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The reactivity of phosphonic esters in aqueous micellar solutions of cationic surfactants

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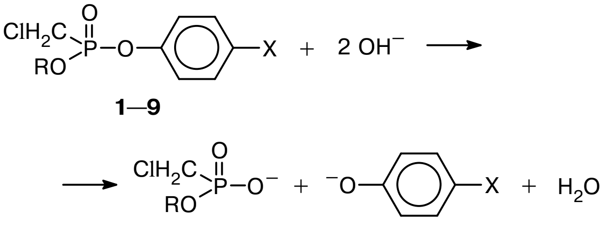
The micellar effect of cationic surfactants in alkaline hydrolysis of *O*-alkyl-*O*-aryl-chloromethyl phosphonates involves a positive contribution of concentrating the reagents and a negative effect of the micellar environment due to a loss in the activation entropy. The reactivity of substrates in micelles depends on both electronic and hydrophobic characteristics of substituents in the aryl group.

Key words: micelles, cetyl-trimethylammonium bromide, kinetics, hydrolysis, substrate specificity, phosphonic esters.

The direct and reverse micelles, microemulsions, and liquid crystals are the simplest analogs of biological systems[1] in which the most efficient, purposeful, and selective mechanism of catalysis operates under mild conditions. Among numerous recent studies of micellar catalysis,[2—5] one can distinguish two main directions: first, a design of novel catalytic nanosystems operating by the "guest—host" mechanism, and second, studies of the effect of highly ordered media on the reaction rates. This study concerns the second aspect. A qualitative analysis of various components of the catalytic effect using true values of the activation enthalpy and entropy in the aqueous and micellar pseudo-phases was carried out to interpret the regularity described in many reports, namely a decrease in the reactivity of compounds upon transfer of the reaction from the aqueous to micellar phase.

Earlier, we have studied the reactivity of a series of phosphonic esters in the reverse micelles of sodium dodecylsulfate and sodium bis(2-ethylhexyl)sulfosuccinates as well as in the direct micelles of cetylpyridinium bromide (CPB).[6—8] A substantial change in the nature of catalytic effect that was found on going from aqueous to non-aqueous media stimulated further studies in this area. In this work, we studied the kinetics of alkaline hydrolysis of a wide series of *O*-alkyl-*O*-aryl-chloromethyl phosphonates (**1—9**) in a micellar solution of cetyltrimethylammonium bromide (CTAB) (Scheme 1). Both hydrophobicity and electronic properties of a substituent in an eliminatied group were varied in the series of compounds **1—7**, and the hydrophobicity of alkoxyl group at the phosphorus atom was varied in substrates **1**, **8** and **1**, **9**.

Scheme 1



R = Et, X = NO_2 (**1**), Br (**2**), H (**3**), Et (**4**), Bu^n (**5**), n-C_8H_{17} (**6**), i-$C_{12}H_{25}$ (**7**);
R = C_6H_{13}, X = H (**8**), NO_2 (**9**)

Experimental

Compounds **1—9** were synthesized according to a previously described procedure.[9] CTAB («Sigma»), CPB, and dodecylpyridinium bromide (DPB) of reagent purity grade were twice crystallized from EtOH. The hydrolysis kinetics was monitored spectrophotometrically on a Specord M-400 instrument at 25 °C by a change in the absorption of the eliminated group. The initial substrate concentration was $5 \cdot 10^{-5}$ mol L^{-1}. The apparent rate constants (k_{app}) were calculated by the formula $\ln(D_\infty - D) = -k_{app}t + \text{const}$, where D and D_∞ are the optical densities of the solution at the moments t and after the reaction was over. The k_{app} values were calculated using the weighed least squares method.

The kinetic data were processed, similarly to works,[6,7] in the framework of a pseudo-phase model using the equation[10]

$$k'_{app} = \frac{k_{2,w} + k_{2,m}/(VK_SK_{OH}C)}{(1 + K_SC)(1 + K_{OH}C)}\,, \qquad (1)$$

where k'_{app} is the apparent second-order rate constant obtained by division of k_{app} by the total concentration of nucleophile; $k_{2,w}$ and $k_{2,m}$ (L mol^{-1} s^{-1}) are the second-order rate constants in the aqueous and micellar pseudo-phases, respectively; K_S and K_{OH} (L mol^{-1}) are the binding constants for a substrate and hydroxide ion; V is the molar volume of a surfactant; C is the concentration of a surfactant minus the critical concentration of micelle formation (CCM).

