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Synthesis and characterizations of well-defined dendrimer-like copolymers with the second and third generation based on polystyrene and poly(L-lactide)

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Abstract

Dendrimer-like copolymers with two and three generations, (polystyrene)$_3$-*b*-(poly(L-lactide))$_6$ (PSt$_3$-*b*-PLLA$_6$) and PSt$_3$-*b*-PLLA$_6$-*b*-PSt$_{12}$ have been successfully prepared using core-first method. The first step of this synthesis is the preparation of three-armed PSt by atom transfer radical polymerization (ATRP) of St using 1,1,1-tri(methylene-α-bromoisobutyryl)propane as initiator. Terminal divergence of the polymers obtained was achieved by the reaction of terminal bromines with branching agent, 2,2-dimethyl-1,3-dioxolane-4-methanol. After deprotection, the polymer with six terminal hydroxyl groups was used in the ring-opening polymerization of LLA. The dendrimer-like copolymer with PLLA as a second generation diverged continuously by the reaction of 6 terminal hydroxyl groups with branching agent, 2,2-bis(methylene-α-bromoisobutyryl)propionyl chloride. The resultant polymer with 12 terminal bromines was used as macroinitiator in the ATRP of St to produce the target dendrimer-like copolymer, PSt$_3$-*b*-PLLA$_6$-*b*-PSt$_{12}$. The structures of polymers obtained from each step were confirmed by their ^{1}H NMR spectra and GPC measurements. DSC results show one $T_g^{PS} = 102\,°C$ for the three-armed PSt, $T_g^{PLLA} = 53\,°C$, $T_c^{PLLA} = 123\,°C$ and $T_m^{PLLA} = 159\,°C$ for the dendrimer-like copolymer with two generations, C(PSt(PLLA)$_2$)$_3$, and $T_g^{PLLA} = 53\,°C$, $T_c^{PLLA} = 114\,°C$ and $T_m^{PLLA} = 166\,°C$ for the copolymer with three generations, C(PSt(PLLA(PSt)$_2$)$_2$)$_3$.

Keywords: Atom transfer radical polymerization; Ring-opening polymerization; Dendrimer-like copolymer

1. Introduction

Dendrimers are spherical macromolecules with a large number of terminal groups on their surface. They have potential applications in many fields, such as in catalysis, drug delivery, anion binding and biomimetics [1–4]. When a linear polymer replaces the organic group between the two branching points in the dendrimers, a type of well-defined dendritic macromolecules, which is called as dendrimer-like star polymers, have been synthesized [5–10]. Most of them were synthesized by a divergent approach via repetitive living ROP. For example, Gnanou

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and his coworkers reported the synthesis of water soluble dendrimer-like copolymers with inner poly(ethylene oxide) and outer poly(acrylic acid) using the core-first approach [8]. In the synthesis, the hydroxyl group was successfully transformed into ATRP initiating sites. However, successful transformation from ATRP to ROP via divergent method in the synthesis of dendrimer-like copolymers has not been reported yet upon our knowledge.

On the selection of three generation polymers, we considered that poly(L-lactide) (PLLA) is a biodegradable and crystalline polymer, and it can be used to produce nontoxic injectable drug carriers for long-term delivery of polypeptides and protein drugs, and the block copolymers containing PLLA have been extensively studied [11–14]. Polystyrene is an amorphous polymers, and poly(LLA-*b*-styrene) (PLLA-*b*-PSt) and poly(LLA-*b*-St-*b*-methyl methacrylate) (PLLA-*b*-PSt-*b*-PMMA) were also prepared by combination of atom transfer radical polymerization (ATRP) and ring-opening polymerization (ROP) [15]. The crystallization temperature ($T_c = 118$ °C) of PLLA is higher than the glass transition temperature ($T_g = 102$ °C) of PSt. The crystallization of PLLA will affect the phase separation, and their self-assembly behaviors were studied [16]. Generally, well-controlled number of branching points can induce different properties in comparison with their linear counterparts [17]. Thus, a new dendrimer-like copolymers with PSt, PLLA and PSt as the first, the second and the third generation are expected to show new properties. To synthesize this type of dendrimer-like copolymers, the transformation of ATRP to ROP initiating sites should be solved.

In the present work, with the aid of appropriate divergent agents, the dendrimer-like copolymers with two and three generations, $C(PSt(PLLA)_2)_3$ and $C(PSt(PLLA(PSt)_2)_2)_3$ have been prepared via the combination of ATRP of St and ROP of LLA, and their thermal behaviors were investigated.

2. Experimental

2.1. Materials

Bis(hydroxymethyl)propionic acid (BHPA, The First Shanghai Chemical Reagent Factory, 98%) was dried in a vacuum oven at 50 °C before use. St (The First Shanghai Chemical Reagent Factory, 95%) was stirred over CaH_2 overnight and distilled before use. CuBr (Shanghai Chemical Reagent Plant, 98%) was purified by stirring in glacial acetic acid, followed by washing with ethanol, and the product was dried in a vacuum oven at 70 °C. 2,2′-Bipyridine (bpy, Aldrich, 99%) was recrystallized from *n*-hexane. L-Lactide (LLA, Aldrich, 98%) was recrystallized from ethyl acetate two times, and then dried under vacuum (0.1 mm Hg) at room temperature for 48 h. 1,1,1,-Trimethylolpropane (TMP, Aldrich, 98%) was recrystallized from toluene. Stannous 2-ethylhexanoate ($Sn(Oct)_2$, Aldrich, 95%), 1,1,4,7,10,10-hexamethyl triethylenetetraamine (HMTETA, Aldrich, 98%) and 2,2-dimethyl-1,3-dioxolane-4-methanol (DMDOM, Aldrich, 98%) were used as received.

2.2. Characterization

^1H NMR spectra were recorded on a Bruker DMX-300 NMR spectrometer; $CDCl_3$ and tetramethylsilane (TMS) were used as solvent and internal standard. The molecular weight and molecular weight distribution (MWD) were determined on a Waters-150C gel permeation chromatograph (GPC) equipped with Ultrastyragel columns (500, 10^3, 10^4 Å) and RI detector at 30 °C, and THF was used as eluent at a flow rate of 1.0 mL/min. Monodispersed polystyrene standards were used in the calibration of molecular weight. DSC spectra were recorded on a Mettler Toledo DSC 822E.

2.3. Synthesis of 1,1,1-tri(methylene-α-bromoisobutyryl)propane (TMBIBP)

Into a 250 mL flask equipped with a magnetic stirring bar and a condenser connected to an anhydrous $CaCl_2$ tube, TMP (13.5 g, 0.1 mol), α-bromoisobutyryl chloride (75 g, 0.4 mol), and chloroform (100 mL) were added. After the mixture was refluxed for 24 h, the chloroform and excess α-bromoisobutyryl chloride were removed by distillation under reduced pressure. The crude product was distilled under reduced pressure two times, and a viscous liquid TMBIBP was collected in 90% yield at 155 °C/0.1 Pa.

^1H NMR (300 MHz, $CDCl_3$), (TMS, ppm): $\delta = 0.98$ [t, 3H, CH_3CH_2], 1.61 [f, 2H, CH_3CH_2], 1.92 [s, 18H, $C(CH_3)_2Br$], 4.19 [s, 6H, $COOCH_2$].

