The catalytic effect of the cationic surfactant—polyethylene imine—water system in the hydrolysis of O-alkyl O-p-nitrophenyl chloromethylphosphonates

D. B. Kudryavtsev,^{a*} R. F. Bakeeva,^a L. A. Kudryavtseva,^b L. Ya. Zakharova,^{b*} and V. F. Sopin^a

 ^aKazan State Technological University, 68 ul. K. Marksa, 420015 Kazan, Russian Federation
^bA. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Research Center of the Russian Academy of Sciences, 8 ul. Akad. Arbuzova, 420088 Kazan, Russian Federation. Fax: +7 (843 2) 75 2253. E-mail: vos@iopc.kcn.ru

The kinetics of the hydrolysis of O-alkyl O- ρ -nitrophenyl chloromethylphosphonates in the cationic surfactant—polyethylene imine—water system was studied. The catalytic effects of the nature of the surfactant and substrate and the surfactant—polyethylene imine ratio were found.

Key words: phosphonates, hydrolysis, kinetics, polymer catalysis, micellar catalysis.

Previously, 1-3 we have studied the influence of direct and reverse micelles, microemulsions, and lyotropic liquid crystals on the rates of the nucleophilic substitution of esters of phosphorus acids. Micellar solutions of surfactants attract attention because they are related to biomimetic structures that function according to the "guest—host" principle.⁴ At the same time, the macro-molecular nature of proteins stimulates an interest in catalytic systems based on synthetic polymers.^{5,6} It can be assumed that the use of mixed surfactant- and polymer-based catalytic systems results in the appearance of additional new effects.

In this work, we studied the hydrolysis of O-alkyl O-p-nitrophenyl chloromethylphosphonates (1, 2) (Scheme 1) in an aqueous solution of polyethylene imine (PEI), micellar solutions of cetyltrimethylammonium bromide (CTAB) and cetyldimethylethylammonium bromide (CDAB), and mixed solutions of the surfactant (Surf) and polyethylene imine. These systems were studied in parallel by conductometry and tensiometry.

Experimental

Compounds 1 and 2 were synthesized by the previously described procedure.⁷ CTAB and CDAB (Sigma) and branched PEI (molecular weight 30000, Aldrich) were used. The hydrolysis kinetics was studied spectrophotometrically on a Specord M-400 instrument in the regime of the pseudo-first order by the change in the absorption of the *p*-nitrophenoxide anion. The rate constants were calculated by the weighted least-squares method. Electroconductivity was measured on a CDM-2-d conductometer (Denmark). Surface tension was determined by the method of ring elimination using a Du Noùy tensiometer at 20 °C.

Scheme 1



 $R = Et(1), n-C_5H_{13}(2)$

The kinetic data for PEI solutions were examined by the equation for the enzyme and micellar catalysis⁸

$$k_{\rm obs} = (k_{\rm w} + k_{\rm m} K_{\rm S}^{*} C) / (1 + K_{\rm S}^{*} C),$$
 (1)

where k_w/s^{-1} and k_m/s^{-1} are the rate constants of pseudo-first order in the aqueous and micellar phases, respectively; K_S/L mol⁻¹ is the reduced binding constant of the substrate; and C is the surfactant concentration minus the critical concentration of association (CCA).

The kinetic data for the surfactant-containing systems were examined in the framework of the pseudo-phase model using the following equation⁹:

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

where $k'_{obs}/L \mod^{-1} s^{-1}$ is the rate constant of the second-order reaction obtained by the dividing of k_{obs} into the total nucleophile concentration; $k_{2,w}/L \mod^{-1} s^{-1}$ and $k_{2,m}/L \mod^{-1} s^{-1}$ are the rate constants of the second-order reaction in the aqueous

Published in Izvestiya Akademii Nauk. Seriya Khimicheskaya, No. 9, pp. 1510-1514, September, 2000.

