Group Interactions in Polyelectrolytes. IX. The Amination Kinetics of Chloromethylated Polystyrene in Binary Mixed Solvents

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(Received May 18, 1974)

All the aminations of chloromethylated polystyrene (CMPS) and benzyl chloride with *i*- and *s*-butylamine in *N*,*N*-dimethylformamide (DMF), in dioxane, and in DMF–dioxane mixtures conformed to the ordinary second-order kinetics. The activation parameters in the pure solvents revealed that the much higher amination rate in DMF than in dioxane was due to both the lower value of $\Delta H^{\neq}$ and the higher value of $\Delta S^{\neq}$ in DMF. The rate of amination in DMF–dioxane was investigated as a function of the composition of the mixed solvent. The observed rate constants in DMF–dioxane mixtures fell substantially on the curves calculated on the basis of Kondo and Tokura's theory concerning reaction rates in binary mixed solvents. It is suggested in this paper that the higher rate of amination in DMF is due to the strong solvation of the activation complex in DMF to form an addition product, and that it is also due to the relative increase in the configurational entropy of the reaction system at the transition state from dioxane to DMF.

The amination of chloromethylated polystyrene (CMPS) with primary and secondary amines in several solvents was studied kinetically by the present author. All the aminations of benzyl chloride, a low-molecular model of CMPS, and most of the aminations of CMPS with primary amines such as butylamines obeyed the ordinary second-order kinetics. The amination rate of CMPS was almost the same as that of benzyl chloride, and there was not much difference in the activation parameters between them.[1] On the other hand, the rate constants were greatly affected by the species of solvent. Although there was very little difference between the rates in dioxane and in methyl ethyl ketone, the rate was markedly enhanced in dipolar aprotic solvents such as *N*,*N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO). It was observed that, in the aminations with 2-aminobutanol and *n*-butylamine, the enthalpy of activation ($\Delta H^{\neq}$) decreased and the entropy of activation ($\Delta S^{\neq}$) increased in DMF or DMSO as compared with those in dioxane.[2] This is probably because of the strong solvation of the polar activated complex in such dipolar solvents.

In the present study, in order to ascertain such a solvent effect, first, CMPS and benzyl chloride were aminated with *i*- and *s*-butylamine in dioxane and their activation parameters were compared with those in DMF. Second, the rate of the aminations were measured in DMF–dioxane mixed solvents. The selective solvent effect of DMF on the rate has been revealed by the fact that the rate increases greatly upon the addition of a small amount of DMF to the dioxane. A theory with regard to the dependence of the reaction rate on the composition of a binary solvent system was proposed by Kondo and Tokura[3] on the basis of the theory of the non-electrolyte solution, and it has been applied to the Menschutkin reaction of alkyl halide with tertiary amine and the benzoylation of amine in a mixed solvent such as benzene–nitrobenzene.[3,4] In the present study, the dependence of the amination rate on the composition of DMF–dioxane has been investigated on the basis of Kondo and Tokura's equation in order to elucidate the effects of solvents on the amination of CMPS.

Experimental

Materials. As the chloromethylated polystyrene (CMPS) we used the samples described in a previous paper (CMPS-9 and CMPS-10).[1] The amines, benzyl chloride, and the solvents, all of a reagent grade, were distilled before use; they were proved to be pure by their refractive indices. All the other chemicals were of a reagent grade.

Kinetic Measurements. The procedures of the kinetic measurements in the amination of CMPS and benzyl chloride were almost the same as those described in a previous paper.[2] The initial concentrations of the chloromethyl group (of CMPS and benzyl chloride) and amine were about 0.040 and 0.400 mol/l respectively. The temperature of the reaction mixture was kept constant (within ±0.1 °C) by means of a thermostat.

