1964 *Macromolecules* **2000,** *33,* 1964−1971

Polymerization of L,L-Dilactide Initiated by Tin(II) Butoxide

Adam Kowalski, Jan Libiszowski, Andrzej Duda,* and Stanislaw Penczek

Department of Polymer Chemistry, Center of Molecular and Macromolecular Studies, Polish Academy of Sciences, Sienkiewicza 112, PL-90-363 Lodz, Poland

Received October 20, 1999; Revised Manuscript Received January 19, 2000

ABSTRACT: The kinetics and mechanism of L,L-dilactide (LA) polymerization, initiated with tin(II) butoxide ($Sn(OBu)_2$) and carried out in THF solvent (from 20 to 80 °C) or in bulk (at 120 °C), were studied. Polarimetric and size exclusion chromatography (SEC) measurements showed that initiation was fast and quantitative; termination and intramolecular transesterification (backbiting) were not observed. According to the ^{1}H NMR and MALDI-TOF spectra analysis, both alkoxide groups in $Sn(OBu)_2$ were converted into poly(L-lactide) (PLA) growing chains, and monomer addition proceeded with the acyl−oxygen bond scission. SEC and osmometric measurements revealed that number-average molar masses (M_n) of PLA chains were equal to the ratio $144.13([LA]_0 - [LA])/2[Sn(OBu)_2]_0$ in the range of M_n from 10^3 up to $\approx 10^6$. Propagation was first order (internally) in LA; it was also approximately first order in initiator (at least for $[Sn(OBu)_2]_0 > 10^{-3}$ mol L^{-1}). The rate constant of propagation (k_p, for one macroalkoxide chain) was equal to 0.5 mol^{-1} L s^{-1} (THF, 80 °C). Agreement of the kinetic plots determined by SEC and polarimetry indicated that racemization did not take place. The $k_p/k_{tr2} = 125$ (where k_{tr2} is the intermolecular transesterification rate constant) was measured at 80 °C, belonging to the highest values from those determined until now.

Introduction

Ring-opening polymerization of lactides (LA) has been systematically studied since the late 1950's.[1−27] The product of this process, polylactide (PLA), is finding various applications, not only as biomedical material but also as commodity thermoplastic.[24,25,28−30] Two classes of initiators—the multivalent metal alkoxides and carboxylates—were mostly used.

All of the multivalent metal (e.g., Al., Fe, Ti, Sn(IV), Y) alkoxides studied until now provide polymerization of cyclic esters practically devoid of termination at moderate temperatures.[25−27] Eventually, $Al(O^iPr)_3$ (in the form of trimer) has become the most versatile initiator for the controlled polymerization of cyclic esters. It provided relatively fast and quantitative initiation, moderately fast propagation, and relatively good selectivity (i.e., high k_p/k_{tr} ratio).[15,16,22,23,26,31] Therefore, $Al(O^iPr)_3$ looked to be ideally suited also for the synthesis of PLA, since apart from a good selectivity it provides, in contrast to the more frequently used tin(II) octoate (cf. below), control of the molar mass of the resulting polyester, by simply adjusting the $([LA]_0 - [LA])/[Al(O^iPr)_3]_0$ ratio.[15,16,23] On the other hand, there is a certain limit of M_n (about 10^5) of PLA that was obtained with $Al(O^iPr)_3$ until now. Reasons for this phenomenon are not yet understood.[16] Also, for the lanthanide alkoxide initiators, providing both very fast and selective propagation, which were introduced more recently,[19,32,33] the reported molar masses do not exceed $M_n \approx 10^5$.

Covalent metal carboxylates, particularly tin(II) 2-ethylhexanoate (tin(II) octoate ($Sn(Oct)_2$)), have been used even more often than metal alkoxides. However, there was no clear-cut evidence of how they initiate polymerization.[5−7,10,13,14,17,20] Among various potential possibilities, either conversion of $Sn(Oct)_2$ into an actual initiator, i.e., tin(II) alkoxide or hydroxide,[6,14] or a direct catalytic action of $Sn(Oct)_2$[5,10,20] was usually considered.

Using MALDI-TOF mass spectrometry, we have more recently shown that macromolecules having OctSn−O−polyester end groups are formed, appearing as such in the spectrum of the cyclic ester/alcohol or water/$Sn(Oct)_2$ reacting mixture.[34,35] Also, results of the kinetic studies indicate formation of the tin(II) alkoxide active species.[36,37] Therefore, at this point we decided to study polymerization of cyclic esters initiated with the Sn(II) alkoxide itself.

Alkoxides of the tetravalent tin ($R_nSn(OR')_{4-n}$, where $n = 3$ or 2) were already applied as initiators in the polymerization of cylic esters.[8,9,11,12,22] This is in contrast to their divalent counterparts which, to the best of our knowledge, have not been systematically studied with the same purpose.

In the present work we report results of the studies of polymerization of LA initiated with tin(II) butoxide ($Sn(OBu)_2$), which provides probably the first example of the fully controlled polymerization of LA for a wide range of molar masses (M_n), from 10^3 to 10^6, of the resulting PLA.

Experimental Section

Substrates and Solvents. L,L-Dilactide (LA, from Boehringer Ingelheim, Austria), crystallized consecutively from dry 2-propanol and toluene, was purified just before use by sublimation in vacuo (10^{-3} mbar, 85 °C) and distributed into the glass ampules equipped with break-seals. Tin(II) butoxide ($Sn(OBu)_2$) was prepared in a two-step synthesis according to ref 38. In the first step $SnCl_2$ was reacted with CH_3OH, in the presence of $(CH_3)_3N$ as the HCl scavenger. The precipitated $Sn(OCH_3)_2$ was then heated with C_4H_9OH; CH_3OH was removed, and the $Sn(OC_4H_9)_2$ formed was finally crystallized from toluene, dried in vacuo, distributed into the thin-walled break-seals, and sealed off. THF and benzene (both from POCh Gliwice, Poland) were kept, after the usual purification, over a liquid Na−K alloy from which they were distilled in vacuo directly into the reaction vessel.

Polymerization Procedures. Polymerizing mixtures were prepared in sealed polarimetric cells or glass ampules using a standard high-vacuum technique.

Determination of the LA Conversion. Conversion of LA was determined using both polarimetry and size exclusion chromatography (SEC) methods. Polarimetric measurements were performed with a Perkin-Elmer 241 MC polarimeter. SEC traces were recorded using a LKB 2150 HPLC pump and two sets of TSK gel columns (G 2000 HXL and 6400 HXL or G 3000 HR and G 6000 HR). A Wyatt Optilab 903 interferometric refractometer and a MALLS Dawn F laser photometer (both Wyatt Technology Corp., Santa Barbara, CA) were

---

* Corresponding author. E-mail: anduda@bilbo.cbmm.lodz.pl.

