifluoromethanesulfonyl)imide. White powder. Yield: 4.92 g (81%). m.p. 107–109 °C. Tₘₛ 331 °C. ¹H NMR (CDCl₃): δ 7.36 (m, 10H, ArH), 4.37 (s, 4H, ArCH₂), 3.17 (m, 4H, NCH₂ ring), 1.97 (m, 4H, NCH₂CH₂ ring), 1.45 (m, 2H, NCH₂CH₂ ring) ppm. ¹³C{¹H} NMR (CDCl₃): δ 133.22, 131.05, 129.57, 126.22, 120.0 (q, JCF = 321 Hz, CF₃), 64.10, 56.02, 20.65, 19.79 ppm. ¹⁹F NMR (CDCl₃): δ -79.19 (s) ppm. m/z (ESI+): 266 (M⁺, 100%), 811 ([2M + NTf₂]⁺), 11. IR (thin film, NaCl): ν 3606(m), 3041(m), 2970(m), 2947(s), 2876(m), 1475(m), 1454(s), 1394(m), 1350(vs), 1327(vs), 1265(s), 1188(vs), 1139(s).

Differential scanning calorimetry (DSC) was performed using a TA Instruments Modulated 2920 DSC. Samples (5–10 mg) were loaded into an aluminum pan and were cooled at 10 °C/min. to -140 °C, equilibrated for 10 min. then warmed at 10 °C/min. to 25 °C. The samples were cycled through this temperature program twice to ensure the reproducibility of the data. Data were analysed using the TA Universal Analysis program.
N,N-Dibutylpyrrolidinium bis(trifluoromethanesulfonyl)imide. White powder. Yield: 4.53 g (88%). m.p. 38–40 °C. T_{dec} 367 °C. ^1H NMR (CDCl₃): δ 3.30 (t, 4H, _J_HH = 7 Hz, NCH₂), 3.00 (4H, NCH₂ ring), 1.99 (m, 4H, NCH₂CH₂ ring), 1.46 (m, 4H, NCH₂CH₂), 1.19 (m, CH₂CH₃), 0.74 (t, 6H, _J_HH = 7 Hz, CH₃) ppm. ^13C^[1]{H} NMR (CDCl₃): δ 115.21 (q, _J_CF = 321 Hz, CF₃), 62.03, 55.95, 24.75, 21.39, 19.13, 12.87 ppm. ^19F NMR (CDCl₃): δ -79.79 (s) ppm. m/z (ESI+): 184 (M⁺, 100%), 642 ([2M + NTF₂]+), 111 IR (thin film, NaCI): v 2966(s), 2982(s), 2947(m), 2887(m), 1468(m), 1398(m), 1059(s), 788(m) cm⁻¹.

N,N-Di-iso-propylpyrrolidinium bis(trifluoromethanesulfonyl)imide. White powder. Yield: 1.14 g (23%). m.p. 90–92 °C. T_{dec} 246 °C. ^1H NMR (CDCl₃): δ 3.89 (sept, _J_HH = 7 Hz, CH₂CH₃), 3.32 (m, 4H, NCH₂ ring), 1.78 (m, 4H, NCH₂CH₂ ring), 1.61 (m, 2H, NCH₂CH₂CH₂ ring), 1.35 (d, 2H, _J_HH = 7 Hz, CH₃CH₂) ppm. ^13C^[1]{H} NMR (CDCl₃): δ 119.71 (q, _J_CF = 321 Hz, CF₃), 60.66, 53.70, 20.52, 19.48, 17.51 ppm. ^19F NMR (CDCl₃): δ -79.05 (s) ppm. m/z (ESI+): 170 (M⁺, 100%), 620 ([2M + NTF₂]+), 592 ([2M + 2NTF₂]+), 17. IR (thin film, NaCI): v 2958(w), 2898(w), 2849(w), 1467(m), 1407(m), 1349(vs), 1213(vs), 793(m), 740(cm⁻¹).

