

Acidity of Frozen Electrolyte Solutions

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Ice is selectively intolerant to impurities. A preponderance of implanted anions or cations generates electrical imbalances in ice grown from electrolyte solutions. Since the excess charges are ultimately neutralized via interfacial (H^+/HO^-) transport, the acidity of the unfrozen portion can change significantly and permanently. This insufficiently recognized phenomenon should critically affect rates and equilibria in frozen media. Here we report the effective ^{19}F NMR chemical shift of 3-fluorobenzoic acid as in situ probe of the acidity of extensively frozen electrolyte solutions. The sign and magnitude of the acidity changes associated with freezing are largely determined by specific ion combinations, but depend also on solute concentration and/or the extent of supercooling. NaCl solutions become more basic, those of $(NH_4)_2SO_4$ or Na_2SO_4 become more acidic, while solutions of the 2-(*N*-morpholino)ethanesulfonic acid zwitterion barely change their acidity upon freezing. We discuss how acidity scales based on solid-state NMR measurements could be used to assess the degree of ionization of weak acids and bases in frozen media.

Introduction

Important chemical, biological, and environmental processes take place at ice interfaces. Recent reports on the dissimilar evolution of nitrous acid from various high-latitude sunlit snowpacks point to site-dependent acidities.^{1–3} Freeze-induced acidity changes are implicated in the inactivation of food, drugs, and tissues during cryogenic storage.^{4–8} Tissue damage is empirically prevented by adding zwitterionic buffers and glycerol or dimethyl sulfoxide prior to freezing,^{9–12} devices that apparently minimize deleterious ion gradients across cell membranes.^{4,10,13}

The seminal finding that ions are marginally, but selectively, incorporated in ice as substitutional dopants during the freezing of electrolyte solutions¹⁴ remained exclusively associated with cloud electrification for decades.^{15–17} Although pH changes in partially frozen phosphate solutions were reported as early as 1959,¹⁸ it was apparently left to Bronshteyn and Chernov to establish the connection between both phenomena,¹⁹ and to Sola and Corti to confirm it experimentally.²⁰ The acidity of extensively frozen electrolyte solutions, in which the unfrozen portion typically consists of a microscopic film wetting polycrystalline ice rather than a separate phase, is, however, not readily accessible to conventional techniques.²¹ Residual molecular mobility in these microfluids, which are known to coexist with ice at temperatures well below the eutectic, provides the potential for active chemistry in the frozen state. It is the local acidity of these fluid phases that determines whether weak, volatile acids or bases can be exchanged between ice and the gas-phase, or whether reactions between ice dopants are inhibited or catalyzed in frozen media at temperatures ranging from a few degrees below the normal freezing point down to ~ 190 K.^{22–28}

Thus, the microscopic acidity of ice may be a key parameter lacking operational definition. We sought to take advantage of the fact that optically opaque polycrystalline ice is transparent to radio frequency waves, and that nuclear magnetic resonance (NMR) signals proceeding from the fluid and solid portions of frozen solutions are readily distinguished by their quite dissimilar line widths,^{29,30} to probe the acidity of frozen solutions at the microscopic scale.³¹ Here we report solid-state MAS NMR measurements of the ^{19}F chemical shift of the weak acid 3-fluorobenzoic acid ($pK_a = 3.93$ in D_2O at 298 K) as in situ probe of the acidity of the residual fluids after the freezing of various electrolyte solutions down to 205 K.^{32–35} We also discuss how to use such measurements to define Hammett-type acidity functions in frozen media.³⁶

Experimental Section

Solutions (90 μL) of the various electrolytes in D_2O (99.5%, Cambridge Isotopes, $T_f = 277$ K) were doped with 10 mM 3-fluorobenzoic acid (FBH, Aldrich), pH adjusted in the range 3 to 5 with 0.1 M SO_4H_2 , if needed, and transferred to a 4 mm diameter NMR zirconia probe, which was then sealed with a Kel-F cap under normal atmospheric conditions. All samples are assumed to contain <5 μM bicarbonate, the main CO_x species in water saturated with atmospheric CO_2 at pH ~ 5.0 , 298 K.³⁷ At such levels, CO_2 is not expected to interfere in present experiments. Solid-state magic-angle-spinning ^{19}F NMR chemical shift measurements on these samples, spun at 5 kHz, were performed using a Bruker DSX 500 MHz spectrometer, operating at 11.70 T, 470.70 MHz, provided with a temperature-controlled cavity.³⁸ ^{19}F chemical shifts were externally referenced to perfluorooctane (C_8F_{18}) in chloroform ($CHCl_3$) on a daily basis. $^{19}\delta(T)$ measurements (vs single temperature reference calibration) are assumed to be accurate within ± 0.01 ppm.^{39,40} Their precision, typically ± 0.02 ppm, reflects

