Reexamination of Hexafluorosilicate Hydrolysis by ^{19}F NMR and pH Measurement

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The dissociation of hexafluorosilicate has been reinvestigated due to recent suggestions that fluorosilicate intermediates may be present in appreciable concentrations in drinking water. ^{19}F NMR spectroscopy has been used to search for intermediates in the hydrolysis of hexafluorosilicate. No intermediates were observable at 10^{-5} M concentrations under excess fluoride forcing conditions over the pH range of 3.5−5. A single intermediate species, assigned as SiF_5^- or its hydrate, was detected below pH 3.5. At moderate pH values of 4 and 5 silica oligomerization in the solutions studied made it difficult to directly determine the hexafluorosilicate equilibrium constant. Under more acidic conditions the average pK_d, or negative log of the dissociation constant K_d, determined by ^{19}F NMR measurements, was 30.6. We also investigated the behavior of hexafluorosilicate in common biological buffer reagents including phosphate/citrate, veronal/HCl buffers, and Ringer's solution. The buffer capacity of all of these systems was found to be insufficient to prevent acidic shifts in pH when hexafluorosilicate was added. The pH change is sufficient explanation for the observed inhibition of acetylcholinesterase that was previously attributed to hexafluorosilicate hydrolysis intermediates.

Introduction

Hexafluorosilicic acid and sodium hexafluorosilicate are the most commonly used compounds for municipal water supply fluoridation (*1*). Their efficacy depends on the hydrolysis of hexafluorosilicate to free fluoride ions. Opponents of fluoridation of water supplies have alleged that incomplete dissociation of hexafluorosilicate results in dangerous reactive intermediates that could pose a public health threat. This argument is used as evidence that use of fluorosilicates as fluoridation agents should be abandoned (*2, 3*).

The exact pathway for hydrolysis of hexafluorosilicate is complex, and several possibilities have been proposed. Though the hydrolysis has been studied since the 1930s, the hydrolysis pathway has not been definitively determined (*4−8*). Recently, the chemistry of this system has been reviewed (*9, 10*). The net reaction can be written as follows:

$$H_2SiF_6(aq) + 4H_2O(l) \rightleftharpoons 6H^+ + 6F^- + Si(OH)_4(aq) \quad (1a)$$

$$SiF_6^{2-}(aq) + 4H_2O(l) \rightleftharpoons 4H^+ + 6F^- + Si(OH)_4(aq) \quad (1b)$$
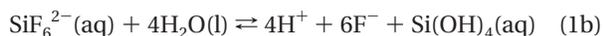
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Fluorosilicic acid is a very strong acid with a second acid dissociation constant, pK_{a2}, of −0.65 (*10*). Thus, except under very acidic conditions the dominant form in solution will be the hexafluorosilicate ion. So the equilibrium reaction is generally considered to be of the form given in eq 1b. However, this equilibrium is further complicated by the weak acidity of hydrofluoric acid and by the oligomerization of silicic acid to discrete oligosilicates and colloidal silica (*11*).

Studies of fluorosilicates have depended heavily on fluoride electrode potentiometry (*5, 12*). The solid-state LaF_3 fluoride electrode can detect free fluoride ion activity at fluoride concentrations down to nearly 10^{-7} M. It does not respond directly to any other fluoride-containing species, including HF, HF_2^-, SiF_6^{2-}, or any potential intermediates in the hydrolysis of hexafluorosilicate. These species can only be inferred from the electrode response as solution conditions such as pH, total fluoride concentration, and concentrations of other co-ions and counterions are varied. The measurement problem is exacerbated by the logarithmic response of the electrode. Generally, authors assume one or another set of intermediates and choose the set that provides the best fit to the experimental data.

Under forcing conditions (low pH, high total fluoride concentration), previous studies have either found evidence of, or fit potentiometric data to, models including various fluorosilicate intermediate species ranging from SiF_5^- to Si-$(OH)_3F$ (*10*). However, all authors do predict complete dissociation under municipal water conditions (pH ∼ 7, initial fluorosilicate concentration equivalent to ∼1 mg/L F^-). In particular, those authors who have studied the system near these conditions have concluded that essentially all fluoride is available as free fluoride ion under these conditions.

The assertion of incomplete hydrolysis of hexafluorosilicate is derived from a study of the effects of fluoride and hydrofluoric acid on inhibition of acetylcholinesterase. The work was reported in the chemistry Ph.D. dissertation of J. Westendorf and in short communications resulting from that work (*12−15*). Westendorf demonstrated that HF rather than F^- was the species that inhibited the enzyme. Various fluoro complexes, such as magnesium hexafluorosilicate, were investigated for their effects by F^- potentiometry. At high (millimolar) fluorosilicate concentrations, enzyme inhibition was observed in veronal, Ringer's, and phosphate/citrate buffers with nominal pHs in the range of 7.0−8.6. Westendorf found that his data fit best with a model that included the presence of hexafluorosilicate intermediates in solution. This finding has been a source of concern for those debating the health effects of ubiquitous water fluoridation.

Our incomplete understanding of the hydrolysis pathway and the known limitations of fluoride electrode potentiometry led us to search for direct evidence of intermediates in the hydrolysis of fluorosilicate dissociation using ^{19}F NMR. NMR does not offer subnanomolar response, but it can provide positive evidence for the presence of hexafluorosilicate and partially hydrolyzed intermediates at the micromolar level. In addition, we observed and modeled the pH changes caused by the addition of magnesium hexafluorosilicate to the buffers used by Westendorf.

