Catalysed hydrolysis of *O*-alkyl *O*-*p*-nitrophenyl chloromethylphosphonates in the cationic surfactant–poly(ethylenimine)–water system

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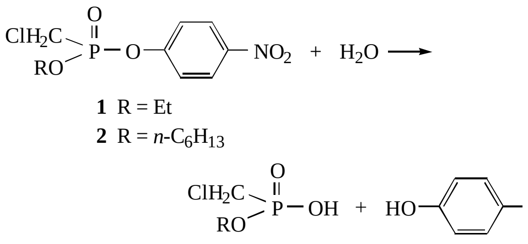
The catalytic effect in the title system was found to depend on the nature of surfactants and substrates and on the surfactant-to-poly(ethylenimine) ratio.

Previously,[1–3] the influence of direct and reverse micelles, microemulsions and liquid crystals on the rate of nucleophilic substitution reactions of phosphorus acid esters has been investigated. Surfactant solutions considered as biomimetic structures acting *via* a host–guest mechanism[4] are of considerable interest. The macromolecular nature of proteins attracted particular interest in the catalytic systems based on synthetic polymers.[5,6] The reactivity in micelles was widely studied, whereas the effects of polyelectrolytes and mixed surfactant–polymer systems on the reaction rate were scarcely examined.

We examined the hydrolysis of *O*-alkyl *O*-*p*-nitrophenyl chloromethylphosphonates **1** and **2** (Scheme 1) in aqueous solutions of poly(ethylenimine) (PEI), micellar solutions of cetyltrimethylammonium bromide (CTAB) and cetyldimethylethylammonium bromide (CDAB) and mixed surfactant–polymer solutions. At present, the behaviour of mixed surfactant–polymer solutions attracts a wide attention.[7–9] Nevertheless, little is known on the interactions in such complex solutions, which become more complicated when reagents are added. Because conductometry is widely used for studying surfactant–polymer interactions,[9] we examined the structural behaviour of the systems used as the reaction medium by conductivity measurements.



Scheme 1

Substrate **1** was prepared as described in ref. 10. Commercial CTAB and CDAB (Sigma), and branched PEI (molecular weight of 30000, Aldrich) were used. Solutions were made in double-distilled water. The reaction was monitored by the absorption of *p*-nitrophenolate at 400 nm using a Specord M-400 spectrophotometer with temperature-controlled cell holders. The substrate concentration (5×10^{-5} mol dm^{-3}) was much lower than the nucleophile concentration. The observed rate constants (k_{obs}) were determined from the equation: $\ln(A_\infty - A) = -k_{obs}t + \text{const}$, where A and A_∞ are the absorbance of micellar solutions at the point t in time and after completion of the reaction, respectively. The k_{obs} values were calculated using the weighted least-squares computing methods from the mean of at least three independent determinations differing by 5%. The electrical conductivity was measured using a CDM-2d conductivity meter (Denmark).

The kinetic data for PEI solutions were treated using the following equation:[11]

$$k_{obs} = \frac{k_w + k_m K'_s C}{1 + K'_s C}, \qquad (1)$$

where k_w and k_m (s^{-1}) are the pseudo-first-order rate constants in the aqueous and micellar phase, respectively, K'_s (dm^3 mol^{-1}) is the binding constant of the substrate, C (mol dm^{-3}) is the PEI concentration below the critical aggregation concentration (c.a.c.).