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Results and Discussion

The reactivity of substrates **1**—**9** in water in the absence of surfactants has been studied earlier.[6] In the CTAB micellar solution, the reactions of compounds **1**—**7** are accelerated up to 25 times due to solubilization of the substrate and electrostatic attraction of OH^- ions to the positively charged micelle surface (Fig. 1, Table 1). The apparent rate constant decreases with weakening the electron-acceptor effect of the substituent X in the series **1**—**3**. The order of the reactivity of the substrates **3**—**7** is opposite to the tendency found in water: the maximal k_{app} was found for substrate **6** (X = n-C_8H_{17}) and the minimal k_{app} was determined for **3** and **4** (X = H, Et). As a whole, the effect of substituents changes as follows: NO_2 > Br > n-C_8H_{17} > i-$C_{12}H_{25}$ > B ≈ Et ≈ H. The findings of quantitative analysis of the kinetic data are presented in Table 1.

The pseudo-phase model (Eq. (1)) makes it possible to calculate the second-order rate constants in the micellar pseudo-phase for a wide series of substrates. The data on reactions in micellar solutions are not available. Fig. 2 shows a linear correlation between the second-order rate constants in the aqueous and micellar pseudo-phases for the substrates **1**—**7**. This fact supports a suggestion that the reaction mechanism does not change when the reaction is transferred from the aqueous into micellar phase. Meanwhile, the correlation between the apparent rate constant k'_{app} and reaction rate constant in water $k_{2,w}$ holds only for substrates **1**—**5** and violates for **6** and **7**. This fact can be explained by 0strengthening the concentrating effect (F_c ~600—650) with increasing the hydrophobicity of a substituent in the phosphonic esters **6** and **7** compared to **3**—**5** (F_c = 150—190) (see Table 1).

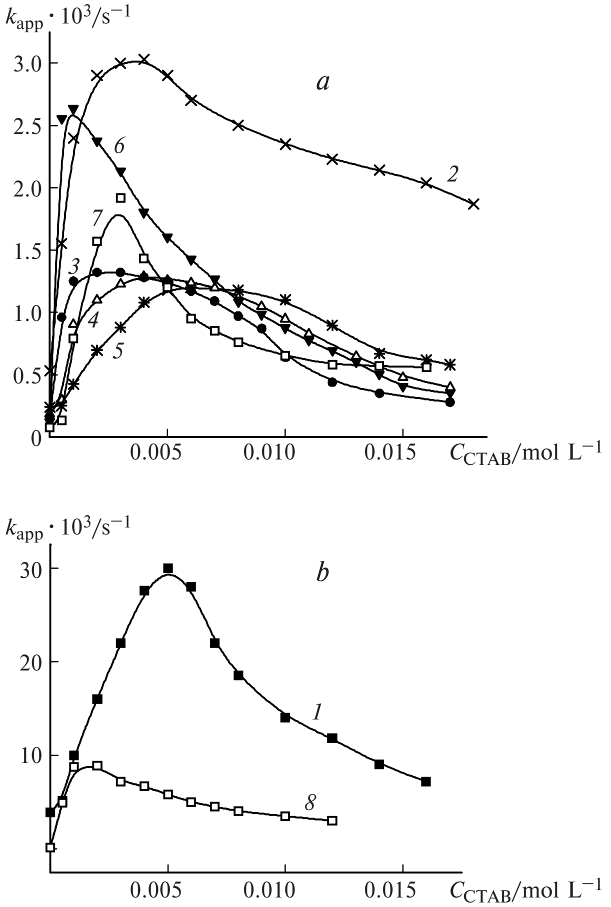

Fig. 1. The apparent rate constants for alkaline hydrolysis of substrates **2**—**7** (*a*) and **1**, **8** (*b*) in micellar CTAB solutions as a function of the surfactant concentration (0.001 mol L^{-1} NaOH, 25 °C); the curve numbers correspond to numeration of substrates in Scheme 1.

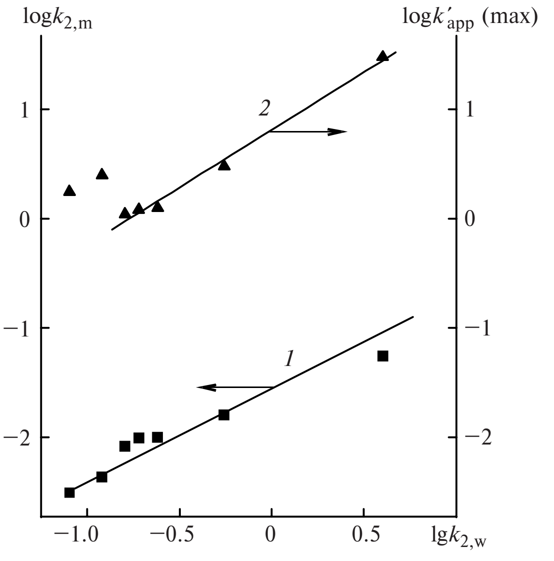

Fig. 2. Correlations between the second-order rate constants for alkaline hydrolysis of substrates **1**—**7** in the micellar and aqueous pseudo-phases (*1*) and those between the apparent rate constant and rate constant in water (*2*), CTAB, 25 °C.

