

Evidence for a Concerted Mechanism in the Solvolysis of Phenyltrimethylsilyl Ethers

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Abstract: The trifluoroethoxide-catalyzed trifluoroethanolysis and the hydroxide-catalyzed hydrolysis of a series of phenyltrimethylsilyl ethers were examined. A Bronsted plot of the logarithm of the second-order rate constant k_{TFE} for reaction with trifluoroethanol against the $\text{p}K_{\text{LG}}$ is not linear. The nonlinear plot might be taken as evidence for a change in rate-determining step of a reaction that proceeds through a pentavalent intermediate. However, the Bronsted plot for the hydroxide-catalyzed hydrolysis, where all the leaving groups are of lower $\text{p}K_{\text{a}}$ than hydroxide, has an identical shape as the Bronsted plot for the trifluoroethanolysis reaction. Therefore, the unusual shape of the Bronsted plots is not due to a change in rate-determining step. It is suggested that the results are most consistent with a one-step concerted mechanism and not with a mechanism involving a pentavalent intermediate.

Introduction

Silicon, unlike carbon, possess d orbitals and is capable of expanding its valence shell, leading to the possible formation of pentavalent species in nucleophilic substitution.¹⁻⁴ Hypervalent or pentavalent silicon has been postulated in a variety of reactions.⁵⁻¹⁰ For example tetravalent silicon compounds containing Si-H, Si-O, and Si-N bonds can be activated for a variety of useful synthetic transformations by their reaction with nucleophilic reagents.^{5,6} It has been suggested that these activated species are pentavalent silicon species. Anionic activation with fluoride ion is well documented and presumably is due to nucleophilic reaction of the fluoride ion with the silicon center to form a reactive pentavalent species.^{5,6,8,9}

Calculations also support the existence of pentavalent silicon species,^{11,12} and pentavalent silicon has been detected in the gas phase.¹² In addition pentavalent silicon salts have been made and characterized by NMR techniques^{13a-f} and X-ray crystallography.^{12,13g-n}

It has not been established if the alcoholysis of silyl ethers occurs by a mechanism that involves the formation of a pentavalent intermediate ($\text{S}_{\text{N}}\text{i-Si}$ mechanism) or by a one-step concerted reaction ($\text{S}_{\text{N}}2\text{-Si}$).^{1,14-18} The $\text{S}_{\text{N}}\text{i-Si}$ and $\text{S}_{\text{N}}2\text{-Si}$ mechanisms can be described by $\text{A}_{\text{N}} + \text{D}_{\text{N}}$ and $\text{A}_{\text{N}}\text{D}_{\text{N}}$ respectively, according to the nomenclature recommended by IUPAC for classifying reaction mechanisms.¹⁹

Solvolytic reactions of silyl ethers typically have large negative

activation entropies; the activation entropies are larger than those for bimolecular substitution at carbon and are consistent with the formation of a pentavalent intermediate.¹⁶

The existence of pentavalent silicon is therefore well established, and the possibility that a pentavalent intermediate exists in the solvolysis of silyl ethers is certainly reasonable and has been proposed. However, solvent isotope effects²⁰ and substituent effects²¹ on the methanolysis of aryloxytriphenylsilanes have led to the suggestion that the methanolysis of aryloxytriphenylsilanes occurs by a one-step concerted reaction. The observation of bifunctional acid-base catalysis for the methanolysis of methylphenylmethoxyphenoxysilane^{18a} and for the trifluoroethanolysis of phenyltrimethylphenoxysilane²² is also consistent with a concerted mechanism.

In this paper we provide evidence that the trifluoroethoxide-catalyzed trifluoroethanolysis and the hydroxide-catalyzed hydrolysis of phenyltrimethylsilyl ethers of general structure **1** occur by a concerted displacement involving a single transition state

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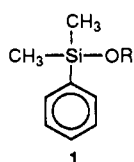
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Table I. Values for k_{TFE} , the Second-Order Rate Constants for the Trifluoroethoxide-Catalyzed Trifluoroethanolysis, Values for k_{OH} , the Second-Order Rate Constants for the Hydroxide-Catalyzed Hydrolysis of Dimethylphenylsilyl Ethers at 30 °C and Constant Ionic Strength, and Values for the $\text{p}K_{\text{LG}}^{\text{c}}$

R in OR leaving group	k_{TFE} (M s) ^a	k_{OH} (M s) ^b	$\text{p}K_{\text{LG}}^{\text{c}}$
2,4,5-Cl ₃ -C ₆ H ₂	3×10^1		6.72 ^d
3-NO ₂ -C ₆ H ₄	7.9	8.8×10^3	8.35
2-Cl-C ₆ H ₄	2.4	7.6×10^2	8.48
3-CN-C ₆ H ₄	7.5	3.0×10^3	8.61
3-Cl-C ₆ H ₄	1.3	1.7×10^3	9.02
CH(CF ₃) ₂	1.3	2×10^3	9.3
4-Br-C ₆ H ₄	1.2	1.2×10^3	9.34
C ₆ H ₅	2.3×10^{-1}	3.4×10^2	9.95
4-CH ₃ -C ₆ H ₄	2.0×10^{-1}	2.0×10^2	10.19
CF ₃ CF ₂ CF ₂ CH ₂	1.1×10^{-1}	2.9×10^2	11.4
CF ₃ CD ₂	1.5×10^{-1}	4.3×10^2	12.43
CHCl ₂ CH ₂	9.0×10^{-2}	1.5×10^2	12.89
HC≡CCH ₂	1.5×10^{-1}	1.9×10^2	13.55
CH ₂ ClCH ₂	2.1×10^{-2}	5.2×10^1	14.31
CH ₃ OCH ₂ CH ₂	5.4×10^{-3}	2.7×10^1	14.82
CH ₃ CH ₂	1.8×10^{-3}	2.4	16
(CH ₃) ₂ CH	3.8×10^{-4}		≈16

