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Ionic Liquids in Synthesis

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Ionic Liquids in Synthesis

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Ionic Liquids in Synthesis

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Contents

	Preface	<i>XI</i>
	Contributors	<i>XV</i>
1	Introduction	<i>1</i>
2	Synthesis and Purification of Ionic Liquids	<i>7</i>
2.1	Synthesis of Ionic Liquids	<i>7</i>
2.1.1	Introduction	<i>7</i>
2.1.2	Quaternization Reactions	<i>9</i>
2.1.3	Anion-exchange Reactions	<i>12</i>
2.1.3.1	Lewis Acid-based Ionic Liquids	<i>12</i>
2.1.3.2	Anion Metathesis	<i>14</i>
2.1.4	Purification of Ionic Liquids	<i>17</i>
2.1.5	Conclusions	<i>19</i>
2.2	Quality Aspects and Other Questions Related to Commercial Ionic Liquid Production	<i>21</i>
2.2.1	Introduction	<i>21</i>
2.2.2	Quality Aspects of Commercial Ionic Liquid Production	<i>22</i>
2.2.2.1	Color	<i>23</i>
2.2.2.2	Organic Starting Materials and other Volatiles	<i>24</i>
2.2.2.3	Halide Impurities	<i>25</i>
2.2.2.4	Protic Impurities	<i>26</i>
2.2.2.5	Other Ionic Impurities from Incomplete Metathesis Reactions	<i>26</i>
2.2.2.6	Water	<i>27</i>
2.2.3	Upgrading of Commercial Ionic Liquids	<i>27</i>
2.2.4	Scaling-up of Ionic Liquid Synthesis	<i>28</i>
2.2.5	HSE data	<i>29</i>
2.2.6	Future Price of Ionic Liquids	<i>30</i>
2.2.7	Intellectual Property Aspects Regarding Ionic Liquids	<i>31</i>
2.3	Synthesis of Task-specific Ionic Liquids	<i>33</i>

3	Physicochemical Properties of Ionic Liquids	41
3.1	Melting Points and Phase Diagrams	41
3.1.1	Introduction	41
3.1.2	Determination of Liquidus Ranges	43
3.1.2.1	Melting points	43
3.1.2.2	Upper limit decomposition temperature	44
3.1.3	Effect of Ion Sizes on Salt Melting Points	45
3.1.3.1	Anion size	46
3.1.3.2	Mixtures of anions	47
3.1.3.3	Cation size	48
3.1.3.4	Cation symmetry	49
3.1.4.1	Imidazolium salts	50
3.1.4.2	Imidazolium substituent alkyl chain length	50
3.1.4.3	Branching	52
3.1.5	Summary	53
3.2	Viscosity and Density of Ionic Liquids	56
3.2.1	Viscosity of Ionic Liquids	56
3.2.1.1	Viscosity measurement methods	56
3.2.1.2	Ionic liquid viscosities	59
3.2.2	Density of Ionic Liquids	65
3.2.2.1	Density measurement	66
3.2.2.2	Ionic liquid densities	66
3.3	Solubility and Solvation in Ionic Liquids	68
3.3.1	Introduction	68
3.3.2	Metal Salt Solubility	70
3.3.2.1	Halometalate salts	70
3.3.2.2	Metal complexes	70
3.3.3	Extraction and Separations	72
3.3.3.1	Anionic extractants	73
3.3.3.2	Organic extractants	73
3.3.4	Organic Compounds	75
3.3.5	Conclusions	79
3.4	Gas Solubilities in Ionic Liquids	81
3.4.1	Introduction	81
3.4.2	Experimental Techniques	83
3.4.2.1	Gas solubilities and related thermodynamic properties	83
3.4.2.2	Stoichiometric technique	84
3.4.2.3	Gravimetric technique	85
3.4.2.4	Gas chromatography	85
3.4.3	Gas Solubilities	86
3.4.3.1	Water vapor	86
3.4.3.2	Other gases	88
3.4.4	Applications	89
3.4.4.1	Reactions involving gases	89
3.4.4.2	Gas separations	90

3.4.4.3	Extraction of solutes from ionic liquids with compressed gases or supercritical fluids	91
3.4.5	Summary	91
3.5	Polarity	94
3.5.1	Chromatographic Measurements	94
3.5.2	Absorption Spectra	96
3.5.3	Fluorescence Spectra	99
3.5.4	Refractive Index	99
3.5.5	Organic Reactions	100
3.5.5.1	Alkylation of sodium 2-naphthoxide	100
3.5.5.2	Diels–Alder reactions	100
3.5.5.3	Photochemical reactions	101
3.5.6	General Conclusions	102
3.6	Electrochemical Properties of Ionic Liquids	103
3.6.1	Electrochemical Potential Windows	104
3.6.2	Ionic Conductivity	109
3.6.3	Transport Properties	118
4	Molecular Structure and Dynamics	127
4.1	Order in the Liquid State and Structure	127
4.1.1	Neutron Diffraction	127
4.1.2	Formation of Deuteriated Samples	128
4.1.3	Neutron Sources	129
4.1.3.1	Pulsed (spallation) neutron sources	129
4.1.3.2	Reactor sources	129
4.1.4	Neutron Cells for Liquid Samples	130
4.1.5	Examples	131
4.1.5.1	Binary mixtures	131
4.1.5.2	Simple salts	133
4.1.6	X-ray Diffraction	134
4.1.6.1	Cells for liquid samples	135
4.1.6.2	Examples	135
4.1.7	Extended X-ray Absorption Fine-structure Spectroscopy	139
4.1.7.1	Experimental	140
4.1.7.2	Examples	142
4.1.8	X-ray Reflectivity	145
4.1.8.1	Experimental set-up	146
4.1.8.2	Examples	146
4.1.9	Direct Recoil Spectrometry (DRS)	147
4.1.9.1	Experimental set-up	148
4.1.9.2	Examples	149
4.1.10	Conclusions	149
4.2	Quantum Mechanical Methods for Structure Elucidation	152
4.2.1	Introduction	152
4.2.3	Ion-pair Models and Possible Corrections	153

