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## ORGANIC SYNTHESIS AND INDUSTRIAL ORGANIC CHEMISTRY

# Effect of Reactant Association on Addition of Tertiary Amines to Acrylic Acid in Aqueous Solutions

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**Abstract**—The formation of betaines by the reaction of tertairy amines (*N,N*-dimethyl-*N*-2-hydroxyethylamine, *N,N*-dimethylaminoethyl methacrylate, *N*-methylmorpholine, *N,N*-dimethylaminopropionitrile, 1,4-diazabicyclo[2.2.2]octane) with acrylic acid in aqueous solutions in a wide concentration range was studied. The concentration effects observed were interpreted taking into account the association of the starting reagents.

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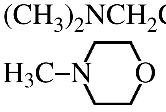
Carboxy betaines are components of many cosmetics and pharmaceutical preparations [1]. In many cases, it is appropriate to prepare β-betains in a single step by nucleophilic addition of tertiary amines to the activated C=C bond in acrylic acid. Water is a convenient solvent for such reactions [2]. Previously, we have examined the reaction of a series of trialkylamines with acrylic acid in dilute and moderately concentrated aqueous solutions [3, 4]. From the practical viewpoint, it is appropriate to use as high concentrations of reactants as possible; however, specific features of betaine formation from amines and acrylic acid in concentrated aqueous solutions have not been studied yet.

Recent papers give more and more indications that (meth)acrylic monomers in aqueous soilutions tend to form stable molecular associates which can strongly affect the chemical properties of these compounds. In particular, studies of the hydrolysis of aminoalkyl and hydroxyalkyl methacrylates (*N,N*-dimethylaminoethyl and 2-hydroxyethyl methacrylates) have shown that the association of the monomers results in abnormal acceleration or inhibition of the reaction in concentrated solutions [5, 6]. Another consequence of the association of amine-containing (meth)acrylic esters or amides in water is the possibility of spontaneous radical polymerization under certain conditions [7, 8]. A study of the radical homopolymerization of acrylic acid (AA) in aqueous solutions also revealed a significant effect of the monomer self-association on the rate constant of chain propagation [9].

In this study, we examined the effect of reactant association on the nucleophilic addition of tertiary amines to AA to give betaines:

$$CH_2{=}CHCOOH + NRR'R'' \rightleftarrows RR'R''\overset{+}{N}CH_2CH_2COO^-,$$

where NRR'R'' = $(CH_3)_2NCH_2CH_2OH$ (DMAE), $(CH_3)_2NCH_2CH_2OCOC(CH_3){=}CH_2$ (DMAEM),



(MeM), $(CH_3)_2N(CH_2)_3CN$ (DMAPN), $N(CH_2CH_2)_3N$ DABCO.

As amines we chose compounds containing, along with the reacting amino group, additional N- and O-containing functional groups: *N,N*-dimethyl-*N*-2-hydroxyethylamine (DMAE), *N,N*-dimethylaminoethyl methacrylate (DMAEM), *N*-methylmorpholine (MeM), *N,N*-dimethylaminopropionitrile (DMAPN), asnd 1,4-diazabicyclo[2.2.2]octane (DABCO). The additional functional groups considerably increase the solubility of amines and their salts in water, which allowed syntheses in aqueous solutions in a wide concentration range. Furthermore, according to [10], the energies of intermolecular associative interactions involving hydroxy, etser, ether, nitrile, and amino groups are essentially different. Therefore, we expected that comparison of the activities of polyfunctional amines in the betaine formation would furnish additional information on the effect of these interactions on the reaction in question.

