Kinetics and Mechanism of the Hydrolysis of Diethyl Thioacetals of Substituted Benzaldehydes in Aqueous Perchloric Acid

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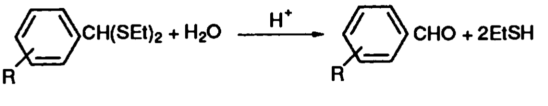
Substituent effects, activation parameters, acidity dependencies and solvent isotope effects suggest that the acid-catalysed hydrolysis of diethyl thioacetals of *meta*- and *para*-substituted benzaldehydes, and of acetophenone, proceed *via* an essentially A1 scheme. The extent of C–S bond cleavage in the transition state may become progressively greater on moving from the least to the most reactive acetals. The use of the excess acidity as a criterion of mechanism is briefly discussed. Activation enthalpies and entropies are significantly larger for the *meta*-substituted acetals. Our results are compared with existing data for the *O,O*- and *O,S*-analogues.

Little is known about the kinetics and mechanisms of the Brønsted acid-catalysed hydrolyses of *S,S*-acetals. There have been one or two isolated measurements with individual compounds, but no systematic study.[1] The hydrolyses are relatively very slow compared with those of the *O,O*- and *O,S*-analogues. We report now on the hydrolyses of the diethyl thioacetals of eight *meta*- and *para*-substituted benzaldehydes and of acetophenone, in aqueous perchloric acid [*e.g.* eqn. (1)].



(1)

Experimental

Materials.—The *S,S*-acetals were either previous samples,[2] or were prepared from ethanethiol and the corresponding benzaldehyde (Aldrich Chemical Co.) by the general method involving boron fluoride catalysis described previously.[3] They were purified by distillation at reduced pressure. Their structures were confirmed by NMR spectroscopy. All hydrolysed to give a >98% yield of the parent benzaldehyde. Perchloric acid was of AnalaR grade, and molarities of stock solutions were determined by iodate titration. Deuterium oxide was the 99.9 at. % Aldrich product, and dioxane the Aldrich spectroscopic grade.

Kinetics.—First-order rate constants, k_{obs}, for loss of *S,S*-acetal (*ca.* 5×10^{-5} mol dm^{-3}) in a series of aqueous perchloric acid solutions were determined at 25 °C. The acetal was added as a solution in dioxane, and reaction mixtures contained 1.0% (v/v) dioxane. The hydrolyses were monitored by observing the appearance of the aldehyde absorption. Good first-order behaviour was normally observed over 3–4 half-lives, and values of k_{obs} were reproducible to within ±5%. Reaction mixtures remained homogenous throughout. Activation parameters were obtained from rate measurements, at a fixed acid concentration, at three or more temperatures. Deuteriated perchloric acid solutions were prepared by adding the appropriate volume of 70% aqueous $HClO_4$ to deuterium oxide. Typical results, and the corresponding reaction conditions, are given in the tables and figures.

Tests[4] for build-up of significant concentrations of hemithioacetals in the reaction mixtures proved negative.

Results

(i) *Dependence of* k$_{obs}$ *on Acid Concentration.*—For each *S,S*-acetal k_{obs} increases more rapidly than does $[H_3O^+]$ ($=[HClO_4]_{stoich}$), especially when $[H_3O^+] > 0.5$ mol dm^{-3}. A typical plot is given in Fig. 1. At 25 °C, plots of ($\log k_{obs} - \log [H_3O^+]$) against the excess acidity, X,[5,6] are straight lines (Fig. 2) the slopes of which change fairly systematically with the reactivity of the acetal.

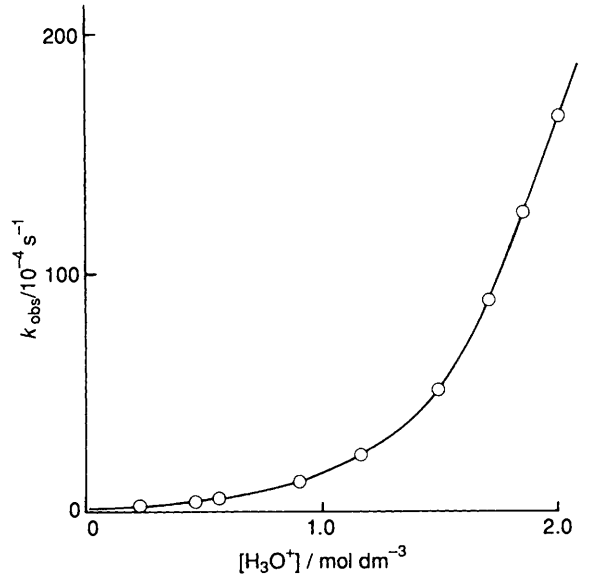


Fig. 1 Plot of k_{obs} against $[H_3O^+]$ for *p*-methylbenzaldehyde *S,S*-diethyl acetal at 25 °C