- 4.2.4 Ab Initio Structures of Ionic Liquids 154
- 4.2.5 DFT Structure of 1-Methyl-3-nonylimidazolium Hexafluorophosphate 155
- 4.2.6 Additional Information Obtained from Semi-empirical and Ab Initio Calculations 156
- 4.3 Molecular Dynamics Simulation Studies 157
 - 4.3.1 Performing Simulations 157
 - 4.3.2 What can we Learn? 159
- 4.4 Translational Diffusion 162
 - 4.4.1 Main Aspects and Terms of Translational Diffusion 162
 - 4.4.2 Use of Translational Diffusion Coefficients 164
 - 4.4.3 Experimental Methods 165
 - 4.4.4 Results for Ionic Liquids 166
- 4.5 Molecular Reorientational Dynamics 168
 - 4.5.1 Introduction 168
 - 4.5.2 Experimental Methods 168
 - 4.5.3 Theoretical Background 169
 - 4.5.4 Results for Ionic Liquids 171
- 5 Organic Synthesis 174**
 - 5.1 Stoichiometric Organic Reactions and Acid-Catalyzed Reactions in Ionic Liquids 174
 - 5.1.1 Stoichiometric Organic Reactions 175
 - 5.1.1.1 Molten salts as reagents 175
 - 5.1.1.2 Reactions in chloroaluminate(III) and related ionic liquids 177
 - 5.1.1.3 Reactions in neutral ionic liquids 181
 - 5.1.2 Acid-Catalyzed Reactions 191
 - 5.1.2.1 Electrophilic substitutions and additions 191
 - 5.1.2.2 Friedel–Crafts alkylation reactions 196
 - 5.1.2.3 Friedel–Crafts acylation reactions 203
 - 5.1.2.4 Cracking and isomerization reactions 208
 - 5.2 Transition Metal Catalysis in Ionic Liquids 213
 - 5.2.1 Why use Ionic Liquids as Solvents for Transition Metal Catalysis? 217
 - 5.2.1.1 Their nonvolatile natures 217
 - 5.2.1.2 New opportunities for biphasic catalysis 218
 - 5.2.1.3 Activation of a transition metal catalyst in ionic liquids 220
 - 5.2.2 The Role of the Ionic Liquid 220
 - 5.2.2.1 The ionic liquid as “innocent” solvent 221
 - 5.2.2.2 Ionic liquid as solvent and co-catalyst 221
 - 5.2.2.3 Ionic liquid as solvent and ligand/ligand precursor 222
 - 5.2.2.4 Ionic liquid as solvent and transition metal catalyst 225
 - 5.2.3 Methods of Analysis of Transition Metal Catalysts in Ionic Liquids 226
 - 5.2.4 Selected Examples of the Application of Ionic Liquids in Transition Metal Catalysis 229
 - 5.2.4.1 Hydrogenation 229

5.2.4.2	Oxidation reactions	232
5.2.4.3	Hydroformylation	234
5.2.4.4	Heck, Suzuki, Stille, and Negishi coupling reactions	241
5.2.4.5	Dimerization and oligomerization reactions	244
5.2.5	Concluding Remarks	252
5.3	Ionic Liquids in Multiphasic Reactions	258
5.3.1	Multiphasic Reactions: General Features, Scope, and Limitations	258
5.3.2	Multiphasic Catalysis: Limitations and Challenges	259
5.3.3	Why Ionic Liquids in Multiphasic Catalysis?	261
5.3.4	Different Technical Solutions to Catalyst Separation through the Use of Ionic Liquids	263
5.3.5	Immobilization of Catalysts in Ionic Liquids	266
5.3.6	Scaling up Ionic Liquid Technology from Laboratory to Continuous Pilot Plant Operation	270
5.3.6.1	Dimerization of alkenes catalyzed by Ni complexes	271
5.3.6.2	Alkylation reactions	275
5.3.6.3	Industrial use of ionic liquids	277
5.3.7	Concluding Remarks and Outlook	278
5.4	Multiphasic Catalysis with Ionic Liquids in Combination with Compressed CO ₂	281
5.4.1	Introduction	281
5.4.2	Catalytic Reaction with Subsequent Product Extraction	282
5.4.3	Catalytic Reaction with Simultaneous Product Extraction	282
5.4.4	Catalytic Conversion of CO ₂ in an Ionic Liquid/scCO ₂ Biphasic Mixture	283
5.4.5	Continuous Reactions in an Ionic Liquid/Compressed CO ₂ System	283
5.4.6	Concluding Remarks and Outlook	287
6	Inorganic Synthesis	289
6.1	Directed Inorganic and Organometallic Synthesis	289
6.1.1	Coordination Compounds	289
6.1.2	Organometallic Compounds	290
6.1.3	Other Reactions	292
6.1.4	Outlook	293
6.2	Making of Inorganic Materials by Electrochemical Methods	294
6.2.1	Electrodeposition of Metals and Semiconductors	294
6.2.1.1	General considerations	294
6.2.1.2	Electrochemical equipment	295
6.2.1.3	Electrodeposition of less noble elements	297
6.2.1.4	Electrodeposition of metals that can also be obtained from water	300
6.2.1.5	Electrodeposition of semiconductors	303
6.2.2	Nanoscale Processes at the Electrode/Ionic Liquid Interface	305
6.2.2.1	General considerations	305
6.2.2.2	The scanning tunneling microscope	305
6.2.2.3	Results	306
6.2.3	Summary	316

