Ionic Liquids in Analytical Chemistry

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Abstract

The role of ionic liquids (ILs) in analytical chemistry is increasing substantially every year. A decade ago there were but a handful of papers in this area of research that were considered curiosities at best. Today, those publications are recognized as seminal articles that gave rise to one of the most rapidly expanding areas of research in chemical analysis. In this review, we briefly highlight early work involving ILs and discuss the most recent advances in separations, mass spectrometry, spectroscopy, and electroanalytical chemistry. Many of the most important advances in these fields depend on the development of new, often unique ILs and multifunctional ILs. A better understanding of the chemical and physical properties of ILs is also essential.

1. INTRODUCTION

Ionic liquids (ILs) are liquids composed entirely of ions. For a salt to be classified as an IL, it must have a melting point of ≤100° C. Ionic liquids are termed room-temperature ionic liquids (RTILs) if they are composed of a salt that is liquid at room temperature. ILs almost always contain an organic ion as either the cation or the anion. Typical cations are based on the imidazolium, pyridinium, ammonium, or phosphonium group. Anions are more likely to be inorganic (such as halides, BF_4, PF_6) than are the cations, but organic anions are also common [examples include trifluoromethanesulfonate (triflate) and bis[(trifluoromethyl)sulfonyl]amide (NTF_2)]. The desired anions of a particular IL are often obtained through metathesis reactions. Given the numerous combinations of cations and anions available, ILs have been touted as "designer" compounds.

ILs are different from the molten salts commonly studied in the mid- to late-twentieth century. Molten salts are generally mixtures of alkali metal salts, which often have limited liquid ranges, thermal stabilities, and variable chemical inertness (1). In contrast, ILs usually contain only one type of cation and anion and can have exceptional stability and inertness over a wide range of temperatures. For this reason, molten salt research is not described in this review. We also draw a distinction between the ILs of today and other so-called ionic liquids that consist of an alkylimidazolium cation and a chloroaluminate anion; the latter are not considered to be water stable, and they can react with other substrates.

Given the volume of scientific literature involving ILs, it is not possible to discuss all of the published work. In this review, we aim to describe early analytical developments that used ILs and to highlight the most important recent advances in separations, mass spectrometry, spectroscopy, and electrochemistry.

2. IONIC LIQUIDS: EARLY HISTORY

The first report of a liquid salt is generally attributed to Paul Walden. In 1914, Walden (2) reported the synthesis of ethylammonium nitrate, which has a melting point of 13–14° C. However, little attention was paid to this report until a synthesis of air- and water-stable ILs based on imidazolium salts was published in 1992 (1). These more stable ILs allowed researchers to study and experiment with them in a variety of applications.

Initially, these new air- and water-stable ILs were applied to the arena of organic synthesis. In 1995, Suarez and coworkers (3) synthesized 1-n-butyl-3-methylimidazolium (BMIM) BF_4 and PF_6 to serve as a solvent for a two-phase catalysis reaction involving rhodium complexes for the hydrogenation of cyclohexene. Later, BMIM BF_4, PF_6, and triflate (trifluoromethanesulfonate) ILs were used in the hydrodimerization of 1,3-butadiene via palladium catalysts in a two-phase system (4, 5). The Welton group (6) found that BMIM BF_4 was an even better solvent than dichloromethane for arene hydrogenation using ruthenium catalysts, although other ruthenium catalysts were insoluble in the IL and were rather ineffective (7). Seddon and coworkers also carried out enzyme-catalyzed reactions in BMIM PF_6 in a biphasic system (8) and later entirely in an IL (9). By 1999, ILs with organic cations that were not based on imidazolium or pyridinium structures began emerging for specific synthesis tasks (10). These studies show how ILs have become such attractive replacements for traditional organic solvents in these applications. However, because synthesis is not the focus of this review, we do not discuss these applications further.

Molten salts with alkylimidazolium cations and chloroaluminate anions were of interest in electrochemical research in the 1980s. However, it became necessary to find alternatives because of the chloroaluminates' instability in water. Fuller and coworkers (11, 12) incorporated 1-ethyl-3-methylimidazolium BF_4, triflate, and PF_6 into a poly(vinylidene fluoride)-hexafluoropropylene copolymer to make a gel electrolyte. These ILs retained the same desirable properties as the earlier chloroaluminate salts, such as high ionic conductivities and wide electrochemical windows, but the former were more water stable. Further developments involving the use of ILs in electrochemical applications are discussed in Section 3.6.

Early applications of ILs also included their use as solvents in liquid-liquid extractions. In 1998, the Rogers group (13) began using ILs as solvents for the extraction of simple, substituted benzene derivatives from water. BMIM BF_4 and PF_6 displayed partitioning behavior similar to that of the traditional octan-1-ol/water system. Although distribution coefficients were higher in the octan-1-ol/water system, the IL possessed an adequate extraction power for practical separations. The authors determined that the uncharged forms of ionizable analytes were more efficiently extracted into the IL layer, similar to their behavior with traditional organic solvents. The appeal of using ILs as replacements for organic solvents thus arises from their negligible vapor pressure.

Dai and coworkers (14) added crown ethers to imidazolium ILs with either PF_6 or NTF_2 [bis[(trifluoromethyl)sulfonyl]amide] anions for the extraction of strontium nitrate from water. When traditional organic solvents were used, the thermodynamically favored complexation of Sr^{2+} was hindered by the thermodynamically unfavored desolvation of the nitrate ion. Alkyl chains on the imidazolium cation and the identity of the anion influenced the distribution coefficient of the Sr^{2+}, with the best-performing IL having a distribution coefficient four orders of magnitude higher than that of traditional organic solvents. Visser et al. (15) also used alkyl-3-methyl imidazolium PF_6 ILs along with organic [1-(pyridylazo)-2-naphthol and 1-(thiazoylazo)-2-naphthol] and inorganic (cyanide, cyanate, thiocyanate, and halides) anions to extract metal cations such as Cd^{2+}, Co^{2+}, Ni^{2+}, Fe^{2+}, and Hg^{2+}. These early papers laid the foundation for a large volume of work describing the use of ILs as extractants.

ILs have also been utilized in another separation technique: gas chromatography (GC). In a 1999 study, Armstrong and coworkers (16) coated GC capillaries with BMIM PF_6 or BMIM Cl. The IL GC columns exhibited a dual nature when separating compounds. Compared to a relatively nonpolar commercial column employed under the same conditions, the IL columns separated nonpolar compounds in much the same way and with similar retention times (16). However, polar compounds such as acids, bases, and compounds capable of hydrogen bonding could also be separated on the IL columns and displayed much different retention behaviors. The ILs were also capable of dissolving large compounds, such as cyclodextrins normally used as chiral GC stationary phases. Additionally, the authors learned more about the nature of the IL stationary phase by using inverse GC and finding the Rohrschneider–McReynolds constants of the IL stationary phase. This work was followed by a more in-depth characterization of 17 RTILs using a linear free-energy approach (17).

The unique properties of ILs led Armstrong et al. (18) to investigate their application as potential liquid matrices for matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS). The low vapor pressure of the ILs allowed them to persist in a vacuum while remaining liquid. Analytes dissolved homogeneously in the IL eliminated the "hot spot" problems encountered with traditional solid matrices. In 2001, the authors tested 18 different IL matrices in the MALDI format. Although all of the ILs possessed great solubility and vacuum stability, their ability to produce gas-phase analyte ions varied. To serve as effective matrices, the ILs needed to have high absorptivity at the correct wavelength as well as the ability to donate protons to the analytes (18).

These early works underlie many of the new developments discussed herein. The initial success of these applications, along with the versatility and unique properties (such as low volatility, low melting points, viscosity, etc.) of ILs, has led to the use of ILs in applications much broader than these initial works. These unique properties are controlled by the structure of the cations and anions as well as which cations are paired with which anions. Monocations can be based on different charge groups. Increasing the number of cations increases the number of structural factors that influence properties of the ILs. Dicationic and tricationic ILs can vary in the type and length of linkage chains connecting the charge groups. The geometry of tricationic liquids (linear versus trigonal) also influences properties. Both dicationic and tricationic ILs can be synthesized to have different types of charged groups, which can greatly affect observed properties. Changing from inorganic to organic anions can also influence these properties. As with the cationic species, increasing the charge groups allows for greater variances in the structure of the anion. By changing the architecture of the ionic parts, ILs can be tuned to the desired properties for use in various analytical applications.

3. RECENT DEVELOPMENTS

3.1. Gas Chromatography

In 2007, Han & Armstrong (19) reviewed the role of ILs in separation techniques including GC. Creating GC stationary phases with high thermal stability is very important if IL stationary phases are to compete with commercial GC stationary phases. GC stationary phases with higher thermal stability were developed using geminal (or dicationic) ILs (20). Dicationic ILs with vinyl groups were cross-linked after being coated on a silica capillary to yield GC stationary phases with very high temperature stability and extremely low column bleed (21). Also, asymmetrical dicationic ILs (22) and tricationic ILs (23) have recently been synthesized. In addition to creating new avenues for tuning chemical properties, these multifunctional ILs have shown exceptional thermal stability and very wide liquid ranges, and they may make intriguing new GC stationary phases. Also highlighted in the review is the development of chiral GC stationary phases using ILs (19). Enantioselectivity was achieved by dissolving cyclodextrin derivatives in ILs, which yielded very high separation efficiencies but achieved lower numbers of separations compared to the output of commercial columns used with the same selectors (24). A chiral stationary phase based on N,N-dimethylphenylephedrine, where the IL itself is the chiral selector, resulted in enantiomeric separations for sulfoxides, alcohols, and epoxides (25). However, this stationary phase racemized or degraded at moderately high temperatures, which highlighted the need for higher-stability chiral IL stationary phases.

