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Reaction of 2-alkylaminomethylphenols with 4-nitrophenyl-bis(chloromethyl)phosphinate in toluene micellar solutions of polyethylene glycol-600 monolaurate

E. P. Tishkova,* R. A. Shagidullina, L. A. Kudryavtseva, I. E. Ismaev, and B. E. Ivanov

A. E. Arbuzov Institute of Organic and Physical Chemistry,
Kazan' Scientific Center of the Russian Academy of Sciences,
8 ul. Akad. Arbuzova, 420083 Kazan', Russian Federation.
Fax: +7 (843 2) 75 2253

The effect of polyethylene glycol-600 monolaurate (PEG-ML) reversed micelles on the reaction of 2-alkylaminomethylphenols (AMP) with 4-nitrophenyl-bis(chloromethyl) phosphinate in toluene has been investigated. PEG-ML increases the observed rate constant of the reaction by more than one order of magnitude. AMP concentration in solution affects the position of the maximum on the concentration dependence of the micellar-catalyzed-reaction rate constants. The reaction rate constant in the micellar phase and the binding constant of the substrate with micelles depend on the alkyl chain length and AMP concentration. Inhibition of the reaction studied is observed in the presence of high PEG-ML concentrations and low AMP concentrations.

Key words: micellar catalysis; inhibition; nonionic surfactant; 2-alkylaminomethylphenol.

ortho-Aminophenols exhibit nucleophilic features to the esters of acids of tetracoordinated phosphorus.[1] In aqueous borate solutions the micelles of the cationic surfactant accelerate the reaction of 4-nitrophenyldimethyl phosphate with 2-dialkylaminomethylphenols.[2] The study of the micellar effect on the reaction of nucleophilic substitution in the 2-alkylaminomethylphenols (AMP) in a nonaqueous low-polar medium is of interest. In the present work we studied the reaction of 2-pentyl- (**1**), 2-octyl- (**2**), 2-dodecyl- (**3**), and 2-hexadecylaminomethylphenols (**4**) with *p*-nitrophenyl-bis(chloromethyl) phosphinate (PNCP) in toluene micellar solutions of polyethylene glycol-600 monolaurate (PEG-ML).

Experimental

2-Alkylaminomethylphenols were synthesized *via* condensation of phenol with paraform and the corresponding amines.[3] The purity of the substances produced was shown by potentiometric titration and by microanalysis. The properties of compounds **1**—**4** are given in Table 1. PNCP was produced following the described procedure.[4] PEG-ML by Ferak was used as it was. Toluene was purified by the standard procedure before use. The reaction kinetics was studied spectrophotometrically using the appearance of the 4-nitrophenol absorption band at 322.6 nm with Specord UV-VIS and SF-26 spectrophotometers. All stock solutions were exposed no less than 4 h before introducing the substrate. Substrate concentration was 10^{-4} *M*. In the kinetic experiments ethanol addition was 0.5 vol. %.

Table 1. Physicochemical properties of AMP

AMP	B.p. or m.p./°C (*p*/Torr)	n_D^{20}	Found / Calculated (%)			Molecular formula
			C	H	N	
1	97—99 (0.02)	1.5110	74.50 74.61	9.57 9.84	7.32 7.25	$C_{12}H_{19}NO$
2	120 (0.02)	1.4910	76.30 76.60	10.90 10.64	6.01 5.96	$C_{15}H_{25}NO$
3	45—47	—	78.59 78.35	11.98 11.34	4.92 4.81	$C_{19}H_{33}NO$
4	60—61	—	79.27 79.54	12.06 11.82	4.13 4.03	$C_{23}H_{41}NO$