2.4. Preparation of three-armed polystyrene $C(PSt\text{-}Br)_3$

Three-armed PSt was prepared by the bulk ATRP of St with TMBIBP as initiator and CuBr/bpy as catalyst/ligand. A typical procedure is as follows. A glass tube with a magnetic stirrer was charged with TMBIBP (267 mg, 0.5 mmol), CuBr (72 mg, 0.5 mmol), bpy (234.3 mg, 1.5 mmol), and St (15.6 g, 0.15 mol). The system was degassed via three freeze–pump–thaw cycles. The polymerization tube was sealed under vacuum, and then it was placed into an oil bath thermostated at 110 °C while stirring. After 2 h, the mixture was cooled down to 0 °C, and the tube was opened. The polymer solution in THF was passed through a short column of neutral alumina to remove the metal salt. After precipitation by adding polymer solution into an excess of methanol, the precipitate was collected by filtration, and then dried in a vacuum oven at 40 °C overnight. The $C(PSt\text{-}Br)_3$ was obtained with $M_n = 10600$ and $M_w/M_n = 1.13$.

^1H NMR (300 MHz, $CDCl_3$), (TMS, ppm): $\delta = 6.30–7.36$ [aromatic protons], 4.35–4.57 [$PhCHBr$], 3.65–3.85 [$COOCH_2$], 1.15–2.25 [CH_2 and CH in main chain, CH_2], 0.74–1.01 [$OOCC(CH_3)_2$].

2.5. Divergent reaction of 3 terminal bromines into 6 terminal hydroxyl groups

Into a dry flask with a magnetic stirrer, sodium (0.12 g, 5 mmol) and toluene (15 mL) were added, and then DMDOM (2.6 g, 25 mmol) was dropwise added under pure nitrogen atmosphere. After stirring for 2 h, $C(PSt\text{-}Br)_3$ (2 g, 0.2 mmol) in 10 mL toluene was dropwise added. The reaction mixture was maintained at 120 °C for 24 h. The reaction solution was passed through a short column of neutral alumina and the eluate was added into an excess of methanol. The precipitate was collected by filtration. The polymer obtained was dried under vacuum at 40 °C overnight, and then was dissolved in a solution of THF/H_2O (v/v = 5/1). Into this solution, the *p*-toluenesulfonic acid monohydrate (0.1 g) was added and the hydrolysis reaction was carried out at 60 °C for 2 h. By adding this polymer solution into methanol, the precipitate was collected by filtration, and then the polymer was dried in vacuum oven at 40 °C overnight to afford purified polymer $C(PSt(OH)_2)_3$.

^1H NMR (300 MHz, $CDCl_3$), (TMS, ppm): 6.23–7.33 [aromatic protons], 4.36–4.57 [$PhCHO$], 3.64–3.84 ($COOCH_2$), 3.45–3.57 [$CH(OH)CH_2OH$], 3.25–3.45 [$CH(OH)CH_2OH$, OCH_2], 1.15–2.25 [CH_2 and CH in main chain, CH_2C], 0.82 [CH_3C], 0.52 [CH_3CH_2].

2.6. Preparation of $C(PSt(PLLA\text{-}OH)_2)_3$

A typical polymerization procedure is as follows. Into a 10 mL two-neck flask equipped with a magnetic stirrer, $C(PSt(OH)_2)_3$ (0.5 g, 0.05 mmol), LLA (0.72 g, 5 mmol) and dry toluene (2 mL) were added, then an exhausting–refilling pure N_2 process was operated three times. The flask was immersed into an oil-bath at 115 °C while stirring for 30 min, and then $Sn(Oct)_2$ (0.13 g, 0.3 mmol) in 1 mL toluene was added. The exhausting–refilling process was carried out again to remove the toluene. The polymerization was carried out at 115 °C for 24 h, and then the reaction flask was cooled to room temperature rapidly. After precipitation by adding polymer solution in CH_2Cl_2 into methanol, the product was collected by filtration and then washed with hot cyclohexane. After dried in a vacuum oven at 40 °C overnight, the $C(PSt(PLLA\text{-}OH)_2)_3$ was obtained with $M_n = 21800$ and $M_w/M_n = 1.15$.

^1H NMR (300 MHz, $CDCl_3$), δ (TMS, ppm): 6.25–7.34 [aromatic protons], 5.03–5.46 [$–OCH(CH_3)CO–$], 4.27–4.48 [$PhCHO$, CH_3CHOH], 3.69–4.07 (CH_2OOC, $CHOOC$), 3.25–3.47 ($CH–CH_2O$), 1.11–2.29 (CH_2 and CH in main chain of PSt, CH_3CH in PLLA, CH_2C), 0.75–1.06 (CH_3, CH_3CH_2).

2.7. Synthesis of 2, 2-bis(methylene-α-bromoisobutyrate)propionyl chloride (BMBIBPC)

The α-bromoisobutyryl chloride (93 g, 0.50 mol), 2,2-bis(hydroxymethyl) propionic acid (30 g, 0.22 mol), and chloroform (150 mL) were added into a 500 mL three-necked flask equipped with a magnetic bar. After the mixture was refluxed for 16 h, chloroform and α-bromoisobutyl chloride remained were removed by distillation under reduced pressure. Thionyl chloride (20 mL, 0.27 mol) was added to the flask, and the mixture was heated at reflux temperature for 5 h. Then the thionyl chloride was distilled off under reduced pressure. The crude product was distilled under reduced pressure two times, and the product, 2,2-bis(methylene-α-bromoisobutyrate) propionyl chloride was collected at 165 °C/0.1 Pa.

^{1}H NMR (300 MHz, $CDCl_3$), δ (TMS, ppm): 4.44 (S, 4H, $2COOCH_2$), 1.92 (S, 12H, $2C(CH_3)_2Br$), 1.50 (S, 3H, CCH_3).

2.8. Divergent reaction of 6 terminal hydroxyl groups into 12 bromines

Into a dry two-necked flask with a magnetic bar, $C(PSt(PLLA\text{-}OH)_2)_3$ (0.4 g, 0.02 mmol), CH_2Cl_2 (5 mL) and $N(C_2H_5)_3$ (0.02 g, 20 mmol) were added under pure nitrogen atmosphere. BMBIBPC (0.55 g, 1.2 mmol) in 3 mL CH_2Cl_2 was dropped into the flask at 0 °C. After 48 h reaction at room temperature, the reaction mixture was filtered and the filtrate was added into petroleum ether. The precipitate was collected by filtration, and the product obtained was dried in a vacuum oven at 40 °C overnight. The polymer with 12 terminal bromines, $C(PSt(PLLABr_2)_2)_3$ was obtained.

^{1}H NMR (300 MHz, $CDCl_3$), δ (TMS, ppm): 6.25–7.24 (aromatic protons), 5.03–5.46 [$OCH(CH_3)CO$], 4.22–4.63 [PhCHO], 3.67–3.88 [$COOCH_2$, CHOOC], 3.20–3.47 [CH_2OCH], 1.92 [$C(CH_3)_2Br$], 1.43–1.71 [$COOCH(CH_3)O$], 1.15–2.10 (CH_2, CH in main chain of PSt).

