Reversible and Irreversible ElcB Mechanisms in the Hydrolysis of 2,2,2-Trifluoroethanesulfonyl Chloride: Carbanion Intermediates in Aqueous Acid[1]

James F. King* and Manjinder Singh Gill

Department of Chemistry, The University of Western Ontario, London, Ontario, Canada N6A 5B7

Received October 10, 1997

Hydrolysis of 2,2,2-trifluoroethanesulfonyl chloride (**1**) is shown to take place by way of the sulfene ($CF_3CH{=}SO_2$), formed by (a) an irreversible E1cB process over the pH range 1.8−5 with water acting as the carbanion-forming base in the lower pH range and hydroxide anion at higher pH, and (b) a reversible E1cB reaction in dilute acid.

Introduction

Current understanding of the mechanisms of the hydrolysis of alkanesulfonyl chlorides may be summarized by first describing the following accepted picture for the hydrolysis of methanesulfonyl chloride.[2,3] (a) In the pH range ~1 to 6.7, the reaction is a direct nucleophilic displacement by attack of water on the sulfonyl sulfur atom with extrusion of chloride anion (S_N2-S reaction). (b) In the pH range 6.7 to 11.8 the hydrolysis involves a rate-determining hydroxide-promoted elimination of HCl (probably E2) to form sulfene ($CH_2{=}SO_2$) which is then quickly trapped by water. (c) Above pH 11.8 similar formation of the sulfene is followed by very fast trapping of the sulfene by hydroxide anion. Except for the transition pH ranges immediately around either pH 6.7 or 11.8 (in which both competing processes are, of course, observed) only one process is in evidence, i.e., there is no significant competition by minor pathways.[3] Most simple alkanesulfonyl chlorides, including ethane- and butanesulfonyl chlorides, phenylmethanesulfonyl chloride, 2-methoxyethanesulfonyl chloride,[3] and even cyclopropanesulfonyl chloride[4] show essentially the same mechanisms. A variation of this mechanism in the form of a reversible E1cB mechanism leading to the sulfene has been put forward for the hydrolysis of dichloromethanesulfonyl chloride.[5]

There are exceptions to the above picture. 2-Hydroxyethanesulfonyl chloride, for example, reacts principally by way of β-sultone with no sign of sulfene formation.[6] Ethenesulfonyl chloride gives no indication of the cumulated sulfene ($CH_2{=}C{=}SO_2$) and reacts with hydroxide anion mostly by direct attack on the sulfur with a small portion of vinylogous nucleophilic attack to form hydroxymethylsulfene ($HOCH_2CH{=}SO_2$).[7] (Trimethylsilyl)methanesulfonyl chloride, on the other hand, reacts with water exclusively by attack at the silicon to form sulfene, and with hydroxide by both silicophilic attack to form sulfene and by elimination of HCl to give trimethylsilylsulfene ($Me_3SiCH{=}SO_2$).[8] 2-Methyl-2-propanesulfonyl chloride, the simplest tertiary alkanesulfonyl chloride, evidently hydrolyzes[9] entirely by way of the *tert*-butyl cation over the pH range 1−13.

In light of the variety of mechanisms displayed in the hydrolysis of sulfonyl chlorides it was not possible to predict with any measure of certainty how the hydrolysis of 2,2,2-trifluoroethanesulfonyl chloride ("tresyl" chloride, **1**) might proceed, and as part of our general study of sulfonyl transfer mechanisms[3−4,6−8] we decided to look at the hydrolysis of **1**.[10]

Results and Discussion

Hydrolysis of **1**, though too fast for our apparatus at 25 °C, was conveniently followed by pH-stat at 1 °C. The observed pH-rate profile for the reaction in 0.05 M KCl, which is shown in Figure 1, has the familiar "hockey stick" shape found with the hydrolyses of the simple alkanesulfonyl chlorides, and which corresponds to the rate law $k_{obs} = k_w + k_{OH}[OH^-]$. A sample of tresyl-1,1-d_2 chloride (**6**), was prepared as in Scheme 1. The pH-rate profile for **6**, also given in Figure 1, shows the same shape but with a new feature, namely a kinetic isotope effect for k_w as well as k_{OH}. For **1**, $k_w = 3.3 \times 10^{-3}$, whereas for **6**, $k_w = 1.50 \times 10^{-3}$ s^{-1}, $(k_w)_H/(k_w)_D = 2.2$; similarly for **1**, $k_{OH} = 1.75 \times 10^7$, and for **6**, $k_{OH} = 3.4 \times 10^6$ M^{-1} s^{-1}, and $(k_{OH})_H/(k_{OH})_D = 5.4$.

