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Reactions of 2-(*p*-Methoxyphenyl)-1,3-dithiolan-2-yl Cation with Water and Other Nucleophiles in Aqueous Solution

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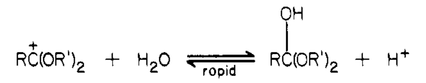
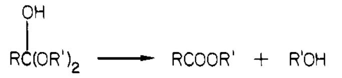
Abstract: 2-(*p*-Methoxyphenyl)-1,3-dithiolan-2-yl cation (**1**) was isolated as a perchlorate and its reaction with water was examined kinetically in 10% aqueous acetonitrile at 30 °C. Hydration of **1** to form a 2-hydroxydithiolane intermediate **2** is rate determining at pH >6, but the decomposition of **2** to lead to a thiolester product becomes a slow step at pH <3. At intermediate pH near the pK_R (4.1) of **1**, both of the steps become partially rate determining. Hydration of **1** is unusually slow as compared with that of the oxygen analogues and is catalyzed by general bases with wide ranges of basicity (pK_a = 1.3–7.7); the Brønsted $\beta = 0.18$. In the presence of nucleophiles like thiol and primary and secondary amines, they can compete with water to form an adduct, **4**. At higher acidity, the nucleophilic reaction becomes a rapid equilibrium which is followed by the slow hydrolysis of **1**; biphasic kinetics were observed.

The chemistry of sulfur-stabilized carbocations has attracted the continuing interest of organic chemists. It has long been admitted that sulfur is a poorer π donor than oxygen[1] as deduced, for example, from $\sigma_P{}^+$ values of CH_3S and CH_3O substituents[2] and frequently cited work[3] on the hydrolysis of chloromethyl sulfide and ether. However, gas phase measurements[4–6] showed that α-thio carbocations are more stable than the α-oxo cations, in accord with the results of ab initio MO calculations.[7,8] Modena and co-workers[9] showed that relative rates of α-thio and α-oxo carbocation-forming reactions range widely from 0.002 to 10 even in solutions.

Dioxo carbocations are important intermediates in the hydrolysis of ortho esters and ketene acetals. The rate-determining step for certain ortho esters has been found to change with a changing acidity of reaction media,[10–13] and in these cases the decay of the carbocation takes place through a rapid equilibrium hydration (reaction 1) followed by a slow decomposition of a hydrogen ortho ester intermediate to form an ester product (reaction 2). However, we have recently found that acyclic dithio carbocations decompose through the rate-determining hydration (see Scheme I) and this reaction is slow enough to compete with β-deprotonation to form a ketene dithioacetal if the cation has a hydrogen atom at the β-carbon.[14–16]

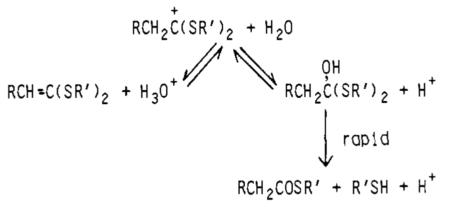


$$\overset{+}{RC}(OR')_2 + H_2O \underset{\text{rapid}}{\rightleftharpoons} \overset{OH}{RC}(OR')_2 + H^+ \qquad (1)$$

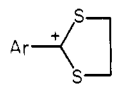


$$\overset{OH}{RC}(OR')_2 \longrightarrow RCOOR' + R'OH \qquad (2)$$

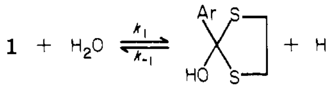
Scheme I



This contrasting behavior of α-thio and α-oxo carbocations prompted us to examine kinetic features of the reactions of an isolated dithio carbocation salt $1{\cdot}ClO_4{}^-$ in aqueous solutions. The present paper describes the results of the reactions of the dithio carbocation **1** with water (hydrolysis) and some other nucleophiles. The rate-determining step of the hydrolysis changes from the hydration of **1** (eq 3) at high pH to the decomposition of a 2-hydroxydithiolane intermediate **2** (eq 4) at low pH. General base catalysis was observed in the pH region where the hydration is a slow step. Primary and secondary amines as well as thiol could compete with water in the nucleophilic reaction and resulted in the rapid, often reversible, formation of the adduct **4** (eq 5).



1, Ar = p-$CH_3OC_6H_4$



(3)

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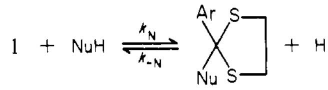
$$2 \xrightarrow{k_2} ArCOS(CH_2)_2SH \qquad (4)$$

3



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Results

Reaction with Water. On addition of a dithiolanyl cation **1** into an aqueous solution, an absorption of **1** (λ_{max} 402 nm) disappears with an accompanying formation of a thiolester **3** (λ_{max} 288 m). An isosbestic point was found at 317 nm during the slower reaction at low pH. Both disappearance of **1** and formation of **3**, monitored