7	Polymer Synthesis in Ionic Liquids	319
7.1	Introduction	319
7.2	Acid-catalyzed Cationic Polymerization and Oligomerization	320
7.3	Free Radical Polymerization	324
7.4	Transition Metal-catalyzed Polymerization	326
7.4.1	Ziegler–Natta Polymerization of Ethylene	326
7.4.2	Late Transition Metal-catalyzed Polymerization of Ethylene	327
7.4.3	Metathesis Polymerization	328
7.4.4	Living Radical Polymerization	329
7.5	Preparation of Conductive Polymers	331
7.6	Conclusions	332
8	Biocatalytic Reactions in Ionic Liquids	336
8.1	Introduction	336
8.2	Biocatalytic Reactions and their Special Needs	336
8.3	Examples of Biocatalytic Reactions in Ionic Liquids	339
8.3.1	Whole-cell Systems and Enzymes other than Lipases in Ionic Liquids	339
8.3.2	Lipases in Ionic Liquids	342
8.4	Conclusions and Outlook	345
9	Outlook	348
	Index	356

Preface

“We prided ourselves that the science we were doing could not, in any conceivable circumstances, have any practical use. The more firmly one could make that claim, the more superior one felt.”

The Two Cultures, C.P. Snow (1959)

A book about ionic liquids? Over three hundred pages? Why? Who needs it? Why bother? These aren't simply rhetorical questions, but important ones of a nature that must be addressed whenever considering the publication of any new book. In the case of this one, as two other books about ionic liquids will appear in 2002, the additional question of differentiation arises – how is this distinctive from the other two? All are multi-author works, and some of the authors have contributed to all three books.

Taking the last question first, the answer is straightforward but important. The other two volumes are conference proceedings (one of a NATO Advanced Research Workshop, the other of an ACS Symposium) presenting cutting-edge snapshots of the state-of-the-art for experts; this book is *structured*. Peter Wasserscheid and Tom Welton have planned an integrated approach to ionic liquids; it is detailed and comprehensive. This is a book designed to take the reader from little or no knowledge of ionic liquids to an understanding reflecting our best current knowledge. It is a teaching volume, admirable for use in undergraduate and postgraduate courses, or for private learning. But it is not a dry didactic text - it is a user's manual! Having established a historical context (with an excellent chapter by one of the fathers of ionic liquids), the volume describes the synthesis and purification of ionic liquids (the latter being crucially important), and the nature of ionic liquids and their physical properties. Central to this tome (both literally and metaphorically) is the use of ionic liquids for organic synthesis, and especially green organic synthesis, and this chapter is (appropriately) the largest, and the *raison d'être* for the work. The book concludes with much shorter chapters on the synthesis of inorganic materials and polymers, the study of enzyme reactions, and an overview and prospect for the area. This plan logically and completely covers the whole of our current knowledge of ionic liquids, in a manner designed to enable the tyro reader to feel confident in using them, and the expert to add to their understanding. This is the first book to

attempt this task, and it is remarkably successful for two reasons. Firstly, the volume has been strongly and wisely directed, and is unified despite being a multi-author work. Secondly, the choice of authors was inspired; each one writes with authority and clarity within a strong framework. So, yes, this book is more than justified, it is a crucial and timely addition to the literature. Moreover, it is written and edited by the key people in the field.

Are ionic liquids really green? A weakly argued letter from Albrecht Salzer in *Chemical and Engineering News* (2002, 80 [April 29], 4-6) has raised this nevertheless valid question. Robin Rogers gave a tactful, and lucid, response, and I quote directly from this: “Salzer has not fully realized the magnitude of the number of potential ionic liquid solvents. I am sure, for example, that we can design a very toxic ionic liquid solvent. However, by letting the principles of green chemistry drive this research field, we can ensure that the ionic liquids and ionic liquid processes developed are in fact green. [. . .] The expectation that real benefits in technology will arise from ionic liquid research and the development of new processes is high, but there is a need for further work to demonstrate the credibility of ionic liquid-based processes as viable green technology. In particular, comprehensive toxicity studies, physical and chemical property collation and dissemination, and realistic comparisons to traditional systems are needed. It is clear that while the new chemistry being developed in ionic liquids is exciting, many are losing sight of the green goals and falling back on old habits in synthetic chemistry. Whereas it is true that incremental improvement is good, it is hoped that by focusing on a green agenda, new technologies can be developed that truly are not only better technologically, but are cleaner, cheaper, and safer as well.”

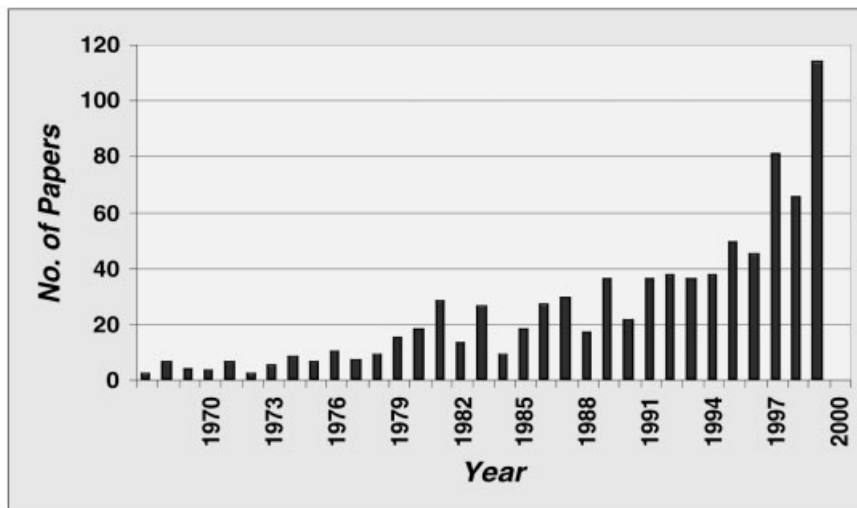


Figure 1: The rise in publications concerning ionic liquids as a function of time, as determined using SciFinder.

