Catalytic effect of supramolecular system based on cationic surfactant and monopodands in nucleophilic substitution of phosphorus esters

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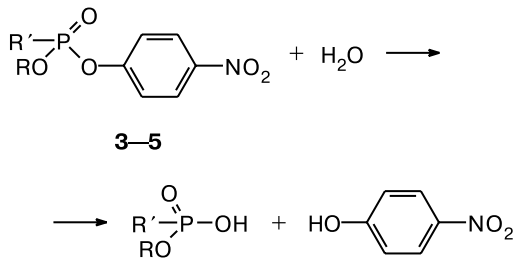
The data are presented on the synthesis of podands with terminal quinoxaline fragments of rings and their influence on both the micellization properties of cetyltrimethylammonium bromide in a water—DMF solution and kinetics of basic hydrolysis of *O*-*p*-nitrophenyl *O*-ethyl chloromethylphosphonate and *O*-*p*-nitrophenyl *O*-hexyl chloromethylphosphonate in the absence and presence of surfactants. The mechanism of the podand effect on the reaction rate depends on the structures of phosphonate and podand. 1,8-Bis(3-ethyl-1,2-dihydro-2-oxoquinoxalin-1-yl)-3,6-dioxaoctane inhibits the basic hydrolysis of the substrates to 3—4 times. In a micellar solution of the surfactant, an approximately 20-fold acceleration of the reaction rate constant is observed. The observed rate constant decreases when podand is added to a micellar solution. The catalytic effect of the polycomponent system is due to concentrating of the reactants. The micellar microenvironment can exert both positive and negative effects on the reactivity of phosphonates.

Key words: podands, phosphorus acid esters, kinetics, hydrolysis, cetyltrimethylammonium bromide, micelles.

The use of polycomponent supramolecular systems as nanoreactors is a promising vehicle in design of catalytic compositions simulating the effect of enzymes. We have previously studied the reactivity of phosphorus acid esters in self-organizing surfactant solutions and the influence of modifiers on the catalytic effect of similar systems. Recognition of the mechanism of changing the catalytic effect by the introduction of organic and inorganic electrolytes,[1] co-surfactants,[2] and polymeric additives[3] made it possible to identify the main factors controlling the reactivity of organophosphorus compounds in supramolecular media and to develop an algorithm for searching efficient polycomponent catalytic systems. In this work, we studied the effect of the system based on cetyltrimethylammonium bromide (CTAB) and podands 1,8-bis(3-ethyl-1,2-dihydro-2-oxoquinoxalin-1-yl)-3,6-dioxaoctane (**1**) and 1,14-bis(3-ethyl-1,2-dihydro-2-oxoquinoxalin-1-yl)-3,6,9,12-tetraoxaoctane (**2**) on the basic hydrolysis rate of *O*-*p*-nitrophenyl *O*-ethyl chloromethylphosphonate (**3**), *O*-*p*-nitrophenyl *O*-hexyl chloromethylphosphonate (**4**), and *O*-*p*-nitrophenyl *O*-ethyl ethyl phosphonate (**5**) in a DMF—water (30 vol.%) mixture (Scheme 1).

Scheme 1



R′ = CH_2Cl, R = Et (**3**), *n*-C_6H_{13} (**4**); R′ = R = Et (**5**)

Podands,[4] in particular, open analogs of crown ethers, attract increasing attention in the recent years due to their accessibility, rather high efficiency, and possibility of controlling complexation abilities in a wide range by changing the structure.[5,6] They are studied as phase-transfer catalysts,[7,8] extracting agents,[9] and components of ion-selective electrodes.[10] However, compounds containing different heterocyclic systems at terminal atoms of the polyether units, which have various functional groups and can be involved in complexation (including π—π-interac-

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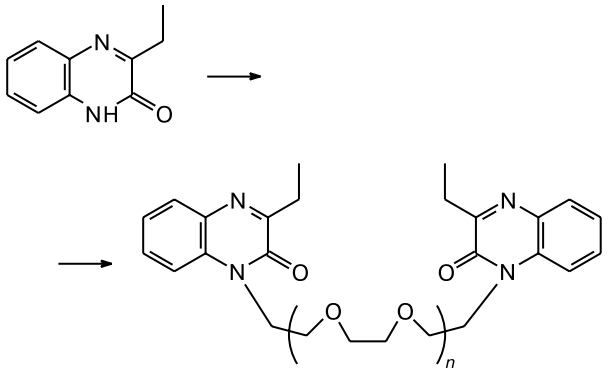
tions with electron-donor and electron deficient π-systems, depending on the π-deficient or π-donating character of the heterocyclic fragments) and also undergo ring closure under certain conditions, are not virtually studied. The properties of chelates and macrocycles based on quinoxaline and its functionalized derivatives are also unknown. In this work, we present the data on the synthesis and catalytic properties of two representatives of monopodands with terminal quinoxaline systems of rings, namely, 1,8-bis(3-ethyl-1,2-dihydro-2-oxoquinoxalin-1-yl)-3,6-dioxaoctane (**1**) and 1,14-bis(3-ethyl-1,2-dihydro-2-oxoquinoxalin-1-yl)-3,6,9,12-tetraoxaoctane (**2**).

Results and Discussion

Compounds **1** and **2** were synthesized in high yields by the reactions of 1,8-dibromo-3,6-dioxaoctane and 1,14-ditosylate-3,6,9,12-tetraoxaoctane with 3-ethylquinoxalin-2(1*H*)-one in the presence of KOH in dioxane (Scheme 2).