^a Ionic strength of 0.05 M with potassium trifluoroacetate. ^b Ionic strength of 0.06 M with sodium chloride. ^c The $\text{p}K_{\text{LG}}$ values are for aqueous solutions, ref 23. ^d Reference 32b.

(S_N2-Si mechanism or A_ND_N) and not by a stepwise mechanism involving a pentavalent intermediate (S_Ni-Si mechanism or A_N+D_N).



- | | |
|---|--|
| a: R = C ₆ H ₅ | i: R = CH ₂ CH ₃ |
| b: R = 4-CH ₃ -C ₆ H ₄ | j: R = CH ₂ CH ₂ OCH ₃ |
| c: R = 4-Br-C ₆ H ₄ | k: R = CH ₂ C≡CH |
| d: R = 3-Cl-C ₆ H ₄ | l: R = CH ₂ CHCl ₂ |
| e: R = 3-CN-C ₆ H ₄ | m: R = CH ₂ CH ₂ Cl |
| f: R = 3-NO ₂ -C ₆ H ₄ | n: R = CH ₂ CF ₂ CF ₂ CF ₃ |
| g: R = 2,4,5-Cl ₃ -C ₆ H ₂ | o: R = CH(CF ₃) ₂ |
| h: R = 2-Cl-C ₆ H ₄ | p: R = CD ₂ CF ₃ |
| | q: R = CH(CH ₃) ₂ |

Results

Table I provides values of the second-order rate constants k_{TFE} for the trifluoroethoxide-catalyzed trifluoroethanolysis of silyl ethers 1a–q at 30 ± 0.5 °C and ionic strength 0.05 M (potassium trifluoroacetate). Values of k_{TFE} were obtained from plots of the observed rate constant k_{obs} vs the concentration of potassium trifluoroethoxide. Table I also gives the second-order rate constants k_{OH} for the hydroxide-catalyzed hydrolysis of most of these silyl ethers. Rate constants for the hydroxide-catalyzed hydrolysis of the silyl ethers were determined in buffered acetonitrile/water solutions (50:50 v/v) at 30 ± 0.5 °C and ionic strength 0.06 M (NaCl). Under these conditions general base catalysis was observed by some buffers. Therefore, the pseudo-first-order rate constants for the hydroxide-catalyzed hydrolysis k'_{OH} were obtained from the intercepts of plots of the observed rate constants k_{obs} measured at a fixed acid/base ratio of the buffer, A/B, vs total buffer concentration, [buffer]_T (see Experimental Section). The second-order rate constants k_{OH} for catalysis by hydroxide were calculated from the slopes of plots of the pseudo-first-order rate constant for catalysis by hydroxide k'_{OH} vs hydroxide concentration. Also reported in Table I are the $\text{p}K_{\text{a}}$ values of the leaving groups ($\text{p}K_{\text{LG}}$) in aqueous solution.²³

Bronsted plots of $\log k_{\text{TFE}}$ vs $\text{p}K_{\text{LG}}$ and of $\log k_{\text{OH}}$ vs $\text{p}K_{\text{LG}}$ are shown in Figures 1 and 2, respectively. The error bars in Figures 1 and 2 are estimated from the slopes of plots of k_{obs} vs the concentration of trifluoroethoxide and from the plots of k'_{OH} vs hydroxide (see Experimental Section). The dotted line in figure 1 represents the $\text{p}K_{\text{a}}$ of trifluoroethanol.

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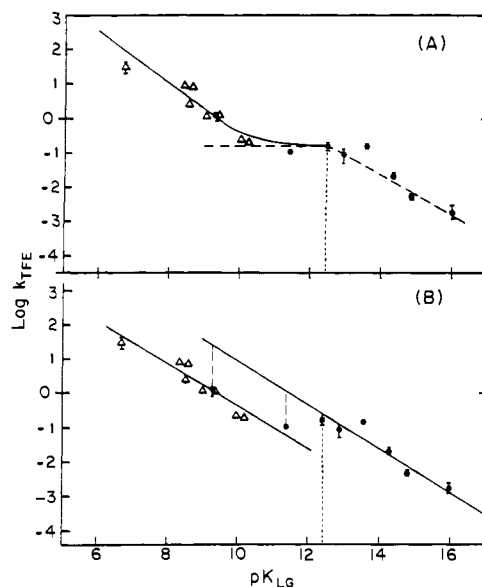


Figure 1. Bronsted-type plots for the trifluoroethoxide-catalyzed trifluoroethanolysis of dimethylphenylsilyl ethers at 30 °C and ionic strength 0.05 M. The circles represent alkoxy leaving groups, and the triangles represent phenoxy leaving groups. Part A is a Bronsted plot with a smooth line drawn through all the experimental points. The dashed line in part A is a calculated line assuming a mechanism involving a change in rate-determining step as described in the text. Part B is a Bronsted plot assuming the same concerted mechanism for both phenoxy and alkoxy leaving groups but with each class of leaving groups being defined by a different correlation.

