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Phase-Transfer Aminolysis of 4-Nitrophenyl Acetate with Amino Acid Salts in the System Liquid–Solid. Kinetics of the Reaction in the Organic Phase

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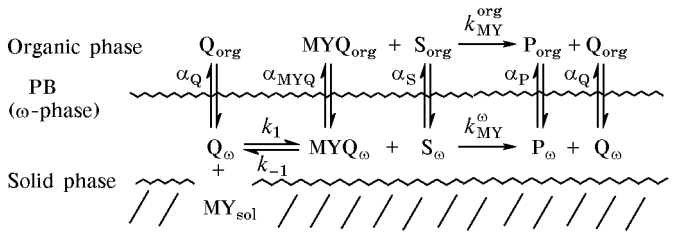
Abstract—In the phase-transfer system solid potassium aminoacetate–crown ether–chlorobenzene, the fraction of the nucleophile–catalyst complex trasferred to the organic phase does not exceed 1% of the amount of the solid phase. Nevertheless, the reactivity of the crown ether complex with potassium aminoacetate is sufficient to ensure the aminolysis to proceed in the organic phase at an appreciable rate.

We previuosly reported [1] that, depending on the reaction conditions (lipophilicity of phase-transfer catalyst, properties of organic phase, and presence of small amounts of water in the system), phase-transfer aminolysis of 4-nitrophenyl acetate with amino acid salts in a liquid–solid (l/s) system can occur at the phase boundary (PB), in the organic phase, or in both these simultaneously. As a first approximation, Scheme 1 illustrates the general reaction pattern in such systems. Here, MY = $NH_2CHRCOO^- M^+$ (M = Na, K); Q is a phase-transfer catalyst (crown ether or quaternary onium salt); S is a substrate (4-nitrophenyl acetate); P is the product ($AcNHCHRCOO^- M^+$ and $4\text{-}NO_2C_6H_4O^- M^+$); *k* stands for the rate constant of the corresponding stage; and α is the partition coefficient between the organic phase and phase boundary for the corresponding species.

In liquid–solid systems containing traces of water or crystallization water in the solid phase, the phase boundary can be regarded as a third phase differing from both bulk solid and bulk organic phases. In terms of phase-transfer catalysis, this phase is referred to as ω-phase [2]. It is assumed that all processes (both sorption and chemical reactions) take place just in the ω-phase. Taking into account that in the present work the solid phase was amino acid salt as monohydrate, the term *ω-phase* will be used to denote PB.

We examined the kinetics of aminolysis of 4-nitrophenyl acetate (S) with solid potassium aminoacetate monohydrate (MY = $NH_2CH_2COOK \cdot H_2O$) in the organic phase of the two-phase system chlorobenzene–MY_{sol} in the presence of 18-crown-6 (Q) at 25°C. The choice of glycine potassium salt as reagent was dictated by the fact that the rate of its reaction with 4-nitrophenyl acetate in the organic phase of the above system is considerably higher than the rate of analogous reaction with glycine sodium salt [1]. Our study was aimed primarily at establishing the relation between the amount of the solid phase and catalyst concentration, on the one hand, and the reaction rate

Scheme 1.



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in the organic phase (k_{MY}^{org} in Scheme 1), on the other. In order to simulate the conditions of aminolysis in the organic phase, extraction of potassium aminoacetate into the bulk organic phase with 18-crown-6 was performed in two ways (*A* and *B*). In the first case (*A*), a portion of the solid salt, specially prepared for kinetic studies, was placed into a solution of 18-crown-6 in chlorobenzene, the mixture was stirred for a strictly specified time (from 1 to 30 min), the organic phase separated, and the concentration of potasium aminoacetate was determined in a portion of the organic phase. Another portion was used to determine the rate of the reaction of the extracted salt with 4-nitrophenyl acetate. Series *A* experiments allowed us to obtain information, on the one hand, on the overall rate of "degradation" of the solid salt through complex formation with crown ether (k_1, k_{-1}) and transfer of the resulting complex into the bulk organic phase (α_{MYQ} in Scheme 1) and, on the other, on the rate of aminolysis of substrate S in the bulk organic phase (k_{MY}^{org}).

