Effect of Molecular Weight on Cloud Point of Aqueous Solution of Poly (ethylene oxide)–Poly (propylene oxide) Alternating Multiblock Copolymer

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Abstract: A poly(ethylene oxide) (PEO)–poly(propylene oxide) (PPO) alternating multiblock (AMB) copolymer with various molecular weights was prepared via precipitation fractionation from an acetone/*n*-hexane mixture. The cloud point (T_c) of the aqueous solution of PEO–PPO AMB copolymer decreased as the number-average molecular weight of the sample increased. This phenomenon is generally observed for certain homopolymer systems having a lower critical solution temperature, such as PEO/water and poly(*N,N*-diethylacrylamide)/water systems. The relationship between the T_c of the solutions and the number of monomer units of the AMB copolymer suggests that the Shultz–Flory theory is applicable to this system.

Key words: multiblock copolymer, thermo-responsive, phase separation, molecular weight dependence

1 Introduction

Thermoresponsive polymers are a class of smart materials. The properties of such polymers change significantly in a controlled fashion under the influence of external stimuli¹. To develop synthetic polymer systems that act as protein mimics is a great challenge for polymer scientists. The block design of copolymers is an effective strategy for preparing protein mimics using synthetic polymers². An alternative way is to control the monomer sequence, which corresponds to the primary structure of proteins³. However, the interaction among the monomers often makes it difficult to predict the macroscopic properties of the final products^{4, 5}. In comparison with monomer sequence control, the block design is advantageous for achieving predictable physicochemical properties of the resultant copolymer and scale-up of the preparation process. Because the individual blocks in the copolymer may retain the characteristics of the homopolymer, the numerous reports on the homopolymers may serve as a block library^{6–19}.

Recently, we investigated the solution properties of amphiphilic alternating multiblock (AMB) copolymers. The AMB copolymer of poly(ethylene oxide) (PEO) and poly(propylene oxide) (PPO), i.e., the PEO–PPO AMB copolymer, exhibits amphiphilic features comparable to those of

Pluronic and Ploxamer. Unique characteristics of the AMB configuration were observed for the unimer morphology in water. Previously, we found that the unimer of PEO–PPO AMB copolymers in water forms a core-corona structure similar to flower micelles²⁰. This may arise from two factors: the hydrophobic interaction among the PPO blocks in the core and the repulsion among the unimers based upon stabilization of the PEO chain at the corona. When the hydrophilic interaction was not sufficiently strong, the unimer of the AMB copolymers could not form a core-corona structure. Indeed, the AMB copolymer of PEO and poly(*N*-isopropylacrylamide) (PNiPAm) adopts a random-coil conformation in water at room temperature, because PNiPAm tends to be well hydrated compared with PPO²¹. Because the PPO blocks are sufficiently hydrophobic to form a unimer micelle, the PEO–PPO AMB copolymer can also be expected to serve as a simple model of multipass transmembrane proteins such as bacteriorhodopsin²¹.

Although the PEO–PPO AMB copolymers possess interesting features as above mentioned, the fundamental aspects have yet to be fully revealed. In this study, we focus on the effect of the molecular weight on the cloud point (T_c) of the copolymers. Based on the literature concerning PEO–PPO–PEO triblock copolymers²², the hydro-

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phobicity of PEO-PPO block copolymers is essentially proportional to the molecular weight of PEO and PPO when the weight fraction of PEO (f_{PEO}) is constant. For the AMB copolymers, however, the molecular weight of the PEO and PPO blocks is fixed, but the number of PEO-PPO repeating pairs varies depending on the total molecular weight. Herein, PEO-PPO AMB copolymers with various molecular weights are prepared by precipitation fractionation. The fractionated samples are used to investigate the T_c of the aqueous solution.

2 Experimental Procedures

2.1 Preparation of PEO-PPO AMB copolymer

The PEO-PPO AMB copolymer was prepared by a dehydrated condensation reaction according to the literature²³. Briefly, α,ω -diamino PPO (JEFFAMINE D-2000; weight-average molecular weight (M_w) = 2,000) was kindly supplied by Huntsman Corporation. α,ω -Disuccinimidyl PEO (SUNBRIGHT DE-100HS; M_w = 10,000) was purchased from NOF Corporation. The reaction was carried out in chloroform solution at 0°C. The crude sample was recovered by dialysis against water, followed by freeze-drying. Precipitation fractionation of the copolymer was performed by phase separation in an acetone/*n*-hexane mixture at 25–50°C. The PEO-PPO AMB copolymer prepared herein is denoted as $(\text{EO}_{220}\text{PO}_{33})_n$, where EO is the ethylene oxide unit, PO is the propylene oxide unit, and n is the number of PEO-PPO repeating units. The characterization details can be found in previous reports^{20, 23}.

