Dihydroxy-Terminated Poly(L-lactide) Obtained by Controlled Ring-Opening Polymerization: Investigation of the Polymerization Mechanism

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Received October 28, 1999; Revised Manuscript Received February 14, 2000

ABSTRACT: Hydroxy telechelic poly(L-lactide)s of different molecular weight have been synthesized by controlled ring-opening polymerization using cyclic tin alkoxides. NMR analysis showed that the propagation proceeded through an insertion mechanism. No free hydroxyl or carboxyl end groups were detected in the polymerization mixture. Complete reaction of the initiator was observed over the entire range of compositions studied. Both tin−oxygen bonds were reactive and participated in the propagation reaction. Peak assignments were obtained by ^{1}H, ^{13}C, distortionless enhancement polarization transfer (DEPT), and heteronuclear multiple quantum coherence−gradient selected (hmqc-gs) nuclear magnetic resonance spectroscopy. The kinetics of the solution polymerization of L-lactide has been investigated and showed a first order in monomer. The external order in initiator has been determined to be $^{3}/_{4}$ for initiator concentrations above 5 mmol/L and to 2 below 2 mmol/L. The molecular weight could easily be adjusted by the monomer-to-initiator ratio, and the molecular weight distribution remained narrow even at high molecular weight (MWD < 1.15). The polymerization products were characterized by size exclusion chomatography (SEC) as well as ^{1}H and ^{13}C NMR.

Introduction

The ring-opening polymerization (ROP) of L-lactide, a cyclic dimer of lactic acid, has become of significant importance in the synthesis of degradable polymers.[1,2] Metal alkoxide or metal carboxylate initiators and catalysts generating controlled ring-opening polymerizations are frequently utilized in synthesis of polymers with predictable molecular weight, narrow molecular weight distribution, and desirable end groups.[3] A diverse variety of functionalized initiators have been developed during the past decade utilized in the production of new biodegradable materials. Extensive work has also been carried out to understand the polymerization mechanism and kinetics of the ROP.[4−6] In particular, considerable progress has been made in elucidating the pseudoionic mechanism (coordination−insertion mechanism).[7]

In our previous papers we have reported on the controlled ring-opening polymerization of 1,5-dioxepan-2-one (DXO) initiated by the cyclic tin alkoxide initiator 1,1,6,6-tetra-*n*-butyl-1,6-distanna-2,5,7,10-tetraoxacyclodecane,[8] which produces dihydroxy-terminated polymers with different molecular weight and moderately narrow molecular weight distribution (MWD ≈ 1.5). The new hydroxy telechelic polymers were then used as macromers in block copolymerization reactions.[9] Hydroxy telechelic polymers have previously been prepared from for example L-lactide and ϵ-caprolactone using other initiator systems.[10,11]

In this paper we report on the investigation of the mechanism and kinetics of controlled ring-opening polymerization of L-lactide leading to hydroxy telechelic polymers to be used in macromer reactions of various nature. The prepolymer molecules can be linked together using chain extension or by utilizing the hydroxy functionalities as macromers for further polymerization.[9] In this process, it is essential that the overall structure and end groups of the macromers are quantitatively and qualititatively controlled. The influence of experimental parameters such as monomer-to-initiator ratio and initiator concentration on the chain length as well as on the end group composition of the poly(L-LA) macromers will be elucidated. The results of NMR analysis will be utilized for determining the structure of the reactive species in the polymerization solution. The results of kinetic experiments will be utilized to understand the action of the initiator in more detail and the mechanism of the lactone and lactide controlled ring-opening polymerization.

Experimental Section

Materials. Dibutyltin oxide (Aldrich Chemie, Germany) and ethylene glycol (Merck, Germany) were obtained commercially and were used as received. Toluene (Merck, Germany) was dried over Na wire before use. Chloroform (Aldrich, Germany), stabilized with 2-methyl-2-butene, was dried by stirring over CaH_2 for at least 24 h prior to distillation under an inert atmosphere. l-Lactide (L-LA) was obtained from Serva Feinbiochemica, Germany. L-LA was purified by recrystallization in dry toluene. The monomer was dried for 20 h under reduced pressure (10^{-2} mbar) at room temperature prior to polymerization.

Initiator. 1,1,6,6-Tetra-*n*-butyl-1,6-distanna-2,5,7,10-tetraoxacyclodecane was prepared from dibutyltin oxide and ethylene glycol as previously described in the literature.[8,12] Characterization by ^{1}H NMR and mass spectroscopy confirmed the formation of the expected structure. The initiator exists in two different forms: as a monomer and as a dimeric compound in equilibrium according to Scheme 1.[13]

Polymerization of L-Lactide. Monomer and initiator was weighed into a previously silanized round-bottomed flask equipped with a magnetic stirring bar inside a drybox (MBraun MB 150B-G-I, Germany). The flask was closed with a three-way valve. A desired amount of solvent was transferred to the flask by a syringe. The reaction vessel was then immersed into the thermostated oil bath for the desired time. All glassware was flame-dried prior to use. The temperature was held constant (±1 °C of preset value) using an Ikatron ETS D3 temperature regulator, IKA Labortechnik, Germany. ^{1}H NMR

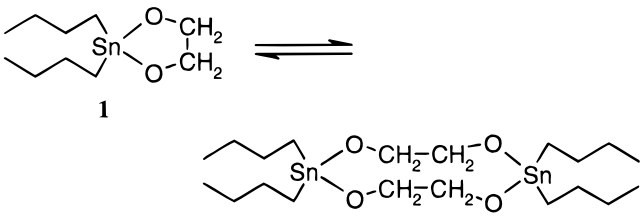
10.1021/ma991811u CCC: $19.00
Published on Web 03/28/2000

