Articles

Acetyltrimethylsilane Keto–Enol System. Determination of the Keto–Enol Equilibrium Constant and Acid Dissociation Constants of the Keto and Enol Forms in Aqueous Solution

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The enol isomer of the prototype α-silyl-substituted ketone, acetyltrimethylsilane, was generated by flash photolytic photooxidation of α-(trimethylsilyl)ethanol in aqueous solution, and its rates of acid- and base-catalyzed ketonization in that medium were determined. These, in combination with rates of enolization of the ketone determined by iodine scavenging, provided the keto–enol equilibrium constant $pK_E = 4.89$, the dissociation constant of the enol ionizing as an oxygen acid $pK_a^E = 11.54$, and the dissociation constant of the ketone ionizing as a carbon acid $pK_a^K = 16.44$. Comparison of these results with corresponding values for simple alkyl-substituted carbonyl compounds shows that α-silyl substitution raises K_E markedly, lowers K_a^E modestly, and raises K_a^K somewhat more strongly. Possible causes of these effects are discussed.

Current interest in the chemistry of silicon and of simple enols has led to the preparation of the first stable α-silyl-substituted enol, β,β-dimesityl-α-(trimethylsilyl)vinyl alcohol, 1 (Mes = 2,4,6-trimethylphenyl).[1] This enol could
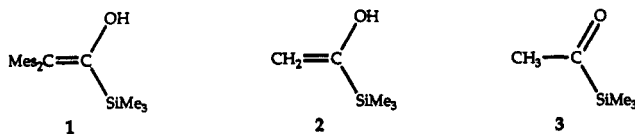
not be converted to its keto isomer under conditions where nonsilyl-substituted analogs could be isomerized, and it was therefore assumed that the enol was the thermodynamically more stable isomer and that the α-silyl group had influenced the keto–enol equilibrium. This assumption was then confirmed by our generation of the prototype α-silyl enol, α-(trimethylsilyl)vinyl alcohol, 2, and equilibration of that substance with its keto isomer, acetyltrimethylsilane, 3: this showed that α-silyl substitution had indeed raised the keto–enol equilibrium constant by several orders of magnitude.[2] We originally described this work only in preliminary form;[2] we now report it in full.

Although α-(trimethylsilyl)vinyl alcohol can be generated and observed in the medium we have used, i.e., aqueous solution, it is nevertheless a short-lived, labile substance in this solvent, and fast reaction techniques are needed for its study. We have used flash photolysis, with photooxidation of α-(trimethylsilyl)ethanol by acetone, eq 1, as the generating reaction; this is a process that we have used successfully before to study a number of other simple enols.[3]
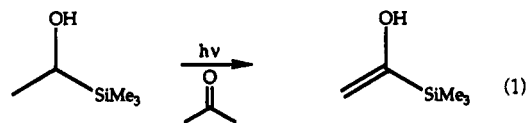
Experimental Section

Materials. Acetyltrimethylsilane was prepared by hydrolysis of ethyl α-(trimethylsilyl)vinyl ether,[4] which was obtained by treating the α-lithio derivative of ethyl vinyl ether with trimethylsilyl chloride.[4,5] α-(Trimethylsilyl)ethanol was synthesized by hydroboration of vinyltrimethylsilane followed by hydrogen peroxide oxidation of the boron adduct;[6] this gave a mixture of α- and β-(trimethylsilyl)ethanols which were separated by gas chromatography.

(Acetyl-d_3)trimethylsilane was prepared from acetaldehyde-d_4 (MSD Isotopes, 99 atom % D) by converting that to its 1,3-dithiane derivative, treating this substance first with butyllithium and then with trimethylsilyl chloride, and finally hydrolyzing the product.[7] Mass spectral analysis of the acetyltrimethylsilane so obtained, however, showed that it had lost 30% of its acetyl group deuterium during these reactions. This material was therefore then subjected to acid-catalyzed exchange with D_2O: a two-phase mixture of 150 mg of the partly deuterated material was stirred rapidly with 25 mL of 0.1 M $DClO_4/D_2O$ for 70 h. Mass spectral analysis showed that the recovered material now had a deuterium content of 99.6 atom % in its acetyl group.

All other materials were best available commercial grades.

Product Study. Acetyltrimethylsilane was detected as the product of photooxidation of α-(trimethylsilyl)ethanol by acetone through conversion to its semicarbazone derivative. A solution of 0.07 M α-(trimethylsilyl)ethanol and 0.04 M acetone in 10 mL of 0.10 M aqueous perchloric acid was subjected to 20 flashes of 320 J each in our conventional flash photolysis apparatus;[8] 1.0 mL of 0.4 M aqueous semicarbazide hydrochloride was then added, and the resulting solution was analyzed by HPLC (Varian

(1) Nadler, E. B.; Rappoport, Z.; Arad, D.; Apeloig, Y. *J. Am. Chem. Soc.* **1987**, *109*, 7873–7875.