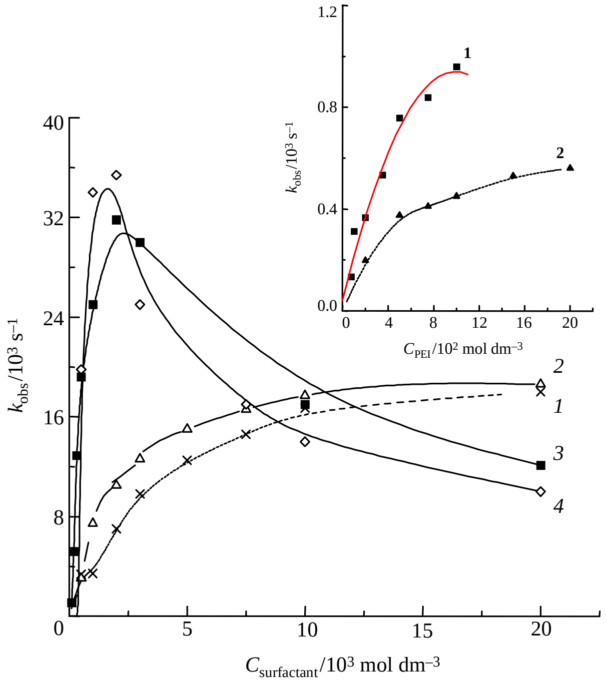


Figure 1 Observed rate constants of hydrolysis of **1** and **2** in the surfactant–water system as a function of surfactant concentration: (*1*) CTAB–**1**, (*2*) CDAB–**1**, (*3*) CDAB–**2**, (*4*) CTAB–**2**. Insert: the observed rate constant of hydrolysis of **1** and **2** in the PEI–water system as a function of PEI concentration.

The kinetic data for the systems based on surfactants were treated in terms of the pseudo-phase model using the equation:[12]

$$k'_{obs} = \frac{k_{2,w} + k_{2,m}K_sK_{Nu}C/V}{(1 + K_sC)(1 + K_{Nu}C)}, \qquad (2)$$

where k'_{obs} (dm^3 mol^{-1} s^{-1}) is the second-order rate constant obtained by dividing the observed pseudo-first-order rate constant k_{obs} by the total nucleophile concentration; $k_{2,w}$ and $k_{2,m}$ (dm^3 mol^{-1} s^{-1}) are the second-order rate constants in the aqueous and micellar phases, respectively; K_s and K_{Nu} (dm^3 mol^{-1}) are the substrate and nucleophile binding constants, respectively; V is the molar volume of the surfactant (assumed equal to 0.3 dm^3 mol^{-1}); C is the surfactant concentration below the critical micelle concentration (c.m.c.).

For comparison, prior to study the kinetics in the mixed surfactant–PEI systems, the hydrolysis of the substrates in individual surfactant and PEI solutions, as well as in water with no catalytic additives, was examined. In unbuffered water, PEI solutions are basic (pH > 9 at concentrations used in the experiment). Under these conditions, basic hydrolysis of the substrates occurs. An increase in the alkyl chain length of the substrates results in a decrease in their reactivity due to an increase in steric hin-

Table 1 Kinetic data treated in terms of the pseudo-phase model.

System	$(k_{obs}/k_w)_{max}$	K_s/dm^3 mol^{-1}	K_{Nu}/dm^3 mol^{-1}	$k_{2,m}$/dm^3 mol^{-1} s^{-1}	F_c^a	F_m^a
1–CTAB	290	233	20	26.9	40	6.7
1–CDAB	283	277	25	23.4	49	5.8
2–CTAB	740	1310	197	5.3	341	1.7
1–CTAB + 0.01 mol dm^{-3} PEI	12.5	422	100	0.0025	149	0.08
1–CTAB + 0.015 mol dm^{-3} PEI	14.2	1670	95	0.0018	207	0.07
1–CTAB + 0.02 mol dm^{-3} PEI	21	1922	251	0.0011	451	0.05
2–CTAB + 0.02 mol dm^{-3} PEI	11.5	3070	270	0.00037	535	0.01
1–CDAB + 0.02 mol dm^{-3} PEI	24.7	1040	460	0.00057	554	0.03
2–CDAB + 0.02 mol dm^{-3} PEI	36.5	2290	535	0.00078	811	0.03

[a] The F_c and F_m values were calculated using the modified equation (2):

$$(k_{obs}/k_w)_{max} = \frac{k_{2,m}}{k_{2,w}} \frac{K_s K_{Nu}}{V(K_s^{1/2} + K_{Nu}^{1/2})^2}.$$

The term on the left expressed as the ratio between the pseudo-first-order rate constants in the micellar system and water describes the maximum acceleration of the reaction. The first term on the right is associated with the influence of the micellar microenvironment (F_m), and the second term reflects concentrating the reagents in micelles (F_c).

drances at the electrophilic phosphorus atom[13] ($k_{2,w}$ are equal to 4.0 and 3.0 dm^3 mol^{-1} s^{-1} for **1** and **2**, respectively).

