

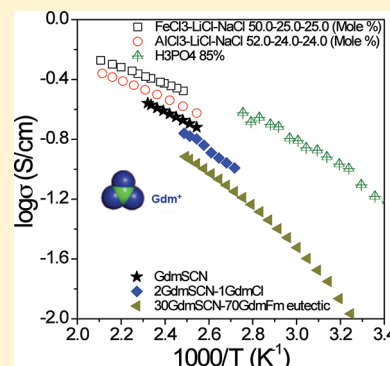
High Conductivity, and “Dry” Proton Motion, in Guanidinium Salt Melts and Binary Solutions

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Supporting Information

ABSTRACT: Salts of the small symmetrical guanidinium cation, which are important protein denaturants in biophysical chemistry, are studied in the ionic liquid state for the first time. Their conductivities prove to be among the highest measured, and their liquid fragilities prove exceptional. We link these features to the large number of exchangeable protons per cation. We present evidence that the unusual properties stem from the increasing delocalization of protons among alternative structural moieties under increasing thermal excitation, and from the associated increase in “dry” proton contribution to the mass transport properties.



INTRODUCTION

The guanidinium cation, $\text{C}(\text{NH}_2)_3^+$, is an elegant symmetrical ion formed by protonation of the imine group on the basic guanidine molecule ($\text{p}K_a = 13$), with subsequent redistribution of the electron density of the double bond to yield three equivalent C–N bonds and a resonance stabilization of the whole entity. Whereas guanidine is readily decomposed to gaseous products, the guanidinium cation is rather stable, and the liquid states of guanidinium cations with stable anions (e.g., chloride, triflate (Tf , CF_3SO_3^-) mesylate (MS , CH_3SO_3^-), etc.) persist far above 200 °C.

We have been interested in the propensity of the salts of this cation for proton conduction by the Grotthus mechanism, since, with six displaceable protons per cation the chance of fluctuations causing detachment and replacement processes with appropriate neighbors would seem unusually high. Thus, we have been exploring the phase transitions, conductivities, etc. of a variety of possible guanidinium salts and their mixtures and report here our findings.

Salts of the guanidinium cation are also of interest to the biochemical community because of their powerful denaturing action on dissolved proteins in many, but not all, cases. The fact that guanidinium sulfate is only a weak denaturant is not fully understood, and the protein stabilization field will profit from a better understanding of the availability and properties of additional guanidinium salts. Due to the unusually basic character of guanidine, a wider range of anions than usual can be utilized in creating salts of which the liquid states are of high ionicity. For instance, the proton transfer to guanidine from the weak acids, HNO_2 , and formic acid, HFm , is sufficient to yield protic ionic liquids, PILs, with high conductivities. Because of

the high ionicities obtained, we adopt the designation Gdm (guanidinium) for the cations of this study, rather than the alternative, Gdn (guanidine) hydro(base anion) terminology, sometimes used.

A number of studies have been carried out previously on salts of imine bases of the guanidinium type, and many of these have yielded ambient temperature liquids of high ionicity.^{1–3} However, they have all involved larger cations, often without exchangeable protons, for example, tetraalkyldimethylguanidinium salts, and so are less interesting to our present search for “dry” proton conductivity. The research presented here will only involve the simple guanidinium cation and some mixtures with comparably simple protic cations.

To assess the extent to which any Grotthus mechanism might contribute to the total conductivity, we need some means of judging conductivity relative to ionic mobility. One much-used possibility, here, is to determine separately the diffusivity of the transferred protons and the carbon centers of (or alkyl protons on) the cations, in order to observe if there is an excess of the former over the latter. Recently, however, evidence has been found of possible artifacts in the assessment of proton mobility in protic ionic liquids caused by previously unrecognized proton exchange effects⁴ usually involving residual water (<0.1 wt %) in the ionic liquid. For this paper, we will therefore continue to use the Walden plot of our earlier papers^{5–7} as the most reliable basis for deciding whether or not a “superionic” component of the conductivity is present.

