Solid-State Postpolymerization of L-Lactide Promoted by Crystallization of Product Polymer: An Effective Method for Reduction of Remaining Monomer

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Received March 28, 1997; Revised Manuscript Received August 5, 1997[⊗]

ABSTRACT: Solid-state postpolymerization of L-lactide was studied by two different ways with 0.1 mol % of stannous 2-ethyl hexanoate as the catalyst. In a two-step method, the ordinary melt polymerization of L-lactide was first performed at temperatures higher than the crystallization temperature (T_c) of poly(L-lactide) (PLLA), and then the postpolymerization was continued around the T_c of PLLA. As PLLA crystallized in the second stage (*e.g.*, when the temperature was changed from 140 to 120 °C), the monomer consumption was found to reach 100% because the monomer and catalyst could be concentrated in the amorphous part. Without the crystallization of PLLA occurring in the postpolymerization, a homogeneous supercooling state was formed to have a remaining monomer ratio exceeding 5 wt %. In the alternative one-step method where the polymerization was continued around the T_c of PLLA, the polymer crystallization was induced during the polymerization to promote the monomer consumption to reach 100%. The kinetic analysis of this polymerization revealed that the rate of monomer consumption is inversely proportional to the square of the amorphous ratio of PLLA, which is opposite to the crystal ratio. However, the molecular weight did not increase with the monomer consumption. This should be because various oligomers are formed in the postpolymerization stage by the ester interchange reaction.

Introduction

Poly(L-lactide) (PLLA) is expected to have wide applications not only as biodegradable plastics,[1] but also as biomedical materials[2−4] because of its excellent mechanical properties and adjustable hydrolyzability. This one-component aliphatic polyester has been prepared by ring-opening polymerization of L-lactide[5−12] or recently established direct polycondensation of L-lactic acid.[13] In the former method using L-lactide, stannous 2-ethyl hexanoate[5] has been used as a standard catalyst mainly because it is highly effective and less toxic. Recently, Kricheldorf et al.[6−11] reinvestigated this tin-catalyzed polymerization and supported the monomer insertion mechanism in which the L-lactide reacts with the hydroxy terminal of PLLA that is activated by coordination to the tin atom.[11] In the initiation step, therefore, the monomer was thought to react with water contaminant present in the system or other hydroxy compounds added as coinitiator.[14] This polymerization system, however, involves the thermodynamic monomer/polymer reaction equilibrium, and the final polymerization product ought to contain a certain amount of remaining monomer corresponding to the equilibrium constant of the polymerization reaction.[15] Since the remaining monomer ratio increases with increasing polymerization temperature, it sometimes exceeds a few percent of the product when melt polymerization is conducted in the bulk state above the melting temperature (T_m) of PLLA (180−200 °C). This remaining monomer has been known to cause unfavorable deterioration of mechanical properties of the processed materials, corrosion of the molding machine, and an unexpected increase of the degradation rate of PLLA. The removal of the remaining monomer, however, is not easy in large scale manufacturing, and in spite of the aforementioned problems, the monomer-containing product would be directly processed for use. Consequently, it has been desired to establish an effective method for removing monomer or increasing monomer conversion in the polymerization. On the basis of this background, we have been interested in the solid-state postpolymerization technique, which has often been adopted for increasing the molecular weight of poly(ethylene terephthalate).[16,17] This technique may possibly be effective also for increasing monomer-to-polymer conversion, because both the monomer and propagating species may be concentrated in the amorphous part in the process of crystallization of the resultant polymer to induce polymer formation. In this paper, the fundamental reaction dynamics in the solid-state postpolymerization of L-lactide is reported to show how effectively the polymerization of L-lactide can be promoted by crystallization of PLLA.

Experimental Section

Measurements. ^{1}H-NMR spectra were measured at 200 MHz on a Varian XL-200 spectrometer in $CDCl_3$ containing 1 vol % of tetramethylsilane (TMS) as the internal reference. The number-average molecular weight (M_n) and the molecular weight distribution (M_w/M_n) were determined by gel permeation chromatography (GPC). The analyzer was composed of a Shimadzu LC-10A pump, a Shodex RI SE-31 RI detector, a Shimadzu C-R7A Chromatopac data processor, a Shodex DEGAS KT-16 degassor, and a Sugai U-620 column oven. A combination of two polystyrene gel columns of Toso TSK gel $G4000H_8$ and $G2500H_8$ was used with chloroform as the eluent at 35 °C. The molecular weight was calibrated according to polystyrene standards. The melting point (T_m) and enthalpy of fusion (ΔH_f) of the polymeric products were determined by differential scanning calorimetry (DSC) on a Mac Science 3100 thermal analyzer at a heating rate of 10 °C/min.

[⊗] Abstract published in *Advance ACS Abstracts,* October 1, 1997.