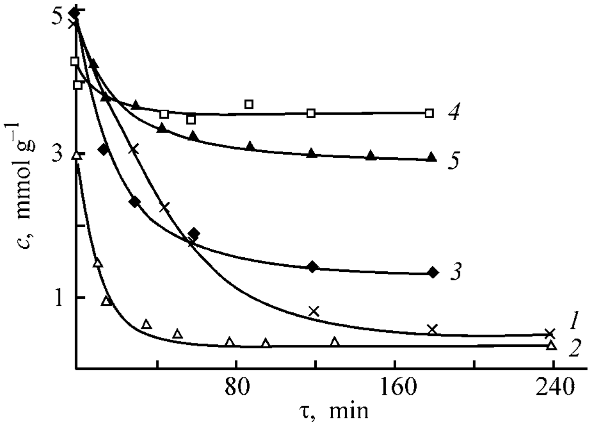


**Fig. 1.** Variation of the reactant concentration *c* with time τ. Amine: (*1*) DMAPN, (*2*) DABCO, (*3*) DMAE, (*4*) DMAEM, and (*5*) MeM; the same for Figs. 2, 3, and 5.

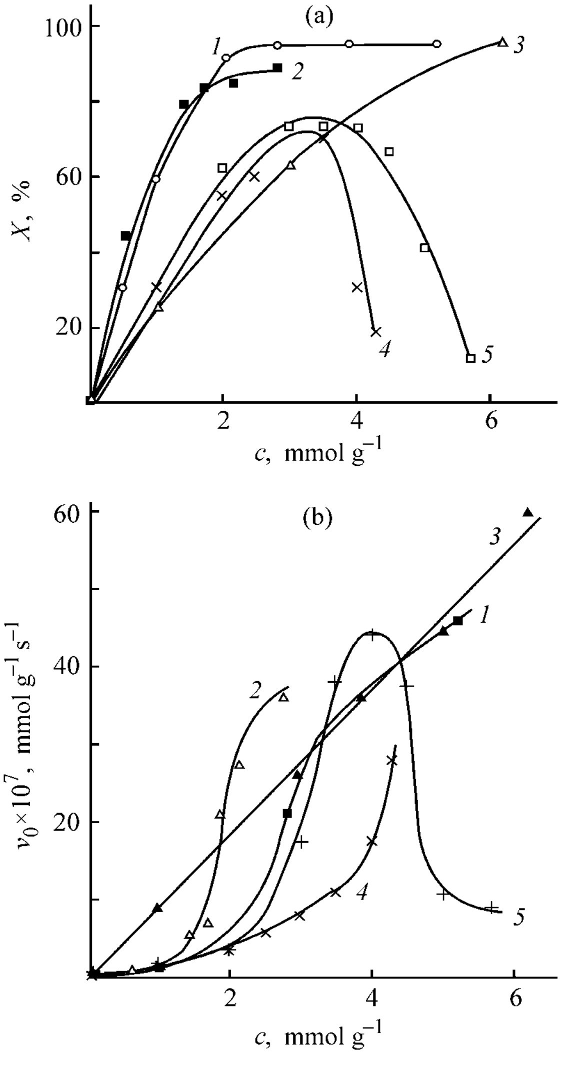


**Fig. 2.** (a) Equilibrium conversion *X* and (b) initial reaction rate $v_0$ vs. the reactant concentration *c*.

## EXPERIMENTAL

The reaction of AA with tertiary amines was performed at 50°C and equimolar ratio of the reactants. Hydroquinone (0.5 wt % relative to AA) was added to the reaction mixtures to prevent radical polymerization. The reactant concentrations in aqueous solution were varied from 1 to 6 mmol g$^{-1}$ (with DABCO, the maximal concentration was 3 mmol g$^{-1}$; at higher concentrations, the system became heterogeneous).

Addition of tertiary amines to AA was monitored by a decrease in the concentration of the C=C bonds determined by bromide–bromate titration. The specific viscosity of the reactants was measured with an Ubbelohde viscometer ($d_c$ 0.34, 0.56, and 0.73 mm; 25°C). The $^1$H NMR spectra were recorded on a Varian Gemini-300 Fourier spectrometer (300 MHz), solvent $D_2O$, reference DMSO.

**3-(*N*,*N*-Dimethyl-*N*-hydroxyethylammonio)propionate.** To 18.2 g of a 76% solution of AA in water, containing 0.07 g of hydroquinone, we added 17.1 g of DMAE. The resulting mixture was heated at 50°C for 5 h. After the reaction completion, water was distilled off in a vacuum, and the residue was washed with acetone. The product was vacuum-dried (20–40°C, 2 mm Hg) to constant weight. Yield 24.8 g (80.1%). The product contained no C=C bonds and no acid groups.

