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Synthesis and Characterization of Dendritic Star Poly(L-Lactide)s

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Summary

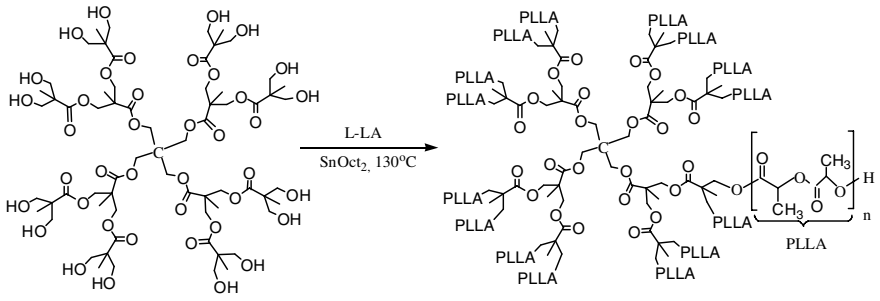
Dendritic star poly(L-lactide)s (PLLAs) were prepared by ring opening polymerization using a hyperbranched aliphatic polyester as the core. The stars were characterized by gel permeation chromatography (GPC) and nuclear magnetic resonance spectroscopy (NMR). The result shows the star PLLAs have narrow molecular weight distribution and the length of arms can be well controlled in terms of the molar ratios of L-lactide to the initiator. The structure and thermal properties of the star polymers were investigated by means of X-ray diffraction (XRD) and differential scanning calorimetry (DSC). XRD shows that the formation of star structure does not alter the structure of crystal of PLLA. The results of DSC indicate that the glass transition temperature (T_g) and the crystallinity of the star polymers increased with increasing the lengths of arms. It is identified that the crystallization of PLLA was effectively suppressed by the formation of star topology.

Introduction

Poly(L-lactide) is an important biodegradable thermoplastic polyester, which has potential applications in wound closure, surgical implants, scaffolds and delivery of drugs [1-3] due to its biodegradability [4,5], biocompatibility and good mechanical properties [6]. However, PLLA possesses some inherent drawbacks such as high crystallinity and low rate of degradation, which greatly limit its application in drug release system [7,8]. Therefore, modifications are necessary before this polymer is successfully used. In general, the modification of structure and properties of PLLA can be achieved *via* copolymerization or physical blending. It was reported that physical blending of PLLA with poly-D,L-lactic acid (PDLLA) or poly(ε-caprolactone) (PCL) can effectively suppress the crystallization of PLLA and thus endow PLLA with improved toughness, which is required for orthopedic or dental applications [9]. Alternatively, LLA was employed to copolymerize with other monomers such as glycolide [10]. Recently, it is recognized that the formation of some specific macromolecular topologies such as star-shaped, comb-shaped and dendritic structures are also favorable to improve the properties of PLLA and to extend the application fields of PLLA.

Dendritic polymers including hyperbranched polymers and dendrimers have attracted considerable attention due to their unique properties such as low melt viscosity, compared to the linear polymer with identical molecular weight [11,12]. The dendritic polymers with functional groups can be used as core molecules to prepare star polymers with numerous arms *via* so-called "core-first" [13,14,15] or "arm-first" [16,17] approaches. The "core-first" approach has been proved to be efficient to access star aliphatic polyesters such as PLLA and PCL *via* sequential ring-opening polymerization [18,19]. Hult, *et al.* synthesized a series of star PCL using a series of hyperbranched polyesters, and studied their properties and potential applications. [20-22]. Nunez, *et al.* extensively studied the crystallisation, melting, crystal unit cell, crystalline superstructure and single crystal morphology of star-branched PCL [19,23,24]. Recently, Xi, *et al.* [25] reported a new star PLLA prepared using a branched poly(amidoamine) (PAMAM) and found that the star PLLA had higher hydrophilicity and faster degradation rate than the linear PLLA with similar molecular weight. These star PLAs have been characterized by liquid chromatography at the critical conditions and by fluorescence [26-28].

In this work, an aliphatic hyperbranched polyester containing 16 hydroxyl groups (Scheme 1) was used as an initiator to prepare star PLLA by ring-opening polymerization. The star PLLA was characterized by gel permeation chromatography (GPC) and nuclear magnetic resonance (NMR). The thermal properties and crystal structure of the star PLLA were systemically investigated by wide-angle X-ray diffraction (WAXD) and differential scanning calorimetry (DSC).



