

# Molecular Organization of Reactants in the Kinetics and Catalysis of Liquid Phase Reactions: IX. The Catalytic Assistance of an Alcohol as a Component of the Medium in the Aminolysis of Esters

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**Abstract**—The kinetics of the reaction of *p*-nitrophenyl acetate with *n*-butylamine is studied in various solvents containing *n*-butanol as a component of the medium. The alcohol is shown to assist the aminolysis by the participation in the proton transfer from the amine molecule to ester. The stoichiometric composition of the poly-molecular complexes of amine with the alcohol participating in the reaction is found from the kinetic data at low concentrations of *n*-butanol and the data on its association in solutions. At high concentrations of the alcohol, the kinetic data are described within the framework of a model that assumes the participation in the reaction of hydroxy groups of the alcohol in the composition of alcohol clusters. The rate of the process is determined by the concentration and sizes of the clusters. The complex kinetics of the catalytic assistance of the alcohol as a component of the medium are quantitatively interpreted according to the concepts on the role of the structural organization of the liquid in the kinetics of molecular reactions in solutions.

## INTRODUCTION

Aminolysis of esters is a typical nucleophilic substitution reaction, whose rate and kinetics are very sensitive to the properties of the medium. These processes usually occur in parallel via several pathways involving amine associates with different compositions (as a rule,  $n \leq 3$ ); however, depending on the donor–acceptor ability of a solvent, the contributions of the reactions of the monomeric, dimeric, and trimeric forms of amine to the apparent rate constant are different [1]. In proton-inert media, the ester aminolysis mainly involves the dimeric and trimeric forms, which are much more reactive than the monomeric form [1, 2]. In this respect, the aminolysis reactions are similar to the reactions of substitution and addition involving aliphatic alcohols, although the equilibrium constants of association of aliphatic alcohols are usually much higher than those of amines [3]. In both cases, an increase in the reactivity of the associates is related to charge redistribution in the system due to the hydrogen bond formation and the possibility for cyclic transition states during the rearrangement of the poly-molecular precursors of reaction products.

Therefore, the aminolysis reactions are characterized by the so-called bifunctional catalysis under the effect of alcohols, carboxylic acids, and other compounds with a mobile hydrogen atom that can be built into the structure of amine associates and participate in the proton transfer along the system of hydrogen bonds by changing the stoichiometric composition of the precursor complexes [4–6].

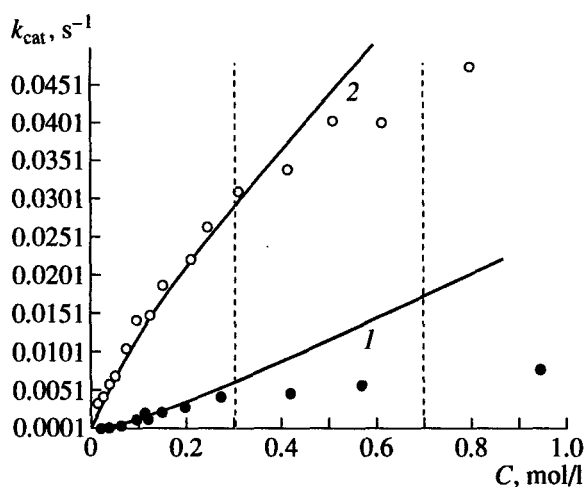
If an alcohol is one of the components of the mixed solvent, the specific features of the structure of the liquid due to the ability of alcohols to form intermolecular associations via hydrogen bonds should reflect the regularities of ester aminolysis in these systems. This work is devoted to the study of the catalytic assistance of *n*-butanol as a component of the medium to the reaction of *n*-butylamine with *p*-nitrophenyl acetate (NPA) and the role of the molecular organization of the solution in the catalysis mechanism.

## EXPERIMENTAL

The kinetics of NPA aminolysis was studied by UV spectroscopy by a change in the absorbance at a wavelength of 350 nm due to *p*-nitrophenol formation during the reaction. The reaction was performed at  $T = 10$ – $60^\circ\text{C}$  in excess amine, whose concentration was 0.0475 and 0.2040 mol/l. The NPA concentration was  $10^{-4}$  mol/l. Under these conditions, the pseudofirst reaction order with respect to NPA was fulfilled until the complete conversion. The solvents, *n*-heptane, benzene, toluene, chloroform, ethyl acetate, dioxane, and *n*-butanol, were purified and dried by the known procedures [7], NPA was recrystallized, and *n*-butylamine was dried and distilled before use.