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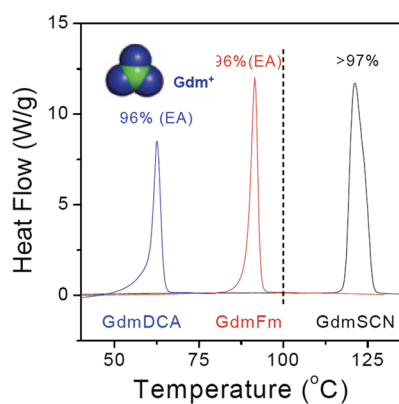


Figure 1. DSC endotherms for the melting of three guanidinium salts of this study. The purities assessed by elemental analysis (EA) (see Table 1) are noted on the figure next to the endotherm peak. See also Tables 1 and 2.

Table 1. Elemental Analysis Data for Some Guanidinium-Based Ionic Liquids

| ILs | C(expt/theor) (wt %) | H(expt/theor) (wt %) | N(expt/theor) (wt %) | purity (%) |
|--------------------|-------------------------|-------------------------|-------------------------|------------|
| GdmDCA | 28.27/28.57 | 4.86/4.76 | 64.44/66.67 | 97 |
| GdmFm | 22.82/22.86 | 6.7/6.66 | 38.24/39.96 | 96 |
| GdmNO ₂ | 12.03/11.3 | 5.8/5.7 | 48.11/52.8 | 92 |

EXPERIMENTAL METHODS

The number of guanidinium salts commercially available, particularly those of monovalent anions needed for high conductivity, is very limited (thiocyanate, chloride, carbonate), and to provide an adequate experimental base for our investigation it has been necessary to generate additional monovalent anion salts in the laboratory. Synthesis of these was in many cases straightforward and yielded stoichiometric products with sharp melting points, though the dicyanamide salt has proved problematical. Initial synthesis attempts employed molecular guanidine prepared by reacting GdmHCl with NaOCH₃ in methanol,⁸ which was then reacted directly with the acid of choice. However, this approach proved unsatisfactory due to an unresolved problem with the purity of the guanidine obtained. Instead, the alternative methods described below were developed.

GdmFm, GdmMS, Gdm trifluoroacetate, TFA, GdmTf, Gdm bis(trifluoromethanesulfonimide), [CF₃SO₂]₂[−], TFSI, GdmH₂PO₄, and GdmHSO₄ were prepared by reacting the carbonate, Gdm₂CO₃, with the appropriate acid. For GdmNO₂ and GdmDCA, it was preferred to use metathetical reactions with starting material guanidinium chloride (Sigma, 99%) and sodium or silver salts of the chosen anion, e.g., NaNO₂ for the nitrite or AgDCA for the dicyanamide DCA.⁹ GdmSCN (Sigma, 97%) was used as received. Finally, GdmFeCl₄ was made by direct reaction of GdmCl with reagent grade FeCl₃ under careful control of temperature.

For characterization, melting endotherms and chemical analyses were carried out. For some representative cases, guanidinium dicyanamide, guanidinium formate, and guanidinium thiocyanate, differential scanning calorimetry (DSC) endotherms, on small (~10 mg) samples, are shown in Figure 1. The sharp melting points are consistent with the elemental analysis results that are listed in Table 1.

Table 2. Glass Temperatures (When Vitrifiable), Melting Point, ΔpK_a and Calculated Purity of the Guanidinium Salts from Elemental Analysis Data

| salts | T_g (°C) | T_m (°C) | ΔpK_a | purity (%) |
|-----------------------------------|------------|------------|-------------------|-------------|
| GdmMS | n.d. | 202 | 15.7 ^a | 97.2 |
| GdmCl | n.d. | 182 | 16.7 ^a | >99 (Sigma) |
| GdmBF ₄ | n.d. | 168 | 14.1 ^a | 97 |
| GdmTf | n.d. | 156 | 26.7 ^a | 95.6 |
| GdmTFAc | n.d. | 155 | 13.7 ^a | 98 |
| GdmLa | −4.98 | 152 | 9.84 ^b | 98.7 |
| GdmSCN | n.d. | 118 | 15.6 ^a | ≥97 (Sigma) |
| GdmH ₂ PO ₄ | n.d. | 107 | 11.7 ^a | 96.1 |
| Gdm FeCl ₄ | n.d. | 99 | ~30 | ~99 |
| GdmTFSI | n.d. | 94 | 17.7 ^a | 95.7 |
| GdmHSO ₄ | n.d. | 93 | 16.7 ^b | 96.4 |
| GdmFm | n.d. | 91 | 9.95 ^a | 95.7 |
| GdmNO ₂ | n.d. | 90 | 10.4 ^b | 92 |
| GdmDCA | n.d. | 60 | 8.6 ^a | 96.5 |