N,N-Diethylpyrrolidinium bis(trifluoromethanesulfonyl)imide. White powder. Yield: 3.87 g (85%). m.p. 92–94 °C. T_{dec} 317 °C. ^1H NMR (CDCl₃): δ 3.41 (m, 4H, NCH₂ ring), 3.27 (t, _J_HH = 7 Hz, NCH₂), 2.15 (m, 4H, OCH₂ ring), 1.29 (t, _J_HH = 7 Hz, CH₃) ppm. ^13C^[1]{H} NMR (CDCl₃): δ 119.87 (q, _J_CF = 321 Hz, CF₃), 62.11, 54.66, 21.74, 8.46 ppm. ^19F NMR (CDCl₃): δ -79.22 (s) ppm. m/z (ESI+): 128
(M, 100%), 536 ([2M + NTEf]+, 17). IR (thin film, NaCl): ν
2995(m), 2925 (w), 2900(w), 1466(m), 1408(m), 1352(vs),
1330(s), 1198(vs), 1141(s), 1056(vs), 790(m), 740(m) cm⁻¹.

4. N,N-Diethylpiperidinium bis(trifluoromethanesulfonyl)imide.
White powder. Yield: 4.13 g (88%). m.p. 99–100 °C. T_dsc 370
°C. 1H NMR (CDCl₃): δ 3.19 (q, 4H, J_HCH = 7 Hz, CH₂N), 3.14
(m, 4H, CH₂N ring), 1.73 (m, 4H, NCH₂CH₂ ring), 1.56 (m, 2H,
NCH₂CH₂ ring), 1.15 (t, 6H, J_HCH = 7 Hz, CH₃) ppm.
13C(1H) NMR (CDCl₃): δ 119.67 (q, J_C'CH = 321 Hz, CF₃), 58.25,
53.11, 20.54, 19.15, 6.50 ppm. 19F NMR (CDCl₃): δ -79.65 (s
ppm. m/z (ESI+): 142 (M⁺, 100%), 564 ([2M + NTEf]+, 26). IR (thin
film, NaCl): ν 2995(w), 2925(m), 2883(w), 1484(m), 1464(m), 1405(m), 1352(vs), 1333(s), 1198(vs), 1139(s), 1054(s),
944(m), 790(m), 739(m) cm⁻¹.

White powder. Yield: 4.04 g (90%). m.p. 113–115 °C (lit. 113
°C). T_dsc 322 °C. 1H NMR (CDCl₃): δ 3.32 (m, 8H, NCH₂ ring),
2.05 (m, 8H, NCH₂CH₂ ring) ppm. 13C(1H) NMR (CDCl₃): δ 119.65 (q, J_C'CH = 321 Hz, CF₃), 62.84, 21.63 ppm. 19F NMR (CDCl₃): δ -79.83 (s) ppm. m/z (ESI+): 126 (M⁺, 100%), 532
([2M + NTEf]+, 46). IR (thin film, NaCl): ν 2980(w), 2944(w),
2902(w), 1463(m), 1350(vs), 1222(s), 1187(vs), 1138(s), 1056(s),
789(m), 739(m) cm⁻¹.

5-Azonaspiro[5.5]decan-2-one.
White powder. Yield: 4.31 g (89%). m.p. 127–129 °C (lit. 130°C). T_dsc 316 °C. 1H NMR (CDCl₃): δ 3.25 (t, 8H, J_HCH = 6 Hz, NCH₃), 1.74
(m, 8H, NCH₂CH₂), 1.61 (dt, 4H, J_HCH = 6 Hz, N-CH₂CH₂H) ppm.
13C(1H) NMR (CDCl₃): δ 119.86 (q, J_C'CH = 321 Hz, CF₃), 59.67,
21.14, 19.16 ppm. 19F NMR (CDCl₃): δ -79.58 (s) ppm. m/z (ESI+): 154 (M⁺, 100%), 588 ([2M + NTEf]+, 30). IR (thin film, NaCl):
ν 2957(w), 2881(w), 1470(m), 1352(vs), 1333(s), 1184(vs), 1138(s), 1053(s), 891(m), 795(m) cm⁻¹.

