

Kinetics of the Hydrolysis of the Potentially Pesticidal *N*-(4-Pyridyl)carbamates in Micellar Solution

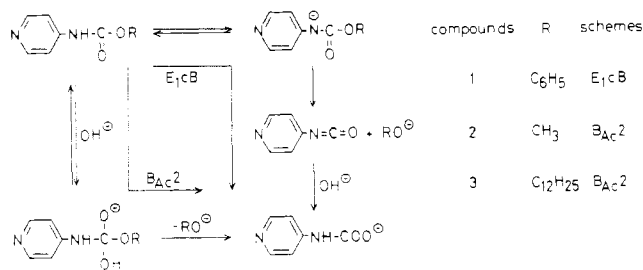
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The kinetics of hydrolysis of the potential pesticides, phenyl, methyl, and dodecyl *N*-(4-pyridyl)carbamates (1-3, respectively), were investigated in micellar H₂O-dioxane solutions containing sodium dodecyl sulfate (SDS) or cetyltrimethylammonium bromide (CTAB) and compared with the kinetics in H₂O-dioxane media. For compounds 1 and 2, the rate constants observed are slightly reduced by the SDS micellar media. On the other hand, the CTAB micellar media speed up the hydrolysis rate for 1, whereas a small decrease is observed for 2. These results can be explained by means of the pseudophase kinetic model coupled with the mechanisms of hydrolysis of these compounds in water-dioxane solution. Lastly, for 3, the micellar SDS or CTAB media inhibit the hydrolysis reaction, which may be attributed to the tensioactive character of these substances.

The carbamates have a variety of biological actions. The aryl esters of the *N*-methyl- and *N,N*-dimethylcarbamic acids such as carbaryl and carbofuran have insecticidal activity while the aliphatic carbanilates such as propham and chlorpropham have herbicidal activity. In human therapeutics, esters of unsubstituted carbamic acid such as meprobamate and mebutamate are used as tranquilizers and muscle relaxants.

We have recently synthesized a series of aryl and alkyl *N*-(4-pyridyl)carbamates with potent herbicidal activity and showed that the E1cB or B_{Ac}2 mechanisms generally found for carbamates (Bergon and Calmon, 1983; Bergon et al., 1985) also apply to these compounds (Matondo et al., 1989). The switch between mechanisms E1cB and B_{Ac}2 depends on the nucleofugal potential of the leaving group RO⁻.



The poor solubility of many pesticides in water means that they are often used in micellar solutions. It is thus important to determine the effects of such media on their kinetics of hydrolysis. We report here the results obtained in anionic and cationic media with three *N*-(4-pyridyl)carbamates of varying hydrophobicity, selected from compounds examined in a previous study (Matondo, 1987) in which the mechanisms were determined, E1cB for 1 and B_{Ac}2 for 2 and 3.

EXPERIMENTAL SECTION

Chemicals. Phenyl, methyl, and dodecyl *N*-(4-pyridyl)carbamates were synthesized by known methods previously described (Matondo, 1987).

Sodium dodecyl sulfate (SDS) and cetyltrimethylammonium bromide (CTAB), used as anionic and cationic surfactants, were analytical reagent grade and were used without further purification. Fresh stock solutions were prepared for each series of experiments.

Nitrogen was bubbled through the distilled water used to make the buffer solutions and the sodium hydroxide solutions. The ionic strength of the solutions was kept constant ($\mu = 1.0$) by addition of KCl.

Apparatus and Kinetic Methods. The time course of the hydrolysis reaction was followed by the change in optical density of substrate or product. This was recorded at a fixed wavelength, 276 nm for 1 and 240 nm for 2 and 3, in a Cary 210 UV spectrophotometer equipped with thermostated sample holder (± 0.1 °C). The hydrolysis reaction was first-order with respect to the substrate.

The observed rate constants k_{obsd} were determined from the relationships

$$\log(A_t - A_\infty) = \log(A_0 - A_\infty) - (k_{\text{obsd}}/2.303)t$$

where A_0 , A_∞ , and A_t are the absorbance readings at time $t = 0$, at the completion of reaction, and at time t , respectively. The rate constants were obtained by a least-squares fit with a regression coefficient of 0.99.

