The Kinetics and Mechanism of the Spontaneous Hydrolysis of 4-Chlorophenyl Isocyanate in Diethyl Ether Solution

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The kinetics of hydrolysis of 4-chlorophenyl isocyanate have been studied at low concentrations in diethyl ether solution at three temperatures. When the ratio [H_2O] : [RNCO] is sufficiently large the final organic product is 4-chloroaniline only, which arises from the loss of carbon dioxide from the initially formed carbamic acid, $RNHCO_2H$. In the presence of a sufficient excess of water, the overall process comprises two consecutive first-order reactions [equation (4)], whose pseudo-first-order rate constants k_1 and k_2 both depend on the third power of the stoicheiometric water concentration. For the first reaction $\Delta H^\ddagger \simeq 22$ kJ mol^{-1} and $\Delta S^\ddagger \simeq -202$ J mol^{-1} K^{-1}; for the second reaction $\Delta H^\ddagger = 22 \pm 1$ kJ mol^{-1} and $\Delta S^\ddagger = -216 \pm 3$ J mol^{-1} K^{-1}. We interpret our results in terms of cyclic transition states involving trimeric water. Ours is the first kinetic investigation to detect the two-stage process of aniline formation.

EARLIER studies[1,2] show that, in the presence of a sufficient excess of water, the hydrolysis of an isocyanate leads to the carbamic acid, which subsequently loses carbon dioxide [equation (1)]. If the ratio [H_2O] : [RNCO] is not sufficiently large, reactions between the primary products and unreacted isocyanate lead to the symmetrical urea [equations (2) and (3)]. The kinetics of hydrolysis have yet to be studied under really satisfactory conditions.[3]

$$RN{=}C{=}O + H_2O \longrightarrow RNHCO_2H \longrightarrow RNH_2 + CO_2 \quad (1)$$

$$RNH_2 + RNCO \longrightarrow (RNH)_2CO \quad (2)$$

$$RNHCO_2H + RNCO \longrightarrow (RNHCO)_2O \longrightarrow (RNH)_2CO + CO_2 \quad (3)$$

In one previous kinetic study Tiger *et al.*[4] examined the hydrolysis of phenyl isocyanate and of methyl isocyanate in aqueous dioxan using high water concentrations (1.5—12 mol dm^{-3}). Having established[2] that no urea formation occurs under these conditions, the authors interpret their measurements in terms of slow carbamic acid formation followed by fast (and therefore kinetically insignificant) loss of carbon dioxide [*cf.* equation (1)]. It is clear from their results that their observed rate constants increase more rapidly than do their stoicheiometric water concentrations. In the light of other work[3] on the alcoholysis of isocyanates and on the hydrolysis of ketens, this fact strongly suggests the involvement of polymeric water in the reaction. However, the authors do not consider this possibility and rationalise their results in terms of a medium effect on the reactivity of monomeric water. In the present kinetic study we have succeeded in examining the hydrolysis of 4-chlorophenyl isocyanate in diethyl ether as solvent at water concentrations sufficient to avoid urea formation but much lower than those used by Tiger *et al.*

EXPERIMENTAL

Materials.—Anhydrous diethyl ether was fractionally distilled from sodium. Karl Fischer titration showed the water concentration in the purified solvent to be $5.0 \pm 0.5 \times 10^{-3}$ mol dm^{-3}. 4-Chlorophenyl isocyanate was purified as before.[5] Water was doubly distilled in an all-glass apparatus.

Kinetic Arrangements.—Stock solutions of the isocyanate in ether were made up by weight. Suitable aliquot portions of these stock solutions, maintained at the chosen reaction temperature, were added to 15 ml volumetric flasks containing weighed amounts of water dissolved in ether also at the reaction temperature. The resulting mixture was made up to the mark with more solvent. Portions of reaction mixtures were quickly transferred to a stoppered spectrophotometer cell (4 cm path) which served as the reaction vessel. The cell was placed in the thermostatted compartment of a Unicam SP 8000 recording spectrophotometer. The blank cell contained solvent. Spectra were scanned at appropriate intervals. The water concentration in a reaction mixture ($10^{-2} <$ [H_2O] < 0.5 mol dm^{-3}) was always in great excess of the initial isocyanate concentration (usually 10^{-5} mol dm^{-3}). The reaction was studied at three temperatures.

