The Kinetics and Mechanism of the Hydrolysis of *p*-Nitrophenyl Isothiocyanate Promoted by Soft Metal Ions

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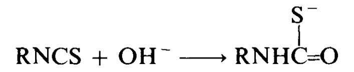
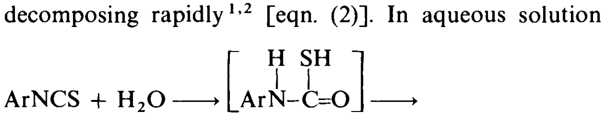
The hydrolysis of *p*-nitrophenyl isothiocyanate in aqueous acid solution is powerfully promoted by the Ag^+ and Hg^{2+} ions. The organic product is *p*-nitroaniline. The mercury-promoted reaction is first order in isothiocyanate and in $[Hg^{2+}]$, and has $\Delta H^\ddagger = 56 \pm 2$ kJ mol^{-1}, $\Delta S^\ddagger = -53 \pm 4$ J K^{-1} mol^{-1}, and $k_{H_2O}/k_{D_2O} = 1.12 \pm 0.05$ at 25.0 °C. The behaviour with silver is similar: promotion is principally first order in $[Ag^+]$, but in H_2O there is evidence for a small kinetic term in $[Ag^+]^2$. $\Delta H^\ddagger = 59 \pm 2$ kJ mol^{-1} and $\Delta S^\ddagger = -88 \pm 3$ J K^{-1} mol^{-1} for the first-order reaction, and $\Delta H^\ddagger = 25 \pm 4$ kJ mol^{-1} and $\Delta S^\ddagger = -202 \pm 12$ J K^{-1} mol^{-1} for the route second order in $[Ag^+]$. Use of D_2O removes the second-order term, and $k_{H_2O}/k_{D_2O} = 1.07 \pm 0.06$ for the route involving one Ag^+ ion. A mechanism of hydrolysis is suggested that involves an isothiocyanate–metal ion pre-equilibrium, followed by a rate-determining attack of water to give the soft metal derivative of the corresponding thiocarbamic acid as a rapidly decomposing intermediate.

The rates of the second-order hydrolytic reactions between hydroxide ions and numerous isothiocyanates have been measured using aqueous alkaline solutions.[1] The product, under sufficiently alkaline conditions, is the anion of the thiocarbamic acid [eqn. (1)]. In neutral aqueous solutions the



$$RNCS + OH^- \longrightarrow RNH\overset{S^-}{\overset{|}{C}}{=}O \qquad (1)$$

hydrolyses are relatively very slow, but proceed faster, and have been studied kinetically for *p*-nitrophenyl isothiocyanate, in H_2O–Me_2SO mixtures.[2] The organic product under such conditions is the corresponding amine, the thiocarbamic acid decomposing rapidly[1,2] [eqn. (2)]. In aqueous solutions of



$$ArNCS + H_2O \longrightarrow \left[Ar\overset{H}{\overset{|}{N}}{-}\overset{SH}{\overset{|}{C}}{=}O\right] \longrightarrow ArNH_2 + COS(\xrightarrow{H_2O} CO_2 + H_2S) \qquad (2)$$

Brønsted acids the hydrolyses are also very slow,[3] and do not appear to have been studied quantitatively. This paper is the first report of the kinetics of hydrolysis of an isothiocyanate at acid pH promoted by soft Lewis acids (Ag^+ and Hg^{2+} ions). The solvent used was 1% (v/v) dioxane–water.

Experimental

The *p*-nitrophenyl isothiocyanate, deuterium oxide (99.8 atom %D), and silver perchlorate were previous samples,[2,4] and stock solutions of mercury(II) perchlorate were prepared as before.[5] Water was doubly distilled. In the experiments using D_2O the solvent contained >98.3 atom %D. All kinetic runs were conducted under pseudo-first-order conditions using an excess of metal ions. Reaction was initiated by addition of a small volume of a stock solution of the isothiocyanate in dioxane; its progress was monitored spectroscopically at *ca.* 380 nm for silver-promotion, and at *ca.* 380 or *ca.* 320 nm for promotion by Hg^{2+} ions. All reaction mixtures contained a small amount of perchloric acid to prevent precipitation of metal oxide or hydroxide, and to maintain a fixed pH. Constant ionic strength was maintained with sodium perchlorate. Our detailed reaction conditions are given in the tables and figures.