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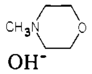
Table I. Catalytic Constants for the General Base Catalyzed Hydration of the Cation 1

base	pK_a[a]	$10^2 k_B$, M^{-1} s^{-1}
H_2O	-1.7[b]	6.08[c]
$Cl_2CHCO_2^-$	1.29	2.15
$NCCH_2CO_2^-$	2.42	2.16
$ClCH_2CO_2^-$	2.86	4.97
$CH_3OCH_2CO_2^-$	3.55	4.98
HCO_2^-	3.75	5.63
$CH_3CO_2^-$	4.76	7.47
$(CH_3)_3CCO_2^-$	5.02	10.6
HPO_3^{2-}	6.42	26.4
HPO_4^{2-}	6.69	24.2
$C_6H_5PO_3^{2-}$	7.16	36.8
$CH_3PO_3^{2-}$	7.69	44.1
MES[d]	6.28	9.27
$NC(CH_2)_2N(CH_3)_2$	7.27	8.78
	7.64	18.3
OH^-	15.7[b]	2.38×10^5
$H_2NCONHNH_2$	3.86[b]	1.4×10^5 [e]
CH_3ONH_2	4.60[b]	8.2×10^4 [e]
$CF_3CH_2NH_2$	5.7[b]	1.3×10^4 [e]

[a] pK_a of the conjugate acid obtained as pH of the buffer of $[BH^+] = [B]$. [b] Values are taken from "Handbook of Biochemistry"; Sober, H. A., Ed.; CRC: Cleveland, OH, 1968. [c] k_1 in s^{-1}. [d] 4-Morpholinoethanesulfonate. [e] Rate constants k_N for the nucleophilic reaction of the base.

by the UV absorbance changes, followed pseudo-first-order kinetics and gave identical rate constants k_{obsd} in most cases. In acetate and succinate buffer solutions of pH 4.5–5.8, however, pseudo-first-order plots (disappearance of **1**) curved downward to form a straight line in the later stage (see below).

Observed rate constants k_{obsd} measured in buffer solutions of phosphate, phosphonates, and tertiary amines in the pH range 6–7.7 increased linearly with buffer concentrations and slopes were dependent only on the conjugate base fraction of the buffer (eq 6). That is, the reaction is catalyzed by general bases. Rate

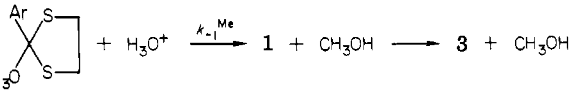
$$k_{obsd} = k_0 + k_B[B] \qquad (6)$$

constants k_{obsd} are given in Table S1 (supplementary material). Catalytic constants k_B for carboxylates were determined at pH 6.7 maintained by a 0.05 M phosphate buffer. Some data were obtained under slightly different conditions (Table S2). All the carboxylates examined are completely ionized at this pH and k_{obsd} increased linearly with carboxylate concentrations, slopes giving catalytic constants. Catalytic constants k_B are summarized in Table I. Primary and secondary amines showed nucleophilic reactivity as described below.

Rate constants k_0 extrapolated to zero buffer concentration as well as k_{obsd} measured in HCl solutions are logarithmically plotted against pH in Figure 1 (open circles). In the pH range 4.5–5.8, where first-order plots curved, rate constants were determined from the slopes of linear parts of the plots in the later stage of the reaction. At pH 3–4.3, very initial parts seemed to deviate from the first-order plots but they were practically linear to give k_{obsd}.

The rate of disappearance of **1** was measured also in a deuterium phosphate buffer solution ($[BH^+] = [B] = 0.005$ M, $\mu = 0.45$) which contained 10 vol % of CH_3CN, giving $k_{obsd} = 4.24 \times 10^{-2}$ s^{-1}. In a similar protium solution of phosphate buffer ($[BH^+] = [B] = 0.005$ M) k_{obsd} was 6.03×10^{-2} s^{-1}; $k_{H_2O}/k_{D_2O} = 1.42$.

Rates of hydrolysis of 2-methoxy-2-(*p*-methoxyphenyl)-1,3-dithiolane **4a** were measured in acetate buffer solutions by following the formation of the thiolester **3** (288 nm) and in formate



(7)

4a

buffer and HCl solutions by following the appearance of the cation **1** (402 nm). Data are given in Table S3. Pseudo-first-order rate constants seemed to increase slightly with buffer concentration but the change was too small to evaluate the catalytic constants. Both rate constants obtained from the appearance of **1** at low pH and from the formation of **3** at high pH showed a unified proportionality to acid concentration (10^{-pH}), giving the second-order rate constant $k_{-1}^{Me} = 9.8 \times 10^2$ M^{-1} s^{-1}.

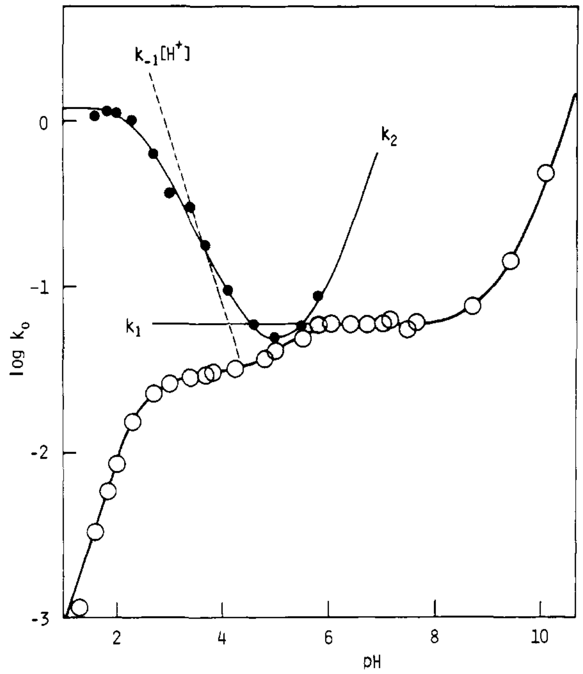


Figure 1. pH–rate profiles for the reaction of **1** with water. Open and closed circles refer to k_0 and calculated values of k_2, respectively.