2.9. Preparation of $C(PSt(PLLA(PSt)_2)_2)_3$

Into a glass tube with a magnetic stirrer, $C(PSt(PLLABr_2)_2)_3$ (0.4 g, 0.02 mmol), CuBr (36 mg, 0.25 mmol), HMTETA (60 mg, 0.25 mmol), St (2.5 g, 24 mmol) and THF (10 mL) were added. The system was degassed via three freeze–pump–thaw cycles. The polymerization tube was sealed under vacuum, and then placed into an oil bath thermostated at 110 °C. After polymerization for a prescribed time, the mixture was cooled down to 0 °C, and the tube was opened. The mixture was diluted with THF, and this polymer solution was passed through a short column of neutral alumina to remove the metal salt. After precipitation by adding polymer solution in THF into methanol, the precipitate was collected by filtration and then dried under vacuum at 40 °C overnight. The polymer, $C(PSt(PLLA(PSt)_2)_2)_3$ was obtained with $M_n = 42200$ and $M_w/M_n = 1.21$.

^{1}H NMR (300 MHz, $CDCl_3$), δ (TMS, ppm): 6.25–7.24 (aromatic protons), 5.04–5.35 [$OCH(CH_3)CO$], 4.30–4.51 [PhCHBr, PhCHO–], 3.76–4.08 [CH_2OOC–, CHOOC], 3.18–3.38 [$CHOCH_2$] 1.19–2.29 [CH_2, CH in main chain of PSt, CH_3 in PLLA], 0.76–1.07 [CH_3CH_2 in TMBIBP, CH_3 in isobutyryl unit].

2.10. Hydrolysis of $C(PSt(PLLA(PSt)_2)_2)_3$

In order to confirm the structure of dendrimer-like copolymers, the hydrolysis of the dendrimer-like polymers was carried out in alkaline solution. A typical hydrolyzed procedure is as follows. Into a flask with a magnetic stirrer, $C(PSt(PLLA(PSt)_2)_2)_3$ (0.2 g) and 10 mL mixture of THF and KOH/H_2O (0.1 M) (v/v = 5/1) were added. After the mixture was refluxed for 24 h, the reaction solution was added into methanol; the precipitate was collected by filtration, and then dried under vacuum at 40 °C overnight. The products should be PSt formed at the first and third polymerization steps.

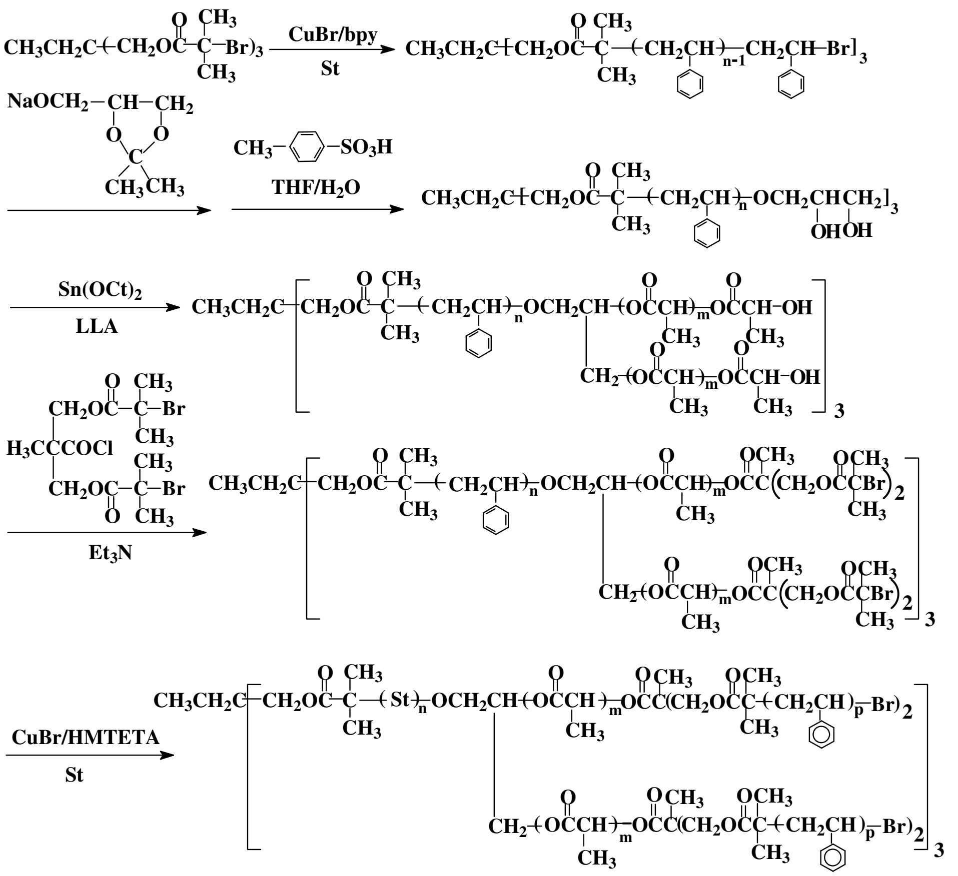
3. Results and discussion

Different from the preparation of dendrimer-like copolymers from EO and *t*-butyl acrylate, application of one type of divergent reaction cannot prepare the copolymers with PSt, PLLA and PSt as the first, the second and the third generation, respectively. Two types of divergent reactions, transformation of terminal Br to hydroxyl and terminal hydroxyl to bromine, are necessary to synthesize the dendrimer-like copolymers $C(PSt(PLLA(PSt)_2)_2)_3$, and the synthetic route is described in Scheme 1.

3.1. Preparation of three-armed PSt stars

The 1,1,1-tri(methylene-α-bromoisobutyryl)propane (TMBIBP) used in this study was prepared by the reaction of 1,1,1-trimethylolpropane (TMP) with α-bromoisobutyryl chloride (BIBC) as shown in Scheme 1. Then this trifunctional initiator was used in the ATRP of St, and the results and conditions are listed in Table 1.

The multi-armed star PSts have been synthesized by ATRP using multifunctional initiators, and the star polymerization of St demonstrated “living” nature [18–20]. The similar results were obtained in this study. The narrowly distributed three-armed star PSts (MWD = 1.11–1.14) were obtained as shown in Fig. 2. Fig. 1(b) represents its typical ^{1}H NMR spectrum. In comparison with that of its precursor in Fig. 1(a), we will find the characteristic signals of PSt at $\delta = 1.15$–2.20 and 6.30–7.36



Scheme 1. Synthesis of $C(PSt(PLLA)_2)_3$ and $C(PSt(PLLA(PSt)_2)_2)_3$ dendrimer-like copolymers.

Table 1
Results and conditions of ATRP of St by TMBIBP/CuBr/bpy[a]

No.	Time (h)	Conversion[b] (%)	M_n(th)[c]	M_n(GPC)[d]	M_n(NMR)[b]	MWD[d]
1	1.5	27	8400	7700	8100	1.11
2	2.0	34	10600	9500	10200	1.13
3	3.0	51	15900	13800	15300	1.14

[a] The polymerization was carried out at 110 °C, $[M]_0/[I]_0/[\mathrm{CuBr}]_0/[\mathrm{bpy}]_0 = 300{:}1{:}1{:}3$ (molar ratio).

[b] Calculated based on ^{1}H NMR data.

[c] $M_n(\mathrm{th}) = ([\mathrm{St}]_0/[I]_0) \times \mathrm{conversion} \times 104 + 581$, where $[\mathrm{St}]_0$ and $[I]_0$ are the initial moles of St and initiator, 104 and 581 are molecular weights of St and TMBIBP.