4. N-Butyl-N-methylpiperidinum bis(trifluoromethanesulfonyl)imide.
Colourless oil. Yield: 3.91 g (83%). m.p. -15 °C (lit. -15°C). T_dsc 330
°C. 1H NMR (CDCl₃): δ 3.49 (s, 4H, J_HCH = 6 Hz, NCH₂), 3.06
(m, 4H, NCH₂CH₂ ring), 2.96 (m, 2H, NCH₂ ring), 2.68 (s, 3H, NCH₃), 1.89 (m, 4H, NCH₂CH₂ ring), 1.41 (m, 2H, NCH₂CH₂), 1.06 (m, 2H, CH₂CH₃), 0.64 (t, 3H,
J_HCH = 7 Hz, CH₃) ppm. 13C(1H) NMR (CDCl₃): δ 119.58 (q, J_C'CH = 321 Hz, CF₃), 64.75, 64.06, 47.82, 25.15, 21.03, 19.06, 12.70 ppm. 19F NMR (CDCl₃): δ -80.03 (s) ppm. m/z (ESI+): 142
(M⁺, 100%), 564 ([2M + Br]+, 40). IR (thin film, NaCl): ν 2968(m), 2941(m), 2880(m), 1466(m), 1350(vs), 1331(s), 1192(vs), 1138(s), 1057(vs), 929(m), 788(m) cm⁻¹.

N-Butyl-N-methylpiperidinum bis(trifluoromethanesulfonyl)imide.
Colourless oil. Yield: 4.22 g (87%). T_dsc -72 °C (lit. -73°C). T_dsc 331 °C. 1H NMR (CDCl₃): δ 3.14 (m, 4H, NCH₃ and NCH₂ ring), 3.08 (m, 4H, NCH₂ ring), 2.81 (s, 3H, NCH₃), 1.68 (m, 4H, NCH₂CH₂ ring), 1.51 (m, 4H, NCH₂CH₂ and NCH₂CH₂ ring), 1.20 (m, 2H, CH₃CH₂), 0.79 (t, 3H, J_HCH = 7 Hz, CH₃) ppm.
13C(1H) NMR (CDCl₃): δ 119.53 (q, J_C'CH = 321 Hz, CF₃), 63.79,
60.82, 46.91, 23.11, 20.15, 19.42, 19.01, 18.32, 12.75 ppm. 19F NMR (CDCl₃): δ -79.88 (s) ppm. m/z (ESI+): 156 (M⁺, 100%), 592 ([2M + Br]+, 32). IR (thin film, NaCl): ν 2964(s), 2880(m),
1468(m), 1350(vs), 1331(vs), 1226(vs), 1196(vs), 1138(vs),
1057(vs), 937(m), 789(m) cm⁻¹.

N,N-Dioctylypiperidinum bromide.
White powder. Yield: 4.09 g (94%). m.p. 149–151 °C (lit. 144–146°C). T_dsc 202 °C. 1H NMR (CDCl₃): δ 3.31 (t, 4H, J_HCH = 6 Hz, NCH₂), 3.07 (m, 4H,
N,N-Dibenzylmorpheopholine

bis[trifluoromethanesulfonylimide]. White powder. Yield: 4.75 g (87%). m.p. 149–151 °C. T$_{dec}$ 265 °C. 1H NMR (CDCl$_3$): δ 3.95 (m, 4H, CH$_2$N ring), 4.00 (m, 4H, CH$_2$N ring), 3.80 (m, 4H, CH$_2$O ring), 1.80 (m, 4H, CH$_2$CH$_2$N), 1.12 (t, $J_{HF}$ = 7 Hz, CH$_3$). 13C{1H} NMR (CDCl$_3$): δ 120.06 (q, $J_{CF}$ = 321 Hz, CF$_3$), 60.66, 61.30, 58.09, 58.15, 15.04, 10.35 ppm. 19F NMR (CDCl$_3$): δ 79.03 (s) ppm. m/z (ESI+): 200 (M$^+$, 100%), 68 (2[M + NTf$_2$$^-$]+), 15. IR (thin film, NaCl): v 3036(s), 1546(s), 1469(s), 1410(w), 1353(s), 1312(s), 1191(s), 1135(s), 1056(s), 969(w), 933(s), 897(m), 791(m), 762(w), 741(s) cm$^{-1}$. 3-Oxa-6-azaspiro[4.5]decan-6-ium