Reactions with Nucleophiles. Primary and secondary amine buffers showed very large effects in the reaction with **1**. Effects of 2,2,2-trifluoroethylamine, methoxyamine, and semicarbazide were examined at pH 6.7 maintained with a 0.05 M phosphate buffer (Table S2). These amines of low pK_a exist mainly in a neutral form at this pH and the disappearance of **1** was remarkably accelerated by very low concentrations of the amines; approximate rate constants k_B (k_N) obtained are included in Table I. In the case of trifluoroethylamine, the absorbance of **1** seemed to remain to some extent after the completion of the primary reaction and a secondary slow reaction seemed to take place.

Effects of morpholine at this pH were also complicated. The reaction was clearly biphasic: The initial rapid reaction was too rapid to follow by a conventional method and the rate of the second slow reaction decreased with increasing concentration of morpholine (Table S2). Similar biphasic decay of **1** was also observed in imidazole buffers but was not examined in detail.

Rates of disappearance of **1** were also measured in the presence of 2-mercaptoethanol (RSH). Organic components (CH_3CN + RSH) of the solution were kept constant at 10% by volume. Results are given in Table S4. The rate increased linearly with [RSH] in acetate buffer solutions. The slope k_N is independent of buffer concentration but increases with pH (Table II). By contrast, a biphasic decay of **1** was observed in the presence of RSH in HCl solutions. The rate of the initial rapid reaction (k_{rapid}) was more than 20 times as great as that of the second slow reaction (k_{slow}) and both could be determined independently by the pseudo-first-order treatments. Rate constants k_{rapid} increased linearly with [RSH] while k_{slow} decreased with [RSH] following a saturation curve (Figure 2). The absorbance change (at 402 nm) due to the rapid reaction ΔA_r increased with [RSH]; that due to the slow reaction ΔA_s accordingly decreased with [RSH].

The rates of hydrolysis of the thiol adduct, 2-((2-hydroxyethyl)thio)-2-(*p*-methoxyphenyl)-1,3-dithiolane (**4b**) (Nu = RS), were also measured under similar conditions. Buffer effects were not observed in formate and acetate buffer solutions. Observed rate constants are logarithmically plotted against pH in Figure

Table II. Rate Constants for the Reaction of 2-Mercaptoethanol with 1

[HCl], M	k_N, M^{-1} s^{-1}	$10^3 k_{-N}$, s^{-1}
0.25	0.156	33.6
0.10	0.173	14.4
0.050	0.222	5.94
0.025	0.294	4.07
0.015	0.384	2.58
0.010	0.543	0.979
4.25[a]	49.4	
4.47[a]	76.2	
4.69[a]	156	

[a] pH of acetate buffer solutions.

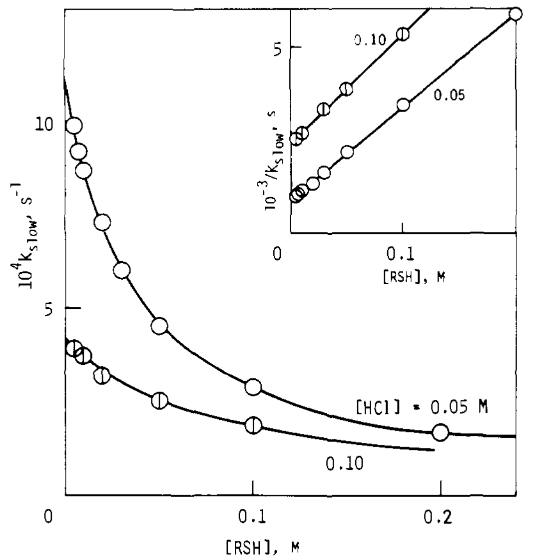


Figure 2. Effects of the concentration of 2-mercaptoethanol on the rate of the slow reaction in HCl solutions at [HCl] = 0.05 (○) and 0.10 M (◐).

3. Acid-catalyzed and spontaneous reactions are obvious from the pH-rate profile.

Discussion

Rate-Determining Step of the Hydrolysis. The decomposition of the dithiolanyl cation **1** in aqueous solutions takes place stepwise through a hydrogen ortho thioester intermediate **2**, leading to thiolester **3** (eq 3 and 4). There are considerable changes in the nature of the kinetics depending on the acidity of the reaction medium. This behavior is accommodated by a change in the rate-determining step of the reaction. The hydration of **1** (eq 3) is rate determining at high pH while the breakdown of the intermediate **2** (eq 4) becomes a slow step in acidic solutions. In between, rates of the two steps become close to each other and first-order kinetics breakds down.