(2) Kresge, A. J.; Tobin, J. B. *J. Am. Chem. Soc.* **1990**, *112*, 2805–2806.

(3) Keeffe, J. R.; Kresge, A. J.; Schepp, N. P. *J. Am. Chem. Soc.* **1988**, *110*, 1993–1995; **1990**, *112*, 4862–4868.

(4) Cunico, R. F., Kuan, C. P. *J. Org. Chem.* **1985**, *50*, 5410–5413.

(5) Soderquist, J. A. *Org. Synth.* **1989**, *68*, 25–31.

(6) Lim, T. F. O.; Meyers, J. K.; Rogers, G. T.; Jones, P. R. *J. Organomet. Chem.* **1977**, *135*, 249–259.

(7) Brook, A. G.; Duff, J. H.; Jones, P. F.; Davis, N. R. *J. Am. Chem. Soc.* **1967**, *89*, 431–434. Corey, E. J.; Seebach, D.; Freedman, R. *J. Am. Chem. Soc.* **1967**, *89*, 434–436.

(8) Chiang, Y.; Hojatti, M.; Keeffe, J. R.; Kresge, A. J.; Schepp, N. P.; Wirz, J. *J. Am. Chem. Soc.* **1987**, *109*, 4000–4009.

9060 Polychrom system with a μBondapac CN column). Elution with 20% CH_3CN/80% H_2O gave a major peak with a retention time of 3.6 min and a minor peak with a retention time of 6.9 min; the substances producing these peaks were identified as the semicarbazones of acetone and acetyltrimethylsilane, respectively, by comparison with chromatograms of authentic samples. The area of the minor peak corresponded to a 0.2% conversion of α-(trimethylsilyl)ethanol to α-(trimethylsilyl)vinyl alcohol, which is consistent with the poor efficiency of the photoreaction indicated by the kinetic studies (vide infra).

Kinetics: Ketonization. Rates of ketonization of α-(trimethylsilyl)vinyl alcohol were measured using enol generated flash photolytically by photooxidation of α-(trimethylsilyl)-ethanol with acetone in an apparatus of conventional design that produced a 2000 J pulse of white light, 50 μs wide, whose details have already been described.[8] Silyl alcohol and acetone were supplied at concentrations ca. 0.01 and 0.05 M, respectively, in aqueous solutions of acid or base from which oxygen had been removed by nitrogen bubbling. The temperature of the reaction solutions was maintained at 25.0 ± 0.05 °C by circulating water from a constant temperature bath through the jacket of the reaction cell. Decay of the enol was monitored at λ = 220 nm, and observed first-order rate constants were obtained by fitting the data to an exponential function; in the case of measurements in acid solutions where the overall decrease in absorbance was biphasic (fast decay of acetone enol followed by slower decay of acetyltrimethylsilane enol), this was accomplished by breaking the trace up into separate faster and slower components.

Kinetics: Enolization. Rates of enolization of acetyltrimethylsilane were determined by trapping the enol with iodine as it formed. Measurements were made in the presence of iodide ion, and the reactions were followed by monitoring the decrease in absorbance at λ = 466 nm due to the triodide ion formed by the rapidly established equilibrium reaction $I_2 + I^- = I_3^-$; Cary Models 118 and 2200 spectrometers were used with cell compartments thermostated to keep the reaction solutions at 25.0 ± 0.05 °C. Initial concentrations of acetyltrimethylsilane (1.9 × 10^{-4} M) were less than initial iodine concentrations ((2.0–6.0) × 10^{-4} M), and reactions were followed for 2–4 half-lives. The data fit the first-order rate law well, and observed first-order rate constants were obtained by least-squares fitting to an exponential function.

Kinetics: Hydrogen Exchange. Rates of exchange of protium of the acetyl methyl group of acetyltrimethylsilane with deuterium in acidified solutions of D_2O were determined by ^{1}H NMR. The half-lives of these exchange reactions were 3–12 h, and they were therefore carried out directly in NMR tubes that were kept immersed in a constant temperature bath (25.0 ± 0.05 °C), except for the brief periods (3–4 min) required to collect the NMR data. NMR measurements were made at 1–2-h intervals at 200 MHz on solutions whose acetyltrimethylsilane concentrations were 4 × 10^{-3} M. Ratios of integrals of the acetyl group signals in the region δ = 2.20–2.30 ppm (this signal was initially a singlet at δ = 2.29 ppm but became a multiplet and moved upfield as exchange progressed) to integrals of the trimethylsilyl group signals at δ = 0.10 ppm were evaluated. These data fit the first-order rate law well, and observed first-order rate constants were obtained by least-squares fitting to an exponential function.

