and adding the sample to an excess of EDTA in a pH 10 buffer solution. The remaining EDTA was back-titrated with 0.005 *M* magnesium sulfate with Eriochrome Black T as the indicator.[6] In preliminary experiments we had verified that EDTA does not complex with benzylmercuric chlorides and that accurate values for mercuric chloride can be obtained in their presence.

The Acid-Catalyzed and Mercuric Ion Catalyzed Hydrolysis of 2-(*para*-Substituted phenyl)-1,3-oxathiolanes

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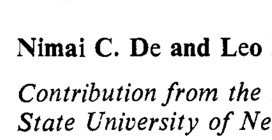
Abstract: The hydrolysis of 2-(*para*-substituted phenyl)-1,3-oxathiolanes to give *para*-substituted benzaldehydes and mercaptoethanol is hydronium ion catalyzed and mercuric ion catalyzed. Mercuric ion catalysis is from 300 to 1600 times more efficient than hydronium ion catalysis. For the acid-catalyzed reactions, $\rho = -1.66$, $\Delta S^{\ddagger} = -17.8$ eu, and the deuterium solvent kinetic isotope effect $k_D/k_H = 2.15$, results consistent with an A2 mechanism involving solvent water in the transition state.

Although there is considerable information concerning the acid-catalyzed hydrolysis of acetals,[1b,2,3] ketals,[3] oxides,[4] ortho esters,[5,6] *para*-substituted phenyl acetals,[7] 2-(*para*-substituted phenyl)-4,4,5,5-tetramethyl-1,3-dioxoalanes,[8] and 2-(substituted phenyl)-3-ethyloxazolidines,[9] relatively little is known about the details of the acid-catalyzed hydrolysis of 2-(*para*-substituted phenyl)-1,3-oxathiolanes (eq 1). Thus the hemithioketal

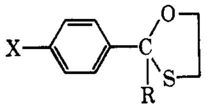


$p\text{-}XC_6H_4CRO + HO(CH_2)_2SH$ (1)

group has been studied primarily from the viewpoint of its synthetic utility as a carbonyl protective group.[10,11] Of biochemical interest is the report of a mammalian thioglycosidase which is capable of catalyzing the hydrolysis of 6-mercaptopurine-β-D-glycothiopyranosides to 6-mercaptopurine and pyranoses.[12] This enzymic reaction is catalyzed by a variety of substances including cupric and mercuric ions and is inhibited by some substances including ethylenediaminetetraacetic acid, results which suggest that the enzyme may have a metal ion requirement and further that the metal ion may function as a super acid in the hydrolysis reaction. This investigation was undertaken in order to gain information about the mechanisms of hydrolysis of oxathiolanes as well as to determine the relative catalytic efficiency of the proton *vs.* mercuric ion in hydrolytic reactions of these substances.

Experimental Section

Reagents. Inorganic salts were Fisher ACS certified reagent chemicals. Organic reagents were purchased from Fisher Co. and were distilled or crystallized before use. Tap-distilled water was redistilled from a Corning AGla still. Deuterium oxide (99.8%) and deuterium chloride in D_2O were purchased from Ciba Co. 2-(Substituted phenyl)-1,3-oxathiolanes were synthesized by the method of Djerrasi, *et al.*[13] A mixture of equimolar quantities of appropriate aldehyde with 2-mercaptoethanol was refluxed in benzene with a trace of *p*-toluenesulfonic acid until the calculated amount of water was collected. The solution was cooled, washed successively with dilute sodium bicarbonate solution and water, and dried with $MgSO_4$. The benzene was distilled out and the residue was purified by vacuum distillation or crystallization from methanol. The physical constants of oxathiolanes are given in Table I.



Apparatus. A Gilford Model 2000 spectrophotometer equipped with thermospacers through which water (±0.1°) from a Tamson T9 water bath was circulated, was used for kinetic measurements. pH measurements were made with a Radiometer PH M22 pH meter with a PHA 630 scale expander and a Radiometer GK2021 B electrode. Ultraviolet spectra were scanned using a Beckman Model DBG spectrophotometer.

Kinetics. Stock solutions of compounds **1–6** were prepared in redistilled acetonitrile. All the reactions were carried out in redistilled water and at a calculated ionic strength of 1 *M* (KCl) unless otherwise stated. The values for the rate constants for the acid and mercuric ion catalyzed reactions were unaffected by changes in μ from 0.1 to 1.0. pH was determined before each run and sometimes after some runs to ensure constancy of pH ±0.02 units. Reactions were started by addition of a microdrop of the appropriate substrate in acetonitrile to a 3-ml cuvette filled to the stopper level with the proper solutions equilibrated at appropriate temperatures (final concentration of substrate = $3\text{–}5 \times 10^{-5}$ *M*).

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(1) (a) To whom inquiries concerning this work should be directed. (b) For a recent review of the mechanism for the hydrolysis of acetals, ketals, and ortho esters, see E. H. Cordes, *Progr. Phys. Org. Chem.*, **4**, 1 (1967).

(2) M. M. Kreevoy and R. W. Taft, Jr., *J. Amer. Chem. Soc.*, **77**, 5590 (1955).

(3) T. H. Fife and L. Hagopian, *J. Org. Chem.*, **31**, 1772 (1966).