As can be seen in Table 1, the main reason for acceleration of the reactions of substrates **1**—**7** is a local increase in the concentration of compounds in the CTAB micelles. The concentrating factor (F_c) decreases initially in the series **1**—**3** in the range of 430—140 and then increases with increasing in the chain length of the substituent in the range of 150—640. This means that the favorable effect of the micellar microenvironment could increase the reaction rate by more than two orders of magnitude. However, a significant decrease in the reactivity upon the transfer of the reaction from the aqueous to micellar phase (F_m < 1) results in a decrease of the micellar effect by 6—25 times (see Table 1).

The reactivity decrease in the micellar pseudo-phase compared to water is typical of most reactions of nucleophillic substitution mediated by a ionic reactant (see reviews[12,13]). The unfavorable effect of the micellar microenvironment contradicts the Ingold—Hughes rule,[14] which predicts benefit of ion-molecular reactions from a decrease in the medium polarity due to charge delocal-

Table 1. The results of the quantitative analysis of the kinetic data (see Figs. *1*, *4*) according to Eq. (1)

Substrate	T/°C	$k_{2,w}$ /L mol^{-1} s^{-1}	$(k_{app}/k_w)_{max}$	K_S /L mol^{-1}	K_{OH} /L mol^{-1}	$k_{2,m}$ /L mol^{-1} s^{-1}	F_c [a]	F_m [a]	F_cF_m
1 [b]	25	4.0	7.5	1775	240	0.055	432	0.014	6
1 [c]	25	4.0	7.0	1190	145	0.10	266	0.026	6.5
1 [d]	25	4.0	35	2020	80	0.78	187	0.19	36
1 [e]	25	4.0	9.5	219	4.2	4.0	10.8	1.0	10.8
	15	2.0	7.0	215	2.0	2.5	6.0	1.2	7.2
	35	6.9	11.1	500	4.0	7.0	10.6	1.1	11.9
	45	14.0	7.8	402	3.0	13.5	8.2	0.99	8.2
2 [b]	25	0.55	5.5	945	135	0.016	240	0.028	6.3
3 [b]	25	0.24	5	400	90	0.01	144	0.042	6.0
4 [b]	25	0.19	7	800	75	0.0098	146	0.053	7.7
5 [b]	25	0.16	9	1675	87	0.0082	190	0.051	9.8
6 [b]	25	0.12	22	2350	350	0.0043	604	0.037	22.5
7 [b]	25	0.08	24	1490	470	0.0031	640	0.039	24.9
8 [b]	25	0.12	74	2800	365	0.014	657	0.117	77
9 [d]	25	3.0	95	7600	337	0.38	766	0.14	109
9 [e]	25	3.0	20	527	24	0.90	55	0.36	19.7
	15	1.7	21	430	30	0.60	57	0.35	20.0
	35	4.5	24	250	29	1.7	52	0.38	20.0
	45	9.9	15	260	31	2.0	57	0.2	15.0

[a] Calculated using the equation $(k_{app}/k_w)_{max} = \dfrac{k_{2,m}}{k_{2,w}} \dfrac{K_S K_{OH}}{V(\sqrt{K_S} + \sqrt{K_{OH}})^2}$. In the right, the value of the maximal acceleration of the reaction is the ratio between the apparent rate constant (k_{app}) and the pseudo-first-order rate constant in water (k_w). The first term in the right expresses the effect of the micellar microenvironment (F_m) on reactivity and the second term expresses the concentrating effect in micelles (F_c).

[b] CTAB, 0.001 mol L^{-1} NaOH.

[c] CTAB, 0.0005 mol L^{-1} NaOH.

[d] CPB, 0.0005 mol L^{-1} NaOH (see Ref 11).

[e] DPB, 0.001 mol L^{-1} NaOH.

ization in the transition state compared to the initial state.

Earlier,[8] we suggested that the violation of the Ingold—Hughes rule in micellar systems is apparent. It seems that the reactivity decrease in micelles is due to a loss in the activation entropy because of a change in the mutual arrangement and the mobility for the molecules of reactants upon a sharp increase in their concentration in the micelles rather than to a decrease in the local polarity.