Results

Ketonization. α-(Trimethylsilyl)ethanol proved to be stable in both acidic and basic aqueous solutions under the conditions of the present ketonization rate measurements: no change in the UV spectrum of this alcohol dissolved in these solutions could be detected even after they had stood overnight. The alcohol was also stable to flash photolysis in 0.10 M $HClO_4$ in the absence of acetone. Flashing in the presence of acetone, however, produced a rapidly decaying transient absorbance that could be attributed to the enols of acetone and acetyltrimethylsilane (vide infra). The photoreaction that produced these enols appeared to be inefficient, as evidenced by the rather weak signal that a single flash

produced and the more or less constant size of the signal generated by several successive flashes of the same solution. Evidently, little substrate was being consumed in a single flash. This made it possible to accumulate data by flashing the same solution several (4–6) times, and that was therefore commonly done.

Flash photolytic rate determinations were performed in dilute aqueous perchloric acid and sodium hydroxide solutions. The transient signals obtained from acid solutions were biphasic, with time constants of the two phases that differed by 2 orders of magnitude. The two phases could therefore be separated readily. The data for each phase obeyed the first-order rate law well, and observed first-order rate constants for each phase were obtained by fitting the separated data to single exponential functions by least-squares analysis. Measurements were made at 25 °C over the acid concentration range $[HClO_4]$ = 0.01–0.1 M at constant ionic strength (0.10 M, $NaClO_4$). Six different concentrations were used, and 5–10 replicate measurements were made at each concentration. The data so obtained are summarized in Tables S1 and S2.[9]

Rate constants for each of the two transient phases determined in this way were accurately proportional to acid concentration, and linear least-squares analysis gave the hydrogen-ion catalytic coefficients k_{H^+} = (5.66 ± 0.27) × 10^3 and 77.8 ± 1.1 M^{-1} s^{-1}.

The photoreaction of an alcohol with a ketone such as that used in the present study is a well-known process[10] in which the photoexcited ketone removes a hydrogen atom from the alcohol to give a pair of ketyl radicals; there is CINDP evidence that the ketyl radicals then disproportionate forming enols.[11] If, as in the present case, the two ketyl radicals are different, eq 2, disproportionation can

$$(2)$$

$$(3)$$
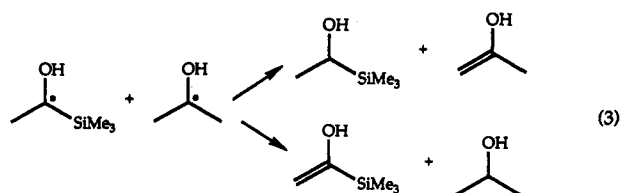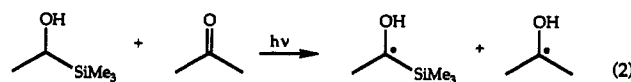
occur in two ways producing two different enols, eq 3. Observation of a biphasic transient decay in the present case is consistent with such a scheme, and the good agreement shown between the catalytic constant for one phase of this decay, k_{H^+} = (5.66 ± 0.27) × 10^3 M^{-1} s^{-1}, and the known rate constant for ketonization of acetone enol catalyzed by the hydrogen ion, $k_{H^+}^K$ = (5.95 ± 0.23) × 10^3 M^{-1} s^{-1},[12] provides additional support for this reaction mechanism. This serves to identify the catalytic coefficient for the other phase of the decay, $k_{H^+}^K$ = (7.78 ± 0.11) × 10^1 M^{-1} s^{-1}, as the rate constant for the ketonization of α-(trimethylsilyl)vinyl alcohol catalyzed by the hydrogen ion.

Rates of ketonization of α-(trimethylsilyl)vinyl alcohol were also measured in D_2O solutions of perchloric acid.

(9) See supplementary material.
(10) See, e.g.: Turro, N. J. *Modern Molecular Photochemistry*; Benjamin/Cummings: Toronto, 1978; Chapter 10.
(11) Blank, B.; Henne, A.; Laroff, G. P.; Fischer, H. *Pure Appl. Chem.* **1975**, *41*, 475–494.
(12) Chiang, Y.; Kresge, A. J.; Schepp, N. P. *J. Am. Chem. Soc.* **1989**, *111*, 3977–3980.
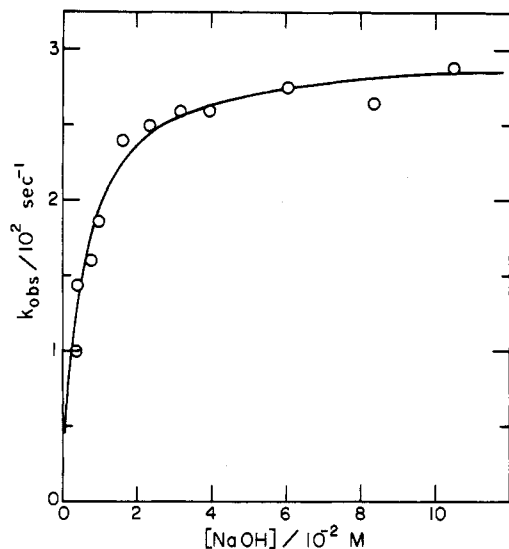
Figure 1. Relationship between sodium hydroxide concentration and observed first-order rate constants for the ketonization of α-(trimethylsilyl)vinyl alcohol in aqueous solution at 25 °C ionic strength = 0.10 M (NaClO₄); each point is the average of four to eight separate determinations. The line shown was obtained by least-squares fitting of the data to eq 5.