Table 1. Ring-Opening Polymerization of L-Lactide with Sn Alkoxide 1/2 as Initiator (Reaction Conducted at 60 °C, Initial Monomer Concentration of 0.5 M)

polym. no.	[M]/[I][a]	reaction time [min]	conversion[b] [%]	yield[c] [%]	$\bar{M}_n$[d]	MWD[d]	$\bar{M}_n$[e]	$\bar{M}_n$[f]
1	51	720	98.4	81.3	12 300	1.05	7 000	7 200
2	100	1475	88.7	83.8	22 600	1.19	11 200	12 800
3	200	3030	94.0	87	32 800	1.22	17 600	27 100
4	250	3600	91.9	88.6	45 800	1.05	29 500	33 100
5	350	6502	97.1	94.7	74 200	1.18		48 900
6	500	9780	98.3	97.1	116 000	1.18	(62 300)	70 800

[a] Concentration initiator calculated from the monomeric species. [b] Calculated from ^{1}H NMR on crude polymerization mixture. [c] Amount of polymer formed after precipitation in methanol. [d] Determined by SEC analysis with polystyrene standards; chloroform was used as eluent. [e] Determined by ^{1}H NMR analysis. [f] Theoretical molecular weight = [M]/[I] × MW(L-LA) × X; MW(L-LA) = monomer molecular weight; X = monomer conversion.

Scheme 1. Equilibrium between the Monomer and the Dimeric Form of the Tin Alkoxide Initiator



and SEC samples, for the kinetic investigation, were withdrawn from the reaction mixture at various times with a flamed syringe under flushing with an inert gas (Ar). The polymer formed was precipitated into cold hexane.

Instrumental Methods. *Nuclear Magnetic Resonance.* The monomer conversion was determined by ^{1}H NMR spectroscopy from the relative intensity of the resonance peaks for the monomer (5.17 ppm) and the polymer methine protons (5.0 ppm), respectively. ^{1}H NMR spectra were obtained using a Bruker AC-400 Fourier transform nuclear magnetic resonance spectrometer (FT-NMR) operating at 400 MHz, T = 25 °C, with chloroform-d_1 ($CDCl_3$) as solvent. A 25 mg sample was dissolved in 0.5 mL of $CDCl_3$ in a 5 mm diameter sample tube. Nondeuterated chloroform was used as an internal standard (δ = 7.26 ppm).

DEPT (distortionless enhancement by polarization transfer) and heteronuclear multiple quantum coherence−gradient selected (hmqc-gs) spectra were obtained by a Bruker DMX-500 Fourier transform nuclear magnetic resonance spectrometer operating at 500.13 and 125.77 MHz, respectively. DEPT (135°) spectra were obtained using a standard Bruker microprogram utilizing 1.3 s acquisition time and 2 s delay. ^1J(C,H) was set to 130 Hz. 2D ^{1}H−^{13}C hmqc-gs spectra were acquired and processed with a standard Bruker microprogram. A total of 20 scans were accumulated with a relaxation delay of 2 s. The spectrum was obtained with 3255.2 Hz spectral width over the F_1 (proton) axis and 24 509.8 Hz along the F_2 (carbon) axis.

The reaction progress was followed in situ by ^{1}H NMR. The monomer and initiator were charged into a silanized round-bottomed flask and closed by a rubber septum inside a drybox. Deuterated solvent, $CDCl_3$, was transferred through the septum with a syringe. The mixture was then transferred to a 5 mm NMR tube equipped with a rubber septum and subsequently frozen in liquid nitrogen to prevent reaction from occurring before insertion into the NMR magnet. The tube was inserted into the heated probe, and a ^{1}H NMR spectrum was recorded every fifth minute in order to follow the disappearance of peaks originating from monomer and occurrence of peaks from the polymer. A reaction temperature of 50 °C in the NMR probe was used.

Size Exclusion Chromatography. Size exclusion chromatography (SEC) was used to monitor the molecular weight change during polymerization. Polymers were analyzed using a Waters 717plus autosampler and a Waters model 510 apparatus equipped with two PLgel 10 μm mixed-B columns, 300 × 7.5 mm (Polymer Labs., UK). Spectra were recorded with an PL-ELS 1000 evaporative light scattering detector (Polymer Labs., UK) connected to an IBM-compatible PC. Millennium^{32} version 3.05.01 software was used to process the data. Chloroform was used as eluent, at a flow rate of 1.0 mL/min. Narrow MWD polystyrene standards were used for calibration, range 1700−706 000 g/mol. SEC measurements were performed on both cyclic and deactivated chains (i.e., into hexane/methanol precipitated chains).

Results and Discussion

A series of polymerization experiments were conducted with the aim to obtain a controlled ring-opening polymerization (ROP) of L-lactide (L-LA) using tin alkoxide 1,1,6,6-tetra-*n*-butyl-1,6-distanna-2,5,7,10-tetraoxacyclodecane as initiator. Results are summarized in Table 1. All polymerizations were carried out in chloroform solution at 60 °C and at an initial monomer concentration of 0.5 M. The monomer-to-initiator ratio ([M]/[I]) was varied between 50/1 and 500/1.

The melting point of poly(L-lactide) has been reported to be approximately 169 °C;[14] however, polymerization at this temperature causes a high extent of side reactions, such as transesterification reactions, to take place. Polymerization conducted in the temperature range 100−140 °C would cause the polymer formed to crystallize out from the melt,[15] resulting in an unsatisfactory control of the synthesis. Moreover, our study showed that the tin initiator **1**/**2** had limited solubility in the monomer melt. The choice of a homogeneous solution as reactive medium and of moderate reaction temperatures was therefore aimed at avoiding all problems connected to the phase separation of the reagents and to limit the number of transesterification reactions.

The results show that polymerization proceeded easily, and high monomer conversions were achieved under the conditions used. The mild reaction conditions resulted in good control of the molecular weight and the molecular weight distribution of the polymer chains. ^{1}H NMR analysis revealed that only poly(L-LA) with hydroxyl end groups were formed after precipitation and termination of the initiator−polymer complex.

