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Catalytic Properties of Supramolecular Systems Based on Polyoxyethylated Calixarenes and Amines

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Abstract—The rate of carboxylic ester cleavage by amphiphilic low-molecular-weight and polymeric amines in the presence of polyoxyethylated calix[4]arenes with different degrees of oxyethylation is determined by the formation of mixed aggregates, by the shift of pK_a of the amine, and the character of the distribution of the reactants in functional micelles. All of the systems show a high substrate specificity. In the case of octyl- and decylamines, the reaction of *p*-nitrophenyl acetate is catalyzed and the reaction of more hydrophobic *p*-nitrophenyl laurate is inhibited. An opposite situation is observed in the systems based on branched polyethyleneimine: the reaction of *p*-nitrophenyl acetate is inhibited and the process involving *p*-nitrophenyl laurate is accelerated.

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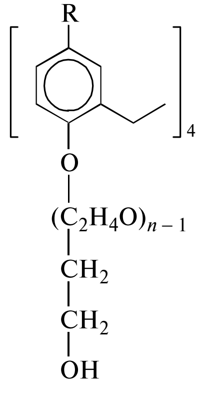
Amphiphilic and polymeric molecules are classified as building blocks whose prototypes are lipids and proteins, which are structure-forming components of biological membranes [1–3]. As their natural analogues, synthetic amphiphiles and polymers show a pronounced tendency to self-organization in solutions. The resulting nanosized supramolecular aggregates can solubilize organic compounds and control their solubility, acid-base properties, reactivity, and other properties by creating a specific microenvironment [4–9]. Therefore, search for new amphiphilic substances and studies of their self-organization in the solution bulk and at interfaces are of considerable interest.

Calix[4]arenes oxyethylated at their lower rim (COs) are new types of amphiphilic compounds, which combine functions of a nonionic surfactant and a cyclophane platform. This is reflected in their aggregation behavior and solubilizing properties [10–12]. Unlike typical surfactants, calixarenes are capable of forming aggregates due to the hydrophobic effect and also due to inclusive interactions involving their cavity [13–16]. Passing to multicomponent compositions containing calixarenes and other amphiphilic compounds and calixarene immobilization on the polymer matrix can initiate other mechanisms of self-organization and impart new functional properties to the system.

Here, we report supramolecular systems based on amphiphilic or polymeric amines and CO with different degrees of oxyethylation having alkyl (*tert*-butyl, *iso*-nonyl) substituents on the upper rim. The structural formulas and designations of the COs are given below.



$R = i\text{-}C_9H_{19}$, $n = 9$ (9CO9), $n = 8$ (9CO8);
$R = t\text{-}C_4H_9$, $n = 16$ (4CO16)

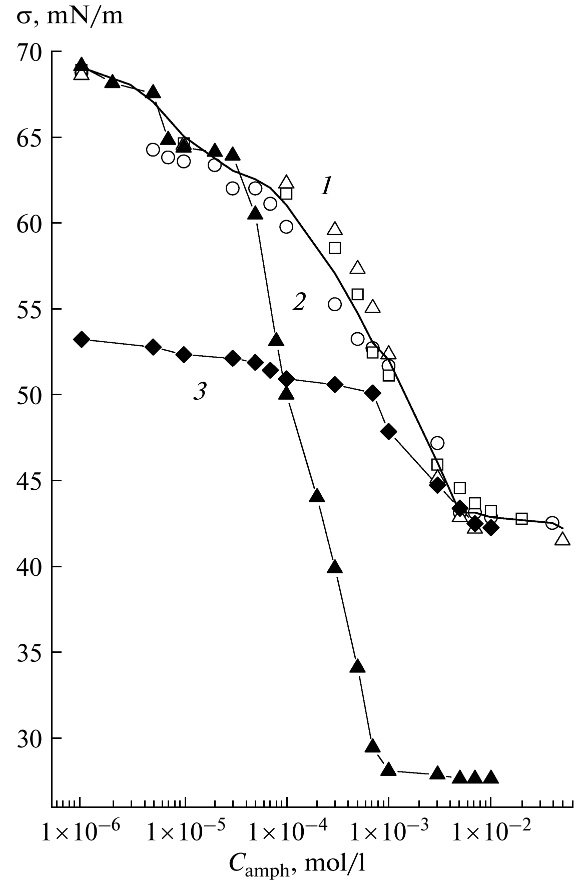


Fig. 1. Surface tension isotherms for the 9CO8-based systems: (*1*) (open circles) individual solution, (open triangles) solution containing an equimolar amount of PEI_{25}, and (open squares) solution containing an equimolar amount of PEI_{25}-12; (*2*) solution containing an equimolar amount of decylamine; (*3*) fixed PEI_{25}-12 concentration (0.005 mol/l).