^a D. R. MacFarlane et al. *Chem. Commun.* **2006**, 1905. ^b pK_a values from “ pK_a Data Compiled by R. Williams”.

The case of Gdm dicyanamide, however, needs some further comment. GdmDCA was made successfully by metathesis using AgDCA and GdmCl with methanol solvent and long reaction time, and the melting point of the product was found to be very sharply defined (see Figure 1). The elemental analysis accorded well with expectations, as seen in Table 1. However, when additional GdmDCA was needed, two repetitions of nominally the same AgDCA-based route that produced the initial satisfactory product failed to produce a pure GdmDCA. We are unable to account for the source of this difficulty. Since the DCA anion is rather unstable, and since the property of principal interest, the conductivity, had been successfully completed with the initial verified product, we abandoned further effort on this compound. We should note, however, that it has the lowest melting point of any of the Gdm salts we have prepared (see Table 2) and that, accordingly, its binary solutions with GdmFm would supercool and vitrify more easily than any of the cases discussed below.

Another salt not normally prepared as a PIL because of the weakness of the related acid is Gdm nitrite. We obtained this salt, by a methathetical reaction route, in a rather impure state (92%) according to elemental analysis, but found it to melt sharply at 92 °C. Preliminary studies of its conductivity showed a very high value, comparable with that of GdmSCN, but the liquid was observed to be slowly decomposing in the molten state, so further study was abandoned. Guanidinium salts with oxidizing cations such as GdmNO₃ are known, but have been deliberately avoided in this work because of the potential for explosion.

The high melting points of the guanidinium salts relative to most common “ionic liquids” are to be noted. They reflect the high symmetry of the guanidinium cation, and the consequent efficient packing and high lattice energies. There are two consequences of note. The first is that glass-forming properties are rare and only encountered in the eutectic region of the binary solutions of lowest melting salts. The second is that, since hygroscopicity is a consequence of effective competition of hydration with lattice energy, only the lowest melting of the present family of salts shows any hygroscopicity. A consequence is that the danger of contamination by water, or incomplete

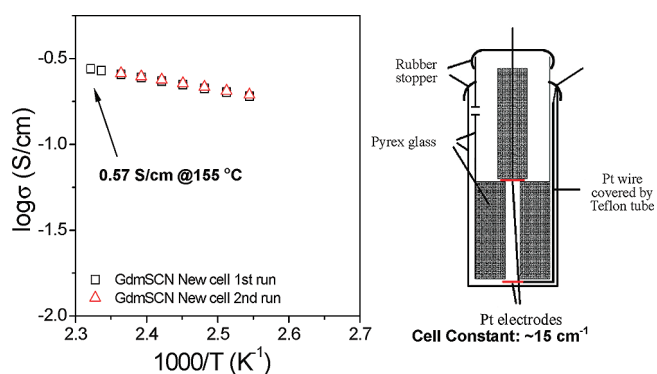


Figure 2. Pyrex glass small-sample conductivity cell for measurements on high conductivity ionic liquids. The precision of conductivity measurements obtained using this cell is shown in the adjacent diagram (for the case of Gdm SCN).

removal of water during salt preparation, is a minor problem in this study relative to most other ionic liquid studies. The measures taken to remove water during preparation, and to avoid its ingress during measurement, are detailed in a Supporting Information file.

Melting Points and Phase Diagrams. Melting points, and binary solution liquidus temperatures and eutectic temperatures, were determined using a Perkin-Elmer DSC7 scanning calorimeter and small samples sealed in aluminum pans. Due to the high cation symmetry, and consequent higher melting points, the majority of pure liquids, and even the binary eutectics, do not supercool readily, and hence few glass temperatures can be reported.

