of the $^{31}P$ spectrum of a mixture of trimethylphosphate and methyl triflate was done on the JEOL FX90Q in the Fourier transform mode with an 85% $D_3PO_4$ reference and lock, and spectra were recorded both with and without proton decoupling. In none of these equilibrium studies was there any rate information, there was no change after the first spectrum was recorded, and the spectra were all as sharp as those with nonreacting systems.

**Calorimetry.** The calorimeter was that used by Turner and co-workers for heats of hydrogenation,[17] modified principally by closing of the hydrogen entry port and by substitution of a Kepco Model PCX-15 regulated power supply for the storage battery for calibration heating power. The methyltrimethoxyphosphonium triflate was dissolved in chloroform, and then after equilibration and an initial rating period, an ampule containing trimethyl phosphite was broken under the solution, and temperature–time recordings were taken until a final rating period was well established. Analogous reactions, but at higher concentrations, showed in the proton NMR complete conversion to dimethylmethylphosphonate and no loss of the catalyzing phosphonium salt. The calculations were conventional,[17] but the precision was not very high. We attribute the difficulty to the hygroscopic nature of trimethyl phosphite (as shown by the fact that the heat evolved seemed greater with older phosphite samples) and to the slowness of the reaction, which made the rate of heat transfer in and out of the calorimeter rather large for simple corrections in the time taken for complete reaction. Six runs yielded the average value $\Delta H = -24.2 \pm 2$ kcal/mol.

(17) Turner, R. B.; Meador, W. R.; Winkler, R. E. *J. Am. Chem. Soc.* **1957**, *79*, 4116.

**Acknowledgment.** We thank the Robert A. Welch Foundation for a grant which supported this work. We thank the National Science Foundation for a Research Equipment grant providing the XL-100 NMR spectrometer and a later grant providing the JEOL FX90Q spectrometer. We thank Mr. Donald Hamp for the spectra reported on this latter instrument.

**Registry No.** $(CH_3O)_3P^+CH_3 \cdot OTF^-$, 64294-66-2; $(CH_3O)_2P^+(CH_3)Ph \cdot OTF^-$, 64294-67-3; $(Ph)_2P^+(CH_3)OCH_3 \cdot OTF^-$, 64294-69-5; $(CH_3O)_2P^+(CH_3)Et \cdot OTF^-$, 64294-72-0; $(Et)_2P^+(CH_3)OCH_3 \cdot OTF^-$, 64294-74-2; $(MeO)_4P^+ \cdot OTF^-$, 78870-31-2; $(PhO)_2P^+(CH_3)OCH_3 \cdot OTF^-$, 64294-70-8; $(PhO)_3P^+OCH_3 \cdot OTF^-$, 78870-33-4; potassium 2,4-dinitrophenoxide, 14314-69-3.

# Mechanism of Acid-Catalyzed Hydrolysis of Phenylketene O,O and O,S Acetals

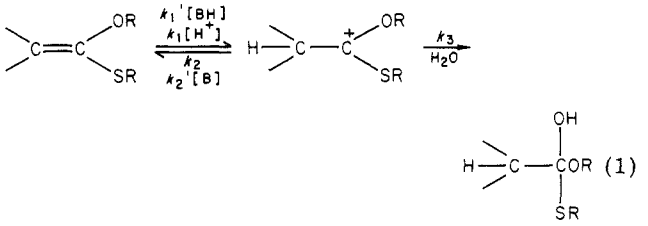
Tadashi Okuyama,* Shoji Kawao, and Takayuki Fueno

*Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560, Japan*

*Received May 7, 1981*

The hydrolyses of a phenylketene O,O acetal (1,1-dimethoxy-2-phenylethene, **1**) and an O,S acetal [(*Z*)-1-methoxy-1-(methylthio)-2-phenylethene, **2**] have been studied kinetically at 30 °C. The observed catalysis by general acids, the deuterium solvent isotope effects ($k_{H_2O}/k_{D_2O} = 5.5$ with **1**), and the lack of nucleophilic acceleration by added 2-mercaptoethanol are in accord with a mechanism involving rate-determining protonation of the double bond. The nonlinear dependence of rate on formate buffer concentration was observed in the hydrolysis of **2**, but it does not seem to be ascribable to a possible change in the rate-determining step in contrast to the previous suggestion.[5]

The acid-catalyzed hydrolysis of ketene acetals occurs through rate-determining protonation of the olefinic function followed by rapid hydration of a carbonium ion intermediate.[1-5] A similar mechanism has been established for the hydrolysis of enol ethers[6-8] and sulfides.[9,10] Ketene O,S acetals were found also to undergo hydrolysis through a similar mechanism in mineral acid solutions.[5,11] However, a possible change in rate-determining step was noted to occur in carboxylic acid buffers.[5] The nonlinear dependence of rate on buffer concentration was ascribed to a change in rate-determining step from the protonation of the doouble bond at low buffer concentrations to the hydration of a carbonium ion intermediate at higher buffer concentrations[5] (eq 1).




A similar mechanistic change in acetate buffers was suggested for the hydrolysis of an unusual cyclic enol ether, 9-methoxyoxacyclonon-2-ene.[12] Considerable efforts have been devoted, so far in vain, to explore this mechanistic change by searching for other examples of enol ether hydrolysis proceeding through rate-determining hydration.[13-18]

We have recently found that a phenylketene S,S acetal undergoes hydrolysis through preequilibrium carbon protonation even in mineral acid solutions.[19] In the present

(1) Kankaanperä, A.; Tuominen, H. *Suom. Kemistil. B* **1967**, *40*, 271.
(2) Gold, V.; Waterman, D. C. A. *J. Chem. Soc. B* **1968**, 839, 849.
(3) Kankaanperä, A.; Aaltonen, R. *Suom. Kemistil. B* **1970**, *43*, 183.
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(5) Hershfield, R.; Yeager, M. J.; Schmir, G. L. *J. Org. Chem.* **1975**, *40*, 2940.
(6) Salomaa, P.; Kankaanperä, A.; Lajunen, M. *Acta Chem. Scand.* **1966**, *20*, 1790.
(7) Kresge, A. J.; Chiang, Y. *J. Chem. Soc. B* **1967**, 53, 58.
(8) Okuyama, T.; Fueno, T.; Nakatsuji, H.; Furukawa, J. *J. Am. Chem. Soc.* **1967**, *89*, 5826.
(9) Okuyama, T.; Nakada, M.; Fueno, T. *Tetrahedron* **1976**, *32*, 2249.
(10) Okuyama, T.; Masago, M.; Nakada, M.; Fueno, T. *Tetrahedron* **1977**, *33*, 2379.
(11) Hershfield, R.; Schmir, G. L. *J. Am. Chem. Soc.* **1972**, *94*, 1263.
(12) Cooper, J. D.; Vitullo, V. P.; Whalen, D. L. *J. Am. Chem. Soc.* **1971**, *93*, 6294.
(13) Kresge, A. J.; Chen, H. J. *J. Am. Chem. Soc.* **1972**, *94*, 2818.
(14) Loudon, G. M.; Berke, C. *J. Am. Chem. Soc.* **1974**, *96*, 4508.
(15) Kresge, A. J.; Chwang, W. K. *J. Am. Chem. Soc.* **1978**, *100*, 1249.
(16) Chiang, Y.; Kresge, A. J.; Young, C. I. *Can. J. Chem.* **1978**, *56*, 461.
(17) Chiang, Y.; Chwang, W. K.; Kresge, A. J.; Szilagyi, S. *Can. J. Chem.* **1980**, *58*, 124.
(18) Burt, R. A.; Chiang, Y.; Kresge, A. J. *Can. J. Chem.* **1980**, *58*, 2199.
(19) Okuyama, T.; Fueno, T. *J. Am. Chem. Soc.* **1980**, *102*, 6590.