[d] Measured by GPC.

corresponding to methylene and methine protons in backbone of PSt, and phenyl protons, respectively. In addition, the signals of methyl protons and ester methylene protons in initiator TMBIBP appear at 0.96 (a) and 3.75 ppm (b), respectively. The signal at 4.40 ppm (e) is ascribed to the terminal methine group next to bromine. Assume that every macromolecule has one initiator residue, the number-average molecular weight (M_n(NMR)) can be calculated according to Eq. (1)

$$M_n(\mathrm{NMR}) = 3(6I_{\mathrm{Ar}}/5I_{0.96}) \times 104 + 581 \qquad (1)$$

Here I_{Ar} and $I_{0.96}$ are the integral values of the signals at $\delta = 6.30$–7.36 and 0.96 ppm, 104 and 581 are the molecular weights of St and TMBIBP, respectively. The results obtained are listed in Table 1.

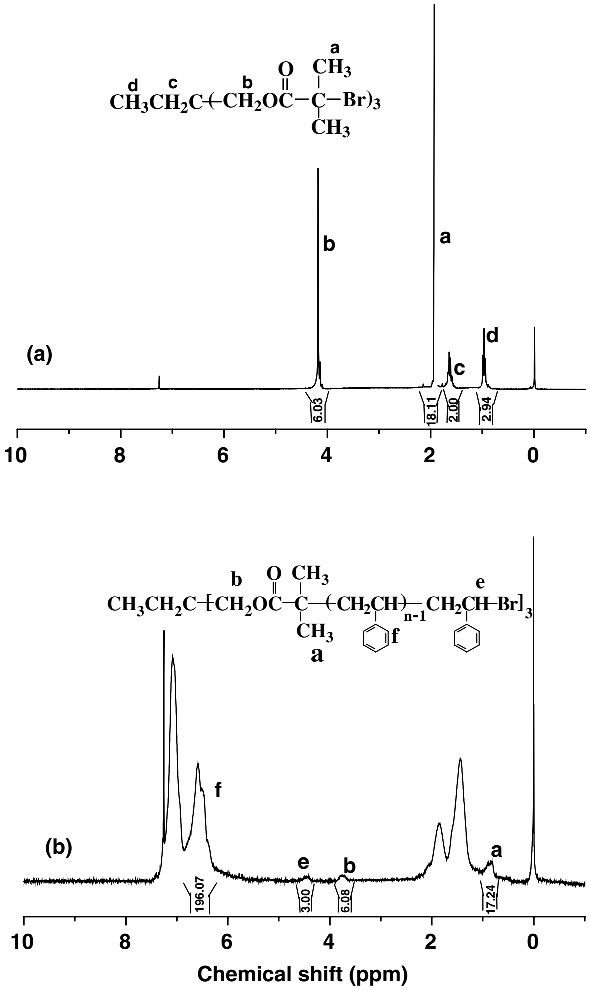


Fig. 1. ^{1}H NMR spectra of (a) TMBIBP and (b) three-armed star, $C(PSt)_3$ (No. 2 in Table 1).

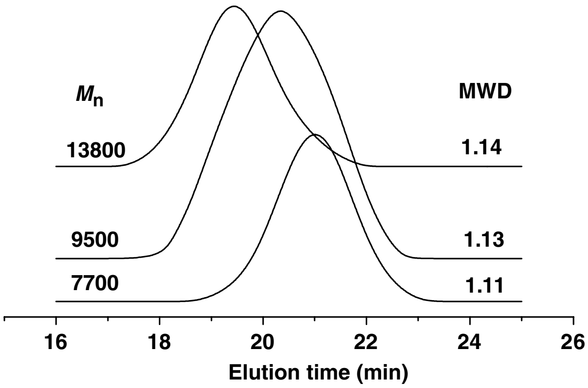


Fig. 2. GPC curves of three star PSts (Nos. 1–3 in Table 1).

The initiation efficiency of TMBIBP is high and we can control the molecular weight of the three-armed PSt by the feed molar ratio of St to initiator and conversion. All values of M_n(GPC) in Table 1 are lower than their M_n(NMR) due to compact structure of the three-armed star PSt.

For ensuring one bromine per each PSt chain, the polymerization was stopped at lower conversion ($\leqslant$51%). From the integration ratio of the signal at 4.40 (e) to that at 3.75 ppm (b), we can estimate the bromine-capped efficiency. This value (6.08/3.00) approaches their proton ratio (6/3), indicating that each PSt chain has almost one terminal bromine group.

3.2. Preparation of dendrimer-like copolymers with two generations $C(PSt(PLLA)_2)_3$

Before preparation of the second generation, a divergent reaction for transformation of the three terminal bromines into six hydroxyl groups is necessary. To ensure easier purification to get the pure dendrimer-like copolymer with two generations, selecting a reaction with higher transformation efficiency is important. We selected 2,2-dimethyl-1,3-dioxolane-4-methanol (DMDOM) as divergent agent because the protection group is easier to be removed in the acidic solution, and higher substitution reaction efficiency of DMDOM with benzyl bromide in $C(PSt\text{-}Br)_3$ was obtained. In order to ensure complete conversion, an excess of DMDPM/Na (molar ratio of DMDOM/$C(PSt\text{-}Br)_3 > 10$) was used, the unreacted DMDOM can be easily removed by passing through a short column of neutral alumina. After treatment of $C(PSt\text{-}DMDOM)_3$ with acidic solution in THF/H_2O (5/1, v/v), the six hydroxyl groups in the three-armed star PSt were recovered. Fig. 3 presents a typical ^{1}H NMR spectrum of $C(PSt(OH)_2)_3$ (No. 2 in Table 1). In comparison with ^{1}H NMR spectrum in Fig. 1(b), the signal at $\delta = 4.40$ ascribed to methine proton next to terminal bromine was replaced by the signal at $\delta = 4.45$ ppm ascribed to methine proton next to oxygen, and the protons of terminal hydroxymethylene and hydroxymethine groups appear at 3.34–3.42 (a) and 3.45–3.57 ppm (b), respectively in Fig. 3(a) except the characteristic signals of PSt. For confirming further the existence of two terminal hydroxyl groups at the each end of PSt chains, ^{1}H NMR spectrum of this sample treated with $(CF_3CO)_2O$ was measured (Fig. 3(b)). The signals a and b are shifted to new positions at $\delta = 4.33$–4.43 and 4.45–4.57 ppm, respectively, confirming further the existence of two hydroxyl