Owing to the low solubility of the *N*-(4-pyridyl)carbamates in water, the rate constants of hydrolysis were determined at a concentration of 5×10^{-5} M in a mixture of water and dioxane (3:1, v/v) containing either 0.1 M sodium hydroxide (pH 13.42) for compounds 2 and 3 or 10^{-2} M sodium borate (pH 9.18) for compound 1.

The pH measurement was carried out by using a Radiometer PHM 64 pHmeter equipped with a Radiometer GK 2321 C electrode.

The critical micellar concentrations (cmc) were determined from surface tension (obtained by means of a Prolabo Tensiomat No. 3 apparatus) versus concentration plots. In water/dioxane (3:1, v/v) at 25 °C in the presence of sodium hydroxide (0.1 M) or sodium borate (10^{-2} M), the cmc values of SDS are 2.50×10^{-5} and 1.25×10^{-5} M, respectively, and the cmc

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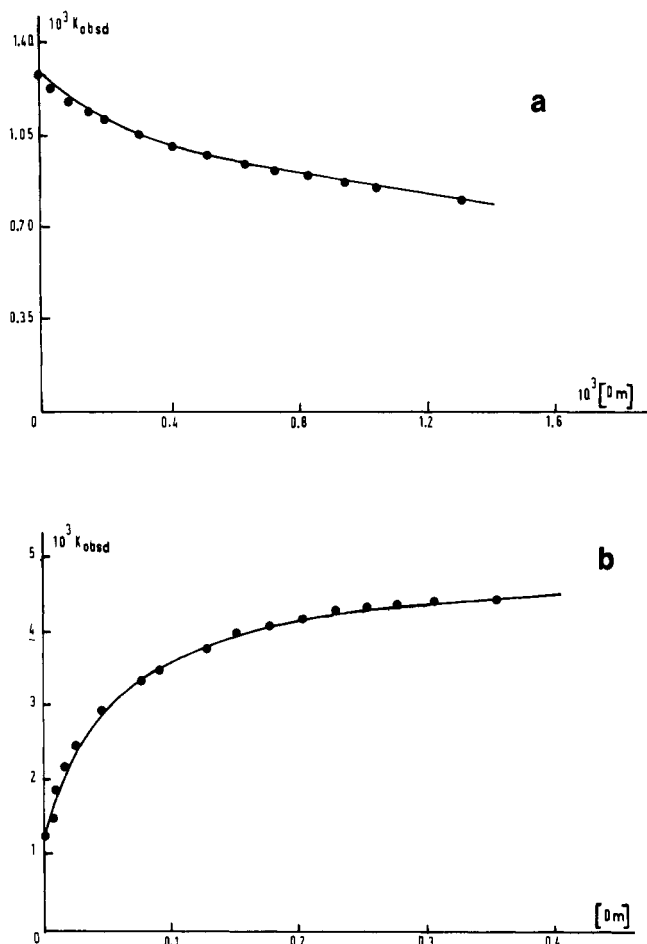


Figure 1. Plot of k_{obsd} vs the micellized surfactant concentration $[D_m]$: (a) influence of SDS on compound 1 in a mixture of water-dioxane (3:1, v/v) at 25 °C; (b) influence of CTAB on compound 1 in a mixture of water-dioxane (3:1, v/v) at 25 °C.

values of CTAB, 3.80×10^{-5} and 2.82×10^{-4} , respectively.

The critical concentration of compound 3 could not be determined due to its rapid hydrolysis.

RESULTS AND DISCUSSION

For compounds 1 and 2, the changes in k_{obsd} at 25 °C as a function of micellized surfactant concentration $[D_m]$ in the various media are plotted on Figures 1a and 2a for SDS micelles and on Figures 1b and 2b for CTAB micelles. $[D_m]$ is given by $[D_m] = [D_T] - cmc$, $[D_T]$ being the total concentration of surfactant in the medium.

For amphiphile 3, the plots k_{obsd} vs $[D_T]$ were used to take into account the comicellization phenomena.