Reaction Products.—Examination of final spectra obtained in kinetic runs showed that with [RNCO] $\simeq 10^{-5}$ mol dm^{-3}. and [H_2O] $> 10^{-2}$ mol dm^{-3} the only organic product was 4-chloroaniline, obtained in effectively quantitative yield. Preparative scale experiments showed that at appreciably higher isocyanate concentrations ($\gtrsim 10^{-4}$ mol dm^{-3}) significant amounts of the symmetrical urea are formed, the exact product composition depending upon [RNCO] and upon the ratio [H_2O] : [RNCO]. For example when [RNCO] $= 6 \times 10^{-4}$ mol dm^{-3} and [H_2O] $= 0.3$ mol dm^{-3} the product is *ca.* 70% 4-chloroaniline and *ca.* 30% 1,3-bis-4-chlorophenylurea. These results are in line with the pattern of earlier work.[1,2] Urea formation did not intrude in our kinetic experiments.

RESULTS AND DISCUSSION

Spectral Changes during Kinetic Runs.—In the accessible region for measurement ($\gtrsim$225 nm) the isocyanate has an absorption maximum centred on 234 nm ($\varepsilon_{\text{max.}}$ 1.6×10^5 mol^{-1} dm^2) and a much weaker absorption band at 277 nm ($\varepsilon_{\text{max.}}$ 1.4×10^4 mol^{-1} dm^2). 4-Chloroaniline has two strong bands. The first partly overlaps the isocyanate absorption at 234 nm and has $\varepsilon_{\text{max.}}$ 1.5×10^5 mol^{-1} dm^2 at 247 nm; the second has its maximum at 302 nm ($\varepsilon_{\text{max.}}$ 2.1×10^4 mol^{-1} dm^2) where the isocyanate absorption is negligible. As reaction proceeds there occurs first a fall in isocyanate absorption (at 234 nm) associated with an isosbestic point at 239 nm and a rise in absorption on its long wavelength side (Figure 1).

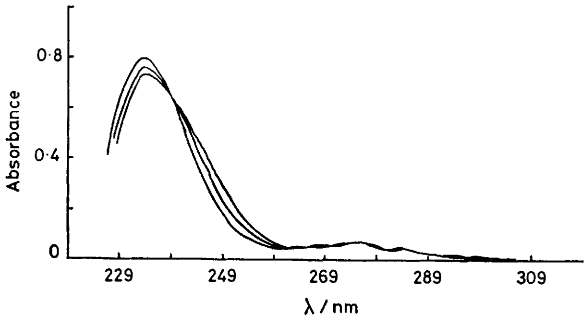


FIGURE 1 Typical initial spectral changes

Negligible aniline is formed at this stage; these changes therefore represent the formation of an intermediate. After this initial period, whose length depends upon the water concentration, aniline begins to be formed in significant amounts (as judged from the absorption at 302 nm) and the isosbestic point at 239 nm is lost. In the final stages of reaction, when the isocyanate concentration has become very small, isosbestic points appear at 245, 269, and 280 nm (Figure 2). These observations are consistent with the reaction sequence of equation (4) in which the intermediate (I) has an absorption maximum between 234 and 244 nm and negligible absorption at 302 nm. It is presumably the carbamic acid [*cf.* equation (1)]. Consistent with this

$$\mathrm{RNCO} \xrightarrow[\mathrm{H_2O}]{k_1} \mathrm{(I)} \xrightarrow{k_2} \mathrm{RNH_2} + \mathrm{CO_2} \qquad (4)$$

interpretation is the fact that (I) absorbs in the same region as the corresponding ester, ethyl 4-chlorophenylcarbamate.[6] The instability of the carbamic acid, the overlapping spectra, and the ratio of the rate constants in equation (4) make it impossible to obtain directly an accurate extinction coefficient for species (I) (or, what is the same thing, its absolute concentration in the reaction mixtures). A normal kinetic analysis[7] of the consecutive reactions (4) is therefore not possible. However, a satisfactory analysis can readily be achieved for the present system by using a slightly modified procedure, as shown below.

