

Synthesis, Characterization, and *In Vitro* Degradation of Star-Shaped P(ϵ -caprolactone)-*b*-Poly(L-lactide)-*b*-Poly(D,L-lactide-*co*-glycolide) from Hexakis [*p*-(hydroxymethyl)phenoxy]cyclotriphosphazene Initiator

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ABSTRACT: Hexaarmed star-shaped hydroxyl-terminated poly(ϵ -caprolactone) (PCL) was successfully synthesized via the ring-opening polymerization of ϵ -caprolactone (CL) with hexakis[*p*-(hydroxymethyl)phenoxy]cyclotriphosphazene initiator and stannous octoate catalyst in bulk. The star-shaped PCL with hydroxy end groups could be used as a macroinitiator for block copolymerization with L-lactide (L-LA). The star-shaped triblock copolymer was synthesized by above-mentioned hydroxyl-terminated star-shaped diblock PCL-*b*-PLLA, D,L-lactide (D,L-LA), and glycolide (GA). IR, ¹H NMR, and GPC analysis showed that the star-shaped block copolymers were successfully synthesized and the molecular weights and the

unit composition of the star-shaped block copolymers were controlled by the molar ratios of monomer to initiator. The triblock copolymer presented a three-phase structure, namely, PCL crystalline, PLLA crystalline, and D,L-PLAGA amorphous domains, which made the triblock copolymer different from the diblock copolymer and star-shaped PCL in crystallizability and thermal behaviors. Then, the *in vitro* degradation behaviors of the copolymers were investigated. © 2007 Wiley Periodicals, Inc. *J Appl Polym Sci* 104: 2310–2317, 2007

Key words: phosphazene; ring-opening polymerization; star-shaped block copolymers; *in vitro* degradation

INTRODUCTION

The construction of polymers with controlled compositions, topologies, and functionalities has been the focus of research in recent years.^{1–3} Among them, star-shaped polymers have attracted considerable attention because of their well-defined structures and unique physicochemical properties different from those of their linear counterparts.^{4–8} Generally, star-shaped polymers can be synthesized by two different routes: one is the arm-first method and the other is the core-first approach using multifunctional initiators.^{9–14} So far, the core-first approach has proven to be a very efficient strategy to form expected structure polymers by ring-opening polymerization. Furthermore, stannous octoate is widely used as a catalyst in ring-opening polymerization because it can produce high yield, molecular weight controlled, and narrow distributed polymers.^{15,16} Trollas and Hedrick synthesized den-

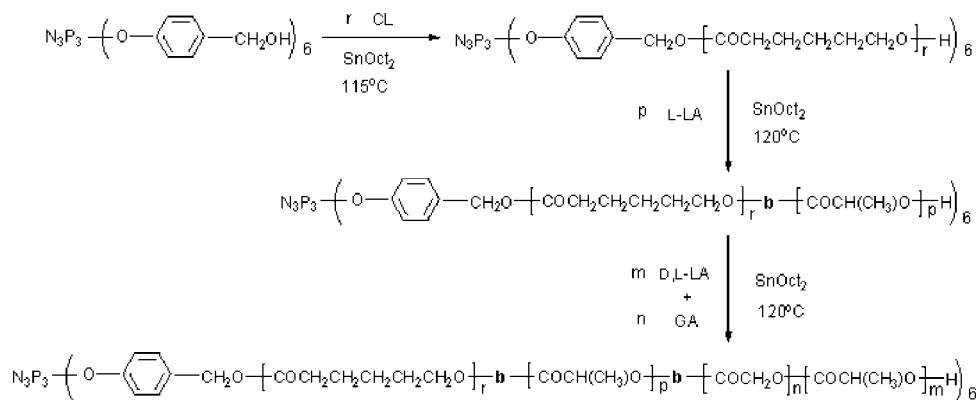
drimer-like star polylactone using a hexahydroxy-functional compound initiator and stannous octoate catalyst.¹⁷ Kim et al. reported the synthesis of star-shaped polylactide with pentaerythritol multifunctional initiator by ring-opening polymerization.^{18,19}