(4) F. A. Long, J. G. Pritchard, and F. E. Stafford, *J. Amer. Chem. Soc.*, **79**, 2362 (1957).

(5) H. Kwart and M. B. Price, *ibid.*, **82**, 5123 (1960).

(6) C. A. Bunton and R. H. DeWolfe, *J. Org. Chem.*, **30**, 1371 (1965).

(7) T. H. Fife and L. K. Jao, *ibid.*, **30**, 1492 (1965).

(8) T. H. Fife, *J. Amer. Chem. Soc.*, **89**, 3228 (1967).

(9) T. H. Fife and L. Hagopian, *ibid.*, **90**, 1007 (1968).

(10) C. Djerassi, M. Shamma, and T. Y. Kau, *ibid.*, **80**, 4723 (1958).

(11) M. L. Wolfrom and K. Anno, *ibid.*, **75**, 1038 (1953).

(12) I. Goodman, J. R. Fouts, E. Bresnick, R. Mengas, and G. H. Hitchings, *Science*, **130**, 450 (1959).

(13) C. Djerassi and M. Gorman, *J. Amer. Chem. Soc.*, **75**, 3704 (1953).

Table I. Physical Constants of Oxathiolanes

Compd	X	R	Bp, °C (mm)	Mp, °C	Found, %: C	H	S
1	H	H	99-100 (1.4)[a]				
2	OCH_3	H	124-126 (0.9)		61.45	6.28	16.25
3	CH_3	H	90-92 (0.2)		66.95	6.59	17.38
4	Cl	H	126-128 (0.95)[b]				
5	NO_2	H		70-71[b]			
6	H	CH_3	80-82 (0.4)[13]				

[a] E. L. Eliel, L. A. Pilato, and V. G. Badding, *J. Amer. Chem. Soc.*, **84**, 2377 (1962). [b] J. R. Marshall and H. A. Stevenson, *J. Chem. Soc.*, 2360 (1959).

Reactions were generally monitored to completion. Pseudo-first-order rate constants were determined by multiplying the slopes of plots of log $(A_\infty - A_0)/(A_\infty - A_t)$ *vs.* time by 2.303 and these plots were linear to at least two half-lives (for **5**) and generally to three half-lives.

Product Analysis. The formation of free aldehydes and 2-mercaptoethanol was proved from the followingex periments. 2-Phenyl-1,3-oxathiolane (3.0 g) was treated with 12.0 ml of 1 *N* HCl in 50 ml of dioxane. The homogeneous solution was kept for 25 min. This was treated with $MgSO_4$ and extracted with ether. The ether extract was washed with water and dried with $MgSO_4$ and the ether was removed. The residue (0.6 g) was dissolved in 20 ml of 95% ethanol to which freshly prepared 2,4-dinitrophenylhydrazine[14] was added. The hydrazone was crystallized from ethanol as crimson-colored crystals, mp 236-237°. The melting point of this hydrazone was compared with that of authentic benzaldehyde and had mp 236-237° (lit.[15] mp 237°). The mixture melting point was not depressed. The residue left after removal of ether was a mixture of benzaldehyde and 2-mercaptoethanol by nmr, infrared, and ultraviolet studies. An nmr study (solvent $CDCl_3$, reference TMS) showed the presence of aromatic protons (multiplets δ 7.2-9.7 ppm), dioxane protons (singlet δ 3.6 ppm), 2-mercaptoethanol protons (multiplets δ 2.5-3.3 ppm), and free aldehydic protons (singlet δ 10.98 ppm). The spectrum also showed a trace amount of unconverted 2-phenyl-1,3-oxathiolane. The infrared spectrum showed OH (3500 cm^{-1} m), aromatic (2900-3000 cm^{-1} (s), 1600 cm^{-1} (s)), and CHO (1700 cm^{-1} (s)) peaks. The ultraviolet spectrum had λ_{max} 245 mμ, identical with that of authentic benzaldehyde.

Results

The hydrolyses of 2-(*para*-substituted phenyl)-1,3-oxathiolanes to give *para*-substituted benzaldehydes and 2-mercaptoethanol (eq 1) were catalyzed both by acid and mercuric ions (eq 2). Under pseudo-first-order

$$\frac{d(p\text{-}XC_6H_4CHO)}{dt} = (k_Ha_H + k_{Hg}[Hg^{2+}])[\text{oxathiolanes}] \quad (2)$$

conditions, $k_{obsd} = k_Ha_H + k_{Hg}[Hg^{2+}]$ where a_H = the hydrogen ion activity measured at the glass electrode and $[Hg^{2+}]$ = the stoichiometric concentration of mercuric ion (mercuric chloride). In the absence of Hg^{2+}, $k_{obsd} = k_Ha_H$ and plots of k_{obsd} *vs.* a_H are linear with slope k_H (Figure 1, Table II).