Data were obtained at five different acid concentrations over the range [DClO₄] = 0.02–0.10 M at constant ionic strength (0.10 M). The results, summarized in Table S1,[9] again showed observed first-order rate constants to be accurately proportional to acid concentration, and linear least-squares analysis gave the catalytic coefficient $k^K_{D^+}$ = (1.84 ± 0.08) × 10¹ M⁻¹ s⁻¹. This, combined with the corresponding rate constant obtained in H₂O solutions, provides the isotope effect k_{H^+}/k_{D^+} = 4.23 ± 0.19.

In contrast to the work in perchloric acid solutions, flash photolysis of α-(trimethylsilyl)ethanol and acetone in dilute aqueous sodium hydroxide produced a transient absorbance which decayed only in a monophasic fashion. This, however, is also consistent with the reaction scheme of eqs 2 and 3, for, in the range of sodium hydroxide concentrations used, acetone enol would be expected[13] to have a lifetime, τ = 20–30 μs, shorter than the width of the flash provided by the conventional flash photolysis system we used (50 μs), and this species would therefore have remained undetected. The monophasic absorbance decay seen in sodium hydroxide solutions may consequently be attributed to the ketonization of α-(trimethylsilyl)vinyl alcohol.

Rates of this reaction were measured at 11 different sodium hydroxide concentrations over the range [NaOH] = 0.003–0.1 M at constant ionic strength (0.10 M); replicate determinations (4–8) were made at each concentration. The data so obtained are summarized in Table S3.[9]

Observed first-order rate constants for this ketonization reaction increased with increasing sodium hydroxide concentration at the lower end of the concentration range employed, but, as Figure 1 shows, this increase leveled off and rate constants approached a limiting value at the high end of the concentration range. This is the behavior expected for ketonization of an enol that takes place through the enolate ion under conditions where significant amounts of the enolate ion are formed, eq 4. The rate law
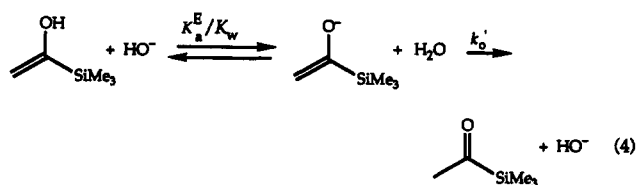
which applies to this reaction scheme is given in eq 5,

$$k_{obs} = \frac{k'_o(K^E_a/K_w)[HO^-]}{(K^E_a/K_w)[HO^-] + 1} \quad (5)$$

where k'_o is the rate constant for "spontaneous" ketonization of the enolate ion by proton transfer from a water molecule, K^E_a is the acid dissociation constant of the enol, and K_w is the autoprotolysis constant of water. Least-squares fitting of the data to this expression gave the relationship shown by the line in Figure 1, which is based upon the parameters k'_o = 299 ± 30 s⁻¹ and K^E_a = (2.94 ± 0.22) × 10⁻¹², pK^E_a = 11.53 ± 0.03.[14]

Another, independent, estimate of the acid dissociation constant K^E_a may be obtained from initial absorbances determined from these rate measurements made in hydroxide ion solutions. This method is based upon the fact that enolate ions absorb more strongly than do the corresponding enols, and transient absorbances extrapolated back to zero time therefore reflect the position of the enol–enolate equilibrium.[15] The expression which relates these initial absorbances, A_o, to K^E_a is given in eq 6, where ϵ_{EH} and ϵ_E are the extinction coefficients of enol

$$A_o = \frac{\epsilon_{EH}[H^+] + \epsilon_E K^E_a}{[H^+] + K^E_a}([EH] + [E]) \quad (6)$$

and enolate ion, respectively, and ([EH] + [E]) is the total enol plus enolate concentration. Least-squares fitting of the data, summarized in Table S4,[9] to this expression gave the result K^E_a = (2.43 ± 0.48) × 10⁻¹², pK^E_a = 11.61 ± 0.09, in good agreement with the constant obtained from the kinetic study, K^E_a = (2.94 ± 0.22) × 10⁻¹², pK^E_a = 11.53 ± 0.03. The weighted average of these two values is K^E_a = (2.85 ± 0.20) × 10⁻¹², pK^E_a = 11.54 ± 0.03.[14]

Absorption maxima of enolate ions, in addition to being stronger than those of corresponding enols, are also generally shifted to longer wavelengths,[15] just as absorption maxima of phenoxide ions appear at longer wavelengths than those of corresponding phenols.[16] This was found to be the case in the present system by using an Optical Multichannel Analyzer (EG & G Princeton Applied Research, Model 1461-1B) to record spectra of the transient species generated in these flash photolysis experiments. The spectrum recorded in 0.10 M aqueous HClO₄, taken after the enol of acetone had completely ketonized but while the enol of acetyltrimethylsilane was still present, showed a maximum at λ = 210 nm, while the spectrum recorded in 0.10 M aqueous NaOH showed a maximum at λ = 240 nm.