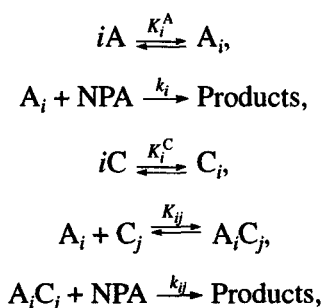
## RESULTS AND DISCUSSION

Taking into account the possibility for the appearance of the self-association of amine and alcohol and



**Fig. 1.** Dependences of  $k_{\text{cat}}$  of the reaction of NPA with *n*-butylamine on the concentration of the alcohol ( $C$ ) in heptane at 28°C: (1)  $[n\text{-BuNH}_2] = 0.0475$  mol/l and (2)  $[n\text{-BuNH}_2] = 0.2040$  mol/l. Solid curves indicate calculation by formula (4). The region of the transition from the homogeneous to microheterogeneous solution is marked by a dotted line.

their heteroassociation in the kinetics of the reaction under study, we can present the kinetic scheme of the NPA aminolysis as follows:



where  $A$  is the amine monomer,  $C$  is the alcohol monomer,  $i$  and  $j$  are the corresponding association degrees,  $A_i$  and  $C_j$  are the associated forms of the amine and alcohol, and  $A_iC_j$  are the mixed heteroassociates, participants of the catalytic reaction.

For the amine concentrations used in the work, the expression for the apparent first-order rate constant

$$k_{\text{app}} = \Sigma k_i[A_i] + \Sigma k_{ij}[A_iC_j] \quad (1)$$

consists of two terms responsible for the noncatalytic reaction in the absence of the alcohol:

$$k_0 = \Sigma k_i[A_i] \quad (2)$$

and the inherent catalytic reaction:

$$k_{\text{cat}} = k_{\text{app}} - k_0 = \Sigma k_{ij}[A_iC_j]. \quad (3)$$

At a constant amine concentration,

$$k_{\text{cat}} = \Sigma \beta_j[C_j], \quad (4)$$

where the coefficients  $\beta_j = \Sigma K_{ij}k_{ij}[A_i]$  characterize the contributions of the pathways involving the alcohol associates with different multiplicities to the catalytic reaction rate constant.

The scheme presented above is valid only at alcohol concentrations where the solution is homogeneous. For kinetic simulation, the data on the constants of alcohol association obtained at low concentrations in independent spectral experiments can be used [3]. When inert heptane is used as a solvent, the transition from the truly homogeneous to microheterogeneous solution occurs at alcohol concentrations of an order of 0.3–0.7 mol/l [8, 9].

Figure 1 shows the plots of  $k_{\text{cat}}$  of the NPA aminolysis in heptane vs. the concentration of *n*-butanol at  $[A_0] = 0.0475$  and 0.2040 mol/l. In this concentration range, *n*-butanol in heptane exists in the monomeric, dimeric, and tetrameric forms, whose concentrations are determined by the corresponding equilibrium constants [3]. Figure 1 shows that while the solution is homogeneous (at an alcohol concentration lower than 0.3 mol/l), the kinetic data are satisfactorily described by equation (4) with  $j = 1, 2$ , and 4. The calculated values of the  $\beta_1$ ,  $\beta_2$ , and  $\beta_4$  coefficients together with the data on the equilibrium constants of di- and tetramerization of the alcohol  $K_2^C$  and  $K_4^C$  [3] are presented in Table 1. The  $\beta_1$ ,  $\beta_2$ , and  $\beta_4$  coefficients were numerically selected to fit equation (4) with these coefficients to the apparent experimental dependences (see, e.g., Fig. 1) at an alcohol concentration lower than 0.3 mol/l.

Although the calculation accuracy of  $\beta_1$ ,  $\beta_2$ , and  $\beta_4$  is not very high, their dependences on the amine concentration provide estimates for the possible composition of the amine–alcohol heteroassociates along the reaction path. For example, when the initial concentration of the amine changes by 4.3 times,  $\beta_1$  changes by  $80 \pm 20$  times, which corresponds to approximately 4.3<sup>3</sup>. This implies that  $\beta_1 \sim [\text{RNH}_2]^3$ ; i.e., the heteroassociates containing the alcohol monomer and three amine molecules are reactive. On the average, a triple to quintuple increase in  $\beta_2$  and  $\beta_4$ , when the amine concentration changes by 4.3 times, indicates the parallel occurrence of the reaction through the complexes containing one amine molecule ( $\beta_2, \beta_4 \sim [\text{RNH}_2]$ ) per two and four alcohol molecules, respectively.

