Kinetics and Mechanism of Cyclic Esters Polymerization Initiated with Tin(II) Octoate. 3.† Polymerization of L,L-Dilactide

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ABSTRACT: Following our previous papers on the mechanism of cyclic esters polymerization induced by tin(II) octoate ($Sn(Oct)_2$) and particularly papers on ϵ-caprolactone (CL), the present work shows that L,L-dilactide/$Sn(Oct)_2$ does not differ mechanistically from the CL/$Sn(Oct)_2$ system. Sn atoms bonded through alkoxide groups to macromolecules were also observed by MALDI−TOF mass spectrometry. Formation of the actual initiator from $Sn(Oct)_2$ and a hydroxy group-containing compound (ROH) was envisaged by kinetic arguments. The appropriate experiments were carried out to show that some "mechanisms" put forward during the past few decades by several research groups were not sufficiently substantiated. Eventually, we conclude that L,L-dilactide/$Sn(Oct)_2$ polymerization proceeds by simple monomer insertion into the ...−Sn−OR bond, reversibly formed in the reaction ...−SnOct + ROH $\rightleftharpoons$ ...−Sn−OR + OctH, where ROH is either the low molar mass co-initiator (an alcohol, hydroxy acid, or H_2O) or a macromolecule fitted with a hydroxy end group. These interconversions take place throughout the whole polymerization process. $Sn(Oct)_2$ itself does not play an active role in the polymerization.

Introduction

Polymerization of L,L-dilactide (LA)[1−18] and ϵ-caprolactone (CL)[19−25] initiated with $Sn(O(O)CCH(C_2H_5)C_4H_9)_2$ (tin(II) octoate, ($Sn(Oct)_2$)) has been systematically studied for a few decades. Several polymerization "mechanisms" were advanced, although at least some of these propositions are based on very limited experimental evidence.

These systems are of particular importance because $Sn(Oct)_2$ is the most often used initiator in preparing various grafts, block copolymers, and multibranched products starting from polymers with hydroxyl groups and using cyclic esters, particularly LA or CL, as monomers.[26−31] Sn(II)-based initiators are also used in industrial (e.g., Cargill/Dow[32]) LA polymerizations, providing the commodity degradable polymer.

Therefore, we decided to study polymerization of LA initiated with $Sn(Oct)_2$ and carried out in THF solvent, either without any co-initiator purposely added or with *n*-butyl alcohol (BuOH) as co-initiator.

Previously Proposed Mechanisms. All of the LA/$Sn(Oct)_2$ polymerization mechanisms can be divided into two categories. The first one[3,4,7,14] assumes that if alcohol or water (ROH) are present, then initiation and propagation involve reaction of three simultaneously interacting compounds—for example, in propagation, a macromolecule fitted with a terminal −OH group, monomer, and $Sn(Oct)_2$. In every propagation step, a macromolecule with an −OH at its end is reformed as a longer one by one monomer unit and one intact $Sn(Oct)_2$, either "free" or complexed, emerges from this step. It is enough to stress that, according to this group of mechanisms, $Sn(Oct)_2$ survives during polymerization as such and is not converted into any other species chemically different from $Sn(Oct)_2$. Thus, the authors consider $Sn(Oct)_2$ to be merely as a catalyst.

Some authors, using other initiators and not studying the mechanism of propagation at all adopted verbally the polymerization mechanism described above, as in a recent paper,[33] in which titanium dichlorodiaryl oxides were used.

The second group of authors assumed that $Sn(Oct)_2$ must be converted into tin(II) alkoxide in order to initiate polymerization.[2,8,13,21] Although this proposition was also not based on sound kinetic and/or spectroscopic data, it clearly differs conceptually from the first group of mechanisms.

Direct reaction of $Sn(Oct)_2$ with LA was also discussed,[7] but even the original authors considered this path as of secondary importance. There are also authors assuming that cationic polymerization emerges from $Sn(Oct)_2$ initiation.[3,6] One of this propositions regarded octanoic acid as an actual initiator.[6]

This paper will show that our experimental data agree well with the tin(II) alkoxide mechanism.

Previous Data on Polymerization of ϵ-Caprolactone Initiated with $Sn(Oct)_2$. We have recently studied polymerization of CL initiated with $Sn(Oct)_2$ in the presence of BuOH and established the following facts:

- The dependence of the rate of polymerization on $[Sn(Oct)_2]_0$ practically levels off, at certain $[Sn(Oct)_2]_0/[BuOH]_0$ ratio higher than 0.5, when $[BuOH]_0$ = constant.[22−24]
- The dependence of the rate of polymerization on $[BuOH]_0$ practically levels off, at certain $[BuOH]_0/[Sn(Oct)_2]_0$ ratios higher than 2, when $[Sn(Oct)_2]_0$ = constant.[22−24]
- MALDI−TOF mass spectra reveal formation of population of macromolecules having an OctSn−O−poly(CL)−Bu structure. The presence of Sn atoms in macromolecules leads to a very characteristic spectra, due to a number of Sn isotopes present in comparable proportions.[22,25]
- Addition of 2-ethylhexanoic acid (octanoic acid (OctH)) to the reaction mixture slows down polymerization.[23]

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† For part 2 of this series: see ref 25.