bis[trifluoromethanesulfonylimide]. Pale yellow solid. Yield: 3.10 g (64%). m.p. 119–121 °C. T$_{dec}$ 359 °C. 1H NMR (CDCl$_3$): δ 3.87 (m, 4H, CH$_2$N ring), 3.60 (m, 4H, CH$_2$N ring), 1.94 (m, 4H, CH$_2$N ring), 1.35 (m, 4H, CH$_2$CH$_2$N), 1.15 (t, $J_{HF}$ = 7 Hz, CH$_3$). 13C{1H} NMR (CDCl$_3$): δ 120.06 (q, $J_{CF}$ = 321 Hz, CF$_3$), 60.32, 59.90, 58.48, 21.08, 19.05 ppm. 19F NMR (CDCl$_3$): δ 79.02 ppm. m/z (ESI+): 156 (M$^+$, 100%), 564 ([2M + NTf$_2$$^-$]+). IR (thin film, NaCl): v 3065(w), 2983(m), 2883(m), 1469(s), 1410(w), 1353(s), 1312(s), 1191(s), 1135(s), 1056(w), 969(w), 933(s), 897(m), 791(m), 762(w), 741(s) cm$^{-1}$. N,N-Dibenzyl-2,3-dihydro-1H-isodolinol bromide. White powder. Yield: 3.04 g (72%). m.p. 257–259 °C (dec). T$_{dec}$ 175 °C. 1H NMR (CDCl$_3$): δ 7.66 (m, 4H, ArH), 7.38 (m, 6H, ArH), 7.24 (m, 4H, ArH), 5.36 (s, 4H, NCH$_2$Ph), 5.12 (s, 4H, ArCH$_2$) ppm. 13C{1H} NMR (CDCl$_3$): δ 133.41, 132.71, 130.77, 129.40, 129.39, 127.97, 123.18, 64.76, 62.47 ppm. m/z (ESI+): 300 (M$^+$, 100%), 60.2 (2[M + Br]$^-$), 8. IR (thin film, NaCl): v 3043(m), 2973(s), 2883(w), 1496(m), 1457(s), 1391(w), 1351(s), 1260(w), 1195(s), 1137(m), 1056(s), 935(w), 876(m), 786(m), 749(vs) cm$^{-1}$. N,N-Dibutyl-2,3-dihydro-1H-isodolinol bromide. Yellow oil. Yield: 5.46 g (96%). T$_{dec}$ -44 °C. T$_{dec}$ 340 °C. 1H NMR (CDCl$_3$): δ 7.57 (m, 4H, ArH), 5.04 (s, 4H, ArCH$_2$), 3.66 (m, 4H, NCH$_2$), 1.89 (m, 4H, NCH$_2$H), 1.59 (m, 4H, CH$_2$CH$_2$N), 1.16 (t, $J_{HF}$ = 7 Hz, CH$_3$). 13C{1H} NMR (CDCl$_3$): δ 132.12, 129.48, 122.91, 119.83 (q, $J_{CF}$ = 321 Hz, CF$_3$), 67.58, 62.42, 25.23, 19.43, 13.14 ppm. 19F NMR (CDCl$_3$): δ -79.40 (s) ppm. m/z (ESI+): 232 (M$^+$, 100%), 743 ([2M + NTf$_2$$^-$]+). IR (thin film, NaCl): v 2966(s), 2937(w), 1546(s), 1469(s), 1410(w), 1353(s), 1312(s), 1191(s), 1135(s), 1056(w), 969(w), 933(s), 897(m), 791(m), 762(w), 741(s) cm$^{-1}$.
50
45
25
20

5.11 g (95%). Tm = 43 °C; Tdec = 365 °C. 1H NMR (CDCl3): δ 7.40–7.25 (m, 4H, ArH), 4.82 (s, 4H, ArCH2), 3.40 (m, 4H, NCH2), 1.71 (m, 4H, CH2CH2), 0.97 (t, JHH = 7 Hz, 6H, CH3) ppm. 13C{1H} NMR (CDCl3): δ 132.11, 129.63, 122.93, 119.91 (q, JCF = 321 Hz, CF3), 67.64, 64.29, 17.06 ppm.