Examination of both our and reported kinetic data[8,11—13,15] shows that a trend to lowering the reactivity (F_m < 1) is typical of systems with efficient binding of reactants, *i.e.*, of the reactions between hydrophobic compounds in aqueous solutions of surfactants possessing high micelle-forming abilities. The kinetic curves k_{app}—C_{sur} for these reactions pass through a maximum. A positive effect of the micellar microenvironment ($F_m \geq 1$) can occur in the systems with a low extent of solubilization of reactants having a plateau on the kinetic curves .

To verify the suggestion on the entropy control of the reactivity, we studied the reaction kinetics for substrates **1** and **9** in DPB micellar solutions at various temperatures. The activation parameters were calculated for the reaction occurring in the absence of the surfactant (ΔH_w, ΔS_w) using the $k_{2,w}$ rate constants and those for the reaction in the micellar pseudo-phase (ΔH_m, ΔS_m) calculated using the $k_{2,m}$ constants (Table 2). For the hydrolysis of compound **1**, the reactivity changes according to the Ingold—Hugues concept. A micellar effect is due to the positive contribution of both factors ($F_m \geq 1$ and F_c changes in the range of 6—11). When the reaction is transferred into micelles, a decrease in

Table 2. The activation parameters (ΔH and ΔS) and rate constants (k/L mol^{-1} s^{-1}) for the alkaline hydrolysis of substrates **1** and **9** in the DPB micellar solutions at different temperatures (T/°C)

Substrate	$k_{2,w}$				$k_{2,m}$				ΔH_w	ΔH_m	ΔS_m	ΔS_w
	15	25	35	45	15	25	35	45	kJ mol^{-1}		J mol^{-1} K^{-1}	
1	2.0	4.0	6.9	14.0	2.5	4.0	7.0	13.5	46.2	39.3	−78.6	−100.6
9	1.7	3.0	4.5	9.9	0.6	0.9	1.7	2.0	40.8	30.0	−98.9	−144.4

the activation enthalpy by 7 kJ mol^{-1} and the activation entropy by 22 J mol^{-1} K^{-1} were found (see Table 2). The reaction of more hydrophobic substrate **9** occur contrary to the Ingold—Hughes concept: only the concentrating factor contributes positively ($F_c \approx$ 52—57) and the micellar microenvironment affects negatively the reactivity ($F_m \approx$ 0.2—0.4). A transfer of the reaction of substrate **9** into the micellar pseudo-phase is accompanied (see Table 2) by a decrease in the activation enthalpy by 10.8 kJ mol^{-1} and the activation entropy by 45.5 J mol^{-1} K^{-1}.

Thus, one can conclude that the transfer of ion-molecular reactions from water to the less polar pseudophase results in a decrease in the activation enthalpy according to the Ingold—Hughes rule. Meanwhile, a passage from diluted aqueous solutions to concentrated solutions with the micellar pseudo-phase, is accompanied by a decrease in entropy apparently at the expence of a decrease in the entropy of mixing, a decrease in the mobility of reactants, *etc.* In the reaction of substrate **1**, changes in the activation enthalpy and entropy are mutually compensated and hence, the reactivity remains practically the same in both pseudo-phases. An increase in the concentrating effect in the reaction of compound **9** results in the more significant loss in the activation entropy, which quantitatively exceeds the gain in the activation enthalpy and manifests itself in an apparent violating the Ingold—Hughes rule.

An increase in the hydrophobicity of a substituent in the alkoxyl group is accompanied by an increase in k_{app} by nearly an order of value (for substrates **3** and **8**, see Fig. 1). The rate growth mentioned in the case of substrate **8** is due to a simultaneous increase in the factors of concentrating and micellar microenvironment (see Table 1). As we have shown previously,[8] an increase in the length of the alkoxyl group in *p*-nitrophenyl esters affects more weakly the rate of alkaline hydrolysis in the CPB micellar solution: k_{app} for substrate **9** this is only twice as high as the k_{app} value for **1**. The difference in k_{app} for phosphonates **1** and **9** in the DPB micelles is still less (Fig. 3). Examination of the kinetic data (see Table 1) leads to a conclusion that in the last two cases, a substantial increase in the binding constants in the reaction of substrate **9** compared to **1** is compensated by a decrease in the $k_{2,m}$ value for substrate **9**. Hence, distinguishing the hydrophobic substrates by micelles depends on both the surfactant nature and substrate structure, particularly on the arrangement of the hydrophobic moiety.