2.2 Size exclusion chromatography (SEC)

The SEC apparatus consisted of a Jasco Intelligent HPLC system equipped with a guard column (SB-G, Shodex), two separation columns (SB-802.5HQ and SB-806MHQ, Shodex), and a refractive index detector (RI-2031Plus, Jasco). *N,N*-Dimethylformamide (HPLC grade, Wako) with 10 mM LiBr was used as the eluent at a flow rate of 0.35 mL min⁻¹, at 60°C. The number-average molecular weight (M_n), M_w , and the polydispersity (M_w/M_n) were evaluated with respect to standard polystyrene samples with ten different peak-top molecular weights in the range of 1.22×10^3 to 2.70×10^6 (STANDARD SM-105, Shodex).

2.3 ¹H NMR and IR spectroscopy

The ratio of EO units to PO units (EO/PO) in the PEO-PPO AMB copolymers was determined from the ¹H NMR spectra recorded on an Ascend 400 (Bruker) instrument at 400 MHz. All spectra were acquired at 25°C using 1.0 wt% D₂O solutions.

2.4 Turbidity measurements

The transmittance of 633 nm light through the polymer

solution was monitored by using a UV-Vis spectrophotometer (V-630iRM, Jasco) equipped with a temperature controller (ETCS-761, Jasco). The sample was heated at a rate of 1.0°C min⁻¹. The cloud point (T_c) was defined by referring to the first derivative of the transmittance curve.

3 Results and Discussion

3.1 Characterization of the fractionated samples

Figure 1 shows the SEC charts of the PEO-PPO AMB copolymers, $(\text{EO}_{220}\text{PO}_{33})_n$, before and after precipitation fractionation. Two peaks at 2270 and 2330 s were apparent in the SEC chart of the last fraction. Thus, we did not analyze this sample (denoted as “residue” in Fig. 1). The SEC charts of fraction 1–3 showed a systematic shift, indicating differences in the M_n of each fraction. The estimated M_n and M_w/M_n values are listed in Table 1. Although fractionation appeared to be successful based on the M_n of each fraction, the M_w/M_n values were still large (1.7–2.4). In general, fractionation of copolymers is more difficult than fractionation of homopolymers because the solubility of copolymers is also influenced by their chemical composition²⁴. To estimate the EO/PO ratio for the fractionated samples, the ¹H NMR spectra were acquired (Fig. 2). The peak at $\delta = 3.7$ ppm arises from the methylene proton of the EO and PO units, while the peak at $\delta = 1.2$ ppm is due to the methyl proton of the PO unit. The intensity ratio of the $\delta = 3.7$ ppm peak to the $\delta = 1.2$ ppm peak ($I_{3.7}/I_{1.2}$) was estimated to be 9.6–9.9. Because the PEO block contains

Fig. 1 SEC charts of the crude and each fractions of the PEO-PPO AMB copolymer.

Table 1 Molecular weight (M_n), polydispersity (M_w/M_n), the ratio of EO units to PO units ($I_{3.7}/I_{1.2}$), and the number of repeating units (n) of PEO-PPO AMB copolymers.

sample	fraction	$M_n (M_w/M_n)^a$	$I_{3.7} / I_{1.2}^b$	n
crude	—	7.2×10^4 (3.3)	—	—
120k ^c	—	1.2×10^5 (1.5)	9.4	6.3
100k	1	1.0×10^5 (2.4)	9.9	5.4
94k	2	9.4×10^4 (1.7)	9.6	5.1
61k	3	6.1×10^4 (1.8)	9.9	3.3

^a Size exclusion chromatography with polystyrene standards.

^b Integrated intensity ratio of the peak at 3.7 ppm to 1.2 ppm obtained from ^1H NMR.

^c The fraction was obtained from a different lot.

220 EO units and the PPO block has 33 PO units, the one-by-one connection of PEO and PPO yields $I_{3.7}/I_{1.2} = 9.5$. Thus, we can assume that the PEO-PPO AMB copolymers contain an equal amount of PEO and PPO blocks and the chemical composition of each fractionated sample is similar.