Experimental Section

^{19}F NMR. All fluoride-containing solutions were prepared in THX volumetric flasks from Jade Scientific and stored in LDPE bottles. NaF, H_2SiF_6, acetic acid, and sodium acetate were purchased from Aldrich. A stock solution of 0.403 F NaF was prepared by weight. A stock solution of 0.218 F H_2SiF_6 was prepared from a 20% to 25% solution of H_2SiF_6 by dilution

with Nanopure (18 MΩ) water and quantified via ^{19}F NMR. Solutions at pH 4 or 5 were buffered with 50−100 mM acetic acid buffer. Solutions for NMR contained 50% v/v D$_2$O.

Hexafluorosilicate-containing solutions for ^{19}F NMR spectroscopy were prepared by dilution from the H$_2$SiF$_6$ stock solution with Nanopure (18 MΩ) water to give a formal concentration of [H$_2$SiF$_6$] = 5.0 × 10^{-4} F. Assuming complete dissociation of the hexafluorosilicate into fluoride, this would result in a [F$^-$] = 3.0 × 10^{-3} F, or 72 ppm F$^-$. Note this is approximately 50 times more concentrated than fluoridated municipal drinking water, which has a range of 1−2 ppm. This higher concentration was chosen so that any partially hydrolyzed intermediates of SiF$_6^{2-}$ might be observed above the noise level of the spectrometer. Additional solutions were prepared with excess fluoride, added as sodium fluoride from the stock solution described above.

The pH of unbuffered solutions characterized by NMR was measured by an Accumet 13-620-221 combination glass electrode/reference electrode using an Accumet AP61 pH meter. The length of time the glass electrode was in contact with the fluoride-containing solutions was minimized to reduce the effects of etching. Each pH measurement was preceded and followed by measuring the pH of Fisher certified pH buffers at pH = 4 and 7.

^{19}F NMR spectra were recorded at 376.304 MHz with a Varian INOVA spectrometer. Fluoride-containing samples were held in Wilmad PTFE−FEP copolymer NMR tube inserts within standard 5 mm NMR tubes. Typical NMR parameters were a flip angle of ∼30°, recycle delay of 0.1−4 s, and 512−1024 scans. Quantitative integrations were obtained from the resulting spectra after baseline correction for background fluorine signal from the NMR probe. Error in peak integrations, which was treated as the major source of error in the ^{19}F NMR concentration measurements, was determined from the limit of detection (concentration of fluorine at a signal-to-noise ratio of 2). Chemical shifts were determined using an external reference of trifluoroacetic acid (−78.5 ppm relative to the usual CFCl$_3$ standard). To ensure that the sensitivity of the ^{19}F NMR spectra did not vary from day-to-day the signal from the same external reference solution was quantified prior to each set of experimental solutions.

Silicomolybdate Test for Soluble Silica. The ASTM silicomolybdate test for soluble silicon (as described in ASTM Standard D 859-05) was used to approximate the concentration of Si(OH)$_4$ in hexafluorosilicate solutions prepared for NMR characterization (16). A 0.1 F silica stock solution was prepared by weighing amorphous fumed silica (Cab-O-Sil M-5, Cabot) and dissolving it in Nanopure (18 MΩ) water raised to a pH > 10 using dilute NaOH solution. A control solution of 1 × 10^{-3} F silica was prepared by dilution from the stock solution with Nanopure water. The test solutions contained 1 × 10^{-3} F hexafluorosilicate and varying concentrations of NaF in 200 mM acetic acid buffer at pH 4. An ammonium molybdate (Merck and Co.) solution was prepared with 1 g of ammonium molybdate dissolved in 10 mL of water at a pH of 7−8. Concentrated (37%) HCl was diluted 1:1 in water to produce an 18.5% HCl solution.

The test solutions were compared to the control, which contained the same total amount of silicon, using the silicomolybdate method. A volume of 1 mL of the ammonium molybdate solution was added to 2.5 mL of the control and test solutions. A volume of 0.5 mL of 18.5% HCl solution was immediately added, and the solution was mixed thoroughly. After 10 min the absorption of the solutions at 452 nm was measured relative to that of Nanopure water. This spectrophotometric method is based on the reaction of ammonium molybdate with soluble silica (Si(OH)$_4$ and possibly small oligomers) to form heteropoly acids yellow in color at low pH. Polymerized silica does not react, and no color is

observed. This method is reported to be analytically useful over a range from 0 to 75 ppm (16).

pH Determination and Modeling of Veronal/HCl, Citrate/Phosphate, and Ringer's Buffer Solutions. Veronal (sodium 5,5-diethylbarbituate)/HCl buffer was prepared at pH 7.6 and 8.6, and citric acid/sodium phosphate buffer solution was prepared at pH 7.6 using standard literature formulations for these buffers (17). Ringer's solution was prepared according to the specifications of Westendorf (12). All solutions were prepared from ACS reagent grade reagents or best available. All containers used were fluorinated high-density polyethylene. A Beckman Phi32 pH meter was used to measure pH. The electrode was a Corning 246530 combination glass electrode/reference electrode. The bottles containing each solution for measurement were brought to 37 °C in a water bath. Temperature was measured before and after each measurement.