Biodegradable polyesters present a class of biomaterials with growing importance, especially in the field of biomedical application.^{20–23} Among them, homopolymers and copolymers of glycolide (GA), lactides (LA), and ϵ -caprolactone (CL) are especially interesting and promising.^{24,25} Poly(ϵ -caprolactone) (PCL) has been used as drug carrier because of its good drug permeability.^{26–28} Poly(L-lactide) (PLLA) has been widely used for bioresorbable devices in drug delivery and tissue engineering owing to its excellent biocompatibility.^{29–31} Moreover, poly(D,L-lactide-*co*-GA) (D,L-PLAGA) has been widely used as biodegradable sutures, implantable screws, intravascular stents, and drug-delivery devices and as temporary scaffolds for tissue.^{32,33} To explore the application of these polymers, considerable investigations have been carried out. Deng et al. reported the synthesis of a novel multiarm block copolymer of PLA and PCL with multifunctional 1-ethylglucopyranoside as an initiator.³⁴ Dong et al. investigated the star-shaped block copoly-

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Scheme 1 Synthesis of star-shaped block copolymer by ring-opening polymerization.

mer PCL-*b*-poly(D,L-lactic acid-*alt*-glycolic acid) with pentaerythritol and trimethylolpropane as initiators, respectively.³⁵ Pennings and coworkers reported the synthesis of star-shaped polylactide-containing block copolymers by ring-opening polymerization with pentaerythritol initiator.³⁶ However, the studies on the synthesis of star-shaped multiblock polyesters using multifunctional initiator are rare and deserve further research.

Phosphazenes possess special properties and play an important role in the chemistry of heteroatom compounds.^{37–42} Among them, phosphazene polymers attracted considerable interest because they could be tailored to possess a variety of physicochemical properties.^{43–45} Allcock and Pucher reported some of phosphazene polymers that could be used as drug carriers for delivery systems.⁴⁶ Cohen et al. synthesized a novel matrix from ionically crosslinkable polyphosphazene.⁴⁷ Cyclotriphosphazenes exhibit useful thermal properties and excellent biocompatibility. Moreover, cyclotriphosphazenes could be used as multifunctional initiators.^{48,49} In our previous study, star-shaped PLA and star-shaped diblock copolymer PCL-*b*-D,L-PLAGA initiated with cyclotriphosphazenes were synthesized.^{50,51} However, there are still some questions should be answered. For instance, (1) whether or not diblock copolymer macroinitiator remains “living”; (2) whether or not this strategy, for synthesis of star-shaped copolymer, can be extended to obtain triblock copolymer; and (3) novel characteristic of thermal properties and *in vitro* degradation of star-shaped triblock copolymer.

The star-shaped PCL-*b*-PLLA-*b*-D,L-PLAGA could expectedly combine the excellent permeability of PCL block, the outstanding biocompatibility and degradability of PLLA block and the higher biodegradability of the D,L-PLAGA block. Therefore, in this article, a series of star-shaped triblock PCL-*b*-PLLA-*b*-D,L-PLAGA copolymers were synthesized by ring-opening polymerization with hexakis[*p*-(hydroxymethyl)phenoxy]cyclotriphosphazene (Scheme 1). The thermal proper-

ties of these polymers were investigated by DSC and TGA analysis. The *in vitro* degradation of these polymers were investigated in phosphate buffer solution (PBS) at pH = 7.4.

EXPERIMENTAL

Materials

CL (99%, Aldrich, MO) was distilled from CaH₂ *in vacuo* under dry N₂. L-Lactide (Purac Biochem, the Netherlands) was purified by recrystallization from toluene twice and dried *in vacuo* at room temperature. D,L-Lactide (D,L-LA) and GA (Purac Biochem) were gifts from Tong Ji University (Shanghai, China) and the purification method was similar to that of L-lactide. Stannous octoate (SnOct₂) (95%, Aldrich, MO) was distilled under reduced pressure before use. Hexakis[*p*-(hydroxymethyl)phenoxy]cyclotriphosphazene was prepared by the reaction of hexachlorocyclotriphosphazene (Aldrich) with the sodium salt of 4-hydroxybenzaldehyde and subsequent reduction of aldehyde groups to alcohol groups by using sodium borohydride.⁵⁰ The melting point of the purified products was 217–218°C. Toluene, hexane, and tetrahydrofuran (THF) (analytic purity, Shanghai Chemical Reagent, China) were distilled from Na and CaH₂ under dry N₂. Chloroform (analytic purity, Shanghai Chemical Reagent) was dried with molecular sieves type 4A before use.