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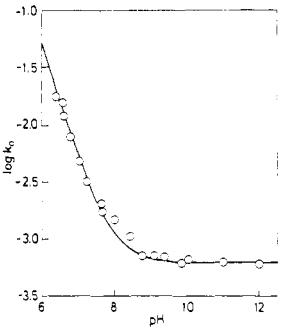
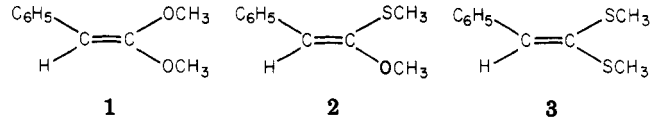



**Figure 1.** pH–rate profile for the hydrolysis of 1.

investigation, the acid-catalyzed hydrolysis of a phenylketene O,O acetal 1 has been examined with special attention to its mechanism, and the hydrolysis of an O,S acetal (2)[11] was reexamined in comparison with the results on the S,S acetal 3.[19]




1 2 3

## Experimental Section

**Materials.** 1,1-Dimethoxy-2-phenylethene (1) was prepared from the corresponding ortho ester,[20] which was made from phenylacetonitrile:[21] bp 112–115 °C (7 mmHg) [lit.[20] bp 123–126 °C (13 mmHg)]; NMR ($CCl_4$) δ 3.67 (s, 3 H), 3.70 (s, 3 H), 4.45 (s, 1 H), 6.9–7.3 (m, 5 H).

(*Z*)-1-Methoxy-1-(methylthio)-2-phenylethene (2) was prepared from 4-phenyl-1,2,3-thiadiazole[22] according to the method of Raap:[11,23] 138–142 °C (5 mmHg) [lit.[23] bp 81–82 °C (0.2 mmHg)]; NMR ($CCl_4$) δ 2.13 (s), 3.63 (s), 5.79 (s), 7.0–7.6 (m); for the *E* isomer δ 2.16 (s), 3.58 (s), 5.74 (s). The configuration was assigned according to Hershfield and Schmir.[11] About 25% of the *E* isomer was present by NMR analysis.

Acetonitrile was distilled from phosphorus pentoxide. Imidazole was recrystallized from benzene. *N*-Methylmorpholine, morpholine, bis(2-hydroxyethyl)amine, 2-hydroxyethyldimethylamine, pyrrolidine, 1,1,1,3,3,3-hexafluoro-2-propanol, 2,2,2-trifluoroethanol, and 2-mercaptoethanol were distilled before use. Other chemicals used for buffer preparations were used as received. Deuterium oxide (Merck) was isotopically pure (>99.75%). Glass-distilled water was used throughout.

**Kinetic Measurements.** Buffer solutions were prepared at room temperature by using a measuring flask and were adjusted to an ionic strength of 0.50 or 0.45 with added KCl. Solutions of 10% aqueous acetonitrile were obtained by bringing 10 parts by volume of $CH_3CN$ to 100 parts with added $H_2O$. Concentrations of stock solutions of acetals 1 and 2 in $CH_3CN$ were both about $5 \times 10^{-3}$ M. The reaction was started by adding 30 μL of the acetal stock solution by use of a microsyringe into a 3-mL buffer solution equilibrated thermally at 30 ± 0.1 °C in a stoppered cuvette inserted in a water-jacketed cell holder. The reaction was followed by the decrease in absorbance at 268 and 280 nm for 1 and 2, respectively. A Shimadzu UV 200 spectrophotometer was employed. The values of the pH of the buffer and reaction solutions were determined with a Hitachi-Horiba F-7 pH meter.

