5010 *J. Org. Chem.* **1994**, *59*, 5010–5016

Mechanism for the General Base Catalyzed Solvolysis of Silyl Ethers

Paul E. Dietze*[1] and Yiying Xu

Department of Chemistry, University of Maryland Baltimore County, Baltimore, Maryland 21228

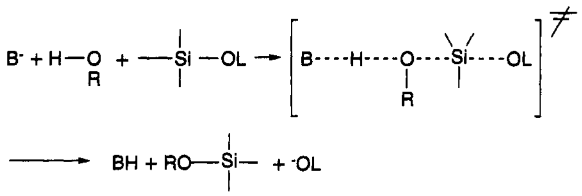
Received April 15, 1994[⊗]

The observed general base catalysis of the solvolysis of dimethylphenylphenoxysilane occurs by a mechanism where the catalyzing base assists by removing a proton from the attacking solvent molecule as the silicon–oxygen bond forms, i.e. true general base catalysis, and not by the kinetically equivalent mechanism of specific base general acid catalysis. This conclusion is based on structure–reactivity relationships with a positive cross interaction coefficient, $p_{xy'} = \partial\beta/-\partial pK_{Nuc} = \partial\beta_{Nuc}/-\partial pK_{Catalyst} = 0.08$, that would be expected for a mechanism involving true general base catalysis.

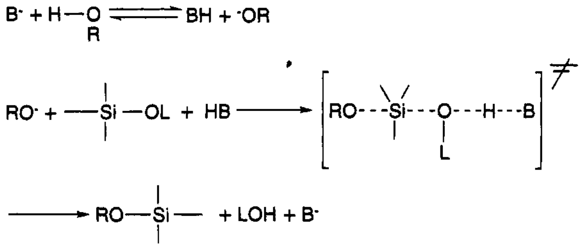
Introduction

The mechanism for solvolysis of silyl ethers in protic solvents has been studied previously and is a subject of much interest.[2] It is well-known that the solvolysis of silyl ethers exhibits general base catalysis.[3–7] The observed general base catalyis could occur by either of two kinetically equivalent mechanisms,[8,9] depicted below in Schemes 1 and 2. Scheme 1 describes the mechanism for true general base catalysis, in which the base catalyst assists in removing a proton from the attacking solvent molecule as the silicon–oxygen bond forms. Scheme 2 depicts the mechanism for specific base general acid catalysis; according to this mechanism, the base catalyst removes a proton from the nucleophilic solvent molecule in a pre-equilibrium step, followed by the rate determining step, in which the conjugate acid of the base catalyst protonates the oxygen of the leaving group as the solvent anion attacks the silicon atom. To our knowledge, there have been no experiments designed to distinguish between these two possibilities. In this paper we report the results of a study on the amine-catalyzed solvolysis of dimethylphenylphenoxysilane in the mixed solvent 80:20 (v/v) ethanol:trifluoroethanol that was designed to distinguish between these two mechanistic alternatives.

Scheme 1



Scheme 2



The solvolysis of silicon compounds is of interest since silicon, although located immediatly below carbon on the periodic table, exhibits quite different behavior in solvolysis reactions when compared to the corresponding reaction of tetravalent carbon compounds.[10] For example, mechanisms involving a cation intermediate are not unusual for the solvolysis of carbon compounds; however, the corresponding reaction for silicon compounds is uncommon.[11] On the other hand, silicon posesses d orbitals, and can expand its valence shell, so there exists the possibility that pentavalent intermediates may be involved in the solvolysis of tetravalent silicon compounds.[10,13] Indeed, many pentavalent silicon species have been synthesized and characterized.[10] However, for tetravalent carbon compounds there is no evidence for the existence of pentavalent species in solvolysis reactions. Another difference between tetravalent carbon and tetravalent silicon, in solvolysis reactions, is the observation that silicon compounds undergo a general base catalyzed addition of solvent in the presence of nucleophilic reagents, rather than direct nucleophilic attack.[3–7] The typical reaction for carbon compounds on the other hand is direct nucleophilic attack; the general base catalyzed addition of solvent is uncommon.[14]

The general base catalyzed solvolysis of silyl ethers has been well-documented.[2–7] In addition it has been demonstrated that the solvolysis of silyl ethers can exhibit general acid catalysis[16,17] and bifunctional catalysis.[17,18]

[⊗] Abstract published in *Advance ACS Abstracts,* August 1, 1994.

[1] Current address: U.S. Food and Drug Administration, Center for Drug Evaluation and Research, Division of Oncology and Pulmonary Drug Products, Office of Drug Evaluation I, HFD-150, 5600 Fischers Lane, Rockville, MD 20852.

[2] For a recent review on mechanisms of nucleophilic attack at silicon, see: Bassindale, A. R., Taylor, P. G. In *The Chemistry of Organosilicon Compounds*; Patai, S., Rappoport, Z., Eds.; John Wiley & Sons Ltd.: New York, 1989; p 839.

[3] Boe, B. *J. Organomet. Chem.* **1976**, *107*, 139.

[4] Boe, B. *J. Organomet. Chem.* **1973**, *57*, 255.

[5] Akerman, E. *Acta. Chem. Scand.* **1956**, *10*, 298.

[6] Modro, A.; Schowen, R. J. *J. Am. Chem. Soc.* **1974**, *96*, 6980.

[7] Schowen, R.; Latham, K. *J. Am. Chem. Soc.* **1967**, *89*, 4677.

[8] Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 3rd ed.; Harper and Row: New York, 1987; p 676.

[9] Jencks, W. P. *Catalysis in Chemistry and Enzymolgy*; McGraw-Hill: New York, 1969; p 182.

