(SO_2 symmetric stretching); ^{13}C NMR ($CDCl_3$)-1.5 (Si(CH_3)$_3$), 8.3 ($NCH_2\underline{C}H_3$), 43.2 ($N\underline{C}H_2Si$), 49.4 ($N\underline{C}H_2CH_3$), 119.6, 123.0, 131.6 and 131.9 (CH aromatic), 133.3 and 144.0 (C aromatic), 170.2 (C=O); mass spec., m/z (rel. intensity) 183 (saccharin M^+, 32), 158 (9), 143 (15), 119 (14), 118 (17), 104 (9), 103 (7), 92 (14), 86 (100), 76 (38), 74 (9), 73 (11); high resolution mass spec., m/z 182.9991 (M^+-$C_8H_{21}NSi$ requires 182.9990).

Spectral data for **5**; ^1H NMR ($CDCl_3$) 1.34 (t, 9H, J=7.3 Hz, $N(CH_2\underline{C}H_3)_2$), 3.19 (q, 6H, J=7.3 Hz, $N(\underline{C}H_2CH_3)_2$), 7.50-7.90 (m, 4H, aromatic); IR (neat) 3600-2200 (broad N^+H stretching), 1635 (C=O stretching), 1280 (SO_2 asymmetric stretching), 1180 cm^{-1} (SO_2 symmetric stretching); ^{13}C NMR ($CDCl_3$) 8.5 ($NCH_2\underline{C}H_3$), 45.9 ($N\underline{C}H_2CH_3$), 120.0, 123.3 131.8 and 132.1 (CH aromatic), 133.5 and 144.3 (C aromatic), 170.3 (C=O); mass spec., m/z (rel. intensity) 183 (saccharin M^+, 100), 120 (35), 119 (25), 104 (26), 103 (16), 101 (16), 92 (23), 86 (80), 82 (25), 74 (13), 64 (17), 58 (20); high resolution mass spec., m/z 182.9990 (M^+-$C_6H_{15}N$ requires 183.0003).

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Effect of Ureas on the Hydrophobic Properties of Aqueous Poly(ethylene oxide) Solutions by Viscometry

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Poly(ethylene oxide) (PEO) in aqueous solutions has a hydrophobic character which can induce the hydrophobic interaction between its nonpolar parts. The hydrophobic properties of aqueous PEO solutions are studied by the viscometry in terms of the water structure-making and -breaking capabilities of added solutes of ureas. The results show that the contracted conformation of PEO of low molecular weight, namely poly(ethylene glycol) (PEG), does not result from the hydrophobic interaction between the nonpolar parts of PEO but it can participate in a hydrophobic interaction between the nonpolar parts of PEO and added ureas solutes with nonpolar groups, which can induce a large hydrodynamic volume and increase the viscosity. On the other hand, the PEO of large molecular weight seems to behave like any other water soluble polymers with nonpolar parts and its conformation in aqueous solutions is well explained in terms of water structure perturbing capabilities of added ureas.

Introduction

Poly(ethylene oxide) is an important water-soluble polymer of industrial and biological interests,[1,2] and a crystalline state has helical conformation that is maintained to a greater or lesser extent in aqueous solutions.[3-5] Furthermore it displays some basic features of proteins so that it can be thought as a simple model compound.[6] The most important feature is that it contains nonpolar hydrophobic region (-CH_2-CH_2-) and polar hydrogen bonding site (-O-). Recent studies suggest that PEO chain has a hydrophobic character,[7-11] which can induce a hydrophobic interaction between the nonpolar groups. The conformation of the PEO chain in aqueous solution will be influenced by the interaction of the hydrophobic nature between the ethylene groups and the polar solvent molecules.

Aqueous solutions of urea and substituted ureas are found to be effective denaturants of proteins.[12,13] The denaturants play a role in the denaturation process by changing the water structure. The change of water structure is explained in terms of water structure-breaking and -making of solutes.[14] The concept of water structure-breaking and -making effect of solutes has been used as a powerful indirect tool for interpreting solute-water interactions in aqueous solution.[15,16]

The hydrophobic groups of PEO can participate in a hydrophobic interaction which is a nonelectrostatic, through the

Table 1. The intrinsic viscosities, $[\eta]$ and k_H values of aqueous PEO solutions of nine different molecular weights at 25℃

