

Part I
Green Synthesis

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1

The Green Synthesis of Ionic Liquids

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1.1

The *Status Quo* of Green Ionic Liquid Syntheses

One of the greatest problems plaguing ionic liquid science is that the terms “green” and “ionic liquid(s)” are often used synonymously. This, however, is both incorrect and deceptive because implicit in the designer classification of ionic liquids [1] is the ability to prepare the salts to possess distinctly non-green characteristics (*viz.* toxic, explosive [2], etc.). What is more, the preparation and purification of the salts are also often extremely dirty, requiring the use of large volumes of harmful organic solvents. It therefore follows that a *bona fide* green ionic liquid synthesis has only occurred if both the ionic liquid product and its preparation comply with all 12 principles of green chemistry as listed below [3, 4].

The Twelve Principles of Green Chemistry

1. It is better to prevent waste than to treat or clean up waste after it has formed.
2. Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product.
3. Wherever practicable, synthetic methodologies should be designed to use and generate substances that possess little or no toxicity to human health and the environment.
4. Chemical products should be designed to preserve efficacy of function while reducing toxicity.
5. The use of auxiliary substances (e.g. solvents, separation agents *etc.*) should be made unnecessary wherever possible and innocuous when used.
6. Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure.

7. A raw material of feedstock should be renewable rather than depleting wherever technically and economically practicable.
8. Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible.
9. Catalytic reagents (as selective as possible) are superior to stoichiometric reagents.
10. Chemical products should be designed so that at the end of their function they do not persist in the environment and break down into innocuous degradation products.
11. Analytical methodologies need to be further developed to allow for real-time, in-process monitoring and control prior to the formation of hazardous substances.
12. Substances and the form of a substance used in a chemical process should be chosen so as to minimize the potential for chemical accidents, including releases, explosions and fires.

To date, many excellent reviews [5–8] have summarized the *status quo* of ionic liquid syntheses, but until the approach discussed here, no publication has exclusively evaluated the state-of-the-art for green ionic liquid syntheses. In addition (and as far as we know), there is also currently no system available to determine whether an existing or planned ionic liquid preparation is green. We therefore thought it was timely not merely to write another ionic liquid synthesis review, but instead to develop a simple, universal method to assess whether an ionic liquid preparation is green or not. In this chapter, we provide a detailed look at our recent approach [9] to gauge the greenness of ionic liquid preparations.

1.2

Ionic Liquid Preparations Evaluated for Greenness

The ionic liquid preparations and purifications that were assessed for greenness are shown in Figure 1.1 and Figure 1.2, respectively. It is important to note that we only considered laboratory scale preparations *i.e.* on scales <2 kg. In particular, we concentrated on the synthesis of ionic liquids containing 1-alkyl-3-methylimidazolium cations, $[C_n\text{mim}]^+$, since the most synthetic data are available in the literature for these types of salts [10]. We also included an evaluation of the pros and cons of using differing energy sources to promote ionic liquid syntheses, *viz.* conductive (conventional) heating, microwave irradiation, ultrasonic irradiation and simultaneous microwave and ultrasonic irradiation.

Although our greenness assessment approach was specifically applied to the methodologies shown in Figures 1.1 and Figure 1.2, in principle the method of analysis can be applied to any type of ionic liquid preparation, such as alkylsulfate [11, 12] and carbene routes [13]. We therefore also evaluated the greenness of the use microstructured reactors for ionic liquid syntheses (Section 1.11).

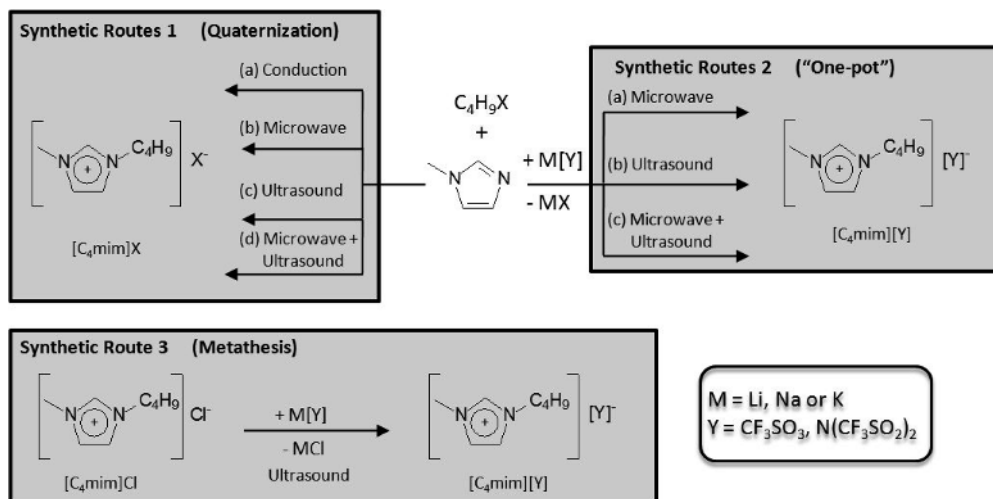


Figure 1.1 Typical ionic liquid synthetic routes [14].

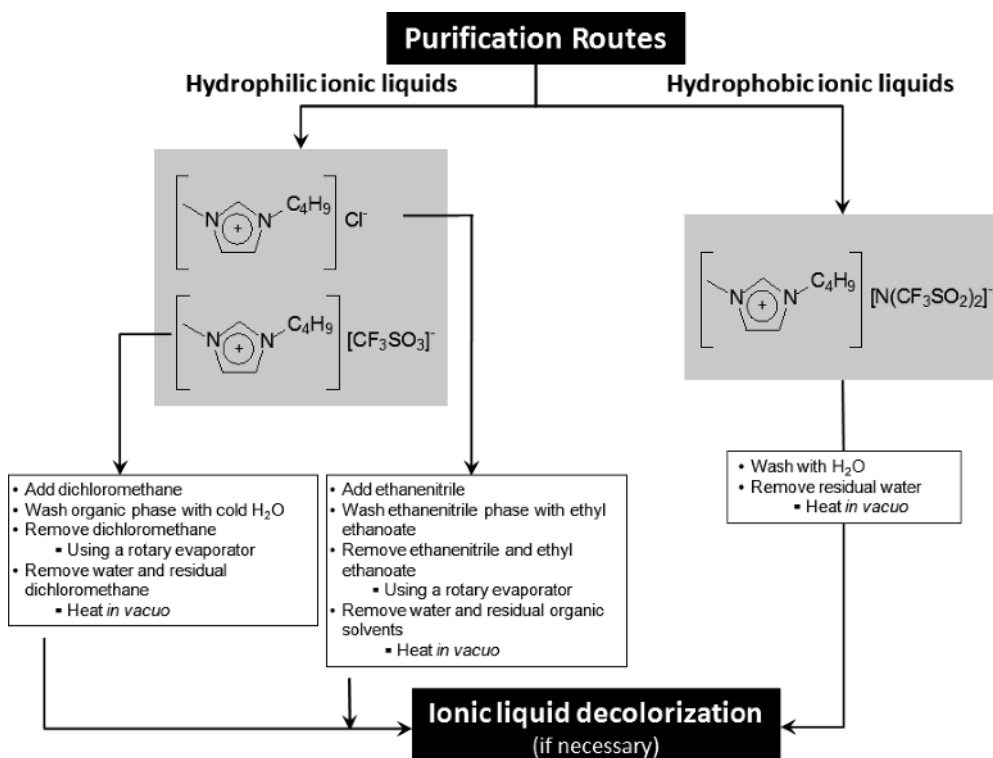


Figure 1.2 Typical ionic liquid purification routes [14].

1.3

Which Principles of Green Chemistry are Relevant to Ionic Liquid Preparations?

The 12 principles of green chemistry [3, 4] and also the 12 principles of green engineering [15] have been formalized over the past two decades by Professor Paul Anastas. Recently, both sets of lengthy principles were condensed by Professor Martyn Poliakoff and co-workers into mnemonics for easy communication, *viz.* PRODUCTIVELY and IMPROVEMENTS [16], as listed below.

The Twelve Principles of Green Chemistry

P Prevents Waste
R Renewable materials
O Omit derivatization steps
D Degradable chemical products
U Use safe synthetic methods
C Catalytic reagents
T Temperature, pressure ambient
I In-process monitoring
V Very few auxiliary substances
E *E*-factor, maximise feed in product
L Low toxicity of chemical products
Y Yes it's safe

The Twelve Principles of Green Engineering

I Inherently non hazardous and safe
M Minimize material diversity
P Prevention instead of treatment
R Renewable material and energy inputs
O Output-led design
V Very simple
E Efficient use of mass, energy, space and time
M Meet the need
E Easy to separate by design
N Networks for exchange of local mass and energy
T Test the life cycle of the design
S Sustainability throughout product life cycle

The first step in conducting our greenness assessments involved a close examination of the 12 principles of green chemistry, which revealed that only eight of the 12 principles were relevant to the ionic liquid syntheses and purifications under scrutiny. The 4th, 7th, 9th and 10th principles are irrelevant to the ionic liquid preparations discussed here, since the 4th, 7th and 10th principles of green chemistry apply to the ionic liquid product itself rather than the procedure, and the 9th principle is associated with catalytic methodologies and hence is also not relevant to the typical ionic liquid preparations discussed here. On the other hand, the 8th, 11th and 12th principles of green chemistry apply to all the ionic liquid syntheses discussed here since:

1. Derivatization (8th principle) is not used in any of the ionic liquid syntheses.
2. In-process monitoring (11th principle), is not applicable to conventional laboratory syntheses, although it does apply to the special case of lab-on-a-chip [17, 18] (see Section 1.11).
3. Ionic liquids, by virtue of their negligible vapor pressure, minimize the potential for chemical accidents such as fires and explosions (12th principle).