Scheme 2



1, **2**

n = 1 (**1**), 2 (**2**)

Reagents, conditions, and yields: 1) KOH, 2) $XCH_2(CH_2OCH_2CH_2OCH_2)_nCH_2X$, dioxane (X = Br, *n* = 1; X = OTs, *n* = 2), Δ; 96% yields (**1**), 75% (**2**).

The absence of the ν_{NH} absorption band of the carbamoyl group in the IR spectrum of the products in the corresponding regions (2800—3100 cm^{-1}) indicates alkylation at the NH group. The ^1H NMR spectrum of the reaction product contains, along with other signals inherent in the quinoxaline fragments (7.72 (dd, *J* = 7.73 Hz, *J* = 1.23 Hz); 7.55 (ddd, *J* = 8.13 Hz, *J* = 7.50 Hz, *J* = 1.23 Hz); 7.47 (dd, *J* = 8.13 Hz, *J* = 1.23 Hz); 7.28 (ddd, *J* = 7.54 Hz, *J* = 7.52 Hz, *J* = 1.23 Hz)), one singlet at 3.49 ppm and two triplet signals at 3.68 ppm (*J* = 5.78 Hz) and 4.38 ppm (*J* = 5.78 Hz) from the methylene groups of the dioxatriethylene unit, which indicates that protons of two methylene groups arranged between two oxygen atoms are magnetically equivalent and confirms the symmetric structure of alkylation product **1**. The ^1H NMR spectrum of compound **2** contains, along with signals of the quinoxaline fragments (doublet signal at 7.79 (*J* = 7.96 Hz) and multiple signals at 7.40—7.50 and 7.20—7.30 ppm), exhibits signals of the tetraoxapentaethylene unit: a singlet signal at 3.49 ppm, two triplet signals at 3.80 (*J* = 5.96 Hz) and 4.44 (*J* = 5.96 Hz), and multiplet signals at 3.50—3.66 ppm.

In this work, we studied the influence of compound **1** on the reactivity of phosphonic acid esters **3** and **4** and considered a possibility of using this compound as a modifier in the composition of the CTAB-based polycomponent catalytic system. Podand **2** and substrate **5** were included into the scope of objects under study for comparison. The effect of additives in micellar systems can be as follows: (i) change in the reactivity of compounds, including that due to the formation of catalytic complexes in a step preceding the chemical reaction, which can be estimated by the activation parameters of the reaction; (ii) change in the binding constants of reactants with the micellar system. An indirect influence can occur: through a change in the aggregation behavior of the system. Therefore, in this work, we studied the hydrolysis kinetics of substrates **3** and **4** at different temperatures in the supramolecular catalytic system and micelle-forming properties of CTAB in the presence of **1**. To obtain a quantitative information on the process in the micellar systems, the kinetic data were analyzed in the framework of the pseudo-phase model of micellar catalysis, which made it possible to estimate the binding constants of the reactants and rate constants in the micellar pseudo-phase.

The plot of the surface tension (γ) of the CTAB—water—DMF and CTAB—**1**—water—DMF systems *vs.* surfactant concentration is presented in Fig. 1. An aqueous solution of DMF (30 vol.%) was chosen because compound **1** is poorly soluble in water. According to the published data, DMF, being an aprotic solvent and distorting the water structure, worsens the micellization of a surfactant and increases the critical micelle concentration (CMC) compared to that in an aqueous solution.[11,12] When 30% (vol.) DMF is added, the CMC of CTAB increases noticeably, which is determined from the break in the γ—logC_{CTAB} plot, from 0.00087 to 0.0067 mol l^{-1}. The introduction of an insignificant amount of podand **1** (0.001 mol L^{-1}), on the contrary, decreases the CMC of CTAB (to 0.0021 mol L^{-1}) (see Fig. 1). It can be assumed that compound **1**, which possesses a low water affinity, forms association sites, promoting micellization and decreasing the CMC of the surfactant. As shown by our tensiometric measurements, compound **1** itself possesses no pronounced surface properties.

Based on the surface tension isotherms (see Fig. 1), we estimated some characteristics of micelles and surface properties of the systems presented in Table 1. The degree

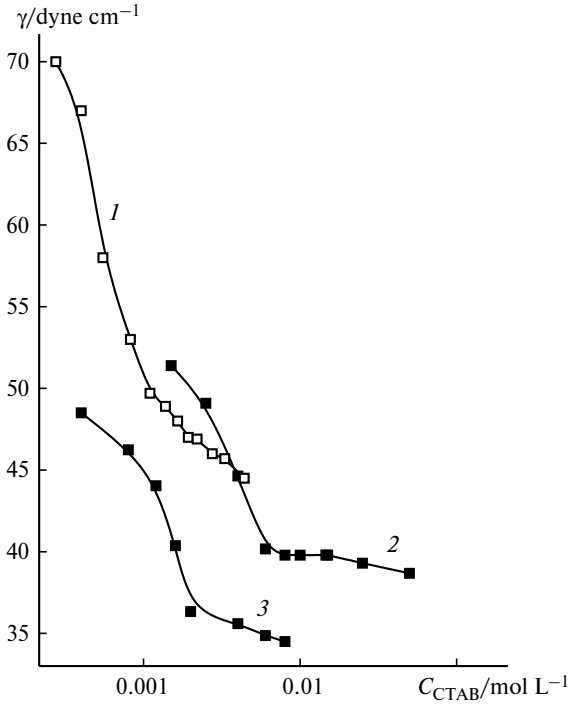


Fig. 1. Plots of the surface tension of CTAB *vs.* surfactant concentration in water (*1*) and a water—DMF mixture in the absence (*2*) and presence (*3*) of compound **1**.

of binding of counterions (β) was determined from the equation[13]

$$2/(1 - \beta) = \tan\alpha_1/\tan\alpha_2, \quad (1)$$

where $\tan\alpha_1$ and $\tan\alpha_2$ are the slope angles of the γ—C_{CTAB} plots before and after the CMC.