In micellar CTAB and CDAB solutions at pH 9.2 (a borate buffer), basic hydrolysis also takes place,[2,14] which is accelerated by cationic micelles by more than two orders of magnitude (Figure 1, Table 1). This acceleration in cationic micelles results from the joint contribution of the microenvironment factor (F_m) and the concentration factor (F_c) (Table 1). The former factor quantitatively expresses a change in the intrinsic rate constant of the reaction in the micellar pseudophase, as compared to water, due to alteration in the microenvironments of reagents with their transfer from a polar aqueous phase (dielectric constant of 81) to a lower polarity micellar phase (dielectric constant ranges from 4 in the micellar core to 36 in the Stern layer).[15,16] The latter factor quantitatively expresses an increase in local concentrations of reagents in the micellar pseudo-phase due to electrostatic attraction of hydroxide ions to positively charged micelles where hydrophobic substrates are incorporated.

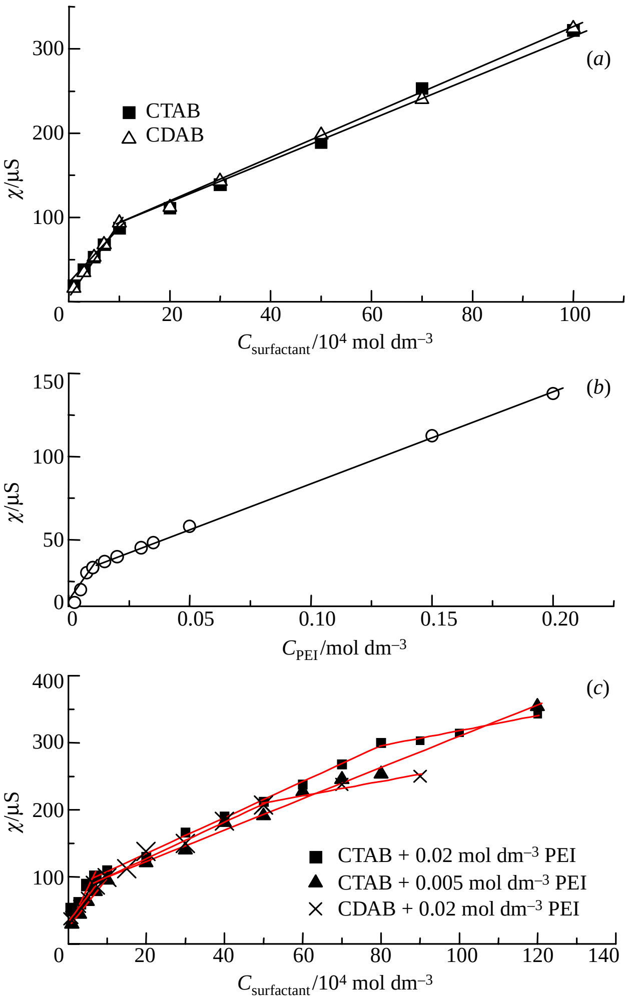


Figure 2 (*a*) Conductivity of the surfactant–water system as a function of surfactant concentration. (*b*) Conductivity of the PEI–water system as a function of PEI concentration. (*c*) Conductivity of the surfactant–PEI–water system as a function of surfactant concentration.

The kinetic data treated in terms of the pseudo-phase model [equation (2)] demonstrate that both the concentration factor and the micellar microenvironment factor make positive contributions to the micellar rate effect (Table 1). A minor effect of the surfactant structure on the reactivity and a pronounced substrate specificity were found in these systems (Figure 1, Table 1). The catalytic effect for substrate **2** is twofold higher than that for **1**, and the k_{obs}–$C_{surfactant}$ curve has a maximum in the case of **2**. The difference between the kinetics of **1** and **2** results from a higher hydrophobicity of the latter. Taking into account the amphiphilic nature of substrate **2**, we examined the behaviour of **2** in solution by conductivity and surface tension measurements; however, no micelle-like aggregates were found. Nevertheless, it is reasonably to assume that highly hydrophobic phosphonate **2** can be involved in the mixed premicellar aggregation with surfactants. This appears from the fact that the catalytic effect is reached at a lower surfactant concentration for **2** as compared to **1** (Figure 1), *i.e.*, a decrease in the c.m.c. is observed.