Found, %: N 8.58.
Calculated, %: N 8.70.

$^1$H NMR spectrum, δ, ppm: 3.34–3.39 ($-CH_2N^+$); 2.85 ($CH_3N^+$); 2.55–2.64 ($-C\underline{H}_2OH$, $-CH_2COO^-$).

The addition of amines to AA is an equilibrium reaction throughout the examined range of initial concentrations of the reactants. Figure 1 shows typical kinetic curves of consumption of the reactants at their high concentrations. Figures 2a and 2b show the dependences of the equilibrium conversion and initial reaction rate on the initial reactant concentration. The following trends can be revealed. As the initial concentrations are raised in the range 0–1.5 mmol g$^{-1}$ for amines containing no oxygen (DMAPN, DABCO), the equilibrium conversion sharply increases, reaches a maximum (88–95%) at the initial concentration of about 2.5 mmol g$^{-1}$, and does not noticeably change with further increase in the concentration.

A different pattern is observed with the oxygen-containing amines. In the experiments with DMAE, the equilibrium conversion monotonically grows with

Inductive ($\sigma^*$) and steric ($R_s$) constants of substituents R, R', R" in the starting amines ($N^*$ is the reaction center)

| Amine | NRR'R" | $\Sigma\ \sigma^*$ | $\Sigma\ -R_s$ |
|---|---|---|---|
| DMAE | $(CH_3)_2N^*CH_2CH_2OH$ | 0.20 | 5.83 |
| DMAEM | $(CH_3)_2N^*CH_2CH_2OCOC(CH_3)=CH_2$ | 0.5 | 6.33 |
| MeM | $CH_3N^*(CH_2CH_2)_2O$ | 0.67 | 6.23 |
| DABCO | $N^*(CH_2CH_2)_3N$ | – | 4.43 |
| DMAPN | $(CH_3)_2N^*CH_2CH_2C\equiv N$ | 0.8 | 6.02 |

the initial solution concentration (with a minor deviation from linearity) and reaches almost 100% at the maximal concentration (actually, for neat reactants without solvent). With DMAEM and MEM, the equilibrium conversion first increases in the initial concentration, passes through a maximum, and then sharply decreases at concentrations exceeding 3.2 mmol $g^{-1}$.

The dependences of the initial rates on the reactant concentration also vary with the amine structure. This dependence is approximately linear with DMAE, passes through a pronounced maximum with MeM, is close to exponential with DMAEM, and is S-shaped with DMAPN and DABCO.

It has been shown previously [3, 4] that, in dilute solutions at approximately equimolar reactant ratio, the relative activity of various tertiary amines in reactions with AA is determined by the steric accessibility and nucleophilicity of the nitrogen atom. To evaluate these parameters for the amines examined in this study, we used the inductive ($\sigma^*$) and steric ($R_s$) constants of substituents, calculated according to [11, 12]. These procedures were developed for systems with a four-coordinate carbon atom as a reaction center. However, previous studies of *N*-alkylation of tertiary amines have shown that this approach also gives adequate results when applied to systems with a nitrogen atom as reaction center [13].

The constants listed in the table show that the amines chosen are similar in the steric accessibility and nucleophilicity of the reaction centers. Therefore, in accordance with the previously developed concepts, the amines should not essentially differ in the reactivity toward AA. Thus, the concentration effects observed cannot be interpreted in terms of the traditional concept of nucleophilic reactions of amines. We attribute the abnormal dependences of the initial rate of betaine formation and equilibrium conversion on the initial reactant concentration to intermolecular interactions of reactant molecules with the formation of various associates.

