

Direct Synthesis with Melt Polycondensation and Microstructure Analysis of Poly(L-lactic acid-co-glycolic acid)

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ABSTRACT: High-molecular-weight poly(L-lactic acid-co-glycolic acid) (PLGA) was prepared through melt polymerization from glycolic acid (GA) and L-lactic acid (L-LA) and then characterized. High resolution ¹H and ¹³C NMR were performed for microstructure analysis of polymer. The solubility in chloroform, compositions, and sequence lengths of PLGA suggest higher reactivity of GA compared with L-LA and shortening GA blocks with reaction time. The racemization of L-LA blocks and transesterification in PLGA are enhanced by increase of GA fractions. PLGA (90/10) samples show crystallization of relatively long L-LA sequences in copolymer chains and the absence of the crystallization of GA blocks. All these results demonstrate the influence of racemization and transesterification on the microstructure of PLGA.

KEY WORDS Direct Synthesis / Microstructure / Poly(L-lactic acid-co-glycolic acid) / Poly(L-lactic acid) / Poly(D, L-lactic acid) /

Aliphatic polyesters derived from lactic acid (LA), glycolic acid (GA), and ϵ -caprolactone (CL) should have promising applications to biodegradable plastic as well as biomedical materials because of their excellent mechanical, processable, biocompatible, and degradable properties.^{1–4} Present in carbohydrate metabolism in nature, LA consists of two optical isomers, L-LA and D-lactic acid (D-LA). The D,L-lactic acid (DL-LA) containing equimolar L-LA and D-LA is racemic. Poly(lactic acid) (PLA) with low molecular weight (M_w) was first prepared by Carothers through the polycondensation of lactic acids⁵ in 1932. Poly(L-lactic acid) (PLLA), Poly(D, L-lactic acid) (PDLLA), and Poly(L-lactic acid-co-glycolic acid) (PLGA) can be prepared *via* both direct synthesis and ring-opening polymerization (ROP). The direct synthesis refers to the polycondensation of LA and/or GA. The ROP refers to the polyaddition of lactides and glycolide,^{3,4,6–14} which are prepared by depolymerizing the oligomers of LA and GA. The synthesis and isolation of these lactones cause PLA polymers high-priced, which prevents commodity applications of PLA.

ROP has been preferred to get polymers with high M_w because of the inability of the direct synthesis to increase polymer M_w . Thus the direct synthesis has been used to prepare low M_w polymers of hydroxy-acids, which can be used in drug delivery systems.^{15–21} In the direct synthesis of PLLA, poly(glycolic acid) (PGA), and PLGA, factors in the obtain of high M_w polymers consist both in driving the dehydration equilibrium to the direction of esterification and in reducing the depolymerization of PLLA to lactide at high temperature

and under vacuum. Since 1995, Ajioka group^{22,23} has developed solution polycondensation of hydroxy-acids, which brought a breakthrough for the direct synthesis. High-molecular-weight PLA and PLGA could be prepared from LA and GA after a relatively long reaction period at 160 °C under high vacuum in diphenyl ether solution. However, the use of solvents leads to the complexity of process control and the purification of end product, which makes these polymers expensive. The Kimura group has attempted to settle the drawbacks of the solution polycondensation. They prepared high M_w PLLA^{24,25} and PGA²⁶ through melt and/or melt/solid polycondensation. However, melt polycondensation in the absence of solvent has been hardly performed to prepare high M_w PLGA so far. Moreover, the microstructure analysis of PLLA, PDLLA, and PLGA obtained through melt polymerization has not been performed.

In the present work, melt polymerization was utilized to prepare PLGA with high M_w . PDLLA and PLLA samples synthesized by the same process are used as the references of racemization for microstructure analysis of PLGA. The effects of the racemization and transesterification on the polymer crystallinity are discussed.

EXPERIMENTAL

Materials

L-LA as a 90 wt% aqueous solution (PH90, pharmaceutical grade) was purchased from Purac Corp. (Netherlands). Aqueous 90 wt% solution of DL-LA (50/50 molar ratio of L-LA/D-LA), glycolic acid

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dihydrate, Tin(II) chloride dihydrate (SnCl_2), *p*-toluenesulfonic acid monohydrate (TSA), diethyl ether, Tin powder, chloroform, and molecular sieve (3 Å) were purchased from Shanghai Chemical Corp. Molecular sieve was activated at 300 °C. All other reagents were used as received.

