Hydrolysis of Aryl and Alkyl Isothiocyanates in Aqueous Perchloric Acid

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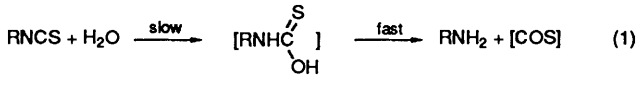
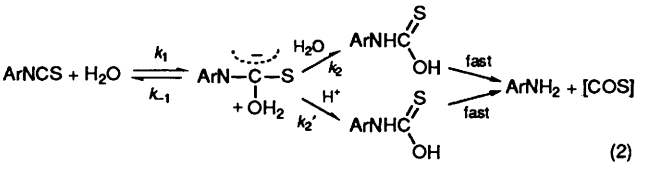
The slow hydrolysis of aromatic and aliphatic isothiocyanates in water is promoted by added perchloric acid. The hydrolysis leads first to the thiocarbamic acid, but this species decomposes rapidly to the (protonated) amine, and is not normally detected. Convenient rates of hydrolysis are obtained at 50 °C when $[HClO_4] \lesssim 6.0$ mol dm^{-3}. The effects of substituents, temperature, and acid concentration on the observed rate constant have been studied. Aliphatic isothiocyanates are somewhat more reactive than aromatic derivatives, but the effect of substituent changes is generally small, with electron release favouring reaction. Substituents close to the nitrogen atom hinder reaction. The value of $\Delta S^{\ddagger}$ is typically −120 to −220 J K^{-1} mol^{-1}, and analysis of the acidity dependence by the excess acidity approach shows $m^{\ddagger} \simeq 0.8$. Addition of water to the isothiocyanate N=C double bond *via* a mechanism involving simultaneous proton transfer to nitrogen and nucleophilic attack by water at carbon with a cyclic transition state is proposed. The carbamic acids formed by the aliphatic isothiocyanates are sufficiently basic for them to be increasingly trapped as their protonated forms when $[HClO_4] > 9.0$ mol dm^{-3}.

Aromatic and aliphatic isothiocyanates are known to hydrolyse [eqn. (1)] very slowly in pure water.[1] In certain dimethyl



(1)

sulfoxide (DMSO)–water mixtures they hydrolyse more rapidly owing to the enhanced nucleophilicity of water in DMSO-rich mixtures.[2] We have recently shown[3] that whereas the addition of 1.0 mol dm^{-3} perchloric acid has a negligible effect on the rate of hydrolysis in pure water, in a DMSO–water mixture such addition leads to significant catalysis: the rate of hydrolysis rises to a limiting value different for each isothiocyanate. We have argued that mechanism (2) underlies this catalysis. The acid



(2)

assists prototropic rearrangement of the zwitterion, and eventually this process becomes so fast that k_1 limits the rate.

We have now found that added acid also promotes the hydrolysis of isothiocyanates in purely aqueous solutions at sufficiently high acid concentrations, and report kinetic studies with a range of aromatic and aliphatic compounds.

Experimental

Materials.—The isothiocyanates, and corresponding amines, were Aldrich or Fisons products. They were normally either redistilled or recrystallised before use. Perchloric acid and dioxane were of AnalaR grade.

Kinetics.—Reaction mixtures were made up from aqueous perchloric acid (*ca.* 6–12 mol dm^{-3}) and a small volume of stock solution of the isothiocyanate in dioxane; mixtures contained <1% dioxane. Reaction was normally followed by observing the fall in isothiocyanate absorption in the region 230–380 and 210–240 nm for the aromatic and aliphatic derivatives, respectively. Loss of isothiocyanate was an accurately first-order process over more than three half-lives, and values of k_{obs}, the observed first-order rate constant, were reproducible to within ±8%. k_{obs} was measured for a range of acid concentrations, normally at 50 °C; the dependence of k_{obs} on temperature was also measured. Details of our concentration and other conditions are in the Tables and Figures. For all the isothiocyanates k_{obs} in the absence of perchloric acid is negligible by comparison with the values observed.