10.1021/ma991751s CCC: $19.00

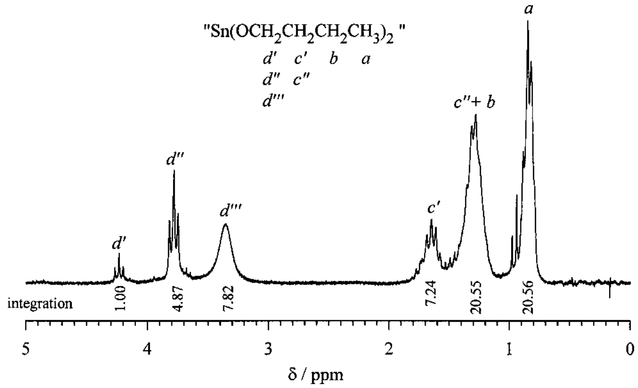


Figure 1. ^{1}H NMR spectrum (200 MHz) of tin(II) butoxide. Conditions: $[Sn(OBu)_2] = 0.1$ mol L^{-1}, C_6D_6 solvent, 80 °C.

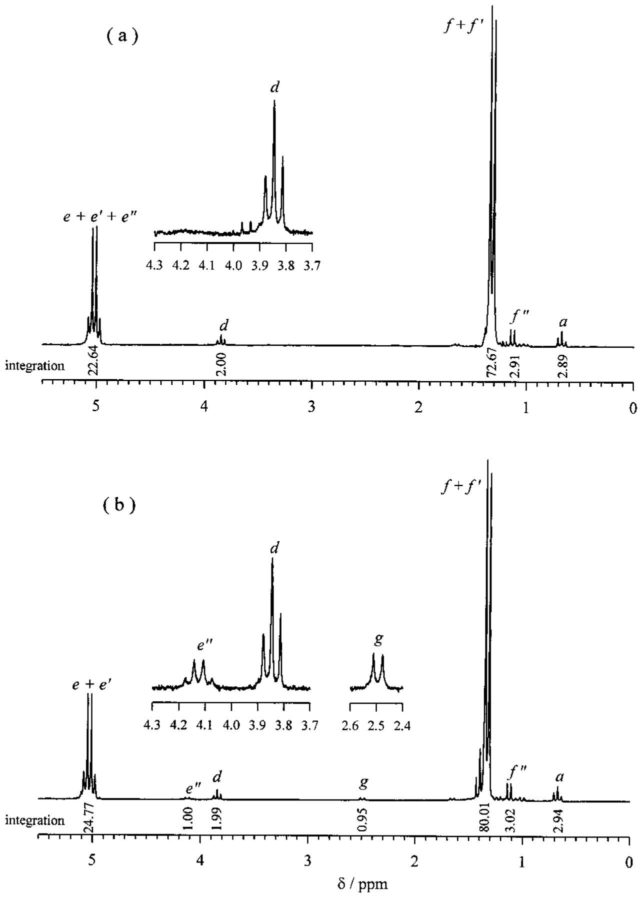


Figure 2. ^{1}H NMR spectra (200 MHz, 25 °C, C_6D_6 solvent) (a) of the living poly(L-lactide) and (b) of the isolated poly(L-lactide) after deactivation of the living polymer with 1 N HCl_{aq}. Conditions of polymerization: $[LA]_0 = 1.0$ mol L^{-1}, $[Sn(OBu)_2] = 3.75 \times 10^{-2}$ mol L^{-1}, C_6D_6 solvent, 80 °C.

applied as detectors in series. Methylene chloride was used as an eluent. A flow rate of 0.8 mL min^{-1} was applied. Simultaneously, the LA monomer conversion was followed using a Perkin-Elmer 241 MC polarimeter. The polymerizing mixtures were transferred into the optical cells under high-vacuum conditions and then sealed off. The optical rotations of the polymerizing mixtures (r) were measured at 578 nm at room temperature. The instantaneous monomer concentrations were determined assuming additivity of the optical rotations for LA (r_m) and PLA (r_p), i.e., $[LA] = [LA]_0(r - r_p)/(r_m - r_p)$.

Determination of Molar Masses (M_n) and Molar Masses Distributions (M_w/M_n). The actual number-average molecular weights (M_n) of PLA were determined using the poly(L-lactide) standards prepared in our laboratory. It was established, however, that in order to get the correct M_n value of PLA, the experimental value, obtained from the SEC traces using polystyrene standards, has to be multipled by 0.68 (at least up to $M_n \leq 2 \times 10^4$, for the set of TSKgel G 2000 HXL and 6400 HXL columns with CH_2Cl_2 as an eluent). The actual number-average molecular weights (M_n) of the deactivated and isolated PLA were occasionally determined on Knauer osmometers (either vapor pressure or high-speed membrane for $M_n \leq 3.5 \times 10^4$ or $\geq 3.5 \times 10^4$, respectively) in dry methylene chloride. The M_w/M_n ratios were determined from the SEC traces. M_n higher than 10^4 were directly determined with a MALLS Dawn F laser giving the actual values of molar masses. For measurements of $M_n > 10^5$ a set of TSKgel G 3000 HR and 6000 HR columns was used.

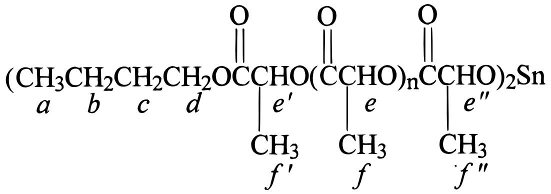
MALDI-TOF Measurements. Mass spectrometry was performed with a Voyager-Elite (PerSeptive Biosystems, Framingham, MA) time-of-flight instrument equipped with a pulsed N_2 laser (337 nm, 4 ns pulse width) and a time delayed extraction ion source. An accelerating voltage of 20 kV was used. Mass spectra were obtained in the reflector mode. The matrix, 2,5-dihydroxybenzoic acid, was dissolved in THF or methylene chloride (10 mg mL^{-1}), and the solution was mixed with the polymerizing mixture (monomer concentration in the feed: 1.0 mol L^{-1}) in a 25:1 v/v ratio. The mixture was dried on stainless steel plate covered by the gold metal target.

NMR Measurements. ^{1}H NMR spectra were recorded in benzene-d_6 solvent on a Bruker AC200 operating at 200 MHz. Benzene was used as an internal standard ($\delta = 7.16$ ppm). The analyzed solutions were prepared and transferred into the NMR tubes under high-vacuum conditions. The NMR tubes were eventually sealed off after degassing and freezing their contents with liquid nitrogen.

Results and Discussion

End Groups Structure of Poly(L-lactide). The ^{1}H NMR spectrum of the $Sn(OBu)_2$ initiator in C_6D_6 at 80 °C (Figure 1) exhibits three groups of signals: a multiplet centered at $\delta = 0.85$ ppm, two multiplets in the range from $\delta = 1.10$ to 1.90 ppm, and two triplets accompanied by one broad peak in the lower field, from $\delta = 3.10$ to 4.30 ppm, with the intensities ratio equal to 3:4:2. We ascribe these absorptions to the CH_3, $b + c$ CH_2, and d CH_2 protons, respectively, in the alkoxide ($CH_3CH_2CH_2CH_2O$) group of $Sn(OBu)_2$. Such an absorption pattern is much more complex then expected for the individual $Sn(OBu)_2$ molecules and can be explained by their aggregation,[38] increasing the number of the magnetically nonequivalent protons. However, in the present work we refrain from discussing the structures of $Sn(OBu)_2$ aggregates.