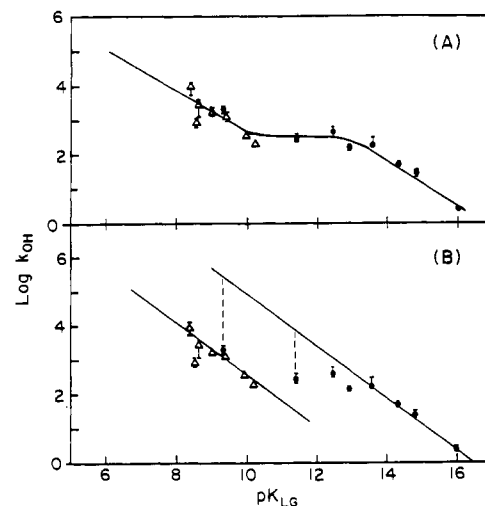
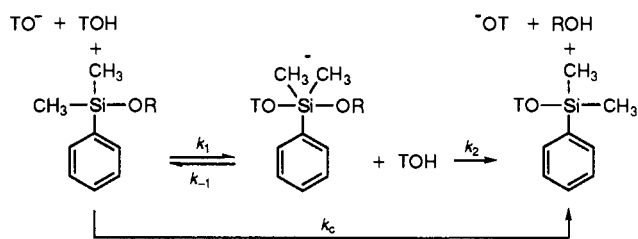


Figure 2. Bronsted-type plots for the hydroxide-catalyzed hydrolysis of dimethylphenylsilyl ethers at 30 °C and ionic strength 0.06 M. The circles represent alkoxy leaving groups, and the triangles represent phenoxy leaving groups. Part A is a Bronsted plot with a smooth line drawn through all the experimental points. Part B is a Bronsted plot assuming the same concerted mechanism for both phenoxy and alkoxy leaving groups but with each class of leaving groups being defined by a different correlation.

Discussion

In order to investigate the mechanism for the alcoholysis of silyl ethers, we chose to study the trifluoroethoxide-catalyzed trifluoroethanolysis of silyl ethers of general structure 1. We chose trifluoroethanol as a solvent, since its $\text{p}K_{\text{a}}$ of 12.43 allowed us to select a variety of leaving groups in the silyl ether of both higher and lower $\text{p}K_{\text{a}}$ than the solvent. In order to span such a wide range of values for $\text{p}K_{\text{LG}}$, both phenoxy and alkoxy leaving groups were required. In Figures 1 and 2 the circles represent alkoxy leaving groups and the triangles represent phenoxy leaving groups.

Scheme I



Previous work has shown that alkoxide acts as a general base to catalyze the addition of an alcohol molecule in these reactions.^{24,25} Two possible mechanisms for the solvolysis of silyl ethers are depicted in Scheme I. In Scheme I, TO^- and TOH represent trifluoroethoxide and trifluoroethanol, respectively, and OR represents the leaving groups.

In the stepwise mechanism k_1 is the microscopic rate constant for trifluoroethoxide acting as a general base to catalyze the addition of a trifluoroethanol molecule to the silyl ether, forming a pentavalent intermediate. The microscopic rate constant k_2 represents collapse of the intermediate to form products. According to the principle of microscopic reversibility, if formation of the intermediate (k_1) is general base catalyzed, then collapse of the intermediate (k_{-1} or k_2) must be general acid catalyzed; therefore, k_2 must involve trifluoroethanol acting as a general acid to donate a proton to the leaving group.²⁶ Indeed, general acid catalysis has been observed in the solvolysis of silyl ethers. The lower part of Scheme I (k_c) represents a one-step, concerted reaction, in which bond formation to the nucleophilic trifluoroethanol molecule and bond breaking to the leaving group occur in a single step.²⁷

If the trifluoroethoxide-catalyzed trifluoroethanolysis of **1a-q** occurs by a stepwise mechanism, involving the formation of a pentavalent intermediate, either formation of the intermediate (k_1 of Scheme I) or collapse of the intermediate to produce products (k_2 of Scheme I) could be rate determining. For leaving groups with $\text{p}K_{\text{LG}}$ greater than the $\text{p}K_{\text{a}}$ of trifluoroethanol, the rate-determining step would be collapse of the intermediate to produce products, k_2 . For leaving groups with $\text{p}K_{\text{LG}}$ lower than the $\text{p}K_{\text{a}}$ of trifluoroethanol, the rate-determining step is formation of the intermediate, k_1 .