According to way *B*, the concentration of potassium aminoacetate in the organic phase was varied by changing the amount of the solid salt MY in the system or the concentration of phase-transfer catalyst Q in chlorobenzene (the mixture was preliminarily stirred for 30 min). This series of experiments allowed us to measure the rate of aminolysis of 4-nitrophenyl acetate in the organic phase at different concentrations of potassium aminoacetate which was extracted with the aid of 18-crown-6.

Figure 1 shows the kinetic curves for the overall complex formation process between potassium aminoacetate and 18-crown-6 and for transfer of the complex from the ω-phase to the bulk organic phase. The shape of the curves suggests saturation in the system, i.e., establishment of complex formation (K_1) and phase-transfer (α_{MYQ}) equilibria (Scheme 1). The initial rates depend on the crown ether concentration and the amount of solid phase.* Without going into kinetic details of the complex formation and extraction processes, the following may be stated (which is useful for further study): when the concentration of solid phase is greater than 5×10^{-3} M and the amount of the catalyst is equivalent, stirring of the two-phase system for 30 min is sufficient for the corresponding equilibria (K_1 and α_{MYQ}) to establish.

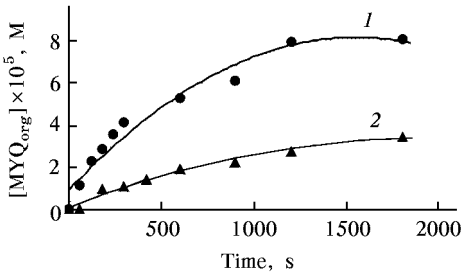

Fig. 1. Plots of potassium aminoacetate concentration in the organic phase ($[MYQ_{org}]$) versus time of stirring of the two-phase system chlorobenzene/$NH_2CH_2COOK\cdot H_2O_{sol}$ in the presence of 18-crown-6 at 25°C: (*1*) [MY] = [Q] = 12.5×10^{-3} M, (*2*) [MY] = [Q] = 6.25×10^{-3} M.

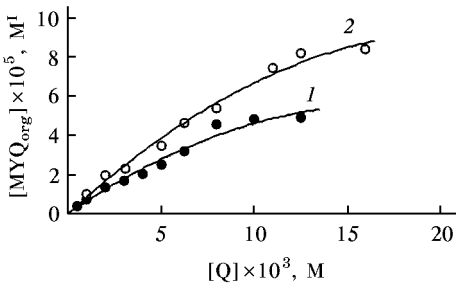

Fig. 2. Plots of potassium aminoacetate concentration in the organic phase ($[MYQ_{org}]$) versus concentration of 18-crown-6 in the system chlorobenzene/$NH_2CH_2COOK\cdot H_2O_{sol}$ at 25°C: (*1*) [MY] = [Q] = 6.25×10^{-3} M; (*2*) [MY] = [Q] = 12.5×10^{-3} M.

Provided that $[MQ_{org}] >> [S_{org}]$, the rate of aminolysis of 4-nitrophenyl acetate in the organic phase is described by pseudofirst-order equation (k^{org}, s^{-1}). Table 1 contains the concentrations of potassium aminoacetate in the organic phase and k^{org} values obtained in series *A* and *B* experiments. The second-order rate constants $k_{MY}^{org} = k^{org}/[MYQ_{org}]$ calculated therefrom do not depend on the time of stirring and the concentrations of the solid phase and 18-crown-6 in the system. The average values of k_{MY}^{org} for series *A* and *B* experiments satisfactorily agree with each other. These results suggest that complexes of potassium aminoacetate with 18-crown-6, transferred to the organic phase, have the same structure.

