Kinetics of the Silver Ion-promoted Hydrolysis of 2-Methyl-2-(substituted phenyl)-1,3-dithianes in 10% Dioxane–Water Mixtures. Implications for Cyclic Acetal Hydrolysis Catalysed by Hydrogen Ions

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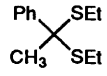
The hydrolysis of 1,3-dithianes derived from *para*-substituted acetophenones is promoted by silver ions. Kinetic study using a 10% (v/v) dioxane–water solvent shows that, when $[Ag^+] \gtrsim 0.2$ mol dm^{-3}, the *p*-NO_2, -Cl, -H and -Me derivatives hydrolyse *via* rapidly-formed 1 Ag^+:1 dithiane-complexes, but that the *p*-MeO derivative forms an unreactive 1:1-complex and hydrolyses *via* a 2 Ag^+:1 dithiane-complex. Comparison of the kinetic parameters with those available for analogous open-chain *S,S*-acetals reveals that cyclisation leads to a substantial ($>10^4$-fold) overall loss of reactivity and that this loss arises both from a lowering of acetal basicity towards Ag^+ and from a slower rate of hydrolysis of the 1:1-complex. The implications for hydrogen ion-catalysed hydrolyses of cyclic acetals are discussed, as are the reasons for the lower reactivity of the cyclic acetals.

Silver ions promote the hydrolysis of thioacetals in dilute aqueous solutions[1,2] [*e.g.*, reaction (1)]. The reactions of open-

$$RC_6H_4CH(SEt)_2 + 2\,Ag^+ + 3H_2O \longrightarrow RC_6H_4CHO + 2EtSAg + 2H_3O^+ \quad (1)$$

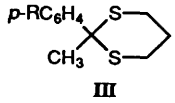
I

chain thioacetals including **I**, **II** and others,[1,3] proceed at



II

convenient rates for kinetic study at moderate silver ion concentrations and are very much faster than the corresponding hydrogen ion-catalysed hydrolyses in dilute aqueous acid.[1] Cyclic thioacetals, however, hydrolyse relatively very slowly and the silver ion-promoted hydrolysis of the cyclic analogues of **I** is inconveniently slow.[4] Up to now no cyclic *S,S*-acetal has been studied entirely satisfactorily from a kinetic viewpoint under silver ion-promotion and it is as yet impossible for any system to compare kinetic parameters available for an open-chain acetal with those for a cyclic analogue. Since acetal **II** was found[3] to be significantly more reactive than **I** (R = H) we considered that appropriate 2-methyl-2-(substituted phenyl)-1,3-dithianes (**III**) might prove to be sufficiently reactive for



III

a R = NO_2 **b** R = Cl **c** R = H **d** R = Me **e** R = MeO

convenient kinetic study. This is so, and we now report on the behaviour of the five acetals **IIIa–e** and show that it has general implications for the acid-catalysed hydrolysis of cyclic acetals.

$$III + 2\,Ag^+ + 3H_2O \longrightarrow RC_6H_4COCH_3 + AgS[CH_2]_3SAg + 2H_3O^+ \quad (2)$$

Experimental

The materials were available from previous work on the hydrogen ion-catalysed hydrolysis of the dithianes,[5] and from other studies on silver ion-promotion.[6] The kinetic methods were those used before.[2,3,6] All the hydrolyses led to an effectively quantitative yield of the acetophenone product. The reactions were followed, using an excess of silver ions, by observing the increase in absorbance of the acetophenone in the region 260–280 nm. Excellent first-order behaviour was found and the observed first-order rate constant, k_{obs}, was reproducible to within ±5% for all the dithianes. Each was studied over a range of silver ion concentrations at fixed pH and ionic strength and at four temperatures. The solvent was 10% (v/v) dioxane–water. Typical results and our concentration and other conditions, are in the Table and Figures. Hydrolysis was negligible in the absence of silver ions.[1]