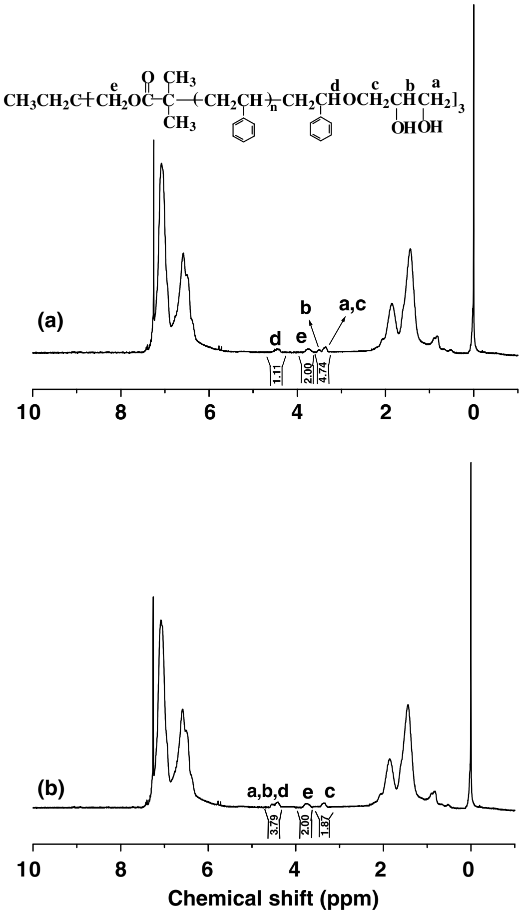


Fig. 3. ^{1}H NMR spectra of (a) three-armed star, $C(PSt(OH)_2)_3$ (No. 2 in Table 1) and (b) after treatment of the three-armed star PSt with $(CF_3CO)_2O$.

groups. Based on the integration ratios of the signals (a + b + c) to e (4.74:2) in Fig. 3(a) and the signals c–e in Fig. 3(b) (1.87:2), we can estimate that there are almost three protons of the terminal methylene and methine groups next to hydroxyl group in every PSt block.

The three-armed star polymer, $C(PSt(OH)_2)_3$ was used as initiator in the ROP of LLA with stannous 2-ethyl hexanoate as catalyst. The reaction conditions and results are listed in Table 2. The GPC trace of the resulting dendrimer-like copolymer $C(PSt(PLLA)_2)_3$ (No. 3 in Table 2) in Fig. 4(a) shows a shoulder peak at the low molecular weight position. If it is the unreacted initiator, it can be removed by precipitation of the crude product in cyclohexane for several times. Certainly, partial product will be lost. The GPC trace of the dendrimer-like copolymer $C(PSt(PLLA)_2)_3$ obtained by purification in cyclohexane is shown in Fig. 4(b). Only a single and symmetrical GPC curve was obtained, indicating that the pure dendrimer-like copolymer, $C(PSt(PLLA)_2)_3$ was obtained. GPC data listed in Fig. 4 and Table 2 demonstrate that all $C(PSt(PLLA)_2)_3$ samples have narrow MWD (1.15–1.18). For confirming further the formation of $C(PSt(PLLA)_2)_3$, their ^{1}H NMR spectra were measured. Fig. 5 represents a typical ^{1}H NMR spectrum (No. 3 in Table 2). Except the characteristic PSt signals, the LLA signals appeared at $\delta = 5.16$ ppm corresponding to ester methine proton. Based on the integration ratio of aromatic signals (I_{Ar}) to ester methine proton signal ($I_{5.16}$), the $M_{n,C(PSt(PLLA)2)3}$(NMR) can be calculated according to Eq. (2)

$$\begin{aligned} M_{n,C(PSt(PLLA)2)3}(\mathrm{NMR}) = {} & (I_{5.16}/2)/(I_{Ar}/5) \\ & \times (144/104) \\ & \times (M_{n,C(PSt)3} - 581) \\ & + M_{n,C(PSt)3}(\mathrm{NMR}) \qquad (2) \end{aligned}$$

Here 144, 104, 581 and $M_{n,C(PSt)3}$(NMR) are the molecular weights of LLA, St, TMBIBP and

Table 2
Results and conditions of ROP of LLA[a]

No.	$[M]_0/[I]_0$ (molar ratio)[b]	Conversion[c] (%)	M_n(th)[d]	M_n(GPC)[e]	M_n(NMR)[c]	MWD[e]
1	0	0	10600	9500	10200	1.13
2	70	92	19500	16800	18900	1.18
3	100	87	22700	18900	21800	1.15
4	130	88	26700	21300	25400	1.15

[a] The copolymerization was carried out at 115 °C for 24 h. The $C(PSt(OH)_2)_3$ (No. 2 in Table 1) was used as macroinitiator; $[Sn(Oct)_2]_0$:$[OH]_0 = 1:1$ (molar ratio).

[b] M = LLA, $I = C(PSt(OH)_2)_3$.

[c] Calculated based on ^{1}H NMR data.

[d] $M_n(th) = ([M]_0/[I]_0) \times conversion \times 144 + 10200$, where 144 and 10200 are molecular weights of LLA and $C(PSt(OH)_2)_3$.

[e] Measured by GPC.

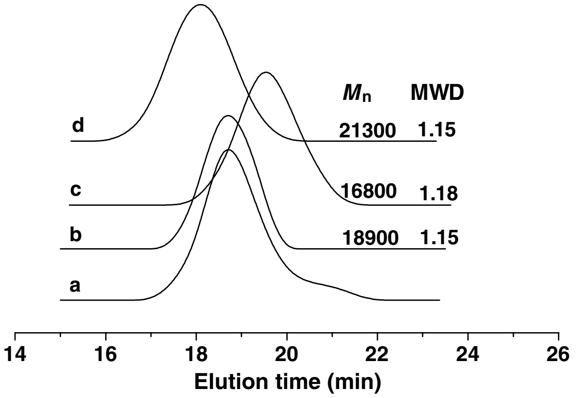


Fig. 4. GPC curves of (a) $C(PSt(PLLA)_2)_3$ (No. 3 in Table 2) before purification, (b) $C(PSt(PLLA)_2)_3$ (No. 3 in Table 2) after purification with cyclohexane, (c) $C(PSt(PLLA)_2)_3$ (No. 2 in Table 2) after purification and (d) $C(PSt(PLLA)_2)_3$ (No. 4 in Table 2) after purification.

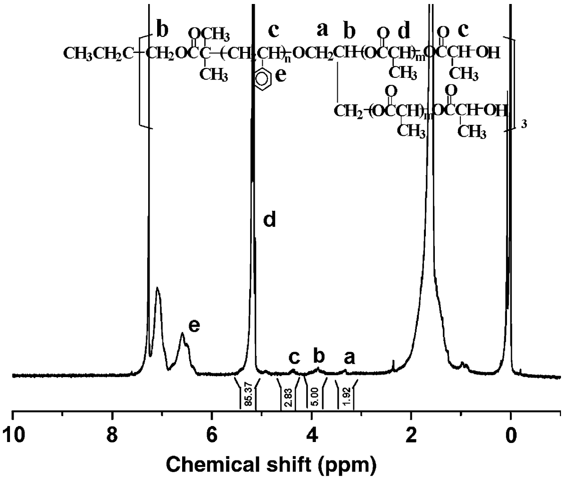


Fig. 5. ^1H NMR spectra of $C(PSt(PLLA)_2)_3$ (No. 3 in Table 2).

$C(PSt)_3$, respectively. The results calculated are listed in Table 2. Based on the integration ratio of the signal of ether methylene at 3.33 ppm (a) to that of ester methylene and methine at 3.87 ppm (b) (Fig. 5), we can judge that all the terminal hydroxyl groups took part in the initiation reaction of LLA. This ratio agrees well with the ratio of their protons (a/b = 2/5). Therefore, we can conclude the formation of $C(PSt(PLLA)_2)_3$.