Low-molecular-weight amines (octyl- and decylamines), branched polyethyleneimine with a molecular weight of 25000 (PEI_{25}), and its derivatives modified with long-chain (dodecyl) radicals (PEI_{25}-12) were studied.

The catalytic effect of supramolecular systems is associated with the transfer of chemical reactions from the solution bulk to nanosized aggregates and is determined by the effect of concentrating and by changes in the microenvironment of interacting particles. For this reason, one of the tasks of this work is to study self-organization in calixarene–amine systems. In addition, a shift of the pK_a of ionogenic compounds can be observed in microheterogeneous systems. In this connection, we studied the influence of calixarenes on the basicity of amines. The data that we obtained served as the basis for evaluation of the catalytic effect of the systems. Oxyethylated calixarene are structurally similar to nonionic surfactants. For this reason, the results obtained in this study were compared with the behavior of supramolecular systems based on oxyethylated phenol Triton X-100 (polyethylene glycol *p*-(1,1,3,3-tetramethylbutyl)-phenyl ether) in order to elucidate the role of the calixarene matrix.

EXPERIMENTAL

COs were synthesized as described in [17]. Commercial long-chain amines (Acros Organics), esters (*p*-nitrophenyl acetate and *p*-nitrophenyl laurate) (Fluka), Triton X-100, and branched PEI_{25} (molecular weight of 25000 g/mol) (Aldrich) were used. Hydrophobized PEI (PEI_{25}-12) was synthesized by reacting PEI_{25} with dodecyl bromide in ethanol [18, 19]. The average molecular weight of the monomeric unit of PEI_{25}-12 was determined by potentiometric titration to be 107 ± 3, which corresponds to a degree of alkylation of ~0.2. The pK_a values of amines and the fraction of nonprotonated amino groups (α) were determined by the potentiometric titration of their solutions with 0.1 M hydrochloric acid using a pH-340 pH meter. The amphiphile concentration was varied between 0 and 0.02 mol/l. Molar concentrations (mol/l) of PEI in terms of monomeric units were used.

The surfactant properties were studied by the ring method on a Du Nouy tensiometer (Kruss). The electric conductivity of solutions prepared in bidistilled water with an electric conductivity of at most 1.8 μS/cm was measured using a CDM-2d instrument (Radiometer Copenhagen).

The reaction kinetics was studied by spectrophotometry on a Specord UV-Vis instrument at 25°C in freshly prepared solutions under pseudo-first-order reaction conditions. A constant pH was maintained by using buffer solutions of sodium tetraborate (pH 9.2 or 10.0). The process was monitored spectrophotometrically as the change in the absorbance of the solution at 400 nm (formation of the *p*-nitrophenolate anion). The initial concentration of the substrate was 5×10^{-5} mol/l, and the conversion was higher than 90%. Apparent rate constants (k_{app}) were determined from the relationship $\log(A_\infty - A_\tau) = -0.434k_{app}\tau + \text{const}$, where A_τ and A_∞ are the absorbances of the solution at the moment τ and after the completion of the reaction. The values of k_{app} were calculated using the least-squares method.

RESULTS AND DISCUSSION

The properties of the mixed compositions are determined, to a considerable extent, by the properties of their components. The aggregation behavior of individual solutions of oxyethylated calixarenes was studied earlier [10, 11]. The values of the critical micelle concentration (CMC) for aqueous solutions of COs with different structures are similar, being 0.0038, 0.0021, and 0.0022 mol/l for 9CO8, 9CO9, and 4CO16, respectively. The surface tension isotherm for 9CO8 is presented as an example in Fig. 1. Note that the CMC of the structurally similar nonionic surfactant Triton X-100 is 0.0002 mol/l [20], one order of magnitude lower than that of the COs. This distinction may arise from different mechanisms of self-organization. Both hydrophobic and inclusive interactions and π–π stacking effects can contribute to the process, and the presence of a large cavity can lead to a specific packing of calixarene molecules. It was shown [11] that COs can form micelle-like aggregates and also lamellar or pile structures.