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The value of k_{obs} of the reaction was calculated by the least-squares method on an Electronika DZ-28 microcomputer by the equation

$$\ln(D_\infty - D) = k_{obs} \cdot \tau + \text{const} ,$$

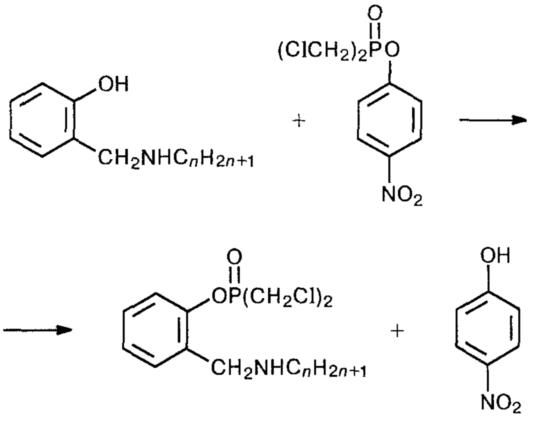
where D and D_∞ are the solution optical densities at the time τ and when the reaction was over, respectively.

The rate constant deviation in the parallel measurements was less than 10 %. ^{31}P NMR spectra were recorded with a Bruker MSL-400 (161.6 MHz) at 35 °C. The chemical shift determination was carried out in toluene with the addition of 1.5 vol. % of ethanol without surfactant and with the addition of 10 vol. % of ethanol in the presence of PEG-ML. Ethanol addition results in the appearance of weak signals at 24.6 and 25.0 ppm in the course of the reaction of **3** with PNCP without and with the surfactant, respectively. These peaks were attributed to a product of the substrate ethanolysis formed concurrently with the main reaction product.

Results and Discussion

The process under study occurs by Scheme 1.

Scheme 1



This scheme was supported by the spectrophotometrically measured formation of 1 mole 4-nitrophenol from 1 mole of the substrate, as well as by the data of ^{31}P NMR. The PNCP peak in the solution of 0.1 *M* **3** without the surfactant is 37.1 ppm, and in the presence of 0.06 *M* PEG-ML it is 38.2 ppm. In the course of the reaction at the same conditions we observed the appearance of a peak close to the parent one at 37.2 and 38.6 ppm, respectively. This peak can be assigned to the nucleophilic substitution product, the phosphorylated AMP. The variations of ^{31}P NMR peak intensities during the reaction of PNCP with **3** in PEG-ML solution are given in Fig. 1. The observed rate constant (k_{obs}) calculated from these data is $3.5 \cdot 10^{-3}$ s^{-1} at 35 °C.

Without surfactant the dependence of k_{obs} on AMP concentration (C_{AMP}) is linear for compounds **1**, **2**, and **4** or close to linear for **3** (Fig. 2) and at 25 °C is described by Eqs. (1) and (2).

$$k_{obs} = k_1 \cdot C_{AMP} , \tag{1}$$

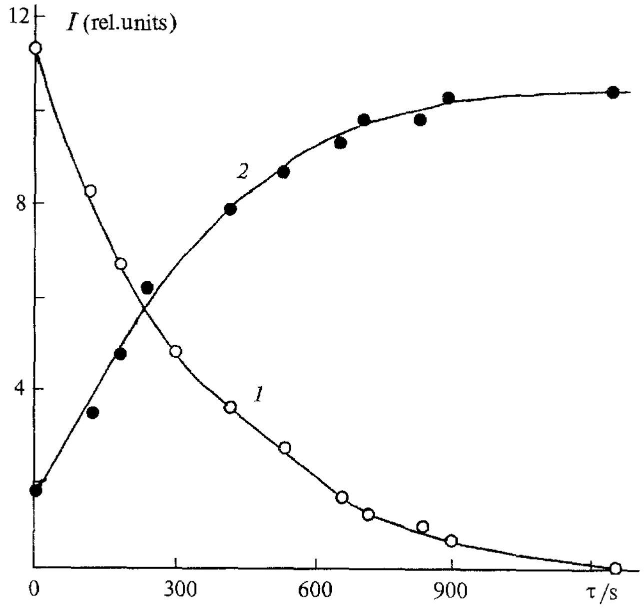


Fig. 1. Variations in ^{31}P NMR intensities of the peaks at δ 38.2 (*1*) and δ 38.6 (*2*) in time in reaction of 0.01 *M* PNCP with 0.1 *M* of **3** in a mixture of toluene—ethanol (90 : 10, v/v) with 0.06 *M* PEG-ML, 35 °C.

