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Aminolysis of Carboxylic Acid Esters in Direct, Bicontinual, and Inverse Microemulsions Based on Cetyltrimethylammonium Bromide

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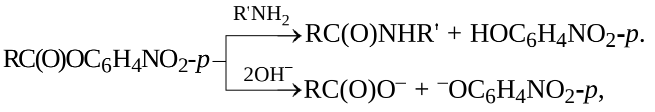
Abstract—The reactivity of primary alkylamines in cleavage of *p*-nitrophenyl esters of carboxylic acids in microemulsions of different structures based on cetyltrimethylammonium bromide was studied. The aminolysis rate considerably increases in going from inverse to direct microemulsions, mainly owing to the concentration of the reactants in the boundary layer.

Detergent microemulsions are macroscopically uniform, thermodynamically stable, self-organizing dispersions with aqueous and hydrocarbon (oil) phases, in which the phase boundary is occupied by molecules of micelle-forming surfactants and cosurfactants. Variation of the water-to-oil volume ratio significantly alters the structure and properties of the microemulsions, with the phase inversion and rearrangement of the phase boundary [1]. Both inverse, bicontinual, and direct microemulsions can be formed, with the system as a whole remaining macrohomogeneous and optically transparent and preserving a high solubilizing capacity toward both polar and nonpolar substances. Unique solubilizing properties of microemulsions, along with exceedingly developed phase boundary surface, provide efficient contact between hydrophilic and hydrophobic reagents and allow successful use of these systems as nanoreactors for various chemical processes. With such systems, it is possible to control not only the reaction rates but even the reaction mechanisms [2–5].

This study continues our previous investigations concerning the catalytic properties of microemulsions in nucleophilic substitutions [5–8]. To reveal how the structure of the reaction medium affects the rate of ester cleavage, we studied the reactions of *p*-nitrophenyl esters of carboxylic acids with primary aliphatic amines in microemulsions consisting of water, cetyltrimethylammonium bromide, *n*-butanol, and *n*-hexane. The content of the surfactant and cosurfactant in the microemulsions was 9.42 wt % each (molar ratio 1 : 5), which made it possible to avoid phase separation when the content of the two other components, water and hexane, was varied in a wide range. For kinetic experiments, we used the microemulsions with the water volume fraction (φ) of 0.77, 0.30, and 0.14, which corresponds to the direct, bicontinual, and inverse structures, respectively [8, 9].

In molecular aqueous solutions, the cleavage of carboxylic acid esters in the presence of primary amines mainly occurs along two pathways: aminolysis (major reaction) and base hydrolysis (side reaction):



$$RC(O)OC_6H_4NO_2\text{-}p \xrightarrow{R'NH_2} RC(O)NHR' + HOC_6H_4NO_2\text{-}p.$$
$$RC(O)OC_6H_4NO_2\text{-}p \xrightarrow{2OH^-} RC(O)O^- + {}^-OC_6H_4NO_2\text{-}p,$$

$$R \text{ and } R' = C_nH_{2n+1}.$$

The kinetic data characterizing the reaction of *p*-nitrophenyl acetate **I** and *p*-nitrophenyl laurate **II** with primary amines in microemulsions of various types are given in Table 1. It is seen from these results that, at equal concentrations of amines (C_{am}), the observed rate constants (k_{obs}) only slightly depend on the hydrophobicity of the amine. At the same time, the rate constants depend on the structure of the microemulsions, increasing in going from the inverse to direct microemulsion. In all the microemulsions studied, acetate **I** is cleaved by a factor of 15–20 more readily than laurate **II**.

The concentration dependences of k_{obs} in the range of amine concentration from 0.005 to 0.04 M in all