Enolization. Rates of enolization of acetyltrimethylsilane were determined in aqueous perchloric acid solutions

(13) Chiang, Y.; Kresge, A. J.; Tang, Y. S.; Wirz, J. *J. Am. Chem. Soc.* **1984**, *106*, 460–462.

(14) This acidity constant is a concentration quotient appropriate to the ionic strength of the measurements: 0.10 M.

(15) Haspra, P.; Sutter, A.; Wirz, J. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 617–619.

(16) Whelland, G. W. *Resonance in Organic Chemistry*; Wiley: New York, 1955; pp 289, 292–293.

using iodine, in the presence of iodide ion and therefore complexed as I_3^-, to scavenge the enol as it formed. Measurements were made over the acid concentration range $[HClO_4] = 0.02–0.10$ M at constant ionic strength (0.10 M), and stoichiometric iodine and iodide ion concentrations were varied as well: $[I_2]_s = (2–6) \times 10^{-4}$ M and $[I^-]_s = (3–20) \times 10^{-4}$ M. The data are summarized in Table S5.[9]

Observed first-order rate constants showed no discernable variation with either iodine or iodide ion concentration, but they were proportional to acid concentration. Linear least-squares analysis gave the hydrogen ion catalytic coefficient $k_{H+}^E = (9.98 \pm 0.24) \times 10^{-4}$ M^{-1} s^{-1}.

Two different isotope effects on this enolization reaction were also determined by measuring rates using a deuterated substrate, $CD_3COSiMe_3$, and by measuring rates with the protio-substrate in D_2O solution. In both cases a range of perchloric acid concentrations was used, and ionic strength was maintained at 0.10 M; observed first-order rate constants in both sets of data (summarized in Table S5)[9] proved to be accurately proportional to acid concentration. Least-squares analysis gave the catalytic coefficients $(k_{H+}^E)_D = (1.81 \pm 0.18) \times 10^{-4}$ M^{-1} s^{-1} for enolization of $CD_3COSiMe_3$ and $k_{D+}^E = (2.09 \pm 0.14) \times 10^{-3}$ M^{-1} s^{-1} for enolization of $CH_3COSiMe_3$ in D_2O. Combination of these results with the catalytic coefficient for enolization of $CH_3COSiMe_3$ in H_2O gave the substrate isotope effect $(k_{H+}^E)_H/(k_{H+}^E)_D = 5.52 \pm 0.56$ and the solvent isotope effect $k_{H+}^E/k_{D+}^E = 0.478 \pm 0.035$.

Hydrogen Exchange. Rates of replacement of protium in the acetyl group of $CH_3COSiMe_3$ by deuterium from the solvent were determined in aqueous (D_2O) perchloric acid solutions. Measurements were made over the concentration range $[DClO_4] = 0.02–0.1$ M, ionic strength $= 0.10$ M, and observed first-order rate constants, summarized in Table S6,[9] proved to be accurately proportional to acid concentration; least-squares analysis of the data gave the hydrogen–ion catalytic coefficient $(k_{D+})_{exch} = (7.09 \pm 0.29) \times 10^{-4}$ M^{-1} s^{-1}.
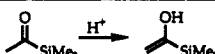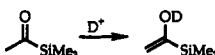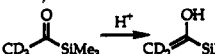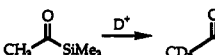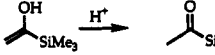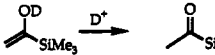
Discussion

Reaction Characteristics. The present investigation is the first detailed study of keto–enol interconversion in a system containing a silyl substituent α to the carbonyl group. Although there is no a priori reason to believe that the processes examined are not the enolization and ketonization reactions they were intended to be, it is nevertheless reassuring that the observations made are all typical of ketones and their enols.
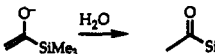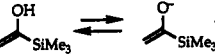
Foremost among these is identification of the keto isomer, acetyltrimethylsilane, as the product of the enol ketonization reaction. This was difficult to accomplish because the enol, formed as it was by an inefficient photooxidation reaction (eq 1), was generated in the presence of a large excess of acetone. Nevertheless, conversion of both ketones to their semicarbazones and separation of the two derivatives by HPLC left no doubt that acetyltrimethylsilane was the reaction product.