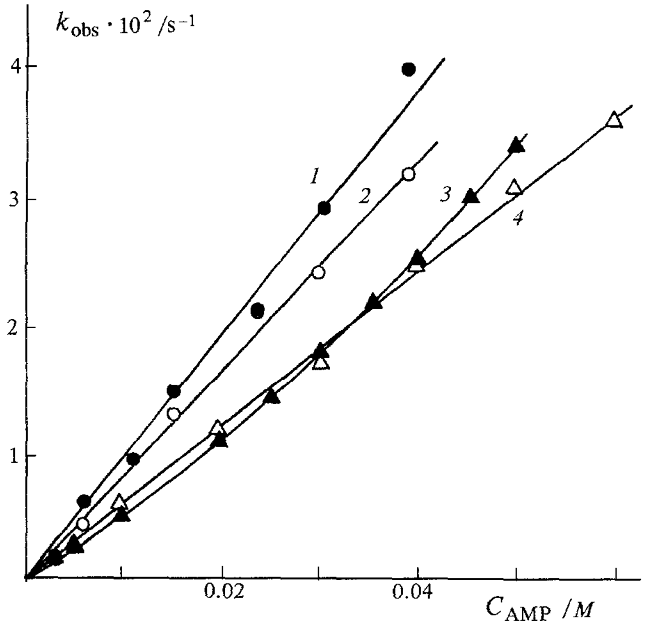


Fig. 2. The observed rate constant of reaction of AMP **1** (*1*), **2** (2), **3** (*3*), and **4** (*4*) with PNCP against AMP concentration, 25 °C.

where the values of k_l (L mol^{-1} s^{-1}) for **1**, **2**, and **4** are 1.02 ± 0.04, 0.85 ± 0.03, and 0.61 ± 0.01, respectively.

$$k_{obs} = k_2 \cdot C_{AMP} + k_3 \cdot C^2_{AMP} , \qquad (2)$$

where for **3** $k_2 = 0.471 \pm 0.004$ L mol^{-1} s^{-1}, $k_3 = 4.2 \pm 0.1$ L^2 mol^{-2} s^{-1}. The constant k_3 in Eq. (2) can be attributed to the catalytic reaction with the second AMP molecule.[4]

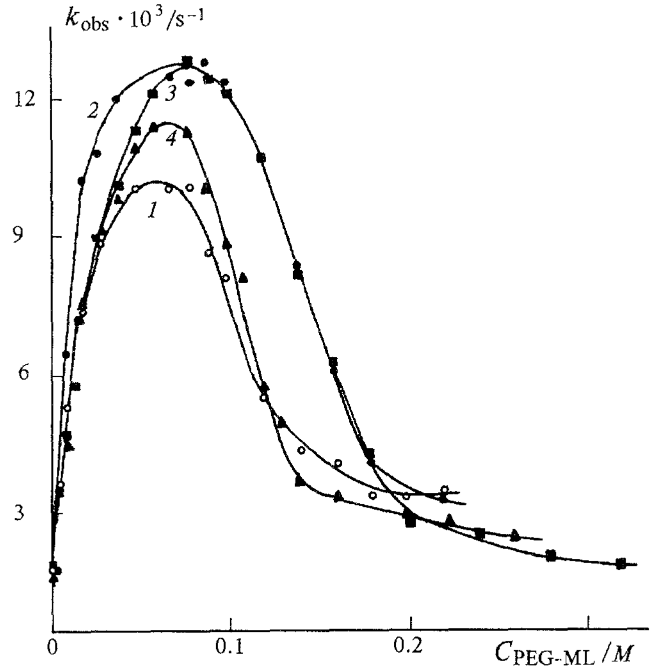


Fig. 3. The observed rate constant of reaction of AMP **1** (*1*), **2** (*2*), **3** (*3*), and **4** (*4*) with PNCP against PEG-ML concentration, C_{AMP} 0.003 *M*, 25 °C.