[10] See citations provided in refs 11 and 12.

[11] Dietze, P. E. *J. Org. Chem.* **1993**, *58*, 5653.

[12] Xu, Y.; Dietze, P. E. *J. Am. Chem. Soc.* **1993**, *115*, 10722.

[13] For a recent review on pentavalent silicon, see: (a) Corriu, R. J. P.; Young, C. J. In *The Chemistry of Organosilicon Compounds*; Patai, S., Rappoport, Z., Eds.; John Wiley & Sons Ltd.: New York, 1989; p 1241. (b) Chuit, C.; Corriu, R. J.; Reye, C.; Young, C. J. *Chem. Rev.* **1993**, *93*, 1371. (c) Also see ref 10.

[14] For examples of general base catalyzed addition to sp^3 hybridized carbon, see: Dietze, P. E.; Jencks, W. P. *J. Am. Chem. Soc.* **1989**, *111*, 340 and references cited within.

[15] Dietze, P. E.; Khattak; J., Fickus, E. *Tetrahedron Lett.* **1991**, *32*, 307.

0022-3263/94/1959-5010$04.50/0

Table 1. Rate Constants, k_{obs}, for the Solvolysis of Dimethylphenylphenoxysilane, the Ratio of Ethyl Ether Product to Trifluoroethyl Ether Product (ROET/ROTFE), and the pK_a of the Amine Catalyst

amine	pK_a[a]	*A/B*[b]	k_{obs} × 10^3 s[d]	ROET/ROTFE[c]
$CH_3(CH_2)_3NH_2$	10.59	0.01/0.01	1.6	0.35 (0.34, 0.36)
		0.02/0.02	2.2	0.53 (0.65, 0.48, 0.50, 0.50, 0.51)
		0.03/0.03	2.3	0.52 (0.56, 0.53, 0.48, 0.53)
		0.04/0.04	3.0	0.63 (0.63, 0.63)
		0.05/0.05	4.0	0.69 (0.69, 0.70, 0.68)
$CH_3OCH_2CH_2NH_2$	9.20	0.01/0.01	3.3	0.41 (0.43, 0.40, 0.41, 0.42)
		0.02/0.02	4.3	0.54 (0.54, 0.53, 0.52, 0.58)
		0.03/0.03	5.5	0.64 (0.64, 0.64, 0.65)
		0.04/0.04	6.3	0.76 (0.77, 0.73, 0.77, 0.79)
		0.05/0.05	7.9	0.80 (0.84, 0.78, 0.79, 0.80)
$HCCCH_2NH_2$	8.15	0.01/0.01	1.5	0.70 (0.76, 0.64, 0.68, 0.72, 0.70)
		0.02/0.02	1.9	0.85 (0.80, 0.86, 0.90, 0.82, 0.86)
		0.03/0.03	2.4	1.21 (1.34, 1.28, 1.10, 1.15, 1.14, 1.19, 1.18, 1.31)
		0.04/0.04	2.8	1.12 (1.21, 1.04, 1.19, 1.08, 1.15, 1.08, 1.06)
		0.05/0.05	3.4	1.67 (1.73, 1.80, 1.53, 1.76, 1.54)
$CF_3CH_2NH_2$	5.70	0.01/0.1	0.55	20.9 (19.8, 21.2, 20.1, 22.5)
		0.02/0.2	0.85	23.1 (22.6, 20.5, 25.3, 24.0)
		0.03/0.3	1.2	24.3 (23.2, 26.2, 25.6, 22.3)
		0.04/0.4	1.5	21.8 (19.4, 23.2, 23.8, 20.7)
		0.05/0.5	1.8	20.2 (24.8, 15.7, 22.0, 15.8, 22.5)

[a] Determined in aqueous solution.[21] [b] Ratio of the protonated form of the amine to the free amine. [c] Average value; in parentheses are reported the individual values used to determine the average. [d] Determined in 80:20 (v/v) ethanol:trifluoroethanol at 30 ± 5 °C buffered with amine–amine hydrochloride buffers at a constant ionic strength of 0.05 M (tetramethylammonium chloride).

Our previous studies, concerning the solvolysis of silyl ethers in protic solvents, have provided evidence that the general base catalyzed solvolysis occurs by a concerted mechanism and does not involve the formation of a pentavalent intermediate.[12] We would now like to establish if the kinetically observed general base catalysis occurs by a mechanism involving true general base catalysis (Scheme 1) or by a mechanism involving specific base general acid catalysis (Scheme 2). Our approach to this problem involves studying the solvolysis of dimethylphenylphenoxysilane, catalyzed by a series of amine buffers of varying pK_a, in the mixed solvent 80:20 (v/v) trifluoroethanol:ethanol, and examining the changes in structure–reactivity relationships that occur upon changing the structure of the reactants.[19]