To summarize, only the 1st, 2nd, 3rd, 5th, 6th, 8th, 11th and 12th principles of green chemistry are relevant to the synthetic procedures discussed here. Although



the principles of green engineering are of course important in determining the greenness of a given chemical reaction, they are more relevant to very large-scale chemical processes and therefore were not included in laboratory-scale (<2 kg) greenness assessments conducted here. As more data become available for industrial-scale ionic liquid preparations, we will expand our greenness assessment methodology to include the 12 principles of green engineering too.

Although, strictly, the 12 principles of green chemistry apply only to synthetic procedures, the 1st, 5th, 6th and 12th principles are relevant to ionic liquid purification procedures and, therefore, we assessed the purification of the salts according to these three principles also.

1.4

Atom Economy and the E-factor

Applying the 12 principles of green chemistry to evaluate the green credentials of ionic liquid syntheses and purifications is very important, but it would have been remiss of us not to include atom economy [19] and the E-factor [20, 21] in the assessments too.

1.4.1

Atom Economy

In simple terms, atom economy (also known as atom efficiency) measures, for a given reaction, how many of the atoms present in the starting materials form part of the final product and it also assumes 100% yield. Atom economy is reported as a percentage value with those reactions closest to 100% reflecting superior atom economies. This means that reactions with very low yields may possess 100% atom economies. For example, the preparation of 1-alkyl-3-methylimidazolium halide salts using quaternization [Routes 1(a)–(d), Figure 1.1] are 100% atom efficient regardless of the yield obtained, since no by-products are formed. On the other hand, ionic liquids prepared using one-pot [Routes 2(a)–(c), Figure 1.1] or metathesis reactions (Route 3, Figure 1.1) will be <100% atom efficient since a stoichiometric amount of MCl waste is generated.

$$\text{Atom economy (\%)} = \frac{\text{molecular weight of desired product (s)}}{\text{molecular weight of all reagents}} \times 100$$

The problem with employing atom economy to evaluate the green credentials of a reaction is that it does not take into account that some reactions with favorable stoichiometries require large excesses of reagents, give poor yields and often generate large amounts of unwanted products. This means that in terms of atom economy, a reaction with a very low yield can still be described as 100% atom efficient. As a result, the E-factor concept was introduced.

1.4.2

The E-factor

In the *E*-factor equation, *all* compounds used in a chemical process that are not contained in the final product are classified as waste. The nature of the *E*-factor equation dictates that the greenest chemical reactions have *E*-factor values close to zero. In brief, the *E*-factor gives a much truer reflection of the greenness of a chemical reaction than atom economy, since all generated waste is accounted for. The ‘ideal’ *E*-factor is reflected in the 2nd principle of green chemistry [3, 4], which states: “*Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product*”.

$$E\text{-factor} = \frac{\text{amount of waste produced in the process (kg)}}{\text{amount of the desired product(s) produced in the process (kg)}}$$

Although every chemical reaction will have its own unique atom economy and *E*-factor value, to simplify discussion, the atom economies and *E*-factors associated with ionic liquid preparations (Figure 1.1) and purifications (Figure 1.2) have been designated as low/medium/high and poor/good/excellent, respectively, since the literature has rarely given enough detail to allow definitive values to be assigned.

1.5

Strengths, Weaknesses, Opportunities, Threats (SWOT) Analyses

In order to simultaneously assess the green credentials of the selected synthesis and purification procedures of ionic liquids in terms of the 12 principles of green chemistry, atom economy and the *E*-factor, we have applied a common tool used in strategic planning, namely Strengths, Weaknesses, Opportunities, Threats (SWOT) analyses [22]. For ionic liquid preparation and purification methods, SWOT analyses involve specifying the objective(s) of a given procedure (e.g. obtaining an ionic liquid that is >99% pure) and identifying the internal and external factors that are favorable and unfavorable to achieving that objective. The SWOT analyses thus give an overview of the advantages or disadvantages of ionic liquid syntheses and purifications. In brief, the SWOT analyses provided here (represented skeletally in Figure 1.3) give a measure of the balance between good and bad for some common ionic liquid preparation and purification procedures and indicate potential directions for cleaning-up the methods.

1.6

Conductive Heating Preparation of 1-Alkyl-3-methylimidazolium Halide Salts

Even the most basic review of the ionic liquid synthesis literature reveals that the preparations of 1-alkyl-3-methylimidazolium halide salts have remained essentially

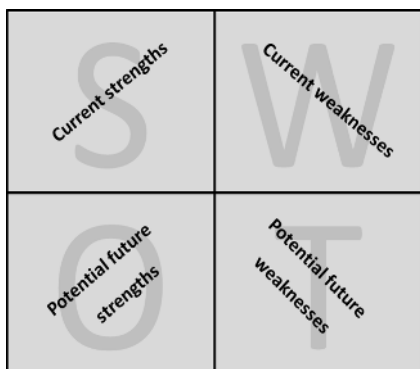


Figure 1.3 Skeletal Strengths Weaknesses Opportunities Threats (SWOT) analysis.

unchanged since they were first reported in 1982 [23, 24]; most reported syntheses still involve reaction of 1-methylimidazole with an excess of 1-haloalkane and are promoted using conductive heating [Route 1(a), Figure 1.1]. From a green chemistry perspective, much room for improvement exists for the syntheses of 1-alkyl-3-methylimidazolium halide salts, particularly regarding the use of more efficient energy sources and reducing/eliminating the need for organic solvents during both synthesis and purification; all these issues are discussed below.

The literature shows that most 1-alkyl-3-methylimidazolium halide salt preparations are executed using traditional heating under reflux, although nowadays an atmosphere of dry dinitrogen is sometimes used (Figure 1.4) since it has been found

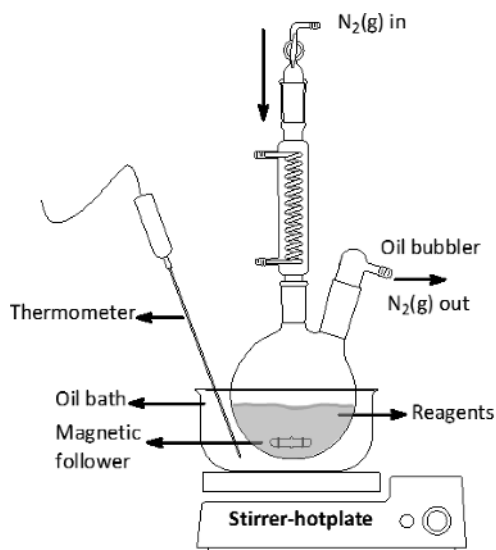


Figure 1.4 Traditional synthesis arrangement for preparing 1-butyl-3-methylimidazolium halide salts.

to promote the production of colorless [8] ionic liquids and also prevents the formation of hydrated halide salts from adventitious water [25] (see Section 1.7).

Almost without exception, reported preparations of 1-alkyl-3-methylimidazolium halide salts use an excess of 1-haloalkane [26], which means that the reactions are not in line with the 2nd principle of green chemistry, which states: “*Synthetic methods should be designed to maximize the incorporation of all materials used in the process into the final product*”. It also means that although the preparations of the halide salts are 100% atom efficient, with every atom of the starting materials incorporated into the final product, their *E*-factors are very poor, since excess 1-haloalkane is required to promote completion of the reactions at a reasonable rate. It also follows that the smaller the excess of 1-haloalkane, the lower the *E*-factor value will be, provided that no organic solvent is used during the preparation. For example, the *E*-factor for the preparation of [C₄mim]Cl (molar mass = 174.1 g mol⁻¹) is 0.106 and 0.005 when a 20% and 1% molar excess of 1-chlorobutane (molar mass = 92.56 g mol⁻¹), respectively, are employed.

$$E\text{-factor (20 mol \% excess C}_4\text{H}_9\text{Cl)} = \frac{0.2 \text{ mol} \times 92.56 \text{ g mol}^{-1}}{1 \text{ mol} \times 174.1 \text{ g mol}^{-1}} = 0.106$$

$$E\text{-factor (1 mol \% excess C}_4\text{H}_9\text{Cl)} = \frac{0.01 \text{ mol} \times 92.56 \text{ g mol}^{-1}}{1 \text{ mol} \times 174.1 \text{ g mol}^{-1}} = 0.005$$

Some reported preparations of 1-alkyl-3-methylimidazolium halide salts also make use of an organic solvent [27, 28] to reduce the viscosity of the reaction mixture and thus improve mass transfer, but also to control the reaction temperature and prevent product scrambling [29]. However, the molecular solvent employed, and also the excess of 1-haloalkane employed, require removal and subsequent disposal, which also does not comply with the 1st principle of green chemistry, which states: “*It is better to prevent waste than to treat or clean up waste after it has formed*”. Therefore, the practice of employing an organic solvent during preparation of 1-alkyl-3-methylimidazolium halide salts further increases the *E*-factor and is highly undesirable. For example, if 100 g of toluene (molar mass = 92.14 g mol⁻¹) is used during the synthesis of [C₄mim]Cl (and using a 20 mol% excess of 1-chlorobutane), the *E*-factor of increases from 0.106 to 0.681:

$$\begin{aligned} E\text{-factor (20 mol \% excess C}_4\text{H}_9\text{Cl} + 100 \text{ g toluene)} \\ = \frac{(0.2 \text{ mol} \times 92.56 \text{ g mol}^{-1} + 100 \text{ g})}{1 \text{ mol} \times 174.1 \text{ g mol}^{-1}} = 0.681 \end{aligned}$$

