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Ring-opening Polymerization of D, L-Lactide by the Single Component Rare Earth Tris(4-*tert*-butylphenolate)s

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Summary

Ring-opening polymerization of $_{D,\ L}$-lactide ($_{D,\ L}$-LA) initiated by single component rare earth tris(4-*tert*-butylphenolate)s has been carried out for the first time. The influences of rare earth element, solvent, temperature, monomer and initiator concentration as well as reaction time on the polymerization were investigated in detail. The kinetics study indicates that the polymerization rate is first order with respect to monomer concentration and initiator concentration, respectively. The overall activation energy of the ring-opening polymerization is 81.7 $kJ.mol^{-1}$. The intensity distribution of the various stereosequence resonances in the NMR spectra reveals that transesterification proceeds slowly during the polymerization at the temperatures $\leq 90\ ^{o}C$. DSC data confirm the random distribution of the polymer. Mechanism studies showed that the $_{D,\ L}$-lactide monomer inserted into the growing chains with the acyl-oxygen bond cleavage.

Introduction

Biodegradable polyesters have raised increasing interest over the past two decades due to their specific applications in the biomedical, pharmaceutical and agricultural field [1-3]. One of the most studied polyesters is polylactide, which is produced from 100 % renewable resources (e.g., corn and sugar beets) and degraded into H_2O, CO_2 and humus. Polylactide and its copolymers have primary advantages such as biodegradability, biocompatibility, processability and good mechanical strength. They are proving to be a viable alternative to petrochemical-based plastics and finding uses in many applications, including paper coating, packaging, fibers, films, and a host of molded articles [4]. In relation to these, various catalysts or initiators (cationic, anionic, coordination, etc.) have been developed for the ring-opening polymerization and copolymerization of lactides [5-6]. However, complete removal of the catalysts residules from the polymer is not possible, and therefore low toxicity catalysts should be used in order to suit the purpose of biomedical application, among which lanthanide-based catalyst have received most current interest due to their high activity, low toxicity and therapeutical application [7-12]. Recently, our group has successfully developed several rare earth catalysts for the ring-opening polymerization and copolymerization of lactides [13-16]. Further studies show that rare earth tris(4-*tert*-

butylphenolate)s (Ln(OTBP)$_3$) are also effective for the polymerization of D, L-lactide (D, L-LA) as a single component initiator. This paper reports the characteristics, kinetics and mechanism of D, L-LA polymerization initiated by Ln(OTBP)$_3$ for the first time.

Experimental

Materials

D, L-Lactide was synthesized according to ref. [17], recrystallized three times from ethyl acetate and dried over P_2O_5 under nitrogen. Toluene and tetrahydrofuran were distilled over the blue benzophenone-Na complex. $CHCl_3$ and CCl_4 were dried and refluxed over P_2O_5 under nitrogen atmosphere. Rare earth oxides (Ln_2O_3) with a purity of 99.99 % were purchased from Shanghai Yaolong factory.

Initiator Preparation

All initiator preparations were performed using Schlenk tubes and vacuum-line techniques under purified nitrogen. Anhydrous rare earth chlorides were prepared by heating the mixture of hydrated rare earth chloride and ammonium chloride under reduced pressure [18]. Ln(OTBP)$_3$ were synthesized according to the literature [19]. The concentrations of rare earth ion in the initiator solution were determined by titration with EDTA.

Polymerization

Polymerizations were carried out in glass ampoules modified from volumetric flasks, each ampoule was heated, evacuated and filled with nitrogen for several cycles before use. Monomer, solvent and initiator solution were added into the ampoule successively. The ampoules were kept thermostated for a designed polymerization time. The reaction mixture was terminated by cold methanol containing 5 % HCl and poured into a large excess of ice-cold methanol. The precipitated polymer was isolated by filtration and dried under vacuum.

Measurements

The 500 MHz ^{1}H NMR and 125 MHz ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker Avance DMX500 spectrometer at room temperature with tetramethylsilane (TMS) as the internal reference. Differential scanning calorimetric (DSC) curves were taken on Perkin-Elmer Pyris 1 in the temperature range from 0 ^{o}C to 110 ^{o}C with a heating rate of 10 ^{o}C.min^{-1}, the midpoint of the heat capacity change was taken as the glass transition temperature (T_g). IR spectra were measured with a Bruker Vector 22 FT-IR Spectrometer using KBr pellets. Gel permeation chromatographic (GPC) measurements were performed on a Waters 208 apparatus with THF as eluent at a flow rate of 1.5 mL / min. Polystyrene standards were used for calibration. The intrinsic viscosity of poly(D, L-LA) was determined in THF at 37.0 ± 0.1 ^{o}C with an Ubbelohde viscosimeter, and the viscosity average molecular weight (M_v) was calculated according to the equation [20]: $[\eta]$ (dL / g) = $1.04 \times 10^{-4} M_v^{0.75}$. Weight-measuring method was employed for the polymerization kinetics study.