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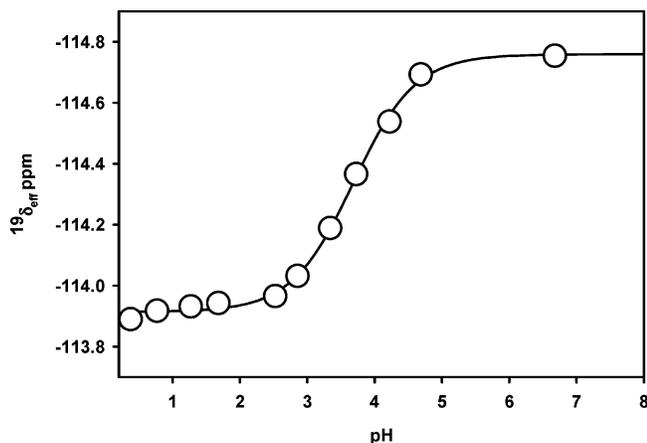


Figure 1. Titration curve of 3-fluorobenzoic acid at 298 K.

instrumental temperature (± 2 K) fluctuations. $^{19}\delta(T)$ measurements are based on 16 spectral scans acquired over ~ 90 s. Solutions were cooled or warmed using various temperature step sequences. Fluid sample supercooling could be enhanced by using sparser cooling step protocols. Chemical shifts measured in frozen samples remained constant over 60 min periods, and did not exhibit thermal hysteresis. The intensity of ^{19}F resonances gradually decreases at sub-freezing temperatures, while their line widths remain nearly constant, until they vanish at temperatures that depend on the type of solute and its initial concentration.

Results and Discussion

Fluorine-containing, weak Brønsted acids or bases are sensitive NMR acidity probes because (1) the fluorine nucleus has a large magnetogyric ratio, (2) its chemical shifts, $^{19}\delta$, span a much wider range than those of the proton and, (3) it is free from interference by solvent proton signals. In the limit of fast (in the NMR time scale) proton exchange between FBH and its conjugated base FBH^- , one measures an effective ^{19}F chemical shift, $^{19}\delta_{\text{eff}}$, the weighted molar average given by eq 1:^{41,42}

$$^{19}\delta_{\text{eff}} = x \, ^{19}\delta_{\text{FB}^-} + (1 - x) \, ^{19}\delta_{\text{FBH}} \quad (1)$$

where x is the degree of FBH dissociation, $^{19}\delta_{\text{FB}^-} = -114.76$ ppm, and $^{19}\delta_{\text{FBH}} = -113.92$ ppm.³² $^{19}\delta_{\text{eff}}$ proves to be sensitive to pH in the range 2 to 5 (Figure 1). The experimental difference, $\Delta = ^{19}\delta_{\text{FBH}^-} - ^{19}\delta_{\text{FBH}} = 0.84$ ppm, agrees well with reported data; the derived $\text{p}K_{\text{a}} = 3.93$ value in D_2O is ~ 0.25 units larger than in H_2O .³² We found that $^{19}\delta_{\text{eff}}$ for a 10 mM FBH solution in deionized water changes less than 0.1 ppm between 298 and 263 K. Notice that less negative $^{19}\delta_{\text{eff}}$ values (lower ordinates in all plots) represent more acidic conditions throughout.