In the presence of mercuric ion, at constant hydrogen ion concentration, plots of k_{obsd} *vs.* $[Hg^{2+}]$ are linear with intercept k_Ha_H and slope k_{Hg} (Figure 2, Table II). The intercept of Figure 2 is within 1% of the calculated value. In this study, the hydrolyses of oxathiolanes were not catalyzed by general acids as chloroacetic acid and acetic acid. Accordingly, plots of k_{obsd} *vs.* $[Hg^{2+}]$ in 0.1 *M* acetate buffer, pH 4.61, are linear with slope k_{Hg} and intercept = 0 (Figure 3). The rate constants, k_{Hg}, determined in HCl and in acetate buffer are 310 and 307 M^{-1} min^{-1}, respectively. The second-order rate constants for the acid-catalyzed and mercuric ion catalyzed hydrolyses of the 1,3-oxathiolanes of this study are given in Table III. (See Table IV for pseudo-first-order constants in acetate buffer.)

Table II. First-Order Rate Constants, k_{obsd}, for the Acid-Catalyzed and Mercuric Ion Catalyzed Hydrolysis of 2-Phenyl-1,3-oxathiolane[a]

a_H	k_{obsd}[b] × 10^2 min^{-1}	$[Hg^{2+}]$ × 10^4, *M*	k_{obsd}[c] × 10^1 min^{-1}
0.087	7.21	0.4	1.12
0.182	13.41	0.6	1.19
0.224	19.4	0.8	1.23
0.342	22.4	1.0	1.27
0.550	37.5	2.0	1.61
0.602	39.5	4.0	2.17
0.650	42.15	6.0	2.93
0.760	51.75	7.0	3.21
		8.0	3.45

[a] Temperature, 30°; solvent, water. [b] Acid-catalyzed reaction, μ = 1.0 *M* KCl. [c] Mercuric ion catalyzed reaction, a_H = 0.149, μ = 0.19 *M* KCl.

Table III. Second-Order Rate Constants for the Acid-Catalyzed k_H and Mercuric Ion Catalyzed k_{Hg} Hydrolyses of 2-(*para*-Substituted phenyl)-1,3-oxathiolanes[a]

Compd	λ_{max}, mμ	k_H,[b] M^{-1} min^{-1}	k_{Hg},[c] M^{-1} min^{-1}	k_D	k_D/k_H
1	250	0.665	3.10 × 10^2	1.33	2.15
2	273	2.52	1.31 × 10^3		
3	255	0.787	1.29 × 10^3		
4	254	0.122	1.10 × 10^2		
5	265	0.0405	1.212 × 10^1		
6	242	0.565			

[a] Temperature, 30°; solvent, water. [b] μ = 1.0 *M* KCl. [c] μ = 0.19 *M* KCl.

Table IV. Pseudo-First-Order Rate Constants, k_{obsd}, for Mercuric Ion Catalyzed Hydrolysis of 2-Phenyl-1,3-oxathiolane in 0.19 *M* Acetate Buffer[a]

$[Hg^{2+}]$ × 10^3, *M*	k_{obsd}, min^{-1}
1.74	0.535
2.32	0.560
2.90	0.932
4.06	1.305
4.65	1.49

[a] pH 4.61; solvent, water; temperature, 30°; μ = 0.1 *M* KCl.

For the hydrolysis of 2-phenyl-1,3-oxathiolane in deuterium oxide the second-order rate constant (Table

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(14) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 3rd ed, John Wiley & Sons, Inc., New York, N. Y., 1948, p 171.

(15) See ref 14, p 229.

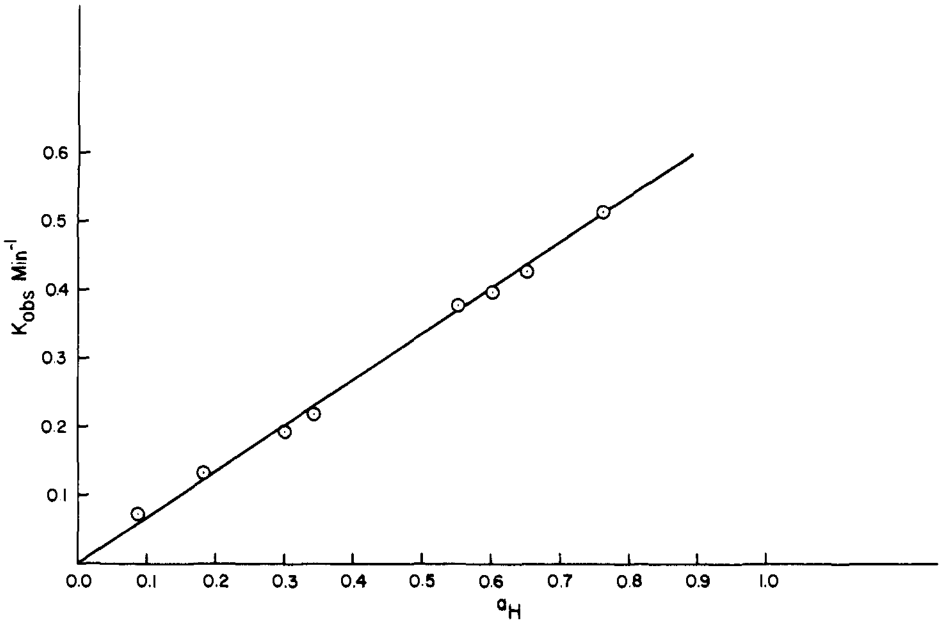

Figure 1. Plot of the pseudo-first-order rate constant, k_{obsd}, *vs.* a_H for the acid-catalyzed hydrolysis of 2-phenyl-1,3-oxathiolane; solvent, H_2O; temperature, 30°; μ = 1.0 (KCl).