Melt Polycondensation of PLGA, PDLLA, and PLLA

The reaction conditions used in the melt polymerization of PLLA²⁴ were employed to prepare PLGA here. A given amount of 90 wt% aqueous solution of L-LA and GA dihydrate were charged into an 100 mL three-necked flask, which was equipped with a mechanical stirrer and a reflux condenser packed with molecular sieve (3 Å). The LA/GA mixture was first dehydrated into the oligomer, whose degree of polymerization is calculated from ¹H NMR to be 6–8. With the addition of SnCl_2 (0.5 wt% of the resultant oligomer) and TSA (equimolar to SnCl_2), the oligomer was gradually heated to 180 °C under mechanical stirring along with pressure reduced to 1300 Pa stepwise. Polymerization was maintained under these conditions for 20 h. The obtained product was dissolved in chloroform and subsequently precipitated into diethyl ether. The resulting solids were filtered and then dried under vacuum at 70 °C. Isolated PLGA was kept in a desiccator in the presence of phosphorus pentoxide. PLGA (90/10) was prepared from L-LA/GA (90/10) (molar ratio in feed being 90/10), while PLGA (70/30) from L-LA/GA (70/30).

The same process was utilized to prepare PDLLA (50/50) and PLLA-1 from DL-LA and L-LA 90 wt% aqueous solution respectively. PLLA-2 was prepared from a prepolymer of L-LA (\bar{M}_n 5690 Daltons) instead of an L-LA oligomer through the melt polymerization. PLLA-1 was a white powder, while PLLA-2 was a slightly yellow to yellow powder. PDLLA (50/50) was a slightly brown powder.

Polymer Characterization

¹³C NMR and ¹H NMR spectra were carried out at a temperature of 300 K on a Bruker DMX-500 NMR spectrometer. All polymer samples were dissolved in deuterated chloroform with tetramethylsilane as internal standard. ¹H NMR spectra were acquired as 1% solution at 500 MHz, while ¹³C NMR spectra were acquired at 125 MHz, with a pulse angle of 25°, acquisition time of 1.6 s, and a delay time of 10 s. FT-IR spectra were recorded on a MANMNA IR-550 spectrometer (Nicolet Corp.). The samples were examined on NaCl discs. For each spectrum, 32 scans were taken at a resolution of 4 cm⁻¹.

X-Ray diffraction (XRD) measurements were per-

formed with a Rigaku D-MAX/Rb Diffractometer (Rigaku Corporation) with Cu-*K*α radiation at a wavelength of 1.54 Å in the 2θ range of 5–50° at 40 kV and 100 mA. The differential scanning calorimetry (DSC) was determined on a DSC2901 thermal analyzer (TA Corp. USA) at a heating rate of 10 °C min⁻¹. Optical rotation $[\alpha]_D^{25}$ was measured at 25 °C on a Perkin–Elmer Md. 243 in an 1 mL cell of 10 cm length with the λ of 578 μ. A sample concentration of 10 g L⁻¹ in chloroform was used in all cases.

Molecular weights of polymers were measured by Waters 1525 HPLC at a concentration of 1 mg mL⁻¹ in tetrahydrofuran (THF) with THF as the mobile phase at 1 mL min⁻¹. Polymer M_w was calculated by the universal calibration method using polystyrene (Shodex M_w 10000, 30000, and 60000) as reference. A Waters Styragel (HR 4E, 5E, 6E, Milford MA) column packed with 5-um particles was used to isolate the M_w fractions, detected by a Waters 2410 RI detector.