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All of these results indicate that polymerization is initiated by the product of reaction of an alcohol and $Sn(Oct)_2$, providing eventually the OctSn−O−poly(CL) growing macromolecules.

The actual active centers can be formed in reactions with adventitious H_2O, hydroxy acids, and some other unknown co-initiators, present as impurities in the polymerizing mixture. Thus, for an alcohol (ROH), two interchange reactions take place

$$\mathrm{Sn(Oct)_2 + ROH \rightleftarrows OctSnOR + OctH} \quad (1a)$$

$$\mathrm{OctSnOR + ROH \rightleftarrows Sn(OR)_2 + OctH} \quad (1b)$$

(where Oct denotes the $C_4H_9(C_2H_5)CHC(O)O$ group) with subsequent propagation by monomer insertion into the −Sn−OR bond(s). The carboxylate-alkoxide equilibria, presented in equations (1) and in the pertinent equations below, are presumably shifted into the carboxylate species side. Whether equilibria (1) are established during polymerization is still an open question.

The present work repeats similar set of experiments taking LA as monomer and shows that there is no principal difference between the mechanism of initiation and the chain growth already established for CL and studied for LA in this work. New evidence based on studies of polymerization conducted in the presence of amines is also provided.

Experimental Section

Substrates and Solvents. L,L-Dilactide (LA, Boehringer Ingelheim, Austria (≥99%)), crystallized consecutively from dry 2-propanol and toluene, was purified just before use by sublimation in vacuo (10^{-3} mbar, 85 °C). The purified monomer was distributed into the glass ampules equipped with breakseals. Tin(II) octoate ($Sn(Oct)_2$, Aldrich (95%, according to our determination)), butyl alcohol (BuOH, Aldrich (99.4+%), and tetrahydrofuran (THF, POCh, Gliwice, Poland (99%)) were purified as described in ref 23. Tin(II) butoxide ($Sn(OBu)_2$) was prepared according to ref 34. Butylamine ($BuNH_2$, Aldrich (99.5%)), 2,6-di-*tert*-butylpyridine (TBPY, Aldrich (97%)), and *o*-dichlorobenzene (POCh, Gliwice, Poland (99%)) were distilled from CaH_2 before use. Chloroform-*d* and benzene-d_6 (Dr. Glaser AG, Basel, Switzerland (99.5+% D)) were used as received.

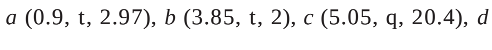
Determination of the LA Conversion. Conversion (α) of LA was determined using both polarimetry and size exclusion chromatography (SEC). Polarimetric measurements were performed with a Perkin-Elmer 241 MC polarimeter at 20 °C. SEC traces were recorded using a LKB 2150 HPLC pump, two sets of TSK Gel columns (G 2000 H_{XL} and 6000 H_{XL} or G 3000 H_{HR} and G 6000 H_{HR} with pore sizes 2.5×10^2 and 10^6 or 1.5×10^3 and 10^6 Å, respectively) at 20 °C. A Wyatt Optilab 903 interferometric refractometer and a MALLS Dawn F laser photometer, equipped with an He−Ne laser emitting at 632.8 nm (both Wyatt Technology Corp., Santa Barbara, CA), were applied as detectors in series. The refractive index increments (d*n*/d*c*) were determined with Wyatt Optilab 903 interferometric refractometer and using DNDC.EVE v 5.20 program (Wyatt Technology Corp., Santa Barbara, CA). For LA and PLA d*n*/d*c* = 0.0310 and 0.0256 mL·g^{-1} (CH_2Cl_2, 20 °C), respectively, were determined. Methylene chloride was used as an eluent at a flow rate of 0.8 mL·min^{-1}. Simultaneously LA conversion was followed using a Perkin-Elmer 241 MC polarimeter. The polymerization mixtures were prepared and transferred into optical cells under high-vacuum conditions, and then the cells were sealed off. The optical rotations of the living polymerization mixtures (or) were measured at 578 nm. The instantaneous monomer concentrations were determined assuming additivity of the optical rotations for LA (or_m) and PLA (or_p), i.e.: $[LA] = [LA]_0 (or - or_p)/(or_m - or_p)$.

Determination of Molar Masses (M_n) and Molar Mass Distributions (Polydispersity Indexes (M_w/M_n)). The actual number-average molar masses (M_n) of PLA were determined using a calibration method described previously for poly(ε-caprolactone).[34] The correct M_n values for PLA can also be obtained after multiplying by 0.68 the M_n determined with polystyrene standards, at least up to M_n 2×10^4, for the set of G 2000 H_{XL} and 6000 H_{XL} columns with CH_2Cl_2 as an eluent. The actual number-average molar masses (M_n) of the deactivated and isolated PLA were occasionally determined with Knauer osmometers: vapor pressure or membrane osmometers 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 values higher than 10^4 were directly determined with a MALLS Dawn F laser photometer and using the ASTRA v 4.70 program (Wyatt Technology Corp., Santa Barbara, CA). For measurements of M_n exceeding 10^5, a set of TSK Gel G 3000 H_{HR} and G 6000 H_{HR} columns was used.