Results

Pseudo-first-order rate constants, k_{obs}, for the solvolysis of dimethylphenylphenoxysilane in 80:20 (v/v) ethanol: trifluoroethanol at 30 ± 0.5 °C and constant ionic strength of 0.05 M, maintained with tetramethylammonium chloride, were determined for a variety of amine/amine hydrochloride buffers. We chose to conduct our study in a single mixed solvent, as oppposed to conducting our study in neat ethanol and neat trifluoroethanol. This is because our study involves comparing the sensitivity, toward the basicity of the catalyst, for the addition of ethanol and for the addition of trifluoroethanol to dimethylphenylphenoxysilane. The pK_a values for the amines were determined in water[21] and it is likely that the pK_a will change on going from water to an alcohol solvent. If the change in pK_a of the amine on going from water to trifluoroethanol is different from the change in pK_a on going from water to ethanol, different sensitivities of the reaction could arise from changes in the pK_a of the catalyst due to the different solvents. By selecting a single solvent system to study the solvolysis reaction, any difference between the sensitivity of ethanol addition and trifluoroethanol addition to the basicity of the catalyst will not be due to differences in solvent. For each amine buffer the concentration of free amine was varied between 0.01 and 0.05 M, except for experiments involving trifluoroethylamine, where the concentration of amine was varied between 0.1 and 0.5 M. In all experiments the ratio of the concentration of the protonated form of the amine to the free form of the amine, *A*/*B*, was kept constant. Typically a ratio of $A/B = 1$ was used except for experiments with trifluoroethylamine, where a ratio for $A/B = 0.1$ was used. Rate constants were determined by monitoring the increase in absorbance at 280 nm due to the formation of phenol or by monitoring the disappearance of the dimethylphenylphenoxysilane using high pressure liquid chromatography (HPLC) as a function of time, as described in the Experimental Section. Pseudo-first-order rate constants, k_{obs}, were obtained from the appropriate semilog plots of absorbance values (UV technique) or peak areas (HPLC technique) vs time (see the Experimental Section). Errors in k_{obs} were estimated by visual inspection of the plots. In several experiments the value for k_{obs} was determined by both methods and each method gave, within experimental error, the same value for k_{obs}. Rate constants were reproducible within ±10%. In Table 1 are reported the rate constants, k_{obs}, and the pK_a values for each of the amine buffers, determined in aqueous solution. Also reported in Table 1 are the ratios of the dimethylphenyl(trifluoroethoxy)silane product to the dimethylphenylethoxysilane product (ROET/ROTFE), determined by HPLC analysis. ROTFE and ROET were the only products detected. The values reported for ROET/ROTFE are the average of at least two measurements determined as early in the reaction as possible; in parentheses are provided the individual

---

(16) Novice, M. H.; Seikaly, H. R.; Seiz, A. D.; Tidwell, T. T. *J. Am. Chem. Soc.* **1980**, *102*, 5834.

(17) Dietze, P. E. *J. Org. Chem.* **1992**, *57*, 6843.

(18) Swain, C. G.; Porschke, K. P.; Ahmed, W.; Schowen, R. L. *J. Am. Chem. Soc.* **1974**, *96*, 4700.

(19) This approach is similar to that used to demonstrate that the observed general acid catalyzed addition of alcohols to formaldehyde involves true general acid catalysis and not the kinetically equivalent specific acid general base catalysis. See Funderburk, L.H.; Aldwin, L.; Jencks, W. P. *J. Am. Chem. Soc.* **1978**, *100*, 5444.

(20) Jencks, W. P. *Chem. Rev.* **1985**, *85*, 511.

(21) Jencks, W. P.; Regenstein, J., In *Handbook of Biochemistry and Molecular Biology*, 3rd ed.; Fassman, G. D., Ed.; CRC: Cleveland, OH, 1975; Physical and Chemical Data, Vol. 1, pp 305–351.

Table 2. Values of the Pseudo-First-Order Rate Constants for Reaction of Ethanol, k^E, and for Reaction of Trifluoroethanol, k^T, with dimethylphenylphenoxysilane

amine	A/B[a]	k^E,[b] s	k^T,[b] s
$CH_3(CH_2)_3NH_2$	0.01/0.01	1.2 (1.1−1.2) × 10^3	0.41 (0.37−0.43) × 10^3
	0.02/0.02	1.4 (1.3−1.6) × 10^3	0.74 (0.66−0.84) × 10^3
	0.03/0.03	1.5 (1.3−1.7) × 10^3	0.79 (0.67−0.90) × 10^3
	0.04/0.04	1.8 (1.6−2.1) × 10^3	1.2 (1.0−1.3) × 10^3
	0.05/0.05	2.4 (2.0−2.5) × 10^3	1.6 (1.4−1.7) × 10^3
$CH_3OCH_2CH_2NH_2$	0.01/0.01	2.3 (2.1−2.5) × 10^4	0.96 (0.88−1.1) × 10^4
	0.02/0.02	2.8 (2.6−3.3) × 10^4	1.5 (1.4−1.8) × 10^4
	0.03/0.03	3.3 (3.2−3.8) × 10^4	2.2 (2.0−2.4) × 10^4
	0.04/0.04	3.6 (3.3−4.0) × 10^4	2.8 (2.5−3.1) × 10^4
	0.05/0.05	4.4 (4.3−5.0) × 10^4	3.5 (3.4−4.0) × 10^4
$HCCCH_2NH_2$	0.01/0.01	0.63 (0.51−0.071) × 10^5	0.90 (0.73−1.0) × 10^5
	0.02/0.02	0.87 (0.80−0.91) × 10^5	1.0 (0.95−1.1) × 10^5
	0.03/0.03	1.3 (0.91−1.4) × 10^5	1.1 (0.88−1.2) × 10^5
	0.04/0.04	1.5 (1.3−1.6) × 10^5	1.3 (1.2−1.5) × 10^5
	0.05/0.05	2.1 (1.9−2.4) × 10^5	1.3 (1.1−1.4) × 10^5
$CF_3CH_2NH_2$	0.01/0.1	0.52 (0.49−0.056) × 10^5	2.5 (2.3−2.8) × 10^7
	0.02/0.2	0.82 (0.80−0.86) × 10^5	3.5 (3.3−4.0) × 10^7
	0.03/0.3	1.1 (0.96−1.2) × 10^5	4.6 (3.7−5.3) × 10^7
	0.04/0.4	1.4 (1.4−1.5) × 10^5	6.6 (5.8−7.5) × 10^7
	0.05/0.5	1.8 (1.6−1.8) × 10^5	8.8 (7.0−11) × 10^7

[a] Ratio of amine hydrochloride to free amine. [b] Values in parentheses are lower and upper limits on the values for k^E and k^T as described in the text. Determined in 80:20 (v/v) ethanol:trifluoroethanol at 30 ± 5 °C buffered with amine−amine hydrochloride buffers at a constant ionic strength of 0.05 M (tetramethylammonium chloride).