The meter was calibrated against Fisher certified pH 4.0, 7.0, and 10.0 buffers at 37 °C. Direct measurement of temperature using a glass thermometer and direct measurement of glass electrode/reference electrode potential changes were employed in lieu of an automatic temperature compensation probe and the internal temperature compensation circuitry of the meter. Data were evaluated using the Nernst equation for 310 K (37 °C).

To solutions of each of the tested buffers solid sodium fluoride or magnesium hexafluorosilicate was added to prepare stock solutions containing 0.04 M total fluoride ion. Aliquots of each of these stock solutions were diluted by addition of the original buffer solution to yield final fluoride concentrations in the range of 0−0.04 M. Observed pH effects were compared to those predicted from calculations made using MINEQL+, v. 4.5, a program widely used in environmental science research (18). The standard equilibrium tables from the MINEQL+ database were used for all calculations. The database contains equilibrium data at 25 °C, so it was necessary to extrapolate the results to 37 °C.

Results and Discussion

^{19}**F NMR.** It was our goal to investigate the dissociation of SiF$_6^{2-}$ under conditions close to those found in municipal drinking water using ^{19}F NMR, a method capable of directly discerning and providing chemical information about the different fluorine-containing species present. Many of the previous studies of this system discussed above were limited to low pH conditions, often at much larger silicon and fluoride concentrations compared to those found in fluoridated drinking water. In this study, a moderate formal concentration of SiF$_6^{2-}$ (5 × 10^{-4} F SiF$_6^{2-}$, leading to a formal concentration of fluoride approximately 50 times that commonly added to drinking water) was used to make it possible to detect potential intermediate hydrolysis species by NMR. We began our study at acidic pH values and then extended them to pH 4 and 5 in an effort to examine the dissociation under conditions closer to those found in municipal water supplies.

The pH dependence of the ^{19}F NMR spectra of 5.0 × 10^{-4} F SiF$_6^{2-}$ solutions between pH 2 and pH 5 was investigated (Figure 1). In these spectra, fluoride and hexafluorosilicate signals were observed at total fluoride concentrations approaching 10^{-5} M. At pH 3.2 or lower a peak at −130.5 ppm is observed that is attributed to SiF$_6^{2-}$. Though the previously reported value for the chemical shift of SiF$_6^{2-}$ is −128.2 ppm, this value was observed in solutions at much higher ionic strength than those described here (19). Since ^{19}F chemical shifts are known to be sensitive to electric field effects, the observed chemical shift difference is expected (20). The hexafluorosilicate peak is not observed at pH ≥ 4 at this fluoride concentration.

A second peak is observed at −129.5 ppm in solutions with a pH < 3 along with the hexafluorosilicate peak. We
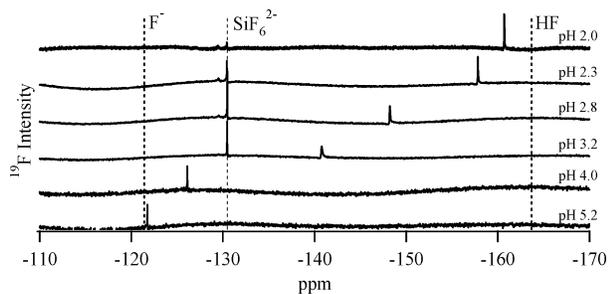
FIGURE 1. ^{19}F NMR spectra of 5×10^{-4} F SiF$_6^{2-}$ solutions at pH values between 2.0 and 5.2. Chemical shifts for the SiF$_6^{2-}$ peak, as well as the chemical shifts of pure HF and NaF, are denoted with vertical dotted lines.

assigned this peak as the hydrolysis intermediate SiF$_5$(H$_2$O)$^-$, as proposed by Kleboth in 1969 (6, 7). This species has been observed previously by ^{19}F NMR by Buslaev and Petrosyants (21). At very low temperatures (-70 °C), two fluorine NMR peaks are observed for this SiF$_5^-$(H$_2$O) for the axial (-134 ppm) and equatorial (-125.5 ppm) fluorides, respectively, in a 1:4 ratio. At room temperature these two peaks would be averaged by fast intramolecular fluoride exchange, producing a single peak at -127.2 ppm under the solution conditions used by Buslaev and Petrosyants. This value is similar to the chemical shift value of the peak we observe, as well as being similar in relative position from the reported SiF$_6^{2-}$ peak. Buslaev and Petrosyants also reported a solvated tetrafluorosilicon species that is stable in alcohol solutions (as SiF$_4$(ROH)$_2$), but is unstable in water, never exceeding 5% of the total fluorosilicate species observed in water. Therefore, the peak at -129.5 ppm was assigned as SiF$_5^-$(H$_2$O). However, the possibility of fluorosilicate species in fast exchange on the NMR time scale compels us to say that further spectroscopic characterization is required to definitively assign this peak.

In addition to the fluorosilicate species a single peak is detected for the dissociated fluoride in all spectra. The chemical shift of the dissociated fluoride peak is known to be strongly pH dependent (22). This peak corresponds to the equilibrium mixture of the F$^-$ and HF.

$$[F]_T = [F^-] + [HF] \tag{2}$$

These species equilibrate at rates faster than the NMR time scale (1–10 ms) and as a result we observe a single peak with an average chemical shift. The pure fluoride ion peak (pH = 6.6) was observed at -121.4 ppm, and the hydrofluoric acid peak (pH = 1) was observed at -164.4 ppm. These chemical shifts were observed for formal concentrations of fluoride of 3.0×10^{-3} F. Again, the relatively low ionic strength explains the subtle differences from previously reported chemical shifts of -121.5 and -166.8 ppm for F$^-$ and HF, respectively (22).

