

Synthesis of Poly(D,L-lactic acid) Modified by Triethanolamine by Direct Melt Copolycondensation and Its Characterization

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ABSTRACT: Using D,L-lactic acid (LA) and multifunctional group compound triethanolamine (TEA) as starting materials, a novel biodegradable material poly(D,L-lactic acid-triethanolamine) [P(LA-TEA)] was directly synthesized by simpler and practical melt polycondensation. The appropriate synthetic condition was discussed in detail. When the molar feed ratio LA/TEA was 30/1, the optimal synthesis conditions were as follows: a prepolymerization time of 12 h; 0.5 weight percent (wt %) SnO catalyst; and melt copolycondensation for 8 h at 160°C, which gave a novel star-shaped poly(D,L-lactic acid) (PDLLA) modified by TEA with the maximum intrinsic viscosity $[\eta]$ 0.93 dL g⁻¹. The copolymer P(LA-TEA) as a different molar feed ratio was characterized by $[\eta]$, Fourier transform infrared

spectroscopy (FTIR), proton nuclear magnetic resonance (¹H-NMR), gel permeation chromatography (GPC), differential scanning calorimetry (DSC), and X-ray diffraction (XRD). Increasing the molar feed ratio of LA/TEA, T_g and M_w increased. However, all copolymers were amorphous, and their T_g (12.2°C–32.5°C) were lower than that of homopolymer PDLLA. The biggest M_w was 9400 Da, which made the biodegradable polymer be potentially used as drug delivery carrier, tissue engineering material, and green finishing agent in textile industry. © 2010 Wiley Periodicals, Inc. *J Appl Polym Sci* 119: 1883–1888, 2011

Key words: biodegradable; copolymerization; drug delivery systems; melt; polycondensation; synthesis

INTRODUCTION

Because of its excellent biodegradability, poly(lactic acid) (PLA) is a representative synthetic polymer based on the resources independent of petrochemicals. Now, the bioplastics, PLA, is a promising general-purpose plastic, which could be used as packaging materials to reduce environmental pollution.^{1,2} At the same time, the excellent biocompatibility make the nontoxic PLA be applied in the biomedicine field, such as medical–surgical suture, injection capsule, bone fixation material, wounds dressing, ophthalmic implantation material, tissue engineering scaffolds, and drug delivery microspheres.^{1,3,4}

However, some shortcomings of PLA limit its extensive application in the biomedicine field. For example, its hydrophilicity should be improved, and one of the conventional methods is the modification of

PLA by the compounds with amino group, especially amino acid.^{5–7} Even so, there is no any report on the modification of PLA with triethanolamine (TEA). At the same time, how to exploit the new potential application of the modified PLA is also noticeable.

TEA is a multifunctional group compound with three hydroxyl groups and an amino group. Its amino basicity, strong hydrophilicity, and hydroxyl reaction performance make it to form ester with a variety of higher fatty acid, and the products are biodegradable surfactants, which could be used as the green softening, fabric conditioning agent, and so on.^{8–11} Therefore, it is possible to get a novel PLA material with the improved hydrophilicity by the modification of TEA.

In this article, based on our previous work on the direct melt polycondensation of LA,^{3,6,12–16} poly(lactic acid-co-triethanolamine) [P(LA-TEA)] was synthesized for the first time using TEA as a comonomer for PLA (Scheme 1), and the copolymer was characterized by means of intrinsic viscosity ($[\eta]$), FTIR, ¹H-NMR, GPC, DSC, and XRD.

EXPERIMENTAL

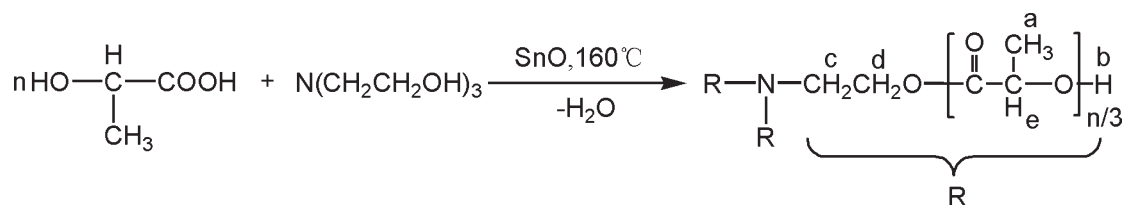
Materials

All chemical reagents, including TEA (analytic reagent), stannous chloride (analytic reagent), D,L-lactic acid (D,L-

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Scheme 1 The synthetic route of P(LA-TEA).

