

ABA Triblock Copolymers from Poly(*p*-dioxanone) and Poly(ethylene glycol)

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ABSTRACT: Poly(*p*-dioxanone)-poly(ethylene glycol)-poly(*p*-dioxanone) ABA triblock copolymers (PEDO) were synthesized by ring-opening polymerization from *p*-dioxanone using poly(ethylene glycol) (PEG) with different molecular weights as macroinitiators in N₂ atmosphere. The copolymer was characterized by ¹H NMR spectroscopy. The thermal behavior, crystallization, and thermal stability of these copolymers were investigated by differential scanning calorimetry and thermogravimetric measurements. The water absorption of these

copolymers was also measured. The results indicated that the content and length of PEG chain have a greater effect on the properties of copolymers. This kind of biodegradable copolymer will find a potential application in biomedical materials. © 2006 Wiley Periodicals, Inc. *J Appl Polym Sci* 102: 1092–1097, 2006

Key words: poly(ethylene glycol); poly(*p*-dioxanone); triblock copolymer; crystallization; thermal stability; water absorption

INTRODUCTION

Poly(*p*-dioxanone) (PPDO) is growing to be recognized substantially due to its expected excellent degradability in addition to the good biocompatibility and physical properties. It is now considered as a candidate not only for medical uses but also for universal uses.^{1–3} However, its hydrophobicity, low crystallization rate, and high cost limit its application in some fields. These problems may be addressed by copolymerization of PDO with other monomers, such as PLA,⁴ PCL,⁵ etc. Polyether has some superior properties such as non-toxicity, flexibility, hydrophibility, and biocompatibility. Therefore, the synthesis of polyester-polyether block copolymers has attracted much attention.^{6–9}

Poly(ethylene glycol) (PEG), one of the most widely used polyethers, accepted by US Food and Drug Administration,¹⁰ is usually used to couple with polyesters. Cerrai et al.¹¹ obtained PLA-PEG-PLA triblock copolymers by bulk ring opening polymerization of L-lactide with PEG at 120–140°C in the absence of a catalyst. Wang and coworkers described the synthesis of poly(ϵ -caprolactone)-PEG block copolymer by copoly-

merization of ϵ -CL and PEG in the presence of Ti(OBu)₄ at high temperature.¹² Wang et al.¹³ synthesized ABA-type block copolymers of PPDO and PEG, and presented the release behavior of DDS consisting of copolymers and Levonorgestrel. However, the copolymerization of PEG having different molecular weights with PPDO has not been reported so far. In this work, a series of PEDO copolymers containing different molecular weight of PEG were synthesized, and their thermal and crystalline behaviors and water absorption were also studied.

EXPERIMENTAL

Materials

p-Dioxanone (PDO), provided by the Pilot Plant of the Center for Degradable and Flame-Retardant Polymeric Materials, was dried over CaH₂ for 48 h, distilled under reduced pressure. PEG 800, 2K, 6K, and 20K were purchased from Kelong Chemical Factory (Chengdu, China), dried under reduced pressure at 50°C for 24 h before use. Stannous octane (Sn(Oct)₂) ($\geq 95\%$) was purchased from Sigma and used without any further purification. After diluting with dry toluene, Sn(Oct)₂ solution was stored in glass ampoules under argon. Ethylene chloride, toluene, and acetone were purchased from Jianjie Chemicals Factory (Chengdu, China) and used without further purification.

Polymerization procedure

Predetermined amount of PEG was added into a flame-dried glass reactor. The reactor was evacuated

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and purged with nitrogen several times. Then the reactor was immersed into a temperature-adjusted oil bath at 80°C. After all of the PEG was melted, (Sn(Oct)₂) was added. Three hours later, when PEG macroinitiator was formed, the calculated amount of PDO was charged into the reactor. When the polymerization was completed, the crude copolymers were dissolved with ethylene chloride and precipitated into an excess amount of cold acetone to remove the unreacted monomers.

Characterization

¹H NMR spectra were recorded in CDCl₃ with 400 MHz NMR spectrometer (INOVA Varian). Thermal analysis was performed with Nethids differential scanning calorimeter (DSC) under an ultrahigh purity nitrogen atmosphere. The equipment was calibrated with indium and tin standards. Samples were heated to 140°C for 5 min to erase all previous thermal history and then were cooled to -80°C at a nominal rate of 10°C/min. The samples were heated again at the same rate up to 140°C. Thermogravimetric measurements (TG) were conducted with a DuPont 2100 system in platinum pans at prescribed heating rates of 10°C/min under a steady flow of nitrogen (80 mL/min).