Results and Discussion

Characteristics of the Polymerization

Ln(OTBP)$_3$ are easily prepared and thermally stable. Five kinds of rare earth initiators have been examined for the polymerization of D, L-LA and the results are summarized in Table 1. From the data, it can be seen that La, Gd and Nd compound are effective initiators for the ring-opening polymerization of D, L-LA. The sequence of catalytic activity and the prepared poly(D, L-LA) molecular weight are as follows: La > Gd > Nd > Y > Er. La(OTBP)$_3$, showing the highest activity, can prepare poly(D, L-LA) over 90 % yield with M_n about 5.0×10^4 and M_w / M_n around 1.6 under the following conditions: [D, L-LA] = 1.0 mol / L, molar ratio of [D, L-LA] / [La] = 1000, 90 °C in toluene.

Table 1. Effect of different rare earth initiators on the polymerization of D, L-lactide

Ln (OTBP)$_3$	[D, L-LA] / [Ln] (molar ratio)	Conversion (%)	$M_v \times 10^{-4}$ (g.mol^{-1})	$M_n \times 10^{-4}$ (g.mol^{-1})	MWD
La	1000	98.1	5.59	5.43	1.64
Gd	1000	50.6	2.72	-----	-----
	500	93.2	4.35	4.12	1.60
Nd	500	41.7	1.32	-----	-----
	250	94.7	2.71	2.58	1.55
Y	500	4.72	-----	-----	-----
	250	20.3	1.02	0.89	1.41
Er	250	-----	-----	-----	-----

Conditions: [D, L-LA] = 1.0 mol / L, 90 °C, 50 min, toluene.

Table 2 shows the effect of different solvents on the polymerization. D, L-LA polymerization in CCl$_4$ was carried out at 105 °C since the monomer is insoluble in CCl$_4$ below that temperature. It can be seen that D, L-LA can effectively polymerize in all solvents examined. The D, L-LA conversion and the molecular weight of poly(D, L-LA) achieved in nonpolar solvent are higher than those in polar solvents, non-polar solvents favor the polymerization, and toluene is the preferred solvent in comparison with the others. These results implies that D, L-LA polymerization initiated by La(OTBP)$_3$ proceeds through a coordination mechanism, not via an ionic mechanism [21].

Table 2. Effect of different solvents on the polymerization of D, L-lactide

Solvents	Temperature (°C)	Time (min)	Conversion (%)	$M_v \times 10^{-4}$ (g.mol^{-1})	$M_n \times 10^{-4}$ (g.mol^{-1})	MWD
Toluene	90	50	97.4	5.69	5.21	1.58
CCl$_4$	105	50	95.7	5.24	5.06	1.69
THF	90	50	88.3	4.76	4.58	1.61
CHCl$_3$	90	50	87.6	4.47	4.36	1.55

Conditions: [D, L-LA] = 1.0 mol / L, [D, L-LA] / [La] = 1000 molar ratio.

The effects of reaction conditions on the D, L-LA polymerization by La(OTBP)$_3$ have been investigated in detail. Data in Table 3 indicate that polymerization variables have great influences on the polymerization. When the polymerization were conducted at 90 °C, the conversion of D, L-LA and the molecular weight of poly(D, L-LA) increase with increasing reaction time and monomer concentration in the test range. Higher concentration of the initiator results in lower molecular weight. Increasing reaction temperature accelerates the polymerization. Thus, the optimum conditions for the D, L-LA polymerization by La(OTBP)$_3$ in toluene can be described as: [D, L-LA] = 1.0 mol.L^{-1}, molar ratio of [D, L-LA] / [La] = 1000, 90 °C, 50 min.