S0024-9297(97)00432-4 CCC: $14.00

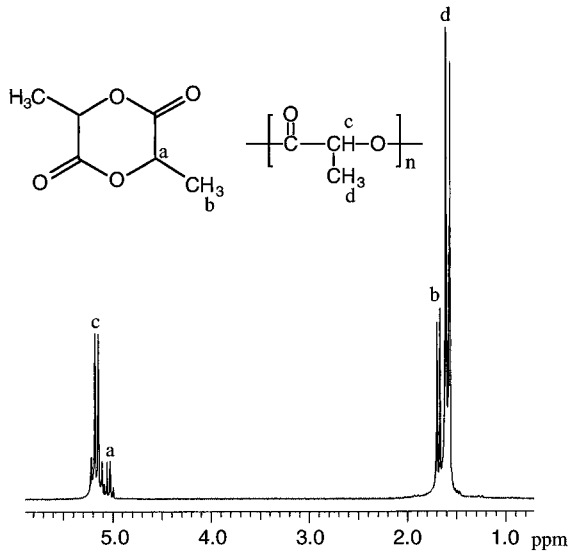


Figure 1. Typical ^{1}H-NMR spectrum of the gross product obtained by the one-step polymerization of L-lactide at 140 °C for 1 h (at 200 MHz in $CDCl_3$).

Materials. L-Lactide was supplied by Purac Biochem (Netherland) and purified by recrystallization from ethyl acetate. Toluene was distilled under a nitrogen atmosphere. Stannous 2-ethyl hexanoate was purchased from Nacalai Tesque Co. (Kyoto) and purified by distillation under high vacuum. It was dissolved in distilled toluene to have a concentration of 0.1 g/mL. An authentic sample of PLLA was prepared by the ordinary bulk polymerization of L-lactide, which was run at 160 °C for 1 h with 0.1 mol % of stannous 2-ethyl hexanoate. The final product was dissolved in chloroform, reprecipitated into an excess of *n*-hexane, filtered, and dried at 80 °C in vacuo. Its molecular weight (M_n) was 100 000.

Solid-State Postpolymerization. Two-Step Method. Into each of several test tubes was charged 1.0 g of L-lactide, and 28.5 μL of the toluene solution of stannous 2-ethyl hexanoate (0.1 mol % relative to L-lactide) was added to it. After evaporation of the toluene in vacuo, each tube was sealed and dipped in a silicone oil bath held at 140 or 170 °C for 1 h to undergo melt polymerization of L-lactide. Then, the tubes were transferred to another oil bath thermostated at 100, 120, or 140 °C to allow the product to solidify. The heating was continued for a prescribed time to undergo solid-state postpolymerization. Then, the tube was cooled to room temperature one by one. Each crude product taken out was subjected to various analyses without purification.

One-Step Method. Ten grams of L-lactide and 285 μL of the catalyst solution (0.1 mol % of stannous 2-ethyl hexanoate relative to L-lactide) were charged into a 50 mL flask. After evaporation of the toluene in vacuo, the mixture was stirred with a magnetic stirrer at a predetermined polymerization temperature for 10 min to have a homogeneous monomer/catalyst liquid mixture. Then, the mixture was evenly divided into four test tubes in a drybox. All of the tubes were heated again at the polymerization temperature. During the heating, the polymerization system turned from liquid to solid with crystallization occurring, and the postpolymerization was continued thereafter. After a prescribed time each tube was opened, and the crude product was analyzed as above.

Determination of Monomer Conversion. Figure 1 shows a typical ^{1}H-NMR spectrum of the polymerization product obtained by the one-step method conducted at 140 °C for 1 h. The methyl signals due to the remaining monomer and PLLA are detected at 1.66−1.70 ppm (signal b) and 1.57−1.60 ppm (signal d), respectively.[18] The remaining monomer ratio was calculated from the integral ratio of these signals according to the equation of $I_b/(I_b + I_d) \times 100$ [represented by wt %] where I_b and I_d denote the integrals of the signals shown by the subscripts, respectively.

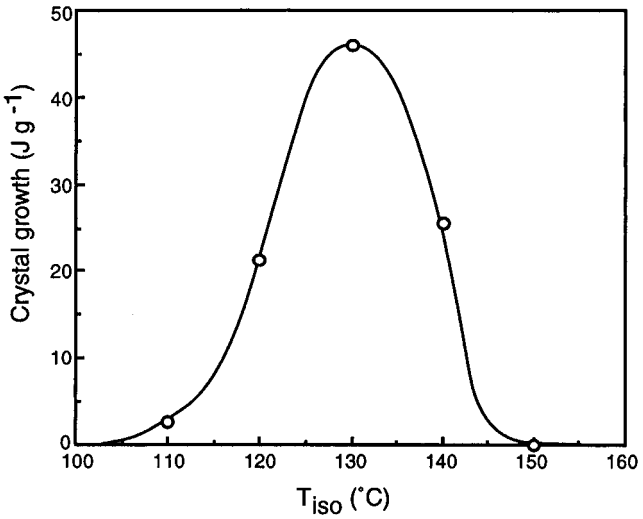


Figure 2. Change in heat of crystallization (ΔH_c) as a function of isothermal crystallization temperature (T_{iso}) of PLLA (M_n = 100 000) as measured by DSC.

Extraction of Oligomers. The crude polymerization products obtained by the one-step method at 120 °C for 3, 7, and 16 h were dissolved in chloroform. Each solution was poured into a large excess of *n*-hexane for reprecipitation of polymer. The precipitate was then filtered off, and the filtrate was evaporated to dryness to obtain the oligomeric product as residue.