Binary system phase diagrams were determined in three cases, using DSC. These were as follows:

- (1) The case of the two commercially available salts GdmSCN (widely used in ribonucleic acid, RNA, purification procedures) and GdmCl (widely used as a chemical denaturant for proteins),
- (2) The case of GdmSCN–GdmFm, because the formate is the lowest-melting Gdm salt of this study except for the dicyanamide. Its preparation yielded a product that could be used, for this initial survey, without further purification. In this system, a narrow range of compositions near the eutectic composition can be supercooled to the glassy state, permitting determination of the glass transition temperature T_g .
- (3) The case with a common and stable anion (SCN^-) based on GdmSCN and the commercially available salt NH_4SCN .

Ionic Conductivities. Conductivities were measured using a Solartron impedance frequency analyzer 1250 with frequency range 10 μHz to 65 kHz. Conductivities were found to be so high in some cases that the simple dip cells used in previous conductivity studies were deemed unsuitable for the determination of conductivities of accuracy sufficient to yield reliable Walden products. To deal with this problem, a new small-sample volume cell of higher cell constant, $\sim 15 \text{ cm}^{-1}$ was constructed. The cell, illustrated in Figure 2, was checked using a standard highly conducting liquid, $\text{LiCl} \cdot 6\text{H}_2\text{O}$, that had been previously characterized by rigorous methods.¹⁰ The precise cell constant was determined using standard 0.1 M KCl solution, usually before each application. Results were the same for continuous heating or cooling but cooling runs were preferred as they yielded a wider range of liquid state data (due to supercooling).

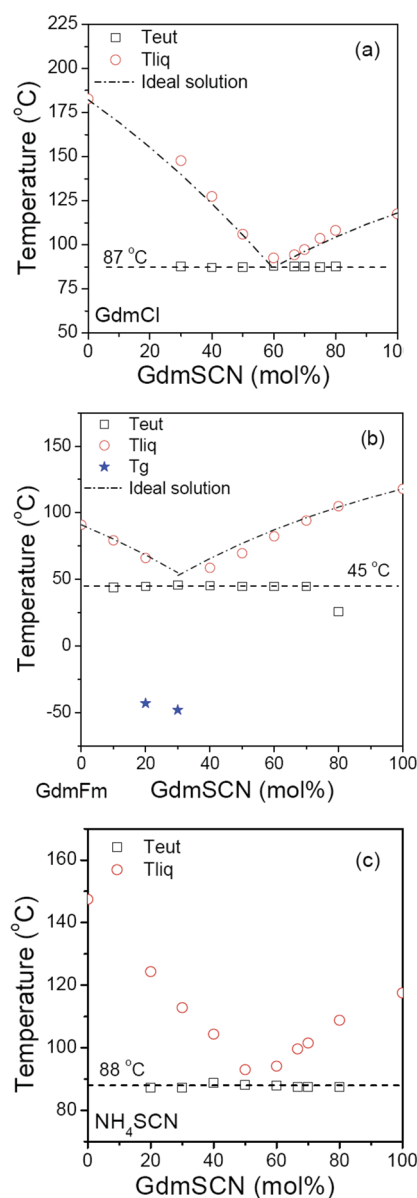


Figure 3. Binary phase diagrams with guanidinium salts. (a) The system GdmCl–GdmSCN. The eutectic lies at 87 °C. (b) The system GdmFm–GdmSCN. Compositions on the GdmFm-rich side of the eutectic supercool readily to the glassy state. The glass temperatures T_g lie near -50 °C. (c) The system NH_4SCN –GdmSCN. The eutectic lies at 88 °C.

Viscosity Measurements. Because of limited sample quantities, it was important to have measuring systems that did not demand large samples. For viscosities, we found that the Brookfield Model RVTDCP rotary viscometer, with cone and plate attachment, was very satisfactory. The instrument requires a sample of volume $< 1 \text{ mL}$ and yields results that are reproducible to $\pm 0.2\%$ and accurate to $\pm 1\%$. Measurements were made using the same sample on which the conductivity had been measured.