When expulsion of the leaving group is rate determining, negative charge develops on the oxygen atom of the leaving group in the transition state. This change in charge as seen by the leaving group on going from the ground state to the transition state will lead to a negative slope, β_{LG} , on a Bronsted plot. When formation of the intermediate is rate determining, much less negative charge develops on the oxygen of the leaving group. For rate-determining formation of the intermediate, the negative charge presumably begins to develop on the silicon center. When formation of the intermediate is rate determining, the developing negative charge is further removed from the substituent(s) on the leaving group, as compared to the case when expulsion of the leaving group is rate determining. The sensitivity of the reaction to the $\text{p}K_{\text{a}}$ of the leaving group, β_{LG} , will therefore be smaller

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(26) When the $\text{p}K_{\text{LG}}$ is higher than 12.6 (the $\text{p}K_{\text{a}}$ of trifluoroethanol), a trifluoroethanol molecule can act as a general base to protonate the leaving group (k_2 of Scheme I). However, for leaving groups with $\text{p}K_{\text{LG}} < 12.6$, a trifluoroethanol molecule can only stabilize the transition state by hydrogen bonding to the leaving group because there is no thermodynamic advantage to proton transfer.

(27) In Scheme I, we indicate that trifluoroethoxide acts as a general base to catalyze the addition of another trifluoroethanol molecule to the silyl ether. It is also possible that the trifluoroethoxide could attack directly. We suggest the general base catalyzed mechanism, since this is the operative mechanism for the methoxide-catalyzed methanolysis of phenoxytriphenylsilanes.²⁴ However, the arguments we make in this paper are equally valid for a mechanism involving nucleophilic catalysis as for a mechanism involving general base catalysis.

than that when expulsion of the leaving group is rate determining. For a stepwise mechanism for the trifluoroethoxide-catalyzed trifluoroethanolysis of silyl ethers **1a-q**, the change in rate-determining step is expected to show up as a change in slope on the Bronsted plot. The change in slope is expected to occur at the $\text{p}K_{\text{a}}$ of trifluoroethanol. Examination of the Bronsted plot in Figure 1 does appear to show a change in slope at the $\text{p}K_{\text{a}}$ of trifluoroethanol (dotted line). For leaving groups of $\text{p}K_{\text{LG}} > 12.43$, the slope of the Bronsted plot, β_{LG} , is about -0.7 , and for leaving groups with $\text{p}K_{\text{LG}} < 12.43$ (but greater than 10, see following paragraph), the slope is zero.

The Bronsted plot for a stepwise mechanism can be described empirically by eq 1.²⁸ In eq 1, k_0 is the rate constant for the

$$\log(k_{\text{TFE}}/k_0) = \beta_2(\text{p}K_{\text{LG}} - \text{p}K_{\text{TFE}}) - \log\left(\frac{[1 + 10^{(\beta_2 - \beta_1)(\text{p}K_{\text{LG}} - \text{p}K_{\text{TFE}})]}{2}\right) \quad (1)$$

virtual reaction where both nucleophile and leaving group have the same $\text{p}K_{\text{a}}$, and β_2 and β_1 are the Bronsted values when k_2 and k_1 are rate determining, respectively. In fact, the points in the Bronsted plot for leaving groups of $\text{p}K_{\text{LG}} > 10$ can be fit reasonably well to eq 1. The dashed line in Figure 1 was calculated according to eq 1 with $\beta_1 = 0.09$, $\beta_2 = -0.71$, and $k_0 = 3.0 \times 10^{-1} \text{ s}^{-1}$. The value of k_0 was obtained from the virtual reaction of **1p**. It can be seen that these values and eq 1 accurately describe the experimental points for leaving groups of $\text{p}K_{\text{LG}} > 10$.

An unusual aspect of the Bronsted plot is that at $\text{p}K_{\text{LG}} < 10$ the plot begins to curve upward. It is difficult to account for this upward curvature according to a stepwise mechanism. Upward curvature in a structure-reactivity relationship is usually indicative of a change in mechanism. Therefore, if the change in slope observed at the $\text{p}K_{\text{a}}$ of trifluoroethanol is due to the fact that the trifluoroethoxide-catalyzed trifluoroethanolysis of silyl ethers undergoes a change in rate-determining step of a stepwise mechanism, involving a pentavalent intermediate, there must be some reason, in order to account for this upward curvature, that the mechanism changes for leaving groups of $\text{p}K_{\text{a}} < 10$.

It is also possible that the same concerted mechanism is followed for both the alkoxy and phenoxy leaving groups but that phenoxy leaving groups, as a whole, are less reactive than alkoxy leaving groups. Such a situation would give rise to separate Bronsted correlations for each class of leaving group, as depicted in Figure 1B. At first, this seems unlikely due to the fact that the alkoxy leaving group hexafluoroisopropoxide ($\text{p}K_{\text{a}} = 9.3$) falls on the same Bronsted line as the one defined by phenoxy leaving groups. However, for the following reasons we believe that the Bronsted correlations for alkoxy leaving groups and phenoxy leaving groups are indeed defined by different lines.

