

# Parallel Developments in Aprotic and Protic Ionic Liquids: Physical Chemistry and Applications

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## ABSTRACT

This Account covers research dating from the early 1960s in the field of low-melting molten salts and hydrates, which has recently become popular under the rubric of “ionic liquids”. It covers understanding gained in the principal author’s laboratories (initially in Australia, but mostly in the U.S.A.) from spectroscopic, dynamic, and thermodynamic studies and includes recent applications of this understanding in the fields of energy conversion and bio-preservation. Both protic and aprotic varieties of ionic liquids are included, but recent studies have focused on the protic class because of the special applications made possible by the highly variable proton activities available in these liquids.

In this Account, we take a broad view of ionic liquids (using the term in its current sense of liquids comprised of ions and melting below 100 °C). We include, along with the general cases of organic cation systems, liquids in which common inorganic cations (like  $\text{Mg}^{2+}$  and  $\text{Ca}^{2+}$ ) strongly bind a hydration or solvation shell and then behave like large cation systems and melt below 100 °C.

Austen Angell obtained his bachelor’s and Masters’ degrees from the University of Melbourne, Australia, and his Ph.D. from Imperial College of Science, University of London. He is currently Regents’ Professor of Chemistry at Arizona State University, Tempe, AZ, having moved to ASU in 1989 after 23 years at Purdue University. His first work in the sub-100 °C ionic liquids field was done at Melbourne University. He has since worked on a wide range of problems related to liquids and glasses, including electrolytes for lithium batteries and most recently ionic liquids for fuel cells and protein folding/preservation studies. He has been especially intrigued by the problem of supercooled water and related liquids in which the phenomenon of polyamorphism is encountered. Awards for research have included the MRS Turnbull Lecture (2006), ACS Joel Henry Hildebrand award for the study of liquids (2004), the Neville Mott award of the *Journal of Non-Crystalline Solids* (1992), and the Morey award of the American Ceramic Society (1990). He has also been the recipient of an Alexander von Humboldt senior research award, and a Fulbright award. He has served on the editorial boards of a number of major journals including the *Journal of Physical Chemistry*, the *Journal of Chemical Physics*, and *Annual Review of Physical Chemistry*. In 1998, he was honored with a special issue of the *Journal of Physical Chemistry*.

Nolene Byrne received her B.E.(Mat)(Hons) in 2003 then a Ph.D. in 2006 from Monash University, Australia, in the area of improved electrolytes for lithium metal batteries. She is currently in a postdoctoral role at Arizona State University, Tempe, AZ. Her research involves the use of ionic liquids as media for improved biopreservation and electrochemical devices.

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We will try to organize a wide variety of measurements on low-melting ionic liquid systems into a coherent body of knowledge that is relevant to the ionic liquid field as it is currently developing.

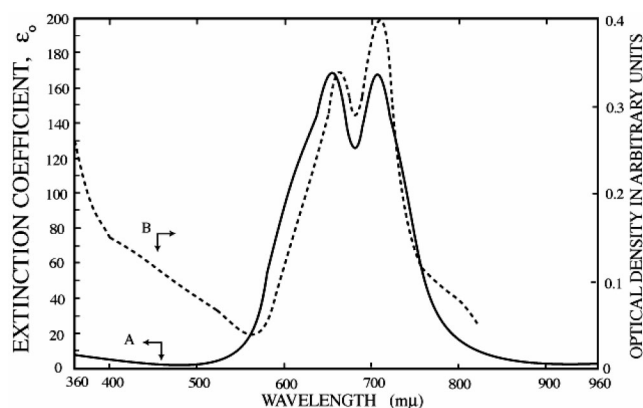
Under the expanded concept of the field, ionic liquid studies commenced in the Angell laboratory in 1962 with a study of the transport properties of the hydrates of  $\text{Mg}(\text{NO}_3)_2$  and  $\text{Ca}(\text{NO}_3)_2$ . These were described as melts of “large weak-field cations”<sup>1</sup> and their properties correlated with those of normal anhydrous molten salts via their effective cation radii, the sum of the normal radius plus one water molecule diameter. This notion was followed in 1966 with a full study under the title “A new class of molten salt mixtures” in which the hydrated cations were treated as independent cation species. The large cations mixed ideally with ordinary inorganic cations such as  $\text{Na}^+$  and  $\text{K}^+$ , to give solutions in which such cohesion indicators as the glass transition temperature,  $T_g$ , changed linearly with composition. The concept proved quite fruitful, and a field (“hydrate melts” or “solvate melts”) developed in its wake in which asymmetric anions like  $\text{SCN}^-$  and  $\text{NO}_2^-$  were used with solvated cations to create a very wide range of systems that were liquid at room temperature, while remaining ionic in their general properties.

The validity of the molten salt analogy was given additional conviction by the observation that transition metal ions such as Ni(II) and Co(II) could be found in the complex anion states  $\text{NiCl}_4^{2-}$  and  $\text{CoCl}_4^{2-}$  when added to the “hydrate melt” chlorides.<sup>2</sup>

Of special interest here was the observation<sup>3</sup> of extreme downfield NMR proton chemical shifts of hydrate protons when the hydrated cation was  $\text{Al}^{3+}$ . These lay much further downfield than did the protons in strong mineral acids at the same concentration, leading to the design of solutions of highly acidic character from salts that would usually be considered neutral. Indeed it was shown in ref 3 that platinum can be dissolved much more rapidly in a hot ionic liquid formed from  $\text{AlCl}_3 \cdot (\text{H}_2\text{O})_6 + \text{Al}(\text{NO}_3)_3 \cdot (\text{H}_2\text{O})_{12}$  than in boiling aqua regia. This scenario of variable proton activity in solvent-free, nominally neutral ionic liquids will be revisited in the context of protic ionic liquids at the end of this Account.