Therefore, the next step of our study was concerned with the association of amines in aqueous solutions in the presence of acids. In these experiments, AA was replaced with acetic acid to preclude betaine formation. We obtained the viscosity–concentration dependences (VCDs) for solutions of amine acetates (Fig. 3). It is known [14] that the occurrence and features of intermolecular interactions in solutions can be judged from the VCDs. Pronounced deviations of the VCDs from the linearity, observed with all the amines, suggest the occurrence of the association. Figure 3 shows that the VCDs of the salts of all the amines except DABCO exhibit pronounced maxima. According to [14, 15], maxima in the viscosity isotherms correspond to the formation of stable complexes in the system. To evaluate the relative capability of the amine salts for association, we cal-

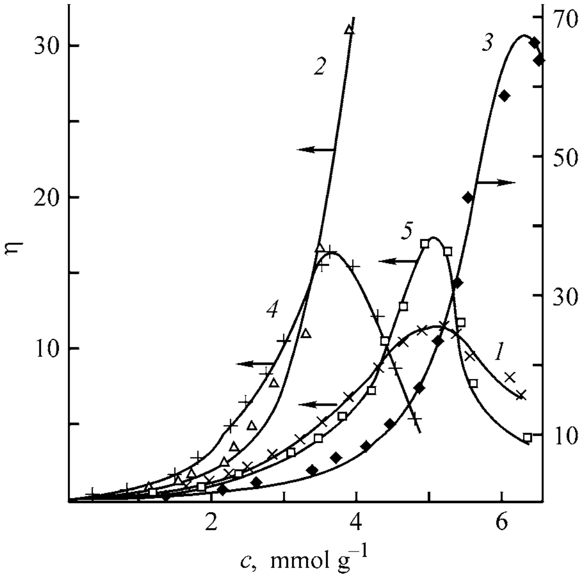


**Fig. 3.** Specific viscosity η of aqueous solutions of amine acetates at 25°C vs. the concentration *c*.

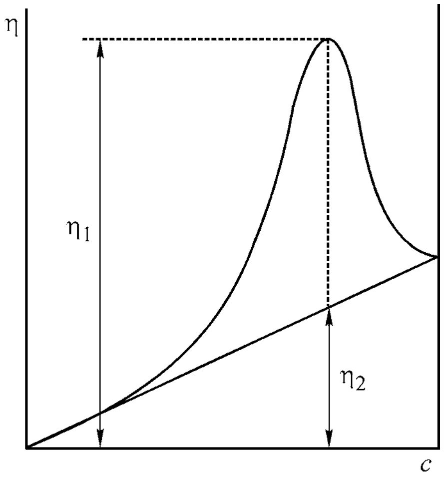


**Fig. 4.** Determination of $\eta_1$ and $\eta_2$ for calculating the association factor $\alpha$.

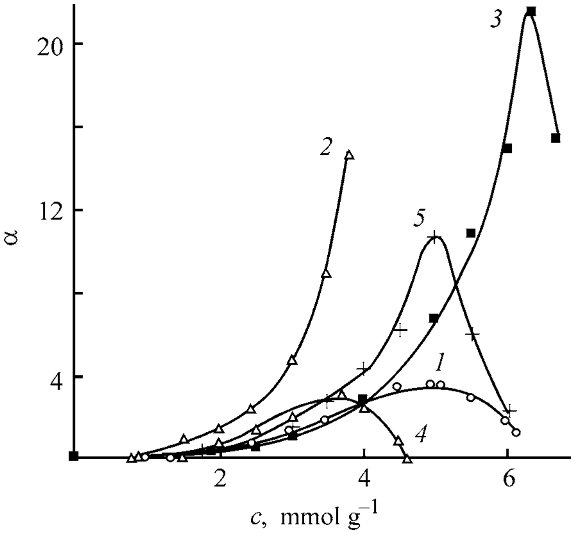


**Fig. 5.** Association factor $\alpha$ at 25°C vs. the concentration of amine acetates, *c*.

culated the association factor $\alpha$ reflecting the extent of deviation of the VCD from the linearity:

$$\alpha = (\eta_1 - \eta_2)/\eta_2,$$

where $\eta_1$ is the actual specific viscosity of an amine salt at a given concentration, and $\eta_2$ is the specific viscosity at the same concentration, estimated by extrapolation of the initial linear portion of the VCD (Fig. 4).

