fluorosulfonate, triphenylvinyl trifluoromethanesulfonate, and triphenylvinyl tosylate was determined by gas chromatographic analysis, column temperature 196°. Triphenylethylene was used as an internal standard. The amount of 1-phenylvinyl acetate produced by the acetolysis of 1-phenylvinyl fluorosulfonate was determined titrimetrically. In all cases, tlc and gc showed only the acetate as a product.

In one instance, triphenylvinyl acetate was isolated in pure form from the acetolysis of triphenylvinyl fluorosulfonate in 93% yield. The fluorosulfonate, 38.8 mg, was dissolved in acetic acid along with 83.0 mg of sodium acetate. This solution was heated to 75° for 2 hr, poured into an equal volume of water, and extracted with ether. The solvent was removed on a rotary evaporator, and the resulting white solid was dried under vacuum for 2 days. This work-up afforded a product, 29.4 mg, whose melting point and mixture melting point were identical with those of triphenylvinyl acetate. The infrared spectrum (Nujol) was superimposable upon that of an authentic sample of triphenylvinyl acetate.

In a similar manner, 1-phenylvinyl acetate was isolated from the acetolysis of 1-phenylvinyl fluorosulfonate. The light yellow oil had an infrared spectrum (neat) that was superimposable upon that of an authentic sample of 1-phenylvinyl acetate.

Acknowledgments. Acknowledgment is made to the donors of the Petroleum Research Fund administered by the American Chemical Society for support of this research. The authors would also like to acknowledge their appreciation to Professors Peterson, Schleyer, and Stang for preprints of pertinent manuscripts. W. M. J. is also grateful to Professor W. B. Person for helpful discussions.

Thioacetal Hydrolysis. The Hydrolysis of Benzaldehyde Methyl S-(Substituted phenyl) Thioacetals

Thomas H. Fife and Edwin Anderson[1]

Contribution from the Department of Biochemistry, University of Southern California, Los Angeles, California.
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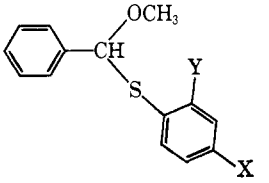
Abstract: The rate constants for acid-catalyzed hydrolysis of a series of benzaldehyde methyl S-(substituted phenyl) thioacetals have been measured at 30° in 20% dioxane–H_2O. General acid catalysis could not be detected with any of these compounds. The value of ΔS^* for the hydronium ion catalyzed hydrolysis of the unsubstituted derivative is −4.8 eu. This reaction is much faster in D_2O than H_2O, the ratio k_D/k_H being 1.51. The ρ value for acid-catalyzed hydrolysis of the series is −1.0. An A1 mechanism is indicated with the carbon–sulfur bond breaking in the rate-determining step. The hydrolysis of the 2,4-dinitrophenyl derivative is pH independent from pH 1.5 to 0.1 *M* NaOH. This reaction proceeds at approximately the same rate in D_2O as in H_2O (k_{D_2O}/k_{H_2O} = 0.90). The pH-independent reaction is therefore very likely a unimolecular decomposition to 2,4-dinitrothiophenoxide ion and a resonance-stabilized carbonium ion.

The generally accepted mechanism for the acid-catalyzed hydrolysis of simple acetals and ketals involves preequilibrium protonation by hydronium ion followed by rate-determining unimolecular decomposition to an alcohol and a resonance-stabilized carbonium ion.[2] Strong electron withdrawal in the leaving group, which greatly reduces the basicity of oxygen and at the same time facilitates breaking of the carbon–oxygen bond, will change the mechanism to one involving partially rate-determining protonation.[3] Replacement of an acetal oxygen by sulfur might therefore also be expected to give rise to a mechanism in which there is partially rate-determining proton transfer since sulfur is much less basic than is oxygen. However, general acid catalysis was not observed in the hydrolysis of 2-(substituted phenyl)-1,3-oxathiolanes.[4,5] Proton transfer from hydronium ion must be essentially complete in the transition state for those compounds.[4] A simple replacement of oxygen by sulfur therefore does not reduce basicity sufficiently to produce clearly a mechanism change. It was thought that it would be of importance to study the hydrolysis of thioacetals of substituted thiophenols so that basicity and ease of bond breaking could be varied systematically by changing the substituent groups in the thiophenol portion of the molecule. Anderson and Capon[6] have