Table 3. Ring-opening polymerization of D, L –lactide by La(OTBP)$_3$ system

[D, L-LA] (mol/L)	[D,L-LA]/[La] (molar ratio)	Temp (°C)	Time (min)	Conv (%)	$M_v \times 10^{-4}$ (g.mol^{-1})	$M_n \times 10^{-4}$ (g.mol^{-1})	MWD
1.0	1000	90	5	17.6	1.12	0.84	1.19
1.0	1000	90	12	35.7	2.01	1.76	1.27
1.0	1000	90	20	54.1	3.14	2.89	1.35
1.0	1000	90	30	70.6	3.99	3.79	1.41
1.0	1000	90	40	86.2	4.62	4.46	1.48
1.0	1000	90	50	98.6	5.61	5.32	1.62
1.0	800	90	50	95.4	4.69	4.37	1.66
1.0	500	90	50	96.6	3.01	2.71	1.71
1.0	250	90	50	93.7	1.81	1.52	1.79
0.9	1000	90	50	90.1	4.89	-----	-----
0.8	1000	90	50	82.1	4.12	-----	-----
0.7	1000	90	50	70.3	3.56	-----	-----
0.6	1000	90	50	58.9	2.96	-----	-----
0.5	1000	90	50	48.1	2.27	-----	-----
1.0	1000	100	35	97.4	5.16	-----	-----
1.0	1000	110	20	95.6	4.38	-----	-----
1.0	1000	120	15	94.2	4.04	-----	-----

Conditions: Toluene.

The stereosequences of the isolated poly(D, L-LA) was analyzed by 125 MHz ^{13}C NMR spectroscopy on the basis of tetrad effect (Figure 1). In the ^{13}C NMR spectra of poly(D, L-LA), the observed resonance can be assigned to stereosequence combinations in the polymer. The assignments are designated as various combinations of “i” isotactic pairwise relationships (RR and SS) and “s” syndiotactic pairwise relationships (RS and SR). The eight possible stereosequence combinations for tetrads are as follows:

i sis → RSSR, SRRS
ii. sii → RSSS, SRRR
iii iis → RRRS, SSSR
iv iii → RRRR, SSSS
v. ssi → RSRR, SRSS
vi iss → RRSR, SSRS
vii. isi → RRSS, SSRR
viii sss → RSRS, SRSR

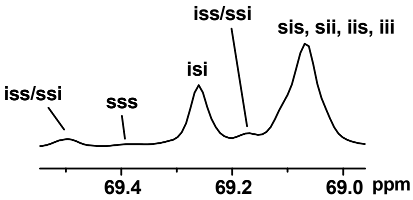


Figure 1. ^{13}C NMR spectra of the methine region of the poly(D,L-LA) obtained by La(OTBP)$_3$ in toluene at 90 ^{0}C after 50min.

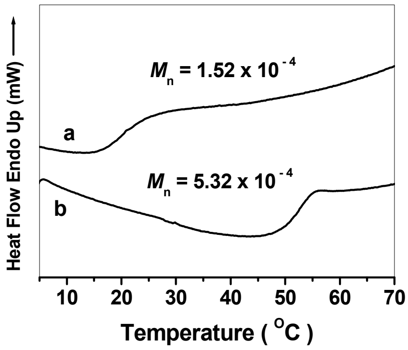


Figure 2. DSC thermograms for poly(D, L-LA)s with different M_n.

A comparison of all signals suggested that the methine carbon is most sensitive to tetrads and best suited for stereosequence analyses. Signals assignments were conducted according to ref. [22-25]. It can be seen that in the methine region the resonance lines due to iss, sss and ssi tetrads, which could be formed exclusively by the transesterification, are observed with very low intensity, indicating that transesterification is slow at temperatures ≤ 90 ^{o}C.

The DSC measurements (Figure 2) reveal that poly(D, L-LA)s prepared with La(OTBP)$_3$ are completely amorphous, suggesting that long isotactic blocks are absent. Glass transition temperature T_g tends to rise with increasing molecular weights, which is in agree with previously published results [26].