New results in GC (published since the 2007 review by Han and Armstrong) have been reported. In one study, polyethylene glycol (PEG)-linked geminal dicationic ILs were used as gas-liquid chromatography (GLC) stationary phases (26). These imidazolium-based dicationic ILs utilized PEG linkage chains rather than the traditional hydrocarbon linkers. Compared with commercial polysiloxane and PEG stationary phases, the PEG dicationic liquids showed unique selectivity and high separation power in separating 24 compounds in a flavor/fragrance mixture (**Figure 1**) (26). Seeley et al. (27) compared a trihexyl(tetradecyl) phosphonium NTF_2 IL column with two other commercially available columns (DB-Wax and HP-50+) for use in two-dimensional GC with a relatively nonpolar commercial column (HP-5). Separations of homologous compounds on the three different configurations showed that the IL column was more polar than the HP-50+ column but less polar than the DB-Wax column. Two-dimensional separations of diesel fuel revealed that the IL column excelled at separating different classes of diesel fuel components (27). A 1,9-di(3-vinylimidazolium)nonane triflate stationary phase was used as the second column in another two-dimensional GC configuration (28). Compared to the commercial DB-Wax column, the IL column showed high selectivity for dimethylmethylphosphonate from pentanol and n-dodecane and was very good at separating all P-O-containing compounds from the other

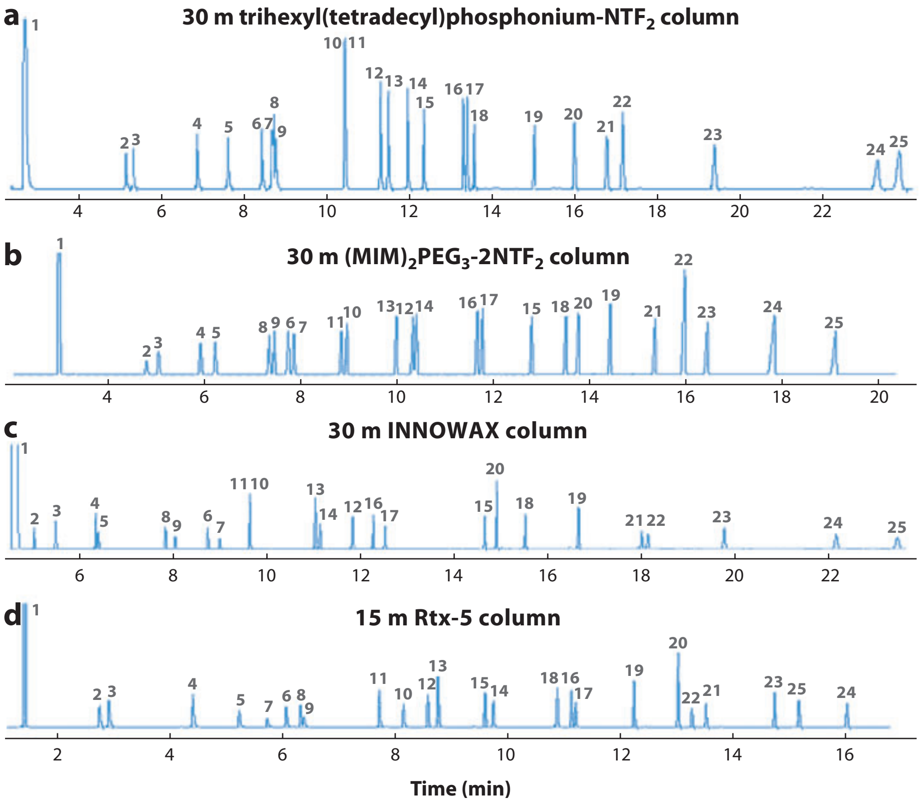

Figure 1

(*a–d*) Separation of a flavor and fragrance mixture with four different columns. 1, dichloromethane; 2, ethyl propionate; 3, methyl butyrate; 4, ethyl butyrate; 5, isopropyl butyrate; 6, allyl butyrate; 7, methyl tiglate; 8, propyl butyrate; 9, ethyl valerate; 10, ethyl hexanoate; 11, isopropyl tiglate; 12, allyl tiglate; 13, propyl tiglate; 14, ethyl heptanoate; 15, furfuryl propionate; 16, hexyl butyrate; 17, ethyl octanoate; 18, furfuryl butyrate; 19, furfuryl pentanoate; 20, hexyl tiglate; 21, furfuryl hexanoate; 22, benzyl butyrate; 23, furfuryl heptanoate; 24, furfuryl octanoate; 25, benzyl tiglate. Gas chromatography separation conditions: 40° C for 3 min, then 10° C min^{-1} to 150° C; 1 ml min^{-1} He; flame ionization detector. Abbreviations: NTF$_2$, bis[(trifluoromethyl)sulfonyl]amide; PEG, polyethylene glycol. Reproduced from Reference 29 with permission from Springer.

31 compounds in a complex mixture. Breitbach & Armstrong (29) characterized 11 phosphonium-based ILs and compared their physicochemical properties to those of analogous ILs, which are based on the more common imidazolium structure. The phosphonium ILs were coated onto capillaries and used as GLC stationary phases. They showed greater thermal stability than did the nitrogen-based imidazolium ILs, making them extremely attractive for GC applications (29). The phosphonium ILs also displayed different selectivity from those of imidazolium ILs and commercial columns.

A mixture of BMIM Cl and BMIM NTF$_2$ was used to improve the selectivity and resolution factors of alcohols and aromatic compounds relative to the neat BMIM NTF$_2$ column (30). By adding chloride ions, the authors changed the retention order of alcohols relative to other compounds in the test mixture. As the chloride ion concentration in the stationary phase increased, the retention times of the alcohols increased as well due to the higher hydrogen-bonding ability of the stationary phase (30). Tran & Challa (31) reported a fullerene-impregnated IL as a potential GC stationary phase. They also attempted to use amino and hydroxyl derivatives as GC stationary phases. By adding fullerene (or its derivatives), the polarity of the resulting stationary phase was altered. Changing the IL used to coat the fullerene also affected the polarity of the stationary phase.

3.2. Liquid-Liquid Extraction

In early applications, ILs were used to replace organic solvents in extraction procedures; these studies were discussed in the review by Han & Armstrong (19). Therefore, we report the progress in this area since then.

When ILs were first used to extract metals, complexing agents were often employed (15); this approach is still in use today. 1-butyl-3-trimethylsilylimidazolium hexafluorophosphate was used to extract lead from aqueous solutions using dithizone as a chelator (32). The lead was then back-extracted into nitric acid solutions for direct analysis by graphite furnace atomic absorption. A mixture of branched alkyl phosphine oxides in C_8MIM (1-octyl-3-methylimidazolium) PF_6 was used to extract scandium (III) from other lanthanides (III) (33). Today, when ILs are used to extract metals from solutions, they can also be used in their pure form. Cerium (IV) was extracted from nitric acid solutions containing thorium (IV) and other trivalent lanthanides using pure C_8MIM PF_6 (34). In some cases, ILs have been developed with special functional groups to aid in the extraction process. Such ILs, termed task-specific ILs, were created for the extraction of Wilkinson's and Jacobsen's catalysts from a homogeneous organic phase (35). Tested functional groups included amino, hydroxyl, thioether, carboxylic, and olefin groups. ILs with longer carbon chains containing amino or thioether functional groups performed the best for extracting the catalysts (35).

ILs have been popularly used as solvents for the extraction of a variety of small molecules. Recently, several hydrophilic ILs were tested for their ability to extract ethanol from a mixture of ethyl acetate and ethanol (36). Ethanol cannot be separated from ethyl acetate via simple distillation due to the formation of a low-boiling azeotrope. 1-allyl-3-methylimidazolium chloride, which is nearly immiscible with ethyl acetate, had the highest extraction efficiency, and ethyl acetate was found to be 99.27% pure after two extractions (36). The IL was recycled using simple distillation. In a related study, anionic dyes were extracted from water solutions using imidazolium-based ILs with either PF_6 or BF_4 anions (37). The pH of the aqueous solution affected the charge on the dyes and thus their extraction efficiency. The authors increased the extraction efficiency by raising the temperature or by using imidazolium cations with longer alkyl chains (37).

A phosphonium IL with a 2,4,4-trimethylpentylphosphinic anion has been shown to be an effective extractant for undissociated lactic acid (38). Lateef and coworkers (39) used ILs to extract decabromodiphenylether and antimony trioxide from a suspension of high-impact polystyrene in ethyl acetate. 1-hexylpyridinium bromide was the most efficient IL at removing flame retardants from polymer suspensions, yielding a plastic that could be fed into recycling streams (39). 1-methyl-3-alkyl imidazolium BF_4 or PF_6 ILs were used to extract five phenols from aqueous solutions (40). The ILs gave distribution coefficients that were one to two orders of magnitude larger than the traditional solvents, dichloromethane and benzene, and in some cases, the ILs selectively extracted one phenol over another (40). ILs are also commonly studied as extractants for various hydrocarbons (41, 42). Use of two immiscible ILs (one based on phosphonium and the other on imidazolium, with NTF_2 as the common anion) did not separate benzene and hexane, the selected test hydrocarbons (41). Under optimal conditions, a centrifugal extractor separated ethylbenzene from octane with 90% efficiency through use of the IL BMIM PF_6 (42).

The removal of aromatic sulfur compounds from fuels using ILs has also been studied (43, 44). Imidazolium-based ILs with alkyl phosphate anions were used to extract 3-methylthiophene, benzothiophene, and dibenzothiophene from gasoline (43). Because most desulfurization work has involved imidazolium ILs, Holbrey and coworkers (44) examined different cations and anions for extraction of dibenzothiophene from dodecane. Polyaromatic quinolinium–based ILs exhibited great extraction potential, but they had to be paired with NTF_2 anions to form low-melting salts. Ethanolate and thiocyanate anions paired with 1-butyl-3-methylpyridinium cations also showed promise as extractants (44). Du and coworkers (45) used BMIM bromide as the extraction solvent in the microwave-assisted extraction of *trans*-resveratrol from the Chinese herb *Rhizma Polygoni Cuspidati*. The anion of the IL was shown to have a significant impact on the extraction ability of the *trans*-resveratrol. The bromide anion gave higher efficiencies than did either chloride or BF_4 BMIM analogs (45).

The use of ILs as extractants for complex biomolecules is increasing. Recent studies have focused upon penicillin G (46), double-stranded DNA (47), hemoglobin (48), and alcohol dehydrogenase enzymes (49). The IL trioctylmethylammonium chloride (TOMAC) more successfully extracted penicillin G than did imidazolium-based ILs, but it was difficult to remove the penicillin from the IL (46). Instead, the authors employed TOMAC as a membrane solution for a supported liquid-membrane system and used chloride concentration as the driving force. The cation in BMIM PF_6 interacted with the oxygen molecules of the phosphates in the DNA, changing the conformation of the DNA and allowing for the quantification of the DNA through ethidium resonance light scattering (47). Coordination between the cation of 1-butyl-3-trimethylsilylimidazolium PF_6 and the ferrous atom in hemoglobin allowed for the extraction of the protein without the need for additives (48). Sodium dodecyl sulfate was used in the back-extraction to remove the protein from the IL extractant. An IL with oligoethyleneglycol units was found to be mostly immiscible with an aqueous solution containing a high amount of potassium phosphate (49). This two-phase system allowed for the extraction of two different alcohol dehydrogenase enzymes from the aqueous solution. The IL stabilized both the enzymes and the hydrophobic substrates, leading to increased conversion rates and higher yields (49).

3.3. Microextraction

ILs have increasingly been used in microextraction techniques. Their negligible vapor pressure and stability at higher temperatures, compared to those of traditional organic solvents, make ILs ideal candidates for liquid-phase microextraction (LPME), especially as headspace (HS) extractants. Recently, BMIM PF_6 was used as the extractant in HS-LPME of phenols (50) and in HS-SDME (single-drop microextraction) of chlorobenzenes (51) from environmental water samples. Both of these optimized methods exhibited excellent linearity and acceptable reproducibility for the selected analytes, which were analyzed by high-performance liquid chromatography (HPLC). However, in both studies, some matrix effects in the environmental samples were observed. Metal ions formed competing complexes with the phenolic analytes, decreasing the ability of the phenols to move into the headspace (50). Adding EDTA (ethylenediaminetetraacetic acid) to the samples appeared to eliminate this interference. For the hydrophobic chlorobenzenes, significant matrix effects were observed only in the effluent water from a wastewater treatment plant (51). It was proposed that adsorption to solid material in the effluent reduced the amount of analyte in the headspace.