3.3. Synthesis of dendrimer-like copolymers, $C(PSt(PLLA(PSt)_2)_2)_3$

Same with the preparation of the second generation, before synthesis of the third generation, a divergent reaction for transformation of the 6 terminal hydroxy groups to 12 ATRP initiating sites is necessary. BMBIBPC was selected as divergent agent because the higher yields for the esterification of alkyl alcohol with –COCl in the presence of Et_3N are generally obtained. In order to ensure complete transformation of terminal hydroxyl groups to ATRP initiating sites, an excess of BMBIBPC was used. The unreacted BMBIBPC can be easily removed by precipitation in the petroleum ether due to its better solubility of BMBIBPC. The conversion efficiency of terminal hydroxyl group to bromine group can be estimated from their ^1H NMR spectrum (Fig. 6(b)). In comparison with ^1H NMR spectrum of $C(PSt(PLLA\text{-}OH)_2)_3$ in Fig. 5, a new signal at 1.92 ppm (c) in Fig. 6(b) is ascribed to the 24 terminal methyl groups in BMBIBPC. Based on the integration ratio (11.35) of the signals c to d, the divergent reaction efficiency (>95%) can be esti-

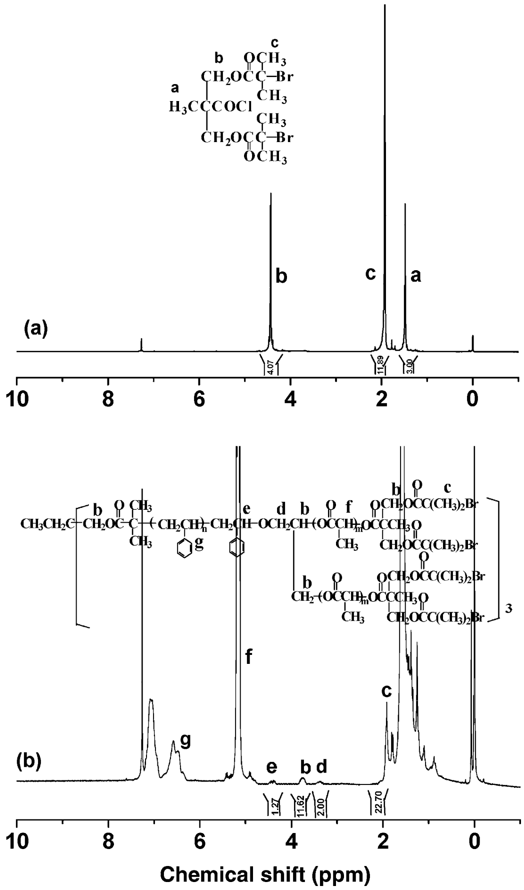


Fig. 6. ^1H NMR spectra of (a) BMBIBPC and (b) $C(PSt(PLLA\text{-}Br_2)_2)_3$ (No. 3 in Table 2).

Table 3
Results and conditions of ATRP of St using $C(PSt(PLLA\text{-}Br_2)_2)_3$/CuBr/HMTETA as initiating system[a]

No.	Time (h)	Conversion[b] (%)	M_n(th)[c]	M_n(GPC)[d]	M_n(NMR)[b]	MWD[d]
1	0	0	22700	18900	21800	1.15
2	2.5	17	43700	36000	42200	1.21
3	3.5	20	47400	38900	45500	1.27

[a] The polymerization was carried out at 110 °C, and $C(PSt(PLLA\text{-}Br_2)_2)_3$ (No. 3 in Table 2) was used as macroinitiator. $[St]_0/[I]_0/[CuBr]_0/[HMTETA]_0 = 1200{:}1{:}1{:}1$ (molar ratio).

[b] Calculated based on ^1H NMR data.

[c] $M_n(\text{th}) = ([St]_0/[I]_0) \times \text{conversion} \times 104 + M_{n,C(PSt(PLLA)2)3}$.

[d] Measured by GPC.

mated. The emphasis is that this value is not accurate because the signal c is partially overlapped.

The resultant dendrimer-like copolymers with 12 terminal ATRP initiating sites, $C(PSt(PLLA\text{-}Br_2)_2)_3$ were used as macroinitiator in the solution ATRP of St with HMTETA/CuBr as ligand and catalyst. The results and conditions are listed in Table 3.

To determine whether the third PSt generation of dendrimer-like copolymers was formed, the GPC curves of two $C(PSt(PLLA(PSt)_2)_2)_3$ samples (Nos. 2 and 3 in Table 3) are shown in Fig. 7(b) and (c). In comparison with the GPC curve of their precursor, $C(PSt(PLLA)_2)_3$ (No. 3 in Table 2) in Fig. 7(a), their molecular weights increase, which must be resulted from ATRP of St. Their ^1H NMR spectra can confirm further the formation of the third PSt generation in dendrimer-like copolymers. Fig. 8 represents a typical ^1H NMR spectrum of $C(PSt(PLLA(PSt)_2)_2)_3$, (No. 2 in Table 3). Relative to the methine proton signal of LLA unit at 5.15 ppm, the aromatic proton signals at $\delta = 6.26$–7.26 ppm increased, which must be the result of ATRP of St. From the integration ratio of the aromatic proton signals $\delta = 6.26$–7.26 ppm to $\delta = 5.15$ ppm, we can calculate the number-average molecular weight [M_n(NMR)] of the dendrimer-like copolymers with three generations according to Eq. (3)

$$M_n(\text{NMR}) = [(I_{Ar}/5)/(I_{5.15})] \times (104/144) \times M_{n,\text{PLLA}} - M_{n,\text{C(PSt)3}} + M_{n,\text{C(PSt(PLLA)2)3}} \qquad (3)$$

Here 104, 144, $M_{n,\text{PLLA}}$, $M_{n,\text{C(PSt)3}}$ and $M_{n,\text{C(PSt(PLLA)2)3}}$ are the molecular weights of St, LLA, PLLA blocks in $C(PSt(PLLA)_2)_3$, $C(PSt)_3$ and $C(PSt(PLLA)_2)_3$. The results obtained are listed in Table 3. The molecular weight can be controlled by the feed molar ratio of St to macroinitiator and conversion. The lower M_n(GPC) than M_n(NMR) is due to the impact structure of this dendrimer-like copolymers in solution.

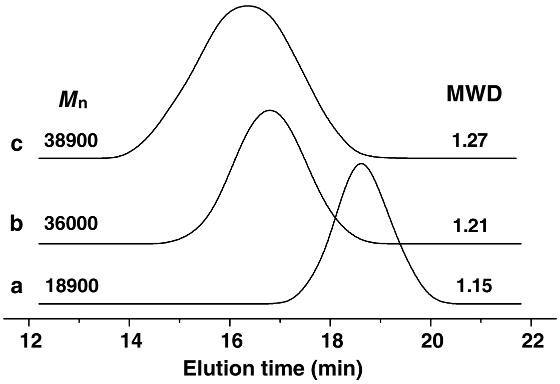


Fig. 7. GPC curves of (a) $C(PSt(PLLA\text{-}Br_2)_2)_3$ (No. 3 in Table 2), (b) $C(PSt(PLLA(PSt)_2)_2)_3$ (No. 2 in Table 3) and $C(PSt(PLLA(PSt)_2)_2)_3$ (No. 3 in Table 3).