Scheme 1. Preparation of star PLLA

Experimental

Materials

L-Lactide (LLA) was obtained from Shanghai Newgenius Biotech Co. Ltd, China. Before use, it was re-crystallized with anhydrous ethyl ester, and then dried *in vacuo* at room temperature. The alipahitic hyperbranched polyester was kindly supplied by Perstorp Specialty Chemicals, Sweden under a trade name of Boltorn H20 and it has a quoted molecular weight of M_n = 1,747 g/mol and 16 terminal hydroxyl groups; its dendritic structure is shown in Scheme 1. Stannous (II) octanoate [$Sn(Oct)_2$] was of analytically pure grade, purchased from Shanghai Reagent Co., Shanghai, China and was used as received. The solvents such as chloroform, tetrahydrofuran (THF), petroleum ether and toluene were obtained from commercial sources. Prior to use, toluene was purified by distillation over CaH_2. All the reagents without special

specification were obtained from Shanghai Reagent Co., Shanghai, China. Linear poly(L-lactide) was supplied by Cargill-Dow Co. with a quoted molecular weight of M_w = 80,000, M_w/ M_n = 1.9.

Synthesis of Star Poly(L-lactide)

The desired amount of Boltorn H20 and L-lactide were charged to a round-bottom flask equipped with a magnetic stirring bar. This flask was connected to a standard Schlenkline system and was degassed and then refilled with highly pure nitrogen. The exhausting-refilling process was repeated three times before liquid reagent was added. The catalyst in toluene solution was added to the system in terms of the ratio of [$Sn(Oct)_2$] to [LLA] of 1/1,000 (wt). The polymerization was carried out at 130°C for 24 hours. The crude product was dissolved in dichloromethane and precipitated with excessive petroleum ether. The precipitates were dried *in vacuo* at 45°C for 24 hours.

Measurement and Characterization

The ^{1}H NMR spectrum was measured using a Varian Mercury Plus 400 NMR spectrometer at room temperature with $CDCl_3$ as solvents. Tetramethylsilane (TMS) was used as an internal reference. The molecular weight and molecular weight distribution were measured on a Waters 150C gel permeation chromatograph equipped with microstyragel columns at 35°C. Tetrahydrofuran (THF) was used as the eluent at a flow rate of 1.0 mL/min, and standard polystyrenes were used as calibration of molecular weights. The calorimetric measurements were performed on a Perkin Elmer Pyris 1 differential scanning calorimeter in a dry nitrogen atmosphere. The instrument was calibrated with standard Indium. The first scans were performed from 0 to 200°C at the heating rate of 20°C/min and were hold at 200°C for 3 min to melt the crystals, followed by quickly quenching to 0°C and then, the second heating scans were carried out from 0 to 200°C at the heating rate of 20°C/min. X-ray diffraction patterns were obtained by using a Rigaku D/max γ X-ray diffractometer equipped with graphite mono-chromatized Cu Kα radiation (λ = 0.154178 nm). The scanning range was from 5 to 60° and a scanning rate of 2°/min was used in all cases.

Results and discussion

In this work, the star PLLAs were prepared *via* ring-opening polymerization of L-lactide and the polymerization was carried out at 130°C for 24 h with $Sn(Oct)_2$ as a catalyst. The hyperbranched aliphatic polyester (Boltorn H20) containing 16 terminal hydroxyl groups was used as an initiator to afford a star topology of PLLA. The PLLA stars with various arm lengths were prepared by controlling the molar ratios of the monomer (LLA) to the initiator. The samples with five arm lengths were denoted as DPLLA1, DPLLA2, DPLLA3, DPLLA4 and DPLLA5 (Table 1). Representatively shown in Figure 1 is the ^{1}H-NMR spectrum of DPLLA1. Since the arm length of DPLLA1 is the shortest among the five samples, and the terminal protons signal of PLLA and protons signal of core molecule can easily be discerned. The resonances at about 1.57 ppm (a) and 5.16 ppm (b) are ascribed to the protons of methyl and methine groups in PLLA main chains, respectively. Moreover, the signal at 4.35 ppm (b'), corresponding to the terminal methine protons of PLLA