The SEC and ^1H NMR results indicate successful precipitation fractionation of the PEO-PPO AMB copolymer. The n value for $(\text{EO}_{220}\text{PO}_{33})_n$ was estimated to range from 3.3 to 5.4. When n -hexane as a poor solvent was added to the acetone solution, the PEO-PPO AMB copolymers precipitated in the order of the molecular weight. Interestingly, this behavior is similar to the precipitation fractionation of homopolymers. Thus, we presumed that the EO/PO for a single chain did not differ in the PEO-PPO AMB copoly-

Fig. 3 Temperature dependence of the transmittance of the 633 nm light passing through the aqueous solution of the PEO-PPO AMB copolymers. The polymer concentration is 1.5 wt% except for the 120k fraction (1.0 wt%).

mers prepared by amide condensation.

3.2 Molecular weight dependence of T_c for the PEO-PPO AMB copolymer in water

The results of the turbidity measurement for the copolymers are shown in Fig. 3. The T_c values were clearly high for the crude sample and the residue. As shown in Fig. 1, the residue contained a certain amount of impurity, corresponding to the peak at 2320 s in the SEC chart. The T_c of the crude sample may also contain a large contribution from the impurity. Thus, we assumed that there is a short PEO-PPO block copolymer in the crude sample and the

Fig. 2 ^1H NMR spectra of the fractionated PEO-PPO AMB copolymers, the crude, and the residue.

Fig. 4 Concentration dependence of the cloud point (T_c) for the aqueous solutions of each PEO-PPO AMB copolymer. The T_c is determined by the transmittance curve measured by the 633 nm light.

residue, resulting in the high T_c . Note that the aqueous solution of the PEO homopolymer with $M_n = 14,000 \text{ g mol}^{-1}$ undergoes phase separation around 107°C ²⁵⁾, whereas the T_c of an aqueous solution of Pluronic F88, for which the EO/PO ratio is similar to that of $(\text{EO}_{220}\text{PO}_{33})_n$ synthesized herein, is over 100°C ²⁶⁾.

Figure 4 shows the molecular weight dependence of T_c for the aqueous solution of the PEO-PPO AMB copolymers. The T_c decreased with increasing M_n , which is typical for polymer solutions that undergo phase separation with a lower critical solution temperature (LCST), such as the PEO/water²⁵⁾ and poly(*N,N*-diethylacrylamide)/water²⁷⁾ systems. On the other hand, poly(*N*-isopropylacrylamide)/water system, which is a quite popular system that undergoes LCST-type phase separation, shows an abnormal M_n dependence on T_c , in which T_c decreases with decreasing M_n ²⁸⁾.

The inset of Fig. 4 shows the plot of $1/T_c$ against $1/N^{0.5} + 1/2N$, where N is the number of monomer units (both of EO and PO) in the AMB copolymer. According to the Shultz-Flory theory²⁹⁾, the critical solution temperature (T_{cp}) of a polymer solution is correlated with the polymerization degree as:

$$\frac{T_0}{T_{cp}} = 1 + \frac{1}{\psi} \left(\frac{1}{\sqrt{N}} - \frac{1}{2N} \right)$$

where T_0 is Flory's theta temperature and ψ is the entropy parameter³⁰⁾. Clearly, T_{cp} is not equal to the T_c measured herein. In a previous paper, however, we reported that the T_c of the aqueous solution of PEO-PPO AMB copolymers is

insensitive to the polymer concentration above T_{cp} , which is located at ca. $0.3 \text{ wt}\%$ ²³⁾. Thus, the T_c measured for the $1.5 \text{ wt}\%$ aqueous solution of the copolymers is expected to be close to the T_{cp} . The intercept of the solid line in the inset gives a value of 39°C , which corresponds to the T_0 of the system. In previous papers, we reported that the micellization temperature of $(\text{EO}_{220}\text{PO}_{33})_6$ is around $41\text{--}50^\circ\text{C}$ ²⁰⁾ and the second virial coefficient, A_2 , of $(\text{EO}_{220}\text{PO}_{33})_8$ approaches zero around 50°C ²³⁾. The results shown here imply that the Shultz-Flory theory is applicable even to PEO-PPO AMB copolymers.

4 Conclusion

We investigated the effect of the molecular weight on the T_c of aqueous solutions of PEO-PPO AMB copolymers with various molecular weights. The PEO-PPO AMB copolymers were obtained by precipitation fractionation. The T_c of the aqueous solution of the PEO-PPO AMB copolymer decreases as the M_n increases. The results imply that the Shultz-Flory theory is applicable to the PEO-PPO AMB copolymer/water system.

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