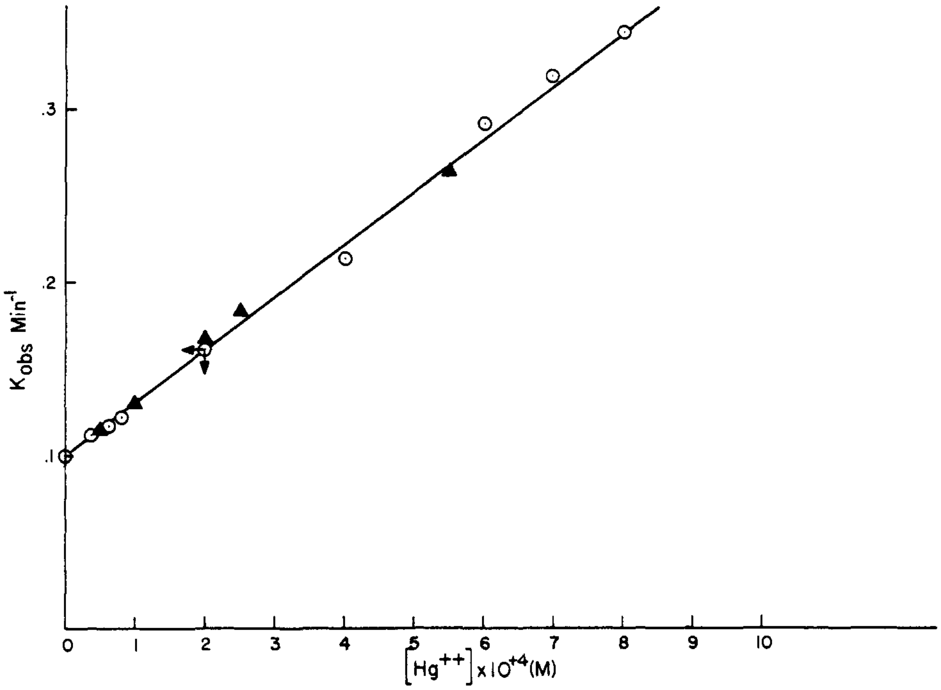

Figure 2. Plot of the pseudo-first-order rate constant, k_{obsd}, *vs.* the concentration of mercuric ion for the hydrolysis of 2-phenyl-1,3-oxathiolane; a_H = 0.149; solvent, H_2O; temperature, 30°; μ = 1.0 (KCl), ▲; μ = 0.19, ○.

III) was evaluated similarly. The values of a_D were calculated by the method of Fife and Bruice.[16]

The Hammett ρ[17] value for the acid-catalyzed reaction is -1.66 ± 0.07 ($r = 0.975$); for the mercuric ion catalyzed reaction $\rho = -2.05 \pm 0.05$ ($r = 0.983$)[18] (Figure 4).

The Arrhenius activation energies (Table V) were calculated from the slopes of plots of log k_H or log k_{Hg} *vs.* $1/T$°K.

Discussion

The 2-(*para*-substituted phenyl)-1,3-oxathiolanes **1–6** undergo acid-catalyzed hydrolysis at slower rates than their oxygen counterparts, the 1,3-dioxolanes.[7] This reactivity difference can be accounted for in several ways. (1) The dioxolanes are likely more basic than the oxathiolanes.[19] (2) Oxygen can better stabilize an α-carbonium ion, or a transition state in which partial onium character is developed, than sulfur.[21]

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[16] T. H. Fife and T. C. Bruice, *J. Phys. Chem.*, **65**, 1079 (1961).

[17] J. D. Roberts and M. C. Caserio, "Basic Principles of Organic Chemistry," W. A. Benjamin, Inc., New York, N. Y., 1965, p 956.

[18] H. H. Jaffé, *Chem. Rev.*, **53**, 253 (1953).

[19] Dimethyl ether, $pK_a = -3.84$, is a stronger base than dimethyl sulfide, $pK_a = -4.25$.[20]

[20] E. M. Arnett, *Progr. Phys. Org. Chem.*, **1**, 223 (1963).