Results and Discussion

Tin-catalyzed ring-opening polymerization of L-lactide is usually conducted in the melt state above the T_m of PLLA.[19] This polymerization system involves thermodynamic monomer/polymer equilibrium, and the monomer-to-polymer conversion cannot be 100% if no side reaction would occur.[15] When the polymerization is carried out at a temperature lower than the T_m of PLLA, the system likely turns to solid state before reaching high conversion. In solid state, however, the polymerization reaction can be favored over the depolymerizing or other side reactions under optimized conditions. 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%. With this idea in mind, the postpolymerization of L-lactide was examined in the solid state where the crystallization of the produced PLLA was favored.

Crystallization of PLLA. In order to determine the crystallization temperature (T_c) of PLLA, its melt-crystallization behavior[20−22] was analyzed by DSC with an authentic sample of PLLA. In the first run, the authentic PLLA sample was heated to 220 °C and held at this temperature for 2 min to have a melt state of PLLA. In the second run the temperature was lowered to the predetermined temperatures (110−150 °C) at a cooling rate of 5 °C/min and kept constant for 30 min for analysis of isothermal crystallization of PLLA. Figure 2 shows the changes in heat of crystallization (ΔH_c) measured from the area of the exothermic peaks of DSC as a function of the isothermal crystallization temperature (T_{iso}). It is known that PLLA crystallizes in the temperature range from 110 to 150 °C and that the crystal growth is the largest at 130 °C. These data suggest that the polymerization temperature should be in the range 120−140 °C for allowing the crystal growth of PLLA during the polymerization of L-lactide.

Table 1. Reaction Conditions and Results of Two-Step Polymerization[a]

run no.	reacn conditions		remaining monomer[b] (%)	ΔH_f[c] (J/g)	ΔH_c[c] (J/g)	ΔH_f-ΔH^c (J/g)	$10^{-4}M_n$[d]	M_w/M_n[d]
	1st step	2nd step						
1	140 °C/1 h		9.5	41.09	18.16	22.93	10.9	1.8
2	140 °C/1 h	100°C/9 h	5.2	52.38	0	52.38	7.6	1.5
3	140 °C/1 h	120 °C/9 h	ND[e]	78.83	0	78.83	7.4	2.0
4	140 °C/1 h	140 °C/9 h	5.7	39.87	19.66	20.21	6.9	2.0
5	170 °C/1 h		7.9	43.68	27.28	16.40	4.0	1.6
6	170 °C/1 h	100 °C/9 h	6.8	32.72	0	32.72	9.3	2.2
7	170 °C/1 h	120 °C/9 h	1.8	55.06	0	55.06	5.2	1.9
8	170 °C/1 h	140 °C/9 h	ND	69.45	0	69.45	8.0	2.3

[a] Catalyst: 0.1 mol % of stannous 2-ethyl hexanoate. [b] Determined by ^{1}H-NMR. [c] Determined by DSC. ΔH_f: heat of crystal fusion of the product. ΔH_c: heat of crystallization of the products. [d] Determined by GPC with chloroform as eluent. [e] ND means "not detected".

Two-Step Method. In this method melt polymerization of L-lactide was conducted at temperatures higher than 140 °C with stannous 2-ethyl hexanoate as the catalyst, and the system was cooled to 100−140 °C to allow crystallization of PLLA. Then, the reaction was further continued in the solid state for a prescribed time. Table 1 summarizes the results of the two-step polymerization at different temperature combinations. When the reaction temperature was identical at 140 °C in the first and the second steps, the system kept a transparent homogeneous state without crystallization of PLLA occurring because of supercooling of the polymer melt containing a certain amount of remaining monomer. In this case, the monomer conversion did not much increase even after a long reaction time, and the final remaining monomer ratio was even higher than 5 wt %. When the temperature was lowered from 140 to 120 °C in the second stage, the produced PLLA crystallized, and the monomer was completely consumed after 9 h. When the reaction temperature was cooled from 170 to 140 °C, the system turned from a homogeneous melt state to the crystalline state, and the remaining monomer ratio gradually decreased to zero. When the temperature of the second step was 120 °C, the remaining monomer ratio was 1.8 wt % after 9 h. On the contrary, when the reaction temperature was lowered to 100 °C from both 140 and 170 °C, the remaining monomer ratio was as high as that of run no. 4 although the system turned to the crystalline state. This may be because the polymerization rate of L-lactide became too slow at 100 °C.

The crystal formation of PLLA during the solid-state polymerization could be analyzed by DSC of the products. Figure 3 shows the DSC curves of the representative polymerization products quenched at room temperature. The transparent products (run nos. 1 and 4) with a significant amount of remaining monomer show an exothermic peak due to the crystallization of PLLA and an endothermic peak around 175 °C due to the crystal fusion of PLLA. These data suggest that the system was kept amorphous throughout the polymerization. The highly crystalline monomer-free product of run no. 3 (white in color) shows only the endothermic peak due to the crystal fusion of PLLA above 185 °C, while the crystalline product of run no. 2 shows the smaller peak at 175 °C. We assumed that the difference between the heat of crystal fusion (ΔH_f) and the heat of crystallization (ΔH_c) would correspond to the amount of crystals having been formed during the polymerization. The values ($\Delta H_f - \Delta H_c$) estimated are also included in Table 1. Even when the apparent crystallization had not been observed during the polymerization, a small difference ($\sim$20 J·g^{-1}) between ΔH_f and ΔH_c was detected. This may be due to the partial crystal formation during the quenching process and the crystal growth during the DSC measurement, particularly through the melt recrystallization of the unstable crystals occurring below T_m. It is known that the crystal growth during the postpolymerization was very large in the monomer-free products and that the remaining monomer ratio decreased with increasing crystal growth.

