Identification of an AS_E2 Mechanism in the Hydrolysis of Cyclic Thioacetals

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2-Phenyl-2-methyl-1,3-dithiane and its *p*-methoxy derivative undergo hydrolysis in concentrated aqueous perchloric acid *via* the AS_E2 mechanism rather than *via* the A1 mechanism.

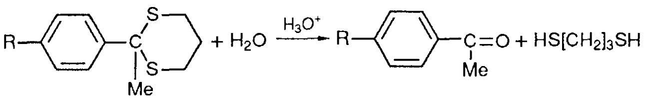
Although the Brönsted acid-catalysed hydrolysis of *O,O*-acetals and ketals is believed to occur most commonly *via* the A1 mechanism, numerous examples of hydrolysis *via* the AS_E2 mechanism have also been reported.[1–3] However, thio-analogues of those *O,O*-acetals that exhibit the AS_E2 mechanism have so far been found not to display this mechanism, and indeed no thioacetal or ketal has yet been found to follow the AS_E2 pattern, except perhaps for one example involving intramolecular catalysis.[4–6] We now report that the hydrolysis of 2-phenyl-2-methyl-1,3-dithiane, and of 2-(4-methoxyphenyl)-2-methyl-1,3-dithiane in aqueous perchloric acid (Scheme 1) shows behaviour indicative of an AS_E2 mechanism.

As in recent work[7] that identified A1 mechanisms for a series of open-chain *S,S*-diethyl dithioacetals, the kinetics of hydrolysis of the dithianes were studied spectroscopically using different temperatures and a series of aqueous perchloric acid solutions ($[H_3O^+]$ *ca.* 3–9 mol dm^{-3}); solvent deuterium isotope effects were also measured. The observed first-order kinetics were well-behaved over at least three

Table 1 Kinetic results for the hydrolysis of dithioketals

Ketal ArCMe(SR)$_2$	Slope of X plot ($m^*m^‡$)	$k_{H^+}/10^{-5}$ dm^3 mol^{-1} s^{-1}	k^D_{obs}/k^H_{obs}	$\Delta H^‡$/kJ mol^{-1}	$\Delta S^‡$/J K^{-1} mol^{-1}
Ar = p-MeOC$_6$H$_4$, RR = –[CH$_2$]$_3$–	0.75	0.42	0.90 ± 0.04[a]		
Ar = Ph, RR = –[CH$_2$]$_3$–	0.92	0.05	0.96 ± 0.04[b]	99 ± 6	0 ± 3
Ar = Ph, R = Et	3.96[c]	260[c]	1.33 ± 0.19[d]	98 ± 5[c]	42 ± 4[c]

[a] 84 atom% D, [L$_3$O$^+$] = 3.7 mol dm^{-3} (L = H or D). [b] 75 atom% D, [L$_3$O$^+$] = 4.9 mol dm^{-3}. [c] Ref. 7. [d] 99 atom% D, [L$_3$O$^+$] = 0.05 mol dm^{-3}.



Scheme 1

half-lives, and no evidence was found for significant build-up of the hemithioacetal intermediate; the observed first-order rate constants, k_{obs}, therefore refer (as usual[2] in acetal hydrolysis) to the first step of the reaction. Our results are summarised in Table 1, which includes also results[7] for the *S,S*-diethyl ketal of acetophenone (A1 mechanism).

Plots, according to the procedure of Cox and Yates,[8] of log k_{obs} – log [H$_3$O$^+$] at 25 °C against X (the excess acidity) lead to good straight lines with slopes $m^*m^‡ < 1$ for the dithianes (Table 1). For S-bases $m^* = 1.3 - 1.6$, so that $m^‡ = 0.5$–0.7 and falls into the region characteristic of the AS_E2 mechanism.[8] For this mechanism for an *S,S*-dithioacetal the solvent deuterium isotope effect, k^D_{obs}/k^H_{obs}, which is found to be 1.3–1.4 for the A1 mechanism,[6,7] might be expected in the light of theory and of experiment for *O,O*-acetals,[2,9] to be *ca.* < 1. Our results indicate k^D_{obs}/k^H_{obs} = 0.90–0.94 for a fully deuteriated solvent (Table 1). A (very approximate) estimate of the Hammett parameter ρ shows it to be similar to that found[7] for the A1 hydrolyses of the open chain *S,S*-analogues (*ca.* –2.9). Work with *O,O*-acetals[2,10] suggests that ρ will be similar for the A1 and AS_E2 mechanisms. Finally, comparison of the activation parameters found for the corresponding A1 hydrolysis of the (much more reactive) *S,S*-diethyl dithioketal of acetophenone with those for 2-phenyl-2-methyl-1,3-dithane shows that much of the difference in rate arises from entropy effects.

Thus for the dithianes the effects of changes in acid concentration, and the isotope effects, both appear incompatible with an A1 mechanism, and rather strongly suggest an AS_E2 scheme. The temperature and substituent effects are compatible with an AS_E2 scheme.

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