The maximum adsorption (surface excess) Γ_{max} was calculated by the Gibbs adsorption equation (2)[14,15]

$$\Gamma_{max} = (1/(4.61RT))\lim_{C\to CMC}(d\pi/d\log C), \quad (2)$$

where π is the surface pressure equal to the difference between the surface tensions of the solvent and solution at a given surfactant concentration: $\pi = \gamma_0 - \gamma$; R is the universal gas constant. The minimum surface calculated per surfactant molecule (A_{min}), free micellization energy ΔG_m, and standard free adsorption energy ΔG_{ad} were calculated using the formulas[15]

$$A_{min} = 10^{18}/N\Gamma_{max}, \quad (3)$$

where N is Avogadro´s number;

$$\Delta G_m = (1 + \beta)RT\ln(CMC), \quad (4)$$

$$\Delta G_{ad} = \Delta G_m - (\pi_{CMC}/\Gamma_{max}). \quad (5)$$

The quantitative parameters (see Table 1) for the CTAB—water system coincide well with the published results.[16,17] According to the data presented, the maximum excess of CTAB in aqueous solutions is higher than that in a water—DMF mixture. The packing of surfactant molecules in the surface layer of aqueous solutions is more compact than that in a mixed solvent, which indicates an increase in the intermolecular repulsion between CTAB monomers in a water—DMF mixture. The free adsorption energy increases when DMF is added to an aqueous solution. A less spontaneous adsorption process in a mixed water—DMF solvent is likely caused by the distortion of the water structure and a decrease in the hydrophobic solvation of hydrocarbon fragments. Similar conclusions are valid for quantitative parameters characterizing micellization of a surfactant, in particular, for the free micellization energy and CMC. The degree of binding of counterions decreases significantly on going from water to a water—DMF mixture. This indicates, most likely, a change in the micelle structure, which becomes more loosened, including a less number of surfactant molecules. The quantitative parameters characterizing the adsorption and micellization of CTAB in a water—DMF solution coincide well with the published data.[11,12] The influence of compound **1** on the parameters presented in Table 1 is less significant than the effect of DMF additives and has an opposite tendency. The introduction of podand **1** into the CTAB—water—DMF system stimulates micellization and results in a more compact packing of surfactant molecules in the surface layer (see Table 1).

In the framework of a kinetic experiment, we studied the basic hydrolysis of phosphonic acid esters **3** and **4** in

Table 1. Quantitative characteristics of the colloidal properties of the CTAB-based organized systems

System	$\Gamma_{max}\cdot 10^6$ /mol m^{-2}	A_{min} /nm^2	π_{CMC} /dyne cm^{-1}	$-\Delta G_m$	$-\Delta G_{ad}$	CMC/ /mol L^{-1}	β
				kJ mol^{-1}			
CTAB—water	3.1	0.53	21.3	30.64	37.5	0.00087	0.76
CTAB—water—DMF	2.1	0.79	11.8	20.0	25.6	0.0067	0.61
CTAB—**1**—water—DMF	2.2	0.73	15.7	25.4	32.5	0.0021	0.66

Note: β is the degree of binding of counterions; Γ_{max} is the maximum adsorption (surface excess); π is the surface tension equal to the difference between the surface tensions of the solvent and solution at a specified surfactant concentration: $\pi = \gamma_0 - \gamma$; A_{min} is the minimum surface calculated per surfactant molecule; ΔG_m is the free energy of micelle formation; ΔG_{ad} is the standard free energy of adsorption.

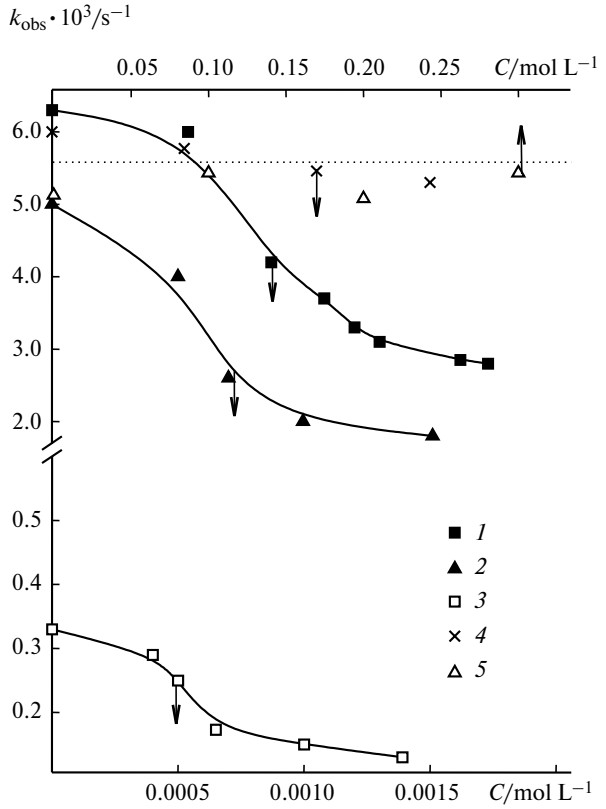


Fig. 2. Kinetics of the basic hydrolysis of substrates **3** (*1*), **4** (*2*), and **5** (*3*) in the presence of monopodand **1**, of substrate **3** in the presence of monopodand **2** (*4*), and of substrate **3** in the presence of 18-crown-6 (*5*); 0.02 *M* NaOH, 30 vol.% DMF, 55 °C.