MALDI−TOF Measurements. Mass spectrometric measurements were performed using 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 time delayed extraction ion source. An accelerating voltage of 20 kV was used. Mass spectra were obtained in the reflector and/or linear mode. The matrix, 2,5-dihydroxybenzoic acid, was dissolved in THF or methylene chloride in concentration equal to 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 a stainless steel plate covered by the gold metal target.

NMR Measurements. ^1H NMR spectra were recorded in benzene-d_6 or chloroform-*d* solvent on a Bruker AC200 operating at 200 MHz. Benzene or chloroform were used as an internal standard ($\delta = 7.16$ or 7.25 ppm).

Polymerization Procedures. Polymerizing mixtures were prepared in sealed polarimetric cells or glass ampules using standard high vacuum technique. A general procedure follows example described below. $Sn(Oct)_2$ (1 mL of 0.75 mol·L^{-1} solution in dry THF) and LA (2.16 g (15 mmol)) were transferred under vacuum into break-seals and sealed after freezing in liquid nitrogen. BuOH (0.11 g (1.5 mmol)) was distilled into thin-walled phial and then sealed after freezing in liquid nitrogen. Break-seals containing $Sn(Oct)_2$/THF solution and LA monomer, and a tube with an immersed BuOH phial, polarimetric cell, and glass ampules were sealed to the reacting (≈30 mL) glass vessel. THF (12.2 mL) was distilled into the resulting reactor, which was then sealed off. The break-seals and phial were broken, and when all components were dissolved at room temperature, the resulting solution was transferred into the polarimetric cell and the glass ampules. The cell and ampules containing the reacting mixture were then sealed off and placed into a thermostat (50 °C). Optical rotation (or) of the reacting mixture was measured at room temperature in the approximately 10 min intervals until it reached a constant value. Then the reacting mixture was injected into a SEC apparatus. Analysis of a SEC trace of the crude reacting mixture gave $M_n = 1.7 \times 10^3$, $M_w/M_n = 1.35$, and 96% of LA conversion (under these conditions $[LA]_{eq} = 0.03$ mol·L^{-1}, which corresponds to 3% of the unconsumed LA).[18] The resulting Bu−PLA−OH was precipitated into cold heptane, separated by filtration, and washed several times with heptane up to the disappearance of the unreacted $Sn(O(O)CCH(C_2H_5)C_4H_9)_2$ proton NMR absorption (e.g., the −C*H*− multiplet at $\delta = 2.1$ ppm, C_6D_6, 20 °C). The mass of the vacuum-dried product and its M_n measured osmometrically were equal to 2.05 g (90% yield) and 1.45×10^3, respectively. ^1H NMR spectrum analysis (C_6D_6, 20 °C) gave the following results (in parentheses are given chemical shifts (δ, in ppm), multiplicities of signals and their relative intensities):



$$\underset{a}{CH_3}CH_2CH_2\underset{b}{CH_2}O[C(O)\underset{c}{CH}(\underset{d}{CH_3})O]_{n-1}C(O)\underset{e}{CH}(\underset{f}{CH_3})O\underset{g}{H}$$

(BuO-(la)$_n$-H)

a (0.9, t, 2.97), *b* (3.85, t, 2), *c* (5.05, q, 20.4), *d* (1.35, d, 65), *e*

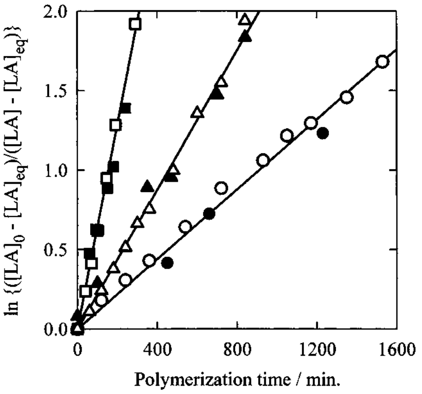


Figure 1. Kinetics of L,L-dilactide polymerization initiated with $Sn(Oct)_2$ without co-initiator added. [LA] measured by polarimetry (□, △, ○) and by SEC (■, ▲, ●). Conditions of polymerization: $[LA]_0 = 1.0$ mol·L^{-1}, THF solvent, 80 °C; $[Sn(Oct)_2]_0$ (in mol·L^{-1}) = 5×10^{-2} (□, ■), 1×10^{-2} (△, ▲), 5×10^{-3} (○, ●). $[LA]_{eq} = 5.5 \times 10^{-2}$ mol·L^{-1}.[18]

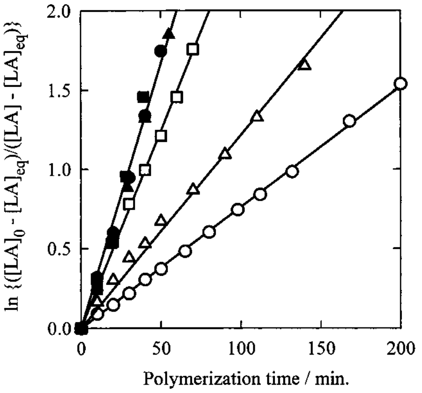


Figure 2. Kinetics of L,L-dilactide polymerization initiated with $Sn(Oct)_2$/BuOH system. [LA] measured by polarimetry. Conditions of polymerization: $[LA]_0 = 1.0$ mol·L^{-1}, $[Sn(Oct)_2]_0 = 5 \times 10^{-2}$ mol·L^{-1}, THF solvent, 50 °C; $[BuOH]_0$ (in mol·L^{-1}) = (○) 0.083, (△) 0.109, (□) 0.240, (●) 0.396, (▲) 1.00, (■) 1.50. $[LA]_{eq} = 3.0 \times 10^{-2}$ mol·L^{-1}.[18]

(3.85, q, 1), *f* (1.1, d, 3.05), *g* (2.5, d, 0.95). M_n calculated on the basis of NMR data is equal to $\approx 1.65 \times 10^3$.