Dependence of Poly(L-LA) Molecular Weight on the Monomer-to-Initiator Ratio. The molecular weight of the polymers formed after precipitation in methanol was determined by ^{1}H NMR and SEC. The absolute number-average molecular weights, determined by ^{1}H NMR, were calculated from the ratio between the methylene group peak originating from the ethylene glycol bridge in the initiator (δ = 4.35 ppm) and the methine proton peak (δ = 5.18 ppm) in the polymer main chain. The molecular weight determined by SEC was much larger than the molecular weight determined by ^{1}H NMR. This was due to the calibration of the SEC by polystyrene standards, which only gave a relative

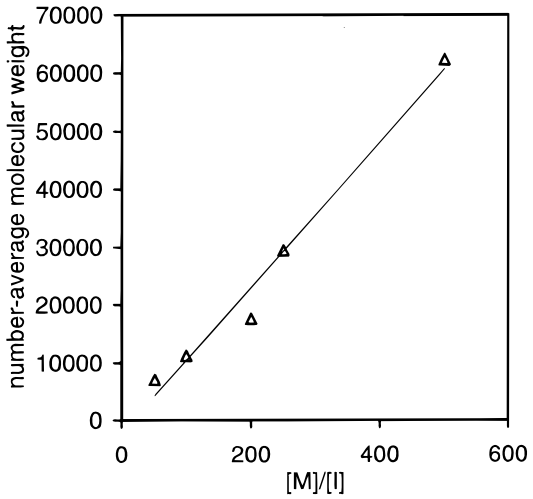


Figure 1. Number-average molecular weight ($\bar{M}_n$) determined by analysis of the $-OCH_2CH_2O-$ content using ^1H NMR spectroscopy as a function of the monomer-to-initiator ratio ([M]/[I]) for the L-lactide polymerization initiated by tin alkoxide **1**/**2** in chloroform at 60 °C, $[M]_0 = 0.5$ mol L^{-1}.

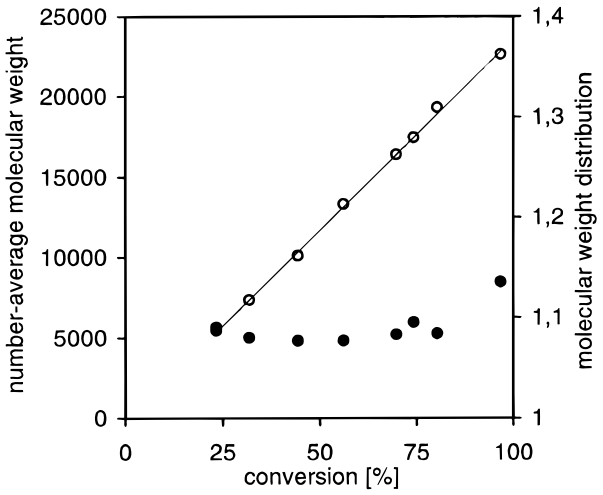


Figure 2. Relationship between the number-average molecular weight (○), molecular weight distribution (●), and the monomer conversion for the polymerization of L-LA in chloroform at 60 °C, initiated by **1**/**2**, $[M]/[I]_0 = 100$, $[M]_0 = 0.5$ mol L^{-1}.

value of the polymer molecular weight. The SEC results were therefore used as a semiquantitative tool to check the peak shape, molecular weight distribution, and the increase in molecular weight during kinetic experiments.

Figure 1 shows the absolute number-average molecular weight, $\bar{M}_n$, dependence on the [M]/[I] ratio. A linear relationship over the entire range of [M]/[I] ratios investigated is observed in agreement with the fact that the number of initiation events, i.e., total number of chains, is a function of the initiator concentration. ($\bar{M}_n$ = [M]/[I] × MW(L-LA) × X; [M]/[I] = monomer-to-initiator molar ratio, MW(L-LA) = molecular weight of the L-LA monomer, X = monomer conversion.) The increase in molecular weight was proportional to the increase in monomer-to-initiator ratio. This relationship held even for the preparation of both low- and high-molecular-weight polyesters, contrary to what has been reported for the bulk polymerization.[16] Moreover, a good correlation was found between the molecular weight values theoretically expected from the [M]/[I] ratio and the experimental values obtained (Table 1).

As shown in Table 1, the [M]/[I] ratio had little influence on the polymer yield. A slight decrease in yield was found at the lower monomer-to-initiator ratios, which was due to fractionation when precipitating the polymer in methanol. The lowest molecular weight chains were removed during precipitation due to formation of a colloid phase in the hexane/methanol mixture. The fractionation also influenced the polymer MWD values given in Table 1, since the SEC analysis was performed on the precipitated polymers. A slightly narrower distribution than actual was determined for the lowest molecular weight samples.

Influence of Monomer Conversion on $\bar{M}_n$ and MWD. The influence of monomer conversion on the $\bar{M}_n$ and MWD was determined by ^1H NMR and SEC. The analyses were performed on the crude reaction mixture; no precipitation or deactivation was executed in order to not influence the results by for example fractionation of the samples. However, some deactivation, i.e., hydrolysis, might take place during preparation of the polymer/chloroform mixture subsequently subjected to SEC analysis. Figure 2 shows the influence of monomer conversion on $\bar{M}_n$ and MWD. It reveals that the $\bar{M}_n$ as determined by SEC follows a linear relationship even at very high conversion, up to 96.8%. This is generally observed in systems propagating in a living manner, e.g., ϵ-caprolactone initiated with aluminum isopropoxide.[17] The linearity of the number-average degree of polymerization, $\overline{DP}$, versus conversion plot indicates that there is less transfer than in other known systems.[4,16] A very limited amount of inter- and intramolecular transesterification reactions occurred, although when high conversion was achieved, some broadening of the MWD took place. It must be emphasized that the MWD was constantly very low for monomer conversions below 95% (MWD < 1.1), with a slight increase toward the end of reaction. No induction period was observed during polymerization, contrary to what is reported for many other metal alkoxide initiator systems.[18] This indicated that the active species was formed instantaneously under the actual experimental conditions; the initiator did not need rearrangement to become reactive and initiate polymerization.