I, X = OCH_3; Y = H
II, X = CH_3; Y = H
III, X = H; Y = H
IV, X = Cl; Y = H
V, X = NO_2; Y = H
VI, X = NO_2; Y = NO_2

(1) Postdoctoral Fellow, Department of Biochemistry, University of Southern California.
(2) E. H. Cordes, *Progr. Phys. Org. Chem.*, 4, 1 (1967).
(3) T. H. Fife and L. K. Jao, *J. Amer. Chem. Soc.*, 90, 4081 (1968).
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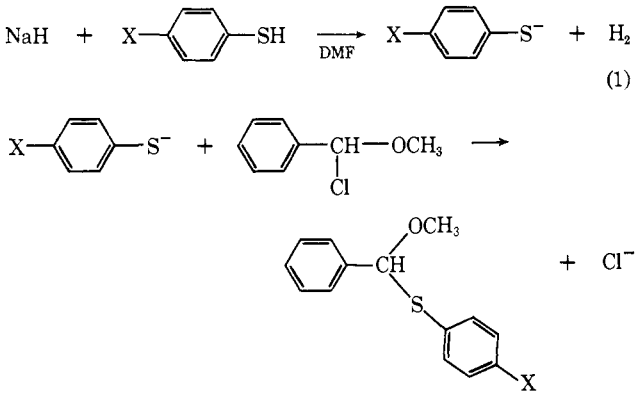
recently reported that the hydrolysis of benzaldehyde methyl phenyl acetal is subject to general acid catalysis. We have, therefore, studied the hydrolysis of the exactly analogous benzaldehyde methyl S-(substituted phenyl) thioacetals, compounds having structures I–VI.

Experimental Section

Materials. The benzaldehyde methyl S-(substituted phenyl) thioacetals were prepared by reacting the appropriate thiophenoxide ion with α-chlorobenzyl methyl ether as in eq 1. α-Chlorobenzyl



(1)

methyl ether was prepared by the action of thionyl chloride on benzaldehyde dimethyl acetal[7] and boiled at 68–70° (1.0 mm). The procedure for preparation of the thioacetals is as follows. The appropriate thiophenol (0.05 mol) in dry DMF (10 ml) was added dropwise to a stirred suspension of sodium hydride (0.05 mol) in dry DMF (35 ml). When hydrogen ceased to be evolved, the solution was cooled to 0° and α-chlorobenzyl methyl ether (0.05 mol) was added. The mixture was diluted threefold with benzene and poured into dilute NaOH solution. The organic layer was separated, washed with dilute NaOH solution, washed with H_2O, and then dried over anhydrous sodium sulfate. The solvent was removed at reduced pressure, and the residue was distilled or crystallized from ethanol or chloroform.

I boiled at 152–154° (0.5 mm), $n^{25}D$ 1.5948. *Anal.* Calcd for $C_{15}H_{16}O_2S$: C, 69.20; H, 6.19; S, 12.32. Found: C, 69.19; H, 6.31; S, 11.96.

II boiled at 140–142° (0.5 mm), mp 30–32°. *Anal.* Calcd for $C_{15}H_{16}OS$: C, 73.73; H, 6.60; S, 13.12. Found: C, 73.58; H, 6.69; S, 12.72.

III boiled at 144–145° (1.8 mm), $n^{25}D$ 1.6193. *Anal.* Calcd for $C_{14}H_{14}OS$: C, 73.00; H, 6.13; S, 13.92. Found: C, 72.81; H, 6.40; S, 14.20.