**Hydrolysis Products of 1 in $D_2O$–$CH_3CN$.** A 0.5-g sample of 1 dissolved in 10 mL of $CH_3CN$ was mixed with 50 mL of $D_2O$ (isotopically pure, >98%, and not buffered) and stirred magnetically for 5 h at 30 °C. The resulted mixture was shaked with three portions of 10 mL of ether. The extract was washed with water and dried over $MgSO_4$. The ether was completely removed under vacuum. The residues were subject to NMR analysis. The $^1H$ NMR spectrum ($CCl_4$) showed signals at 3.43 (br s, 1 H), 3.52 (s, 3 H), and 7.23 ppm (s, 5 H), which are consistent with methyl phenylacetate-α-$d_1$.

Table I. Catalytic Constants for the Hydrolysis of 1

| no. | HA | $pK_{HA}$[a] | $k_{HA}$, $M^{-1}$ $s^{-1}$ | $n$[b] |
|---|---|---|---|---|
| 1 | $H_3O^+$ | (−1.7) | $5.20 \times 10^4$ | 4 |
| 2 | $CH_3CO_2H$[c] | 4.60 | $3.32 \times 10^2$ | 1 |
| 3 | $H_2PO_4^-$ | 6.60 | $1.31 \times 10^2$ | 1 |
| 4 | imidazolium | 7.05 | 2.09 | 5 |
| 5 | *N*-methylmorpholinium | 7.67 | 1.55 | 1 |
| 6 | $TrisH^+$ | 8.20 | $2.41 \times 10^{-1}$ | 3 |
| 7 | morpholinium | 8.48 | $4.18 \times 10^{-1}$ | 1 |
| 8 | $(HOCH_2CH_2)_2NH_2^+$ | 8.94 | $2.37 \times 10^{-1}$ | 1 |
| 9 | $B(OH)_3$ | 9.18 | $4.00 \times 10^{-2}$ | 4 |
| 10 | $HOCH_2CH_2NH(CH_3)_2^+$ | 9.39 | $2.8 \times 10^{-1}$ | 1 |
| 11 | $(CF_3)_2CHOH$ | 9.47 | 1.52 | 1 |
| 12 | $HOCH_2CH_2SH$[d] | 9.7 | $4.18 \times 10^{-1}$ | 2 |
| 13 | $HCO_3^-$ | 9.85 | $4.7 \times 10^{-1}$ | 1 |
| 14 | $(C_2H_5)_3NH^+$ | 10.1 | $8.7 \times 10^{-3}$ | 1 |
| 15 | pyrrolidinium | 11.4 | $8.82 \times 10^{-3}$ | 1 |
| 16 | $CF_3CH_2OH$[d] | (12.4) | $9.40 \times 10^{-3}$ | 1 |
| 17 | $H_2O$ | (15.7) | $6.24 \times 10^{-4}$[e] | 2 |
| 18 | $D_2O$[f] | | $1.14 \times 10^{-4}$[e] | 1 |

[a] Taken as the pH of the half-neutralized buffer solution at 30 °C and $\mu = 0.5$. Values in parentheses are taken from: "CRC Handbook of Biochemistry"; Sober, H. A., Ed.; Chemical Rubber Co: Cleveland, OH, 1968. [b] Number of pH's employed to determine $k_{HA}$. [c] Measured by the stopped-flow method. [d] Measured in aqueous solutions containing 10 vol % organic phase ($CH_3CN$ + HA) at $\mu = 0.45$. [e] First-order rate constant in $s^{-1}$. [f] Measured in 0.01 M NaOD.

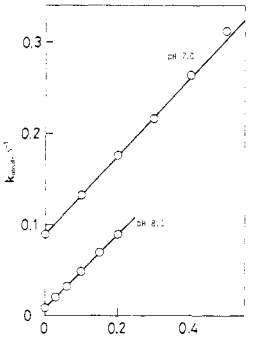



**Figure 2.** Effects of 2-mercaptoethanol on the hydrolysis rate of 1 at pH 7.0 ([imidazole]$_t$ = 0.1 M) and at pH 8.1 ([Tris]$_t$ = 0.1 M) in aqueous solutions containing 10 vol % organic phase ($CH_3CN$ + $HOCH_2CH_2SH$). The ionic strength was maintained at 0.45 with KCl.