NMR Assignment of Species in Solution. To identify the reactive species involved in solution polymerization and to obtain NMR assignments, conventional ^1H and ^{13}C NMR spectra of the reaction mixture were recorded as well as the ^{13}C DEPT (135°) spectrum and the 2D $^1H-^{13}C$ hmqc-gs spectrum.

Signals were sorted according to the number of protons attached to carbons using the DEPT mode of spectral data collection. In DEPT (135°) spectra, the carbons attached to an odd number of hydrogens (methine ($-CH-$) and methyl carbons ($-CH_3$)) produce signals with positive amplitudes while carbons coupled to an even number (methylene carbons ($-CH_2-$)) give signals with negative amplitudes. Figure 3 shows the DEPT (135°) spectrum of the reaction mixture after ca. 60% of the initiator was activated. The alkyl group methylene carbons from the initiator show signals around δ = 27.0, 27.4, 27.6, and 27.9 ppm. The $-OCH_2-CH_2O-$ carbon signal produces two peaks at δ = 63.1 and 63.6 ppm. The methine carbon signals from the polymer main chain and the monomer appear at δ = 69.05 ppm and δ = 72.9 ppm, respectively. Peaks were assigned (partly based on the literature)[10] as shown in Figure 3.

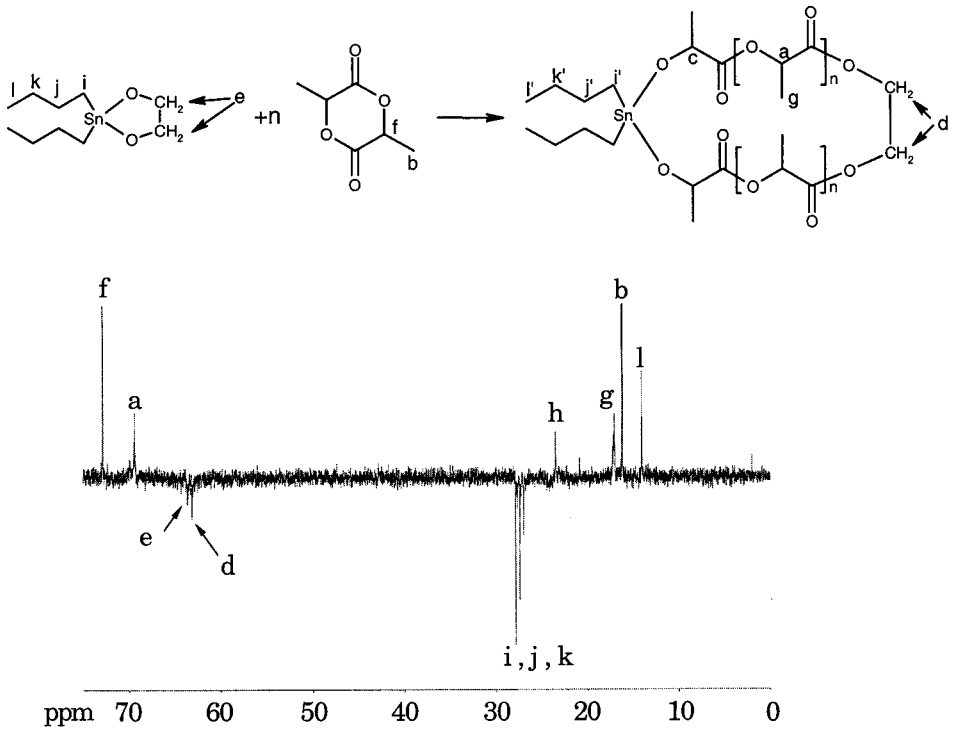


Figure 3. DEPT spectrum of the active reaction mixture after 60% of the initiator has reacted. Polymerization conducted in $CDCl_3$ at 60 °C, $[M]_0 = 0.5$ mol L^{-1}, $[M]/[I] = 7$.

The correlation between the proton and carbon spectrum can be determined with the help of the $^1H-^{13}C$ hmqc-gs spectrum. This technique reveals the direct coupling between the ^{13}C and ^1H nucleus. Figure 4 shows a 2D $^1H-^{13}C$ hmqc-gs spectrum of the active reaction mixture, $[M]/[I] = 7$. This method was used to determine which peaks originate from the −O−CH− end groups, i.e., the part of the chain closest to the tin, and the peaks emerging from the $-OCH_2CH_2O-$ group incorporated in the polymer main chain. In Figure 4 a cross-peak appears at $\delta = 3.63$ ppm/$\delta = 63.6$ ppm which was assigned to the $-OCH_2CH_2O-$ group in the initiator. The peak emerging at $\delta = 4.34$ ppm/$\delta = 63.1$ ppm originated from a $-CH_2-$ group as determined by DEPT analysis and was therefore concluded to be the $-OCH_2CH_2O-$ group from the initiator, which is incorporated into the polymer main chain. The peak at $\delta = 4.65$ ppm/$\delta = 70.0$ ppm corresponds to the −OCH− group connected to tin; the group covalently coupled to the tin atom is shifted upfield in the proton spectrum.

Figure 5 shows the conventional ^1H NMR spectrum of the reaction mixture after approximately 55% of the initiator was reacted and the peak assignment. It is clear that the ^1H NMR spectrum of the reaction mixture is rather complex and that 2D hmqc-gs simplifies the interpretation of the proton spectrum. From the hmqc-gs spectroscopy the ^1H NMR spectrum was completely assigned.

Initiator Efficiency. The polymerization progress and the reaction of the initiator were investigated by running the polymerization of L-LA in chloroform-d_1 ($CDCl_3$) in a silanized NMR tube. The purpose was to determine whether all of the initiator reacted and participated in propagation and whether both Sn−O bonds were active in propagation. Reaction was followed in situ by ^1H NMR; the probe was heated to 50 °C.