The conclusions on the composition of the main pathways of aminolysis are indirectly confirmed by the temperature dependences of the corresponding  $\beta_j$  coefficients. It is known [3] (see also Table 1) that the equilibrium constants of formation of the associates with a low multiplicity (dimers) are substantially less temperature-dependent than the equilibrium constants of trimerization (and even more so tetramerization). This is related to an increase in the strength of the hydrogen bond as the chain length of the associate increases [10]. The activation energy of the noncatalytic aminolysis reactions are usually lower than 10 kcal/mol [6, 11],

**Table 1.** Kinetic parameters of the reaction of NPA with *n*-butylamine in heptane in the presence of *n*-butanol at  $C < 0.3$  mol/l

Parameter	[BuNH <sub>2</sub> ], mol/l			
	0.0475	0.2040		
	T, °C			
	28	10	28	60
$K_2^C$ , l/mol [3]	0.93	1.30	0.93	0.50
$K_4^C$ , l <sup>3</sup> /mol <sup>3</sup> [3]	450	2500	450	9.5
$\beta_1$ , l mol <sup>-1</sup> s <sup>-1</sup>	0.002 ± 0.001	0.2 ± 0.05	0.15 ± 0.05	0.03 ± 0.01
$\beta_2$ , l mol <sup>-1</sup> s <sup>-1</sup>	0.06 ± 0.03	0.8 ± 0.1	0.3 ± 0.2	0.7 ± 0.2
$\beta_4$ , l mol <sup>-1</sup> s <sup>-1</sup>	0.08 ± 0.03	0.3 ± 0.1	0.25 ± 0.10	0.2 ± 0.1

and the apparent rate constants change by at most three times as the temperature is varied within 10–60°C. When the alcohol dimers and tetramers with the amine monomer form reactive heteroassociates, the  $\beta_2$  and  $\beta_4$  coefficients should be poorly dependent on the temperature, whereas the  $\beta_1$  coefficient including the concentration of the amine trimer should substantially decrease with an increase in the temperature. Indeed, the data in Table 1 show that the  $\beta_2$  and  $\beta_4$  coefficients, taking into account a low accuracy of their calculation by the experimental data, slightly depend on the temperature, whereas  $\beta_1$  changes by almost an order of magnitude.

The study of the regularities of the catalytic assistance of the alcohol as a component of the medium over a wide range of concentrations providing the microheterogeneity of the aminolysis solution is most interesting. We have developed new concepts on the kinetics of molecular reactions in such solutions as the system of close-packed spherical clusters with a characteristic size  $r$  formed by the chains of hydrogen bonds with one of the reactants (alcohol) being both a constituent of a cluster and a component of the mixed solvent [8, 9]. According to the proposed model, in the microheterogeneity region at  $C > C_{cr}$ , where  $C_{cr}$  is the critical concentration of the alcohol at which the system undergoes microsplitting, the alcohol almost entirely exists in the form of clusters, and the reactivity of its OH groups depends on the structure of the clusters. The cluster size  $r$  is the power function of the concentration of the alcohol molecules in its composition [8, 9]:

$$r \sim (C/C_{cr})^{-\gamma}. \quad (5)$$

If the reaction involving the OH groups of the associates, which are in the composition of the alcohol clusters, occurs in the microheterogeneous medium, the apparent rate constant should be proportional to the concentration of alcohol clusters and their surface area. Assuming that the solution is a system of close-packed spherical clusters, their concentration is proportional to

the reciprocal cluster volume  $(1/r^3)$ , and the surface area of the cluster is proportional to  $r^2$  [8, 9]. Then,

$$k_{app} \sim (1/r^3)r^2 \sim 1/r \sim (C/C_{cr})^\gamma. \quad (6)$$

The exponent  $\gamma$  calculated from the experimental data as the apparent order of the molecular reaction involving the alcohol represents the quantitative parameter that characterizes the influence of the structural organization of the liquid on the reaction rate [8, 9]. For the structurally sensitive reaction of isocyanates with alcohols, whose apparent order with respect to the alcohol concentration varied in a wide interval depending on the solvent nature, we obtained [12] the values of the exponent  $\gamma$  for various binary systems containing *n*-butanol as a component of the mixed solvent. If a different reaction, for example, the aminolysis of NPA, is performed in the same systems, then we can obtain useful information on the catalysis mechanism and the role of the alcohol as a component of the medium in this process using the  $\gamma$  values of the standard reaction and comparing with them the apparent orders  $\delta$  with respect to the alcohol that accomplishes the catalytic assistance on the aminolysis.

