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EFFECT OF POLYMER AS COSOLVENT ON CHEMICAL REACTIONS IN SOLUTION—II

EFFECTS OF POLYOXYETHYLENE AND POLYSTYRENE ON THE REACTION OF DANSYL CHLORIDE WITH PRIMARY AMINO-ENDED POLYOXYETHYLENE IN CHLOROFORM

A. Okamoto, A. Hayashi and I. Mita
Institute of Interdisciplinary Research, Faculty of Engineering, University of Tokyo, 4-6-1, Komaba, Meguro-ku, Tokyo 153, Japan

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Abstract—The second-order rate constants for the reaction of 5-dimethylamino-1-naphthalenesulphonyl chloride (dansyl chloride) with primary amino-ended polyoxyethylene in chloroform were measured in the presence of polymers such as polyoxyethylene and polystyrene and compared with those in the presence of low molecular weight models, diethoxyethane and toluene respectively. Both polymers exhibit the polymer effect which is characterized by acceleration of the reaction depending on the degree of polymerization of the polymer cosolvent and on the fraction of the cosolvent. The effect by polymer cosolvents on chemical reactions between a low molecular weight species and a polymer is explained generally in terms of the thermodynamics of polymer solutions.

INTRODUCTION

Solid-phase synthesis has been successfully used for the preparation of a wide range of peptides and facilitated a number of synthetic organic transformations [1, 2]. Recently, linear or "soluble" polymers have been used as polymeric reagents or catalysts for a number of syntheses [2]. Although it is more than 25 years since polymer-mediated syntheses were put into practice, few systematic kinetic studies of such reactions have been made. On the other hand, the rate of polymerization is sometimes enhanced by the presence of polymers. This is the so-called template or matrix effect on polymerization [3]. In these systems, a characteristic effect by polymer catalysts, reagents, or matrices is called a "polymer effect when it differs from those found with low molecular weight models.

In our previous study on chemical reactions between low molecular weight species [4], we found a polymer effect for polyoxyethylene (POE) and polystyrene (PS) as polymer cosolvents on the reaction of dansyl chloride with butylamine in organic solvents. The polymer cosolvent effect was explained in terms of thermodynamics of polymer solution. We also claimed that the thermodynamical polymer effect should not be neglected in such chemical reactions in the presence of polymers as mentioned above.

In this paper, we report on the polymer cosolvent effect on reactions between a low molecular weight species and a polymer. Effects of POE and PS as polymer cosolvents on the rate of reaction of dansyl chloride with primary amino-ended POE (POE-NH_2) have been examined and compared with those of low molecular weight models such as diethoxyethane and toluene respectively. The reactions were followed by the increase in fluorescence intensity of the product. The polymer cosolvent effect for reactions between a low molecular weight species and a polymer is compared with the effect on reactions between two low molecular weight species and discussed in general terms from the thermodynamical viewpoint of polymer solution. Further, thermodynamic parameters for the reaction system estimated from the polymer effect are discussed briefly.

EXPERIMENTAL

Materials

5-Dimethylamino-1-naphthalenesulphonyl chloride (dansyl chloride; DNSCl) was obtained from Tokyo Kasei Co. and used without further purification. The solvents used (Wako Pure Chemical Industries Co.) were "Dotite Spectrosol" grade chloroform (CF) and toluene (Tol.), and used as received. Diethoxyethane (DEE) was distilled before use. Commercially available polyoxyethylene (POE90; $\bar{M}_n = 4100$, $\bar{M}_w/\bar{M}_n = 1.17$) and α-methoxy-polyoxyethylene (POE5; $\bar{M}_n = 240$, $\bar{M}_w/\bar{M}_n = 1.47$) were used after the hydroxyl groups were acetylated to suppress their side-reactions with DNSCl [4]. Polystyrene (PS) samples were so-called monodisperse standards, PS170 ($\bar{M}_n = 17{,}500$, $\bar{M}_w/\bar{M}_n = 1.05$; from Pressure Chemical Co.) and PS8 ($\bar{M}_n = 840$, $\bar{M}_w/\bar{M}_n = 1.10$; from Tokyo Soda Manufacturing Co.) and used as received.