Water absorption: PEDO copolymer chips were immersed in distilled water at 37°C for 24 h, then taken out and the surplus surface water removed by filter paper. Water absorption was calculated according to the following equation:

$$\text{Water absorption (\%)} = (m_1 - m_2)/m_2 \times 100\%$$

where m_1 and m_2 are the weights of wet and dry samples, respectively.

RESULTS AND DISCUSSION

Synthesis of PPDO-*b*-PEG-*b*-PPDO copolymers

PPDO-*b*-PEG-*b*-PPDO triblock copolymers (PEDO) with different molecular weights of PEG (PEG800,

PEG2K, PEG6K, and PEG20K) were synthesized via ring-opening polymerization of PDO monomer initiated by PEG macroinitiator with Sn(Oct)₂ as catalyst. The same mole ratio (1500:1) of PDO to the hydroxyl group of PEG with different molecular weights was used so as to keep the length of PPDO chain fixed. A typical reaction mechanism has been studied and proposed in several articles.^{7,14-18} Since the two terminal hydroxyl groups of the PEG have equal reactivities towards monomers, the PEG molecules can act as a macroinitiator for the ring-opening polymerization of cyclic lactones to form ABA-type copolymers. This mechanism of polymerization has been studied and clearly demonstrated for the synthesis of ABA triblock copolymer based on PEG (as B block) and various lactones such as LLA, ε-caprolactone, and copolymer of lactide and glycolide (as A block).^{7,13,14,16-19} Keeping these ideas in mind, the similar method can be extended to the present block copolymerization of PDO with PEG macroinitiator, since the bulk polymerization of PDO and PEG by Sn(Oct)₂ catalyst can proceed via a similar activated complex. Because there is the possibility of ring-opening polymerization of PDO with Sn(Oct)₂, which is initiated by moisture in the system besides PEG, the feed order becomes very important in this reaction. In present work, PEG was first added in reactor, and Sn(Oct)₂ was added after all of the PEG was melted. When PEG macroinitiator was formed, PDO was charged into the reactor. It can effectively avoid producing PPDO homopolymer by this way. The relevant data of copolymers, which were named as PEDO800, PEDO2K, PEDO6K, and PEDO20K in terms of the different molecular weight of PEG, were listed in Table I.

The inherent viscosities ([η]) of copolymers were determined by capillary viscosity measurements using an Ubbelohde viscometer and solutions of PEDO samples in phenol/1,1,2,2-tetrachloroethane (2:3 w/w) at 25°C. We were not able to obtain GPC traces of the copolymers in view of their poor solubility in the solvents commonly employed to perform gel permeation chromatography (GPC) at

TABLE I
Copolymerization of PDO with PEG

Sample	$f_{\text{PDO}}^{\text{a}}$ (%)	Conversion of PDO (wt %)	$F_{\text{PDO}}^{\text{b}}$ (%)	M_n^{c}	$[\eta]^{\text{d}}$ (dL/g)
PEDO800	98.45	89.16	98.24	44,600	0.56
PEDO2K	96.15	88.51	95.68	44,300	0.61
PEDO6K	89.35	88.79	88.11	44,500	0.77
PEDO20K	71.52	88.48	68.94	44,500	0.83

^a Weight fraction of PDO in the feed.

^b Weight fraction of PDO in the copolymers.

^c Molecular weight of PPDO block calculated by the conversion of PDO.

^d In phenol/1,1,2,2-tetrachloroethane(2:3 w/w) at 25°C.

ambient temperatures. The solubility of PEDO synthesized in present work is somewhat like that of the PPDO homopolymer. Only low molecular weight of PPDO can be dissolved in common solvents such as chloroform, while high molecular weight of PPDO can only be dissolved in a few kinds of solvents like phenol/1,1,2,2-tetrachloroethane (2 : 3 w/w). The same problem exists in PEDO copolymers with high content of PPDO. Likewise, PEDO could not be dissolved in chloroform at all and so their components cannot be calculated exactly by ^1H NMR. In this article, the constitutions of PEDO were roughly evaluated via the conversion of PDO, and the length of PPDO component was also calculated in theory.

From Table I, we can see that the conversions of PDO are high and nearly same in the cases of different feed ratios and so the weight fraction in the feeds should be nearly consistent with that in the products. According to our primal expectation, the average molecular weight of PPDO blocks in the copolymers has no obvious difference. Consequently, the inherent viscosities of PEDO copolymers increase with the increase of molecular weight of PEG blocks.