The above applications used HPLC to analyze the compounds extracted by the ILs, allowing for the direct injection of the extracted analytes and ILs into the analysis system. However, the nonvolatility of ILs, which is normally an asset, becomes a liability when combining LPME

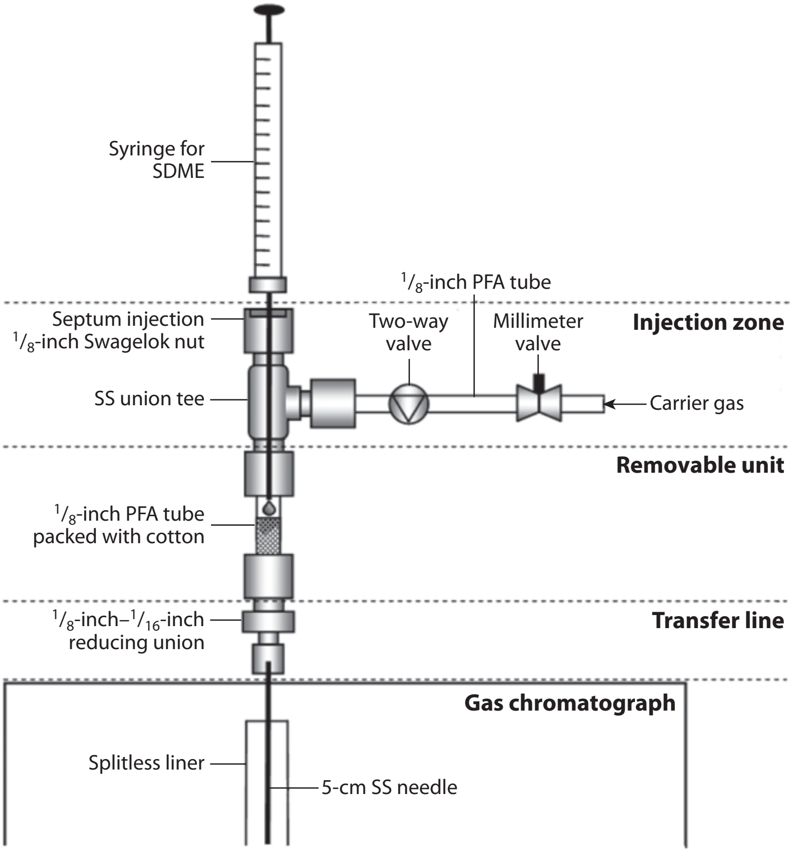

Figure 2

Schematic diagram of the interface developed for direct introduction of ionic liquid containing extracted analytes. Abbreviations: PFA, perfluoroalkoxi; SDME, single-drop microextraction; SS, stainless steel. Reproduced from Reference 52 with permission from the American Chemical Society.

(including SDME) and GC. Aguilera-Herrador and coworkers (52) developed a removable interface that permits the introduction of extracted analytes from SDME into the GC system while preventing the IL from entering the column. **Figure 2** shows the developed interface, which has three zones: an injection zone, a removable zone, and a transfer zone. The new interface is located directly above the GC injector to allow heat from the injector to be transmitted to the injection zone of the new interface. The removable section is packed with cotton and is made removable by Swagelok® nuts on the ends of the perfluoroalkoxi tube. Porcelain insulators allow the new injection system to reach thermal equilibrium and to maintain a constant injection temperature. Aguilera-Herrador et al. chose dichloromethane, *p*-xylene, and *n*-undecane as representative compounds and extracted them with BMIM PF_6 with acceptable relative standard deviation values (52). Recently, IL-based HS-SPME was combined with cataluminescence (CTL) detection for analysis of acetone in human plasma (53). The solid support was filter paper saturated with various ILs. BMIM CO_2CF_3 provided the highest acetone signal at the CTL detector.

3.4. Ionic Liquids as MALDI Matrices

Early use of ILs as MALDI matrices led to new applications of ILs. In the first application, IL matrices were compared to conventional solid matrices, such as α-cyano-hydroxycinnamic acid, on the basis of their ability to ionize traditional analytes such as insulin, bradykinin, and PEG (18). Later, the Armstrong group (54) tested IL matrices for ionizing oligonucleotides. However, the best ionic matrices for the oligonucleotides were solids, not liquids. Thus, even though higher signal intensities could be reached with the new ionic matrices, homogeneity problems such as hot spots occurred as with conventional solid matrices (55).

In early studies, IL matrices were also tested for small-molecule ionization. Through use of amino acids, sugars, and vitamins as analytes, IL matrices were made from sinapinic, α-cyano-hydroxycinnamic, and 2,5-dihydroxybenzoic acids as well as equimolar amounts of organic bases such as pyridine, 1-methylimidazole, and tributylamine (55). Compared to conventional solid matrices, the IL matrices yielded better linearity, smaller standard deviations, and decreased analysis time. Li & Gross (56) also achieved good calibrations and linearity with macromolecules using IL matrices. They also noticed that the slope of the calibration curve correlated inversely with the weight of the peptide studied.

Although the papers described above focused on the use of organic salts of classical MALDI solid matrices, Tholey and coworkers (57) used a different approach to analyzing small molecules via MALDI-MS. Using more traditional ILs, the authors achieved ionization by adding the classical solid matrices to the ILs. The homogeneity of the analyte in this mixture of ILs and solid matrix was not high, but this type of approach may be useful for the quantification of analytes produced by enzymatic reactions in ILs (57). However, most work involving IL MALDI matrices continues to utilize the organic salts of traditional solid matrices. Other matrix additives to IL matrices have also been used to increase detectability (58).

Time-of-flight mass spectrometers were used in the MALDI applications discussed above. The choice of mass analyzer can affect the quality of the spectra observed. The longer analysis times of MALDI FT-MS (Fourier transform mass spectrometry) resulted in more fragmentation of peptides and oligonucleotides when IL matrices, rather than traditional solid matrices, were used (59). However, for phospholipids, the use of IL matrices actually resulted in the suppression of fragmentation.

Recent research on IL MALDI matrices has focused on the analysis of peptides/proteins (60–62), saccharides (63–65), and modified lipids (66, 67). α-cyano-hydroxycinnamic acid combined with pyridine at a ratio of 2:1 led to better signal-to-noise ratios, reduced chemical noise, and reduced matrix clusters for most peptides than did pure α-cyano-hydroxycinnamic acid or an equimolar mixture of α-cyano-hydroxycinnamic acid and pyridine (60). Compared to pure α-cyano-hydroxycinnamic acid, the optimized 2:1 mixture also led to more sequence coverage and higher match scores for a protein excised from a two-dimensional gel for identification. IL matrices were successfully used to monitor peptide products from a trypsin-catalyzed digestion of several proteins (61). The presence of multiple peptide products led to large variations due to peak suppression in peptide signals for some analytes. Addition of a peptide internal standard only worsened the problem. Thus, the authors (61) advocated an internal standard-free approach to quantification for this type of application. Analyte suppression in multianalyte peptide mixtures was also observed when a 2,5-dihydroxybenzoic acid/pyridine IL matrix was used for a multianalyte peptide mixture (62). However, the IL matrix gave cleaner spectra for the peptides than did the classical solid matrix alone.

The imidazolium salt of α-cyano-hydroxycinnamic acid and the butylammonium salt of 2,5-dihydroxybenzoic acid were used to produce sodium adducts of sulfated oligosaccharides for analysis by MALDI-MS (63). Prior to this new method, the standard procedure was to create adducts between the oligosaccharides and various basic peptides, which was time consuming. However, the saccharides did undergo some fragmentation with the loss of the labile SO_3 group using the new IL-based matrices. Through use of a new IL matrix with a bis-1,1,3,3-tetramethylguanidinium cation and an α-cyano-4-hydroxycinnamate anion, the loss of the SO_3 group from dermatan and chondroitin sulfate was reduced even though the saccharides were detected as sodium adducts (64). The guanidinium α-cyano-4-hydroxycinnamate IL and cesium salt were also used for MALDI-MS analysis of glycoaminoglycan disaccharides as cesium salts (65). The cesium salts of the disaccharides prevented loss of the SO_3 groups more effectively than did lithium, sodium, potassium, and rubidium salts. Also, Fukuyama and coworkers (66) developed a guanidinium-based IL MALDI matrix with *p*-coumaric acid as the anion for analysis of various oligosaccharide forms. In addition to showing great sensitivity for sulfated, sialyated, and neutral oligosaccharides, this new IL matrix was particularly effective in negative-ion mode for the detection of glycopeptides from a digest of ribonuclease B. **Figure 3** shows the ion intensities for a classic MALDI matrix [2,5-dihydroxybenzoic acid (DHB)] and the two IL matrices. The higher signal intensities from the entire spot are quite noticeable when IL matrices are used. Tissot et al. (67) used both a crystalline matrix (norharmane) and an IL matrix (imidazolium α-cyano-4-hydroxycinnamate) to characterize glycoaminoglycan polysaccharides. The IL matrix exhibited less sulfate loss compared to the crystalline matrix, making it useful in determining the total number of sulfate groups. The crystalline matrix was useful for determining the length of the backbone and the number of acetyl groups.

IL matrices and classical solid matrices were both evaluated for the analysis of lipids isolated from biological samples, yielding two different outcomes. For the analysis of a chlorosulfolipid from *Ochromonas danica*, the IL matrix 1-butylamine α-cyano-4-hydroxycinnamate provided higher signal-to-noise ratios than did the only crystalline matrix to give a signal (68). The IL matrix was then used for characterization of the chlorosulfolipid. However, when a sulfolipid from *Porphyridium purpureum* was used as the analyte, the classical matrix 2,5-dihydroxybenzoic acid provided the best signal compared to two IL matrices using α-cyano-4-hydroxycinnamate as the anion (69). These results highlight the fact that the choice of MALDI matrix continues to be analyte dependent.

3.5. Spectroscopy

There is a large volume of work in the field of spectroscopy involving ILs as solvents for the study of other species. In this section, we discuss early research on ILs in spectroscopy and highlight a few analytical applications.

Spectroscopy has been used to understand the solvation characteristics of ILs (70–76). Karmakar & Samanta (70) used time-resolved fluorescence data to show that the solvation of coumarin 153 was biphasic (i.e., with fast and slow components) and dependent on the monitoring wavelength. They also estimated that the IL BMIM BF_4 was as polar as 2-propanol. Later, coumarin 153 was used as a fluorescent probe by the Petrich group (71, 72) in time-resolved fluorescence studies, which indicated that at least half of the solvation reorientation around the probe was completed within 100 ps in bulk ILs. Dynamic solvation studies were performed on the micelles formed by ILs when water was used as the bulk solvent. Initial results with an imidazolium-based IL indicated that the organic cation still forms the majority of the early solvation when the IL is present in the form of micelles, as well as when the IL is the bulk solvent (73). However, later results using phosphonium ILs showed that this was not the case and that the calculated solvation time is highly dependent on the construction of the solvation correlation function (74).