Low-molecular-weight amines containing hydrophobic radicals are prone to micelle formation in water: octylamine in neutral form is characterized by a CMC value of 0.008 mol/l, while the CMC of decylamine is 0.00095 mol/l [21]. In the case of polyamines, the tensiometric data indicate that unsubstituted PEI_{25} is surface-inactive, whereas hydrophobized PEI_{25}-12 exhibit properties of a typical surfactant (Fig. 2). The concentration of PEI_{25}-12 corresponding to the inflection in the surface tension isotherm (critical aggregation concentration CAC_1 = 0.0012 mol/l) indicates the commencement of aggregation in the system. The inflection in the conductivity versus concentration curve is observed in the same region, and another one (CAC_2) occurs at a higher concentration of ~0.01 mol/l (Fig. 2, inset). It is likely that, at low polymer concentrations, aggregation occurs due to interactions inside one polymer molecule. An increase in the polymer concentration increases the probability of intermolecular interactions, including hydrogen bond formation, which results in the formation of aggregates containing several macromolecules.

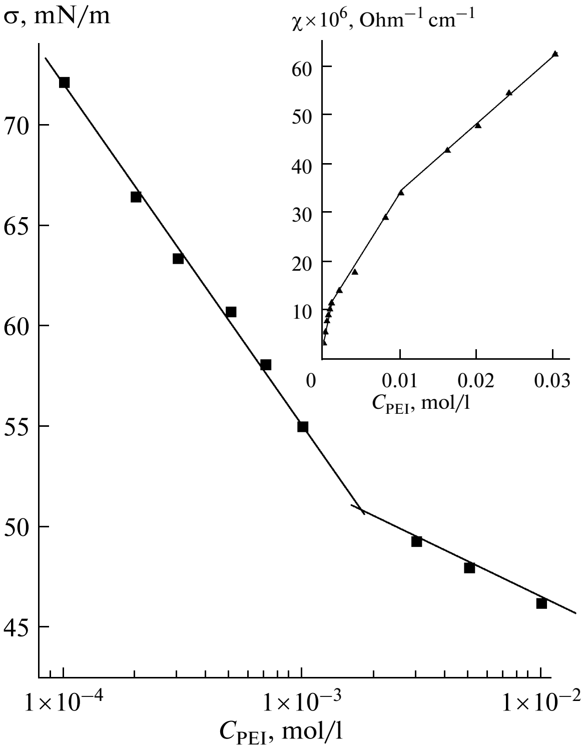


Fig. 2. Surface tension isotherm for an aqueous solution of PEI_{25}-12; 25°C. Inset: concentration dependence of the electric conductivity of aqueous solutions of PEI_{25}-12; 25°C.

In binary systems, nonmicellizing hydrophilic amines (both low-molecular-weight butylamine and polymeric PEI_{25}) do not shift the CMC of the calixarenes (Fig. 1). In the systems based on PEI_{25}-12 and 9CO8, the CMC determined from the surface tension isotherm both at a constant molar ratio of components (1 : 1) and at a fixed PEI concentration (0.05 mol/l) also insignificantly differs from the CMC of the individual calixarene. These results are in agreement with the known facts that the addition of a polymer to solutions of nonionic surfactants does not usually decrease the CMC [22]. This was confirmed in our recent study of the surface properties of the Triton X-100–PEI system [23]. Decylamine exerts the most significant effect on

Fraction of the neutral form of amines (α) in aqueous solutions at pH 9.2 in the presence and in the absence of CO

CO	α			
	Octylamine	Decylamine	PEI_{25}	PEI_{25}-12
No surfactant	0.02	0.13	0.92	0.96
9CO9 (C = 0.01 M)	0.11	0.39	0.92	0.97
4CO16 (C = 0.01 M)	0.12	0.38	0.91	0.96