the CTAB—**1**—water—DMF system at different temperatures. In addition, the catalytic effects of individual components were estimated: a micellar solution of CTAB and compound **1**. The results are presented in Figs. 2 and 3. As follows from the data in Fig. 2, compound **1** exerts an inhibition effect on the basic hydrolysis of **3** and **4**. The kinetic data for the basic hydrolysis of *O*-*p*-nitrophenyl *O*-ethyl ethylphosphonate (**5**) are presented in Fig. 2 for comparison. These data make it possible to estimate the influence of the chloromethyl fragment of substrates **3** and **4** on their binding and reaction in a catalytic complex. The shapes of the kinetic plots (see Fig. 2) for all substrates indicate the formation of a complex involving compound **1** and phosphonates **3**—**5** in a step preceding the reaction. The process in the "host—guest" catalytic complex makes it possible to use Eq. (6) for analysis of the kinetic data. This equation is widely used for enzymatic processes and micelle-inhibited reactions.[18]

$$k_{obs} = \frac{k_0 + k_{cat} K'_S C}{1 + K'_S C}, \qquad (6)$$

where k_0 and k_{cat} (s^{-1}) are the pseudo-first-order rate constants in the absence of compound **1** and in the catalytic complex, respectively; K'_S (L mol^{-1}) is the binding constant of the substrate; C (mol L^{-1}) is the concentration of compound **1** involved in the formation of the catalytic complex. The results of quantitative analysis are presented in Table 2.

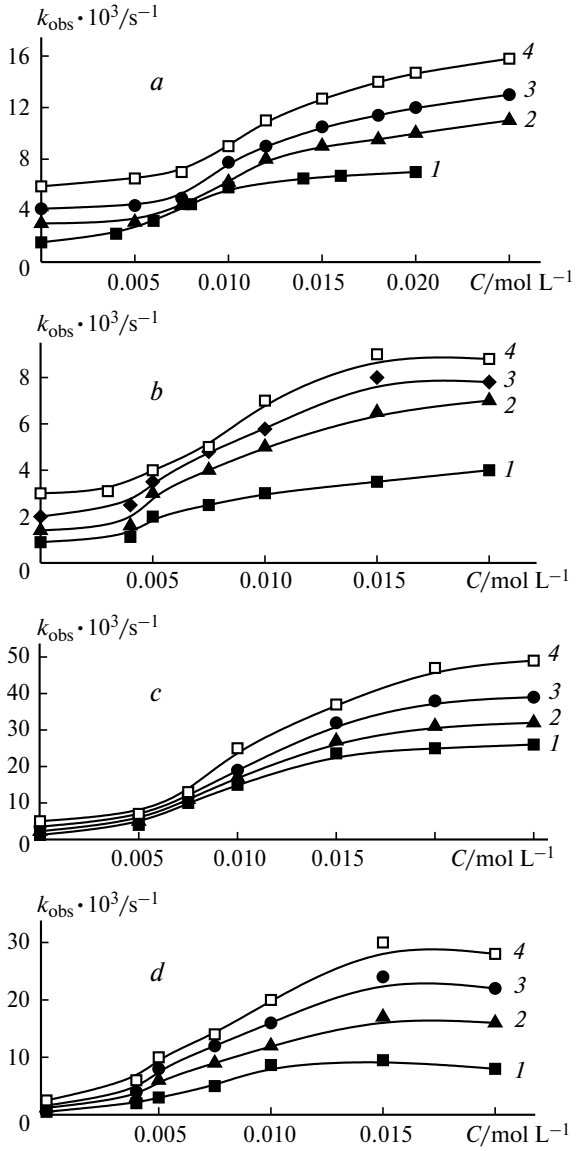


Fig. 3. Plots of the observed rate constants of basic hydrolysis of **3** (*a*, *b*) and **4** (*c*, *d*) in the absence (*a*, *c*) and presence (*b*, *d*) of **1** *vs.* surfactant concentration at different temperatures (0.02 *M* NaOH, 30 vol.% DMF): 25 (*1*), 35 (*2*), 45 (*3*), and 55 °C (*4*).