The higher pH region of the pH-rate profile is interpreted in terms of rate-determining hydration of cation **1**. Initial absorbances of **1** extrapolated to zero time were equal to those expected for the initial concentration of **1** even at a pH several units higher than the pK_R ($pK_1 = 4.1$) of **1**. The rate constant k_0 must reflect

$$k_0 = k_1 + k_1'[OH^-] \qquad (8)$$

the nucleophilic attack by water ($6 < pH < 9$) and by hydroxide ion ($pH > 9$) as seen in Figure 1. The formation of the product **3** monitored at 288 nm followed good first-order kinetics and gave a k_{obsd} identical with that obtained from the disappearance of **1**. No accumulation of any intermediate was observed. The water reaction was found to be catalyzed by general bases as will be discussed below.

Breaks of the pH-rate profile at intermediate pH are complicated and we could not define pK_1 ($K_1 = k_1/k_{-1}$) from the profile. The value of k_{-1} can be estimated from the rate constant for a similar reaction of the methoxy derivative **4a** to generate cation **1** (eq 7). From the relative rates of similar reactions of dioxolane derivatives,[10,17] k_{-1} was taken to be equal to $0.8 k_{-1}^{Me}$:$k_{-1} = 7.8 \times 10^2$ M^{-1} s^{-1}. The value of pK_1 is thus estimated to be about 4.1.

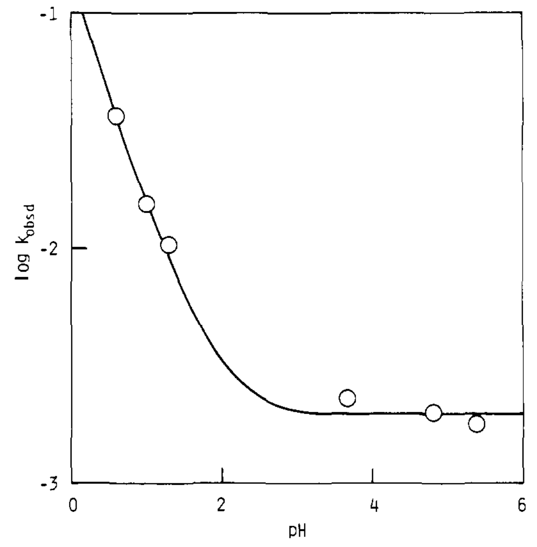


Figure 3. pH-rate profile for the hydrolysis of **4b** in 10 vol % CH_3CN-H_2O at $\mu = 0.45$ (KCl) and 30 °C.

The acid inhibition observed at pH < 3 must be ascribed to the decreasing concentration of the intermediate **2** in equilibrium. The rate-determining step must be the decomposition of **2**.

$$k_0 = K_1 k_2/(K_1 + [H^+]) \qquad (9)$$

However, the break of the profile near pH 3 cannot be ascribed to pK_1, which should be at least one pH unit higher. The break may be attributed to a change in the k_2 value with changing pH. Using the value $pK_1 = 4.1$ and eq 9, k_2 values were calculated from k_0 and plotted against pH with closed circles in Figure 1.

Above pH 3 the equality of eq 9 breaks down because k_1, $k_{-1}[H^+]$, and k_2 become close to each other in their magnitude. In such a situation, pseudo-first-order plots curve and the kinetic equation to describe the curve is rather complex.[18] The decrease in substrate concentration as a function of time is expressed by a linear combination of two exponential terms, one of which declines more rapidly leaving the other term as a main contributor after a certain reaction time;[18] this must correspond to the linear part of the first-order plots observed in the later stage of the reaction, the slope being described by eq 10.[18,19] In the pH range

$$k_{obsd} = \tfrac{1}{2}\{k_1 + k_{-1}[H^+] + k_2 - [(k_1 + k_{-1}[H^+] + k_2)^2 - 4k_1k_2]^{1/2}\} \qquad (10)$$

3–6, k_2 values are evaluated by eq 10[20] as plotted in Figure 1. The values of k_2 seem to increase both above and below pH 5.

The rate of dehydration of **2** ($k_{-1}[H^+]$) is shown by a broken line in Figure 1. All the rates of the three processes involving the intermediate **2** converge to the same value around pH 4 and the observed kinetics were complicated in this pH region. At pH > 6, hydration of **1** becomes rate determining because the decay of **2** is catalyzed by hydroxide ion. Below pH 3, on the other hand,

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(19) Below pH 5 the difference of the two exponential factors is large enough and the ultimate slope was easily determined. Near pH 6 the preexponential factor for the one term becomes negligibly small. In between (pH 5–5.8), the definition of the ultimate slope was rather difficult but it was determined from the last 20% reaction.

(20) Equation 10 is transformed to $k_2 = k_{obsd}(k_{obsd} - k_1 - k_{-1}[H^+])/(k_{obsd} - k_1)$. The calculated values of k_2 may be accurate to within ±50% at pH 5–5.8 but are much better at lower pH.

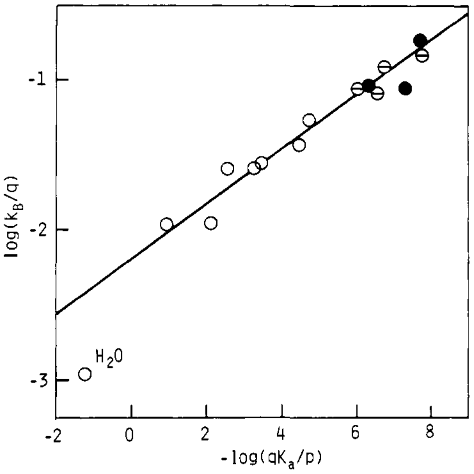


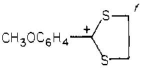
Figure 4. Brønsted plot for the general base-catalyzed hydration of **1**: ○, carboxylates; ⊖, phosphate and phosphonates; ●, tertiary amines.