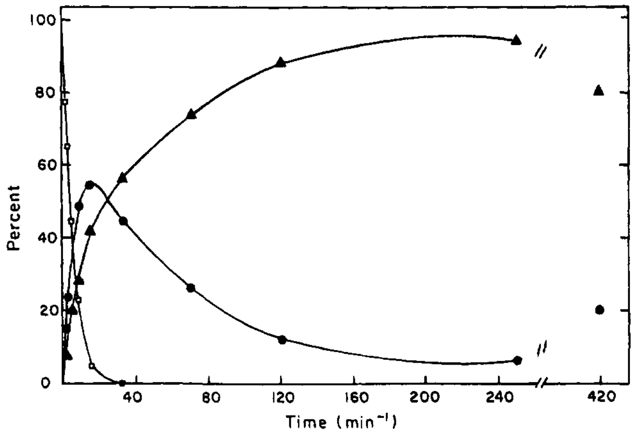


Figure 1. Plot of the fraction of total products against time for the butylamine-catalyzed reaction of dimethylphenylphenoxysilane in 80:20 v/v ethanol:trifluoroethanol containing 0.05 M butylamine and 0.05M butylamine hydrochloride at 30 ± 0.5 °C. Dimethylphenylphenoxysilane, □; ROET, ▲; and ROTFE, ●.

measurements for each experiment. It was demonstrated for each buffer system that the ratio of ROET/ROTFE remained constant during the time that product ratios were established. If the reaction was allowed to go to completion and monitored for longer periods of time the ratio ROET/ROTFE would eventually level off and remain at a value of approximately 5, which is the same as the molar concentration of trifluoroethanol to ethanol. In Figure 1 is shown a plot of the percentages of dimethylphenylphenoxysilane, ROET, and ROTFE as a function of time for the butylamine-catalyzed reaction of dimethylphenylphenoxysilane in 80:20 v/v ethanol:trifluoroethanol with A/B = 0.05 M/0.05 M. It can be seen in Figure 1 that the ratio ROET/ROTFE obtained from the intercept is similar to those obtained in individual measurements.

The value for k_{obs} is given by the following equation:

$$k_{obs} = k^T + k^E \tag{1}$$

where k^T and k^E are the pseudo-first-order rate constants for the reaction of dimethylphenylphenoxysilane with trifluoroethanol and ethanol, respectively, and where k^T and k^E are given by eqs 2 and 3:

$$k^T = k^T{}_O[\mathrm{TFE}] + k^T{}_B[\mathrm{B}][\mathrm{TFE}] \tag{2}$$

$$k^E = k^E{}_O[\mathrm{EtOH}] + k^E{}_B[\mathrm{EtOH}][\mathrm{B}] \tag{3}$$

In eqs 2 and 3 $k^T{}_O$ and $k^E{}_O$ are the second-order rate constants for the uncatalyzed reaction of dimethylphenylphenoxysilane with trifluoroethanol and ethanol, respectively, and $k^T{}_B$ and $k^E{}_B$ are the third-order rate constants for the base-catalyzed reaction of trifluoroethanol and ethanol with dimethylphenylphenoxysilane, respectively.

The product ratio ROET/ROTFE is given by:

$$\mathrm{ROET/ROTFE} = k^E/k^T \tag{4}$$

Combining eqs 1 and 4 gives eqs 5 and 6.

$$k^T = \frac{k_{obs}}{(1 + \mathrm{ROET/ROTFE})} \tag{5}$$

$$k^E = \frac{k_{obs}}{(1 + \mathrm{ROTFE/ROET})} \tag{6}$$

Using eqs 5 and 6, the values for k^T and k^E can be obtained for any experiment using the measured value for k_{obs} and the experimentally determined product ratio. In Table 2 are reported values of $k^T$and k^E for each experiment. Upper limits and lower limits on the values of k^T and k^E were obtained using the upper and lower limits for the value of k_{obs} and the smallest and largest experimentally determined values for the product ratios in each experiment.

According to eq 2, a plot of k^T vs [B] will have a slope of $k^T{}_B$[TFE], the pseudo-second-order rate constant for the amine-catalyzed addition of trifluroethanol to dimethylphenylphenoxysilane, and an intercept of $k^T{}_O$[TFE], the pseudo-first-order rate constant for the uncatalyzed addition of trifluoroethanol. Similarly, values of $k^E{}_B$[EtOH], the pseudo-second-order rate constant for

Table 3. Values of the Pseudo-Second-Order Rate Constant for the Amine-Catalyzed Addition of Trifluoroethanol, $k^T{}_B$[TFE], and of Ethanol, $k^E{}_B$[EtOH], to Dimethylphenylphenoxysilane[a]

amine	$k^T{}_B$[TFE], M s	$k^E{}_B$[EtOH], M s
$CH_3(CH_2)_3NH_2$	2.9×10^{-2} $[(2.2-3.7) \times 10^{-2}]$	2.7×10^{-2} $[(1.7-4.0) \times 10^{-2}]$
$CH_3OCH_2CH_2NH_2$	4.9×10^{-3} $[(3.8-6.6) \times 10^{-3}]$	5.7×10^{-3} $[(5.4-7.0) \times 10^{-3}]$
$HCCCH_2NH_2$	1.2×10^{-4} $[(1.0-2.0) \times 10^{-4}]$	3.7×10^{-4} $[(3.6-5.9) \times 10^{-4}]$
$CF_3CH_2NH_2$	1.4×10^{-6} $[(1.1-2.3) \times 10^{-6}]$	3.1×10^{-5} $[(2.7-3.4) \times 10^{-5}]$

[a] Values in brackets lower and upper limits on the values for $k^T{}_B$[TFE] and $k^E{}_B$[EtOH].