The chemical shift of the dissociated fluoride (F$^-$/HF) peak is given from the pH of the solution by the following equations.

$$\delta_{obs} = \alpha_F \delta_F + (1 - \alpha_F)\delta_{HF} \tag{3a}$$

$$\alpha_F = \frac{K_{HF}}{[H^+] + K_{HF}} \tag{3b}$$

In Figure 2 a plot of ^{19}F NMR chemical shifts for the dissociated fluoride peak in various solutions are plotted versus the pH values determined by potentiometry (glass electrode). The theoretical curve predicted by eq 3a is also shown in Figure 2. The value of the HF acid dissociation constant determined
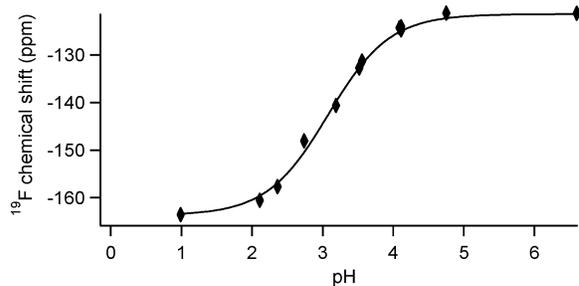
FIGURE 2. Plot of ^{19}F chemical shift observed against pH measured by potentiometry for a series of unbuffered fluoride-containing solutions with formal fluoride concentrations between 3 and 18 mF (◆). The solid line represents the analytic fit of the chemical shift vs pH data to eq 3a. Chemical shift was calibrated to CFCl$_3$ using an external reference.

from the analytic fit is p$K_{HF} = 3.08 \pm 0.02$, which is consistent with other literature values. The hydronium ion concentration, and therefore pH, of fluoride-containing solutions can therefore be determined from the ^{19}F NMR spectrum using the chemical shift of the fluoride/hydrofluoric acid peak with eq 4, while the full width at half-maximum of the NMR peak, $\sim$0.09 ppm, provides an error estimate of error$_{pH} \leq \pm0.03$ for pH values between $\sim$1.5–4. Therefore, the pH of each solution reported in this section is determined using the NMR method.

$$[H^+] = K_{HF}\left(\frac{\delta_F - \delta_{obs}}{\delta_{obs} - \delta_{HF}}\right) \tag{4}$$

In cases where peaks assigned to SiF$_6^{2-}$ and F$^-$/HF are observed in the ^{19}F NMR spectra (at pH < 4.0) the dissociation constant, K_d, can be calculated. The formal concentration of hexafluorosilicate was kept at Si$_T = 5.0 \times 10^{-4}$ F in all solutions. The formal concentration of total fluoride is therefore $F_T =$ 6Si$_T$ or 3.0×10^{-3} F. The relative peak areas observed in the ^{19}F NMR spectra of the undissociated SiF$_6^{2-}$, SiF$_5^-$, and the dissociated fluoride, as either F$^-$ or HF, were used to determine the concentrations of the species in the dissociation equilibrium according to the equations below.

$$[F]_T = F_T\frac{A_F}{A_T} \tag{5}$$

$$[SiF_6^{2-}] = \frac{1}{6}F_T\frac{A_{SiF_6^{2-}}}{A_T} \tag{6}$$

$$[SiF_5^-] = \frac{1}{5}F_T\frac{A_{SiF_5^-}}{A_T} \tag{7}$$

In the equations above A is the integrated peak area, $[F]_T$ is the concentration of dissociated fluoride (F$^-$ and HF), and F_T is the total formal fluoride concentration present in the solution. The concentration of free fluoride ion can be derived from $[F]_T$ since the pH of the solution is known.

$$[F^-] = \alpha_F[F]_T \tag{8}$$

Silicic acid is the only species not directly determined from the ^{19}F NMR spectra. It can be calculated from the silicon mass balance equation

$$[Si(OH)_4] = Si_T - [SiF_6^{2-}] - [SiF_5^-] \tag{9}$$

where Si$_T = 5.0 \times 10^{-4}$ F. This assumption neglects the possible oligomerization of silicic acid. At low pH, less than 4, it is known that acid-mediated hydrolysis of polymerized silica will oppose oligomerization (11).

TABLE 1. ^{19}F NMR Data, Fluoro-Species Concentrations, and pK_d Determined at Low pH Values[a]

	relative area[b]			concentration (mM)[c]				
pH[d]	F$^-$/HF	SiF$_6^{2-}$	SiF$_5^-$	[F$^-$][e]	[HF][f]	[SiF$_6^{2-}$][g]	[SiF$_5^-$][g]	pK_d[h]
1.96 ± 0.03	0.67	0.16	0.17	0.14 ± 0.02	1.9 ± 0.2	0.08 ± 0.03	0.10 ± 0.04	30.3 ± 0.6
2.28 ± 0.02	0.50	0.38	0.12	0.21 ± 0.03	1.3 ± 0.2	0.19 ± 0.03	0.07 ± 0.04	31.1 ± 0.6
2.84 ± 0.02	0.41	0.45	0.14	0.45 ± 0.08	0.8 ± 0.1	0.23 ± 0.03	0.09 ± 0.04	31.5 ± 0.7
3.15 ± 0.02	0.61	0.39	0	1.0 ± 0.1	0.8 ± 0.1	0.20 ± 0.04	0 ± 0.04	30.4 ± 0.7