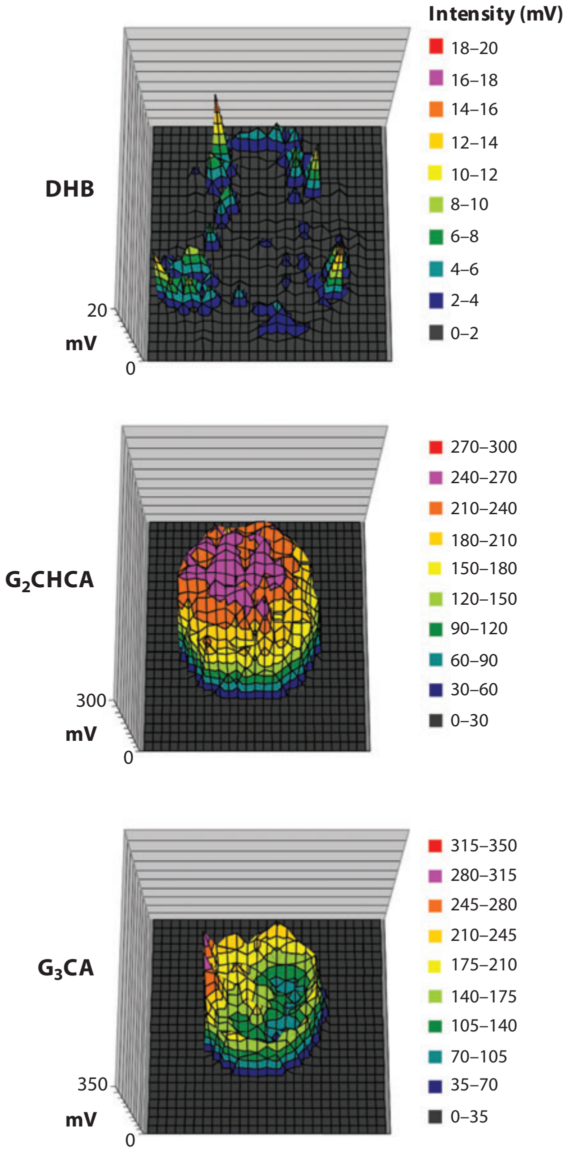

Figure 3

Ion-intensity distributions of the analyte-matrix surface (810 μm × 810 μm) using 2,5-dihydroxybenzoic acid (DHB) and guanidinium ionic liquid matrices (G_2CHCA and G_3CA) for sodium neocarratetraose-41,3-di-O-sulfate. Reproduced from Reference 66 with permission from the American Chemical Society.

Steady-state ultraviolet (UV) and time-resolved fluorescence measurements were used to show that chiral ILs made using imidazole and chloromethyl methyl ether cause small but reproducible stereodifferentiation in the fluorescence lifetimes of naproxen and an analog (both of which are chiral) (75). These results are believed to represent the first time chiral ILs have induced such a change in photophysical properties. Bhattacharya & Samanta (76) conducted excited-state proton-transfer dynamics in room-temperature ILs using 7-hydroxyquinoline as the probe molecule. A small amount of methanol was required to observe the proton transfer. The amount of methanol was found to change the viscosity of the bulk solution and to change the kinetics of the proton transfer, but the microenvironments can have a different viscosity from that of the bulk solution (76).

Long thought to be optically transparent materials, imidazolium-based ILs were shown to exhibit significant absorbance in the UV region and a surprising amount of fluorescence in the visible spectrum (77–79). Some of this absorbance in the UV spectrum may be caused by colored impurities thought to exist at the parts-per-billion level (but with high molar absorptivities) (80). The fact that two methods for decolorizing ILs have been developed gives credence to this assumption (81, 82). The first method, decolorization, employs (*a*) a chromatography column (50 cm × 36 mm inner diameter) filled bottom to top with celite to trap charcoal particles, (*b*) flash chromatographic silica gel for the decolorizing/removal of polar and inorganic impurities, and (*c*) activated charcoal for decolorizing (81). This technique achieved excellent results for the NTF_2, PF_6, and BF_4 anions, but it is not recommended for ILs capable of strong hydrogen bonding or ILs that interact with charcoal. Although this method greatly reduced the color of the ILs, the effect on the fluorescence from ILs was only reduced, not eliminated. Thus, only some of the colored impurities give rise to this background fluorescence. Optical studies (mentioned above) indicate that this background fluorescence may be inherent to the ILs themselves (77–79). Another method was developed for the purification of ILs through use of solid-phase extraction with an octyldecylsilyl sorbent (82). This method is capable of purifying ILs capable of hydrogen bonding, but it works better for ILs with shorter alkyl chains. Removal of fluorescence-causing impurities was not tested.

Tran & Lacerda (83) used near-infared spectrometry to determine the binding behavior of analytes to cyclodextrins dissolved in 1-butyl-3-methylimidazolium chloride. The binding constants of phenol with α-, β-, and γ-cyclodextrin increased with the size of the cyclodextrin cavity when done in the IL. But for α- and β-cyclodextrin, the binding constants were an order of magnitude lower than the corresponding binding constants in D_2O. (γ-cyclodextrin binding constants were not determined in D_2O.) The authors postulated that the lower binding constants achieved in the IL resulted from the aromatic cation interfering with the inclusion of the phenol, which would confirm a previous report to this effect by Armstrong and coworkers (24).

Spectroscopy has also been used to study the solvation effect of ILs on proteins. Denaturation of *Candida antarctica* lipase B (CaLB) (84) and the thermostability of monellin (85) were studied by FT-IR (Fourier transform infrared) spectroscopy and fluorescence, respectively. ILs consisting of (*a*) either BMIM or ethylammonium cations and (*b*) nitrate, lactate, or ethylsulfate anions sufficiently dissolved the CaLB, but the reaction rates were ten times slower than those in BMIM BF_4 or PF_6, which do not dissolve CaLB (84). The slower reaction rates were attributed to denaturation of the enzyme in the ILs, which was confirmed by FT-IR spectroscopy. Fluorescence emission blueshifts of a tryptophan residue in the monellin indicated that the protein compacted as temperatures rose when the protein was dissolved in 1-buytyl-1-methylpyrrolidinium NTF_2, which contained a nominal amount of water (2% by volume) (85).

X-ray photoelectron spectroscopy (XPS) of liquids is not commonly performed because liquids tend to evaporate under the high-vacuum conditions necessary for analysis. However, ILs have negligible vapor pressure even under high-vacuum conditions and therefore can be studied by XPS. Smith and coworkers (86) found that the IL 1-ethyl-3-methyl imidazolium ethylsulfate exhibited good photoelectron flux, and because of its ionic composition, it did not suffer from differential charging effects. XPS was sensitive enough to easily detect a silicon impurity in the IL, which was thought to have originated from the septum of the storage vial. XPS was also used to confirm the instability of a palladium catalyst in the IL.

ILs are also being studied as potential nuclear magnetic resonance (NMR) solvents. However, unless the ionic liquids are deuterated, ^{1}H signals from the IL can be observed throughout the spectral range, especially when the ILs have long hydrocarbon chains. Giernoth & Bankman (87) employed diffusion-ordered NMR spectroscopy to filter out the signals for IL solvents. In this method, the signal from the IL—which is more viscous and slower to diffuse than the solute being studied—can be almost totally suppressed if the difference between the diffusion coefficients is large enough. The application of this suppression method was demonstrated for the ternerization of dimethylsulfide with methyl iodide. With the solvent signal suppressed, the signals from the two reactants were clearly visible, although the product cation signal was absent due to the presence of a diffusion coefficient similar to that of the IL (88). The Rogers group was able to study the composition of ripening banana pulp using conventional high-resolution ^{13}C NMR because the signals from the BMIM Cl did not overlap with the signals from the carbohydrates. The IL was found to dissolve the banana pulp with essentially no additional sample preparation, and signals from the anomeric carbons were used to estimate the molar composition ratios of the carbohydrates.

BMIM PF_6 served as both the extraction solvent and the analysis medium in the spectrophotometric determination of germanium in water samples (89). The germanium forms a red-colored complex with methylbenzeneazosalicylfluorone in the presence of Triton X-100 and is extracted into the IL layer. Linearity was achieved between 0 and 16 ng ml^{-1} with a detection limit of 0.2 ng ml^{-1}. Results obtained through use of this spectrophotometric method agreed extremely well with an established electrothermal atomic absorption spectroscopy method (89).

Optical spectroscopy was explored for the speciation of several uranyl complexes that were dissolved in either BMIM NTF_2 or 1-butyl-3-methyl pyrrolidinium NTF_2 (90). The molecular symmetry of a uranyl complex yielded a characteristic vibrational fine structure of absorption spectra. However, extended X-ray absorption fine-structure spectroscopy was necessary to determine the coordination number or interatomic distances of the complexes.

Scanning electrochemical microscopy (SECM) was attempted in BMIM BF_4 and PF_6 (91). These ILs, especially when purified, have much higher viscosities than do the aqueous or organic solvents in which SECM is usually conducted, requiring scientists to use smaller electrodes and slower approach speeds to achieve similar image quality (91). Thus, although it is possible to replace the other solvents with ILs, conducting SECM in ILs remains a challenge.

3.6. Electrochemistry

For many years, chemists used molten salts and chloroaluminate salts in their electrochemical applications. Although there are some areas of research where these salts are still the preferred "ionic solvents," the use of RTILs in electrochemistry has become widespread. The studies we discuss in this section focus on analytical applications from the wealth of electrochemistry literature. For a more extensive overview of all electrochemical applications, see the review by Tsuda & Hussey (92).

Construction and development of new electrodes involving ILs have been undertaken by several research groups (93–99). 1-octyl-3-methylimidazolium PF_6 was mixed with multiwalled carbon nanotubes to create a thin gel film to cover a glassy carbon disk electrode (93). This electrode was then used to detect dopamine in the presence of both ascorbic acid and uric acid using cyclic voltammetry or differential pulse voltammetry. In this method, the anodic peaks of ascorbic acid are moved to more negative potentials with the modified electrode, and the anodic peaks for uric acid are shifted to more positive potentials, leading to the determination of dopamine without interference. The detection limit for dopamine with differential pulse voltammetry was 1×10^{-7} M (93).

Replacing the nonconducting organic binder (such as paraffin) in carbon paste electrodes has been a much more popular use of ILs in the fabrication of electrodes (94–97). The IL n-octylpyridinium PF_6 was used as the binder to form a carbon composite electrode (94). This electrode exhibited better characteristics than those of other carbon-based electrodes, including but not limited to low background, low cost, ease of preparation, favorable electrochemical response, and resistance to fouling. Additionally, the electrode demonstrated high selectivity for biomolecules, which was exploited for the simultaneous determination of dopamine, ascorbic acid, and uric acid using differential pulse voltammetry (95). Analysis in complex matrices found in human serum and urine samples was also demonstrated. A similar electrode was constructed for the detection of dopamine, but the IL used in this case was N-butylpyridinium PF_6 (96). An IL carbon paste electrode for the detection of calcium dobesilate was made using 1-pentyl-3-methylimidazolium PF_6 (97). Compared to a traditional carbon paste electrode, this IL electrode exhibited higher selectivity, faster electron transfer, and better reversibility, leading to a detection limit of 4×10^{-7} M for the angioprotective agent.