LA) (analytic reagent), were purchased from Guangzhou Chemical Reagent Factory (Guangzhou, China), and used without further purification.

Instrumental Analysis and Measurements

$^1\text{H-NMR}$ spectra were recorded with a Varian NMR system 400 MHz (USA) with CDCl_3 as solvent and TMS as internal standard. IR spectra were obtained from an FTIR spectrometer (Bruker Vector 33, Ettlingen, Germany) by the KBr salt slice method.

The intrinsic viscosity ($[\eta]$) of PLA modified by TEA was determined with Ubbelohde viscometer (Cannon-Ubbelohde, State College, PA) by the single-point method using CHCl_3 as solvent at 25°C . According to the literatures,^{17–19} the relative molecular weight and molecular weight distribution of the modified PLA were determined by gel permeation chromatography (Waters 1515 pump, Torrance, CA) with tetrahydrofuran as solvent and with polystyrene as reference at 35°C and a flow velocity of 1 mL min^{-1} .

DSC was performed with Perkin-Elmer DSC7 thermal analyzer (Perkin-Elmer, Cetus Instruments, Norwalk, CT) at a heating rate of $10^\circ\text{C min}^{-1}$ under an argon atmosphere (flow velocity, 20 mL min^{-1}). XRD was investigated with Rigaku D/max-1200X X-ray diffractometer (Dandong, China) using $\text{Cu-K}\alpha$ radiation with a wavelength of $1.5406 \times 10^{-10} \text{ m}$, and scanning range $2\theta = 5^\circ\text{--}45^\circ$ at a scanning speed of 0.3 deg min^{-1} .

Melt Copolymerization

According to our previous research on the melt homopolymerization/copolymerization of LA,^{3,6,12–16} LA and TEA should be prepolymerized before copolymerization. After LA and TEA were uniformly mixed as preplanned molar feed ratio, the mixture was directly dehydrated for a preplanned time at 140°C under 4000 Pa in a flask equipped with mechanical stirring and thermometer.

After prepolymerization, the selected catalyst was added in according to the weight percent (wt %) of dehydrated reactants. Then, the melt copolymerization was carried out at a certain temperature (140°C – 180°C) and an absolute pressure of 70 Pa for 4–12 h. When the reaction finished, the product was purified by the dissolution in CHCl_3 and the subse-

quent precipitation by CH_3OH , and a white powder ordinarily yielded after drying *in vacuo*.

RESULTS AND DISCUSSION

Optimal Synthetic Conditions for P(LA-TEA)

The optimal synthetic conditions for P(LA-TEA), including the influences of catalyst kinds, prepolymerization time, polymerization time, and temperature on the $[\eta]$ of P(LA-TEA), was first investigated. Catalyst played an important role in the direct melt polycondensation of LA, and usually tin catalysts gave the best effect for their good dispersibility in the reaction system.^{20–22} The influences of different catalysts on reaction are shown in Table I, and the results are similar to those of the reported literatures.^{12–16,20–22} Although the reaction catalyzed by zinc chloride (Table I, Run 3) gave the biggest yield (65.3%), the $[\eta]$ was smaller than that using SnO as the catalyst (Run 2). Thus, SnO was selected for the following experiments because the catalyst was most likely to generate bigger molecular weight.

According to the report by Moon et al.,²⁰ during the melt polymerization of LA, the prepolymerization was very important for the dehydration. The influences of different prepolymerization time on reaction are shown as Table II. It was obvious that the $[\eta]$ reached a maximum after the reaction lasted for 12 h (Run 5). When the prepolymerization time was less than 12 h, the prepolymerization was insufficient (Table II, Run 4). Once the time was more than 12 h, the total polycondensation time was too long to get larger $[\eta]$ (Table II, Run 6) mainly because of the thermal decomposition of the product.²³ Thus, the appropriate time should be 12 h.