## Results

**Phenylketene *O,O*-Dimethyl Acetal (1).** The rates of hydrolysis of 1 were measured spectrophotometrically in aqueous solutions (containing 1% $CH_3CN$) of an ionic strength of 0.50 at 30 °C. The hydrolysis of 1 is catalyzed by hydronium ion and general acids. Water catalysis is evident in the pH–rate profile shown in Figure 1. Catalytic constants are summarized in Table I. The effects of added 2-mercaptoethanol on the hydrolysis rate of 1 at pH 7.0 and 8.1 were examined by keeping the volume percent of organic phase ($CH_3CN$ + $HOCH_2CH_2SH$) constant at 10%. The rate increased linearly with thiol concentration (Figure 2). The slopes are identical within experimental error (0.428 $M^{-1}$ $s^{-1}$ at pH 7.0 and 0.408 $M^{-1}$ $s^{-1}$ at pH 8.1). The hydrolysis product obtained in $D_2O$–$CH_3CN$ was monodeuterated, $C_6H_5CHDCOOCH_3$.

**Phenylketene *O,S*-Dimethyl Acetal (2).** The hydrolysis of 2 was carried out at 30 °C in an aqueous solution containing 10% $CH_3CN$, the ionic strength being maintained at 0.45. The sample of 2 used for kinetic measurements contained about 25% of the *E* isomer,

(20) McElvain, S. M.; Davie, W. R. *J. Am. Chem. Soc.* **1951**, *73*, 1400.
(21) McElvain, S. M.; Stevens, C. L. *J. Am. Chem. Soc.* **1946**, *68*, 1917.
(22) Raap, R.; Micetich, R. G. *Can. J. Chem.* **1968**, *46*, 1057.
(23) Raap, R. *Can. J. Chem.* **1968**, *46*, 2251.

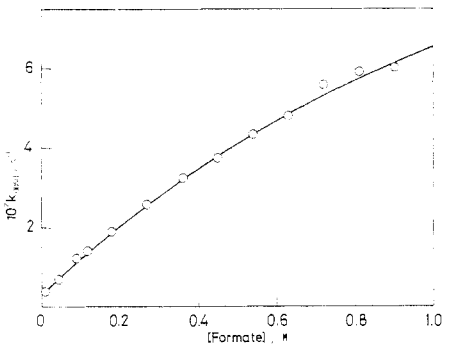



**Figure 3.** Effects of the formate buffer concentration on the hydrolysis rate of 2 at pH 3.70.

**Table II. Rate Constants ($10^2 k_{obsd}$, $s^{-1}$) for the Hydrolysis of 2 in the Presence of 2-Mercaptoethanol in Formate Buffers of pH 3.70 ± 0.03**

| $[HOCH_2CH_2SH]$, M | $[formate]_t$, M | | |
|---|---|---|---|
| | 0.36 | 0.63 | 0.90 |
| 0 | 3.21 | 4.88 | 6.58 |
| 0.05 | | 4.90 | 6.55 |
| 0.10 | 3.20 | 4.96 | 6.48 |
| 0.15 | 3.27 | 4.99 | 6.49 |
| 0.20 | 3.28 | 5.06 | 6.52 |
| 0.25 | 3.30 | | 6.50 |
| 0.30 | 3.26 | 4.99 | 6.64 |
| 0.35 | 3.23 | | 6.76 |
| 0.40 | 3.21 | 4.97 | 6.67 |
| 0.45 | | | 6.66 |
| 0.50 | 3.22 | 5.02 | 6.72 |

which reacts about 3 times as fast as 2 (*Z* isomer), as observed previously.[11] Since rate constants for the more reactive and less abundant component (the *E* isomer) calculated from biphasic first-order plots were less reliable,[11] kinetic analyses presented here are limited to those obtained with the less reactive and more abundant isomer (2).

