2472 *J. Chem. Eng. Data* **2007,** *52,* 2472−2476

Viscosity *B*-Coefficients and Activation Parameters of Viscous Flow for Hexanedioic Acid in Aqueous Poly(vinyl alcohol) Solution

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Viscosity and density for the ternary solution of hexanedioic acid dissolved in poly(vinyl alcohol) (PVA) + water at the temperatures (293.15, 298.15, 303.15, 308.15, and 313.15) K are reported in this paper. A linear relation between the viscosity and the concentration of hexanedioic acid is observed, and the viscosity *B*-coefficient is extracted. The activation free energy for the viscous flow of the solution is found from the slope of the linear equation by using the Eyring−Feakins equation. By investigating the concentration effect, we have found that with the increase of PVA concentration the activation free energy of viscous flow first decreases and then increases. This implies that PVA promotes the diffusion of hexanedioic acid at lower concentration but demotes the diffusion of hexanedioic acid at higher concentration.

Introduction

The effective components of drugs are mainly hydrophobic organic compounds. Many drugs show a rather low solubility and dissolution rate in water. Therefore, the dissolution enhancement and release rate control for hydrophobic drugs in aqueous solution is an important task in pharmaceutical technology because it leads to a better bioavailability and more bioefficiency.[1,2] Poly(vinyl alcohol) (PVA) is commonly used as a component to form hydrogels. PVA hydrogels have been used in a number of biomedical applications and drug delivery matrices.[3,4] This is because of their inherent nontoxicity, good biocompatibility, as well as rubbery and swelling nature in aqueous solutions. The drug release rate in the hydrogel system is basically governed by the restrictive effect of the polymer on drug mobility due to either a reduction in free volume or an increase in medium viscosity. This process generally shows an inverse relationship between release rate and viscosity, which is predicted by the Stokes−Einstein equation. Consequently, the viscosity has been widely used as a predictor for resistance to diffusion.[5,6]

This work is a continuation of our studies on the viscosities and molecular diffusion for the system of hydrophobic molecules in a model pharmaceutical environment.[5] Experiments have been made for hexanedioic acid in PVA aqueous solutions.

Experimental Section

Materials. PVA is of reagent grade. Its polymerization degree is 1750. Hexanedioic acid, analytical grade, was purified by recrystallization from acetone and then dried under vacuum at 393.15 K over 10 h. They were received from the Shanghai Chemical Reagent Inc. Water was obtained by distilling deionized water from alkaline $KMnO_4$ solution to remove any organic matter.

Density and Viscosity Measurement. PVA aqueous solutions with given concentrations were prepared. The concentration of PVA is controlled in a dilute range to interrupt the formation of hydrogel. Hexanedioic acid was dissolved in PVA aqueous solutions to form the ternary solution. Densities were measured with an Anton Paar DMA 602 vibrating tube densimeter with an uncertainty of $\pm$ 0.00002 $g\cdot cm^{-3}$. The temperature of the cell was controlled by circulation of water from a water bath with the temperature within ± 0.01 K. The densimeter was calibrated by using degassed water and dry air as calibration substances. Viscosities were measured by means of a suspended level Ubbelohde viscometer. The efflux time of the fluid was measured with a digital stopwatch to ± 0.01 s. The viscometer was kept in a water thermostat controlled to ± 0.01 K. Viscometers were calibrated by water as described in our previous work.[5] Two viscometers were used in the experiments. Detection was performed at least in six replicates for each composition at each temperature. The estimated relative standard deviation for η was ± 0.1 %. The reference data for density and viscosity calibration are from ref 7. Other experimental details and procedures are the same as those described in a previous work.[5]

Results and Discussion

Density, Viscosity, and the B-Coefficients of Viscous Flow. The densities and viscosities of binary solutions PVA (2) + water (1) are given in Table 1. A linear relation between the viscosity and PVA concentration is observed within the concentration range, which is given by[8]

$$\ln \eta_r = \ln(\eta_{12}/\eta_1) = Bc_2 \tag{1}$$

where η_r is the relative viscosity; c_2 is the concentration of PVA; and η_1 and η_{12} are the viscosity of water and aqueous PVA solution, respectively.