^{a} Si$_T$ = 5.0 × 10^{-4} F for all samples. ^{b} Relative peak areas were determined by integrating the F$^-$/HF, SiF$_6^{2-}$, and SiF$_5^-$ ^{19}F NMR peak areas for each sample. ^{c} Errors in concentration values were propagated from the error in the NMR peak integration. ^{d} pH was measured by the ^{19}F NMR chemical shift of the F$^-$/HF peak according to eq 4, with the error determined as described in the text. ^{e} The concentration of F$^-$ was determined from the F$^-$/HF relative peak area and the measured pH value using eqs 5 and 8. ^{f} The concentration of HF was determined by [HF] = [F]$_T$ − [F$^-$]. ^{g} The concentrations of SiF$_6^{2-}$ and SiF$_5^-$ were determined by eqs 6 and 7, respectively. ^{h} pK_d, the negative log of the dissociation constant K_d, was determined using eq 9 to determine Si(OH)$_4$ and eq 10 for the K_d.

TABLE 2. ^{19}F NMR Data and Fluoro-Species Concentrations, Determined at pH 4 and 5 for Representative Solutions, and SiF$_6^{2-}$ Concentrations Calculated Assuming a K_d Value Consistent with Low pH Data[a]

		relative area[b]		concentration (mM)		
mF [NaF]	pH[c]	F$^-$/HF	SiF$_6^{2-}$	[F$^-$][d]	[SiF$_6^{2-}$][e]	[SiF$_6^{2-}$]$_{calc}$[f]
0	3.98 ± 0.02	1	0	2.7 ± 0.2	0	0.04
2.5	4.15 ± 0.03	1	0	5.1 ± 0.4	0	0.24
3.75	4.10 ± 0.03	0.94	0.06	5.8 ± 0.4	0.07	0.30
5	4.06 ± 0.02	0.93	0.07	6.7 ± 0.5	0.10	0.40
7.5	4.08 ± 0.02	0.92	0.08	8.8 ± 0.6	0.13	0.48
10	4.08 ± 0.02	0.91	0.09	10.8 ± 0.7	0.19	0.50
15	4.13 ± 0.03	0.96	0.04	16 ± 1	0.12	0.50
20	4.14 ± 0.03	0.96	0.04	20 ± 1	0.16	0.50
30	4.16 ± 0.03	0.97	0.03	30 ± 2	0.18	0.50
10	5.1 ± 0.2	1	0	12.9 ± 0.9	0	0.07
15	5.2 ± 0.2	1	0	18 ± 1	0	0.23
20	5.2 ± 0.2	0.96	0.04	22 ± 1	0.14	0.25
25	5.2 ± 0.2	0.97	0.03	27 ± 2	0.14	0.38
30	5.1 ± 0.2	0.97	0.03	32 ± 2	0.15	0.45

^{a} Si$_T$ = 5.0 × 10^{-4} F for all samples. ^{b} Relative peak areas were determined by integrating the F$^-$/HF and SiF$_6^{2-}$ ^{19}F NMR peak areas for each sample. ^{c} pH was measured from the ^{19}F NMR chemical shift of the F$^-$/HF peak using eq 4, with the error determined as described in the text. ^{d} The concentration of F$^-$ was determined from the F$^-$/HF relative peak area and the measured pH value using eqs 5 and 8. The error was propagated from the uncertainty in the NMR peak integration. ^{e} The concentration of SiF$_6^{2-}$ was determined by eq 6. The error was determined from the uncertainty in the NMR peak integration, and the standard deviation obtained for each value is ±3 × 10^{-5}. ^{f} [SiF$_6^{2-}$]$_{calc}$ was calculated assuming K_d = 2.4 × 10^{-31} and full availability of all silicon present in each sample.

The K_d for the equilibrium reaction given in 2b can now be calculated using the concentrations of species derived from the NMR data in eqs 5−9.

$$K_d = \frac{[\text{Si(OH)}_4][\text{H}^+]^4[\text{F}^-]^6}{[\text{SiF}_6^{2-}]} \quad (10)$$

The dissociation constants for SiF$_6^{2-}$ were calculated from the ^{19}F NMR peak areas for a series of solutions prepared at low pH values (Table 1). The large standard deviations reported are primarily due to the high relative error in the SiF$_6^{2-}$ and Si(OH)$_4$ determinations due to the relatively low Si$_T$ concentration of the solutions. The experimental values of the SiF$_6^{2-}$ dissociation constant K_d reported here, average pK_d (negative log K_d) = 30.6, are consistent with the values previously reported by other authors and tabulated by Gmelin (23). We did not attempt to determine the equilibrium constant for the intermediate hydrolysis step, SiF$_6^{2-}$ to SiF$_5^-$.

