

PROGRESS OF POLYMERIZATION OF *D,L*-LACTIDE THROUGH DIFFERENTIAL SCANNING CALORIMETRY AND GEL PERMEATION CHROMATOGRAPHY

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Abstract

Melt polymerization conditions for *D,L*-lactide initiated with tetraphenyltin were studied with regard to polymer molecular weight. The present study was undertaken to investigate the progress of polymerization of *D,L*-lactide through differential scanning calorimetry (DSC), and also to explore the correlation between melt polymerization conditions and molecular weight. The physical characteristics, such as glass transition temperature (T_g) of the polymer and melting transition (T_m) of *D,L*-lactide are correlated with GPC data. DSC data shows that the T_m of *D,L*-lactide is 122.8 at 150°C polymerization time. ΔH_f is 83.2 J g⁻¹, and T_g of polymer is untraceable. At 180°C the T_m is 101.4°C, ΔH_f is 34 J g⁻¹, and T_g is around 29.5°C. The drop in T_m and ΔH_f clearly shows the conversion of *D,L*-lactide to polymer. The maximum increment to molecular weight of polymer is achieved at 160°C and 8 h. After a short induction period, the slow polymerization of *D,L*-lactide resulted in maximal molecular weight followed by an almost constant value of molecular weight.

Keywords: *D,L*-lactide, tetraphenyltin

Introduction

Biodegradable aliphatic polyesters have over the last several years been explored as biomaterial – in prosthetic components, surgical sutures, and vehicles for drug delivery [1–10].

Poly(lactide) appears to be a biocompatible material which degrades to non-toxic, naturally occurring metabolites. Although poly(lactide) may be prepared by the direct condensation of *L*(+) and *D*(-) lactic acid [11–12], the preferred method for the preparation of high molecular weight poly(lactide) is the ring opening polymerization of cyclic dimer, lactide, initiated with appropriate initiator, such as, tin chloride [13], Zn [9], stannous octoate [14], or tetraphenyltin

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[15]. While the preparation of poly(lactide) has been well documented, little information is available on the regulation of its molecular weight, as the variables involved – the type and concentration of the catalyst, reaction time, temperature and concentration of lactic acid etc. have not been examined in sufficient detail for their effects to be quantified [16–17].

The present study was undertaken to investigate the progress of polymerization of *D,L*-lactide initiated with tetraphenyltin through differential scanning calorimetry (DSC) and to explore the correlation between melt polymerization conditions and molecular weight of the polymer weight obtained.

Experimental

D,L-lactide acid was procured from Sigma. Tetraphenyltin was supplied by Aldrich, and was recrystallized from dichloromethane before use.

D,L-lactide was prepared according to the procedures of Kulkarni *et al.* [1] using antimony trioxide as the depolymerization catalyst. Poly (*D,L*-lactide) was obtained by the ring opening polymerization as described by Kulkarni *et al.* [1] and Kohn *et al.* [15] using tetraphenyltin. A series of polymerization ampules were prepared as follows. Ampules were cleaned and dried 24 h before filling with *D,L*-lactide and tetraphenyltin. Each ampule was connected via an adaptor to a purge valve system with access to vacuum. They were subjected to three cycles of heating and cooling in order to remove dissolved air and sealed under vacuum. The ampules were then subjected to different reaction conditions. For studying the effect of reaction time, ampules were maintained, for example, at $150 \pm 1^\circ\text{C}$ in a stirred oil bath; and representative ampules removed and quenched at different time intervals. For temperature dependence studies, similar experiments were carried out at different temperature settings. The solid contents of ampules were used for physical characterization of the polymer prepared at different sets of experiments using differential scanning calorimeter. The retrieved ampules were stored at 20°C , and the contents dissolved in tetrahydrofuran. Aliquots were used for gel permeation chromatography.

A TA Instruments DSC 10 Differential Scanning Calorimeter was used to record thermal transitions. The samples were crimped in aluminium pans and heated at 2°C min^{-1} . Peak temperature and heat of fusion were determined after calibration with an indium standard.

Gel Permeation Chromatographic (GPC) measurements were performed with a Waters model 500 GPC system using three analytical columns packed with ultrastayragel of porosity ratings 10^4 , 10^3 , and 500 \AA in series. The operational conditions were flow rate, 1 ml min^{-1} ; solvent, THF; temperature, 30°C ; sample concentration, $\sim 0.5\%$. A differential flow through refractometer was used as a detector. A linear molecular weight elution volume curve was obtained for polystyrene standards in tetrahydrofuran over the molecular weight range 10^3 to 10^6 , and was used to derive the weight average molecular weight, M_w and the number average molecular weight, M_n .