Several ILs were tested for use in a composite electrode (consisting of a suspension of gold nanoparticles, single-walled carbon nanotubes, and the IL that was used to create a film over a glassy carbon electrode) for the determination of the antibiotic chloamphenicol (98). The best results were achieved with the most hydrophobic cation and anion pair. Thus, 1-octyl-3-methylimidazolium PF_6 provided the highest peak currents, which was thought to be the result of higher accumulations of the antibiotic in the film. The detection limits, after 150 s on an open circuit, was determined to be 5.0×10^{-9} M (98). IL-polymer films using the NTF_2 salts of dodecylethyldiphenylphosphonium or 1-butyl-2,3-dimethylimidazolium cations were coated on miniature, planar, screen-printed electrodes for use as ion-selective electrodes (99). The phosphonium-based electrode gave near-Nernstian response for both anions and cations, whereas the imidazolium-based electrode responded only to cations. Detection limits were higher for these modified electrodes than for similar ion-selective electrodes with liquid inner-filling solutions (99). However, the modified solid electrodes were thought to be more suitable for use in miniaturized applications.

Electrodes also have been constructed for the study of biomolecules through use of ILs as materials for immobilization (100–102). Chitosan and BMIM BF_4 were used to immobilize hemoglobin over a glassy carbon electrode, and this system was used to explore both electron transfer between the protein and the glassy carbon electrode and other bioactivities (100). A similar electrode was fashioned using horseradish peroxidase immobilized in a gelatin-N,N-dimethylformamide-IL gel over a glassy carbon electrode (101). Again, 1-octyl-3-methylimidazolium PF_6 was chosen as the IL for construction of the electrode, as the less-hydrophobic BMIM BF_4 and PF_6 yielded smaller peak currents. A hydrophobic phosphonium NTF_2 IL was also tested, and it produced results similar to those obtained from the 1-octyl-3-methylimidazolium PF_6. Cytochrome *c* was immobilized over a basal plane graphite electrode with gold nanoparticles and 1-ethyl-3-methyl imidazolium BF_4 (102). Reduction peak currents were linearly proportional to the concentration of oxygen present, leading to the possible application of this electrode as an oxygen sensor.

The IL 1-ethyl-3-methylimidazolium NTF_2 was used as the solvent for the electrochemical detection of ammonia using hydroquinone (103). It was tested as a solvent to achieve conditions that were more tolerant of humidity and moisture. Analogous sweep shapes were observed in both the IL and DMF (N,N-dimethylformamide), but the reversibility of the reaction in DMF was better (103). The electrochemical oxidation of ammonia was also studied in both propylene carbonate and in three ILs in studies aimed at developing an ammonia gas sensor (104). Analytical detection of ammonia was highest in propylene carbonate through the indirect oxidation of ammonia with hydroquinone. Direct oxidation of ammonia was better in the ILs than in the propylene carbonate, but analytical detection in the ILs remained an order of magnitude higher than in the indirect hydroquinone method in propylene carbonate. The better detection limits in propylene carbonate were thought to be attributable to the high viscosity of the ILs (104). The use of ILs in various sensors is reviewed in Section 3.7, below.

Electrochemical methods have been employed to recover metals from nuclear wastewater and other effluents (105, 106). Tsuda and coworkers (105) studied the feasibility of carrying out cesium recovery from IL-based extractants by electrochemical reduction in the presence of water and air, which represented actual conditions. Compared to dry ILs, the presence of water reduced the effectiveness of the electrochemical reduction by almost a third, and the presence of oxygen either greatly hindered or completely prevented the recovery of the cesium. By sparging the IL extractant with nitrogen, both the water content and the oxygen content were reduced to levels that permitted the recovery of cesium by electrochemical reduction. Electrochemical recovery of other nuclear metallic contaminants from tissue paper was also attempted (106). BMIM Cl dissolved a maximum of 15–17% by weight of the contaminated tissue paper containing uranium (VI) nitrate and palladium (II) chloride. The paper-IL mixture was extremely viscous, and electrodeposition had to be carried out at elevated temperatures for both the palladium and the uranium. The addition of DMSO (dimethyl sulfoxide) resulted in only a slight increase in the recovery amount of palladium, whereas it prevented the electrodeposition of uranium as uranium oxide (106).

The micro liquid-liquid interface created between a hydrophobic IL and an aqueous phase at a capillary tip has been studied using voltammetry (107). A very small amount of current circumvents the high solution resistance created by the viscous IL. Ion transfer across the liquid-liquid interface can be studied using this method, which may have implications for extraction and other applications (107).

Electrochemical processes of various analytes also have been carried out in ILs. The electrochemical properties of sulfur dioxide (108) and hydrogen sulfide (109) were studied with traditional electrochemical methods such as cyclic voltammetry and chronoamperometry. These studies are representative of the many papers in the literature that characterized various analytes using ILs, rather than traditional choices, as solvents.

3.7. Ionic Liquid–Based Sensors and Other Instrumentation

Early sensors involving ILs tended to be electrochemically based (110–112). A supported membrane electrode made by filling the pores of polyethylene with 1-ethyl-3-methylimidazolium BF_4 was developed for use as an oxygen sensor (110). Via potential-step chronoamperometry, a change in oxygen concentration was detected. However, the IL was prone to absorbing water, which could render the electrode responses irreproducible in humid environments. A hydrogen peroxide biosensor was created by mixing BMIM BF_4 with tetraethyl orthosilicate to create a sol-gel doped with horseradish peroxidase and ferrocene, then covering a glassy carbon electrode with the sol-gel mixture (111). This IL sol-gel electrode gave faster response times than did the silica sol-gel electrode alone, and it exhibited high affinity for the hydrogen peroxide. A membrane-free sensor based on a two–electrode cell design also was proposed (112). Several ILs were examined to create a film over the working electrode, which eliminated the need for the membrane. Because of the ILs' high viscosity, diffusion of oxygen through the ILs was on par with oxygen diffusion through similarly constructed sensors with gas-permeable membranes. However, the response time of the IL was slower than the response times for most of the membrane electrodes (112). Application of such a sensor would be limited to conditions in which the electrolyte solutions of the membrane sensors volatilize.

More recent sensors have utilized various methods for detection of analyte molecules. Incorporating ILs into the sensor films of quartz crystal microbalances has been a popular method for creating sensors (113–115). One sensing film was synthesized by partially filling the nanopores from anodized alumina with the NTF_2 salt of an imidazolium- or ammonium-based IL. The nanopores prevented problems related to viscoelasticity and dewetting from interfering with the changes in response caused by the adsorption of gas vapor (113). Six organic solvents (THF, cyclohexane, i-octane, methanol, toluene, and acetonitrile) were used as test analytes. In another approach, a gas sensor array was made by adding 1-ethyl-3-methyl imidazolium BF_4 in varying concentrations to a plasma-polymerized film of D-phenylalanine (114). Methanol, ethanol, *n*-propanol, and *n*-butanol were used to test the discrimination ability of the sensor array. Adding the IL changed the interactions (i.e., lipophilicity, polarizability, and hydrogen bonding) between the polymer film and the alcohols, inducing variances large enough to discriminate between the alcohols.

Another gas sensor array was developed using seven ILs as the sensing thin films (without any other support) on quartz crystal microbalances (115). To maximize solvent-analyte interactions, the seven ILs were chosen from the imidazolium, phosphonium, and ammonium cation families and had various anions to create a diverse array. Ethanol, heptane, benzene, and dichloromethane were used as test analytes. Great linearity was achieved for concentration curves for ethanol, heptanes, and benzene, but the high volatility of dichloromethane created nonlinear deviations at high temperatures (115). Linear discriminant analysis was used to analyze the sensing patterns and identify the analytes. There was only one failure in 28 samples of unknown concentrations.

ILs have also been used for the development of optical sensors. Because BMIM Cl dissolves both cellulose and the metal complexant 1-(2-pyridylazo)-2-naphthol, these two compounds were homogeneously combined to prepare a mercury (II) sensor (116). The IL–1-(2-pyridylazo)-2-naphthol–cellulose mixture was spread to create a thin film, then the IL was rinsed away. The resulting film was used for determining the presence of mercury (II), but only in the absence of other metals such as zinc and copper. The films were used up to five times after stripping the sensor with acetic acid. However, noticeable dye leaching was observed with each stripping process. Using more selective complexing agents and chemically bonding the agent to the cellulose must be achieved to improve the performance of this sensor (116). Through use of complexed ruthenium–doped BMIM BF_4 or Br, a fluorescence-based oxygen-sensitive solution was developed for potential use in an optical oxygen sensor (117). Nonadecafluorodecanoic acid was added to enhance the amount of dissolved oxygen in the IL. With the perfluorochemical additive, the authors obtained high oxygen sensitivity, complete linearity from 0% to 100% oxygen, and high stability for the sensing solution.

Microfluidic devices designed with parallel cochannels for temperature control have employed BMIM PF_6 and NTF_2 as heat transfer liquids (118). The temperature of the ionic liquids is increased through the use of Joule heating from the supplied ac current. ILs were chosen because aqueous solutions of potassium chloride reached the boiling point too easily, causing arcing and damage to the chip. This approach to temperature control allowed the authors to maintain a steady temperature ($\pm 0.2°$ C) for long periods of time (118).

In a very interesting application, two IL-based liquid-in-glass thermometer prototypes were constructed (119). Tris(2-hydroxyethyl)methylammonium methylsulfate was the IL used to create a thermometer for standard applications, and trihexyl(tetradecyl)phosphonium NTF_2 was used as the filling liquid for a specialty thermometer covering a very wide temperature range. Because both ILs are colorless, an intense red color was added by doping the ILs with trihexyl(tetradecyl)phosphonium Direct Red 81 ionic solid. Even at 1% by weight (which gives a color that is extremely intense), the addition of the dye had minimal impact on the change in volume of the ILs (119). Pyrex tubes with an inner diameter of 1.2 mm were used as the glass portion of the thermometer. The freezing and boiling points of water were the two fixed points on the degree scale. Both proof-of-concept thermometers gave good temperature agreement with the boiling points of other liquids, a very promising result given the primitive construction of the thermometer.

3.8. Other Analytical Applications

There are other analytical applications in which ILs have been dissolved in various solvents. Because the dissolved salts do not maintain the same unique physical properties as undiluted ILs, we do not discuss these applications in this review. However, some of these applications, particularly in HPLC and capillary electrophoresis, have been described elsewhere (120, 121). Dissolved multifunctional ILs have also been utilized in conjunction with electrospray ionization MS for the ultrasensitive analysis of anions in the positive-ion mode. The method was first developed for the MS determination of perchlorate (122). In this method, the dicationic-based reagents paired with perchlorate ions to give ion complexes of an overall positive charge. This allowed determination of perchlorate via the positive-ion mode, where arcing is less problematic; this method also reduced interference from the hydrogen sulfate ion, which has almost the same mass as perchlorate. This method was then used to determine the amounts of perchlorate, iodide, and thiocyanate in milk (123), human urine (124), and seaweed and seawater (125). The method was examined for the determination of a number of other ions (126), and other dicationic reagents were explored for their ability to provide sensitive detection (127). Tricationic IL reagents were also developed for the analysis of divalent anions (128). Even lower detection limits were obtained using tandem MS in conjunction with the di- and tricationic reagents (126–128). ILs dispersed in aqueous solvents have also been applied as extraction solvents (129–131). These are just a few examples of the applications in which ILs can be used as dissolved salts to solve analytical problems.