Primary amino-ended polyoxyethylenes (POE-NH_2) were prepared as follows from commercially available samples of POE and α-methoxy-polyoxyethylene having two or one OH group per chain respectively (from Aldrich Chemical Co. and Iwai Chemical Co.) [4]. Isocyanato-ended polymers, prepared by the reaction of the polymer with a large excess of hexane-diisocyanate, were reacted with *t*-butyl alcohol to give polymer with the primary NH_2 group protected by the *t*-butoxycarbonyl group. The protective group was finally removed to obtain POE-NH_2. The amine content was determined by quantitative fluor-

Table 1. Reaction conditions and second-order rate constants for POE-NH$_2$–DNSCl reactions without cosolvent

POE-NH$_2$	$\bar{M}_n$ ($\bar{M}_w/\bar{M}_n$)	No. of NH$_2$ groups chain	$[\mathrm{DNSCl}]_0/10^{-5}$ M	$\frac{[\mathrm{NH_2}]_0}{[\mathrm{DNSCl}]_0}$	$k_2/M^{-1}\,s^{-1}$
1	1000 (2.3)	0.22	2.2	7.7	0.32
2	3000 (2.7)	0.01	0.90	2.6	0.40
3	4300 (1.3)	0.27	0.96	24	0.34
4	5300 (1.6)	0.01	0.86	2.0	0.23
5	8800 (9.3)	0.31	0.99	72	0.22
6	10,000 (2.6)	0.73	2.2	10	0.26
7	63,000 (2.2)	0.10	0.77	5.8	0.23
8	915,000 (9.6)	1.28	0.96	9.0	0.23

Samples 1 and 6 were prepared from α-methoxy-POE (from Aldrich Chemical Co.), 2, 4, 5 and 7 from POE (from Aldrich Chemical Co.), and 8 from POE (from Iwai Chemical Co.).

escence analysis after converting the NH$_2$ group to the fluorescent dansyl amide using dansyl chloride. Molecular weight and molecular weight distribution of the polymer were measured with a gel permeation chromatograph (Toyo Soda HLC-802UR with columns of G5000PW and G3000PW) using a u.v. detector (365 nm). The characteristics of the polymers are listed in Table 1.

Kinetic measurement

The reactions were followed by the increase in fluorescence intensity at the peak wavelength of the reaction products (500 nm) and the fluorescence measurements were performed without degassing by a JASCO FP-550 spectrofluorometer using a quartz cell with a cap. The fluorescence intensity was corrected by subtracting the value obtained in a blank solution without DNSCl. The final fluorescence intensity was measured after two days and was also corrected. Second-order rate constants were calculated from the observed pseudo first-order rate constants for systems with excess amine.

RESULTS AND DISCUSSION

Reactions of POE-NH$_2$ with DNSCl in chloroform without cosolvent

First, the reaction of POE-NH$_2$ with 5-dimethylamino-1-naphthalenesulphonyl chloride (DNSCl) to form a sulphonamide was studied in chloroform without cosolvent. The reaction was followed by fluorometry because the product is fluorescent while the reactants are not. We have confirmed that the reaction of primary amino group with DNSCl is strictly second-order [5]. In the previous study [4], we found that the presence of POE accelerates the reaction of the sulphonyl chloride with amine by two factors, *viz.* cosolvent effect of the polymer and coordination effect by the oxygen atoms in the polymer. The polymer cosolvent effect is, however, negligible at such dilutions as in these experimental conditions (2×10^{-5}–5×10^{-2} g/dl), and the coordination effect due to the oxygen atoms in POE-NH$_2$ itself, i.e. an intramolecular coordination effect, should alone be observed. Table 1 lists the reaction conditions and the second-order rate constants, k_2, for the reaction in CF at 40°. The values of k_2 in Table 1 are constant and about 7.5 times larger than that for the reaction of butylamine with DNSCl under the same conditions [5]. This difference may be due to the intramolecular coordination effect. The effect reflects the effective overall concentration C_{eff} of the monomeric units (—C_2H_4O—) in the POE chain around the terminal amino group of POE-NH$_2$. Table 1 shows that the effect is saturated already at the lowest degree of polymerization 24 of POE-NH$_2$. In our study on the intramolecular quenching of triplet anthryl group by phenyl groups in α-anthryl-polystyrene [6], it was found that C_{eff} of phenyl groups in the polymer around the anthryl group is saturated at a degree of polymerization over 25. This is consistent with the result in the present study. Further, the values of k_2 are in fair agreement with that of k'_2 for the reaction of butylamine with DNSCl in CF at 40° with *ca.* 20 vol% of DEE where the acceleration due to coordination seems to be saturated ($k'_2 = 2.3 \times 10^{-1}$ M^{-1} s^{-1} [4]). Consequently, C_{eff} of oxyethylene units around the end amino group is about 6 M, i.e. a concentration of 20 vol% of DEE. This value is roughly consistent with C_{eff} of PS in benzene [6] and of polyacrylamide in aqueous solution obtained by Goodman *et al.*[7]. Finally, the acceleration effect due to coordination need not to be considered for the reaction of POE-NH$_2$ with DNSCl in the presence of POE as a polymer cosolvent, because the effect is already saturated and unaltered by change of the volume fraction of the polymer cosolvent. Only the polymer effect of the polymer cosolvent can be focussed in the reaction system.