Figure 6 shows the ^1H NMR spectra for the polymerization of L-LA in chloroform-d_1, at a very low monomer-to-initiator ratio = 8. A spectrum was taken every 20 min, and the plot shows the first 10 runs. In the ^1H NMR spectrum recorded in $CDCl_3$, signals originating from −CH groups attached to free hydroxyl end groups is normally found at 4.35 ppm.[19] Figure 6 shows no peaks at this shift, only a $-CH_2-$ group according to DEPT (135°), indicating that the polymerization does not proceed by or involve formation of free hydroxyl chain ends. The peak at 4.65 ppm was assigned to the −O−CH group attached directly to the tin atom.

As illustrated by Figure 6, the signal from the unreacted initiator at 3.63 ppm gradually disappeared and was completely absent after 80 min reaction; the peak from the $-OCH_2CH_2O-$ group incorporated in the polymer backbone was simultaneously emerging at 4.35 ppm. The initiator was completely reacted after 50% monomer conversion, which corresponds to an average degree of polymerization of 4. These results clearly demonstrate the initiator was entirely consumed under the present experimental conditions. From the chemical structure of the tin alkoxide it is given that the number of possible polymerization sites/Sn is 2. Consequently, both active sites on the tin atom were determined to be active during polymerization. A literature report had conversely shown that although the tin alkoxide (**1**/**2**) was an efficient initiator for the polymerization of L-lactide in bulk,[20] the reaction of the initiator was not complete at low [M]/[I] ratios. Upon hydrolysis of the polymer−initiator complex, the structure of the end groups was transformed into hydroxyl groups; as determined by NMR of the precipitated polymer, a peak from the free $-CH-OH$ group appeared at 4.35 ppm.

Mechanism. From the above-reported results it must be concluded that the L-lactide is inserted into the Sn−O bond of the initiator through the selective cleavage of the acyl−oxygen bond of the monomer. We propose a mechanism in which the monomer was inserted into the tin−oxygen bond. The reaction pathway is schematized

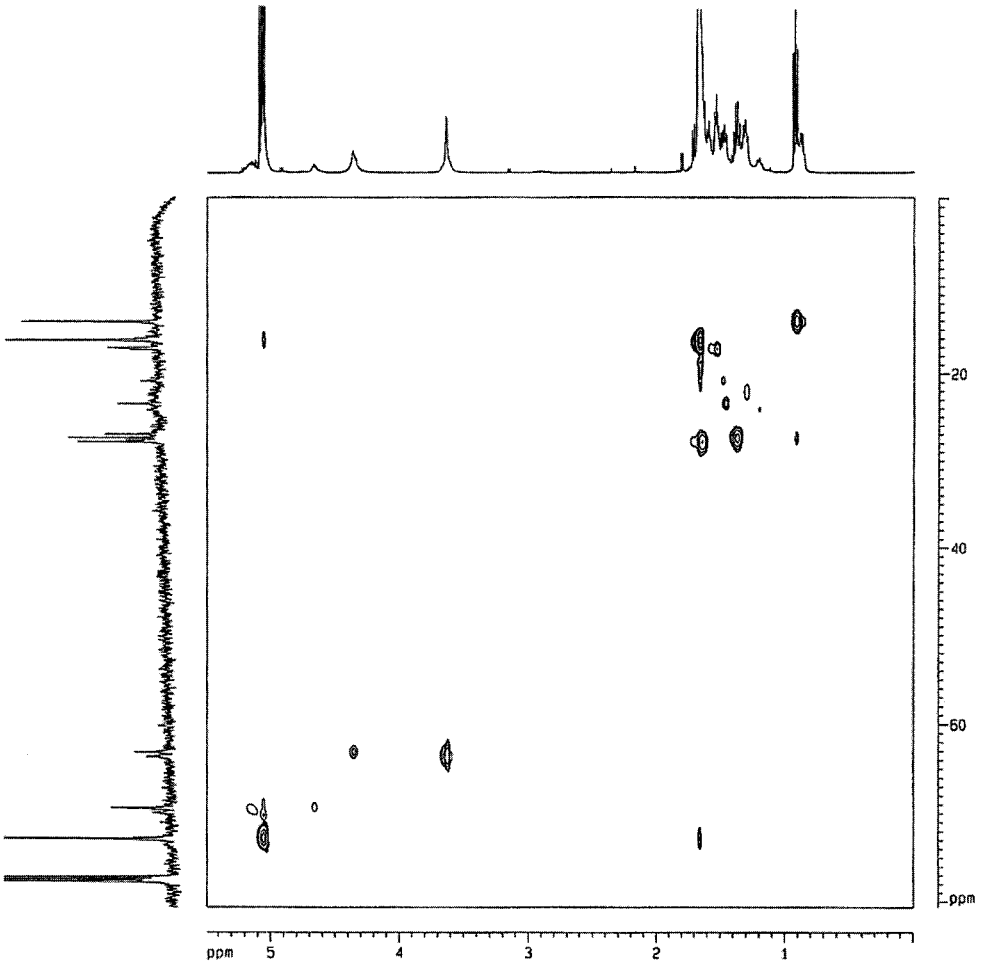


Figure 4. 2D hmqc-gs spectrum of the active reaction mixture. Polymerization conducted in $CDCl_3$ at 60 °C, $[M]_0 = 0.5$ mol L^{-1}, $[M]/[I] = 7$. F1 = conventional proton spectrum; F2 = conventional ^{13}C spectrum.

for L-lactide in Scheme 2, which is in agreement with the mechanism proposed by Kricheldorf for the bulk polymerization.[16]