The influences of different melt polymerization temperature on reaction are shown as Table III. Obviously, the optimal temperature was 160°C (Table III, Run 3). The lower temperature was disadvantageous for the polycondensation to remove the produced water from the reaction system. Increasing the temperature to 160°C yielded the biggest $[\eta]$ (0.93 dL g^{-1}). When the temperature was higher than 160°C , the side reactions such as oxidation and thermal degradation, especially the latter markedly took place.^{13–16,23} So, the $[\eta]$ decreased markedly

TABLE I
The Influences of Catalysts on Reaction^a

Run	Catalysts	$[\eta]$ (dL g ⁻¹)	Yield (%)
1	SnCl ₂	0.25	60.4
2	SnO	0.73	49.7
3	ZnCl ₂	0.51	65.3
4	ZnO	0.36	57.5
5	TSA	0.34	63.3

^a All runs were polymerized with a molar feed ratio LA/TEA of 30/1, a prepolymerization temperature of 140°C, a prepolymerization time of 8 h, a polycondensation temperature of 160°C, a polycondensation time of 8 h, and a catalyst quantity of 0.5 wt % (weight percent).

(Table III, Run 4). Even when the temperature was 180°C, the product became brown and viscous.

The influences of melt polycondensation time on the $[\eta]$ of P(LA-TEA) are shown in Table IV. It could be seen that the $[\eta]$ reached a maximum after the reaction lasted for 8 h (Table IV, Run 3). When the time was too shorter, polymerization was not sufficient. However, once the reaction time was longer than 8 h, the thermal degradation and/or oxidation of the polymer became serious,^{13–16,23} which made the $[\eta]$ dropped and the color of the purified product become yellow or brown. In these cases, 8 h was selected as the appropriate time in our experiments.

Therefore, when the molar feed ratio of LA/TEA was the same as 30/1, the optimal synthetic conditions for P(LA-TEA) was as follows: catalyst 0.5 wt % SnO, prepolymerization time 12 h, and the melt copolycondensation at 160°C for 8 h. Using the product synthesized at this conditions as a sample, the structure of P(LA-TEA) was characterized by FTIR and ¹H-NMR.

Structure Characterization of P(LA-TEA)

The structure of P(LA-TEA) was characterized using FTIR. Even the molar feed ratio LA/TEA was different, the IR data of the serial P(LA-TEA) were almost same. The data of P(LA-TEA) synthesized at the

TABLE II
The Influences of Prepolymerization Time on Reaction^a

Run	Time (h)	$[\eta]$ (dL·g ⁻¹)	Yield (%)
1	4	0.34	54.6
2	6	0.60	63.3
3	8	0.73	49.7
4	10	0.88	60.4
5	12	0.93	48.7
6	14	0.55	76.0

^a All runs were polymerized with a molar feed ratio LA/TEA of 30/1, a prepolymerization temperature of 140°C, a polycondensation temperature of 160°C, a polycondensation time of 8 h, and 0.5 wt % SnO as the catalyst.

TABLE III
The Influences of Melt Polymerization Temperature on Reaction^a

Run	Temperature (°C)	$[\eta]$ (dL g ⁻¹)	Yield (%)
1	140	0.25	64.3
2	150	0.27	68.2
3	160	0.93	48.7
4	170	0.44	77.9
5	180	0.42	72.1

^a All runs were polymerized with a molar feed ratio LA/TEA of 30/1, a prepolymerization temperature of 140°C, a prepolymerization time of 12 h, a polycondensation time of 8 h, and 0.5 wt % SnO as the catalyst.

molar feed ratio LA/TEA of 30/1 were obtained as follows. IR (KBr, cm⁻¹): 753.65, the absorption of —CH₂CH₂— in TEA segment; 1091.43, 1194.39, strong, the absorption of C—O—C in ester group and C—N in TEA segment; 1382.11, 1456.26, the absorption of the saturated C—H in copolymer, including CH₃, CH₂, and CH; 1755.77, strong, the absorption of ester carbonyl C=O in copolymer; 2946.20, 2996.15, the absorption of the saturated C—H in copolymer, including CH₃ and CH₂; 3405.79, weak, the absorption of terminal OH in copolymer (Fig. 1).