Results and discussion

With the method of preparation of poly(lactide) used, it is evident that the polymerization time, temperature, and a fixed quantity of catalyst have significant effect on the molecular weight of the polymer.

DSC heating scans of poly(lactide) prepared at 150°C temperature and at different time intervals are given in Fig. 1. It shows the conversion of dimer *d,l*-lactide, and an appearance of polymer. *D,L*-lactide has a melting transition, T_m around 125°C, and heat of fusion ΔH_f , is around 135 J g⁻¹. Figure 1 (curve a) shows the decrease in both T_m and ΔH_f , and there is no occurrence of glass transition (T_g). On increasing reaction time, 2 h (curve b), T_m and ΔH_f decrease sharply (data in Table 1), and T_g of polymer is traceable. With further increase in polymerization time, T_m is not detectable, and glass transition temperature increases further. The similar trend (Fig. 2) is observed, when polymerization is carried at 160°C and for different time periods. At 180°C, the trend is some what different (Fig. 3). Even at 1 h T_m is not traceable, and T_g of polymer is around 40°C. It remains same, even if reaction time is increased to 8 h. The combined effect of time and temperature are presented in Table 1. It shows the conversion of *D,L*-lactide and molecular weight achieved by the polymer in different polymerization conditions.

The physical characteristics, like T_g of the polymer and T_m of *D,L*-lactide are correlated with GPC data. It is evident from Table 1 that with the increase in polymerization temperature from 150 to 180°C (ampule kept in oil bath for 1 h), the conversion of *D,L*-lactide to poly(lactide) increases from 23% to 82%, and molecular weight of polymer achieved is around 34000. DSC data shows that the T_m of *D,L*-lactide is 122.8°C at 150°C, area under the peak (ΔH_f) is 83.2 J g⁻¹, and T_g of polymer is untraceable. At 180°C, the T_m is 101.4°C, ΔH_f is 34 J g⁻¹, and T_g is around 29.5°C. The depression in T_m and ΔH_f clearly indicates the conversion of *D,L*-lactide to polymer. A similar trend was observed, when the reaction time

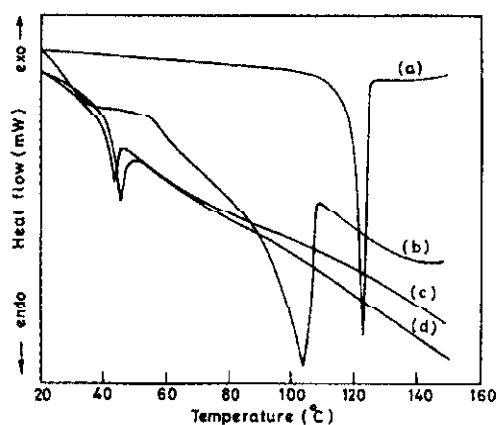


Fig. 1 DSC heating scans of poly(*D,L*-lactide) prepared at 150°C; (a) 1 h, (b) 2 h, (c) 4 h, (d) 8 h

Table 1 DSC and GPC data of poly (*D,L*-lactide)

$T/^\circ\text{C}$	Parameters	Time/h			
		1	2	4	8
150	\overline{M}_w	18144	26622	33456	42338
	%	I-23	I-69	I-83	I-92.7
	Conversion	II-77	II-31	II-17	II-7.3
	T_g/T_m	$T_m=122.8$	$T_m=105.5$	$T_m=\text{ND}$	$T_m=\text{ND}$
	($^\circ\text{C}$)	$\Delta H_f=83.2$	$\Delta H_f=33$	$T_g=37$	$T_g=42$
	$\Delta H_f/\text{J g}^{-1}$	$T_g=\text{ND}$	$T_g=29.8$		
160	\overline{M}_w	23739	45679	72374	85075
	%	I-51	I-85.3	I-92.5	I-94.8
	Conversion	II-49	II-14.7	II-7.5	II-5.2
	T_g/T_m	$T_m=116$	$T_m=\text{ND}$	$T_m=\text{ND}$	$T_m=\text{ND}$
	($^\circ\text{C}$)	$\Delta H_f=48.5$	$T_g=40.2$	$T_g=42.2$	$T_g=43$
	$\Delta H_f/\text{J g}^{-1}$	$T_g=29.5$			
170	\overline{M}_w	26599	31909	57495	57289
	%	I-53.3	I-88	I-95	I-91.7
	Conversion	II-46.7	II-12	II-5	II-8.3
	T_g/T_m	$T_m=101.4$	$T_m=\text{ND}$	$T_m=\text{ND}$	$T_m=\text{ND}$
	($^\circ\text{C}$)	$\Delta H_f=34$	$T_g=36$	$T_g=40.4$	$T_g=40.8$
	$\Delta H_f/\text{J g}^{-1}$	$T_g=29.8$			
180	\overline{M}_w	34634	35474	38738	39056
	%	I-82	I-86.5	I-87	I-92
	Conversion	II-18	II-13.5	II-13	II-8
	T_g/T_m	$T_g=39.8$	$T_g=39.2$	$T_g=39.8$	$T_g=39.6$
	($^\circ\text{C}$)				