Synthesis of star-shaped PCLs

A typical polymerization procedure was as follows: CL (6.21 g, 54.4 mmol), hexakis[*p*-(hydroxymethyl)phenoxy] cyclotriphosphazene (0.396 g, 0.453 mmol), catalytic amount of tannous octoate in dried toluene, and a magnetic stirring bar were added into a dried glass tube. The copolymerization and the purification process were carried out by a similar approach as mentioned in our previous work.⁵¹ Namely, the poly-

merization tube was connected to a Schenkline, where an exhausting-refilling process was repeated thrice. The tube was immersed into an oil bath at 115°C with stirring. The tube was then cooled to room temperature after polymerization for 24 h. The crude product was dissolved in chloroform microfiltered through a 0.45- μm -pore membrane filter and then precipitated in hexane for three times. The purified polymer was dried in a vacuum oven until constant weight. $M_{n,\text{NMR}} = 14,100$; $M_{n,\text{GPC}} = 11,000$; $M_w/M_n = 1.083$, IR (KBr, cm^{-1}): 3390–3610 ($\nu_{\text{O-H}}$), 2940 ($\nu_{\text{C-H}}$), 2862 ($\nu_{\text{C-H}}$), 1730 ($\nu_{\text{C=O}}$). ^1H NMR (CDCl_3 , δ , ppm): 7.16 (d, CH in), 6.88 (d, CH in), 5.04 (s, CH_2O), 4.05 (m, CH_2O in PCL), 3.64 (t, terminal CH_2O in PCL), 2.31 (m, COCH_2 in PCL), 1.64 (m, CH_2 in PCL), 1.38 (m, CH_2 in PCL).

Synthesis of star-shaped PCL-*b*-PLLA

A typical example is given below. PCL with hydroxy end groups obtained above (2.23 g, 0.155 mmol), L-lactide (2.68 g, 18.6 mmol), and a magnetic stirring bar were put into a dried tube. The tube was then connected to a Schenkline, where an exhausting-refilling process was repeated three times. The tube was put into an oil bath at 120°C with vigorous stirring for 5 min. Then, catalytic amount of tannous octoate catalyst in dry toluene was added to the melt mixture, and the exhausting-refilling process was carried out again to remove the toluene. The tube was put into an oil bath at 120°C with stirring and cooled to room temperature after reaction for 24 h. The resulting product was dissolved in chloroform, microfiltered through a 0.45- μm -pore membrane filter, and then precipitated in hexane for three times. The purified polymer was dried in a vacuum oven until constant weight. $M_{n,\text{NMR}} = 27,800$; $M_{n,\text{GPC}} = 23,700$; $M_w/M_n = 1.229$, IR (KBr, cm^{-1}): 3406–3590 ($\nu_{\text{O-H}}$), 2948 ($\nu_{\text{C-H}}$), 2862 ($\nu_{\text{C-H}}$), 1760 ($\nu_{\text{C=O}}$), 1728 ($\nu_{\text{C=O}}$). ^1H NMR (CDCl_3 , δ , ppm): 7.16 (d, CH in), 6.88 (d, CH in), 5.16 (s, CH in PLLA and CH_2O), 4.36 (t, terminal CH in PLLA), 4.05 (m, CH_2O in PCL), 2.31 (m, COCH_2 in PCL), 1.64 (m, CH_2 in PCL and CH_3 in PLLA), 1.38 (m, CH_2 in PCL).

Synthesis of star-shaped PCL-*b*-PLLA-*b*-poly(*D,L*-LA-*co*-GA)

A typical example is as follows: hydroxy-functional PCL-*b*-PLLA (1.26 g, 0.041 mmol), *D,L*-LA (0.356 g, 2.46 mmol), GA (0.286 g, 2.46 mmol), and a magnetic stirring bar were put into a dried tube. By a similar approach as described earlier and after adding stannous octoate catalyst, the tube was immersed into an oil bath at 120°C with stirring for 24 h. The resulting product was dissolved in chloroform, microfiltered through a 0.45- μm -pore membrane filter, and then precipitated in hexane for three times. The purified

polymer was dried in a vacuum oven until constant weight. $M_{n,\text{NMR}} = 40,900$; $M_{n,\text{GPC}} = 34,200$; $M_w/M_n = 1.292$, IR (KBr, cm^{-1}): 3406–3620 ($\nu_{\text{O-H}}$), 2946 ($\nu_{\text{C-H}}$), 2868 ($\nu_{\text{C-H}}$), 1762 ($\nu_{\text{C=O}}$), 1726 ($\nu_{\text{C=O}}$). ^1H NMR (CDCl_3 , δ , ppm): 7.18 (d, CH in), 6.86 (d, CH in), 5.16 (s, CH in PLLA and CH_2O), 4.82 (m, CH_2 in PGA), 4.34 (t, terminal CH in PDLLA), 4.28 (s, terminal CH in PGA), 4.05 (m, CH_2O in PCL), 2.31 (m, COCH_2 in PCL), 1.64 (m, CH_2 in PCL and CH_3 in PLLA), 1.38 (m, CH_2 in PCL).