The ^{1}H NMR spectrum of the living $LA/Sn(OBu)_2/C_6D_6$ polymerization mixture (Figure 2a) shows, apart from the strong signals coming from the PLA chain (doublets of CH_3 protons, $\delta \approx 1.35$ ppm, and a quartet of CH protons centered at $\delta \approx 5.02$ ppm),[8,15] two small well-resolved triplets at $\delta \approx 0.67$ and 3.85 ppm with the intensity ratio 3:2, respectively. These triplets can be ascribed to protons a and d (cf. $(PLA{-}O)_2Sn$ structure shown below) in the end group of the growing PLA macromolecule.



$$(\underset{a}{CH_3}\underset{b}{CH_2}\underset{c}{CH_2}\underset{d}{CH_2}O\overset{O}{\overset{\|}{C}}\underset{\underset{f'}{CH_3}}{\underset{|}{\overset{e'}{C}H}}O(\overset{O}{\overset{\|}{C}}\underset{\underset{f}{CH_3}}{\underset{|}{\overset{e}{C}H}}O)_n\overset{O}{\overset{\|}{C}}\underset{\underset{f''}{CH_3}}{\underset{|}{\overset{e''}{C}H}}O)_2Sn$$

((PLA-O)$_2$Sn)

Table 1. Molar Masses (M_n) and Their Distributions (M_w/M_n) for Poly(L-lactide) Prepared with $Sn(OBu)_2$[a]

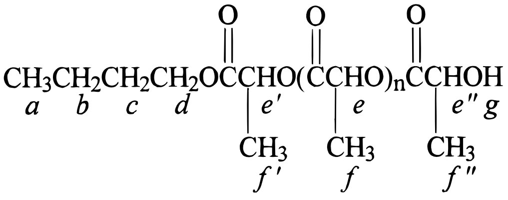
$[LA]_0$, mol L^{-1}	$[Sn(OBu)_2]_0$, mol L^{-1}	time, min	conv[b]	M_n(calcd)[c]	M_n(SEC)[d]	M_w/M_n (SEC)
1.0[e]	2.9×10^{-3} $(+1.4 \times 10^{-1}$ BuOH)	400	0.95	1.01×10^3	1.19×10^3 (0.97×10^3)[g]	1.15
1.0	5.0×10^{-2}	5	0.90	1.37×10^3	1.67×10^3	1.25
1.0[f]	3.75×10^{-2}	30	0.99	1.98×10^3	2.02×10^3	1.84
1.0	1.17×10^{-2}	5	0.91	5.62×10^3	4.04×10^3	1.25
1.0	5.0×10^{-3}	90	0.94	1.40×10^4	1.32×10^4	1.80
3.0	9.75×10^{-3}	4	0.87	1.93×10^4	1.79×10^4	1.15
1.0	2.68×10^{-3}	15	0.92	2.48×10^4	3.05×10^4 (2.79×10^4)[g]	1.28
3.0	5.95×10^{-3}	8	0.93	3.38×10^4	3.03×10^4	1.56
1.0	1.8×10^{-3}	20	0.86	3.44×10^4	4.35×10^4	1.12
1.0	1.16×10^{-3}	40	0.94	5.95×10^4	6.00×10^4 (6.18×10^4)[h]	1.85
3.0	3.0×10^{-3}	400	0.88	6.34×10^4	7.22×10^4	1.32
1.0	7.6×10^{-4}	700	0.75	7.13×10^4	5.91×10^4	1.25
3.0	2.16×10^{-3}	300	0.90	9.01×10^4	7.83×10^4	1.42
1.0	4.9×10^{-4}	800	0.68	1.0×10^5	1.07×10^5 (1.13×10^5)[h]	1.15
3.0	3.8×10^{-4}	10290	0.84	4.78×10^5	5.54×10^5	1.37
8.1[i]	5.5×10^{-4}	1140	1.00	1.061×10^6	9.68×10^5 (9.53×10^5)[h]	1.36

[a] Polymerizations carried out in THF as a solvent at 80 °C if it is not otherwise indicated. [b] Conversion of a LA monomer $(([LA]_0 - [LA])/[LA]_0)$. [c] $M_n(\text{calcd}) = 144.13([LA]_0 - [LA])/[OBu]_0 + 74.11$. [d] Absolute values, either based on PLA standards ($M_n \le 2 \times 10^4$) or obtained with a laser light scaterring detector ($M_n > 10^4$). [e] Polymerization conducted with butyl alcohol as a transfer agent (BuOH concentration given in parentheses). [f] Polymerization with C_6D_6 as a solvent; after 30 min at 80 °C the "living" reaction mixture was kept at 20 °C. [g] Measured by vapor pressure. [h] Measured by membrane osmometry. [i] Polymerization conducted in bulk at 120 °C.

Another small signal, doublet at $\delta \approx 1.13$ ppm, comes from the CH_3 group f'' in a direct vicinity of the Sn(II) alkoxide active center. It is remarkable that integrations of protons a and f'' are close to one another. Signals of the methylene protons b and c of the end group coincide with the main-chain doublet f; quartets of the methine protons e, e', and e'' are also overlapped. (A similar observation has been noted for polyester chains fitted with other metal (Y,[19] Al[31]) alkoxides.) The weak quartet at $\delta \approx 3.95$ ppm corresponds to the unreacted LA, present in the equilibrium concentration ($\approx 10^{-2}$ mol L^{-1} at 25 °C[21]).

Assuming that one molecule of initiator starts growth of exactly one $(PLA-O)_2Sn$ macromolecule carrying two PLA chains, the expected molar mass of one PLA arm can be calculated from the feed composition. For the analyzed polymerizing mixture $[LA]_0 = 1.0$ mol L^{-1} and $[Sn(OBu)_2]_0 = 3.75 \times 10^{-2}$ mol L^{-1}. Thus, $M_n(\text{calcd}) = 1980$ (cf. third entry in Table 1). On the other hand, assuming that the resulting $(PLA-O)_2Sn$ has a structure shown above, the ratio of the intensities of the main-chain to the end groups signals allows this molar mass to be determined. Intensities of the respective signals taken from the ^1H NMR spectrum in Figure 2a give $M_n(\text{NMR}) = 1872$.

Hydrolysis at mild conditions (e.g., with 1 N HCl_{aq} at room temperature) of the $(PLA-O)_2Sn$ macromolecule should give two chains of the hydroxy-terminated PLA (PLA−OH).



$$\underset{a}{CH_3}\underset{b}{CH_2}\underset{c}{CH_2}\underset{d}{CH_2}O\overset{O}{\overset{\|}{C}}\underset{\underset{f'}{CH_3}}{\underset{|\,e'}{C}}HO(\overset{O}{\overset{\|}{C}}\underset{\underset{f}{CH_3}}{\underset{|\,e}{C}}HO)_n\overset{O}{\overset{\|}{C}}\underset{\underset{f''}{CH_3}}{\underset{|\,e''}{C}}HO\underset{g}{H}$$

(PLA-OH)

The ^1H NMR spectrum of the hydrolyzed and then precipitated PLA−OH is presented in Figure 2b. Protons to signals assignment is given directly in the spectrum. Most characteristic is an appearance of the quartet e'' and doublet g (both absent in the spectrum of chains fitted with −OSnO− units; cf. Figure 1a), having comparable intensities, with chemical shifts typical for the $PLA-C(O)CH(CH_3)-OH$ terminal protons ($\delta \approx 4.13$ and 2.50 ppm, respectively).[15] There is also a good agreement between integration of a and f'' signals. For this sample $M_n(\text{NMR}) = 2051$ and $M_n(\text{SEC}) = 2018$ were determined.