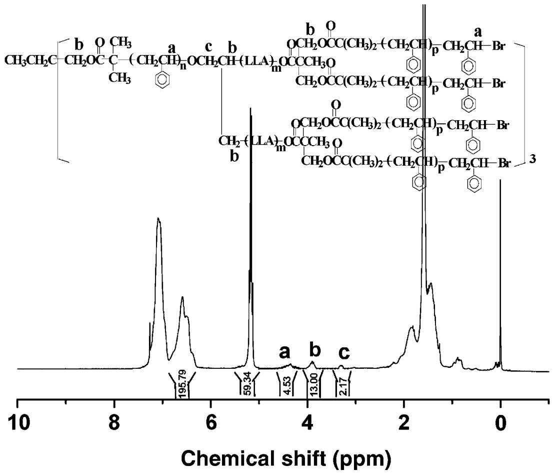


Fig. 8. ^1H NMR spectrum of $C(PSt(PLLA(PSt)_2)_2)_3$ (No. 2 in Table 3).

By analysis of the hydrolyzed product of $C(PSt(PLLA(PSt)_2)_2)_3$, we can find that the third generation has 12 PSt sub-chains. The copolymer $C(PSt(PLLA(PSt)_2)_2)_3$ was hydrolyzed in a mixture of THF and KOH/H_2O (v/v = 5:1), only one hydrolyzed product was obtained by precipitation from

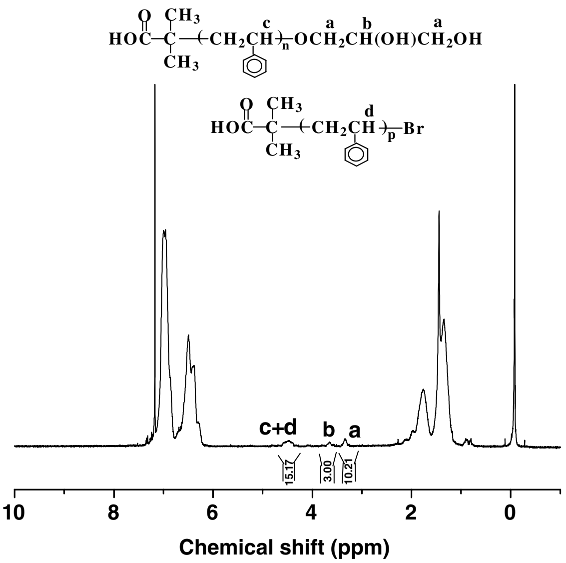


Fig. 9. ^1H NMR spectrum of the product obtained from hydrolysis of $C(PSt(PLLA(PSt)_2)_2)_3$ (No. 2 in Table 3) in alkaline solution.

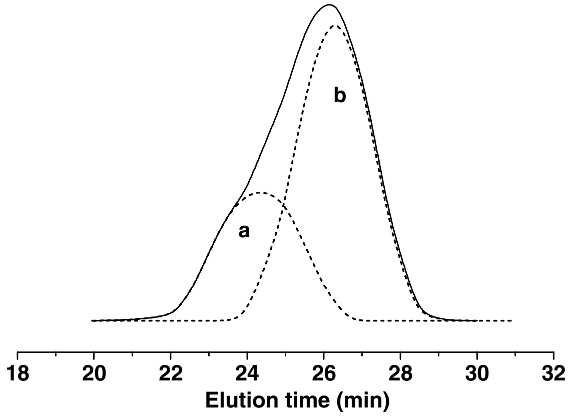
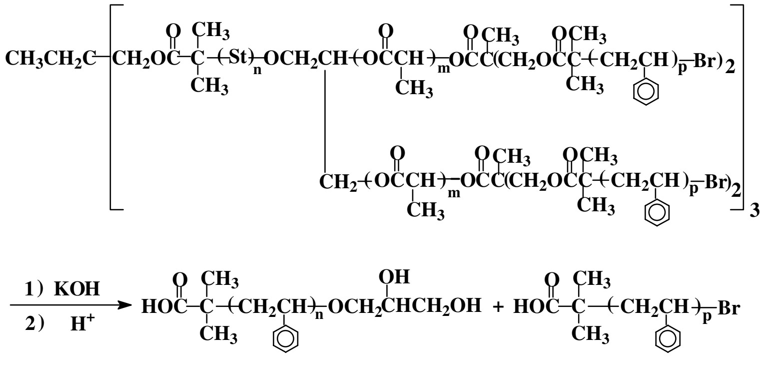


Fig. 10. GPC curve of the hydrolysis product of $C(PSt(PLLA(PSt)_2)_2)_3$ (No. 2 in Table 3) in alkaline solution.

methanol since hydrolysis of the PLLA block yielded low molecular weight compounds. From its ^1H NMR spectrum in Fig. 9, we can conclude that this hydrolyzed product is PSt. According to hydrolysis reactions in Scheme 2, there are two PSt portions, one is from the first generation with M_n(NMR) (3400) of each PSt sub-chain. Other is from the third PSt generation with M_n(NMR) (1710) of each PSt block. PLLA was hydrolyzed into soluble products that were lost during the precipitation from methanol. From its typical GPC shown in Fig. 10, we could see a shoulder peak at the high molecular weight position. By simulation, this GPC curve is composed of two GPC curves as shown in Fig. 10. The curve a at higher molecular weight position is ascribed to the PSt from the first generation. The curve b belongs to PSt from the third generation. The integration ratio (1:2) of curves a to b is consistent with their weight ratio (3400 × 3/1710 × 12), confirming further the formation of $C(PSt(PLLA(PSt)_2)_2)_3$.

3.4. Thermal behaviors

Theoretically, for block copolymers with amorphous and crystallizable blocks, three physical events, which are the microphase separation of the diblock copolymers, the crystallization of the crystallizable blocks and the vitrification of amorphous blocks, compete each other or override one over another in forming the final phase and crystalline morphologies [21]. Probably, the same will happen in this dendrimer-like copolymers composed of PSt and PLLA blocks. In this study, we investigated the thermal phase transitions using DSC measurements at heating rate of 20 °C /min and cooling rate of 10 °C/min. Their DSC data are listed in Table 4. As



Scheme 2. Hydrolysis reactions of $C(PSt(PLLA(PSt)_2)_2)_3$ dendrimer-like copolymer.

Table 4
DSC data of $C(PSt)_3$, $C(PSt(PLLA)_2)_3$ and $C(PSt(PLLA(PSt)_2)_2)_3$ obtained from heating and cooling process

Polymers[a]	Heating process at heating rate of 20 °C/min						Cooling rate: 10 °C/min		
	M_n(NMR)	T_g[b] (°C)	T_c (°C)	ΔH_c (J/g)	T_m (°C)	ΔH_m (J/g)	T_g^{PS} (°C)	T_c (°C)	ΔH_c (J/g)
$C(PSt)_3$	10200	103					92		
$C(PSt(PLLA)_2)_3$	22500	53	123	31.2 (58.6)[c]	159	−41.2 (−77.5)[c]	47	97	26.0 (48.9)[c]
$C(PSt(PLLA(PSt)_2)_2)_3$	43000	53	114	14.0 (50.8)[c]	166	−18.2 (−66.3)[c]	50	103	10.8 (39.2)[c]

[a] The polymer samples: $C(PSt)_3$ (No. 2 in Table 1), $C(PSt(PLLA)_2)_3$ (No. 3 in Table 2) and $C(PSt(PLLA(PSt)_2)_2)_3$ (No. 2 in Table 3).

[b] T_g for C(PSt)3 is T_g of PSt, for $C(PSt(PLLA)_2)_3$ and $C(PSt(PLLA(PSt)_2)_2)_3$, it is T_g of PLLA.