Figure 1 shows the ^1H NMR spectra of PEDO6K. Although the composition of copolymer cannot be calculated exactly due to the incomplete solubility of copolymers in the chloroform, the peaks of three kinds of hydrogen in PPDO were still observed, and their chemical shifts are at 4.33 (2H, t) (c), 4.16 (2H, s) (a), 3.78 ppm (2H, t) (b), respectively. A proton peak of PEG was also observed at 3.65 ppm (d). This confirms the structure of the copolymer.

The thermal properties and crystallization of copolymers

Thermograms of PEDO with different molecular weights of PEG are shown in Figure 2, and the relevant data are listed in Table II. Clearly, the content and length of PEG chains do have an effect on the thermal properties and crystallization behaviors of copolymers. As shown in Figure 2, PEDO800 and PEDO2K only have one melting point. PEG segments in molecule chains of these two samples are very short and the content of PEG block is very low. Therefore, the PEG segments dispersed in copolymers can hardly form regular crystal by ordering process in a small domain. While the molecular weight of original PEG increased, the PEG block in copolymer became longer and the content of PEG segment also increased. When the content of PEG chains increases to a certain extent, the density of isolated domains can be far greater than that of available heterogeneities, thus creating appropriate conditions for homogeneous nucleation.^{20,21} So it is also reasonable that PEDO6K and PEDO20K have two independent melting peaks, which are very close to those of PEG and PPDO homopolymers, and they could be regarded as the melting points of PEG and PPDO, respectively.

It also can be found in Figure 2 that PEDO800 finished its crystallization during the cooling scan, and no cold crystallization was observed in the following heating scanning. Moreover, the T_c of PEDO800 (Table II) is much higher than that of the other samples. Even the small amount of PEG segments (1.76%) in PEDO800 cannot form the own crystal, but it can act as the nucleation agent during the crystallization

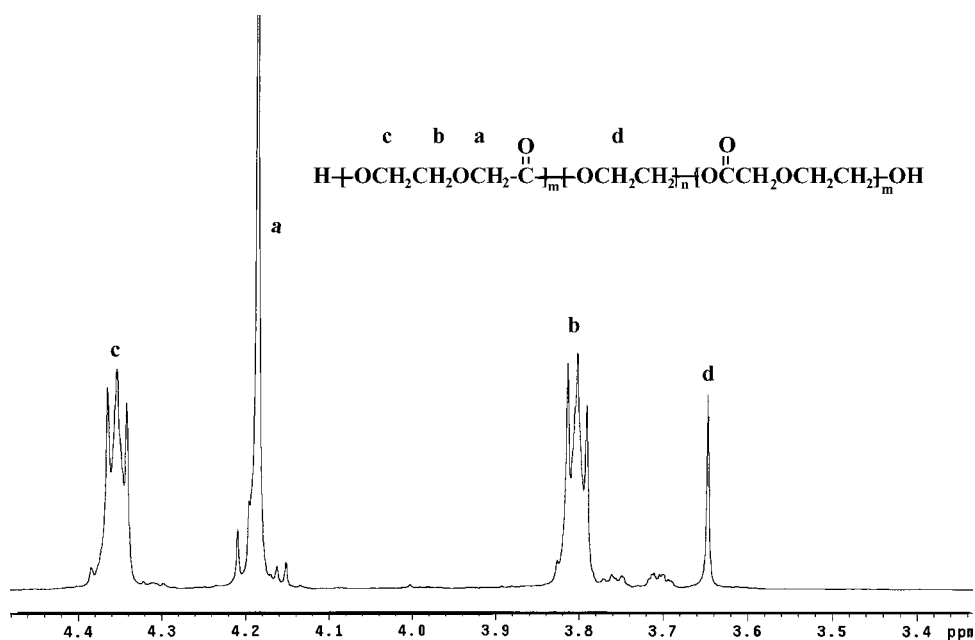


Figure 1 ^1H NMR spectra of PPDO-*b*-PEG-*b*-PPDO copolymer.