Kinetics and Mechanism of the Polymerization

Kinetics of the D, L-LA polymerization by La(OTBP)$_3$ has been investigated in toluene at 90 ^{o}C. Figure 3 shows the typical monomer consumption-time dependence of polymerization reaction in semi-logarithmic coordinates at [La] = 1.0 × 10^{-3} M. Figure 4 indicates the dependence of polymerization rate on initiator concentration (lnR_p vs. ln[La]). From these data, it can be concluded that the polymerization rate is first order with respect to the monomer concentration and initiator concentration, respectively. Therefore, the polymerization of D, L-LA initiated by La(OTBP)$_3$ proceeds according to the overall kinetic law of the form:

$$R_p = k_p[\text{D, L-LA}][\text{La(OTBP)}_3] \qquad \textbf{(1)}$$

where k_p is the polymerization rate constant. At 90 ^{o}C, when the monomer concentration is 1.0 mol.L^{-1}, the k_p is 40.4 L.mol^{-1}.min^{-1}. This equation is exactly the same as that derived by Teyssie for the polymerization of D, L-LA initiated by Al(OiPr)$_3$ in toluene at 70 ^{o}C , the k_p value being lower in the latter case (0.6 L.mol^{-1}.min^{-1}) [27]. The relationship between the lnR_p and the reciprocal of polymerization temperature (1 / T) has been plotted (Figure 5). According to the Arrhenius equation, the apparent activation energy is 81.7 kJ.mol^{-1}, which is higher than that for the La(OTBP)$_3$ polymerization of ε-caprolactone but comparable to that of the La(OTBP)$_3$ polymerization of 2,2-dimethyltrimethylene carbonate [28-29].

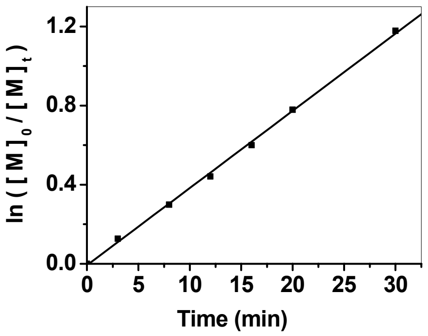


Figure 3. ln([M]$_0$/[M]$_t$) as a function of time. Conditions: [D, L-LA] = 1.0 mol / L, [D, L-LA] / [La] = 1000, 90 ^{0}C, toluene.

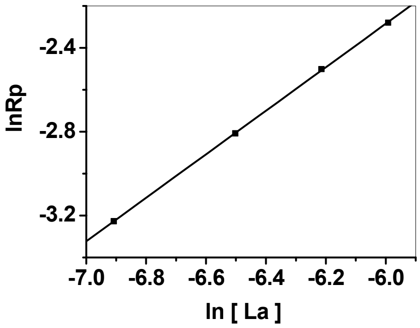


Figure 4. The plot of lnR_p vs. ln[La].

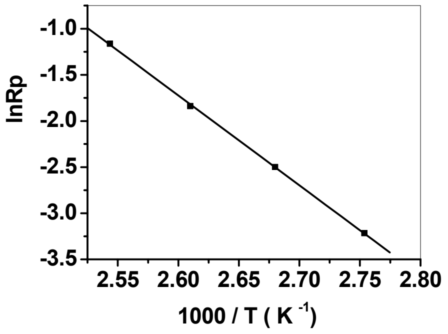


Figure 5. Effect of reaction temperature on the rate of propagation.

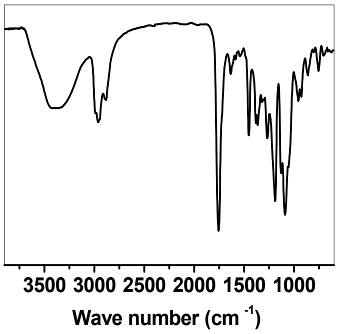


Figure 6. IR spectrum of D, L-LA oligomer.

A differentiation between a propagation involving acyl-oxygen cleavage and alkyl-oxygen cleavage is difficult to achieve via kinetic methods, whereas end group analyses could provide sufficient information about the ring-opening mode of the monomer. In order to determine the mechanism, stoichiometric amounts of La(OTBP)$_3$ and D, L-LA were reacted in toluene at 90 °C. The reaction mixture with 100% conversion was terminated by isopropanol and the prepared oligomer was analyzed by IR and ^{1}H NMR spectra. The IR spectrum (Figure 6) shows a broad absorption in the region of 3400 cm^{-1}, which is characteristic of the hydroxyl functions. In ^{1}H NMR spectrum (Figure 7), the doublet at δ 1.22 and the peaks at δ 4.34 are assignable to the methyl protons of the isopropoxycarbonyl end group and the methine proton neighboring the hydroxyl end group. It is interesting to note that the two CH-quadruplets of the –CH(CH$_3$)OH end group are attributed to the asymmetric methyne group in the D, L-LA monomer unit.