SiF$_6^{2-}$ is not observed by ^{19}F NMR at pH higher than 3.2 for 5 × 10^{-4} F SiF$_6^{2-}$ solutions. To extend this investigation to higher pH excess fluoride was added as NaF to hexafluorosilicate solutions at pH 4 or pH 5. The ^{19}F NMR spectra obtained for a series of pH 4.0 solutions (0.1 M buffer strength) containing varying amounts of NaF are shown in Figure 3. A similar series of spectra was collected for solutions at pH 5 (data not shown). The major peak in all spectra is the F$^-$/HF peak, which appears at a chemical shift of −124.9 ppm. At the higher fluoride concentrations the SiF$_6^{2-}$ species is
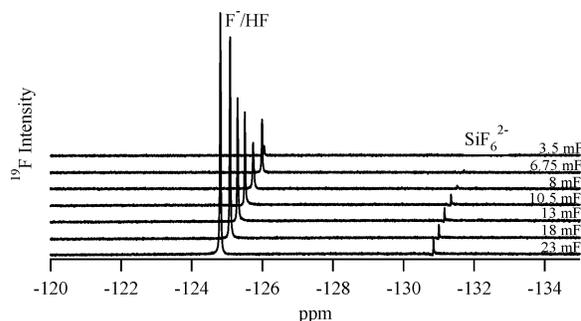
FIGURE 3. ^{19}F NMR spectra of a series of solutions containing 5 × 10^{-4} F silicon and varying excess fluoride formal concentrations. Total fluoride formal concentrations are indicated at the right edge of each plot. The pH of all solutions was ∼4, and the acetic acid/acetate buffer concentration was 100 mM in all cases except the 3.5 mF solution, which had a 50 mM buffer concentration.

observed as a minor peak at approximately −130.8 ppm. No other fluorosilicate species is observed.

The ^{19}F NMR spectra shown in Figure 3 reveal a consistently lower amount of SiF$_6^{2-}$ than would be expected from the equilibrium constants obtained for solutions at pH < 3.5. Table 2 reports the NMR integration results at pH values of 4 and 5 for the SiF$_6^{2-}$ and the F$^-$/HF signals along with the amount of SiF$_6^{2-}$ expected assuming an equilibrium constant of 2.4 × 10^{-31}, the average K_d value obtained under low pH conditions. The observed SiF$_6^{2-}$ is consistently below the

expected value in all cases, and at large formal concentrations of fluoride this value appears to level off, undergoing no further significant changes with added fluoride.

One explanation for the low SiF_6^{2-} concentrations at pH 4 and 5 is that the total amount of silicon participating in the equilibrium reaction was reduced by polymerization of silicic acid to form colloidal silica. The formation of colloidal silica is known to be pH dependent. Mechanisms for both acid- and base-catalyzed depolymerization occur at pH < 4 and pH > 10, but near neutral pH values colloidal silica is quite stable (*11*). This effect may be exacerbated by the preparation of our solutions from a stock solution of H_2SiF_6 ~400 times more concentrated in silicon than our final solutions.

To test this hypothesis, the silicomolybdate test for soluble silicon was performed on SiF_6^{2-} solutions prepared from the same stock solution used to prepare the ^{19}F NMR samples. Solutions of 1×10^{-3} F SiF_6^{2-} at pH 4, with and without 15 mM NaF added, were compared to a control solution of 1×10^{-3} M fumed silica. The hexafluorosilicate solutions gave identical responses, within 1 standard deviation of each other, yielding $16 \pm 2\%$ of the heteropoly acid formation of the control solution. There was no significant difference between the solution with excess fluoride added and the one without, suggesting that SiF_6^{2-} formation does not significantly affect the results of the silicomolybdate test. This result confirms that a significant portion of the silicon present in these pH 4 solutions is not soluble and is therefore not available to participate in the hexafluorosilicate dissociation equilibrium.

The precise fate of silicon as a dissociation product might prove useful for examining this problem further. Several fluorosilicate intermediates have been observed in acidic solutions using ^{29}Si NMR (*24*). However, the NMR sensitivity of [29]Si is approximately 4×10^{-4} that of ^{19}F due to the low natural abundance of [29]Si and lower magnetogyric ratio. The detection limit of ^{29}Si NMR in solution, recently reviewed by Knight and Kinrade (*25*), is 800 ppm silicon at 9.3T. This means that in order to see possible minor intermediates we would have to use approximately 0.25 M Si_T, 1×10^4 times more concentrated than the hexafluorosilicate levels in fluoridated municipal water.

The results of this ^{19}F NMR study confirm the importance of studying the hydrolysis of hexafluorosilicate ion under different conditions to fully characterize the behavior of this system. While our results at low pH values (<3.5) are in good agreement with previous studies and confirm the presence of a hydrolysis intermediate consistent with the pentafluorosilicate ion, very different results were obtained from investigation of solutions at pH 4 or higher. No fluorosilicate intermediates were observed, even under conditions of excess fluoride ion added. In addition, silica polymerization at moderate pH removed silicon from this equilibrium process, resulting in a greater proportion of dissociated fluoride at moderate pH than expected from previously reported values of the dissociation constant. The results of this study do not contradict previous findings that at pH ~ 7 and at typical drinking water formal fluoride concentration, hexafluorosilicate dissociation to produce free fluoride ions will be essentially complete.