In vitro degradation of star-shaped polymers

Films of linear PCL and star-shaped polymers were cast from 6% chloroform solution (w/v). Residual solvents (chloroform) were removed *in vacuo* at room temperature for 72 h until a constant weight was obtained. The film thickness was found to be 0.2 mm. The films of the polymers were placed in tubes filled with immersed in PBS (pH = 7.4). The tubes were placed in a water bath at 37°C for 33 days. At the given time intervals, the samples were washed with distilled water, and dried *in vacuo* to constant weight at room temperature. The degradation was investigated by detecting weight loss.

Characterization

Fourier transform infrared spectroscopic (FTIR) analyses were performed on a Paragon 1000 FTIR spectrometer (PerkinElmer, MA) with potassium bromide discs. ^1H spectra were obtained from a Varian Mercury Plus-400 NMR spectrometer (Varian, CA) with CDCl_3 as solvent. Chemical shifts were relative to tetramethylsilane at $\delta = 0$ ppm for protons. The molecular weight and molecular weight distribution were measured on a Waters gel permeation chromatography equipped with three Waters Styragel columns (HR3 + HR4 + HR5) at 30°C. THF was used as an eluent and narrow-distributed polystyrene standards were used as calibrations. Differential scanning calorimetric (DSC) analysis was investigated on a Pyris1 DSC (PerkinElmer) with a heating rate of 10°C/min from –10 to 200°C under N_2 atmosphere. Thermogravimetric analysis was carried out on a TGA7/DX thermogravimetric analyzer with a heating rate of 10°C/min under N_2 atmosphere.

RESULTS AND DISCUSSION

Synthesis of star-shaped PCLs macroinitiator

Hexaarmed star-shaped PCLs with hydroxy end groups were successfully synthesized from the polymerization of CL with the hydroxyl-terminated cyclo-triphosphazene initiator and the stannous octoate catalyst in bulk at 115°C. The polymers were charac-

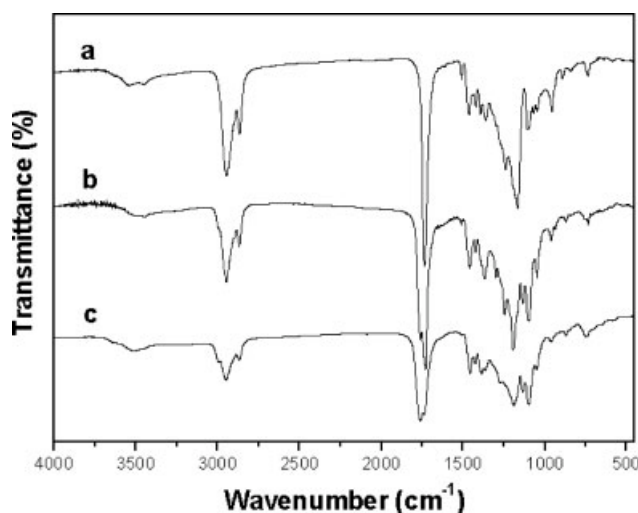


Figure 1 IR spectra of star-shaped poly(ϵ -caprolactone) (PCL) (a), star-shaped diblock copolymer PCL-*b*-PLLA (b), and star-shaped triblock copolymer PCL-*b*-PLLA-*b*-D,L-PLAGA (c).

terized by FTIR spectroscopy [Fig. 1(a)], ^1H NMR spectroscopy, and GPC analysis. From Figure 2, the methylene proton signal showed that PCL was terminated by hydroxy end groups. Moreover, the molecular weight determined by ^1H NMR spectroscopy was calculated from the integration ratio between the methylene protons in the repeat units (g) and the methylene protons in the terminal unit (h).