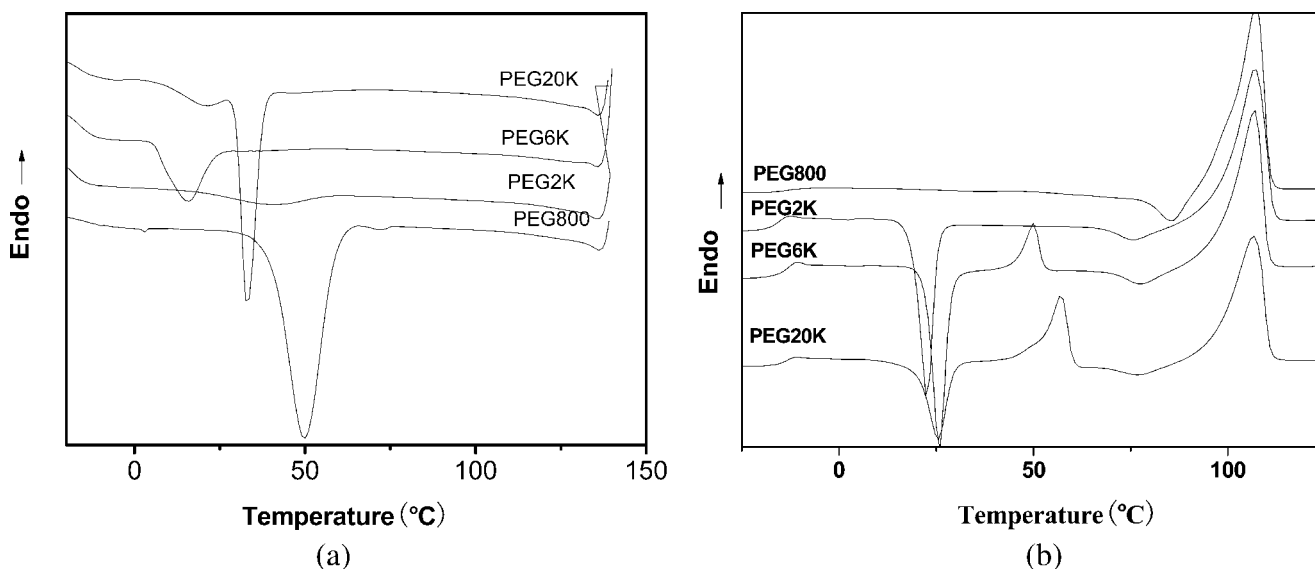


Figure 2 DSC cooling scans (a) and subsequent heating scans (b) of copolymers (10°C/min).

of PPDO chains. With the increase of the PEG content, the nucleation effect decreased. Otherwise, when PEG chains became long enough, they began to tangle with the PPDO chains, which prevented the chains from getting into the lattice, decreasing the growing rate of the crystal and so PEDO2K did not exhibit the clear T_c peak during the cooling scan. While the length of PEG reaches to 6K, PEG chains are long enough to form their own domains, and even they can influence the motion of PPDO chains. On the other hand, the effect of entanglement of PEG with PPDO becomes weak as the miscibility of two polymers becomes poor with the increase of their molecular weights (as shown in Table II, only one T_g belonging to PPDO homopolymer can be observed, for example, despite much higher PEG contents in PEDO6K than in PEDO2K). As a result, the T_c of PEDO6K is clearer than that of PEDO2K, although the value of T_c decreases to a minimum of 15.55°C. However, when PEG chains continue elongating to some extent, the ordering process becomes easier, and the crystallizability increases, resulting in the increase of T_c of PEDO20K again.

TABLE II
Results from DSC of Copolymers and PPDO Homopolymer

Sample	T_g (°C)	T_c (°C)	T_m (°C)	
			PPDO	PEG
PEDO800	-12.72	49.81	107.17	-
PEDO2K	-15.15	40.94	106.98	-
PEDO6K	-14.22	15.55	106.78	49.98
PEDO20K	-14.19	33.03	106.58	76.58

Thermal stability of copolymers

The weight loss curves obtained at a heating rate of 10°C/min under nitrogen for the different triblock copolymers and PPDO homopolymer are shown in Figure 3, and the relevant data are listed in Table III. From Figure 3, we can see that PEDO 800 has one weight loss stage, the same as PPDO homopolymer. With the increase of PEG molecular weight/weight fraction in the copolymer PEDO, however, the decomposing behaviors become quite different: there appeared a second weight loss stage, in which the weight loss decreases with the increase of PEG molecular weight/weight fraction in the copolymer PEDO until the residues become zero at about

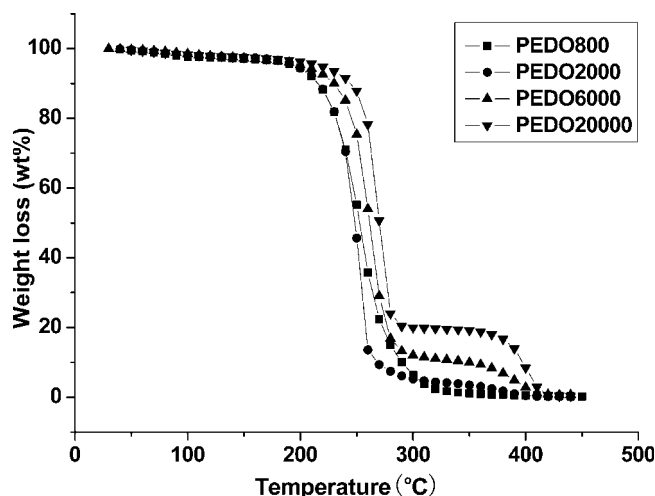


Figure 3 TGA of PPDO homopolymer and PEDO triblock copolymers.