IV boiled at 163–164° (1.4 mm), $n^{25}D$ 1.6042. *Anal.* Calcd for $C_{14}H_{13}ClOS$: C, 63.53; H, 4.95; Cl, 13.36; S, 12.12. Found: C, 63.35; H, 4.85; Cl, 13.52; S, 12.35.

V melted at 72–74°. *Anal.* Calcd for $C_{14}H_{13}NO_3S$: C, 61.07; H, 4.76; N, 5.09; S, 11.65. Found: C, 60.78; H, 4.88; N, 5.10; S, 11.64.

VI melted at 129–130°. *Anal.* Calcd for $C_{14}H_{12}N_2O_5S$: C, 52.49; H, 3.78; N, 8.75; S, 10.01. Found: C, 52.25; H, 4.02; N, 8.63; S, 9.76.

Dioxane was purified by the method of Fieser[8] and was stored frozen in brown bottles. Deuterium oxide (99.8%) was from Bio-Rad Co.

Kinetic Measurements. The rates of hydrolysis were measured on a Cary 15 spectrophotometer by following the appearance of benzaldehyde or in the case of VI, the appearance of 2,4-dinitrothiophenoxide ion. Temperature was maintained constant (±0.05°) by circulating water from a Precision Scientific Temptrol 154 water bath through a Thelma thermostated cell. Stock solutions of the thioacetals in dioxane were prepared. To initiate the reactions 20 μl was added with a Hamilton syringe to 1.4 ml of solution in the cuvette. Pseudo-first-order rate constants (k_{obsd}) were calculated as the slopes of plots of ln $((OD_\infty - OD_0)/(OD_\infty - OD_t))$ *vs.* time by a rigorous least-squares procedure on an IBM-360-40 computer.

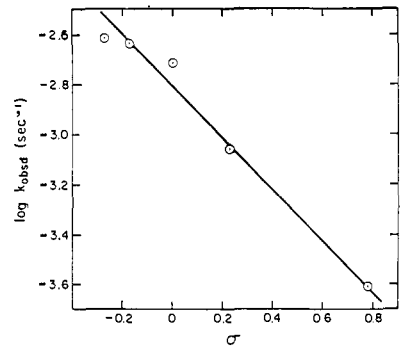


Figure 1. Plot of log k_{obsd} for hydrolysis of benzaldehyde methyl S-(4-substituted phenyl) thioacetals in 20% dioxane–H_2O with 0.1 *M* HCl at 30° *vs.* σ, the Hammett substituent constant.

In isopropyl alcohol–HCl solutions (99.4% isopropyl alcohol, 0.1 *M* HCl) the liberation of thiophenol was followed by reaction with an alkaline solution of 5,5′-dithiobis(2-nitrobenzoic acid) (VII).[9] A solution (100 ml) containing 10^{-3} *M* VII in isopropyl alcohol–0.1 *M* HCl, was equilibrated in a constant-temperature bath at 30.0°. After 30 min, 2.5 μl of the appropriate thioacetal was injected into the solution which was then vigorously mixed. A 2-ml sample of solution was withdrawn at appropriate time intervals and quenched and developed with 1 ml of 10% aqueous ammonia solution. The absorbance of the anion of 2-nitro-5-thiolbenzoic acid was measured at 412 mμ.

Rate constants were also determined by measuring the rate of liberation of methanol by glpc analysis. The isopropyl alcohol–0.1 *M* HCl solution (10 ml) containing the internal standard (6 μl of ethanol) was allowed to equilibrate in a constant-temperature bath at 30.0°. After 30 min, the thioacetal (100 μl) was injected into the solution, and the solution was then vigorously mixed. Samples (0.1 ml) were quenched with concentrated aqueous ammonia solution (0.05 ml), and 1 μl was injected into a Varian Aerograph 200 gas–liquid partition chromatograph, equipped with dual FID detectors and a 1-m Porapak Q column at 120°. Flow rates (cc/min) were hydrogen 25; nitrogen 25; and air 250. Relative retention times were methanol 1.2; ethanol 1.8; and isopropyl alcohol 3.2. The observed first-order rate constants were calculated from least-squares plots of ln $((H_{CH_3OH}/H_{EtOH})_\infty - (H_{CH_3OH}/H_{EtOH})_t)$ *vs.* time.