Some studies on the fundamental properties of ILs have also been published recently (132, 133). A study on the electrowetting of ILs was conducted to determine the characteristics of ILs that may make them useful for application as electrowetting components in dielectric-based microfluidic devices (132). **Figure 4** illustrates the basic process of electrowetting by an IL on a

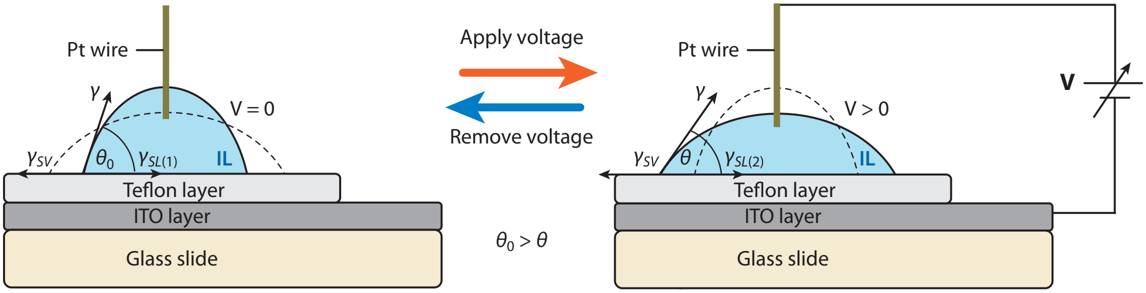

Figure 4

A schematic showing electrowetting on dielectric for an ionic liquid (IL). The contact angle (θ) of the drop decreases with increasing voltage (V), and it returns to its original angle when the voltage is off. γ, γ_{SV}, and γ_{SL} are the surface tensions associated with the liquid/vapor, solid/vapor, and solid/liquid interfaces, respectively. ILs can sometimes show different contact angles at negative versus positive voltages, which makes them different from other liquids. Compared to most common electrowetting solvents, ILs are less susceptible to evaporation, fouling, and thermal degradation. Abbreviation: ITO, indium tin oxide.

dielectric surface. The figure shows that ILs may be useful in microfluidic devices, among other applications (132). GC was used to find the enthalpies and entropies of the transfer of a homologous series of *n*-alkanes (133). This theoretical study allowed for the estimation of dielectric constants and interionic distances of the ILs. On the basis of their findings, the authors proposed a basic solvation model for the alkanes (133).

4. CONCLUSIONS

ILs are versatile, tunable materials that can be used to great advantage in chemical analysis. Their negligible vapor pressure; high thermal, air, and water stability; variable solvent interactions; and synthetic tunability allow them to be used in many different applications. Some applications of ILs, such as liquid-liquid extraction and GC, are more mature than others (e.g., sensors). Simple monocationic ILs and some MALDI matrices are already commercially available. In both cases, the cost of the ILs themselves is essentially negligible compared to labor costs for analysis. However, IL solvents remain more expensive than traditional solvents. Multicationic ILs are starting to become commercially available in finished products (such as GC stationary phases). However, the use of ILs in all areas of analytical chemistry is relatively new, and opportunities for discovery and optimization abound. These new discoveries are impossible to predict, but they will likely require an increased understanding in how IL structure determines the properties of the ILs. ILs will probably play an increasingly important role in analytical chemistry in the foreseeable future.

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LITERATURE CITED

1. Wilkes JS, Zaworotko MJ. 1992. Air and water stable 1-ethyl-3-methylimidazolium based ionic liquids. *J. Chem. Soc. Chem. Commun.* 1992:965–67
2. Walden P. 1914. Molecular weights and electrical conductivity of several fused salts. *Bull. Acad. Sci. St. Petersburg* 1914:405–22
3. Suarez PAZ, Dullius JEL, Einloft S, de Souza RF, Dupont J. 1995. The use of new ionic liquids in two-phase catalytic hydrogenation reaction by rhodium complexes. *Polyhedron* 15:1217–19
4. Dullius JEL, Suarez PAZ, Einloft S, de Souza RF, Dupont J. 1998. Selective catalytic hydrodimerization of 1,3-butadiene by palladium compounds dissolved in ionic liquids. *Organometallics* 17:815–19
5. Silva SM, Suarez PAZ, de Souza RF, Dupont J. 1998. Selective linear dimerization of 1,3-butadiene by palladium compounds immobilized into 1-n-butyl-3-methyl imidzaolium ionic liquids. *Polymer Bull.* 40:401–5
6. Boxwell CJ, Dyson PJ, Ellis DJ, Welton T. 2002. A highly selective arene hydrogenation catalyst that operates in ionic liquid. *J. Am. Chem. Soc.* 124:9334–35
7. Ellis DJ, Dyson PJ, Parker DG, Welton T. 1999. Hydogenation of non-activated alkenes catalysed by water-soluble ruthenium carbonyl clusters using a biphasic protocol. *J. Mol. Catal. A* 150:71–75
8. Cull SG, Holbrey JD, Vargas-Mora V, Seddon KR, Lye GJ. 2000. Room-temperature ionic liquids as replacements for organic solvents in multiphase bioprocess operations. *Biotechnol. Bioeng.* 69:227–33

9. Lau RM, van Rantwiik F, Seddon KR, Sheldon RA. 2000. Lipase-catalyzed reactions in ionic liquids. *Org. Lett.* 2:4189–91
10. Davis JH Jr, Forrester KJ. 1999. Thiazolium-ion based organic ionic liquids (OILs). Novel OILs which promote the benzoin condensation. *Tetrahedron Lett.* 40:1621–22
11. Fuller J, Breda AC, Carlin RT. 1997. Ionic liquid–polymer gel electrolytes. *J. Electrochem. Soc.* 4:L67–L70
12. Fuller J, Breda AC, Carlin RT. 1998. Ionic liquid–polymer gel electrolytes from hydrophilic and hydrophobic ionic liquids. *J. Electroanal. Chem.* 459:29–34
13. Huddleston JG, Willauer HD, Swatloski RP, Visser AE, Rogers RD. 1998. Room temperature ionic liquids as novel media for "clean" liquid-liquid extraction. *Chem. Commun.* 1998:1765–66
14. Dai S, Ju YH, Barnes CE. 1999. Solvent extraction of strontium nitrate by a crown either using room-temperature ionic liquids. *J. Chem Soc. Dalton Trans.* 1999:1201–2
15. Visser AE, Swatloski RP, Griffin ST, Hartman DH, Rogers RD. 2001. Liquid/liquid extraction of metal ions in room temperature ionic liquids. *Sep. Sci. Technol.* 36:785–804
16. Armstrong DW, He L, Liu Y-S. 1999. Examination of ionic liquids and their interaction with molecules, when used as stationary phase in gas chromatography. *Anal. Chem.* 71:3873–76
17. Anderson JL, Ding J, Welton T, Armstrong DW. 2002. Characterizing ionic liquids on the basis of multiple salvation interactions. *J. Am. Chem. Soc.* 124:14247–54
18. Armstrong DW, Zhang L-K, He L, Gross ML. 2001. Ionic liquids as matrixes for matrix-assisted laser desorption/ionization mass spectrometry. *Anal. Chem.* 73:3679–86
19. Han X, Armstrong DW. 2007. Ionic liquids in separations. *Acc. Chem. Res.* 40:1079–86
20. Anderson JL, Ding R, Ellern A, Armstrong DW. 2005. Structure and properties of high stability germinal dicationic ionic liquids. *J. Am. Chem. Soc.* 127:593–604
21. Anderson JL, Armstrong DW. 2005. Immobilized ionic liquids as high-selectivity/high-temperature/high-stability gas chromatography stationary phases. *Anal. Chem.* 77:6453–62
22. Payagala T, Huang J, Breitbach ZS, Sharma PS, Armstrong DW. 2007. Unsymmetrical dicationic ionic liquids: manipulation of physicochemical properties using specific structural architectures. *Chem. Mater.* 19:5848–50
23. Sharma PS, Payagala T, Wanigaskara E, Wijertne AB, Huang J, Armstrong DW. 2008. Trigonal tricationic ionic liquids: molecular engineering of trications to control physiochemical properties. *Chem. Mater.* 20:4182–84
24. Berthod A, He L, Armstrong DW. 2001. Ionic liquids as stationary phase solvents for methylated cyclodextrins in gas chromatography. *Chromatographia* 53:63–68
25. Ding J, Welton T, Armstrong DW. 2004. Chiral ionic liquids as stationary phase in gas chromatography. *Anal. Chem.* 76:6819–22
26. Huang K, Han X, Zhang X, Armstrong DW. 2007. PEG-linked germinal dicationic ionic liquids as selective, high-stability gas chromatographic stationary phases. *Anal. Bioanal. Chem.* 289:2265–75
27. Seeley JV, Seeley SK, Libby EK, Breitbach ZS, Armstrong DW. 2008. Comprehensive two-dimensional gas chromatography using a high-temperature phosphonium ionic liquid column. *Anal. Bioanal. Chem.* 390:323–32
28. Reid VR, Crank JA, Armstrong DW, Synovec RE. 2008. Characterization and utilization of a novel triflate ionic liquid stationary phase for use in comprehensive two-dimensional gas chromatography. *J. Sep. Sci.* 31:3429–36
29. Breitbach ZS, Armstrong DW. 2008. Characterization of phosphonium ionic liquids through a linear solvation energy relationship and their use as GLC stationary phases. *Anal. Bioanal. Chem.* 390:1605–17
30. Baltazar QQ, Leininger SK, Anderson JL. 2008. Binary ionic liquid mixtures as gas chromatography stationary phases for improving the separation selectivity of alcohols and aromatic compounds. *J. Chromatogr. A* 1182:119–27
31. Tran CD, Challa S. 2008. Fullerene-impregnated ionic liquid stationary phases for gas chromatography. *Analyst* 133:455–64
32. Zaijuin L, Qiping P, Haixia S. 2007. Use of a novel medium, the ionic liquid 1-butyl-3-trimethylsilylimidazolium hexafluorophosphate, for liquid-liquid extraction of lead in water and its determination by graphite furnace atomic absorption spectrometry. *J. AOAC Int.* 90:1191–96

