Linear and Branched Architectures from the Polymerization of Lactide with Glycidol

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ABSTRACT: Samples of polylactide (PLA) were synthesized by initiating lactide ring opening with glycidol using $Sn(Oct)_2$ catalyst. Under low-temperature solution polymerization conditions, epoxide ring opening is precluded, leading to predominately linear epoxide capped PLA. With high-temperature bulk polymerization, simultaneous lactide and epoxide ring opening leads to hyperbranched polyesters characterized by linear PLA segments separating glycerol branch points. Molecular weights and extent of branching were determined by gel permeation chromatography (GPC), and the presence of branching was confirmed by solution viscosity measurements and g' calculations. Solution polymerizations yielded linear samples with controlled number-average molecular weights in the range 4800−19 200 g/mol. Number-average molecular weights of branched samples from bulk polymerization ranged from 19 800 to 100 800 g/mol. The branched samples exhibited relatively low polydispersity indices (PDI) in the range 1.48−2.00. Glass transition temperatures of branched samples were determined by differential scanning calorimetry and were found to be lower compared with literature values for linear PLA of similar molecular weight.

Introduction

Polylactides (PLA) are well-known biodegradable, biocompatible polyesters produced by ring opening of lactide monomer. A combination of favorable degradation and mechanical properties with good biocompatibility makes PLA a popular candidate for various medical applications including sutures, drug delivery systems, and internal bone fixation.[1−4] Additionally, the monomer is derived from renewable resources, making it a desirable alternative to fossil fuel based plastic products from both environmental and economic perspectives. Thus, PLA has recently gained significant attention due to the prospects of replacing traditional commodity products such as those in the packaging industry.[2,4−10] The properties of linear PLA, however, are not optimal to facilitate widespread substitution of fossil fuel based plastics at this time. Physical properties are dependent on a number of different characteristics, including enantiomeric ratios, the nature of comonomer species, and structural architecture.

The introduction of branching to the PLA backbone is one highly effective approach to tailor the physical properties. Star branched PLA has been investigated by numerous synthetic approaches.[11−15] Other types of branched PLA including comb-branched[16−21] and cross-linked[22,23] structures have also received abundant attention. However, there are only three unique synthetic examples of hyperbranched polymers containing PLA.[24−27]

A number of research groups have extensively studied hyperbranched polyesters having either aromatic or aliphatic repeat units, and several reviews describe their synthesis and properties.[28−31] Several literature examples describe hyperbranched polyesters made from lactones, although examples incorporating lactide are limited.[24−27] ϵ-Caprolactone has been functionalized with hydroxyl groups to form both AB_2 and AB_3 monomers that have been homopolymerized to form hyperbranched polyesters.[32−34] A latent AB_3 derivative of ϵ-caprolactone has been employed in homopolymerizations in addition to copolymerization with unsubstituted ϵ-caprolactone monomer using $Sn(Oct)_2$ catalyst in a single step.[33] More often, however, linear oligomeric polyester segments formed by lactone ring-opening polymerization (ROP) are integrated into "linear-hyperbranched hybrids" and "dendrimer-like stars". The linear polyester chains separate branch points via copolymerization with an AB_2 monomer, typically through the combination of ROP of cyclic lactone monomer with the polycondensation of a suitable AB_2 initiator. Studies dominating the literature employ bis(hydroxy)carboxylic acids copolymerized with cyclic lactones.[25,32,33,35] There are several different well-designed approaches to these copolymerizations, each resulting in unique structures. Protected AB_2 macromonomers were prepared by ring-opening of lactide by 2,2-bis(hydroxymethyl)benzyl propionate, which were subsequently hydrogenated to the corresponding acid and polymerized via polycondensation.[36] Frey et al. have demonstrated a single-step approach through simultaneous copolymerization of ϵ-caprolactone, δ-valerolactone, and L,L-lactide with 2,2-bis(hydroxymethyl)butyric acid in the bulk with $Sn(Oct)_2$.[25,37,38] An alternative to an AB_2 monomer containing an acid group was demonstrated in a copolymerization study combining lactide with mevalonolactone in a one-pot reaction using $Sn(Oct)_2$ catalyst.[27] The mevalonolactone acts as a latent comonomer, where the "second" hydroxyl group is inactive until the six-membered lactone ring is attacked. We focus on a similar approach utilizing simultaneous dual ROP through copolymerization of a latent AB_2 cyclic monomer with lactide. However, we introduce the copolymerization of two ring systems of completely different structure.

We are interested in investigating the simultaneous ring opening of lactide and hydroxy-functionalized epoxides. One such hydroxy-functionalized epoxide is 2,3-epoxy-1-propanol (glycidol). The first reports of glycidol polymerization were in 1966.[39] Thereafter, several groups produced linear polyglycidol where branching was considered an undesirable side reaction.[40,41] More recently, glycidol has been the subject of numerous studies investigating formation of hyperbranched

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polyethers, termed "polyglycerols".[42,43] Several studies have combined hyperbranched polyglycerols formed from glycidol polymerization with lactone ROP in successive steps.[43−45] This approach leads to starlike structures with a hyperbranched polyglycerol core that acts as multifunctional initiator for linear polyester arms. In this manner, the number of initiating hydroxyl groups in the core can be controlled, as can the length of the arms. Single-step copolymerization of lactide and glycidol is absent in the literature. Our approach leads to randomly branched structures with linear PLA segments separating glycerol branch points. The success of our investigation relies on the initiation of lactide ring opening by the primary hydroxyl on glycidol in conjunction with the ring opening of the epoxide group by the PLA chain end hydroxyl, in which both mechanisms are catalyzed by $Sn(Oct)_2$.