Results and Discussion

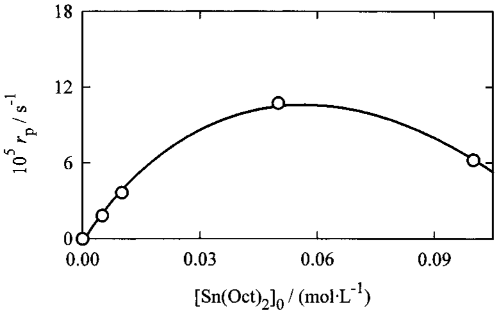


Figure 3. Dependence of the rate of polymerization of L,L-dilactide ($r_p = -d([LA] - [LA]_{eq})/([LA] - [LA]_{eq})\,dt = \ln\{([LA]_0 - [LA]_{eq})/([LA] - [LA]_{eq})/t$ on $[Sn(Oct)_2]_0$. Conditions of polymerization are given in the caption for Figure 1.

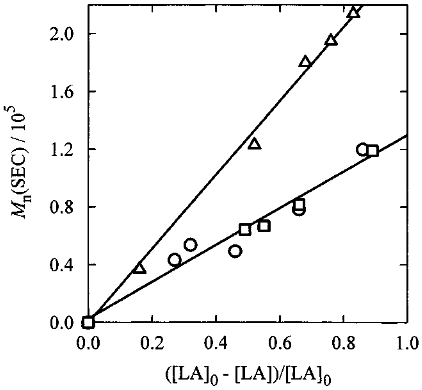


Figure 4. Dependence of molar masses (M_n) of poly(L-lactide) measured by SEC (RI and light scattering detectors in series) on degree of monomer conversion. Conditions of polymerization: $[LA]_0 = 1.0$ mol·L^{-1}, THF solvent; $[Sn(Oct)_2]_0$ (in mol·L^{-1}) = 5×10^{-2} (□), 1×10^{-2} (△), 5×10^{-3} (○); temperature 80 °C.

Kinetics of L,L-Dilactide Polymerization Initiated with Tin Octoate. The kinetics of polymerization was studied by measuring monomer conversion by size exclusion chromatography (SEC) and polarimetry as described in the Experimental Section. Figure 1 shows that both methods give similar results. This not only indicates the correctness of the experimental procedure but also shows that no important racemization takes place throughout polymerization. Kinetic plots, obtained for polymerizations carried out with either BuOH added or not, gave straight lines in the semilogarithmic coordinates (Figures 1 and 2). Thus, the number of growing chains does not change appreciably during polymerization at the applied condition. In Figure 3 the dependence of the relative polymerization rate ($r_p = -d[LA]/[LA]dt = \ln\{([LA]_0 - [LA]_{eq})/([LA] - [LA]_{eq})\}/t$, where *t* denotes polymerization time) on $[Sn(Oct)_2]_0$ is given. At lower $[Sn(Oct)_2]_0$, and without any co-initiator introduced purposely, the rate increases almost linearly with $[Sn(Oct)_2]_0$ until $[Sn(Oct)_2]_0 \approx 0.025$ mol·L^{-1}; then further increase of r_p is less steep, and after reaching a maximum, it eventually decreases with further increasing $[Sn(Oct)_2]_0$. This result means that the adventitious co-initiator, i.e., any compound containing hydroxyl group (ROH) able to form $-$SnOR species from $Sn(Oct)_2$ in the carboxylate$-$alkoxide exchange reactions (cf. eq 2) does exist in both the solvent/monomer mixture and in $Sn(Oct)_2$ itself. Thus, above a certain $[Sn(Oct)_2]_0$ any further increase in rate is only due to the co-initiator present in $Sn(Oct)_2$. A slight retarding effect is probably caused either by the OctH acid introduced as an impurity with $Sn(Oct)_2$ and/or by aggregation at higher concentration of $Sn(Oct)_2$.

Our system contains approximately 10^{-3} mol·L^{-1} of the adventitious ROH co-initiator. This estimation was based on molar masses (M_n) of polymers obtained for conditions given in Figure 4, assuming that one molecule of co-initiator starts the growth of one macromolecule. In another experiment, when equimolar quantities of LA and $Sn(Oct)_2$ were reacted ($[LA]_0 = 1.0$ mol·L^{-1}, $[Sn(Oct)_2]_0 = 1.0$ mol·L^{-1}, THF solvent at 80 °C), PLA having $M_n = 7 \times 10^3$ was formed. Thus, the total concentration of co-initiator was equal to 0.02 mol·L^{-1}.