In the reactions of the simplest alkanesulfonyl chlorides a sizable primary kinetic isotope effect (KIE) was observed for k_{OH}, but there was no KIE for the k_w term, in accord with the proposed mechanism. It should also be noted that the rate constants for **1** are faster than the

* Corresponding author: Telephone 519-679-2111 ext 6348; Fax 519-661-3022; e-mail scijfk@uwoadmin.uwo.ca

(1) Organic sulfur mechanisms. 42. Part 41: King, J. F.; Yuyitung, G.; Gill, M. S.; Stewart, J. C.; Payne, N. C. *Can. J. Chem.*, in press.

(2) (a) Gordon, I. M.; Maskill, H.; Ruasse, M. F. *Chem. Soc. Rev.* **1989**, 123−151. (b) Kice, J. L. *Adv. Phys. Org. Chem.* **1980**, *17*, 65−181.

(3) King, J. F.; Lam, J. Y. L.; Skonieczny, S. *J. Am. Chem. Soc.* **1992**, *114*, 1743−1749.

(4) King, J. F.; Lam, J. Y. L.; Ferrazzi, G. *J. Org. Chem.* **1993**, *58*, 1128−1135.

(5) Seifert, R.; Zbirovský, M.; Sauer, M. *Collect. Czech. Chem. Commun.* **1973**, *38*, 2477−2483.

(6) King, J. F.; Khemani, K. C. *Can. J. Chem.* **1989**, *67*, 2162−2172.

(7) King, J. F.; Hillhouse, J. H.; Skonieczny, S. *Can. J. Chem.* **1984**, *62*, 1977−1995.

(8) King, J. F.; Lam, J. Y. L. *J. Org. Chem.* **1993**, *58*, 3429−3434.

(9) King, J. F.; Lam, J. Y. L.; Dave, V. *J. Org. Chem.* **1995**, *60*, 2831−2834.

(10) Part of the work reported in this paper has been presented in preliminary form at (a) the 23rd Ontario-Quebec Physical-organic Minisymposium, Hamilton, Ont., Nov 1995, (b) the Fourth International Conference on Heteroatom Chemistry (ICHAC-4), Seoul, Korea, July 1995, cf. King, J. F.; Gill, M. S.; Klassen, D. F. *Pure Appl. Chem.* **1996**, *68*, 825−830.

S0022-3263(97)01872-0 CCC: $15.00
Published on Web 01/22/1998

Table 1. Selected Pseudo-First-Order Rate Constants for the Hydrolysis of the Isotopomers of 2,2,2-Trifluoroethanesulfonyl Chloride

substrate	reaction medium (temp, °C)	pH/pD[a]	method	k_{obs} (s^{-1})
1	H_2O, 0.05 M KCl (1.0)	2.5	pH-stat	3.67×10^{-3}
6	H_2O, 0.05 M KCl (1.0)	2.5	pH-stat	1.50×10^{-3}
1	H_2O:CD_3CN, 80:20 (4.5)	2.5	pH-stat	9.5×10^{-3}
1	H_2O:CD_3CN, 80:20 (4.5)	2.5	^{19}F NMR	1.0×10^{-2}
1	D_2O:CD_3CN, 80:20 (4.5)	2.5	^{19}F NMR	2.0×10^{-3}
1	D_2O:CD_3CN, 80:20 (4.5)	1.82	^{19}F NMR	1.80×10^{-3}
6	H_2O:CD_3CN, 80:20 (4.5)	2.5	^{19}F NMR	5.5×10^{-3}
1	2 M H_2SO_4 in H_2O:CD_3CN, 80:20 (4.5)	–	^{19}F NMR	1.21×10^{-3}
1	2 M D_2SO_4 in D_2O:CD_3CN, 80:20 (4.5)	–	^{19}F NMR	2.4×10^{-4}

[a] pH meter reading for solutions with ordinary water; pH meter reading +0.37 for D_2O-containing media.