Average molecular weight	$[\eta]$ (dL/g)	k_H
6.0×10^5	4.1	0.45
3.0×10^5	2.8	0.43
2.0×10^5	1.3	0.44
1.0×10^5	0.90	0.46
1.0×10^4	0.24	1.7
8.0×10^3	0.20	1.8
3.4×10^3	0.10	4.4
2.0×10^3	0.068	7.0
1.0×10^3	0.038	19

structuring of water around the nonpolar parts of PEO (hydrophobic hydration).[15,17,18] The compact random coil conformation[19] will be formed by the hydrophobic interaction between the nonpolar groups and may be disappeared if water structure breaking solute, such as urea, is added. The hydrophobic properties of PEO in aqueous solution are studied with the method of viscosity in terms of the water structure-making and -breaking capabilities of the series of urea solutes.

Experimental

Several PEO's of different average molecular weight were purchased from Aldrich Chemical Co. and they were dissolved in triply distilled water as a solvent. The viscosities were measured with an Ubbelohde viscometer at 25± 0.01℃. The intrinsic viscosities, $[\eta]$ (dL/g), were determined by extrapolating plots of $\ln \eta_r/c$ and η_{sp}/c against concentration c(g/dL) to infinite dilution where η_r and η_{sp} are the relative and specific viscosity, respectively, and both plots gave the same intercept.[19,20] The A.C.S. reagent grade, urea (U), thiourea (TU), methylurea (MU), 1,3-dimethylurea (DMU), and tetramethylurea (TMU), were used as received from Aldrich Co. The aqueous solutions of ureas were prepared from dissolving them into water and then PEO was dissolved in them. The intrinsic viscosities of PEO in aqueous solutions of ureas were measured by the same method as mentioned above.

Results and Discussion

The experiments for PEO's of nine different molecular weights were performed to determine the intrinsic viscosities and Huggins coefficients of PEO in aqueous solutions, and the results are shown in Table 1. The Huggins coefficients (k_H) are obtained from the following Huggins equation.[20]

$$\frac{\eta_{sp}}{c}=[\eta]+k_H[\eta]^2c \quad (1)$$

The value of k_H is often near 0.35 and approximately 2.0 for flexible random coil polymer molecules in good solvents and for uncharged sphere-like molecules,[21] respectively, and increases as the solvent power to polymer molecules decreases.[21,22] From the estimation of Huggins coefficients in Table 1, we can classify the PEO with nine different molecular weights in aqueous solutions into two groups. One is the commonly named poly(ethylene glycol)[1] (PEG) having k_H value higher than 1, which means roughly the polymer chain is largely contracted in a small volume space. The other is named poly(ethylene oxide) having k_H value about 0.4, which means that it is a common random coiled polymer in good solvents. As the molecular weight of PEO decreases, the chain is more contracted in a small volume space, of which phenomenon is more distinct for PEO's of low molecular weight, namely PEG, showing the successive increase of the k_H value.

Table 2. The intrinsic viscosities, $[\eta]_{ureas}$, of PEO in 0.2 M aqueous ureas solutions at 25℃

Urea solutes	$[\eta]_{ureas}$ (dL/g)	
	8.0×10^3[a]	1.0×10^5[a]
Thiourea (TU)	0.205	0.954
Urea (U)	0.210	0.944
Methylurea (MU)	0.219	0.931
1,3-dimethylurea (DMU)	0.238	0.927
Tetramethylurea (TMU)	0.225	0.908

[a] Average molecular weights of PEO.

Table 3. The excess apparent molal heat capacities[28], ϕC_p^0 (excess), of ureas, and intrinsic viscosity ratios, $[\eta]_{ureas}/[\eta]$, of PEO in 0.2 M aqueous ureas solutions at 25℃

Urea solutes	ϕC_p^0 (excess)[a]	$[\eta]_{ureas}/[\eta]$	
		8.0×10^3[b]	1.0×10^5[b]
Thiourea (TU)	+17.4	1.03	1.06
Urea (U)	−5.8	1.05	1.05
Methylurea (MU)	10.7	1.10	1.034
1,3-dimethylurea (DMU)	25.6	1.19	1.03
Tetramethylurea (TMU)	50.1	1.13	1.01

[a] Obtained from reference (28) and unit in cal $deg^{-1}mol^{-1}$. [b] Average molecular weights of PEO.