Most of the interest in the field lies with room temperature liquids in which the cations are indeed of organic origin, and the story takes up naturally with these because of the manner in which the organic cation ionic liquids can be put to use in providing excellent complex anions for spectroscopic study. A good example is that shown in Figure 1 from the work of Gruen and McBeth<sup>4</sup> in whose laboratory one of us first encountered melts such as pyridinium chloride,  $\text{PyHCl}$ , and first used them in the (unpublished) study of Ni(II) complexes in low-melting systems such as  $\text{PyHCl-ZnCl}_2$ . We were impressed by the sharp changes in electronic spectra of Ni(II), reflecting

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**FIGURE 1.** Electronic (visible) spectrum of  $\text{Ni}^{2+}$  dissolved at  $10^{-4}$  mol/L in pyridinium chloride. Reprinted with permission from ref 4.

distinct and different structures, which were produced by small changes in solution composition.

The knowledge that these liquids could be used for molten salt studies at low temperatures quickly became useful when the new science of high-pressure physical chemistry using the diamond anvil high-pressure cell (DAC) burst on the scene. Little was known at that time of the effect of pressure on ion coordination.

The DAC was then only available for room-temperature studies, and a room-temperature molten chloride for the application of this newly invented high-pressure technique was needed. Even these days, ambient-temperature ionic liquid chlorides are not common, but Angell and Abke-meier<sup>5</sup> found that ethanolaminium chloride could serve as the ambient-temperature noncrystallizing component that induced ambient-temperature stability on mixtures with ethylammonium chloride. This chloride ion melt proved ideally suited for the study of transition metal ion spectra up to 3.5 GPa, pressure being calibrated in the range to 0.3 GPa by observing the glass transition spectroscopically and relating it to independently determined  $T_g$  values from high-pressure differential thermal analysis (DTA) studies.

$\text{Ni(II)}$  electronic spectra of good quality, shown in Figure 2, were obtained, and the conversion from  $\text{NiCl}_4^{2-}$  at ambient pressure to  $\text{NiCl}_6^{4-}$  at higher pressures was observed. Impressively simple, the change with pressure of the equilibrium constant

$$d \ln K_{\text{eq}} / dP = -\Delta V / RT \quad (1)$$

for the process  $\text{NiCl}_4^{2-} + 2\text{Cl}^- \rightarrow \text{NiCl}_6^{4-}$ , yielded a  $\Delta V$  within 10% of the volume of 2 mol of chloride ion.<sup>5</sup>

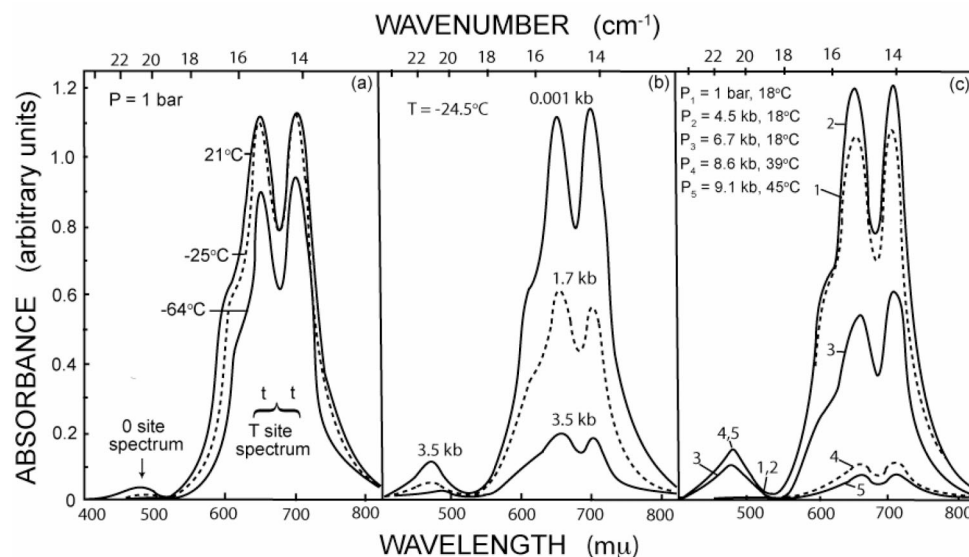
## Role of Complex Anions in the Development of Ambient Temperature Air- and Water-Stable Ionic Liquids

While the latter study of transition metal spectra used organic cation ionic liquids as a tool for the study of complex ions, Hodge and co-workers<sup>6</sup> used complex anions in organic cation salts for the study of ionic liquid properties, indeed properties that have found recent applications.

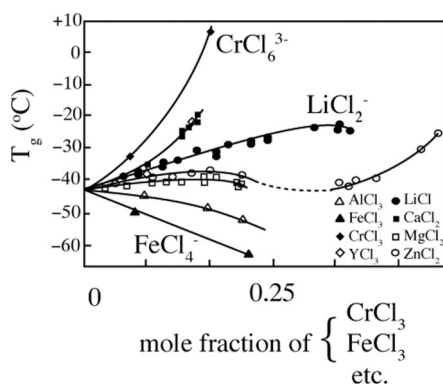
The dramatically different effects of complexation on the liquid viscosity are well illustrated by a 1976 study<sup>6</sup> that used the lower-melting  $\alpha$ -methyl derivative of pyridinium chloride as the source of the Lewis base chloride. Data seen in Figure 3 show that the cohesive energy of an ionic liquid is lowered most strongly when chloride ions are complexed by  $\text{FeCl}_3$  to produce the large singly charged  $\text{FeCl}_4^-$  anion. This observation leads to the prediction that, among ionic liquids of a given cation, the tetrachloroferrate salt should be the most fluid and also most conductive, even more so than the well-studied ionic liquids containing  $\text{AlCl}_4^-$  anions.<sup>7</sup> The veracity of this expectation is demonstrated in Figure 4 for salts of the butylmethylimidazolium cation taken from a very recent study by Xu et al.<sup>8</sup> For the 25 °C conductivity, the tetrachloroferrate is half an order of magnitude above any others in the group. The increase of ionic mobility by complexation seen here is no different in principle from the use of  $\text{BeF}_2$  additions to alkali fluoride melts utilized in the molten salt reactor technology that had provided much of the driving force, and also funding, for molten salt studies in the 1950–1970 period. There, the addition of 1 mol of  $\text{BeF}_2$  replaced two high charge intensity fluoride anions with a doubly charged anion of much larger dimensions, for a net decrease in cohesion.