The inhibition of basic hydrolysis of substrates **3**—**5** is a consequence of their efficient binding with compound **1** (see Table 2). The mechanism of decreasing k_{obs} can proceed through the trivial separation of reactants when one of them (substrate) is bound to the catalyst and the hydrophilic hydroxide ion remains in a solution. This assumption is unfavored by the fact that the inhibition effect

Table 2. Results of quantitative analysis of the kinetic data (see Fig. 2) using Eq. (6)

Substrate	$k_{2,0}$* /L mol^{-1} s^{-1}	K'_S /L mol^{-1}	k_{cat} /s^{-1}	k_0/k_{cat}
3	0.3	3060±122	0.0019±0.00007	3.1
4	0.25	7555±377	0.0013±0.00006	3.8
5	0.016	3740±187	0.000078±0.000004	4.1

* $k_{2,0}$ is the second-order reaction rate constant in the absence of compound **1**.

would be proportional to the binding constants of substrates, *i.e.*, the maximum inhibition effect belongs to compound **4**, which is not confirmed by experimental data. A more detailed information on the mechanism of inhibition can be obtained by analysis of the activation parameters of the reaction. The decrease in the basic hydrolysis rate of **3** in the presence of **1** is caused by losses of the activation entropy, although the activation enthalpy somewhat decreases (Table 3). It is most likely that the binding of substrate **3** results in a more favorable orientation of reactants, whose probability is rather low, which is expressed as a decrease in the activation entropy of the process. The variant described for a compensation change in the activation parameters is characteristic of catalytic processes, in particular, for nucleophilic and enzymatic catalysis when the catalyst involvement in the transition state increases the order of the reaction, and hence, results in a loss of the activation entropy.[19] An alternative explanation is an assumption on the stabilization of the transition state due to efficient solvation, which can be accompanied by a decrease in the activation entropy due to the structurization of solvent molecules around the transition state.

Somewhat different results were obtained by analysis of the kinetic data on the hydrolysis of **4**. The inhibition of the reaction in the presence of **1** is caused by an increase in the activation enthalpy, and the entropy factor becomes more favorable. In this case, we can speak about a negative influence of the microenvironment of reactants or worsening of their mutual orientation upon catalytic complex formation.

Table 3. Activation parameters of the basic hydrolysis of phosphonates **3** and **4** in the absence and presence of compound **1**

Substrate	Concentration of podand **1**/mol L^{-1}	ΔH /kJ mol^{-1}	$-\Delta S$ /J mol^{-1} K^{-1}
3	0	32.6±1.6	155.9±7.8
3	0.001	29.8±1.5	170.6±8.5
4	0	35.6±1.8	148.1±7.4
4	0.001	46.3±2.3	128.5±6.4

This work is one of the first attempts to study the influence of podands on the reactivity of phosphorus acid esters. Hence, in the kinetic study, we checked different assumptions that can elucidate the mechanism of effects of these compounds. In particular, we studied the hydrolysis kinetics of phosphonate **3** in the presence of the podand with a longer spacer (**2**) and in the presence of 18-crown-6. Neither compound **2**, nor crown ether exert effects on the reaction rate (see Fig. 2). Therefore, we can conclude that the geometric factor (spacer size, flexibility of the structure, and an opened character of the latter) plays a role in the mechanism of podand effect. The absence of the effect of crown ethers confirms that the influence of compound **1** on the hydrolysis in a solvent that solvates well ions occurs due to hydrophobic and dispersion interactions with the substrate molecule rather than due to capturing of sodium cations.

We also studied by spectrophotometry the absorption of *p*-nitrophenol in borate and methylmorpholine buffers at *p*-nitrophenol—**1** ratios of 2 : 1; 1 : 1; 1 : 2; 1 : 20 (mol.). It was established that additives of **1** have no influence on the position of the band of the *p*-nitrophenoxide anion (400 nm) and do not change pK_a of *p*-nitrophenol. This fact indicates that the reaction of *p*-nitrophenol, which is a structural analog of the fragment of the substrate molecule, with compound **1** involves no phenolic hydroxide. It should be assumed that the interaction of phosphonates **3**—**5** with podand **1**, as in the case of biological systems, is multi-centered and involves aromatic fragments of both molecules (contribution of hydrophobic and dispersion forces and π—π-interactions), electron-releasing atoms of podand **1**, and electrophilic sites of substrates. According to the classification taking into account the degree of mutual involvement of "host" and "guest" molecules in bond formation,[20] the phosphonate—podand **1** complex should be assigned, probably, to the "nest" type when at least half a surface of the "guest" contacts with the "host." For a more surface-type contact ("roost" type), it would be difficult to explain the influence of the cavity size on the process rate and high binding constants of phosphonates (see Table 2).

The influence of CTAB micelles on the basic hydrolysis rate of the substrates in the absence of **1** is shown in Fig. 3, *a*, *c*. As expected, in cationic micelles, the reaction is accelerated compared to a molecular solution. The maximum reaction rate increases 4- and 20-fold for substrates **3** and **4**, respectively. It should be noted that the basic hydrolysis of phosphonates in the CTAB—DMF—water system occurs in a different way than that in an aqueous solution of CTAB. The main distinction is that the system, in the first case, is equilibrated in several hours and, therefore, the reaction was carried out after prolong settling. The k_{obs} values in mixed water—DMF solutions are underestimated compared to those in aqueous systems both in the absence of surfac-

Table 4. Results of quantitative analysis of the kinetic data (see Fig. 3) using Eq. (7)