The 5th principle of green chemistry states that: “*The use of auxiliary substances (e.g. solvents, separation agents, etc.) should be made unnecessary wherever possible and innocuous when used*”, which means that ideally, no solvent should be used during preparation, but, if a solvent is to be used, it must be green and recycled. In order to align with the 1st, 2nd and 5th principles of green chemistry and have low *E*-factor

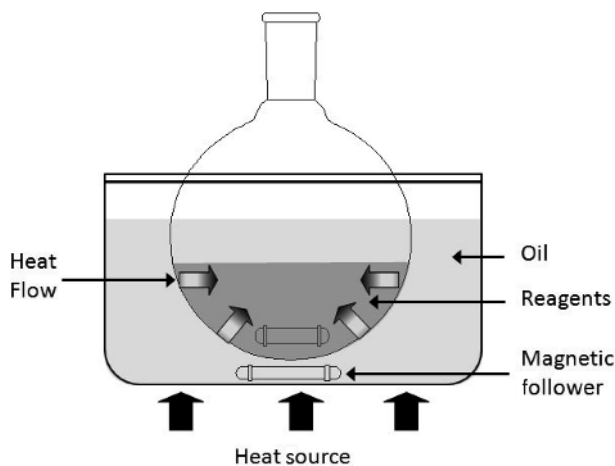
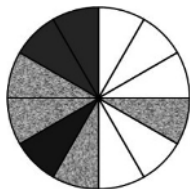


Figure 1.5 Schematic representation of conventional heating using an oil bath as external heat source.

values, neither excess 1-haloalkane nor organic solvent should be employed during the synthesis of 1-alkyl-3-methylimidazolium halide salts.

The use of conductive heating (usually an oil bath or heating mantle) to prepare 1-alkyl-3-methylimidazolium halide salts also does not align with the 6th principle of green chemistry, which states: “*Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure*”. Therefore, since conductive heating is slow, it is also energy inefficient because the transfer of heat from the heat source to the reaction mixture depends on the thermal conductivities of all the materials that must be penetrated such as the flask and solvent (Figure 1.5). In addition, the traditionally heated reactions are kinetically limited by the boiling point of the 1-haloalkane employed and can take several days, whereas microwave promoted reactions do not share these limitations (see below). The conductively heated preparations of 1-alkyl-3-methylimidazolium halide salts are also not performed at room temperature but usually at $\sim 75^\circ\text{C}$, which does not align with the second part of the 6th principle of green chemistry.

When all the above-mentioned negatives that are associated with the traditional syntheses of 1-alkyl-3-methylimidazolium halide ionic liquids are considered, it is safe to say that their preparations are not green. Indeed, of the eight relevant principles of green chemistry, they only comply with the three principles (8th, 11th and 12th) which apply to all the ionic liquid syntheses discussed here anyway. On the other hand, the *E*-factors for the preparations fall between good and excellent provided that excess 1-haloalkane is kept to a minimum and no harmful organic solvent is used and/or recycled during the preparation. Overall, however, the conductively heated preparations of 1-alkyl-3-methylimidazolium halide



salts possess a lot of room for improvement, as indicated by their SWOT analysis (see Section 1.7.1).

1.7

Purification of 1-Alkyl-3-methylimidazolium Halide Salts

The purification of 1-alkyl-3-methylimidazolium halide salts (Figure 1.6) is generally dirty, with poor *E*-factors, since the excess 1-haloalkane, unconverted 1-methylimidazole and any solvent used during their preparation require removal and are therefore out of line with the 5th principle of green chemistry.

In our laboratories, removal of the excess 1-haloalkane and unconverted 1-methylimidazole is typically achieved by first adding a solvent such as ethanenitrile to the crude ionic liquid mixture and then repeatedly washing this phase with ethyl ethanoate. Once the washing process is complete, the two organic solvents are removed under reduced pressure (using a rotary evaporator). Since the amount of organic solvent used for the purification and also excess reagents are classified as waste in the *E*-factor equation, the more of each that is used, the higher the *E*-factor for a given purification procedure will be.

In less experienced groups, the purification of 1-alkyl-3-methylimidazolium halide salts is usually performed on the bench and therefore the salts absorb water from the atmosphere that also requires removal. It must be noted, however, that this adventitious water cannot be completely removed from ionic liquids containing halide anions (especially chloride) as they form, typically, very stable hydrates (Figure 1.7 [25]).

Therefore, if water-free ionic liquids containing halide ions are desired, their preparation and purification must be conducted under strictly anhydrous conditions from start to finish, for example, using Schlenk techniques. Nevertheless, some adventitious water can be removed by heating 1-alkyl-3-methylimidazolium halide salts under reduced pressure at $\sim 70^\circ\text{C}$ for several hours. Almost needless to say,

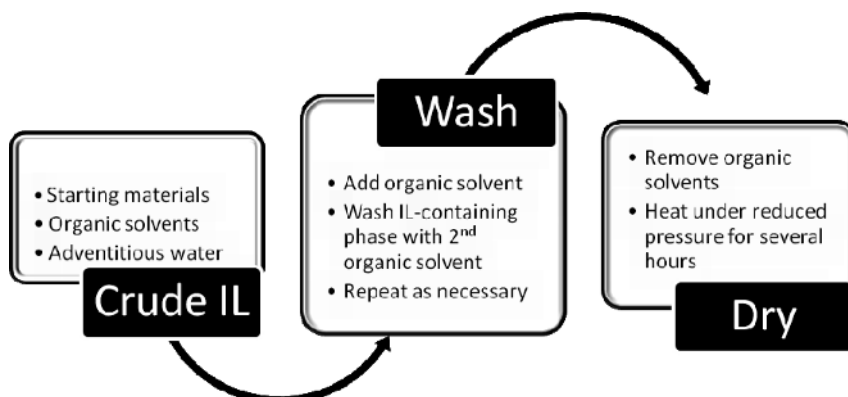
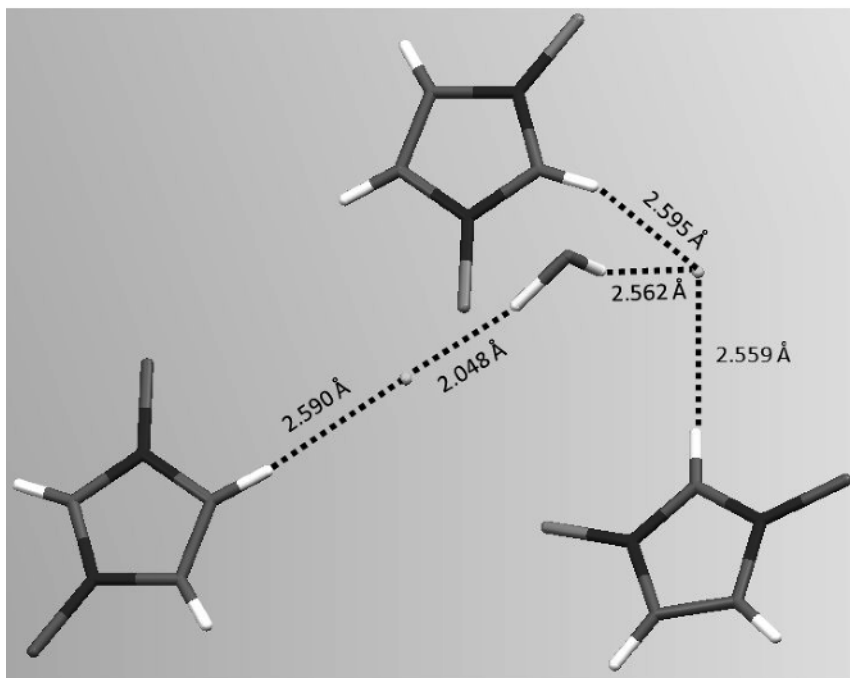


Figure 1.6 Schematic diagram of the purification of $[\text{C}_4\text{mim}]\text{X}$ ionic liquids.

(a)



(b)

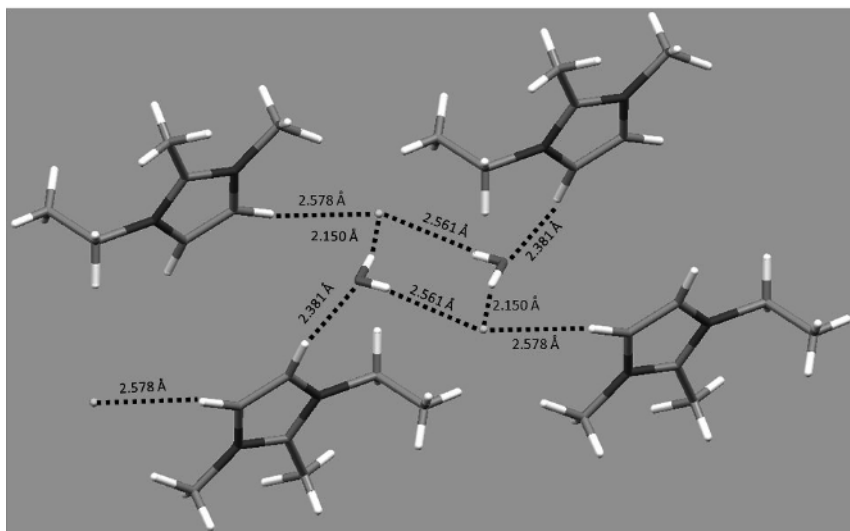


Figure 1.7 Structures of 1,3-dimethylimidazolium chloride hemihydrate (a) and 1,2-dimethyl-3-ethylimidazolium chloride hemihydrate (a) showing hydrogen bonding (dashed lines) [25] as determined by single crystal X-ray diffraction.

removing water in this way requires a large energy input and thus contributes further to the green inefficiency (*via* non-compliance with the 6th principle of green chemistry) of the purification of 1-alkyl-3-methylimidazolium halide salts. Indeed, the purification of 1-alkyl-3-methylimidazolium halide salts, as summarized in Figure 1.6, complies with none of the relevant principles of green chemistry.