The hydrolysis of 2 is subject to acid catalysis, the rate being proportional to acid concentration in HCl solutions ([HCl] < 0.1 M). The rate constant $k_{H^+}$ obtained (15.3 $M^{-1}$ $s^{-1}$) is slightly greater than that reported previously.[11] General-acid catalysis is observed in formate and acetate buffers. In formate buffers of pH 3.7, plots of $k_{obsd}$ vs. buffer concentration showed downward curvature as shown in Figure 3. Effects of added 2-mercaptoethanol were examined in formate buffers of different concentrations, keeping the volume percent of the organic phase ($CH_3CN$ + $HOCH_2CH_2SH$) constant at 10%. Results given in Table II show negligible effects of added thiol on the rate.

## Discussion

**O,O Acetal 1.** The phenylketene O,O acetal 1 is one of the most reactive olefins which undergoes water-catalyzed hydrolysis as is evident in the pH–rate profile of Figure 1. The reactivity of 1 relative to (*Z*)-1-methoxy-2-phenylethene is of the order of $10^7$.[24] That is, an α-methoxy substitution accelerates the hydrolysis of the vinyl ether by a factor of $10^7$. A β-phenyl substitution seems to reduce the reactivity of a ketene acetal by a factor of about $10^2$.[25]

(24) The rate constant $k_{H^+}$ for the hydrolysis of (*Z*)-1-methoxy-2-phenylethene was estimated to be $2.7 \times 10^{-3}$ $M^{-1}$ $s^{-1}$ at 25 °C.[16]

(25) The rate constant $k_{H_2O}$ for ketene diethyl acetal was found to be $8.9 \times 10^{-2}$ $s^{-1}$ at 25 °C[1], and ketene dimethyl acetal may be less reactive than the diethyl acetal as is the case for ethyl and methyl vinyl ethers.[26-28]

(26) Ledwith, A.; Woods, H. J. *J. Chem. Soc. B* **1966**, 753.

(27) Kresge, A. J.; Chen, H. L.; Chiang, Y.; Murrill, E.; Payne, M. A.; Sagatys, D. S. *J. Am. Chem. Soc.* **1971**, *93*, 413.

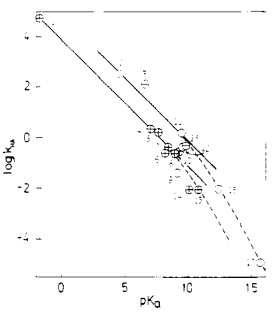



**Figure 4.** Brønsted plots for the hydrolysis of 1. The numbers indicate the general acids listed in Table I.

The Brønsted plots for the general-acid catalysis are illustrated in Figure 4. Plots span over 17 $pK_a$ units, including $H_3O^+$ and $H_2O$, and seem to conform to two parallel lines one logarithmic unit apart, the slope ($-\alpha$) changing from −0.53 to −1.0 with increasing $pK_a$. One line is based on positively charged acids (crossed circles) while the other is based on neutral (open circles) and negatively charged acids (barred circles).[29] That is, positively charged catalysts are less effective owing to repulsive, energy-raising, electrostatic interactions at the transition state. Such electrostatic effects of catalysts in vinyl ether hydrolysis were previously found and closely investigated.[31-33] Positive deviations of anionic catalysts are not apparent in the present study because of a great variety in their structural type and the small number of catalysts examined. The curved Brønsted relation is not uncommon in vinyl ether hydrolysis involving rate-determining protonation[15,32-34] and may be accommodated by the Marcus theory.[33,35]