According to the results from Hegarty and Frost (1973) and Broxton (1984), we assumed that, for the compounds studied, similar mechanisms took place in the micellar medium as in the water-dioxane system. The results can thus be explained by means of the pseudophase kinetic model proposed by Menger and Portnoy (1967) and developed by Bunton (1979), Romsted (1982), and Vera and Rodenas (1986a,b). These authors consider the total volume of the micelles as a separate phase uniformly distributed in the aqueous phase and the reaction occurring in both phases according to the following scheme

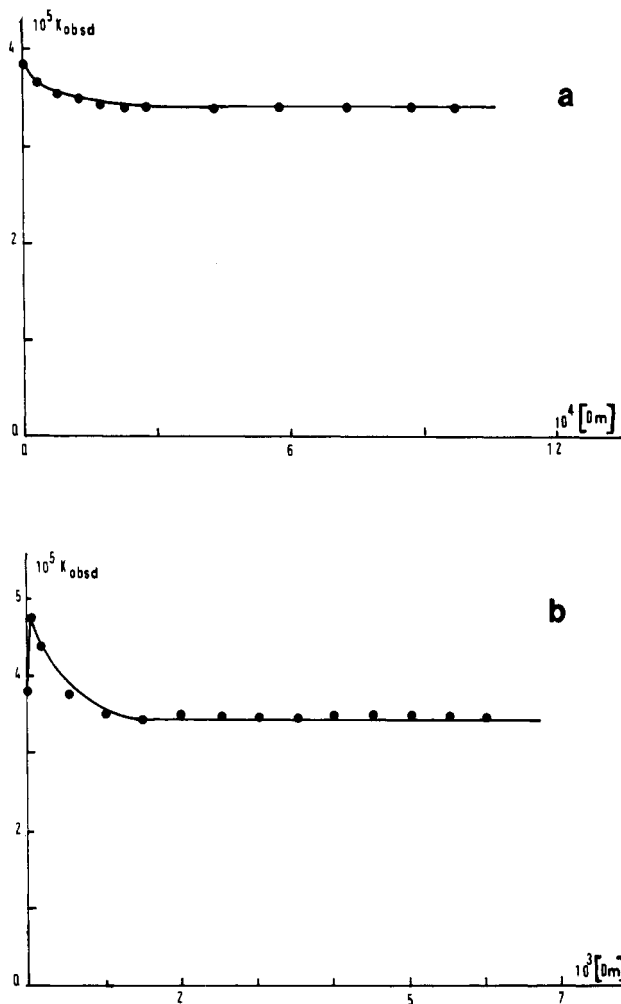
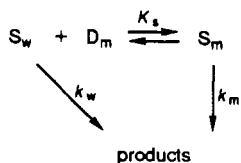


Figure 2. Plot of k_{obsd} vs the micellized surfactant concentration $[D_m]$: (a) influence of SDS on compound 2 in a mixture of water-dioxane (3:1, v/v) at 25 °C; (b) influence of CTAB on compound 2 in a mixture of water-dioxane (3:1, v/v) at 25 °C.

with $K_s = [S_m]/[S_w][D_m]$. w and m signify the aqueous and micellar phases respectively. D_m is the micellized surfactant, S_m the substrate in the micelles, and S_w the substrate in the water. K_s is the equilibrium constant; k_w and k_m are the rate constants in the aqueous and micellar phases, respectively.

The rate law is expressed as

$$v = k_{obsd}[S_T] = k[OH^-_T][S_T] = k_w[S_w] + k_m[S_m]$$

with

$$[S_T] = [S_w] + [S_m] \quad [OH^-_T] = [OH^-_m] + [OH^-_w]$$

$$k_{obsd} = \frac{k_w + k_m K_s [D_m]}{1 + K_s [D_m]} \tag{1}$$

For a pseudo-first-order reaction in which OH^- act as a nucleophile, the relation (1) is useable with $k_w = k'_w[OH^-_w]$ being the apparent pseudo-first-order rate constant in the aqueous phase and $k_m = k'_m[OH^-_m]/[D_m]$ the apparent pseudo-first-order constant in the micelle medium. Since $k_{obsd} = k[OH^-_T]$ and $[OH^-_m]/[D_m] = m_{OH^-}$, k_{obsd} can be expressed by

$$k_{obsd} = \frac{1}{1 + K_s [D_m]} [k'_w [OH^-_T] + (k'_m K_s - k'_w) m_{OH^-} [D_m]] \tag{2}$$

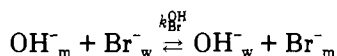
Moreover, when the OH^- and Br^- ions compete for access