In this work, having this problem statement in mind, we studied the kinetics of the reaction of *n*-butylamine with NPA in various solvents at the alcohol concentrations  $C > C_{cr}$ ; i.e., in the microheterogeneity region of binary solutions. In all cases, the amine concentration was much lower than the alcohol concentrations, so that its influence on the structure of the solution can be neglected.

Figures 2 and 3 show that the power law (6) for the apparent rate constant of the aminolysis at the alcohol concentration  $C > C_{cr}$  is well fulfilled. The  $\delta$  coefficients, which formally correspond to the aminolysis reaction order with respect to the alcohol, can be found from the slope of the straight lines and compared to the  $\gamma$  coefficients determined in the independent experiments on the kinetics of the standard reaction in the same media [12]. Table 2 presents the  $\delta$  and  $\gamma$  values.

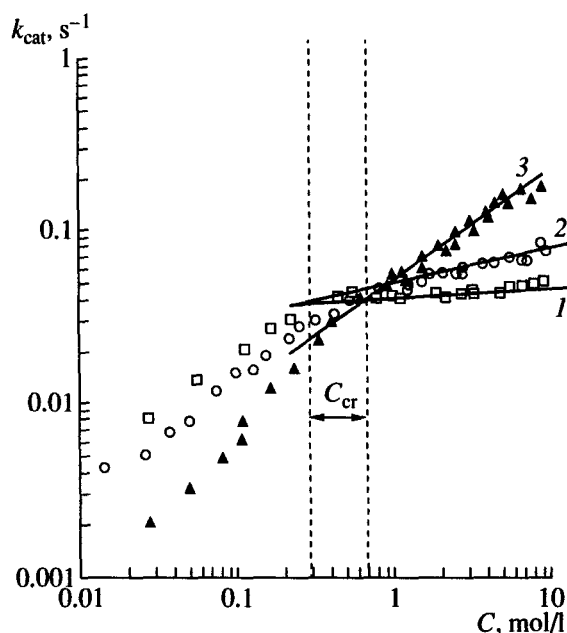


Fig. 2. Dependence of  $k_{cat}$  of the reaction of NPA with *n*-butylamine on the concentration of *n*-butanol ( $C$ ) in heptane at temperatures (1) 10, (2) 28, and (3) 60°C in the logarithmic coordinates;  $[n\text{-BuNH}_2] = 0.2040$  mol/l. The region of the transition from the homogeneous to microheterogeneous solution is marked by a dotted line.

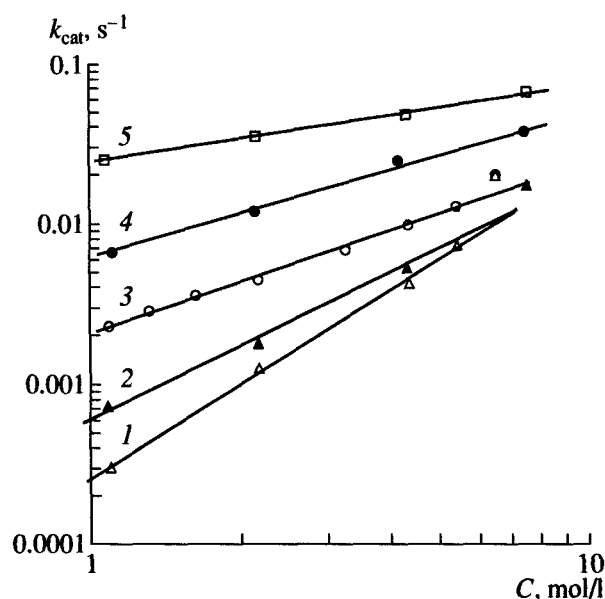
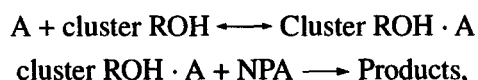


Fig. 3. Dependences of  $k_{cat}$  of the reaction of NPA with *n*-butylamine on the concentration of *n*-butanol at  $C > C_{cr}$  in (1) ethyl acetate, (2) chloroform, (3) benzene, and heptane-ethyl acetate mixtures with the content of the latter (4) 35 and (5) 10 vol % in the logarithmic coordinates;  $[n\text{-BuNH}_2] = 0.2040$  mol/l,  $T = 28^\circ\text{C}$ .