Substrate	Concentration of **1** /mol L^{-1}	T /°C	$k_{2,0}$* /L mol^{-1} s^{-1}	$k_{obs,max}/k_0$	K_S	K_{Nu}	$k_{2,m}$ /L mol^{-1} s^{-1}	F_c	F_m	$F_c \cdot F_m$
					L mol^{-1}					
3	0	25	0.08	4.8	430±21	20±1.0	0.0075±0.0004	45.1	0.10	4.4
3	0	35	0.15	3.7	420±21	18±0.9	0.012±0.0006	41.2	0.10	4.3
3	0	45	0.21	3.1	410±21	15±0.7	0.017±0.0008	35.2	0.08	2.8
3	0	55	0.30	2.7	400±20	13±0.6	0.022±0.0011	31.1	0.07	2.3
4	0	25	0.06	20.6	530±26	10±0.5	0.05±0.0025	25.8	0.79	20.4
4	0	35	0.11	13.9	450±22	8±0.4	0.075±0.0037	20.8	0.65	13.5
4	0	45	0.17	11.1	400±20	7±0.4	0.11±0.0055	18.2	0.63	11.4
4	0	55	0.25	9.8	390±20	7±0.4	0.13±0.0065	18.1	0.52	9.4
3	0.001	25	0.04	4.4	450±22	23±1.1	0.004±0.0002	51.0	0.09	4.5
3	0.001	35	0.07	5.0	490±24	25±1.2	0.006±0.0003	55.4	0.08	4.7
3	0.001	45	0.1	3.9	510±25	22±1.1	0.008±0.0004	50.3	0.08	4.0
3	0.001	55	0.15	2.9	540±27	17±0.8	0.0105±0.0005	40.9	0.07	2.9
4	0.001	25	0.02	19.0	1260±63	2.5±0.1	0.06±0.003	7.6	2.4	18.3
4	0.001	35	0.06	14.2	3500±175	3.8±0.2	0.07±0.003	11.9	1.17	13.8
4	0.001	45	0.08	9.6	3800±190	4.7±0.2	0.08±0.004	14.6	0.64	9.3
4	0.001	55	0.12	7.5	4500±225	5.0±0.3	0.097±0.005	15.6	0.485	7.6

*$k_{2,0}$ is the second-order reaction rate constant in the absence of a surfactant.

tants and in micellar solutions (see Tables 2 and 4). This is probably caused by a change in the solvation (stabilization) of the transition state of the reaction and the effective concentration of hydroxide ions. When compound **1** is added to a micellar solution of CTAB, k_{obs} decreases approximately 1.5-fold for both substrates (see Fig. 3, *b*, *d*).

To obtain a quantitative information on factors determining the effect of micelles and a modifier, the kinetic data were analyzed using the following equation[21]:

$$k'_{obs} = \frac{k_{2,0} + (k_{2,m}/V)K_S K_{Nu} C}{(1 + K_S C)(1 + K_{Nu} C)}, \quad (7)$$

where k'_{obs} (L mol^{-1} s^{-1}) is the second-order rate constant obtained by the division of k_{obs} into the total nucleophile concentration; $k_{2,0}$ and $k_{2,m}$ (L mol^{-1} s^{-1}) are the second-order rate constants in aqueous and micellar phases, respectively; K_S and K_{Nu} (L mol^{-1}) are the binding constants of the substrate and nucleophile; V is the molar volume of the surfactant accepted to be 0.3 L mol^{-1}; C (mol L^{-1}) is the surfactant concentration minus CMC.

Under the condition that the reaction in the micellar pseudo-phase contributes mainly to the observed rate constant, *i.e.*, the condition $k_{2,m}K_S K_{Nu}/V > k_{2,0}$ is fulfilled, the maximum acceleration of the reaction ($k_{obs,max}/k_0$) can be described by expression (8), which is simplified and transformed Eq. (7).[21]

$$k_{obs,max}/k_0 = \frac{k_{2,m}}{k_{2,0}} \frac{K_S K_{Nu}}{V(\sqrt{K_S} + \sqrt{K_{Nu}})^2}, \quad (8)$$

where $k_{obs,max}$ is the maximum value of the experimental rate constant of the pseudo-first order (see Fig. 3), and k_0 is the pseudo-first-order reaction rate constant in the absence of a surfactant. Equation (8) makes it possible to characterize quantitatively the main components of the micellar effect: the first term in the right part (F_m) characterizes the influence of changing the microenvironment of reactants on going from the aqueous to micellar phase, the second term (F_c) characterizes the effect of concentrating reactants in micelles, and their product is numerically equal to the acceleration of the reaction in micelles.

The K_S, K_{Nu}, and $k_{2,m}$ constants can be found from Eq. (7), which is transformed, for this purpose, into the following equation[23]:

$$C/(k'_{obs} - k_{2,0}) = \alpha + \beta C \frac{k'_{obs}}{k'_{obs} - k_{2,0}} + \gamma C^2 \frac{k'_{obs}}{k'_{obs} - k_{2,0}}, \quad (9)$$

where $\alpha = V/(k_{2,m}K_S K_{Nu})$; $\beta = \alpha(K_S + K_{Nu})$; $\gamma = \alpha K_S K_{Nu}$.

The graphical solution of Eq. (9), which was described in detail in Refs. 21—23, makes it possible to calculate the desired parameters. In this work, the K_S, K_{Nu}, and $k_{2,m}$ values were determined by a specific program based on Eq. (9), and the calculated parameters are presented in Table 4. The F_c and F_m values are numerically equal to the terms in the right part of Eq. (8) and are also presented in Table 4. In addition, the kinetic plots for different temperatures were analyzed to estimate the activation parameters of the reaction in the micellar pseudo-phase (Table 5).