Figure 2 illustrates the dependence of the concentration of the potassium aminoacetate–18-crown-6 complex in the organic phase $[MYQ_{org}]$ on the overall concentration of crown-ether [Q] in the system. The molar ratio of the solid salt and crown ether in the mixture $[MY_{sol}]/[Q]$ changes from 12.5 to 0.5 (Table 1). Increase in the concentration of the complex in the organic phase is observed when [MY] >

* Hereinafter, the substrate and catalyst concentrations are given relative to the volume of the organic phase. The concentration of the solid phase in the system is also given in arbitrary volume units (M).

Table 1. Kinetics of aminolysis of 4-nitrophenyl acetate with potassium aminoacetate in the organic phase of the system chlorobenzene/$NH_2CH_2COOK \cdot H_2O_{sol}$ in the presence of 18-crown-6 at 25°C

$[MY_{sol}] \times 10^3$, M	$[Q_{org}] \times 10^3$, M	$\frac{[MY_{sol}]}{[Q_{org}]}$	Time of stirring, min	$[MYQ_{org}] \times 10^5$, M	$k^{org} \times 10^4$, s^{-1}	k^{org}_{MY}, $l\ mol^{-1}\ s^{-1}$	α_{MYQ}	Number of runs
			Series *A*					
12.5	12.5	1	1–30	1.13–8.6	0.608–4.60	5.62 ± 0.17	154	9
6.25	6.25	1	3–30	0.95–3.42	0.410–1.90	5.53 ± 0.22	182	7
			Series *B*					
12.5	1–16	12.5–0.8	30	1.00–8.41	0.750–4.90	6.30 ± 0.27	147	9
6.25	0.5–12.5	12.5–0.5	30	0.44–5.00	0.286–3.62	7.05 ± 0.44	147	10

[Q] up to a [MY]:[Q] ratio of 1:1. When this ratio becomes the reverse, i.e., [MY] < [Q], the organic phase is saturated with the complex. Such a situation implies that the equilibrium described by the constant K_1 is completely displaced toward the MYQ complex. Therefore, we are able to calculate the partition coefficient of MYQ between the ω-phase (PB) and the organic phase ($\alpha_{MYQ} = [MYQ]^{\omega}/[MYQ_{org}]$) using the following equations:

$$\alpha_{MYQ} = \frac{[MY_{sol}] - [MYQ_{org}]}{[MYQ_{org}]} \text{ at } [MY_{sol}] < [Q]; \quad (1)$$

$$\alpha_{MYQ} = \frac{[Q] - [MYQ_{org}]}{[MYQ_{org}]} \text{ at } [MY_{sol}] > [Q]. \quad (2)$$

The α_{MYQ} values were calculated from the data in Table 1 obtained when the system was preliminarily stirred for 30 min (series *B*). Regardless of the ratio

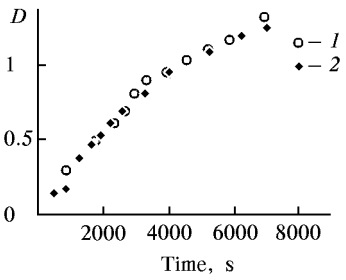

Fig. 3. Kinetic curves for the aminolysis of 4-nitrophenyl acetate with the solid potassium aminoacetate–18-crown-6 complex in benzene at 25°C (*1*) without preliminary stirring of a mixture of the complex with benzene and (*2*) with preliminary stirring before addition of the substrate; [MYQ] = 6.25×10^{-3} M, [S] = 6.25×10^{-5} M.

$[MY_{sol}]/[Q]$, the α_{MYQ} values remain satisfactorily constant. The absolute value of α_{MYQ} (147) indicates that less then 1% of the complex MYQ (relative to its overall amount in the system) is transferred into the organic phase. Nevertheless, its reactivity is sufficiently high for the reaction in the organic phase to occur at a measurable rate.