The rate law for reaction of ketones with halogens is also characteristic.[17] Ketones themselves do not react with halogens, but their enol isomers do, and halogenation therefore takes place by prior formation of the enol. Enols,
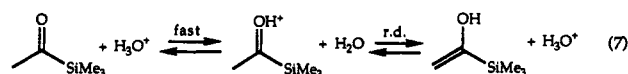
Table I. Summary of Rate and Equilibrium Constants for the Keto–Enol Interconversion of Acetyltrimethylsilane and α-(Trimethylsilyl)vinyl Alcohol in Aqueous Solution at 25 °C[a]

process	constant
(keto → enol, H$^+$)	$k_{H+}^E = 9.98 \times 10^{-4}$ M^{-1} s^{-1}
(keto → enol-OD, D$^+$)	$k_{D+}^E = 2.09 \times 10^{-3}$ M^{-1} s^{-1}
(CD_3 keto → CD_2 enol, H$^+$)	$(k_{H+}^E)_D = 1.81 \times 10^{-4}$ M^{-1} s^{-1}
(CH_3 keto → CD_3 keto, D$^+$)	$(k_{D+})_{exch} = 7.09 \times 10^{-4}$ M^{-1} s^{-1}
(enol → keto, H$^+$)	$k_{H+}^K = 7.78 \times 10^1$ M^{-1} s^{-1}
(enol-OD → keto, D$^+$)	$k_{D+}^K = 1.84 \times 10^1$ M^{-1} s^{-1}
(enolate → keto, H$_2$O)	$k_O' = 2.99 \times 10^2$ M^{-1} s^{-1}
(keto ⇌ enol)	$K_E = 1.28 \times 10^{-5}$; p$K_E = 4.89$
(enol ⇌ enolate + H$^+$)	$K_a^E = 2.85 \times 10^{-12}$ M; p$K_a^E = 11.54$
(keto ⇌ enolate + H$^+$)	$K_a^K = 3.66 \times 10^{-17}$ M; p$K_a^K = 16.44$

[a] Ionic strength $= 0.10$ M ($NaClO_4$); acidity constants are concentration quotients applicable at this ionic strength.

moreover, are very reactive toward halogens,[18] and halogenation of the enol therefore occurs in a rapid step after the rate-determining enol-formation stage. This leads to a rate law independent of halogen concentration. Such was the case here: rates of reaction of acetyltrimethylsilane with iodine were measured at different iodine concentrations, but this produced no change in reaction rate.

Isotope effects on hydronium-ion catalyzed keto–enol interconversions are also diagnostic. This reaction occurs by a two-step mechanism, which, in the enolization direction, involves equilibrium protonation of the keto oxygen atom followed by rate-determining removal of another hydrogen from the α-carbon atom, eq 7;[19] the

$$\text{(keto)} + H_3O^+ \underset{\text{fast}}{\rightleftharpoons} \text{(protonated)} + H_2O \underset{\text{r.d.}}{\rightleftharpoons} \text{(enol)} + H_3O^+ \quad (7)$$

reverse, ketonization reaction, therefore, consists of rate-determining proton transfer from the hydronium ion to the substrate. Reactions with equilibrium proton transfer

(17) Bell, R. P. *The Proton in Chemistry*, 2nd ed.; Cornell University Press: Ithaca, NY, 1973; pp 171–173.

(18) Hochstrasser, R.; Kresge, A. J.; Schepp, N. P.; Wirz, J. *J. Am. Chem. Soc.* **1988**, *110*, 7875–7876. Tapuhi, E.; Jencks, W. P. *J. Am. Chem. Soc.* **1982**, *104*, 5758–5765.

(19) For a recent review of the evidence, see: Keeffe, J. R.; Kresge, A. J. *The Chemistry of Enols*; Rappoport, Z., Ed.; Wiley: New York, 1990; Chapter 7.

Table II. Comparison of the Acetyltrimethylsilane Keto–Enol System with Related Analogs[a]

| system	pK_E	pK_a^E	pK_a^K	$k_{H+}^E/10^{-4}$ M^{-1} s^{-1}	$k_{H+}^K/10$ M^{-1} s^{-1}	ref
	4.89	11.54	16.44	9.98	7.78	this work
	6.23	10.50	16.73	0.168	3.30	8
	8.33	10.94	19.27	0.279	595.	12, 13
	8.76			0.131	750.	3

[a] Aqueous solution, 25 °C, ionic strength = 0.10 M (NaClO$_4$); acidity constants are concentration quotients applicable at this ionic strength.

from the hydronium ion prior to the rate-determining step generally give inverse solvent isotope effects ($k_H/k_D < 1$), whereas those on rate-determining proton transfer from the hydronium ion generally are in the normal direction ($k_H/k_D > 1$).[20] It is gratifying, therefore, that the present study found an inverse isotope effect on what was intended to be the enolization of acetyltrimethylsilane, k_{H+}/k_{D+} = 0.48, and a normal isotope effect on what was intended to be the ketonization of its enol, k_{H+}/k_{D+} = 4.2.