pH Behavior of Veronal and Citrate/Phosphate Buffers. Westendorf's proposed hydrolysis intermediates have been a source of concern for some advocacy groups. In an attempt to account for the differences between our NMR findings and Westendorf's potentiometry results, we measured the pH changes caused by addition of NaF and MgSiF₆ to citrate/phosphate buffers, veronal/HCl buffer, and Ringer's solution. These buffers were used by Westendorf in his work describing the inhibition of acetylcholinesterase in the presence of magnesium hexafluorosilicate and are commonly used by biochemists to mimic biological systems. In both the veronal and citrate/phosphate buffers, the concentrations of the acids
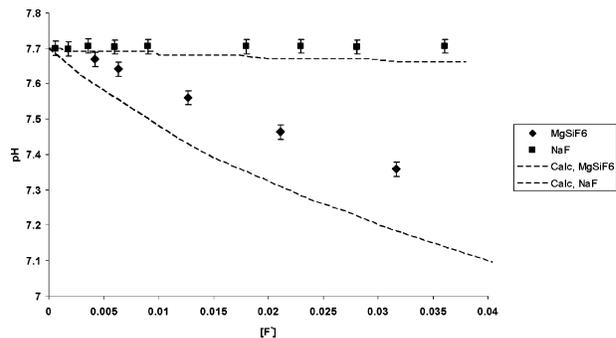
FIGURE 4. Measured (points) and calculated (dotted lines) pH values of citrate/phosphate buffer upon addition of fluoride in the form of sodium fluoride and magnesium hexafluorosilicate.
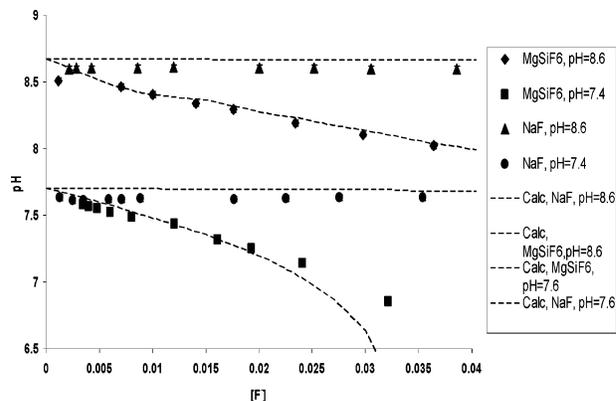
FIGURE 5. Measured (points) and calculated (dotted lines) pH values of veronal/HCl buffer upon addition of fluoride in the form of sodium fluoride and magnesium hexafluorosilicate.
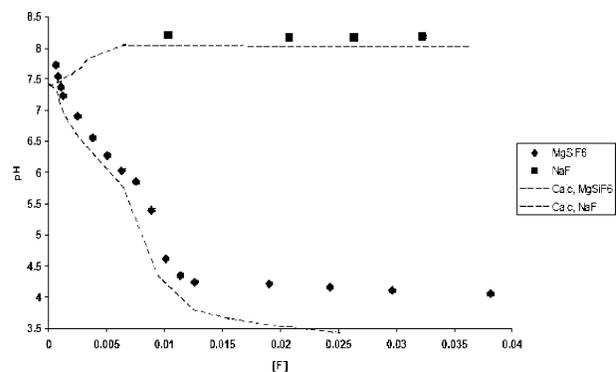
FIGURE 6. Measured (points) and calculated (dotted lines) pH values of Ringer's solution upon addition of fluoride in the form of sodium fluoride and magnesium hexafluorosilicate.

and their conjugate bases are high compared to the concentrations of reactants in typical biochemical studies. Ringer's solution is not truly a buffer but is instead a formulation that approximates the electrolyte composition of human blood. The types and concentrations of additives in Ringer's solution can vary across researchers. We monitored the pH effects in Westendorf's formulation (*12*) in order to test Urbansky's suggestion that the buffer capacity may not have been adequate to ensure that the pH remained constant (*10*).

The results of our study are shown in Figures 4−6. In each system the results were compared to calculations performed in MINEQL+. All equilibria included in the MINEQL+ calculations are given in Supporting Information Table 1. As hexafluorosilicate is added, the pHs of the buffered solutions are lowered. The changes are smallest in the citrate/phosphate buffer and largest in Ringer's solution. By contrast,

the pH remains constant or increases slightly upon addition of sodium fluoride. Note that, in all but one case, MINEQL+ accurately predicted the pH changes to within 0.1 pH unit. Only in the Ringer's solution at high fluoride concentrations did the MINEQL+ calculation diverge from the observed values.

Our studies show that all three of the buffers have inadequate buffer capacities to maintain constant pH in the presence of hexafluorosilicate. While Westendorf understood that the dissociation of hexafluorosilicate would cause an acidic change in pH, his analysis did not account for the magnitude of this effect in these commonly employed buffers. The descriptions of his research do not say that he actually measured the pH of his buffer solutions, although the measurement protocols for fluoride ion potentiometry are described in detail in his dissertation.

Westendorf's studies demonstrated that HF, rather than F^-, is the active inhibitor of acetylcholinesterase. He attributed continued inhibition in the presence of hexafluorosilicate to undissociated intermediates as he assumed a constant pH and, thus, a constant ratio of HF/F^- concentrations. However, our data indicate that Westendorf's solutions had inadequate buffer capacity to maintain a constant pH in the presence of hexafluorosilicate. The addition of magnesium hexafluorosilicate causes a decrease in pH and a resultant shift in equilibrium from F^- to HF. This simple change in pH can explain the observed inhibition of the enzyme in the presence of magnesium hexafluorosilicate. Westendorf's findings must be reinterpreted in light of these new data.