2.32 (m, 4H, NCH2CH2), 1.77 (m, 2H, NCH2CH2), 1.40 (m, 2H, CH2CH2), 0.96 (t, 3H, JHH = 7 Hz, CH3CH2) ppm. 13C{1H} NMR (CDCl3): δ 131.95, 129.68, 123.47, 119.82 (q, JCF = 321 Hz, CF3), 69.41, 65.03, 50.11, 25.76, 19.46, 13.26 ppm. 19F NMR (CDCl3): δ -79.01 (s) ppm (m/z (ESI+) = 190 (M⁺, 100%), 660 ([2M + NTF2]⁺ - 1)), IR (thin film, NaCl): ν 3080(br m), 2970(s), 2943(m), 2881(m), 1483(s), 1428(m), 1351(vs), 1189(vs), 1139(vs), 1057(vs), 983(s), 945(m), 872(w), 817(m), 792(s), 760(s), 741(s) cm⁻¹.

5.11 g (84%). m.p. 81–83 °C. Tg = 83 °C. 1H NMR (CDCl3): δ 7.32 (m, 4H, ArH), 3.18 (s, 3H, NC3), 1.67 (m, 2H, NCH2), 1.35 (t, 6H, JHH = 7 Hz, 6H, CH3) ppm. 13C{1H} NMR (CDCl3): δ 132.69, 129.63, 123.07, 119.89 (q, JCF = 321 Hz, CF3), 67.27, 61.49, 57.86, 25.29, 19.57, 13.32, 8.97 ppm. 19F NMR (CDCl3): δ -78.94 (s) ppm (m/z (ESI+) = 188 (M⁺, 100%), 656 ([2M + NTF2]⁺ - 2)), IR (thin film, NaCl): ν 3080(br m), 2970(s), 2943(m), 2881(m), 1483(s), 1428(m), 1351(vs), 1189(vs), 1139(vs), 1057(vs), 983(s), 945(m), 872(w), 817(m), 792(s), 760(s), 741(s) cm⁻¹.

5.48 g (91%). m.p. 74–76 °C. Tg = 391 °C. 1H NMR (CDCl3): δ 7.37 (m, 4H, ArH), 4.79 (s, 4H, ArCH2), 3.69 (m, 4H, NCH2), 2.32 (m, 4H, NCH2CH2) ppm. 13C{1H} NMR (CDCl3): δ 132.11, 129.68, 123.07, 119.89 (q, JCF = 321 Hz, CF3), 67.52, 63.89, 21.52 ppm. 19F NMR (CDCl3): δ -79.09 (s) ppm (m/z (ESI+) = 174 (M⁺, 100%), 628 ([2M + NTF2]⁺ - 15)), IR (thin film, NaCl): ν 3061(m), 2998(m), 2900(w), 1482(m), 1466(s), 1351(vs), 1269(s), 1198(vs), 1140(vs), 1058(vs), 976(m), 941(w), 907(m), 790(s), 739(vs) cm⁻¹.

Acknowledgements

The Australian Research Council supported this research. The authors would also like to thank John Morris Scientific Pty Ltd for the generous loan of the Biotage Initiator 2.5 microwave system.

Notes and references


\[
\begin{align*}
R^1NH &+ Br\text{-}CH_X\text{-}CH\text{-}Br \\
\text{ii} \rightarrow \text{LiNTf}_2
\end{align*}
\]

**35 EXAMPLES**

REACTION TIME: 20-60 min

YIELDS: 64-95%