Kinetics of Lactide Ring-Opening Polymerization. To understand the action of the initiator in more detail and the mechanism of the lactone and lactide controlled ring-opening polymerization, we carefully investigated the kinetic behavior of the initiator. Polymerization of L-lactide was monitored in time by the manual sampling followed by ^1H NMR analysis to determine the monomer conversion. Figure 7 shows the semilogarithmic plot of $-\ln([M]/[M]_0)$ versus the reaction time, t, for the polymerization of L-lactide using the tin alkoxide system. $[M]_0$ is the initial monomer concentration and [M] the concentration of the unreacted monomer at time t. As the plot shows, the polymerization was first order in monomer when initiated in chloroform at 60 °C. No induction period was observed, and the polymerization started immediately. The linearity of the plot of $-\ln([M]/[M]_0)$ versus the reaction time was systematically observed, and it illustrates that no termination reactions occurred during polymerization; i.e., the number of propagating chains remained constant throughout reaction. It has been shown that the nature of metal, alkoxide groups, solvent, and temperature does not influence the first order in monomer.[21] The kinetic equation thus is as follows:

$$-\mathrm{d}[M]/\mathrm{d}t = k_{app}[M] \quad (1)$$

The aggregation of active centers in the metal alkoxide initiated ROP of lactones or lactides is a commonly reported phenomenon.[22,23] In the studied systems, reactivity of aggregated and nonaggregated species differs substantially, and as a consequence, the kinetics of polymerization is influenced. Most commonly, the propagation proceeds via the nonaggregated species while the aggregated complex is temporarily terminated and thus inactive toward polymerization. The kinetic scheme describing this system have recently been proposed as shown below:[22]

$$(P_n^*)_m \overset{K_{da}}{\rightleftharpoons} m P_n^* \quad (2)$$

$$P_n^* + M \xrightarrow{k_p} P_{n+1}^* \quad (3)$$

where P_n^*, (P_n^*), and M denote nonaggregated center, aggregated active center, and monomer, respectively. K_{da} is the aggregation equilibrium constant, k_p the propagation rate constant, and m the degree of aggregation.

To solve the kinetic equations corresponding to this system, Penczek and co-workers have recently proposed a method to analyze the degree of aggregation from the curved plots $\ln(k_{app})$ versus $\ln[I]_0$.[24] (k_{app} is the apparent rate constant $= (\ln[M]/[M]_0)/t$, $[I]_0$ = initial initiator concentration.) Equation 4 has been proposed for this system:

$$(k_{app})^{1-m} = -m/K_{da}(k_p)^{m-1} + k_p[I]_0 (k_{app})^{-m} \quad (4)$$

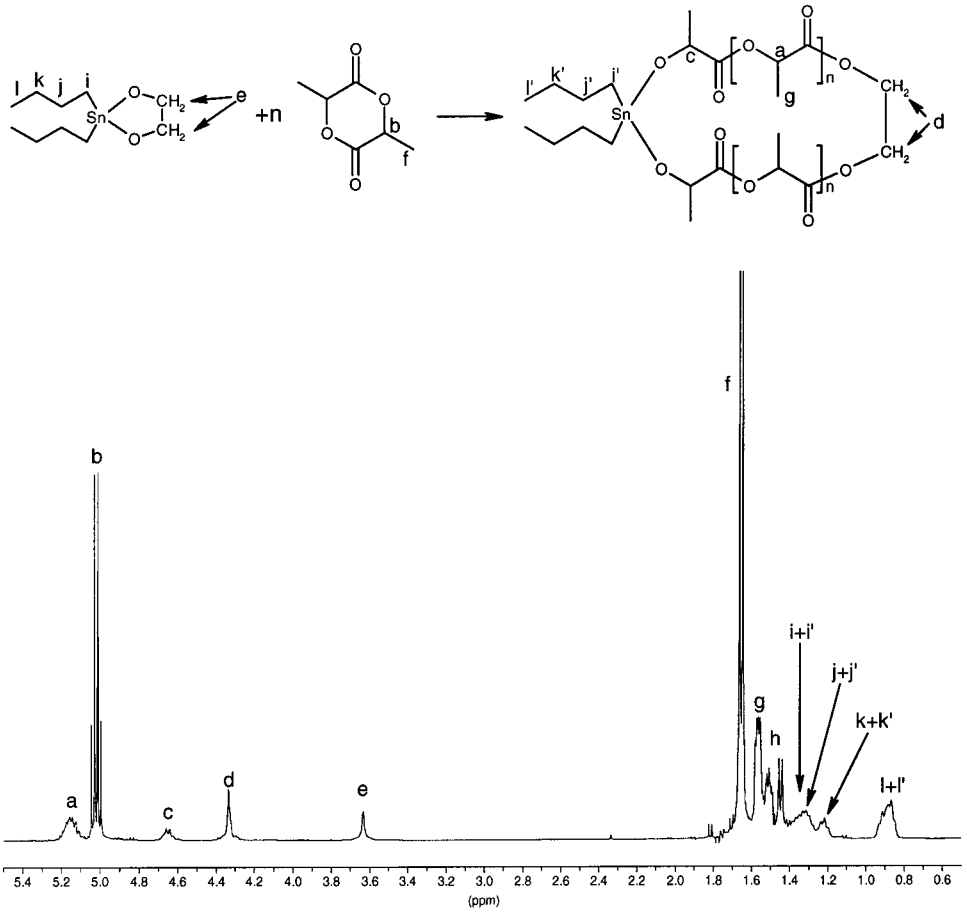


Figure 5. ^{1}H NMR spectrum of the reaction mixture and the peak assignment. Polymerization initiated with tin alkoxide **1**/**2** in chloroform at 60 °C, [M]/[I] = 7, $[M]_0$ = 0.5 mol L^{-1}.