Synthesis of star-shaped diblock PCL-*b*-PLLA copolymers

The star-shaped hydroxyl-terminated PCL could act as macroinitiator for the block copolymerization with L-lactide in bulk at 120°C. As shown in Figure 1(a,b), the main difference of IR spectrum between the star-shaped diblock copolymer and star-shaped PCL was in the carbonyl absorption band region. The carbonyl absorption band of diblock copolymer became wide and split into two peaks. The peak at 1760 cm^{-1} corresponded to the carbonyl absorption of PLLA units, while the peak at 1728 cm^{-1} was assigned to the car-

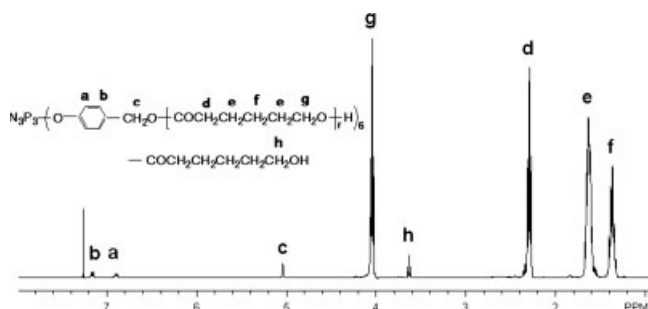


Figure 2 ^1H NMR spectrum of star-shaped poly(ϵ -caprolactone) (PCL).

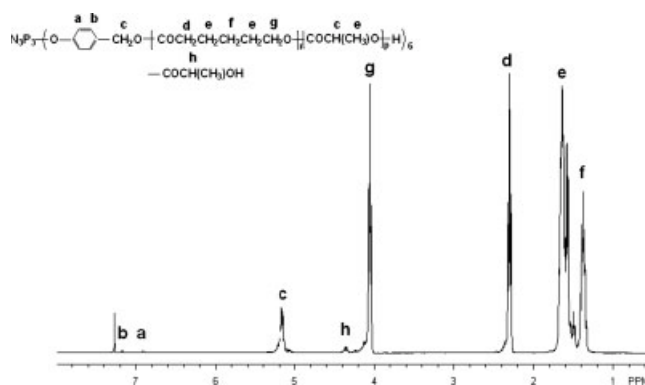


Figure 3 ^1H NMR spectrum of star-shaped diblock copolymer PCL-*b*-PLLA.

bonyl absorption of PCL units. This could prove that the PCL chain existed in the diblock copolymer as a block. ^1H NMR spectrum of star-shaped diblock copolymer was shown in Figure 3. The peak assigned to methylene protons ($\delta = 3.64$ ppm, h in Fig. 2) disappeared, and the new peak at 4.36 ppm for the produced end groups of PLLA was observed. This indicated that the terminal hydroxyl groups of the macroinitiator successfully initiated the polymerization of L-LA. The average chain length was determined by comparison of the signal intensity ratios of methine protons of the PLLA (c) to the terminal methine protons (h).

Synthesis of star-shaped triblock PCL-*b*-PLLA-*b*-poly(D,L-LA-co-GA) copolymers

The star-shaped triblock copolymer was synthesized by above-mentioned diblock hydroxyl-terminated copolymer, D,L-LA, and GA. IR spectrum of this polymer was shown in Figure 1(c). When compared with that of diblock polymer, the carbonyl absorption band of triblock polymer became wide. The peak at 1762 cm^{-1} corresponded to the carbonyl absorption of PGA units

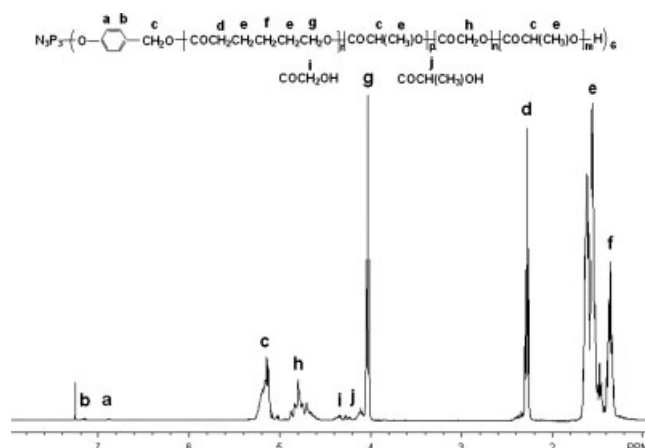


Figure 4 ^1H NMR spectrum of star-shaped triblock copolymer PCL-*b*-PLLA-*b*-D,L-PLAGA.