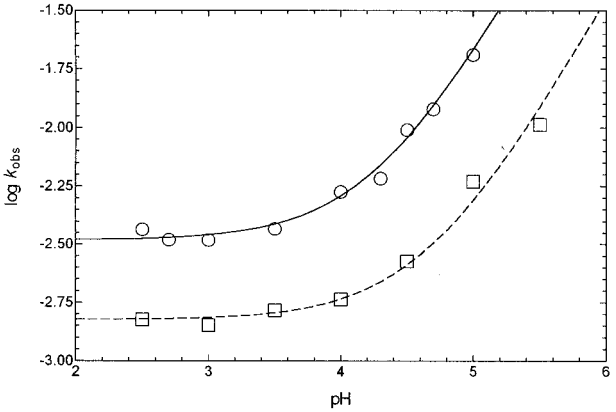
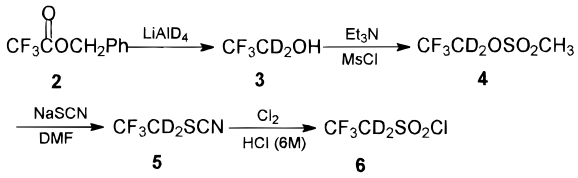


Figure 1. pH-rate profiles for the hydrolysis in 0.05 M KCl at 1.0 °C of trifluoroethanesulfonyl chloride (**1**) (circles and solid line) and trifluoroethanesulfonyl-d_2 chloride (**6**) (squares and broken line). The points are experimental and the lines calculated from the equation log k_{obs} = log(k_w + k_{OH}[OH^-]) taken with following rate constants derived from nonlinear least-squares fitting of the points: for **1**, $k_w = 3.3 \times 10^{-3}$ s^{-1} and $k_{OH} = 1.75 \times 10^7$ M^{-1} s^{-1}; for **6** $k_w = 1.50 \times 10^{-3}$ s^{-1} and $k_{OH} = 3.4 \times 10^6$ M^{-1} s^{-1}.

Scheme 1



corresponding values for other alkanesulfonyl chlorides[3] (at 25 °C), which is consistent with the intervention of different mechanisms in the hydrolysis of **1**.

Further information was obtained by following the hydrolysis and deuteriolysis of **1** and **6** by ^{19}F NMR spectrometry; to obtain concentrations of **1** (or **6**) sufficiently high for convenient determination of the spectra, an 80:20 mixture of H_2O:CD_3CN (or D_2O:CD_3CN) was used as solvent. *For all of the reactions above pH 1.8, the product was the monodeuterated anion $CF_3CHDSO_3^-$ with a trace of the anion corresponding to no H−D exchange ($CF_3CH_2SO_3^-$ or $CF_3CD_2SO_3^-$) in accord with the intermediacy of the sulfene, $CF_3CH{=}SO_2$*; there was no sign of H−D exchange in the starting material. Table 1 lists the rate constants (obtained at 4.5 °C) by ^{19}F NMR, as well as a pH-stat determination, along with two of the earlier pH-stat results (at 1 °C in 0.05 M KCl) for comparison; the ^{19}F NMR and pH-stat k_{obs} values are identical within experimental uncertainty. Comparison of the rate constants for **1** and **6** (in H_2O:CD_3CN) indicates a primary kinetic isotope effect (KIE) of 1.8.