(HOC*H*(CH_3)-) of star PLLA can be also identified. The resonance at about 1.22 ppm (c+c') and 4.20 ppm (d+d') were respectively assigned to the protons of methyl groups and methylene groups of Boltorn H20. In addition, the terminal methylene protons signals at about 3.45 ppm of Boltorn H20 (HOCH_2-) disappeared in this spectrum. The fact that the resonance of the protons from the core molecule Boltorn H20 is discernible is an indicative of the presence of dendritic structural units in the polymer. The ^{1}H NMR spectroscopy indicates that the resulting products were combined the structural features from Boltorn H20 and PLLA. It should be pointed out that the NMR spectra of the star PLLAs can not be employed to estimate the molecular weights of the polymers since there are some overlaps between the resonance of the methine protons of PLLA and that of methylene protons of core moiety. In addition, the terminal methine protons signal [HOC*H*(CH_3)-] of star PLLA with higher molecular weight is hard to be identified. In this work, the molecular weights of the star PLLA were determined by means of gel permeation chromatography (GPC).

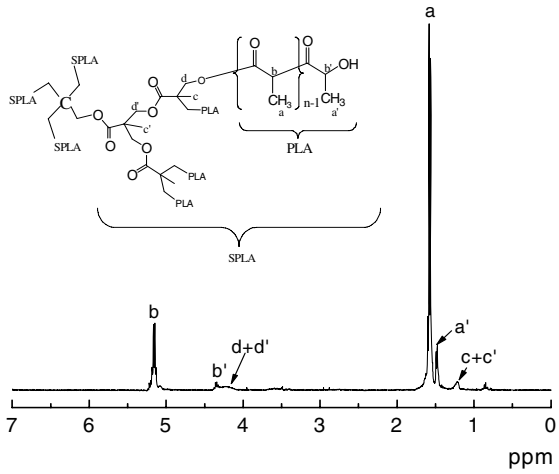


Fig. 1. ^{1}H-NMR spectrum of DPLLA1

Shown in Figure 2 are the GPC curves of the star PLLAs and the results of polymerization were summarized in Figure 3 and Table 1. From Figure 3, the molecular weight of the star PLLA linearly increased with increasing the molar ratios of LLA to Boltorn H20, indicating that the molecular weight of star PLLA can be well controlled in terms of the feed ratios. It is noted that from Table 1, the arm lengths of the star PLLA determined by GPC are close to the predicted. It should be pointed out that actual molecular weight of PLA could be considerably lower than those determined with polystyrene calibration in GPC measurement [29,30] since star polymers possess lower hydrodynamic volume than the linear counterpart with identical molecular weights. Therefore, while the molecular weights of star polymers are measured by means of GPC, the values of lower molecular weights could be obtained than their linear counterparts. Moreover, star topology of these polymers could complicate the measurements of GPC. The interactions between terminal functional groups of star-shaped polymers and stationary phase of GPC are

pronounced for the stars with low molecular weights. In this case, the GPC results could give the values of molecular weights than their linear counterparts. The above two factors could simultaneously contribute to the experimental values of molecular weights. It is the above factors affecting the GPC measurements that result in the molecular weights of star-shaped polymer measured by GPC can be lower or higher than the predicted depending on molecular weights of star polymers [31-33]. It is of interest to note that in the present case, the values of the molecular weights for the star-shaped polymer measured by GPC are quite close to the values predicted in terms of feed ratios and yields. The symmetry and unimodal peaks of GPC curves (Figure 2) suggest that no detectable homopolymers were formed during the ring-opening polymerization. It should be pointed out that the observation that the polydispersity values of all these dendritic star PLAs are in the range of 1.2 to 1.3 unnecessarily indicates that the molecular weight distribution of the individual arm lengths is also narrow [11,34].

Table 1. Characterization of dendrimer-like PLLA synthesized by ring-opening polymerization of L-lactide using hyperbranched polyester initiators and $Sn(Oct)_2$ catalyst in bulk at 130°C, 24 hours. [LLA]/[$Sn(Oct)_2$] = 1000/1.