The aliphatic isothiocyanates are more reactive than the aromatic compounds, and were studied over a wider range of acidity. Their kinetic behaviour follows the pattern characteristic of the aromatic isothiocyanates when $[HClO_4] \lesssim 8.5$ mol dm^{-3} (Table 1) but at the highest perchloric acid concentrations studied the absorption rises initially, rather than falling, and the isothiocyanate spectrum centred at *ca.* 215–235 nm is converted into a new absorption band with a maximum at *ca.* 240–247 nm. This is probably due to the trapping of the intermediate monothiocarbamic acid as an unreactive protonated form[4] [eqn. (4)] and is being investigated further. The effect does not interfere when $[HClO_4] \lesssim 8.5$ mol dm^{-3}. A very similar effect was found previously for the hydrolysis of the (more stable) dithiocarbamic acids in concentrated sulfuric acid.[4] In the present systems the trapping of a substantial fraction of the carbamic acid in an unreactive form leads to a reduction in the overall rate of amine formation at the highest acidities where the loss of carbamic acid, rather than its rate of formation, becomes the slow phase of the hydrolysis.

Reaction Products.—As expected from previous work[1,2] [eqn. (1)] the organic product was in all cases the corresponding (protonated) amine. Final absorbances corresponded closely to those obtained from appropriate mixtures of acid and amine. The amine could also be isolated in preparative-scale experiments by careful neutralisation of reaction mixtures.

Results and Discussion

Values for k_{obs} at 50 °C for the various isothiocyanates at

Table 1 Dependence of k_{obs} on $[HClO_4]$ for ArNCS and RNCS

$[HClO_4]$/ mol dm^{-3}	$k_{obs}/10^{-3}$ s^{-1}							
	p-NO_2	o-Cl	*p*-F	*p*-H	*p*-MeO	*p*-Me	*m*-Me	*o*-Me (75 °C)
RC_6H_4NCS								
11.50	6.5	7.7	13	19	20	28	30	
11.00	2.9	2.4	5.5	8.0	7.8	11	12	
10.87	2.1	1.7	4.9	7.0			9.2	11
10.50	1.1					6.7		5.9
10.20	0.53	0.41	1.2	1.9	2.0	3.0		3.6
9.80	0.35	0.12	0.65				1.6	1.8
9.40	0.20	0.05			0.60	0.74		0.75
9.00	0.15		0.25	0.35	0.46			0.56
8.50	0.10		0.12	0.17	0.26	0.27	0.32	0.30
8.00	0.042				0.13	0.13	0.14	
$m^*m^{\ddagger}$	0.74	1.3	0.86	0.86	0.73	0.86	0.84	0.86
RNCS	Me	$PhCH_2$	Bu^t					
8.18	2.6	2.6	1.2					
7.90	2.0	2.00	1.0					
7.50	1.4	1.2	0.45					
7.30	1.1	0.88						
7.02	0.77	0.68	0.15					
6.70	0.48	0.50	0.11					
6.12	0.24	0.24	0.05					
$m^*m^{\ddagger}$	0.69	0.70	0.94					

[a] $[ArNCS]_{initial} \simeq 3 \times 10^{-5}$ mol dm^{-3}; $[RNCS]_{initial} \simeq 3 \times 10^{-4}$ mol dm^{-3}; $T = 50.0$ °C unless otherwise specified.

Table 2 Effects of temperature on k_{obs}[a]