Aqueous solutions of ureas are effective denaturants of proteins[12,13] and they are made by the addition of ureas into water and the concentrations of them are controlled to maintain 0.2 mol/L. The intrinsic viscosities of PEO's of two different average molecular weight (8.0×10^3 for PEG and 1.0×10^5 for PEO) in aqueous ureas solutions are determined by the aforementioned method. The results are presented in Table 2. Comparing the intrinsic viscosities of PEO in water (Table 1) and in aqueous ureas solutions (Table 2), it is noticeable that the values of intrinsic viscosity are higher in aqueous ureas solutions than in water, which may be consequence of the fact that the addition of ureas causes the disruption of nonelectrostatic interactions of hydrophobic groups of PEO in water. By altering the water structure, ureas lower the tendency of nonpolar groups to make hydrophobic interactions.

Bonner *et al.*[23] reported the apparent molal heat capacities for some ureas and substituted ureas, and calculated excess apparent molal heat capacities, ϕC_p^0 (excess) (cal deg^{-1} mol^{-1}), which is a measure of the water stucture perturbing capability of solutes, *i.e.*, the decrease in the quantity ϕC_p^0

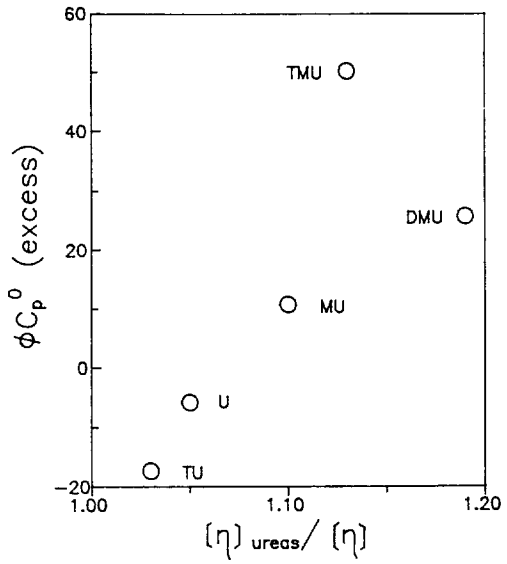

Figure 1. The relation between excess apparent molal heat capacities, ϕC_p^0 (excess) (cal deg^{-1}mol^{-1}), of ureas, and intrinsic viscosities, $[\eta]$ (dl/g), of PEO of 8.0×10^3 average moleculat weight in 0.2 M aqueous solutions of ureas at 25℃.

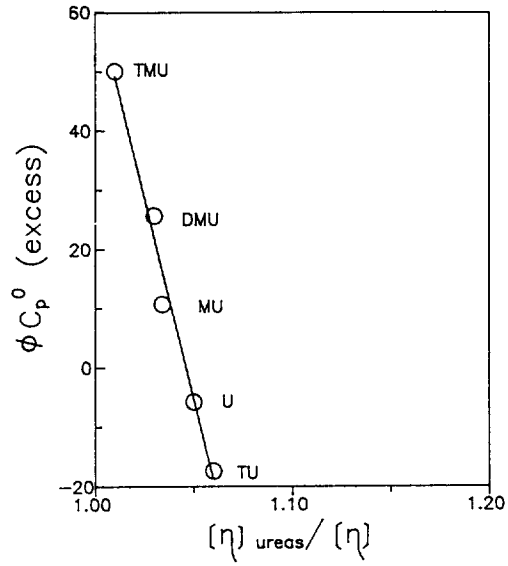

Figure 2. The linear relation between apparent molal heat capacities, ϕC_p^0 (excess) (cal deg^{-1}mol^{-1}), of ureas, and intrinsic viscosities, $[\eta]$ (dl/g), of PEO of 1.0×10^5 average moleculat weight in 0.2 M aqueous solutions of ureas at 25℃.

(excess) enhances the water structure breaking effect, which is given in Table 3. To study the degree which the ureas perturb the water structure, the intrinsic viscosities of PEO in aqueous ureas solutions, $[\eta]_{ureas}$, are related to the intrinsic viscosity of PEO in pure water, $[\eta]$. The intrinsic viscosity ratio, $[\eta]_{ureas}/[\eta]$, for two different molecular weights of PEO are obtained and summarized in Table 3. The intrinsic viscosity ratio, $[\eta]_{ureas}/[\eta]$, is related to the ϕC_p^0 (excess) with respect to the water structure perturbation. The results are shown in Figures 1 and 2 for PEG and PEO, respectively.