$k_{-1}[H^+]$ becomes greater than k_2 and the k_2 step is rate determining. In the pH ranges 3–4 and 4–6, the rate constant k_2 is respectively near to $k_{-1}[H^+]$ and k_1, and the kinetics of the disappearance of **1** was accordingly complicated. The linear part of the first-order plots could however be analyzed reasonably by eq 10. Simulation of the whole curve of the first-order plots seemed to be difficult because the kinetic zero time is hard to define owing to the rapidity of the reaction.

General Base Catalysis of Hydration. Hydration of cation **1** was found to be catalyzed by a variety of general bases. They include carboxylates, phosphate, phosphonates, and tertiary amines, pK_a values of their conjugate acids ranging from 1.3 to 7.7. The Brønsted plot of catalytic constants vs. pK_a gives a single straight line with a slope $\beta = 0.180 \pm 0.012$ (Figure 4). Most of the bases are anionic but neutral (tertiary) amines do not seem to deviate appreciably from the line, suggesting that possible electrostatic effects on the cation–anion reaction are small. A general absence of observable coulombic effects was in fact noted before for the reaction between stable carbocations and anionic nucleophiles.[21] The reactivity of hydroxide ion is some 600-fold greater than that predicted from the Brønsted relationship, as is usually the case for general base catalyzed reactions of water. Hydroxide ion is reacting as a nucleophile. Primary amines were also found to be $\sim 10^3$ times more effective than the general bases.

Examples of general base catalysis observed in the hydration of carbocations are so far limited. Hydration of stable cations like dimethylamino-substituted triphenylmethyl[22,23] and trianisylmethyl cations[24] was found to be catalyzed by strong bases (tertiary amines). Earlier workers failed to detect such catalysis in the reaction of the latter cation and believed that it was not subject to general base catalysis in accord with a generally accepted mechanism of the reverse reaction, alochol dehydration being specific acid catalyzed.[25-27] However, it has recently been found that the dehydration of diferrocenylphenylmethanol and tropyl alcohol to give stable carbocations is catalyzed by carboxylic acids.[28] Furthermore, hydration of a less stable carbocation, 1-methoxy-1-(*p*-methylphenyl)ethyl cation, was found to be catalyzed even by weak bases like carboxylates by means of the competitive trapping experiments.[29] These previous results are summarized in Table III together with the present results. Although some of the Brønsted coefficients β based on the limited number of catalytic bases are not reliable, the magnitude of β tends to increase with increasing stability (pK_R) of the cation in accord with the previous interpretation in terms of three-dimensional energy diagrams.[28]

Table III. General Base Catalysis of Hydration of Carbocation[a]

cation	pK_R	k_{H_2O}, s^{-1}	β	ref
$[p\text{-}(CH_3)_2NC_6H_4]_2C^+C_6H_5$	6.94	2.1×10^{-4}	0.65^b	23
tropylium	4.75		0.29^c	28
tropylium[d]	4.02	5.5	0.2^c	28
$Fc_2C^+C_6H_5$[d,e]	4.18	2.8×10^{-4}	0.12^c	28
 [f]	4.1	6.08×10^{-2}	0.18	present work
$(p\text{-}CH_3OC_6H_4)_3C^+$	0.82	1.2×10	0.3^b	28
$(p\text{-}CH_3C_6H_4)(CH_3O)C^+CH_3$	−4.1	5×10^7	0.09^g	29

[a] In aqueous solution at 25 °C. [b] Obtained from three basic amines. [c] Estimated from α for the reverse reaction. [d] Obtained in 1:1 CH_3CN–H_2O (w/w). [e] Diferrocenylphenylmethyl cation. [f] In 10 vol % CH_3CN–H_2O at 30 °C. [g] Obtained by the competitive trapping experiments.

Solvent isotope effects leading to $k_{H_2O}/k_{D_2O} = 1.42$ were observed in dilute phosphate buffer solutions. These effects must mostly come from the uncatalyzed reaction of water with **1**. Similar isotope effects were previously found for trianisylmethyl[25] and ferrocenylmethyl[30] cations ($k_{H_2O}/k_{D_2O} \simeq 1.2$). These results are compatible with the observed general base catalysis. The rate-determining step of the reaction involves a transfer of proton (from the attacking water to a general base). The fractionation factor considerations[31] on the assumption that any proton is not transferred during the reaction predict $k_{H_2O}/k_{D_2O} = 0.5$ as a result of secondary isotope effects. Observed normal isotope effects must be a composite of the primary effects arising from the proton transfer and the secondary effects. Observations consistent with this argument were found for the reverse reaction (acid-catalyzed dehydration of alcohols)[25,28,30] and similar reactions.[32]

Reactions with Nucleophiles. Apparent catalytic constants k_B obtained for primary amines are 10^3–2×10^4 times those expected for general base catalysis. This large effect undoubtedly comes from the nucleophilic reaction of the amines with **1** (eq 5).[33] The excess reactivity is greater for semicarbazide and methoxyamine (α-effect nucleophiles) than for trifluoroethylamine.