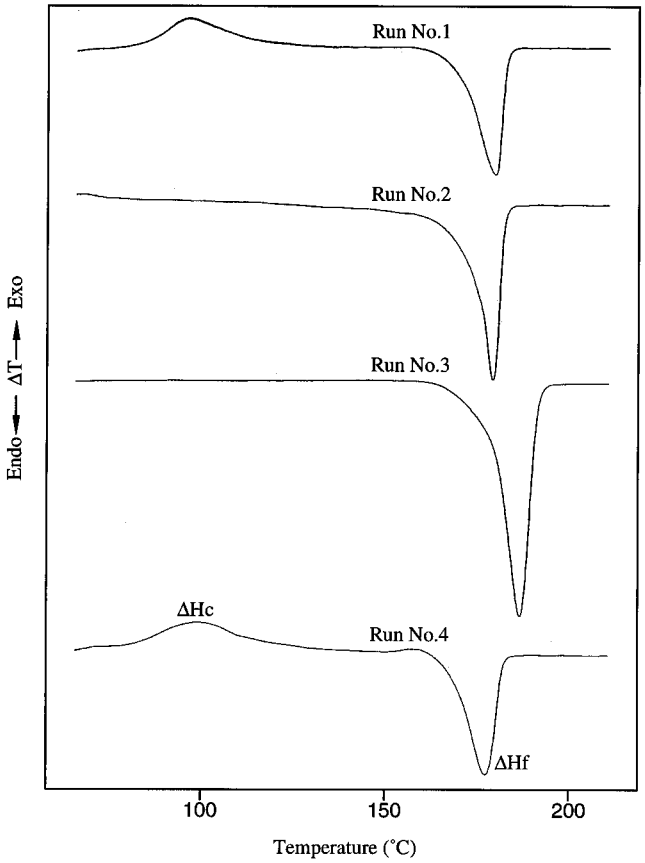


Figure 3. DSC curves of the polymerization products indicated (see Table 1 for run no.).

In this polymerization catalyzed by stannous 2-ethyl hexanoate, the contaminant moisture and impurities coming from the monomer and the catalyst solution are considered to initiate the polymerization, and the initial concentration of the initiating species would be slightly different in each run. Therefore, the difference in molecular weight of the polymerization products cannot be discussed. However, their GPC data in Table 1 suggested that the increase in molecular weight of PLLA should be very small even with increasing monomer consumption in the solid-state postpolymerization.

One-Step Method. A source mixture of monomer and catalyst was first prepared and divided into several batches to make the aforementioned monomer/initiator ratio uniform in each batch. They were then subjected

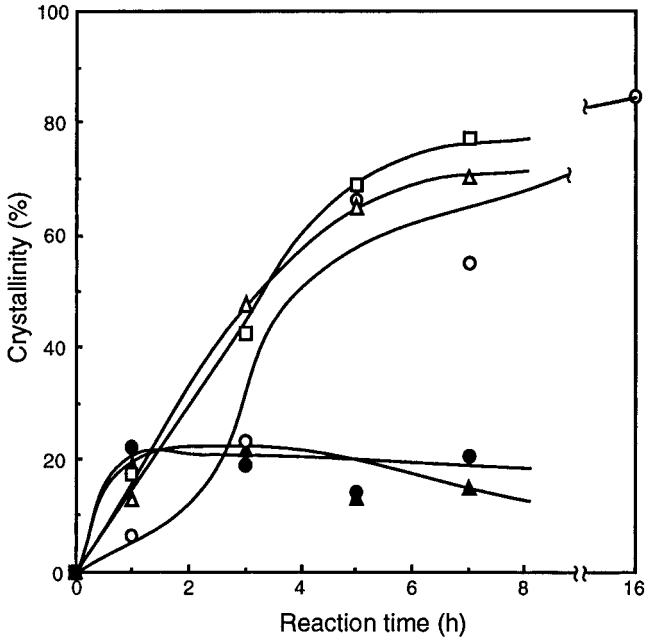


Figure 4. Time courses of crystallinity of the polymerization product in the one-step polymerization of L-lactide at 120 °C (○), 130 °C (△), 140 °C (□), 150 °C (●), and 160 °C (▲).

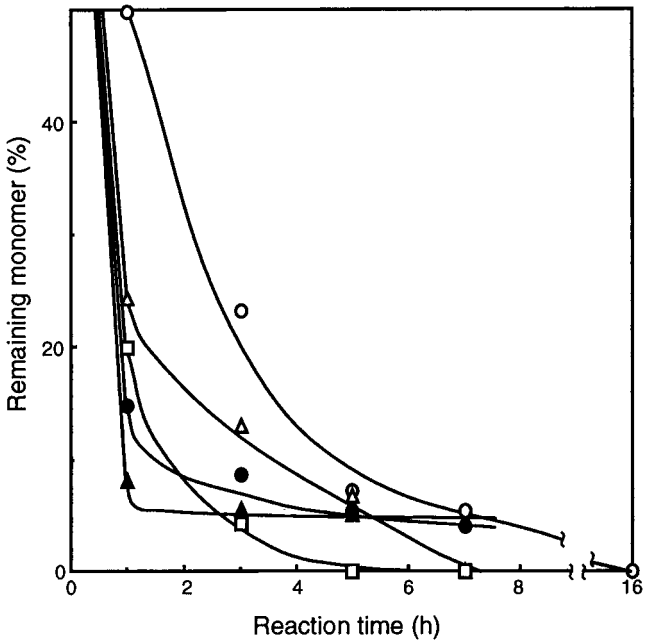


Figure 5. Time courses of monomer consumption in the one-step polymerization of L-lactide at 120 °C (○), 130 °C (△), 140 °C (□), 150 °C (●), and 160 °C (▲).