The fluorinated anion salts (containing  $\text{BF}_4^-$  and  $\text{PF}_6^-$ ) that are most frequently cited in connection to practical applications of the ambient-temperature ionic liquids, are to be understood in the same terms (unfortunately, the tetrachloroferrate anion is slowly hydrolyzed by water, and the applications of ambient temperature ionic liquids generally require the presence of water-stable anions). Fluorinated species in addition to being water-stable have the advantage of being unpolarizable and so minimize the effect of van der Waals contributions to the liquid cohesion. The importance of this characteristic of fluorinated anions to ionic liquid properties was first emphasized in a 1983 study of binary solutions of ionic liquid halides with lithium halides by Cooper.<sup>9</sup> There it was predicted that the replacement of iodide anions by the equivalent number of  $\text{BF}_4^-$  anions would lead to an increase of ambient temperature conductivity, which was then proven true (unfortunately only in a “note added in proof” in ref 9) by some 2 orders of magnitude.<sup>9,10</sup> Cooper’s further extensive syntheses and measurements on viscosity and conductivity of a family of tetraalkylammonium tetrafluoroborate salts remained unpublished (for over 2 decades) until 2003.<sup>8</sup>

In the meantime, Cooper and O’Sullivan<sup>11</sup> reported, in 1992, the first systematic study of ambient-temperature water-stable ionic liquids, using triflate and related anions combined with imidazolium type cations. This announcement, presented at one of the Electrochemical Society’s International Molten Salt Conferences and eventually published in its proceedings,<sup>11</sup> was immediately followed by a communication by Wilkes and co-workers<sup>12</sup> who had been working on similar salts, and the field of high-fluidity, water-stable ionic liquids was launched.



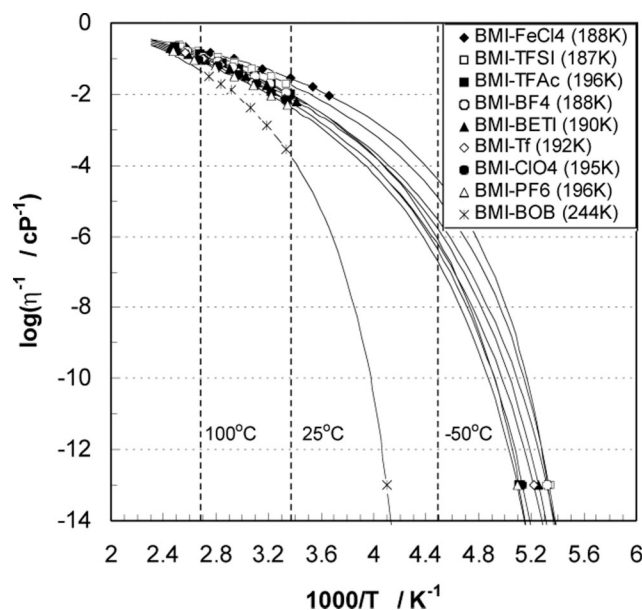
**FIGURE 2.** Electronic spectra (d-d transitions) of Ni(II) in a chloride environment both at 1 atm pressure and variable temperature down into the glass state (panel a) as a function of pressure up to 0.3 GPa at 24.5 °C and as a function of both up to 0.91 GPa, showing conversion from tetrahedral to octahedral coordination at high pressures and low temperatures. Reprinted with permission from ref 5. Copyright 1973 American Chemical Society.



**FIGURE 3.** Variation of  $T_g$  of the simple chloride glass former  $\alpha$ -methylpyridinium chloride on chloride complexation with various Lewis acids. Adapted from ref 6 by permission.

### Ionicity of Ionic Liquids: Relation to Vapor Pressure and Conductivity

The “ionicity” of aprotic ionic liquids is the property that is responsible for their characteristic low vapor pressures. Low vapor pressure is the single most important property of this class of liquid, the property that, more than any other, is responsible for high level of interest in the field. However there is very little written about what exactly is involved in achieving high ionicity.<sup>13</sup> If the ions created in forming the ionic liquid were to remain locked together in pairs, the liquids would not be found to be of very low vapor pressure, and their conductivities would also be poor. They would just represent an unusual group of polar liquids. Indeed there are cases of aprotic ionic liquids in which for one reason or another the ions are largely paired up, and these are characterized by a high vapor pressure and a poor conductivity (see below). To obtain the low vapor pressures for which ionic liquids are generally reputed, the ions must distribute themselves in a uniform manner each ion surrounded by a symmetrical shell of

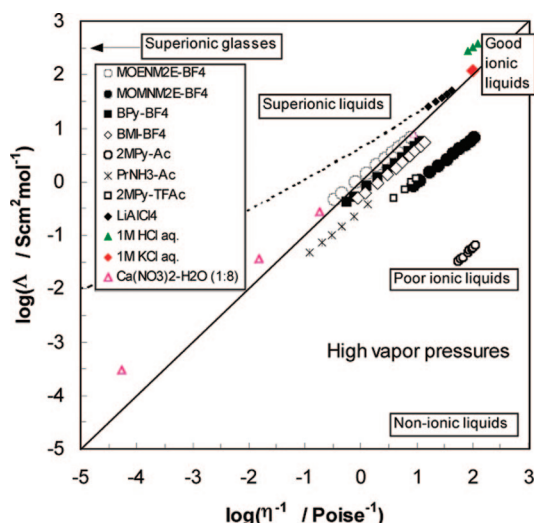


**FIGURE 4.** Fluidity data for a number of salts of the butylmethylimidazolium cation, showing that the tetrachloroferrate is more fluid than any of the fluorinated anion salts, in accord with its lowest  $T_g$  seen here ( $\log \eta^{-1} = 10^{-13}$ ) and in the Figure 6 legend. Reproduced with permission from ref 8. Copyright 2003 American Chemical Society.