Robin's response is insightful. It reflects, in part, the burgeoning growth of papers in this area (see Figure 1) combined with the inevitable (and welcomed) rise in new researchers entering the area. However, with increasing activity comes the inevitable increasing "garbage" factor. In recent years we have (unfortunately) seen papers reporting physical data on ionic liquids that were demonstrably impure, liquids reported as solids and solids reported as liquids because of the impurity level, communications "rediscovering" and publishing work (without citation) already published in the patent literature, the synthesis of water-sensitive ionic liquids under conditions that inevitably result in hydrolysis, and academically weak publications appearing in commercial journals with lax refereeing standards. I truly believe that this book will help combat this; it should, and will, be referred to by all workers in the field. Indeed, if the authors citing it actually read it too, then the garbage factor should become insignificantly small!

In conclusion, this volume reflects well the excitement and rapid progress in the field of ionic liquids, whilst effectively providing an invaluable hands-on instruction manual. The lacunae are emphasised, and the directions for potential future research are clearly signposted. Unlike Snow in his renowned *Two Cultures* essay, many of us (Mamantov, Osteryoung, Wilkes, and Hussey, to name but a few of the founding fathers) who entered this area in its early (but not earliest!!) days prided ourselves that the science we were doing could not fail to have a practical use. Whether that use was battery applications, fuel cells, electroplating, nuclear reprocessing, or green industrial synthesis, we all believed that ionic liquids (or room-temperature molten salts, as they were then commonly known) offered a unique chemical environment that would (*must*) have significant industrial application. Because of this, we suffered then (and to some extent now) from the disdain of the "pure" scientists, who failed (and still fail) to appreciate that, if selecting an example to study to illustrate a fundamental scientific principle, there is actually some merit in selecting a product manufactured at the one million ton per annum level, rather than an esoteric molecule of no use and even less interest. Unfortunately, the pride and superiority Snow refers to is still alive and well, and living in the hearts of some of the academic establishment. I believe that this book will help tackle this prejudice, and illustrate that useful practical applications and groundbreaking fundamental science are not different, opposing areas, but synergistic sides of the same coin.

K.R. Seddon
May, 2002

A note from the editors

This book has been arranged in several chapters that have been prepared by different authors, and the reader can expect to find changes in style and emphasis as they go through it. We hope that, in choosing authors who are at the forefront of their particular specialism, this variety is a strength of the book. The book is intended to be didactic, with examples from the literature used to illustrate and explain. Therefore, not all chapters will give a comprehensive coverage of the literature in the area. Indeed, with the explosion of interest in some applications of ionic liquids comprehensive coverage of the literature would not be possible in a book of this length. Finally, there is a point when one has to stop and for us that was the end of 2001. We hope that no offence is caused to anyone whose work has not been included. None is intended.

Acknowledgements

We would like to sincerely thank everyone who has been involved in the publication of this book. All of our authors have done a great job in preparing their chapters and it has been a pleasure to read their contributions as they have come in to us. When embarking on this project we were both regaled with stories of books that never saw the light of day because of missed deadlines and the general tardiness of contributors. All of our colleagues have met their commitments in the most timely and enthusiastic manner. We are truly grateful for them making our task so painless. We would also like to thank the production team at VCH-Wiley, particularly Dr. Karen Kriese.

Finally, in a project like this, someone must take responsibility for any errors that have crept in. Ultimately we are the editors and this responsibility is ours. So we apologise unreservedly for any mistakes that have found their way into the book.

P. Wasserscheid, T. Welton
August, 2002

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Introduction

John S. Wilkes

Ionic liquids may be viewed as a new and remarkable class of solvents, or as a type of materials that have a long and useful history. In fact, ionic liquids are both, depending on your point of view. It is absolutely clear though, that whatever “ionic liquids” are, there has been an explosion of interest in them. Entries in Chemical Abstracts for the term “ionic liquids” were steady at about twenty per year through 1995, but had grown to over 300 in 2001. The increased interest is clearly due to the realization that these materials, formerly used for specialized electrochemical applications, may have greater utility as reaction solvents.

For purposes of discussion in this volume we will define ionic liquids as salts with a melting temperature below the boiling point of water. That is an arbitrary definition based on temperature, and says little about the composition of the materials themselves, except that they are completely ionic. In reality, most ionic liquids in the literature that meet our present definition are also liquids at room temperature. The melting temperature of many ionic liquids can be problematic, since they are notorious glass-forming materials. It is a common experience to work with a new ionic liquid for weeks or months to find one day that it has crystallized unexpectedly. The essential feature that ionic liquids possess is one shared with traditional molten salts: a very wide liquidus range. The liquidus range is the span of temperatures between the melting point and boiling point. No molecular solvent, except perhaps some liquid polymers, can match the liquidus range of ionic liquids or molten salts. Ionic liquids differ from molten salts in just where the liquidus range is in the scale of temperature.

There are many synonyms used for ionic liquids, which can complicate a literature search. “Molten salts” is the most common and most broadly applied term for ionic compounds in the liquid state. Unfortunately, the term “ionic liquid” was also used to mean “molten salt” long before there was much literature on low-melting salts. It may seem that the difference between ionic liquids and molten salts is just a matter of degree (literally); however the practical differences are sufficient to justify a separately identified niche for the salts that are liquid around room temperature. That is, in practice the ionic liquids may usually be handled like ordinary solvents. There are also some fundamental features of ionic liquids, such as strong

ion–ion interactions that are not often seen in higher-temperature molten salts. Synonyms in the literature for materials that meet the working definition of ionic liquid are: “room temperature molten salt”, “low-temperature molten salt”, “ambient-temperature molten salt”, and “liquid organic salt.”