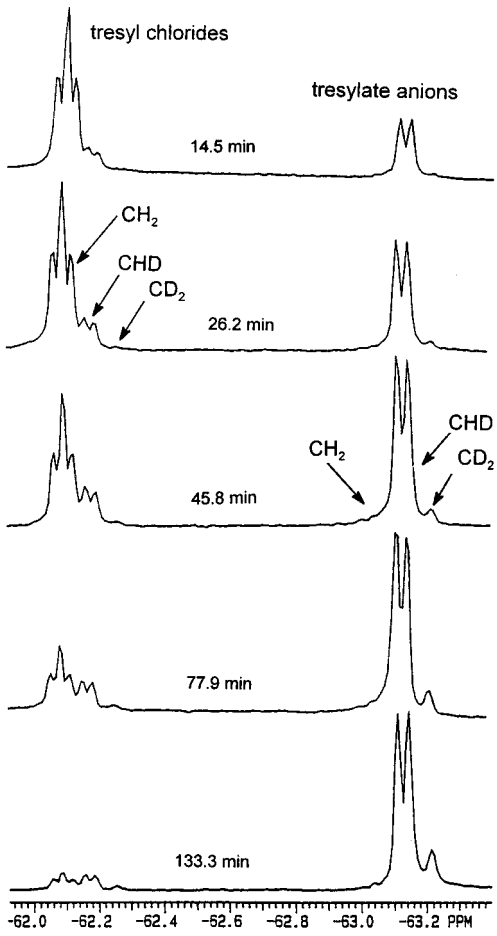
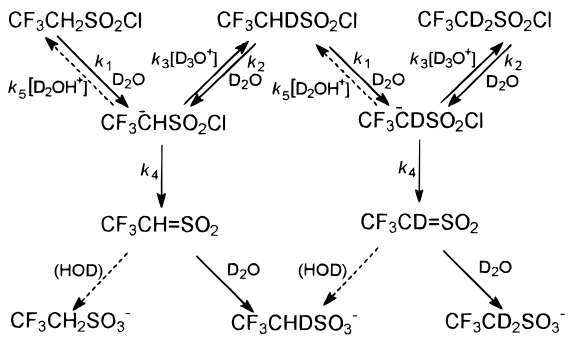


Figure 2. ^{19}F NMR spectra of the reaction product as a function of time for the hydrolysis of **1** in an 80:20 mixture of 2 M D_2SO_4 and CD_3CN at 4.5 °C.

Interestingly, the solvent KIE on going from H_2O:CD_3CN to D_2O:CD_3CN is large, k_H/k_D = 5.0.

A new feature appeared in the ^{19}F NMR spectra obtained by following the reaction of **1** in 2 M D_2SO_4 in D_2O (plus CD_3CN), shown in Figure 2. As is readily evident, each isotopomer of tresyl chloride and the tresylate anion is easily distinguished. As with the spectra observed at higher pH's, there is only the smallest trace of $CF_3CH_2SO_3^-$, again in accord with the intermediacy of the sulfene, $CF_3CH{=}SO_2$. What is new in Figure 2, however, is the set of peaks due to the isotopomers of tresyl chloride, CF_3CHDSO_2Cl (doublet) and $CF_3CD_2SO_2Cl$ (singlet), in addition to the expected hydrolysis products, $CF_3CHDSO_3^-$ and $CF_3CD_2SO_3^-$; a control experiment showed the complete absence of H−D exchange in the tresylate anion under these conditions.

Scheme 2



These observations are most simply accounted for by assuming formation of a discrete carbanion by reaction with H_2O (or D_2O), and its reversal (as required by microscopic reversibility) by H_3O^+ (or D_3O^+). In other words (a) the reaction in 2 M D_2SO_4 (and presumably that in 2 M H_2SO_4 as well) is a reversible E1cB process leading to the sulfene, and (b) that in the pH range 2 to ~4.3, in which no H−D exchange in **1** or **6** is seen, is an irreversible ElcB reaction; in both of these cicumstances the carbanion is generated by attack of H_2O (or D_2O). By extension the reaction at higher pH (>4.3), i.e., the k_{OH} term, must also be an irreversible ElcB reaction giving the sulfene, with the only difference being that the carbanion is formed by attack of hydroxide anion. The nature of the sulfene trapping step has not been studied, though trapping by water would seem to be the most likely route to the tresylate anion under (most of) the conditions of these experiments. The mechanism of the low pH hydrolysis (k_w term) is shown in Scheme 2.

Computer simulation[11] based on this mechanism was carried out with the following parameters: k_1 3.5×10^{-4} s^{-1}; k_3:k_4:k_5 1:3:1; KIE in sulfene trapping 3; [D_3O^+] 2 M; 99.8 atom % excess D. As my be seen from Figures 3 and 4, the correspondence between prediction and the results of the ^{19}F NMR experiment is good, except perhaps for the relatively large amount of undeuterated tresylate anion ($CF_3CH_2SO_3^-$) found over what is predicted by the simulation. Simulation using a larger value for the protium concentration in the D_2SO_4 than that indicated by the suppliers gives a very good fit to the points for $CF_3CH_2SO_3^-$. Though this could simply mean that there is more protium in the D_2SO_4−D_2O solution than expected from the label, it is also conceivable that the H−D exchange processes involving the carbanion, $CF_3\bar{C}HSO_2Cl$, may be very fast relative to the mixing processes and the concentration of D_2OH^+ in the vicinity of any carbanion may well be higher than that corresponding to true equilibration of all species, with the result that protiation of the carbanion may be much greater than expected on the basis of complete mixing before sulfene trapping.