1066-5285/00/4909-1501 \$25.00 © 2000 Kluwer Academic/Plenum Publishers

and micellar phases, respectively; $K_S/L \mod^{-1}$ and $K_{Nu}/L \mod^{-1}$ are the binding constants of the substrate and nucleophile, respectively; V is the molar volume of the surfactant; and C is the surfactant concentration minus the critical concentration of micelle formation (CCM).

We used the modified form of Eq. (2)

$$(k_{\rm obs}/k_{\rm w})_{\rm max} = \frac{k_{2,\rm m}}{k_{2,\rm w}} \cdot \frac{K_{\rm S}K_{\rm OH}}{V(\sqrt{K_{\rm S}} \div \sqrt{K_{\rm OH}})^2}$$
,

in which the first cofactor in the right part (F_m) characterizes the influence of a change in the microenvironment of the reactants when the reaction is transferred from the aqueous to micellar phase, and the second cofactor (F_c) characterizes the effect of the concentrating of the reactants in micelles. This allows the contributions of different factors to the micellar effect to be quantitatively estimated. In this equation, K_{OH} is the binding constant of the substrate with the OH⁻⁻ ion.

Results and Discussion

The alkaline hydrolysis of phosphonates 1 and 2 in an aqueous solution occurs in the absence of the surfactant and PE1 at pH 9–10. When the hydrophobicity of the alkoxy group increases, the reactivity of the substrates decreases due to an increase in the steric hindrances for the attack at the phosphoryl group ($k_{2,w} = 4.0$ and 3.0 L mol⁻¹ s⁻¹ for compounds 1 and 2, respectively).¹⁰

In micellar solutions of CTAB and CDAB at pH 9.2 (borate buffer), cationic micelles accelerate alkaline hydrolysis¹¹ by at least two orders of magnitude (Fig. 1). The analysis of the kinetic data in the framework of the pseudo-phase model of micellar catalysis using Eq. (2) showed that both the concentrating of the reactants and the micellar microenvironment make positive contributions to the micellar effect (Table 1). The concentrating effect (F_c) exceeds the medium effect (F_m) by 6–8 and 35–40 times for phosphonates 1 and 2, respectively. The nature of the head group of the surfactant weakly affects the reactivity of the substrates in these systems, and hydrolysis is characterized by a pronounced substrate specificity (see Fig. 1, Table 1). The catalytic effect for hydrophobic substrate 2 exceeds more than



Fig. 1. Observed rate constants (k_{obs}) of the alkaline hydrolysis of compounds 1 (1, 2) and 2 (3, 4) in the surfactant—H₂O system at pH 9.2 as functions of the surfactant concentration: Surf = CTAB (1, 3) and CDAB (2, 4). The observed rate constants of the hydrolysis of compounds 1 (1') and 2 (2') in the PEI—H₂O system as functions of the PEI concentration are presented in insert.

twofold that observed for substrate 1. The plot k_{obs} -{Surf} for phosphonate 2 has a pronounced maximum, which is due to the much higher binding constants of this substrate as compared to those of phosphonate 1.

The general base catalysis of phosphonic esters in the presence of PEI has previously been found.¹² which is confirmed by the value of the deuterium isotope effect of \sim 2. In aqueous solutions, PEI is partially protonated, depending on the pH. The cationic centers that formed induce a decrease in the basicity of the amine due to the

Table 1. The results of analysis of the kinetic data (see Fig. 1) by Eq. (2)