When an additive is absent, the catalytic effect is mainly caused by the factor of reactant concentrating, whereas the micellar environment exerts a negative effect ($F_m < 1$) in all cases. The binding constants of sub-

Table 5. Activation parameters of the basic hydrolysis of phosphonates **3** and **4** in the micellar pseudo-phase of the CTAB—water—DMF system in the absence and presence of compound **1**

Substrate	Concentration of podand **1**/mol L^{-1}	ΔH /kJ mol^{-1}	$-\Delta S$ /J mol^{-1} K^{-1}
3	0	26.7±1.3	195.6±9.8
3	0.001	23.4±1.2	211.8±10.6
4	0	24.0±1.2	188.7±9.4
4	0.001	10.3±0.5	233.6±11.7

strates **3** and **4** are virtually the same, although the hydrophobicity of the latter is much higher. This alignment of substrate binding can be caused by a low efficiency of micellization in a DMF—water solution, resulting in the formation of small aggregates with a weak solubilizing ability.

A higher reactivity of compound **4** in a micellar solution in the absence of the podand (see Table 4) is caused by the fact that phosphonate **3** is characterized by a sharp decrease in the second-order rate constant on going from the volume to micellar phase: the F_m values for compounds **4** are 6—8 times higher than those for **3**. The negative influence of the microenvironment of both substrates (see Tables 3 and 5) is caused by a decrease in the activation entropy when the reaction is transferred to micelles, although the activation enthalpy decreases.

In the presence of compound **1**, the kinetic behavior of substrates **3** and **4** in micellar solutions differs substantially. In the case of compound **3**, the mechanism of micellar effect remains almost unchanged when **1** is introduced, which is indicated by an insignificant change in the F_c and F_m values (see Table 4). The binding constants of reactants remain virtually unchanged in the individual CTAB micelles and mixed CTAB—**1** systems, while the decrease in the second-order rate constants on going from the pseudo-phase volume to micelles is approximately an order of magnitude in the absence and presence of **1**. The decrease in the reactivity, as in the absence of an additive, is caused by a loss of the activation entropy (see Table 5). Similar tendencies of changing the quantitative characteristics of reactivity in the micellar system can indicate that the introduction of the podand, in the case of substrate **3**, exerts no effect on the distribution of reactants between the pseudo-phases, *i.e.*, the substrate **3**—podand **1** catalytic complex is formed in the micellar pseudo-phase and decreases $k_{2,m}$.

Substrate **4** is characterized by a considerable increase in the binding constant in a mixed system, achieving an order of magnitude. In addition, the micellar microenvironment factor changes rather sharply with temperature, indicating that the second-order rate constants in the volume and micellar pseudo-phases change *via* different mechanisms. As mentioned above, for the reaction in the absence of a surfactant, the inhibition effect of an additive is caused by an unfavorable change in the activation enthalpy of the reaction, and the activation entropy becomes more positive (see Table 2). On the contrary, in the micellar pseudo-phase in the presence of compound **1**, the activation enthalpy decreases favorably accompanied by losses of the activation entropy (see Table 5). Probably, in this case, a catalytic complex of substrate **4** with podand **1** is preliminarily formed and then solubilized by the CTAB micelles, which increases the binding constants of the substrate and decreases the binding constants of the nucleophile. The observed hydrolysis rate constant of substrate **3** decreases, when podand **1** is introduced in a micellar solution of CTAB, due to a decrease in the reactivity of the substrate in the micellar pseudo-phase characterized by $k_{2,m}$, while the influence of podand **1** on the hydrolysis of phosphonate **4** occurs *via* a change in binding of the reactants with micelles.

Thus, analysis of Tables 2—5 suggests the following. The mechanisms of basic hydrolysis of **3** and **4** in the absence of a surfactant and compound **1** are identical, which is indicated by close ΔH and ΔS values for both phosphonates. The calculated activation parameters correspond to the bimolecular nucleophilic substitution at tetracoordinate phosphorus.[24] The mechanisms of inhibition effect of **1** on the hydrolysis of **3** and **4** in the absence of a surfactant differ, and that for **3** is caused by an unfavorable change in the activation entropy, while in the case of **4**, the mechanism is caused by an increase in the activation enthalpy of the reaction. The mechanism of catalytic effect of CTAB micelles in the absence of **1** is identical for substrates **3** and **4** and occurs through the positive contribution of the concentrating factor and the negative contribution of the microenvironment factor. In a mixed CTAB—**1**—water—DMF system, the catalytic effect is caused by concentrating the reactants in the supramolecular system, and the influence of the micellar microenvironment can change from negative (for substrate **3**) to positive (for substrate **4**).

Experimental

IR spectra of the compounds synthesized were recorded on a Bruker Vector-22 FTIR spectrometer (in Nujol). ^{1}H NMR spectra were obtained on a Bruker MCL-400 spectrometer (400.13 MHz) in CD_3OD for compound **1** and in CD_3COCD_3 for compound **2** (internal standard). Melting points were determined on a Boetius heating stage.

1,8-Bis(3-ethyl-1,2-dihydro-2-oxoquinoxalin-1-yl)-3,6-dioxaethane (1). A mixture of 3-ethylquinoxalin-2(1*H*)-one (3.00 g, 17 mmol), KOH (1.5 g, 27 mmol), and dioxane (40 mL) was heated at the boiling point for 1—3 min, then 1,8-dibromo-3,6-dioxaoctane (2.6 g, 9.4 mmol) in dioxane (10 mL) was added,