Results

In Table I rate constants are given for hydrolysis of the benzaldehyde methyl S-(4-substituted phenyl) thioacetals in 20% dioxane–H_2O at 30° with 0.1 *M* HCl. In Figure 1 is shown a plot of log k_{obsd} *vs.* σ, the Hammett substituent constant.[10] The slope is −1.0 (r = 0.989). The rate constant for hydrolysis of III in 20% dioxane–D_2O is also given in Table I. The

Table I. Rate Constants for Hydrolysis of Benzaldehyde Methyl S-(4-Substituted Phenyl) Thioacetals in 20% Dioxane–H_2O at 30°, with 0.1 *M* HCl, μ = 0.1

Compd	4 Substituent	$k_{obsd} \times 10^3$, sec^{-1}	$k_H \times 10^2$, l. mol^{-1} sec^{-1}
I	OCH_3	2.42	2.42
II	CH_3	2.32	2.32
III	H	1.92	1.92
IV	Cl	0.876	0.876
V	NO_2	0.263	0.203
III (D_2O)[a]	H	3.41	2.89
V (D_2O)[a]	NO_2	0.38	

[a] 0.118 *M* DCl in D_2O.

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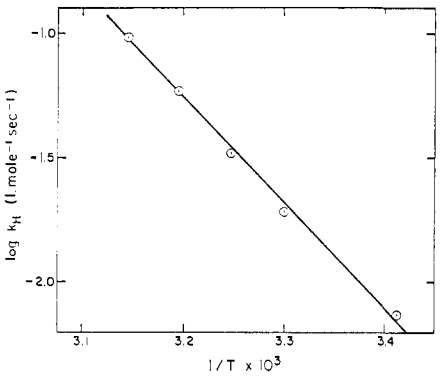


Figure 2. Plot of log k_H for hydrolysis of benzaldehyde methyl S-phenyl thioacetal in 20% dioxane-H_2O *vs.* $1/T$°K.

reaction is much faster in solvent containing D_2O than H_2O, the ratio k_D/k_H being 1.51.

Rate constants were also determined for solvolysis of II and IV in isopropyl alcohol–0.1 *M* HCl at 30° by (a) observing the appearance of thiophenol spectrophotometrically, and (b) by observing the appearance of methanol with glpc analysis. These constants were for II; $k_{spect} = 6.9 \times 10^{-4}$ sec^{-1} and $k_{glpc} = 7.3 \times 10^{-4}$ sec^{-1}; while in the case of IV, $k_{spect} = 1.4 \times 10^{-4}$ sec^{-1} and $k_{glpc} = 1.7 \times 10^{-4}$ sec^{-1}.

The rate constants for hydrolysis of III and V in formic acid–formate buffers (20% dioxane-H_2O) at 45° are given in Table II. Increasing the concentration of formic acid at constant pH has no effect on the rate constant. Thus, these compounds are not susceptible to general acid catalysis.

Table II. Rate Constants for Hydrolysis of Benzaldehyde Methyl S-Phenyl Thioacetal and Benzaldehyde Methyl S-(4-Nitrophenyl) Thioacetal in Formate Buffers in 20% Dioxane-H_2O at 45° and μ = 0.25 with KCl

Compd	HCOOH, *M*	pH	$k_{obsd} \times 10^4$, sec^{-1}	$10k_H$, l. mol^{-1} sec^{-1}
V[a]	0.75	3.40[a]	2.80	
	0.45	3.40	2.82	
	0.09	3.37	3.03	
III	0.75	3.40	0.383	0.963
	0.45	3.40	0.419	1.05
	0.09	3.37	0.436	1.02

[a] The hydrolysis of V is almost pH independent at this pH (at 30°, $k_0 = 6 \times 10^{-5}$ sec^{-1}).