Since a positively charged amino group of the adduct **4** dissociates very easily as observed with amide acetals,[34] the addition of the amine would be reversible at such pH where a certain amount of the adduct is in a protonated form at equilibrium. Under such conditions biphasic reaction should be observed for the disappearance of **1**; the rapid attainment of equilibrium 5 (involving a protonated form of the adduct **4**) is followed by the slow hydrolysis of **1**. Relative contributions from the two reactions depend on the fraction of **1** present after the rapid reaction (at equilibrium). In the reaction of less basic amines like methoxyamine and semicarbazide, the equilibrium favoring the adduct formation results in a negligibly small fraction of **1** present, and thus the second slow reaction was not observed.[35] In the case of trifluoroethylamine the second reaction seemed to be observable with a small change in absorbance.

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Table IV. Kinetic Parameters for the Reaction of **1** with 2-Mercaptoethanol

acetate buffer	$k_t'K_{RSH} = (3.49 \pm 0.48) \times 10^{-3}\ s^{-1}$
rapid reaction	$k_t'K_{RSH} = (3.96 \pm 0.13) \times 10^{-3}\ s^{-1}$
	$k_t = 0.136 \pm 0.007\ M^{-1}\ s^{-1}$
	$k_{-t} = 0.134 \pm 0.004\ M^{-1}\ s^{-1}$
slow reaction	
[HCl] = 0.05 M	$K_N = 1.28 \pm 0.03$
	$k_o = (1.01 \pm 0.16) \times 10^{-3}\ s^{-1}$
[HCl] = 0.10 M	$K_N = 1.02 \pm 0.06$
	$k_o = (3.98 \pm 0.02) \times 10^{-4}\ s^{-1}$
absorbance change	
[HCl] = 0.05 M	$K_N = 1.16 \pm 0.03$
[HCl] = 0.10 M	$K_N = 0.973 \pm 0.060$
reaction of 4b	$k_{-t} = 0.15\ M^{-1}\ s^{-1}$
	$k_{-t}' = 2.0 \times 10^{-3}\ s^{-1}$

With more basic morpholine (pK_a = 8.4), the reaction was clearly biphasic at pH 6.7 and the slow reaction was accompanied by a significant absorbance change. Curved dependence of the rate constants k_{slow} was analyzed according to eq 11 where the equilibrium constant $K_N = [\mathbf{4}][H^+]/[\mathbf{1}][NuH]$. An approximate value obtained for morpholine is: $K_N = 4.8 \times 10^{-4}$.

$$k_{slow} = k_0[H^+]/([H^+] + K_N[NuH]) \qquad (11)$$

The nucleophilic reaction of 2-mercaptoethanol (RSH) with **1** was examined in more detail. In acetate buffer solutions, equilibrium 5 favors formation of the adduct **4b** (Nu = RS). The observed rapid reaction must be formation of **4b**. Apparent second-order rate constants k_N for the thiol reaction increase with pH, suggesting that the contribution from the thiolate ion RS^- (k_t') is significant in this reaction (eq 12).

$$k_N = k_t + k_t'K_{RSH}/[H^+] \qquad (12)$$

where k_t and K_{RSH} are the rate constants for the reaction of the neutral thiol and the dissociation constant of RSH, respectively. Plots of k_N against $1/[H^+]$ gave a straight line, a slope of which is $k_t'K_{RSH}$ (Table IV). The contribution from the neutral thiol (k_t) was found to be negligible in this pH region; this is compatible with the observed lack of buffer catalysis. At still higher pH, e.g., in phosphate buffers, acceleration was large with a very low concentration of thiol ([RSH] < 10^{-4} M) as expected for the thiolate reaction.

In acidic (HCl) solutions, a biphasic decay of **1** was observed in the presence of RSH, which is consistent with a mechanism involving the rapid equilibrium formation of **4b** (k_{rapid}) followed by the slow hydrolysis of **1** (k_{slow}). The observed rate constant k_{rapid} should thus be a sum of rate constants for the forward and the reverse reactions (eq 13).

$$k_{rapid} = k_N[RSH] + k_{-N} \qquad (13)$$

The linearities of eq 13 give k_N as a slope and k_{-N} as an intercept (Table II). These rate constants obey eq 12 and 14, respectively.

$$k_{-N} = k_{-t}[H^+] + k_{-t}' \qquad (14)$$

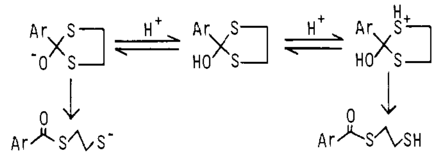
where k_{-t} and k_{-t}' refer to the acid-catalyzed and spontaneous dissociation of 4b, respectively. Least-squares treatments of the data gave rate constants listed in Table IV.

Rates of the slow reaction decrease with increasing [RSH] owing to the decrease in the concentration of **1** in equilibrium (eq 11 with NuH = RSH). Least-squares analyses of $1/k_{slow}$ vs. [RSH] (inset of Figure 2) gave kinetic parameters summarized in Table IV. The values of K_N of about unity obtained are in good agreement with the value ($K_N = k_t/k_{-t} = 1.01$) calculated from the rate constants obtained in the rapid reaction. The values of k_0 agree with k_{obsd} in the absence of RSH.