Solvent deuterium isotope effects of $k_{H_2O}/k_{D_2O} = 5.5$ are in accord with a mechanism involving rate-determining protonation. Furthermore, first-order plots for the reaction in $D_2O$ were excellently linear. If the protonation were a prior equilibrium, a deuterium incorporation into the substrate 1 would occur, and the rate should change as the reaction proceeds, as previously found for the S,S acetal 3.[19] The product obtained from the reaction in $D_2O$–$C_6H_5CN$ was monodeuterated (methyl phenylacetate-$\alpha$-$d_1$) as expected for the mechanism (eq 2). Any extensive deuteration by the protonation–deprotonation equilibrium was not detected by the NMR analysis.

$$1 \xrightarrow{D_2O} C_6H_5\overset{\overset{D}{|}}{C}\overset{\overset{H}{|}}{C}OOCH_3 \qquad (2)$$

Thiols are strongly nucleophilic and can compete well with water even in aqueous solutions.[36] If a nucleophilic reaction is involved in the rate-determining step of the reaction, added thiols should accelerate the reaction as observed previously with 3 (eq 3).[19] This provides a good diagnostic probe as to whether the nucleophilic hydration is involved in the rate-determining step of the reaction in acidic aqueous solutions; most of other nucleophiles are

(28) Okuyama, T.; Fueno, T. *J. Org. Chem.* **1974**, *39*, 3156.

(29) Boric acid (no. 9 of Figure 4) has often been an ineffective catalyst as a general acid owing to its unique dissociation pattern.[30]

(30) Kankaanperä, A.; Salomaa, P. *Acta Chem. Scand.* **1969**, *23*, 712.

(31) Kresge, A. J.; Chiang, Y. *J. Am. Chem. Soc.* **1973**, *95*, 803.

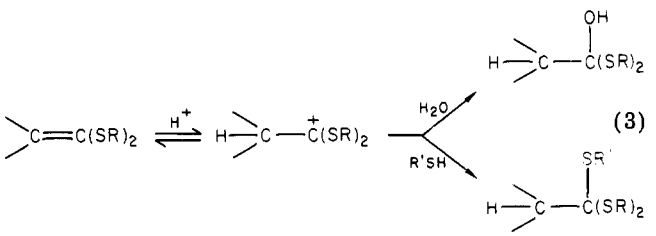
(32) Chwang, W. K.; Eliason, R.; Kresge, A. J. *J. Am. Chem. Soc.* **1977**, *99*, 805.

(33) Kresge, A. J. *Chem. Soc. Rev.* **1973**, *2*, 475.

(34) Chiang, Y.; Chwang, W. K.; Kresge, A. J.; Robinson, L. H.; Sagatys, D. S.; Young, C. I. *Can. J. Chem.* **1977**, *56*, 456.

(35) Marcus, R. A. *J. Phys. Chem.* **1968**, *72*, 891.

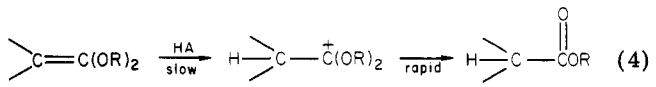
(36) Ritchie, C. D.; Gandler, J. *J. Am. Chem. Soc.* **1979**, *101*, 7318.



(3)

protonated in acidic solutions and lose their nucleophilicity.

Thus, the effects of added 2-mercaptoethanol on the hydrolysis rate of 1 were examined. The rate did increase linearly with the thiol concentration (Figure 2). However, this cannot result from the nucleophilic reaction of the thiol. Thiol-dependent catalytic constants are constant independent of the identity of the buffer used and of pH of the buffer solution. If the nucleophilic attack were rate determining, the apparent catalytic constant for the thiol would have been affected by the preequilibrium constant which is dependent on the acid concentrations. Since the catalytic constant falls reasonably on the plots of Brønsted relation (no. 12 of Figure 4), the acceleration observed must be ascribed to the rate-determining protonation by the thiol ($pK_a = 9.7$) as a general acid. All these results agree with the conventional mechanism involving rate-determining protonation of the double bond by general acids[1-5] (eq 4).