to polymerization at a constant temperature around the T_c of PLLA to allow the system to turn to the solid state during the reaction. Each of the gross products obtained at different reaction times was then analyzed by DSC, as described above. The apparent crystallinity (crystal content of PLLA) of the gross products was evaluated from the ($\Delta H_f - \Delta H_c$) value, assuming the theoretical heat of crystal fusion of PLLA as 93.0 J·g^{-1}.[21−23] Figure 4 shows the time-dependent changes in apparent crystallinity of the products at various polymerization temperatures. When the temperature was held at 120, 130, and 140 °C, the polymerization system spontaneously turned from the liquid state to the crystalline state, and the apparent crystallinity increased with the reaction time. While at 130 and 140 °C, the increase reached a plateau beyond 7 h; it continued until 16 h at 120 °C, where the final apparent crystallinity was over 80%. Fast crystallization was observed even at 140 °C, where little crystallization had occurred in the two-step method, because a small amount of polymer, produced during the monomer/catalyst mixing, deposited by cooling and remained as fine particles in the system to provide the crystal nucleators for crystallization of PLLA. On the other hand, when the reaction temperature was held at 150 and 160 °C, the system remained in the amorphous state with opaque color, and the apparent crystallinity was around 20%. This value can also be attributed to the crystal formation during the quenching process in the DSC measurement.

Figure 5 shows the time courses of the monomer consumption at different reaction temperatures. At 120, 130, and 140 °C, where the apparent crystallinity of PLLA increased with reaction time, the remaining monomer was slowly consumed up to zero. At 150 and 160 °C, in return, where the crystallinity did not increase, the monomer consumption stopped, and the final remaining monomer ratio exceeded 5%. These data also support the fact that the monomer conversion increases with the polymer crystallization. Figure 6 shows the time courses of the molecular weight of PLLA at various reaction temperatures. At every reaction temperature, the molecular weight increased initially,

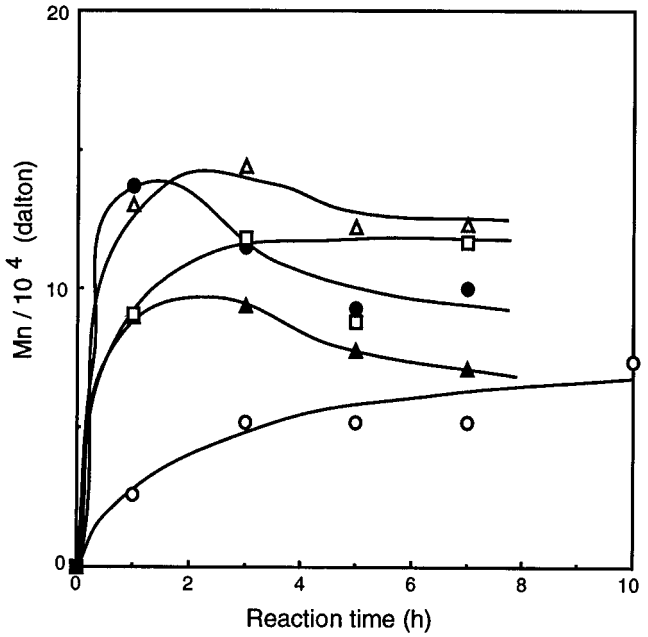


Figure 6. Time courses of molecular weight of the polymerization product in the one-step polymerization of L-lactide at 120 °C (○), 130 °C (△), 140 °C (□), 150 °C (●), and 160 °C (▲).

reached the maximum, and decreased gradually. In spite of the continuous monomer consumption even after 3 h at 120−140 °C (Figure 3), no increase was observed in molecular weight in the solid-state postpolymerization. This result strongly suggests the formation of oligomers with the monomer consumption.

Oligomer Formation and Polymerization Mechanism. The product of the one-step polymerization at 120 °C was fractionated by reprecipitation with a chloroform (solvent)/*n*-hexane (precipitant) system. A very small amount of oligomeric fraction was isolated from the supernatant obtained after the reprecipitation. Figure 7 shows the typical GPC chromatograms of the oligomeric fractions isolated from the polymerization products prepared at different polymerization times. It is known that only L-lactide was contained in the

