The Kinetics and Mechanism of the Silver Ion-promoted Hydrolysis of Thiolurethanes in Aqueous Solution

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The hydrolysis of thiolurethanes p-$RC_6H_4NHCOSEt$ (**1**, R = Cl, H, OMe) in dilute aqueous acid is promoted by silver ions. The promoted hydrolysis involves the slow decomposition of low concentrations of complexes of 2 Ag^+ : 1-thiolurethane stoichiometry, which are formed from relatively stable 1 : 1-complexes. The (positively charged) 1 : 1-complex (**2**) undergoes N-H dissociation to give a formally neutral 1 : 1-complex, **3**. The 2 : 1-complexes are formed from both **2** and **3**. The formation constants, K_1, and the acid dissociation constants, K_a, of (**2**, R = Cl, H, MeO) have been obtained from a kinetic analysis using a range of silver and hydrogen ion concentrations, and different temperatures. The results suggest that the 2 : 1-complexes undergo nucleophilic attack by water in an overall A2-like process. Thiolurethanes **1** are *ca.* 10^5-fold more reactive in Ag^+ ion-promoted hydrolysis than are the corresponding ethyl thiolbenzoates.

We reported recently[1] on the thallium(III) ion-promoted hydrolysis of thiolurethanes (thiol carbamates) **1** in dilute aqueous acid [eqn. (1)], and showed that it could occur *via* an elimination mechanism involving an isocyanate intermediate,

$$\underset{\mathbf{1}}{p\text{-}RC_6H_4NHCOSEt} + Tl^{3+} + 2H_2O \xrightarrow[\text{slow}]{H_3O^+} [ArNHCO_2H] + EtSTl^{2+} + H_3O^+$$
$$\Big\downarrow \text{fast}$$
$$ArNH_3^+ + CO_2 + EtSTl^{2+} + H_2O \quad (1)$$

or *via* a mechanism analogous to an $A_{AC}1$ hydrolysis. We have now examined the silver ion-promoted hydrolysis of (**1**, R = Cl, H, MeO) under similar conditions [eqn. (2)].

$$p\text{-}RC_6H_4NHCOSEt + Ag^+ + H_2O \xrightarrow{H_3O^+} ArNH_3^+ + CO_2 + EtSAg \quad (2)$$

Experimental

All the chemicals were previous samples.[1,2] The kinetic methods used were those used for the thallium ion-promotion, and reactions were monitored by noting the fall in urethane absorption. Final spectra indicated a very high yield of product. As in the Tl^{3+} ion-promoted hydrolysis, the initial spectra provided no extra evidence for the complex formation between thiolurethane and Ag^+ ions proposed in the Discussion section on the basis of the kinetic evidence. Presumably little spectral change occurs on complex formation. Unfortunately the reactions were too fast to obtain reliable initial spectra under concentration conditions where significant amounts of complex could be expected to be present. In the absence of soft metal ions, thiolurethanes **1** hydrolyse relatively slowly at pH < 7. Measurements were made, mostly at constant ionic strength ($NaClO_4$), over a range of silver and hydrogen ion concentrations ($HClO_4$) and at different temperatures. At very low values of $[H_3O^+]$ the presence of silver ions affects $[H_3O^+]$; we therefore used $[H_3O^+] > 10^{-3}$ mol dm^{-3}, and checked low hydrogen ion concentrations by pH measurements. Our observed first-order rate constants, k_{obs}, were usually reproducible to within ± 12% and often to within ± 5%. All reaction mixtures remained homogeneous throughout a run. Typical results are given in the Figures and Tables. The p-chloro-derivative was studied in most detail. Excellent yields of amine were obtained in preparative-scale experiments using conditions similar to those of the kinetic runs.

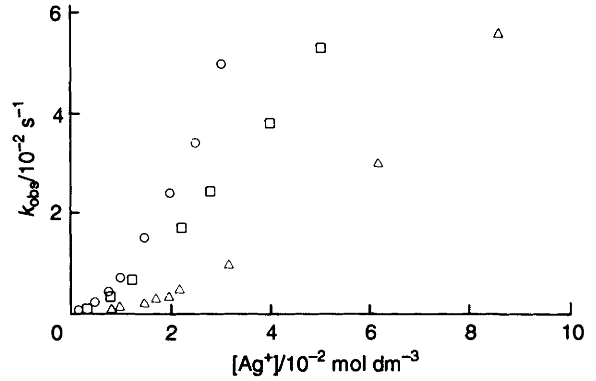


Fig. 1 Effect of $[Ag^+]$ on k_{obs} at 25 °C: ○: R = H ($[H_3O^+]$ = 8.5 × 10^{-3} mol dm^{-3}); □: R = MeO ($[H_3O^+]$ = 0.010 mol dm^{-3}); △: R = Cl ($[H_3O^+]$ = 0.197 mol dm^{-3}); $[\mathbf{1}]_{initial} \approx 1 \times 10^{-5}$ mol dm^{-3}. Ionic strength = 0.495 mol dm^{-3}.