RESULTS AND DISCUSSION

Synthesis and Molecular Weights of Copolymers

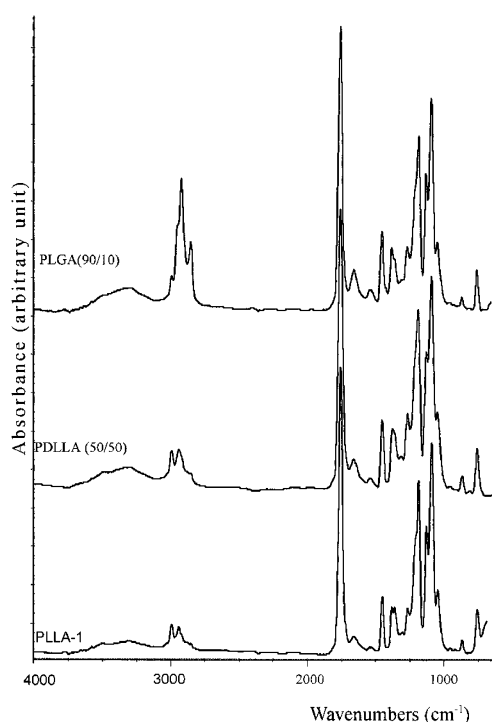
According to Kimura,²⁴ the SnCl_2 /TSA catalyst system (Sn(II)/TSA) is effective for increasing M_w of PLLA and preventing discoloration and racemization of PLLA in melt polymerization. Thus the Sn(II)/TSA catalyst system was used in the present work to prepare PLGA, PLLA, and PDLLA with melt polycondensation in the absence of solvent. The FT-IR spectra of PLLA, PDLLA, and PLGA are given in Figure 1. The spectra of PLLA and PDLLA show a well-defined absorption at 1755 cm⁻¹ due to the ester carbonyl, peaks at 1200–1000 cm⁻¹ to the C–O stretch, and peaks at 2850–2960 cm⁻¹ to the stretch of CH and CH₃ groups.^{16,27,28} The wide band at 3300 cm⁻¹ owing to hydrogen-bonded OH groups denotes the existence of OH end groups in polymer chains. PLGA spectrum is similar to that of PLLA except for a medium band at 2926 cm⁻¹ due to CH₂ of GA in the L-LA/GA copolymer.

Solubility in chloroform, M_w , compositions, and yields of polymers were detected. All results are given in Table I. All L-LA/GA oligomers are soluble in chloroform. PLGA solubility decreases with reaction time, and PLGA becomes insoluble after the oligomer polymerized for 6 h. With further reaction time, the solubility of PLGA increases again, and PLGA becomes soluble eventually. PLGA solubility decreases with GA content in polymers. Poly(glycolide) and copolymers of glycolide with long glycolide blocks are usually insoluble in most common solvents including chloroform. PLGA solubility indicates higher reactivity of

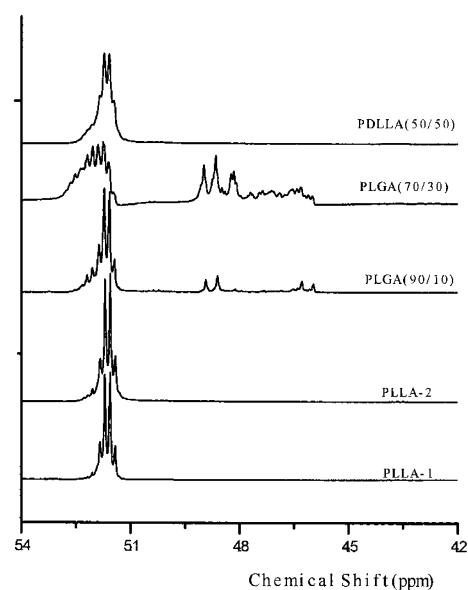
Table I. The results of PLLA, PLGA, and PDLLA prepared by the direct synthesis through melt polymerization

Samples	\overline{M}_n^a kDa	MWD ^a	f_G^b %	F_G^b %	Yield ^c %	Solubility ^d	Appearance
PLLA-1	23.6	1.31	0	0	53.82	+++	White powder
PLLA-2	31.4	1.40	0	0	51.21	+++	Slight yellow powder
PLGA (90/10)	54.7	1.28	10.0	12.12	45.44	++	White fibril
PLGA-1 (90/10) ^e	25.2	1.29	10.0	13.80	44.83	++	White powder
PLGA (70/30)	25.5	1.75	30.0	32.20	42.64	+	Yellow solid
PDLLA (50/50)	18.0	1.30	0.0	0	40.20	++++	Slight brown powder

^a \overline{M}_n calculated from GPC. Da is the abbreviation of dalton. Molecular weight distribution (MWD) is equal to $\overline{M}_w/\overline{M}_n$. ^b f_G and F_G were molar fractions of GA in feed and in copolymers respectively. F_G was calculated from ¹H NMR spectra. ^cYield(%) of polymers were calculated by the ratio of isolated polymer to initially charged reagents. ^dSolubility in chloroform of polymers decreased from ++++ to +. ^ePLGA-1 (90/10), copolymer prepared after the oligomer of L-LA/GA (90/10) was polymerized for 12 h.