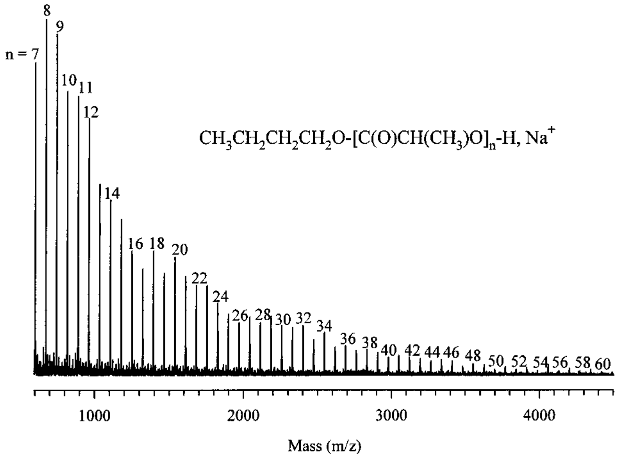
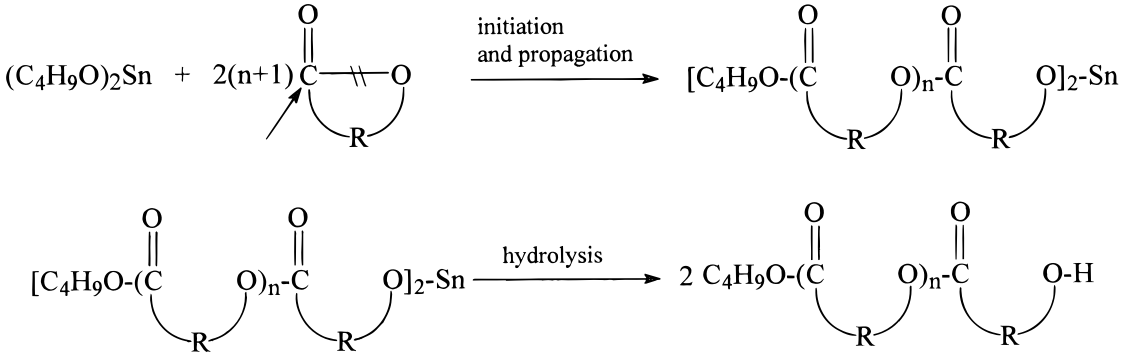


Figure 3. MALDI-TOF spectrum of the living poly(L-lactide). $\text{Mass}(m/z) = M_{BuOH} + nM_{la} + M_{Na^+}$ (where $M_{BuOH} = 74$, $M_{la} = 72$, $M_{Na^+} = 23$. Conditions of polymerization are given in the caption for Figure 2.

The MALDI-TOF spectrum of the isolated PLA−OH (Figure 3) shows almost exclusively peaks corresponding to the $C_4H_9O(C(O)CH(CH_3)O)_nH$ population doped with Na^+. Interestingly, there are no signals coming from PLA macromolecules terminated with CH_3O end groups. This observation strongly indicates that during the initiator synthesis CH_3O groups in $Sn(OCH_3)_2$ were quantitatively substituted by the C_4H_9O groups (cf. Experimental Section) giving pure $Sn(OC_4H_9)_2$.

Scheme 1



(1)

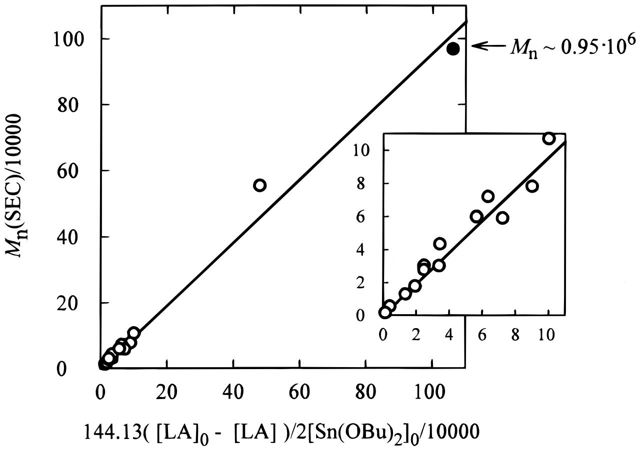


Figure 4. Dependence of molar mass (M_n) of poly(L-lactide) measured by SEC on M_n calculated from the feed composition; M_n(calcd) = 144.13($[LA]_0$ − [LA])/2$[Sn(OBu)_2]_0$. Conditions of polymerization: (○) $[LA]_0$ from 1.0 to 3.0 mol L^{-1}, THF solvent, 80 °C; (●) polymerization in bulk, 120 °C.

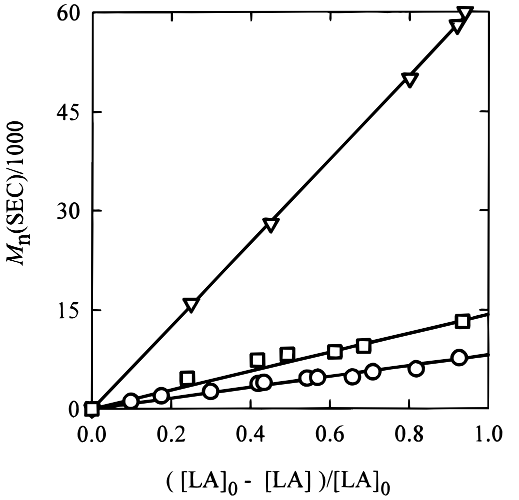


Figure 5. Evolution of molar masses (M_n) of poly(L-lactide) with degree of monomer conversion. Conditions of polymerization: $[LA]_0$ = 1.0 mol L^{-1}, THF solvent; $[Sn(OBu)_2]_0$ (in mol L^{-1}) = 1.16 × 10^{-3} (▽), 5 × 10^{-3} (□), 8.9 × 10^{-3} (○); temperature: 80 °C (▽, □), 20 °C (○). Points experimental, lines calculated assuming that every alkoxide group starts growth of one PLA chain.

Concluding, the analysis presented above shows that polymerization of LA initiated with $Sn(OBu)_2$ proceeds as with other covalent metal alkoxides. Namely, (a) initiation is quantitative, (b) each alkoxide group of initiator starts growth of one macromolecule and is transformed into the polyester end group, and (c) elementary reaction of the polymer chain growth formally proceeds as the nucleophilic attack of the alkoxide active species on the monomer carbonyl carbon atom followed by the acyl−oxygen bond scission, e.g., Scheme 1 where R stands for $CH(CH_3)C(O)OCH(CH_3)$ group.