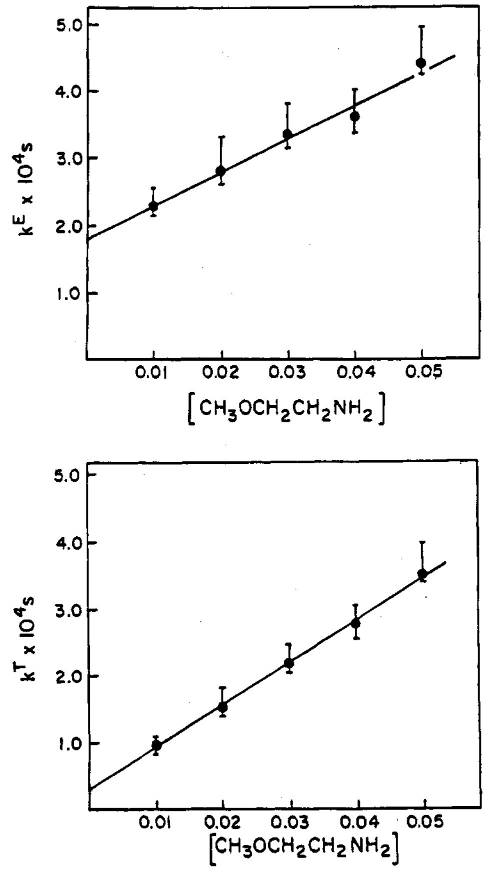


Figure 2. Plot of the pseudo-first-order rate constant for the reaction of trifluoroethanol, k^T, and of ethanol, k^E, with phenyldimethylphenoxysilane vs the concentration of methoxyethylamine for reaction in 80:20 v/v trifluoroethanol: ethanol buffered with 1:1 methoxyethylamine:methoxyethylamine hydrochloride and constant ionic strength of 0.05 M (tetramethylammonium chloride) at 30 ± 0.5 °C.

the amine-catalyzed addition of ethanol, and $k^E{}_O$[EtOH], the pseudo-first-order rate constant for the uncatalyzed addition of ethanol, can be determined using eq 3. Values of $k^T{}_B$ and $k^E{}_B$ for each amine are reported in Table 3, and errors are estimated from examination of the slopes of the plots of k^T and k^E vs [B]. A typical plot of k^T vs [B] and of k^E vs [B] is shown in Figure 2.

Discussion

Previously we provided evidence that the alcoholysis of phenyldimethylphenoxysilane occurs by a concerted mechanism where bond formation to the attacking alcohol takes place concurrently with bond breaking to the leaving group.[12] In addition, it is well-established that the addition of solvent is general base catalyzed.[2-7] The data in Table 1 demonstrate that the values for k_{obs} increase with increasing concentration of the buffer, as expected for general base catalysis. What has not yet been established is the mechanism for the observed catalysis. The results of the experiments reported above and discussed below provide evidence that the mechanism for the observed catalysis is true general base catalysis as described in Scheme 1 and not the kinetically equivalent mechanism of specific base general acid catalysis as described in Scheme 2.

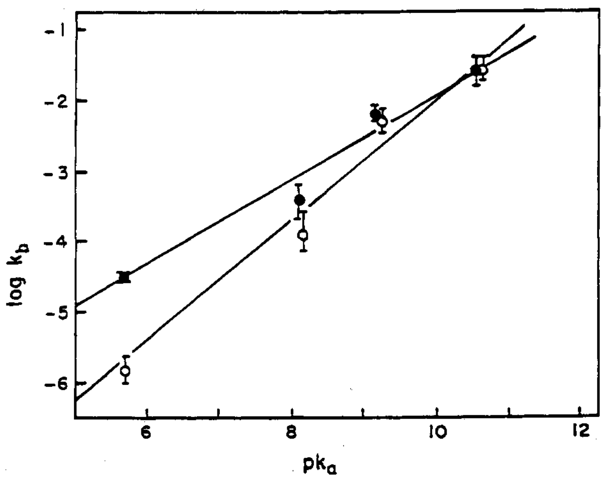


Figure 3. Brönsted plot for the general base catalyzed addition of ethanol (●), and trifluoroethanol (○) to phenyldimethylphenoxysilane. The catalysts in order of increasing pK_a are trifluoroethylamine, propargylamine, methoxyethylamine, and butylamine.

Brönsted plots of log $k^T{}_B$[TFE] and of log $k^E{}_B$[EtOH] vs the pK_a of the base catalyst are provided in Figure 3. The slopes of these plots, β_{TFE} and β_{EtOH} , are 0.89 and 0.59, respectively. The values for β_{TFE} and β_{EtOH} are a measure of the sensitivity of the reaction to the pK_a of the base catalyst for the general base catalyzed addition of trifluoroethanol and ethanol to phenyldimethylphenoxysilane, respectively. The Brönsted plots for the general base catalyzed addition of trifluoroethanol and ethanol to phenyldimethylphenoxysilane indicate that the sensitivity of the reaction to the pK_a of the catalyzing base is larger for trifluoroethanol than for ethanol. That the slopes of the Brönsted plots for trifluoroethanol addition and for ethanol addition are different is clearly illustrated by a plot of (log $k^E{}_B$ − log $k^T{}_B$) vs the pK_a of the base catalyst (Figure 4). If there was no difference in the sensitivity, all of the points in Figure 4 would fall on a line of slope zero.