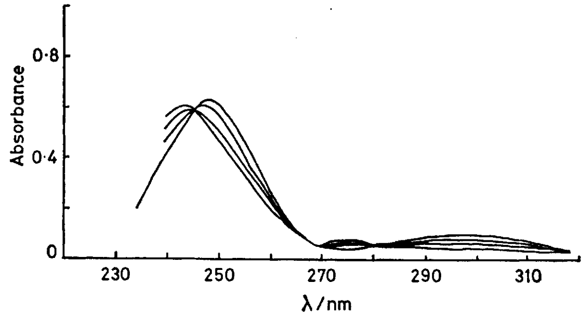


FIGURE 2 Typical final spectral changes

Rate Constants.—The analysis is facilitated by the fact that in equation (4) we find that k_1 is significantly greater than k_2 under all conditions. Also 4-chloroaniline formation can be followed unambiguously at 302 nm. At any given water concentration after the initial stages [when the principal process occurring is the relatively rapid formation of (I)] a plot of ln $(A_\infty - A_t)$ against time, where A_t and A_∞ are the absorbances at 302 nm at time *t* and at infinity, respectively, is rectilinear (Figure 3). Thus over the latter part of the reaction the formation of the aniline is a simple first-order process. For this phase we have equation (5). Values of k_2, calculated from the slope of plots such as Figure 3, are

$$\begin{aligned} \mathrm{d[RNH_2]}/\mathrm{d}t &= k_2(\mathrm{[RNH_2]_\infty} - \mathrm{[RNH_2]}_t) \\ &= k_2(\mathrm{[RNCO]_0} - \mathrm{[RNH_2]}_t) \\ &= k_2\{\mathrm{[RNCO]}_t + [\mathrm{(I)}]_t\} \\ &\simeq k_2[\mathrm{(I)}]_t = -\mathrm{d}[\mathrm{(I)}]/\mathrm{d}t \qquad (5) \end{aligned}$$

in the Table. They were reproducible to within ±5%. Similar behaviour is found at each temperature. It is clear that k_2 depends strongly on the stoicheiometric water concentration, $\mathrm{[H_2O]_S}$, and at 25 °C a plot of log k_2 against log $\mathrm{[H_2O]_S}$ is rectilinear with slope 2.98 (*r* 0.998). Furthermore, a plot of $k_2/\mathrm{[H_2O]_S}^2$ against $\mathrm{[H_2O]_S}$ is rectilinear and passes through the origin with slope 3.92×10^{-3} mol^{-3} dm^{9} s^{-1} (*r* 0.995). Hence, equation (6) holds.

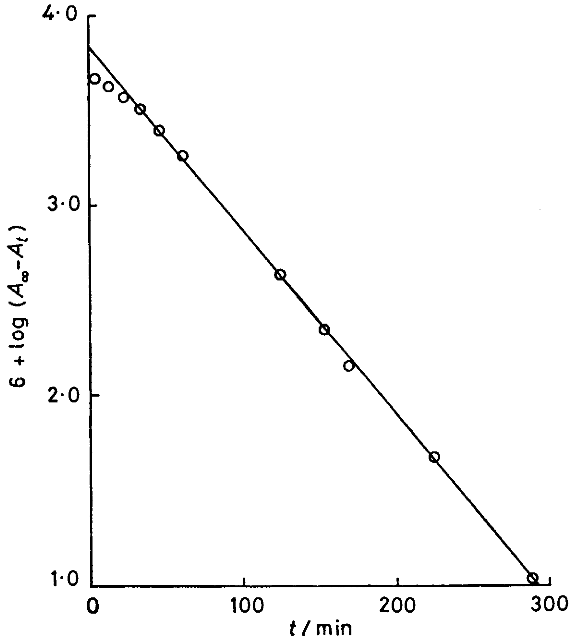


FIGURE 3 Typical first-order plot. $\mathrm{[RNCO]_0}$ 1.24×10^{-5} mol dm^{-3}; $\mathrm{[H_2O]_S}$ 0.344 mol dm^{-3}; temperature 25 °C; *A* absorbance at 302 nm

$$k_2 = k_3\mathrm{[H_2O]_S}^3 \qquad (6)$$

Lillford and Satchell[8] found no evidence for the formation of polymeric water species in significant amounts in ether solution at water concentrations $\lesssim 0.3$ mol dm^{-3};