Experimental Section

Materials. All solvents were from Mallinckrodt. Toluene (99.5%) was washed with concentrated H_2SO_4, aqueous 5% $NaHCO_3$, and finally water until neutral and then distilled over CaH_2 under an argon atmosphere directly prior to use. HPLC grade tetrahydrofuran (THF) (>99.8%), lab grade methylene chloride (99%), and lab grade hexanes (98%) were used without further purification. L-Lactide (97%), obtained from Purac, was recrystallized from toluene and dried under vacuum (70 mtorr) for 24 h prior to use. D-Lactide (∼95%) was donated from Chronopol (Golden, CO) and purified as for L-lactide. $Sn(Oct)_2$ (95%) and glycidol (96%), purchased from Aldrich, were each fractionally distilled under vacuum (70 mTorr) and stored for short periods in sealed flasks under an argon atmosphere at 5 °C before use. All glassware, ground-glass syringes, and needles were oven-dried at 160 °C for at least 24 h and cooled under argon directly prior to use. Glassware was further flame-dried under an argon purge after assembly. Gastight syringes were dried over $CaSO_4$ in a vacuum desiccator (70 mTorr) for 24 h directly prior to use.

Characterization. Molecular weights were determined by gel permeation chromatography (GPC) at 30 °C. The instrument is a Hewlett-Packard model 1084B liquid chromatograph connected to a calibrated Waters R401 differential refractometer and a Wyatt Technology miniDAWN multiangle laser light scattering (MALLS) detector. Two Hewlett-Packard Plgel 5μ Mixed-D columns with linear range of molecular weight from 200 to 400 000 g/mol were used in series with THF as eluent at a flow rate of 1.0 mL/min. Molecular weights were determined by light scattering using Windows-based Astra 4.90.07 software supplied by Wyatt Technology. A value of 0.042 mL/g[46] was used for the refractive index increment (d*n*/d*c*) of all PLA samples. This d*n*/d*c* value was validated using Astra software to determine the integration of the entire elution peak using a calibrated refractive index detector and assuming 100% sample elution. The different PLA architectures did not have a noticeable effect on the d*n*/d*c*. Intrinsic viscosities were measured in THF at 30 °C using a size 50 Cannon-Ubbelohde viscometer. At least four concentrations of each sample were measured, and the reduced and inherent viscosities were plotted to zero concentration to obtain the intrinsic viscosity as the average of the two intercepts. Glass transition temperatures (T_g) were measured by differential scanning calorimetry (DSC) using a Perkin-Elmer Pyris 1 instrument. The instrument was calibrated with an indium standard. T_g's were taken as the midpoint of the inflection of the heat capacity curve as determined by the baseline tangents. ^{1}H NMR spectra were obtained using a 400 MHz Chemagnetics CMX Infinity spectrometer. $CDCl_3$ was used as the solvent, and the peak positions are reported with respect to TMS.

Polymerization. All polymerizations were conducted using a mixture of 80% L-lactide and 20% d-lactide.