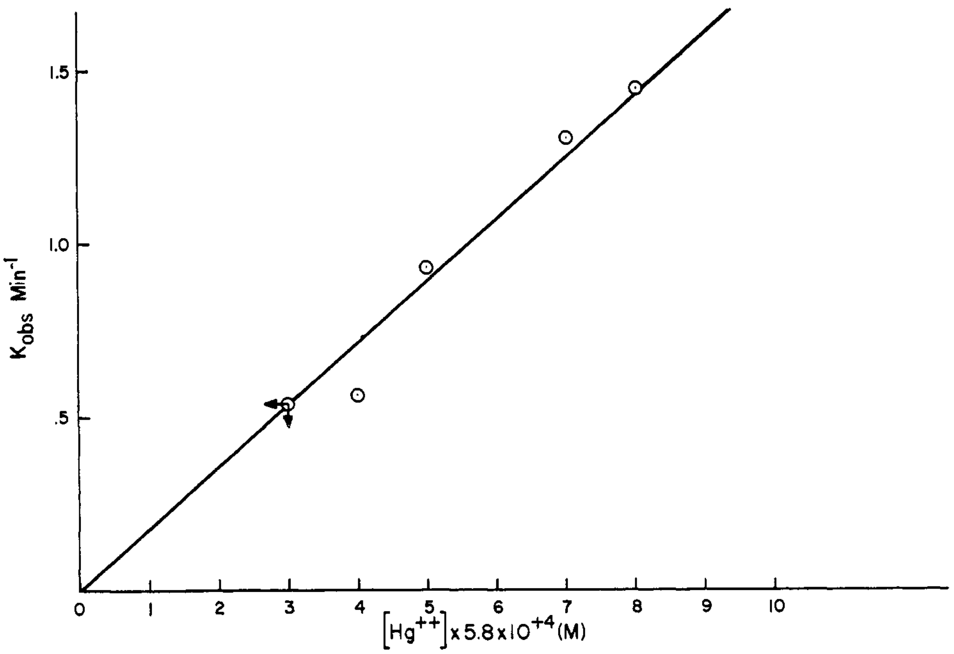

Figure 3. Plot of the pseudo-first-order rate constant, k_{obsd}, *vs.* the concentration of mercuric ion in 0.1 *M* acetate buffer, for the hydrolysis of 2-phenyl-1,3-oxathiolane; pH 4.62; solvent, H_2O; temperature, 30°; μ = 0.1 (KCl).

Thus ethoxyacetylenes undergo acid-catalyzed hydration faster than thioethoxyacetylenes[22] and α-chloromethyl ethers undergo hydrolysis faster than α-chloromethyl thioethers.[23] Presumably these reactions involve stabilization of positive charge at the α-carbon atom *via* electron donation by O and S. (3) Sulfur likely imposes additional steric constraint in **1–6** *vs.* the dioxolanes which could influence the mechanism of the hydrolytic reactions as well as the relative rates of the reactions. The steric involvement could itself take several forms. (a) The protonation of **1–6** could be hindered owing to the size of S *vs.* O. (b) The transition state for the solvolysis of **1–6** may be destabilized more relative to the ground state than the dioxolanes. Assuming protonation of **1–6** is accompanied by the development of some carbonium ion character at C_2 which can be stabilized in part by overlap of sulfur p or hybridized pd orbitals, the ground-state distorted envelope conformation[24] of the oxathiolanes will assume a more nearly planar conformation resulting in destabilizing interactions between the C_2 substituents and the "sulfonium" sulfur atom. (c) Assumption of a more nearly planar transition state as in b above requires that in addition to increased 1,2 interactions at C_4 and C_5 the interactions between the C_2 substituents and the hydrogen atoms at C_4 and C_5 will increase relative to the ground state.[24] Thus Pasto, *et al.*,[24] have shown by nmr studies that the oxathiolanes exist in a distorted envelope conformation and that strong ground-state interactions exist between the pseudoaxial hydrogen atoms at C_4 and C_5 and the 2 substituents.

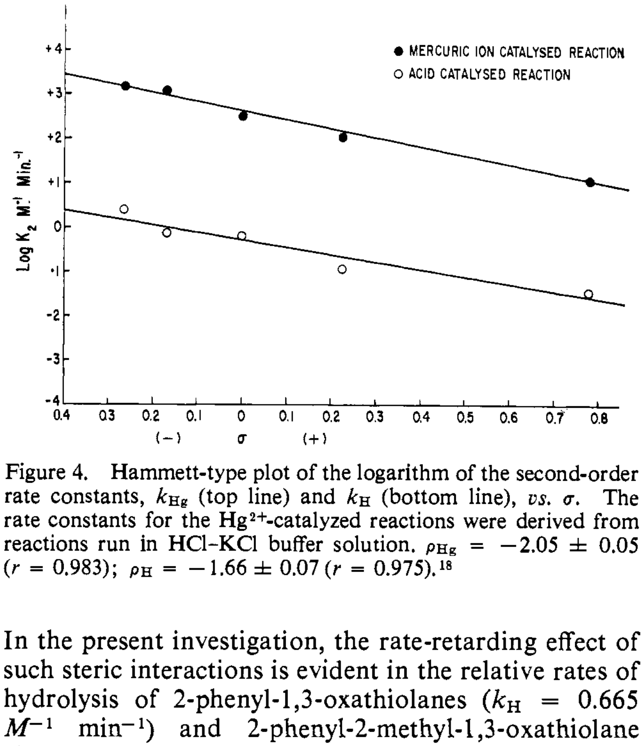

Figure 4. Hammett-type plot of the logarithm of the second-order rate constants, k_{Hg} (top line) and k_H (bottom line), *vs.* σ. The rate constants for the Hg^{2+}-catalyzed reactions were derived from reactions run in HCl-KCl buffer solution. $\rho_{Hg} = -2.05 \pm 0.05$ (r = 0.983); $\rho_H = -1.66 \pm 0.07$ (r = 0.975).[18]

In the present investigation, the rate-retarding effect of such steric interactions is evident in the relative rates of hydrolysis of 2-phenyl-1,3-oxathiolanes (k_H = 0.665 M^{-1} min^{-1}) and 2-phenyl-2-methyl-1,3-oxathiolane (k_H = 0.565 M^{-1} min^{-1}).