Polymer effect by POE as polymer cosolvent

Figure 1 shows cosolvent effects on the second-order rate constants for the reaction of POE-NH$_2$ ($\bar{M}_n$ = 10,000) with DNSCl in chloroform at 40° by three kinds of cosolvents, *viz.* POE with higher molecular weight (POE90), POE with lower molecular weight (POE5), and DEE as a dimer model of POE. Previously [4] we found that the addition of DEE increases the rate of reaction of DNSCl with butylamine in CF. The acceleration by DEE has been attributed to the coordination of two oxygen atoms in the molecule. In the present case, however, the second-order rate constant of the reaction decreases almost monotonously with increasing amount of DEE. This is not unexpected because the coordination is already accomplished intramolecularly as described in the preceding chapter. The decrease in the rate of the reaction is simply due to the decrease in polarity of the reaction medium as a whole with increasing amount of DEE as a nonpolar cosolvent. On the contrary, POE accelerates the reaction until the volume of POE is equal to that of CF. The accelerating effect of POE depends on the molecular weight of the polymer. The molecular weight dependence of the acceleration effect produced by POE becomes more distinct with increasing volume fraction of the polymer cosolvent.

Polymer effect by PS as polymer cosolvent

Figure 2 shows cosolvent effects on the second-order rate constants for the reaction of POE-NH_2 ($\overline{M}_n = 10{,}000$) with DNSCl in chloroform at 40° by three kinds of cosolvents, *viz.* PS with higher molecular weight (PS170), PS with lower molecular weight (PS8), and toluene as a monomer model of PS. For the reaction of DNSCl with butylamine in CF, neither of the cosolvents accelerates the reaction [4]. In the present study, on the contrary, the second-order rate constant of the reaction remains almost constant or rather increases with increasing volume fraction of the cosolvents. The acceleration effect by PS depends on the molecular weight of the polymer and the molecular weight dependence becomes more distinct with increasing volume fraction of the polymer cosolvent.

Thermodynamical expression of polymer effect by polymer cosolvent

In our previous paper [4], the polymer effect by polymer cosolvent on reactions between two low molecular weight species was explained in terms of the thermodynamics of polymer solution and was expressed as

$$\ln\left(\frac{k_2^m}{k_2^n}\right) = \left(\frac{1}{n} - \frac{1}{m}\right)(2\chi''_{CX} - \chi''_{CA} - \chi''_{CB})v_C, \quad (1)$$

where $k_2^m(k_2^n)$ is the second-order rate constant for the reaction with polymer of degree of polymerization m (n), A and B designate reactants, X activated complex P products, C polymer cosolvent, and v_C is the volume fraction of the polymer cosolvent

The parameter χ''_{ij} was introduced in the form [4]

$$\chi_{ij}/m_i = \chi'_{ij} + \chi''_{ij}/m_i, \quad (2)$$

where χ_{ij} is a general pair-interaction parameter between components i and j in the expression for free energy of mixing of polycomponent system defined according to Flory and m_i is the degree of polymerization of the ith component and is regarded as the ratio of the molar volume of the ith component to the common unit molar volume. The term χ'_{ij} and χ''_{ij} are independent of m_i. It should be noted that for polymers with high mol. wt ($m_i \rightarrow \infty$) χ''_{ij}/m_i is neglected and χ'_{ij} (or according to Flory $m_i\chi'_{ij}$) is regarded as the pair-interaction parameter. In our case, however, the term χ''_{ij} functions efficiently in the polymer effect of polymer cosolvent as shown in Eqn 2.