Preparative experiments led to high (>92%) yields of *p*-nitroaniline and formation of the metal sulphide [eqns. (3) and (4), Ar = p-$NO_2C_6H_4$–, *cf.* eqn. (2)]. For all the kinetic runs

$$ArNCS + 2Ag^+ + 4H_2O \longrightarrow ArNH_2 + Ag_2S + CO_2 + 2H_3O^+ \qquad (3)$$

$$ArNCS + Hg^{2+} + 4H_2O \longrightarrow ArNH_2 + HgS + CO_2 + 2H_3O^+ \qquad (4)$$

involving mercury-promotion the reaction mixtures remained homogeneous throughout a run, and the kinetic behaviour was accurately first order for more than three half-lives. The final absorbances at 380 nm at low Hg^{2+} and H_3O^+ concentrations indicated a high yield of *p*-nitroaniline. At the higher Hg^{2+} and H_3O^+ concentrations used the increase in absorption at *ca.* 380 nm due to *p*-nitroaniline formation is much reduced owing to protonation, and to complexation with mercury ions, and for many of the mercury-promoted reactions the loss of isothiocyanate was monitored directly (at *ca.* 320 nm). For silver-ion promotion the strong absorption of silver ions precluded measurements near 320 nm, but measurements at 380 nm were always possible. There was some precipitation of silver sulphide during the silver-promoted runs, but this did not interfere seriously with the kinetic measurements, and good first-order plots were obtained covering most of the reaction. There was no evidence of autocatalytic acceleration of the reaction by the precipitate.[6] Values of k_{obs}, the observed first-order rate constant, were reproducible to within ±6% with Hg^{2+} ions, and to within ±10% with Ag^+ ions. The spontaneous hydrolyses were always negligible compared with the promoted reactions.

Results and Discussion

(*i*) *Mercury*(II)-*ion Promotion.*—The results obtained with this ion have a simple pattern so we deal with them first. Values of k_{obs} obtained by following the loss of isothiocyanate, or the formation of amine product were the same, within experimental error. The use of various concentrations of Hg^{2+} ions in H_2O, at fixed values of $[H_3O^+]$ and ionic strength, and at three temperatures led to results shown in Fig. 1. This figure also contains results for D_2O solutions at 25.0 °C. It is clear that

Table 1 Effects of ionic strength, $[H_3O^+]$ and $[Cl^-]$. $[ArNCS]_{initial} = 2 \times 10^{-5}$ mol dm^{-3}.

T/°C	$[M^{II}]$/mol dm^{-3}	I/mol dm^{-3}	$[H_3O^+]$/mol dm^{-3}	$k_{obs}/10^{-3}$ s^{-1} [a]	$[Cl^-]$/mol dm^{-3}
(*a*) Promotion by mercury(II) ions					
Effect of ionic strength					
24.8	5.50×10^{-3}	0.024	7.14×10^{-3}	5.8	
		0.059		5.9	
		0.112		6.5	
		0.289		7.6	
		0.500		9.0	
		0.738		9.6	
		1.27		10.9	
Effect of $[H_3O^+]$					
24.8	5.50×10^{-3}	0.500	3.34×10^{-3}	9.0	
			7.14×10^{-3}	9.0	
			2.26×10^{-2}	9.0	
			5.00×10^{-2}	8.6	
			9.90×10^{-2}	8.6	
			1.96×10^{-1}	8.6	
			2.94×10^{-1}	8.4	
Effect of $[Cl^-]$					
24.8	9.40×10^{-3} [b]	0.500	1.20×10^{-2}	3.4	9.4×10^{-3} [c]
	2.17×10^{-2} [b]			8.2	2.17×10^{-2} [c]
(*b*) Promotion by silver(I) ions					
Effect of ionic strength					
25.7	8.20×10^{-2}	0.090	1.00×10^{-2}	0.53	
		0.170		0.54	
		0.260		0.55	
		0.500		0.60	
		0.740		0.65	
		1.14		0.69	
Effect of $[H_3O]^+$					
25.7	6.56×10^{-2}	0.500	1.0×10^{-2}	0.48	
	6.56×10^{-2}		1.0×10^{-1}	0.46	
	16.6×10^{-2}		1.0×10^{-2}	1.25	
	16.6×10^{-2}		5.90×10^{-2}	1.34	
	45.8×10^{-2}		1.00×10^{-2}	4.2	
	45.8×10^{-2}		1.90×12^{-2}	4.1	

[a] k_{obs} = observed first-order rate constant. [b] $[Hg^{2+}]_{stoich}$. [c] $[Cl^-]_{stoich}$.