Enolization of a ketone also generally shows a substantial primary substrate isotope effect, inasmuch as a carbon-hydrogen bond of the substrate is broken in the rate-determining step. This also proved to be so in the present case: comparison of rates of reaction of CH$_3$COSiMe$_3$ and CD$_3$COSiCH$_3$ gave k_H/k_D = 5.5.

Finally, exchange of α-hydrogens of ketones generally occurs through enol formation followed by reketonization, and this implies a relationship between enolization and exchange rate constants. If, as was the case in the present study, exchange is followed by monitoring total loss of all hydrogens in a methyl group, specific rates of exchange should be one-third of rates of enolization. (See the Appendix of this paper for a derivation of this relationship.) This expectation was also met in that the catalytic coefficient for exchange of hydrogen from acetyltrime-thylsilane in D$_2$O solution was found to be $(k_{D+})_{exch}$ = (7.09 ± 0.29) × 10^{-4} M^{-1} s^{-1}, in good agreement with one-third of the rate of enolization of this substance in that medium, $^1/_3 k_{D+}^E$ = $^1/_3$(2.09 ± 0.14) × 10^{-3} M^{-1} s^{-1} = (6.97 ± 0.46) × 10^{-4} M^{-1} s^{-1}.

Enol Chemistry. The equilibrium constant for keto-enol isomerization in the acetyltrimethylsilane system may be obtained as the ratio of the hydrogen-ion catalytic coefficients for the enolization and ketonization reactions, $K_E = k_{H+}^E/k_{H+}^K$. The result is K_E = (1.28 ± 0.04) × 10^{-5}, pK_E = 4.89 ± 0.01. This equilibrium and the ionization of the enol as an acid, for which an acid dissociation constant, K_a^E, was determined from the present kinetic measurements in sodium hydroxide solutions, form two legs of a thermodynamic cycle whose third member is ionization of acetyltrimethylsilane as a carbon acid, eq 8. An equilibrium constant for this carbon acid ionization may therefore
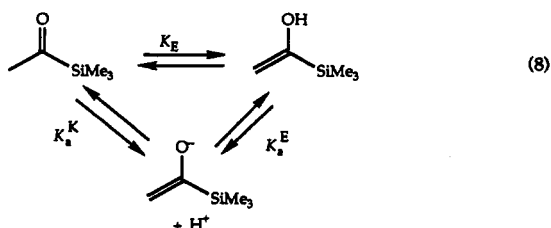
be obtained as the product of the other two constants, $K_a^K = K_E K_a^E$ = (3.66 ± 0.28) × 10^{-17}, pK_a^K = 16.44 ± 0.03. These results are compared with values for related systems in Table II.

It may be seen that α-silyl substitution raises the keto-enol equilibrium constant by a substantial amount: by 1.3 pK units relative to α-hydrogen and by 3.8–3.9 pK units relative to α-methyl[21] or *tert*-butyl. This difference is reflected in an increased rate of enolization of the silyl compound and, except in the case of the comparison with hydrogen, a decreased rate of ketonization as well; each of these changes is in the direction that will raise K_E.

Insight into the cause of this increase in K_E upon α-silyl substitution may be gained from the results of some recent ab initio molecular orbital calculations of energy differences between keto and enol isomers.[22] These calculations predict an increase in K_E upon α-silyl substitution, and, although they pertain to the gas phase, they are nevertheless in reasonably good quantitative agreement with our experimental result for aqueous solution. These calculations show that the principal cause of this increase in K_E is destabilization of the keto isomer by the α-silyl substituent, but there is also a significant, though smaller, stabilization of the enol isomer; both of these changes serve to lower the energy gap between ketone and enol and thus raise the value of K_E.

The comparisons provided by Table II show further that α-silyl substitution has a modest weakening effect on the acid strength of the enol of acetyltrimethylsilane: pK_a^E is 1.0 greater than that for the enol of acetaldehyde and 0.6 greater than that for the enol of acetone. This may be attributed to the electropositive nature of silicon which can be expected to destabilize the enolate ion; a similar acid-weakening effect of the silyl substituent has been observed on the acid strength of m-(trimethylsi-lyl)phenol.[23]

The effect of α-silyl substitution on the carbon acidity of the ketone, on the other hand, is in the opposite direction: pK_a^K for acetyltrimethylsilane is 0.3 lower than that for acetaldehyde and 3.1 lower than that for acetone. These differences are probably produced by α-silyl de-stabilization of the ketone: this would raise the initial state of the ionization reaction, thereby making the ketone

(8)

(20) Keeffe, J. R.; Kresge, A. J. *Techniques of Chemistry, Volume VI; Investigation of Rates and Mechanisms of Reactions*; Bernasconi, C. F., Ed.; Wiley: New York, 1986; Part I, Chapter XI.