The data of the hexanedioic acid (3) + water (1) binary solution can be found from our previous work.[5] The data for hexanedioic acid (3) dissolved in five PVA (2) + water (1) solutions are given in Tables 2 and 3, respectively. Because the ionization constants K_1 and K_2 for hexanedioic acid are $3.71\cdot10^{-5}$ and $3.87\cdot10^{-6}$ at 298.15 K, respectively,[7] and the

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10.1021/je700401r CCC: $37.00

Table 1. Densities ρ/g·cm^{-3} and Viscosities η/10^{-3}Pa·s of PVA (2) + Water (1) Binary Solutions

$1000m_2$	T/K					$1000m_2$	T/K				
mol·kg^{-1}	293.15	298.15	303.15	308.15	313.15	mol·kg^{-1}	293.15	298.15	303.15	308.15	313.15
			ρ/g·cm^{-3}						η/10^{-3}Pa·s		
0	0.99817	0.99702	0.99561	0.99401	0.99221	0	1.002	0.8903	0.7972	0.7192	0.6529
2.293	0.99819	0.99705	0.99564	0.99403	0.99224	2.293	1.008	0.8957	0.8013	0.7244	0.6579
4.948	0.99822	0.99706	0.99566	0.99405	0.99227	4.948	1.018	0.9036	0.8096	0.7309	0.6635
5.714	0.99823	0.99708	0.99568	0.99407	0.99229	5.714	1.020	0.9062	0.8113	0.7325	0.6656
6.835	0.99825	0.99709	0.99569	0.99409	0.99229	6.835	1.024	0.9089	0.8133	0.7344	0.6674
7.961	0.99826	0.99711	0.99571	0.99410	0.99230	7.961	1.028	0.9121	0.8166	0.7376	0.6691
10.23	0.99828	0.99713	0.99573	0.99412	0.99234	10.23	1.037	0.9195	0.8226	0.7431	0.6740
45.90	0.99868	0.99754	0.99613	0.99445	0.99268	45.90	1.175	1.037	0.9255	0.8335	0.7546
91.67	0.99918	0.99801	0.99659	0.99495	0.99315	91.67	1.382	1.211	1.078	0.9652	0.8708
138.5	0.99969	0.99852	0.99709	0.99539	0.99357	138.5	1.623	1.418	1.257	1.119	1.005
184.0	1.00017	0.99896	0.99757	0.99589	0.99402	184.0	1.898	1.648	1.459	1.293	1.154
246.9	1.00089	0.99966	0.99821	0.99649	0.99464	246.9	2.362	2.035	1.797	1.579	1.403

Table 2. Density ρ/g·cm^{-3} of the Hexanedioic Acid (3) + PVA (2) + Water Ternary Solution