Results and Discussion

The following pattern of results was found: under otherwise fixed conditions (i) the dependence of k_{obs} on $[Ag^+]$ is more than first-order, and tends to second-order at low values of $[Ag^+]$ (*e.g.* Fig. 1), (ii) an increase in $[H_3O^+]$ leads to a decrease in k_{obs} (*e.g.* Fig. 2), (iii) the effect of a change in p-substituent on k_{obs} is rather small, but depends upon $[H_3O^+]$, (iv) an increase in ionic strength has only a small effect on k_{obs} (Table 1), and (v), an increase in temperature leads to an increase in k_{obs} (*e.g.* Fig. 3). The results in Fig. 1, and other similar sets of results for the three thiolurethanes obtained at different hydrogen ion concentrations and temperatures, obey eqn. (3) (*e.g.* Figs. 3–5). In eqn. (3) a and b are constants whose values depend upon the

$$k_{obs} = a[Ag^+]^2/(1 + b[Ag^+]) \quad (3)$$

urethane, on $[H_3O^+]$, and on the temperature; both a and b decrease as $[H_3O^+]$ is increased. This pattern of results, the conclusions reached in the study of the thallium(III) ion-promoted hydrolysis,[1] and previous studies[3,4] of silver ion-promotion of reactions of other organosulfur compounds, lead us to suggest the following outline mechanism for the present reactions.

Table 1 Rate constants, equilibrium constants and the effects of temperature

(a) Derived parameters

R in p-$RC_6H_4NHCOSEt$	T/°C	K_1[a]/dm^3 mol^{-1}	K_a[b]/10^{-2}	$k_{iv}K_2$[c]/dm^3 mol^{-1} s^{-1}	k_vK_3[d]/dm^3 mol^{-1} s^{-1}
Cl	13.8	3.3	2.9	1.5	1.8
	25.1	2.3	4.4	3.5	3.6
	37.9	1.8	6.7	7.4	6.9
	51.8	1.4	9.0	15	13.6
H	25.0	9.4	1.4	1.9	3.8
MeO	25.0	25	0.35	1.0	4.0

For R = Cl: [a] $\Delta H_1^\circ = -17 \pm 3$, $\Delta S_1^\circ = -50 \pm 9$. [b] $\Delta H_a^\circ = 23 \pm 3$, $\Delta S_a^\circ = 52 \pm 7$. [c] $\Delta H_{iv}^\ddagger + \Delta H_2^\circ = 44 \pm 6$, $\Delta S_{iv}^\ddagger + \Delta S_2^\circ = -90 \pm 13$. [d] $\Delta H_v^\ddagger + \Delta H_3^\circ = 38 \pm 4$, $\Delta S_v^\ddagger + \Delta S_3^\circ = -106 \pm 12$. Units of ΔH kJ mol^{-1}, ΔS J K^{-1} mol^{-1}.

(b) Effects of ionic strength for (**1**, R = OMe) at 24.9 °C[a]

Ionic strength/ mol dm^{-3}	$k_{obs}/10^{-2}$ s^{-1}
0.032	1.4
0.052	1.45
0.126	1.5
0.313	1.6
0.496	1.7

[a] [Thiolurethane]$_{initial}$ ≃ 3×10^{-5} mol dm^{-3}; $[H_3O^+] = 0.010$ mol dm^{-3}; $10^2[Ag^+] = 2.24$ mol dm^{-3}.