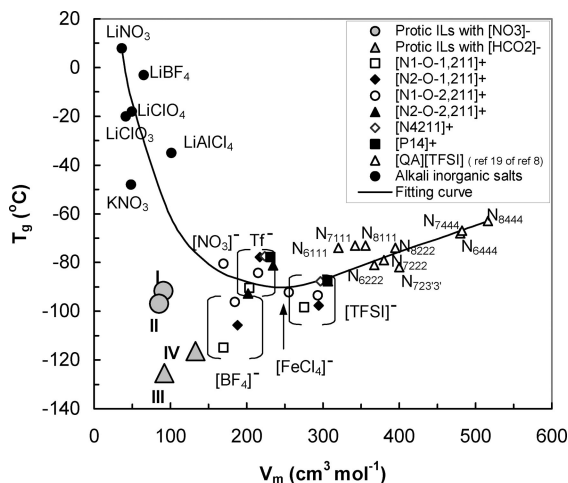
the opposite charge. This is the distribution that minimizes the electrostatic potential energy, developing the liquid equivalent of the ionic crystal Madelung energy.<sup>14</sup> It is the difficulty of overcoming this electrostatic free energy to produce individual ion pairs that is responsible for the low vapor pressures of “good” ionic liquids.

An example of an ion-paired aprotic salt (unsymmetrical charge shell) is shown in Figure 5, which is a plot based on the classical concept, due to Walden, that ionic mobility is determined by the viscous friction of the liquid dragging on the ion as it attempts to move under the electrochemical force exerted by the DC electric field. This





**FIGURE 5.** Walden Plot for ionic liquids and other molten salt and hydrate systems. Position of ideal line is fixed by data for KCl in 1 M aqueous solution. “Good” ionic liquids cluster on the ideal line. For exceptions, see text. Reprinted with permission from ref 15.



**FIGURE 6.** Glass transition temperatures of protic ILs in relation to the plot for aprotic salts of weakly polarizable anions from ref 8. Protic ILs are large shaded symbols (see ref 8 for details). Adapted from ref 8.

salt, methoxymethyl-dimethyl-ethyl-ammonium tetrafluoroborate (MOMNM2E-BF<sub>4</sub> or [N<sub>1-O-1,211</sub>][BF<sub>4</sub>]) is seen, among the aprotic cases, to be that most clearly belonging to the “poor ionic liquids” domain<sup>15</sup> in Figure 5. It would have a high vapor pressure relative to others because it never developed the full Madelung potential. The precise reason why the cation and anion like to associate in this salt is not fully established, but it is probably due to the electron depletion of the methylene group between O and N<sup>+</sup> yielding acid protons that H-bond to BF<sub>4</sub> fluorines in some lock-and-key manner.

The only “poorer” ionic liquid than [N<sub>1-O-1,211</sub>][BF<sub>4</sub>] in Figure 5 is a “protic” ionic liquid in which the drive to transfer the proton and create two ions is very weak. Protic ionic liquids as a class are given extensive discussion in a later section as they are among the most interesting and versatile of ionic liquids.

Figure 5 can be used to classify liquids between the groups “ionic” (whose members lie near the diagonal line), “subionic” (whose members lie below the line in the region labeled as “poor” ionic liquids), and superionic (whose members lie above the line by virtue of having some ionic species, usually small and low-charged, that can “slip through the cracks” in a nanoscopic sense and thus escape the full viscous drag of the surrounding medium).

## Cohesive Energy of Ionic Liquids

The salts that develop the full Madelung potential are, by the above understanding, those that will have the largest cohesive energy (for given ionic sizes). Generally they will be the cases that have ions of comparable size and uniform shape so that they pack well and occupy a small volume. However salts that conform to this description will in general find it easy to crystallize into some high lattice energy structure and will have high melting points. They will therefore not be among the group known as “ionic liquids”. To qualify as ionic liquids there must be some factor that lowers the lattice energy and thereby lowers the melting point. The “good” ionic liquids then must be those with some optimum departure from high symmetry, achieved by judicious (or serendipitous) choice of ion shape and interaction factors.

Those that achieve a sufficiently low melting point will then fail to crystallize and, on further cooling, will terminate in the glassy state. The temperature at which the liquid vitrifies,  $T_g$ , provides a second measure of the liquid cohesion. The plot is expected to have a minimum where decreasing Coulomb attractions balance increasing van der Waals attractions. Such a minimum is indeed found<sup>8</sup> in the vicinity of a volume that corresponds to a charge concentration of  $\sim 4$  M (Figure 6).

The case of the “poor” ionic liquid [N<sub>1-O-1,211</sub>][BF<sub>4</sub>], in which the cations and anions are largely paired, is of interest in this connection. This aprotic ionic liquid was seen, in Figure 10 of ref 8 to have the lowest cohesion, by the  $T_g$  criterion, of any aprotic IL. This is fully consistent with its poorly developed Madelung potential. It is only underlain by the protic cases, I–IV, discussed below.

## Aprotic Ionic Liquid Applications: Lithium Battery Electrolytes

Despite the interest widely expressed in ionic liquid-based lithium battery electrolytes, we omit reference to our recent studies in this area. This application is limited by a fundamental problem, discussed in ref 9 and illustrated in Figure 3, where it is seen that all small cations, including Li<sup>+</sup>, get trapped as anionic complexes (by outcompeting the large solvent cations) and hence must lose mobility. This problem is reduced by use of fluorinated anions<sup>9</sup> but not overcome.