m_3	ρ/g·cm^{-3}				
mol·kg^{-1}	T/K = 293.15	T/K = 298.15	T/K = 303.15	T/K = 308.15	T/K = 313.15
			c_{PVA}/g·dm^{-3} = 0.2175		
0	0.99822	0.99706	0.99566	0.99405	0.99227
0.01523	0.99871	0.99757	0.99616	0.99452	0.99275
0.02836	0.99905	0.99796	0.99658	0.99493	0.99314
0.05568	1.00002	0.99878	0.99741	0.99572	0.9939
0.08252	1.00078	0.99958	0.99816	0.99645	0.99471
0.1106	1.00174	1.00052	0.99901	0.99735	0.99548
0.1427	1.00275	1.00155	1.00008	0.99831	0.99641
			c_{PVA}/g·dm^{-3} = 0.2512		
0	0.99823	0.99708	0.99568	0.99407	0.99229
0.01430	0.99872	0.99753	0.99617	0.99456	0.99271
0.02821	0.99909	0.99793	0.99650	0.99486	0.99304
0.05560	1.00001	0.99883	0.99740	0.99578	0.99391
0.08252	1.00083	0.99956	0.99816	0.99653	0.99454
0.1099	1.00170	1.00045	0.99892	0.99726	0.99542
0.1376	1.00257	1.00138	0.99988	0.99810	0.99617
			c_{PVA}/g·dm^{-3} = 0.3005		
0	0.99825	0.99709	0.99569	0.99409	0.99229
0.01382	0.99863	0.99749	0.99606	0.99445	0.99265
0.02754	0.99909	0.99791	0.99644	0.99483	0.99303
0.05500	0.99999	0.99873	0.99730	0.99559	0.99378
0.08233	1.00084	0.99961	0.99811	0.99643	0.99455
0.1097	1.00161	1.00040	0.99892	0.99722	0.99531
0.1365	1.00252	1.00125	0.999721	0.99801	0.99611
			c_{PVA}/g·dm^{-3} = 0.3500		
0	0.99826	0.99711	0.99571	0.99410	0.99230
0.01380	0.99867	0.99750	0.99611	0.99449	0.99262
0.02753	0.99907	0.99784	0.99648	0.99484	0.99302
0.05490	0.99994	0.99872	0.99728	0.99560	0.99377
0.08180	1.00078	0.99951	0.99806	0.99638	0.99451
0.1095	1.00164	1.00040	0.99892	0.99723	0.99531
0.1370	1.00248	1.00121	0.99974	0.99803	0.99608
			c_{PVA}/g·dm^{-3} = 0.4499		
0	0.99828	0.99713	0.99573	0.99412	0.99234
0.01386	0.99869	0.99750	0.99611	0.99449	0.99263
0.02769	0.99907	0.99787	0.99647	0.99485	0.99302
0.05521	0.99994	0.99875	0.99729	0.99560	0.99377
0.08220	1.00078	0.99951	0.99806	0.99638	0.99454
0.1102	1.00165	1.00040	0.99894	0.99721	0.99532
0.1372	1.00246	1.00121	0.99971	0.99801	0.99607

Table 3. Viscosity η/10^{-3}Pa·s of the Hexanedioic Acid (3) + PVA (2) + Water Ternary Solution

m_3	η/10^{-3}Pa·s				
mol·kg^{-1}	T/K = 293.15	T/K = 298.15	T/K = 303.15	T/K = 308.15	T/K = 313.15
			c_{PVA}/g·dm^{-3} = 0.2175		
0	1.018	0.9036	0.8096	0.7309	0.6635
0.01523	1.019	0.9050	0.8138	0.7353	0.6687
0.02836	1.024	0.9065	0.8153	0.7370	0.6710
0.05568	1.032	0.9137	0.8220	0.7470	0.6795
0.08252	1.041	0.9212	0.8311	0.7508	0.6839
0.1106	1.055	0.9377	0.8423	0.7621	0.6933
0.1427	1.064	0.9470	0.8514	0.7672	0.6982
			c_{PVA}/g·dm^{-3} = 0.2512		
0	1.020	0.9061	0.8113	0.7326	0.6656
0.01430	1.022	0.9075	0.8134	0.7356	0.6701
0.02821	1.028	0.9105	0.8190	0.7414	0.6757
0.05560	1.034	0.9193	0.8246	0.7479	0.6796
0.08252	1.044	0.9256	0.8322	0.7545	0.6836
0.1099	1.055	0.9377	0.8405	0.7605	0.6929
0.1376	1.064	0.9467	0.8501	0.7672	0.6978
			c_{PVA}/g·dm^{-3} = 0.3005		
0	1.024	0.9088	0.8133	0.7344	0.6674
0.01382	1.032	0.9143	0.8193	0.7396	0.6722
0.02754	1.035	0.9200	0.8224	0.7419	0.6738
0.05500	1.046	0.9273	0.8301	0.7480	0.6788
0.08233	1.058	0.9379	0.8382	0.7562	0.6861
0.1097	1.067	0.9467	0.8474	0.7627	0.6924
0.1365	1.079	0.9573	0.8546	0.7703	0.6985
			c_{PVA}/g·dm^{-3} = 0.3500		
0	1.028	0.9120	0.8166	0.7376	0.6691
0.01380	1.033	0.9170	0.8215	0.7402	0.6724
0.02753	1.039	0.9220	0.8255	0.7449	0.6754
0.05490	1.049	0.9304	0.8328	0.7509	0.6813
0.08180	1.061	0.9404	0.8423	0.7584	0.6883
0.1095	1.073	0.9507	0.8498	0.7667	0.6950
0.1370	1.082	0.9597	0.8575	0.7738	0.7014
			c_{PVA}/g·dm^{-3} = 0.4499		
0	1.037	0.9194	0.8225	0.7431	0.674
0.01386	1.044	0.9246	0.8273	0.7458	0.6767
0.02769	1.049	0.9293	0.8301	0.7499	0.6799
0.05521	1.060	0.9385	0.8399	0.7567	0.6872
0.08220	1.070	0.9467	0.8477	0.7652	0.6928
0.1102	1.082	0.9581	0.857	0.7725	0.7010
0.1372	1.094	0.9685	0.8657	0.7805	0.7072