Our definition of an ionic liquid does not answer the general question, “What is an ionic liquid?” This question has both a chemical and a historical answer. The details of the chemical answer are the subject of several subsequent chapters in this book. The general chemical composition of ionic liquids is surprisingly consistent, even though the specific composition and the chemical and physical properties vary tremendously. Most ionic liquids have an organic cation and an inorganic, polyatomic anion. Since there are many known and potential cations and anions, the potential number of ionic liquids is huge. To discover a new ionic liquid is relatively easy, but to determine its usefulness as a solvent requires a much more substantial investment in determination of physical and chemical properties. The best trick would be a method for predicting an ionic liquid composition with a specified set of properties. That is an important goal that awaits a better fundamental understanding of structure–property relationships and the development of better computational tools. I believe it can be done.

The historical answer to the nature of present ionic liquids is somewhat in the eye of the beholder. The very brief history presented here is just one of many possible ones, and is necessarily biased by the point of view of just one participant in the development of ionic liquids. The earliest material that would meet our current definition of an ionic liquid was observed in Friedel–Crafts reactions in the mid-19th century as a separate liquid phase called the “red oil.” The fact that the red oil was a salt was determined more recently, when NMR spectroscopy became a commonly available tool. Early in the 20th century, some alkylammonium nitrate salts were found to be liquids [1], and more recently liquid gun propellants based on binary nitrate ionic liquids have been developed [2]. In the 1960s, John Yoke at Oregon State University reported that mixtures of copper(I) chloride and alkylammonium chlorides were often liquids [3]. These were not as simple as they might appear, since several chlorocuprous anions formed, depending on the stoichiometry of the components. In the 1970s, Jerry Atwood at the University of Alabama discovered an unusual class of liquid salts he termed “liquid clathrates” [4]. These were composed of a salt combined with an aluminium alkyl, which then formed an inclusion compound with one or more aromatic molecules. A formula for the ionic portion is $M[Al_2(CH_3)_6X]$, where M is an inorganic or organic cation and X is a halide.

None of the interesting materials just described are the direct ancestors of the present generation of ionic liquids. Most of the ionic liquids responsible for the burst of papers in the last several years evolved directly from high-temperature molten salts, and the quest to gain the advantages of molten salts without the disadvantages. It all started with a battery that was too hot to handle.

In 1963, Major (Dr.) Lowell A. King (Figure 1.1) at the U.S. Air Force Academy initiated a research project aimed at finding a replacement for the LiCl/KCl molten salt electrolyte used in thermal batteries.

Figure 1.1: Major (Dr.) Lowell A. King at the U.S. Air Force Academy in 1961. He was an early researcher in the development of low-temperature molten salts as battery electrolytes. At that time “low temperature” meant close to 100 °C, compared to many hundreds of degrees for conventional molten salts. His work led directly to the chloroaluminate ionic liquids.



Since then there has been a continuous molten salts/ionic liquids research program at the Air Force Academy, with only three principal investigators: King, John Wilkes (Figure 1.2), and Richard Carlin. Even though the LiCl/KCl eutectic mixture has a low melting temperature (355 °C) for an inorganic salt, the temperature causes materials problems inside the battery, and incompatibilities with nearby devices. The class of molten salts known as chloroaluminates, which are mixtures of alkali halides and aluminium chloride, have melting temperatures much lower than nearly all other inorganic eutectic salts. In fact NaCl/AlCl₃ has a eutectic composition with a melting point of 107 °C, very nearly an ionic liquid by our definition [5]. Chloroaluminates are another class of salts that are not simple binary mixtures, because the Lewis acid-base chemistry of the system results in the presence of the series of the anions Cl⁻, [AlCl₄]⁻, [Al₂Cl₇]⁻, and [Al₃Cl₁₀]⁻ (although fortunately not all of these in the same mixture). Dr. King taught me a lesson that we should take heed of with the newer ionic liquids: if a new material is to be accepted as a technically useful material, the chemists must present reliable data on the chemical and physical properties needed by engineers to design processes and devices. Hence, the group at the Air Force Academy, in collaboration with several other groups, determined the densities, conductivities, viscosities, vapor pressures, phase equilibria, and electrochemical behavior of the salts. The research resulted in a patent for a thermal battery that made use of the NaCl/AlCl₃ electrolyte, and a small number of the batteries were manufactured.

Early in their work on molten salt electrolytes for thermal batteries, the Air Force Academy researchers surveyed the aluminium electroplating literature for electrolyte baths that might be suitable for a battery with an aluminium metal anode and chlorine cathode. They found a 1948 patent describing ionically conductive mixtures of AlCl₃ and 1-ethylpyridinium halides, mainly bromides [6]. Subsequently, the salt 1-butylpyridinium chloride/AlCl₃ (another complicated pseudo-binary)



Figure 1.2: Captain (Dr.) John S. Wilkes at the U.S. Air Force Academy in 1979. This official photo was taken about when he started his research on ionic liquids, then called “room-temperature molten salts.”



Figure 1.3: Prof. Charles Hussey of the University of Mississippi. The photo was taken in 1990 at the U.S. Air Force Academy while he was serving on an Air Force Reserve active duty assignment. Hussey and Wilkes collaborated in much of the early work on chloroaluminate ionic liquids.

was found to be better behaved than the earlier mixed halide system, so its chemical and physical properties were measured and published [7]. I would mark this as the start of the modern era for ionic liquids, because for the first time a wider audience of chemists started to take interest in these totally ionic, completely nonaqueous new solvents.

The alkylpyridinium cations suffer from being relatively easy to reduce, both chemically and electrochemically. Charles Hussey (Figure 1.3) and I set out a program to predict cations more resistant to reduction, to synthesize ionic liquids on the basis of those predictions, and to characterize them electrochemically for use as battery electrolytes.

Figure 1.4: Dr. Michael Zaworotko from Saint Mary's University in Halifax, Nova Scotia. He was a visiting professor at the U.S. Air Force Academy in 1991, where he first prepared many of the water-stable ionic liquids popular today.