TABLE I
Results of Star-Shaped Block Copolymerization

Sample	[OH]/[CL]/[L-LA]/ [D,L-LA]/[GA]	$M_{n,th}^a$	$M_{n,NMR}^b$	$M_{n,GPC}^c$	M_w/M_n^c	Conversion (%)
1	1/20/0/0/0	14,400	14,100	11,000	1.083	99
2	1/40/0/0/0	27,100	24,900	21,100	1.252	96
3	1/20/20/0/0	30,500	27,800	23,700	1.229	93
4	1/20/10/0/0	22,600	20,800	17,500	1.118	95
5	1/40/30/0/0	49,900	45,100	37,500	1.301	88
6	1/40/15/0/0	39,000	34,800	29,700	1.286	92
7	1/20/20/10/10	45,200	40,900	34,200	1.292	94
8	1/40/30/20/10	71,500	62,900	54,100	1.330	89
9	1/20/10/10/10	36,900	32,300	28,700	1.276	92
10	1/20/10/20/10	45,100	40,600	34,000	1.304	93
11	1/40/15/10/10	53,000	47,500	41,200	1.325	90
12	1/40/15/20/10	61,100	53,600	46,200	1.338	91

THF was used as eluent.

^a $M_{n,th} = [\text{monomer}]/[\text{OH}] \times 6 \times M_{\text{monomer}} \times \text{Conversion} (\%) + M_{\text{initiator}}$, $M_{n,th}$ denotes the average number molecular weight of star-shaped copolymer.

^b $M_{n,NMR}$ was determined by ^1H NMR spectroscopy of star-shaped copolymer.

^c $M_{n,GPC}$ and M_w/M_n were determined by GPC analysis with polystyrene standards.

within D,L-PLAGA block. A typical ^1H NMR spectrum of star-shaped triblock copolymer was shown in Figure 4. The new peaks at 4.34 and 4.28 ppm for the end groups of D,L-PLAGA block could be observed, while the peak assigned to methine protons ($\delta = 4.36$ ppm, h in Fig. 3) disappeared. The polymerization degree was estimated by comparison of the signal intensity ratios of methylene protons (h) and methine protons (c) in the repeat units to those of methylene protons (i) and methine protons (j) in the terminal units.

From Table I, it could be seen that the number-average molecular weight of the resulting star-shaped PCL, star-shaped PCL-*b*-PLLA, and star-shaped PCL-*b*-PLLA-*b*-D,L-PLAGA linearly increased with the molar ratio of monomer to initiator, which indicated that the hydroxyl-terminated phosphazene could be used as effective propagation centers. Moreover, the molecular weight determined by NMR was much closer to the theoretic value than that obtained by GPC. For star-shaped polymer, the GPC analysis always underestimates the molecular weight because it has smaller hydrodynamic volume than that of linear polystyrene having the same molecular weight.⁵² However, the GPC analysis could monitor the purity of polymers and polydispersion of molecular weight. The GPC traces (Fig. 5) of star-shaped PCL, PCL-*b*-PLLA, and PCL-*b*-PLLA-*b*-D,L-PLAGA were symmetrical and monomodal, which indicated that these polymers were pure star-shaped block polymers and no mixture of star and linear polymers were formed.

Thermal properties of star-shaped block copolymers

The properties of star-shaped block copolymers were presented in Table II. According to the DSC data, melting point (T_{m1}) and the degree crystallinity (X_{c1})

of star-shaped PCL were lower than those of linear one, which could be attributed to the crystalline imperfection mainly because of the short chain length of the star-shaped PCL arms and the branched structure of star-shaped PCL. Star-shaped diblock copolymer PCL-*b*-PLLA showed different thermal properties when compared with star-shaped PCL owing to the presence of PLLA block segments existed in star-shaped diblock copolymer PCL-*b*-PLLA. It is well-known that PLLA was crystalline polymer. Therefore, there were two melting endotherms for the diblock copolymer and this showed the existence of different crystalline domains of PCL block and PLLA block. It was found that the melting endotherms of both blocks changed with the composition of the copolymers. The