System	$(k_{obs}/k_w)_{max}$ /L mol ⁻¹	<i>K</i> _S /L mol ⁻¹	$K_{\rm Nu}$ /L mol ⁻¹ s ⁻¹	k _{2,m}	F _c	<i>F</i> _m
1+CTAR	290	233	20	26.9	40	6.7
1+CDAB	283	233	25	23.4	49	5.8
2+CTAB	737	8170	47	9.6	159	3.9
2+CDAB	662	4343	48	9.5	139	3.7
1+CTAB+0.01 mol 1. ⁻¹ PE1	12.5	422	100	0.0025	149	0.08
1+CTAB+0.015 mol L ⁻¹ PEI	14.2	1670	95	0.0018	207	0.07
1+CTAB+0.02 mol L ⁻¹ PE1	21	1922	251	0.0011	451	0.05
2+CTAB+0.02 mol L ⁻¹ PEI	11.5	3070	270	0.00037	535	0.01
1+CDAB+0.02 mol L ⁻¹ PE1	24.7	1040	460	0.00057	554	0.03
2+CDAB+0.02 mol L ⁻¹ PEI	36.5	2290	535	0.00078	811	0.03

inductive effects and electrostatic interaction. The hydrolysis of phosphonates is catalyzed by uncharged amino groups, which participate in the activation of the H₂O molecule by the mechanism of general base catalysis. Cationic centers can increase the contribution of alkaline hydrolysis of the substrate to the observed rate constant due to electrostatic interaction with the OH⁻ ions. The titration of branched PEI (M = 30000) showed that, depending on the pH (5.5–8.5), *i.e.*, on the protonation degree, the pK_a^{eff} value ranged from 6.3 to 7.75. A similar influence of the pH on pK_a of branched PEI (M = 80000) has been described previously.¹²

Unlike the kinetic data for short-chain polyamines, analogs of PE1.¹³ the plot of the observed rate constant (k_{obs}) on the PEI concentration in water has a nonlinear profile characteristic of enzyme and micellar catalyses (see insert in Fig. 1).⁵ The observed rate constant in solutions of PEI is higher for substrate 1 than that for 2, which agrees with the behavior of these phosphonates in aqueous alkaline solutions, ¹⁰ although, as shown by us previously, ¹⁴ the reactivity increases in micellar solutions of the substrate increases.

The nonlinear profile of the plot k_{obs} -[PE1] (see insert in Fig. 1) and the data on the electroconductivity (χ) of the PE1 solution (Fig. 2) suggest the possibility of PE1 aggregation due to the formation of hydrogen bonds



Fig. 2. Electroconductivity (χ) of the surfactant—PEI-H₂O system as a function of the surfactant concentration: *I*, CTAB+0.02 mol L⁻¹ PEI: 2, CTAB+0.005 mol L⁻¹ PEI; *3*, CDAB+0.02 mol L⁻¹ PEI. The electroconductivity of the PEI-H₂O system as a function of the PEI concentration is presented in insert.



Fig. 3. Observed rate constants (k_{obs}) of the hydrolysis of compounds 1 (1-4) and 2 (5) in the CTAB-PEI-H₂O system as functions of the CTAB concentration: [PEI]/mol L⁻¹ = 0.010 (1), 0.015 (2), 0.020 (3, 5), and 0.025 (4). The observed rate constants of the hydrolysis of phosphonates 1 (1') and 2 (2') in the CDAB-PEI-H₂O system as functions of the CDAB concentration at [PEI] = 0.02 mol L⁻¹ in the micellar phase (1', 2') and liquid-crystalline E-phase (3') are presented in insert.

and small globules. The CCA value found from the inflection point on the plot in the coordinates χ -log[PEI] amounts to 10^{-2} mol L⁻¹.

Analysis of the kinetic data for the PEI-H₂O system by Eq. (1) gave $k_m = 1.07 \cdot 10^{-3} \text{ s}^{-1}$, $K'_S = 50 \text{ L mol}^{-1}$ for compound 1 and $k_m = 0.63 \cdot 10^{-3} \text{ s}^{-1}$, $K'_S =$ 47.7 L mol⁻¹ for compound 2. The low binding constants of the substrates can most likely be explained by a low degree of PEI aggregation.