As was noted in the Introduction, there is one report of a sulfonyl chloride hydrolysis by way of an E1cB process. Seifert, Zbirovsky, and Sauer[5] concluded that the hydrolysis of dichloromethanesulfonyl chloride in dioxane:water mixtures takes place via the reversible E1cB reaction. The key pieces of evidence were (a) rate suppression by added acid and (b) the observation of H−D exchange in recovered sulfonyl chloride after partial reaction in D_2O:dioxane. This behavior was quite different from that seen by the same authors with methanesulfonyl or chloromethanesulfonyl chlorides, which showed the normal reactions described earlier. Like all studies of sulfonyl chloride hydrolysis carried out up to that time (and later), their experiments were conducted without pH control, and hence most of the reactions must be regarded as having taken place in aqueous media of somewhat varying acidities. We estimate that in the experiment which led to recovered Cl_2CDSO_2Cl, 90% of the reaction took place with [D_3O^+] in the range 0.02 to 0.22 M. Under their conditions the reversible E1cB reaction is evidently operating, but the mechanism of hydrolysis under less acidic conditions is simply not known. Further study is in order, not only of dichloromethanesulfonyl chloride, but also of both the large solvent isotope effect and the effect of acid on the rate of ionization of **1**, and we hope to be able to report on these points at a later date.

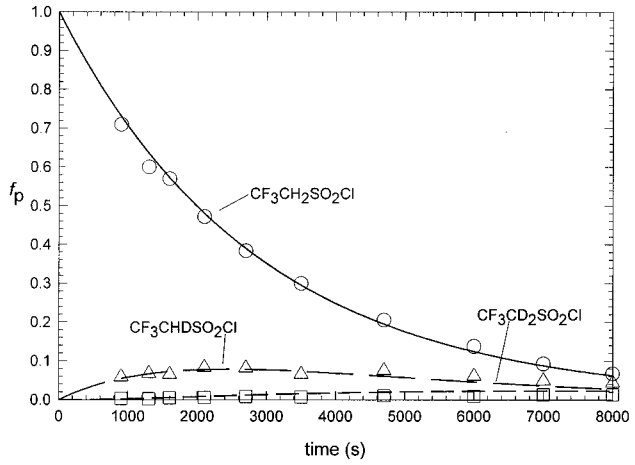


Figure 3. Quantities of the isotopomers of trifluorethanesulfonyl chloride (measured as a fraction of the total original **1**) as a function of time in the hydrolysis of **1** in an 80:20 mixture of 2 M D_2SO_4:CD_3CN at 4.5 °C. The points were obtained from ^{19}F NMR spectra (shown partly in Figure 2) and the lines from computer simulation of the mechanism shown in Scheme 2 using $k_1 = 3.5 \times 10^{-4}$ s^{-1}, k_3:k_4:k_5 = 1:3:1, KIE = 3 for trapping of the sulfene, [D_2O] = 2 M, and deuterium content of the D_2O, 99.8 atom % excess D.[11]

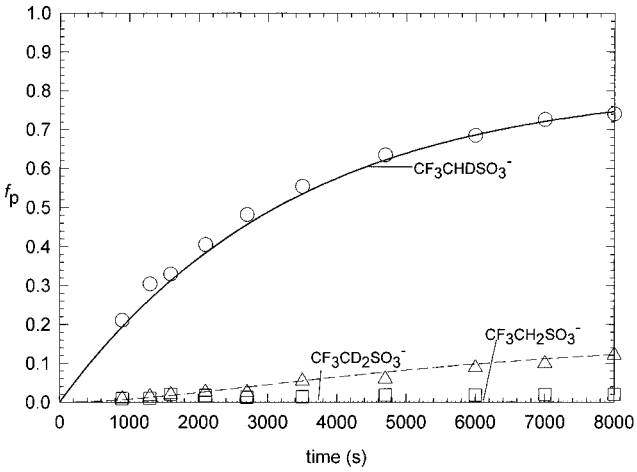


Figure 4. Amounts of the isotopomers of trifluoroethanesulfonate anion in the same reaction of **1** in D_2SO_4:CD_3CN at 4.5 °C; further details are in the caption to Figure 3.