More detailed analysis of the propagation step will be given elsewhere.

Molar Masses of Poly(L-lactide). A series of LA polymerizations initiated with $Sn(OBu)_2$ have been carried out in THF solvent at 80 °C. Monomer and initiator concentrations in the feed and the monomer conversion degrees (($[LA]_0$ − [LA])/$[LA]_0$) at which molar masses (M_n) were measured by SEC are given in Table 1. For a few polymerizations osmometric measurements are also reported, showing good agreement with the chromatographic readings. The extent of polymerization was determined from polarimetry and/or from the polymer and monomer peak areas in SEC traces of the polymerization mixture. For each experiment M_n has also been calculated from the feed composition. A plot of M_n(SEC) versus M_n(calcd) is given in Figure 4. Although there is some scatter of the experimental points, the resulting linear relationship with a slope of 0.96 supports a conclusion drawn in the previous section that practically each butoxide group initiates the growth of one PLA chain. Moreover, for a given polymerization M_n(SEC) increase linearly with monomer conversion (Figure 5), being in a close agreement with the calculated dependence. These molar mass data show that in polymerization of LA initiated with $Sn(OBu)_2$ M_n of the resulting PLA can be controlled in a wide range of values from 10^3 to 10^6 by adjusting the $[LA]_0$/$[Sn(OBu)_2]_0$ ratio. This is the first result of this kind in the area of cyclic esters polymerization.

Particularly rewarding was the first fully controlled synthesis of PLA with $M_n \approx 10^6$ in the bulk process at 120 °C; polymerization time 19 h (cf. last entry in Table 1 and Figure 6). During polymerization polymer crystallized out of the melt ($T_m \approx$ 180 °C[6,7]). According to our SEC and ^1H NMR measurements, the monomer was consumed quantitatively, despite the fact that the equilibrium concentration of LA ($[LA]_{eq}$) at 120 °C (in 1,4-dioxane as a solvent)[21] is equal to 0.13 mol L^{-1} (for LA in bulk it is equivalent to 1.6 mol %). Thus, eventually a free volume remaining for the liquid monomer gradually decreases, and although $[LA] \approx [LA]_{eq}$ the molar fraction of the unreacted LA falls down.

Although short PLA chains ($M_n \leq 10^3$) can also be prepared in the LA/$Sn(OBu)_2$ system, the synthesis requires a high amount of the initiator. It is therefore more convenient to apply much lower concentrations of the $Sn(OBu)_2$ initiator and to use an alcohol as a

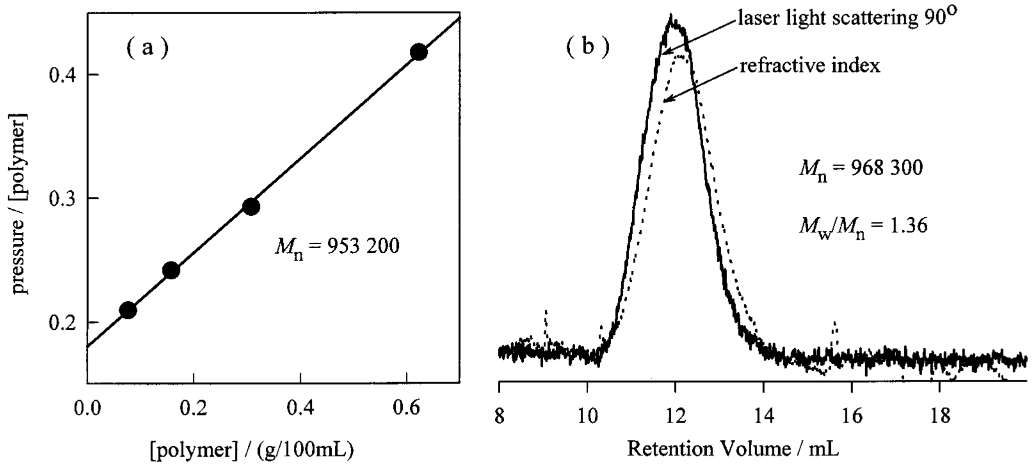


Figure 6. Determination of M_n of a high molar mass poly(L-lactide), prepared in bulk at 120 °C (6.8×10^{-3} mol % of $Sn(OBu)_2$ initiator) (a) by membrane osmometry and (b) by size exclusion chromatography. Conditions of measurements: cf. Experimental Section.

transfer agent. Sn(II) alkoxide exchanges with alcohol (e.g., BuOH) effectively, and the molar mass of PLA is controlled by the $([LA]_0 - [LA]_{eq})/(2[Sn(OBu)_2]_0 + [BuOH]_0)$ ratio. An example of a such synthesis is evidenced in the first entry in Table 1.

PLA's having $M_n > 10^5$ in a controlled way (i.e., planned as such) could not be prepared until now, although such polymers were prepared earlier with adventitious concentration of impurities.[6,7] To achieve some control, for example in tin(II) 2-ethylhexanoate (tin octoate ($Sn(Oct)_2$)) co-initiated polymerization of LA, the "calibration" curves—molar mass versus $[LA]_0/[Sn(Oct)_2]_0$ ratio or molar mass versus polymerization temperature—had to be prepared for the substrates of a standardized purity. Eventually, PLA with $M_v \approx 10^6$ has been obtained at 100 °C (the lowest investigated temperature) after 384 h. At higher temperatures the uncontrolled decrease of M_n was observed.[6,7]

Although for other initiators, such as Al,[15,16,23] Y,[19,32,33] and Sn(IV),[8,9,11] alkoxides or $Sn(Oct)_2$/alcohol (or water) system[20] molar masses of PLA can be directly predicted by the monomer to initiator concentrations ratio, this control is limited to $M_n \leq 10^5$. Reasons for this situation are not fully understood at present.

Molar Mass Distributions of Poly(L-lactide). Polydispersity indexes (M_w/M_n) of PLA's prepared with $Sn(OBu)_2$ (Table 1) are higher than those expected for the living irreversible polymerization with fast initiation and propagation only. Moreover, M_w/M_n increase with LA conversion; this is shown in a more systematic way in Figure 7 by the example of two polymerizations conducted at 25 and 80 °C. Since termination does not take place in the LA/$Sn(OBu)_2$ system, reversibility of polymerization[39,40−43] and/or chain transfer to polymer with chain scission (via transesterification reactions)[22,41,42] can be responsible for this phenomenon. The pertinent kinetic reactions are given in Scheme 2, where la and la* denote the lactoyl repeating unit ($C(O)CH(CH_3)O$) and involved active species ($C(O)CH(CH_3)O{-}SnO{-}PLA$; k_p and k_d are the rate constants of propagation and depropagation; k_{tr1} and k_{px} are the rate constants of the unimolecular transesterification (backbiting) and of propagation of the cyclic x-mer; respectively; and k_{tr2} is the rate constant of the bimolecular transesterification (segmental exchange).