Results and Discussion

Amination in Dioxane. The aminations of CMPS and benzyl chloride with *i*- and *s*-butylamine in dioxane conformed to the ordinary second-order kinetics, and the rate constant was computed on the basis of the following equation:

$$kt = \frac{1}{(a-b)} \ln \frac{b(a-x)}{a(b-x)} \tag{1}$$

where a and b are the initial concentrations of the amines and the chloromethyl group respectively, and where x is the concentration of hydrochloride formed after a certain time, t. The rate constants measured at different temperatures are listed in Table 1, where k_P and k_B are the rate constants of CMPS and benzyl chloride respectively. The table also lists the activation energy, E_a, and the frequency factor, A, as computed by means of the least-squares method. The activation parameters, $\Delta H^{\neq}$, $\Delta S^{\neq}$, and $\Delta G^{\neq}$, which were computed on the basis of the equations described in a previous paper,[2] are tabulated in Table 2. (Since the errors in $\Delta G^{\neq}$ are much smaller than those in $\Delta H^{\neq}$ and $\Delta S^{\neq}$, they are omitted from the table.)

As has been described in a previous paper,[1] the amination rates with butylamines are $k_P > k_B$ in dioxane, and $k_P < k_B$ in DMF. All the values of $\Delta H^{\neq}$ decreases from benzyl chloride to CMPS; however, $\Delta S^{\neq}$ decreases

Table 1. Amination of CMPS and benzyl chloride with *i*- and *s*-butylamine in dioxane

Amine	Temp °C	Rate constants $\times 10^3$, l/mol·min		E_a kcal/mol	log A[c]
		k_P[a]	k_B[b]		
i-Butyl	50	2.06	1.24		
	60	3.90	2.30	(k_P) 13.0±0.2	6.08±0.10
	70	7.13	4.15		
	80	11.6	7.37[d]	(k_B) 13.2±0.1	6.00±0.05
	90	19.1	11.8		
s-Butyl	60	2.04	1.04		
	70	3.65	1.93	(k_P) 13.2±0.1	5.98±0.07
	80	6.46	3.35	(k_B) 13.4±0.1	5.82±0.10
	90	10.6	5.56		

a) Rate constant of CMPS. b) Rate constant of benzyl chloride. c) A is expressed by l/mol min. d) The value at 80.3 °C.

Table 2. Thermodynamic quantities for 25 °C in the amination of CMPS and benzyl chloride in dioxane

Amine	Chloride	$\Delta H^{\ddagger}$ kcal/mol	$\Delta S^{\ddagger}$ e.u.	$\Delta G^{\ddagger}$ kcal/mol
i-Butyl	CMPS	12.3±0.2	−40.8±0.5	24.5
	Benzyl	12.5±0.1	−41.2±0.2	24.7
s-Butyl	CMPS	12.6±0.1	−41.3±0.3	24.9
	Benzyl	12.8±0.1	−42.0±0.3	25.4

slightly from benzyl chloride to CMPS in dioxane, and it increases a little in DMF. This difference in $\Delta S^{\ddagger}$ between CMPS and benzyl chloride is general for DMF and DMSO,[1,2] and it is considered to be characteristic of dipolar aprotic solvents.

On the other hand, the rates in DMF are much larger than those in dioxane; $\Delta H^{\ddagger}$ decreases and $\Delta S^{\ddagger}$ increases from dioxane to DMF. Similar changes in the activation parameters were also found in the amination with *n*-butylamine and 2-aminobutanol when the solvent was changed from dioxane to DMF or DMSO.[2] The decrease in $\Delta H^{\ddagger}$ is considered to be due to the strong solvation of the activation complex in a dipolar aprotic solvent; that is, it corresponds to the enthalpy of the formation of an addition product as a result of the interaction of the activation complex with the solvent. The increase in $\Delta S^{\ddagger}$ may be ascribed to the relative increase in the configurational entropy of the reaction system at the transition state from dioxane to a dipolar aprotic solvent.

