

Effect of Association on Nucleophilic Addition of (Meth)acrylic Aminoamides to Acrylic Acids in Aqueous Solutions

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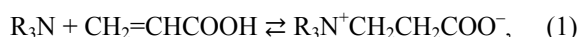
Received October 26, 2017

Abstract—Reactions of nucleophilic addition of *N*-(3-dimethylaminoalkyl)(meth)acrylamides to acrylic, *N*-acryloylaminoacetic, and 2-acrylamido-2-methylpropanesulfonic acid with the formation of betaines revealed an unusual dependence of the initial rate and equilibrium conversion on concentration of the reagents. The observed effects were explained by structural features of the reagents and the products.

Keywords: *N*-(3-dimethylaminoalkyl)metacrylamides, acrylic acid, *N*-acryloylaminoacetic acid, 2-acrylamido-2-methylpropanesulfonic acid, betaines

DOI: 10.1134/S1070363218040059

Synthetic water-soluble polymers containing betaine motifs are used as amphoteric thickeners [1], flocculants [2], additives to paper and textile materials [3], components of detergents and cosmetics [4]. Monomers for their preparation are synthesized in one step by nucleophilic addition of tertiary amines to acrylic acids: acrylic acid **1**, *N*-acryloylaminoacetic acid **2**, 2-acrylamido-2-methylpropanesulfonic acid **3** [5–7].



It was shown that in aqueous, alcohol solutions or without solvent such reactions proceed under mild conditions and are not accompanied by side transformations [5–9]. For the presence of vinyl groups in betaines formed by reactions (1)–(3) to be active in radical polymerization, as starting amines, (meth)acrylic monomers with sterically non-hindered tertiary amino groups can be used, like *N*-(3-dimethylaminopropyl)acrylamide **4**, *N*-(3-dimethylaminopropyl)methacrylamide **5**, *N*-(1,1-dimethyl-3-dimethylaminopropyl)acrylamide **6** [9]. Compounds **4–6** contain the same

amine fragment CH₂CH₂N(CH₃)₂ and differ by the presence or absence of methyl substituents in positions 3 and 6 with respect to the amine nitrogen. Earlier, for these compounds sharply different dependencies were revealed of initial rates on starting concentrations of the reagents for nucleophilic reactions with participation of amino groups: the quaternization with ethylene chlorohydrin [10] or chloroacetic acid [11] by the Menshutkin reaction.

The goal of the present work was to elucidate and analyze the dependence of the initial rates and equilibrium conversions on the initial concentrations of the reagents (at their constant ratio) in nucleophilic addition reactions of amines **4–6** to acrylic acids **1–3** in aqueous solutions. Amines **4–6** have p*K*_a values of 9.23, 9.39, and 9.25 [12], practically the same sum of induction constants of the substituents at nitrogen atom Σσ* (0.1724, 0.1726, 0.1725), but different sum of steric constants Σ*R*_S: 4.72, 4.95, 5.31.

The addition of amines to electron-deficient C=C bonds is known to increase with the nucleophilicity of amine and steric accessibility of its reaction center [8, 13]. However, because of the reaction of neutralization, amines and carboxylic acids, when simultaneously present in aqueous solutions, exist in various equilibrium forms: as unbound molecules,

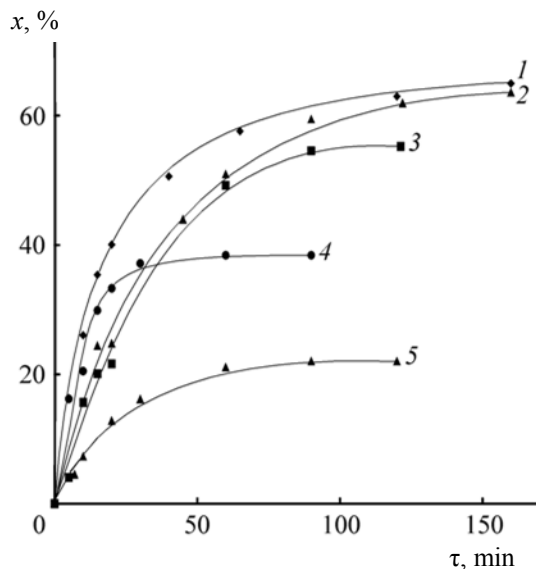


Fig. 1. Dependence of conversion of acids (1–3) 1, (4) 2, (5) 3 on time in the reactions with amines 4–6. Initial concentration of amine, mmol/g: (1–3) 3.0, (4, 5) 1.0.