Isothiocyanate	$[HClO_4]$/mol dm^{-3}	T/°C	$k_{obs}/10^{-3}$ s^{-1}	$\Delta H^{\ddagger}$/kJ mol^{-1}	$\Delta S^{\ddagger}$/J K^{-1} mol^{-1}
MeNCS	7.90	30.5	0.29	78 ± 5	−119 ± 12
		40.0	0.84		
		50.0	2.0		
$PhCH_2NCS$	7.50	40.0	0.43	80 ± 6	−116 ± 10
		50.0	1.2		
		60.0	2.9		
o-$CH_3C_6H_4NCS$	10.2	52.0	0.23	92 ± 6	−135 ± 12
		67.5	1.0		
		75.0	2.4		
p-$NO_2C_6H_4NCS$	11.0	25.0	0.23	83 ± 6	−144 ± 15
		34.0	0.53		
		50.0	2.9		
p-FC_6H_4NCS	11.5	30.5	3.2	60 ± 5	−217 ± 20
		37.0	4.8		
		50.0	13		
p-$CH_3C_6H_4NCS$	11.5	25.0	3.2	68 ± 5	−190 ± 16
		34.0	7.5		
		50.0	28		
m-$CH_3C_6H_4NCS$	11.0	25.0	1.5	66 ± 6	−190 ± 18
		34.0	3.5		
		50.0	12		

[a] Calculation of $\Delta S^{\ddagger}$ uses (very approximate) second-order rate constant obtained[6] by extrapolation of plots of log k_{obs} − log$[H_3O^+]$ *vs.* X (*e.g.* Fig. 1) to $X = 0$.

different perchloric acid concentrations are given in Table 1. For aliphatic isothiocyanates only the range below 8.2 mol dm^{-3} is included. Some effects of temperature change, and the corresponding activation parameters, are in Table 2. Typical (rectilinear) plots of log k_{obs} − log $[H_3O^+]$ *vs.* X, where X is the excess acidity,[5] are shown in Fig. 1. The slopes of these plots are rather similar for almost all the isothiocyanates and are given in Table 1. These various results show that: (*i*) hydrolysis is strongly acid-promoted, with no levelling-off of k_{obs} at high acidity; (*ii*) the effect on k_{obs} of substituent changes in the aryl isothiocyanates are small with electron-release slightly favouring the reaction; (*iii*) the aliphatic derivatives, methyl and benzyl isothiocyanate, are *ca.* 20–40 times more reactive than are the aromatic derivatives when $[HClO_4] \simeq 8.0$ mol dm^{-3}; (*iv*) substituents close to the isothiocyanate nitrogen atom impede hydrolysis (methyl more than chloro); and (v) formation

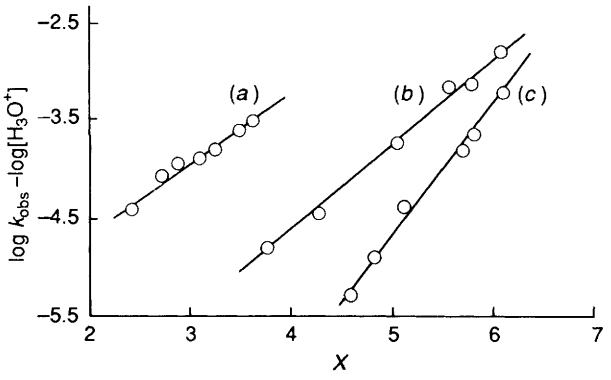


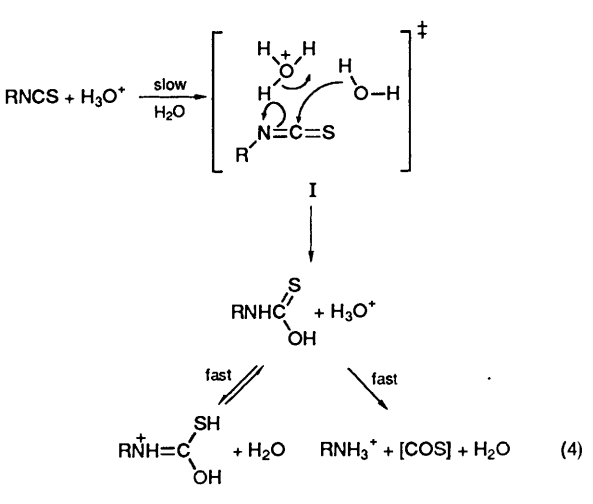
Fig. 1 Plots of $\log k_{obs} - \log[H_3O^+]$ *vs.* excess acidity. For k_{obs} see the text; X values refer[5] to *ca.* 25 °C: (*a*), $PhCH_2NCS$; (*b*), PhNCS; (*c*), *o*-ClC_6H_4NCS