Amination in DMF–Dioxane Mixtures. The amination of CMPS and benzyl chloride in DMF–dioxane conformed to the second-order rate equation. Figure

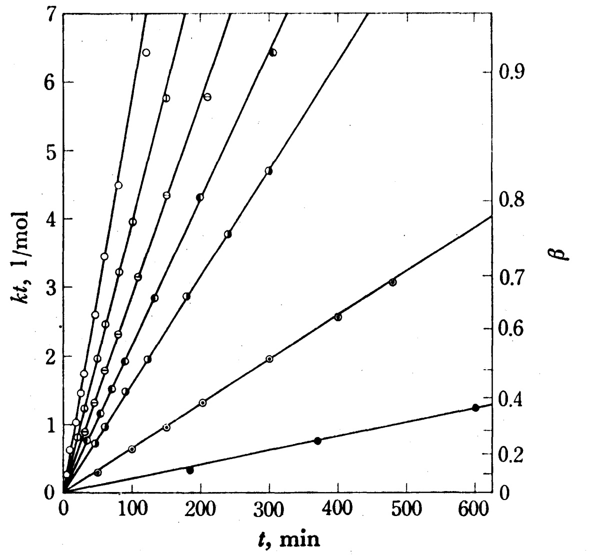

Fig. 1. The amination of CMPS with *s*-butylamine at 60 °C in DMF–dioxane systems of different DMF mole fractions (x_1).
○: x_1=1, ⦶: x_1=0.8, ⊖: x_1=0.65, ◐: x_1=0.50, ◑: x_1=0.35, ⊙: x_1=0.15, ●: x_1=0.

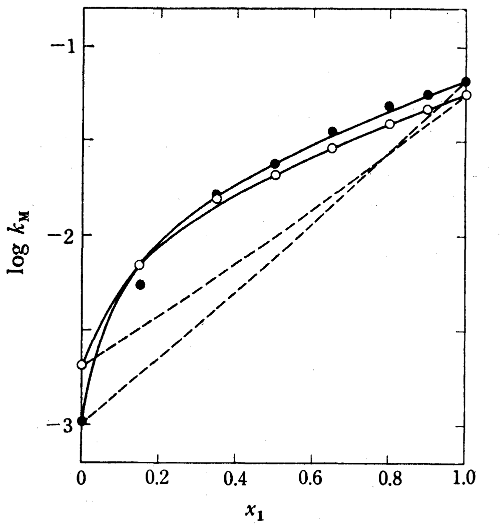

Fig. 2. Plot of log k_M *vs.* mole fraction of DMF, x_1, for the amination of CMPS (○) and benzyl chloride (●) with *i*-butylamine in DMF–dioxane mixture at 50 °C.
——: Calculated on the basis of Eq. (4)
……: Calculated on the basis of Eq. (3)

Table 3. Amination rate constants of CMPS and benzyl chloride in DMF-dioxane mixture, $10^2 k$ (l/mol min)

Amine	Chloride	Temp °C	Mole fraction of DMF (x_1)							
			0	0.15	0.35	0.50	0.65	0.80	0.90	1
i-Butyl	CMPS	50	0.206	0.871	1.76	2.80	4.01	5.46	6.42	7.72
	Benzyl	50	0.124	0.758	2.11	3.44	5.05	6.93	8.43	9.97
s-Butyl	CMPS	60	0.204	0.641	1.58	2.11	2.91	4.01	4.72	5.72
	Benzyl	60	0.104	0.545	1.60	2.44	3.57	4.95	5.72	6.67