The kinetic data for phosphonates 1 and 2 in mixed PEI-Surf-H₂O systems are presented in Fig. 3. In these systems, general base catalysis occurs (deuterium isotope effect ~2, as in the absence of the surfactant). The titration of PEI showed that, in the presence of the surfactant, the pK_a value was shifted toward high values. The Surf: PEI ratio substantially affects the reactivity of the substrates. At the PEI concentration of 0.02 mol L⁻¹, the observed rate constant of the hydrolysis of phosphonate 1 increases strongly, although it slightly changes at lower and higher PEI concentrations. Probably, at



Fig. 4. Surface tension (σ) of solutions of CTAB in the absence of additives (1) and in the presence of PEI (2-6) as a function of the logarithm of the surfactant concentration: [PEI]/mol L⁻¹ = 0.010 (2), 0.015 (3), 0.020 (4), 0.025 (5), and 0.030 (6). For convenience, the plots are spaced along the ordinate.

 $[PEI] = 0.02 \text{ mol } L^{-1}$, mixed CTAB-PEI micelles begin to form, in which the most favorable conditions for the reaction are created. This is indicated by a sharp increase in the binding constant of PEI at its concentration of 0.02 mol L^{-1} (see Table 1). The conductometric data (see Fig. 2) indicate that PEI additives slightly affect the CCM of CTAB and CDAB. It is of interest that, at $[PEI] = 0.02 \text{ mol } L^{-1}$ in the Surf-PEI-H₂O system, one more inflection in the plots χ -[Surf] is observed, along with the inflection point in the conductometric curves corresponding to the CCM of the cationic surfactants (0.0007-0.001 mol L⁻¹), at concentrations of CTAB and CDAB equal to 0.008 and 0.005 mol L^{-1} , respectively. This is most likely due to the formation of new structures involving the surfactant and PEI. Note that the [Surf] values in the inflection point coincide with the region of surfactant concentrations corresponding to the maxima in the k_{obs} -[Surf] plot for substrate 1.

The detailed study of the surface properties of the CTAB-PEI-H₂O system by the surface tension method (Fig. 4) showed that its aggregating properties noticeably change at [PEI] = $0.02 \text{ mol } L^{-1}$. At [PEI] < 0.02 mol L⁻¹, CCM of CTAB changes slightly and amounts to $\sim 7 \cdot 10^{-4}$ mol L⁻¹; at [PEI] = 0.02 mol L⁻¹, CCM increases to $\sim 1.2^{\circ} 10^{-3}$ mol L⁻¹ and remains unchanged with further increase in the PEI concentration. This agrees with the aforemade assumption that at [PEI] = 0.02 mol L⁻¹ mixed Surf-PEI aggregates characterized by a high CCM value are formed.

It is seen in Fig. 3 that the nature of the substrate and the structure of the head groups of the surfactant noticeably affect the reaction rate in the Surf-PEI-H2O system. The reactivity of phosphonate 1 in the CDAB-PEI-H₂O system is twofold lower than that in the CTAB-PEI- H_2O system, whereas for compound 2 k_{obs} is threefold higher in the CDAB-containing system. We may conclude from the data in Table 1 that in the Surf-PEI-H₂O system the increase in the reaction rate is due to the concentrating of the reactants in the mixed Surf-polymer associates that formed ($F_c \approx 150-800$), and the micellar microenvironment of the reactants decreases the reactivity by 12-100 times as compared to the reaction in water. The combined effect of these factors accelerates the reaction by ~40 times (see Table 1). As follows from the data in Table 1, compensating changes in the binding constant of the reactants and the rate constant in the micellar phase are observed. The binding constants of the more hydrophobic substrate 2 are higher than those for phosphonates in the systems with both CTAB and CDAB. The $k_{2,m}$ values for substrate 2 in the CDAB-PEI system are also higher, due to which k_{obs} for phosphonate 2 in this system is higher than that for 1. The opposite tendency is observed in the CTAB-PEI system because, in this case, $k_{2,m}$ for substrate 1 is higher than that for 2.