The large negative ρ values generally associated with the acid-catalyzed hydrolysis of acetals ketals, ortho esters, etc.[1b] is taken as evidence for the A1 mechanism. In the present study a ρ value of −1.66 was obtained (Figure 4), considerably less than the −3.25 to −4 range reported for the oxygen series[1b,3] and less than the −2.0 value reported for the tetramethyldioxolanes.[8] A possible interpretation of this result is that there is less carbonium ion character in the transition state in the hydrolysis of 1,3-oxathiolanes than in the hydrolysis of acetals, ketals, etc. In fact, the A1 mechanism predicts an even greater dependence on electron-donating substituents (larger negative ρ) in

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[21] The hydrolyses of acetals, ketals, etc. are characterized by large, negative ρ values indicating that the transition state for these reactions, using this criterion of mechanism, has carbonium ion character which can be stabilized in part by oxygen atoms.

[22] W. Drenth and H. Hogeveen, *Rec. Trav. Chim. Pays-Bas*, **79**, 1002 (1960).

[23] (a) H. Bohme, H. Fisher, and R. Frank, *Ann.*, **563**, 54 (1949); (b) H. Bohme, *Ber.*, **74**, 248 (1949).

[24] D. J. Pasto, F. M. Klein, and T. W. Doyle, *J. Amer. Chem. Soc.*, **89**, 4368 (1967).

Table V. Temperature-Dependent Second-Order Rate Constants and Arrhenius Activation Parameters for the Hydrolysis of Compounds **1** and **6** in 0.1 M HCl[a]

Temp, °C		**1**	**6**	**1**
		k_H, M^{-1} min^{-1}	k_H, M^{-1} min^{-1}	k_{Hg},[b,d] M^{-1} min^{-1}
20		0.220	0.219	1.695×10^2
30		0.665	0.556	3.10×10^2
40		1.14	1.13	5.02×10^2
	$\Delta H^{\ddagger}$,[c,e] kcal/mol	14.9 ± 0.2	12.6 ± 0.6	7.5 ± 0.6
	$\Delta S^{\ddagger}$,[c] eu	−17.8 ± 0.8	−24.7 ± 0.4	−30.0 ± 1.7
		$r = 0.995$	$r = 0.998$	$r = 0.972$

[a] Solvent, water; $\mu = 1.0$. [b] $\mu = 0.1$ M KCl. [c] $E_a = \Delta H^{\ddagger} + RT$ (W. J. Moore, "Physical Chemistry," 3rd ed, Prentice-Hall, Inc., Englewood Cliffs, N. J., 1963, p 297), $\Delta F^{\ddagger} = -2.303RT \log (k_2h/TK)$, $\Delta F^{\ddagger} = \Delta H^{\ddagger} - T\Delta S^{\ddagger}$; temperature, 30° k_2 in M^{-1} sec^{-1}, h = Plank's constant, k = Boltzmann constant. [d] k_{Hg} values for mercuric ion catalyzed hydrolysis were calculated by using eq 2, knowing the values of k_Ha_H previously determined at different temperatures with $a_H = 0.1$. [e] The uncertainties in the values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are the standard deviations (S) derived from the least-squares regression lines for which the corresponding correlation coefficients r are given.

the oxathiolanes allowing that sulfur is less effective than oxygen as an electron donor to carbon (*vide supra*). Accordingly an A2 mechanism is favored for the hydrolysis of the oxathiolanes using this criterion of mechanism.

Consistent with the A2 mechanism of hydrolysis are the small entropy values obtained for the acid-catalyzed hydrolysis of **1** (−17.8 eu) and **6** (−24.7 eu Table V). These values may be compared to those of 2-phenyl-1,3-dioxolane (−8.9 eu)[7] and 2-phenyl-2-methyl-1,3-dioxolane (−8.6 eu)[3] for which the A1 mechanism is assumed and to 2-phenyl-4,4,5,5-tetramethyl-1,3-dioxolane (−14.2 eu)[8] for which the A2 mechanism is assumed. In general, reactions proceeding *via* the A1 mechanism are attended by zero or positive entropy values.[25]

The deuterium solvent kinetic isotope effect, $k_D/k_H = 2.15$ (Table III), for **1** is outside the theoretical range 1.3–1.7 predicted by Long[26] for reactions proceeding *via* the A2 mechanism. However, it is considerably less than the theoretical value of 2.7 or greater predicted for reactions proceeding *via* the A1 mechanism. The experimental value for k_D/k_H can be compared with that determined for the hydrolysis of 2-phenyl-1,3-dioxolane (2.75)[3] by the A1 mechanism and for the hydrolysis of the 4,4,5,5-tetramethyl derivative (2.4)[8] for which the A2 mechanism is postulated. We believe the deuterium solvent kinetic isotope effect for **1** to be consistant with the A2 mechanism.