The absorbance change due to the rapid reaction, ΔA_r, corresponds to the equilibrium concentration of **4b** and that due to the slow reaction, ΔA, corresponds to the concentration of **1**. This leads to the relationship of eq 15. This correlation gives again K_N close to unity as listed in Table IV. All the three independent analyses of the kinetic and spectral observations gave consistent results as to K_N; this strongly supports the proposed mechanism of the reaction.

$$\Delta A_r/\Delta A_s = (K_N/[H^+])[RSH] \qquad (15)$$

Scheme II



Finally, the rate constants for the dissociation, k_{-t} and k_{-t}', were obtained directly from the hydrolysis of the isolated adduct **4b** and are given in Table IV. The value of k_{-t} agrees well with that obtained in the rapid reaction. The rate constant k_{-t}' can be evaluated as $k_{-t}' = k_t'K_{RSH}/K_N = 3.4 \times 10^{-3}\ s^{-1}$, which is somewhat too large as compared with the value obtained directly.

Nucleophilic reactivity of thiolate ion was found to be large toward carbocations, about 10^4 times that of hydroxide ion, as compared with that toward carbonyl groups, the thiolate/hydroxide rate ratio being near unity.[37] In the present reaction, the value k_t' is evaluated to be $1.9 \times 10^7\ M^{-1}\ s^{-1}$ assuming pK_{RSH} = 9.7; the thiolate/hydroxide rate ratio (k_t'/k_1') is thus estimated to be 0.8×10^4, which is in good agreement with those found for triarylmethyl cations.[37] Reactivity of the neutral thiol toward trianisylmethyl cation was found to be $1/(2 \times 10^7)$ that of the thiolate ion,[37] the thiolate/thiol rate ratio being 1.4×10^8 in the present reaction. In another way, reactivity of the neutral thiol is compared with that of water. The thiol/water rate ratio (in M^{-1}) is estimated to be 0.65 toward trianisylmethyl cation[27,37] and it is 2.3 toward **1**. Similar thiol/water rate ratios were found to be 1.0 and 6 toward bis(methylthio)methyl[16] and 1,3-dithianyl[38] cations, respectively, during the hydrolysis of ketene dithioacetals. The nucleophilic reactivity of 2-mercaptoethanol toward the positive carbon is $1/10^7$–10^8 of the thiolate ion or 0.6–6 (M^{-1}) of water. In nucleophilic reactions in aqueous solutions, the neutral thiol becomes the reactive species below pH 2–3, 7–8 pH units below pK_a of the thiol, and the neutral thiol (e.g., 0.1 M) can compete with water even in acid solutions.[39]

Decomposition of Hydroxydithiolane. The pH–k_2 profile for the decomposition of a 2-hydroxy-1,3-dithiolane **2**, as seen in Figure 1, involves both acid- and hydroxide-ion-catalyzed regions. The acid-catalyzed increase in rate, however, levels off near pH 2. This leveling off of the acid catalysis at higher acidity is unusual for the simple reaction. This feature of the profile comes from the constancy at pH 3–4 and the reduction below pH 3 of the observed rate constants k_{obsd}. Even if the estimated value of pK_1 (and so k_{-1}) is varied to some extent (±0.5), calculated profiles of pH–k_2 always show a similar tendency that the acid catalysis levels off near pH 2. Furthermore, a similar pH–rate profile was observed for the decomposition of another cyclic hydrogen ortho thioester, a 2-hydroxy-1,3-dithiane, during the hydrolysis of 2-methylene-1,3-dithiane.[38] Thus, the unusual feature of the profile seems to be real. The breakdown of the tetrahedral intermediate **2** cannot be described simply by acid- and base-catalyzed reactions (Scheme II). We cannot think of any reasonable mechanism for this reaction, but some transport process may be involved in the rate-determining step.[40]

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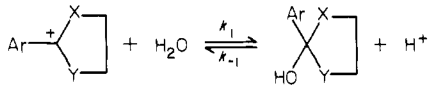
Table V. Rate Constants for Reaction 16

cation	pK_1	k_1, s^{-1}	k_{-1}, M^{-1} s^{-1}	reaction conditions
1	4.1	6.08×10^{-2}	7.8×10^{2}	30 °C, $\mu = 0.45$[a]
6[b]	1.8	4.6×10	2.9×10^{3}	25 °C, $\mu = 1.0$
5[c]	1.1 (1.8)[d]	1.2×10^{3}	1.5×10^{4}	25 °C, $\mu = 0.1$

[a] 10 vol % CH_3CN-H_2O. [b] Reference 17. [c] Reference 10. [d] $\mu = 1.0$.

Comparison with Oxygen Analogues. Reactions of the oxygen analogues, dioxolanyl **5**[10] and oxathiolanyl cations **6**,[17] with water have been investigated as generated from their methoxy derivatives.