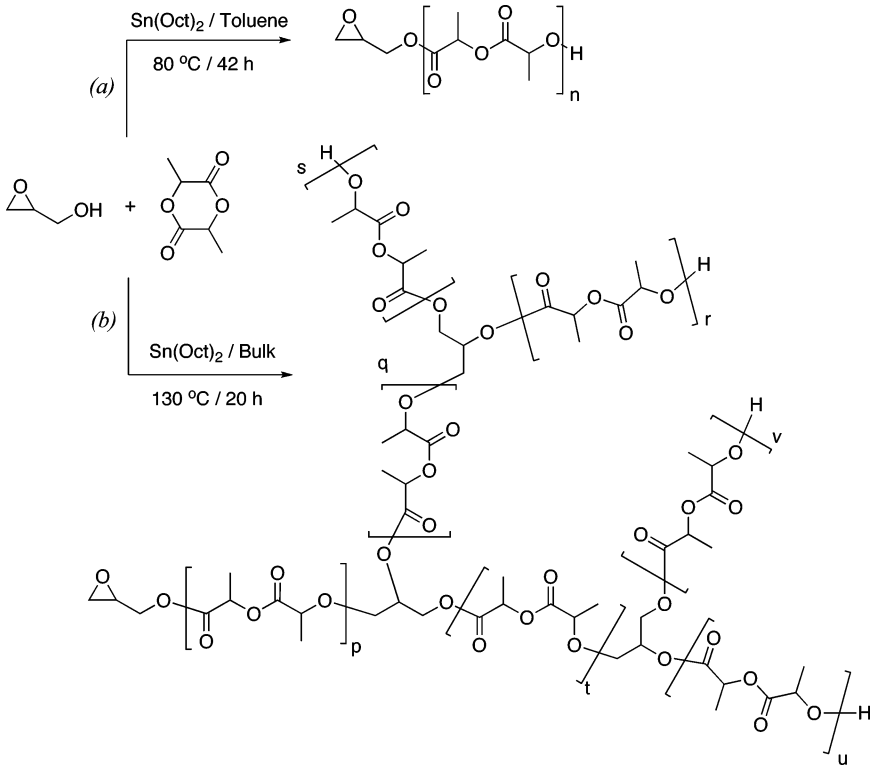
Initiation of Lactide with Glycidol in Solution. Small sample sizes were used (≈3.75 g of lactide), necessitating dilute initiator and catalyst stock solutions in toluene. The stock solutions were pressurized under argon and freshly prepared within 4 h of reaction commencement. The following describes the preparation of sample **1a**: L-lactide (3.00 g, 20.8 mmol) and D-lactide (0.75 g, 5.2 mmol) were weighed into a 50 mL flame-dried, two-neck, round-bottom flask containing a Teflon-coated magnetic stir bar. A flame-dried condenser was connected to one neck, and the second neck was sealed with a rubber septum. A vacuum line was attached to the condenser and vacuum was applied (70 mTorr) for 4 h. The flask was filled with argon, and then toluene (30 mL; 1.3 M in lactide) was added via a ground glass syringe, after which the reaction flask was immersed in an oil bath at 80 °C with rapid stirring. A dilute solution of initiator was prepared by mixing 1.0 mL of glycidol (1.12 g, 15.1 mmol) with 5.0 mL of toluene, resulting in a 2.5 M solution. 207 μL (0.52 mmol of glydicol) of the stock solution was added to the reaction flask using a gastight syringe, which corresponds to a monomer-to-initiator ratio of 50. A 0.061 M solution of catalyst was prepared by mixing 0.126 g of $Sn(Oct)_2$ (0.31 mmol) with 5.0 mL of toluene. 85 μL (0.0052 mmol of $Sn(Oct)_2$) of the stock solution was introduced to the reaction, corresponding to a monomer-to-catalyst ratio of 5000. The temperature was maintained for 42 h, after which the hot solution was precipitated directly into a 10-fold excess of cold hexanes. Polymer samples were isolated by filtration and then dried at room temperature under vacuum for 24 h. A 60% conversion was calculated from GPC measurements, which correlates well with the conversion based on ^{1}H NMR spectroscopy. The molecular weight as measured by GPC (with MALLS detector) is 4800 g/mol, with a PDI of 1.44. ^{1}H NMR [deuterated chloroform ($CDCl_3$) as solvent with respect to tetramethylsilane (TMS) at 0.00, ppm]: PLA: δ 1.5−1.65 ppm (m, CH_3); δ 5.15−5.25 ppm (m, C*H*); glycidol residue: δ 3.75−3.85 ppm (m, C*H*), δ 2.7−2.9 ppm (m, CH_2); residual lactic acid: δ 1.45−1.49 ppm (d, CH_3); δ 4.34−4.37 ppm (q, C*H*); residual lactide: δ 1.67−1.69 ppm (d, CH_3); δ 5.01−5.06 ppm (q, C*H*).

Copolymerization of Lactide and Glycidol in the Bulk. Bulk reactions were performed with the same catalyst, monomer, and initiator ratios as for solution polymerizations. The experimental details for the preparation of sample **2a** are provided: L-lactide (2.87 g, 19.9 mmol) and D-lactide (0.72 g, 5.0 mmol) were weighed into a 50 mL flame-dried, single-neck, round-bottom flask containing a Teflon-coated magnetic stir bar. After drying the monomer under vacuum and purging with argon, the flask was sealed with a rubber septum and further purged with argon. The mixture was then melted by placing into an oil bath heated to 130 °C, immediately after which the glycidol initiator (200 μL of 2.5 M solution; 0.50 mmol) and $Sn(Oct)_2$ catalyst (82 μL of 0.061 M solution; 0.0050 mmol) were introduced sequentially through the septum via gastight syringes. The temperature was maintained for 20 h, during which stirring ceased due to the viscosity increase caused by polymerization. The flask was cooled to room temperature, and the polymer was dissolved in 20 mL of warm methylene chloride and then precipitated into a 10-fold excess of cold hexanes. A 95% conversion was calculated from GPC measurements. The number-average molecular weight as measured by GPC−light scattering is 19 800 g/mol, with a PDI of 1.76. ^{1}H NMR [$CDCl_3$ as solvent with respect to TMS at 0.00, ppm]: PLA: δ 1.5−1.65 ppm (m, CH_3); δ 5.15−5.25 ppm (m, C*H*); glycidol residue: δ 3.75−3.85 ppm (m, C*H*), δ 2.7−2.9 ppm (m, CH_2); residual lactic acid: δ 1.45−1.49 ppm (d, CH_3); δ 4.34−4.37 ppm (q, C*H*); residual lactide: δ 1.67−1.69 ppm (d, CH_3); δ 5.01−5.06 ppm (q, C*H*).