experimental concentration c_3 is much lower, the ionization process of hexanedioic acid was assumed to be negligible. The correlation of η_{123} with c_3 follows a linear relation, eq 2, with a standard deviation less than 0.002.

$$\eta_{123}/\eta_{12} = \eta_r = 1 + Bc_3 \qquad (2)$$

Here, we treat (1) + (2) as a solvent and hexanedioic acid as a solute. The B-coefficients are determined by a least-squares regression method with a mean uncertainty of 0.005. The values of B are given in Table 4. Formally, B is dependent only upon temperature. However, B will vary with the concentration of the PVA aqueous solution. Figure 1 shows the effect of temperature and PVA concentration on B-coefficients.

The B-coefficient originally introduced as an empirical term has been found to depend upon solute−solvent interactions. The values of (dB/dT) for groups can provide direct evidence regarding their structure making or breaking effect in solution.[5] The value of (dB/dT) is positive for hydrophilic structural

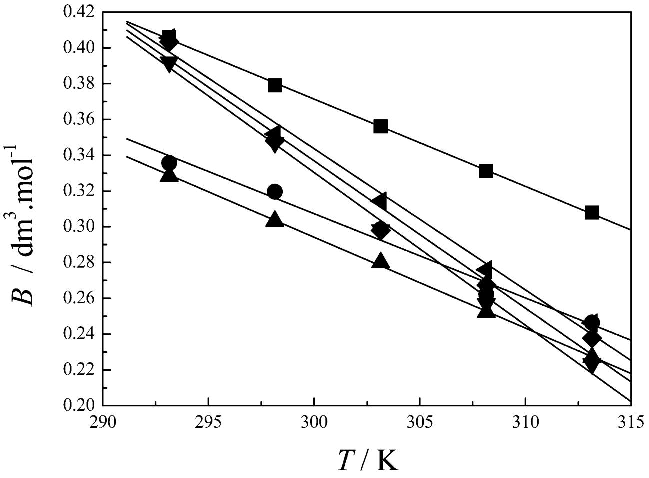

Figure 1. Temperature effect on the B-coefficient of viscous flow of hexanedioic acid in aqueous PVA solution. ■, $c_{\mathrm{PVA}} = 0$ g·dm^{-3}; ●, 0.2175 g·dm^{-3}; ▲, 0.2512 g·dm^{-3}; ▼, 0.3005 g·dm^{-3}; solid arrow pointing left, 0.35 g·dm^{-3}; solid arrow pointing right, 0.4499 g·dm^{-3}; lines, linear correlation.