TABLE III
Results from TGA and DTG of the Copolymers

Sample	1st stage			2nd stage		
	T_{d1}^{a1} (°C)	T_{max} (°C)	ΔW^{C1} (wt %)	T_d^{a2} (°C)	T_{max} (°C)	ΔW^{C2} (wt %)
PPDO	221.17	249.07	—	—	—	—
PEDO800	229.76	254.66	96.32	—	—	—
PEDO2K	237.09	254.53	94.08	260.33	390.00	5.92
PEDO6K	245.00	260.41	85.85	275.42	394.60	14.15
PEDO20K	258.06	268.35	77.50	278.17	400.04	22.50

a1 and a2 represents the temperature at the inflection points corresponding to 1st and 2nd stage degradation, respectively. ΔW^{C1} , the total weight loss percentage at the end of 1st stage; and ΔW^{C2} , the total weight loss percentage during the 2nd stage.

400°C. Nishida et al.²² showed that in the degradation of PPDO homopolymer, cyclic degradation products were produced due to transesterification reactions and were easier to volatilize to gas phase, leading to a weight loss. Therefore, with the decrease of PPDO content in the copolymers, the probability of cyclization decreases, resulting in the slow decomposition of the copolymers in the second weight loss stage.

The inflection point temperatures of the first stage degradation, (T_{d1}), which are important for practical applications, are found to increase slightly with increasing the weight fraction of PEG in the copolymers. T_{d1} also ascends with the increase of PEG molecular weight. The weight losses, ΔW^{C1} and ΔW^{C2} of the copolymer PEDO during the two stages, which conform to their weight percentage of PPDO and PEG respectively, suggest that the degradation in the first stage is primarily due to the PPDO blocks, and the degradation in the second stage is due to the PEG blocks. Moreover, in first stage, the temperature at which the decomposing rate is the maximum increases with the increase of PEG molecular weights. That is to say that the copolymers have higher thermal stability than PPDO.

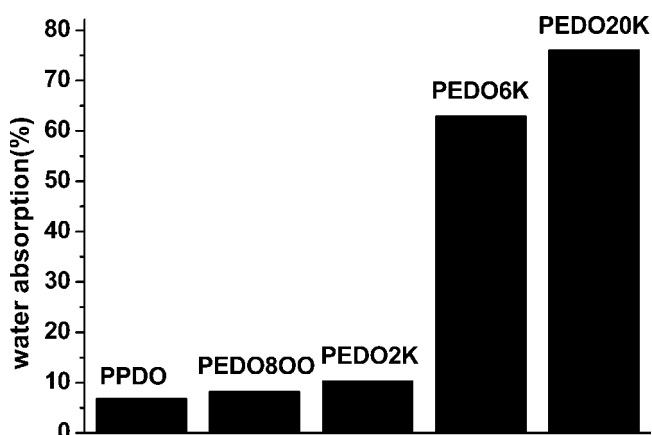


Figure 4 Effect of PEG molecular weight on water absorption behavior of PEDO copolymers and PPDO homopolymer at 37°C.

The water absorption of the copolymer

The water absorption of the copolymers with different molecular weight of PEG and PPDO homopolymer is shown in Figure 4. The water absorption of PPDO is smaller (6.85%) than that of various copolymers, for the introduction of hydrophilic PEG chain to the copolymers enhanced their water absorption. With the increase of PEG molecular weight, the water absorption of the copolymers also increases. For example, the water absorption of the copolymers increase from 8.27% for PEDO800 to 76.10% for PEG20K. The water absorption of copolymers is ascribed to the existence of hydrophilic PEG segments in the amorphous domains. The water can penetrate easily into the amorphous phase but hardly into the crystalline phase.²³ Therefore, The water absorption of copolymers is related to two factors: one is the content and the length of PEG chains; the other is the crystallinity of the copolymers.

CONCLUSION

A series of ABA triblock copolymers with different length of PEG blocks can be synthesized via the initiated polymerization of PDO by different molecular weight of PEG as macroinitiators in the existence of Sn(Oct)₂ as a catalyst. The molecular weight of PEG and its content have great effects on the thermal and crystalline behaviors, the thermal stability and the water absorption of the copolymers. Therefore, all the above properties can be adjusted via controlling the composition and size of both PPDO and PEG blocks of the triblock copolymers.

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