33. Sun X, Wu D, Chen J, Li DQ. 2007. Separation of scandium (III) from lanthanides (III) with room temperature ionic liquid based extraction containing Cyanex 925. *J. Chem. Technol. Biotechnol.* 82:267–72
34. Zuo Y, Liu Y, Chen J, Li DQ. 2008. The separation of Cerium (IV) from nitric acid solutions containing thorium (IV) and Lanthanides (III) using pure [C_8mim]PF_6 as extracting phase. *Ind. Eng.Chem. Res.* 47:2349–55
35. Li M, Wang T, Pham PJ, Pittman CU Jr, Li T. 2008. Liquid phase extraction and separation of noble organometallic catalysts by functionalized ionic liquids. *Sep. Sci. Technol.* 43:828–41
36. Zhang DL, Deng YF, Li CB, Chen J. 2007. Separation of ethyl acetate-ethanol azeotropic mixture using hydrophilic ionic liquids. *Ind. Eng. Chem. Res.* 47:1995–2001
37. Pei YC, Wang JJ, Xuan XP, Fan J, Fan M. 2007. Factors affecting ionic liquids based removal of anionic dyes from water. *Environ. Sci. Technol.* 41:5090–95
38. Martak J, Schlosser S. 2007. Extraction of lactic acid by phosphonium ionic liquids. *Sep. Purif. Technol.* 57:483–94
39. Lateef H, Grimes SM, Morton R, Mehta L. 2008. Extraction of components of composite materials: ionic liquids in the extraction of flame retardants from plastics. *J. Chem. Technol. Biotechnol.* 83:541–45
40. Fan J, Fan Y, Pei Y, Wu K, Wang J, Fan M. 2008. Solvent extraction of selected endocrine-disrupting phenols using ionic liquids. *Sep. Purif. Technol.* 61:324–31
41. Arce AA, Earle MJ, Katdare SP, Rodriguez H, Seddon KR. 2008. Application of mutually immiscible ionic liquds to the separation of aromatic and aliphatic hydrocarbons by liquid extraction: a preliminary approach. *J. Phys. Chem. Chem. Phys.* 10:2538–42
42. Zhu J-Q, Chen J, Li C-Y, Fei W-Y. 2007. Centrifugal extraction for separation of ethylbenzene and octane using 1-butyl-3-methylimidazolium hexafluorophosphate ionic liqud as extractant. *Sep. Purif. Technol.* 56:237–40
43. Nie Y, Li C, Sun A, Meng H, Wang Z. 2006. Extractive desulfurization of gasoline using imidazolium-based phosphoric ionic liquids. *Energy Fuels* 20:2083–87
44. Holbrey JD, Lopez-Martin I, Rothenberg G, Seddon KR, Silvero G, Zheng X. 2008. Desulfurization of oils using ionic liquids: selection of cationic and anionic components to enhance extraction efficiency. *Green Chem.* 10:87–92
45. Du F-Y, Xiao X-H, Li G-K. 2007. Application of ionic liquids in the microwave-assisted extraction of *trans*-reveratrol from *Rizma Polygoni Cuspidati*. *J. Chromatogr. A* 1140:56–62
46. Matsumoto M, Ohtani T, Kondo K. 2007. Comparison of solvent extraction and supported liqud membrane permeation using an ionic liquid for concentrating penicillin G. *J. Membr. Sci.* 289:92–96
47. Wang J-H, Cheng DH, Chen X-W, Du Z, Fang Z-L. 2007. Direct extraction of double-stranded DNA into ionic liquid 1-butyl-3-methylimidazolium hexafluorophosphate and its quantification. *Anal. Chem.* 79:620–25
48. Cheng D-H, Chen X-W, Shu Y, Wang J-H. 2008. Selective extraction/isolation of hemoglobin with ionic liquid 1-butyl-3-trimethylsilylimidazolium hexafluorophosphate (BtmsimPF_6). *Talanta* 75:1270–78
49. Dreyer S, Kragl U. 2008. Ionic liquids for aqueous two-phase extraction and stabilization of enzymes. *Biotechnol. Bioeng.* 99:1416–24
50. Ye C, Zhou Q, Wang X, Xiao J. 2007. Determination of phenols in environmental water samples by ionic liquid–based headspace liquid-phase microextraction coupled with high-performance liquid chromatography. *J. Sep. Sci.* 30:42–47
51. Vidal L, Psillakis E, Domini CE, Grane N, Marken F, Canals A. 2007. An ionic liquid as a solvent for headspace single drop microextraction of chlorobenzenes from water samples. *Anal. Chim. Acta* 584:189–95
52. Aguilera-Herrador E, Lucena R, Cardenas S, Valcarcel M. 2008. Direct coupling of ionic liquid based single-drop microextraction and GC/MS. *Anal. Chem.* 80:793–800
53. Yang P, Lau C, Liu X, Lu J. 2007. Direct solid-support sample loading for fast cataluminescence determination of acetone in human plasma. *Anal. Chem.* 79:8476–85
54. Carda-Broch S, Berthod A, Armstrong DW. 2003. Ionic matrices for matrix-assisted laser desorption/ionization time-of-flight detection of DNA oligomers. *Rapid Commun. Mass Spectrom.* 17:553–60

55. Zabet-Moghaddam M, Heinzle E, Tholey A. 2004. Qualitative and quantitative analysis of low molecular weight compounds by ultraviolet matrix-assisted laser desorption/ionization mass spectrometry using ionic liquid matrices. *Rapid Commun. Mass Spectrom.* 18:141–48
56. Li Y, Gross ML. 2004. Ionic-liquid matrices for quantitative analysis by MALDI-TOF mass spectrometry. *J. Am. Soc. Mass Spectrom.* 15:1833–37
57. Zabet-Moghaddam M, Kruger R, Heinzle E, Tholey A. 2004. Matrix-assisted laser desorption/ionization mass spectrometry for the characterization of ionic liquids and the analysis of amino acids, peptides, and proteins in ionic liquids. *J. Mass Spectrom.* 39:1494–505
58. Tholey A. 2006. Ionic liquid matrices with phosphoric acid as matrix additive for the facilitated analysis of phosphopeptides by matrix-assisted laser desorption/ionization mass spectrometry. *Rapid Commun. Mass Spectrom.* 20:1761–68
59. Jones JJ, Mariccor S, Batoy AB, Wilkins CL, Liyanage R, Lay JO Jr. 2005. Ionic liquid matrix-induced metastable decay of peptides and oligonucleotides and stabilization of phospholipids in MALDI-FTMS analyses. *J. Am. Soc. Mass Spectrom.* 16:2000–8
60. Zabet-Moghaddam M, Heinzle E, Lasaosa M, Tholey A. 2006. Pyridinium-based ionic liquid matrices can improve the identification of proteins by peptide mass-fingerprint analysis with matrix-assisted laser desorption/ionization mass spectrometry. *Anal. Bioanal. Chem.* 384:215–24
61. Tholey A, Zabet-Moghaddam M, Heinzle E. 2006. Quantification of peptides for the monitoring of protease-catalyzed reactions by matrix-assisted laser desorption/ionization mass spectrometry using ionic liquid matrixes. *Anal. Chem.* 78:291–97
62. Vaidyanathan S, Gaskell S, Goodacre R. 2006. Matrix-suppressed laser desorption/ionization mass spectrometry and its suitability for metabolome analyses. *Rapid Commun. Mass Spectrom.* 20:1192–98
63. Laremore TN, Murugesan S, Park T-J, Avci FY, Zagoreski DV, Linhart RJ. 2006. Matrix-assisted laser desorption/ionization mass spectrometric analysis of uncomplexed highly sulfated oligosaccharides using ionic liquid matrices. *Anal. Chem.* 78:1774–79
64. Laremore TN, Zhang F, Linhardt RJ. 2007. Ionic liquid matrix for direct UV-MALDI-TOF-MS analysis of dermatan sulfate and chondroitin sulfate oligosaccharides. *Anal. Chem.* 79:1604–10
65. Laremore TN, Linhardt RJ. 2007. Improved matrix-assisted laser desorption/ionization mass spectrometric detection of glycoaminoglycan disaccharides as cesium salts. *Rapid Commun. Mass Spectrom.* 21:1315–20
66. Fukuyama Y, Nakaya S, Yamazaki Y, Tanaka K. 2008. Ionic liquid matrixes optimized for MALDI-MS of sulfated/sialylated/neutral oligosaccharides and glycopeptides. *Anal. Chem.* 80:2171–79
67. Tissot B, Gasiunas N, Powell AK, Ahmed Y, Zhi Z, et al. 2007. Towards GAG glycomics: analysis of highly sulfated heparins by MALDI-TOF mass spectrometry. *Glycobiology* 17:972–82
68. Darsow KH, Lange HA, Resch M, Walter C, Buchholz R. 2007. Analysis of a chlorosulfolipid from *Ochromonas danica* by matrix-assisted laser desorption/ionization quadrupole ion trap time-of-flight mass spectrometry. *Rapid Commun. Mass Spectrom.* 21:2188–94
69. Naumann I, Darsow KH, Walter C, Lange HA, Buchholz R. 2007. Identification of sulfoglycolipids from the alga *Porphyridium purpureum* by matrix-assisted laser desorption/ionization quadrupole ion trap time-of-flight mass spectrometry. *Rapid Commun. Mass Spectrom.* 21:3185–92
70. Karmakar R, Samanta A. 2002. Solvation dynamics of coumarin-153 in a room-temperature ionic liquid. *J. Phys. Chem. A* 106:4447–52
71. Chowdhury PK, Halder M, Sanders L, Calhoun T, Anderson JL, et al. 2004. Dynamic solvation in room-temperature ionic liquids. *J. Phys. Chem B* 108:10245–55
72. Headley LS, Mukherjee P, Anderson JL, Ding R, Halder M, et al. 2006. Dynamic solvation in imidazolium-based ionic liquids on short time scales. *J. Phys. Chem. A* 110:9549–54
73. Mukherjee P, Crank JA, Halder M, Armstrong DW, Petrich JW. 2006. Assessing the roles of the constituents of ionic liquids in dynamic solvation: comparision of an ionic liquid in micellar and bulk form. *J. Phys. Chem. A* 110:10725–30
74. Murkerjee P, Crank JA, Sharma PS, Wijeratne AB, Adhikary R, et al. Dynamic salvation in phosphonium ionic liquids: comparsion of bulk and micellar systems and considerations for the construction of the salvation correlation function, C(t). *J. Phys. Chem B* 112:3390–96