We had no good way to predict if they would be liquid, but we were lucky that many were. The class of cations that were the most attractive candidates was that of the dialkylimidazolium salts, and our particular favorite was 1-ethyl-3-methylimidazolium [EMIM]. [EMIM]Cl mixed with AlCl_3 made ionic liquids with melting temperatures below room temperature over a wide range of compositions [8]. We determined chemical and physical properties once again, and demonstrated some new battery concepts based on this well behaved new electrolyte. We and others also tried some organic reactions, such as Friedel–Crafts chemistry, and found the ionic liquids to be excellent both as solvents and as catalysts [9]. It appeared to act like acetonitrile, except that it was totally ionic and nonvolatile.

The pyridinium- and the imidazolium-based chloroaluminate ionic liquids share the disadvantage of being reactive with water. In 1990, Mike Zaworotko (Figure 1.4) took a sabbatical leave at the Air Force Academy, where he introduced a new dimension to the growing field of ionic liquid solvents and electrolytes.

His goal for that year was to prepare and characterize salts with dialkylimidazolium cations, but with water-stable anions. This was such an obviously useful idea that we marveled that neither we nor others had tried to do it already. The preparation chemistry was about as easy as the formation of the chloroaluminate salts, and could be done outside of the glove-box [10]. The new tetrafluoroborate, hexafluorophosphate, nitrate, sulfate, and acetate salts were stable (at least at room temperature) towards hydrolysis. We thought of these salts as candidates for battery electrolytes, but they (and other similar salts) have proven more useful for other applications. Just as Zaworotko left, Joan Fuller came to the Air Force Academy, and spent several years extending the catalog of water-stable ionic liquids, discovering better ways to prepare them, and testing the solids for some optical properties. She made a large number of ionic liquids from the traditional dialkylimidazolium cations, plus a series of mono- and trialkylimidazoliums. She combined those cations with the water-stable anions mentioned above, *plus* the additional series of bromide, cyanide, bisulfate, iodate, trifluoromethanesulfonate, tosylate, phenyl-

phosphonate, and tartrate. This resulted in a huge array of new ionic liquids with anion sizes ranging from relatively small to very large.

It seems obvious to me and to most other chemists that the table of cations and anions that form ionic liquids can and will be extended to a nearly limitless number. The applications will be limited only by our imagination.

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2 Synthesis and Purification of Ionic Liquids

James H. Davis, Jr., Charles M. Gordon, Claus Hilgers, and Peter Wasserscheid

2.1 Synthesis of Ionic Liquids

Charles M. Gordon

2.1.1 Introduction

Despite the ever-growing number of papers describing the applications of ionic liquids, their preparation and purification has in recent years taken on an air of “need to know”. Although most researchers employ similar basic types of chemistry, it appears that everyone has their own tricks to enhance yields and product purity. This chapter is an attempt to summarize the different methods reported to date, and to highlight the advantages and disadvantages of each. The purity of ionic liquids is also an area of increasing interest as the nature of their interactions with different solutes comes under study, so the methods used for the purification of ionic liquids are also reviewed. The aim is to provide a summary for new researchers in the area, pointing to the best preparative methods, and the potential pitfalls, as well as helping established researchers to refine the methods used in their laboratories.

The story of ionic liquids is generally regarded as beginning with the first report of the preparation of ethylammonium nitrate in 1914 [1]. This species was formed by the addition of concentrated nitric acid to ethylamine, after which water was removed by distillation to give the pure salt, which was liquid at room temperature. The protonation of suitable starting materials (generally amines and phosphines) still represents the simplest method for the formation of such materials, but unfortunately it can only be used for a small range of useful salts. The possibility of decomposition through deprotonation has severely limited the use of such salts, and so more complex methods are generally required. Probably the most widely used salt of this type is pyridinium hydrochloride, the applications of which may be found in a thorough review by Pagni [2].

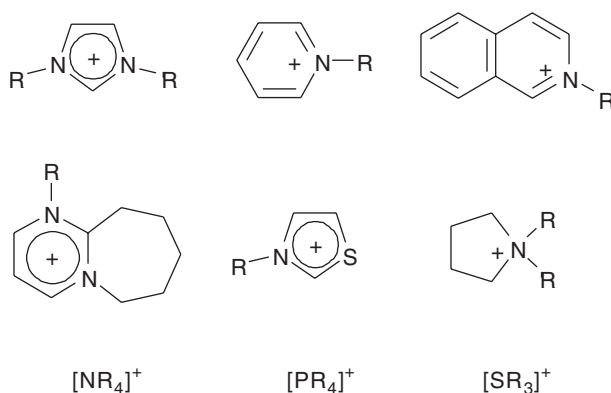


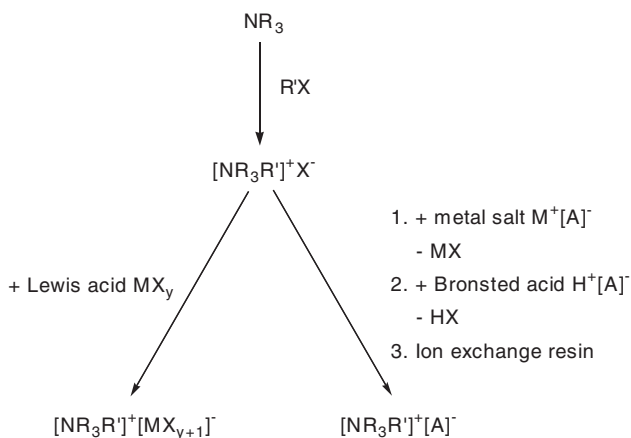
Figure 2.1-1: Examples of cations commonly used for the formation of ionic liquids.

Thus, most ionic liquids are formed from cations that do not contain acidic protons. A summary of the applications and properties of ionic liquids may be found in a number of recent review articles [3]. The most common classes of cations are illustrated in Figure 2.1-1, although low melting point salts based on other cations, such as complex polycationic amines [4] and heterocycle-containing drugs [5], have also been prepared.

The synthesis of ionic liquids can generally be split into two sections: the formation of the desired cation, and anion exchange where necessary to form the desired product (demonstrated for ammonium salts in Scheme 2.1-1).