Results and Discussion

In recent years we have studied the kinetics and mechanisms of the silver ion-promoted hydrolyses of a wide range of organo-sulfur compounds and a common mechanistic pattern has emerged.[6] For open-chain *S,S*-acetals such as **I** and **II** this mechanism can be written[2,3] as in eqns. (3)–(7).

$$RC_6H_4CH(SEt)_2 + Ag^+ \rightleftharpoons RC_6H_4CH(SEt)(SEt)(Ag^+) \quad \text{fast, } K_1 \quad (3)$$

I IV

$$IV + Ag^+ \rightleftharpoons RC_6H_4CH(SEt)(SEt)(Ag^+)(Ag^+) \quad \text{fast, } K_2 \quad (4)$$

V

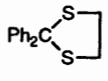
$$IV + (2H_2O) \longrightarrow RC_6H_4CH(SEt)(OH) + EtSAg + H_3O^+ \quad \text{slow, } k_1 \quad (5)$$

VI

$$V + (2H_2O) \longrightarrow VI + EtSAg_2^+ + H_3O^+ \quad \text{slow, } k_2 \quad (6)$$

$$VI \xrightarrow{Ag^+/H_2O} RC_6H_4CHO + EtSAg + H_3O^+ \quad \text{fast} \quad (7)$$

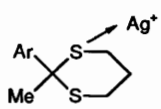
For open-chain thioacetals, as for most organo-sulfur compounds studied,[6] both 1:1- and 2:1-Ag^+–substrate complexes are formed rapidly (to extents dependent upon the substrate, silver ion concentration, *etc.*) and both lead *via* slow steps to the hydrolysis product. With *S*,*S*-acetals, as for other substrates containing two S atoms, more than one type of 2:1-complex can exist, but the most reactive complex is considered to be that with both Ag^+ ions on the same *S*-atom.[1,7] Normally little 2:1-complex is formed and only the product k_2K_2 (and not independent k_2 and K_2 values) is accessible from the kinetic analysis. However, independent values of k_1 and K_1 have been determined for a number of systems, including substrates such as **I** and **II**. In certain systems and concentration ranges just one complex dominates reaction. Thus for acetals **I** contributions from the 2:1-complexes are negligible[2,3] when $[Ag^+] \lesssim 0.025$ mol dm^{-3}, whereas for **VII** the extensively-formed 1:1-complex



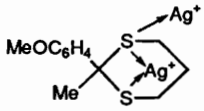
VII

is unreactive and hydrolysis proceeds *via* a small quantity of the 2:1-complex(es).[7] Acetals **I** are the only thioacetals, prior to the present substrates **III**, for which substituent effects on K_1 and k_1 have been measured.[1,2]

We find that the behaviour of **III** fits into the pattern described above. At all the silver ion concentrations and temperatures studied the results (*e.g.* Fig. 1) for **IIIa–d** are compatible with the significant involvement of just a 1:1-Ag^+–acetal complex (*e.g.* **VIII**). For this situation the corresponding



VIII



IX

rate equation derived from the general mechanism (3)–(7), with **III** replacing **I**, is eqn. (8). For acetals **IIIb–d** values of k_1 and

$$k_{obs} = k_1K_1[Ag^+]/(1 + K_1[Ag^+]) \quad (8)$$

or

$$\frac{1}{k_{obs}} = \frac{1}{k_1K_1[Ag^+]} + \frac{1}{k_1} \quad (9)$$

K_1 at the different temperatures can be obtained from the rectilinear plots of $1/k_{obs}$ against $1/[Ag^+]$, or of $[Ag^+]/k_{obs}$ against $[Ag^+]$ (*e.g.* Fig. 2). For the *p*-NO_2 derivative **IIIa**, K_1 is too small to produce significant curvature in plots of k_{obs} against $[Ag^+]$ (*e.g.* Fig. 1) so that k_1 and K_1 cannot be separated for this acetal. Our derived values of k_1 and K_1 (or k_1K_1) are in Table 1.