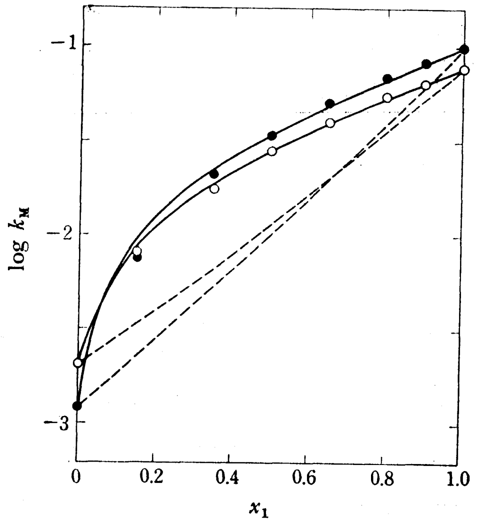

Fig. 3. Plot of $\log k_M$ *vs.* mole fraction of DMF, x_1, for the amination of CMPS (○) and benzyl chloride (●) with s-butylamine in DMF-dioxane mixture at 60 °C.
——: Calculated on the basis of Eq. (4)
……: Calculated on the basis of Eq. (3)

1, as an example, shows the plots of *kt* against *t* for the amination of CMPS with *s*-butylamine at 60 °C, where *kt* represents the right-hand term in Eq. (1) and where $\beta = x/b$. Table 3 lists the rate constants, computed on the basis of Eq. (1), of the amination with *i*-butylamine at 50 °C and those with *s*-butylamine at 60 °C.

The logarithms of the rate constant in DMF–dioxane, denoted here as $\log k_M$, are plotted against the mole fraction of DMF in the mixed solvent, denoted as x_1, in Figs. 2 and 3. In the figures, the observed values (expressed by the circles) are on the straight lines represented by Eq. (2), which are omitted in the figures;

$$\log k_M = x_1 \log k_1 + x_4 \log k_4 \qquad (2)$$

where x_1 and x_4 $(=1-x_1)$ are the mole fractions of DMF and dioxane respectively in the DMF–dioxane system and where k_1 and k_4 are the rate constants in pure DMF and pure dioxane respectively. It is shown in the figures that the addition of a small amount of DMF to dioxane increases the rate constant markedly. This result, along with that described in the preceding section, suggests that the activated complex in the mixed solvent interacts selectively with DMF to form the solvated activated complex.

With regard to a reaction in a binary mixed solvent, Kondo and Tokura[3] calculated thermodynamically the Henry constant of each species in the reaction system; they derived theoretically the relation between the rate constant and the composition of the solvent mixture on the basis of molecular models. In the first model, where two reactants, A and B, and the activation complex, M^*, yield regular solutions with Solvent 1 (S_1) and Solvent 4 (S_4), the rate constant in the mixed solvent, k_M, is expressed by:

$$\log k_M = x_1 \log k_1 + x_4 \log k_4 - x_1 x_4 \alpha_{14}/2.303 \qquad (3)$$

where α_{14} is an empirical coefficient which is related to the interaction between S_1 and S_4.

In the second model, where A and B yield regular solutions with both the solvents, but where M^* reacts selectively with S_1 to form an addition product, denoted here as MS_1^*, k_M is given by:

$$\log k_M = x_1 \log k_1 + x_4 \log k_4 - [x_1 \log (K+1) - \log (x_1 K+1) + x_1 x_4 \alpha_{14}/2.303] \qquad (4)$$

where K is the equilibrium constant, expressed on the basis of the mole fractions of the species, in the formation of MS_1^* from M^* and S_1.

In the present study, x_1 and x_4 are the mole fractions of DMF and dioxane respectively, and k_1 and k_4, the rate constants in pure DMF and pure dioxane respectively. The coefficient, α_{14}, is related to the molar excess free energy of mixing in the binary system, $\Delta G_M{}^E$, by means of the following equation:

$$\Delta G_M{}^E RT = \alpha_{14} x_1 x_4 \qquad (5)$$

while $\Delta G_M{}^E$ can be obtained from the equilibrium vapor-pressure data in the system. The data in the DMF–dioxane system were presented by Quitzch;[5] the values of $\Delta G_M{}^E$ and α_{14} calculated from the data are shown in Fig. 4. At $x_1=0.5$, $\alpha_{14}(50\ °C)=0.403$ and α_{14}-(60 °C)=0.390. The values of α_{14} and k_M at $x_1=0.5$ were introduced into Eq. (4) in order to obtain the K values, which are shown in Table 4. Then, the values of α_{14} and K were introduced into Eqs. (3) or (4) in order to calculate $\log k_M$ as a function of x_1. In Figs. 2 and 3, the broken lines and solid lines are those calculated on the basis of Eqs. (3) and (4) respectively. The observed values, expressed by the circles, are substantially on the lines calculated on the basis of Eq. (4). This agreement suggests that the activated complex is solvated selectively with DMF in DMF–dioxane.

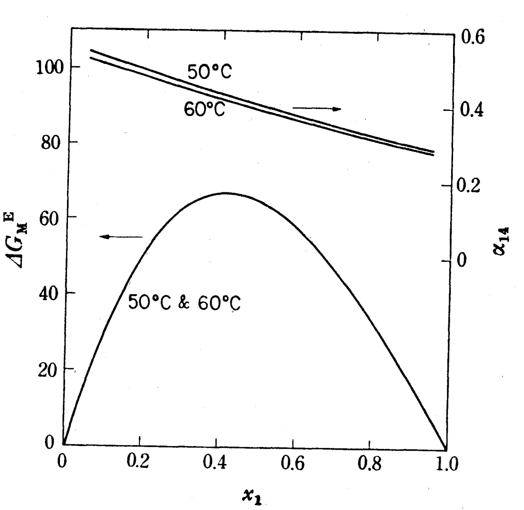

Fig. 4. Excess free energy of mixing, $\Delta G_M{}^E$, and the coefficient, α_{14}, for the DMF-dioxane system.

Enhancement of the Amination Rate in a Dipolar Aprotic Solvent and Comparison of the Rate between CMPS and Benzyl Chloride. In Table 4, K is an equilibrium constant of the $M^* + S_1 \rightleftarrows MS_1^*$ reaction, which is expressed on the basis of mole fraction; this was then transformed to an equilibrium constant expressed

TABLE 4. EQUILIBRIUM CONSTANT IN THE SOLVATION OF THE ACTIVATED COMPLEX AND THERMODYNAMIC QUANTITIES

Amine	Chloride	Temp °C	K	K_c l/mol	$\Delta G^{\neq\mathrm{solv}}$ kcal/mol	$\Delta H^{\neq\mathrm{solv}}$ kcal/mol	$T\Delta S^{\neq\mathrm{solv}}$ kcal/mol	$T\delta\Delta S^{\neq\mathrm{conf}}$ a) kcal/mol
i-Butyl	CMPS	50	21.2	1.73	−0.4	−1.4	−1.0	1.9
	Benzyl	50	43.8	3.57	−0.8	−1.4	−0.6	2.0
s-Butyl	CMPS	60	15.7	1.28	−0.2	−1.1	−0.9	2.0
	Benzyl	60	38.5	3.14	−0.8	−1.2	−0.4	2.0

a) $T\delta\Delta S_i^{\neq\mathrm{conf}}$ represents $T(\Delta S_1^{\neq\mathrm{conf}}-\Delta S_4^{\neq\mathrm{conf}})$.

on the basis of the molar concentration, $K_c=[\mathrm{MS_1}^{\neq}]/[\mathrm{M}^{\neq}][\mathrm{S_1}]$, by means of the following equation:

$$K = K_c/V_{\mathrm{soln}} \tag{6}$$

where V_{soln} is the molar volume of the solution defined as:[3]

$$V_{\mathrm{soln}} = (\sum_i m_i V_i)/\sum_i m_i \tag{7}$$

where m_i is the moles of a component, i, of the solution and where V_i is partial molar volume of the component. Provided that the solute components are negligible, V_{soln} (DMF–dioxane)=0.0816 l/mol at $x_1=0.5$ (at 25 °C). The values of K_c calculated on the basis of Eq. (6) are shown in Table 4. The free energy of solvation of the activated complex with DMF (S_1), $\Delta G^{\neq\,\mathrm{solv}}$, in Table 4 is calculated from the K_c values.