(16)

Ar = *p*-methoxyphenyl

5, X = Y = O

6, X = O; Y = S

The rate constants, k_1 and k_{-1}, evaluated at 25 °C are summarized in Table V together with those for **1** (X = Y = S) obtained at 30 °C. Although reaction conditions for kinetic measurements are somewhat different for each cation, a comparison of the data shows clearly the following trends. Relative stabilities (compared with the hydroxy derivative) decrease in the order X, Y = S,S > S,O > O,O, though the difference between the latter two seems to be small. *Both* rate constants for hydration (k_1) and dehydration (k_{-1}) decrease with increasing stability of the cation. The sulfur-substituted cation is more stable but *less easily* generated from the hydroxy derivative than the oxygen cation is. This may be another example of unusual reactivities of sulfur-stabilized carbocations.[9] Although we cannot think of any explanation of these unusual observations at the moment, they may have some connection with the phenomena referred to by "symbiotic effects".[41,42] A central atom prefers bonding to groups of the same kind.[43] Ortho-ester-type adduct may be more easily formed than ortho thioester with mixed substituents.

In any case, the marked stability of the dithiolanyl cation **1** is due to the remarkably slow rate of hydration;[44] i.e., the difference in k_1 is much greater than that in k_{-1}. This eminent tendency of dithio carbocations to react very reluctantly with water may be responsible for some apparently unusual reactivities related to these cations. The rate-determining step of the hydrolysis of these cations is often the hydration step[15,16] for this reason although oxygen analogues are hydrolyzed through this step as a rapid equilibrium (eq 1 and 2).[10-13] Reversibility of the protonation of ketene dithioacetals observed during their hydrolysis (Scheme I)[14-16,38] may be ascribed to slowness of hydration rather than rapidity of the protonation.

Experimental Section

Materials. 2-(*p*-Methoxyphenyl)-1,3-dithiolane was prepared from 1,2-ethanedithiol and anisaldehyde using boron trifluoride etherate as catalyst.[45] Triphenylmethyl perchlorate was obtained from triphenylmethanol by the method of Dauben et al.[46]

2-(*p*-Methoxyphenyl)-1,3-dithiolan-2-yl perchlorate ($\mathbf{1}\cdot ClO_4^-$) was obtained as yellow crystallines by the reaction of the dithiolane with triphenylmethyl perchlorate:[47,48] UV ($HClO_4$) λ_{max} 402 nm; ^{1}H NMR (CF_3CO_2H) δ 4.12 (s, 3 H), 4.36 (s, 4 H), 7.20 (d, 2 H), 8.25 (d, 2 H); ^{13}C NMR (CF_3CO_2H) 225.5 (C^+), 44.2 (CH_2), 57.9 (CH_3), 174.3, 136.8, 126.6, 118.1 ppm from Me_4Si.

2-Methoxy-2-(*p*-methoxyphenyl)-1,3-dithiolane (**4a**) was prepared by the reaction of **1** with methoxide ion. A sample of **1** was added to methanol in which sodium had been dissolved in advance. Products were extracted with ether, washed with water, and dried over $MgSO_4$. The ether was completely removed under vacuum. The residues showed an NMR spectrum and kinetic behavior consistent with the structure. ^{1}H NMR (CCl_4) δ 3.37 (s, 3 H), 3.45 (s, 4 H), 3.76 (s, 3 H), 6.71 (d, 2 H), 7.54 (d, 2 H).

2-((2-Hydroxyethyl)thio)-2-(*p*-methoxyphenyl)-1,3-dithiolane (**4b**) was obtained by the reaction of **1** with 2-mercaptoethanol in acetonitrile solution. The adducts were extracted with ether and the ether was removed under vacuum. The residues showed kinetic and spectral behavior consistent with the structure. ^{1}H NMR (CCl_4) δ ~2 (s, 1 H), 2.60 (t, 2 H), 3.45 (br s and t, 6 H), 3.74 (s, 3 H), 6.74 (d, 2 H), 7.62 (d, 2 H).

Methylphosphonic acid was prepared by hydrolysis of methylphosphonyl dichloride.[49,50] Substituted acetic acids, 3-(dimethylamino)propionitrile, morpholine, *N*-methylmorpholine, and 2-mercaptoethanol were distilled before use. Formic acid, phenylphosphonic acid, and other salts were commercially obtained and used without purification.

Kinetic Measurements. Procedures were similar to those described previously.[15,16] Buffer solutions were prepared by bringing 10 parts by volume of CH_3CN (or an RSH solution in CH_3CN) and necessary amounts of chemicals to 100 parts with water, the ionic strength being adjusted at 0.45 with KCl. Stock solutions of **1**, **4a**, and **4b** were obtained as CH_3CN solutions. The reaction was started by introducing 10–30 μL of the stock solution of the substrate from a microsyringe into 3 mL of the buffer solution in a cuvette at 30 ± 0.1 °C. The reaction of **1** was monitored by following the decrease in absorbance at 402 nm or, in some cases, absorbance increase at 288 nm on a Shimadzu UV 200 spectrophotometer. The reaction of **4** was followed by the increase in absorbance at 288 nm at high pH in the same way. The rapid reaction of **4** at low pH was monitored by the appearance of an absorption at 402 nm on a Union RA 1100 stopped-flow spectrophotometer. The pH values were determined as before[15] by using a Hitachi-Horiba F-7 pH meter.

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Registry No. 1, 88200-30-0; **4a**, 88180-48-7; **4b**, 88180-49-8; deuterium, 7782-39-0; 2-mercaptoethanol, 60-24-2.

Supplementary Material Available: Rate constants for the decay of **1** in buffer solutions (Tables S1 and S2), for the hydrolysis of **4a** (Table S3), and for the reaction of **1** with 2-mercaptoethanol (Table S4) (4 pages). Ordering information is given on any current masthead page.

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