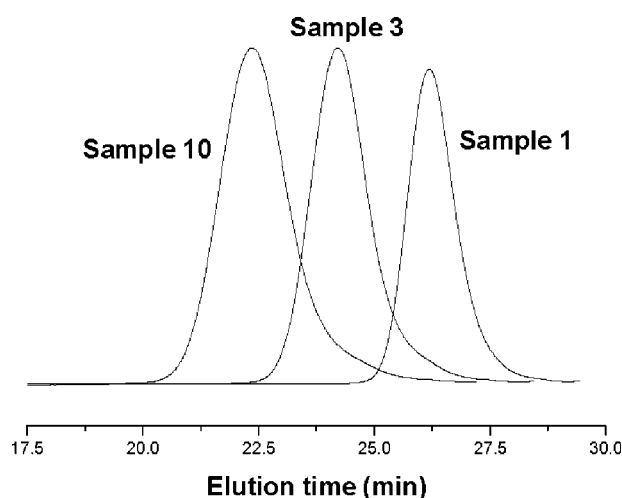


Figure 5 GPC traces of star-shaped PCL (Sample 1), star-shaped PCL-*b*-PLLA (Sample 3), and star-shaped PCL-*b*-PLLA-*b*-D,L-PLAGA (Sample 10).

TABLE II
Thermal Properties of Star-Shaped Block Copolymer

Sample	T_{m1} (°C) ^a	T_{m2} (°C) ^b	ΔH_1 (J/g) ^c	ΔH_2 (J/g) ^d	X_{c1} (%) ^e	X_{c2} (%) ^f	T_{onset} (°C) ^g	T_{max} (°C) ^h
Linear PCL	61.0		76.3		54.7		376.9	396.5
1	52.8		50.6		36.3		357.7	398.8
2	57.5		56.9		40.8		385.4	413.5
3	44.9	136.8	15.6	6.4	11.2	6.8	263.8	315.6
4	45.6	134.9	20.5	4.3	14.7	4.6	261.9	310.9
5	48.1	139.2	22.5	7.9	16.1	8.4	267.4	328.7
6	49.8	137.1	28.6	3.9	20.5	4.2	264.6	317.6
7	38.6	131.8	4.0	1.2	2.9	1.3	264.9	314.7
8	49.3	136.6	7.8	2.1	5.6	2.2	268.1	329.4
9	42.2	130.5	6.7	0.7	4.8	0.8	262.5	312.5
10	37.5	129.6	4.3	0.5	3.1	0.5	262.3	311.6
11	46.2		10.9		7.8		265.8	318.9
12	45.6		8.8		6.3		267.8	320.1

Samples are the same as Table I (Samples 1–12).

^a T_{m1} denotes the onset melting point of PCL-block segments.

^b T_{m2} denotes the onset melting point of PLLA-block segments.

^c Heat of melting of crystalline PCL-block segments. Calculated from the heat of melting using the melting of 139.5 J/g of 100% crystalline PCL.

^d Heat of melting of crystalline PLLA-block segments. Calculated from the heat of melting using the melting of 93.6 J/g of 100% crystalline PLLA.

^e The degree of crystallinity of PCL-block segments.

^f The degree of crystallinity of PLLA-block segments.

^g T_{onset} is the onset decomposition temperature.

^h T_{max} is the temperature corresponding to the maximum rate of weight loss.

X_{c1} and X_{c2} of PCL and PLLA block were 11.2 and 6.8%, respectively, for Sample 3, whereas the X_{c1} and X_{c2} of PCL and PLLA block were 14.7 and 4.6%, respectively, for Sample 4. Meanwhile, the crystallinity of PCL block of PCL-*b*-PLLA decreased sharply ($X_{c1} = 16.1\%$, Sample 5) when compared with star-shaped PCL ($X_{c1} = 40.8\%$, Sample 2). These could be interpreted by the fact that the introduction of the PLLA block into the copolymers worsened the conditions for crystallization of the PCL and the crystallizability of PLLA was also seriously affected because of the presence of PCL. The crystallinity of PCL and PLLA block segments in the star-shaped triblock copolymer PCL-*b*-PLLA-*b*- D,L -PLAGA was further hindered with the introduction of amorphous D,L -PLAGA segments. The X_{c1} and X_{c2} of PCL and PLLA block decreased to 4.8 and 0.8%, respectively (Sample 9). Moreover, the degree of crystallinity of PLLA block even could not be detected for Samples 11 and 12. The branched structure of the block polymer and the presence of D,L -PLAGA segments together resulted in the crystallinity imperfection, which led to the obvious decrease of crystallinity of PCL and PLLA segments existed in star-shaped triblock copolymer. All the information obtained from DSC data further proved that the PCL-*b*-PLLA-*b*- D,L -PLAGA copolymer contained three kinds of blocks, namely, PCL block, PLLA block, and D,L -PLAGA block. According to the TGA data in Table II, the onset decomposition temperature (T_{onset}) of the star-shaped PCL was lower than that of linear PCL, which should be ascribed to the