$[H_2O]_S$ will therefore be equivalent to the concentration of water monomers. From equation (7) it follows that

$$3H_2O \overset{K_T}{\rightleftharpoons} (H_2O)_3 \qquad (7)$$

the concentration of water trimers, $[H_2O]_T$, is $K_T[H_2O]_S^3$. Our results for k_2 therefore suggest that trimeric water may be involved as a catalyst in the conversion of (I) to 4-chloroaniline and carbon dioxide [equation (8)]. For

$$(I) + (H_2O)_3 \xrightarrow{k_T} RNH_2 + CO_2 + (H_2O)_3 \qquad (8)$$

$$-d[(I)]/dt = k_T[(I)][H_2O]_T = k_TK_T[H_2O]_S^3\,[(I)] = k_3[H_2O]_S^3\,[(I)] \qquad (9)$$

this reaction we have equation (9) as found experimentally. Values of k_3 obtained from plots of $k_2/[H_2O]_S^2$ against $[H_2O]_S$ are 3.03×10^{-3} (r 0.995), 3.92×10^{-3} and 4.65×10^{-3} (r 0.997) mol^{-3} dm^9 s^{-1} at 17, 25, and 30 °C, respectively. These values were used to calculate the enthalpy and the entropy of activation by computing the linear least squares fit to the equation $\ln(k_3/T) = \ln(k/h) - \Delta H^‡/RT + \Delta S^‡/R$. We find $\Delta H^‡ = 22 \pm 1$ kJ mol^{-1} and $\Delta S^‡ = -216 \pm 3$ J mol^{-1} K^{-1}.

Dependence of k_2, $t_{max.}$, and k_1 on water concentration. Units of k_1 and k_2 are s^{-1}, of $[H_2O]_S$ mol dm^{-3}, and of $t_{max.}$ s. Values of $[H_2O]_S$ include residual water in purified solvent

$10^2[H_2O]_S$	10^5k_2	$10^{-3}t_{max.}$	10^5k_1
(i) At 17.0 °C			
21.6	3.03	13	15
30.8	9.35	3.9	55
35.9	14.3	2.1	112
40.1	19.3	1.8	120
42.6	23.8	1.6	126
(ii) At 25.0 °C			
8.68	0.273	135	1.6
12.9	0.873	45	4.5
15.3	1.38	30	6.8
18.4	2.27	15	15
24.5	5.62	7.8	25
28.8	9.22	4.5	45
33.4	14.9	2.4	88
34.4	16.6	2.2	98
36.9	19.5	2.1	96
41.6	27.8	1.4	145
(iii) At 30.2 °C			
17.6	2.50	13.5	16
22.0	5.05	7.2	30
30.2	12.4	3.0	71
31.0	14.2	2.6	81
35.4	20.6	1.6	142

To obtain k_1 in equation (4) attention must be focused on the initial stages of the reaction and on the spectral region 230—260 nm. Here all three species [(I), RNCO, RNH_2] contribute to the absorbance, but the knowledge of the concentration of aniline present at any time permits estimation of $t_{max.}$, the time taken for (I) to reach its maximum concentration; $k_2t_{max.}$ then leads [7] to k_1/k_2 and hence k_1. Typical results are in the Table. Values of k_1 were reproducible to within ±15%.

We find that (i) like k_2, k_1 depends upon $[H_2O]_S^3$ (at 25 °C the plot of log k_1 against $\log[H_2O]_S$ has slope 2.9 (r 0.997) and the plot of $k_1/[H_2O]_S^2$ against $[H_2O]_S$ passes through the origin with a slope 2.07×10^{-2} mol^{-3} dm^9 s^{-1} (r 0.968), and (ii) $k_1/k_2 \simeq 5$—6 and shows no significant variation with temperature. The first step of equation (4) must therefore be associated with a $\Delta H^‡$ value very similar to that of the second step, but with a $\Delta S^‡$ value which is (slightly) more positive ($\Delta S^‡ \simeq -202$ J mol^{-1} K^{-1}).

The satisfactory nature of our overall analysis can be seen from the plots of Figure 4, where experimental values of the ratio $[RNH_2]_t : [RNCO]_0$ are compared with the values predicted theoretically [7] by our derived values of k_2 and k_1/k_2. Good agreement of this sort is obtained for all runs and computerised curve-fitting confirms that $k_1/k_2 = 5.6 \pm 0.4$. Use of this value to calculate k_1 from k_2, and thence [RNCO], [(I)], and $[RNH_2]$ at a given time, shows that the carbamic acid has its maximum absorption at 238 nm with $\varepsilon_{max.}$ 1.5×10^5 mol^{-1} dm^2.