Results and Discussion

Design of Hyperbranched Polymer. Our approach to PLA branching is based on the effective copolymerization of epoxide and lactide using a single catalyst in one step. Although numerous authors report the sequential polymerization of epoxides and lactide to form ABA and ABC block copolymers,[47−50] we found only two studies involving direct copolymerization. Ethylene oxide and lactide have been copolymerized in a single step performed at 60 °C in toluene using various

Scheme 1. Synthesis of Glycidol−Lactide (Co)polymers under Different Conditions[a]



[a] (Co)polymerization reactions catalyzed by $Sn(Oct)_2$ lead to (*a*) linear epoxide-capped PLA from solution polymerization in toluene at 80 °C or (*b*) hyperbranched poly(glycidol-*co*-lactide) from bulk polymerization at 130 °C.

dual catalyst systems, including $Sn(Oct)_2$ and $Al(R)_3$ where R is either isobutyl or ethyl.[51] Additionally, terpolymers were formed in single-step polymerizations involving lactide, 4,4′-hexafluoroisopropylidenephenol (6F-Bis-A), and the diglycidyl ether of bisphenol A (DGEBA) at 110 °C in various solvents,[52] using a complex of KCl/18-crown-6 as catalyst. Results of this study varied widely under different conditions, and high MW polymer was obtained only when the molar feed ratio was 1:1:1. The authors did not address the mechanism, and the exact composition of polymer resulting from this epoxide/lactide copolymerization was not determined. We have attempted to identify conditions that will promote the simultaneous ring-opening of lactide and the epoxide group of glycidol to form branched polymers.

$Sn(Oct)_2$ has been shown to catalyze polymerization of lactide and various lactones under different temperature conditions.[12,27,53,54] $Sn(Oct)_2$ does not initiate lactide ring opening alone. Addition of an alcohol forms a tin alkoxide, which propagates ROP by an insertion coordination mechanism.[55−57] Since the tin alkoxide is the initiating species, the theoretical molecular weights of linear polymers are dependent solely on hydroxyl concentration relative to lactide and are calculated as follows assuming the absence of epoxide ring opening (eq 1):

$$M_{n(theo)} = \frac{[LA]_0}{[I]} M_{LA} x_{LA} \quad (1)$$

where $[LA]_0$ and [I] are the initial concentrations of lactide and glycidol monomer, respectively, M_{LA} is the molecular mass of lactide, and x_{LA} is the fractional conversion of lactide monomer. Equation 1 neglects the small contribution to molecular weight from the initiating species (74 g/mol).

Polymer molecular weight is therefore strongly indicative of secondary structure in the case of poly(glycidol-*co*-lactide). The two possible structure−molecular weight relationships are represented as follows (eqs 2 and 3):

$$\bar{M}_{n(expt)} \leq \bar{M}_{n(theo)} \rightarrow \text{linear} \quad (2)$$

$$\bar{M}_{n(expt)} > \bar{M}_{n(theo)} \rightarrow \text{coupled (branched)} \quad (3)$$

The first represents the case in which the alcohol initiates lactide ROP in the absence of epoxide ring opening. We propose the structure shown in Scheme 1a, namely linear PLA capped with an epoxide group. Experimental data that adhere to eq 3 suggest that epoxide ring opening has occurred in conjunction with alkoxide-initiated lactide ROP, leading to molecular weights in excess of those theorized using eq 1, and thus define at a minimum linear chains coupled together leading to a branched structure (Scheme 1b). Reaction conditions are proposed as a means to control ring opening and thus architecture.

It has been demonstrated that lactide ring-opening proceeds in toluene at temperatures of 75 °C in the presence of alcohol and $Sn(Oct)_2$ catalyst, although 100% monomer conversion was not attainable.[54] Contrarily, nucleophilic attack on the oxirane ring associated with glycidol is generally favored at bath temperatures exceeding 100 °C.[58,59] Bicak et al. have demonstrated nucleophilic ring opening of maleic anhydride by the hydroxyl group of glycidol at 70 °C.[58] They report that due to the exothermic nature of the reaction, the mixture actually reaches 80 °C, yet epoxide ring opening does not occur. They were able to isolate the monoglycidyl maleate from a 1:1 reaction of glycidol with maleic anhydride. Subsequent reaction at 120 °C led to epoxide ring opening and polymerization ensued. Both steps of the polymerization were performed in dimethoxyethane without catalyst. Accordingly, we conducted polymerizations under different reaction conditions to control the epoxide ring opening. Low-temperature solution polymerizations with glycidol initiator were designed in order to avoid epoxide ring opening, leading to linear epoxide-capped PLA

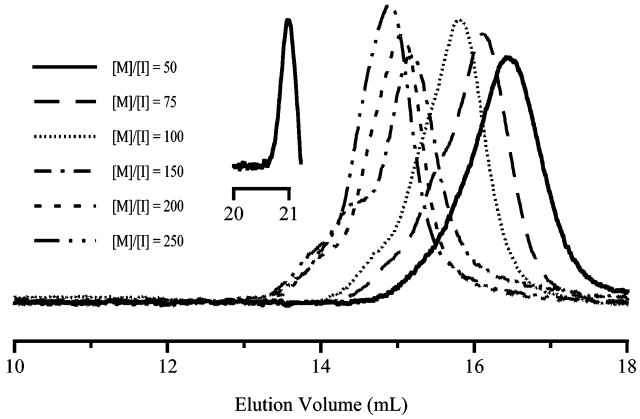


Figure 1. GPC plots of linear epoxide-capped PLA formed in solution (co)polymerization of glycidol and lactide in toluene at 80 °C with varying monomer-to-initiator ratios ([M]/[I]) from 50 to 250. Inset depicts residual monomer for sample [M]/[I] = 50.

with low polydispersity. High-temperature bulk polymerizations were designed to promote epoxide ring opening, leading to hyperbranched PLA.