Table 4. B-Coefficient/dm^3·mol^{-1} of Viscous Flow for Hexanedioic Acid Dissolved in Aqueous PVA Solution

c_{PVA}	B/dm^3·mol^{-1}				
g·dm^{-3}	T/K = 293.15	T/K = 298.15	T/K = 303.15	T/K = 308.15	T/K = 313.15
0	0.406	0.379	0.356	0.331	0.308
0.2175	0.336	0.320	0.299	0.262	0.247
0.2512	0.328	0.303	0.280	0.252	0.227
0.3005	0.392	0.347	0.298	0.257	0.223
0.3500	0.403	0.348	0.298	0.268	0.238
0.4499	0.406	0.352	0.314	0.276	0.246

breaking groups, and for a hydrophobic structural making group, the value of (dB/dT) is negative. In Figure 1, the (dB/dT) is negative. This is an indication that the hydrophilic groups of hexanedioic acid contribute less than the hydrophobic groups.

Volumetric Properties of Solution. The densities of five ternary systems are linear functions of m_3, respectively.

$$\rho_{123} = \rho_{12} + \alpha m_3 \tag{3}$$

The partial molar volume of solute 3 at infinite dilution, $V_{m_3}{}^0$, can be estimated by eq 4.

$$V_{m_3}{}^0 = \frac{M_3}{\rho_{12}} - \frac{1000\alpha}{\rho_{12}{}^2} \tag{4}$$

where m_3 is the molality of hexanedioic acid in solution (mol·kg^{-1}); ρ_{123} and ρ_{12} represent the densities of the solution (1 + 2 + 3) and (1 + 2), respectively; and M_3 is the molecular weight of component 3. The value of α is obtained from eq 3 by a least-squares regression method. The effect of PVA concentration on $V_{m_3}{}^0$ is shown in Figure 2.

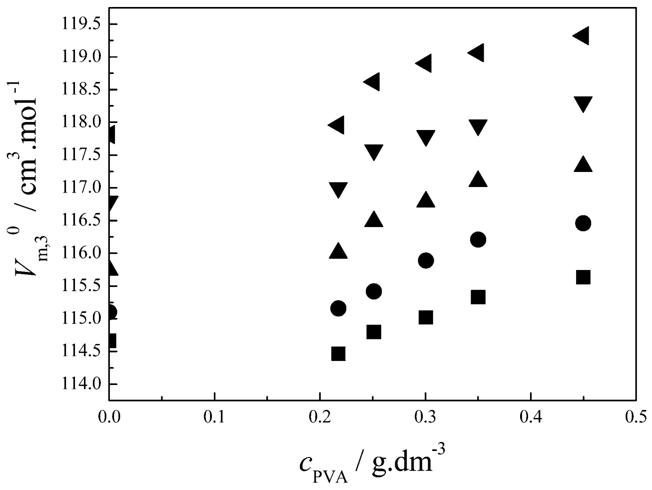

Figure 2. Partial molar volume, $V_{m_3}{}^0$/cm^3·mol^{-1}, of hexanedioic acid in aqueous PVA solution and concentration of PVA, c_{PVA}/g·dm^{-3}, at temperatures: ■, 293.15 K; ●, 298.15 K; ▲, 303.15 K; ▼, 308.15 K; solid arrow pointing left, 313.15 K.

Activation Parameters of Viscous Flow. The relationship of activation parameters of viscous flow with the B-coefficient is described by the Eyring−Feakins equation.

$$B = (V_{m_{12}} - V_{m_3}{}^0) + (V_{m_{12}}/RT)(\Delta G^{\ddagger}_{m_3} - \Delta G^{\ddagger}_{m_{12}}) \tag{5}$$