Figure 2 shows $^{19}\delta_{\text{eff}}$ vs T for a 1.0 M $(\text{NH}_4)_2\text{SO}_4$ solution in D_2O that was cooled from 298 to 243 K in discrete steps, and then warmed to 298 K. It is apparent that: (1) the initial solution freezes without significant supercooling at ~ 270 K [1 mol L^{-1} $(\text{NH}_4)_2\text{SO}_4$ is 1.06 molal and fully dissociated; it roughly freezes at $T_{\text{f}} \sim 277$ K $-\lambda \times 3.18$ m = 270.6 K; $\lambda = 2.01$ K molal $^{-1}$ is the D_2O cryoscopic constant], (2) the remaining liquidus becomes more acidic as the temperature drops and, (3) the system closely retraces its acidity, i.e., $^{19}\delta_{\text{eff}}(T)$, upon warming. Figure 3 displays further measurements extending to 205 K, i.e., about 50 K below the eutectic at $T_{\text{e}} \sim 258$ K,^{43,44} obtained under three different cooling protocols. The lower bounds to the temperature ranges covered in present experiments are solely limited by NMR signal detection. The real acidity changes that would develop in the absence of the probe are anticipated to be

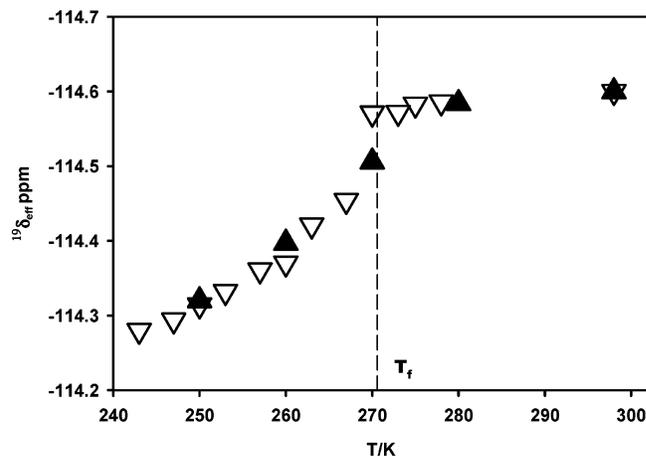


Figure 2. Effective fluorine chemical shift of the 3-fluorobenzoic acid (FBH) probe, $^{19}\delta_{\text{eff}}$, in a [1 M $(\text{NH}_4)_2\text{SO}_4$ in D_2O + 10 mM FBH] solution cooled from 298 K down to 243 K (∇), and then warmed (\blacktriangle). $T_{\text{f}} \sim 270.6$ K is the cryoscopically depressed freezing point of the sample solution.

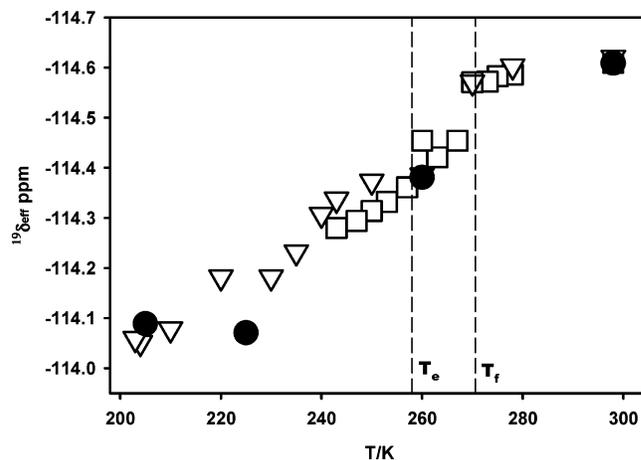


Figure 3. $^{19}\delta_{\text{eff}}$ vs T upon cooling the solution of Figure 2 along three different (∇), (\square) and (\bullet) cooling step sequences. $T_{\text{e}} \sim 258$ K, is the eutectic temperature of $[(\text{NH}_4)_2\text{SO}_4 + \text{D}_2\text{O}]$.

somewhat larger than those actually observed in these experiments, depending on the relative concentrations of solute and probe, because FBH, as a weak acid, provides limited buffering action.