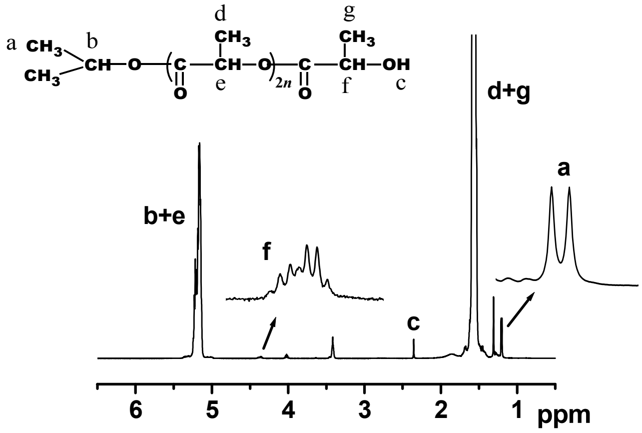
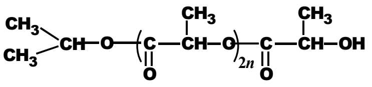


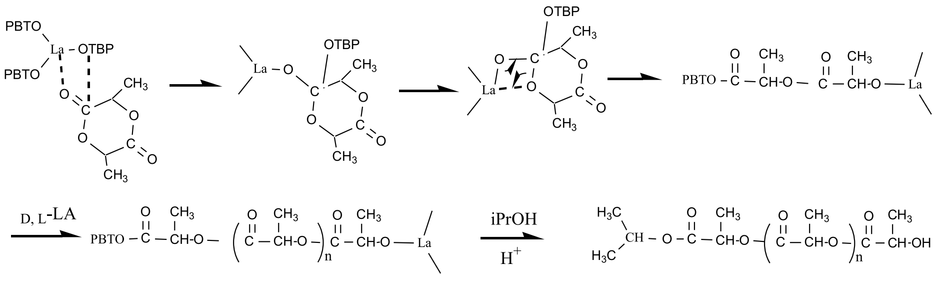
Figure 7. ^{1}H NMR of poly(D, L-LA) terminated by isopropanol.

According to the ^{1}H NMR, the structure of the polymer terminated with isopropanol can be described as follows:



$$(CH_3)_2CH-O-\left(\overset{\overset{O}{\|}}{C}-\overset{CH_3}{\overset{|}{C}}H-O\right)_{2n}-\overset{\overset{O}{\|}}{C}-\overset{CH_3}{\overset{|}{C}}H-OH$$

The isopropoxy group was clearly incorporated into the living chain during the termination and that the polymerization of D, L-LA proceeded exclusively by acyl-oxygen cleavage of the monomer. It has been demonstrated that L-LA polymerization initiated by La(OTBP)$_3$ proceeds through a coordination mechanism [30], since poly(L-lactide) obtained by La(OTBP)$_3$ possess 100% optical purity, which is a characteristic result of the coordination polymerization [24,27,31], while cationic and anionic polymerization of L-LA cause racemization [32,33]. By analogy with the mechanism for L-LA polymerization by La(OTBP)$_3$ and on the end-group analysis basis, it can be concluded that D, L-LA can be polymerized by La(OTBP)$_3$ according to a coordination mechanism with the selective cleavage of the acyl-oxygen bond of the monomer (Scheme 1).



Scheme 1. Mechanism of the polymerization of D,L-LA initiated by La(OTBP)$_3$.

Conclusions

Single component rare earth tris(4-*tert*-butylphenolate)s are effective initiators for the ring-opening polymerization of $_{\mathrm{D,\ L}}$-LA. La(OTBP)$_3$ has higher activity and gives higher molecular weight poly($_{\mathrm{D,\ L}}$-LA). The kinetics study of La(OTBP)$_3$ system shows that the polymerization rate has the first-order in monomer concentration and initiator concentration and the overall activation energy amounts to 81.7 kJ.mol^{-1}. NMR spectrum reveals that transesterification occurs slowly at the temperatures $\leq 90\ ^{o}$C. DSC measurements confirm the random structure of the polymer. Mechanism analysis indicate that $_{\mathrm{D,\ L}}$-lactide polymerization initiated by rare earth tris(4-*tert*-butylphenolate)s proceeds via a coordination mechanism with selective acyl-oxygen bond cleavage of the monomer.

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