Rate constants for hydrolysis of III in 20% dioxane-H_2O (0.1 *M* HCl) at a series of temperatures (±0.05°) are given in Table III. A plot of log k_H *vs.* $1/T$°K is presented in Figure 2. The value of ΔH^* is 18.8 ± 0.3 kcal/mol, while ΔS^* has the value −4.8 ± 0.9 eu.

Table III. Rate Constants for Hydrolysis of Benzaldehyde Methyl S-Phenyl Thioacetal in 20% Dioxane-H_2O with 0.1 *M* HCl at Various Temperatures, μ = 0.1

Temp, °C	$k_{obsd} \times 10^4$, sec^{-1}	$k_H \times 10^3$, l. mol^{-1} sec^{-1}
20	7.35	7.35
30	19.2	19.2
35	32.8	32.8
40	58.8	58.8
45	96.3	96.3

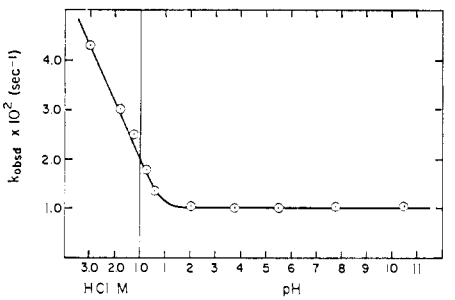


Figure 3. Plot of k_{obsd} for hydrolysis of benzaldehyde methyl S-(2,4-dinitrophenyl) thioacetal in 20% dioxane-H_2O at 30° *vs.* pH or HCl concentration.

The errors in ΔH^* and ΔS^* were calculated from the standard error of a plot of ln k_{obsd} *vs.* $1/T$.

In Table IV are given rate constants for hydrolysis of the 2,4-dinitrophenyl derivative VI at various pH values. A plot of k_{obsd} *vs.* pH or HCl concentration is shown in Figure 3. The reaction is independent of acid concentration from 0.1 *M* NaOH to 0.05 *M* HCl. At acid concentrations greater than 0.05 *M* the rate increases with increasing acidity due to hydronium ion catalysis. The pH-independent reaction proceeds at nearly the same rate in 20% dioxane-D_2O as 20% dioxane-H_2O, the ratio k_{D_2O}/k_{H_2O} being 0.90.

Table IV. Rate Constants for Hydrolysis of Benzaldehyde Methyl S-(2,4-Dinitrophenyl) Thioacetal in 20% Dioxane-H_2O at 30°

Buffer	pH	mμ[a]	$k_{obsd} \times 10^2$, sec^{-1}
0.1 *M* NaOH[b]		414.6	1.05
Carbonate[b]	10.48	414.6	1.06
Borate (D_2O)[b]	10.33 (pD)	414.6	0.957
Tris[b]	7.75	414.6	1.06
Acetate[b]	5.51	414.6	1.02
Formate[b]	3.71	414.6	1.11
0.01 *M* HCl[b]		252	1.07
0.05 *M* HCl[b]		252	1.03
0.3 *M* HCl		252	1.37
0.6 *M* HCl		252	1.80
1.2 *M* HCl		252	2.52
1.8 *M* HCl		252	3.01
3.0 *M* HCl		252	4.29

[a] Wavelength at which the reaction was followed. [b] μ = 0.1.