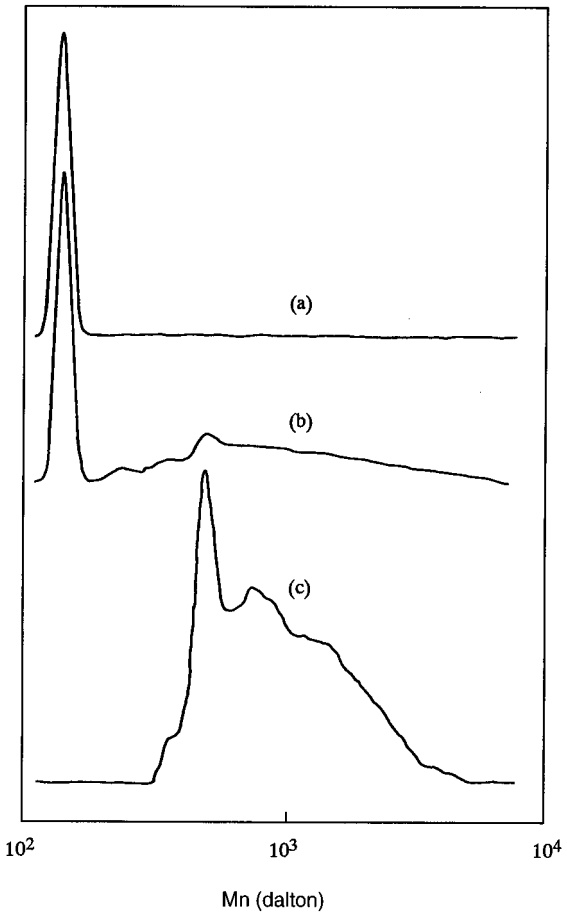
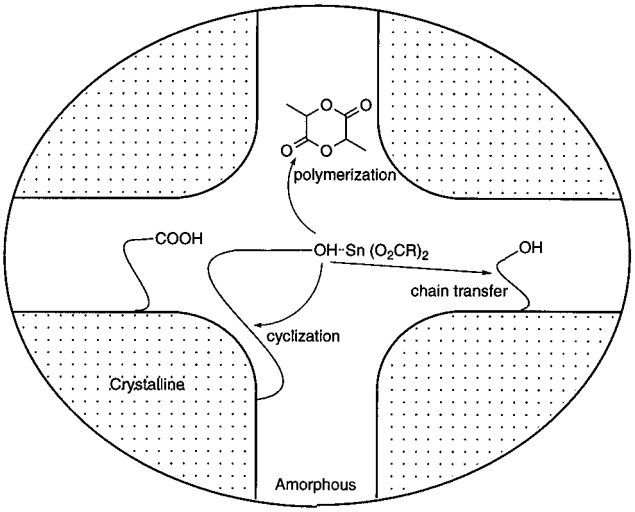


Figure 7. Typical GPC curves of the low molecular weight fractions obtained by the one-step polymerizations of L-lactide at 120°C for (a) 3 h, (b) 7 h, and (c) 16 h. The scale of molecular weight is with respect to the polystyrene standards.

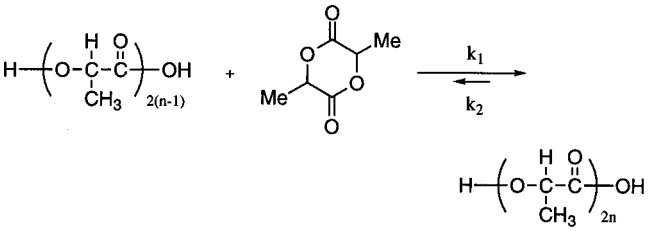
fraction at the polymerization time of 3 h, where the monomer consumption was not complete. When the polymerization time was 7 h, both the monomer and oligomer peaks were detected. At this stage, the monomer consumption proceeded to a degree over 95%, judging from the results of Figure 5. When the polymerization time reached 16 h, only the oligomer was contained in the fraction. These data support that the monomer is consumed to form oligomers in the solid-state postpolymerization. Therefore, the monomer consumption in the later stage did not contribute to the increase of the molecular weight of the polymer.

Scheme 1 shows a schematic mechanism of post-polymerization in the solid state. When the monomer conversion is low, the reaction system is homogeneous in a monomer melt of L-lactide.[11,14] With further monomer consumption, the crystallization of PLLA takes place, and the monomer, catalyst, and the active sites (or the polymer ends) are concentrated in the amorphous region present between the PLLA crystals. Then, the monomer consumption is driven to reach 100%. With decreasing monomer concentration, however, the main-chain ester groups of the polymer tail present in the amorphous phase are allowed to react with the end group to promote cyclization[24] and chain transfer,[22] by which various cyclic and linear oligomers can be formed. With these two processes (monomer consumption and oligomerization) balanced, the number average molecular weight of PLLA should be maintained almost constant with a slight increase in molecular weight distribution.