(ii) *Effects of Substituents on Acetal Reactivity.*—Extrapolation of the straight lines in Fig. 2 to $X = 0$ permits[6] an (approximate) comparison of the reactivities of the acetals in dilute acid solution. The derived second-order (catalytic) rate constants, k_{H^+}, at 25 °C are given in Table 1. They show that the least reactive of these open-chain *S,S*-acetals are the derivatives of *m*- and *p*-nitrobenzaldehydes, and the most reactive are the acetals of *p*-methoxybenzaldehyde and of acetophenone. The latter hydrolyse at convenient rates in dilute acid (< 1.0 mol dm^{-3}) whereas the former required 2.5–6.0 mol dm^{-3} acid. The overall spread of reactivities involves a factor of *ca.* 1000.

A Hammett plot of $\log k_{H^+}$ *vs.* σ is shown in Fig. 3; its best slope ρ is *ca.* −2.9. This slope is similar to that (−3.3) reported for the hydrolyses of the *O,O*-analogues in aqueous solution.[7] The points for the *m*- and *p*-nitro, and for the *p*-methoxy derivatives fall somewhat off the Hammett plot in Fig. 3, but the

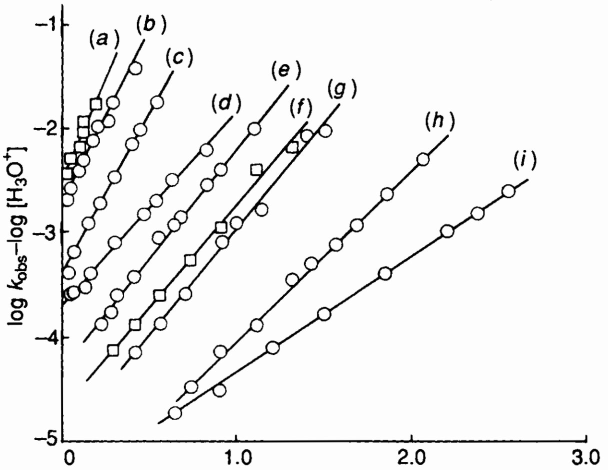


Fig. 2 Plots of log k_{H^+} − log [H_3O^+] against the excess acidity, X. T = 25.0 °C. (a) Acetophenone, (b) = p-MeO, (c) = p-Me, (d) = H, (e) = p-Cl, (f) = m-Cl, (g) = m-CF_3; (h) = p-NO_2; (i) = m-NO_2 derivative of benzaldehyde S,S-diethyl acetal

Table 1 Derived parameters for hydrolyses of diethylthioacetals at 25 °C in aqueous perchloric acid containing 1% (v/v) dioxane[a]

Acetal	$k_{H^+}/10^{-5}$ dm^3 mol^{-1} s^{-1} [b]	$m^*m^‡$ [c]	$m^‡$
$RC_6H_4CH(SEt)_2$			
R = p-NO_2	0.25	1.60	1.2
m-NO_2	0.37	1.07	0.82
m-CF_3	0.80	2.17	1.7
m-Cl	1.23	2.16	1.7
p-Cl	5.20	2.19	1.7
p-H	19.1	1.94	1.5
p-CH_3	37.0	3.10	2.4
p-OCH_3	195	3.35	2.6
Ph(Me)C(SEt)$_2$	260	3.96	3.1

[a] For m^* and $m^‡$ see text. [b] k_{H^+} = second-order rate constant in dilute acid (from intercepts of plots in Fig. 2). [c] $m^*m^‡$ from slopes of plots in Fig. 2

fit is significantly improved (except for the point for R = H) by using a plot[8] against σ^+ (Fig. 3, ρ^+ *ca.* −1.9). A Hammett plot of four points for some O,S-analogues[9] (p-H, p-OMe, p-NMe_2, p-N^+HMe_2) gives ρ = *ca.* −2.3, but the rate constants calculated for the p-NMe_2 and p-OMe compounds involve assumptions.

