Determination of Stability Constants of Stannous Fluoride Complexes by Potentiostatic Titration

K. G. NELSON [x] **and K. N. AMIN** *

Abstract □ The stability constants for stannous fluoride complexes were determined by potentiostatic titration. The method involves incremental additions of fluoride wherein each addition is followed by titration with stannous such that there is no change in the electromotive force developed between the fluoride ion and the reference electrodes. The values obtained were $\beta_1 = 4 \times 10^3$, $\beta_2 = 1.1 \times 10^7$, and $\beta_3 = 1 \times 10^9$. The results of this work suggest that the potentiostatic method would be useful for determining stability constants in complexation systems involving an ion for which a specific ion electrode is available.

Keyphrases □ Stannous fluoride complexes—determination of stability constants, potentiostatic titration □ Titration, potentiostatic—determination of stability constants of stannous fluoride □ Stability constants—stannous fluoride complexes, potentiostatic titration

Stannous fluoride is well recognized as a topically applied anticaries agent. Past work (1–3) has demonstrated that the various products formed from the reaction of stannous fluoride and hydroxyapatite are $Sn_3F_3PO_4$, $Sn_4(PO_4)_2(OH)_2 \cdot H_2O$, $SnHPO_4$, and CaF_2, depending on the experimental conditions. A thorough description of the solution chemistry of stannous fluoride is needed for an understanding of the reactions and for the construction of stability fields for this system.

DISCUSSION

Stannous ion forms three soluble complexes with fluoride in aqueous solution. The stoichiometry of these complexes is SnF^+, SnF_2, and SnF_3^-. Their stability constants have been determined by potentiometric titration (4) and by polarography (5), but there are wide discrepancies in the reported values.

Kankare (6) recently reported a novel potentiostatic technique for determining dissociation constants of weak acids (or bases). Briefly, this method involves the titration of incremental increases of the weak acid with a strong base such that the electromotive force of the glass–reference electrode system remains constant. This procedure permits certain mathematical simplifications in data analysis and circumvents problems associated with the liquid junction potential and non-Nernstian electrode response. The potentiostatic technique could be useful for studying equilibria in systems containing an ion for which there exists a specific ion electrode.

The purposes of this study were: *(a)* to provide a set of stability constants for the stannous fluoride complexes to help clarify the discrepancy in reported values, and *(b)* to demonstrate the applicability of the potentiostatic technique to the study of a metal-ion complex system.

THEORETICAL

In an aqueous solution of pH 4 or below containing stannous and fluoride ions, the equilibria shown in Scheme I prevail.

$$Sn^{+2} + iF^- \rightleftharpoons SnF_i^{(2-i)} \qquad i = 1,2,3$$

Scheme I

The corresponding complexation stability constants are:

$$\beta_i = \frac{[SnF_i^{(2-i)}]}{[Sn^{+2}][F^-]^i} \qquad \text{(Eq. 1)}$$

There are two additional equilibria involving fluoride ions (Scheme II).

$$HF \rightleftharpoons H^+ + F^- \qquad K_{HF} = \frac{[H^+][F^-]}{[HF]}$$

$$HF_2^- \rightleftharpoons HF + F^- \qquad K_{HF_2} = \frac{[HF][F^-]}{[HF_2^-]}$$

Scheme II

Let the total amount (in moles) of stannous be s, the total amount of the fluoride be f, and the volume be V. Then the mass balance equations are as follows:

$$\frac{f}{V} = \sum_{i=1}^{3} i\beta_i[Sn^{+2}][F^-]^i + [F^-] + [HF] + 2[HF_2^-] \qquad \text{(Eq. 2)}$$

$$\frac{s}{V} = \sum_{i=1}^{3} \beta_i[Sn^{+2}][F^-]^i + [Sn^{+2}] \qquad \text{(Eq. 3)}$$

Rearranging Eq. 2 and dividing by Eq. 3 give:

$$Z = \frac{f - V\left[[F^-] + \frac{[F^-][H^+]}{K_{HF}} + \frac{2[F^-]^2[H^+]}{K_{HF}K_{HF_2}}\right]}{s} = \frac{\sum_{i=1}^{3} i\beta_i[F^-]^i}{1 + \sum_{i=1}^{3} \beta_i[F^-]^i} \qquad \text{(Eq. 4)}$$

where z may be considered the degree of complexation of fluoride with stannous.