(11) For the simulation program see Gill, M. S., Ph.D. Thesis, The University of Western Ontario, April, 1996; pp 201−202; *Chem. Abstr.* **1997**, *127*, 148846s.

Though carbanion formation with water (rather than hydroxide ion) acting as the base is well-precedented in, for example, the ionization in water of such very strong carbon acids as 2-(dicyanomethylene)-1,1,3,3-tetracyanopropane[12] and tris(methylsulfonyl)methane,[13] the hydrolysis of **1** is to the best of our knowledge the first clearly demonstrated example of reversible and irreversible E1cB reactions induced by water. We were fortunate in this instance to be able to induce H−D exchange under acidic conditions, and hence to observe the alteration in the reaction from $(E1cB)_{irr}$ to $(E1cB)_{rev}$, thereby providing an easy way to distinguish the $(E1cB)_{irr}$ and E2 processes.

Experimental Section

Laboratory procedures, spectra determination, and pH-stat rate measurements were carried out as previously described,[14] except that a Neslab ULT-80 low-temperature bath circulator was used for rate measuurements at 1.0 °C. 2,2,2-Trifluoroethanesulfonyl chloride (**1**) was either purchased from Aldrich Chemical Co. Inc. and used as supplied, or prepared by the following variation on the literature[15] procedure. Aqueous 6 M HCl (20 mL) in an ice bath was saturated with Cl_2, and CF_3CH_2SCN[15] (1.81 g, 12.8 mmol) was quickly added to the stirred solution. The reaction mixture was stirred for 8 min with a constant flow of Cl_2. Workup, followed by distillation under reduced pressure, gave **1** (1.28 g, 53%) as a clear liquid. ^{1}H NMR δ 4.43 (q, J = 8 Hz, 2H); ^{19}F NMR δ −62.09 (t, J = 8 Hz); reported ^{1}H NMR (neat) δ 4.37 (q, J = 9 Hz, 2H).[16] Authentic 2,2,2-trifluoroethanesulfonic acid was prepared by stirring a mixture of **1** (283 mg, 1.55 mmol) and water (5 mL) for 1.5 h and then removing the water under reduced pressure leaving tresic acid as a clear liquid (202 mg, 80%); ^{1}H NMR (D_2O/DSS) δ 3.88 (q, J = 10 Hz, 2H); ^{19}F NMR δ −63.4 (t, J = 10 Hz); reported[16] ^{1}H NMR (D_2O) δ 3.87 (q, J = 10 Hz, 2H).

2,2,2-Trifluoroethanesulfonyl-1,1-*d*$_2$ Chloride (6). Benzyl trifluoroacetate (**2**) (15 g, 73.5 mmol) from a literature preparation[17] (in 80% yield) was added dropwise to a slurry of $LiAlD_4$ (2 g, 48 mmol) in dry ether (80 mL) under N_2, over a period of 40 min, and the mixture was stirred for 1 h at rt. Excess reducing agent was destroyed by dropwise addition of water, followed by addition of 20% H_2SO_4 (50 mL). The reaction mixture was extracted with dichloromethane (200 mL). Fractional distillation using a Vigreux column (12 cm) gave fractions that contained **3** (5 g, 67%) with a little diethyl ether. ^{1}H NMR δ 3.5 (br, s, OH); ^{19}F NMR δ −77.86 (s). Triethylamine (3.08 g, 30.4 mmol) was added to a stirred solution of **3** (2.7 g, 26.5 mmol) in dry ether (75 mL) in an ice bath, and methanesulfonyl chloride (3.34 g, 29 mmol) was added dropwise from an addition funnel over a period of 15 min. The reaction mixture was stirred for 3.5 h; workup with dichloromethane followed by washing with ice cold water and HCl (10%), drying, and evaporation of the organic phase followed by fractional distillation gave **4** (2.8 g, 62%) as a clear liquid. ^{1}H NMR δ 3.15 (s), ^{13}C NMR δ 38.0, 63.6 (4 × 5, J_{CF} = 38.1 Hz, J_{CD} = 23.4 Hz), 121.2 (q, J = 277.5 Hz), ^{19}F NMR δ −74.47 (s). A solution of sodium thiocyanate (3.6 g, 44.4 mmol) in DMF (25 mL) was heated till the head temperature reached 150 °C (6 mL of DMF collected). To the cooled reaction mixture was added **4** (2 g, 11.1 mmol), and the reaction mixture slowly distilled over a period of 2 h. The distillate was taken up in pentane (100 mL), and the solution was washed with water (4 × 50 mL). The pentane layer was dried over anhydrous $MgSO_4$ and the solvent carefully distilled off to give **5** (600 mg, 37.8%) as a light yellow liquid; ^{19}F NMR δ −66.7 (s). Conversion of **5** to **6** followed the preparation of **1**; **5** (520 mg, 3.63 mmol) gave **6** (355 mg, 53%) as a clear liquid. The ^{1}H NMR spectrum showed only signals due to the presence of traces of DMF; ^{19}F NMR δ −62.36 (s).