Solution Polymerization. The solution polymerizations were carried out at 80 °C for 42 h in toluene. Lactide samples were prepared in an 80:20 L:D ratio in order to produce amorphous materials that could be easily characterized using THF as eluent in GPC measurements. Studies of glycidol polymerization catalyzed by $Sn(Oct)_2$ are absent from the literature. Figure 1 shows the GPC plots corresponding to six samples produced using various [M]/[I] ratios.

The general trend of increasing molecular weight with increasing $[M]_0/[I]$ ratio is clearly demonstrated in the GPC plots. The trend exhibits the dependence of molecular weight on initial hydroxyl concentration as opposed to $Sn(Oct)_2$ concentration, which was the same in each experiment.

GPC chromatograms reveal monomer conversion based on the relative area of the polymer and lactide monomer peaks. The elution volume of lactide monomer was determined by GPC analysis of lactide alone and can be separated from the solvent peak that elutes above 21.2 mL. The peak associated with residual lactide monomer for one of the samples is shown in the inset of Figure 1, and monomer elutes at the same volume in each sample. Conversion was calculated by dividing the polymer peak area by the sum of the polymer and monomer peak areas. This approach assumes the same d*n*/d*c* for PLA and lactide monomer. Conversion was also determined by ^{1}H NMR spectroscopy by comparing the methine peaks due to lactide at 5.01−5.06 ppm with the methine peaks due to PLA at 5.15−5.25 ppm to yield similar values to that determined by GPC analysis (Figure 2). The residual lactide was readily removed by vacuum sublimation. The results for the series of six reactions are presented in Table 1.

Ring−chain equilibrium is established during polymerization, the extent of which determines the maximum monomer conversion. For example, Kalmi et al. observed maximum conversion of ≈65% in toluene at 75 °C using $Sn(Oct)_2$ with *n*-butanol initiator.[54] Thus, if maximum conversion is considered on the basis of $[M]_0$, the final molecular weight can be controlled precisely by adjusting the $[M]_0/[I]$ ratio. Any experimental error is attributed to the purity of the starting materials with respect to protic impurities. Longer reaction times did not lead to higher conversion. Results reported by Kalmi et al. show that the upper conversion limit is reached after ∼20 h under the given conditions. A small shoulder on the low elution volume side of the peak is observed in some samples, which may indicate a small amount of epoxide ring opening during the long reaction times.

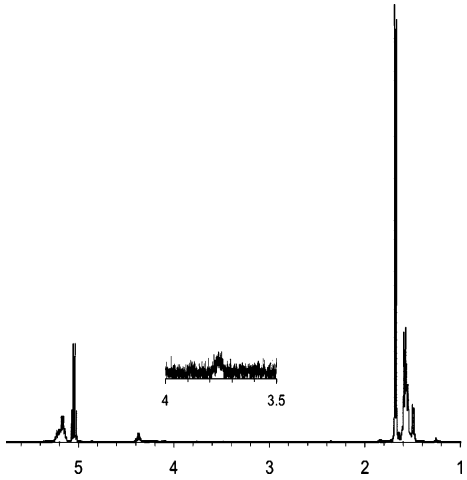


Figure 2. ^{1}H NMR spectrum for 1a. Inset shows the expanded region.

Table 1. Characterization Data for the Linear Epoxide-Capped PLA from Solution Polymerization in Toluene at 80 °C

expt ID	$[M]_0/[I]^a$	x^b	$M_{n(theo)}$,^{c} g/mol	M_n,^{d} g/mol	$M_w/M_n{}^d$
1a	50	0.60	4 300	4 800	1.44
1b	75	0.69	7 500	6 600	1.18
1c	100	0.74	10 700	10 400	1.14
1d	150	0.85	18 400	14 900	1.23
1e	200	0.67	19 300	16 100	1.28
1f	250	0.70	25 200	19 200	1.25

[a] $[M]_0$ = initial lactide molar concentration; [I] = glycidol concentration. [b] Fractional conversion of lactide monomer as measured by GPC chromatogram. [c] Calculated from eq 1. [d] GPC-MALLS measurement.

Conversions based on GPC plots correlate directly to experimental molecular weights as described by eq 1 and confirm the predicted structure in Scheme 1a, namely linear PLA chains capped with epoxide groups from the glycidol initiator. Experimental molecular weights that are smaller than theoretical values indicate that the number of polymer chains is slightly greater than the number of glycidol molecules introduced. The presence of protic impurities offers a potential explanation for this phenomenon.

The experimental number-average molecular weights of samples from solution polymerizations in our study range from 4800 to 19 200 g/mol with an average conversion of ≈70%. As is typical with such reactions, the polydispersities remained low, ranging from 1.14 to 1.44, indicative of the living character established for linear polyester formation using $Sn(Oct)_2$ catalyst.

Application of ^{1}H NMR spectroscopy was done in an attempt to independently determine the molecular weight by measuring the relative ratio of lactide repeat units to peaks associated with the glycidol initiator. The signal for the protons associated with the glycidol initiator is less than 1.5% relative to the protons of the lactide repeat unit; thus, the sensitivity did not provide adequate results even for the two lowest molecular weight samples (1a and 1b).

The results ultimately demonstrate that the epoxide group is essentially unreactive toward ROP under the low-temperature reaction conditions. These polymers represent latent AB_2 macromonomers, leaving open the possibility for further reaction under catalytic conditions tailored toward ROP of epoxide species. However, the main objective of the current work was to define conditions where ring opening of the epoxide occurs concurrently leading to branched polymer.