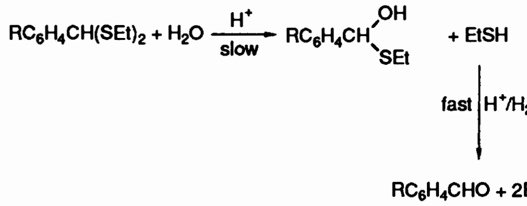
Our k_{H^+} values estimated for dilute acid solutions at 25 °C (Table 1) can be compared with those reported for the O,O- and O,S-analogues under similar conditions.[7,9,10] We find the (approximate) relative reactivity ratios O,O- : O,S- : S,S- to be 1–8 × 10^5:3–4 × 10^3:1. These new ratios are similar to those exhibited by the few existing data,[1] and so confirm them; most existing comparisons refer to cyclic rather than to open-chain acetals.

(iii) *Activation Parameters*.—Our results are in Table 2. There can be seen to be a gradual increase in $\Delta H^‡$ for the *para*-derivatives of the benzaldehyde S,S-acetals from *ca.* 88 to 92 kJ mol^{-1} on moving from strongly electron-releasing to strongly electron-withdrawing substituents, with the p-Cl derivative out of line. As $\Delta H^‡$ increases there is an accompanying decrease in $\Delta S^‡$ from *ca.* −1.5 J mol^{-1} K^{-1} for the p-methoxy derivative to *ca.* −44 J mol^{-1} K^{-1} for the p-nitro acetal. The most striking feature of the results is that the *meta*-derivatives all exhibit much larger values of $\Delta H^‡$ and more positive $\Delta S^‡$ values than might have been expected from the results for the *para*-derivatives. For the O,O-analogues of the *para*-derivatives in 50% dioxane–water[11] $\Delta H^‡$ lies in the range 59–84 kJ mol^{-1}, with $\Delta S^‡$ = *ca.* 4 J mol^{-1} K^{-1}. Activation parameters do not appear to be available for the *meta*-substituted O,O-acetals.

(iv) *Solvent Isotope Effects*.—The details of these experiments are in Table 3. The most reactive compounds have k^D/k^H = *ca.* 1.3 (at [L_3O^+] = *ca.* 0.05 mol dm^{-3}) whereas the least reactive may have k^D/k^H = *ca.* 1.5 (at [L_3O^+] = 2.34 mol dm^{-3}).

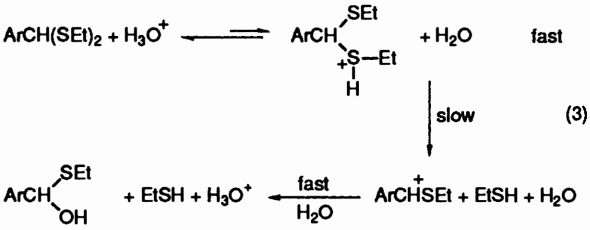
Discussion

Since we find no evidence for the build-up of hemi-thioacetals in the reaction mixtures (see Experimental), and becuase O,S-acetals are appreciably more reactive towards acid-catalysed hydrolysis than are the corresponding S,S-acetals, it seems reasonable to assume, as we shall,[12] that the reactions we have followed correspond to the first step of eqn. (2). Studies



(2)

of this step for open-chain benzaldehyde O,O-acetals show[7] that it can display general-acid catalysis, and its mechanism is believed to range from the usual[13] A1 type [eqn. (3)], for acetals

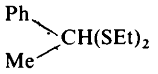


(3)

not showing general-acid catalysis, to variations[7,14] on the A-S_E2 type for those acetals that do exhibit general acid catalysis to some degree. In short there probably exists a range of transition states. General-acid catalysis has to date appeared to be absent from the hydrolyses of all thioacetals[1,15] and open-chain O,S-acetals have, for want of evidence to the contrary, been assumed normally to react *via* the A1 mechanism.[9] We have not tested directly for general-acid catalysis with our present, mostly rather unreactive, S,S-acetals. The measurements we have made, however, as the discussion will show, perhaps suggest that some progressive variation exists in the mechanism of hydrolysis of these compounds on moving from the most to the least reactive.