Note a considerable effect of the nature of the head group in a surfactant on the reactivity of the compounds under study. Figure 4 presents the kinetic data for substrate **1** in the CTAB, CPB, and DPB micelles. Comparison of the maximal values of k_{app} for CPB and CTAB at the same concentration of alkali (see Fig. 4) shows that the k_{app} value in the CPB micellar solutions is nearly 7 times higher. Analysis of the kinetic data using Eq. (1) indicates that such a difference in the reactivity is due to the more favorable effect of the micellar environment of the CPB aggregates on the reaction transition state compared to the CTAB micelles. Table 1 demonstrates that $k_{2,m}$ for substrate **1** in the CPB micelles is nearly an order of magnitude higher than $k_{2,m}$ for this substrate in the CTAB micellar pseudophase, whereas the concentrating factors change scarcely. An increase in the chain length of the surfactant, as a rule, increases the micellar effect.[16] The same trend is found when the kinetic data in the micellar solutions of DPB and CPB are compared. An increase in the micellar effect by 4 times (for substare **1**) and by 5 times (for substrate **9**) when the chain length of the surfactant by

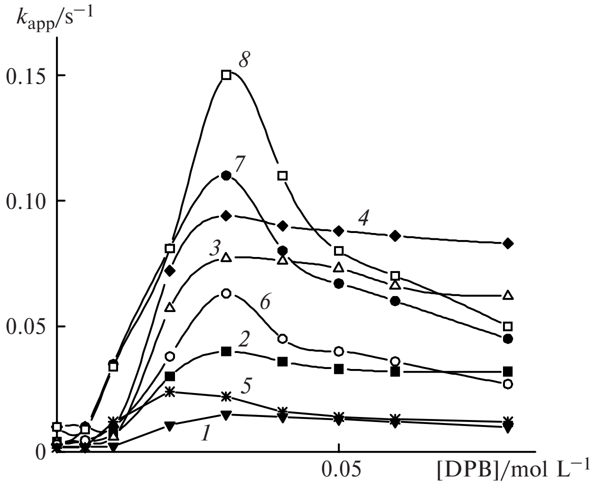

Fig. 3. The apparent rate constants for alkaline hydrolysis of substrates **1** (*1—4*) and **9** (*5—8*) in the DPB micellar solutions at different temperatures in the presence of 0.001 mol L^{-1} NaOH at 15 (*1, 5*), 25 (*2, 6*), 35 (*3, 7*) and 45 °C (*4, 8*), respectively.

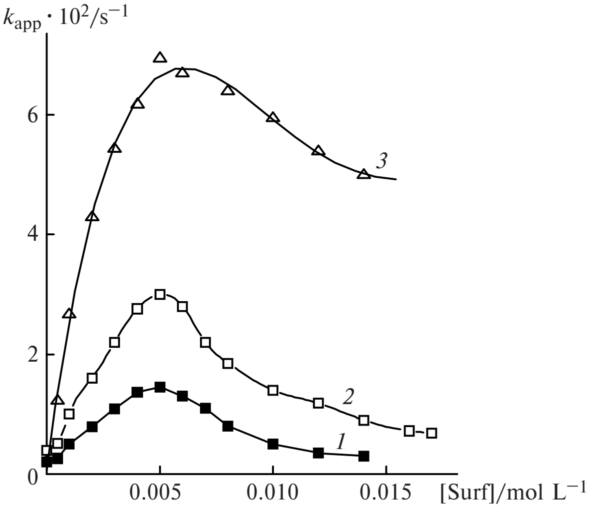

Fig. 4. The apparent rate constants for alkaline hydrolysis of substrates **1** in the micellar solutions of surfactants (Surf): *1,* CTAB, 0.0005 mol L^{-1} NaOH, *2,* CTAB, 0.001 mol L^{-1} NaOH, *3,* CPB, 0.0005 mol L^{-1} NaOH.

four methylene groups is due to an increase in the concentrating factor in the CPB micelles by 12—17 times and the compensating decrease in the factor of a micellar microenvironment by 3—5 times (see Table 1).

Thus, the mechanism of the catalytic effect of the CTAB micelles in the alkaline hydrolysis of a wide series of phosphonic esters was studied. A significant effect of the substrate structure, the nature of the head group, and the chain length on the reactivity was found. A widely reported trend of a decrease in the reactivity of compounds in the micellar pseudo-phase was critically examined for the first time, and this phenomenon was interpreted on the basis of calculations of the activation parameters for the reaction in both preudo-phases.

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