The structure of P(LA-TEA) was also characterized with ¹H-NMR. Though the molar feed ratio LA/TEA was different, the chemical shift data of CH, CH₂, and CH₃ were similar. Using P(LA-TEA) synthesized at the molar feed ratio LA/TEA of 30/1 as a representative (Fig. 2), the data of ¹H-NMR were obtained as follows. ¹H-NMR (CDCl₃ as solvent and TMS as internal standard, δ , ppm): 1.55, H_a, CH₃ in LA unit; 2.84, H_b, terminal OH in copolymer; 3.76, H_c, NCH₂ in TEA segment; 4.17, H_d, OCH₂ in TEA segment; 4.37, H_e, CH in terminal LA segment; 5.17, H_e, CH in LA unit.²⁴ Therefore, the structure of P(LA-TEA) was demonstrated by FTIR and ¹H-NMR as the illustrated in Scheme 1.

GPC Characterization of P(LA-TEA)

The GPC results showed that when LA/TEA was 30/1, the GPC flow curve had only a single

TABLE IV
The Influences of Melt Polymerization Time on Reaction^a

Run	Time (h)	$[\eta]$ (dL g ⁻¹)	Yield (%)
1	4	0.28	76.0
2	6	0.47	76.0
3	8	0.93	48.7
4	10	0.70	64.3
5	12	0.33	91.0

^a All runs were polymerized with a molar feed ratio LA/TEA of 30/1, a prepolymerization temperature of 140°C, a prepolymerization time of 12 h, a polycondensation temperature of 160°C, and 0.5 wt % SnO as the catalyst.

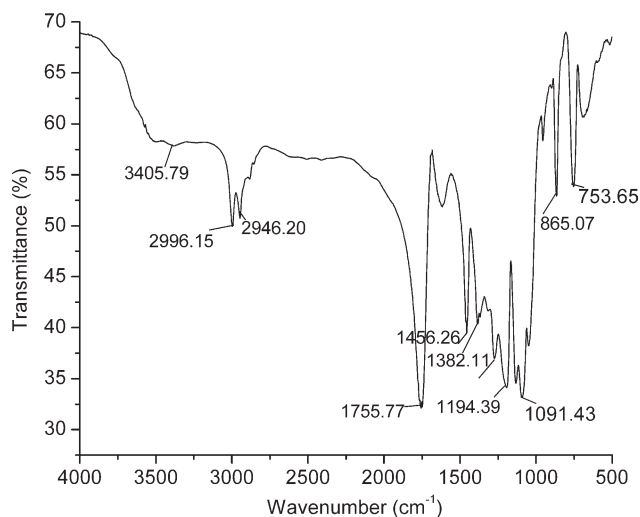


Figure 1 FTIR spectrum of P(LA-TEA) synthesized as the molar feed ratio LA/TEA of 30/1.

symmetrical peak, and polydispersity index (PDI) value ($M_w/M_n = 1.33$) was less than 2 (in fact, all PDI was less than 2, Table V). These indicated that the melt copolycondensation of LA and TEA indeed only gave the copolymer P(LA-TEA) and did not produce homopolymer poly(D,L-lactic acid) (PDLA).¹³ Of course, the low PDI (especially Run 1 in Table V) also showed a selectivity of the reaction toward the formation of similar chain length macromolecules and potentially the higher susceptibility of longer chains to decompose. At the same time, M_w of copolymer determined by GPC was 4000 Da, and M_n was 3000 Da.

Usually, when the PLA biodegradable polymers were used as drug delivery material, their molecular weights were not more than 30,000 Da.^{3,6,25} As reported in the literature, the PLAs material with molecular weight of 1800 Da could be applied in drug delivery, even the PLA polymers with molecular weight of only 900 Da could be used as drug delivery material.^{6,26,27} The molecular weight of P(LA-TEA) synthesized here by using direct melt copolycondensation was overwhelmingly higher than 900 Da. Therefore, its molecular weight meets the requirement for drug delivery applications.