Considering that the unfrozen portion becomes increasingly more concentrated at lower temperatures, the acidity of initially acidic ($\text{pH} \sim 4.4$) solutions should naturally drop further, in the absence of concomitant phenomena, upon freezing. The acidity changes expected from concentration effects are, however, smaller than the ones observed.²⁰ Furthermore, they could not possibly occur below the eutectic. $^{19}\delta_{\text{eff}}$ vs T results for the freezing of 1 M NaCl solutions (Figure 4) definitively eliminate the possibility that the acidity changes are simply due to concentration effects, although they may still make a minor contribution. In this case the unfrozen solutions become more basic at lower temperatures, an effect that appears to be magnified in the more dilute sample that freezes with minimal supercooling. Since $^{19}\delta_{\text{eff}}$ measured in these partially frozen solutions do not detectably change (during the 60 min periods) following freezing, they are ascribed to thermally and chemically equilibrated systems. Acidity changes, either toward more acid or basic conditions, are observed down to the lowest temperatures, which in some cases fall below the corresponding eutectics. This is an indication that the mechanism responsible for these changes is still active under conditions in which the

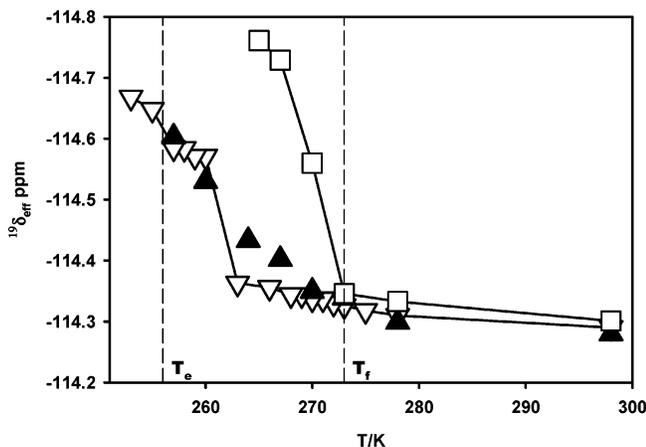


Figure 4. $^{19}\delta_{\text{eff}}$ vs T upon cooling (∇) a [1 M NaCl in D_2O + 10 mM FBH] solution, and then warming it up (\blacktriangle). $T_f \sim 273$ K and $T_e \sim 256$ K for a 1 M NaCl solution in D_2O . (\square) $^{19}\delta_{\text{eff}}$ measured upon cooling a [5 mM NaCl in D_2O + 10 mM FBH] solution.

frozen samples should be presumed to consist exclusively of bulk solid phases. Notice that, although $^{19}\delta_{\text{eff}}$ vs pH is a sigmoidal function bound by $^{19}\delta_{\text{FB}^-} = -114.76$ ppm and $^{19}\delta_{\text{FBH}} = -113.92$ ppm (Figure 1), limiting $^{19}\delta_{\text{eff}}$ values may not be always approached asymptotically in $^{19}\delta_{\text{eff}}$ vs T plots because there are no obvious restrictions on actual pH vs T functions. Furthermore, NMR signals may simply vanish at temperatures at which acidity changes are still operative.

It should be emphasized that even binary solutions may contain microfluids at temperatures below the eutectic point.⁴⁵ The existence of these fluids does not violate, however, the Gibbs phase rule because the thermodynamic state of highly disperse microcrystalline ice, in contrast with single ice crystals, needs to be defined by an interfacial tension, γ , in addition to T and P , as intensive variables. Since an additional intensive variable allows for an extra degree of freedom, the eutectic ceases to be an invariant point in the phase diagram of a binary mixture once interfaces are taken into account.^{46,47} Chemical activity,⁴⁸ or inactivity, below the eutectic should be considered, therefore, insufficient evidence against a fluid reaction medium.