1.7.1

SWOT Analysis: Conductively Heated Preparation of 1-Alkyl-3-Methylimidazolium Halide Salts and Their Subsequent Purification

Examination of the SWOT analysis for the preparation of 1-alkyl-3-methylimidazolium halide salts using conductive heating and their subsequent purification (Figure 1.8) shows that the overall methodology is dirty. Nevertheless, the procedure possesses some strengths, *viz.* the processes are well established, simple, can be performed in even the most basic of laboratories to produce the salts on a small to medium scale (<1 kg) and possess 100% atom economies. On the other hand, both the preparations and purifications share the weakness of poor *E*-factors, since extensive purification is necessary to remove the excess of the 1-haloalkane employed, which generates large volumes of solvent waste. Further weaknesses are that large-scale preparations (>1 kg) and purifications are laborious and the use of conductive heating to promote the reactions, and also remove some residual water and organic solvents, is slow and energy inefficient. All the above-mentioned weaknesses show that opportunities exist to develop a greener methodology to

<p>i. Well-established methodology</p> <p>ii. Simple</p> <p>iii. Useful for laboratory scale preparations</p> <p>iv. High atom economy</p>	<p>i. Long syntheses</p> <p>ii. Excess 1-haloalkane used</p> <p>iii. Poor <i>E</i>-factor</p> <p>iv. Inconvenient for large-scale procedures</p> <p>v. Laborious purification</p> <p>vi. Large volumes of waste solvent generated</p>
<p>i. Green process development</p> <p>ii. Eliminate/reduce use of organic solvents</p> <p>iii. Identify green solvent replacements</p>	<p>i. REACH legislation</p> <p>ii. Starting material cost rises</p>

Figure 1.8 SWOT analysis: conductively heated preparation of 1-alkyl-3-methylimidazolium halide salts and their subsequent purification.

prepare pure 1-alkyl-3-methylimidazolium halide salts using conductive heating and thus reduce the costs of their manufacture, especially on large scales.

At present, the implementation of REACH (Registration, Evaluation, Authorization and restriction of CHemicals [30]) legislation is a threat to the continued low-cost manufacture of many chemicals, but especially for new products, since they require a large initial financial investment. Therefore, research scientists aiming to develop any new industrial-scale ionic liquid synthesis need to be extremely familiar with REACH legislation in order to achieve their aim. A further threat that exists for the synthesis of 1-alkyl-3-methylimidazolium halide salts using conductive heating is that starting material costs will undoubtedly rise and, therefore, the challenge facing chemists is to render preparations greener and concomitantly cheaper.

1.8

Ionic Liquid Syntheses Promoted by Microwave Irradiation

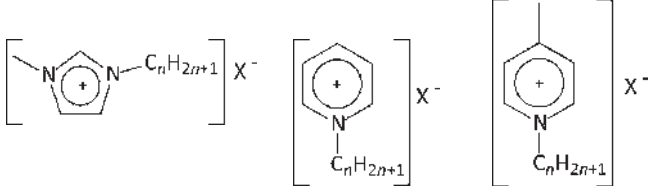
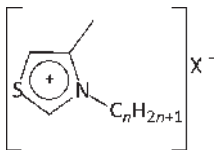
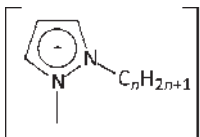
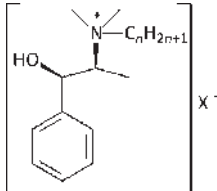
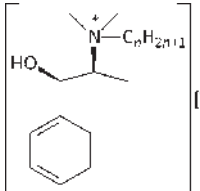
It has long been recognized that much more efficient energy sources exist to promote chemical reactions compared with conductive heating. In particular, microwave irradiation [31–35] has started to attract attention for the preparation of ionic liquids [Routes 1(b) and 2(a), Figure 1.1]. Some ionic liquids that have been prepared to date using microwave-assisted methodologies are shown in Table 1.1.

Microwave heating is governed by two mechanisms [34], dipole rotation and ionic conduction (Figure 1.9). Microwave heating by dipole rotation commonly occurs when molecules with high dielectric constants or polarities constantly and very rapidly realign to the fluctuating microwave field. Heating by an ionic conduction mechanism occurs because the ions present in a reaction medium (e.g. ionic liquid reaction mixture) begin to move under the influence of the electric field of the microwave irradiation, resulting in an increased collision rate and, therefore, the rapid conversion of kinetic energy into heat. Furthermore, microwaves penetrate a reaction medium directly as opposed to conductively heated reactions, provided the reaction vessel consists of a microwave-transparent material such as quartz and therefore, unlike conductive heating, preparation speeds are not limited by all the thermal conductivities of the materials to be penetrated (see Figure 1.5).

The promotion of 1-alkyl-3-methylimidazolium halide syntheses using microwave irradiation is favored by an ionic conduction heating mechanism since ionic liquids absorb microwave irradiation excellently. As an ionic liquid product is generated during a synthetic procedure, it absorbs microwave energy, which speeds up the reaction. Obviously, the more ionic liquid product has formed, the faster the reaction will proceed. In brief, microwave irradiation represents a far more efficient mode of heating to prepare ionic liquids than conductively heated syntheses. In addition, all microwave-assisted ionic liquid preparations align with the 6th principle of green chemistry by virtue of reduced preparation times and vastly reduced energy consumption (see Section 1.8.1).

At present, the implementation of microwave irradiation to prepare ionic liquids continues to evolve, but a question that remains unanswered is: How much greener

Table 1.1 Some ionic liquids prepared using microwave irradiation.

Ionic liquid	References
 <p data-bbox="557 475 864 533"> $n = 3, 4, 6, 8 \text{ or } 10$ $X = \text{Cl, Br or I}$ </p>	[31, 33]
 <p data-bbox="557 742 696 797"> $n = 4, 6, 8 \text{ or } 10$ $X = \text{Br or I}$ </p>	 <p data-bbox="1025 624 1057 647">[31]</p>
 <p data-bbox="557 1057 722 1133"> $n = 4, 8, 10 \text{ or } 16$ $X = \text{Br}$ $Y = \text{PF}_6 \text{ or } \text{CF}_3\text{SO}_3$ </p>	 <p data-bbox="1025 915 1057 939">[36]</p>

are microwave-promoted preparations than traditional methods? From a very simplistic standpoint, tremendous energy savings have already been demonstrated for laboratory-scale ionic liquid syntheses [31, 33], since microwave-promoted reactions occur far more rapidly than the same preparations performed using conductive heating. For example, the synthesis of $[\text{C}_4\text{mim}]\text{Cl}$ performed in a microwave oven at 300 W and taking 20 min to complete uses 99 W h ($0.33 \text{ h} \times 300 \text{ W}$) of energy, whereas the same preparation uses 14 400 W h ($24 \text{ h} \times 600 \text{ W}$) if performed employing an isomantle that operates at 600 W for 24 h [33]. Simplistically, this represents a 145-fold energy efficiency improvement when using microwave irradiation compared with conductive heating. This significant energy saving strongly aligns with the 6th principle of green chemistry by keeping the energy input of the syntheses to a minimum.

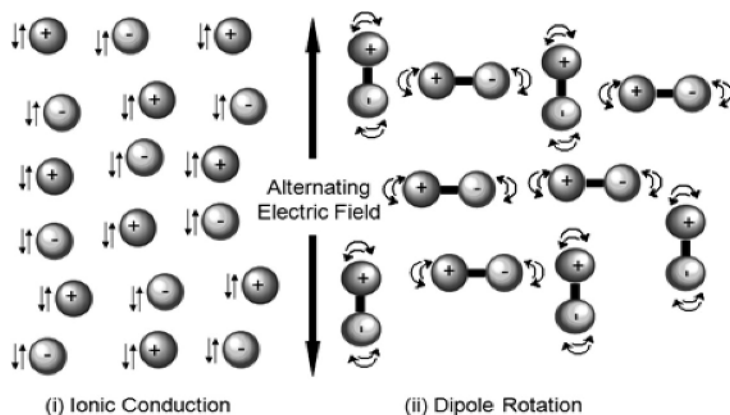


Figure 1.9 Schematic of microwave heating mechanisms: (i) ionic conduction and (ii) dipole rotation [34].

The first papers describing microwave syntheses of ionic liquids employed domestic microwave ovens that offered no temperature and pressure control and thus gave irreproducible results [35, 37, 38]. Since then, more reliable results have been obtained using commercial microwave reactors (Figure 1.10), which have allowed the temperature and pressure of reactions to be moderated, rendering the procedures far safer and more reproducible than their domestic predecessors [39].