This change in slope of the Brönsted correlation with changing pK_a of the nucleophilic alcohol is the behavior expected for a mechanism involving true general base catalysis as depicted in Scheme 1[8,9] and can be qualitatively described using a three-dimensional energy contour diagram.[21] In Figure 5 is depicted a three-dimensional energy contour diagram for the true general base catalyzed addition of an alcohol, ROH, to a silyl ether such as phenyldimethylphenoxysilane. In Figure 5 the base catalyst is represented by B. In Figure 5 the reactants are located in the lower left hand corner of the diagram and the products in the upper right hand corner. The X axis of Figure 5 represents the amount of proton transfer as measured by β, the Y axis measures the amount of

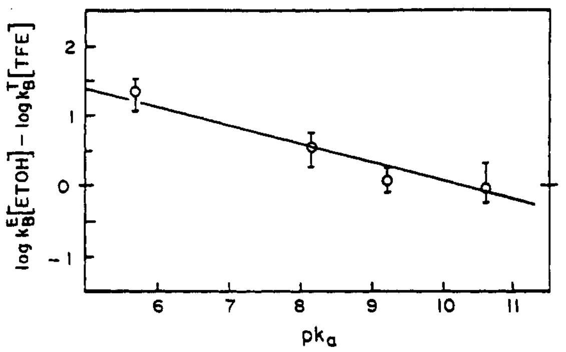


Figure 4. Plot of the difference between the logarithm of the rate constants for general base catalyzed addition of ethanol to phenyldimethylphenoxysilane and the logarithm of the rate constants for general base catalyzed addition of trifluoroethanol to phenyldimethylphenoxysilane vs the pK_a of the catalyst.

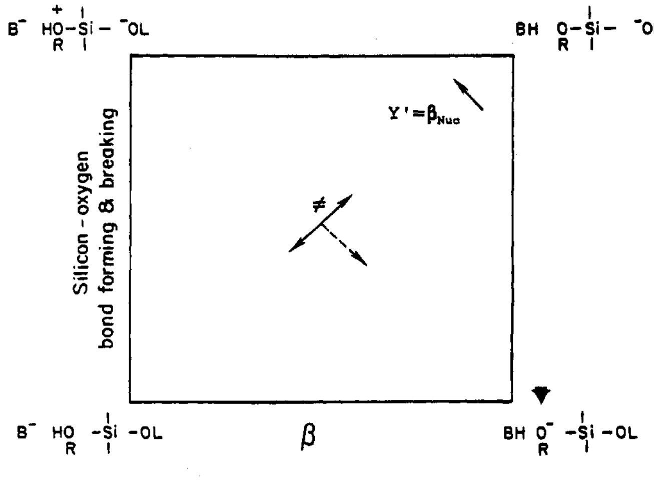


Figure 5. Reaction coordinate energy diagram for the general base catalyzed reaction of alcohols with silyl ethers according to the mechanism described in Scheme 1. Proton transfer is represented on the horizontal axis by β, silicon—oxygen bond formation and cleavage are represented on the verticle axis, and charge development on the nucleophilic alcohol, as measured by β_{Nuc}, is represented along the diagonal coordinate from the lower right hand corner to the upper left hand corner of the figure.

silicon-oxygen bond formation and/or bond breaking, and a diagonal axis from the lower right hand corner to the upper left hand corner, labeled Y', represents charge development on the central oxygen atom of the attacking alcohol as measured by β_{Nuc}. This diagonal axis, Y', ranges from a full negative charge on the attacking alcohol in the lower right hand corner to a full positive charge on the attacking alcohol in the upper left hand corner and is determined by the relative amounts of proton transfer to the base catalyst and bond formation to the silicon atom. There is no charge on the attacking alcohol along the diagonal line from reactants to products. In Figure 5 energy contour lines have been omitted for clarity and the transition state has been arbitrarily placed in the middle of the diagram. Now, consider the effect of changing the attacking alcohol from ethanol to trifluoroethanol. Changing the alcohol to one with a more electron withdrawing group will stabilize the alkoxide structure, RO$^-$. This can be represented by lowering the lower right hand corner of the diagram relative to the upper left hand corner, as indicated by the heavy arrow. This will cause the transition state to slide downhill perpendicular to the reaction coordinate, an anti-Hammond effect, as indicated by the dashed line. The new transition state will thus show an increase in the value of β for proton removal. The value of β will be larger for the less nucleophilic alcohol so that the value of β will be larger for trifluoroethanol than for ethanol, $\beta_{\mathrm{TFE}} > \beta_{\mathrm{EtOH}}$. This structure–reactivity behavior, consistent with what is observed experimentally, can be described by the cross interaction coefficient $p_{XY'} = \partial\beta/-\partial pK_{\mathrm{Nuc}} = \partial\beta_{\mathrm{Nuc}}/-\partial pK_{\mathrm{Catalyst}} = +0.08$.[20]

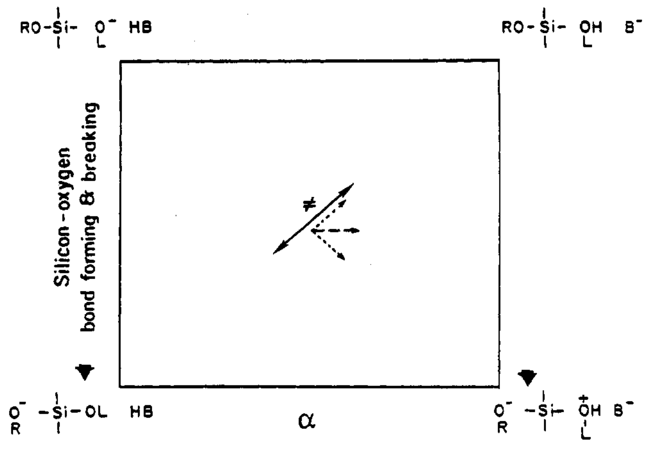


Figure 6. Reaction coordinate energy diagram for the general base catalyzed reaction of alcohols with silyl ethers according to the mechanism described in Scheme 2. Proton transfer is represented on the horizontal axis by α and silicon—oxygen bond formation and cleavage is represented on the verticle axis.