Table 2. The observed rate constants of the reaction of **3** with PNCP at different PEG-ML concentrations, 25 °C

$C_{PEG\text{-}ML}$ /*M*	$k_{obs} \cdot 10^2$/s^{-1}		$C_{PEG\text{-}ML}$ /*M*	$k_{obs} \cdot 10^2$/s^{-1}	
	0.006 *M* **3**	0.01 *M* **3**		0.006 *M* **3**	0.01 *M* **3**
0	0.28	0.52	0.12	3.8	7.4
0.005	0.67	1.1	0.14	3.8	7.4
0.01	1.0	1.6	0.15	3.6	—
0.015	1.3	2.1	0.16	3.2	7.4
0.02	1.6	2.5	0.17	3.1	—
0.03	2.0	3.4	0.18	—	7.5
0.04	2.4	4.4	0.20	2.3	7.6
0.05	2.7	4.9	0.22	—	7.2
0.06	3.1	5.6	0.24	—	6.9
0.07	3.3	6.2	0.26	1.0	6.5
0.08	3.4	6.6	0.28	—	6.4
0.09	3.6	6.9	0.32	0.56	5.6
0.10	3.7	7.0			

The existence of PEG-ML in solution results in a substantial (more than an order) increase in the rate constant of the AMP reaction with PNCP (Fig. 3, Table 2). This can be attributed to the catalytic effect of the non-ionic surfactant on the reaction studied. It is known that in toluene at 36 °C the PEG-ML critical concentration of micellization (CCM) lies in the range of $5 \cdot 10^{-4}$—$2 \cdot 10^{-3}$ *M* (CCM-1), and at concentrations 0.07—0.1 *M* (CCM-2) and 0.21—0.24 *M* (CCM-3) the structural reorganization of the micellar aggregates occurs.[5] The micellar catalysis also affects the shape of the k_{obs} dependence on the surfactant concentration with a sharp rise in the region of CCM-1 following the passage through a maximum. The maximum position depends on the AMP concentration in the solution. We observed $k_{obs}{}^{max}$ at the higher values of C_S as the AMP concentration increased. As is known, the maximum in the concentration dependence can be a result of reagent dilution in the micellar phase as its volume increases.[6] It appears that increasing AMP concentration in solution makes the dilution more difficult, and this results in a shift of k_{obs} maximum values of the micelle catalyzed reaction to high PEG-ML concentrations.

We determined the parameters of the micelle catalyzed reaction by least-square treatment of the kinetic data (see Fig. 3, Table 2) in the surfactant concentration range from CCM-1 to CCM-2 using the equation[7]

$$\frac{k_{obs} - k_0}{k_m - k_{obs}} = K_{bond} \cdot (C_S - C_m) ,$$

where k_0 and k_m are the reaction rate constants in bulk solution and in the micellar phase, respectively, K_{bond} is the substrate binding constant with the surfactant micelles, C_m is CCM. K_{bond} and C_m depend on the alkyl chain length and AMP concentration (Table 3). The values of k_m and K_{bond} vary nonlinearly with an increase in the AMP alkyl chain length. At equal nucleophile concentrations an increase in k_m and a decrease in K_{bond} occur only for AMP with n = 5, 8, 12. For compound **4,** in comparison with **3,** the reverse trend takes place. An increase in the concentration of **3** in solution results in an increase in k_m and a reduction in K_{bond} (see Table 3).