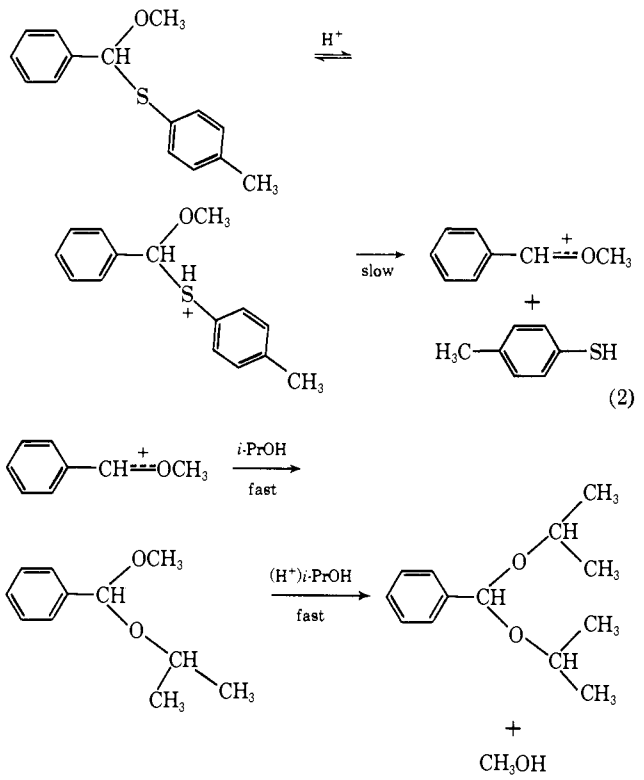
Discussion

General acid catalysis cannot be observed in the hydrolysis of 2-(substituted phenyl)-1,3-oxathiolanes.[4,5] The most likely mechanism for the hydronium ion catalyzed reaction involves preequilibrium protonation followed by a unimolecular, rate-determining ring cleavage step.[4] Thus, there is considerable ionic character in the transition state as shown by the highly negative value of ρ and the positive deviation produced by the *p*-methoxy substituent in the plot of the logarithms of the rate constants *vs.* σ, the Hammett substituent constant. When 50% dioxane-H_2O is the solvent a reasonable correlation with σ^+ is obtained. Also, there is a linear correlation between the logarithms of the rate constants and H_0, the Hammett acidity function, and the reaction is much faster in D_2O than H_2O. It was considered that in the reaction

sulfur was protonated with a subsequent carbon–sulfur bond-breaking step.[4] An adjoining oxygen would, of course, stabilize the intermediate carbonium ion much better than would sulfur,[11] and the direction of ring opening in similar reactions is governed by carbonium ion stability.[12] The alternative possibility in which oxygen is protonated followed by C–O bond breaking was thought to be less likely but was not rigorously excluded.

There is considerably less ambiguity in the position of bond cleavage with the present series of compounds. Thus, the ρ value of -1.0 is very similar to that observed in the hydrolysis of 2-(substituted phenoxy)tetrahydropyrans in 50% dioxane–H_2O (-0.9) and in the hydrolysis of substituted phenyl β-D glycosides[13,14] (-0.66 and -0.48), where the phenyl group is undoubtedly the leaving group. Electronic effects should be fairly similar if with the thioacetals it is the C–S bond that is breaking in the transition state. The fast pH-independent hydrolysis of the dinitrophenyl derivative VI shows clearly that C–S bond breaking is occurring with that compound since such a reaction can only be explained on the basis of the excellence of the 2,4-dinitrothiophenoxide ion leaving group.

The very similar first-order rate constants obtained for liberation of methanol and for liberation of the appropriate thiophenol in isopropyl alcohol shows conclusively that it is the C–S bond that is initially breaking. The rate-determining step in the sequence must be cleavage of the C–S bond with ultimate formation of benzaldehyde isopropyl methyl acetal which would solvolyze rapidly. If the C–O bond was broken preferentially then the solvolysis product would still be a thioacetal, and the appearance of thiophenol would therefore be quite slow in comparison to methanol since thioacetals are much less reactive than analogous acetals.