Acknowledgments

Supporting Information Available

Supporting Information Table 1 containing aqueous species equilibria and formation constants considered in the MINEQL+ calculations of addition of NaF or MgSiF$_6$ to buffer solutions used by Westendorf; Supporting Information Table 2 containing solid and gaseous species equilibria and formation constants considered in the MINEQL+ calculations of addition of NaF or MgSiF$_6$ to buffer solutions used by Westendorf. This material is available free of charge via the Internet at http://pubs.acs.org.

Literature Cited

(1) *Water Fluoridation A Manual for Engineers and Technicians*; U.S. Department of Health and Human Services: Atlanta, GA, 1986.

(2) Coplan, M. J.; Masters, R. D. Silicofluorides and fluoridation. *Fluoride* **2001**, *34* (3), 161−164.

(3) Masters, R. D.; Coplan, M. J.; Hone, B. T.; Dykes, J. E. Association of silicofluoride-treated water with elevated blood lead. *Neurotoxicology* **2000**, *21* (6), 1091−1100.

(4) Rees, A. G.; Hudleston, L. J. The decomposition of the fluorosilicate ion in aqueous and in aqueous salt solutions. *J. Chem. Soc.* **1936**, 1334−1338.

(5) Busey, R. H.; Schwartz, E.; Mesmer, R. E. Fluorosilicate equilibria in sodium chloride solutions from 0 to 60 °C. *Inorg. Chem.* **1980**, *19*, 758−761.

(6) Kleboth, K. Fluoro complexes of silicon in aqueous solution. II. Formation and properties of tetrafluorosilicic acid. *Monatsh. Chem.* **1969**, *100* (3), 1057−1068.

(7) Kleboth, K. Theory of the distillation of fluorine as fluorsilicic acid. *Monatsh. Chem.* **1969**, *100* (3), 1494−1498.

(8) Ciavatta, L.; Iuliano, M.; Porto, R. Fluorosilicate equilibria in acid solution. *Polyhedron* **1988**, *7* (18), 1773−1779.

(9) Urbansky, E. T.; Schock, M. R. Can fluoridation affect lead(II) in potable water? Hexafluorosilicate and fluoride equilibria in aqueous solution. *Int. J. Environ. Stud.* **2000**, *57* (5), 597−637.

(10) Urbansky, E. T. Fate of fluorosilicate drinking water additives. *Chem. Rev.* **2002**, *102* (8), 2837−2853.

(11) Iler, R. K. *The Chemistry of Silica: Solubility, Polymerization, Colloid and Surface Properties, and Biochemistry*; Wiley: New York, 1979.

(12) Westendorf, J. The Kinetics of Acetylcholinesterase Inhibition and the Influence of Fluoride and Fluoride Complexes on the Permeability of Erythrocyte Membranes. Doctoral Dissertation, University of Hamburg, Hamburg, Germany, 1975.

(13) Knappwost, A.; Westendorf, J. Hemmung von cholinesterasen durch fluorokomplexe des siliciums und des eisens. *Naturwissenschaften* **1974**, *61*, 275.

(14) Knappwost, A.; Westendorf, J. Zur hemmung der acetylcholinesterase durch fluroid. *Naturwissenschaften* **1974**, *61*, 274−275.

(15) Knappwost, A.; Westendorf, J. Fluroionen-aufnahme und vagotonie. *Naturwissenschaften* **1973**, *60*, 353−354.

(16) Neofotistou, E.; Demadis, K. D. Use of antiscalants for mitigation of silica (SiO$_2$) fouling and deposition: fundamentals and applications in desalination systems. *Desalination* **2004**, *167*, 257−272.

(17) Dean, J. A. *Lange's Handbook of Chemistry*, 13th ed.; McGraw-Hill Book Company: New York, 1985.

(18) Schecher, W. D.; McAvoy, D. C. MINEQL+: A software environment for chemical equilibrium modeling. *Comput. Environ. Urban Syst.* **1992**, *16* (1), 65−76.

(19) Connick, R. E.; Poulson, R. E. F-19 nuclear magnetic resonance of various metal−fluoride complexes in aqueous solution. *J. Phys. Chem.* **1959**, *63* (4), 568−569.

(20) Saika, A.; Slichter, C. P. A note on the fluorine resonance shifts. *J. Chem. Phys.* **1954**, *22*, 26.

(21) Buslaev, Y. V.; Petrosyants, S. P. Composition of fluoro complexes of aluminum and fluosilicic acid in aqueous solutions. *Sov. J. Coord. Chem. (Engl. Trans.)* **1980**, *5* (2), 123−129.

(22) Bodor, A.; Toth, I.; Banyai, I.; Szabo, Z.; Hefter, G. T. 19F NMR Study of the equilibria and dynamics of the Al3$^+$/F$^-$ system. *Inorg. Chem.* **2000**, *39*, 2530−2537.

(23) *H2SiF6*, 8th ed.; Springer-Verlag: New York, 1995; Vol. Supplement B8.

(24) Axon, S. A.; Klinowski, J. Nuclear-magnetic-resonance studies of the synthesis of silicalite by the fluoride method. *J. Chem. Soc., Faraday Trans.* **1993**, *89* (23), 4245−4248.

(25) Knight, C. T. G.; Kinrade, S. D. Silicon-29 nuclear magnetic resonance spectroscopy detection limits. *Anal. Chem.* **1999**, *71* (1), 265−267.