In the general case, two models of the catalytic assistance of the alcohol in a microheterogeneous medium can be presented (Fig. 4).

**Model I.** Any OH group of the associate in the composition of the alcohol cluster can accomplish the catalytic assistance on the proton transfer from an amino group to a NPA molecule. On the assumption that almost all of the alcohol is present in the composition of the clusters, the kinetic scheme of the aminolysis assisted by the OH groups of the alcohol inside a cluster or on the cluster surface (ROH cluster) can be written as follows:



where A is the amine molecule.

The concentration of the reactive amine molecules in the composition of the clusters  $[\text{cluster ROH} \cdot \text{A}]$  is related to the content of the alcohol molecules in the solution ( $C$ ) according to the law [8, 9]:

$$[\text{Cluster ROH} \cdot \text{A}] \sim C^\gamma. \quad (7)$$

The probability  $p$  that an associate contains an amine molecule instead of one alcohol molecule is

$$p = [\text{Cluster ROH} \cdot \text{A}] / C. \quad (8)$$

According to formula (8), the rate constant of the aminolysis catalyzed by the alcohol which is in the composition of the cluster is

$$k_{cat} \sim pC^\gamma \sim C^\gamma [\text{Cluster ROH} \cdot \text{A}] / C \sim C^{2\gamma-1}. \quad (9)$$

Thus, according to model I, the formally apparent order of the aminolysis with respect to the alcohol is the following:

$$\delta = 2\gamma - 1. \quad (10)$$

**Model II.** The catalytic assistance is performed only by the terminal OH groups of the associates in the cluster composition that form a hydrogen bond with the amine molecule. The mean chain length (the number of monomeric units  $n$ ) of the associate is related to the alcohol concentration as  $n^2 \sim C$  [8, 9]; hence,

$$n \sim C^{0.5}. \quad (11)$$

Therefore, the concentration of the terminal groups is

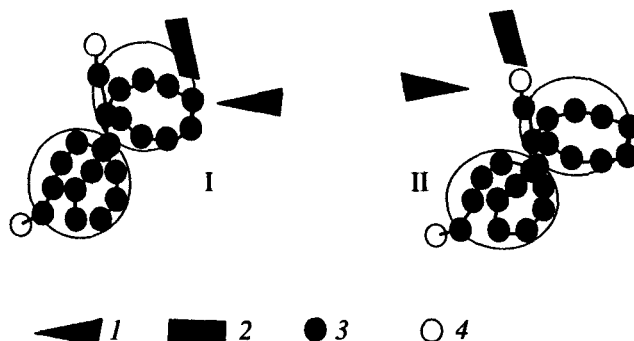


Fig. 4. Models I and II of the catalytic assistance of the alcohol in the aminolysis of NPA in the microheterogeneous medium; (1) ester molecule; (2) amine molecule; (3) alcohol molecule in the composition of the associate entered into the cluster; and (4) terminal alcohol molecule in the associate.

**Table 2.** Parameters  $\gamma$  of the addition of *n*-butane to *m*-Cl-phenyl isocyanate [12] and  $\delta$  of the reaction of NPA with *n*-butylamine in various solvents in the presence of *n*-butanol as a component of the medium; [BuNH<sub>2</sub>] = 0.2040 mol/l