The Bronsted correlation for the hydroxide-catalyzed hydrolysis of the same silyl ethers is shown in Figure 2. It is obvious that the Bronsted correlation of Figure 2 has the same shape as the Bronsted correlation for the trifluoroethoxide-catalyzed trifluoroethanolysis (Figure 1). In fact, the changes in slope are observed at the same values for $\text{p}K_{\text{LG}}$ as are observed in the trifluoroethanolysis reaction. Now, for the hydroxide-catalyzed reaction, formation of the intermediate (k_1 of Scheme I) will be rate determining, since hydroxide is of higher $\text{p}K_{\text{a}}$ than all of the leaving groups in **1**. Therefore, the changes in slope of the Bronsted correlation for the hydroxide-catalyzed hydrolysis will not be due to a change in rate-determining step. It seems likely that whatever factors lead to the change in slope of the Bronsted correlation for the hydroxide-catalyzed reaction are also responsible for the change in slope observed in the Bronsted correlation for the trifluoroethoxide-catalyzed reaction. In fact a plot of $\log k_{\text{TFE}}$ vs $\log k_{\text{OH}}$ is linear and shows no evidence for a change in

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slope, as would be expected for the trifluoroethoxide-catalyzed trifluoroethanolysis reaction occurring by a stepwise mechanism that involves a change in rate-determining step but with rate-determining formation of the intermediate for the hydroxide-catalyzed reaction.

The conclusion that the change in slope for the trifluoroethoxide-catalyzed reaction is not due to a change in rate-determining step suggests that the reaction is not occurring by a stepwise mechanism. The results are most consistent with bond formation to the attacking alcohol and bond breaking to the leaving group occurring simultaneously. The reaction can best be described as occurring by a one-step concerted mechanism (S_N2 -Si or A_ND_N mechanism). The absence of a break in a structure-reactivity relationship due to a change in rate-determining step has been offered as evidence for a concerted mechanism with a single transition state for nucleophilic substitution at other centers, such as the reaction of nucleophiles with phosphorylated pyridines,²⁹ phosphinate and sulfonate esters,³⁰ isoquinoline-*N*-sulfonates,³¹ acetate esters,³² and formate esters.³³

The data represented in the Bronsted correlations of Figures 1 and 2 are better described by two separate correlations, with one line for phenoxy leaving groups and another line for alkoxy leaving groups (Figures 1B and 2B). The slopes of the lines for the phenoxy leaving groups and for the alkoxy leaving groups are the same. This indicates that both phenoxy and alkoxy leaving groups see the same change in charge density on going from the ground state to the transition state, consistent with a one-step concerted displacement for all leaving groups.

However, phenoxy ethers react, as a group, slower than alkoxy ethers. The pK_a of phenols is determined in part by resonance, and resonance delocalization of charge can lag behind bond cleavage.³⁴ This would account for compounds with phenoxy leaving groups being less reactive compared to those with alkoxy leaving groups, leading to separate correlation lines. This would be another example where there is an imbalance in the degree to which different processes may proceed in the transition state.³⁴

Two alkoxy groups, hexafluoroisopropoxide and heptafluorobutoxide, show negative deviations from the line defined by the other alkoxy groups (dashed lines in Figures 1B and 2B). This deviation is presumably due to the fact that the other alkoxy groups used to define the line for alkoxy leaving groups in Figures 1B and 2B are all substituted ethanols, while hexafluoroisopropoxide and heptafluorobutoxide are more bulky groups than the simple substituted ethanols. The fact that hexafluoroisopropoxide falls on the line defined by phenoxide leaving groups is merely coincidental. Steric factors are known to be important for substitutions at silicon.^{1,35} The rate of reaction for the trifluoroethoxide-catalyzed trifluoroethanolysis of **1q**, with isopropoxide as the leaving group, also appears to show a deviation from the Bronsted correlation defined by substituted ethanol leaving groups. However, the deviation for isopropoxide is not as large as the deviation observed for hexafluoroisopropoxide as a leaving group, presumably due to the greater steric bulk of a CF_3 group relative

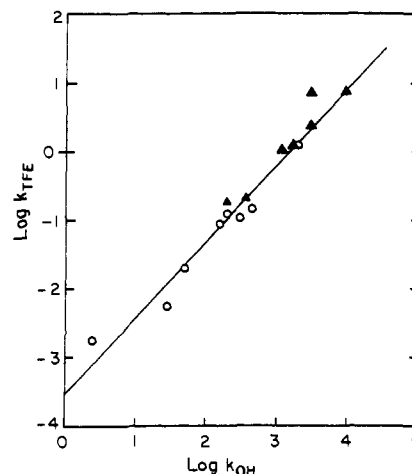


Figure 3. Comparison of the logarithm of the rate constant for the hydroxide-catalyzed hydrolysis of dimethylphenylsilyl ethers against the logarithm of the rate constant for the trifluoroethoxide-catalyzed trifluoroethanolysis. The circles represent alkoxy leaving groups, and the triangles, phenoxy leaving groups.

to a CH_3 group.³⁶ In addition the fact that the points for hexafluoroisopropoxide and heptafluorobutoxide leaving groups do not deviate from the plot of $\log k_{TFE}$ vs $\log k_{OH}$ (Figure 3) suggests that any deviations observed on the Bronsted plots are caused by the same factors for both reactions.