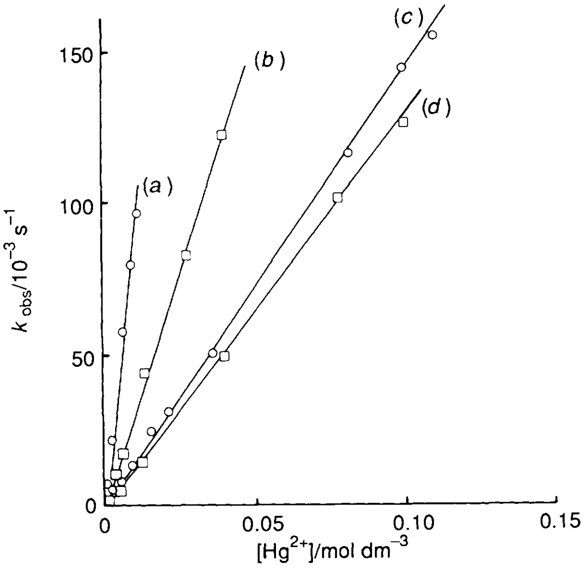
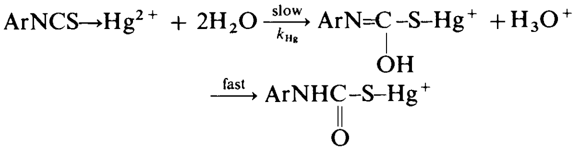


Fig. 1 Promotion by Hg^{2+} ions. $[ArNCS]_{initial}$ = *ca.* 2×10^{-5} mol dm^{-3}; $[H_3O^+]$ = 0.05 mol dm^{-3}; ionic strength = 0.50 mol dm^{-3}. (*a*) 48.4 °C; (*b*) 34.6 °C; (*c*) 24.8 °C (H_2O); (*d*) 24.8 °C (D_2O).

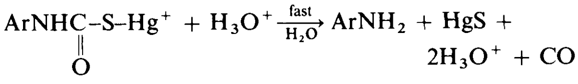
the hydrolysis is accurately first order in $[Hg^{2+}]$ with no evidence of the saturation effects often met in mercury-ion promotion.[7–9] *p*-Nitrophenyl isothiocyanate is evidently a much weaker *S*-base than are typical *S*-acetals, diphenyl disulphide, and thiobenzamide.[7–9] Effects of changes in $[H_3O^+]$, and in ionic strength, are shown in Table 1; the relevant derived second-order rate constants, isotope effect and activation parameters are listed in Table 2.

The results for mercury are compatible with the mechanism of eqns. (5) and (6), in which the decomposition of the intermediate mercury derivative of the thiocarbamic acid is assumed to be fast. Were this decomposition the slow step, since it involves proton transfer, k_{obs} might be expected to be increased by increase in $[H_3O^+]$, which is contrary to experiment.

$$ArNCS + Hg^{2+} \overset{fast}{\rightleftharpoons} ArNCS{\rightarrow}Hg^{2+} \quad K_{Hg} \qquad (5)$$



$$ArNCS{\rightarrow}Hg^{2+} + 2H_2O \xrightarrow[k_{Hg}]{slow} ArN{=}\underset{\substack{|\\OH}}{C}{-}S{-}Hg^+ + H_3O^+ \xrightarrow{fast} ArNH\underset{\substack{\|\\O}}{C}{-}S{-}Hg^+ \qquad (6)$$



$$ArNH\underset{\substack{\|\\O}}{C}{-}S{-}Hg^+ + H_3O^+ \xrightarrow[H_2O]{fast} ArNH_2 + HgS + 2H_3O^+ + CO_2$$

Table 2 Derived second-order rate constants, isotope effects and activation parameters. k = second-order rate constant = average of $k_{obs}/[Hg^{2+}]$; k_1 and k_2 from Fig. 3 (see the text).

