Kinetics and mechanism of phosphorylation of monoethanolamine in reversed micelles of a cationic surfactant

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The reactions of monoethanolamine with 4-nitrophenyl esters of tetracoordinated phosphorus acids in chloroform in the presence of 2-hydroxyethyldimethylpentadecylammonium bromide were studied. The effective rate constants of the reactions are increased by more than two orders of magnitude in the presence of the micelle-forming cationic surfactant. The latter also favors the formation of the product of *O*-phosphorylation of monoethanolamine and leads to the appearance of a new ionic form of the 4-nitrophenol—monoethanolamine complex.

Key words: micellar catalysis, surfactant; monoethanolamine; esters of phosphorus acids.

The monoethanolamine molecule has two nucleophilic centers and can undergo phosphorylation at the N and O atoms.[1—3] The rate constants of the reactions and the ratio of the products of *N*- and *O*-phosphorylation of monoethanolamine with 4-nitrophenyl esters of phosphorus acids depend on the nature of the medium. In dipolar aprotic solvents, both reaction centers of the monoethanolamine molecule are involved in phosphorylation to the same extent, whereas in low-polarity solvents, phosphorylation at the O atom predominates.[3] Micellar aggregates can exert an additional effect on this process. It is known that in aqueous solutions, micelle-forming surfactants affect both the rate and the ratio of the directions of nucleophilic substitution in esters of four-coordinate phosphorus acids.[4] It was of interest to study the effect of reversed micelles of the cationic surfactant on the reaction of 4-nitrophenyl esters of phosphorus acids with monoethanolamine in a non-aqueous low-polarity medium.

In this work, we studied the reactions of monoethanolamine with 4-nitrophenyl bis(chloromethyl)-phosphinate (**1**) and 4-nitrophenyl ethylchloromethyl-phosphonate (**2**) in chloroform in the presence of 2-hydroxyethyldimethylpentadecylammonium bromide.

Experimental

Esters **1** and **2** were synthesized according to a known procedure.[5,6] 2-Hydroxyethyldimethylpentadecylammonium bromide was prepared by quaternization of 2-dimethylaminoethanol with pentadecylammonium bromide (see Ref. 7). Monoethanolamine was distilled before use. Chloroform was purified according to the standard procedure.[8]

The kinetics of the reaction was studied on Specord UV-VIS and SF-26 spectrophotometers using the intensity of the absorption band of 4-nitrophenol at 315—329 nm in the absence of the surfactant and the intensity of the absorption band of the 4-nitrophenoxide ion at 423—440 nm in the presence of the surfactant. The observed first-order rate constants (k) were calculated by the least-squares method on an Elektronika D3-28 microcomputer. The ^{31}P NMR spectra were recorded on a Bruker MSL-400 instrument (162 MHz) at 35 °C; the number of scans was 400. The initial concentrations of the reagents (mol L^{-1}) were 0.0015 (**1**) and 0.31 (monoethanolamine) in the absence of the surfactant and 0.003 (**1**) and 0.31 (monoethanolamine) in the presence of a 0.1 *M* 2-hydroxyethyldimethylpentadecylammonium bromide solution.

Results and Discussion

Phosphorylation of monoethanolamine can afford products **3** and **4**.

$$ClCH_2(R)P(O)OC_6H_4NO_2 + HOCH_2CH_2NH_2 \longrightarrow$$

$$\longrightarrow ClCH_2RP(O)OCH_2CH_2NH_2 \quad \mathbf{3}$$

$$\longrightarrow ClCH_2RP(O)NHCH_2CH_2OH \quad \mathbf{4}$$

R = $ClCH_2$ (**1**), EtO (**2**)

Previously, it has been demonstrated that when monoethanolamine reacted with 4-nitrophenyl phenyl(chloromethyl)phosphonate in chloroform, only *O*-phosphorylation of the nucleophile occurred.[3] We have found that this direction of the reaction predominated also in the case of ester **1**. According to the data of

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^{31}P NMR spectroscopy, in the absence of the surfactant in chloroform, products **3** (δ ^{31}P 41.4) and **4** (δ ^{31}P 25.0) were formed in yields of 69% and 31%, respectively. In the presence of 2-hydroxyethyldimethylpentadecylammonium bromide, the reaction shifted further to the products of *O*-phosphorylation, which were obtained in yields of 86% (δ ^{31}P 41.4) and 14% (δ ^{31}P 22.9), respectively.