A detailed explanation of eq 5 and the activation parameters can be found in the literature.[5,9,10] $V_{m_3}{}^0$ and $V_{m_{12}}$ are the partial molar volume of solute 3 at infinite dilution in a ternary solution and the average molar volume of binary solution 1 + 2, respectively. The $\Delta G^{\ddagger}_{m_{12}}$ is the average molar free energy of activation for binary solution 1 + 2. $\Delta G^{\ddagger}_{m_{12}}$ was calculated from their viscosity η_{12}. Figure 3 shows the linear relation of $\Delta G^{\ddagger}_{m_{12}}$ with m_2. The $\Delta G^{\ddagger}_{m_3}$ is the contribution from per mole of the solute 3 in the ternary solution and was calculated from eq 5. The effect of PVA concentration on $\Delta G^{\ddagger}_{m_3}$ is shown in Figure 4. A minimum value can be found for the curves of $\Delta G^{\ddagger}_{m_3}$ vs c_{PVA}. The physical meaning of $\Delta G^{\ddagger}_{m_3}$ is connected with the diffusion of solute 3 in solution.[9] Figure 4 implies that, in dilute aqueous PVA solution, the diffusion of solute 3, hexanedioic acid, will become easier with increasing PVA concentration, while the $\Delta G^{\ddagger}_{m_3}$ decreases. However, when more PVA is added into the solution, the diffusion will become difficult when $\Delta G^{\ddagger}_{m_3}$ increases.

Table 5. Activation Parameters for Viscous Flow of $\Delta H^{\ddagger}_{m_{12}}$/kJ·mol^{-1}, $T\Delta S^{\ddagger}_{m_{12}}$/kJ·mol^{-1}, $\Delta H^{\ddagger}_{m_3}$/kJ·mol^{-1}, and $T\Delta S^{\ddagger}_{m_3}$/kJ·mol^{-1}

c_{PVA}/g·dm^{-3}		T/K = 293.15	T/K = 298.15	T/K = 303.15	T/K = 308.15	T/K = 313.15
	$\Delta H^{\ddagger}_{m_{12}}$/kJ·mol^{-1}	$T\Delta S^{\ddagger}_{m_{12}}$/kJ·mol^{-1}				
0	16.1	6.82	6.96	7.08	7.19	7.29
0.2175	16.1	6.76	6.89	7.01	7.12	7.22
0.2512	16.1	6.73	6.86	6.98	7.09	7.18
0.3005	16.1	6.75	6.88	7.00	7.11	7.21
0.3500	16.1	6.77	6.91	7.03	7.13	7.24
0.4499	16.2	6.81	6.94	7.06	7.17	7.27
	$\Delta H^{\ddagger}_{m_3}$/kJ·mol^{-1}	$T\Delta S^{\ddagger}_{m_3}$/kJ·mol^{-1}				
0	221	144	147	149	152	154
0.2175	212	145	145	148	152	154
0.2512	227	160	163	165	168	171
0.3005	374	299	304	309	314	319
0.3500	362	285	292	298	301	305
0.4499	347	270	276	280	285	288

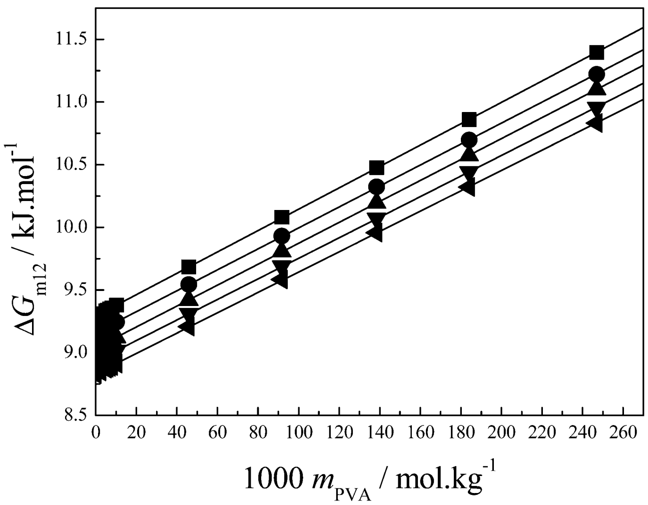

Figure 3. Average activation free energy, $\Delta G^{\ddagger}_{m_{12}}$/kJ·mol^{-1}, of aqueous PVA solution changes with the concentration of PVA, m_{PVA}/mol·kg^{-1}, at temperatures: ■, 293.15 K; •, 298.15 K; ▲, 303.15 K; ▼, 308.15 K; solid arrow pointing left, 313.15 K; lines, linear correlation.