Contribution of a reversibility of the polymerization to the molar mass broadening is of a minor importance due to the relatively low equilibrium monomer concentration of LA (e.g., 0.055 mol L^{-1} at 80 °C[21]), as was shown recently in our laboratory.[42,43]

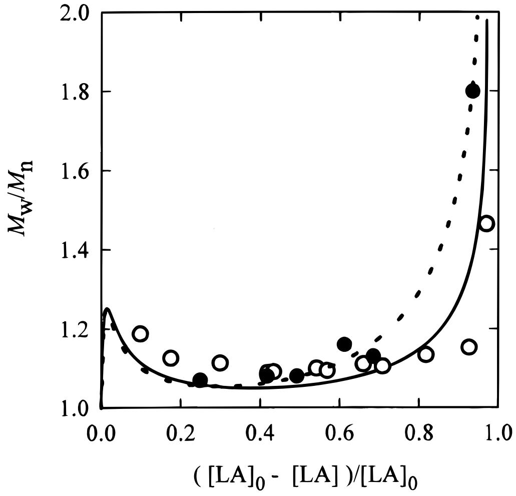


Figure 7. Dependence of polydispersity indexes (M_w/M_n) of poly(L-lactide) on degree of monomer conversion. Conditions of polymerization: $[LA]_0$ = 1.0 mol L^{-1}, THF solvent; $[Sn(OBu)_2]_0$ (in mol L^{-1}) = 5×10^{-3} (●), 8.9×10^{-3} (○); temperature: 80 °C (●), 20 °C (○). Points experimental, lines computed from the kinetic scheme 2 (omitting eq 2b), assuming k_p/k_{tr} = 125 and 200 (dotted and solid line, respectively).

Both MALDI-TOF measurements (Figure 3) and molar mass dependencies on the LA monomer conversion, obtained by SEC (Figures 4 and 5), allow excluding the presence of the macrocylics fraction. Nevertheless, the observed increase of M_w/M_n with monomer conversion as well as appearance of PLA chains containing an odd number of lactoyl units in the MALDI-TOF spectra can be explained in terms of eq 2b, assuming that cyclic even-membered oligomers are formed by backbiting and then propagate relatively fast, which would result in their low concentration (i.e., below MALDI and SEC detection threshold). This problem is currently under study in our laboratory.

Thus, in further analysis we assume that broadening of the PLA molar masses distribution with monomer conversion results exclusively from bimolecular transesterification (eq 2c). Using an approach that we developed recently in a series of papers,[22,41−43] we have determined, from the experimental plots of M_w/M_n

Scheme 2

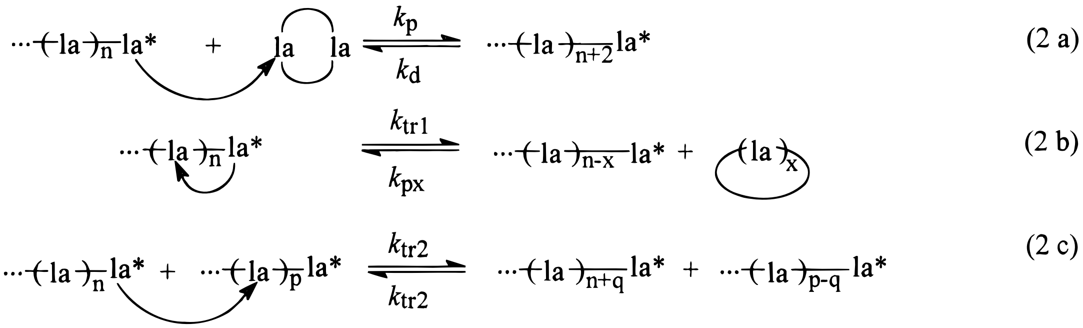


Table 2. Comparison of the Rate Costants of Propagation (k_p) and of Selectivity Parameters (k_p/k_{tr2}) for L,L-Dilactide Polymerizations Initiated with Multivalent Metal Alkoxides[a]

initiator	Bu_3SnOMe	$Bu_2Sn(OEt)_2$	$Sn(Oct)_2$/ROH	$Sn(OBu)_2$	$Al(O^iPr)_2)_3$	$Y(OR)_3$
k_p, mol^{-1} L s^{-1}	3.5×10^{-4}	1.5×10^{-2}	$(\approx 10^{-1})^b$	5×10^{-1} $(4 \times 10^{-3})^c$	4.7×10^{-3} $(7.5 \times 10^{-5})^c$	$(6 \times 10^{-2})^d$ $(1 \times 10^{1})^e$
ref	22,44	44	37	this paper	23	19, 33
k_p/k_{tr2}	20	60	200	125	100	no data
ref	22, 44	44	22	this paper	22	no data

[a] Polymerizations carried out in THF as a solvent at 80 °C if not otherwise indicated. [b] Estimated on the basis of the kinetic and molar mass data from ref 37. [c] THF, 20 °C. [d] CH_2Cl_2, 25 °C; R = $CH_2CH_2OCH(CH_3)_2$. [e] CH_2Cl_2, 22 °C; R = 2,6-di-*tert*-butylphenoxide group, polymerization conducted in the presence of $(CH_3)_2CHOH$.

versus $([LA]_0 - [LA])/[LA]_0$ given in Figure 7, the ratios k_p/k_{tr2} equal to 200 and 125 at 25 and 80 °C, respectively. These values reveal high selectivity of active species in the $Sn(OBu)_2$-initiated LA polymerization as is seen from the comparison with k_p/k_{tr2} determined for other initiators, such as alkoxide derivatives of tin(IV) or aluminum (Table 2). Only $Sn(Oct)_2$ co-initiated polymerization behaves similarly.

High molar mass PLA prepared in bulk has a low polydispersity index (M_w/M_n) equal to 1.36, even after "complete" consumption of the monomer. Since segmental exchange proceeds via reaction betwen two macromolecules, this result can be explained by a limited mobility of poly(L-lactide) chains in the crystalline phase (cf. ref 16).

Kinetics of L,L-Dilactide Polymerization Initiated with $Sn(OBu)_2$. Polymerizations were studied with $[LA]_0 = 1$ mol L^{-1} and $[Sn(OBu)_2]_0$ from 7.5×10^{-4} to 5×10^{-3} mol L^{-1} and in the temperature range from 20 to 80 °C in THF as a solvent. Instantaneous concentration of LA ([LA]) was followed by polarimetry and/or by SEC. The dependencies of $\ln\{([LA]_0 - [LA]_{eq})/([LA] - [LA]_{eq})\}$ as a function of time give straight lines, at least up to 95% of the monomer conversion (Figures 8 and 9). Thus, initiation is fast and quantitative, and termination is practically absent. Moreover, kinetic curves measured by polarimetry and SEC are the same, what indicates that there is no racemization of LA monomer.

The relative polymerization rate ($r_p = -d[LA]/[LA]dt = t^{-1} \ln\{([LA]_0 - [LA]_{eq})/([LA] - [LA]_{eq})\}$, where t denotes polymerization time) depends on the starting concentration of initiator in an untypical way (Figure 10). It appears that at low initiator concentration the rate is relatively lower. On the other hand, each alkoxide group starts growth of exactly one PLA chain, and therefore $[Sn(OBu)_2]_0$ could be used as a measure of the total concentration of the active centers. Thus, in the range of $[Sn(OBu)_2]_0$ above 10^{-3} mol L^{-1} the order of propagation in active centers is close to 1. However, at the lower concentration range it is higher than 1 (dotted line in Figure 10).