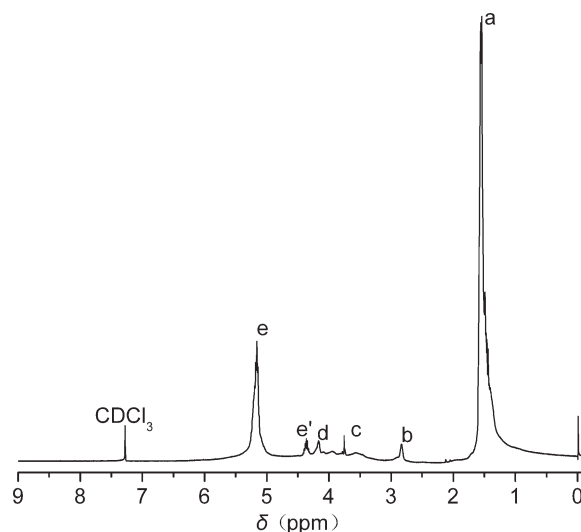


Figure 2 $^1\text{H-NMR}$ spectrum of P(LA-TEA) synthesized as the molar feed ratio LA/TEA of 30/1.

The PLA material has a good biodegradability, and it owns ester group, which is useful for the finishing agent in textile industry. And the compounds with higher molecular weight will be helpful to improve the thermal stability of the finishing agent.^{28–30} Therefore, the copolymer P(LA-TEA) could be used not only as drug delivery carrier but also as a high-security “green” finishing agent in the textile industry and other fields. Especially, when LA/TEA was 15/1, the minimum of all M_n (2300 Da, Run 1 in Table V) is in favor of the application in the field of textile finishing (the molecular weight of the finishing agent based on TEA in current exploitation was between 900 and 1200 Da).^{8–11}

Influences of Molar Feed Ratio on P(LA-TEA)

Under the aforementioned optimal synthetic conditions, serial P(LA-TEA) with different feed molar ratios were directly synthesized by simpler and practical melt polycondensation, and the results were shown as Table V. It could be seen that both $[\eta]$ and M_w basically increased with the increasing of LA/TEA. When LA/TEA was 180/1, the M_w of copolymer

TABLE V
The Influences of Molar Feed Ratio on Copolymer^a

Run	LA/TEA	$[\eta]$ (dL g ⁻¹)	M_n (Da)	M_w (Da)	M_w/M_n	T_g (°C)	Yield (%)
1	15/1	0.66	2300	2700	1.17	12.2	54.9
2	30/1	0.93	3000	4000	1.33	26.9	48.7
3	60/1	0.98	3800	5800	1.53	26.7	61.4
4	120/1	1.00	3200	4700	1.47	27.6	56.3
5	180/1	1.29	5300	9400	1.77	32.5	45.3

^a All runs were polymerized with a prepolymerization temperature of 140°C, a prepolymerization time of 12 h, a polycondensation temperature of 160°C, a polycondensation time of 8 h, and 0.5 wt % SnO as the catalyst.

P(LA-TEA) was 9400 Da, the biggest of all, meeting the requirements for drug delivery.^{3,6,25–27}

On the DSC curve, the glass-transition temperature (T_g) was observed for all samples synthesized at different monomer feed ratios (Fig. 3), and the corresponding data of T_g were also listed in Table V. It was obvious that, no matter what different molar feed ratio was, T_g of the copolymer P(LA-TEA) (in fact a three-arm PDLLA, Scheme 1), was lower than that of linear PDLLA ($T_g = 54.6^\circ\text{C}$, $T_m = 120.0^\circ\text{C}$)^{3,13} due to the introduction of TEA segment as a core of the star polymer.^{4,16,31,32} However, no peak of melting temperature (T_m) was detected on the DSC curve (Fig. 3).