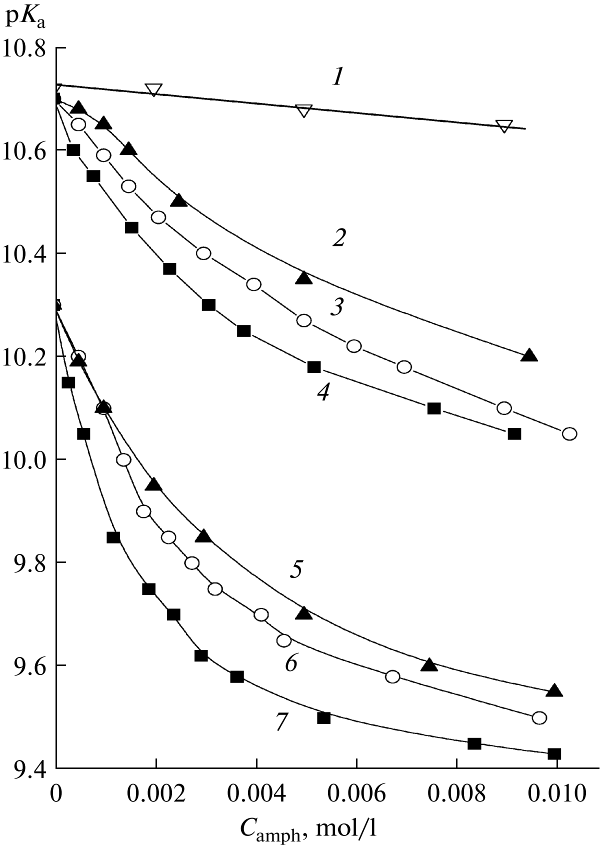
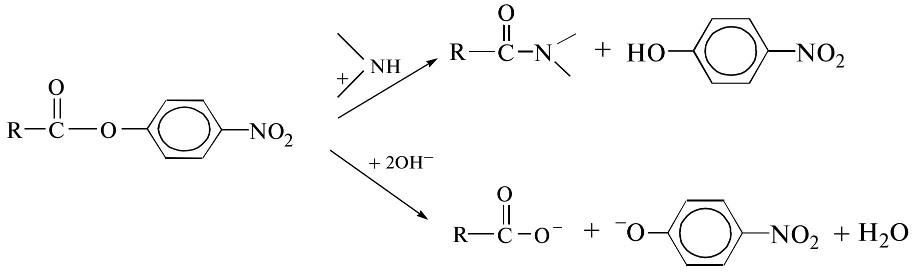


Fig. 3. Plot of pK_a of amines versus the amphiphile concentration in the amine–nonionic amphiphile binary systems: (*1*) butylamine–9CO8, (*2*) octylamine–Triton X-100; (*3*) octylamine–9CO8, (*4*) octylamine–4CO16, (*5*) decylamine–Triton X-100, (*6*) decylamine–9CO8, and (*7*) decylamine–4CO16; C_{amine} = 0.005 mol/l, 25°C.

the character of the surface tension isotherm of the COs. It affects both the slope of the curve and the CMC value: at the 1 : 1 molar ratio of the components, the 9CO8–decylamine system is characterized by CMC = 0.0007 mol/l. It should be mentioned that this system can strongly decrease the the water–air interfacial tension (Fig. 1).

The formation of mixed aggregates in the systems based on the calix[4]arenes and low-molecular-weight hydrophobic amines decreases the pK_a of the latter (Fig. 3, table). The higher the hydrophobicity of the amine, the stronger this influence; however, the role of the change in the calixarene structure is insignificant. A decrease in the pK_a of amines is accompanied by an increase in the fraction of their neutral form (α) at a given pH of the solution. For both unsubstituted and alkylated PEIs, the addition of a CO almost does not change the value of α (table), which probably reflects the weak binding between the components of the system. For more basic, long-chain amines, the formation of mixed aggregates is facilitated by the possibility of stronger hydrogen bonding between the amine and the calixarene.

It is the neutral form of amines that manifests the nucleophilic properties observed in chemical reactions. Accordingly, a decrease in pK_a usually accelerates processes involving amines. In this work, we studied the influence of CO–amine binary systems on nucleophilic substitution in carboxylic esters, namely, *p*-nitrophenyl acetate (PNPA) and *p*-nitrophenyl laurate (PNPL). In weakly alkaline media, this process proceeds via two routes. The main route is aminolysis, which, in the case of branched PEIs, involves the terminal primary amino groups and secondary amino groups included in the main chain. In addition, alkaline and neutral hydrolyses can occur. The scheme of the process is presented below.