Polymerization with Added BuOH. Figure 5 shows another set of kinetic plots, obtained for polymerizations carried out with butyl alcohol (BuOH) added as co-initiator. In one series of experiments the starting concentration of $Sn(Oct)_2$ was kept constant ($[Sn(Oct)_2]_0 = 0.05$ mol·L^{-1}) and $[BuOH]_0$ was varied (Figure 5a). First, at lower starting concentrations of BuOH, the rate increases proportionally to $[BuOH]_0$. When a certain $[BuOH]_0/[Sn(Oct)_2]_0$ ratio is reached, the rate becomes

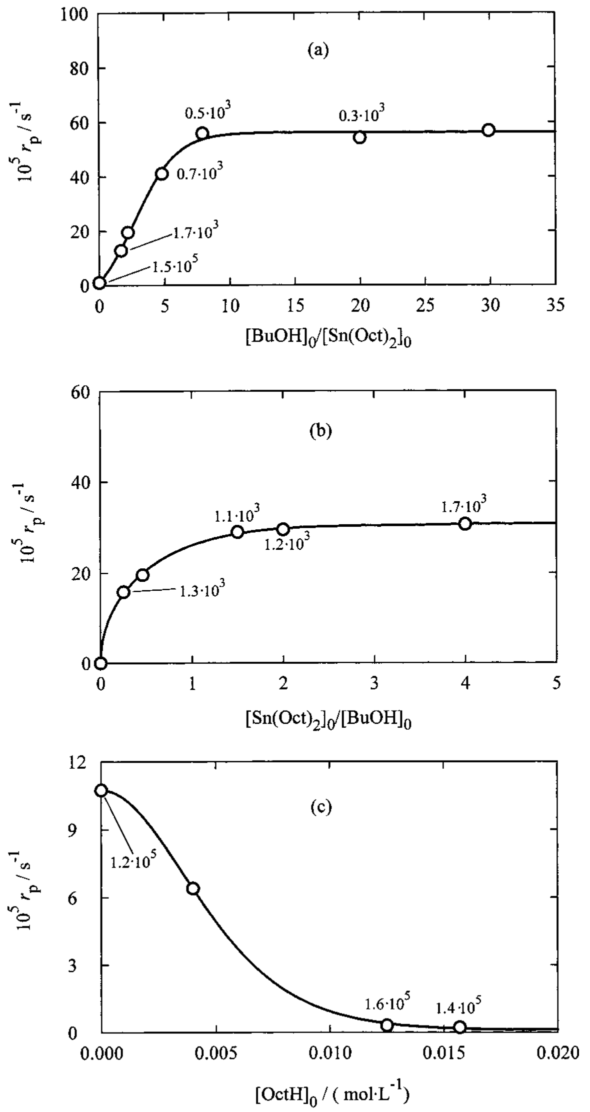


Figure 5. Dependence of the rate of polymerization of L,L-dilactide ($r_p = -d([LA] - [LA]_{eq})/([LA] - [LA]_{eq})\ dt = \ln\{([LA]_0 - [LA]_{eq})/([LA] - [LA]_{eq})/t$) initiated with $Sn(Oct)_2/BuOH$ system: (a) $[BuOH]_0/[Sn(Oct)_2]_0$ ratio with $[Sn(Oct)_2]_0 = 0.05$ mol·L^{-1}; (b) $[Sn(Oct)_2]_0/[BuOH]_0$ ratio with $[BuOH]_0 = 0.1$ mol·L^{-1}; (c) $[OctH]_0$ with $[Sn(Oct)_2]_0 = 0.05$ mol·L^{-1}. Conditions: $[LA]_0 = 1.0$ mol·L^{-1}, THF solvent, temperature 50 °C (a, b) or 80 °C (c). Values in the figures give molar masses (M_n) of the resulting PLA's.

independent of $[BuOH]_0$. Moreover, with increasing $[BuOH]_0$, molar masses (M_n) decrease (cf. M_n values in Figure 5a). This is because BuOH plays a double role, of co-initiator and of transfer agent, e.g.,

- formation of an initiator

$$Sn(Oct)_2 + BuOH \rightleftharpoons OctSnOBu + OctH \quad (2a)$$

- reversible chain transfer

$$OctSnO{-}(la)_n{-}OBu + BuOH \rightleftharpoons OctSnOBu + HO{-}(la)_n{-}Bu \quad (2b)$$

(where la denotes the lactoyl repeating unit ($CH(CH_3)$-$C(O)O$)).

A similar dependence was observed when for a set of kinetic measurements, $[BuOH]_0$ was kept constant and $[Sn(Oct)_2]_0$ was increased in every following kinetic experiment (Figure 5b). First, the rate increased with increasing $[Sn(Oct)_2]_0$. After a certain $[Sn(Oct)_2]_0/[BuOH]_0$ ratio was reached, practically no more increase of rate was observed. The reasoning is similar as for the previous set of experiments. Increase of rate results from shifting equilibrium 2a to the right-hand side until almost all of the BuOH is converted into tin(II) alkoxide. Further increase of $[Sn(Oct)_2)]_0$ does not provide, however, any more active species. In this set of experiments, carried out at constant $[BuOH]_0$, the M_n values of PLA's do not practically depend on $[Sn(Oct)_2)]_0$ and are controlled by the $([LA]_0 - [LA])/[BuOH]_0$ ratios; molar masses are given directly in Figure 5b.