**Figure 1.** FT-IR spectra of PLLA, PDLLA (50/50), and PLGA (see the text).

GA in comparison with L-LA. Thus in the L-LA/GA copolymerization, GA can be polymerized preferentially, leading to the formation of long GA blocks. With longer polymerization time, L-LA will be built in polymer chains when GA is depleted, which can increase the solubility of PLGA. Thus L-LA and GA monomers are not randomly incorporated in polymer chains, as observed in the ring-opening copolymerization of lactide and glycolide.^{1,2,8,13} ROP at high temperature and high vacuum results in the racemization of L-lactide units and transesterification, which increase with initiator basicity, reaction time, and reaction temperature.⁶ Similarly at high temperature and vacuum, melt polycondensation of PLGA can also induce the racemization of L-LA units and transesterification. The transes-

**Figure 2.** ¹H NMR spectra (500 MHz) of PLLA, PDLLA (50/50), and PLGA (methine region in LA and methene region in GA) obtained in CDCl₃ solutions.

terification will reduce both GA and LA block lengths gradually, which will promote PLGA solubility and lower PLGA crystallinity.

The number average molecular weight (\overline{M}_n) and molecular weight distribution (MWD) of the polymers were detected through GPC (shown in Table I). PLGA (90/10) with the highest M_w among these polymers shows a narrow MWD. MWD of PLGA increases with GA fractions and decreases slightly with reaction time. The compositions of PLGA were determined by ¹H NMR spectra. Figure 2 gives typical methine regions in the ¹H NMR spectra of PLLA, PDLLA, and PLGA samples. The molar fraction of GA moiety in PLGA can be calculated from the integrated area of peaks at 5.15 ppm due to methine protons in LA units^{17,29,30} and that of peaks at 4.60–4.90 ppm owing to methylene protons in GA blocks in PLGA.^{7,9,15} Assigning I_L to integrated peak area at 5.15 ppm, I_G integrated

Table II. Crystallinities and sequence lengths of copolymers prepared by the direct synthesis through melt polymerization

Samples	F_G^a %	T_g °C	T_m °C	Crystallinity ^b %	$[\alpha]_D^{25}$	Racemization ^c %	Average block lengths	
							L_L	L_G
PLLA-1	0	58.4	155.7	57.69	-146	6.76	-	-
PLLA-2	0	58.2	149.6	38.71	-132	19.40	-	-
PLGA-1 (90/10) ^d	13.80	ND ^e	ND	ND	-131	25.82	17.52	2.84
PLGA (90/10)	12.12	57.1	116.3	28.48	-125	29.31	17.47	2.40
PLGA (70/30)	32.20	52.8	ND	ND	-112	48.84	5.45	2.60
PDLLA (50/50)	0	48.4	104.8	14.05	-58	40.00	-	-

^a F_G , molar fraction of GA in copolymers, calculated from ¹H NMR. ^bCalculated from DSC curve according to ref 45.

^cCalculated from carbonyl signals in ¹³C NMR spectra. ^dPLGA-1 (90/10), prepared from the oligomer of L-LA/GA (90/10) after polymerized for 12 h. ^eND, not detected.

peak area of at 4.6–4.9 ppm, and F_G molar fraction of GA respectively, F_G can be calculated according to the following relationships, $F_G = I_G/(2I_L + I_G)$. The molar fraction of GA in PLGA is higher than that in the monomer feed, even though it decreases with reaction time as shown in Table I. GA fractions indicate that GA has higher reactivity than L-LA, which is consistent with that of the PLGA solubility.