It is worth noting that whereas the first reports describing microwave-assisted ionic liquid syntheses focused on their preparation *via* quaternization [Route 1(b), Figure 1.1], later reports [38, 40, 41] showed that a one-pot approach [Route 2(a), Figure 1.1] could also be used. Since the microwave-assisted procedures require much smaller 1-haloalkane excesses (~ 1 mol%) compared with conventional

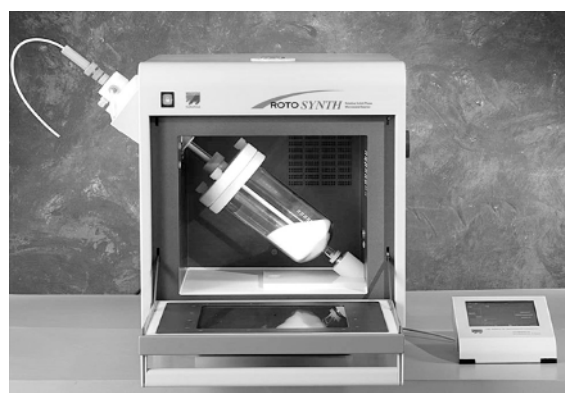
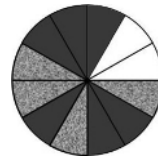


Figure 1.10 Commercially available microwave reactors for solid- and solution-phase batch synthesis. Photograph courtesy of Milestone srl, Sorisole, BG, Italy.



preparations (up to 400 mol% [26]), they align well with the 1st principle of green chemistry and their *E*-factors are far superior to those of traditional synthesis routes, especially if no organic solvent is used during the synthesis. In other words, if no organic solvent is used during synthesis, the preparations also align with

the 2nd principle of green chemistry and the best *E*-factors for the preparations are obtained. In brief, the microwave-assisted preparations of 1-alkyl-3-methylimidazolium halide salts comply with seven of the eight relevant principles of green chemistry (1st, 2nd, 5th, 6th, 8th, 11th and 12th) whereas the analogous one-pot microwave-assisted syntheses align with six (1st, 5th, 6th,



8th, 11th and 12th). It must be noted that although the one-pot microwave-assisted ionic liquid syntheses generate a stoichiometric amount of MX waste (e.g. NaCl), the waste salt is far less harmful/toxic and straightforward to dispose of than 1-haloalkane waste and therefore the methodology aligns reasonably well with the 1st principle of green chemistry too.

1.8.1

Microwave-assisted Versus Traditional Ionic Liquid Preparations

The superior *E*-factors and energy efficiencies of microwave-assisted syntheses of ionic liquids show that they are far greener than conductively heated preparations. However, the “degree of greenness” depends on (i) the type of quaternization being performed, since the kinetics of the reaction typically follow the order $C_nH_{2n+1}Cl < C_nH_{2n+1}Br < C_nH_{2n+1}I$, (ii) the 1-haloalkane excess required to achieve complete conversion to product, (iii) the scale of the reaction and (iv) if any solvent is necessary to reduce the viscosity and/or reduce product scrambling [29]. The proviso for the use of solvent in terms of green chemistry is that the solvent itself will have to be green (e.g. ethanol) and/or recycled to uphold the overall green credentials of a given preparation.

The preparation of ionic liquids on scales >2 kg also requires special consideration, as this is moving from bench scale to semi-pilot plant scale. However, at the semi-pilot plant scale, the 12 principles of green engineering [15] must also be considered, but as already mentioned, this falls outside the scope of this review. Nevertheless, current indications are that continuous flow reactors (Figure 1.11) represent the way forward to producing ionic liquids on large scales [37, 42].

1.8.2

SWOT Analysis: Microwave-promoted Syntheses of Ionic Liquids

The SWOT analysis for the preparation of ionic liquids using microwave irradiation is shown in Figure 1.12. The greatest green strengths of performing microwave-assisted ionic liquid preparations on a laboratory scale are the energy reduction by virtue of reduced reaction times and low 1-haloalkane excesses. Further strengths are that (i) different microwave reactors [35] can be employed to execute the preparations



Figure 1.11 Commercially available microwave reactors for continuous flow synthesis. Photograph courtesy of Milestone srl, Sorisole, BG, Italy.

on different scales [37], (ii) syntheses can be performed solvent free, (iii) the reactions are 100% atom efficient and (iv) they have excellent (low) *E*-factor values compared with traditional preparations. All the before mentioned strengths render the microwave-promoted syntheses of ionic liquids as very green indeed.

<ul style="list-style-type: none"> i. Rapid ii. Energy efficient iii. Flexible reaction scales iv. Solvent-free synthesis v. High atom economy vi. Excellent <i>E</i>-factor 	<ul style="list-style-type: none"> i. Lack of energy efficiency data ii. Expensive apparatus iii. Ionic liquid discoloration iv. Ionic liquid decomposition v. Mass transfer issues vi. Scale-up very expensive
<ul style="list-style-type: none"> i. Green process development ii. Quantitative energy input data iii. Reactor design iv. Intellectual property 	<ul style="list-style-type: none"> i. Expensive operation ii. <i>In-situ</i> reaction monitoring iii. Safety controls

Figure 1.12 SWOT analysis for the preparation of ionic liquids using microwave irradiation.

The weaknesses associated with microwave-assisted preparation of ionic liquids are that:

1. Lack of energy efficiency data of syntheses makes an exact comparison with other methodologies difficult.
2. Microwave reactors are expensive compared with traditional synthesis apparatus.
3. Discolored ionic liquids are sometimes obtained at temperatures $>75^{\circ}\text{C}$ [43, 44].
4. Ionic liquids decompose if overheated [29, 31, 45].
5. The high viscosity of ionic liquids can produce mass transport problems during synthesis.
6. The scale-up of the syntheses is very expensive.

Despite the above-mentioned weaknesses, opportunities exist for the development of green microwave reactor technology to produce ionic liquids. One major opportunity is green process development by establishing quantitative energy input data to assess definitively the greenness of microwave-assisted preparations versus other methodologies. Another opportunity is the design and manufacture of custom-made reactors to produce ionic liquids on large scales [42]. Both of these opportunities may generate valuable intellectual property and could also reduce the cost of producing ionic liquids on large scales.

The greatest threat to the development of microwave technology to produce ionic liquids on large scales by continuous flow is that it proves too expensive. Further threats include the inability, *via* design constraints, to incorporate *in situ* reaction monitoring (which aligns with the 11th principle of green chemistry) and the inability (albeit unlikely) to incorporate safety controls in industrial reactors to produce ionic liquids on large scales (which aligns with the 12th principle of green chemistry).

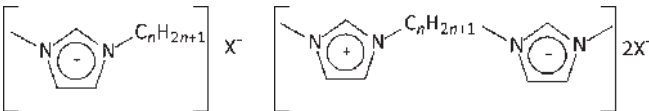
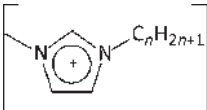
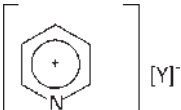
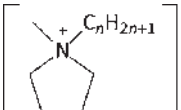
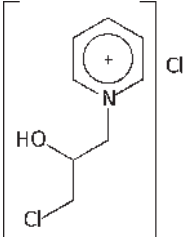
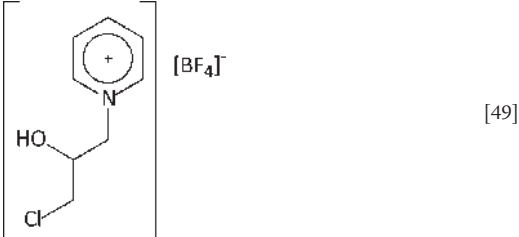
1.9

Syntheses of Ionic Liquids Promoted by Ultrasonic Irradiation

At about the same time that the first reports describing the microwave-assisted preparations of ionic liquids were published, reports also began to appear describing ultrasound-promoted preparations of ionic liquids [46, 47]. Some of the ionic liquids that have been prepared to date using ultrasonic irradiation are shown in Table 1.2.

The promotion of chemical reactions with ultrasound is due to a physical phenomenon known as cavitation, which is the formation, growth and implosive collapse of bubbles in a liquid [51]. The collapse or implosion of such bubbles results in some fascinating physical effects, which include the formation of localized “hotspots” in an elastic liquid and reduction of particle size [52, 53]. In terms of ionic liquid synthesis, the formation of hotspots favors quaternizations [Route 1(c), Figure 1.1], whereas the reduction of particle size favors both quaternizations and metathesis [Route 3, Figure 1.1] [47], since improved mass transport overcomes the viscosity issues generally associated with ionic liquid syntheses. Together, hotspot formation, particle size reduction and the reduced preparation times compared with traditional methods all speed up ionic liquid syntheses and thus represent a

Table 1.2 Some ionic liquids prepared using ultrasonic irradiation.

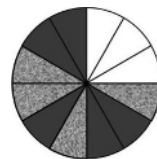
Ionic liquid	References	
 <p data-bbox="164 402 293 456">$n = 3, 4, 6$ or 8 $X = \text{Cl}, \text{Br}$ or I</p> <p data-bbox="435 402 542 456">$n = 4, 6$ or 8 $X = \text{Br}$ or I</p>	[47]	
 <p data-bbox="164 626 332 711">$n = 4, 5$ or 6 $Y = \text{BF}_4, \text{PF}_6, \text{BPh}_4$ or CF_3SO_3</p>	 <p data-bbox="435 626 564 711">$n = 4, 5, 6$ or 8 $Y = \text{PF}_6$</p>	 <p data-bbox="680 626 770 693">$n = 4$ or 8 $Y = \text{PF}_6$</p> <p data-bbox="915 535 989 558">[46, 48]</p>
	 <p data-bbox="915 844 954 868">[49]</p>	

significant green advantage, especially if the preparations are performed solvent free. Indeed, it is worth noting that at present, the majority of papers describing ultrasound-promoted syntheses of ionic liquids have focused on ‘one-pot’ reactions [Route 2(b), Figure 1.1].