Table I. Values of k_w , k_m , K_a , and $[S_m]/[S_T]^a$ for Compounds 1 and 2 in the Different Media

substrate	H ₂ O/dioxane	SDS			CTAB		
	k_{1w} , s ⁻¹	k_w , s ⁻¹	K_a , M ⁻¹	$[S_m]/[S_T]$	k_m , s ⁻¹	K_a , M ⁻¹	$[S_m]/[S_T]$
1	1.28×10^{-3}	0.80×10^{-3}	4.65×10^2	0.18	5.02×10^{-3}	18.89	0.84
2	3.85×10^{-5}	3.40×10^{-5}	1.20×10^2	0.06	6.35×10^{-6}	46.60	0.05

^a $[S_m]$ used corresponds to beginning of the level in the plot $k_{\text{obsd}} = f([D_m])$. ^b k_{1w} = rate constant in H₂O-dioxane medium (Matondo et al., 1989).

to the charged micellar surface, Romsted (1984) assumes that the interactions are governed by an ion-exchange equilibrium such as



Considering that the β fraction of the neutralized micellar surface is constant ($\beta = 0.8$ for a halogenated counterion; Romsted, 1982), m_{OH} is expressed versus $K_{\text{Br}}^{\text{OH}}$ from the equation (3).

$$m_{\text{OH}}^2 + m_{\text{OH}} \left[\frac{[\text{OH}_T^-] + k_{\text{Br}}^{\text{OH}}[\text{Br}_T^-]}{(K_{\text{Br}}^{\text{OH}} - 1)[D_m]} - \beta \right] - \frac{\beta[\text{OH}_T^-]}{(K_{\text{Br}}^{\text{OH}} - 1)[D_m]} = 0 \quad (3)$$

The experimental results can be fitted to eq 1 or 2, and k_w , k_m , and K_a are determined by simulation technique. Table I shows the values of k_w , k_m , K_a , and $[S_m]/[S_T]$ for compounds 1 and 2.

For these compounds, the presence of SDS micelles has little influence. The shapes of curves 1a and 2a and the value of k_w (compared to k_{1w} in H₂O/dioxane) show that the reaction essentially takes place in the aqueous pseudophase. The reduction in k_{obsd} (Figures 1a and 2a) is attributed to micelle-substrate association in agreement with E1cB or B_{Ac}2 mechanisms. For compound 1, such associations hinder ionization of substrate S to S⁻ and, for compound 2, inhibit the reaction between S and OH⁻ because of the repulsion between the ions and the negatively charged micelles.

For compound 1, the rates of hydrolysis in CTAB micellar medium are determined at pH 9.18, lower than the pK_a value of this substance ($pK_a \approx 12$) estimated in comparison with the pK_a of 2,2,2-trichloroethyl N-(4-pyridyl)carbamate ($pK_a = 12.84$; Matondo et al., 1989) as was observed for phenyl and 2,2,2-trichloroethyl N-acetylcarbamates (Bergon and Calmon, 1976). Under these conditions, the increase in k_{obsd} (Figure 1b) probably results, on the one hand, from an increase of S⁻ concentration in the micellar cationic pseudophase in agreement with the behavior of various substances as phenols and acetonitriles (Minch et al., 1975). The 4-fold higher rate of hydrolysis ($k_m \approx 4k_w$; Table I) can be accounted for by an association between S⁻ and the cationic micelles, which tend to favor the transition state, probably due to the poor polarity of the Stern layer (with respect to the polarity of the water) where the reaction takes place (Dunlap and Cordes, 1968).

On the other hand, the increase in k_{obsd} could also be explained by a catalytic micellar decomposition of S⁻ giving the isocyanate and phenol forms. This result is in good agreement with those relative to the E1cB hydrolysis of the 2-nitrophenyl cyanoacetate in micellar media with pH values smaller than the pK_a value of this compound (Al-Lohedan and Bunton, 1981).

For compound 2, curve 2b is characteristic of an ion exchange (Br⁻ and OH⁻) at the surface of the CTAB micelles. With small quantities of Br⁻ ions in the medium,