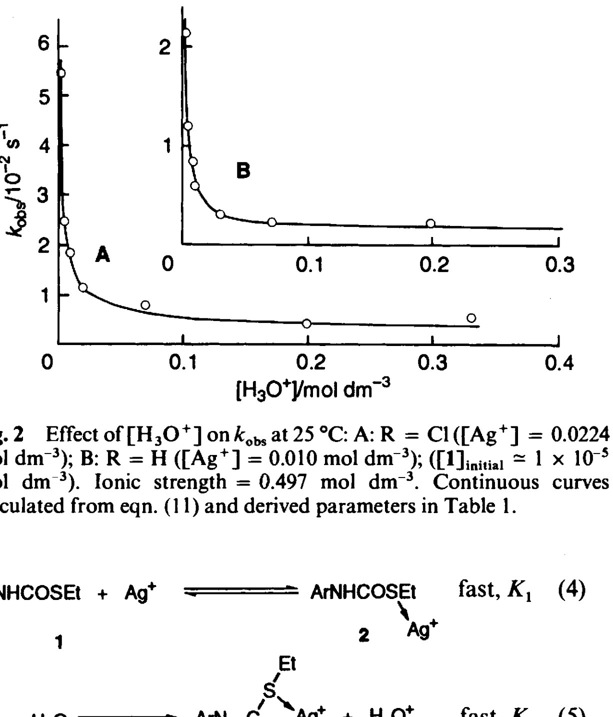
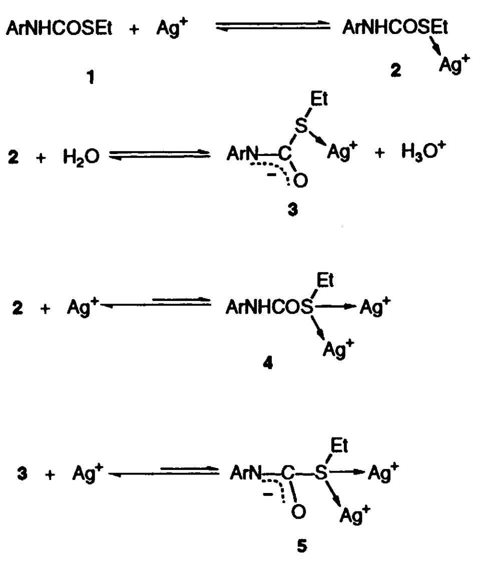


Fig. 2 Effect of $[H_3O^+]$ on k_{obs} at 25 °C: A: R = Cl ($[Ag^+] = 0.0224$ mol dm^{-3}); B: R = H ($[Ag^+] = 0.010$ mol dm^{-3}); ($[\mathbf{1}]_{initial} \simeq 1 \times 10^{-5}$ mol dm^{-3}). Ionic strength = 0.497 mol dm^{-3}. Continuous curves calculated from eqn. (11) and derived parameters in Table 1.



fast, K_1 (4)

fast, K_a (5)

fast, K_2 (6)

fast, K_3 (7)

$$\mathbf{4}\,(+2H_2O) \longrightarrow ArNHCO_2H + EtSAg_2^+ + H_3O^+ \qquad \text{slow, } k_{iv} \quad (8)$$

$$\mathbf{5}\,(+H_2O) \longrightarrow ArNHCO_2H + EtSAg_2^+ \qquad \text{slow, } k_v \quad (9)$$

$$ArNHCO_2H \xrightarrow{H_3O^+/H_2O} ArNH_3^+ + CO_2 \qquad \text{fast} \quad (10)$$

The corresponding rate eqn. is (11), which has the same form as eqn. (3) with $a = (k_{iv}K_1K_2 + k_vK_1K_3K_a/[H_3O^+])$ and $b = K_1(1 + K_a/[H_3O^+])$

$$k_{obs} = (k_{iv}K_1K_2 + k_vK_1K_3K_a/[H_3O^+])[Ag^+]^2/\{1 + K_1(1 + K_a/[H_3O^+])[Ag^+]\} \quad (11)$$

Clearly a and b will decrease as $[H_3O^+]$ is increased, as found. At high values of $[H_3O^+]$, $a \sim k_{iv}K_1K_2$ and $b \sim K_1$. The typical plots of eqn. (3), expressed as (12), shown in Figs. 3–5 illustrate by their curvature that b can be significant, and that

$$\frac{k_{obs}}{[Ag^+]} = \frac{a[Ag^+]}{(1 + b[Ag^+])} \quad (12)$$

a non-neglible amount of 1:1-complex (**2** + **3**) is formed at high values of $[Ag^+]$, particularly at low and intermediate values of $[H_3O^+]$. That the curves pass through the origin shows that the results do not follow an eqn. of the form of (13). Eqn. (13) would be expected if the 1 : 1-complexes (as well as the 2:1 complexes) decomposed directly to products at a significant speed. The $2Ag^+$: 1 thiolurethane complexes **4**, and especially **5**,

$$\frac{k_{obs}}{[Ag^+]} = \frac{c + a[Ag^+]}{(1 + b[Ag^+])} \quad (13)$$

may exist in a form with one of the Ag^+ ions attached to the N-atom. Such a structure would seem unlikely to facilitate C–S cleavage, but could aid nucleophilic attack on the carbonyl carbon atom (see below). However, there exist now[3,4] many examples of promoted reactions involving two Ag^+ ions attached to the same S atom.