Acetal **IIIe** behaves differently from **IIIa–d**, but also fits into Scheme (3)–(7). For this acetal K_1 is much larger, but the kinetic behaviour shows that the 1:1-complex is relatively unreactive and that hydrolysis proceeds *via* a small amount of 2:1-complex. The rate equation corresponding to this situation is (10). We find that when $[Ag^+] \lesssim 0.2$ mol dm^{-3} eqn. (10) simplifies to (11) and plots of $[Ag^+]^2/k_{obs}$ against $[Ag^+]$ yield

$$k_{obs} = k_2K_1K_2[Ag^+]^2/(1 + K_1[Ag^+] + K_1K_2[Ag^+]^2) \quad (10)$$

$$k_{obs} = k_2K_1K_2[Ag^+]^2/(1 + K_1[Ag^+]) \quad (11)$$

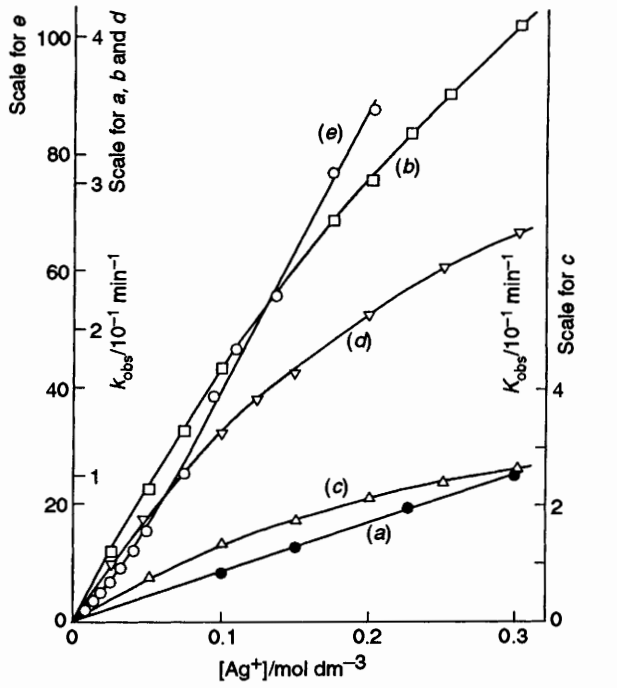


Fig. 1 Examples of dependence of k_{obs} on $[Ag^+]$: (*a*) *p*-NO_2 at 55.7 °C; (*b*) *p*-Cl at 45.1 °C; (*c*) *p*-H at 35.1 °C; (*d*) *p*-Me at 25.3 °C; (*e*) *p*-MeO at 54.7 °C

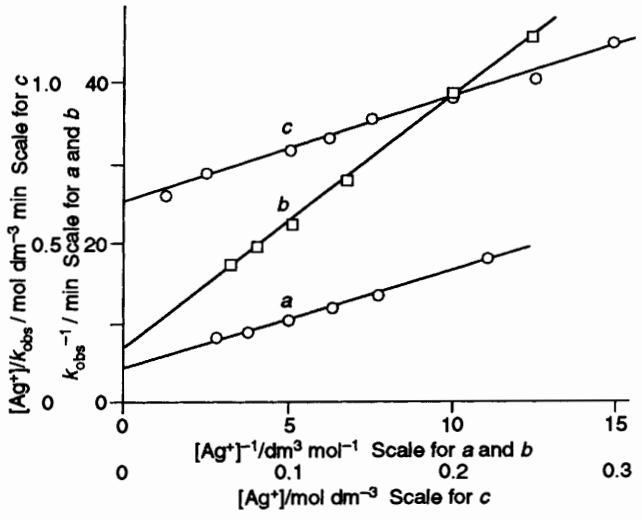


Fig. 2 Typical plots of eqn. (9): (*a*) *p*-H at 26.0 °C; (*b*) *p*-Cl at 25.0 °C; (*c*) *p*-Me at 25.3 °C