RESULTS AND DISCUSSION

Basic characterization data for the pure salts prepared and characterized in this study are provided in Tables 1 and 2. The melting point of the majority of the salts studied are not low

enough to qualify the liquids as ILs by the familiar, but quite arbitrary, criterion $T_m < 100\text{ }^\circ\text{C}$. However, the eutectic temperatures of the different possible binary systems bring the binary liquids into the “ionic liquid” range.

The salt guanidinium formate is of special interest because, like ice, it melts with a decrease in volume. This can lead to problems during remelting where cracking of the container vessel can occur unless the melting is carefully caused to proceed from the top down. This substance deserves much further study.

Binary Phase Diagrams. Phase diagrams for three binary systems are shown in Figure 3a–c. They all seem to be of the simple eutectic type. The dashed lines show the depression of freezing points calculated from the measured heats of fusion with the ideal solution melting point depression law. This was applied without using the dilute solution approximation but treating the heat of fusion of the solvent as a constant.

Ionic Conductivities. Conductivities of the eutectic compositions seen in the phase diagrams are shown alongside those of some of the pure salts in Figure 4, as identified in the legend.

The conductivities are very high at $100\text{ }^\circ\text{C}$ but drop off very rapidly with decreasing temperature as expected from the high glass transition temperature. To assess how the conductivities rank in the hierarchy of known high-conducting ionic liquids we make a comparison, in Figure 5, with the conductivity of two of

the best-conducting systems reported to date for ionic liquid systems, including an aqueous LiCl solution near its composition of maximum conductivity. We include the mineral acid case of $\text{H}_3\text{PO}_4 \cdot \text{H}_2\text{O}$ (85 wt % H_3PO_4) because of its relevance to current fuel cell technology.

The high-temperature conductivities are seen to surpass those of almost all previous studies and again to reach the values typical of aqueous solutions. This is remarkable in view of the relatively high values of the glass temperatures ($-50\text{ }^\circ\text{C}$ vs $-91.5\text{ }^\circ\text{C}$ for EAN⁷), seen in Figure 3, for the only system in which the glassy state could be accessed. Advantage may be taken of this case to assess, using T_g/T scaling, the fragility of the guanidinium thiocyanate–formate eutectic by comparison of the viscosities of this eutectic solution with those of other glass-forming ionic liquids. Viscosity data are also needed for the purpose of ascertaining, via Walden plots, whether the high conductivity is partly to be explained by the much-sought-after “dry” proton hopping mechanism.

VISCOSITIES AND FRAGILITIES

The raw viscosity data are displayed in Figure 6a and their comparison with other liquids is made on the scaled Arrhenius plot in Figure 6b which contains some of the data on PILs presented in ref 7. It is seen from Figure 6b that the fragility is extraordinarily high. Indeed it is the highest of any ionic liquid studied to date. The high fragility is not to be associated with the high conductivity per se, however, since the only system that is distinctly more conductive, the aqueous system $\text{LiCl} \cdot 6.7\text{H}_2\text{O}$, is known to be rather nonfragile—closer to glycerol than to the guanidinium salts.^{12,13} A possibility to be considered is that the freeing-up of protons, such that they can explore a distribution of independent sites, contributes to the configurational entropy of the liquid, and thereby¹⁴ to the fragility. This will be further explored after considering the relation of the ionic mobilities (as represented by the equivalent conductivity) to the liquid viscosity. The aberrant-appearing data for GdmFm in Figure 6a may be related to its anomalous (water-like) volume-of-melting behavior noted earlier. The viscosity of water is known to increase at an anomalously high rate near and below its melting point. GdmFm deserves a dedicated study.

Using the density equations listed in Table 3, we obtain the equivalent conductivities Λ from the specific conductivities of

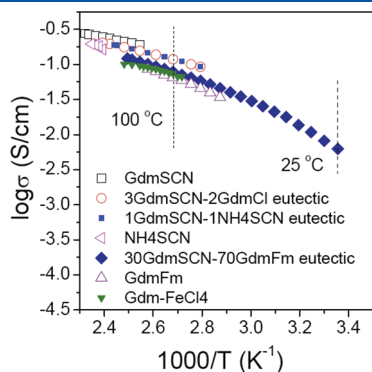


Figure 4. Conductivities of three eutectic solutions of Figure 3, and comparison with some of the individual salt conductivities. Data acquired during continuous slow cooling. We include the large, weak-base anion case of guanidinium tetrachloroferrate, which has been the most conductive in other studies,¹¹ for comparison.