Rearrangement of Eq. 4 gives:

$$f = sZ + V\left[[F^-] + \frac{[H^+][F^-]}{K_{HF}} + \frac{2[H^+][F^-]^2}{K_{HF}K_{HF_2}}\right] \qquad \text{(Eq. 5)}$$

At constant fluoride-ion and hydrogen-ion concentrations, the unique condition for a potentiostatic titration, Eq. 5 predicts a linear relationship between f and s. A modification of this expression is necessary, however, due to the increase in V during the titration. At any time during the titration:

$$V = V_0 + \frac{s}{C_s} + \frac{f}{C_f} \qquad \text{(Eq. 6)}$$

where V_0 is the initial volume, and C_s and C_f are the concentrations of the stannous and fluoride titrant solutions, respectively. By substituting Eq. 6 into Eq. 5 and letting:

$$X = [F^-] + \frac{[F^-][H^+]}{K_{HF}} + \frac{2[F^-]^2[H^+]}{K_{HF}K_{HF_2}} \qquad \text{(Eq. 7)}$$

the following equation can be obtained:

$$f = s\frac{Z + X/C_s}{1 - (X/C_f)} + \frac{V_0X}{1 - (X/C_f)} \qquad \text{(Eq. 8)}$$

Table I—Potentiostatic Data

Experiment	pH	Fluoride, moles × 10^5				Stannous, moles × 10^5			m	r^a
		f_0	f_1	f_2	f_3	s_1	s_2	s_3		
1	3.22	1.0	11.04	5.0	8.97	12.103	6.0611	10.9	0.8261	0.99999
2	3.24	1.75	10.0	5.21	—	9.0976	4.3604	—	1.1255	0.99980
3	3.26	2.5	10.01	5.01	7.41	6.98	3.58	5.405	1.4058	0.99993
4	3.30	4.0	10.0	5.0	6.07	6.275	2.991	3.624	1.6335	0.99990
5	3.38	6.0	10.0	5.13	3.89	5.411	2.818	2.006	1.8527	0.99996
6	3.46	8.0	10.0	7.2	—	4.73	3.50	—	2.0912	0.99997
7	3.53	10.0	10.0	5.0	—	4.734	2.266	—	2.1382	0.99994
8	3.62	14.0	6.13	—	—	2.723	—	—	2.251	—

[a] Correlation coefficient.

Table II—Stability Constants for Stannous Fluoride Complexes at 25°

Sources	Methods	Ionic Strength	β_1	β_2	β_3
Hall–Slater (4)	Potentiometric	0.85[a]	1.80×10^6	5.79×10^8	1.77×10^9
Bond–Taylor (5)	Polarographic	1.00[a]	1.0×10^4	7.0×10^6	2.70×10^9
This work	Potentiostatic	0.10	4.0×10^3	1.1×10^7	1.0×10^9

[a] Sodium perchlorate.

which is of the linear form:

$$f = sm + b \qquad \text{(Eq. 9)}$$

Plotting fluoride consumption *versus* stannous consumption for the potentiostatic titration directly gives m = slope and b = intercept, from which X and Z can be easily calculated. Since pH can be obtained experimentally and K_{HF} and K_{HF_2} are reported constants, fluoride concentration, $[F^-]$, can be calculated from X by Eq. 7. Sets of Z and $[F^-]$ are thus obtained from potentiostatic titrations and are used to calculate the stability constants through a rearrangement of Eq. 4:

$$Z = \sum_{i=1}^{3} (i - Z)[F^-]^i \beta_i \qquad \text{(Eq. 10)}$$

EXPERIMENTAL

Materials and Apparatus—The source of fluoride was a standard solution[1] containing 0.1 ± 0.0005 mole of sodium fluoride/liter. Stannous sulfate was prepared by the method described by Donaldson and Moser (7). The remaining chemicals were reagent grade and were used without further purification except potassium dichromate, which was recrystallized twice from water. All solutions were prepared using boiled, double-distilled water stored under a nitrogen atmosphere.