The excess acidity concept has proved useful in the hands of Cox and Yates,[6,16] for identifying (or suggesting) mechanisms of acid catalysis in strongly acidic media. Most applications so far refer to sulphuric acid solutions. The essence of the method is that (for substrates that are only slightly protonated by the medium) a plot, covering a reasonable acidity range, of log k_{obs} − log [H_3O^+] against X (the excess acidity function[5]) should be a curve for an A2 mechanism, but rectilinear for an A1 or A-S_E2 mechanism. The slopes of such plots have been found, or are suggested to be, significant in identifying mechanism. In the theory underlying the method,[6] the slope is $m^*m^‡$, where m^* is a parameter characteristic of the particular

Table 2 Effects of temperature

Acetal	T/°C	$k_{\mathrm{H}^+}/10^{-5}$ dm^3 mol^{-1} s^{-1} [a]	$\Delta H^‡$/kJ mol^{-1} [b]	$\Delta S^‡$/J K^{-1} mol^{-1} [b]
$RC_6H_4CH(SEt)_2$				
R = p-NO$_2$	25.0	0.25	92 ± 4	−44 ± 3
	30.0	0.44		
	35.0	0.78		
	40.0	1.48		
	45.0	2.59		
m-NO$_2$	25.0	0.37	102 ± 5	−7 ± 0.5
	35.0	1.50		
	45.0	5.31		
m-CF$_3$	25.0	0.80	112 ± 7	32 ± 4
	32.2	1.70		
	35.0	3.10		
	45.2	12.6		
m-Cl	25.9	1.40	115 ± 5	48 ± 3
	32.0	4.00		
	37.8	9.10		
	42.2	15.0		
p-Cl	25.0	5.20	96 ± 3	−6 ± 0.5
	30.0	10.6		
	35.0	19.0		
	40.0	36.3		
	45.0	61.8		
p-H	25.0	19.1	90 ± 3	−13 ± 0.5
	35.0	71.1		
	40.0	122		
	45.0	216		
p-CH$_3$	25.0	37.0	89 ± 3	−11 ± 1
	35.0	141		
	40.0	255		
	45.0	360		
p-OCH$_3$	25.0	195	88 ± 3	−1.5 ± 0.5
	35.0	680		
	40.0	1320		
	45.0	2050		
	25.0	260	98 ± 5	42 ± 4
	32.0	745		
	39.0	1929		
	43.0	2803		

[a] k_{H^+} = second-order rate constant. For $T > 25.0$ °C k_{H^+} was calculated from k_{obs} assuming that X, and the dependence of k_{obs} upon X, are the same as at 25.0 °C. The error introduced by these assumptions is uncertain although it is likely to be small.[5,21] [b] The error limits given refer to the reproducibility of the experimental results.

Table 3 Solvent isotope effects measured at 25 °C in aqueous perchloric acid containing 1% dioxane

Acetal	$[L_3O^+]$/dm^3 mol^{-1} [a]	$k^{\mathrm{H}}_{\mathrm{obs}}/10^{-4}$ s^{-1}	$k^{\mathrm{D}}_{\mathrm{obs}}/10^{-4}$ s^{-1}	at. %D	$k^{\mathrm{D}}/k^{\mathrm{H}}$
p-MeOC$_6$H$_4$CH(SEt)$_2$	0.057	1.15	1.49	99.4	1.30 ± 0.10
Ph(Me)CH(SEt)$_2$	0.047	1.22	1.62	99.4	1.33 ± 0.10
m-NO$_2$C$_6$H$_4$CH(SEt)$_2$	2.34	0.42	0.60	87.1	1.43 ± 0.15[c]
p-NO$_2$C$_6$H$_4$CH(SEt)$_2$	2.34	0.32	0.42	87.1	1.31 ± 0.10[c]

[a] L = H or D. [b] $k^{\mathrm{H}}_{\mathrm{obs}}$ ($k^{\mathrm{D}}_{\mathrm{obs}}$) = observed first-order rate constant in the light (or heavy) medium (average of two determinations). [c] Had $k^{\mathrm{D}}/k^{\mathrm{H}}$ for the nitrobenzaldehyde acetals been measured using a heavy medium containing 100 at. % D their value would probably have been *ca.* 14% larger.[22]

substrate (to which the proton is being transferred), and $m^‡$ a parameter related to the type of transition state involved. Average values of m^* for different classes of basic substrate (O-, N-, S-bases, *etc.*) are available;[5,6] these average values are quite similar for sulphuric and perchloric acid solutions, but the extent to which m^* will vary within a class of bases is rather uncertain.[17] Normally m^* will not be known for a particular substrate, and then division by the average m^* value will be necessary to obtain $m^‡$ from the slopes of plots such as those in Fig. 2. If $m^‡ > 1$ an A1 mechanism is indicated, whereas if $m^‡ < 1$ A-S$_E$2 is suggested (by tests with reactions of supposedly known mechanisms[6]). For S-bases m^* = *ca.* 1.3.