Scheme 1. Mechanism of the Post-polymerization of L-Lactide in the Solid State



Scheme 2. Equilibrium Polymerization of L-Lactide



Kinetic Analysis of Solid-State Postpolymerization. As described in Scheme 1, the propagation is driven by the successive reaction of L-lactide with the hydroxy terminal of PLLA. This propagation is in equilibrium with the reverse back-biting reaction to regenerate L-lactide. Therefore, the rate of monomer consumption[15,25] can be depicted by eq 1, where k_1 and

$$-\mathrm{d}M/\mathrm{d}t = k_1\mathrm{MP} - k_2P \qquad (1)$$

k_2 denote the second-order and first-order rate constants for the propagation and back-biting reaction, respectively, and M and P are the concentrations of L-lactide and the propagating hydroxy groups (see Scheme 2). In the solid state reaction, the reaction system can be separated into the crystalline and amorphous regions, and the monomers and end groups should be segregated into the amorphous phase. Therefore, it can be assumed that the reaction is allowed only in the amorphous region. If the volume change is very small and the concentration of the propagating hydroxy groups of PLLA is constant during the polymerization and crystallization, eq 1 can be transformed to eq 2, where a is

$$-\mathrm{d}M/\mathrm{d}t = k_1MP/(1-a)^2 - k_2P/(1-a) \qquad (2)$$

the crystallinity of the product PLLA in the system. Here, if the volume of the reaction system is assumed to be kept constant at the initial volume, the concentrations of monomer and propagating species in the amorphous phase can be shown by $M/(1-a)$ and $P/(1-a)$, respectively. For easier calculation, the equilibrium constant of the polymerization and the equilibrium monomer concentration are expressed by K and M_e, respectively. Then, the following relations are obtained.

$$K = k_2/k_1 = M_e/(1-a) \qquad (3)$$

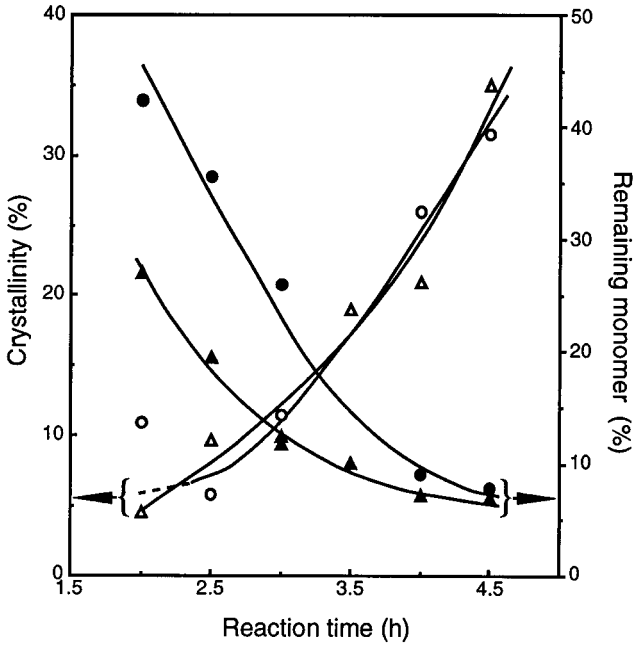


Figure 8. Time courses of monomer consumption (●, 120 °C; ▲, 130 °C) and crystallinity (○, 120 °C; △, 130 °C) of the polymerization product in the one-step polymerizations of L-lactide at 120 and 130 °C.

When this is put into eq 2, eq 4 can be derived. This

$$-\mathrm{d}M/\mathrm{d}t = k_1P(M - M_e)/(1- a)^2 \qquad (4)$$

equation suggests that the rate of monomer consumption is inversely proportional to $(1 - a)^2$, which is the amorphous ratio. Therefore, the polymerization rate is

$$-\ln\{(M/M_0 - M_e/M_0)/(1 - M_e/M_0)\} = k_1P\int 1/(1- a)^2\,\mathrm{d}t \qquad (5)$$

enhanced with the increasing degree of crystallization of the resultant PLLA. Integration of eq 4 from time 0 to t and from M_0 to M gives eq 5. When $(1 - a)^2$ is plotted against t, the right term of eq 5 ($\int(1 - a)^{-2}\,\mathrm{d}t$) can be estimated by the graph integration. The value of $(M - M_e)/(M_0 - M_e)$ can be plotted against $\int(1 - a)^{-2}\,\mathrm{d}t$. Figure 8 shows the experimental data taken for this kinetic analysis. Their kinetic plots according to eq 5 are shown in Figure 9, where the equilibrium monomer conversions M_e/M_0 in the imaginary homogeneous polymerizations at 120 and 130 °C are set at 0.012 and 0.017, respectively. A linear relation was supported at each temperature, although the real value of P was unknown in the present analysis. Because the slope is higher at 130 °C than at 120 °C, it may be supported that the rate constant increases with reaction temperature. When the crystallinity of the polymerization products was over 30% at high monomer conversion (>95%), the plot deviated from the linear relation. It should probably be due to the enlarged experimental error. The linear plots shown in Figure 9 strongly support that the monomers, propagating species, and catalyst are allowed to migrate into the amorphous phase with crystallization occurring and that the polymerization rate of L-lactide in the amorphous phase is almost identical with that in the melt state of the monomer.