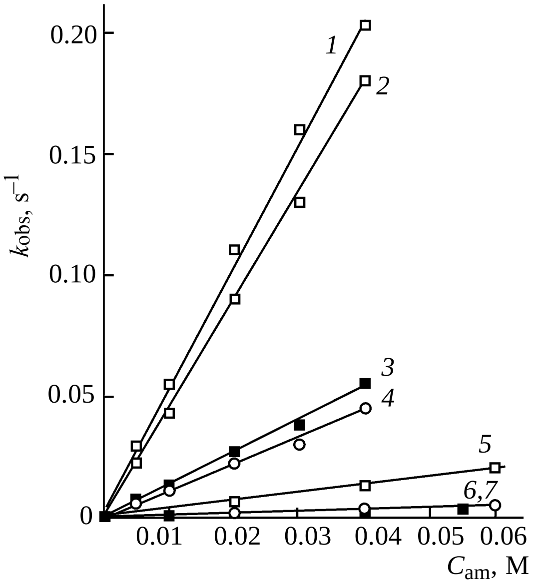


Fig. 1. Influence of the amine concentration on the observed rate constant k_{obs} of cleavage of carboxylic acid esters in microemulsions based on cetyltrimethylammonium bromide: (*1*) hexylamine, *p*-nitrophenyl acetate, φ 0.77; (*2*) decylamine, *p*-nitrophenyl acetate, φ 0.77; (*3*) decylamine, *p*-nitrophenyl acetate, φ 0.30; (*4*) decylamine, *p*-nitrophenyl acetate, φ 0.14; (*5*) decylamine, *p*-nitrophenyl laurate, φ 0.77; (*6*) decylamine, *p*-nitrophenyl laurate, φ 0.30; and (*7*) decylamine, *p*-nitrophenyl laurate, φ 0.14.

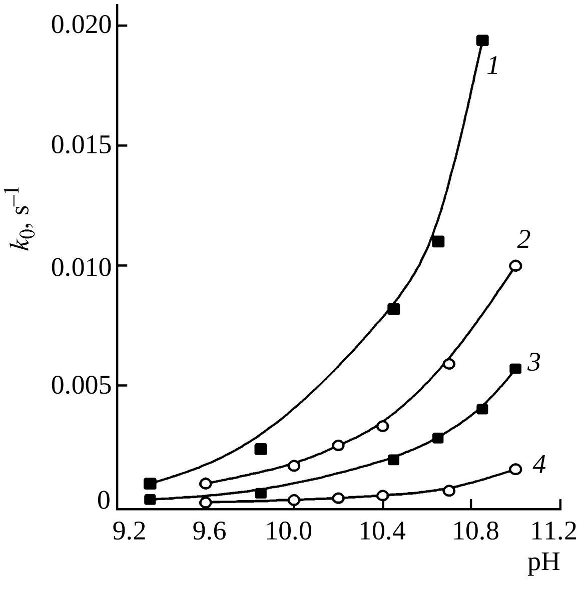


Fig. 2. Rate constant of hydrolysis of carboxylic acid esters in microemulsions based on cetyltrimethylammonium bromide as a function of pH: (*1, 3*) *p*-nitrophenyl acetate and (*2, 4*) *p*-nitrophenyl laurate; φ: (*1, 2*) 0.77 and (*3, 4*) 0.30.

the microemulsions studied are linear and pass virtually through the origin (Fig. 1). This fact indicates that the contribution of base hydrolysis to the ester cleavage is insignificant. This contribution can be quantitatively estimated from the kinetics of hydrolysis of esters **I** and **II** at the same pH as those of the microemulsions containing amines. Depending on the basicity of the amine and its concentration in the system, the apparent pH values of the microemulsions, determined with a pH meter, are in the range 9.8–10.5. The highest pH was observed with hexylamine at its 0.04 M content in the direct microemulsion. The pH dependences of the observed rate constant of the base hydrolysis of esters (k_0) in various microemulsions are shown in Fig. 2. In the systems under consideration, the contribution of hydrolysis to the overall rate of cleavage of the carboxylic acid esters does not exceed 10%; nevertheless, it should be taken into account at low amine concentrations or at high pH.

We have shown previously that the hydrolysis of carboxylic acid esters is usually characterized by a high activation energy, whereas in aminolysis of these compounds the rate constants only weakly depend on temperature [5]. A kinetic study of the cleavage of ester **I** at different temperatures in various microemulsions based on cetyltrimethylammonium bromide in alkaline media and in the presence of amines allowed evaluation of the activation energy (E_a) of hydrolysis and aminolysis (Table 2).