Despite the apparent green advantages of ultrasound-assisted ionic liquid preparations, a phenomenon which renders these preparations inadequate is that, almost without exception, ionic liquids discolor and decompose when exposed to ultrasonic irradiation for the time required to obtain acceptable conversions [50, 51]. Needless to say, this decomposition of ionic liquids is a severe disadvantage to the successful and widespread implementation of the technology and, from a green chemistry perspective, does not align with the 1st principle of green chemistry since very dirty purification and decolorization of the salts are required, which also give very poor *E*-factors. In addition, in a recent review, the highest reported tabulated yield to produce 1-alkyl-3-methylimidazolium halide and similar salts without halide anions are 95% and 90%, respectively [52]. This contrasts with yields of >99%

obtained by thermally induced and microwave-assisted preparations, rendering ultrasound-assisted ionic liquid syntheses far less green.

Although ultrasound-assisted preparations of 1-alkyl-3-methylimidazolium ionic liquids [Routes 1(c) and 2(b), Figure 1.1] comply with five of the eight relevant principles of green chemistry (namely the 5th, 6th, 8th, 11th and 12th), they do not follow the 1st and 2nd principles, since they give poor yields (compared with thermal and microwave routes) and the ionic liquid products require extensive purification. As a result, ultrasound-assisted ionic liquid syntheses also have poor *E*-factors and therefore are not as green as their microwave-assisted analogues.



1.9.1

SWOT Analysis: Ultrasound-promoted Syntheses of Ionic Liquids

The SWOT analysis for the preparation of ionic liquids promoted by ultrasonic irradiation (Figure 1.13) reveals that its unique strength (compared with traditional and microwave-assisted syntheses) is improved mass transport. However, almost without exception, the preparations have very poor *E*-factors (high values) due to the discolored ionic liquid products, requiring extensive purification and decolorization efforts that produce large volumes of organic solvent and solid waste (see above). In addition to the major weakness of a poor *E*-factor, other weaknesses of ultrasound-assisted ionic liquid syntheses include the lack of quantitative energy efficiency data, the cost of the apparatus and lack of demonstrated large-scale production. It must be

<ul style="list-style-type: none"> i. Rapid ii. Energy efficient iii. Good mass transport iv. Solvent-free synthesis v. High atom economy 	<ul style="list-style-type: none"> i. Lack of energy efficiency data ii. Expensive apparatus iii. Ionic liquid discoloration iv. Ionic liquid decomposition v. Scale-up not demonstrated vi. Poor <i>E</i>-factor
<ul style="list-style-type: none"> i. Green process development ii. Quantitative energy input data iii. Reactor design iv. Intellectual property 	<ul style="list-style-type: none"> i. Ionic liquid discoloration ii. Ionic liquid decomposition iii. <i>In-situ</i> reaction monitoring iv. Safety controls

Figure 1.13 SWOT analysis for the preparation of ionic liquids using ultrasonic irradiation.

pointed out that ionic liquid discoloration is far more severe under ultrasonic conditions than under microwave irradiation and, furthermore, the salts decompose under even mild ultrasonic conditions [51].

The greatest opportunities that exist for ultrasound-promoted ionic liquid syntheses are (i) to develop green procedures that do not lead to the discoloration and decomposition of ionic liquids and (ii) to determine the true energy efficiency of the preparations compared with other methodologies by collecting quantitative energy input data, thus allowing the opportunity for (iii) reactor design and (iv) generating valuable intellectual property.

It must be reiterated that ultrasound-assisted ionic liquid preparation will probably only find commercial application if its severe shortcomings (or threats in terms of the SWOT analysis) are overcome by future research and development efforts. Such research and development efforts will, similarly to microwave-assisted preparations, have to include safety controls and *in situ* reaction monitoring to align with the 11th and 12th principles of green chemistry.

1.10

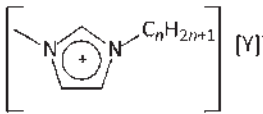
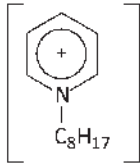
Simultaneous Use of Microwave and Ultrasonic Irradiation to Prepare Ionic Liquids

Recent studies have shown that the simultaneous use of microwave and ultrasonic irradiation promote ionic liquid syntheses [Routes 1(d) and 2(c), Figure 1.1] [40, 52–54]. Some ionic liquids that have been prepared to date using this technology are shown in Table 1.3, which were obtained using one-step [Route 1(d), Figure 1.1], two-step [Route 1(a) then Route 3, Figure 1.1] as well as one-pot [Route 2(c), Figure 1.1] procedures.

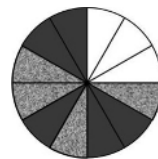
The simultaneous use of microwave and ultrasonic irradiation to prepare ionic liquids should offer the cumulative benefits of the individual irradiations, *viz.* excellent coupling of microwaves with ionic liquids plus improved mass transport. Therefore, the time and energy saved using microwave and ultrasonic irradiation simultaneously would represent a significant green advantage, especially if the syntheses are performed solvent free. However, using this technology to prepare 1-alkyl-3-methylimidazolium halide ionic liquids [Route 1(d), Figure 1.1] gives very poor yields (<5%) and can also take significantly longer than using microwave or ultrasound irradiation alone [40]. Therefore, the combined use of microwave and ultrasonic irradiation to prepare 1-alkyl-3-methylimidazolium halide salts has very poor *E*-factors and requires significantly more energy than using the individual types of irradiation alone, rendering the syntheses dirty. In addition, a major problem that is anticipated for all ionic liquid syntheses using microwave and ultrasonic irradiation simultaneously is that discolored ionic liquid products will be obtained, requiring extensive decolorization, which will further negatively affect the *E*-factors.

Although the simultaneous microwave/ultrasound-assisted preparations of 1-alkyl-3-methylimidazolium halide [Route 1(d) Figure 1.1] and non-halide [Route 2(c), Figure 1.1] salts comply with the five of the eight relevant principles of green

Table 1.3 Some ionic liquids prepared using simultaneous microwave and ultrasonic irradiation.

Ionic liquid	Reference
 <p data-bbox="306 420 503 511"> $n = 4 \text{ or } 8$ $Y = \text{BF}_4, \text{PF}_6, \text{CF}_3\text{SO}_3$ or NTF_2 </p>	[40]
 <p data-bbox="271 720 464 766"> $Y = \text{BF}_4, \text{PF}_6, \text{CF}_3\text{SO}_3$ or NTF_2 </p>	[53]

chemistry (namely the 5th, 6th, 8th, 11th and 12th), they do not follow the 1st and 2nd principles, since they give poor yields (compared with thermal and microwave routes) and the ionic liquid products require extensive purification. In addition, the *E*-factors of the preparations are poor due to the need to decolorize the ionic liquid products.



1.10.1

SWOT Analysis: Simultaneous Use of Microwave and Ultrasonic Irradiation to Prepare Ionic Liquids

The simultaneous use of microwave and ultrasonic irradiation to prepare ionic liquids offers both the best and worst of the individual technologies and the SWOT analysis shows that this indeed true (Figure 1.14).

The expected strengths of the technology include (i) rapid preparations with (ii) good energy efficiencies compared with traditional methods, (iii) improved mass transport (*versus* conductive heating and microwave-assisted preparations), (iv) the potential to perform the transformations solvent free and (v) high atom economies. At present, however, the limited number of studies describing syntheses have shown that the technology works best for one-pot preparations [Route 2(c), Figure 1.1] and is less successful for preparing ionic liquids containing halide anions [40]. The SWOT analysis clearly shows, without laboring the point, that at present, combined microwave/ultrasound irradiation technology has no obvious advantages or disadvantages.

<ul style="list-style-type: none"> i. Rapid ii. Energy efficient iii. Good mass transfer iv. Solvent-free synthesis v. High atom economy 	<ul style="list-style-type: none"> i. Ionic liquid discoloration ii. Ionic liquid decomposition iii. Extremely specialized apparatus iv. Expensive apparatus v. Lack of energy efficiency data vi. Scale-up not demonstrated vii. Poor <i>E</i>-factor viii. Low yield
<ul style="list-style-type: none"> i. Green process development ii. Quantitative energy input data iii. Reactor design iv. Intellectual property 	<ul style="list-style-type: none"> i. Ionic liquid discoloration ii. Ionic liquid decomposition iii. <i>In-situ</i> reaction monitoring iv. Safety controls

Figure 1.14 SWOT analysis for the preparation of ionic liquids using simultaneous ultrasound and microwave irradiation.

1.11

Preparation of Ionic Liquids Using Microreactors

An exciting novel technology to prepare ionic liquids that has very recently emerged is the use of microstructured reactors (or microreactors), which function under continuous flow conditions [55–60]. In very simple terms, and as their name suggests, microstructured reactors are small reactors that can fit in the palm of the hand and their discerning feature is that they possess multiple parallel channels (microchannels) with diameters of ~ 10 – 100 μm [61–63]. Two microreactors that have been used to prepare 1-ethyl-3-methylimidazolium ethylsulfate ($[\text{C}_2\text{mim}][\text{EtSO}_4]$) [56, 58] and 1-butyl-3-methylimidazolium bromide ($[\text{C}_4\text{mim}]\text{Br}$) [59] respectively, have their microchannels arranged in parallel either on a stack of plates (Figure 1.15 [58, 64]) or within a tube [56].

