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Melt/solid polycondensation of L-lactic acid: an alternative route to poly(L-lactic acid) with high molecular weight

S.-I. Moon[a], C.-W. Lee[b], I. Taniguchi[a], M. Miyamoto[a], Y. Kimura[a,*]

[a]*Department of Polymer Science and Engineering, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606-8585, Japan*
[b]*Department of Innovative Industrial and Technology, Hoseo University, Baebang-Myun, Asan, Chungnam 336-795, South Korea*

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Abstract

A high polymer of poly(L-lactic acid)(PLLA) is successfully obtained by the melt/solid polycondensation of L-lactic acid (LA) catalyzed by a tin chloride dihydrate/*p*-toluenesulfonic acid binary system. In this process, a polycondensate with a molecular weight of 20,000 Da is first prepared by ordinary melt-polycondensation, crystallized by heat-treatment around 105°C, and heated at 140 or 150°C for 10–30 h for further polycondensation. A high-quality polymer of PLLA can be obtained in high yield in a relatively short reaction time and its molecular weight exceeds 500,000 Da which is comparable with that of the PLLA obtained by the lactide method but has never been attained by the simple melt-polycondensation. © 2001 Elsevier Science Ltd. All rights reserved.

Keywords: Polymer synthesis; Poly(L-lactic acid); Solid-state post-polycondensation

1. Introduction

Poly(L-lactic acid) (PLLA) is expected to have wide applications not only as a biodegradable plastic but also as a biomedical material [1–4] because of its excellent mechanical properties and adjustable hydrolyzability. This one-component aliphatic polyester has usually been prepared by ring-opening polymerization of L-lactide [5,6]. Recently, it has become accepted that the polycondensation of L-lactic acid (LA) can also give PLLA with a significantly high molecular weight [7]. In our former study [8], we succeeded in preparing a high polymer of PLLA by direct melt-polycondensation of LA by using Sn(II) compounds activated by proton acids as the co-catalysts. These binary catalyst systems were quite effective in conducting the polycondensation without serious racemization and discoloration of the resultant polymer, whose molecular weight reached about 100,000 Da. However, when the melt-polycondensation was conducted above T_m of PLLA at reduced pressure, the polymer yield became about 60% relative to the starting LA because of the evaporation of lactide formed by the ring (L-lactide)/chain (PLLA) equilibrium. Furthermore, the molecular weight remained around 100,000 Da, being much lower than that of the PLLA obtained by the ring-opening polymerization of L-lactide. In this paper, therefore, we examined the melt/solid polycondensation of LA in which the melt-polycondensate of LA was subjected to solid-state polycondensation below T_m of PLLA. In solid-state, the polymerization reaction can be favored over the depolymerization or other side reactions. Particularly, in the process of crystallization of the resultant polymer, both monomer and catalyst can be segregated and concentrated in the noncrystalline part to allow the polymer formation to reach 100% [9]. Scheme 1 shows the whole process of this melt/solid polycondensation of LA. As a result, the molecular weight of PLLA reached over 600,000 Da in a relatively short reaction time, demonstrating that the present melt/solid process is comparable to ring-opening polymerization.

2. Experimental

As described in our former paper, LA was dehydrated into oligo(L-lactic acid) (OLLA) whose degree of polymerization (DP) was 8.0 on an average. It was mixed with tin(II) chloride dihydrate ($SnCl_2$) (0.4 wt% relative to OLLA) and *p*-toluenesulfonic acid (TSA) (an equimolar ratio to $SnCl_2$). Then, the mixture was heated to 180°C under mechanical stirring. The pressure of the reaction system was reduced stepwise to 10 Torr in 1 h, at which pressure the reaction was continued for 5 h. At the end of this reaction, the polycondensate was cooled down to form a white solid. It was

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* Corresponding author. Tel.: +81-75-724-7804; fax: +81-75-712-3956.
E-mail address: ykimura@ipc.kit.ac.jp (Y. Kimura).