of the transition state involves a large decrease in entropy. The slopes of the plots *vs.* X average *ca.* 0.83. In the application by Cox and Yates[6] of excess acidity dependencies to mechanisms of acid catalysis these slopes equal the product of parameters $m^*m^\ddagger$. The value of m^* is not known for isothiocyanates, but since they undergo protonation on their nitrogen atom[7] m^* is almost certainly >1, and probably *ca.* 1.4. This suggests that $m^\ddagger$, the parameter characteristic of transition state structure,[6] is normally <0.8 (and perhaps as small as 0.6) and points to a slow proton transfer mechanism.[6]

A simple slow proton transfer[8] to nitrogen to give the carbamyl cation [eqn. (3)] seems unlikely to be the mechanism

$$RNCS + H_3O^+ \xrightarrow{slow} RN(H)-\overset{+}{C}-S + H_2O \xrightarrow{fast} \text{products} \qquad (3)$$

of promotion for at least two reasons.[8] (i) The small effects produced by substituent changes suggest opposed substituent effects (as for example in acid-catalysed ester hydrolysis), although with the demands of protonation being the dominant effect; (ii) the very negative values of $\Delta S^\ddagger$ suggest that one, or more, additional water molecules are in the transition state. All the facts may be compatible with the mechanism of eqn. (4). The



(4)

elimination of water from thiocarbamic acids is not a known reaction, but the mechanism suggested[9] for the elimination of hydrogen chloride from carbamyl chlorides implies a concerted, cyclic addition to the N=C bond for the reverse. And one explanation[10] of the acid-catalysed hydration of ketenes involves a transition state like **I**.

In eqn. (4) addition would be perpendicular to the molecular plane. That minimises steric effects, but work on similar additions to ketenes shows that even in perpendicular attack steric effects are not negligible[11,12] and are compatible with the effects found here (Table 1). A cyclic transition state is likely to have important steric requirements. In view of the $\Delta S^\ddagger$ values the cycle may involve a second water molecule for most aryl isothiocyanates. (Eight-membered rings are most favourable energetically[13]).

An alternative explanation of the present results in terms of a conventional A2 mechanism (pre-equilibrium protonation of nitrogen followed by slow attack of water at the thiocarbamyl carbon atom) cannot be excluded, but seems less attractive in view of the probable value of $m^\ddagger$, and because attack by water on a reactive carbamyl cation seems unlikely to be a slow step. We have not attempted to distinguish between slow proton transfer and pre-equilibrium protonation by using a deuteriated solvent because the discriminating power of the solvent isotope in strongly acidic media is uncertain.[14]

We have previously[2] pointed out that additions to isothiocyanates involving synchronous nucleophilic attack at carbon and proton transfer to nitrogen are probably much less common than in the analogous additions to isocyanates and ketenes;[15] relatively difficult proton transfer to nitrogen is probably the principal reason that the spontaneous hydrolyses and alcoholyses of isothiocyanates are relatively so very slow. However, it now appears that in sufficiently strongly acidic conditions important acceleration *via* proton transfer to nitrogen is possible for isothiocyanates. Whatever the true details there clearly exist at least two mechanisms of acid-promotion available for isothiocyanates: catalysed prototropy following nucleophilic attack at carbon by good nucleophiles [eqn. (2)]; and the direct protonation of nitrogen synchronous with, or preceding, nucleophilic attack at carbon in very acidic media.

Qualitative comparison of our results for MeNCS with those observed[16] (in the pH region) for MeNCO shows that the isothiocyanate is *ca.* 10^7 times less susceptible to acid catalysis in water than its *O*-analogue. As noted above, very large factors are also found in comparisons[2] of the spontaneous hydrolyses of isocyanates and isothiocyanates.

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