branched structure and short-chain length of the star-shaped PCL. However, the maximum decomposition temperature (T_{max}) of the star-shaped PCL was higher than that of linear one, which should be attributed to the thermally stable cyclotriphosphazene core. To the diblock star-shaped copolymer PCL-*b*-PLLA and triblock copolymer PCL-*b*-PLLA-*b*- D,L -PLAGA, the T_{onset} and T_{max} were lower than those of the star-shaped PCL (for example, the T_{onset} and T_{max} of Sample 9 were 262.5 and 312.5°C, respectively) owing to the comparative thermal instability of PLLA block and D,L -PLAGA block in the copolymers.

In vitro degradation of polymers

The degradation behaviors of star-shaped PCL, PCL-*b*-PLLA, PCL-*b*-PLLA-*b*- D,L -PLAGA, and linear PCL ($M_n \approx 20,000$) were investigated by immersing them in PBS solution (pH = 7.4) maintained at 37°C. The weight losses of these polymers during the degradation period were shown in Figure 6. At 37°C, the degradation of linear PCL was very slow (for instance, the residual weight was 98.1% after degradation for 33 days), which should be attributed to it being a highly crystalline polymer with a degree of crystallinity about 54.7%. The degradation rate of star-shaped PCL was faster than that of the linear one. This was attributed to the lower degree of crystallinity of the star-shaped PCL (36.3%). To star-shaped block copolymer PCL-*b*-PLLA, the degradation rate was obviously faster than that of star-shaped PCL, which should be

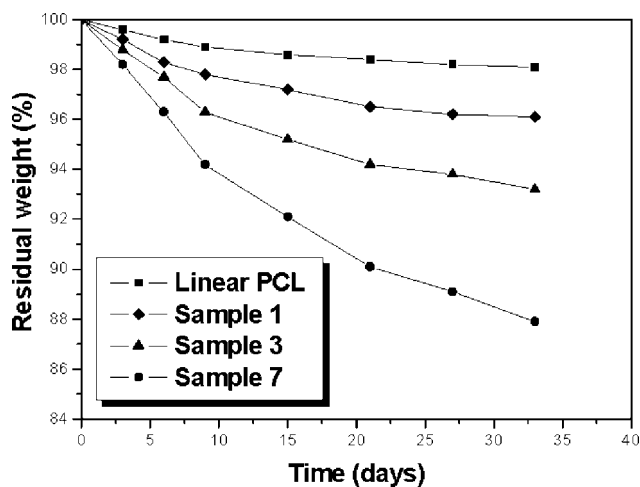


Figure 6 The change in the residual weight of linear PCL, star-shaped PCL (Sample 1), star-shaped PCL-*b*-PLLA (Sample 3), and star-shaped PCL-*b*-PLLA-*b*-_{D,L}-PLAGA (Sample 7) in phosphate buffer solution (PBS) at 37°C.

ascribed to the much lower crystalline of the copolymer than that of PCL because of the presence of the PLLA block. To triblock star-shaped copolymer PCL-*b*-PLLA-*b*-_{D,L}-PLAGA, the degradation rate was much faster than those of linear PCL, star-shaped PCL, and star-shaped PCL-*b*-PLLA. For example, the residual weight was 87.9% after degradation for 33 days. All of these should be attributed to the branched structure of the copolymer and the presence of amorphous copolymer _{D,L}-PLAGA, which led to the lowering of crystallinity of triblock copolymer. Therefore, the water molecule pervaded the molecule of copolymer was faster than those of the linear PCL, star-shaped PCL, and PCL-*b*-PLLA, which promoted the hydrolytic degradation of the copolymer.

CONCLUSIONS

The novel star-shaped triblock copolymer PCL-*b*-PLLA-*b*-_{D,L}-PLAGA initiated with hexakis[*p*-(hydroxymethyl)phenoxy]cyclotriphosphazene was successfully synthesized via the block copolymerization of hydroxyl-terminated star-shaped diblock copolymer PCL-*b*-PLLA. The molecular weights and the unit compositions of the star-shaped block copolymers were controlled by the molar ratios of monomer to initiator. The triblock copolymer presented a three-phase structure, namely, PCL crystalline, PLLA crystalline, and _{D,L}-PLAGA amorphous domains, which made the triblock copolymer different from the diblock copolymer and star-shaped PCL in crystallizability, thermal behaviors, and the *in vitro* degradation behaviors at 37°C.

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