The sign of the acidity changes observed during the freezing of $(\text{NH}_4)_2\text{SO}_4$ and NaCl solutions are those expected from the corresponding electric polarizations previously detected by Workman and Reynolds,¹⁴ who found the ice phase to be positively and negatively charged, relative to the liquid, respectively, and from Bronshteyn and Chernov's theory of freezing hydrolysis.¹⁹ The polarizations arise from the preferential incorporation of NH_4^+ vs SO_4^{2-} and of Cl^- vs Na^+ into the ice matrix as substitutional dopants. This phenomenon is related to the selective transport of ions across membranes, the most fundamental event in living organisms.¹³ Acidity changes in the unfrozen solution ensue the restoration of electroneutrality via H^+ migration out of or into ice, respectively. Sodium ions, which are preferentially rejected from ice vs chloride (cf. Figure 4), still behave as NH_4^+ , the leading chaotropic cation, vis-à-vis the strongly hydrated, kosmotropic SO_4^{2-} (Figure 5).⁴⁹ In full accord with this view, solutions of 2-(*N*-morpholino)ethanesulfonic acid (MES), a zwitterionic buffer with $\text{p}K_1 = 0.87$, $\text{p}K_2 = 6.10$,⁵⁰ freeze with a minimal ($\Delta^{19}\delta_{\text{eff}} \sim -0.02$ ppm) change in acidity about pH 3 (Figure 6). Zwitterionic buffers may not induce significant acidity changes upon freezing because the covalently linked cationic and anionic centers cannot be separated across the ice/solution interface.

The interpretation of acidity measurements in concentrated solutions at low-temperature involves some precision.^{51,52} While

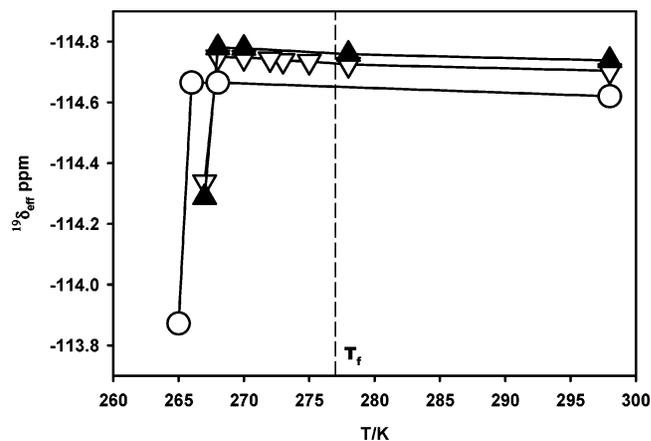


Figure 5. $^{19}\delta_{\text{eff}}$ vs T upon cooling a [5 mM Na_2SO_4 in D_2O + 10 mM FBH] solution along three different (∇), (\blacktriangle), and (\circ) cooling step sequences.

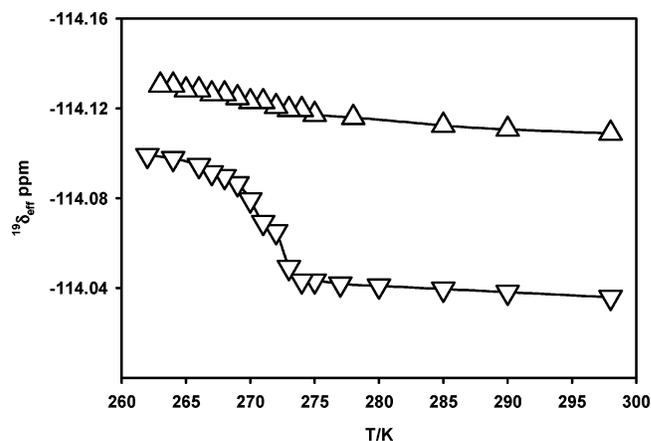


Figure 6. $^{19}\delta_{\text{eff}}$ vs T upon cooling 2-(*N*-morpholino)ethanesulfonic acid (MES) solutions in D_2O . (Δ) 5 mM. (∇) 1 M. MES is a zwitterion in the range $2 \lesssim \text{pH} \lesssim 5$.