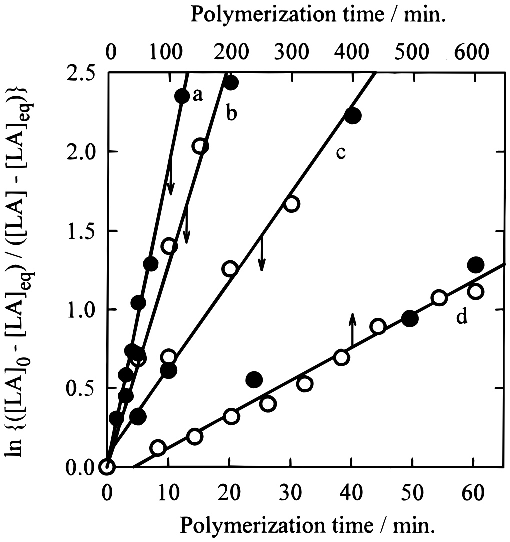


Figure 8. Kinetics of L,L-dilactide polymerization initiated with $Sn(OBu)_2$. [LA] followed by SEC (●) and/or by polarimetry (○). Conditions of polymerization: $[LA]_0 = 1.0$ mol L^{-1}, THF solvent, 80 °C; $[Sn(OBu)_2]_0$ (in mol L^{-1}) = 5×10^{-3} (a), 2×10^{-3} (b), 1.16×10^{-3} (c), 7.5×10^{-4} (d). The values of $[LA]_{eq}$ are taken from ref 21.

Our former experience with the kinetic studies allowed to exclude termination by the reaction of active centers with impurities as an origin of the observed change of the kinetic order in the vicinity of $[Sn(OBu)_2]_0 = 10^{-3}$ mol L^{-1}. A plausible explanation can be based on an assumption that there is an equilibrium between the nonaggregated (unimeric) and aggregated Sn(II) alkoxide active centers and that the latter are more reactive toward a LA monomer than the unimeric ones. In other systems we studied until now the reverse dependence was observed: the aggregates were less or not reactive at all.[23] In the further discussion of the polymerization rates parameters determined for $[Sn(OBu)_2]_0 > 10^{-3}$ mol L^{-1} range, governing the first order in active centers will be used.

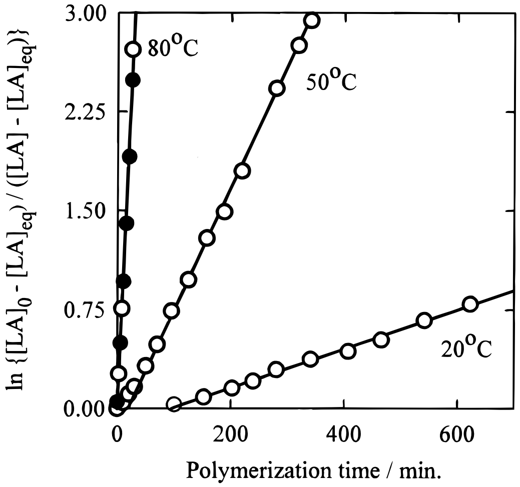


Figure 9. Kinetics of L,L-dilactide polymerization initiated with $Sn(OBu)_2$ and carried out at various temperatures. [LA] followed by SEC (●) and/or by polarimetry (○). Conditions of polymerization: $[LA]_0 = 1.0$ mol L^{-1}, THF solvent, $[Sn(OBu)_2]_0 = 3 \times 10^{-3}$ mol L^{-1}. The values of $[LA]_{eq}$ are taken from ref 21.

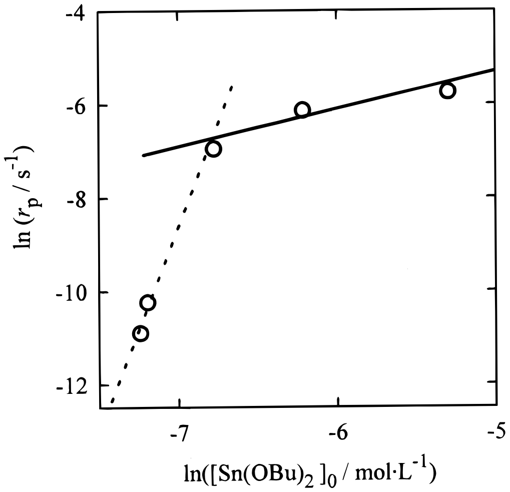


Figure 10. Dependence of the rate of LA polymerization initiated with $Sn(OBu)_2$ on the initiator concentration in the feed. Conditions of polymerization are given in the caption for Figure 8.

The values of the rate constants of propagation (k_p) collected in Table 2 reveal that k_p determined in this work ($k_p = 5 \times 10^{-1}$ mol^{-1} L s^{-1} (THF, 80 °C)) is comparable with the rate coefficient estimated for polymerization initiated with the $Sn(Oct)_2$/ROH system[37] and is much higher than k_p determined also by us for $R_3Sn(OR')$[22] and $R_2Sn(OR')_2$.[44]

Higher reactvity of the Sn(II) compounds in comparison with their Sn(IV) counterparts may be explained by the better steric accessibility of the tin atom in the divalent derivative as well as its more pronounced ability to coordinate the approaching monomer molecule. The positive induction effect of the alkyl groups on Sn(IV) additionally decreases its reactivity toward nucleophilic agents. Large difference of reactivities between Sn(II) dialkoxides and Al trialkoxides[23] (10^2 times in favor of Sn(II)) comes mostly from the difference of ionic radii of both metal atoms, resulting in a stronger polarization of the tin−oxygen bond.

However, the highest rates of LA polymerization reported until now were found for even more polarized yttrium alkoxides.[19,32,33] For example, in the $Y(OCH_2CH_2OCH(CH_3)_2)_3$ initiated polymerization $k_p = 6 \times 10^{-2}$ mol^{-1} L s^{-1} was determined (in CH_2Cl_2 solvent, at 25 °C)[33] (cf. $k_p = 4 \times 10^{-3}$ mol^{-1} L s^{-1} with $Sn(OBu)_2$ under the comparable conditions). Polymerization initiated with a tris(2,6-di-*tert*-butylphenoxy)yttrium/2-propanol mixture reveals an even higher rate:[19] $k_p = 1 \times 10^1$ mol^{-1} L s^{-1}. It would be of interest to compare these rate constants with the anionic polymerization, but reliable data are not available.

Conclusions

Polymerization of LA initiated with $Sn(OBu)_2$ proceeds as with other multivalent metal alkoxides, i.e., it is a living process (no irreversible transfer and/or termination); both alkoxide groups in $Sn(OBu)_2$ molecule start growth of the PLA chain, and monomer reacts with acyl−oxygen bond scission. However, to the best of our knowledge, this is the first system providing a full control of LA polymerization in a range of molar masses (M_n) of the resulting PLA up to $\approx 10^6$.