Table 2. Characterization Data for the Hyperbranched PLA Copolymers from Bulk Polymerization at 130 °C

expt ID	$[M]_0/[I]^a$	x^b	$M_{n(theo)}$,[c] g/mol	M_n,[d] g/mol	M_w/M_n[d]
2a	50	0.95	6 900	19 800	1.76
2b	75	0.98	10 600	37 000	1.49
2c	100	0.94	13 600	44 000	2.00
2d	150	0.92	19 900	52 400	1.56
2e	200	0.95	27 400	60 200	1.84
2f	250	0.93	33 500	101 000	1.48

[a] $[M]_0$ = initial lactide molar concentration; [I] = glycidol concentration. [b] Fractional conversion of lactide monomer as measured by GPC chromatogram. [c] Calculated from eq 1. [d] GPC-MALLS measurement.

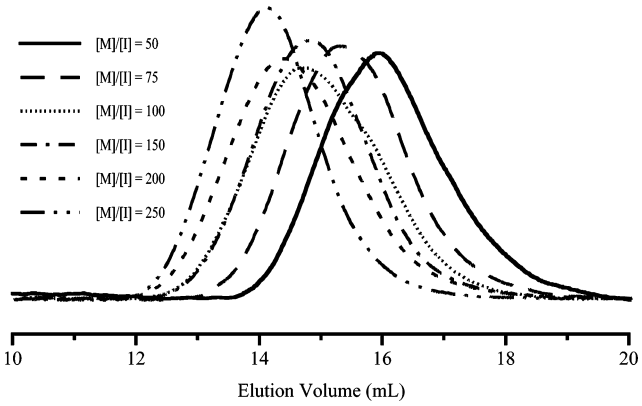


Figure 3. GPC plots of branched polymer samples from bulk copolymerization of glycidol and lactide at 130 °C with varying monomer-to-initiator ratios ([M]/[I]) ranging from 50 to 250.

Bulk Polymerization. The bulk polymerizations were carried out at 130 °C for 20 h using $Sn(Oct)_2$ as catalyst. The results for a series of six experiments are shown in Table 2. This procedure does two things: (1) it averts the necessity of solvent, and (2) it promotes epoxide ring opening that leads to branching.

The GPC plots for the six samples are shown in Figure 3. An additional advantage of bulk polymerizations of lactides is the higher monomer conversions compared to solution polymerization,[56,54] in which the polymer−monomer equilibrium lies further toward monomer. The standard entropy and enthalpy of L-lactide polymerization were previously measured in bulk and in 1,4-dioxane at 1 M concentration.[60] Based on these values, a reaction temperature of 130 °C corresponds to $[M]_{eq}$ of 0.15 mol/L (≈1.7 wt %).[61] Thus, bulk lactide polymerizations conducted at 130 °C lead essentially to quantitative monomer consumption, as shown in Table 2.

^{1}H NMR spectroscopy corroborates the high conversion, indicating minimal signal intensity corresponding to residual lactide monomer (Figure 4). Again, the ability to quantify the ratio of polylactide relative to glycidol and ring-opened glycidol units by ^{1}H NMR spectroscopy is hampered by the relatively low concentration of glycidol in the polymerizations.

The GPC plots illustrate systematic variation of molecular weight based on [M]/[I] ratios similarly to solution polymerizations. Molecular weights, however, indicate the simultaneous ring-opening of lactide and glycidol monomer through the relationship between the theoretical and experimental M_n values in eq 3. The results indicate the linking of linear PLA segments, although the extent of linking is apparently limited to ∼66% conversion of epoxide ring-opening ($M_{n(expt)}/M_{n(theo)} \approx 3$) under the given conditions. Further evidence of the occurrence of epoxide ring-opening was obtained by a different approach. Two samples were prepared in the same manner as the bulk polymerizations described in the Experimental Section. A

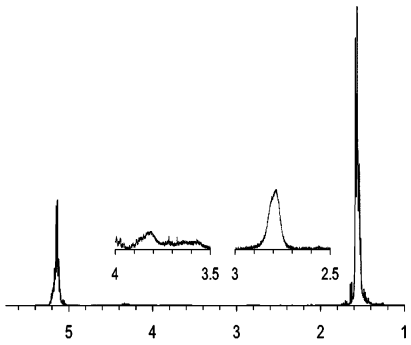


Figure 4. ^{1}H NMR spectrum for 2a. Inset shows the expanded region.

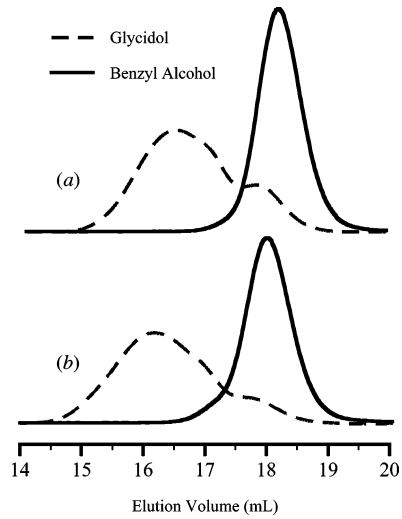


Figure 5. GPC plots for bulk polymerizations using the two different initiators glycidol and benzyl alcohol at a monomer to initiator ratio of 50 at different times: (a) after 1 h and (b) after 2 h at 130 °C.