The mercuric ion catalyzed[27] hydrolysis of **1**–**5** is from 300 to 1600 times more efficient than the hydronium ion catalyzed reaction. Likely the mechanism of the hydrolytic reaction is also A2 with $\Delta S^{\ddagger} = -30.0$ eu (Table V) and $\rho = -2.06$ (Figure 4). The lower value for ρ (*cf.* −1.66 for the acid-catalyzed reaction) suggests more carbonium ion character in the transition state for the Hg^{2+}-catalyzed reaction than for the H_3O^+-catalyzed reaction. Mercury(II) is likely a stronger acid toward sulfur than hydronium ion is toward oxygen[29] (*cf.* the dissociation constant for Hg(II)-thioglycolate complex[28] with the ionization constant for alcohols) which predicts a higher equilibrium concentration of Hg(II)–oxathiolane complex than of H_3O^+–oxathiolane complex. This coupled with the possibility that the Hg(II)–oxathiolane complex, if it carries more than unit charge, can better polarize the carbon–sulfur bond for scission in the transition state may account for the exhalted activity of Hg(II) over H_3O^+. General acid catalysis is a term usually applied in the Brønsted sense of acids and includes catalysis by proton donors excluding lyoxonium species. However the Lewis definition of an acid accommodates metal ions within the category of general acid catalysts. The finding of such catalysis in the present study is by no means unique. Thus catalysis by metal ions in the halogenation of ketones[31] and in the decarboxylation of oxaloacetic acid[32] could involve acid catalysis of enolization. Similarly, the metal ion catalyzed hydrolysis of thiol esters[33] could be viewed as a special example of general acid catalysis. It is attractive to think that enzymes might utilize such "super" acids in catalysis as well as the usual Brønsted general acids available from the peptide chain. Possibly the mammalian thioglycosidase mentioned previously utilizes metal ions as acid catalysts.

The value for ρ, the deuterium solvent isotope effect and the Arrhenius activation parameters support a reaction mechanism consistent with the A2 formulation which involves the participation of water in the transi-

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(25) L. L. Schaleger and F. A. Long, *Advan. Phys. Org. Chem.*, **1**, 1 (1963).

(26) F. A. Long, *Ann. N. Y. Acad. Sci.*, **84**, 596 (1960).

(27) Strictly speaking, mercuric ion is noncatalytic in the sense that it is presumably consumed in the reaction, the mercaptoethanol product being present as its salt. Here mercuric ion catalysis refers to catalysis by some form of Hg^{2+} (ligand)$_n^{n-}$ such as $HgCl_2$ or $HgCl_4^{2-}$; nothing concerning the nature of the complex is implied by the use of Hg^{2+} in the discussion. With regard to the possibility that $HgCl_2$ or $HgCl_4^{2-}$ is the catalytic species, the small dissociation constant for the equilibrium $HgCl_4^{2-} \rightleftarrows Hg^{2+} + 4Cl^-$, 8.3×10^{-16}, does not mean that Hg^{2+} can not be the catalytic species; it is in equilibrium with all ligands in solution and the equilibrium can be displaced if the stability constant for the oxathiolane–Hg^{2+} (ligand)$_n^{n-}$ complex is greater than that for $HgCl_4^{2-}$, etc. Stricks, Kolthoff, and Heyndrickx[28] have determined the dissociation constant for the Hg(II)–thioglycolic acid complex to be *ca.* 10^{-45}. While this model is only an approximation to the oxathiolane system, it serves to illustrate the strong association between divalent sulfur and Hg(II).

(28) W. Stricks, I. M. Kolthoff, and A. Heyndrickx, *J. Amer. Chem. Soc.*, **76**, 1515 (1954).

(29) In this study it is assumed that protonation occurs primarily on oxygen and mercuration occurs primarily on sulfur. This is by analogy to the work of Pearson[30] and others concerning the hard–soft acid–base concept. A tenet of the concept is that hard acids react preferentially with hard bases (H_3O^+, ROR) and soft acids react preferentially with soft bases (Hg^{2+}, RSR). Also, in this investigation it was established that 2-phenyl-1,3-dithiolane is practically inert toward 1 M HCl and that 2-phenyl-1,3-dioxolane is inert toward $HgCl_2$. The second-order rate constant for the acid-catalyzed hydrolysis of 2-phenyl-1,3-dioxolane (250 mμ, pH 2.55–3.30, 5k_{obsd}, μ = 1.0 M (KCl), solvent = H_2O, t = 30 ± 0.1°) is 208.5 M^{-1} min^{-1}. The hydrolysis of this compound is indifferent to $HgCl_2$ (k_{obsd} min^{-1}; [$HgCl_2$], M): 0.231, 4.87×10^{-5}; 0.231, 1.95×10^{-4}; 0.231, 2.83×10^{-4}, pH = 2.96, μ = 1.0 M (KCl), solvent = H_2O, t = 30 ± 0.1°. The pseudo-first-order rate constant for hydrolysis of the dioxolane by H_3O^+, pH 2.96 is 0.229 min^{-1}.

(30) R. G. Pearson, *J. Amer. Chem. Soc.*, **85**, 3533 (1963).

(31) K. Pedersen, *Acta Chem. Scand.*, **2**, 252, 385 (1948).

(32) J. F. Speck, *J. Biol. Chem.*, **178**, 315 (1948).

(33) T. C. Bruice in "Organic Sulfur Compounds," N. Kharasch, Ed., Pergamon Press, New York, N. Y., 1961, Chapter 35.

tion state. In the above-mentioned solvolysis of 2-

$$S + H^+ (Hg^{2+}) \underset{}{\overset{\text{fast}}{\rightleftarrows}} SH^+ (SHg^{2+})$$

$$SH^+ (SHg^{2+}) + H_2O \xrightarrow{\text{slow}} \text{products}$$

phenyl-4,4,5,5-tetramethyldioxolane (A2), Fife[8] observed general acid catalysis of hydrolysis by formic acid. This finding coupled with the magnitude of ρ, k_D/k_H, and $\Delta S^{\ddagger}$ for that study suggests the possibility of a concerted protonation and nucleophilic attack by water on the substrate. In the present study no evidence of catalysis by chloroacetic acid or acetic acid was detected. Thus proton transfer to oxathiolanes is virtually complete prior to the rate-determining step.