The activation energies are apparent quantities and depend on the thermodynamic parameters of the intermediate equilibrium processes. Hydrolysis of ester **I** in all the microemulsions is characterized by high activation energies, exceeding E_a of this reaction in water (45.8 kJ mol^{-1} [5]). The activation energy of the aminolysis in microemulsions is considerably lower than that of hydrolysis, although it is essentially nonzero, in contrast to that of the process in molecular solutions (Table 2). Thus, at the same pH, the contribution of base hydrolysis to the cleavage of esters

Table 1. Observed rate constants (k_{obs}, s^{-1}) of the reactions of carboxylic acid esters **I** and **II** with amines in microemulsions of various types (25°C, C_{am} 0.04 M)

Amine	φ 0.14		φ 0.30		φ 0.77	
	I	**II**	**I**	**II**	**I**	**II**
Hexylamine	0.059	0.0027	0.068	0.0035	0.20	0.014
Octylamine	0.050	0.0023	0.065	0.0036	0.19	0.014
Decylamine	0.045	0.0025	0.055	0.0033	0.18	0.013
Cetylamine	0.030	0.0028	0.038	0.0039	0.18	0.011

Table 2. Influence of temperature and composition of the microemulsion on the observed rate constants of hydrolysis and aminolysis of *p*-nitrophenyl acetate

Parameter	*t*, °C	Base hydrolysis			Aminolysis		
		φ 0.14	φ 0.30	φ 0.77	φ 0.14	φ 0.30	φ 0.77
k_0, k_{obs} s^{-1}	25	0.00010	0.0007	0.0010	0.023	0.028	0.09
	32	0.00043	0.0015	0.0021	0.025	0.032	0.13
	44	0.00078	0.0029	0.0046	0.033	0.044	0.14
E_a, kJ mol^{-1}		80.6	57.4	62.7	16.2	18.9	17.3

[a] The rate constant of base hydrolysis was determined in microemulsions with a buffer solution of sodium tetraborate (pH 9.2) as aqueous phase.

Table 3. Second-order rate constants ($k_{2,\varphi}$, l mol^{-1} s^{-1}) of aminolysis of carboxylic acid esters **I** and **II** in the nonaqueous phase of microemulsions of various compositions (25°C)[a]

Amine	φ 0.14		φ 0.30		φ 0.77	
	I	**II**	**I**	**II**	**I**	**II**
Hexylamine	1.27	0.058	1.15	0.060	1.27	0.090
Octylamine	1.07	0.050	1.10	0.061	1.20	0.088
Decylamine	0.97	0.053	0.94	0.056	1.13	0.081
Cetylamine	0.65	0.060	0.65	0.097	0.73	0.066

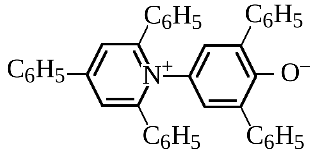
[a] k_2 of aminolysis of acetate **I**, l mol^{-1} s^{-1}: in hexane, 0.018 (hexylamine) and 0.02 (cetylamine); in butanol, 0.28 (hexylamine) and 0.33 (cetylamine).

increases with temperature. Hence, in oil/water microemulsions, the temperature, along with the concentration of the hydroxide ion and amine, can be an important parameter governing the amide : acid ratio in the final reaction product.

From the dependences of k_{obs} of the cleavage of **I** and **II** on the amine concentration (Fig. 1), using the equation $k_2 = (k_{obs} - k_0)/C_{am}$, we can calculate the second-order rate constants of aminolysis (k_2) averaged over the emulsion volume. Low-polarity long-chain amines are virtually insoluble in water and concentrate in the oil phase or at the phase boundary. The second-order rate constants determined for the nonaqueous part of the microemulsions [$k_{2,\varphi} = (1 - \varphi)k_2$] allow the effect of this factor on the reaction rate to be taken into account; these quantities should reflect changes in the microenvironment in the reaction zone (factor of the medium).

The $k_{2,\varphi}$ values obtained (Table 3) appeared to be similar for all the types of microemulsions. This fact suggests that, irrespective of the microemulsion structure, the reaction occurs in areas of similar micropolarity. To estimate preliminarily the site of localization of the reaction components, we determined k_2 of aminolysis of ester **I** in nonpolar hexane and low-polarity butanol (see note to Table 3), which appeared to be considerably lower than $k_{2,\varphi}$ in microemulsions. Hence, in microemulsions the reaction occurs in a relatively polar boundary layer. Within this layer, the reaction zone can probably shift somewhat toward the oil or aqueous phase depending on the hydrophobicity of the reactants. This is suggested, e.g., by an increase in $k_{2,\varphi}$ of aminolysis of acetate **I** in going from cetylamine to hexylamine (Table 3).