By special experiment, using preliminarily synthesized $NH_2CH_2COOK \cdot H_2O$ complex with 18-crown-6, we have confirmed that stirring of the system liquid–solid for 30 min is sufficent for the formation of the MYQ complex at the phase boundary (in the ω-phase; see Experimental). Figure 3 shows the kinetic curves for the reaction of the solid MYQ complex with 4-nitrophenyl acetate in benzene, which were obtained when the substrate was added to the hetereogeneous system preliminarily stirred for 30 min and when the complex and the substrate were added to benzene simultaneously. The kinetic curves and the rate constants calculated therefrom fully coincide with each other: $k \times 10^{-4} = 1.63 \pm 0.05$ and 1.49 ± 0.08 s^{-1}, respectively.

In this connection, quite demonstrative are the kinetic data for the aminolysis of 4-nitrophenyl acetate after activation of the two-phase system potassium aminoacetate–organic solvent in the presence of 18-crown-6 over a period of 30 min (k_{MY}, Table 2) and those obtained using preliminarily synthesized potassium aminoacetate–18-crown-6 complex as solid phase (k_{MYQ}, Table 2). The apparent rate constants of the heterophase aminolysis of 4-nitrophenyl acetate under the above conditions, the reactant concentrations being equal, satisfactorily coincide with each other in different organic solvents employed as organic phase.

Thus we have found that the two-phase system $NH_2CH_2COOK \cdot H_2O$/organic solvent, containing 18-crown-6 as phase-transfer catalyst, gives rise to formation of a solid complex which is distributed between the organic phase and ω-phase with a very low degree of extraction into the organic phase (<1%). The process of solid phase activation is complete in about 30 min (at concentrations of the salt and catalyst equal to or greater than 5×10^{-3} M). The complex is formed almost quantitatively at a MY_{sol}/Q molar ratio of 1 : 1. This means that the complex formation constant K_1 in Scheme 1 is high: it exceeds a value of at least 1000 l/mol.

EXPERIMENTAL

Potassium aminoacetate monohydrate was synthesized as described in [3]. For kinetic measurements, the salt was ground in a vibrational ball mill to a grain size of 20 ± 10 μm. The grain size was controlled with the aid of an MIM-80 metallographic microscope.

The crown ether complex with potassium aminoacetate was synthesized by the known procedure [4] by melting the reactants under vigorous stirring. For kinetic measurements, the solid complex was ground to the same grain size as that of potassium aminoacetate monohydrate.

The concentration of potassium aminoacetate in the organic phase was determined by the ninhydrin method [5]. Solvents were purified by standard procedures [6]. The procedure for measurement of the rate of aminolysis of 4-nitrophenyl acetate with potassium aminoacetate was described in detail in [7]. The kinetics of the overall process including complex formation between potassium aminoacetate and 18-crown-6 and extraction of the complex into the organic phase were studied using the same sampling setup as in the study of the kinetics of aminolysis [7].

Table 2. Rate constants of aminolysis of 4-nitrophenyl acetate in the systems $NH_2CH_2COOK \cdot H_2O$/organic solvent in the presence of 18-crown-6 (k_{MY}, s^{-1})[a] and solid potassium aminoacetate–18-crown-6 complex/organic solvent (k_{MYQ}, s^{-1})[b] at 25°C

Solvent	$k_{MY} \times 10^4$, s^{-1}	$k_{MYQ} \times 10^4$, s^{-1}
Toluene	2.69 ± 0.13	2.36 ± 0.07
Benzene	1.75 ± 0.08	1.63 ± 0.05
Chlorobenzene	10.5 ± 0.4	12.6 ± 0.1
Tetrachloroethylene	1.38 ± 0.05	0.995 ± 0.017
Dichloroethane	5.53 ± 0.23	4.57 ± 0.29
Acetonitrile	7.47 ± 0.56	6.35 ± 0.41
Dioxane	5.86 ± 0.08[c]	7.12 ± 0.62[d]

[a] [MY] = [Q] = 6.25×10^{-3} M.
[b] [MYQ] = 2.5×10^{-4} M.
[c] [MY] = [Q] = 6.25×10^{-4} M.
[d] [MYQ] = 6.25×10^{-4} M, [S] = 6.25×10^{-5} M.

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