Solvent	<i>T</i> , °C	$\gamma$ [12]	$\delta$
Heptane	10	0.75 ± 0.03	0.05 ± 0.02
"	28	0.80 ± 0.03	0.25 ± 0.03
"	60	0.95 ± 0.03	0.65 ± 0.05
Heptane/ethyl acetate (5/95 vol %)	28	1.00 ± 0.05	0.35 ± 0.05
" (10/90 vol %)	"	1.05 ± 0.05	0.50 ± 0.05
" (15/85 vol %)	"	1.1 ± 0.1	0.60 ± 0.05
" (20/80 vol %)	"	1.3 ± 0.1	0.60 ± 0.05
" (25/75 vol %)	"	1.4 ± 0.1	1.0 ± 0.1
" (35/65 vol %)	"	1.45 ± 0.10	1.1 ± 0.1
" (50/50 vol %)	"	1.6 ± 0.1	1.35 ± 0.05
" (65/35 vol %)	"	1.7 ± 0.1	1.7 ± 0.1
" (75/25 vol %)	"	1.8 ± 0.1	1.9 ± 0.2
" (85/15 vol %)	"	1.9 ± 0.1	2.2 ± 0.3
Benzene	"	1.00 ± 0.05	1.0 ± 0.1
Chloroform	"	1.4 ± 0.1	1.4 ± 0.1
Ethyl acetate	"	2.1 ± 0.2	2.5 ± 0.5
Dioxane	"	2.8 ± 0.5	3.0 ± 0.5

$$C_{\text{term}} = C/n \sim C^{0.5}, \quad (12)$$

The probability that any alcohol molecule in the associate can be at the end of the chain is

$$p_{\text{term}} = C_{\text{term}}/C \sim C^{-0.5}, \quad (13)$$

Then, by analogy with the derivation of formula (9):

$$[\text{Cluster ROH} \cdot \text{A}] \sim p_{\text{term}} C^\gamma \sim C^{\gamma-0.5}, \quad (14)$$

Taking into account formula (14), expression (9) for the catalytic rate constant in model II takes the following form:

$$k_{\text{cat}} \sim C^\gamma [\text{Cluster ROH} \cdot \text{A}]/C \sim C^{2\gamma-1.5}. \quad (15)$$

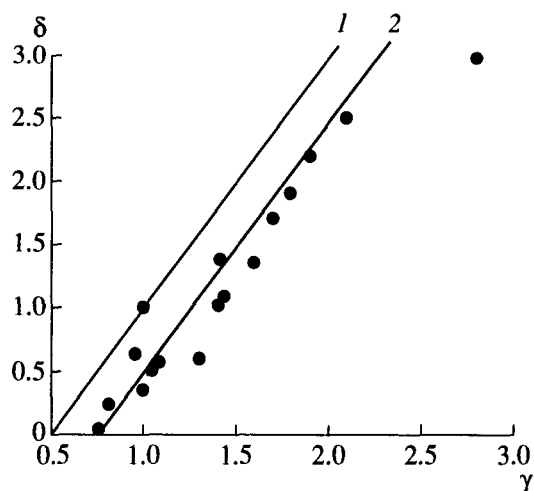
It is seen that, in this case, the apparent reaction order with respect to the alcohol is

$$\delta = 2\gamma - 1.5. \quad (16)$$

Thus, according to formulas (10) and (16), models I and II result in different orders of the catalytic reaction with respect to the alcohol in the microheterogeneous medium. A difference of 0.5 orders of magnitude is not high; however, it permits an attempt to discriminate between this or other models on the basis of the available experimental data (Figs. 2, 3; Table 2).

Figure 5 presents the relationship between the exponents  $\delta$  and  $\gamma$  resulting from models I and II and the corresponding experimental data in various solvents containing up to ~80% *n*-butanol as a component of the medium. It is seen that model II describes the experimental data better than model I; i.e., in the microheterogeneous medium, the catalytic assistance is mainly

accomplished, most likely, by the terminal groups of the associates in the composition of the alcohol clusters. This is indirectly confirmed by the data in Fig. 2, which presents the concentration dependences of the aminolysis rate constants at different temperatures in *n*-heptane. In dilute, truly homogeneous solutions at  $C < C_{\text{cr}}$ , a higher reaction rate at low temperatures is related to a higher concentration of the associates that are more reactive species than the monomers. When we



**Fig. 5.** Exponent  $\delta$  as a function on the exponent  $\gamma$ . Straight line 1: dependence predicted by formula (9); straight line 2: dependence predicted by formula (13).

switch to the microheterogeneous medium, the inversion of the temperature dependence of the catalytic rate constant takes place at an alcohol concentration of  $C > C_{cr}$ . As the temperature increases, the chain length of the alcohol associates decreases, which is accompanied by an increase in the concentration of the terminal group accomplishing the catalytic assistance in the aminolysis according to model II.

#### ACKNOWLEDGMENTS

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