The observed structure-reactivity behavior is opposite to that expected for the specific base general acid catalyzed mechanism described in Scheme 2 and depicted by the three-dimensional energy contour diagram depicted in Figure 6.[8,9] In Figure 6 the X axis represents the amount of proton transfer, as measured by α, and the Y axis represents bond formation to the attacking alcohol, as measured by β_{Nuc}. Changing to an alcohol with a more electron withdrawing group, such as changing from ethanol to trifluoroethanol, will stabilize the alkoxide structure, RO$^-$, and can be represented by lowering the lower edge of the diagram relative to the upper edge, as indicated by the heavy arrows. Such a change will cause the transition state to slide downhill perpendicular to the reaction coordinate, an anti-Hammond effect, and uphill parallel to the reaction coordinate, a Hammond effect, as indicated by the dotted lines. The overall effect is the sum of the two vectors and the transition state will move to a new position as indicated by the dashed line. The new transition state will show an increase in the value for α. For a given series of catalysts α is equal to $1 - \beta$ so that an increase in α corresponds to a decrease in β. If the mechanism of catalysis were specific base general acid catalysis a decrease in the value of β would be observed when the attacking alcohol is changed to one of lower nucleophilicity, i.e. $\beta_{\mathrm{TFE}} < \beta_{\mathrm{EtOH}}$, this is contrary to what is observed experimentally. Therefore, the increase in β for proton removal that is observed when the pK_a of the nucleophilic alcohol is decreased provides evidence that the observed general base catalysis of silyl ether solvolysis occurs by a mechanism that involves true general base catalysis and not by the kinetically equivalent mechanism of specific base–general acid catalysis.[19]

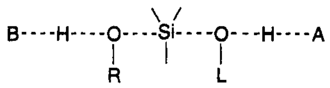


Figure 7.

This observation supports our earlier suggestion[17] that general acid catalysis, general base catalysis, and bifunctional catalysis in the solvolysis of phenyldimethylphenoxysilane all occur by slight modification of a similar mechanism. We provided evidence that the observed bifunctional catalysis of phenyldimethylphenoxysilane solvolyis involved a molecule of acid catalyst protonating the leaving group in the transition state as a molecule of base catalyst removed a proton from the attacking solvent molecule.[17] The transition state for bifunctional catalysis is depicted in Figure 7. In Figure 7, ROH is the alcohol solvent, OL is the leaving group, B is the base catalyst, and AH is the acid catalyst.

We suggested[17] that the observed general base catalysis occurred by a similar mechanism except that the acid catalyst was replaced by another molecule of solvent (AH in Figure 7 is replaced by ROH); however, this solvent molecule only stabilizes the negative charge developing on the leaving group by hydrogren bonding since there is no thermodynamic advantage for proton transfer. This mechanism proposed to account for the observed general base catalyzed alcoholysis of phenyldimethylphenoxysilane is true general base catalysis. The results of this study are consistent with that proposal.

In conclusion, the alcoholysis of phenyldimethylphenoxysilane is characterized by a positive cross interaction coefficient $p_{XY'} = \partial\beta/-\partial pK_{Nuc} = \partial\beta_{Nuc}/-\partial pK_{Catalyst}$. The observation of a positve $p_{XY'}$ coefficient provides support that the mechanism for catalysis is true general base catalysis and not specific base general acid catalysis.

Experimental Section

Methods. High-performance 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-μm NOVA-PAK C_{18} 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 NMR specrometer. 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. 2,2,2-Trifluoroethanol, ethanol, methanol, butylamine, 2-methoxyethylamine, 2,2,2-trifluoroethylamine, 2,2,2-trifluoroethylamine hydrochloride, acetic acid, potassium acetate, phenol, and phenyldimethylsilyl chloride were commercially available and used without further purification. Propargylamine was commercially available and distilled prior to use. Tetramethylammonium chloride was commercially available and recrystallized from ethanol/acetone.

Butylamine hydrochloride and methoxyethylamine hydrochloride were prepared by adjusting the pH of an aqueous solution of the amine to a pH of 7 with 1.0 M HCl. The water was removed under vacuum and the resulting wet solid recrystallized from ethanol/ether and dried in a vacuum desiccator overnight. The pH of an aqueous solution of the salt was 7.

Dimethylphenylphenoxysilane was prepared from phenyldimethylsilyl chloride according to published procedure[4] and was distilled under vacuum. The dimethylphenylphenoxysilane gave an ^{1}H NMR and mass spectra consistent with the desired product and was determined 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 was stable under the reaction conditions used in this study and in fact could be used as an internal standard (see below).