Figure 5 shows the dependences of $\alpha$ on the amine salt concentration. It is seen that DABCO and DMAE show the strongest tendency toward association, and DMAEM and DMAPN, the weakest tendency. Thus, the amines chosen are similar in the nucleophilicity and steric accessibility of reaction centers in the isolated molecules, but strongly differ in the tendency toward association in the presence of acids. In this context, it is reasonable to assume that the factor responsible for significant differences in the betaine formation kinetics is the effect of the association on the local concentration, accessibility, and reactivity of active centers of the reactants. Our results show that the association can both accelerate and inhibit the reaction.

In particular, it is known [16] that form linear aggregates alcohols in aqueous solutions. It is reasonable to assume that DMAE or its salt, containing a hydroxy group, also tend to form such associates. Apparently, the local concentration of the reactants in such associates increases, which facilitates their reaction. As a result, the concentration, initial rate, and equilibrium conversion proportionally increase.

Shibalovich et al. [17] measured the surface tension of aqueous solutions of DMAEM and its salts and showed that these compounds exhibit surface activity even in relatively dilute solutions. Hence, associates of micellar rather than linear type are more probable for DMAEM salts. It should be noted that, at concentrations less than 1.8 mmol $g^{-1}$ (relatively dilute solutions), the dependences of the specific viscosity and reaction rate on the amino ester concentration are approximately linear. At concentrations exceeding 2 mmol $g^{-1}$, both the viscosity of the reaction mixtures and the initial reaction rate sharply increase, i.e., the association of the starting amine salts favorably affects the betaine formation. A sharp decrease in the equilibrium conversion in highly concentrated solutions (>3.5 mmol $g^{-1}$) is apparently due to formation in the course of the reaction of stable heteroassociates of the starting reactants and betaines, in which the mutual arrangement of the unchanged amino groups and C=C bonds is unfavorable for the reaction.

Data for the MeM–AA system show that, in this case, the reaction rate and viscosity of the system grow virtually linearly as the reactant concentration is raised to 2 mmol $g^{-1}$, and in the concentration range 2–4 mmol $g^{-1}$ the growth accelerates. With a further increase in the concentration, the initial rate, equilibrium conversion, and viscosity sharply decrease. This fact may be due to the formation in highly concentrated solutions of stable homoassociates of the starting amine salts and heteroassociates of amine salts with the forming betaines, with the mutual arrangement of the amino group and C=C bond in these associates being unfavorable for the reaction.

With DABCO and DMAPN containing no oxygen atoms, the molecular "packing" in the homo- and heteroassociates is favorable, according to the experimental data, for the betaine formation. Therefore, with an increase in the initial concentration to above $1.0 - 1.5$ mmol $g^{-1}$, the initial reaction rate and viscosity of the mixture demonstrate virtually synchronous accelerated growth, without a decrease in the equilibrium conversion.

## CONCLUSIONS

(1) The effect of the initial reactant concentration on the nucleophilic addition of tertiary amines to acrylic acid in aqueous solutions was examined.

(2) With an increase in the initial reactant concentration, the initial reaction rate grows linearly (*N*,*N*-dimethyl-*N*-2-hydroxyethylamine), exponentially (*N*,*N*-dimethylaminoethyl methacrylate), in the S-shaped mode (*N*,*N*-dimethylaminopropionitrile, 1,4-diazabicyclo[2.2.2]octane), or passes through a maximum followed by a sharp decrease (*N*-methylmorpholine).

(3) With an increase in the initial reactant concentration, the equilibrium conversion monotonically grows to reach maximal values (*N*,*N*-dimethyl-*N*-hydroxyethylamine, *N*,*N*-dimethylaminopropionitrile, 1,4-diazabicyclo[2.2.2]octane) or passes through a maximum followed by a sharp decrease (*N*,*N*-dimethylaminoethyl methacrylate, *N*-methylmorpholine).

(4) Salts of tertiary amines in aqueous solutions tend to form associates; their structure determines the course of the reaction of betaine formation.

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