It has been shown¹⁵ that, at concentrations of CDAB lower than 0.1 mol L^{-1} in aqueous solutions, a metastable liquid-crystalline mesophase is formed first, and beginning at 0.4 mol L^{-1} , the stable hexagonal phase (E-phase) is formed. The kinetic data for the hydrolysis of phosphonate 1 in the CDAB—PEI--H₂O system, under the conditions of E-phase formation, are presented in the insert in Fig. 3. A decrease in the observed rate constant with an increase in the ordering degree of the solution can be seen.

Thus, the catalytic effect in the Surf-PE1- H_2O system is mainly determined by the factor of concentrating of the reactants, and the micellar microenvironment has a negative effect. The reactivity of the substrates depends on the nature of the surfactant and substrate and the Surf : PE1 ratio.

References

- L. Ya. Zakharova, F. G. Valeeva, L. A. Kudryavtseva, and E. P. Zhil'tsova, Mendeleev Commun., 1999, 125.
- E. P. Tishkova and L. A. Kudryavtseva, *Izv. Akad. Nauk,* Ser. Khim., 1996, 298 [Russ. Chem. Bull., 1996, 45, 284 (Engl. Transl.)].

- 3. R. F. Bakeeva, L. Yu. Tartykova, L. A. Kudryavtseva, R. M. Mukhamadeyeva, R. R. Shagidullin, and A. Kh. Plyamovaty. Mol. Mat., 1994, 3, 279.
- 4. J. H. Fendler, Chem. Rev., 1987. 87, 877.
- 5.1. V. Berezin and K. Martinek, Osnovy fizicheskoi khimii fermentativnogo kataliza [Fundamentals of the Physical Chemistry of Enzyme Catalysis]. Vysshaya Shkola, Moscow, 1977, 279 pp. (in Russian).
- 6. A. Arcelli and C. Concilio, J. Org. Chem., 1996, 61, 1682.
- 7. D. F. Toy and K. H. Rattenbury, US Pat. 2922810, 1960; Chem. Abstrs., 1960. 54, 9848.
- 8. F. M. Menger and C. E. Portnoy, J. Am. Chem. Soc., 1967, 89, 4698.
- 9. K. Martinek, A. K. Yatsimirsky, A. V. Levashov, and I. V. Beresin, Micellization, Solubilization, and Microemulsions, Ed. K. L. Mittal, Plenum Press, New York-London, 1977, 489.
- 10. N. A. Loshadkin, in Toksichnye efiry kislot fosfora [Toxic Esters of Phosphorus Acids], Mir, Moscow. 1964, 460 (in Russian).

- 11. L. Ya. Zakharova, S. B. Fedorov, L. A. Kudryavtseva, V. E. Bel'skii, and B. E. Ivanov, Izv. Akad. Nauk, Ser. Khim., 1993, 2161 [Russ. Chem. Bull., 1993, 42, 1329 (Engl. Transl.)].
- 12. R. F. Bakeeva, L. A. Kudryavtseva, V. E. Bel'skii, and B. E. Ivanov, Zh. Obshch. Khim., 1983, 53, 1058 [J. Gen. Chem. USSR, 1983, 53 (Engl. Transl.)].
- 13. R. F. Bakeeva, V. E. Bel'skii, L. A. Kudryavtseva, A. T. Chetveryakova, and B. E. Ivanov, Izv. Akad. Nauk SSSR, Ser. Khim., 1987, 756 [Bull. Acad. Sci. USSR, Div. Chem. Sci., 1987, 36 (Engl. Transl.)].
- 14. Ya. Zakharova, R. A. Shagidullina, F. G. Valeeva, and L. A. Kudryavtseva, Mendeleev Commun., 1999, 201.
- 15. R. F. Bakeeva, L. A. Kudryavtseva, G. Eme, E. M. Kosacheva, V. E. Bel'skii, D. B. Kudryavtsev, R. R. Shagidullin, and V. F. Sopin, Izv. Akad. Nauk, Ser. Khim., 1998, 1499 [Russ. Chem. Bull., 1998, 47, 1454 (Engl. Transl.)].

Received January 5, 2000