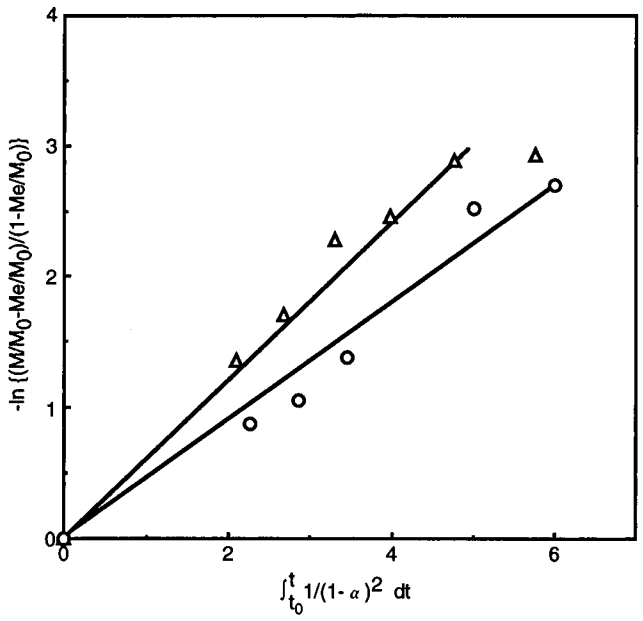


Figure 9. Kinetic plots for the solid-state polymerizations of L-lactide at 120 and 130 °C: (○) M_e/M_0 (120 °C) = 1.2%; (△) M_e/M_0 (130 °C) = 1.7%.

Conclusions

Solid-state polymerization of L-lactide was conducted by the one-step and two-step methods with 0.1 mol % of stannous 2-ethyl hexanoate as the catalyst. It was found that the remaining monomer ratio exceeds 5% owing to the monomer/polymer equilibrium if no crystallization of PLLA is promoted during the reaction. The monomer consumption could reach 100% with satisfactory polymer crystallization, because the monomer and catalyst should be concentrated in the amorphous part. The molecular weight of produced PLLA, however, did not increase, because various oligomers are formed in the stage of postpolymerization by ester interchange reaction. The fundamental data obtained here would contribute to the determination of the reaction conditions for the solid-state postpolymerization of L-lactide to reduce the remaining monomer in the product.

References and Notes

(1) Kulkarni, R. K.; Moore, E. G.; Hegyeli, A. F.; Leonard, F. *J. Biomed. Mater. Res.* **1971**, *5*, 169.
(2) Van Sliedregt, A.; De Groot, K.; Van Blitterswijk, C. A. *J. Mater. Sci. Mater. Med.* **1993**, *4*, 213.
(3) Nakamura, T.; Hitomi, S.; Watanabe, S.; Shimizu, Y.; Jamshidi, K.; Hyon, S.-H.; Ikada, Y. *J. Biomed. Mater. Res.* **1989**, *23*, 1115.
(4) Bergsma, J. E.; Rozema, F. R.; Bos, R. R. M.; Boering, G.; De Bruijn, W. C.; Pennings, A. J. *J. Biomed. Mater. Res.* **1995**, *29*, 173.
(5) Leenslag, J. W.; Pennings, A. J. *Makromol. Chem.* **1987**, *188*, 1809.
(6) Kricheldorf, H. R.; Boettcher, C.; Tonnes, K.-U. *Polymer* **1992**, *33*, 2817.
(7) Kricheldorf, H. R.; Sumbel, M. *Eur. Polym. J.* **1989**, *25*, 585.
(8) Kricheldorf, H. R.; Kreiser-Saunders, I. *Makromol. Chem.* **1990**, *191*, 1057.
(9) Kricheldorf, H. R.; Lee, S.-R. *Polymer* **1995**, *36*, 2995.
(10) Kricheldorf, H. R.; Dunsing, R. *Makromol. Chem.* **1986**, *187*, 1611.
(11) Kricheldorf, H. R.; Kreiser-Saunders, I.; Boettcher, C. *Polymer* **1995**, *36*, 1253.
(12) Eguiburu, J. L.; Berridi, M. J. F.; Roman, J. S. *Polymer* **1995**, *36*, 173.
(13) Ajioka, M.; Enomoto, K.; Suzuki, K.; Yamaguchi, A. *J. Environ. Polym. Degrad.* **1995**, *3*, 225.
(14) Zhang, X.; Macdonald, D. A.; Goosen, M. F. A.; Mcauley, K. B. *J. Polym. Sci., Polym. Chem.* **1994**, *32*, 2965.

(15) Duda, A.; Penczek, S. *Macromolecules* **1990**, *23*, 1636.
(16) Chang, S.; Sheu, M.-F.; Chen, S.-M. *J. Appl. Polym. Sci.* **1983**, *28*, 3289.
(17) Zhi-Lian, T.; Gao, Q.; Nan-Xun, H.; Sironi, C. *J. Appl. Polym. Sci.* **1995**, *57*, 473.
(18) Lillie, E.; Schulz, R. C. *Makromol. Chem.* **1975**, *176*, 1901.
(19) Jamshidi, K.; Eberhart, R. C.; Hyon, S.-H.; Ikada, Y. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1987**, *28*, 236.
(20) Vasanthakumari, R.; Pennings, A. J. *Polymer* **1983**, *24*, 175.
(21) Kalb, B.; Pennings, A. J. *Polymer* **1980**, *21*, 607.
(22) Tsuji, H.; Ikada, Y. *Polymer* **1995**, *36*, 2709.
(23) Fischer, E. W.; Sterzel, H. J.; Wegner, *G. Kolloid-Z. Z. Polym.* **1973**, *251*, 980.
(24) Montaudo, G.; Montaudo, M. S.; Puglisi, C.; Samperi, F.; Spassky, N.; LeBorgne, A.; Wisniewski, M. *Macromolecules* **1996**, *29*, 6461.
(25) Dubois, P.; Jacobs, C.; Jerome, R.; Teyssie, P. *Macromolecules* **1991**, *24*, 2266.

MA9704323