or

$$\frac{[Ag^+]^2}{k_{obs}} = \frac{1}{k_2K_1K_2} + \frac{[Ag^+]}{k_2K_2} \quad (12)$$

values of K_1 and k_2K_2 (*e.g.* Fig. 3). Such plots would not be rectilinear at low $[Ag^+]$ values were the 1:1-complex contributing importantly to decomposition. Over much of the concentration range $[Ag^+]$ = 0–0.2 mol dm^{-3} the results fit the equation k_{obs} = const. $[Ag^+]$, showing that the 1:1-complex is effectively fully-formed (*i.e.* $K_1[Ag^+] \gg 1$) but this equilibrium makes itself felt at relatively low values of $[Ag^+]$ (*e.g.* Fig. 1). When $[Ag^+] \gtrsim 0.2$ mol dm^{-3} some deviation from eqn. (11) occurs, probably owing to the increasing importance of the term $K_1K_2[Ag^+]^2$ in (10). The deviations are too small for accurate values of K_2 to be determined, but calculations based on the full eqn. (10) indicate that K_2 = 0.3 ± 0.2 and 0.2 ± 0.15 dm^3 mol^{-1} at 25 and 45 °C, respectively. Our other derived constants for **IIIe** are in Table 1, which also contains some

Table 1 Derived constants and activation parameters[a]

R	T/°C	K_1	10^3k_1	$10^3K_1k_1$	$\Delta H_1°$	$\Delta S_1°$	$\Delta H_1^‡$	$\Delta S_1^‡$	K_2k_2
(i) Acetals **III**									
NO_2	25.0			0.4[b]					
	45.2			2.2	$(\Delta H_1° + \Delta H_1^‡)$		61		
	50.2			3.5	$(\Delta S_1° + \Delta S_1^‡)$		−81		
	55.7			5.2					
	60.8			8.0					
Cl	25.0	2.1	2.5		−33	−104	102	47	
	35.1	1.2	10						
	45.1	0.90	33						
	55.4	0.58	140						
H	26.0	4.3	3.2						
	35.1	2.8	9.7		−30	−90	88	1	
	44.9	2.1	32						
	54.6	1.4	76						
Me	25.3	2.4	11						
	35.3	1.9	30		−17	−49	78	−21	
	45.0	1.6	83						
	55.2	1.3	208						
MeO	25.1	98							0.084
	35.2	70			−24	−43			0.19 $(\Delta H_2° + \Delta H_2^‡)$ 60
	45.3	53							0.41 $(\Delta S_2° + \Delta S_2^‡)$ −65
	54.7	41							0.83
(ii) Acetals **II**									
H	25.0	1000	500						
(iii) Acetals **I**									
NO_2	25.0	1.5	3.0						
H	25.0	300	16						
Me	25.0	230	160		−41	−92	91	45	
MeO	25.0	160	3000		−26	−43	73	10	

[a] Units: k_1 and k_2/s^{-1}; K_1 and K_2/dm^3 mol^{-1}; ΔH/kJ mol^{-1}; ΔS/J K^{-1} mol^{-1}; T/°C. For all systems $[H_3O^+]$ = 0.05 mol dm^{-3}; ionic strength = 0.50 mol dm^{-3}; $[\text{acetal III}]_{initial}$; ~2 × 10^{-6}–2 × 10^{-5} mol dm^{-3}. Acetals **I** and **II** studied using 1% (v/v) dioxane–water as solvent,[2,3] acetals **III** in 10% dioxane–water. This change in solvent has been shown[4] to have a quite small effect on reactivity in metal ion-promoted hydrolyses. [b] Estimated from results at higher temperature. Errors in derived parameters normally ≲ ± 10%.