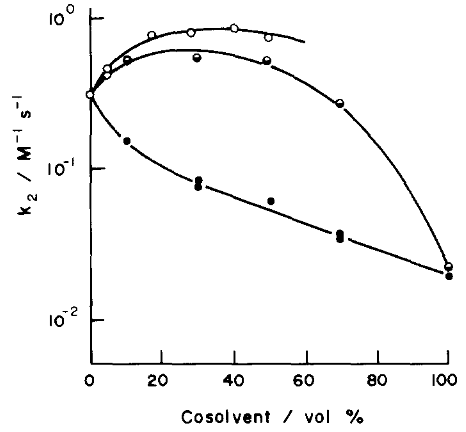

Fig. 1. Plot of k_2 vs v_C for the reaction of POE-NH_2 with DNSCl in CF at 40° with cosolvents: POE90 (○), POE5 (◒) and DEE (●).

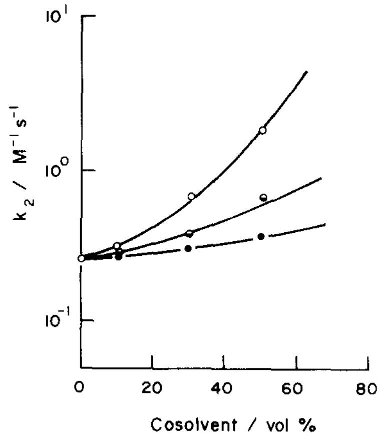

Fig. 2. Plot of k_2 vs v_C for the reaction of POE-NH_2 with DNSCl at 40° with cosolvents PS170 (○), PS8 (◒) and Tol. (●).

According to Patterson [8], pair-interaction parameter χ_{ij}/m_i is given in terms of two contributions, an interactional term $\chi_{I,ij}$ and a free volume term $\chi_{F,ij}$. Although $\chi_{I,ij}$ is constant for polymers i and/or j of the same chemical nature with different chain lengths, $\chi_{F,ij}$ is not always constant for polymer with not very

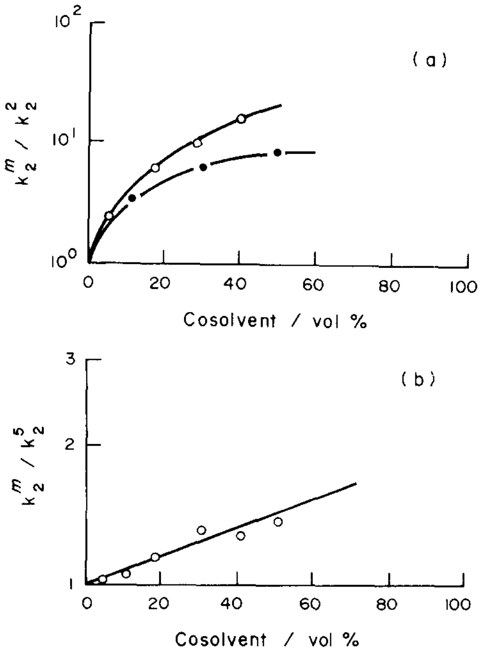

Fig. 3. Plot of ln (k_2^m/k_2^n) vs v_C for the reaction of POE-NH_2 with DNSCl in CF at 40° with cosolvents POE90, POE5 and DEE: (a) POE90/DEE (○) and POE5/DEE (●); (b) POE90/POE5.

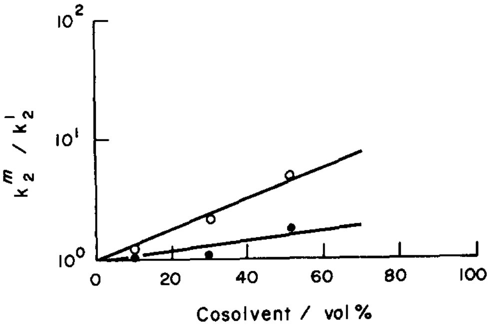

Fig. 4. Plot of ln (k_2^m/k_2^n) vs v_C for the reaction of POE-NH_2 with DNSCl in CF at 40° with cosolvents PS170, PS8 and Tol.: PS170/Tol. (○) and PS8/Tol. (●).

high molecular weight because $\chi_{F,ij}$ is mainly due to the difference of size or chain length between components i and j. We can express $\chi_{F,ij}$ to a first approximation as $\chi_{F,ij} = \chi^0_{F,ij}\ (1 - 1/m_i)$, because the free volume contribution increases with increasing molecular weight of polymer i and is usually neglected for a system of low molecular weight species ($\chi_{F,ij}$ vanishes at $m_i = 1$). Consequently we have

$$\frac{\chi_{ij}}{m_i} = \chi_{I,ij} + \chi^0_{F,ij} - \frac{\chi^0_{F,ij}}{m_i}. \tag{3}$$

From Eqns 2 and 3 we obtain the relations $\chi'_{ij} = \chi_{I,ij} + \chi^0_{F,ij}$ and $\chi''_{ij} = -\chi^0_{F,ij}$.