Note that this choice of objects of investigation makes it possible to simulate a set of factors characteristic of enzyme catalysis. In these systems, polymeric and higher monomeric amines act both as reactants and as structure-forming components, thus forming functional micelles. These aggregates allow one to attain the maximum reactant concentrating effect. Another important factor, which plays the key role in biocatalysis, is the shift of the pK_a of ionogenic groups (amino groups in our case) in micellar systems. Kinetic studies of a reaction of two substrates differing in hydrophobicity make it possible to evaluate the substrate specificity, one of the most important parameters of the efficiency of catalytic systems.

Kinetic studies of ester cleavage in the presence and absence of an amine (at a fixed pH) make it possi-

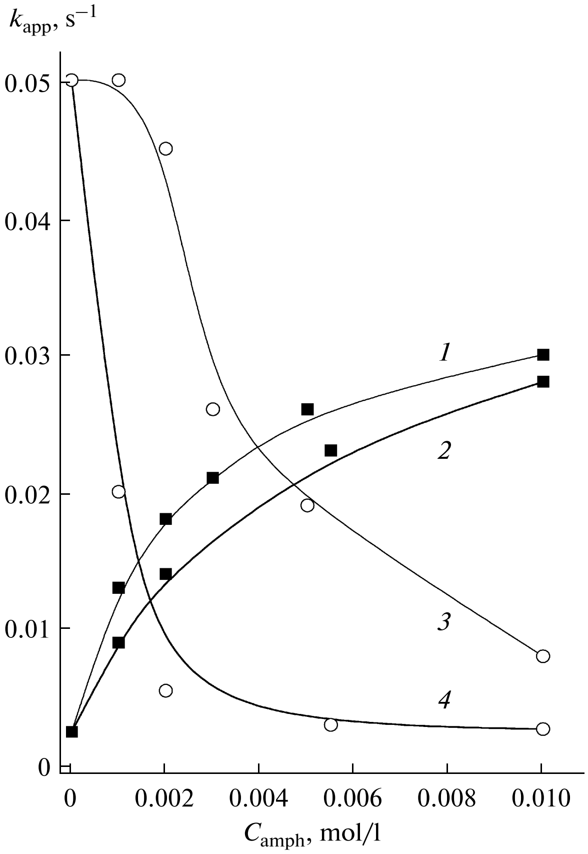


Fig. 4. Apparent rate constant for the reactions of carboxylic esters with decylamine versus the amphiphile concentration in the decylamine–nonionic amphiphile binary systems: (*1*) PNPA–Triton X-100, (*2*) PNPA–9CO9, (*3*) PNPL–Triton X-100, and (*4*) PNPL–9CO9; C_{amine} = 0.0025 mol/l, pH 9.2, 25°C.