(2)

The D_2O solvent isotope effect ($k_D/k_H = 1.93$) observed in hydrolysis of 2-(*p*-methoxyphenyl)-1,3-oxathiolane[4] and the ratio of 1.51 in the hydrolysis of III with the present series are considerably less than generally obtained in A1 acetal hydrolysis reactions where ratios from 2.7 to 3.0 are normally seen.[15,16] These low solvent isotope effects would perhaps be in accord with a mechanism involving partially rate-determining protonation by hydronium ion, but this is not likely in view of the lack of general acid catalysis and the large amount of carbonium ion character in the transition state in the case of the oxathiolanes.[4] Thus, with both types of compounds proton transfer must be essentially complete. The smaller solvent isotope effects are probably reflecting the differences arising from protonation of sulfur rather than oxygen which have been previously observed.[17] It is of interest in this regard that for hydrolysis of the dianion of S-(2-carboxyphenyl) phosphorothioate, where proton transfer to sulfur must be nearly complete in the transition state in view of the pK_a of the leaving group, $k_{H_2O}/k_{D_2O} = 1.2$,[18] whereas a ratio of about unity (0.9–1.0) is usually seen in the hydrolysis of oxygen phosphate esters probably proceeding through zwitterion intermediates.[19–21] Thus, it can be calculated that the expected lowering of the k_D/k_H ratio due to protonation of sulfur rather than oxygen is 20–30%, giving a value in fair accord with the solvent isotope effects observed in thioacetal hydrolysis.

The ΔS^* of -4.8 eu for hydrolysis of III is also in accord with an A1 mechanism. 2-Phenyl-1,3-oxathiolane had a ΔS^* considerably more negative (-13.2 eu).[4] This is probably due to the cyclic nature of the oxathiolanes. Similarly, the A1 hydrolysis of 1,3-dioxolanes gives ΔS^* values 8–10 eu more negative than for benzaldehyde diethyl acetals.[15,16] Several explanations for this are possible,[15,22] and probably apply also to the differences in ΔS^* for the cyclic oxathiolane and the noncyclic III. The evidence then points to an A1 mechanism for hydrolysis of the benzaldehyde methyl S-phenyl thioacetals with C–S bond breaking to give the most highly stabilized carbonium ion (eq 3).

The ΔS^* and D_2O solvent isotope effect are also in accord with an A2 mechanism in which water attacks the protonated thioacetal. Such a mechanism was, however, ruled out in oxathiolane hydrolysis since substitution of a methyl group at the reaction center enhances the rate of the reaction. The acid-catalyzed hydrolysis of thioglycosides has also been considered

(11) For example, chloromethylethyl ether hydrolyzes 1600 times faster than chloromethylethyl sulfide in aqueous dioxane: H. Bohme, H. Fischer, and R. Frank, *Ann.*, **563**, 54 (1949); H. Bohme, *Chem. Ber.*, **74**, 248 (1941).
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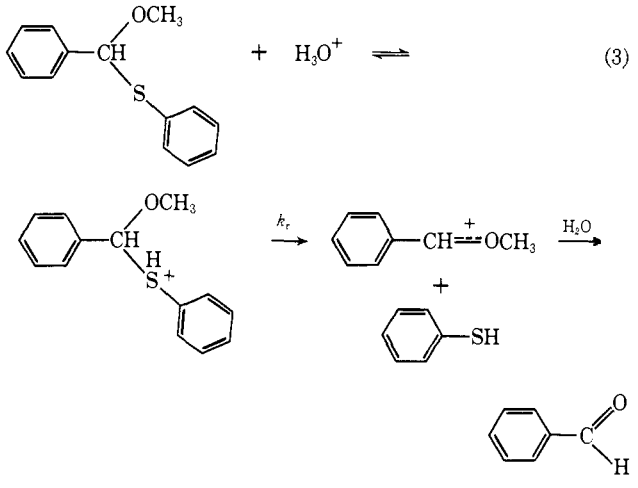
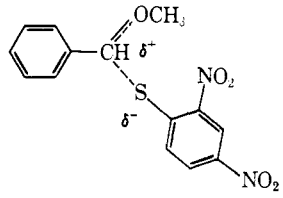


(3)

to be an A1 process.[23] Therefore, even with compounds giving rise to a relatively unstable glycosyl carbonium ion, where an A2 mechanism would be more likely, there is no evidence for that type of mechanism.