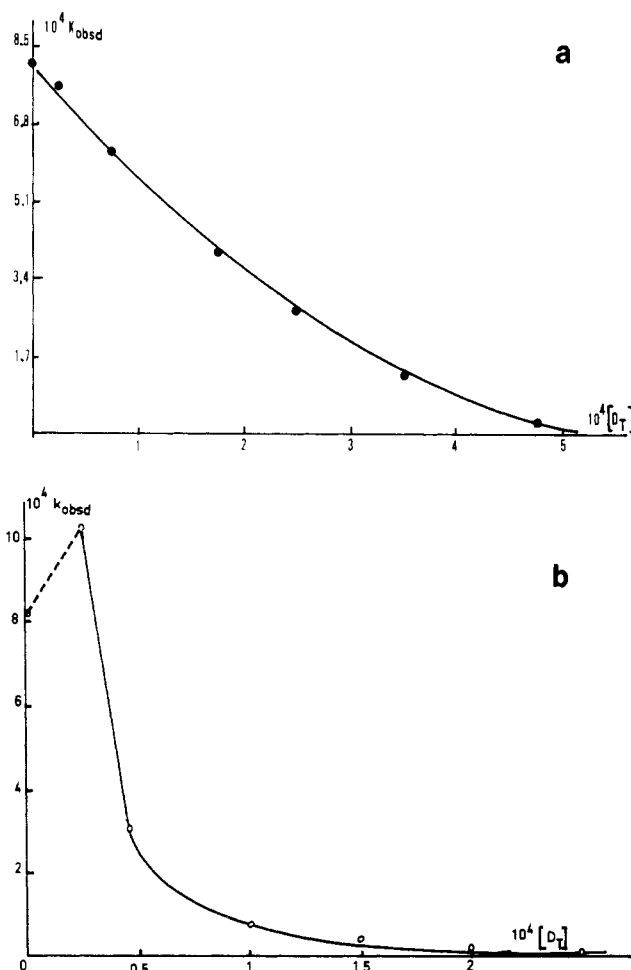


Figure 3. Plot of k_{obsd} vs the total surfactant concentration $[D_T]$: (a) influence of SDS on compound 3 in a mixture of water-dioxane (3:1, v/v) at 25 °C; (b) influence of CTAB on compound 3 in a mixture of water-dioxane (3:1, v/v) at 25 °C.

the excess OH⁻ ions readily react with the substrate in the positively charged micelles (rising part of the curve). As the number of Br⁻ ions increases, competition between OH⁻ and Br⁻ for access to the positive charges on the micelles is in favor of Br⁻ and the rate of reaction falls. When the quantity of Br⁻ ions is such that $[D_m] > 2 \times 10^{-3}$ M, the reaction takes place essentially in the aqueous pseudophase (level part of the curve). The calculated exchange constant $K_{\text{Br}}^{\text{OH}} = 0.051$ is indicative of a weak association between OH⁻ and the micelles. This value is close to that found by Bunton (1979).

Lastly, the K_a and $[S_m]/[S_T]$ values obtained are in good agreement with the poor hydrophobic character of compound 2 as compared to that of compound 1.

The amphiphilic structure of compound 3 causes the peculiar behavior observed. Although the pseudophase model may still apply, eq 2 can no longer be employed for calculation of the kinetic parameters, as it includes $[D_m]$, the concentration in the SDS or CTAB micelles. With compound 3, mixed-micelles substrate/CTAB or

substrate/SDS are formed. The fact that the substrate is readily hydrolyzed, forming a product that is itself a surfactant, complicates the situation and makes quantitative analysis of the aggregation phenomena more difficult. Curves a and b in Figure 3 can thus only be interpreted qualitatively.

Figure 3a shows a rapid fall in reaction rate in the presence of SDS micelles, indicating a significant association between the substrate and the negatively charged micelles hindering the reaction with OH^- . For SDS concentration above 5×10^{-5} M, all the substrate appears to be associated with the micelles and the reaction does not take place. This graph can be compared to Figure 2a for the nonsurfactant compound 2.

Figure 3b is similar to Figure 2b, although the maximum is found at a CTAB concentration (2.5 M) lower than the critical micellar concentration of pure CTAB. This indicates the presence of comicelles of CTAB and substrate 3. Competition between Br^- and OH^- ions for access to the positively charged micelles is partly responsible for the slowing of the rate as $[\text{D}_T]$ increases. Complete inhibition of the reaction is thus due to total comicellization of the substrate, thereby hindering access of OH^- ions to the reactive site.

In conclusion, these results throw more light on the mechanism of hydrolysis of *N*-(4-pyridyl)carbamates. Especially, the behavior in micellar media is consistent with the E1cB or B_{Ac}2 mechanism proved in aqueous media. The study also shows that it is possible to increase, reduce, and even prevent hydrolysis in micellar media, either by altering the substituent group on the carbamate or by changing the surfactant. These results open new perspectives for the formulation of pesticides belonging to this chemical class.

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