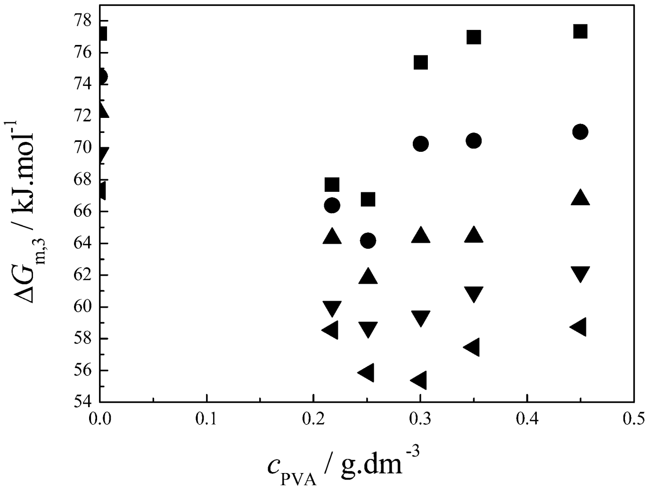

Figure 4. Effect of PVA concentration, c_{PVA}/g·dm^{-3}, on the activation free energy of viscous flow, $\Delta G^{\ddagger}_{m_3}$/kJ·mol^{-1}, at temperatures: ■, 293.15 K; ●, 298.15 K; ▲, 303.15 K; ▼, 308.15 K; solid arrow pointing left, 313.15 K.

According to thermodynamic relations, the molar activation enthalpy, $\Delta H^{\ddagger}_{m_3}$, and the molar activation entropy, $\Delta S^{\ddagger}_{m_3}$, of solute 3 in solution can be calculated from eqs 6 and 7

$$\Delta H^{\ddagger}_{m_3} = [\partial(\Delta G^{\ddagger}_{m_3}/T)/\partial(1/T)]_p \tag{6}$$

$$\Delta S^{\ddagger}_{m_3} = (\Delta H^{\ddagger}_{m_3} - \Delta G^{\ddagger}_{m_3})/T \tag{7}$$

Approximately linear curves of $(\Delta G^{\ddagger}_{m_3}/T)$ vs $(1/T)$ are shown in Figure 5. $\Delta H^{\ddagger}_{m_3}$ is obtained from the curve slopes. Then, $T\Delta S^{\ddagger}_{m_3}$ is calculated from $\Delta H^{\ddagger}_{m_3}$ and $\Delta G^{\ddagger}_{m_3}$. In a similar way, $\Delta H^{\ddagger}_{m_{12}}$ and $\Delta S^{\ddagger}_{m_{12}}$ of the PVA + water binary solution are calculated from their $\Delta G^{\ddagger}_{m_{12}}$. $\Delta G^{\ddagger}_{m_{12}}$ values are linear functions of temperature. The activation parameters of viscous flow are listed in Table 5. The effect of PVA concentration on the activation parameters $T\Delta S^{\ddagger}_{m_3}$, $\Delta H^{\ddagger}_{m_3}$, $T\Delta S^{\ddagger}_{m_{12}}$, and $\Delta H^{\ddagger}_{m_{12}}$ is shown in Figure 6. Because the temperature effect on $\Delta S^{\ddagger}_{m_3}$ and $\Delta S^{\ddagger}_{m_{12}}$ is much weaker, only the data at 298.15 K are shown for comparison. It can be observed from Figure 6 that $\Delta H^{\ddagger}_{m_3} > T\Delta S^{\ddagger}_{m_3} \gg \Delta H^{\ddagger}_{m_{12}} > T\Delta S^{\ddagger}_{m_{12}}$. The values of $\Delta H^{\ddagger}_{m_{12}}$ and $T\Delta S^{\ddagger}_{m_{12}}$ change little with the increase in c_{PVA}. However, the values of $\Delta H^{\ddagger}_{m_3}$ and $\Delta S^{\ddagger}_{m_3}$ increase sharply at $c_{PVA} = 0.2512$ g·dm^{-3} up to a top point and then decrease slightly.