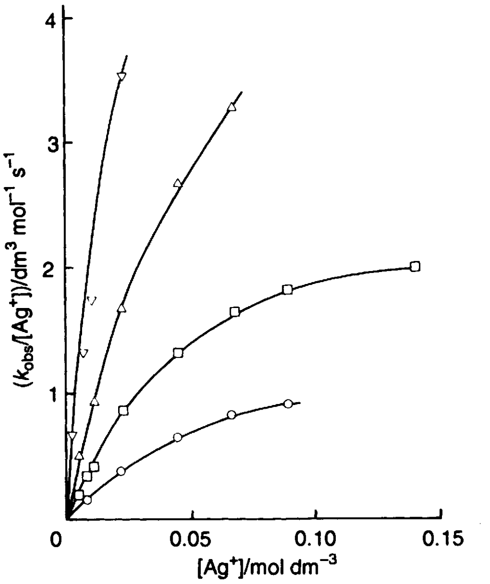


Fig. 3 Plots of eqn. (12) for (**1**, R = Cl): $[H_3O^+]$ = 0.010 mol dm^{-3}. Ionic strength = 0.495 mol dm^{-3}. ○: 13.8 °C; □: 25.1 °C; △: 37.9 °C; ▽: 51.8 °C.

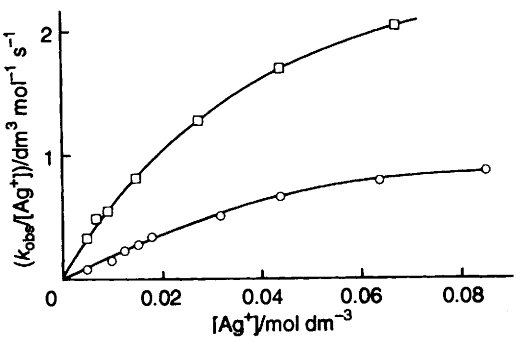


Fig. 4 Plots of eqn. (12) for (**1**, R = H): *T*: 25.1 °C. Ionic strength = 0.495 mol dm^{-3}. □: $[H_3O^+]$ = 0.010 mol dm^{-3}; ○: $[H_3O^+]$ = 0.197 mol dm^{-3}.

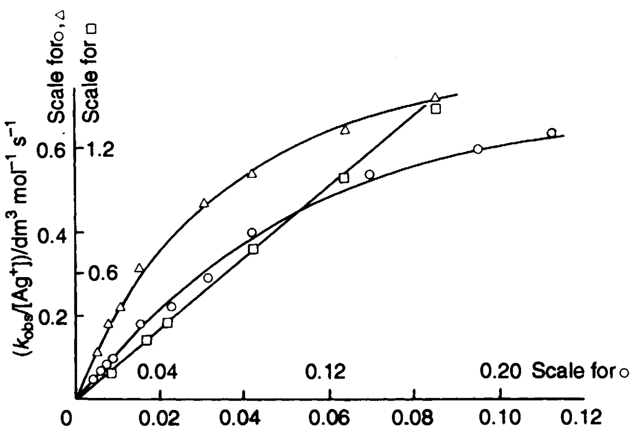


Fig. 5 Plots of eqn. (12) for (**1**, R = OMe, Cl): $[H_3O^+]$ = 0.197 mol dm^{-3}. Ionic strength = 0.495 mol dm^{-3}; △: (**1**, R = OMe) at 25 °C; ○: (**1**, R = Cl) at 13.9 °C; □: (**1**, R = Cl) at 37.9 °C.