For the homopolymer PDLLA synthesized through direct melt polycondensation of D,L-LA, a lower crystallinity could be detected.^{3,13} Once TEA segment was introduced into the star polymer P(LA-TEA) as a core, it could be found that, no diffraction peak could be observed (Fig. 4), and all P(LA-TEA) were amorphous. This conclusion was very coincident with the earlier mentioned DSC characterization. This indicated that TEA segment in P(LA-TEA) has contributed greatly to the aptness of P(LA-TEA) to be amorphous. Fortunately, lower or no crystallinity is more beneficial for PLA biodegradable materials to be applied in the biomedical fields, especially drug delivery carrier materials, because there will be no residual microcrystalline after degradation *in vivo*.^{3,12,25}

CONCLUSIONS

Using multifunctional group compound TEA as a modified comonomer, P(LA-TEA) was synthesized by direct melt copolymerization of D,L-LA and TEA. The novel copolymer P(LA-TEA) is expected used in

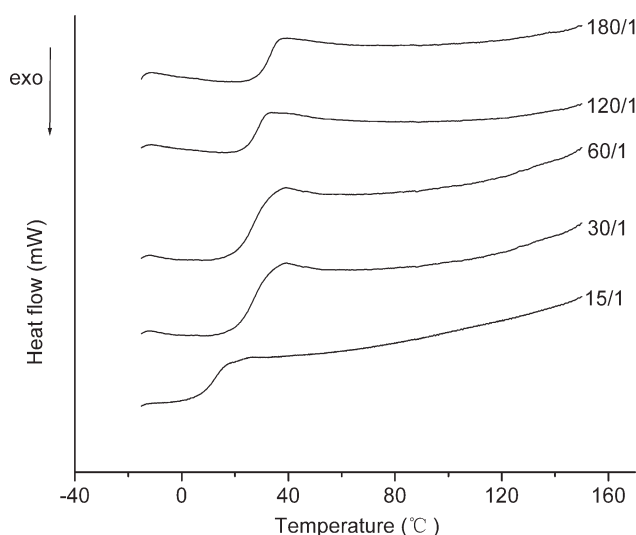


Figure 3 DSC curves of P(LA-TEA) synthesized as different molar feed ratio LA/TEA.

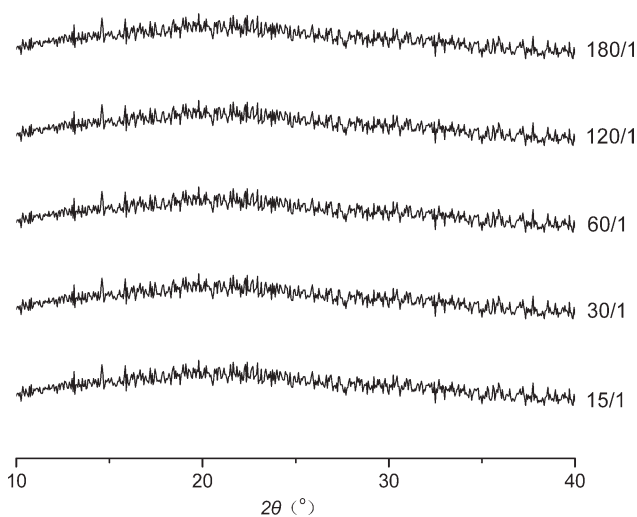


Figure 4 XRD spectra of P(LA-TEA) synthesized as different molar feed ratio LA/TEA.

the biomedical fields, such as drug delivery carrier, tissue engineering material, as well as in other fields, such as a finishing agent with high security and high biodegradability.^{28–30} If the copolymer is further converted into a polymeric quaternary ammonium salt, it also may be a good fabric softener and could be used in leather processing.⁸

When the molar feed ratio LA/TEA was 30/1, the optimal synthetic conditions for P(LA-TEA) were discussed. Using SnO (0.5 wt %) as the catalyst, after 12 h prepolymerization at 140°C and 4000 Pa, the polycondensation at temperature 160°C and absolute pressure 70 Pa for 8 h gave the copolymer P(LA-TEA) with the biggest $[\eta]$ of 0.93 dL g^{-1} . P(LA-TEA) synthesized at different molar feed ratios was systematically characterized by $[\eta]$, FTIR, $^1\text{H-NMR}$, GPC, DSC, and XRD. When LA/TEA was 180/1, the biggest M_w of copolymer was 9400 Da. All copolymers were amorphous and had lower T_g than homopolymer PDLLA.

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