Racemization and Sequence Length of PLGA

The microstructures of polyester chains appear to affect biodegradable and mechanical properties of polymers. The microstructures of copolyesters are influenced by the kind of monomer, initiator and transesterification in the ROP. In Figure 2, the methine region at 5.15 ppm of PDLLA (50/50) shows two indistinctly resolved quartets caused by racemic LA units, which is similar to poly(D, L-lactide) with more or less racemic structure.^{17,30} In comparison with PDLLA (50/50), PLLA-1 spectrum shows a less intense quartet in down-field at the methine region because of slight racemization of L-LA units. Because of long reaction time, PLLA-2 shows more racemization than PLLA-1. PLGA samples with CH signals similar to those of PDLLA possess more racemic structure than PLLA-2. The racemization of PLGA increases greatly with GA fractions. The optical rotation of the obtained polymers decreases with prolonged reaction time and increasing GA fractions in the copolymers as shown in Table II. All these results indicate that the addition of GA increases the racemization of LA blocks. CH₂ signals of PLGA in Figure 2 appear as a nine-line multiplet attributed to various pentads, whose intensity is greatly affected by the transesterification in poly(lactide-co-glycolide).^{7,9,15} In the melt polymerization of PLLA with Sn(II)/TSA as catalyst,²⁴ terminal groups of PLLA are coordinated with the catalyst center of Sn(II). TSA as a ligand fills the open coordination sites of the catalyst, so side reaction leading to the discoloration and racemization of PLLA is pre-

vented. In L-LA/GA copolymerization, GA terminal groups with higher reactivity could be coordinated with the catalyst preferentially. Thus the coordination of L-LA and TSA could be hindered to increase side reaction. Consequently, racemization and discoloration of PLGA increase with GA fractions.

High-resolution ¹³C NMR spectroscopy has been successfully used to characterize the microstructures of homo- and copolymers derived from L-LA,¹⁷ GA,¹⁸ lactides,^{8,27} glycolide,^{6,7} and CL.^{31–36} Carbonyl signals are more suitable to analyze monomer block lengths in copolymers, because they are more sensitive to sequence effect than other signals such as methyl, methylene, and methine.^{8,18,34} The methine signals at 68.5–69.5 ppm are useful for determination of the racemization of PDLLA and PLLA.^{34,37} Carbonyl positions of L-LA and GA blocks are shown in Figure 3. Figure 4 shows the carbonyl regions at 165–170 ppm of the ¹³C NMR spectra of the obtained polymers. Assignments of signals due to the isotactic (i) and syndiotactic (s) sequences of the lactate units are shown in Figure 4 according to the literature.^{24,38–41} The degree of racemization of polymer was calculated from the integral ratio of these sequence signals (see Table II). PDLLA (50/50) spectrum shows predominantly isotactic polymer chains with racemization of 40.0%, which is much different from that of poly(D,L-lactide) prepared by ROP process.^{34,37} PDLLA (50/50) is optically active, levorotary, *i.e.*, with predominant L-LA units. PDLLA prepared from DL-LA with tin powder as catalyst or without a catalyst is racemic.^{17,18,21,22} This means that L enantiomer is preferentially polymerized by Sn(II)/TSA catalyst in the present conditions. Thus stereoselective polymerization of DL-LA exists, as in the case of D,L-lactide reported by Spassky.³⁸

Carbonyl carbon signals in the ¹³C NMR spectra of PLGA were designated in comparison with those of PLLA, PDLLA, and poly(L-lactide-co-glycolide).^{6–9,18} In PLGA spectra, a new peak at 169.44 ppm appears and increases with GA fractions, which results