## Protic Ionic Liquids: Properties and Applications

In contrast to the systems on which most of the work in the ionic liquid field has been performed (represented here by data in Figure 4), the protic ionic liquids are formed very simply by proton transfer from an inorganic acid to a Bronsted base. The base is usually organic in character, but there are also inorganic examples. The salt hydrazinium nitrate was reported in 1971 to have a melting point of only 70 °C,<sup>16</sup> and hydrazinium formate and hydrazinium acetate are both molten below 100 °C and can easily be studied through room temperature down to their glass transition temperatures.<sup>16</sup> The electrical conductance of hydrazinium formate at room temperature (measured in 1970 but only reported in the open literature in 2003<sup>17</sup>) is higher than that of any aprotic ionic liquid and is among the highest known. Many eutectic mixtures of ammonium salts are liquid below 100 °C, and these have recently been shown to be very interesting in application as fuel cell electrolytes,<sup>18</sup> as will be discussed further below. And of course there are the hydronium compounds such as hydronium triflate, which is congruently melting,  $T_m = 35$  °C, and has a very high electrical conductivity. Triflic acid and other superacids will presumably protonate many inorganic molecules that would not normally be considered as having cationic forms, so there are likely to be many additional inorganic protic ionic liquids recognized in the future. However the organic bases are far more versatile for protic ionic liquid formation.

There are organic bases not only from the primary, secondary or tertiary amines, but also with nitrogen atoms in heterocyclic rings (which may or may not be resonance stabilized).<sup>19</sup> There are also protonatable phosphorus analogs available, and sulfur-, selenium-, and iodine-based examples also exist.

An important aspect of protic ionic liquids is that the properties of the ionic liquid formed on proton transfer depend very strongly on the relative strengths of the acid and base between which the proton is transferred.<sup>20</sup> While the concentration of protonated species is always very high, of order 5–10 M in most cases, the properties may vary from strongly acidic to strongly basic in character, as is readily seen by simple tests with proton sensitive probes, such as the common indicator ions. For instance, a wide pH range litmus paper registers bright pink in contact with triethylammonium triflate but dark blue in contact with triethylammonium acetate. The systematic and quantitative measurement of basicity in these solvent-free liquids is a recent achievement.

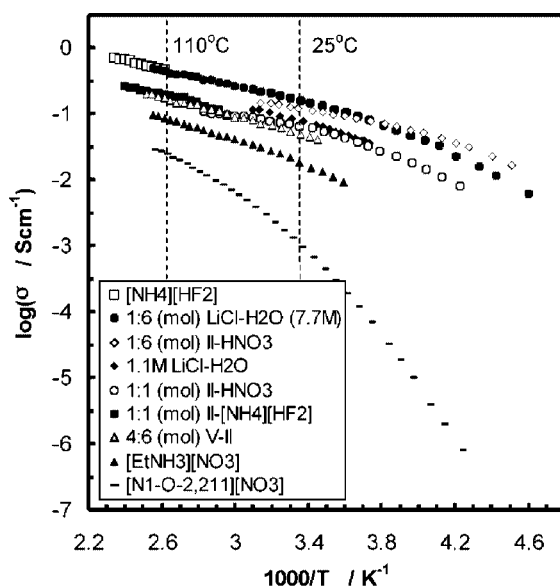
In order to assist the prediction of protic ionic liquid properties, the authors<sup>20,21</sup> have generalized the Gurney proton energy level diagram<sup>22</sup> not just to deal with proton transfers between acid and base species in an aqueous environment but, rather, to describe the energy changes when a proton moves between any proton donor and proton acceptor pair in the absence of any solvent at all. So far, for lack of alternatives, levels in the diagram relative to that of the  $\text{H}_3\text{O}^+/\text{H}_2\text{O}$  level have been based on the

	Occupied	Vacant	pK <sub>a</sub>	E (eV)	
Acid Electrolytes	HSbF <sub>6</sub>	SbF <sub>6</sub> <sup>-</sup>			
	HBOb	BOB <sup>-</sup>			
	HTFSI	TFSI <sup>-</sup>			
	HTf	Tf <sup>-</sup>	-14	0.83	
	HSO <sub>3</sub> F	SO <sub>3</sub> F <sup>-</sup>			
	HClO <sub>4</sub>	ClO <sub>4</sub> <sup>-</sup>	-10	0.59	
	HSO <sub>3</sub> SO <sub>3</sub> H	HSO <sub>3</sub> SO <sub>3</sub> <sup>-</sup>	-9	0.53	
	HPO <sub>2</sub> F <sub>2</sub>	PO <sub>2</sub> F <sub>2</sub> <sup>-</sup>			
	<b>HNO<sub>3</sub></b>	<b>NO<sub>3</sub><sup>-</sup></b>	<b>-1.30</b>	<b>0.08</b>	
	CH <sub>3</sub> SO <sub>3</sub> H	CH <sub>3</sub> SO <sub>3</sub> <sup>-</sup>	-0.60	0.04	
	2-fluoropyridineH <sup>+</sup>	2-fluoropyridine	-0.43	0.03	
	CF <sub>3</sub> COOH	CF <sub>3</sub> COO <sup>-</sup>	-0.25	0.01	
	H <sub>3</sub> O <sup>+</sup>	H <sub>2</sub> O	0	0	
Neutral Electrolytes	HSbF <sub>6</sub>	SbF <sub>6</sub> <sup>-</sup>	2.12	-0.13	
	1,2,4-lH-triazoleH <sup>+</sup>	1,2,4-lH-triazole	3.00	-0.18	
	HF	F <sup>-</sup>	3.20	-0.19	
	HCOOH	HCOO <sup>-</sup>	3.75	-0.22	
	CH <sub>3</sub> COOH	CH <sub>3</sub> COO <sup>-</sup>	4.75	-0.28	
	ImH <sup>+</sup>	Im	6.99	-0.41	
	hydrazineH <sup>+</sup>	hydrazine	7.96	-0.47	
		NH <sub>4</sub> <sup>+</sup>	NH <sub>3</sub>	9.23	-0.55
		<b>EtNH<sub>3</sub><sup>+</sup></b>	<b>EtNH<sub>2</sub></b>	<b>10.63</b>	-0.63
	Bu <sub>3</sub> NH <sub>2</sub> <sup>+</sup>	Bu <sub>3</sub> NH	11.25	-0.67	
	H <sub>2</sub> O	OH <sup>-</sup>	14	-0.83	
Basic Electrolytes					
	NH <sub>3</sub>	NH <sub>2</sub> <sup>-</sup>			
	OH <sup>-</sup>	O <sub>2</sub> <sup>-</sup> (Na <sup>+</sup> )	28	-1.66	