The micropolarity of the phase boundary in microemulsions based on cetyltrimethylammonium bromide was characterized with the $E_T(30)$ solvatochromic probe, 2,6-diphenyl-4-(2,4,6-triphenylpyridinio-1)-phenoxide existing in alkaline solutions in the form of a zwitter ion:



This compound is very sensitive to the polarity of the medium, in contrast to other spectroscopic probes [10]. The $E_T(30)$ probe is used for characterizing the polarity of not only homogeneous solutions but also microheterogeneous media, in particular, micellar solutions and microemulsions [11, 12]. A combination of the hydrophilic and lipophilic properties ensures the localization of $E_T(30)$ in the phase boundary layer [13, 14]. The hydroxy group of the probe, dissociated in an alkaline solution, will interact electrostatically with the head groups of a cationic surfactant, and the hydrophobic moiety will be oriented toward the oil phase. Such localization and orientation in the microemulsions under consideration can also be presumed for long-chain amines exhibiting pronounced amphiphilic properties.

The influence of the water content in the system on the parameter E_T is shown in Fig. 3. Three portions of the plots can be distinguished. In the initial portion ($\varphi < 0.22$), E_T is independent of the water content in the system. Then, in the narrow interval $0.22 < \varphi < 0.25$ (which corresponds to a transition from the inverse to bicontinual emulsion, as we determined previously by a number of physical methods [8]), E_T sharply increases. At $\varphi > 0.25$, E_T becomes again independent of the volume fraction of water, since the probe used is apparently insensitive to further structural rearrangements in the system and does not allow detection of the transition from the bicontinual to direct microemulsion. We have determined the interval of this transition previously (φ 0.4 – 0.5) by viscometry and ^{1}H NMR spectroscopy with pulse magnetic field gradient and confirmed it by the method of chemical kinetics [8]. This fact emphasizes once again that it is appropriate to use an integrated approach when studying the structural properties of microemulsions.

A comparison of the E_T values in hexane (31.0), *n*-butanol (50.2), water (63.1) [10], and the systems under consideration (52.2–53.2) shows that the probe is localized in the boundary layer containing butanol and certain amount of water.

In the presence of *n*-decylamine, the dependence of E_T on the water content in the microemulsions is different (Fig. 3). This amine makes the probe more sensitive to structural changes. In this case, we can distinguish in the plot the portions corresponding to the existence of inverse ($\varphi < 0.2$), bicontinual ($0.5 > \varphi > 0.25$), and direct ($\varphi > 0.6$) microemulsions, which is consistent with the data from [8]. We have shown previously that introduction of long-chain amines into microemulsions based on cationic surfactants results in the redistribution of the components between the phases [15]. Changes in E_T depending on the decylamine concentration (Fig. 3) reflect, apparently, the rearrangements occurring in the system and resulting in changes in the microenvironment of the probe. In the presence of decylamine, the intervals of the phase transitions slightly shift toward higher water content. We have detected such a shift previously in conductometric studies and attributed it to a change in the porosity and flexibility of the boundary layer with variation of the cosurfactant (butanol) concentration [16].

A comparison of the results of the solvatochromic and kinetic experiments shows that microemulsions with the volume fraction of water of 0.77, 0.30, and 0.14 in the presence of decylamine are characterized by virtually equal E_T values (Fig. 3) and similar bimolecular rate constants of aminolysis in the nonaqueous phase (Table 3). For the reaction of decylamine with *p*-nitrophenyl acetate in a microemulsion with φ 0.25, characterized by the highest E_T (53.15), we obtained $k_{2,\varphi}$ as high as 1.56 $\mathrm{l\,mol^{-1}\,s^{-1}}$.

Thus, the influence of the microenvironment (factor of the medium) is reflected in $k_{2,\varphi}$ of the aminolysis of the esters. At the same time, the apparent rate constants of the process are governed by the concentrating effect: With the same amount of an amine, in emulsions of different types, k_{obs} is the higher, the smaller the nonaqueous phase volume (Table 1). Hence, to attain the highest rates of aminolysis of carboxylic acid esters, preference should be given to direct microemulsions.