Products of Deuteriolysis of 1 and Hydrolysis of 6. In D_2O. A sample of **1** (10 mg, 0.055 mmol) in CD_3CN:D_2O, 20:80, after 15 min showed ^{1}H, ^{13}C, and ^{19}F NMR signals assignable almost entirely to monodeutrated $CF_3CHDSO_3^-$, with a small amount (≤2%) of $CF_3CH_2SO_3^-$. Similar spectra were obtained for the reaction in pH 2−7 range; $CF_3CHDSO_3^-$: ^{1}H NMR (D_2O/DSS) δ 3.86 (qt, J = 9 Hz, J = 2.3 Hz, 1H); ^{13}C NMR (D_2O/DSS) δ 54.9 (qt, J = 30 Hz, J = 21 Hz), 125.3 (q, J = 275.5 Hz); ^{19}F NMR (D_2O/$CFCl_3$) δ −63.49 (d, J = 9 Hz). **In H_2O.** Similar reaction of **6** (10 mg, 0.054 mmol) in CD_3CN:H_2O, 20:80, mixtures in pH range 2−7 after 15 min showed signals assignable mostly to $CF_3CHDSO_3^-$ and a trace of $CF_3CD_2SO_3^-$.

Procedure for Hydrolysis Rate Measurements. Aqueous KCl (50 mL, 0.05 M) solution was brought to 1 °C and the desired pH using 0.1 M H_2SO_4 or 0.1 M NaOH. To the above stirred solution was added a solution of **1** (or **6**) (3.72 mg, 0.02 mmol) in THF (50 μL), and the pH of the solution was kept constant with NaOH (0.1 M). The rate of hydrolysis was monitored by recording the volume of the titrant (NaOH) added with time. Plots of $\ln(V_\infty - V_t)$ versus time were constructed from the volume of sodium hydroxide titrant added. The pseudo-first-order rate constants were then obtained from the slopes of straight lines; the results are shown in Figure 1 and listed in Table S1 (see also Table 1). The pH-stat measurements at 4.5 °C were carried out similarly except that a mixture of CH_3CN (10 mL) and aqueous KCl solution was kept at 4.5 °C in a Haake FJ constant temperature circulating bath, and a solution of **1** (3.11 mg, 0.017 mmol) in dry CH_3CN was used for each run.

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada for financial support of this study.

Supporting Information Available: Rate constants for the hydrolysis of **1** and **6** at 1 °C and of **1** in H_2O:CH_3CN 80:20 at 4.5 °C (1 page). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO971872V

(12) Middleton, W. J.; Little, E. L.; Coffman, D. D.; Engelhardt, V. A. *J. Am. Chem. Soc.* **1958**, *80*, 2795−2806.
(13) Schwartzenbach, G.; Felder, E.; *Helv. Chim. Acta* **1944**, *27*, 1701−1711.
(14) King, J. F.; Gill, M. S. *J. Org. Chem.* **1996**, *61*, 7250−7255.
(15) Crossland, R. K.; Wells, W. E.; Shiner, V. J., Jr. *J. Am. Chem. Soc.* **1971**, *93*, 4217−4219.
(16) Bunyagidj, C.; Piotrowska, H.; Aldridge, M. H. *J. Org. Chem.* **1981**, *46*, 3335−3336.
(17) Oliverio, V. T.; Sawicki, E. *J. Org. Chem.* **1955**, *20*, 363−367.