contact and solvent-separated ion pairs, dissociated ions. The equilibria between these forms depend on initial concentrations of the reagents, ionic strength of the solutions, and other factors. Binding of molecules of the reagents to salts sharply decreases the acid activity and nucleophilic properties of the amino group, which is converted to the ammonium one [13]. The transfer of proton to the negatively charged α -carbon atom of the activated alkene, finalizing the nucleophilic addition, can also follow different routes. As a result, as was shown by the example of addition of pyridine to acid 4 [14], adequate kinetic equation must include several different reaction rates, with the understanding that a set of constant values calculated for certain conditions can be unsuitable for the other conditions (for example, for the increase of concentration of the reagents from 0.05 to 1.0 M). Therefore in this work as a criterion of the influence of initial concentrations of amines 4–6 having very similar structure of the amine reaction center on the kinetics of their addition to acids 1–3 we have chosen readily measurable experimental parameters: initial rates and attained equilibrium conversion.

Judged from practical equity of the values of pK_a and $\Sigma\sigma^*$ of amines 4–6 and only small variation of steric hindrances ΣR_s , their activity in nucleophilic addition reactions with the same electron-deficient alkenes must be similar. However, the experimental results have shown that as in the Menshutkin reaction

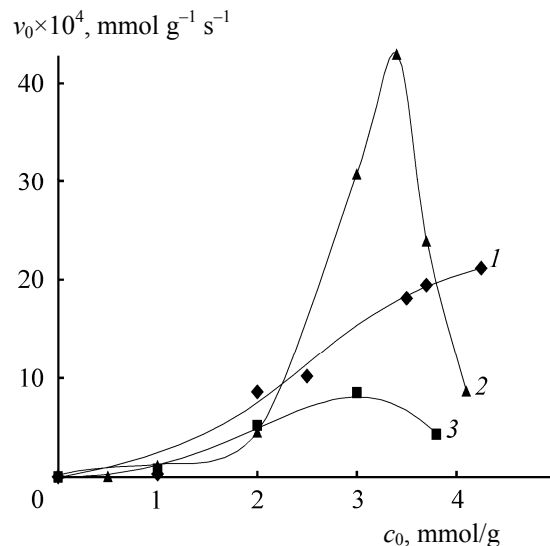


Fig. 2. Effect of initial concentrations of the reagents on the initial rates of addition of amines 4–6 to acid 1.

compounds 4–6 strongly differ by manifestation of concentration effects.

Figure 1 shows typical kinetic curves, which demonstrate that reactions (1)–(3) in the systems under investigation reach the equilibrium in 1–3 h.

Based on the kinetic curves extrapolated to zero time the initial reaction rates were determined at different concentrations of the reagents with their constant ratio (Figs. 2, 3). In doing so, unusual concentration plots were obtained. In dilute solutions (concentration of the reagents up to 1.0 mmol/g), the initial rates of addition of amines 4–6 to acids 1–3 are slightly different. However, with the increase of initial concentrations of the reagents, the activity of amines becomes substantially different, the difference being dependent on the range of concentrations. For example, in concentration of 1.5 mmol/g, amine 5 shows the least activity as compared to 4 and 6, at c_0 3.0 mmol/g it shows the highest activity, and at c_0 ~4.0 mmol/g the rate of addition of amine 5 is intermediate between those of 4 and 6.

The shapes of the initial rate dependences on concentration for reactions of amines 4–6 are also different. In the case of amine 5, the curve has a clearly expressed maximum, for 6 the maximum is smoothed (although corresponds to approximately the same concentration, 3.0–3.5 mmol/g). The dependence of the rate of addition of amine 4 on concentration has

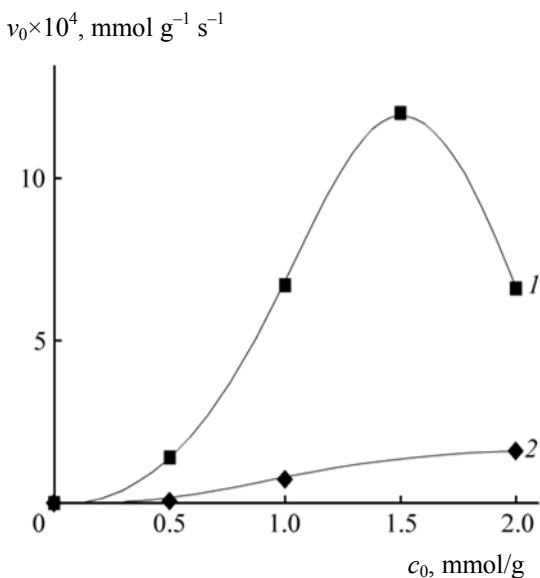


Fig. 3. Effect of initial concentrations of unsaturated acids on the initial rates of addition of amine 5 to acids (1) 2 and (2) 3.

an S-shaped form with sharp increase of the rate in the concentration interval 1.0–3.5 mmol/g.