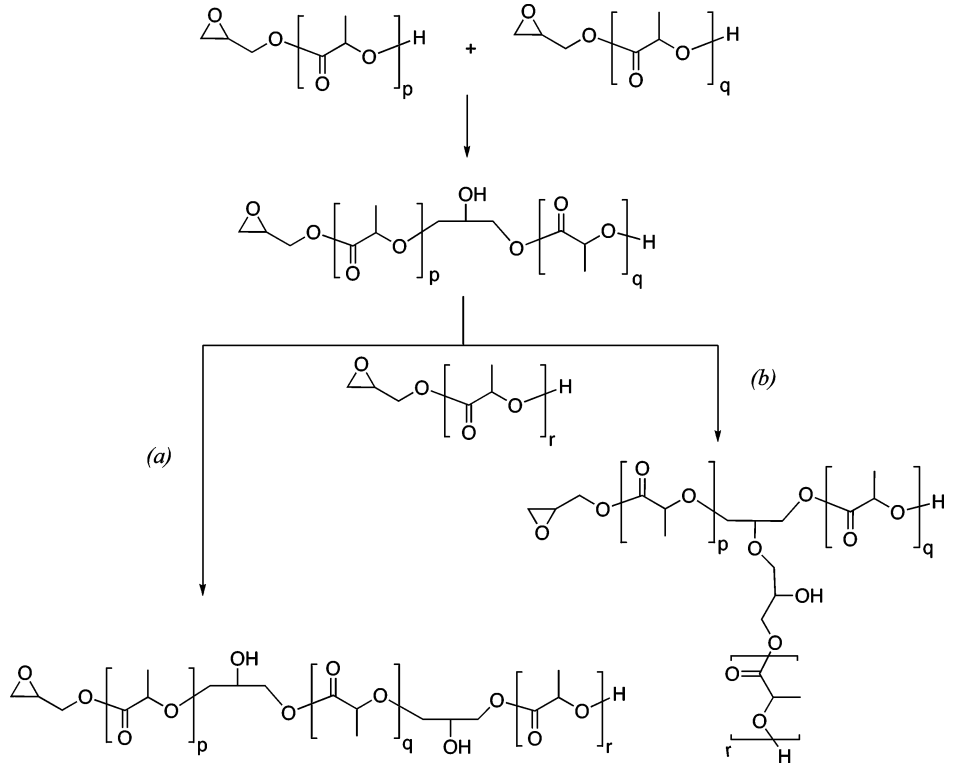
Table 3. Characterization Data for Bulk PLA Polymerizations Initiated by Benzyl Alcohol and Glycidol ([M]/[I] = 50; $M_{n(theo)}$ = 6850)

initiating species	rxn time, h	M_n, g/mol	M_w/M_n
benzyl alcohol	1	4394	1.10
	2	5052	1.29
glycidol	1	6980	1.88
	2	14770	1.34

monofunctional initiator (benzyl alcohol) was introduced to one, while the other was initiated with glycidol. The monomer-to-initiator ratio in both cases was 50 ($M_{n(theo)} \approx 6900$). Samples were withdrawn via syringe from each reaction after 1 and 2 h at 130 °C. Figure 5 shows the GPC plots attributed to these samples.

The plots suggest several things regarding the poly(glycidol-*co*-lactide) polymerizations. First, the shift in elution volume to lower values compared to PLA formed from monofunctional initiator indicates that linkage of PLA chains is occurring as a result of epoxide ring opening. Second, a qualitative description of the relative rates of ring opening of the lactide and epoxide rings can be inferred. The molecular weights determined by light scattering for the benzyl alcohol initiated samples at 1 and 2 h suggest that lactide ROP proceeds relatively rapidly and is nearing completion after just 2 h. The quantitative results are presented in Table 3 and reinforce this implication. For the glycidol initiated samples, residual linear polymer is observed at ∼18 mL, and the relative amount decreases from 1 to 2 h. Furthermore, the amount of higher molecular weight material at low elution volume increases from 1 to 2 h, and the peak

Scheme 2. Possible Structures from Linking of Linear Epoxide-Capped PLA in Which (*a*) Only the Primary Hydroxyl Is Active or (*b*) Both the Primary and Secondary Hydroxyl Groups Are Active toward ROP



continues to shift to lower elution volume, indicating an increase in molecular weight with time and slower reaction of the epoxide relative to lactide.

The epoxide ring opening in the bulk polymerization has been established, but the results in Table 2 imply two potential polymer structures, and samples may consist of a mixture of each possibility. Scheme 2 demonstrates the two possible pathways and their corresponding products.

Pathway (*a*) in Scheme 2 would result from an inactive secondary hydroxyl group associated with the ring-opened epoxide group, whereupon only the PLA chain-end hydroxyl is active toward further epoxide ring opening. Alternatively, structure (*b*) represents the scenario in which the secondary hydroxyl group resulting from glycidol ring opening is active in nucleophilic attack on another epoxide-capped PLA segment. The latter circumstances lead to a branched structure, whereas the former result in a linear structure via the linkage of several linear segments with periodic pendant hydroxyl groups separating linear PLA fragments. The final structure in Scheme 2b represents the result of two epoxide ring-opening reactions between linear epoxide-capped PLA oligomers, leading to the branched structure. Subsequent epoxide ring opening leads to hyperbranched architectures.