In some cases only the first step is required, as with the formation of ethylammonium nitrate. In many cases the desired cation is commercially available at reasonable cost, most commonly as a halide salt, thus requiring only the anion exchange reaction. Examples of these are the symmetrical tetraalkylammonium salts and trialkylsulfonium iodide.

This chapter will concentrate on the preparation of ionic liquids based on 1,3-dialkylimidazolium cations, as these have dominated the area over the last twenty



Scheme 2.1-1: Typical synthesis paths for the preparation of ionic liquids (adapted from Ref. 3c).

years. The techniques discussed in this chapter are generally applicable to the other classes of cations indicated in Figure 2.1-1, however. The original decision by Wilkes et al. to prepare 1-alkyl-3-methylimidazolium ([RMIM]⁺) salts was prompted by the requirement for a cation with a more negative reduction potential than Al(III) [6]. The discovery that the imidazolium-based salts also generally displayed lower melting points than the 1-alkylpyridinium salts used prior to this cemented their position as the cations of choice since then. Indeed, the method reported by Wilkes et al. for the preparation of the [RMIM]Cl/AlCl₃-based salts remains very much that employed by most workers to this day.

2.1.2

Quaternization Reactions

The formation of the cations may be carried out either by protonation with a free acid as noted above, or by quaternization of an amine or a phosphine, most commonly with a haloalkane. The protonation reaction, as used in the formation of salts such as ethylammonium nitrate, involves the addition of 3 M nitric acid to a cooled, aqueous solution of ethylamine [7]. A slight excess of amine should be left over, and this is removed along with the water by heating to 60 °C in vacuo. The same general process may be employed for the preparation of all salts of this type, but when amines of higher molecular weight are employed, there is clearly a risk of contamination by residual amine. A similar method has been reported for the formation of low melting point, liquid crystalline, long alkyl chain-substituted 1-alkylimidazolium chloride, nitrate, and tetrafluoroborate salts [8]. For these a slight excess of acid was employed, as the products were generally crystalline at room temperature. In all cases it is recommended that addition of acid be carried out with cooling of the amine solution, as the reaction can be quite exothermic.

The alkylation process possesses the advantages that (a) a wide range of cheap haloalkanes are available, and (b) the substitution reactions generally occur smoothly at reasonable temperatures. Furthermore, the halide salts formed can easily be converted into salts with other anions. Although this section will concentrate on the reactions between simple haloalkanes and the amine, more complex side chains may be added, as discussed later in this chapter. The quaternization of amines and phosphines with haloalkanes has been known for many years, but the development of ionic liquids has resulted in several recent developments in the experimental techniques used for the reaction. In general, the reaction may be carried out with chloroalkanes, bromoalkanes, and iodoalkanes, with the reaction conditions required becoming steadily more gentle in the order Cl → Br → I, as expected for nucleophilic substitution reactions. Fluoride salts cannot be formed in this manner.

In principle, the quaternization reactions are extremely simple: the amine (or phosphine) is mixed with the desired haloalkane, and the mixture is then stirred and heated. The following section refers to the quaternization of 1-alkylimidazoles, as these are the most common starting materials. The general techniques are similar, however, for other amines such as pyridine [9], isoquinoline [10], 1,8-diazabicyclo[5,4,0]-7-undecene [11], 1-methylpyrrolidine [12], and trialkylamines [13], as

well as for phosphines. The reaction temperature and time are very dependent on the haloalkane employed, chloroalkanes being the least reactive and iodoalkanes the most. The reactivity of the haloalkane also generally decreases with increasing alkyl chain length. As a general guide, in the author's laboratory it is typically found necessary to heat 1-methylimidazole with chloroalkanes to about 80 °C for 2–3 days to ensure complete reaction. The equivalent reaction with bromoalkanes is usually complete within 24 hours, and can be achieved at lower temperatures (ca. 50–60 °C). In the case of bromoalkanes, we have found that care must be taken with large-scale reactions, as a strong exotherm can occur as the reaction rate increases. Besides the obvious safety implications, the excess heat generated can result in discoloration of the final product. The reaction with iodoalkanes can often be carried out at room temperature, but the iodide salts formed are light-sensitive, requiring shielding of the reaction vessel from bright light.

A number of different methodologies have been reported, but most researchers use a simple round-bottomed flask/reflux condenser experimental setup for the quaternization reaction. If possible, the reaction should be carried out under dinitrogen or some other inert gas in order to exclude water and oxygen during the quaternization. Exclusion of oxygen is particularly important if a colorless halide salt is required. Alternatively, the haloalkane and 1-methylimidazole may be mixed in Carius tubes, degassed by freeze-pump-thaw cycles, and then sealed under vacuum and heated in an oven for the desired period. The preparation of salts with very short alkyl chain substituents, such as [EMIM]Cl, is more complex, however, as chloroethane has a boiling point of 12 °C. Such reactions are generally carried out in an autoclave, with the chloroethane cooled to below its boiling point before addition to the reaction mixture. In this case, the products should be collected at high temperature, as the halide salts are generally solids at room temperature. An autoclave may also be useful for the large-scale preparation of the quaternary salts.

In general, the most important requirement is that the reaction mixture be kept free of moisture, as the products are often extremely hygroscopic. The reaction may be carried out without the use of a solvent, as the reagents are generally liquids and mutually miscible, while the halide salt products are usually immiscible in the starting materials. A solvent is often used, however; examples include the alkyl halide itself [6], 1,1,1-trichloroethane [14], ethyl ethanoate [15], and toluene [16], although no particular advantage appears to accrue with any specific one. The unifying factor for all of these is that they are immiscible with the halide salt product, which will thus form as a separate phase. Furthermore, the halide salts are generally more dense than the solvents, so removal of excess solvent and starting material can be achieved simply by decantation. In all cases, however, after reaction is complete and the solvent is decanted, it is necessary to remove all excess solvent and starting material by heating the salt under vacuum. Care should be taken at this stage, as overheating can result in a reversal of the quaternization reaction. It is not advised to heat the halide salts to temperatures greater than about 80 °C.