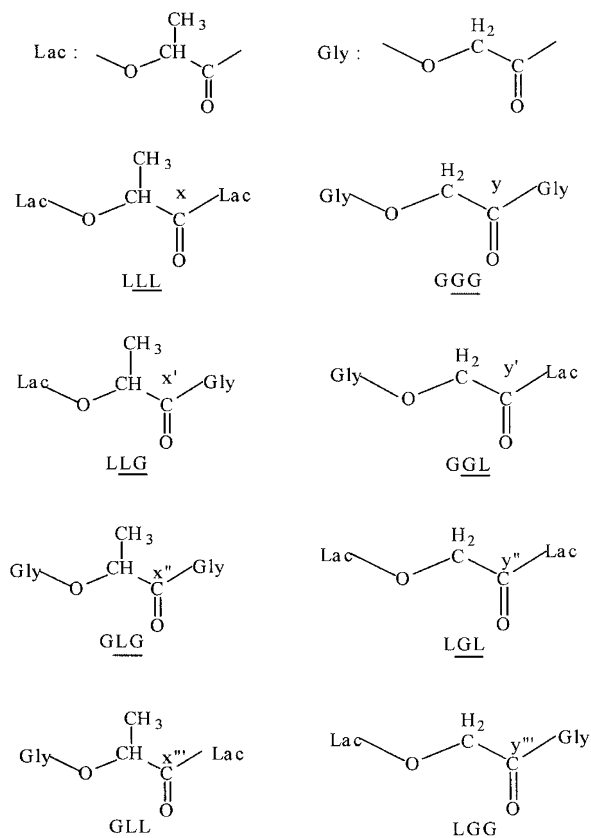


Figure 3. Labeling of different carbonyl units of poly(L-lactic acid-co-glycolic acid).

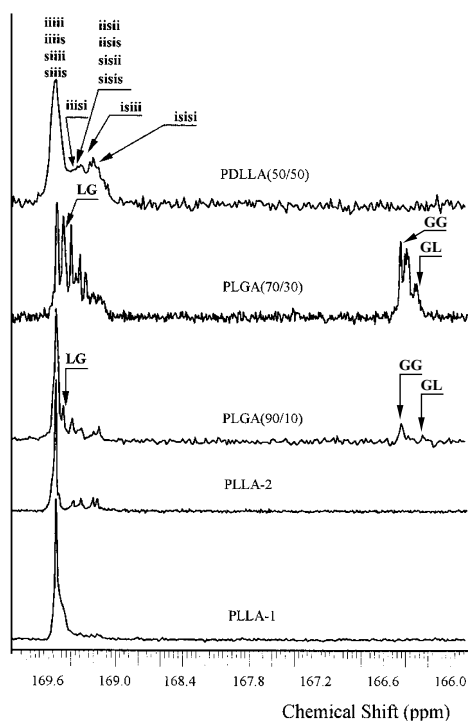


Figure 4. ¹³C NMR spectra (125 MHz) of PLLA, PDLLA (50/50), PLGA (carbonyl region) obtained in CDCl₃ solutions.

from LG blocks. The intensity of carbonyl signals due to the racemic units in PLGA increases with GA fractions. Racemization of PLGA indicates that the racem-

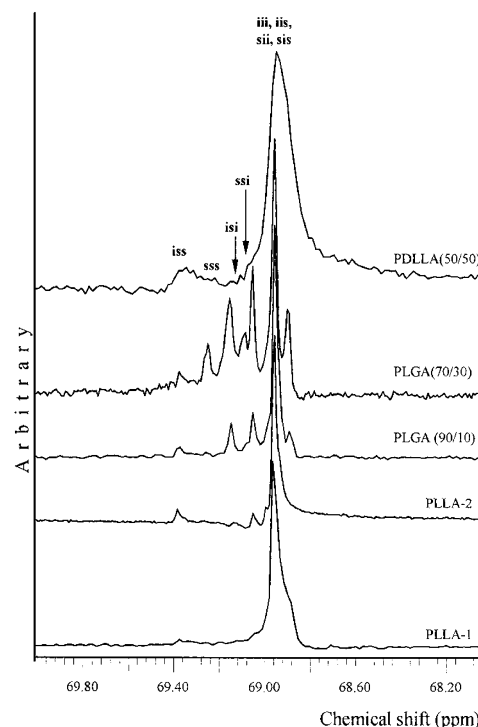


Figure 5. ¹³C NMR spectra (125 MHz) of PLLA, PDLLA, PLGA (methine region) obtained in CDCl₃ solutions.

ization of LA blocks increases with GA fraction and reaction time. Racemization makes it complicated to determine signal assignments of PLGA accurately.

Methine signals at 68.5–69.5 ppm in Figure 5 are designated in comparison with poly(D, L-lactide) and poly(L-lactide).^{34,37} The spectrum of PLLA-2 shows more intense signals due to tetrads such as iss, sss, isi, and ssi than that of PLLA-1, which confirms the effect of reaction time on the PLLA racemization. The PDLLA spectrum with a strong signal at 68.94 ppm due to tetrads of iii, iis, sii, and sis indicates stereoselective polymerization of DL-LA, which is consistent with the above results. The intensities of peaks due to iss, sss, isi, and ssi increase greatly with GA contents, which is further evidence of promoted racemization of LA blocks in the presence of GA. A new peak at 68.84 ppm can be caused by GA block, because it appears and increases with increasing GA fractions in PLGA.