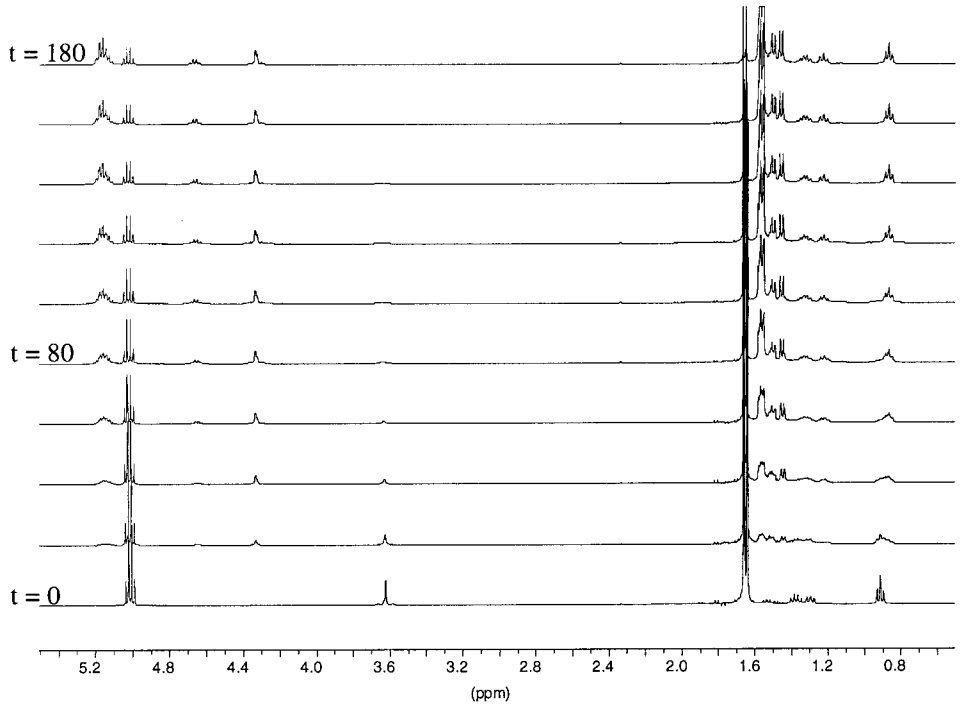
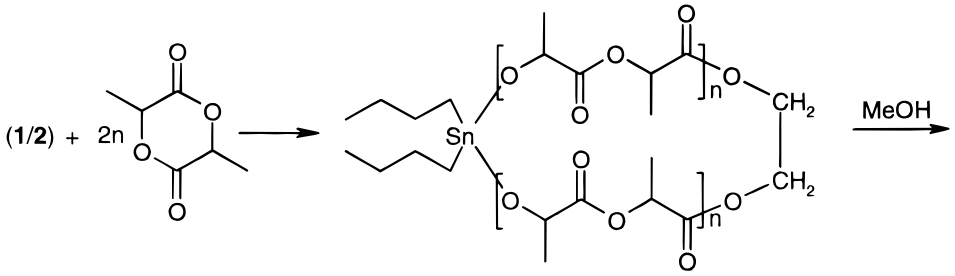


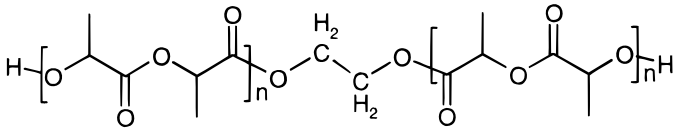
Figure 6. ^{1}H NMR spectra for the reaction progress of the polymerization of L-LA in deuteriochloroform, monomer-to-initiator ratio = 8, [M]/[I] = 8, $[M]_0$ = 0.25 mol L^{-1}.

This equation is valid for polymerization in which a fast reversible aggregation of the active centers takes place.

If the polymerization is concluded to be first order in initiator, the k_{app}/[I] ratio must be constant as long as the number of active sites is independent of the initiator concentration. However, when polymerization proceeds with reversible aggregation (temporary termination), the plot is often curved, due to a change of proportions of aggregated and nonaggregated species.

Scheme 2. Proposed Reaction Pathway for the Synthesis of Hydroxyl Telechelic Poly(L-lactide)





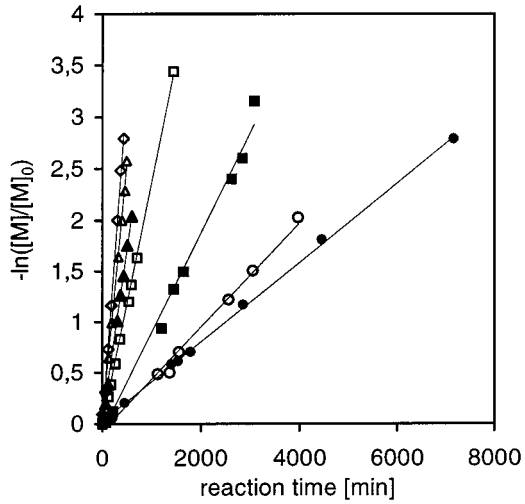


Figure 7. Semilogarithmic plots of L-lactide monomer conversion expressed as $\ln[M]_0/[M]$ versus the reaction time for the polymerization initiated by the tin alkoxide system at different initiator concentrations, as monitored by ^{1}H NMR spectroscopy in $CDCl_3$ (25 °C). M/I = (◇) 25, (△) 35, (▲) 50, (□) 100, (■) 250, (○) 360,and (●) 400.

Table 2. Apparent Rate Constants for the Polymerization of L-Lactide with Sn Alkoxide $^1/_2$ as Initiator[a]

$[M]/[I]_0$	$[I]_0$ [mol/dm^3] × 10^3	k_{app} [min^{-1}]
25	20.0	6.8
35	14.2	5.1
50	10.0	3.5
100	5.0	2.4
250	2.0	0.98
360	1.39	0.51
400	1.25	0.39

[a] Reaction was conducted at 60 °C; an initial monomer concentration of 0.5 M was used.

Since the polymerization proceeded without any induction period, the apparent rate constant was easily determined from the slope of the linear dependence in Figure 7. Table 2 summarizes the apparent rate constants, $k_{app} = -(\ln[M]/[M]_0)/t$, obtained for the different initiator concentrations, $[I]_0$. The k_{app} values range from 0.39 min^{-1} at $[M]/[I] = 400$ up to 6.8 min^{-1} at $[M]/[I] = 25$.