Further characterization was warranted in order to confirm the structure of the bulk samples. Intrinsic viscosity measurements present a convenient experimental indication of polymer structure if Mark−Houwink−Sakurada parameters are readily available. Branched structures adopt a more compact structure in solution that corresponds to smaller hydrodynamic volumes. The solution viscosities of hyperbranched polymers are influenced by the extent of branching relative to linear polymers of comparable molecular weight.[30,62,63] A contraction factor, g', displayed in eq 4 has been established to compare the intrinsic viscosities [η] of branched and linear polymers of equal molecular weight as a ratio.

Table 4. Intrinsic Viscosities, Contraction Factors (g'), and Glass Transition Temperatures (T_g) for the Hyperbranched PLA Copolymers from Bulk Polymerization at 130 °C

expt ID	M_w,[a] g/mol	$[\eta]_{calc}$,[b] mL/g	$[\eta]_{expt}$,[c] mL/g	g'	T_g,[d] °C
2a	34 900	0.34	0.23	0.68	47
2b	55 100	0.48	0.35	0.71	50
2c	88 000	0.68	0.47	0.68	51
2d	81 700	0.65	0.50	0.77	52
2e	111 000	0.81	0.63	0.78	54
2f	149 000	1.01	0.76	0.75	54

[a] Weight-average molecular weight from GPC-MALLS. [b] Calculated from eq 5 using MHS constants from the literature.[46] [c] Extrapolation from viscometry. [d] DSC measurement.

$$g' = [\eta]_{branched}/[\eta]_{linear} \quad (4)$$

Intrinsic viscosities of polymers produced in the bulk were determined in THF at 30 °C. Mark−Houwink−Sakurada (MHS) parameters k and a for linear PLA initiated with monofunctional alcohol (benzyl alcohol) have been determined to be 1.742×10^{-4} dL/g and 0.736, respectively.[46] Intrinsic viscosity values for linear PLA samples with the same molecular weight as the bulk samples ($[\eta]_{linear}$ in eq 4) were calculated from the MHS relationship (eq 5) using experimental M_w for bulk poly(glycidol-*co*-lactide) samples determined by GPC-MALLS.

$$[\eta]_{linear} = k\bar{M}_w{}^a \quad (5)$$

Values of g' are shown in Table 4. Values significantly lower than unity are observed, and the extent of branching in our bulk samples can be estimated. Although the number-average molecular weights indicate only 66% conversion of epoxide ring opening based on $M_{n(expt)}/M_{n(calc)} \approx 3$ (Table 2), a mixture of structural architectures is postulated. Previous studies have

demonstrated typical g' values corresponding to star-branched structures with various arm numbers comprised of polystyrene, polyisoprene, polybutadiene,[64] and polylactide.[65] Typical values associated with three-arm stars are on the average of 0.82 for polystyrene,[66] whereas four-arm and six-arm polystyrene stars exhibit average g' values of 0.76[67] and 0.63,[68] respectively. Values of g' calculated by Cao et al. for star-branched PLA samples with three, four, five, and six arms were 0.96, 0.91, 0.86, and 0.84, respectively.[65] Our bulk PLA samples exhibit g' values between 0.68 and 0.78. Consequently, we conclude that the samples contain a significant portion of structures that represent high degrees of branching. Taking the 66% conversion value based upon the number-average degree of branching would imply that, on average, the structures represent 3-arm stars (Scheme 2b) as opposed to hyperbranched structures. However, considering the polydispersities of 1.48−2.00, our bulk polymerization samples obviously consist of a mixture of branched PLA polymers containing molecules with a variety of structural architectures. Therefore, the degree of branching of some portion of the samples is validly represented by structures similar to that shown in Scheme 1b.

Thermal behavior of polymers offers insight into structure and physical properties. Table 4 summarizes the DSC analysis of the copolymers formed in the bulk. T_g systematically increased with increasing molecular weight. T_g of the branched samples are lower than typical values of linear PLA from L-lactide reported in the literature, which are around 60 °C for $M_n \approx 50$ kg/mol.[27,44] Linear PLA produced from a mixture of D- and L-stereoisomers displays a lower T_g relative to that produced from only the L-isomer due to the amorphous nature. However, branching can also have a marked effect on T_g based on the larger number of functional end groups relative to linear samples. The effect of both number and type of functional groups in hyperbranched polymers and their effect on T_g have been the subject of several papers.[69,70] The T_g behavior in these samples is consistent with additional free volume from the increase in chain end concentration relative to linear polymers of equivalent molecular weight.

Conclusion

This investigation establishes a one-pot method for copolymerization of lactide with glycidol, using different temperature conditions to control the occurrence of epoxide ring opening that leads to hyperbranching. Epoxide ring opening was prevented in low-temperature solution polymerizations, resulting in essentially linear PLA functionalized with an epoxide group. These latent AB_2 macromonomers have the potential for further polymerization under conditions tailored specifically toward epoxide ring opening, and this possibility is being explored. Simultaneous ring opening of epoxide and lactide rings was achieved at higher polymerization temperatures. Intrinsic viscosity behavior reflected the branched architecture of the copolymers formed in bulk polymerizations. Thus, $Sn(Oct)_2$ is an effective catalyst for lactide and epoxide ring opening, where the epoxide reactivity can be systematically controlled through thermal manipulation. The structures formed in this investigation illustrate a novel approach to forming polymers with unique and promising physical properties. The approach provides materials and techniques that may ultimately aid in advancing the applications of biodegradable, biocompatible PLA.

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