For reactions between A attached to a polymer chain and a low molecular weight species B in the presence of polymer cosolvent C, the polymer effect by the polymer cosolvent is expressed from Eqn 2 as

$$\ln\left(\frac{k_2^m}{k_2^n}\right) = \left(\frac{1}{n} - \frac{1}{m}\right)(\chi''_{CA} - \chi''_{CB})v_C, \tag{4}$$

where χ''_{CX} is considered equal to χ''_{CA} because χ''_{CX} and χ''_{CA} mainly reflect the chemical nature of chains of polymers with X and A. Compared with Eqn 2, Eqn 4 expresses the polymer effect more definitely by virtue of the second term in which an ambiguous χ''_{CX} related to the interaction between cosolvent and activated complex, is eliminated. The polymer with A has an end-group A which is chemically different from the monomeric units in the polymer. Then the effect of the end-group on the interactional term $\chi_{I,ij}$ must be considered generally. The effect of the end-group on the interactional parameter $\chi_{I,CA}$ between polymer cosolvent and reactive polymer can however be neglected when the degree of polymerization of the polymer with A is high. This is the case for POE-NH_2; the degree of polymerization of POE-NH_2 is *ca.* 230.

Data in Fig. 1 are plotted in the form ln (k_2^m/k_2^n) $- v_C$ according to Eqn 4 (Fig. 3a). The plots are not linear. Since the behaviour of DEE is distinct from that of POE as shown in Fig. 1, DEE may not be a proper model for POE in this case; in other words, the pair-interaction between POE and POE-NH_2 may not be the same as that between DEE and POE-NH_2. Figure 3(b) shows ln $(k_2^m/k_2^n) - v_C$ plot for which POE5 is taken as a reference. The plot is linear in accordance with Eqn 4. The slope of the line in Fig. 3(b) gives a value of 3.7 for the χ''_{ij} term. Because in these reaction systems the chemical natures of chains of both reactant POE-NH_2 and polymer cosolvent POE are identical, χ''_{CA} can be considered zero. Then χ''_{CB} is equal to -3.7 and $\chi^0_{F,CB}$ ($= -\chi''_{CB}$) to 3.7.

According to Patterson [8], for usual polymer–solvent system the effect of a difference in free volumes of the two component results in a positive free volume contribution to chi parameter. The value of $\chi^0_{F,CB}$ obtained here is positive and is qualitatively in accord with the positive free volume contribution.

Figure 4 shows $\ln(k_2^m/k_2^n) - v_C$ plot from the data in Fig. 2. Equation 4 is also found to be valid in this system. The numbers of experiments with polymers of different chain length are not enough for detailed discussion on the variation of the slope with $(1/n - 1/m)$. By using the slopes of lines in Fig. 4 and values of $(1/n - 1/m)$, we obtained values 3.0 and 1.3 for $\chi''_{CA} - \chi''_{CB}$. In these reaction systems, the chemical natures of reactant POE-NH_2 and polymer cosolvent PS are different. Then χ''_{CA} cannot be considered zero.

In conclusion, the polymer effect by polymer cosolvent on chemical reactions between a polymer and a low molecular weight species is demonstrated for the reaction of POE-NH_2 with DNSCl in CF with polymer cosolvents POE and PS. The polymer effect by the polymer cosolvents is explained by the thermodynamics of polymer solution (Eqn 4). The validity of Eqn 5 with respect to the term v_C was justified as shown in Figs 3(b) and 4. Such a thermodynamical polymer effect must be considered in reactions in the presence of polymers: reactions with polymeric reagents or catalysts, template or matrix polymerization, polymer reactions for nondilute polymer concentration, etc. A study on the validity of Eqn 4 with respect to the term $(1/m - 1/n)$ will be presented in the near future.

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