Carbonyl signals of GA block at 166.40 ppm show two peaks attributed to GG and GL units respectively^{6–9,18} (see Figure 4). From intensity ratios of the two carbonyl signals, the average lengths of GA blocks (L_G) and L-LA blocks (L_L) were calculated according to the eq 1. All results are shown in Table II. L_G/L_L can be checked by the ¹H NMR spectroscopically determined composition served as control, according to eq 2.^{6–9,18}

$$L_L = \frac{I_{LL} + I_{LG}}{I_{LG}} \quad L_G = \frac{I_{GG} + I_{GL}}{I_{GL}} \quad (1)$$

$$\frac{n_G}{n_L}({}^1\text{H NMR}) = \frac{L_G}{L_L}({}^{13}\text{C NMR}) \quad (2)$$

Where n_L and n_G are the LA and GA molar fraction in the copolymers respectively. n_L/n_G (${}^1\text{H NMR}$) is in fair agreement with L_G/L_L (${}^{13}\text{C NMR}$), which supports the validity of each signal intensity. The random copolymers of L-LA/GA may possess random sequences with L_G near to 1. From the lengths of L-LA and GA blocks, the present reaction conditions obviously bring out a sequential block copolymer of L-LA/GA instead of a random copolymer. Both L_L and L_G decrease with reaction time in PLGA (90/10). L_L decreases with GA fractions in PLGA, while L_G increases. Considering the solubility and ${}^1\text{H NMR}$ spectra of PLGA, it is reasonable that transesterification and differences of reactivity between LA and GA exist in the melt copolymerization. The copolymerization of L-lactide with CL or glycolide^{1,2} has shown similar results. The lengths of the GA and LA blocks in copolymers decrease continuously, and may be equilibrated eventually by the transesterification.

Crystallinity of Copolymers

Figure 6 gives typical DSC thermograms of the polymers obtained. PLLA-1 curve shows a glass transition temperature (T_g) at 58.4 °C and an endothermic peak due to the crystal fusion at the melting temperature (T_m) of 155.7 °C. T_m of PLLA-1 is relatively lower than that of poly(L-lactide) (T_m 175 °C) prepared by ROP.^{28,35} The lower T_m results from low crystallinity and imperfect crystallization of PLLA, caused by some racemic sequences in PLLA chains. PLLA-2 with higher racemization shows lower T_m than PLLA-1. The enthalpy of fusion for a large crystal of poly(L-lactide) with infinite size corresponds to 93 J g⁻¹.⁴² In the present research, the crystallinity of PLLA-1 was 57.69%, similar to PLLA reported by Kimura.²⁴ Racemization of PLLA can be made sure on the basis of the relation between melting temperature and racemic content of poly(L-lactide).⁴³

Poly(D, L-lactide) prepared *via* ROP is amorphous (T_g at 45–55 °C and no T_m),³⁵ while PDLLA (50/50) in the present work shows T_g at 48.4 °C, T_m at 104.8 °C, and crystallinity of 14.05%. The partial crystallization of PDLLA (50/50) can be caused by stereoselective polymerization, which is consistent with ${}^1\text{H}$ and ${}^{13}\text{C}$ NMR spectral analysis and optical rotation. Neat poly(glycolide) is substantially crystalline material with T_m of 222 °C and small T_g at 45 °C, while poly(glycolide-co-L-lactide) with 12.3% glycolide units showed T_m at 166.4 °C and T_g at 40.4 °C.^{8,12,13} In the present work, PLGA (90/10) with 12.12% GA units shows T_g at 57.1 °C, T_m at 116.3 °C,