Reversed micelles affect also the reaction rate. In chloroform, the dependences of the observed first-order rate constants of the reactions of monoethanolamine (MEA) with esters **1** and **2** on the concentration of the nucleophile are nonlinear (Fig. 1) and are described by the following equation:

$$k = k_1 C_{MEA} + k_2 C_{MEA}^2. \quad (1)$$

The values of k_1 and k_2, which were calculated using this equation by the least-squares method, are given in Table 1. The second-order concentration term for the nucleophile in Eq. (1) can be due to the participation of the second monoethanolamine molecule in the reaction analogously to that described previously in Ref. 5. In the presence of 2-hydroxyethyldimethylpentadecylammonium bromide, the effective first-order rate constant increases substantially (Fig. 2). This effect depends on the concentration of the surfactant at high concentrations of which the value of k reaches a limiting value. Such dependence is typical of micellar-catalyzed processes. The obtained data are described by the following equation:

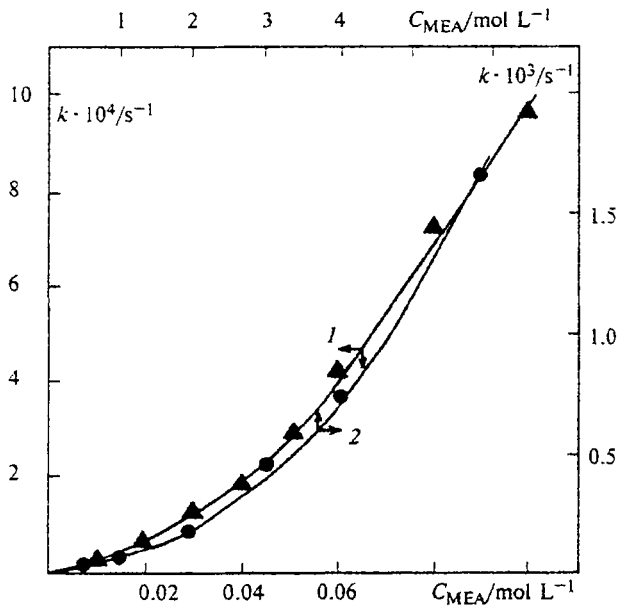

Fig. 1. Dependences of the observed rate constants of the reactions (k) of monoethanolamine with esters **1** ($5 \cdot 10^{-5}$ mol L^{-1}) (*1*) and **2** (10^{-4} mol L^{-1}) (*2*) on the concentration of monoethanolamine in chloroform at 25 °C.

$$k = \frac{k_m K_{bond} C_{surfactant} + k_0}{1 + K_{bond} C_{surfactant}}, \quad (2)$$

where k_m and k_0 are the rate constants of the reaction in the micellar phase and in the bulk of the solvent, respectively, K_{bond} is the constant of bonding of the substrate with micelles of the surfactant, and $C_{surfactant}$ is the concentration of the surfactant in the solution taking into account the data on the critical micelle concentration (Cmc).[9] Analysis of the concentration dependences of the rate constants by the least-squares method using Eq. (2) in $1/(k_0 - k) - 1/C_{surfactant}$ coordinates allows one to calculate the values of k_m and K_{bond} (Table 2). An increase in the concentration of monoethanolamine results in an increase in the values of k_m and K_{bond}. An increase in the temperature causes an increase in the value of k_m and affects only slightly the value of K_{bond}.

The character of the dependence of the observed rate constant of the reaction on the concentration of amine also changes in the presence of 2-hydroxyethyldimethylpentadecylammonium bromide. From the data in Table 3 it follows that for the reactions of monoethanolamine with esters **1** and **2** in micellar solutions of 2-hydroxyethyldimethylpentadecylammonium bromide, the dependences of k_m on the concentration of the