The slopes of the Bronsted correlations, β_{LG} , in Figures 1B and 2B are both about 0.7. This suggests that in the transition state the oxygen on the leaving group sees approximately 70% of a full negative charge and that oxygen silicon bond cleavage has progressed to a substantial degree in the transition state. However, it is important to realize that, in order to get a realistic measure of charge on going from the ground state to the transition state, the Bronsted value must be "standardized" against a calibrating equilibrium, β_{Eq} , that is directly related to the reaction being studied.³⁷ Such a "standardized equilibrium" is not available for this reaction. It is possible that the oxygen of the leaving group has, in the ground state, a partial positive charge so that the overall change in charge as seen by the leaving group on going from the ground state to products could be greater than 1. β_{Eq} will therefore also be greater than 1. Results from substitution reactions at silicon in polar aprotic solvents suggest that this may indeed be the case.³⁸ If this is the case, the Bronsted value $\beta_{LG} = 0.7$ would overestimate the degree of bond breaking in the transition state; the value of $\beta_{LG} = 0.7$ can therefore only be taken as an upper limit for the amount of silicon-leaving group bond breaking in the transition state.

In summary, it appears that the solvolysis of silyl ethers such as **1** occurs by a one-step concerted mechanism (S_N2 -Si or A_ND_N mechanism) and not by a stepwise mechanism involving the formation of a pentavalent intermediate (S_{Ni} -Si or $A_N + D_N$ mechanism). The change in slope at $pK_a = 12.4$ observed for the trifluoroethoxide-catalyzed trifluoroethanolysis of silyl ethers **1a-q** is not due to a change in rate-determining step of a reaction that proceeds through a pentavalent intermediate, since the same change in slope is observed for the hydroxide-catalyzed hydrolysis, where a change in rate-determining step does not occur. The unusual shapes of the Bronsted correlations for solvolysis of **1** are best accounted for by the fact that phenoxides as a group are poorer leaving groups than alkoxides and the fact that steric factors are important.

(36) This is obvious when one compares the Taft steric factor, E_s , for a CH_3 and a CF_3 group. The E_s values for a CH_3 and a CF_3 group are 0.00 and -1.16, respectively. See: Taft, R. W., Jr. In *Steric Effects in Organic Chemistry*; Newman, M. S., Ed.; John Wiley and Sons: New York, 1956; Chapter 13.

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Experimental Section

Methods. Gas chromatographic analyses were performed on a Shimadzu Model 14A gas chromatograph with a 10m AT-35 0.54-mm i.d. capillary column or on a Varian 2400 series gas chromatograph with a 6' \times 1/8" 5% DC-550 on 100/200 mesh Chromosorb HPW column. The gas chromatographs were equipped with flame ionization detectors and were interfaced to a Shimadzu Model CR 601 integrator. High-pressure liquid chromatography (HPLC) was performed on a Shimadzu HPLC system equipped with a Model SPC-6A variable-wavelength detector, a Model C-R6A electronic integrator, and a Waters reverse-phase 5- μ m NOVA-PAK C₁₈ column in a radial compression module. Mass spectral analyses were performed on a Hewlett Packard Model 5988A GC/MS/DS. NMR spectra were recorded on a GE QE-300 or on a IBM NR/80 NMR spectrometer. pH measurements were made on a Radiometer PHM precision pH meter at room temperature with a glass combination electrode containing saturated potassium chloride, standardized with aqueous buffers.

Materials. The silyl ethers were synthesized according to the procedure of Boe¹⁴ and were distilled under vacuum. All of the silyl ethers gave NMR and mass spectra consistent with the desired product and were demonstrated to be better than 80% pure, the only impurity being tetramethyldiphenylsiloxane, as indicated by NMR and GC/MS analysis. It was shown that the tetramethyldiphenylsiloxane impurity was inert under the reaction conditions used in this study and in fact could be used as an internal standard (see below). Trifluoroacetic acid, acetonitrile, 2,2,2-trifluoroethanol-*d*₃, phenyldimethylsilyl chloride, and all of the phenols and alcohols used to make the silyl ethers were commercially available and were used without further purification.

Sodium carbonate, sodium hydrogen carbonate, sodium chloride, methoxyethylamine, and 1.0 N standardized HCl used to make solutions were commercially available and used without further purification.

A stock trifluoroethoxide solution (0.1 M) was prepared by dissolving potassium metal in trifluoroethanol. The potassium metal was cleaned by rinsing with pentane followed by rinsing with trifluoroethanol. The concentration of potassium trifluoroethoxide was determined by titration with standardized 0.1 M HCl.

Potassium trifluoroacetate was prepared by adjusting the pH of an aqueous solution of trifluoroacetic acid to approximately 1.5 with 1 M KOH. The water was removed under vacuum, and the resulting wet solid was recrystallized from 2-propanol. The recrystallized potassium trifluoroacetate was dried overnight in a vacuum desiccator. The pH of an aqueous solution of the salt was 7.