It is of great interest that general acid catalysis cannot be detected in the hydrolysis of the benzaldehyde methyl S-phenyl thioacetals since pronounced general acid catalysis is seen in the hydrolysis of the exactly analogous oxygen acetals.[6] The general acid catalysis of the hydrolysis of 2-(substituted phenoxy)tetrahydropyrans with a strongly electron-withdrawing substituent in the leaving group is due to reduced basicity and increased ease of C–O bond breaking with those compounds in comparison to normal acetals.[3] The second-order rate constants for formic acid catalysis increase as electron withdrawal in the leaving group increases ($\rho = +0.9$), in contrast to the negative ρ of -0.9 for hydronium ion catalysis.[3,24] Therefore, bond breaking is of considerably greater importance when a weak acid is the catalyst. With 2-(*p*-nitrophenoxy)tetrahydropyran the reaction at pH values greater than 4 is pH independent,[3,24] the facility of this reaction being brought about by the excellent leaving group. Consequently, although reduction in basicity is certainly important, the predominant structural feature in giving rise to general acid catalysis with those compounds is ease of C–O bond breaking. Pronounced general acid catalysis and a fast pH-independent reaction is also observed in the hydrolysis of tropone diethyl ketal.[25] In that case the leaving group is poor, but bond breaking has been made very easy by the great stability of the carbonium ion intermediate. Accordingly, with the thioacetals, even though basicity has been greatly reduced, general acid catalysis is not observed since bond breaking has not been facilitated to a great enough extent. It would be expected that carbon–sulfur bond breaking would actually be more difficult than breaking an analogous C–O bond.[26] These considerations are seen most clearly with the *p*-nitrophenyl derivative V where in addition to the lowered basicity due to sulfur a further reduction is brought about by the electron-withdrawing substituent, and yet general acids are without effect. However, the D_2O solvent isotope effect is smaller in the case of V than with the unsubstituted derivative, k_D/k_H being 1.3, suggesting that V is perhaps a borderline case.

Introduction of a second nitro substituent into the leaving group as in VI produces a dramatic effect. Now, as seen in Figure 3, the hydrolysis reaction is pH independent from approximately pH 1.5 to 13. This behavior is, of course, similar to that seen with 2-(*p*-nitrophenoxy)tetrahydropyran[3] and tropone diethyl ketal,[25] and, as with those compounds, the D_2O solvent isotope effect is about unity. The pH-independent reaction is, therefore, most likely a unimolecular decomposition brought about, as in the previous examples, by the ease of bond breaking. In the case of VI, however, general acid catalysis can still not be



detected, although a careful search was made with chloroacetate buffers. This is undoubtedly due to the inability of such catalysis to compete with the rapid pH-independent reaction. Even hydronium ion catalysis does not become noticeable until a concentration of almost 0.3 *M* is reached. It is therefore not surprising that much weaker acids are without effect. It would be predicted, however, on the basis of these data that general acid catalysis would be observed with a thioacetal having a leaving group intermediate between *p*-nitrothiophenoxide and 2,4-dinitrothiophenoxide so that bond breaking would still be relatively easy, and therefore protonation by a weak acid could occur, but not so facile that the pH-independent reaction overwhelms catalysis.

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(25) E. Anderson and T. H. Fife, *ibid.*, 91, 7163 (1969).
(26) For example, hemithioacetals form more readily than do hemiacetals and are much more stable: E. Campaigne in "Organic Sulfur Compounds," N. Kharasch, Ed., Pergamon Press, New York, N. Y., 1961, p 134.