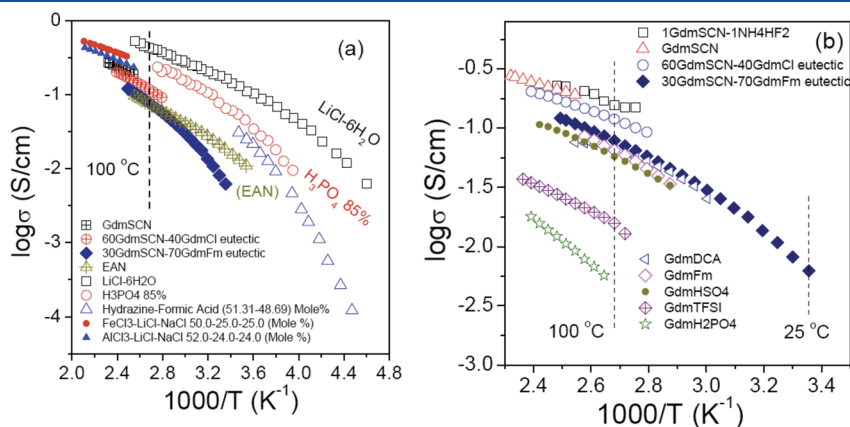


Figure 5. (a) Comparison of the conductivities of guanidinium salts and eutectic mixtures with other systems known for their high conductivities. The chloroaluminates, chloroferrates, and $\text{H}_3\text{PO}_4(\text{aq})$ all have a “fast species” contribution. (b) Conductivities of other guanidinium salts of this study.

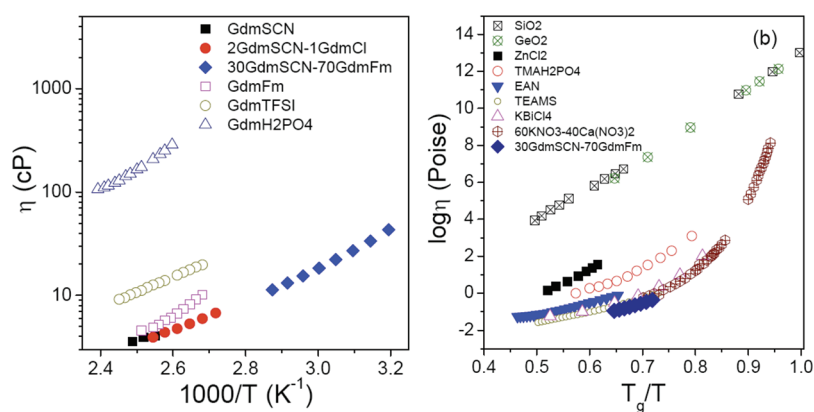


Figure 6. (a) Viscosity data for individual salts and some eutectic mixtures. Note the anomalous behavior of GdmFm. (b) Comparison of the viscosity data for the glassforming eutectic of (a) with those of other glassformers on a reduced Arrhenius plot for fragility assessment.

Table 3. Densities (ρ) of Guanidinium Salts and Their Binary Mixtures as a Function of Temperature

| compound | density (g/cm ³) |
|-----------------------------------|--|
| GdmSCN | $(1.706 - 1.342 \times 10^{-3} (T/K))$ |
| GdmFm | $(1.529 - 8.117 \times 10^{-4} (T/K))$ |
| GdmH ₂ PO ₄ | $(1.941 - 9.758 \times 10^{-4} (T/K))$ |
| GdmTFSI | $(2.017 - 1.107 \times 10^{-3} (T/K))$ |
| 2GdmSCN–1GdmCl | $(1.460 - 7.072 \times 10^{-4} (T/K))$ |
| 30GdmSCN–70GdmFm | $(1.421 - 5.444 \times 10^{-4} (T/K))$ |