Solvent	T/°C	k dm^3 mol^{-1} s^{-1}	k_1 dm^3 mol^{-1} s^{-1}	k_2/dm^6 mol^{-1} s^{-1}	k_{H_2O}/k_{D_2O}	$\Delta H^‡$/ kJ mol^{-1}	$\Delta S^‡$/J mol^{-1} K^{-1}
(a) Promotion by mercury(II) ions							
H_2O	24.8	1.45			1.12 ± 0.05	56 ± 2	−53 ± 4
	34.6	3.1					
	48.4	8.3					
D_2O	24.8	1.30					
(b) Promotion by silver(I) ions							
H_2O	25.0		6.3×10^{-3}	8.0×10^{-3}	1.07 ± 0.06	59 ± 2 ($\Delta H^‡_1$)	−88 ± 4 ($\Delta S^‡_1$)
	35.1		1.55×10^{-3}	1.4×10^{-2}		25 ± 4 ($\Delta H^‡_2$)	−202 ± 12 ($\Delta S^‡_2$)
	49.2		4.05×10^{-2}	1.92×10^{-2}			
D_2O	25.0		5.9×10^{-3}				

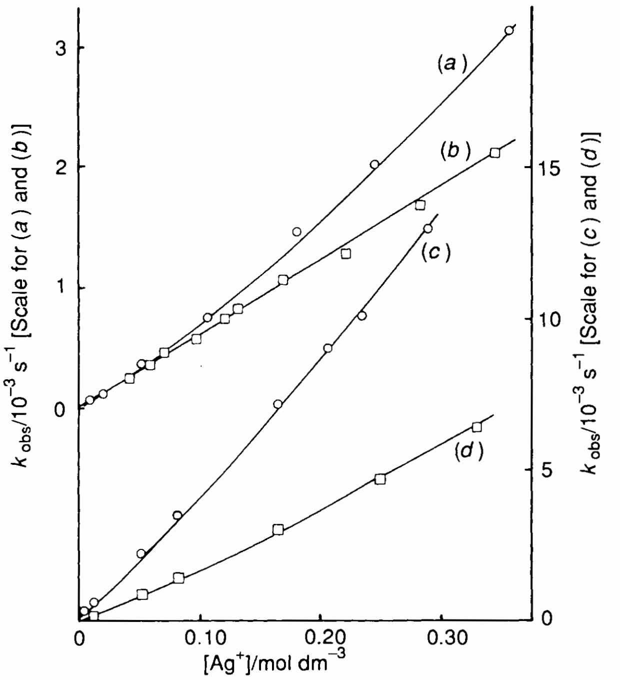


Fig. 2 Promotion by Ag^+ ions. $[ArNCS]_{initial}$ = $ca.$ 2×10^{-5} mol dm^{-3}; $[H_3O^+]$ = 0.01 mol dm^{-3}; ionic strength = 0.50 mol dm^{-3}. (a) 25.0 °C (H_2O); (b) 25.0 °C (D_2O); (c) 49.2 °C; (d) 35.1 °C.

With equilibrium (5) lying well to the left, the corresponding rate equation is (7), as required by the observed orders.