Previously,[17] we found the general basic catalysis of phosphates in the presence of PEI. In aqueous solutions, PEI is partly protonated depending on pH. The cationic centres formed result in a decrease in the amine basicity due to induction effects and electrostatic interactions. The hydrolysis is catalysed by uncharged amino groups activating the water molecules. In addition, the cationic centres, because of their electrostatic interactions with hydroxide ions, can increase the contribution of alkaline hydrolysis to the observed rate constant.

The observed rate constant of hydrolysis in aqueous PEI solutions for substrate **1** is higher than that for **2** (Figure 1, insert), while in cationic micelles an increase in the reactivity with the substrate hydrophobicity was observed.[3,18] Unlike short-chain homologues, which demonstrate a linear k_{obs}–C_{amine} relationship,[19] the dependence of the observed rate constant on C_{PEI} is non-linear, which is typical of enzymatic and micellar catalysis. The non-linear k_{obs}–C_{PEI} plot can be considered as a kinetic argument in favour of the hypothesis that the aggregation of PEI occurs {this is also confirmed by the conductivity data for the PEI solutions [Figure 2(*b*)]}. The c.a.c. detected as a point of inflection in the conductivity–C_{PEI} plot is equal to 0.01 mol dm^{-3}. Kinetic data for the hydrolysis in the presence of PEI (Figure 1), demonstrate an acceleration of the reaction, as compared to water, for the **1** or **2** by a factor of 5–36 or 5–20, respectively, depending on the PEI concentration. The following data were obtained using equation (1): $k_m = 1.07\times10^{-3}$ s^{-1}, $K'_s = 50$ dm^3 mol^{-1} and c.a.c. = 1.05×10^{-3} mol dm^{-3} (for **1**); $k_m = 6.33\times10^{-4}$ s^{-1}, $K'_s = 48$ dm^3 mol^{-1}, c.a.c. = 9×10^{-3} mol dm^{-3}