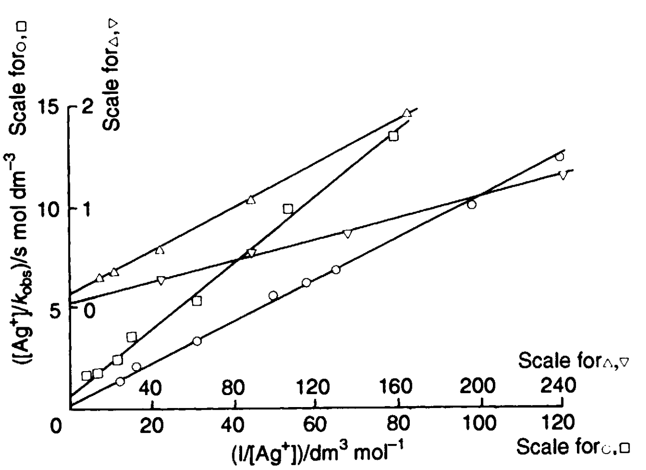


Fig. 6 Plots of eqn. (14) for (**1**, R = Cl). At $[H_3O^+]$ = 0.197 mol dm^{-3}: ○ = 25.1 °C, □ = 13.8 °C. At $[H_3O^+]$ = 0.010 mol dm^{-3}; △ = 37.9 °C, ▽ = 51.8 °C.

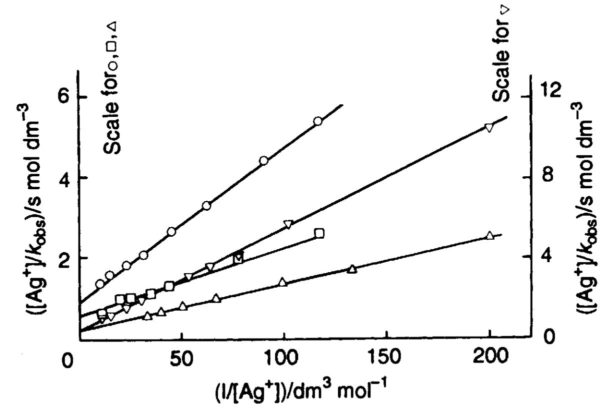


Fig. 7 Plots of eqn. (14) for (**1**, R = H, OMe) at 25 °C. For (**1**, R = OMe) ○: $[H_3O^+]$ = 0.197 mol dm^{-3}; □: $[H_3O^+]$ = 0.010 mol dm^{-3}. For (**1**, R = H) △: $[H_3O^+]$ = 8.5 × 10^{-3} mol dm^{-3}; ▽: $[H_3O^+]$ = 0.197 mol dm^{-3}. Ionic strength = 0.495 mol dm^{-3}.

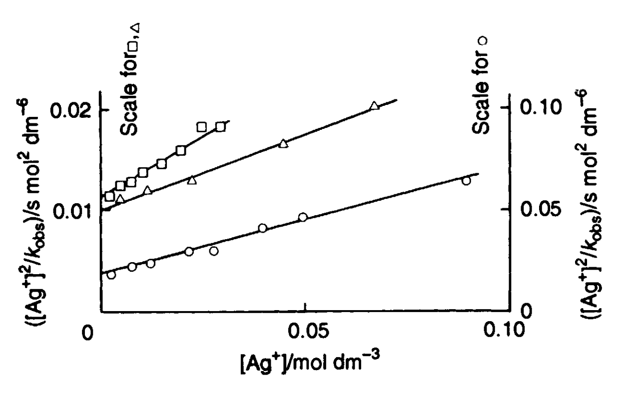


Fig. 8 Typical plots of eqn. (15). ○ (**1**, R = OMe): $[H_3O^+]$ = 0.010 mol dm^{-3}, *T* 25 °C; △ (**1**, R = Cl): $[H_3O^+]$ = 0.010 mol dm^{-3}, *T* 37.9 °C. □ (**1**, R = H): $[H_3O^+]$ = 8.5 × 10^{-3} mol dm^{-3}, *T* 25 °C; ionic strength = 0.495 mol dm^{-3}.

Values of *a* and *b* at different fixed values of $[H_3O^+]$ and temperature, were conveniently obtained by using plots of eqn. (14) or (15), the reciprocals of eqn. (12). Such plots (*e.g.* Figs. 6–8) were normally good straight lines. Since when $[H_3O^+]$ is large, $b \sim K_1$, whereas when $[H_3O^+]$ is small $b \simeq K_1K_a/[H_3O^+]$, and at intermediate values $b = K_1(1 +$

$$\frac{[Ag^+]}{k_{obs}} = \frac{1}{a[Ag^+]} + \frac{b}{a} \qquad (14)$$

$$\frac{[Ag^+]^2}{k_{obs}} = \frac{1}{a} + \frac{b[Ag^+]}{a} \qquad (15)$$

$K_a/[H_3O^+]$), it is therefore possible to calculate K_1 and K_a from experiments at different hydrogen ion concentrations. The main measurements were made with $[H_3O^+] = 0.197$, 0.010 and 5.80×10^{-3} mol dm^{-3}. Our derived values of K_1 and K_a are given in Table 1. These values can be used, together with the values of a, to calculate the products of constants $k_{iv}K_2$ and k_vK_3 (Table 1). Our experiments at different temperatures were mostly confined to the *p*-chloro-derivative, and led to ΔH and ΔS values for the equilibria (4) and (5), and to values corresponding to $k_{iv}K_2$ and k_vK_3 (Table 1).