\overline{M}_w – weight average molecular weight of polymer

I – peak 1 corresponds to polymer

II – peak 2 corresponds to *D, L*-lactide

T_m – melting transition of *D, L*-lactide

T_g – glass transition of polymer

ΔH_f – heat of fusion of *D, L*-lactide

ND – not detectable

was increased to 2 h. The molecular weight, instead of increasing in a linear fashion with temperature, increases up to 160 $^\circ\text{C}$ and then decreases. DSC data also supports the observation that above 160 $^\circ\text{C}$ the T_g of the polymer decreases. Increasing reaction time beyond 2 h and polymerization temperature above 160 $^\circ\text{C}$ similarly results in the formation of lower molecular weight polymer.

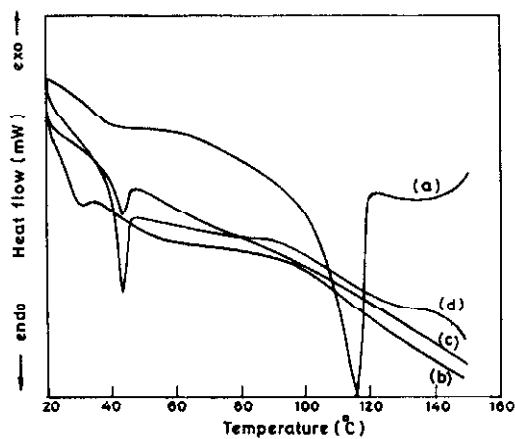


Fig. 2 DSC heating scans of poly(*D,L*-lactide) prepared at 160°C; (a) 1 h, (b) 2 h, (c) 4 h, (d) 8 h

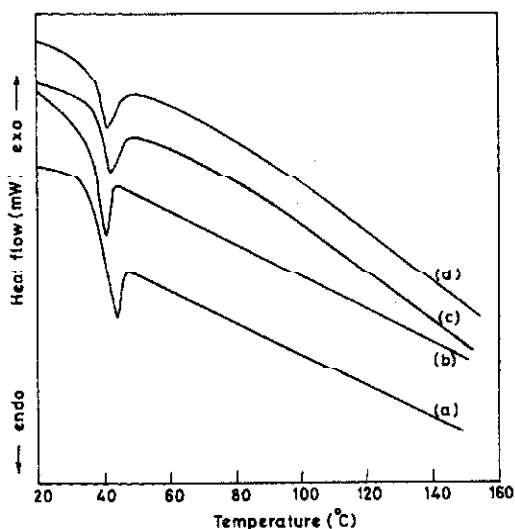


Fig. 3 DSC heating scans of poly(*D,L*-lactide) prepared at 180°C; (a) 1 h, (b) 2 h, (c) 4 h, (d) 8 h

Table 1 shows that when the reaction temperature is maintained at 150°C, and the time of polymerization increased from 1 h to 8 h, the conversion of *D,L*-lactide to polymer increases from 23 to 92.7%. The molecular weight also increases from 18000 to 42000. DSC data also supports the observation that the reaction has indeed progressed. ΔH_f decreases from 83.2 J g⁻¹ (1 h) to 33 J g⁻¹ (2 h), and T_g of the polymer also increases with the increase in time. The maximal increment in molecular weight of the polymer is achieved at 160°C and at 8 h. Above 180°C the molecular weight of the polymer remains almost unchanged, even on increasing the time of polymerization.

Data analysis of Table 1 and other experiments suggest that after an induction period (<1 h) there is a rapid rise in molecular weight during the first 8 h. In this period, above 90% of the *D,L*-lactide is converted to the polymer. This conversion is slow in the first 2 h. The maximum molecular weight is achieved between 10–12 h. At this stage, the conversion of *D,L*-lactide is above 95%. In the next few hours a fairly constant molecular weight is achieved. In order to achieve higher molecular weight of poly(lactide) with minimum batch to batch variation, three factors were considered essential: (1) use of freshly recrystallized *D,L*-lactide from dried ethyl acetate, (2) allow for three cycles of heating and cooling in ampules to remove dissolved air/moisture in vacuum and, (3) high vacuum (>0.01 mm/Hg) sealing of the ampule.

Conclusions

The results of melt polymerization of *D,L*-lactide indicate the polymer molecular weight can be predicted with variation ± 5000 , provided the great precautions (as described above) are taken during synthesis.

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