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Table 1
Typical results of the melt/solid polycondensation at various stages (nd = not detected)

Step	Time (h)	Temp. (°C)	Vacuum (Torr)	Polymer recovery[a] (%)	M_w[b] (10^4 Da)	M_w/M_n[b]	T_g[c] (°C)	T_m[c] (°C)	Crystallinity[d] (%)
Melt-polycondensation[e]	5	180	10	96	1.3	1.9	48	157	53
Heat-treatment[f]	1	105	0.5	97	1.6	1.6	nd	159	63
	2	105	0.5	96	1.5	1.5	nd	158	66
Solid-state polycondensation[g]	10	150	0.5	88	32	3.4	nd	178	85
Solid-state polycondensation[h]	10	150	0.5	89	26	4.7	nd	179	89

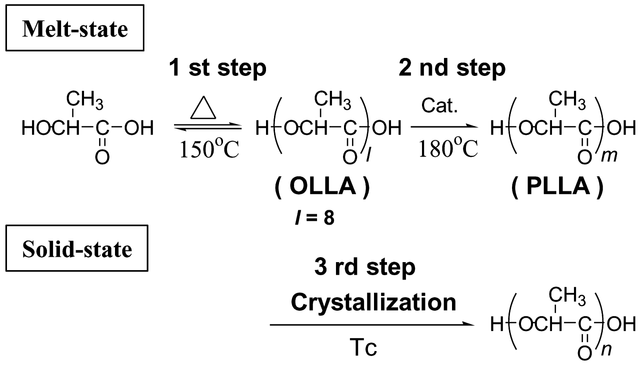
[a] Based on OLLA.
[b] Determined by GPC relative to polystyrene standards with chloroform as the eluent.
[c] Measured by DSC (heating rate: 10°C/min).
[d] Based on enthalpy of fusion; measured by DSC (first scan).
[e] For OLLA (20 g) with $SnCl_2 \cdot 2H_2O$ (60 mg) and TSA (50 mg).
[f] For the melt-polycondensate (ca. 4 g).
[g] After the heat-treatment for 1 h.
[h] After the heat-treatment for 2 h.

then crushed into granules and evenly divided into four test tubes. Each tube was preheated at 105°C for 1 or 2 h in vacuo. During this preheating, the product was crystallized and became resistive to fusion even when heated at a higher temperature. Then, solid-state post-polycondensation was continued at 150°C at 0.5 Torr. At 10 h intervals, each one of the tubes was opened and the product was subjected to various analyses in its as-formed state.

3. Results and discussion

Table 1 shows the polymerization results at various stages of the melt/solid polycondensation. After the melt-polycondensation of OLLA, an amorphous PLLA product with a molecular weight of 13,000 Da was obtained in high yield (>99%). The DSC thermogram of this melt-polycondensate showed a clear crystallization exotherm around 100°C as well as a broad melting endotherm of the PLLA crystals at 135–160°C. Both peak temperatures were significantly lower in comparison with those of the ordinary PLLA (T_c = 130°C, T_m = 170–180°C) because of its low molecular weight. Since the crystallization exotherm was known to extend up to 107°C, the melt-polycondensate was heat-treated at 105°C for 1 or 2 h for its crystallization. The polycondensate obtained after this heat-treatment became crystalline and did not reveal a crystallization exotherm in its DSC curve, showing a clear melting endotherm at 158°C. The crystallinity of the polycondensate was 29 and 30% after 1 and 2 h of heat-treatment, respectively, as determined from the heat of fusion [10]. Since the heat-treated polycondensates did not melt up to 150°C, the solid-state post-polycondensation was conducted at 150°C for a different length of time (10 h) to obtain a high polymer without discoloration. Fig. 1 shows the changes in the molecular weight (open marks) and the crystallinity (closed marks) of PLLA as a function of the reaction time at the solid-state post-polycondensation. In both polycondensates that had been heat-treated for 1 and 2 h, the molecular weight reached the highest molecular weight after 20 h in reaction time, but decreased sharply beyond 20 h. The highest molecular weight of 670,000 Da was obtained for the sample that was heat-treated for 2 h. A comparison of this result with the changes in the crystallinity of PLLA reveals that the increase in crystallinity is parallel to the increase in molecular weight [10].[1] When the reaction time was over 20 h, the crystallinity decreased significantly, as did the molecular weight.

The GPC curve of the intermediate melt-polycondensate showed a broad curve around 13,000 Da in molecular weight while that of the polycondensate heat-treated for 2 h showed a curve in a higher-molecular-weight region (~15,000 Da). As the solid-state post-polycondensation progressed, the main GPC peak shifted to the higher-molecular-weight region. Besides the main peak, a small peak



Scheme 1.

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[1] The crystallinity was evaluated by the heat of crystal fusion measured by DSC according to the theoretical heat of fusion (203.4 J/g) of the ideal PLLA crystals reported before [10]. This value was estimated from the melting endotherm appearing at 184°C.