Kinetics. Rate constants for reaction of **1** catalyzed by trifluoroethoxide were determined at 30.0 ± 0.5 °C under pseudo-first-order conditions with alkoxide generally in >10-fold excess over the silyl ether ($\mu = 0.05$ with potassium trifluoroacetate). However, for very fast reactions some experiments were conducted with only a 5-fold excess of the trifluoroethoxide. The rate constants from these experiments agree well with the rate constants obtained at higher trifluoroethoxide concentrations (i.e. >10-fold excess). Reactions with phenol leaving groups were run by adding a small amount of the silyl ether (0.4–1.0 μ L) to 2 mL of a trifluoroethanol solution containing a known concentration of potassium trifluoroethoxide. Pseudo-first-order rate constants, k_{obs} , were determined by measuring the increase in absorbance due to the formation of the phenolate anion as a function of time using a Shimadzu UV-160 spectrophotometer equipped with a thermostated cell holder. Reactions were monitored at 280, 283, 285, 280, 300, 290, 300, and 290 nm for **1a–h**, respectively. The spectrophotometer was interfaced to a personal computer, and the pseudo-first-order rate constants k_{obs} were obtained by nonlinear regression analysis of absorbance vs time data. Reactions were generally followed for more than three half-lives. The nonlinear regression analysis calculated the best end point. For reactions that were followed to completion, the observed end points always agreed well with the calculated end points. Good pseudo-first-order kinetics were followed, and semilog plots of $(A_{\infty} - A_t)$ vs time were linear. Rate constants were generally reproducible within 10%.

For alcohol leaving groups **1i–p**, pseudo-first-order rate constants k_{obs} were obtained by adding 0.5–1.0 μ L of the silyl ether to 0.5 mL of a trifluoroethoxide solution and using gas chromatography to measure the peak area of the silyl ether as a function of time. Peak areas were normalized relative to an internal standard. Either mesitylene (0.2 μ L added to the reaction mixture) or tetramethyldiphenylsiloxane was used as an internal standard. For very fast reactions requiring analysis by gas chromatography, 10- μ L aliquots of the reaction mixture were removed at given time intervals and quenched in 10 μ L of 0.06 M acetic acid in

trifluoroethanol at -78 °C. The solutions at -78 °C were then warmed to 0 °C in an ice/water mixture prior to injection on the gas chromatograph. For the silyl ethers with leaving groups of higher pK_a than that of trifluoroethanol, it was not necessary to use an excess of trifluoroethoxide, since the alkoxide leaving group is a stronger base than trifluoroethoxide and becomes protonated by the trifluoroethanol solvent, regenerating the trifluoroethoxide; some reactions were run with only a 2- or 3-fold excess of trifluoroethoxide relative to the silyl ether. For **1n** and **1o**, where the leaving group is of lower pK_a than trifluoroethanol, reactions were carried out with trifluoroethoxide in >5-fold excess over the silyl ether. The slope of a semilog plot of peak area of silyl ether relative to standard against time gave k_{obs} . Semilog plots were linear for over three half-lives. Rate constants were generally reproducible within 10%. The only product observed by gas chromatography was the (2,2,2-trifluoroethoxy)dimethylphenylsilane.

Rate constants for **1p** were determined by following the loss of deuterium from the deuterated dimethylphenyl(trifluoroethoxy)silane as a function of time by gas chromatography–mass spectrometry (GC/MS). A 1- μ L volume of the reaction mixture was injected onto a 30 m \times 0.257 mm J&W fused-silica DB-5 capillary column operated at an initial temperature of 80 °C for 3 min followed by temperature programming at 10 °C/min to a final temperature of 220 °C. The mass spectrometer was operated in the electron impact mode. The peaks of interest are the parent peaks of the dimethylphenyl(trifluoroethoxy)silane (m/z of 234) and of the deuterated dimethylphenyl(trifluoroethoxy)silane (m/z of 236). The intensities of these peaks were measured by single-ion monitoring of m/z 234 and 236 using the average scans taken over the entire GC peak after appropriate background correction. The ratio of 236/(234 + 236) gives the percent of deuterated dimethylphenyl(trifluoroethoxy)silane. The slopes of semilog plots of the percent deuterated dimethylphenyl(trifluoroethoxy)silane vs time were used to obtain k_{obs} .

Second-order rate constants k_{TFE} were obtained from the slopes of plots of k_{obs} vs concentration of trifluoroethoxide. Typically five concentrations of trifluoroethoxide were used. Plots of k_{obs} vs trifluoroethoxide concentration were linear with intercepts of zero.

The pseudo-first-order rate constants for the hydrolysis of **1** k_{obs} were determined by adding a small amount of the silyl ether (0.4–1.0 μ L) to 2.4 mL of a buffered 1:1 v/v acetonitrile/water solution maintained at 30.0 ± 0.5 °C and at constant ionic strength of 0.06 M. For compounds having a phenolate leaving group, the pseudo-first-order rate constants for hydrolysis k_{obs} were obtained by measuring the increase in absorbance due to the formation of the phenolate anion as a function of time. Reactions were monitored at 280 nm for **1a–d,h**, 325 nm for **1e**, and 350 nm for **1f**. The absorbance vs time data was collected and treated in the same way as described above for the trifluoroethanolysis reaction.