(21) This comparison includes a statistical factor of 2 to account for the fact that acetone can react in two directions.

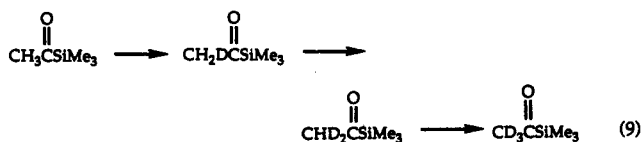(22) Apeloig, Y.; Arad, D.; Rappoport, Z. *J. Am. Chem. Soc.* 1990, *112*, 9131–9140.

(23) Benkeser, R. A.; Krysiak, H. R. *J. Am. Chem. Soc.* 1953, *75*, 2421–2425.

a stronger acid. Such an initial state effect is consistent with the greater difference in pK_a^K seen when the comparison is made with acetone than with acetaldehyde, inasmuch as methyl groups stabilize the ketone, producing an initial state effect in the opposite direction from that provided by a silyl group, and the two methyl groups of acetone will have a greater effect than the single methyl of acetaldehyde.

It was pointed out at the beginning of this paper that the first α-silyl-substituted enol to be synthesized, β,β-dimesityl-α-(trimethylsilyl)vinyl alcohol, 1, could not be converted to its keto isomer and that it was therefore assumed that the enol was the more stable isomer in this system. The present results support this assumption in that application of the factors by which K_E for acetyltrimethylsilane is greater than K_E for acetaldehyde, acetone, or methyl *tert*-butyl ketone to the known K_E values for the corresponding analogs of 1 produces estimates of K_E for 1 all of which exceed $K_E = 100$.

Appendix

Rate Law for Hydrogen Exchange. Replacement of protium by deuterium in the acetyl group of acetyltrimethylsilane will take place in three stages, as shown in eq 9. When this exchange is conducted using a dilute solution of the substrate in D_2O, the amount of deuterium available will be very much greater than the amount of protium, and each reaction step will be essentially nonreversible. The system can then be represented by a series of first-order nonreversible reactions, eq 10. The set of differential equations governing this kinetic scheme can be solved and

$$\underset{\substack{\text{O}\\\|\\CH_3CSiMe_3}}{} \longrightarrow \underset{\substack{\text{O}\\\|\\CH_2DCSiMe_3}}{} \longrightarrow$$

$$\underset{\substack{\text{O}\\\|\\CHD_2CSiMe_3}}{} \longrightarrow \underset{\substack{\text{O}\\\|\\CD_3CSiMe_3}}{} \qquad (9)$$

$$A \overset{k_1}{\rightarrow} B \overset{k_2}{\rightarrow} C \overset{k_3}{\rightarrow} D \qquad (10)$$

explicit expressions relating the concentrations of A, B, and C to time, t, may be obtained, eq 11.[24]

If k is taken to be the rate constant for the first step of the process in eq 9, then, neglecting secondary isotope

$$[A] = [A]_o e^{-k_1 t} \qquad (11)$$

$$[B] = [A]_o \left\{ \frac{k_1}{(k_2 - k_1)} \right\} (e^{-k_1 t} - e^{-k_2 t})$$

$$[C] = [A]_o \left[\left\{ \frac{k_1 k_2}{(k_2 - k_1)(k_3 - k_1)} \right\} e^{-k_1 t} + \left\{ \frac{k_1 k_2}{(k_1 - k_2)(k_3 - k_2)} \right\} e^{-k_2 t} + \left\{ \frac{k_1 k_2}{(k_1 - k_3)(k_2 - k_3)} \right\} e^{-k_3 t} \right]$$

effects, the rate constants for the subsequent steps will be $^2/_3 k$ and $^1/_3 k$ and the relationships of eq 12 result. The

$$k_1 = k; \; k_2 = 2k/3; \; k_3 = k/3 \qquad (12)$$

total protium content of the system is given by eq 13, and

$$[H] = A + {}^2/_3 B + {}^1/_3 C; \; [H]_o = [A]_o \qquad (13)$$

combination of eqs 11–13 then leads to eq 14. This is a

$$[H] = [H]_o e^{-1/_3 k t} \qquad (14)$$

first-order expression whose rate constant is $^k/_3$; it shows that the total loss of all protium from the acetyl group of $CH_3COSiMe_3$ will be a first-order process whose observed first-order rate constant is equal to one-third of the specific rate of the first stage of the overall process, $CH_3COSiMe_3 \rightarrow CH_2DCOSiMe_3$. If exchange occurs by an enolization-ketonization mechanism, then the rate constant for exchange will be one-third of the rate constant for enolization.

(24) Capellos, C.; Bielski, B. H. *Kinetic Systems*; Wiley-Interscience: New York, 1972; pp 46–49.