We have also compared the concentration effects in the addition of amine 5 to acids 1–3. The products of reactions (2) and (3) are, respectively, methacrylic carboxy- and sulfobetaines with two monosubstituted amide groups. Acids 2 and 3 at an equimolar ratio of the reagents are inferior in activity in the addition of amines to acid 1, therefore, their reactions were performed with excess of amines. It is worth noting, that, when using acids 2 and 3 at $c_0 > 2$ mmol/g, the homogeneity of the systems was violated. In view of this, the effect of initial concentrations of the reagents was investigated in more narrow intervals than in reaction with acid 1.

It turned out that for the addition of amine 5 to acid 2 the concentration dependence of the initial rate passes through a maximum, and there is an interval of initial concentrations of the reagents in which v_0 first sharply increases and then quickly decreases. The maximally reached initial rates correspond to much lower values of c_0 than in the case of addition of amine 5 to acid 1 (1.5 as compared to 3.5 mmol/g). For the system 5–3, the maximum on the plot $v_0-f(c_0)$ is lacking and monotonous growth of the initial rate close to linear is observed.

As follows from the data on equilibrium conversions reached in all investigated systems, the effect of the total initial concentration of the reagents is retained

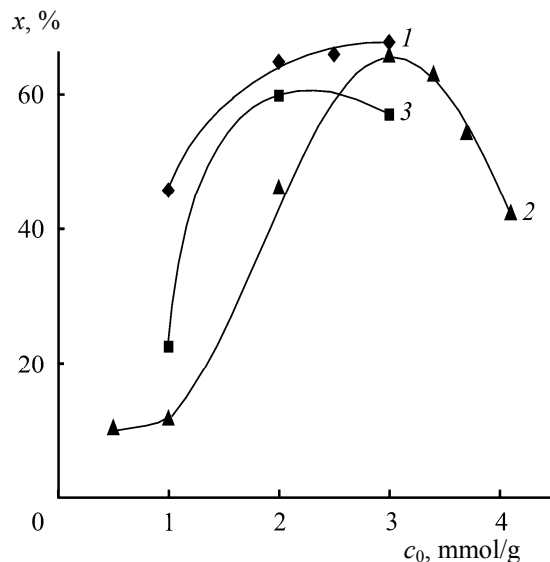


Fig. 4. Effect of initial concentration of the reagents on the equilibrium conversion for addition of amines (1–3) 4–6 to acid 1.

for carrying out the process up to deep conversion (Figs. 4, 5). Therewith in all five systems the growth of c_0 values first gives rise to a substantial shift of the equilibrium toward the product formation, the equilibrium conversion increases 1.5–6.5 times. However, in three systems, with further increase in the initial concentrations of the reagents a decrease in equilibrium conversions was detected. Most clearly it was manifested in system 5–1, where the initial concentration of the reagents could be increased up to

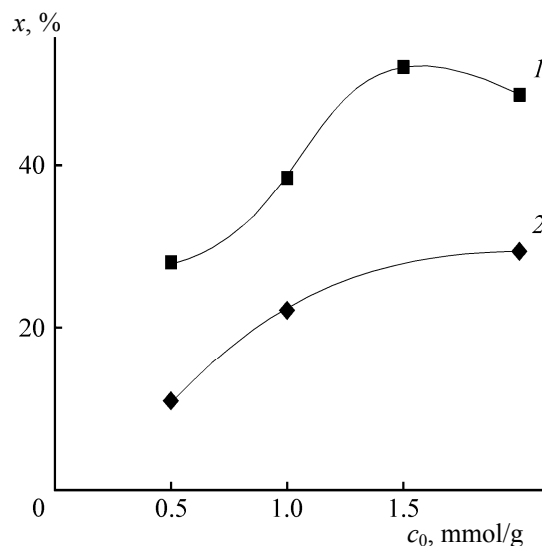


Fig. 5. The effect of initial concentrations of unsaturated acids on equilibrium conversions in addition of amine 5 to acids (1) 2 and (2) 3.

4 mmol/g with retention of homogeneity of the system. In other cases, the highest initial concentrations were as low as 2 mmol/g (5–2, 5–3) or 3 mmol/g (4–1, 6–1); note that for acrylic aminoamides the reason for such limitation was not the violation of homogeneity but spontaneous polymerization of the monomers occurring when the conversion reached > 20% in solutions with higher c_0 (even when concentration of the inhibitor of radical polymerization, hydroquinone, was substantially increased).