$$-d[ArNCS]/dt = k_{Hg}K_{Hg}[Hg^{2+}][ArNCS] = k_{obs}[ArNCS] \quad (7)$$

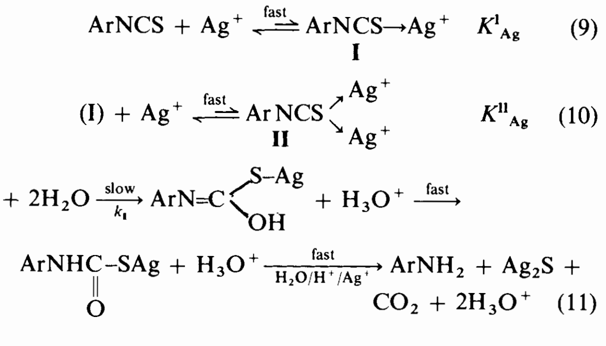
Previous work[10] on soft-metal-ion promotion shows that when the substrate–metal ion pre-equilibrium lies well to the left, as does eqn. (5), increases in ionic strength lead to some increase in k_{obs} (owing probably to an increase in the equilibrium constant). This is compatible with results in Table 1. The values of the activation parameters and the isotope effect (Table 2) will reflect changes in both K_{Hg} and k_{Hg}. For weak S-bases there is some evidence[4] that a change from H_2O to D_2O as the solvent might increase K_{Hg}, while for step (6) k_{Hg} would be expected to decrease,[11] so that a rather small net isotope effect is expected, as found. Assuming the mechanism (5)–(6), the observed activation parameters (Table 2) represent ($\Delta H_5 + \Delta H_6^‡$) and ($\Delta S_5 + \Delta S_6^‡$). The observed values are qualitatively compatible with expectations for weakly basic S-substrates.[8,12]

The acceleration provided by 1.0 mol dm^{-3} of Hg^{2+} ions is $> 10^6$ when compared with the spontaneous rate of hydrolysis. The k_{obs} values obtained in the presence of added Cl^- ions (Table 1) indicate that $HgCl^+$ (formed almost stoichiometrically) is $ca.$ four times less effective in promoting hydrolysis than is Hg^{2+}. The effectiveness of these two species has in the past usually proved to be more nearly equal.[7,13]

(ii) *Silver-ion Promotion.*—Typical results for k_{obs} for variation of $[Ag^+]$ at fixed values of $[H_3O^+]$ and ionic strength are shown in Fig. 2. For H_2O as the solvent there is evidence, particularly at the two lower temperatures, of a greater-than-first-order dependence on $[Ag^+]$, although the effect is small. The results can be analysed for contributions from both first- and second-order terms in $[Ag^+]$ using plots of eqn. (8) (Fig. 3). The first-order term makes the dominant contribution at each temperature. For the D_2O solutions (25.0 °C) only a simple first-order dependence on $[Ag^+]$ was found. Values for k_1, k_2 and the corresponding activation parameters (for H_2O), are in Table 2. Effects on k_{obs} of changes in $[H_3O^+]$ and ionic strength are in Table 1; these effects are small, but there is some increase in k_{obs} with ionic strength.

$$k_{obs} = k_1[Ag^+] + k_2[Ag^+]^2$$
$$\text{or } k_{obs}/[Ag^+] = k_1 + k_2[Ag^+] \quad (8)$$

Reaction paths involving two silver ions are common in silver-ion-promoted reactions, especially for weakly basic S-substrates,[13–15] and therefore postulation of such a path is inherently reasonable for the present system, but it is surprising that it is not detected for D_2O solutions. Considering our suggestions for mercury-ion promotion, and the foregoing findings for silver ions, we tentatively suggest the mechanism given by eqns. (9)–(12) for silver-ion promotion. The corresponding rate equation is (13), as found experimentally [eqn. (8)].



$$ArNCS + Ag^+ \overset{\text{fast}}{\rightleftharpoons} \underset{\mathbf{I}}{ArNCS{\rightarrow}Ag^+} \qquad K^{I}_{Ag} \quad (9)$$

$$(I) + Ag^+ \overset{\text{fast}}{\rightleftharpoons} \underset{\mathbf{II}}{ArNCS}\begin{smallmatrix}\nearrow Ag^+ \\ \searrow Ag^+\end{smallmatrix} \qquad K^{II}_{Ag} \quad (10)$$

$$I + 2H_2O \xrightarrow[k_1]{\text{slow}} ArN{=}C\begin{smallmatrix} S{-}Ag \\ OH \end{smallmatrix} + H_3O^+ \xrightarrow{\text{fast}}$$

$$ArNH\underset{\underset{O}{\|}}{C}{-}SAg + H_3O^+ \xrightarrow[H_2O/H^+/Ag^+]{\text{fast}} ArNH_2 + Ag_2S + CO_2 + 2H_3O^+ \quad (11)$$