Addition of 2-ethylhexanoic acid (octanoic acid (OctH)) to the system decreases the rate of polymerization and practically does not influence the M_n (Figure 5c). Similar phenomena were observed by McAuley[13] and in our group for CL.[23] The rates decrease because growing chains are converted into the dormant ones by displacing the alkoxide active chain from tin atom. The higher the concentration of added acid the lower the instantaneous concentration of growing (active) chains:

$$\underset{\text{growing chain}}{OctSnO{-}(la)_n{-}Bu} + OctH \rightleftharpoons OctSnOct + \underset{\text{dormant chain}}{HO{-}(la)_n{-}Bu} \quad (3)$$

Moreover, octanoic acid and/or $Sn(Oct)_2$ are responsible for esterification of hydroxyl chain ends (see below, section related to the MALDI−TOF spectra of PLA):

$$OctH + HO{-}(la)_n{-}Bu \overset{Sn(Oct)_2}{\rightleftharpoons} Oct{-}(la)_n{-}Bu + H_2O \quad (4a)$$

$$Sn(Oct)_2 + H_2O \rightleftharpoons OctSnOH + OctH \quad (4b)$$

$$OctSnOH + mLA \rightleftharpoons OctSnO{-}(la)_n{-}Bu \quad (4c)$$

This reaction (eq 4a) decreases the total concentration of macromolecules able to grow (active or dormant) by forming the dead macromolecules ($Oct{-}(la)_n{-}Bu$). Some new initiating species may be formed in the reaction of the esterification byproduct, H_2O, with the unreacted $Sn(Oct)_2$ (eqs 4b and 4c). Thus, reaction 4 increases the number of the growing species increasing polymerization rate this way. In parallel reactions, carboxylic acid (OctH and $...{-}(la)_m{-}H$) is formed and inhibits polymerization. Which of these two effects prevails is not yet clear; however, the linearity of the semilogarithmic kinetic plots (Figures 1 and 2) suggests that within kinetic measurements they compensate each other. When $[Sn(Oct)_2]_0$ is low these phenomena are of minor importance.

Esterification and formation of the octanoic ester end groups are much less important in the polymerization of LA than in the polymerization of CL.[25] Actually, even with the relatively high $[Sn(Oct)]_0$, the population of macromolecules with octanoic ester end groups was much lower than in the polymerization of CL, under the otherwise identical conditions (cf. the MALDI−TOF spectra discussed below). However, concentration of the esterified macromolecules at the final equilibrium would presumably be close to $2[Sn(Oct)_2]_0$.

The Identity of Systems: $Sn(OBu)_2/OctH$ (I) and $Sn(Oct)_2/BuOH$ (II). Formation of tin(II) alkoxide from $Sn(Oct)_2$ and an alcohol is a reversible reaction. The rates of exchange and the position of equilibria are not

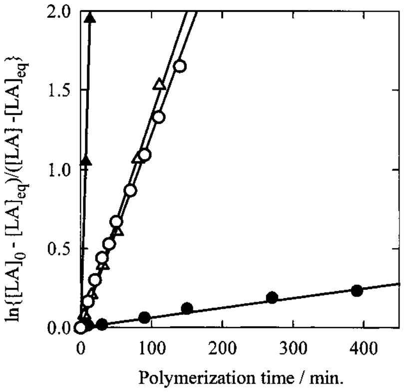


Figure 6. Comparison of the kinetics of LA polymerization initiated by $Sn(OBu)_2$ (▲), $Sn(OBu)_2$/OctH (△), $Sn(Oct)_2$/BuOH (○), and $Sn(Oct)_2$ (●). Conditions of polymerization: $[LA]_0 = 1.0$ mol·L^{-1}, $[Sn(OBu)_2]_0 = [Sn(Oct)_2]_0 = 0.05$ mol·L^{-1}, $[OctH]_0 = [BuOH]_0 = 0.10$ mol·L^{-1}, THF solvent, 50 °C.

yet established and are under study in our group. However, the influence of this interconversion on the polymerization kinetics can be approached from two sides as is shown below:

$$\mathrm{Sn(Oct)_2 \overset{ROH}{\leftrightarrows} OctSnOR + OctH \overset{ROH}{\leftrightarrows} ROSnOR + 2OctH} \qquad (5a)$$

$$\mathrm{Sn(OR)_2 \overset{OctH}{\rightleftarrows} OctSnOR + ROH \overset{OctH}{\rightleftarrows} OctSnOct + 2ROH} \qquad (5b)$$

Therefore, we compared rates of polymerization of two systems, namely that initiated with $Sn(Oct)_2$ + BuOH and that initiated with $Sn(OBu)_2$ + OctH. This comparison is shown in Figure 6.

Polymerization with $[Sn(Oct)_2]_0 = 0.05$ mol·L^{-1} with no alcohol added is very slow. It is certainly co-initiated by compounds containing the hydroxyl group, adventitiously present in the system as impurities. Assuming that one molecule of co-initiator gives rise to one macromolecule, the concentration of the co-initiator, calculated from $M_n = 1.5 \times 10^5$ mol·L^{-1}of the resulting polymer, is equal to $\approx 10^{-3}$ mol·L^{-1} in this set of experiments ($[LA]_0 = 1.0$ mol·L^{-1}, THF, 80 °C).