Polymerization is relatively fast ($k_p = 5 \times 10^{-1}$ mol^{-1} L s^{-1} in THF solvent at 80 °C), the only faster systems being the rare earth alkoxides.

Although tin(II) alkoxide active species belong to the most reactive ones in LA polymerization, they provide a low extent of the intermolecular transesterification manifested by high ratio of the rate constants of propagation to that of transesterification: $k_p/k_{tr2} = 125$ (THF, 80 °C).

Acknowledgment. The financial support of the Polish State Committee for Science (KBN), Grant 3 T09B 105 11, is gratefully acknowledged.

References and Notes

(1) Kleine, J.; Kleine, H.-H. *Makromol. Chem.* **1959**, *30*, 23.
(2) Dietrich, W.; Schulz, R. C. *Angew. Makromol. Chem.* **1971**, *15*, 109.
(3) Schindler, A.; Gaetano, K. D. *J. Polym. Sci., Polym. Lett. Ed.* **1988**, *26*, 47.
(4) Chabot, F.; Vert, M.; Chapelle, S.; Granger, P. *Polymer* **1983**, *24*, 53.
(5) Schwach, G.; Coudane, J.; Engel, R.; Vert, M. *J. Polym. Chem., Part A: Polym. Chem.* **1997**, *35*, 3431.
(6) Leenslag, J. W.; Pennings, A. J. *Makromol. Chem.* **1987**, *188*, 1809.
(7) Nijenhuis, A. J.; Grijpma, D. W.; Pennings, A. J. *Macromolecules* **1992**, *25*, 6419.
(8) Kricheldorf, H. R.; Berl, M.; Scharnagl, N. *Macromolecules* **1988**, *21*, 286.
(9) Kricheldorf, H. R.; Boettcher, C.; Toennes, T.-U. *Polymer* **1992**, *33*, 2817.
(10) Kricheldorf, H. R.; Kreiser-Saunders, I.; Boettcher, C. *Polymer* **1995**, *36*, 1253.
(11) Kricheldorf, H. R.; Lee, S. R.; Bush, S. *Macromolecules* **1996**, *29*, 1375.
(12) Kricheldorf, H. R.; Damrau, D.-O. *Makromol. Chem.* **1997**, *198*, 1753; **1997**, *198*, 1767.
(13) Dahlman, J.; Rafler, G. *Acta Polym.* **1993**, *44*, 103.
(14) Zhang, X.; MacDonald, D. A.; Goosen, M. F. A.; McAuley, K. B. *J. Polym. Sci., Part A: Polym. Chem.* **1994**, *32*, 2965.
(15) Dubois, P.; Jacobs, C.; Jérôme, R.; Teyssié, P. *Macromolecules* **1991**, *24*, 2266.
(16) Degée, Ph.; Dubois, Ph.; Jérôme, R. *Macromol. Chem. Phys.* **1997**, *198*, 1973.
(17) Degée, P.; Dubois, P.; Jacobsen, S.; Fritz, H.-G.; Jérôme, R. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 2413.
(18) Montaudo, G.; Montaudo, M. S.; Puglisi, C.; Samperi, F.; Spassky, N.; Le Borgne, A.; Wisniewski, M. *Macromolecules* **1996,** *29*, 6461.
(19) Stevels, W. M.; Ankoné, M. J. K.; Dijkstra, P. J.; Feijen, J. *Macromolecules* **1996**, *29*, 6132.

(20) In't Veld, P. J. A.; Velner, E. M.; van de Witte, P.; Hamhuis, J.; Dijkstra, P. J.; Feijen, J. *J. Polym. Sci., Part A: Polym. Chem.* **1997**, *35*, 219.
(21) Duda, A.; Penczek, S. *Macromolecules* **1990**, *23*, 1636.
(22) Baran, J.; Duda, A.; Kowalski, A.; Szymanski, R.; Penczek, S. *Macromol. Symp.* **1997**, *123*, 93.
(23) Kowalski, A.; Duda, A.; Penczek, S. *Macromolecules* **1998**, *31*, 2114.
(24) Kharash, G. B.; Sanchez-Riera, F.; Severson, D. K. In *Plastics from Microbes;* Mobley, D. P., Ed.; Hanser Publishers: Munich, New York, 1994; p 93.
(25) Hartmann, H. In *Biopolymers From Renewable Resources*; Kaplan, D. L., Ed.; Springer: Berlin, 1998; p 367.
(26) Mecerreyes, D.; Jérôme, R.; Dubois, P. *Adv. Polym. Sci.* **1998**, *147*, 1.
(27) Duda, A.; Penczek, S. In *Polymers from Renewable Resources; Polyesters of Biomedical and Environmental Importance*; Scholz, C., Gross, R., Leatham, G., Eds.; ACS Symp. Ser.; Oxford University Press: Oxford, 2000.
(28) Zhang, X.; Wyss, U. P.; Pichora, D.; Goosen, M. F. A. *J. Macromol. Sci., Pure Appl. Chem.* **1993**, *A30*, 933.
(29) Sinclair, R. G. *J. Macromol. Sci., Pure Appl. Chem.* **1996**, *A33*, 585.
(30) Lunt, J. *Polym. Degrad. Stab.* **1998**, *59*, 145.
(31) Duda, A.; Penczek, S. *Macromolecules* **1995**, *28*, 5981.
(32) McLain, S. L.; Ford, T.; Drysdale, M. E. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1992**, *33* (2), 463; **1994**, *35* (2), 534.
(33) Simic, V. Polymerisation et Copolymerisation d'Esters Cycliques a l'Aide de Derives de Terres Rares. Ph.D. Thesis, de l'Universite Pierre et Marie Curie (Paris VI), Paris, France, 1998.
(34) Kowalski, A.; Libiszowski, J.; Duda, A.; Penczek, S. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1998**, *39* (2), 74.
(35) Kowalski, A.; Duda, A.; Penczek, S. *Macromolecules* **2000**, *33*, 689.
(36) Kowalski, A.; Duda, A.; Penczek, S. *Macromol. Rapid Commun.* **1998**, *19*, 576.
(37) Duda, A.; Penczek, S.; Kowalski, A.; Libiszowski, J. *Macromol. Symp.* (RO(M)P '99, Mons (Belgium) Volume), **2000**, in press.
(38) Gsell, R.; Zeldin, M. *J. Inorg. Nucl. Chem.* **1975**, *37*, 1133.
(39) Nanda, V. S.; Jain, S. C. *Eur. Polym. J.* **1970**, *6*, 1517.
(40) Tonoyan, A. O.; Davtyan, S. P.; Rozenberg, B. A.; Irzhak, V. I.; Enikolopyan, N. S. *Dokl. Akad. Nauk SSSR* **1970**, *193*, 862.
(41) Penczek, S.; Duda, A.; Szymanski, R. *Macromol. Symp.* **1998**, *132*, 441.
(42) Szymanski, R. *Macromol. Theory Simul.* **1998**, *7*, 27.
(43) Duda, A. *Polimery (Warsaw)* **1998**, *43*, 132.
(44) Baran, J.; Duda, A.; Penczek, S. Unpublished results.

MA991751S