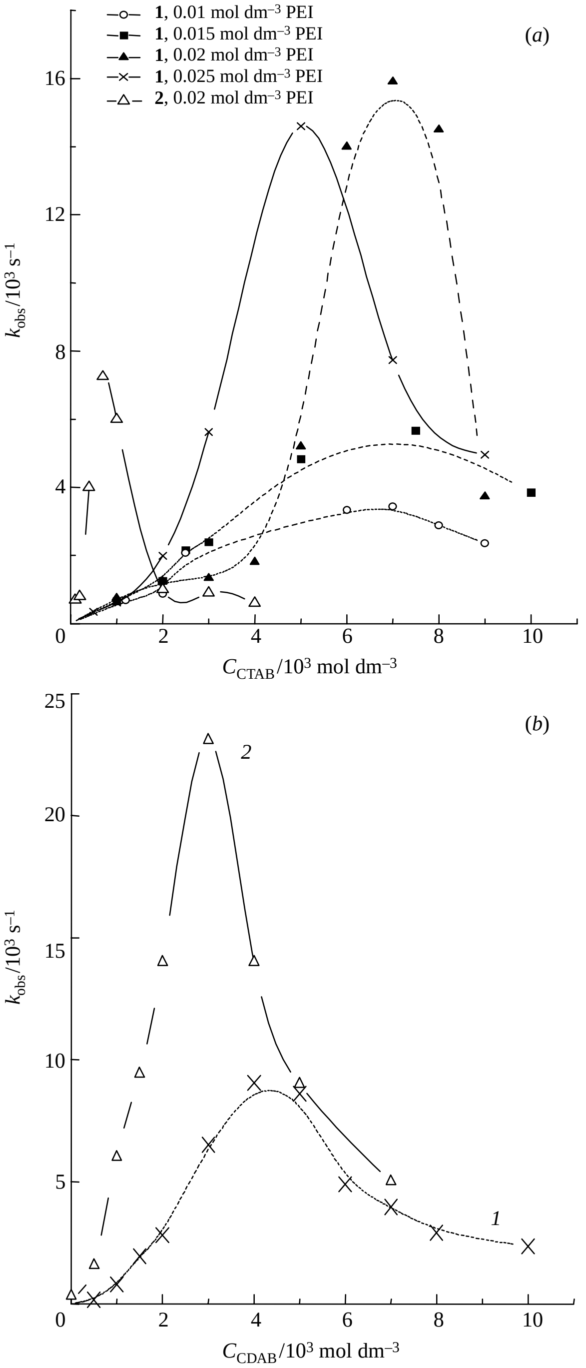


Figure 3 (*a*) Observed rate constants of hydrolysis of **1** and **2** in the CTAB–PEI–water system as a function of CTAB concentration. (*b*) The observed rate constant of hydrolysis of (*1*) **1** and (*2*) **2** in the CDAB–PEI–water system as a function of CDAB concentration at 0.02 mol dm^{-3} of PEI.

(for **2**). The low values of K'_s are probably due to a low degree of PEI aggregation.

The kinetic data for **1** and **2** in the mixed surfactant–PEI solutions are shown in Figure 3. The surfactant-to-PEI ratio considerably influences the reactivity of the substrates. At a PEI concentration of 0.02 mol dm^{-3}, a substantial increase in the observed rate constant of **1** occurs. As can be seen in Figure 2, aggregation occurs in the individual surfactant and PEI solutions, which can be identified as break points in the conductivity–$C_{surfactant}$ or C_{PEI} plots. There is one break point only in the individual surfactant and PEI solutions, which is treated as the c.m.c. for CTAB and CDAB direct micelles and as c.a.c. for the PEI solutions. At $C_{PEI} < 0.02$ mol dm^{-3}, an identical behaviour is observed in the mixed surfactant–PEI system, *i.e.*, only one break point is detected, whereas the second break point appears at the $C_{PEI} = 0.02$ mol dm^{-3}. According to published data,[9] the first break point in the mixed surfactant–polymer systems called as c.a.c., marks a concentration at which small micelle-like aggregates of the surfactant bound to the polymer begin to form. The second break point above the c.a.c. is taken to be the polymer saturation point (p.s.p.), where the saturation of the polymer with the surfactant occurs. Apparently, a sharp increase in the reactivity in the mixed system at 0.02 mol dm^{-3} reflects a change in the structural behaviour of the mixed systems in the presence of 0.02 mol dm^{-3} PEI.

As can be seen in Figure 3, the nature of the substrate and the structure of the surfactant head group influence the reaction rate. The reactivity of **1** in the mixed CDAB–PEI–water system is twice as low as that in the CTAB–PEI–water system, while k_{obs} for **2** is higher by a factor of three in the CDAB-based system. Table 1 suggests that concentrating the reagents is mainly responsible for the catalysis in the surfactant–PEI–water system (F_c ranged within the limits 150–800 depending on the PEI concentration), whereas a microenvironment exerts a negative effect resulting in a reduction of the reaction rate in comparison with water by a factor of 12–100 depending on the PEI concentration. As a result, a maximum 40-fold acceleration of the reaction is observed. When the CTAB-to-PEI ratio is increased, compensatory changes in the binding constants of the reagents and in the $k_{2,m}$ values occur. For more hydrophobic substrate **2**, higher K_s values were obtained in the case of both of the surfactants; this fact, as well as a higher $k_{2,m}$ value for **2** as compared to that for **1** in the CDAB–PEI–water system, is responsible for the higher reactivity of **1** in the CDAB-based system. The opposite is true in the CTAB–PEI–water system because of higher $k_{2,m}$ in the case of **1** as compared to **2**.

Thus, the catalysis in mixed polymer–micellar systems is mainly determined by the concentrating factor, while a microenvironment makes a negative contribution to the micellar rate effect. The reactivity depends on the nature of surfactants and substrates and on the surfactant-to-polymer ratio.

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