For the alcohol leaving groups, pseudo-first-order rate constants for hydrolysis were obtained by monitoring the rate of disappearance of the silyl ether relative to a standard (tetramethyldiphenylsiloxane) as a function of time by HPLC analysis of the reaction mixture. To 1 mL of buffered acetonitrile/water solution maintained at 30.0 ± 0.5 °C and at constant ionic strength of 0.06 M was added 1.5 μ L of the silyl ether, and the mixture was shaken. At various time intervals an aliquot of the reaction mixture was removed, quenched in an equal volume of 0.06 M acetic acid/0.06 M potassium acetate in 50:50 v/v CH₃CN/H₂O, and injected on the HPLC. HPLC analysis of the reaction mixture was accomplished with a flow of 0.8 mL/min for the initial 18 min, after which the flow was increased to 1 mL/min. The solvent system was 75/25 CH₃CN/H₂O for 13 min followed by gradient elution to 100% CH₃CN over a time of 5 min; the solvent system was maintained at 100% CH₃CN for 3 min. There was only one product detected by HPLC in the reaction mixtures, presumably the phenyldimethylsilane.

For very fast reactions, 75 μ L of the reaction mixture was removed at a given time interval and quenched in 75 μ L of 0.06 M acetic acid/0.06 M potassium acetate in methanol at -78 °C. The quenched solutions were then warmed to 0 °C in an ice/water bath prior to injection on the HPLC. The peak areas of the silyl ether and of tetramethyldiphenylsiloxane were obtained by electronic integration of their UV absorbances at 280 nm. The peak area of the silyl ether was normalized against the peak area of the tetramethyldiphenylsiloxane. The pseudo-first-order rate constants for hydrolysis k_{obs} were obtained from semilog plots of the peak area of the silyl ether relative to the peak area of the tetramethyldiphenylsilane vs time. Reactions were generally followed for greater than three half-lives and gave linear semilog plots typically containing at least seven data points. The rate constants for the hydrolysis of **1o** was very fast and could only be estimated from two- or three-point semilog

plots, the first data point being at $t = 0$ and the later data point(s) being obtained after 5–30 s.

For silyl ethers **1a–c,i–p**, a $\text{NaHCO}_3/\text{Na}_2\text{CO}_3$ buffer was used. Reaction mixtures were prepared by combining known volumes of a 0.03 M Na_2CO_3 solution (1:1 v/v $\text{H}_2\text{O}/\text{CH}_3\text{CN}$) with a known volume of a 0.03 M $\text{NaHCO}_3/0.03$ M NaCl solution (1:1 v/v $\text{H}_2\text{O}/\text{CH}_3\text{CN}$). The pH of the resulting solution was determined before and after the reaction and showed little change, usually decreasing slightly (less than 0.02 pH units) during the course of the reaction. It was demonstrated that under these conditions buffer catalysis was negligible. Buffer solutions at a fixed ratio of acidic to basic form of the buffer, A/B, when diluted gave the same value for k_{obs} after dilution as before dilution. For example, ratios of A/B of 0.018 M/0.0018 M and of 0.009 M/0.0009 M both provided a value of k_{obs} of $3.9 \times 10^{-4} \text{ s}^{-1}$ for the hydrolysis of **1l**. After dilution of the buffer, the pH was observed to decrease slightly (less than 0.1 pH units). Small amounts of 0.06 M HCl were added to the more basic solution in order to decrease the pH of this solution to the same value as that of the more dilute solution. The pH of a solution was calculated according to eq 2

$$\text{pH} = \text{pH}_{\text{app}} - 0.58 \quad (2)$$

where pH_{app} is the pH reading measured in 50:50 v/v $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with ionic strength 0.06 M (NaCl). Equation 2 was obtained from the observed pH readings pH_{app} of 0.03, 0.01, 0.005, and 0.002 M NaOH in 1:1 v/v $\text{H}_2\text{O}/\text{CH}_3\text{CN}$ with ionic strength 0.06 M (NaCl).

Values of the second-order rate constants k_{OH} were obtained from the slope of plots of the pseudo-first-order rate constants k'_{obs} vs $[\text{OH}^-]$. Plots of k'_{obs} vs $[\text{OH}^-]$ generally consisted of five data points covering a range of about 1 pH unit.

For silyl ethers **1d–h** a 0.03 M methoxyethylamine/0.03 M methoxyethylamine hydrochloride buffer in 50:50 v/v $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ with constant ionic strength of 0.06 M (NaCl) was used and the reactions were monitored in the same way as described above for the $\text{Na}_2\text{CO}_3/\text{NaHCO}_3$ buffer system. However, for the amine buffer plots of the observed rate constant k_{obs} vs total buffer concentration, $[\text{buffer}]_{\text{T}}$, at a constant A/B ratio (and constant pH maintained by additions of small amounts of 0.06 M HCl to correct for effects on the measured pH from dilution with 0.06 M NaCl) had positive slopes, indicating that general base catalysis by the buffer is important. The pseudo-first-order rate constants k'_{obs} in the absence of buffer at a given pH were obtained from the intercepts of plots of k_{obs} vs $[\text{buffer}]_{\text{T}}$. These plots typically contained five data points covering a range for $[\text{buffer}]_{\text{T}}$ of 0.005–0.03 M. Plots of k'_{obs} vs $[\text{OH}^-]$ had slopes of k_{OH} ; these plots typically contained five data points spanning at least 1 pH unit.

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