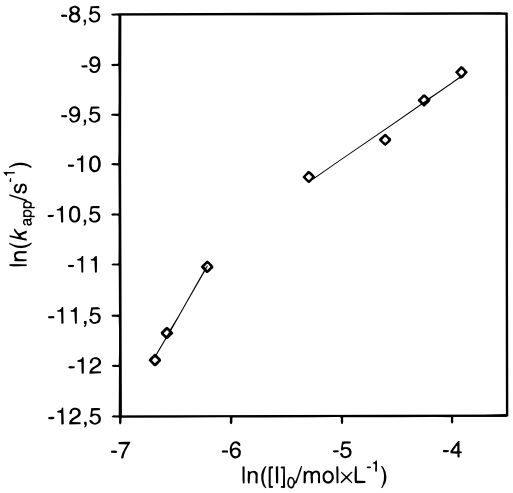


Figure 8. External orders in initiator. Dependence of the logarithm of the apparent rate constant, $\ln(k_{app})$, on the logarithm of the initiator concentration, $\ln([I]_0)$. Polymerizations were conducted at 60 °C, and an initial monomer concentration of 0.5 mol L^{-1} was used.

To determine the degree of aggregation of active species, i.e., the reciprocal of the external order in initiator, $\ln(k_{app})$ was plotted versus $\ln([I]_0)$ according to eq 4 (Figure 8). The plot shows two different steps. The slopes change with initiator concentration; this indicates a variation in the ratio of aggregated and nonaggregated species. If the polymerization reaction was first order in initiator, a straight-line relationship would hold between $\ln(k_{app})$ and the logarithm of the initiator concentration, as long as the number of active sites was independent of the initiator concentration.[25] Contrary to the order in monomer, the order in initiator is largely dependent on the structure of the metal alkoxide and the degree of association.

The degree of aggregation of the initiator decrease from the value $\approx^4/_3$ at $[I]_0 \approx 5$ mmol L^{-1} and higher to the value $^1/_2$ at initial initiator concentrations $[I]_0 \approx 2$ mmol L^{-1} and lower. This change in the degree of aggregation was attributed to the change of proportions of aggregated and nonaggregated species. However, the fractional orders in degree of aggregation might imply that cyclic initiators do not follow the kinetic equations

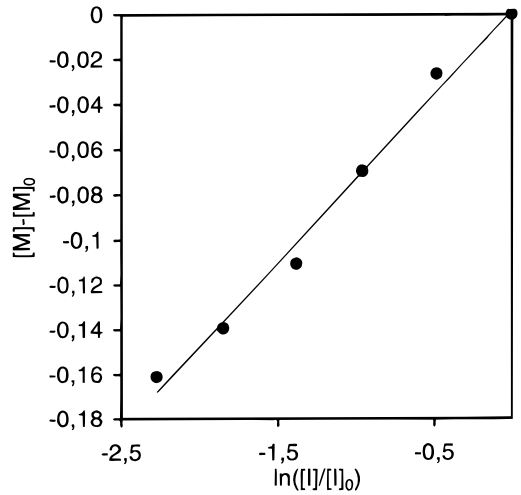


Figure 9. $[M] - [M]_0$ as a function of $\ln([I]/[I]_0)$. Polymerization conditions as described in Figure 6.

proposed for regular metal alkoxides. It has previously been reported for ϵ-caprolactone polymerization initiated with $(C_2H_5)_2Al-OC_2H_5$ that the degree of aggregation increase from ca. 1 at lower concentrations to 2−3 at higher concentrations.[26]

The ratio between the rate of propagation and the rate of initiation, k_p/k_i, was determined from the NMR spectra shown in Figure 6, assuming no aggregation at the first approximation. This system is described by reactions 4 and 5:

$$M + I \xrightarrow{k_i} P^* \tag{5}$$

The following kinetic equations can be derived for such a system:[27]

$$-\frac{dI}{dt} = k_i[M][I] \tag{6}$$

$$-\frac{dM}{dt} = k_i[M][I] + k_p[M]([I]_0 - [I]) \tag{7}$$

By dividing eq 7 with eq 6 and integrating the resulting equation, the following will be obtained:

$$[M] - [M]_0 = \left(1 - \frac{k_p}{k_i}\right)([I] - [I]_0) + \frac{k_p}{k_i}[I]_0 \ln([I]/[I]_0)$$

Figure 9 shows $[M] - [M]_0$ plotted versus $\ln([I]/[I]_0)$. The value of $k_p/k_i[I]_0$ was determined from the slope of the line shown in Figure 9. The k_p/k_i ratio was calculated to be 2.4 by inserting the known initial initiator concentration.

Conclusions

L-Lactide can be ring-opening polymerized directly to high molecular weight hydroxy telechelic poly(L-lactide) macromolecules. In the controlled polymerization of telechelic polymers, the molecular weight of the resulting polymer depends on the amount of initiator added. Quantitative reaction of the initiator was achieved at a very low degree of polymerization at moderate temperature and mild reaction conditions. These controlled ring-opening polymerization reactions proceeded with a negligible amount of side reactions, such as chain transfer or termination as shown by the narrow molecular weight distribution. NMR spectroscopy of the reaction mixture revealed the existence of tin alkoxide end groups before precipitation and hydroxyl-terminated end groups after precipitation and termination in methanol. The polymerization was shown to follow a "coordination−insertion" mechanism, where both tin alkoxide groups were active in propagation. The kinetics was first order in monomer. The degree of aggregation changed with the initiator concentration, due to aggregation/deaggregation of the active species.

Acknowledgment. The authors thank the Swedish Research Council for Engineering Sciences (TFR) for financial support of this work. We also gratefully acknowledge Elisabetta Ranucci for stimulating discussions.

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MA991811U