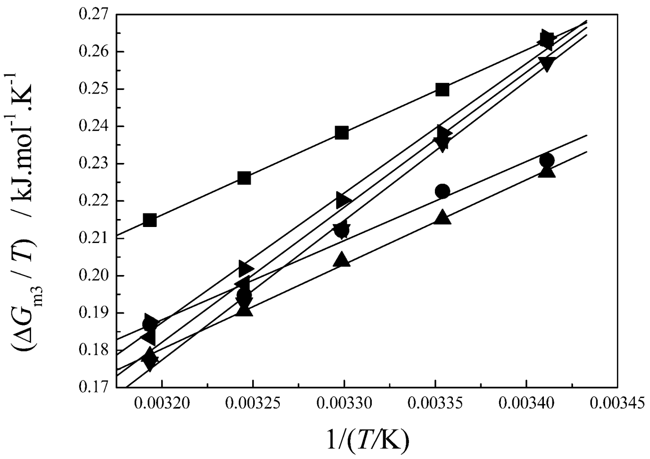

Figure 5. Values of $(\Delta G^{\ddagger}_{m_3}/T)$/kJ·mol^{-1}·K^{-1} changing with 1/(T/K) at: ■, $c_{PVA} = 0$ g·dm^{-3}; ●, 0.2175 g·dm^{-3}; ▲, 0.2512 g·dm^{-3}; ▼, 0.3005 g·dm^{-3}; solid arrow pointing left, 0.35 g·dm^{-3}; solid arrow pointing right, 0.4499 g·dm^{-3}; lines, linear correlation.

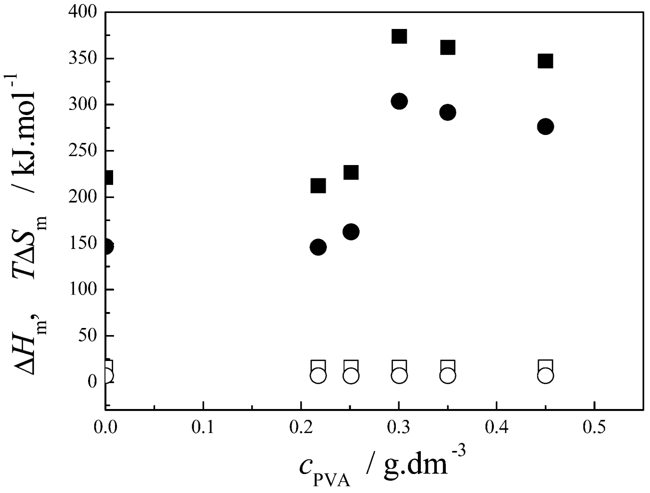

Figure 6. Change with c_{PVA}/g·dm^{-3} at T = 298.15 K of: ■, $\Delta H^{\ddagger}_{m_3}$/kJ·mol^{-1}; ●, $T\Delta S^{\ddagger}_{m_3}$/kJ·mol^{-1}; □, $\Delta H^{\ddagger}_{m_{12}}$/kJ·mol^{-1}; and ○, $T\Delta S^{\ddagger}_{m_{12}}$/kJ·mol^{-1} .

A conclusion can be obtained from the above discussion. When a small amount of PVA is added to an aqueous solution, the activation free energy of solute 3 decreases, which implies enhanced solute diffusion. When more PVA is added, the activation free energy of solute 3 increases, which implies impeded solute diffusion. At the transition point, the corresponding activation enthalpy and entropy increase sharply.

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Received for review July 16, 2007. Accepted August 22, 2007. Tong-Chun Bai acknowledges the support of the Key Academic Discipline of Organic Chemistry of Jiangsu Province of China.

JE700401R