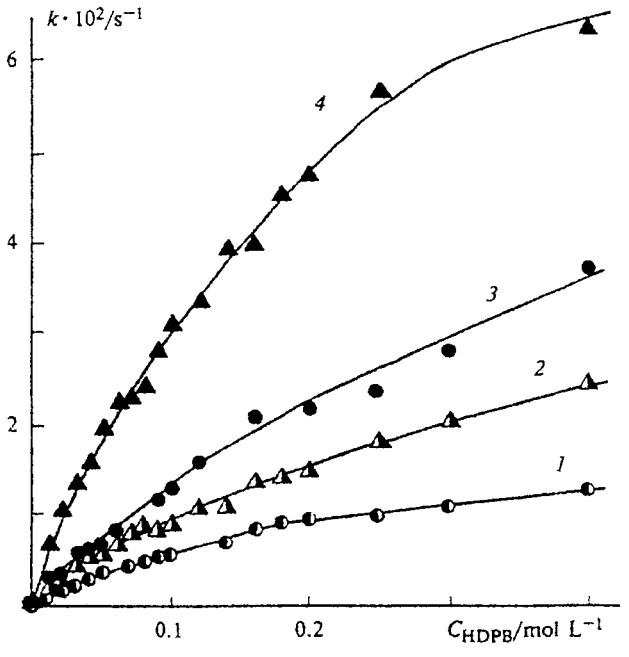

Fig. 2. Dependences of the observed rate constant of the reaction (k) of monoethanolamine with ester **1** (10^{-4} mol L^{-1}) in chloroform in the presence of 2-hydroxyethyldimethylpentadecylammonium bromide on the concentration of the surfactant at 25 °C (*1*, *4*), 40 °C (*2*), and 50 °C (*3*); C_{MEA}/mol L^{-1} is 0.01 (*1*—*3*) and 0.05 (*4*).

Table 1. Rate constants of the reaction of monoethanolamine with esters **1** and **2** in chloroform at 25 °C in the presence of 2-hydroxyethyldimethylpentadecylammonium bromide (HDPB)

Substrate	$C_{substrate} \cdot 10^{-4}$ / mol L^{-1}	C_{HDPB} / mol L^{-1}	$k_1 \cdot 10^{-3}$ / L mol^{-1} s^{-1}	$k_2 \cdot 10^{-3}$ / L mol^{-2} s^{-1}	k_2/k_1
1	0.5	—	1.65	90.3	55.0
2	1.0	—	0.0278	0.0406	1.5
1	2.0	0.01	165.0	—	—
1	2.0	0.05	413.0	—	—
2	1.0	0.25	0.779	0.616	0.8

Table 2. Characteristics of the reaction of monoethanolamine with ester **1** (10^{-4} mol L^{-1}) in chloroform in the presence of HDPB*

C_{MEA} /mol L^{-1}	T/°C	$k_m \cdot 10^{-2}/s^{-1}$	K_{bond} /mol^{-1} L
0.01	25	1.8	5
0.05	25	6.0	13
0.01	40	3.1	5
0.01	50	5.1	3

* Cmc_{HDPB} < 0.005 mol L^{-1}.

Table 3. Dependences of the observed rate constants of the reactions of monoethanolamine with esters **1** ($2 \cdot 10^{-4}$ mol L^{-1}) and **2** (10^{-4} mol L^{-1}) in the presence of HDPB on the concentration of monoethanolamine in chloroform at 25 °C

C_{MEA} /mol L^{-1}	$k_1 \cdot 10^{-2}/s^{-1}$ C_{HDPB} = 0.01*	$k_1 \cdot 10^{-2}/s^{-1}$ C_{HDPB} = 0.05*	$k_2 \cdot 10^{-2}/s^{-1}$ C_{HDPB} = 0.25*
0.005	—	0.254	—
0.01	0.15	0.45	—
0.015	0.26	0.6	—
0.02	0.28	0.81	—
0.03	—	1.1	—
0.04	0.57	—	—
0.05	—	2.0	—
0.06	0.9	2.4	—
0.08	1.1	3.4	—
0.1	1.2	—	0.0075
0.15	2.0	—	—
0.2	2.7	—	0.013
0.25	3.8	—	—
0.3	4.8	—	—
0.35	5.4	—	—
0.4	6.3	—	0.04
0.5	8.6	—	—
0.6	10.5	—	0.084
0.7	11.0	—	—
0.8	13.0	—	0.12
2.0	—	—	0.41
3.0	—	—	0.75