**FIGURE 7.** The proton energy level diagram for predicting the ionicities of ionic liquids resulting from the falling of a proton from an occupied level (on an acid molecule) to a vacant level (on a basic molecule or on a divalent anion, in the latter case the counteraction(s) must remain to balance the new anion charge). Reprinted with permission from ref 21. Copyright 2007 American Chemical Society.

known aqueous  $pK_a$  values, but this is of course only approximate because of the different dehydration energies of acid and base species in passing from aqueous to anhydrous systems. The approximate values will in time be replaced by energy levels based on NMR chemical shift studies<sup>23</sup> and other direct protic ionic liquids measurements, for instance, vapor pressure changes,<sup>20</sup> and particularly on voltages obtained from appropriate electrochemical measurements. The latter are just beginning.<sup>24,25</sup>

An example of the energy level diagram is provided in Figure 7.<sup>21</sup> It is constructed, following Gurney, by grouping acid and conjugate base forms of each molecule or ion together at a free energy level (in electronvolts) based on the arbitrary assignment of 0 eV to the couple  $\text{H}_3\text{O}^+/\text{H}_2\text{O}$ . The right-hand member of the couple is described as possessing an unoccupied quantized proton energy level, while the left-hand member has this level “occupied”. The proton in the occupied level of any couple can “fall into” the vacant level of any couple lower on the diagram. When the occupied level of a couple lies on a neutral molecule, the fall of its proton to the unoccupied level of a couple at a lower level leaves behind a negatively charged species and creates a new positive species from the neutral

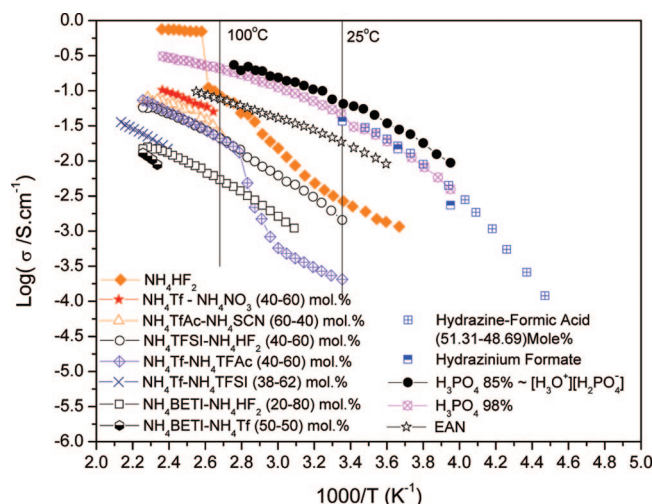


**FIGURE 8.** Conductivities of various protic ionic liquids (and one aprotic case,  $[N_{1-O-2,211}][BF_4]$ ) compared with those of aqueous LiCl solutions to show how the aqueous solutions are no longer unique with respect to high ionic conductivity. II is dimethylammonium nitrate; V is methoxypropylammonium nitrate. Reprinted from ref 17 with permission of AAAS.

molecule into whose unoccupied proton level it fell, and an ionic liquid is created if the melting point of the product is below 100 °C, as is frequently the case. The relation between the level values is based on  $E = -\Delta G/F = 2.303RT\Delta pK_a/F$ .

We can now group the products of such proton transfers together into three protic electrolyte categories, acid, neutral, and basic. **Acid** protic electrolytes result when the proton falls from an occupied level on a superacid to a vacant level on a weak base, for example from triflic acid to fluoroaniline or to water, as in common aqueous acids. **Neutral** electrolytes arise when the proton falls from a moderately strong acid like nitric or methanesulfonic acid to a strong base like ethylamine or cyclopentylamine. Provided the proton falls across a gap of 0.7 eV or more, the electrolyte is a “good” ionic liquid, meaning the proton resides on the base for at least 99% of the time. Finally, **basic** electrolytes, for example, the product of proton transfer from a weak acid such as acetic acid to a base such as ethylamine, will give a poor ionic liquid. To obtain a truly basic ionic liquid, the cation of an initial proton transfer process yielding a product like Ethylammonium nitrate (EAN) must be combined with the product of second proton transfer process that yields a basic anion like  $OH^-$  or  $NH_2^-$  by some metathetical reaction, for example,  $[CH_3CH_2NH_3^+][Cl^-] + NaOH \rightarrow [CH_3CH_2NH_3^+][OH^-] + NaCl$ . Such compounds tend to be high melting and have been little explored to date. The properties of low melting liquids produced by reducing the charge density of the anion by complexation, for example, with a weak Lewis acid, such as  $Al(OH)_3$ , have yet to be explored.

The ionic conductances of some protic ionic liquids are shown in Figure 8 along with those of aqueous LiCl



**FIGURE 9.** Arrhenius plot of the ionic conductivities of a collection of inorganic protic salts and salt mixtures (hydrazinium formate, ammonium bifluoride, and various ammonium salt mixtures). Comparison is made with ethylammonium nitrate and two phosphoric acids of different water content. Except for hydrazinium salts, the inorganic PILs are less highly conducting. High conductivity in solid state is shown for two cases.