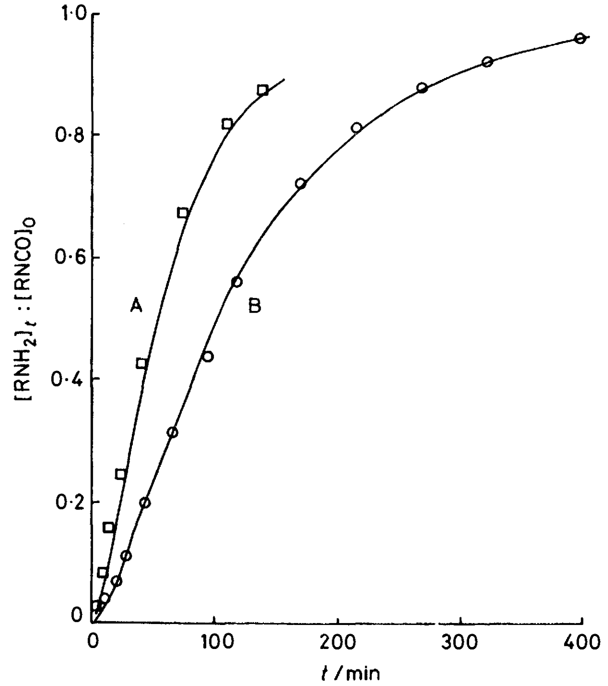
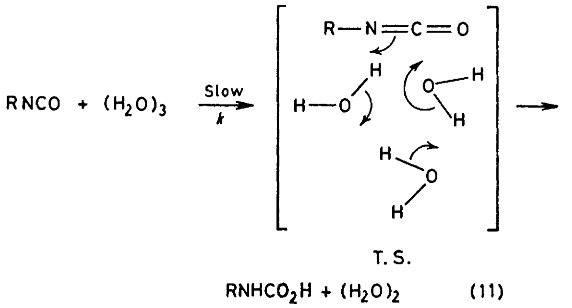
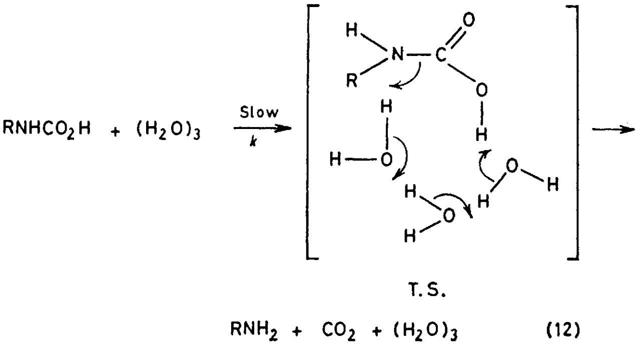


FIGURE 4 Calculated and theoretical values of $[RNH_2]_t : [RNCO]_0$. The continuous lines represent the theoretical values and the points are the experimental values. For A (at 25 °C) $k_2 = 2.78 \times 10^{-4}$ s^{-1} and $k_1/k_2 = 5.2$; for B (at 30 °C) $k_2 = 1.42 \times 10^{-4}$ s^{-1} and $k_1/k_2 = 6.0$

Detailed Mechanism.—As shown above, the kinetic dependences on $[H_2O]_S^3$ are compatible with the involvement of trimeric water. We choose to interpret the results in this way since such an interpretation (*a*) is in general keeping with much recent work on the alcoholysis of isocyanates and other similar reactions in aprotic solvents [3] and (*b*) seems more likely than an interpretation in terms of a medium effect on the monomer reactivity arising from increased polarity of the solvent. In our experiments the water concentration was never greater than 0.8% (w/w) of the solvent. Moreover, in ether-like solvents, water and alcohol monomers (and dimers) have been considered [3,5] likely to be less reactive than the trimers since the former are hydrogen-bonded to the solvent whereas the latter are probably cyclic and can more readily open to form cyclic transition states. Our detailed scheme for the hydrolysis is therefore equations (10)—(12). We identify the intermediate (I) with the carbamic acid although it might perhaps be its tautomer, R-N=C(OH)$_2$. Our observed activation parameters are very similar to those previously found characteristic of his type of cyclic mechanism involving polymeric species.[3] Moreover the bonding changes implicit in the two transition states are at least compatible with reaction (12) being slower than reaction (11). Ours is the first kinetic study to detect the intermediate carbamic acid. but previous qualitative evidence [1] does suggest that its decomposition is slower than its formation, as now found. Why Tiger *et al.*[4] assume the contrary is not clear, Precisely to what stage of the reaction their measurements actually refer can only be conjectured, but our results suggest they were following the rate of aniline formation.

$$3\,H_2O \rightleftharpoons (H_2O)_3 \qquad \text{Fast} \qquad (10)$$





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