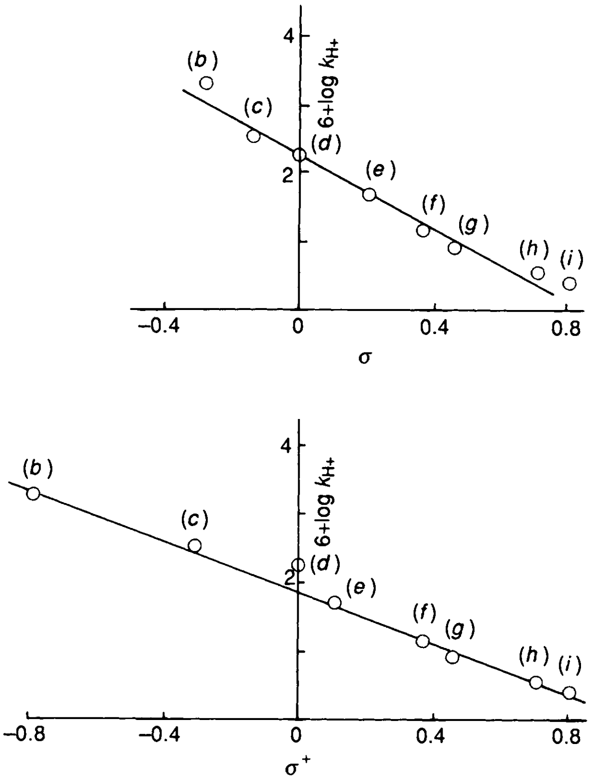


Fig. 3 Plots of log k_{H^+} against σ and σ^+. Values of σ and σ^+ from O. Exner, *Correlation Analysis of Chemical Data*, Plenum Press, London, 1988. Letter code as for Fig. 2.

For the present sytems the slopes $m^*m^\ddagger$ vary fairly systematically from high values (>3) for reactive acetals to values near unity for the least reactive (Table 1). If we can assume that m^* is roughly constant for all the *S,S*-acetals, then $m^\ddagger$ must vary in a parallel way (Table 1). Previous work with other systems suggests that m^* is unlikely to vary as much as the observed slopes, so the derived $m^\ddagger$ values perhaps point to some change in detailed mechanism on passing along the reactivity series. This seems reasonable. Most of our $m^\ddagger$ values are >1, so that our results using the excess acidity approach indicate a predominantly A1 type of mechanism for the various hydrolyses, with perhaps some decrease in A1 character on moving from the most to the least reactive acetals.

The activation parameters (Table 2) are also compatible with an A1 mechanism for all the acetals. $\Delta S^\ddagger$ is nowhere particularly negative, and sometimes positive, a situation characteristic of acid-catalysed reactions with unimolecular rate-determining steps.[18] The high enthalpies of activation, and relatively positive $\Delta S^\ddagger$ values, found for the *meta*-substituted compounds, and for the acetophenone acetal, suggest to us less solvation of the transition state for the slow step, and a generally looser transition state, with more separation of the cleaving fragments, in these cases. For the *para*-substituted compounds we tentatively suggest that our results are compatible with some progression towards transition states with a loose structure (more C–S cleavage), and more strongly bound protons, on moving from the less to the more reactive acetals. These suggestions are rather different to conclusions reached for the *O,O*-analogues,[7–12] although there the involvement of the A-S$_E$2 mechanism complicates the picture. We do not envisage A-S$_E$2 schemes for the most reactive *S,S*-acetals. Nor do we find any evidence for A2 mechanisms.

That the plot against σ^+ is a little more successful than that against σ (Fig. 3) supports an essentially A1 mechanism,[13] and suggests that these *S,S*-acetal hydrolyses as a whole have transition states with more carbenium ion character than do those of the *O,O*-derivatives; more indeed than those of most of the acid-catalysed acetal hydrolyses studied hitherto.[12]

The solvent deuterium isotope effects (Table 3), being >1, are certainly compatible[19] with a pre-equilibrium (A1) type of mechanism. Interpretation of the slightly larger values probable for the least reactive acetals (had they been obtained using 100 at. % D) is complicated by the known tendency of similar isotope effects to increase significantly with the concentration of the acid catalyst.[19] Values of k^D/k^H = *ca.* 1.3 have been obtained previously for the hydrolysis of an *O,S*-acetal for which initial *S*-protonation is probably involved.[20] Since pre-equilibrium mechanisms (A1 or A2) involving *O,O*-acetals normally[1,13] have $k^D/k^H > 2$, the solvent isotope effect may prove a convenient way of distinguishing between initial C–O or C–S cleavage in the acid-catalysed hydrolyses of *O,S*-acetals.[1]

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