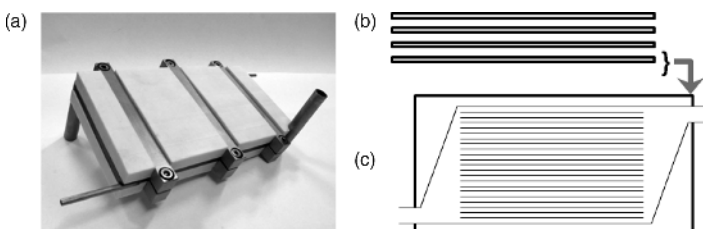
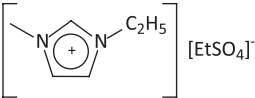
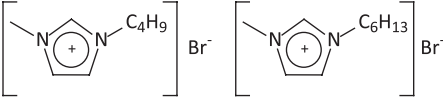
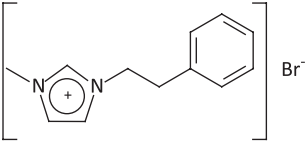


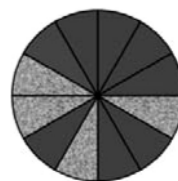
Figure 1.15 (a) Photograph of a microstructured reactor showing the arrangement of (b) four parallel plates and (c) a schematic of a single plate. Photograph courtesy of IMM, Mainz [64].

Table 1.4 Ionic liquids reported to date using microstructured reactors

Ionic liquid	References
	[56–58, 66]
	[59, 60]
	[60]

Using the above-mentioned tubular- and stacked plate-type microstructured reactors, respectively, 1-ethyl-3-methylimidazolium ethylsulfate has been obtained with an excellent conversion rate of $X = 0.998$ [58], and 1-butyl-3-methylimidazolium bromide was obtained with a purity of $>99\%$ [56], demonstrating both the product yield and purity advantages of using microreactors [60]. In other words, ionic liquids can be prepared quickly and virtually without the need for purification by employing custom-made microstructured reactors. More examples of ionic liquids that have been prepared to date using microstructured reactors are shown in Table 1.4.

The key to the green advantages of using microstructured reactors is their microchannels, which allow for much better mass and heat transfer rates to prepare ionic liquids much faster than is possible with any other batch-type preparative method. In addition, excellent energy efficiency and reduced operational costs are achieved in the microstructured reactors, because heat exchange is far superior to that in traditional reactors, hotspot formation is prevented, higher reaction temperatures are possible and reaction volumes are reduced [58]. Since the salts are also obtained in high purities, purification using harmful organic solvents is not needed, which means that these types of preparations have excellent E -factors and are very green indeed. In fact, of all the preparative methodologies assessed here, the use of microstructured reactors to prepare the salts is the only technique that complies with all eight relevant principles of green chemistry, namely the 1st, 2nd, 3rd, 5th, 6th, 8th, 11th and 12th.



In practical terms, the advantages of using microstructured reactors become even clearer when it is considered that 9.3 kg per day of $>99\%$ pure 1-butyl-3-methylimidazolium bromide [59] is realistically achievable. To the best of our

knowledge, not even the most efficient batch-type industrial-scale ionic liquid preparations can compete with this greenness and efficiency. It is also worth highlighting that the high pressure stability of some microstructured reactors (up to 100 bar) means that they can permit continuous flow even at viscosities up to 10 000 MPa. Yet another advantage of this technology is that custom-made reactors are currently commercially available [64] and patented [65].

It must be pointed out that we have assumed that the *E*-factors associated with the preparation of ionic liquids using microreactors are excellent because of the high purity of the products obtained (e.g. >99% [59]). However, due to the nature of the apparatus (i.e. reagent delivery to a microreactor *via* pumps), reaction stoichiometries are not given in the literature. We have therefore presumed that these stoichiometries are 1 : 1 based on reported product purities of >99%. If, however, reaction stoichiometries are not 1 : 1, then we must remove one of the green credentials, namely the 2nd principle of green chemistry, which means that only seven of the eight relevant principles of green chemistry will apply (see Section 1.11).

1.11.1

SWOT Analysis: Preparation of Ionic Liquids Using Microreactors

The SWOT analysis for the preparation of ionic liquids using microstructured reactors (Figure 1.16) unambiguously shows that the strengths of the technology (as discussed in Section 1.11) heavily outweigh its weaknesses. Indeed, the only

<ul style="list-style-type: none"> i. Energy efficient ii. Excellent mass and heat transport iii. Solvent-free synthesis iv. High atom economy v. Excellent E-factor vi. Flexible reactor design vii. Flexible reaction scales viii. Convenient reactor size ix. Excellent conversion rates x. High product purity 	<ul style="list-style-type: none"> i. Time consuming syntheses ii. Delicate reactor construction
<ul style="list-style-type: none"> i. Green process development ii. IL-specific reactor manufacture 	<ul style="list-style-type: none"> i. Cost of reactor manufacture ii. Time of reactor manufacture

Figure 1.16 SWOT analysis: preparation of ionic liquids using microreactors.

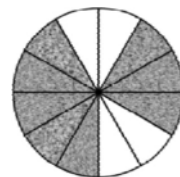
weakness of the technology is that some reported ionic liquid preparations take a long time to achieve good conversions when working at lower temperatures [56]. In addition, manufacture of the reactors is delicate and specialized, requiring laser welding, for example [58], to prevent potential problems such as leaking.

The opportunities of the technology are green process development and the market niche for the design and manufacture of suites of microstructured reactors for specific ionic liquid preparations or sets of preparations. The only threat that we see for the future widespread implementation of the technology is that microstructured reactors are currently still specialized pieces of apparatus that are expensive and time-consuming to manufacture.

1.12

Purification of Ionic Liquids with Non-halide Anions

Ionic liquid purification procedures can be divided into two main categories: purification of hydrophobic ionic liquids and purification of hydrophilic ionic liquids (Figure 1.2). To simplify discussion for the former and latter categories, we have selected two stereotypical salts as representatives, 1-butyl-3-methylimidazolium bisether amide, $[C_4mim][NTf_2]$, and 1-butyl-3-methylimidazolium trifluoromethanesulfonate, $[C_4mim][OTf]$. It must be noted that 1-alkyl-3-methylimidazolium halide salts fall in the above-mentioned hydrophilic category, but their purification and associated green performance have already been discussed in Section 1.7). As already discussed in Section 1.3, only the 1st, 5th 6th and 12th principles of green chemistry are relevant to ionic liquid purification. Regardless of whether a one- or two-step methodology is employed to prepare $[C_4mim][NTf_2]$ and $[C_4mim][OTf]$ (Figure 1.1) a stoichiometric amount of MX waste (usually NaCl) is generated. If not removed from the ionic liquid product, the presence of the metal halide waste will severely affect the physical properties of the ionic liquid [7, 14].



The removal of MX from both $[C_4mim][NTf_2]$ and $[C_4mim][OTf]$ is achieved by washing the crude ionic liquid product with water, although the ease with which this is achieved and the respective green performances vary considerably.

Although a stoichiometric amount of MX waste is generated during two-step ionic liquid syntheses, it is not toxic waste and therefore does not require incineration. Furthermore, the metal halide waste is also not contaminated with organics, which means that both one- and two-step syntheses to produce $[C_4mim][NTf_2]$ and $[C_4mim][OTf]$ closely align with the 1st principle of green chemistry.

1.12.1

Purification of Hydrophobic Versus Hydrophilic Ionic Liquids

In order to remove MX from hydrophilic $[C_4mim][OTf]$, dichloromethane, a dense solvent, is usually added to the crude ionic liquid mixture. The dichloromethane is

added since the ionic liquid preferentially dissolves therein, allowing repeated washing of the ionic liquid-containing phase with cold water to remove the MX waste more easily. The residual dichloromethane and also the water that remains in the ionic liquid as a result of the washing procedure require removal, which is achieved by first using a rotary evaporator and then drying the salt *in vacuo* at $\sim 70^\circ\text{C}$ for many hours, which is extremely energy inefficient. Almost needless to say, the use of dichloromethane to purify $[\text{C}_4\text{mim}][\text{OTf}]$ is an extremely dirty practice since it is a toxic solvent that is detrimental to both humans and the environment [67]. Furthermore, the larger the volume of dichloromethane used, the poorer is the *E*-factor of the procedure.

The removal of MX from hydrophobic $[\text{C}_4\text{mim}][\text{NTf}_2]$ is far easier than its removal from $[\text{C}_4\text{mim}][\text{OTf}]$ because it does not readily mix with water and, therefore, washing the salt with water to extract MX is both faster and more efficient. This purification is also greener, since no organic solvent is required as is the case for hydrophilic salts to aid with the removal of MX. In principle, the water phase can also be recycled by distillation and reused, although some contaminated ionic liquid, now severely contaminated with MX, will remain, since even hydrophobic ionic liquids exhibit mutual solubility with water [68]. Moreover, the water must be removed in order to obtain the pure salt; this is achieved by drying the salt *in vacuo* at $\sim 70^\circ\text{C}$ for many hours, which is extremely energy inefficient.