From Table 3 and Figure 1, the values of intrinsic viscosity ratio for PEO having molecular weight of 8.0×10^3, namely PEG, are lower for urea (U) and thiourea (TU) which are stronger water structure-breaking solutes[24,25] than for any other ureas. The experimental results are opposite to the expectation of the more increase of intrinsic viscosity ratio due to the breaking of structured water near the hydrophobic groups of PEO and reducing the hydrophobic interactions between them by the addition of water structure-breaking solutes (U and TU). So the conformation of PEO of this molecular weight is different from that of the common polymers[24-27] having the hydrophobic groups. The more increase of intrinsic viscosity ratios of PEO in aqueous solutions are observed as the increase of the content of hydrophobic groups of ureas (MU, DMU and TMU), which may result from the increase of hydrodynamic volume of PEO due to the hydrophobic interactions[24] between the hydrophobic parts of PEO and the hydrophobic groups of added ureas. PEO of low molecular weight, namely PEG, in aqueous solutions can induce the hydrophobic interactions between the hydrophobic parts of PEO and added solutes having hydrophobic groups.

What does it happen for PEO of large molecular weight? The conformation seems to be like a common neutral random coil in good solvents from the k_H value of 0.35 (Table 1). The hydrophobic parts of PEO can participate in a hydrophobic interaction between them by the water structuring near the nonpolar groups. PEO of large molecular weight will behave like many other common water-soluble polymers[24-27] with hydrophobic groups and the conformations will be affected by the concept of water-structuring capabilities. The linear relationship between the intrinsic viscosity ratios of PEO of 1.0×10^5 molecular weight in aqueous solutions of ureas and the excess apparent molal heat capacities is obtained (Figure 2), and the conformations of PEO in aqueous solutions may be directly affected by the water structure breaking and making capabilities, which are more common phenomena for neutral water-soluble polymers[24-27] with hydrophobic groups. The water structure breaking solutes, such as TU and U, can break the structured water around the hydrophobic groups, reduce the strength of hydrophobic interaction between them, and the chain is more extended and the viscosity of PEO solution must increase, which is observed in Figure 2. As the hydrophobicity of added solutes of ureas increases, the water around the hydrophobic groups of PEO is more structured (hydrophobic hydration). Since it promotes the hydrophobic interaction between the hydrophobic groups of PEO,[15,16,21] the chain is more or less contracted and the values of intrinsic viscosity ratio are gradually lowered, which is directly related to the capabilities of water-structuring of ureas.

If the chain has higher hydrophobicity, then it is more contracted by the hydrophobic interaction between the hydrophobic groups in the chain. And it is extended and has a higher value of intrinsic viscosity ratio when the water structure perturbing solutes are added. The values of intrinsic viscosity ratio of PEO in aqueous ureas solutions are in the range of 1.01 and 1.07 (Table 3), which are far lesser than the values (1.2-1.9) of isotactic poly(2-hydroxyethyl methacrylate) (PHEMA)[24] with viscosity average molecular weight of 5.1×10^4 in similar concentrations of aqueous ureas solutions studied. Isotactic PHEMA, which is soluble in wa-

ter, is one of the synthetic polymers containing both hydrophobic and hydrophilic groups capable of forming interchain hydrogen bonds as well as bonds with water molecules. The hydrophobic groups of isotactic PHEMA participate in a hydrophobic interaction.[19,24,25] PEO behaves in the similar manner to isotactic PHEMA, but the overall hydrophobicity of it is smaller than isotactic PHEMA as can be seen in the lower values of intrinsic viscosity ratio.

From the above discussions, we conclude; i) The low molecular weight PEO, namely PEG, have a compact conformation, which does not result from the hydrophobic interaction between the hydrophobic groups of PEO. PEG can have a hydrophobic interaction between the hydrophobic groups and added solutes, which is not a desirable property of PEG to be used as the materials of artificial organs.[2,8,9] ii) PEO of large molecular weight may behave like many other water-soluble polymers having a random coil conformation, which has the structured water region around the nonpolar parts (hydrophobic hydration) and can participate in a hydrophobic interaction between them. iii) PEO has a hydrophobic groups which participate in a hydrophobic interaction, but it exhibits generally a lower hydrophobicity than isotactic PHEMA in water.

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