(4)

**O,S Acetal 2.** Hydrolysis of the phenylketene O,S acetal 2 has previously been investigated, and a mechanism involving rate-determining protonation was concluded on the basis of independent pH–rate and pH–product profiles.[11] However, the nonlinear dependence of rate on formate buffer concentration was noted and ascribed to a change in rate-determining step.[5] We reexamined the buffer effects on the hydrolysis rate of 2 to see if the noted mechanistic change is actually occurring.

The curved buffer dependence was observed (Figure 3) as noted before.[5,11] The curvature formally fits eq 5 with

$$k_{obsd} - k_{H^+}[H^+] = \frac{(k_{max} - k_{H^+}[H^+])[B]_t}{K_{app} + [B]_t} \quad (5)$$

$k_{max} = 0.173\ s^{-1}$ and $K_{app} = 1.82$ M, where $k_{H^+} = k_1k_3/(k_2 + k_3)$, $k_{max} = k_1'k_3(1 - \alpha)/k_2'\alpha$, $K_{app} = (k_2 + k_3)/k_2'\alpha$, and $\alpha = [B]/[B]_t$. The notation of $k_1$, $k_2$, $k_3$, $k_1'$, and $k_2'$ is given in eq 1.

Now in order to probe a possible mechanistic change, effects of added thiol were examined in formate buffers. The results summarized in Table II indicate that the rate is hardly affected by added 2-mercaptoethanol even in 0.9 M ($K_{app}/2$) formate buffer. The rate increase observed is less than 3% of the rate in the absence of thiol. This cannot be ascribed to a mechanism involving rate-determining nucleophilic hydration.[37] A similar but stronger curvature in buffer dependence, which is no doubt due to the mechanistic change, was found in the hydrolysis of a simple ketene S,S acetal (1,1-dimethylthioethene), and at the buffer concentration of $K_{app}/2$ a large acceleration by added thiol was observed.[38]

The observed nonlinear dependence of the rate on buffer concentration cannot always be taken as evidence for a mechanistic change. In some cases this must be ascribed to some other factors. Association of carboxylic acids, once considered to be such a factor, has been disregarded.[39,40] Solvent effects may be responsible for the present observation. Hydrolysis rates of 2 and similar substrates[4,38] sharply decrease with the increasing fraction of organic phase of the solvent.

Finally, it would be of interest to compare reactivities of 1–3. The ketene O,O acetal 1 and O,S acetal 2 are, respectively, $4.1 \times 10^5$ and $1.2 \times 10^2$ times as reactive as the S,S acetal 3. That is, when the methylthio groups of 3 are substituted with methoxy groups one by one, the first substitution enhances the reactivity of 3 by a factor of only $10^2$, and the second one further activates 2 by a factor as great as $3 \times 10^3$. These unusual reactivities must be closely related with the observed mechanistic change in the hydrolysis of 3. A methylthio group may effectively stabilize the olefinic linkage owing to the S 3d orbitals as compared with a methoxy group. This olefin-stabilizing effect would be responsible for the unusual reactivity as well as for the mechanistic change. Detailed energetic considerations will be presented elsewhere.

**Acknowledgment.** We thank A. Oshio for his partial assistance in the experimental work and Professor G. L. Schmir for useful comments.

**Registry No.** 1, 13049-41-7; 2, 70101-41-6.

(37) 2-Mercaptoethanol ($pK_a = 9.7$) is too weak an acid to significantly accelerate the reaction of 2 at pH 3.7 as observed with a very reactive substrate 1 at pH 7–8.

(38) Okuyama, T.; Kawao, S.; Fueno, T., to be submitted for publication.

(39) See footnote 26 of ref 5.

(40) Hershfield, R.; Schmir, G. L. *J. Am. Chem. Soc.* **1973**, *95*, 8032.