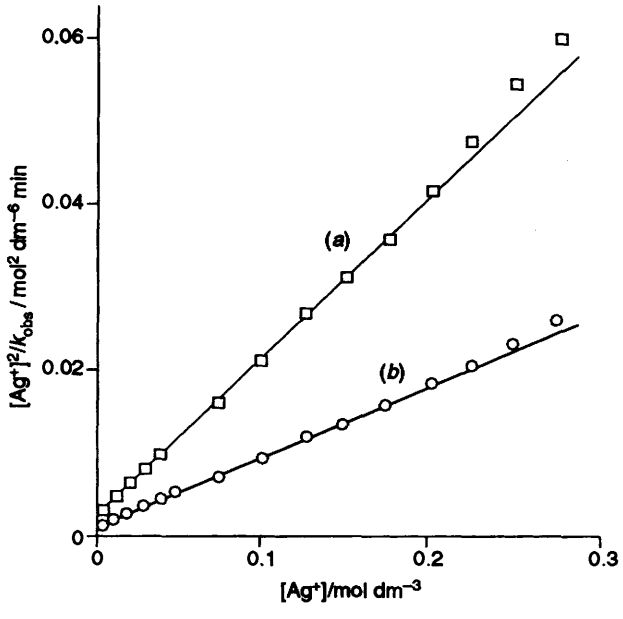


Fig. 3 Plots of eqn. (12) for **IIIe**: (*a*) 25.1; (*b*) 35.2 °C

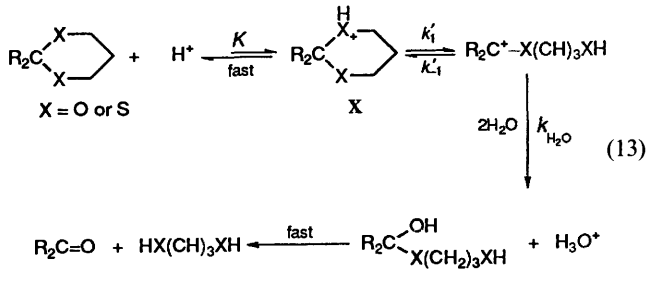
activation parameters for all the acetals and results[2,3] found for acetals **I** and **II** at 25 °C.

Table 1 shows that, apart from *p*-MeO, the substituents R in **III** produce a pattern of effects on K_1 and k_1 reminiscent of those found with the open-chain acetals **I** studied previously, although the effect of the NO_2 group is not as marked.[2,3] For both **I** and **III** electron-release has a similar but complex effect on K_1 despite the substantially smaller absolute values found for **III**. The two sets of results appear to be reflecting similar electronic effects and previously we tentatively suggested[2] that back-donation from, as well as electron-acceptance by, Ag^+ is important in determining K_1. The unexpectedly large value of K_1 found for the *p*-MeO derivative **IIIe** suggests that in this case the 1 : 1-complex is chelated (see **IX**) and therefore more stable. The results in Table 1 show that in general acetals **III** form 1 : 1-complexes much less easily than do **I** and **II**; $\Delta H°$ (the enthalpy of formation) appears to be less negative for **III**. We attribute this fall in basicity to the cyclisation. In contrast to the open-chain acetals, in 1,3-cyclic *S*,*S*-compounds[8] the relevant orbitals on the two S atoms have restricted orientations and it is possible that changes in the principal molecular configurations available can materially affect basicity. Our evidence suggests it, as do previous results for the mercury(II) and thallium(III) ion-promoted hydrolyses of similar cyclic *S*,*S*-acetals.[4] The soft basicity of these compounds is apparently more affected by the effect of cyclisation on mutual S-orbital orientation than by changes in electron-release by a *para*-substituent R. This is a stereoelectronic effect and it may be that such effects on acetal reactivity are more widespread than previously seemed likely.[9,10]