Table 3. The parameters of the micellar catalyzed reaction of AMP with PNCP in toluene solution of PEG-ML, 25 °C

AMP	C_{AMP} /*M*	$k_m \cdot 10^2$ /s^{-1}	C_{bond} /*M*$^{-1}$	$C_m \cdot 10^4$ /*M*
1	0.003	1.3	69	32
2	0.003	1.6	54	11
3	0.003	2.1	20	7.7
4	0.003	1.7	30	1.6
3	0.006	6.2	14	8.4
3	0.01	16	8	9.1
3*	0.003	2.3	19	7.2
3**	0.003	2.3	18	9.4

* *T* = 40 °C. ** *T* = 55 °C.

Table 4. The observed rate constants of the reaction of **3** with PNCP in PEG-ML micellar solutions at different AMP concentrations, 25 °C

C_{AMP}	$k_{obs} \cdot 10^2/s^{-1}$					
$\cdot 10^2/M$	Without surfactant*	0.04 *M* PEG-ML	0.12 *M* PEG-ML	0.2 *M* PEG-ML	0.26 *M* PEG-ML	0.32 *M* PEG-ML
0.05	0.024	0.018	—	—	—	—
0.1	0.048	0.078	0.015	0.0084	0.0063	0.0057
0.15	0.072	0.21	0.036	—	—	—
0.2	0.096	0.4	0.086	0.048	0.03	0.019
0.25	0.12	0.57	0.16	—	—	—
0.3	0.15	1.0	1.0	0.16	0.11	0.074
0.4	0.2	—	1.8	0.28	0.18	0.12
0.5	0.25	1.8	3.1	0.67	0.34	0.26
0.6	0.3	—	3.7	2.1	1.0	0.55
0.7	0.35	—	4.6	2.4	1.5	0.75
0.8	0.4	—	5.5	3.5	2.4	1.2
0.9	0.46	—	6.4	4.5	3.7	2.3
1.0	0.51	4.1	7.4	7.6	6.5	5.6

* k_{obs} are calculated by Eq. (2).

Table 5. The observed rate constants of the reaction of **1**, **2**, and **4** with PNCP in PEG-ML micellar solutions at different AMP concentrations, 25 °C

C_{AMP}/M	$k_{obs} \cdot 10^2/s^{-1}$		
	1	**2**	**4**
0.0015	0.085	0.12	0.054
0.003	0.53	0.5	0.67
0.0045	1.6	1.8	1.9
0.006	3.0	3.5	4.0
0.0075	4.4	5.1	5.4
0.009	6.1	7.3	6.6
0.0105	7.3	8.9	8.4

The character of the dependence of the observed rate constant on the AMP concentration is defined by the surfactant concentration (Tables 4 and 5). A dependence close to linear occurs only for the low values of C_S (0.04 *M* of PEG-ML, see Table 4). For higher surfactant concentrations the slight dependence of k_{obs} on the concentration of **3** is characteristic of the initial part of the curve, but then a dramatic increase in k_{obs} occurs (see Tables 4 and 5). The peculiarity of the curves described is the existence of regions not only of the catalytic action of surfactant micelles but of inhibition action as well (see Table 4). Micellar inhibition of the reaction at the initial part of the curves appears to be a result of reagent separation due to the weak affinity of AMP molecules to the micellar core. Inhibition is most pronounced for high surfactant concentrations (see Table 4).