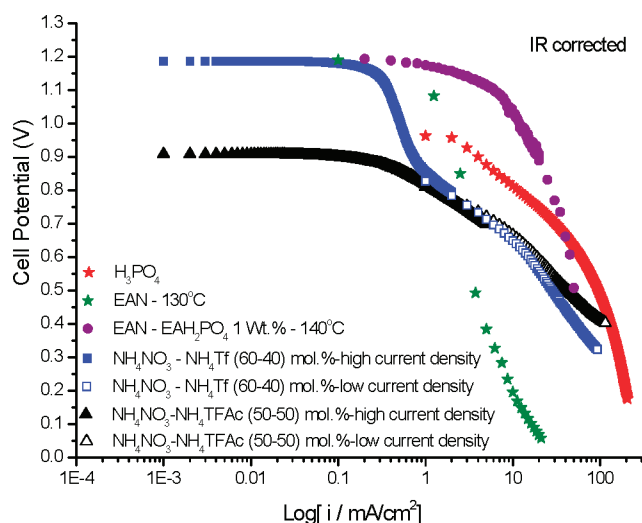
to show that for some salts like dimethylammonium nitrate<sup>17</sup> the conductivities at ambient temperature can be as high as those found in aqueous solutions. The conductivity of an aprotic ionic liquid with low glass temperature,  $[N_{1-O-2,211}][BF_4]$ , is included for comparison.

## Inorganic Protic Ionic Liquids

The smallest organic cation that can be obtained in an ionic liquid of the organic cation type is the methylammonium cation,  $CH_3NH_3^+$ . It is of interest to know whether, by passing to protic salts of the inorganic type, in which the cations are, for instance, ammonium or hydrazinium, even higher conductivities can be obtained. Hydrazinium nitrate and hydrazinium formate (having melting points below 100 °C)<sup>16</sup> were earlier cited as examples of inorganic ionic liquids, and the conductivity of hydrazinium formate was found to be extremely high,<sup>18</sup> though the finding remained unpublished until very recently. The conductivity of ammonium bifluoride, although not strictly an IL (having a melting point of 125 °C), is even higher.<sup>17</sup> Now we can add the conductivities of a number of ammonium salt mixtures, whose eutectic temperatures fall well in the IL range, to the collection of inorganic ionic liquids. The conductivity data for these systems<sup>18</sup> are shown in Figure 9.

In Figure 9, the conductivities, while indeed very high, do not reach the values of the best organic cation ILs except in the case of the hydrazinium formate. The case of ammonium bifluoride is exceptional, and it is possible that this unusual liquid, extensively used as a cleaning and a fluorinating agent in inorganic fluoride chemistry<sup>26</sup> may be a “dry” proton conductor.





**FIGURE 10.** IR-corrected polarization curves for hydrogen/oxygen fuel cells utilizing inorganic and organic cation ionic liquid electrolytes. Reproduced from ref 18 by permission.

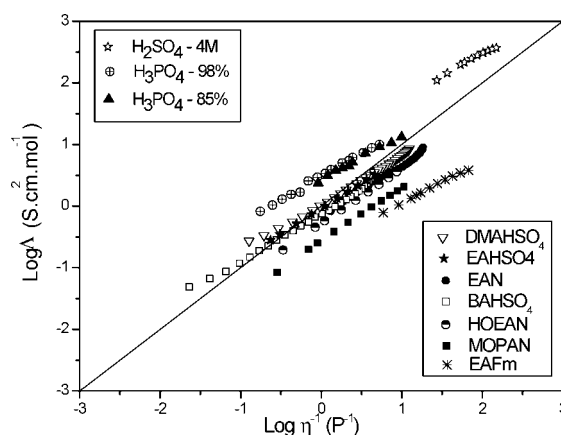
### Protic Ionic Liquids As Fuel Cell Electrolytes

It is astonishing that protic ionic liquids had been known for nearly a century before it was realized<sup>27,28</sup> that they could serve as the proton carriers in fuel cell electrolytes. In fact, they can serve very well in this role and can provide electrolytes of a type that are simply not available in systems in which water acts as acid or base in the proton transfer process.

It is even more astonishing that until 2006 it had not been realized that mixtures of **inorganic** salts (namely, the ammonium salts) can be used as protic electrolytes for fuel cells running above 80 °C (hydrazinium salts could be used to much lower temperatures). Applied as fuel cell electrolytes, the ammonium salts give more stable performance than electrolytes containing organic cations. The IR-corrected polarization curves for some inorganic electrolyte fuel cells are shown in Figure 10, using the logarithmic current ("Tafel plot") form. The plateau current at the theoretical voltage can now be extended out to 50 mA·cm<sup>-2</sup> in some inorganic systems to be described in future articles, beyond the previously recognized limits. The increase in efficiency relative to the phosphoric acid cell is about 20%, and the implied reduction in generated heat may be very important in some applications, which do not require high power.

While the ionic liquids offer the possibility of higher efficiency cells, the phosphoric acid (PA) cell has a significant advantage in kinetics. The kinetic advantage lies in the higher conductivity of the phosphoric acid, which is a molecular liquid that exhibits not only considerable autoionization but also "dry" proton mobility. This superprotonic component, which is illustrated in Figure 11, is unfortunately not present in the protic ionic liquids, which mostly lie on or below the "ideal" Walden line.<sup>8</sup> It may be necessary to compromise on power output for the sake of energy efficiency, though the NH<sub>4</sub>HF<sub>2</sub> data in Figure 9 suggest that breakthroughs may eventuate.

In an initial report on the relation of fuel cell voltage output to other properties of the PILs,<sup>18</sup> we noted a