Samples	[L-LA]/[I][a]	$M_{n,GPC}$	$M_{n,GPC}^{arm,b}$	$M_{n,th}$[c]	$M_{n,th}^{arm,d}$	M_w/M_n[e]	Yield (%)
DPLLA1	111/1	17,800	1112	17,174	1073	1.20	96.4
DPLLA2	278/1	38,800	2424	39,550	2472	1.19	94.5
DPLLA3	556/1	75,600	4725	78,710	4919	1.31	96.2
DPLLA4	833/1	119,700	7484	119,710	7482	1.30	98.3
DPLLA5	1111/1	157,700	9858	149,750	9359	1.25	92.5

[a] molar ratios of monomer to initiator;
[b] the arm length of DPLLA measured by GPC, $M_{n,GPC}^{arm} = M_{n,GPC}^{arm}/16$;
[c] $M_{n,th}$ means the theoretical number-average molecular weight, $M_{n,th} = [LLA]/[I] \times M_{LLA} \times Yield + M_{boltorn,\ H20.}$;
[d] the arm length of DPLLA calculated by the theoretical number-average molecular weight, $M_{n,th}^{arm} = M_{n,th}/16$;
[e] molecular weight distribution determined by GPC.

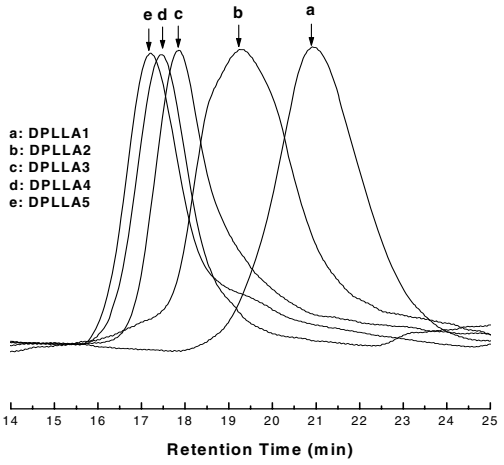


Fig. 2. GPC curves of star PLLA

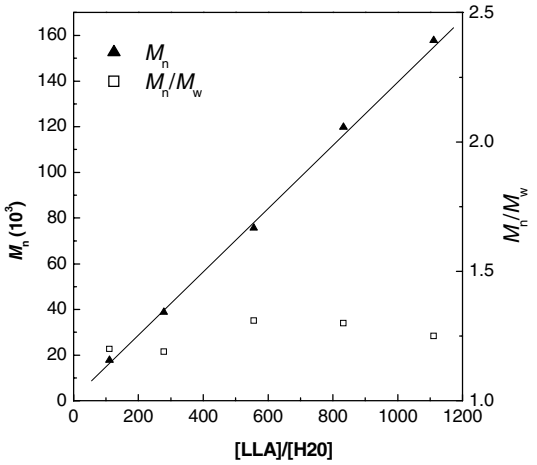


Fig. 3. Plots of molecular weight and molecular weight polydispersity for the star PLLA as functions of molar ratio of LLA to the initiator.

Figure 4 shows the X-ray diffraction patterns of linear PLLA (LPLLA) and DPLLA3. LPLLA shows an intense diffraction peak at 8.4° and two smaller ones at 9.5° and 11.2°, which corresponds to the typical diffraction of PLLA [35]. It is noted that the similar XRD patterns were obtained for star PLLA, indicating that the formation of star topology does not alter the structure of PLLA crystals. However, the intensity of diffraction peak for star PLLA is obviously lower than that of LPLLA, due possibly to the lower crystallinity for the star PLLA.

The thermal properties of the star PLLA were investigated by means of DSC. Shown in Figure 5a are the first heating scans for the as-prepared samples. The glass transition temperature (T_g) of DPLLA1 was *c.a.* 30°C, which is quite lower than that of the linear control PLLA (*c.a.* 60°C). With increasing the arm length, the T_g's of the