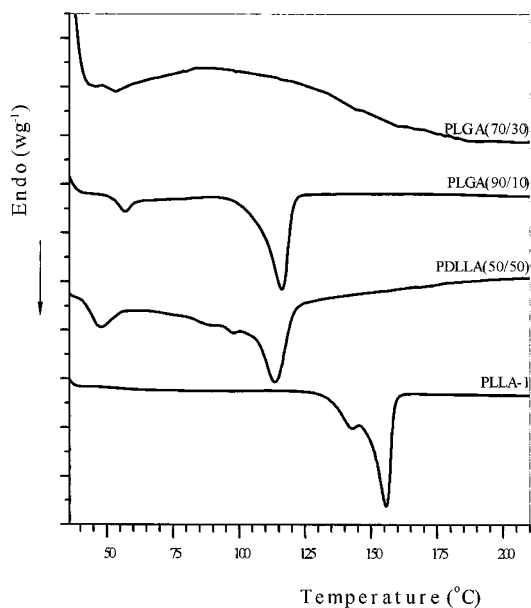


Figure 6. DSC thermograms of PLLA-1, PDLLA (50/50), and PLGA (see the text).

and crystallinity of 28.48% according to PLLA.⁴² The crystallization of PLGA chains yields smaller and less perfect crystallites, because the crystal lattice of L-LA blocks tends to exclude GA units, and incorporation causes lattice defects. When the molar fraction of GA in feed is more than 20%, the amorphous copolyester is formed because crystallization is reduced by the decrease of the L-LA block length. Additionally, the racemization promoted by the addition of glycolic acid monomer could also perform important role on the decrease of T_m and crystallinity of PLGA.⁶ Thus DSC measurements show good agreement with NMR sequence analysis.

X-Ray diffractograms of the obtained polymers are given in Figure 7. The diffraction curve of PLLA-1 shows a sharp and intense peak at 16.84 degree 2θ due to 020 reflection. Other peaks can be observed at 14.90, 19.21, and 22.45 degree 2θ due to 101, 023, 121 reflection respectively.^{15,18,28,44,45} These values coincide with observed values of the α structure of poly(L-lactide). PGA with \overline{M}_n of 2900 prepared by direct synthesis shows reflections at 2θ of 22.2° and 28.9°.¹⁵ The diffraction spectrum of PLGA (90/10) consists of a relatively intense reflection at 16.84 degree 2θ and two less resolved peaks at 14.90, 19.21 degree 2θ due to the crystallization of L-LA sequences, but no crystallization of GA sequences can be detected. The crystallization of PLGA (90/10) indicates the presence of relatively long LA sequences in the polymer chains, as confirmed by ${}^{13}\text{C}$ NMR analysis. PLGA (70/30) becomes amorphous, because the length of L-LA blocks is lessened by increasing GA content through transesterification. All results are consistent with those of ${}^1\text{H}$

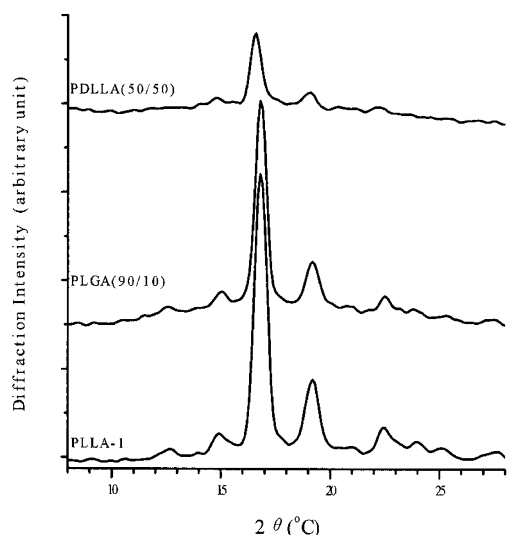


Figure 7. X-Ray diffractogram of PLLA-1, PDLLA (50/50), and PLGA (90/10).

NMR, ^{13}C NMR, and DSC determinations.

CONCLUSION

Direct synthesis was utilized to prepare PLLA, PDLLA, and PLGA with high M_w and narrow MWD through melt polycondensation in the presence of Sn(II)/TSA catalyst system. In the copolymerization of L-LA with GA, the reactivity of GA is higher than that of L-LA. The solubility in chloroform of PLGA decreases with GA content in feed, while the racemization of copolymers is promoted by increasing GA fractions. PDLLA (50/50) displays predominantly isotactic polymer chains because of partial stereoselective polymerization of racemic DL-LA. Transesterification occurs in the copolymerization of L-LA with GA, which lessens the sequence length of GA and L-LA. Racemization and transesterification result in short sequence length and lower crystallinity, as verified by DSC and XRD measurements. Present reaction conditions bring out sequential block copolymers instead of random copolymers of L-LA/GA.

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