Therefore, in all five investigated systems strong concentration effects are revealed. When analyzing the reasons of these effects it is necessary to underline sharp differences in the addition of aminoamides with the same structure of the amine reaction center to acid **1**, as well as the fact that in the investigated systems both the reagents and the products have potential centers for associative interactions. It is well known that the amine, acidic, and amide groups are active in formation of hydrogen bonds; the presence of charged ammonium, carboxylate and sulfonate groups must cause strong ionic interactions in the reagents and products. The studied aminoamides were earlier shown to actively form associates in aqueous solutions [15], the effect of association on physical properties of the solutions being notably different.

This allows a conclusion that the concentration effects in reactions (1)–(3) are due to associative interactions with participation of the reagents. In recent years more and more data appear in the literature that under certain conditions such interactions may play an important role in the kinetics of homogeneous liquid-phase reactions with participation of the reagents capable of association. This allowed developing, in particular, adequate kinetic models for some reactions of alcohols [16, 17]. The method of simulation had shown [18] that the rate constants for the reactions in liquid-phase systems capable of association may increase or decrease with concentration of the associated reagents depending on the equilibrium constant and the ratio of the rate constants for free and associated molecules. In the case of participation in association of not only the reagents but also the reaction products, the concentration dependences at a deep conversion may differ from those for initial rates.

The obtained results are indicative of this very behavior in the investigated systems. Note also that association may affect not only redistribution of the electron density in the molecules of the reagents, which determines the variation of their reactivity. One

of factors determining the kinetic specific features of the reactions can be alteration of accessibility of the reaction centers connected with the structure of the associates. Therefore, the formation of associates may either favor or prevent the contact between the reaction centers. The model of formation in concentrated aqueous solutions of ammonium salts of vinyl type of monomeric associates favoring the reactions with participation of the C=C bonds was first suggested rather long ago on the basis of the data on spontaneous polymerization [19]. Occurring of spontaneous polymerization in some systems we investigated is also indicative of a possibility of formation of similar associates in them.

The obtained results show that the occurrence of reactions (1)–(3) with participation of amines **1**–**3** is strongly affected by associative interactions depending on the structure of the reagents. With increased initial concentrations, the role of noncovalent pre-reaction interactions increases. At low conversion the main factor is association of the reagents, while at high conversion the association of the products of the reaction makes its contribution. This determines the differences in concentration effects measured for the initial rates and for equilibrium conversions of reactions (1)–(3).

EXPERIMENTAL

Acid **1** (“Acrylate” Ltd.), amine **4**, and acid **3** (Aldrich) were used without additional purification. Acid **2** and amine **1** were synthesized by the Schotten-Baumann reaction from acryloyl chloride and aminoacetic acid or *N,N*-dimethylpropanediamine [12, 20]. Amine **3** was prepared by the Ritter reaction using the described procedure [21].

The addition of amines **4**–**6** to acid **1** was performed at 50°C with an equimolar ratio of the reagents; the reaction of amine **5** with acid **3**, at 70°C and molar ratio of the reagents 1.5 : 1.0; the reaction of amine **5** with acid **3**, at 50°C and the ratio of 1.2 : 1.0. Initial concentrations of the reagents varied from 0.5 mmol/g to maximally possible (up to the limit of solubility or carrying the reaction in mass). To exclude radical polymerization of the monomers, hydroquinone (0.5% of the monomer) was introduced to the reaction mixtures. The degree of conversion in reactions (1)–(3) was calculated from variation of concentration of the C=C bonds, which was determined by bromide-bromate titration.

Steric and inductive effects of the substituents at nitrogen atom in the molecules of tertiary amines **4–6** were characterized by parameters ΣR_S and $\Sigma \sigma^*$ calculated from Eqs. (4) and (5) using the Galkin–Cherkasov method [22, 23].

$$\sigma^* = \sum_{i=1}^n \frac{(\sigma_A)_i}{r_i^2}, \quad (4)$$

$$R_S = 30 \log \left[1 - \sum_{i=1}^n \frac{R_i^2}{4r_i^2} \right]. \quad (5)$$

where $(\sigma_A)_i$ denotes the ability of the i th atom of the substituent to manifestation of inductive effect (by the Taft's scale of inductive constants; inductive effect of alkyl substituents was taken to be zero), R_i is the covalent radius of the i th atom, Å, r_i is the distance of the i th atom from the reaction center, Å.

ACKNOWLEDGMENTS

This work was performed with the financial support from the Ministry of Education and Science (State contract 10.2326.2017/PCh) and the Program of development of R.E. Alekseev Nizhny Novgorod State Technical University.

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