A potentiometric titrator[2] was used as a null-point detector for the potentiostatic titration, as a pH meter, and as a potentiometer for the stannous analysis. For these applications a fluoride-ion electrode[3], a glass electrode[4], and a platinum electrode[5], respectively, were used in conjunction with a silver–silver chloride low leak reference electrode[6]. The titration vessel consisted of a 50-ml capacity plastic beaker[7], which was maintained at 25° with a constant-temperature water bath[8].

The stannous sulfate solution was delivered with a micrometer syringe[9] or an ultraprecision micrometer buret[10]. An automatic buret[11] was used for dispensing the fluoride and potassium dichromate solutions and was capable of delivering 1-μl volumes. The micrometer buret and syringe volumes could be read with an accuracy of 0.1 μl. A Teflon-coated stirring bar and a magnetic stirrer[12] were used to agitate the solution.

Method—A 25-ml volume of the titration medium, consisting of 0.03333 M sodium sulfate and 0.005% concentrated sulfuric acid, was pipetted into the titration vessel. A continuous flow of nitrogen was maintained over the solution. A small, accurately known amount of fluoride, f_0, was added and the potential was allowed to stabilize. The end-point for the titration was set at this potential on the titrator.

Aliquots of the fluoride solution were then added corresponding to amounts f_1, f_2, and f_3. Each addition of fluoride was followed by a titration back to the adjusted end-point with corresponding amounts of stannous s_1, s_2, and s_3. The stannous sulfate solution was freshly prepared for each experiment by dissolving 400 mg in 2 ml of water and filtering through a membrane[13] filter of 0.22-μm pore size. After each experiment the titration mixture was subjected to stannous analysis by the method of Collins and Nebergall (8) to ensure that the amount of stannous present would be accurately known.

The pH was monitored by means of a duplicate experiment. It was determined after the initial fluoride addition and at the completion of the titration. There was no noticeable or measurable change in pH.

RESULTS

The data obtained from the potentiostatic titrations (Table I) were processed by performing a least-squares calculation on the cumulative additions of fluoride and stannous. The linearity predicted by theory (Eq. 8) is quite satisfactory as displayed by the correlation coefficients. The slopes and intercepts (f_0) shown were used to determine sets of Z and $[F^-]$ by means of Eqs. 7–9 and using $K_{HF_2} = 2.59 \times 10^{-1}$ (9) and $K_{HF} = 9.312 \times 10^{-4}$ (10).

To determine the concentration stability constants from the sets of Z and $[F^-]$, it was first assumed for experiments 1–3 that $[SnF_3^-]$ was sufficiently small that it could be ignored. Values for β_1 and β_2 were then calculated by solving simultaneous equations (i = 1, 2 in Eq. 10). This value of β_1 was used in a modified Leden's method (11) to get a better estimate for β_2. The procedure involved plotting $\log [Z - (1 - Z)\beta_1]/(2 - Z)$ *versus* $\log [F^-]$ for the data of experiments 1–4. If the $[SnF_3^-]$ is sufficiently low, this plot should have a slope of two. Such was the case so that the intercept was used to obtain the better estimate of β_2. By using β_1 and β_2, the method of Leden was used to determine β_3. The stability constants

[1] Orion Catalog No. 94-09-06, Orion Research Inc., Cambridge, Mass.
[2] Radiometer TTTlc, Radiometer A/S, Copenhagen, Denmark.
[3] Model 94-09A, Orion Research Inc., Cambridge, Mass.
[4] pH electrode No. 39301, Beckman Instruments, Inc., Fullerton, Calif.
[5] Beckman Instruments, Inc., Fullerton, Calif.
[6] Perma probe solid-state reference electrode No. 39406, Beckman Instruments, Inc., Fullerton, Calif.
[7] TPX, No. 1203, Nalgene Labware, Rochester, N.Y.
[8] Model FK, Haake Instruments, Inc., Rochelle Park, N.J.
[9] Agla, Burroughs Wellcome & Co., London, England.
[10] Catalog No. 7876, Roger Gilmont Instruments, Inc., Great Neck, N.Y.
[11] ABU 1B, B150, Radiometer A/S, Copenhagen, Denmark.
[12] Sargent-Welch Scientific Co., Skokie, Ill.
[13] GSWP 013, Millipore Corp., Bedford, Mass.