Polymerization initiated with $[Sn(OBu)_2]_0 = 0.05$ mol·L^{-1} was 2.4×10^2 times faster than that with $Sn(Oct)_2$ "alone" and the measured (SEC) molar mass of the resulting PLA is $M_n(SEC) = 1.5 \times 10^3$. This is practically equal to the value (M_n(calcd) = 1515), calculated assuming that polymerization proceeds on both alkoxide groups of $Sn(OBu)_2$,[35] and it was 10^2 times lower than that with $Sn(Oct)_2$.

In the next two experiments, $[Sn(Oct)_2]_0$ and $[Sn(OBu)_2]_0$ were equal to one another (0.05 mol·L^{-1}), and 0.1 mol·L^{-1} each of BuOH and OctH was added, respectively. As it is seen in Figure 6, polymerization rates in the $Sn(Oct)_2$ + BuOH and $Sn(OBu)_2$ + OctH systems are practically the same. Thus

$$\text{(I)} \quad [\mathrm{Sn(Oct)}]_0 = 0.05 \text{ mol·L}^{-1} \text{ and } [\mathrm{BuOH}]_0 = 0.1 \text{ mol·L}^{-1}$$

$$r_p = 2.0 \times 10^{-4}\cdot\mathrm{s}^{-1}; \quad M_n(\mathrm{SEC}) = 1.41 \times 10^3$$

and

$$\text{(II)} \quad [\mathrm{Sn(OBu)_2}]_0 = 0.05 \text{ mol·L}^{-1} \text{ and } [\mathrm{OctH}]_0 = 0.1 \text{ mol·L}^{-1}$$

$$r_p = 2.2 \times 10^{-4}\ \mathrm{s}^{-1}; \quad M_n(\mathrm{SEC}) = 1.45 \times 10^3$$

give identical rates and M_n (M_n(calcd) = 144.13($[LA]_0 - [LA]_{eq}$)/$[OBu]_0$ + 74.1 = 1514). This means that the stationary state concentrations of the actually growing species (or their equilibrium concentrations) are the same and controlled by the interconversions shown below.

system I

$$\mathrm{Sn(Oct)_2 + BuOH \leftrightarrows OctSnOBu + OctH} \qquad (6a)$$

$$\mathrm{OctSnOBu + BuOH \leftrightarrows Sn(OBu)_2 + OctH} \qquad (6b)$$

$$\mathrm{...{-}SnOBu} + n\mathrm{LA} \rightleftarrows \mathrm{...{-}SnO{-}(la)}_n\mathrm{{-}Bu} \qquad (6c)$$

system II

$$\mathrm{Sn(OBu)_2 + OctH \rightleftarrows OctSnOBu + BuOH} \qquad (7a)$$

$$\mathrm{OctSnOBu + OctH \rightleftarrows Sn(Oct)_2 + BuOH} \qquad (7b)$$

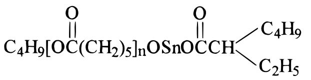
$$\mathrm{...{-}SnOBu} + n\mathrm{LA} \rightleftarrows \mathrm{...{-}SnO{-}(la)}_n\mathrm{{-}Bu} \qquad (7c)$$

The identity of these two systems clearly indicate that interconversions in system I and system II give the same concentrations of growing species and that if there are two or more different species then their proportions are also identical.

We refrain in this paper from discussing a more general problem: what are the conditions sufficient and necessary for the two systems, such as I and II, to be identical. For the practical purpose of the present work it has been sufficient that the concentration of Sn compounds were identical (0.05 mol·L^{-1}) in both systems and the other components taken in the identical excess.

We have shown previously that in the $Sn(OBu)_2$-initiated polymerization all of the alkoxide groups are engaged in the PLA chain growth.[35] Since the observed rate for experiment with OctH added to $Sn(OBu)_2$ is approximately 10 times lower (cf. Figure 6), it means that equilibria a and b in eq 7 are shifted into the right-hand side and that approximately 90 mol % of tin(II) alkoxide became temporarily deactivated. The same reasoning applies to the $Sn(Oct)_2$ + BuOH system. However, the system $Sn(Oct)_2$ + BuOH would "never" reach the rate observed with $Sn(OBu)_2$ alone, because there will "always" be a certain concentration of OctH, continuously converting a certain proportion of growing (active) species into the dormant ones.