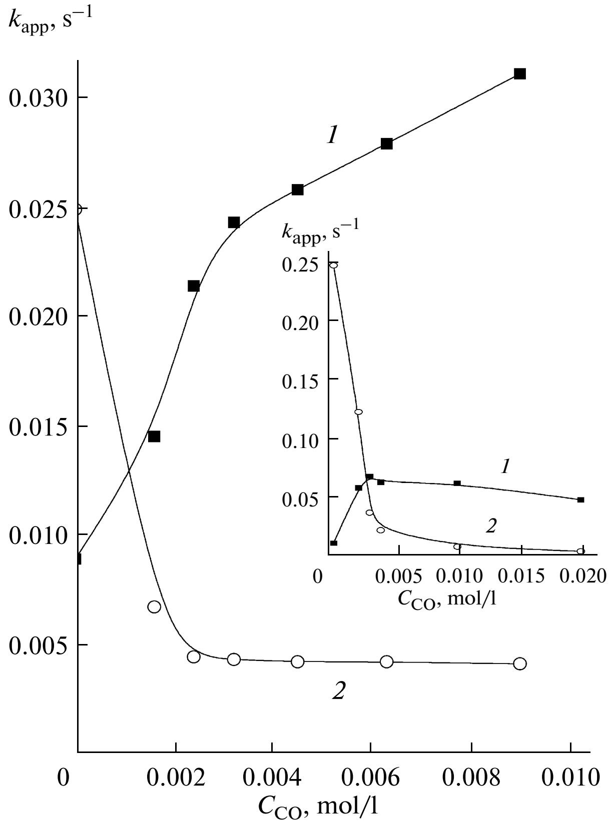


Fig. 5. Apparent rate constant for the reactions of octylamine with (*1*) PNPA and (*2*) PNPL versus the calixarene concentration in the binary system octylamine–9CO9; C_{amine} = 0.0025 mol/l, pH 10, 25°C. Inset: apparent rate constant for the reactions of decylamine with (*1*) PNPA and (*2*) PNPL versus the calixarene concentration in the decylamine–9CO9 binary system; C_{amine} = 0.0025 mol/l, pH 10, 25°C.

ble to separate the contributions from aminolysis and hydrolysis to the overall process rate. Figures 4–6 illustrate the influence of COs on the apparent rate constant (k_{app}) of PNPA and PNPL cleavage in the systems containing both low-molecular-weight and polymeric amines, specifically, unsubstituted PEI_{25} and alkylated PEI_{25}-12. The rate constant for the alkaline hydrolysis of PNPA was preliminarily estimated by spectrophotometry at pH 9.2 (borate buffer) in the absence of amines. The addition of 9CO9 exerts an insignificant effect on the process rate: k_{app} decreases from 0.0005 to 0.0004 s^{-1}. Thus, under our experimental conditions, the contribution from hydrolysis can be ignored. Therefore, the curves presented in Figs. 4–6 reflect the influence of the COs on aminolysis. However, passing to a more alkaline medium can increase the contribution from hydrolysis, and this should be taken into account.

The influence of calixarenes on the aminolysis rate depends on the structures of the amine and substrate. The rate constant of the reaction of PNPA with low-molecular-weight amines containing hydrophobic radicals (decylamine) in solutions of 9CO9 increases. This possibly reflects the decrease in the pK_a of the amines and the increase in the fraction of their neutral form. A similar dependence is observed for the aminolysis of PNPA in solutions of Triton X-100 (Fig. 4). In spite of the decrease in the pK_a of decylamine in CO micelles, the reaction of decylamine with PNPL is inhibited (Fig. 4). Laurate is self-associated in aqueous solutions, resulting in the screening of the active sites of the substrate and making it anomalously less reactive than PNPA [24]. Some amphiphilic reactants, including hydrophobic amines, can form mixed aggregates with PNPL. In these aggregates, the two reactants are in intimate contact, resulting in high process rates [25]. The addition of a CO to the system containing highly reactive association species of decylamine and PNPL is accompanied by the formation of new multicomponent mixed micelles and by the sepa-