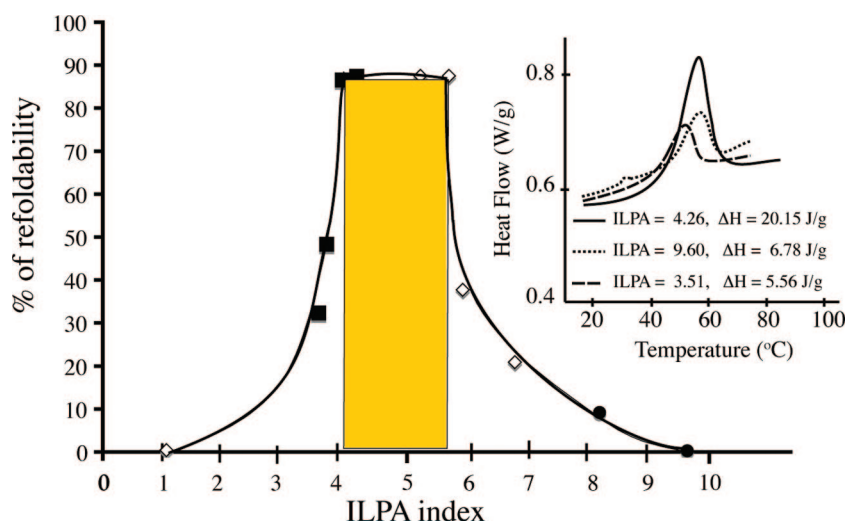


**FIGURE 11.** Walden plot showing the behavior of equivalent conductivity expected from precise correlation with liquid viscosity solid line, with examples of subionic behavior in some protic salt cases and superprotonic behavior in some acid + water systems. Reprinted with permission from ref 21. Copyright 2007 American Chemical Society.

relation between the output voltage and the difference in pK<sub>a</sub> values for the acid and base components of the electrolyte. The voltage increased strongly with increasing ΔpK<sub>a</sub> and reached the theoretical value when the ΔpK<sub>a</sub> value for the electrolyte reached about 14. There is now an urgent need to develop direct measures of the free energy of proton transfer for the anhydrous case.

### In Situ Measures of Proton Transfer Energetics and Relative Proton Activities in Ionic Liquids

Two steps have now been taken toward direct proton transfer energy characterization. The first<sup>23</sup> has been to study the NMR proton chemical shift for the proton that has been transferred to the base nitrogen but is still being counterattracted by the conjugate base of the acid from which it came. The stronger the "pull" from the conjugate base (which means the smaller the free energy of transfer), the more deshielded will be the N–H proton. The more deshielded the proton, the further downfield its resonance frequency will lie relative to a standard reference, for example, C(CH<sub>3</sub>)<sub>4</sub>. Thus the N–H chemical shift (δN–H) can serve as an in situ probe of the proton transfer energy. We find immediately that it does not enjoy a linear relation with the value of ΔpK<sub>a</sub> but rather gives a relationship similar to that between the fuel cell open circuit voltage (OCV) and the ΔpK<sub>a</sub> value.<sup>18</sup> The second step has been to develop a method of measuring directly the voltage necessary to displace a proton from its normal site on a nitrogen onto the anion from which it originally came. This will be described elsewhere.<sup>29</sup> A preliminary correlation of voltage output from a modified glass electrode with the N–H proton chemical shift discussed in the next section, has been given in an abstract for the Ionic Liquids meeting (COIL 2, Yokohoma, July 2007). These direct measures have already found application in another recently developing application of ionic liquids, namely, the stabilization of biomolecules discussed in the next section.



**FIGURE 12.** Refolding fraction (defined by the ratio of areas under the DSC unfolding endotherms of second to first upscans) as function of PA represented by the ILPA index (Ionic Liquid Proton Activity) which is a substitute for pH. The ILPA value is determined using a modified glass electrode, to be described elsewhere. The values depend on the reference electrode and liquid junction potential corrections, so they are only provisional in this figure. It correlates linearly with the N–H proton chemical shift  $\delta(\text{N-H})$ . Insert shows the unfolding endotherms in the most stable domain compared with those on either side. Closed markers are single component solutions and open diamonds are 1:1 binary mixtures of EAN–TEATf, EAN–TEATfAc, and EAN–EAFm.

## Proton Activity and Protein Stabilization in PILs

An exciting new role for ionic liquids may lie in the storage and manipulation of sensitive biomolecules. Fujita et al.<sup>30</sup> have recently reported that the protein cytochrome *c* is remarkably stabilized in solution in a nontoxic dihydrogen phosphate IL, and we have found<sup>31</sup> that lysozyme in 200 mg/mL concentration is still folded after 3 years in ambient solutions with large ethylammonium nitrate concentrations. The source and full extent of this stability is not yet properly understood.

It is well-known from standard biological concentration solution studies that each protein has pH range in which its native state is most preferred and that deviations from that pH range can affect its folding energy and its stability against such undesirable behavior as aggregation, and recently, fibrillization. It might be expected that the proton activity of the solvent will exert a strong effect on the stability of proteins in the ionic liquid protective solution, and this is verified by our findings,<sup>32</sup> which are shown in Figure 12. In Figure 12, the proton activity is represented by the  $\delta(\text{N-H})$  while, for stability on the vertical axis, we use a refoldability index pending the necessary long-term assessments.

The refoldability index is the percentage of the initial enthalpy of unfolding obtained after lowering the temperature to allow thermally denatured molecules to refold and then remeasuring the unfolding enthalpy. The difference between the two is a measure of the fraction of the protein lost to the aggregation process and is found to be 3%. The stability index is then given by the ratio (second unfolding enthalpy)/(first unfolding enthalpy) and is 0.97, or 97%, under favorable circumstances. The “% refoldability” for hen egg lysozyme is shown as a function of the proton activity measured electrochemically with a modified glass electrode to be described elsewhere. The

output voltage of this device is used to define an “ILPA” index which correlates linearly with the N–H chemical shift ( $\delta(\text{N-H})$ ) determined for the solution in which the lysozyme was dissolved, in Figure 12. The presence of an ILPA range equivalent to about 2 pH units, in which the same high refoldability index is obtained is quite striking. The refoldability index varies as a function of water content at constant ionic liquid content. But when the  $\delta(\text{N-H})$  of the solution is measured, it is found that the  $\delta(\text{N-H})$  has also changed with water content, and it is evidently only the proton activity that is important. The solution in which the 3 years stability was recorded<sup>31</sup> happened to have been formulated near the center of the maximum stability zone of Figure 12 for lysozyme.

Different proteins have different favorable proton activity stability ranges. We hope to establish these optimum conditions for many normally fragile biomolecules so that they can be preserved indefinitely at ambient temperatures, thereby opening the door to unrefrigerated shipping and storage of drugs and other biologically important materials.

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