75. Adhikary R, Bose S, Mukherjee P, Thite A, Kraus GA, et al. 2008. Influence of chiral ionic liquids on the excited-state properties of naproxen analogs. *J. Phys. Chem. B* 112:7555–59
76. Bhattacharya B, Samanta A. 2008. Excited-state proton-transfer dynamics of 7-hydroxyquinoline in room temperature ionic liquids. *J. Phys Chem. B* 112:10101–6
77. Paul A, Mandal PK, Samanta A. 2005. How transparent are the imidazolium ionic liquids? A case study with 1-methyl-3-butylimidazolium hexfluorophosphate, [bmim][PF_6]. *Chem. Phys. Lett.* 402:375–79
78. Paul A, Mandal PK, Samanta A. 2005. On the optical properties of the imidazolium ionic liquids. *J. Phys. Chem. B* 109:9148–53
79. Samanta A. 2006. Dynamic stokes shift and excitation wavelength dependent fluorescence of dipolar molecules in room temperature ionic liquids. *J. Phys. Chem. B* 110:13704–16
80. Anderson JL, Armstrong DW, Wei G-T. 2006. Ionic liquids in analytical chemistry. *Anal. Chem.* 78:2892–2902
81. Earle MJ, Gordon CM, Pechkova NV, Seddon KR, Welton T. 2007. Decolorization of ionic liquids for spectroscopy. *Anal. Chem.* 79:758–64
82. Tang F, Wu K, Ding L, Yuan J, Liu Q, et al. 2008. Purification of undiluted ionic liquids from trace-colored impurities for spectroscopy by octadecylsilyl solid-phase extraction. *Sep. Purif. Technol.* 60:245–60
83. Tran CD, Lacerda SHDP. 2002. Determination of binding constants of cyclodextrins in room-temperature ionic liquids by near-infared spectrometry. *Anal. Chem.* 74:5337–41
84. Lau RM, Sorgedrager MJ, Carrea G, van Rantwijk F, Secundo F, Sheldon RA. 2004. Dissolution of *Candida antarctica* lipase B in ionic liquids: effects on structure and activity. *Green Chem.* 6:483–87
85. Baker SN, McCleskey TM, Pandey S, Baker GA. Fluorescence studies of protein thermostability in ionic liquids. *Chem. Commun.* 2004:940–41
86. Smith EF, Garcia IJV, Briggs D, Licence P. 2005. Ionic liquids in vacuo: solution-phase X-ray photoelectron spectroscopy. *Chem. Commun.* 2005:5633–35
87. Giernoth R, Bankman D. 2005. Application of diffusion-ordered spectroscopy (DOSY) as a solvent signal filter for NMR in neat ionic liquids. *J. Eur. Org. Chem.* 2005:4529–32
88. Fort DA, Swatloski RP, Moyna P, Rogers RD, Moyna G. 2006. Use of ionic liquids in the study of fruit ripening by high-resolution 13C NMR spectroscopy: 'green' solvents meet green bananas. *Chem. Commun.* 2006:714–16
89. Xia Z, Zaijun L, Rui Y, Huizhen L. 2006. A novel room temperature ionic liquid extraction spectrophotometric determination of trace germanium in natural water with methylbenzeneazosalicylfluorone. *Anal. Lett.* 39:863–77
90. Nockeman P, Servaes K, van Deun R, van Hecke K, van Meervelt L, et al. 2007. Speciation of uranyl complexes in ionic liquids by optical spectroscopy. *Inorg. Chem.* 46:11335–44
91. Carano M, Bond AM. 2007. Prospects for the application of scanning electrochemical microscopy in ionic liquids. *Aust. J. Chem.* 60:29–34
92. Tsuda T, Hussey CL. 2007. Electrochemical applications of room-temperature ionic liquids. *Electrochem. Soc. Interface* 16:42–49
93. Zhao Y, Gao Y, Zhan D, Liu H, Zhao Q, et al. 2005. Selective detection of dopamine in the presence of ascorbic acid and uric acid by a carbon nanotubes/ionic liquid gel modified electrode. *Talanta* 66:51–57
94. Maleki N, Safavi A, Tajabadi F. 2006. High-performance carbon composite electrode based on an ionic liquid as a binder. *Anal. Chem.* 78:3820–26
95. Safavi A, Maleki N, Moradlou O, Tajabadi F. 2006. Simultaneous determination of dopamine, ascorbic acid, and uric acid using carbon ionic liquid electrode. *Anal. Biochem.* 359:224–29
96. Sun W, Yang M, Jiao K. 2007. Electrocatalytic oxidation of dopamine at an ionic liquid modified carbon paste electrode and its analytical application. *Anal. Bioanal. Chem.* 389:1283–91
97. Zheng J, Zhang Y, Yang P. 2007. An ionic liquid-type carbon paste electrode for electrochemical investigation and determination of calcium dobesilate. *Talanta* 73:920–25
98. Xiao F, Zhao F, Li J, Yan R, Yu J, Zeng B. 2007. Sensitive voltammetric determination of chloramphenicol by using single-walled carbon nanotube–gold nanoparticle–ionic liquid composite film modified glassy carbon electrodes. *Anal. Chim. Acta* 596:79–85
99. Chernyshov DV, Khrenova MG, Pletnev IV, Shvedene NV. 2008. Screen-printed ion-selective electrodes covered with membranes containing ionic liquids. *Medeleev Commun.* 18:88–89

100. Lu X, Hu J, Yao X, Wang Z, Li J. 2006. Composite system based on chitosan and room-temperature ionic liquid: direct electrochemistry and electrocatalysis of hemoglobin. *Biomacromolecules* 7:975–80

101. Yan R, Zhao F, Li J, Xiao F, Fan S, Zeng B. 2007. Direct electrochemistry of horseradish peroxidase in gelatin–hydrophobic ionic liquid gel films. *Electrochim. Acta* 52:7425–31

102. Xu J-S, Zhao G-C. 2008. A third-generation biosensor based on the enzyme-like activity of cytochrome c on a room temperature ionic liquid and gold nanoparticle composite film. *Int. J. Electrochem. Sci.* 3:519–27

103. Giovanelli D, Buzzeo MC, Lawrence NS, Hardacre C, Seddon KR, Compton RG. 2004. Determination of ammonia based on the electro-oxidation of hydroquinone in dimethylforamide or in the room temperatre ionic liquid, 1-ethyl-3-methylimidazolium bis(trifluoromethylsulfonyl)imide. *Talanta* 62:904–11

104. Ji X, Banks CE, Silvester DS, Aldous L, Hardacre C, Compton RG. 2007. Electrochemical ammonia gas sensing in nonaqueous systems: a comparision of propylene carbonate with room temperature ionic liquids. *Electroanalysis* 19:2194–201

105. Tsuda T, Hussey CL, Luo H, Dai S. 2006. Recovery of cesium extracted from simulated tank waste with an ionic liquid: water and oxygen effects. *J. Electrochem. Soc.* 153:D171–76

106. Rao CJ, Venkatesan KA, Nagarjan K, Srinivasan TG, Rao PRV. 2007. Treatment of tissue paper containing radioactive waste and electrochemical recovery of valuables using ionic liquids. *Electrochim. Acta* 53:1911–19

107. Tsujioka N, Imakura S, Nishi N, Kakiuchi T. 2006. Voltametry of ion transfer across the electrochemically polarized micro liquid-liquid interface between water and a room-temperature ionic liquid, tetrahexylammonium *bis*-(trifluoromethylsulfonyl)imide, using a glass capillary micropipette. *Anal. Sci.* 22:667–71

108. Barrosse-Antle LE, Silvester DS, Aldous L, Hardacre C, Compton RG. 2008. Electroreduction of sulfure dioxide in some room-temperature ionic liquids. *J. Phys. Chem. C* 112:3398–404

109. O'Mahony AM, Silvester DS, Aldous L, Hardacre C, Compton RG. 2008. The electrochemical reduction of hydrogen sulfide on platinum in several room temperature ionic liquids. *J. Phys. Chem. C* 112:7725–30

110. Wang R, Okajima T, Kitamura F, Ohsaka T. 2004. A novel amperometric O_2 gas sensor based on supported room-temperature ionic liquid porous polyethylene membrane-coated electrodes. *Electroanalysis* 16:66–72

111. Liu Y, Shi L, Wang M, Li Z, Liu H. 2005. A novel room temperature ionic liquid sol-gel matrix for amperometric biosensor application. *Green Chem.* 7:655–58

112. Buzzeo MC, Hardacre C, Compton RG. 2004. Use of room temperature ionic liquids in gas sensor design. *Anal. Chem.* 76:4583–88

113. Goubaidoulline I, Vidrich G, Johannsmann D. 2005. Organic vapor sensing with ionic liquids entrapped in alumina nanopores on quartz crystal resonators. *Anal. Chem.* 77:615–19

114. Seyama M, Iwaski Y, Tate Y, Sugimoto I. 2006. Room-temperature ionic-liquid-incorporated plasma-deposited thin films for discriminative alcohol-vapor sensing. *Chem. Mater.* 18:2656–62

115. Jin X, Yu L, Garcia D, Ren RX, Zeng X. 2006. Ionic liquid high-temperature gas sensor array. *Anal. Chem.* 78:6980–89

116. Poplin JH, Swatloski RP, Holbrey JD, Spear SK, Metlen A, et al. 2007. Sensor technologies based on a cellulose supported platform. *Chem. Commun.* 2007:2025–27

117. Topal SZ, Ertekin K, Topkaya D, Alp S, Yenigul B. 2008. Emission based oxygen sensing approach with tris(2,2′-bipyridyl)-ruthenium (II) chloride in green chemistry reagents: room temperature ionic liquids. *Microchim. Acta* 161:209–216

118. de Mello AJ, Habgood M, Lancaster NL, Welton T, Wootton RCR. 2004. Precise temperature control in microfluidic devices using Joule heating of ionic liquids. *Lab Chip* 4:417–19

119. Rodriguez H, Williams M, Wilkes JS, Rogers RD. 2008. Ionic liquids for liquid-in-glass thermometers. *Green Chem.* 10:501–7

120. Pandey S. 2006. Analytical applications of ionic liquids: a review of recent efforts. *Anal. Chim. Acta* 556:38–45

121. Berthod A, Ruiz-Angel MJ, Carda-Broch S. 2008. Ionic liquids in separation techniques. *J. Chromatogr. A* 1184:6–18

122. Martinelango PK, Anderson JL, Dasgupta PK, Armstrong DW, Al-Horr RS, Slingsby RW. 2007. Gas-phase ion association provides increased selectivity and sensitivity for measuring perchlorate by mass spectrometry. *Anal. Chem.* 77:4829–35
123. Dyke JV, Kirk AB, Martinelango PK, Dasgupta PK. 2006. Sample processing method for the determination for perchlorate in milk. *Anal. Chim. Acta* 567:73–78
124. Martinelango PK, Gumus G, Dasgupta PK. 2006. Matrix interference free determination of perchlorate in urine by ion association–ion chromatography–mass spectrometry. *Anal. Chim. Acta* 567:79–86
125. Martinelango PK, Tian K, Dasgupta PK. 2006. Perchlorate in seawater: bioconcentration of iodide and perchlorate by various seaweed species. *Anal. Chim. Acta* 567:100–7
126. Soukup-Hein RJ, Remsburg JW, Dasgupta PK, Armstrong DW. 2007. A general, positive ion mode ESI-MS approach for the analysis of singly charged inorganic and organic anions using dicationic reagents. *Anal. Chem.* 79:7346–45
127. Remsburg JW, Soukup-Hein RJ, Crank JA, Breitbach ZS, Payagala T, Armstrong DW. 2008. Evaluation of dicationic reagents for their use in detection of anions using positive ion mode ESI-MS via gas phase ion association. *J. Am. Soc. Mass Spectrom.* 19:261–69
128. Soukup-Hein RJ, Remsburg JW, Breitbach ZS, Sharma PS, Payagala T, et al. 2008. Evaluating the use of tricationic reagents for the detection of doubly charged anions in the positive ion mode by ESI-MS. *Anal. Chem.* 80:2612–16
129. Zhou Q, Bai H, Xie G, Xiao J. 2008. Temperature-controlled ionic liquid dispersive liquid phase microextraction. *J. Chromatogr. A* 1177:43–49
130. Baghdadi M, Shemirani F. 2008. Cold-induced aggregation microextraction: a novel sample preparation technique based on ionic liquids. *Anal. Chim. Acta* 613:56–63
131. Pino V, Anderson JL, Ayala JH, Gonzalez V, Afonso AM. 2008. The ionic liquid 1-hexadecyl-3-methylimidazolium bromide as novel extracting system for polycyclic aromatic hydrocarbons contained in sediments using focused microwave-assisted extraction. *J. Chromatogr. A* 1182:145–52
132. Nanayakkara YS, Moon H, Payagala T, Wijeratne AB, Crank JA, et al. 2008. Fundamental study on electrowetting by traditional and multifunctional ionic liquids: possible use in electrowetting components in dielectric-based microfluidic applications. *Anal. Chem.* 80:7690–98
133. Berthod A, Kozak JJ, Anderson JL, Ding J, Armstrong DW. 2007. Ionic liquid–alkane association in dilute solutions. *Theor. Chem. Acc.* 177:127–35

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