[c] The values in the parentheses are the correction values of ΔH_c and ΔH_m based on Eqs. (4) and (5).

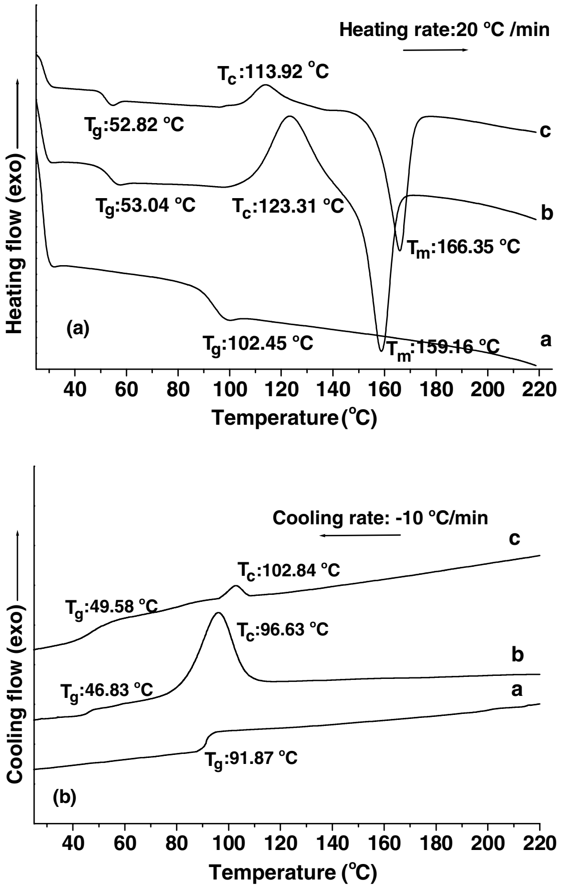


Fig. 11. DSC curves of (a) $C(PSt)_3$ (No. 2 in Table 1), (b) $C(PSt(PLLA)_2)_3$ (No. 3 in Table 2) and (c) $C(PSt(PLLA(PSt)_2)_2)_3$ (No. 2 in Table 3) in the heating process of (a) at heating rate: 20 °C/min; and in the cooling process of (b) at cooling rate: 10 °C/min.

shown in Fig. 11(a), in the heating curve (a) of $C(PSt)_3$, there is only one glass transition temperature (T_g) of PSt at 103 °C. But for the dendrimer-like copolymer with two generations $C(PSt(PLLA)_2)_3$ (b), there are three phase transition temperatures: one T_g^{PLLA} of PLLA block at 53 °C, another exothermic crystallization temperature T_c^{PLLA} at 123 °C and crystallize melting temperature T_m^{PLLA} of crystalline PLLA at 159 °C. The T_g of PSt is overlapped by crystallization of PLLA. For the dendrimer-like copolymer with three generations, $C(PSt(PLLA(PSt)_2)_2)_3$, its heating curve (c) shows three phase transition temperatures also: $T_g^{PLLA} = 53$ °C; $T_c^{PLLA} = 114$ °C and $T_m^{PLLA} = 166$ °C. As shown in Fig. 11(b), in the cooling curve (a) of $C(PSt)_3$, there is one T_g^{PS} of PSt at 92 °C. However, the cooling curve (b) of the dendrimer-like copolymer with two generations shows two phase transition temperatures: one T_g^{PLLA} of PLLA at 47 °C, other T_c^{PLLA} at 97 °C. For the dendrimer-like copolymer with three generations, its cooling curve (c) shows two phase transition temperatures also: $T_g^{PLLA} = 50$ °C; $T_c^{PLLA} = 103$ °C. If the dendrimer-like copolymers have the spheric shape similar to dendrimer, the crystalline PLLA should be in the middle layer of spheric ball. The crystallization of PLLA must be affected by the confined space between the inner and outer PSt domains in the case of $C(PSt(PLLA(PSt)_2)_2)_3$. For $C(PSt(PLLA)_2)_3$ with PSt as core and PLLA as shell, the crystallization of PLLA will be not restricted by amorphous PSt domain. Thus it is understandable that PLLA in $C(PSt(PLLA)_2)_3$ has higher T_c and lower T_m in comparison with the $C(PSt(PLLA(PSt)_2)_2)_3$ in heating flow, while in cooling flow, PLLA of $C(PSt(PLLA)_2)_3$ has lower T_c than those in $C(PSt(PLLA(PSt)_2)_2)_3$. We also measured the ΔH_m and ΔH_c of PLLA block and the results are listed in Table 4. Because the content of PLLA in the three generations dendrimer-like copolymer is much lower than that in the two generations copolymer, we corrected the ΔH_m and ΔH_c of $C(PSt(PLLA)_2)_3$ according to Eq. (4) and that of $C(PSt(PLLA(PSt)_2)_2)_3$ according to Eq. (5)

$$\Delta H_m(\Delta H_c)(\mathrm{corr}, C(PSt(PLLA)_2)_3) = \Delta H_m(\Delta H_c)/((21800 - 10200)/21800) \tag{4}$$

$$\Delta H_m(\Delta H_c)(\mathrm{corr}, C(PSt(PLLA(PSt)_2)_2)_3) = \Delta H_m(\Delta H_c)/((21800 - 10200)/42200) \tag{5}$$

where 10200, 21800 and 42200 are $M_{n,C(PSt)3}$(NMR), $M_{n,C(PSt(PLLA)2)3}$(NMR) and $M_{n,C(PSt(PLLA(PSt)2)2)3}$(NMR), respectively. The results are listed in Table 4. Obviously, the absolute values of ΔH_m(correction) and ΔH_c(correction) of PLLA in C(PSt(PLLA)$_2$)$_3$ are higher than those of C(PSt(PLLA(PSt)$_2$)$_2$)$_3$ in both heating and cooling flows. Thus the crystallization of PLLA in C(PSt(PLLA)$_2$)$_3$ is better in comparison with that in C(PSt(PLLA(PSt)$_2$)$_2$)$_3$, because the PLLA between two PSt domains can not be well crystallized.

4. Conclusion

The dendrimer-like copolymers with two and three generations have been successfully synthesized by ATRP of St in the preparation of the first and the third generations, and ring-opening polymerization of LLA in the preparation of the second generation. The divergence at the chain ends of the first and the second generation polymers can be realized by the reaction of terminal bromine with divergent reagent, DMDOM/Na and by the esterification reaction of terminal hydroxyl group with BMBIBPC respectively. In order to ensure the divergent reactions as complete as possible, using excess of the divergent agents in the reactions is necessary, and the unreacted divergent agents can be removed during precipitation of the polymers in an appropriate solvent. The reactivity difference of the primary and secondary hydroxyl groups in C(PSt(OH)$_2$)$_3$ was not observed in the ring-opening polymerization of LLA. DSC studies demonstrate that the absolute values of ΔH_m and ΔH_c of C(PSt(PLLA)$_2$)$_3$ are higher than those of C(PSt(PLLA(PSt)$_2$)$_2$)$_3$ in both heating and cooling flows, which implies that the crystallization of PLLA in C(PSt(PLLA)$_2$)$_3$ is better than that in C(PSt(PLLA(PSt)$_2$)$_2$)$_3$.

Acknowledgement

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