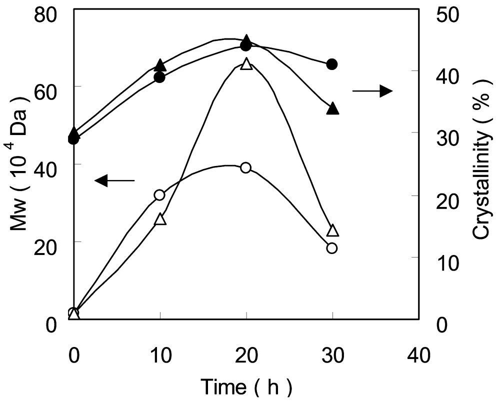
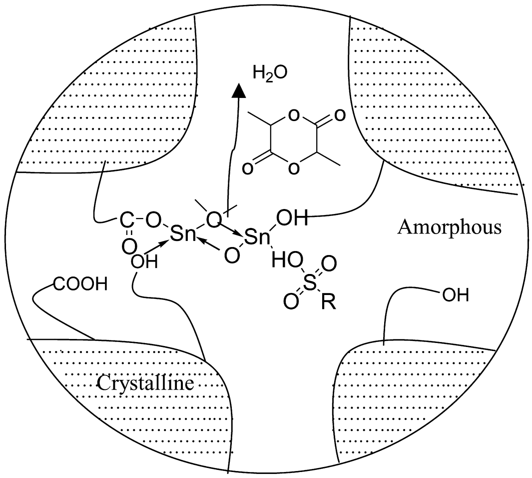


Fig. 1. Changes in the molecular weight (open marks) and the crystallinity (closed marks) of PLLA as a function of the reaction time in the solid-state post-polycondensation ($SnCl_2 \cdot 2H_2O$/TSA = 1.0, 150°C, 0.5 Torr) for the melt-polycondensates heat-treated for 1 h (circles) and 2 h (triangles).



Scheme 2.

also appeared at a relatively lower-molecular-weight region. This bimodal nature suggests that the chain elongation had proceeded in a heterogeneous manner while allowing the crystallization of the polymer. The polycondensation system of LA involves two thermodynamic equilibria: the dehydration/hydration equilibrium for ester formation and the ring/chain equilibrium for lactide formation (Scheme 1). In our melt-polycondensation method the former dehydration reaction was successfully activated by the catalysis of the $SnCl_2$–TSA binary system (1:1 in molar ratio) without being accompanied by serious discoloration of the polymeric product. However, the long-time heating in the melt state of PLLA induced lactide formation and relevant polymer decomposition rather than polycondensation, and the DP of PLLA reached a plateau (around 100,000 Da in molecular weight) in the later stage. In the present method, the PLLA product obtained in the middle stage of melt-polycondensation was subjected to solid-state post-polycondensation around the T_c of PLLA to continue the dehydrative polycondensation. At this reaction temperature, lactide formation and other side reactions could efficiently be suppressed because the reaction equilibrium declined in the direction of polymer formation. In fact, a colorless product with high T_m (187°C), for which no racemization was detected by ^{13}C NMR spectroscopy, was obtained in a yield of around 90%. Furthermore, the crystallization of the polymer chains could effectively undergo the segregation and concentration of the polymer tails and catalyst in the amorphous parts with the enhancing of polycondensation. Although the reaction rate is usually slowed down in such solid-state reactions, the present dehydration reaction was not significantly hindered by the increase in crystallinity. This should be attributed not only to the high activity of our binary catalyst even at low temperature but also to the high mobility of the PLLA chains in the amorphous phase.

Scheme 2 shows a plausible mechanism of the solid-state post-polycondensation of PLLA catalyzed by the binary catalyst. Although the structure of the catalytic site is still unknown, the polymer terminals can be concentrated in the amorphous region and connected with each other effectively by esterification. The polymer chains thus elongated can participate in crystallization around the crystal-amorphous borders. The polymer chains held in the initial crystals have difficulty in reacting with the neighboring chains and remain as the relatively low-molecular-weight parts that were observed by the bimodal GPC curves. The increase in crystallinity can continue until the crystallinity exceeds 43–45% [10].[1] At this stage, the ester-forming rate among the polymer terminals becomes too slow and the intramolecular ester-exchange reaction may overcome the chain extension to form the cyclics together with the linear fragments. This process can reasonably be supported by the observed decrease in molecular weight and crystallinity of the polycondensates obtained after heating for a period of time exceeding 30 h.

4. Conclusions

Melt/solid polymerization of LA was carried out by heating the low-molecular-weight polymer (melt-polycondensate) at temperatures above T_g, yet below T_m of PLLA. The characteristics of this method are that a high-quality polymer can be obtained in high yield in a relatively short reaction time and that the molecular weight of PLLA exceeds 500,000 Da which has never been obtained by the simple melt-polycondensation of LA. This direct process can be a new route to the synthesis of the high polymer of PLLA, and an even alternative to the currently adopted lactide method.

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