If the activated complex is solvated merely with DMF in DMF–dioxane, the enthalpy of the solvation of the activated complex, $\Delta H^{\neq\,\mathrm{solv}}$, will be the difference between the enthalpy of activation in DMF, $\Delta H_1^{\neq}$, and that in dioxane, $\Delta H_4^{\neq}$. The $T\Delta S^{\neq\mathrm{solv}}$ values in Table 4 were thus calculated. Although there is very little difference in $\Delta H^{\neq\mathrm{solv}}$ values between CMPS and benzyl chloride, the $T\Delta S^{\neq\mathrm{solv}}$ of CMPS is a little lower than that of benzyl chloride. This difference may be attributed to the steric hindrance to the solvation in CMPS; that is, the formation of the addition product from the activation complex and the solvent molecules is obstructed by the neighboring groups of the polymer.

Although the values of $\Delta S^{\neq\mathrm{solv}}$ are negative, the values of $(\Delta S_1^{\neq}-\Delta S_4^{\neq})$ can be seen to be positive by comparing Table 7 in Ref. 1 with Table 2 in the present paper. Since the activated complex in the amination is ionic or rather polar, there must be a large difference in the configurational entropy of the reaction system at the transition state between the system containing such a polar solvent as DMF (the solubility parameter, $\delta=12.11$) and the system containing dioxane ($\delta=9.88$). Accordingly, $(\Delta S_1^{\neq}-\Delta S_4^{\neq})$ is assumed to be composed of those two terms:

$$\Delta S_1^{\neq} - \Delta S_4^{\neq} = \Delta S^{\neq\,\mathrm{solv}} + (\Delta S_1^{\neq\,\mathrm{conf}}-\Delta S_4^{\neq\,\mathrm{conf}}) \tag{8}$$

where $\Delta S_i^{\neq\mathrm{conf}}$ is the change in the configurational entropy of the reaction system containing a solvent, i (i is 1 or 4), from its initial state to its transition state. Thus, we obtain the following relation:

$$(\Delta G_1^{\neq}-\Delta G_4^{\neq}) - \Delta G^{\neq\,\mathrm{solv}} = T(\Delta S_1^{\neq\,\mathrm{conf}}-\Delta S_4^{\neq\,\mathrm{conf}}) \tag{9}$$

The difference between $(\Delta G_1^{\neq}-\Delta G_4^{\neq})$ and $\Delta G^{\neq\mathrm{solv}}$, therefore, corresponds to the difference in the configurational entropy changes of the reaction systems. Since the $\Delta S_i^{\neq\mathrm{conf}}$ term is not directly related to the solvation of the activated complex, the values of $(\Delta S_1^{\neq\mathrm{conf}}$—$\Delta S_4^{\neq\mathrm{conf}})$, unlike those of $\Delta S^{\neq\mathrm{solv}}$, will be almost the same for DMPS and benzyl chloride. The numerical values of $T(\Delta S_1^{\neq\mathrm{conf}}$—$\Delta S_4^{\neq\mathrm{conf}})$ calculated on the basis of Eq. (9) are shown in Table 4; they are the same for all the cases shown in the table, as had been expected.

The results of the present study suggest that the remarkable increase in the amination rate from dioxane to DMF is caused not only by the decrease in the activation energy, which is equal to the solvation energy of the activated complex with DMF, but also by the large relative increase in the configurational entropy of the reaction system at the transition state from the reaction in dioxane to that in DMF.

The author wishes to express his thanks to Dr. Masaya Yanagita for his valuable discussions. He is also grateful to Mr. Yasunori Uchiyama for his helpful assistance in preparing the polymer and in carrying out the measurements.

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