The halide salts are generally solids at room temperature, although some examples – such as e.g. the 1-methyl-3-octylimidazolium salts – remain viscous oils even at room temperature. Crystallization can take some time to occur, however, and

many salts remain as oils even when formed in good purity. Purification of the solid salts is best achieved by recrystallisation from a mixture of dry acetonitrile and ethyl ethanoate. In cases of salts that are not solid, it is advisable to wash the oil as best as possible with an immiscible solvent such as dry ethyl ethanoate or 1,1,1-trichloroethane. If the reactions are carried out on a relatively large scale, it is generally possible to isolate product yields of >90 % even if a recrystallisation step is carried out, making this an extremely efficient reaction. A drybox is not essential, but can be extremely useful for handling the salts, as they tend to be very hygroscopic, particularly when the alkyl chain substituents are short. In the author's experience, solid 1-alkyl-3-methylimidazolium halide salts can form as extremely hard solids in round-bottomed flasks. Therefore, if a drybox is available the best approach is often to pour the hot salt into shallow trays made of aluminium foil. Once the salt cools and solidifies, it may be broken up into small pieces to aid future use.

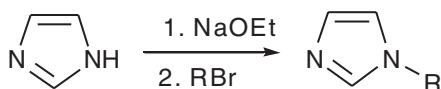
The thermal reaction has been used in almost all reports of ionic liquids, being easily adaptable to large-scale processes, and providing high yields of products of acceptable purity with relatively simple methods. An alternative approach involving the use of microwave irradiation has recently been reported, giving high yields with very short reaction times (minutes rather than hours) [17]. The reaction was only carried out for extremely small quantities of material, however, and it is unlikely that it could be scaled up with any great feasibility.

By far the most common starting material is 1-methylimidazole. This is readily available at a reasonable cost, and provides access to the majority of cations likely to be of interest to most researchers. There is only a limited range of other N-substituted imidazoles commercially available, however, and many are relatively expensive. The synthesis of 1-alkylimidazoles may be achieved without great difficulty, though, as indicated in Scheme 2.1-2.

A wider range of C-substituted imidazoles is commercially available, and the combination of these with the reaction shown in Scheme 2.1-2 permits the formation of many different possible starting materials. In some cases, however, it may still be necessary to carry out synthesis of the heterocycle from first principles. For reasons of space, this topic is not covered here.

Relatively little has been reported regarding the determination of the purity of the halide salts other than by standard spectroscopic measurements and microanalysis. This is largely because the halide salts are rarely used as solvents themselves, but are generally simply a source of the desired cation. Also, the only impurities likely to be present in any significant quantity are unreacted starting materials and residual reaction solvents. Thus, for most applications it is sufficient to ensure that they are free of these by use of ^1H NMR spectroscopy.

The removal of the haloalkanes and reaction solvents is generally not a problem, especially for the relatively volatile shorter chain haloalkanes. On the other hand,



Scheme 2.1-2: Synthesis of alkylimidazoles.

the presence even of small quantities of unreacted 1-methylimidazole (a coordinating base) could cause problems in many applications. Furthermore, its high boiling point (198 °C) means that it can prove difficult to remove from ionic liquids. Holbrey has reported a simple colorimetric determination based on the formation of the blue $[\text{Cu}(\text{MIM})_4]^{2+}$ ion, which is sensitive to 1-methylimidazole in the 0–3 mol% concentration range [18]. Although this does not solve the problem, it does allow samples to be checked before use, or for the progress of a reaction to be monitored.

It should be noted that it is not only halide salts that may be prepared in this manner. Quaternization reactions between 1-alkylimidazoles and methyl triflate [14], tri-alkylamines and methyl tosylates [19], and triphenylphosphine and octyl tosylate [20] have also been used for the direct preparation of ionic liquids, and in principle any alkyl compound containing a good leaving group may be used in this manner. The excellent leaving group abilities of the triflate and tosylate anions mean that the direct quaternization reactions can generally be carried out at ambient temperatures. It is important that these reactions be carried out under an inert atmosphere, as the alkyl triflates and tosylates are extremely sensitive to hydrolysis. This approach has the major advantage of generating the desired ionic liquid with no side products, and in particular no halide ions. At the end of the reaction it is necessary only to ensure that all remaining starting materials are removed either by washing with a suitable solvent (such as ethyl ethanoate or 1,1,1-trichloroethane) or *in vacuo*.

2.1.3

Anion-exchange Reactions

The anion-exchange reactions of ionic liquids can really be divided into two distinct categories: direct treatment of halide salts with Lewis acids, and the formation of ionic liquids by anion metathesis. These two approaches are dealt with separately, as quite different experimental methods are required for each.

2.1.3.1 Lewis Acid-based Ionic Liquids

The formation of ionic liquids by treatment of halide salts with Lewis acids (most notably AlCl_3) dominated the early years of this area of chemistry. The great breakthrough came in 1951, with the report by Hurley and Weir on the formation of a salt that was liquid at room temperature, based on the combination of 1-butylpyridinium with AlCl_3 in the relative molar proportions 1:2 ($X = 0.66$) [21].¹ More recently, the groups of Osteryoung and Wilkes have developed the technology of room temperature chloroaluminate melts based on 1-alkylpyridinium [22] and $[\text{RMIM}]^+$ cations [6]. In general terms, treatment of a quaternary halide salt Q^+X^- with a Lewis acid MX_n results in the formation of more than one anion species, depending on the relative proportions of Q^+X^- and MX_n . Such behavior can be illus-

1 Compositions of Lewis acid-based ionic liquids are generally referred to by the mole frac-

tion (X) of monomeric acid present in the mixture.