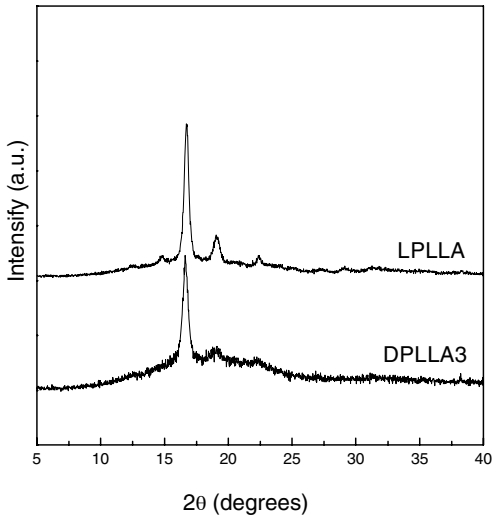


Fig. 4. X-ray diffraction patterns of linear PLLA and DPLLA3

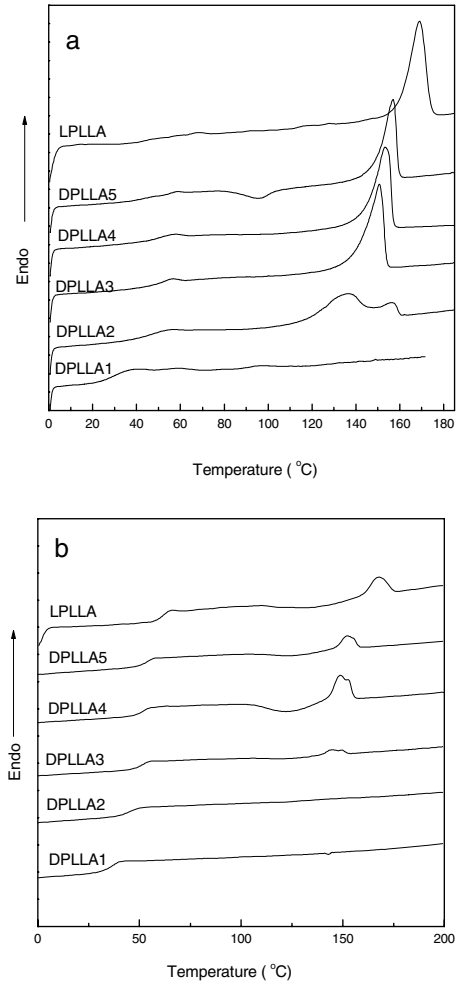


Fig. 5. DSC Curves of star PLLAs. (a): the first heating scan; (b): the second heating scan for the quenched samples.

star PLLA increased and attained a constant value. It is worth noticing that the star PLLA displayed lower T_g's than the linear counterpart with the comparable molecular weights. The glass transition temperatures are close to that of control PLLA only for the star polymers with sufficiently high molecular weights (*e.g.*, DPLLA4 and DPLLA5). The behavior of glass transition temperature could be responsible for the specific topology of star PLLA. In the star polymers; there exist more free ends of chains than the linear counterpart with the same molecular weight. These free ends contribute to the increase in free volume of polymers and thus lower glass transition temperatures are displayed.

Returning to Figure 5a, it is seen that DPLLA1 did not show crystallinity. Nonetheless, the melting transitions were detected for the dendritic stars with the higher molecular weights, indicating the presence of PLLA crystals. For DPLLA2, the dual melting transitions at 136°C and 156°C were observed under the commonly used

heating rate (*e.g.*, 20°C/min) for the quenched sample. The dual melting behavior is attributed to melting of the initial crystals followed by re-crystallization and final melting of the crystals grown during the heating scan [36]. The fact that the dual melting transitions occurred even during the fast heating process implies that the crystallization rearrangement was slowed down by the formation of the star-shaped topological structure. For DPLLA3, DPLLA4 and DPLLA5, only single sharp melting transitions were observed and the melting temperatures (T_m) increase with increasing the length of arms, indicating that the crystallinity of the star PLLA increases with increasing the lengths of arm. However, the crystallinity of the dendritic stars is much lower than that of their linear counterpart with the comparable molecular weight.
Figure 5b shows the DSC curves of the second scans for the quenched samples. For DPLLA2, it is noted that no melting transition was displayed in the DSC curve although the melting transition was discernible in the DSC curve of the as-prepared sample, suggesting that the crystallization of DPLLA is quite too slow to be detected. For the star PLLA with the higher molecular weight (*viz*. DPCLA3 and DPCLA4), the intensity of the melting peaks also became lower than those in the first scanning, which is in marked contrast to the linear counterpart with identical molecular weights.

Conclusions

The star PLLA was successfully prepared by ring opening polymerization with an aliphatic hyperbranched polyester as the core. The molecular weight of the star PLLA can be controlled in terms of the molar ratios of the monomer (LLA) to the initiator. The star PLLAs were characterized by means of nuclear magnetic resonance spectroscopy (NMR), gel permeation chromatography (GPC), X-ray diffraction (XRD) and differential scanning calorimetry (DSC). The X-ray diffraction indicates that the formation of star topological structure does not alter the structure of crystals of PLLA, but the degree of crystallization of the star PLLA is lower than that of the linear counterpart with identical molecular weights. The glass transition temperature and the crystallization of the star PLLA increase with increasing the molecular weights of the samples. It is noted that the crystallization of PLLA can be effectively suppressed by the formation of the star structure.

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