Table III—Comparison of Calculated and Experimental Values of Z

Experimental	Calculated
0.822	0.826
1.117	1.213
1.391	1.426
1.607	1.684
1.808	1.872
2.025	1.988
2.055	2.069
2.132	2.184

obtained along with those reported in the literature are given in Table II.

It can be seen that there is wide discrepancy in the reported stability constant for SnF^+. The reported value (4) was determined by regression analysis. In a review article, Bond (12) cautioned against applying statistical analysis of complexation data without appropriate weighing of the data relative to the known chemistry of the system. Using Leden's method, Bond calculated the following stability constants from the data of Hall and Slater (4): $\beta_1 = 3 \times 10^4$, $\beta_2 = 1.5 \times 10^8$, and $\beta_3 = 2 \times 10^{10}$. Thus, the new β_1 is in closer agreement with the value reported by Bond and Taylor (5), but they expressed uncertainty in their reported value because of curvature in their Leden plot.

The agreement in reported values of β_3 is satisfactory considering the differences in experimental methods, computational analyses, and ionic strengths. The β_2 values reported range over two orders of magnitude, with the one determined in this work occupying an intermediate position. If the values are transformed to association constants for the sequential reaction shown in Scheme III, then the respective constants for the current work would be 4×10^3, 2.75×10^3, and 9.09×10^1.

$$SnF_{i-1}^{(3-i)} + F^- \rightleftharpoons SnF_i^{(2-i)} \qquad i = 1, 2, 3$$

Scheme III

The respective constants of Bond and Taylor (5) would be 1.2×10^4, 4×10^2, and 6.02×10^2. It can be seen that the latter values are not sequentially in order, which is physically unrealistic.

To assess whether stability constants are satisfactory, it has been suggested that a point-by-point comparison be made between experimental and calculated values (12). Such a comparison is shown in Table III. The stability constants reported in this work are quite satisfactory by this criterion and give a much better fit than if other reported sets of β are used.

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* Present address: College of Pharmacy, Howard University, Washington, DC 20001

[x] To whom inquiries should be directed.

Dehydration of Tetracycline

K. D. SCHLECHT *[x] **and C. W. FRANK** [‡]

Abstract □ The dehydration of tetracycline at the C-5a–C-6 position as a function of acidity was investigated at various temperatures. The rate was first order with respect to tetracycline and with respect to $[H^+]$. Rate constants and an activation energy are reported. Tetracycline was unstable in dilute acid.

Keyphrases □ Tetracycline—dehydration kinetics, effect of acidity at various temperatures □ Dehydration kinetics—tetracycline, effects of acidity at various temperatures □ Stability—tetracycline, dehydration, effects of acidity at various temperatures

Tetracyclines have been subjected to numerous reactions to aid in elucidating their structures; one reaction involves dehydration at the C-5a–C-6 position in the presence of warm mineral acids (1–4). When tetracycline [4-(dimethylamino)-1,4,4a,5,5a,6,11,12a-octahydro-3,6,10,12,12a-pentahydroxy-6-methyl-1,11-dioxo-2-naphthacenecarboxamide] (I) is dehydrated, anhydrotetracycline [4-(dimethylamino)-1,4,4a,5,12,12a-hexahydro-3,10,11,12a-tetrahydroxy-6-methyl-1,12-dioxo-2-naphthacenecarboxamide] (II) is formed; II has aromatic character in both the C- and D-rings.

The benzylic C-6 position of I has a tertiary hydroxyl, which is *trans* to the adjacent C-5aH, thereby making the hydroxyl very acid labile and anhydro formation an easy process. Recently, the ease of anhydro formation has been used in the analysis of tetracyclines. Generally, I and its main degradation products [II, 4-epitetracycline (III), and 4-epianhydrotetracycline (IV)] can be separated by TLC, treat-