In brief, the purification procedure of $[\text{C}_4\text{mim}][\text{OTf}]$, is far less efficient than that of its cousin $[\text{C}_4\text{mim}][\text{NTf}_2]$, since a significant amount of the ionic liquid is “lost” to the organic phase and higher levels of MX also remain in the purified ionic liquid. This is evidenced by the lower chloride content levels achievable for $[\text{C}_4\text{mim}][\text{NTf}_2]$ [69] than for $[\text{C}_4\text{mim}][\text{OTf}]$ [14, 70]. In addition, less energy is required to remove residual water from $[\text{C}_4\text{mim}][\text{NTf}_2]$ than for $[\text{C}_4\text{mim}][\text{OTf}]$ by heating the salts *in vacuo*, as the former should, by definition, hold less water than the latter. Although the purification of these ionic liquids does not comply with the relevant principles of green chemistry (namely the 1st, 5th, 6th and 12th), the hydrophilic ionic liquid processes are much greener than the hydrophobic processes, both in total isolated yield and in avoidance of organic solvents.

1.12.2

SWOT Analyses: Purification of Hydrophobic and Hydrophilic Ionic Liquids

The SWOT analyses for the purification of $[\text{C}_4\text{mim}][\text{NTf}_2]$ and $[\text{C}_4\text{mim}][\text{OTf}]$ show that the former procedure is the greener (Figure 1.17). This is mainly due to the purification of $[\text{C}_4\text{mim}][\text{OTf}]$ requiring the use of dichloromethane (Section 1.12), which is an extremely harmful compound. Another major reason why the purification of $[\text{C}_4\text{mim}][\text{OTf}]$ is dirty is because much greater losses of the ionic liquid to the water phase occur compared with the purification of $[\text{C}_4\text{mim}][\text{NTf}_2]$ and it also requires longer heating *in vacuo* to remove residual water.

(a)

<ul style="list-style-type: none"> i. Simple ii. Fast iii. Efficient iv. Good <i>E</i>-factor 	<ul style="list-style-type: none"> i. Minimal ionic liquid losses to water phase ii. Stoichiometric amounts of MX waste iii. Heating <i>in vacuo</i>
<ul style="list-style-type: none"> i. Process optimization ii. Scale-up 	<ul style="list-style-type: none"> i. MX disposal

(b)

<ul style="list-style-type: none"> i. Simple 	<ul style="list-style-type: none"> i. Poor <i>E</i>-factor ii. Toxic dichloromethane used iii. Large ionic liquid losses to water phase iv. Stoichiometric amounts of MX waste v. Extensive heating <i>in vacuo</i> vi. Laboratory scale only
<ul style="list-style-type: none"> i. Process optimization ii. Scale-up 	<ul style="list-style-type: none"> i. Waste disposal

Figure 1.17 SWOT analyses for the purification of (a) $[\text{C}_4\text{mim}][\text{NTf}_2]$ and (b) $[\text{C}_4\text{mim}][\text{OTf}]$.

1.13

Decolorization of Ionic Liquids

All practicing ionic liquid synthetic chemists know that the salts are sometimes obtained as pale yellow to black products. Ionic liquids containing halide anions are particularly susceptible to discoloration and the cause of the color can be transferred to subsequent ionic liquids prepared by metathesis (Route 3, Figure 1.1). Although chromophores are the suspected discoloration culprits [71], the true cause, and indeed the types of chromophores responsible, remain a mystery. To date, attempts to isolate the chromophores by column chromatography have failed to provide enough material for identification. This failure indicates the extremely low levels of the chromophores in ionic liquids (probably ppb levels of materials with molar extinction coefficients of $>10^6 \text{ l mol}^{-1} \text{ cm}^{-1}$). It is worth noting that even some of the most intensely colored ionic liquids are usually analytically pure to NMR and mass spectrometric techniques.

The color of an ionic liquid is usually not detrimental when using the salts as solvents (provided that they contain minimal levels of other impurities such as chloride and/or water), but colorless ionic liquids are essential for spectroscopic studies in order to eliminate interference from the suspected chromophoric impurity resonances that usually appear in the aromatic region of UV-Vis spectra.

Colorless ionic liquids may be obtained in two ways: careful reaction preparation and execution or post-synthesis, using decolorization. The former is the method of choice, achieved by purification of all starting materials and diligent monitoring of the reaction temperature to avoid overheating ($\sim <75^\circ \text{C}$), which is known to produce colored ionic liquids. On the other hand, post-synthesis decolorization may be effected using a decolorizing column (Figure 1.18), a method that has recently been developed and which is scrutinized here for “greenness” in terms of the relevant principles of green chemistry (1st, 5th 6th and 12th) and also the *E*-factor.

1.13.1

SWOT Analysis: Decolorization of Ionic Liquids

It is almost unnecessary to do a SWOT analysis to establish that the decolorization of ionic liquids is not green (Figure 1.19). This is because from a green chemistry perspective, the toxicity of dichloromethane alone outweighs all strengths associated with the methodology and, since large volumes of the toxic solvent are also used during the process, it makes the decolorization procedure even dirtier, with an extremely poor *E*-factor.

It is important to note that the “column decolorization” of ionic liquids is not only environmentally unfriendly, but it will also probably only be applied in academia to obtain small quantities of ionic liquids destined for spectroscopic studies. Nevertheless, the method is simple and efficient on the laboratory scale but, in contrast, it uses a lot of dichloromethane and also produces solid waste (Celite, silica and activated charcoal) that need to be disposed of. On the upside, much research opportunity exists to render the methodology green and also to identify the nature

(a)



(b)

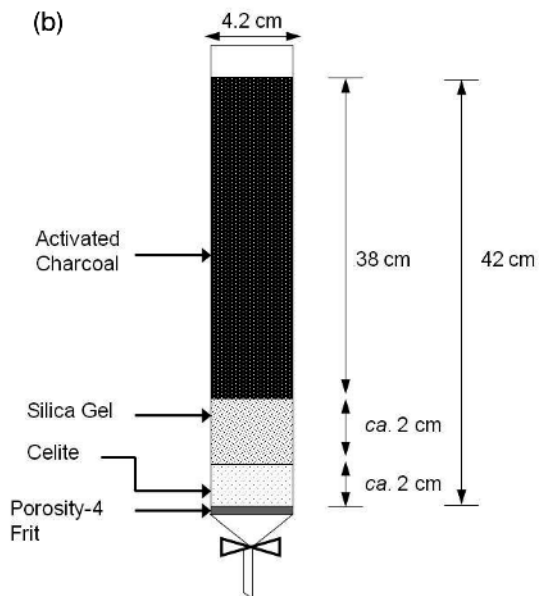
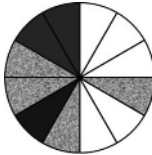

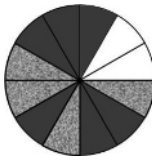

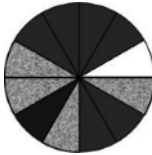

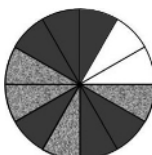


Figure 1.18 Experimental apparatus for decolorizing ionic liquids [71].

<ul style="list-style-type: none"> i. Simple ii. Efficient 	<ul style="list-style-type: none"> i. Extremely poor <i>E</i>-factor ii. Large volumes of toxic dichloromethane used iii. Time consuming iv. Solid waste generated v. Only laboratory-scale use
<ul style="list-style-type: none"> i. Explore greener alternatives ii. Identify chromophore 	<ul style="list-style-type: none"> i. Psychological barrier to use of colored ionic liquids



Figure 1.19 SWOT analysis for ionic liquid decolorization.

Table 1.5 Greenness summary of ionic liquid preparative methods.

Methodology	E-factor	Atom economy	Principles of green chemistry complied with (total number and type) ^a
Route 1(a)	Good–excellent	High	3 (8th, 11th, 12th) 
Route 1(b)	Excellent	High	7 (1st, 2nd, 5th, 6th, 8th, 11th, 12th) 
Route 1(c)	Poor	Low–high	5 (5th, 6th, 8th, 11th, 12th) 
Route 1 (d)	Poor	High	5 (5th, 6th, 8th, 11th, 12th) 
Route 2(a)	Poor–good	Low–medium	7 (1st, 2nd, 5th, 6th, 8th, 11th, 12th) 
Route 2(b)	Poor	Low–Medium	5 (5th, 6th, 8th, 11th, 12th) 
Route 2(c)	Very poor	Low–medium	5 (5th, 6th, 8th, 11th, 12th) 

(Continued)

Table 1.5 (Continued)

Methodology	E-factor	Atom economy	Principles of green chemistry complied with (total number and type) ^a	
Route 3	Poor	Low-medium	3 (8th, 11th, 12th)	
Microstructured reactors	Excellent ^b	Excellent	8 (1st, 2nd, 3rd, 5th, 6th, 8th, 11th, 12th)	

^a4th, 7th, 9th and 10th principles of green chemistry do not apply.

^bBut see Section 1.11.

and identity of the chromophore. Until these opportunities exist, the threat to the methodology is the psychological barrier that exists for many ionic liquid researchers, especially those new to the field, to use colored ionic liquids.

1.14

Conclusion

The greenness of the synthetic procedures and purification methodologies assessed in this critical review are summarized in Table 1.5.

To maintain green credibility, ionic liquids must be green both in application and in their synthesis. The above discussions clearly illustrate that ionic liquid synthesis and purification can certainly be considered as green if microwave-assisted synthesis and microstructured reactors are employed. It is also clear that the purification of hydrophobic ionic liquids is intrinsically greener than that of hydrophilic ionic liquids.

With current trends towards the design of non-toxic, biodegradable ionic liquids, the new challenges become to develop improved purification procedures for hydrophilic ionic liquids alongside a universal requirement for the development of *in situ* on-line analytical monitoring for industrial-scale syntheses. Overall, the judgment provided here for the synthesis and purification of ionic liquids is “green, but not green enough”.

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