The various parameters derived for the three thiolurethanes collected in Table 1 not only reasonably reproduce the observed rate constants (see Fig. 2), but, accepting the suggested mechanism, are related to each other in chemically intelligible ways. First, as expected, the equilibrium constants (K_1) for formation of the 1:1 adducts **2** at 25 °C fall as the electron-withdrawing power of the *p*-substituent increases; a Hammett plot shows $\rho \simeq -1.9$. Secondly, also as expected, the acid dissociation constant (K_a) of **2** increases with electron-withdrawal by the *p*-substituent; now $\rho \simeq 2.0$. It is interesting that the product K_1K_a is not only largely independent of the *p*-substituent, but also, at least for the chloro-derivative, insensitive to temperature ($K_1K_a = 0.11 \pm 0.02$ over the range 14–52 °C). This latter effect arises from the rather symmetrical values of ΔH (Table 1) for the two equilibria. K_3, the association constant for the reaction of Ag^+ with the (overall) neutral complex **3**, would be expected to be larger (perhaps much larger) than K_2, the corresponding constant for reaction with **2**. Since we find (especially for the *p*-chloro compound) that $k_vK_3 \simeq k_{iv}K_2$, it follows that probably $k_{iv} > k_v$. That also is a chemically sensible result: the departure of the leaving group (or nucleophilic attack at the carbonyl carbon atom) would be expected to be easier for **4** than for **5**. At 25 °C, the product k_vK_3 is approximately independent of the *p*-substituent, whereas $k_{iv}K_2$ falls significantly with increase in electron-release by R. Increase in electron-release should increase both K_2 and K_3; it must therefore decrease both k_{iv} and k_v. Since electron-release would be expected to facilitate the cleavage of the C–S bond in **4** and **5**, it seems that nucleophilic attack on the carbonyl carbon atom is the dominant effect controlling the values of k_{iv} and k_v. This conclusion is compatible with the (negative) values of ΔS found for the products $k_{iv}K_2$ and k_vK_3 (for the *p*-chloro derivative, Table 1). Judging by the ΔS° values for K_1 and from previous experience[5,6] of ΔS° values for Ag^+ adduct formation with very weakly basic *S*-substrates, such large negative values of ΔS would not be expected for K_2 and K_3 alone. This suggests that $\Delta S^\ddagger$ is negative for the slow steps, which in turn suggests that the decomposition is not unimolecular (as in the Tl^{3+} ion-promotion)[1] but involves nucleophilic attack by one or more water molecules. We therefore tentatively propose an A2-like mechanism for the Ag^+ ion-promoted hydrolyses of these thiolurethanes. The various opposing effects of substituents on the reactions account for the overall rather small effect of substituents on k_{obs}. In the Tl^{3+} ion-promoted hydrolyses[1] the corresponding K_1 values vary from *ca.* 100 to 200 mol^{-1} dm^3, and K_a is *ca.* 0.1–0.2. Thus the Tl^{3+} ion produces more powerful effects than does Ag^+, but the influence of R is smaller (Table 1).

The thiolurethanes **1** are *ca.* 10^5-fold more reactive in Ag^+ ion-promoted hydrolysis than are the corresponding ethyl thiolbenzoates[7] (RC_6H_4COSEt). Both types of ester display A2-like mechanisms, and an important reason for the difference in reactivity is that much more 1:1-complex formation occurs with the thiolurethanes. In the wide range of silver-ion promoted reactions of organo-sulfur compounds that has been studied kinetically[3,4] the present system is only the third to display effectively exclusive reaction *via* the $2Ag^+$:1-S-substrate complex; the other examples are the hydrolyses of phosphonothiolates,[8] and of thio acetals such as $Ph_2C(SCH_2CO_2H)_2$ which only form complexes of $2Ag^+$:1 thioacetal stoicheiometry owing to chelation effects.[9]

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