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The Synthesis and Acid-Catalyzed Rearrangement of 3,3-Dimethoxy-1,5-dimethyltetracyclo[3.2.0.0^{2,7}.0^{4,6}]heptane[1]

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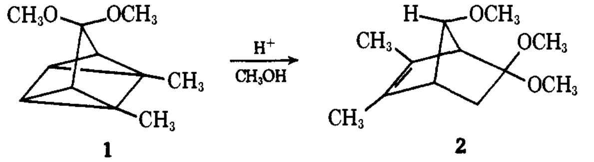
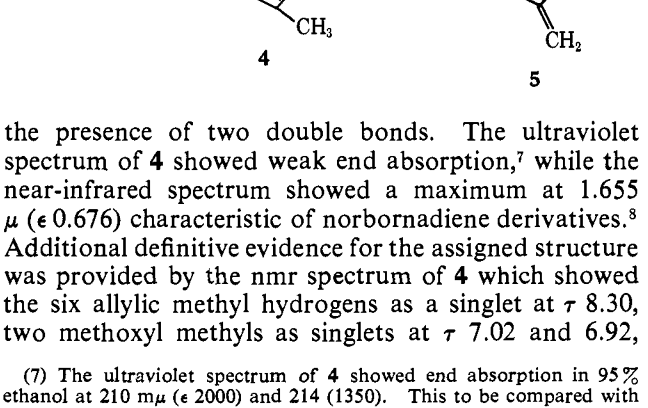
Abstract: 7,7-Dimethoxy-2,3-dimethylbicyclo[2.2.1]heptadiene was prepared and photochemically converted into 3,3-dimethoxy-1,5-dimethyltetracyclo[3.2.0.0^{2,7}.0^{4,6}]heptane by both photosensitized and direct irradiation. The photoproduct was extremely sensitive to mildy acidic conditions, yielding a dehydronorcamphor derivative virtually instantly on exposure to 0.01% methanolic sulfuric acid. The mechanistic implications of this unusual rearrangement are discussed.

Although "quadricyclane" derivatives[5] have become relatively well-known compounds (as illustrated by some 25 publications in the area), a dearth of information exists concerning the reactions of this highly strained ring system. In relation to our long-standing interest in carbonium ion chemistry we were particularly concerned about the nature and ultimate fate of carbonium ions generated on the quadricyclane skeleton. This paper presents our findings on the reactions of 3,3-dimethoxy-1,5-dimethyltetracyclo[3.2.0.0^{2,7}.0^{4,6}] heptane (**1**), a quadricyclane derivative which rapidly rearranges to 5,5-dimethoxy-*anti*-7-methoxy-2,3-dimethylbicyclo[2.2.1]hept-2-ene (**2**) in weakly acidic methanol.



1 **2**

The known triene, **3**, prepared by a modification of the procedure of Hoch[6] served as the origin of our synthetic work. Dechlorination of **3** with sodium tetrahydrofuran–*t*-butyl alcohol gave a mixture of **4** and **5** in 38 and 24% yields, respectively. 7,7-Dimethoxy-2,3-dimethylbicyclo[2.2.1]heptadiene, **4**, which arose *via* a novel 1,4 reduction of the conjugated diene system was of prime importance to our synthetic approach. Hence, the structure of **4** was substantiated in several ways. Catalytic reduction of **4** over palladium on carbon resulted in the rapid uptake of 1 mol of hydrogen followed by the relatively slow addition of 1 additional mol of hydrogen indicating the presence of two double bonds. The ultraviolet spectrum of **4** showed weak end absorption,[7] while the near-infrared spectrum showed a maximum at 1.655 μ (ϵ 0.676) characteristic of norbornadiene derivatives.[8] Additional definitive evidence for the assigned structure was provided by the nmr spectrum of **4** which showed the six allylic methyl hydrogens as a singlet at τ 8.30, two methoxyl methyls as singlets at τ 7.02 and 6.92,



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[1] For a preliminary report on part of this work, see P. G. Gassman, D. H. Aue, and D. S. Patton, *J. Am. Chem. Soc.*, **86**, 4211 (1964).

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[5] The term "quadricyclane" is the commonly accepted name for the tetracyclo[3.2.0.0^{2,7}.0^{4,6}]heptane ring system. For the systematic nomenclature and numbering details, see J. Meinwald and J. Crandall, *J. Am. Chem. Soc.*, **88**, 1292 (1966).

[6] P. E. Hoch, *J. Org. Chem.*, **26**, 2066 (1961).

[7] The ultraviolet spectrum of **4** showed end absorption in 95% ethanol at 210 mμ (ϵ 2000) and 214 (1350). This to be compared with norbornadiene which shows end absorption at 214 mμ (ϵ 1480).

[8] P. G. Gassman and W. M. Hooker, *J. Am. Chem. Soc.*, **87**, 1079 (1965).