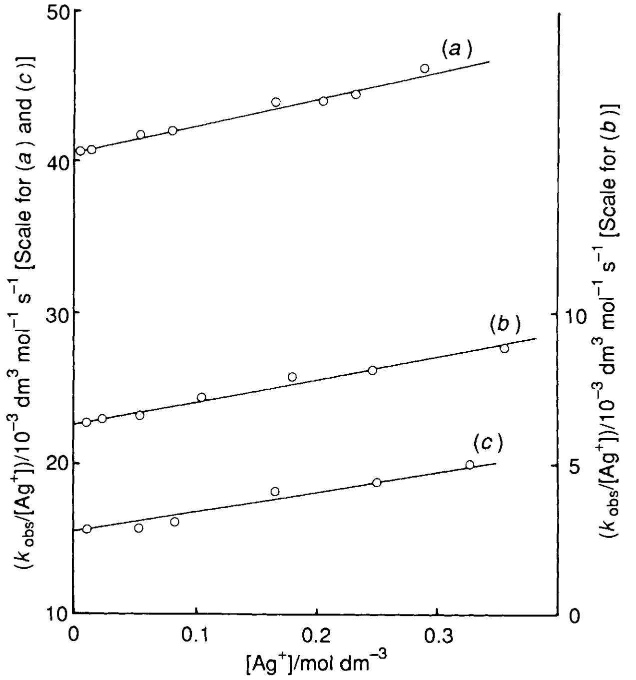
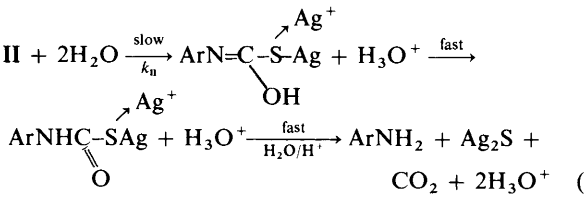


Fig. 3 Plots of eqn. (8) for silver-ion promotion. (*a*) 49.2 °C; (*b*) 25.0 °C; (*c*) 35.1 °C.



$$\mathrm{II} + 2H_2O \xrightarrow[k_{II}]{\text{slow}} ArN{=}C(OH){-}S(\rightarrow Ag^+){-}Ag + H_3O^+ \xrightarrow{\text{fast}}$$

$$ArNHC(=O){-}S(\rightarrow Ag^+)Ag + H_3O^+ \xrightarrow[H_2O/H^+]{\text{fast}} ArNH_2 + Ag_2S + CO_2 + 2H_3O^+ \quad (12)$$

$$-d[ArNCS]/dt = (k_1K^{I}_{Ag}[Ag^+] + k_{II}K^{II}_{Ag}[Ag^+]^2)[ArNCS]$$

or

$$k_{obs} = k_1[Ag^+] + k_2[Ag^+]^2 \quad (13)$$

By comparison with mercury-ion promotion, the route involving one Ag^+ ion has a larger value for $(\Delta H_9 + \Delta H^{\ddagger}{}_{11})$ and a more negative value for $(\Delta S_9 + \Delta S^{\ddagger}{}_{11})$. For the route with two silver ions the enthalpy term is much smaller and the entropy term much more negative (Table 2). These effects could be compatible with eqns. (9)–(12). At 25 °C, under similar conditions, Hg^{2+} ions are *ca.* 200-times more effective in promoting hydrolysis than are Ag^+ ions. This factor is commonly larger for other reactions.[13]

If our analysis for silver-ion-promotion in terms of two paths is correct, the isotope effect $(k_1)_{H_2O}/(k_1)_{D_2O}$ = *ca.* 1.07, and is similar to that for Hg^{2+} ions. The principal net effect of the change to D_2O appears to be the suppression of the route involving two silver ions. We plan to examine the generality of this finding using other silver-ion-promoted reactions known to exhibit second-order terms.

Although $NO_2C_6H_4NCS$ is a significantly weaker *S*-base than are, for example, $NO_2C_6H_4CH(SEt)_2$ or Ph_2S_2, its overall reactivity towards promoted hydrolysis is comparable to that of the *S*-acetal, and *ca.* 100 times greater than that of the disulphide. This circumstance probably arises because the slow step for the isothiocyanate reaction involves attack of water at a (weak) carbon–sulphur double bond rather than at a saturated carbon atom as in the other hydrolyses.

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Paper 0/03996I
Received 3*rd September* 1990
Accepted 2*nd October* 1990