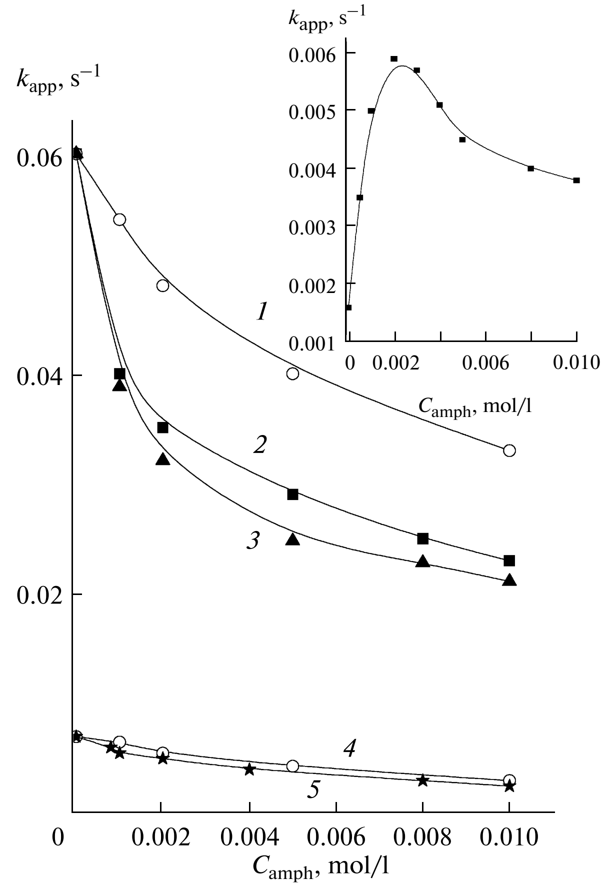


Fig. 6. Apparent rate constant for the aminolysis of PNPA versus the amphiphile concentration in the PEI–nonionic amphiphile binary systems: (*1*) PEI_{25}-12–Triton X-100, (*2*) PEI_{25}-12–9CO8; (*3*) PEI_{25}-12–9CO9; (*4*) PEI_{25}–9CO9, and (*5*) PEI_{25}–Triton X-100; 0.01 mol/l PEI, pH 9.2, 25°C. Inset: apparent rate constant of the reaction of PNPL with PEI_{25}-12 (0.01 mol/l) versus the 9CO9 concentration; pH 9.2, 25°C.

ration of molecules of decylamine and the substrate, making their interaction difficult and thus slowing down the reaction. A decreases in the process rate is also observed in the interaction of PNPL with decylamine in solutions of Triton X-100, but the inhibiting effect of this surfactant is somewhat weaker than that of the COs. Octylamine behaves similarly in CO solutions; however, the influence of the calixarene on aminolysis is not so pronounced in this case. The fivefold acceleration of the reaction of octylamine with PNPA and the fivefold deceleration of its reaction with PNPL can be achieved in CO solutions at pH 10.0 (Fig. 5). Under the same conditions, the reaction of decylamine with PNPA is accelerated by a factor of 6 and the reaction between decylamine and PNPL is slowed down by a factor of 50 (inset in Fig. 5).

The influence of 9CO9 and Triton X-100 is almost absent for the reactions of the substrates with hydrophilic amines, for example, butylamine. The same insignificant influence of nonionic amphiphiles is observed in the case of the hydrophilic polyamine, which is exemplified by the PNPA–PEI_{25} system (Fig. 6).

A quite different situation is observed in the reaction of esters with hydrophobized PEI_{25}-12, as compared to low-molecular-weight hydrophobic amines: in the presence of nonionic amphiphiles, the aminolysis of PNPA is inhibited (by a factor of 1.5 and 3 for 9CO9 and Triton X-100, respectively), while this process for PNPL is somewhat accelerated (Fig. 6). The influence of the CO and nonionic surfactant on the pK_a of the polyamine is nearly absent (table); i.e., in this case, the change in the fraction of the neutral form of amine is not the cause the change in the aminolysis rate.

The influence of micelles on the process rate is determined by two main factors [4]: concentrating of the reactants and the change in their microenvironment. The functional micelles considered in this work contain reactive nucleophilic groups, and, in the case of PNPL, the substrate molecules are also involved in aggregation. Probably, the character of distribution and localization and the fraction of reactants in mixed ensembles play an important role in these functional micelles. Therefore, the inhibition of the reaction of PEI_{25}-12 with PNPA in solutions of nonionic surfactants reflects the redistribution of PNPA between individual aggregates of the polymer and mixed PEI_{25}-12–CO aggregates in which the fraction of nucleophilic groups decreases with an increase in the calixarene content.

In the case of PNPL, the low rate constant for the reaction of the substrate in the absence of CO (point on the ordinate axis) can be due to the low reactivity of aggregated PNPL and the inability of PEI_{25}-12 to decompose individual micelles of the substrate and activate the substrate. The increase in the rate constant in the PEI_{25}-12–9CO9 binary system is probably caused by the formation of functional aggregates involving both reactants. The extremum in this dependence can be due to the dilution of the reactants because of the increase in the micelle concentration and the decrease in the fraction of reactive components in the micelles.

Thus, supramolecular systems were formed from amphiphilic oxyethylated calixarenes and from higher or polymeric amines. They exhibit the properties of functional catalysts in nucleophilic substitution in carboxylic esters. A high substrate specificity of the process was observed: acceleration (by approximately one order of magnitude) of the reaction of PNPA and inhibition (by a factor of up to 50) of the reaction of PNPL in the case of decylamine. The opposite situation is observed in the PEI-based systems: inhibition of the reaction of PNPA and acceleration of the process involving PNPL.

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