The dependences of the effective values of the activation energy (E_a) and the activation entropy ($\Delta S^{\neq}$), calculated from the temperature dependences of k_{obs} at 25, 40, and 55 °C (see Figs. 3 and 4) on PEG-ML concentration are of a complex shape (Fig. 5). This is a result of the occurrence of three concurrent processes — the reaction in the bulk solution, the reaction in the

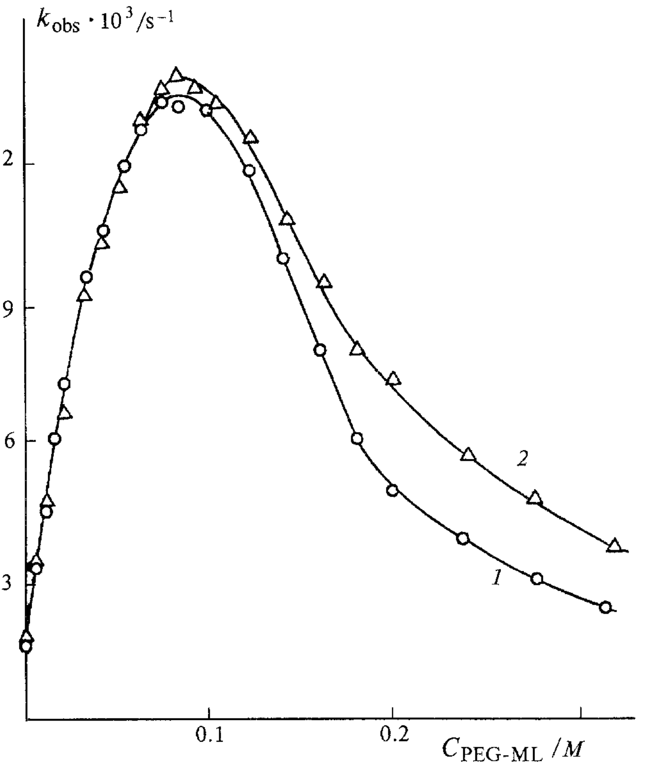


Fig. 4. The observed rate constant of reaction of 0.003 *M* of **3** with PNCP against PEG-ML concentration at 40 (*1*) and 55 (*2*) °C.

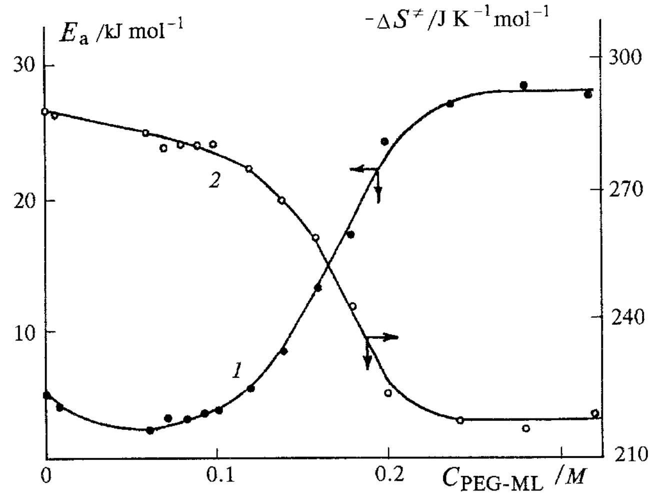


Fig. 5. The activation energy (*1*) and the activation entropy (*2*) of the reaction of 0.003 *M* of **3** with PNCP against PEG-ML concentration, 25 °C.

micellar phase, and reagent solubilization. Each of these processes makes a contribution to the activation parameter values determined, and the contribution magnitude depends on the surfactant concentration.[8,9] When the surfactant concentration is below C_m, the process thermodynamics is mainly defined by the reaction parameters in the bulk solution. When $C_S \approx C_m$, solubilization makes a substantial contribution. At high surfactant concentrations the thermodynamic parameters determined are close to those for the micellar phase. Structural reorganization of the micelles can play some role,[5] because according to the literature[10] variation of the surfactant aggregate shape can influence the reagent solubilization, its location, and the local mobility inside the micellar associates.

The results obtained indicate that the effect of PEG-ML micelles on the reaction of AMP with PNCP is determined by the concentrations of AMP and the surfactant in solution. The micelles inhibit or catalyze the reaction as a function of the ratio of AMP and the surfactant concentration.

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