and the resulting mixture was refluxed for 5 h. Then the reaction mixture was poured into water, and the crystals precipitated were filtered off and washed with a solution of KOH and water. Compound **1** was obtained in 96% yield (3.5 g), m.p. 115—117 °C (acetone). ^{1}H NMR, δ: 1.30 (t, 6 H, Me, J = 7.40 Hz); 2.90 (q, 4 H, C$\underline{H}_2$Me, J = 7.40 Hz); 3.51 (s, 4 H, OCH_2CH_2O); 3.68 (t, 4 H, NCH_2C$\underline{H}_2$O, J = 5.78 Hz); 4.38 (t, 4 H, NC$\underline{H}_2$CH_2O, J = 5.78 Hz); 7.32 (dd, 2 H, H(6) or H(7), quinox., J = 8.23 Hz, J = 6.29 Hz); 7.29 (ddd, 2 H, H(6) or H(7), quinox., J = 8.09 Hz, J = 6.71 Hz, J = 1.38 Hz); 7.49 (ddd, 2 H, H(6) or H(7), quinox., J = 8.33 Hz, J = 6.94 Hz, J = 1.39 Hz); 7.54 (dd, 2 H, H(8), quinox., J = 8.09 Hz, J = 0.92 Hz); 7.74 (dd, 2 H, H(5), quinox., J = 7.86 Hz, J = 1.14 Hz). IR, ν/cm^{-1}: 460, 717, 748, 873, 1029, 1075, 1092, 1115, 1177, 1224, 1262, 1313, 1354, 1424, 1496, 1569, 1604, 1650. Found (%): C, 67.76; H, 6.45; N, 12.26. $C_{26}H_{30}N_4O_4$. Calculated (%): C, 67.51; H, 6.54; N, 12.11.

1,14-Bis(3-ethyl-1,2-dihydro-2-oxoquinoxalin-1-yl)-3,6,9,12-tetraoxatetradecane (2). A mixture of 3-ethylquinoxalin-2(1*H*)-one (1.00 g, 5.6 mmol), KOH (0.5 g, 8.9 mmol), and dioxane (20 mL) was heated with boiling for 1—3 min, and a solution of 1,14-ditosylate-3,6,9,12-tetraoxatetradecane (1.6 g, 2.9 mmol) in dioxane (5 mL) was added. The resulting mixture was refluxed for 3 h, poured into water, and extracted with toluene (3×20), and then the solvent was evaporated with a water jet pump. Compound **2** was obtained as an oil, which was dissolved in *tert*-butyl methyl ether (20 mL) and filtered through a column (300×15 mm) packed with silica gel (5 g). The filtrate was washed with *tert*-butyl methyl ether (100 mL), and the solvent was evaporated. Analytically pure crystalline compound **2** was obtained in 75% yield (1.2 g), m.p. 33—34 °C (butyl methyl ether). ^{1}H NMR, δ: 1.26 (t, 6 H, Me, J = 736 Hz); 2.87 (q, 4 H, C$\underline{H}_2$Me, J = 7.36 Hz); 3.42 (s, 4 H, N$(CH_2)_2$-O$(CH_2)_2$OC$\underline{H}_2$C$\underline{H}_2$O$(CH_2)_2$O$(CH_2)_2$N); 3.46—3.51 (m, 4 H, N$(CH_2)_2$OCH_2C$\underline{H}_2$O$(CH_2)_2$OC$\underline{H}_2$CH_2O$(CH_2)_2$N); 3.53—3.57 (m, 4 H, N$(CH_2)_2$OC$\underline{H}_2$CH_2O$(CH_2)_2$OCH_2C$\underline{H}_2$O$(CH_2)_2$N); 3.80 (t, 4 H, NCH_2C$\underline{H}_2$O$(CH_2)_2$O$(CH_2)_2$O$(CH_2)_2$OC$\underline{H}_2$-CH_2N, J = 5.96 Hz); 4.46 (t, 4 H, NC$\underline{H}_2$CH_2O$(CH_2)_2$-O$(CH_2)_2$O$(CH_2)_2$OCH_2C$\underline{H}_2$N, J = 5.96 Hz); 7.31 (ddd, 2 H, H(6) or H(7), quinox., J = 8.04 Hz, J = 7.01 Hz, J = 1.40 Hz); 7.53 (ddd, 2 H, H(6) or H(7), quinox., J = 8.40 Hz, J = 7.04 Hz, J = 1.40 Hz); 7.63 (d, 2 H, H(8), quinox., J = 8.04 Hz); 7.75 (dd, 2 H, H(5), quinox., J = 8.08 Hz, J = 1.40 Hz). IR, ν/cm^{-1}: 464, 599, 637, 717, 751, 878, 952, 974, 1021, 1038, 1090, 1119, 1182, 1249, 1311, 1354, 1433, 1571, 1602, 1650. Found (%): C, 65.36; H, 7.15; N, 10.26. $C_{30}H_{38}N_4O_6$. Calculated (%): C, 65.44; H, 6.96; N, 10.17.

Compounds **3**—**5** were synthesized according to a known procedure.[25] Cetyltrimethylammonium bromide (Sigma) was used as received. The hydrolysis kinetics was studied spectrophotometrically on a Specord M-400 instrument in the pseudo-first order mode by a change in the absorbance of the *p*-nitrophenoxide anion (λ = 400 nm). The observed rate constants were determined from the dependence

$$\ln(A_\infty - A) = -k_{obs}t + \text{const},$$

where A and A_∞ are the absorbancies of the solution at the moment t and at the end of the reaction, respectively. They were calculated by the weighing least-squares method, and arithmetic mean values of three measurements differed by at most 5% were used in the calculation. The surface tension was determined by the ring method using the Du Nouy tensiometer[26] at 20 °C.

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