the $\text{p}K_a$ values of weak acids are nearly temperature independent ($\Delta H_a \sim 2$ kJ mol⁻¹), K_w is rather sensitive to temperature ($\Delta H_w \sim 56.6$ kJ mol⁻¹).⁵³ Thus, the neutral point of supercooled water at 240 K occurs at pH 8.4. The ionic strength, I , changes attending massive freezing may also affect the activity coefficients, γ , of ions and neutrals and, hence, acid dissociation equilibria.⁵⁴ However, if one intends to assess the degree of dissociation of a weak acid, e.g., HONO, in frozen electrolyte solutions, most of these effects tend to cancel out. Let us consider how $^{19}\delta_{\text{eff}}$ vs T measurements for FBH could be used to estimate the degree of dissociation of the cosolute nitrous acid, HONO, a weak acid whose $\text{p}K_a$ overlaps the range of $^{19}\delta_{\text{eff}}$ variations. From eq 1, and the definitions of K_N and K_P , the thermodynamic dissociation equilibrium constants for HONO ($\text{p}K_a = 2.8$)⁵⁵ and the probe FBH, eqs 2 and 3, one obtains eq 4:

$$K_N = \frac{[\text{H}^+][\text{NO}_2^-] \gamma_{\text{H}^+} \gamma_{\text{NO}_2^-}}{[\text{HONO}] \gamma_{\text{HONO}}} \quad (2)$$

$$K_P = \frac{[\text{H}^+][\text{FB}^-] \gamma_{\text{H}^+} \gamma_{\text{FB}^-}}{[\text{FBH}] \gamma_{\text{FBH}}} \quad (3)$$

$$\frac{[\text{HONO}]}{[\text{NO}_2^-]} = \frac{\gamma_{\text{NO}_2^-} \gamma_{\text{FBH}}}{\gamma_{\text{HONO}} \gamma_{\text{FB}^-}} \frac{^{19}\delta_{\text{FB}^-} - ^{19}\delta_{\text{eff}}}{^{19}\delta_{\text{eff}} - \delta_{\text{FBH}}} \frac{K_P}{K_N} \quad (4)$$

which gives $[\text{HONO}]/[\text{NO}_2^-]$, the ratio of undissociated to

dissociated HONO, as a function of experimental $^{19}\delta_{\text{eff}}$ data. The relationship $[\text{HONO}]/[\text{NO}_2^-]$ vs $^{19}\delta_{\text{eff}}$ will be, in general, determined by the initial overall composition of the solution and T . Notice that the first factor in the right-hand side of eq 4 is expected to be nearly independent of I and T due to a mutual cancellation of effects between the γ 's for the corresponding anions and undissociated acids. This approximation is akin to the fundamental assumption underlying the validity of the Hammett acidity functions, H_0 , that would be obtained from (spectrophotometric) $[\text{FBH}]/[\text{FB}^-]$ measurements:³⁶

$$H_0 = \text{p}K_{\text{P}} - \log([\text{FBH}]/[\text{FB}^-]) = \text{p}K_{\text{P}} - \log \frac{^{19}\delta_{\text{FB}^-} - ^{19}\delta_{\text{eff}}}{^{19}\delta_{\text{eff}} - \delta_{\text{FBH}}} \quad (5)$$

Equation 5, which is usually recast as $H_0 = -\log h_0$ in terms of $h_0 = a_{\text{H}^+} \gamma_{\text{FB}^-} / \gamma_{\text{FBH}}$, implies that $h_0 \rightarrow [\text{H}^+]$ and $H_0 \rightarrow \text{pH}$ in dilute aqueous solutions. Thus, if H_0 is known for a given solvent system, the degree of protonation of any base Z^- can be evaluated from $\text{p}K_{\text{ZH}}$ (or of a neutral base Z and $\text{p}K_{\text{ZH}^+}$) via eq 5. Experiments performed with a series of bases generally confirm that $\gamma_{\text{Z}^-} / \gamma_{\text{ZH}}$ is nearly independent of Z in concentrated acid solutions at a given temperature.^{36,53} On the other hand, extensive data on the thermodynamics of protolytic reactions indicate that the strength of weak acids is mainly controlled by their dissociation enthalpies, rather than by dissociation entropies.^{53,56} Therefore, the temperature dependences of K_{a} for acids of comparable strength are expected to be similar, i.e., their ratios, such as $K_{\text{P}}/K_{\text{N}}$, the last factor in the right-hand side of eq 4, are expected to be weakly temperature dependent. Considering that the chemical shifts of FBH/FB^- as well as of the reference standard have very weak temperature dependences ($<0.001 \text{ ppm K}^{-1}$),^{39,40} we conclude that eqs 4 and 5 establish the basis for estimating the extent of dissociation of weak acids in frozen solutions.

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