The exact comparison between similarly-substituted open-chain and cyclic thioacetals provided (Table 1) by the results for **II** and **IIIc** reveals (*i*) the substantially (≳10^4-fold) lower reactivity of the cyclic compound under the same conditions at low silver ion concentrations (*i.e.* when $k_{obs} \propto k_1K_1$) and (*ii*)

the fact that this lower reactivity arises from comparable reductions in both K_1 and k_1. The cyclic compound is not only less basic, its 1 : 1-complex is less readily hydrolysed. It is noteworthy that a similar (*ca.* 10^4–10^5-fold) difference in overall reactivity (as indicated by k_{H^+}, the second-order catalytic rate constant) is also found on comparing the hydrogen ion-catalysed hydrolyses[5,11] of these and other[12] *S,S*-acetals. The factor gets progressively smaller as O-atoms are introduced: for *O,S*-acetals it is *ca.* 10^2–10^3 whereas cyclic (5- or 6-ring) *O,O*-acetals are only *ca.* 10–10^2-fold less reactive than their open-chain analogues in hydrogen ion-catalysed hydrolyses.[1] This sequence has not been commented upon before. In hydrogen ion-catalysis[1,13] it is as yet impossible to separate the effect of cyclisation on acetal basicity from that on the decomposition of the protonated acetal (k_{H^+} is the equivalent in the hydrogen ion reaction of the product of constants k_1K_1 in the Ag^+ reaction) so that silver ion-promotion provides extra information. Our present results strongly support the suggestion[5] that in the hydrogen ion-catalysed hydrolyses too, both basicity and rate of breakdown to product are affected by cyclisation.

Why does the deceleration factor get larger as S atoms are introduced? There may be at least three reasons. Firstly, 1,3-oxathiolanes, -oxathianes, -dithiolanes and -dithanes have different geometries[8] from their *O,O*-analogues owing to the greater size of the S atom and to the comparatively great length of C–S bonds. Perhaps their basicity is lowered more, compared with that of the open-chain acetals, than is that of the more symmetrical 1,3-dioxolanes and dioxanes. Secondly, a similar stereoelectronic effect may reduce the rate of cleavage of C–O (or C–S) bonds in the protonated cyclic *S*-acetals more than in the *O,O*-analogues. Thirdly, cyclic acetals, unlike open-chain acetals, can in principle recyclise after C–X cleavage[1,9,14,15] [*e.g.* eqn. (13)]. This intramolecular process (k_{-1}') may always



(13)

be rapid, but be most important when the free XH group is SH, because then a soft centre is attacking another soft centre (≡C^+). This possible recyclisation for cyclic acetals means that their hydrolyses may normally be affected by the rate of attack by water, perhaps as in eqn. (13), for which the rate equation is (14). Eqn. (13) represents a sort of mixture of conventional A1

$$k_{obs} = Kk_1' \times k_{H_2O}[H_2O]/(k_{-1}' + k_{H_2O}[H_2O]) \quad (14)$$

and A2 schemes.[1] Except at high acidity (where the water activity is affected) the acid dependence of k_{obs} may be dominated by that of Kk_1'. If k_{-1}' is very large, reaction could[1,12,14] involve direct (A2) attack of water on the protonated acetal (**X**). For silver-ion promotion of *S,S*-acetal hydrolysis similar general considerations should apply as for hydrogen ion-catalysis when a comparison of open-chain with cyclic reactivity is involved; our finding of a similar rate retardation is therefore reasonable, if perhaps fortuitous. A mechanism of promoted hydrolysis for **IIIa–d** analogous to (13), but with Ag^+ replacing H^+, seems possible, although recyclisation is likely to be less important with an –SAg group. The activation parameters for k_1 (Table 1) show similar trends for both **I** and **III** on increasing electron-release by R; for **I** an A1-like mechanism was favoured[2] for all except the *p*-NO_2 derivative (A2). Another indication that the present silver ion-promoted hydrolyses may involve slow unimolecular breakdown is that they are substantially (> 100-fold) faster than those of 2-phenyl-1,3-dithianes:[4] an extra 2-methyl group is found to produce comparatively small rate accelerations (or even decelerations) with other cyclic acetals where A2 schemes are postulated.[1]

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