Kinetics and Product Studies. Reaction solutions were prepared by combining known volumes of stock solutions of the amine/amine hydrochloride, 0.05 M/0.05 M in 80:20 ethanol:trifluoroethanol with a known volume of 0.05 M tetramethylammonium chloride to give a final volume of 2.5 mL. For trifluoroethylamine the stock buffer solution of amine/amine hydrochloride was 0.5 M/0.05 M. The stock solutions were prepared by weighing a known amount of the amine and a known amount of the amine hydrochloride into a volumetric flask and filling to volume with a previously prepared 80:20 (v/v) ethanol: trifluoroethanol solution. The tetramethylammonium chloride solution was prepared in a similar way. The 80:20 (v/v) ethanol:trifluoroethanol solution was prepared by combining 80 mL of ethanol and 20 mL of trifluoroethanol accurately measured using a pipet. For the reactions catalyzed by trifluoroethylamine and propargylamine, the reaction solutions were prepared in a cuvette and placed in a thermostated cell holder of the spectrophotometer. After temperature equilibration (30 ± 0.5 °C), 0.4–0.6 μL of dimethylphenylphenoxysilane was added, the cuvette shaken and the appearance of phenol monitored as a function of time at 280 nm. The spectrophotometer was interfaced to a personal computer and the pseudo-first-order rate constants, k_{obs}, were obtained by a nonlinear regression analysis of absorbance vs time data. Reactions were followed for more than 3 half-lives except for the slowest reactions, which were followed for 2 half-lives. The nonlinear regression analysis calculated the best end point. For reactions that could be followed to completion, the observed end points always agreed well with calculated end points. Good pseudo-first-order kinetics were followed and semilog plots of $(A_\infty - A_t)$ were linear. Rate constants were generally reproducible within better than 12%.

For reactions catalyzed by butylamine and methoxyethylamine pseudo-first-order rate constants, k_{obs}, were obtained by monitoring the disappearance of phenyldimethylphenoxysilane as a function of time by HPLC. A 1.0-mL sample of reaction solution was placed in a 4-mL glass vial. The vial was closed tightly with a Teflon-sealed cap and placed in a constant temperature bath at (30 ± 0.5 °C). After temperature equilibration, 2.0 μL of dimethylphenylphenoxysilane was added to the vial and the vial shaken. At various time intervals, 75-μL aliquots of the reaction mixture were removed and quenched in 75 μL 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 and injected on the HPLC. The area of the peak corresponding to dimethylphenylphenoxysilane was normalized relative to the standard tetramethyldiphenylsiloxane (see above). HPLC analysis of the reaction mixture was accomplished with a flow of 0.8 mL/min for the initial 19 min, after which the flow was increased to 1.0 mL/min. The solvent system was 65:35 $CH_3CN:H_2O$ for 13 min followed by gradient elution to 100% CH_3CN over a time of 6 min, and then maintained at 100% CH_3CN for 3 min. The slope of a semilog plot of of peak area of dimethylphenylphenoxysilane relative to the standard against time gave k_{obs}. Semilog plots were linear for over 3 half-lives. Rate constants were generally reproducible within 12%. For several experiments with propargylamine buffers, k_{obs} was determined by both the UV procedure and by the HPLC procedure. Both techniques gave the same value for k_{obs} within experimental error. The only observed products by HPLC were ROET and ROTFE.

The ratio of ROET relative to ROTFE for the amine-catalyzed reactions of dimethylphenylphenoxysilane (ROPh) in 80:20 v/v ethanol:trifluoroethanol (EtOH:TFE) was determined by HPLC analysis of the reaction mixtures. To 1 mL of 80:20 EtOH:TFE, placed in a glass vial closed with a Teflon-sealed cap, containing a known concentration of the amine buffer and maintained at 30 ± 0.5 °C was added 2 μL of dimethylphenylphenoxysilane and the mixture shaken. At various times, early in the reaction, 75 μL of the reaction mixture was removed and quenched in 75 μL of 0.06 M acetic acid/0.06 M potassium acetate in methanol at −78 °C (0.15 M acetic acid/0.15 M potassium acetate was used to quench the trifluoroethylamine-catalyzed reactions). The appropriate control experiments demonstrated that the quenched solution at −78 °C did not undergo any additional reaction during the time required for analysis. The quenched solutions were then warmed to 0 °C in an ice/water bath and injected on the HPLC apparatus. HPLC analysis of the reaction mixture was accomplished with the same set of conditions as described above for the kinetic experiments. The only products detected by HPLC were ROET and ROTFE. Peak areas of ROPh, ROET, and ROTFE were obtained by electronic integration of their UV absorbance at 254 nm. The peak areas of ROET and ROTFE were corrected by their relative response factors when determining the product ratio ROET/ROTFE. The relative response factors were determined by the following procedure: 1 μL of ROPh was added separately to 1 mL of trifluoroethanol and to 1 mL of ethanol and the solutions were allowed to sit overnight at 30 ± 0.5 °C. On the following day each solution was injected on the HPLC apparatus, the peak corresponding to ROPh had completely disappeared, and the only peak observed corresponded to either ROET or ROTFE. The area of the ROET peak or of the ROTFE peak was normalized relative to the internal standard (tetramethyldiphenylsiloxane). The response factor for each peak was then obtained by comparing their normalized peak areas to the normalized peak area of dimethylphenylphenoxysilane. The normalized area for dimethylphenylphenoxysilane relative to the internal standard tetramethyldiphenylsiloxane was determined by placing 1 μL of ROPh (containing tetramethyldiphenylsiloxane, see above) in 1 mL of CH_3CN and analyzing the mixture with HPLC. The same sample of dimethylphenylphenoxysilane was used in all experiments. Each measurement of peak area relative to the peak area of the tetramethyldiphenylsiloxane was determined four times. The relative response factors for ROPh, ROET, and ROTFE were found to be 3.5, 1.0, and 1.3, respectively.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work and to the University of Maryland for an institutional DRIF grant.