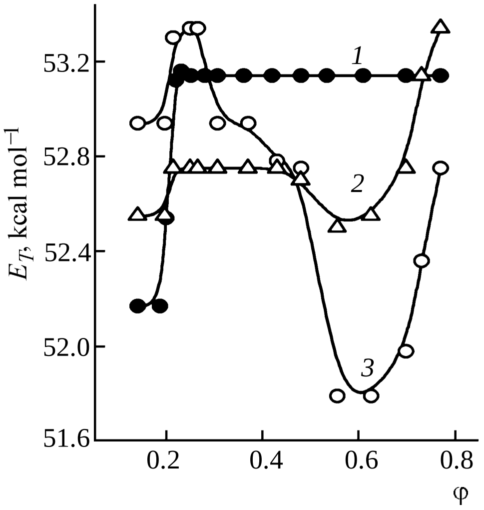


Fig. 3. E_T as a function of water content in microemulsions based on cetyltrimethylammonium bromide: (*1*) no amine, (*2*) 0.02 M decylamine, and (*3*) 0.04 M decylamine.

At the same time, when using microemulsions as reaction medium, there may be a problem with their limited solubilizing capacity for long-chain amines, especially in the case of direct microemulsions. We determined by potentiometric titration the amount of amines that can be added to a homogeneous microemulsion without causing visible changes (Table 4). We found that the solubility of amines in the microemulsions drastically decreased with an increase in the length of the hydrocarbon substituent in the amine. It is also seen that the solubilizing capacity of the bicontinual microemulsion is approximately three times higher than that of the direct microemulsion. The solubility of amines in inverse microemulsions is so high that it cannot be estimated by visual observation of the state of the microemulsion.

It should be noted that acidification of the medium, which is commonly used to increase the solubility of amines in aqueous solutions and is accompanied by amine protonation, leads to an opposite result in the case of microemulsions. Such an effect is due to the unfavorable influence of the electrostatic repulsion between the positivelly charged head groups of the surfactant and protonated nitrogen atom of the amine, preventing incorporation of the amine in the boundary layer.

Table 4. Solubilizing capacity of microemulsions for long-chain primary amines

Amine	Amine content, M (%)	
	φ 0.77	φ 0.30
Octylamine	0.194 (2.50)	0.88 (11.3)
Decylamine	0.135 (2.12)	0.40 (6.87)
Dodecylamine	0.097 (1.70)	0.243 (4.50)
Cetylamine	0.033 (0.71)	0.10 (2.10)

EXPERIMENTAL

Microemulsions were prepared from commercial cetyltrimethylammonium bromide (Sigma) containing ~99.9% main substance; the surfactant was used without additional purification. Butanol and hexane were purified by standard procedures. Solutions were prepared in double-distilled water.

For the kinetic studies, we used *p*-nitrophenyl esters of carboxylic acids (Fluka), recrystallized by common procedures. The reaction kinetics was studied spectrophotometrically (Specord UV-Vis) in temperature-controlled cells, using freshly prepared microemulsions. The reaction progress was monitored by variation of the optical density of the solutions at λ 400 nm (formation of *p*-nitrophenolate anion). The initial concentration of the substrate was 5×10^{-6} M, and the conversion was more than 90%.

The observed pseudo-first-order rate constants k_{obs} were determined by the least-squares method from the relationship $\log(D_\infty - \mathrm{D}\tau) = -0.434 k_{\mathrm{obs}}\tau + \mathrm{const}$, where D_τ and D_∞ are the optical densities of the solutions at time τ and after the reaction completion.

The optical density of the solutions and the electronic absorption spectra of $E_T(30)$ in the visible and UV ranges were measured with a Hewlett–Packard-8452A spectrophotometer in 1-cm quartz cells (Perkin–Elmer). The empirical parameter was calculated by the formula $E_T(\mathrm{kcal\ mol^{-1}}) = 2.859 \times 10^{-3}\nu$, where ν is the frequency ($\mathrm{cm^{-1}}$), from the experimental wavelengths of the absorption maxima of the probe, which were determined with an error of ±1 nm. The E_T values plotted in Fig. 3 have the generally accepted dimension of $\mathrm{kcal\ mol^{-1}}$ [10].

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