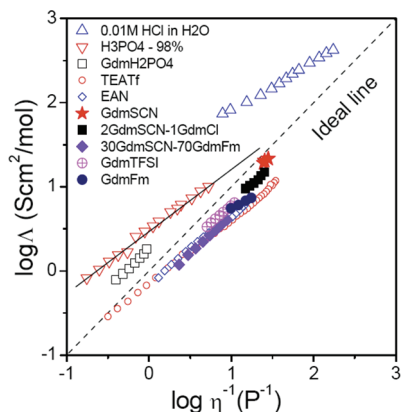


Figure 7. Walden plot for a selection of the guanidinium salts of this study and two systems (dilute aqueous HCl and hydrated phosphoric acid) known for the presence of extensive decoupled proton hopping. The ideal line is based on data for dilute KCl solution (see refs 7 and 11).

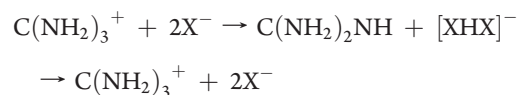
Figures 3 and 4, by

$$\Lambda = \sigma V_{\text{eq}}$$

where V_{eq} is the equivalent volume (the molar volume in the present systems), and display them against the fluidities (in inverse Poise units) in the Walden plot (Figure 7). Figure 7 contains data for two systems that are known for the presence of a substantial “free” proton hopping contribution, (1) hydrated phosphoric acid (H_3PO_4) containing a small amount of water, and (2) supercooled dilute aqueous HCl,¹⁵ which represents, at

the extreme of $-30\text{ }^\circ\text{C}$, the most pronounced case of Grotthuss proton hopping known to the authors.

In Figure 7 it is seen that, with the exception of the H_2PO_4^- salt, which has been found to be superprotonic in previous studies^{7,16} (though only at temperatures where the viscosity is high), all data points for salts studied in this work fall below the ideal line. However, the points for guanidinium thiocyanate fall closer to the line than do those of any previous salt that we, or any others, have reported at such high conductivities. Even the case of 98% H_3PO_4 , well-known for its proton-hopping contributions to conductivity,¹⁷ barely exceeds the value for GdmSCN when extrapolated to the same high conductivity. Thus, there is something exceptional about this salt, and it is closely followed by the eutectic solutions for which there are more extensive data (Figures 5 and 6). Remembering the exceptional *fragility* of the solutions containing this salt (see Figure 6), it is indeed tempting to conclude that their behavior is influenced by a population of protons that have the freedom to move between cations via temporary occupation of sites on the anion (transient reformation of the original proton donor acid), or in a transient dianion $[\text{XHX}]^-$. The transient dianion path, which we can represent by the following sequence



should be of lower energy. The existence of dianions as probable, and even preferred, states was illustrated in an earlier article⁵ in which it was shown that, for certain proton-transfer energies (ΔpK_a values), the maximum boiling point in the binary system, Brønsted base + Brønsted acid, occurred at the dianion $[\text{XHX}]^-$ stoichiometry. Intermediate energy sites, such as the above, that may arise via fluctuations in the molecule ion coordinates in the natural course of thermal motions can be taken advantage of with much higher probability when (as with $\text{C}(\text{NH}_2)_3^+$) the cation presents six equally probable “launch points” for its protons, than when there is only a single exchangeable proton per cation.

CONCLUDING REMARK

We have given evidence for an unusually high nonelectronic conductivity in liquid guanidinium salts. With the exception of aqueous solutions, this level has only previously been reached by systems in which there is a “fast” species contribution to the

conductivity (Li^+ or H^+), see Figure 4). It is tempting to conclude that a “dry” proton mobility is a feature of conductivity in the Gdm cation-containing systems. Higher levels of decoupling at the same high conductivity can probably only be obtained by shifting the composition into ranges of higher acidity, which will require change of both acid and base $\text{p}K_{\text{a}}$ values.

■ ASSOCIATED CONTENT

S Supporting Information. Experimental details on the synthesis and purity (particularly with respect to water vulnerability) of the guanidinium salts of this study are provided in separate file. This material is available free of charge via the Internet at <http://pubs.acs.org>.

■ ACKNOWLEDGMENT

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