* The concentration of HDPB is given in mol L^{-1}.

nucleophile are approximately linear. The absence of the squared term in the case of the reaction of ester **1** and the insignificant contribution of this term in the case of the reaction of **2** (see Table 1) may be evidence that in micelles, the process occurs in the microenvironment, which differs substantially from that in the pure solvent. Previously,[5] it has been found that when 4-nitrophenyl esters of phosphorus acids undergo nucleophilic substitution in nonaqueous media, the decrease in the contribution of the squared term depends directly on the proton-accepting ability of the solvent. In this case, the first order with respect to the nucleophile can result from the fact that the molecule of the solvent is involved in the reaction instead of the second molecule of the reagent.[5] It is known that in micellar nonaqueous solutions, transfer of the reagents from the bulk of the solvent to polar nuclei of the micelles occurs.[10] The nucleus of the micelle of 2-hydroxyethyldimethylpentadecylammonium bromide is formed by groups containing hydroxyethyl fragments and counterions (Br^- anions), which can form a hydrogen bond and can be involved in the process due to which the k_2/k_1 ratio in Eq. (1) changes substantially (see Table 1).

In addition to the kinetic effects, the influence of micelles is also manifested in the change in the optical

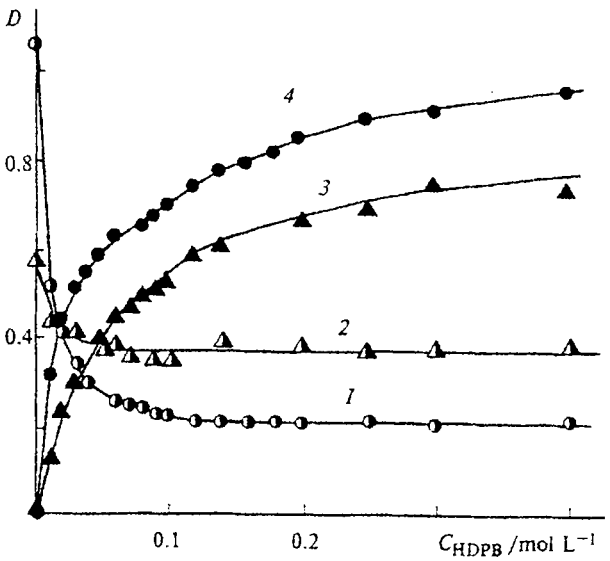

Fig. 3. Dependences of the optical density (D) of the complex of 4-nitrophenol (NP) with monoethanolamine in chloroform in the presence of 2-hydroxyethyldimethylpentadecylammonium bromide on the concentration of the surfactant at 315 nm (*1*, *2*) and 440 nm (*3*, *4*) 25 °C; C_{MEA}/mol L^{-1} is 0.01 (*2*, *3*) and 0.05 (*1*, *4*); $C_{NP} = 10^{-4}$ mol L^{-1}; d = 1 cm.

properties of solubilized particles. The optical density of the absorption band at 430—460 nm increases and the intensity of the band at 315—322 nm decreases as the concentration of the surfactant increases. The higher the concentration of monoethanolamine, the larger these changes (Fig. 3).

It is known that in the presence of amines, 4-nitrophenol can form a complex, which contains a hydrogen bond, and a ionic pair. In solvents with a low dielectric permeability (ε = 2—7), the equilibrium

is shifted to the nonionic structure.[11] The appearance and the increase in the optical density of the absorption band at 430—460 nm in the system under study may be a result of the fact that localization of 4-nitrophenol and monoethanolamine in the polar nucleus of the micelle leads to the shift of the equilibrium to the ionic pair. This phenomenon becomes more pronounced as the concentration of monoethanolamine increases, which is, apparently, due both to an increase in the bonding of the substrate (see Table 2) and to a change in the polarity of nuclei of reversed micelles when the nuclei are saturated with molecules of the nucleophile.

The obtained data indicate that the micelle-forming cationic surfactant allows one to change the rate of phosphorylation of monoethanolamine with 4-nitrophenyl esters of four-coordinate phosphorus acids in a nonaqueous low-polarity medium, affect the mechanism, and shift the equilibrium of the 4-nitrophenol—monoethanolamine complex that formed in the system.

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