MALDI−TOF Mass Spectra of PLA's Prepared with $Sn(Oct)_2$. In the polymerization of CL described by us previously,[25] MALDI−TOF mass spectrometry allowed determining, the presence of tin atoms in macromolecules. The presence of macromolecules with the structure


$$\mathrm{C_4H_9[O\overset{O}{\overset{\|}{C}}(CH_2)_5]_nOSnO\overset{O}{\overset{\|}{C}}CH\begin{cases}C_4H_9\\C_2H_5\end{cases}}$$

(Bu-(cl)$_n$-OSnOct)

is one of the proofs for polymerization proceeding on the tin−alkoxide bond (−Sn−O−polymer). Besides, for po-

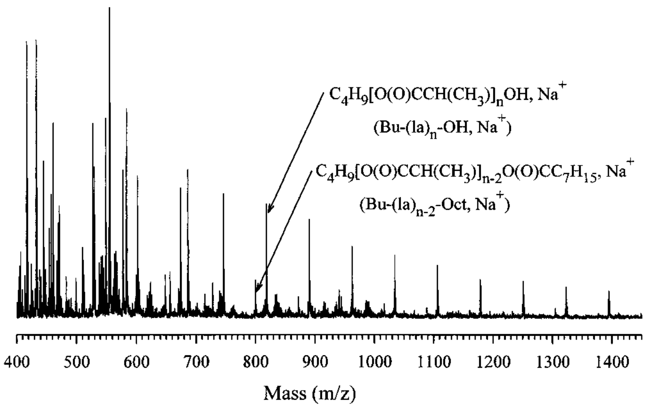
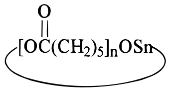


Figure 7. MALDI–TOF spectrum of the L,L-dilactide/Sn(Oct)$_2$/BuOH reacting mixture (reflector mode, virgin sample—without NaI added). Polymerization conditions: $[\mathrm{LA}]_0 = 1.0$ mol·L^{-1}, $[\mathrm{Sn(Oct)_2}]_0 = 1.0$ mol·L^{-1}, $[\mathrm{BuOH}]_0 = 0.15$ mol·L^{-1}; THF solvent, 80 °C.

lymerizations carried out with H_2O as co-initiator a series of cyclics containing tin atoms were also observed:



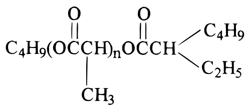
$\mathrm{[O\overset{\overset{O}{\|}}{C}(CH_2)_5]_nOSn}$ ((cl) $_n$OSn)

In the present work on LA polymerization, as in the previous analysis of the MALDI–TOF mass spectra of CL/Sn(Oct)$_2$/BuOH reacting mixtures,[25] tin-containing species could only be detected in the lower *m*/*z* region and for a high enough $[\mathrm{Sn(Oct)_2}]_0$. The pertinent spectrum (Figure 7), recorded for the virgin reacting mixture (without NaI added), shows that at 80 °C Bu−(la)$_n$−OH chains are mostly formed. Apart from sharp signals coming from the latter species the broader “multiplets” are also seen and could be ascribed to the tin-containing derivatives. Some of these characteristic signals are expanded in Figure 8 and compared with the patterns computed for the assumed structures. A large number of tin isotopes present in comparable proportions makes these patterns unique, and they cannot be mistaken with other species, from which the tin atoms are absent.[25]

For example, signals due to OctSnOSnOBu, H$^+$ ($m/z = 470.96$; Figure 8a), OctSnOSnO−(la)$_1$−Bu, H$^+$ ($m/z = 542.81$; Figure 8b), OctSnOSnO−(la)$_1$−Bu, Na$^+$ ($m/z = 564.98$; Figure 8c), and OctSnO−(la)$_4$−Bu, H$^+$ ($m/z = 625.16$; Figure 8d) clearly appear in the spectrum. Then, comes a short series of the tin-containing species being a part of $m/z = 72$ (see signals appearing at 840, 912, and 984). More detailed inspection in their structure revealed that each of those patterns is composed of signals coming from LA oligomers fitted with various tin−alkoxide and distannoxane groups. However, such a detailed analysis of the MALDI–TOF spectra is out of the scope of the present paper.

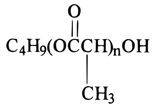
All of these populations with Sn atoms are much less clearly seen at the higher molar masses than these observed for the OctSnO−(cl)$_n$−Bu series.[25] It is certainly due to the much higher hydrolytical stability of the primary alkoxides of tin (i.e., in the growing PCL) than the secondary alkoxides (i.e., in the growing PLA). Nevertheless, all of the provided evidence leaves no doubt that the OctSnO−(la)$_n$−Bu species are present, as previously observed the OctSnO−(cl)$_n$−Bu species in the polymerization of CL.

The most intense signals in the MALDI–TOF spectra, recorded for LA/Sn(Oct)$_2$/BuOH polymerization mixtures (Figure 9), come from the following PLA chains:



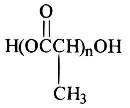
$\mathrm{C_4H_9(O\overset{\overset{O}{\|}}{C}\underset{\underset{CH_3}{|}}{C}H)_nO\overset{\overset{O}{\|}}{C}CH\begin{smallmatrix}C_4H_9\\ C_2H_5\end{smallmatrix}}$

(Bu-(la) $_n$-Oct, (B))



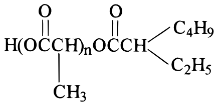
$\mathrm{C_4H_9(O\overset{\overset{O}{\|}}{C}\underset{\underset{CH_3}{|}}{C}H)_nOH}$

(Bu-(la) $_n$-OH, (C))



$\mathrm{H(O\overset{\overset{O}{\|}}{C}\underset{\underset{CH_3}{|}}{C}H)_nOH}$

(H-(la) $_n$-OH, (D))



$\mathrm{H(O\overset{\overset{O}{\|}}{C}\underset{\underset{CH_3}{|}}{C}H)_nO\overset{\overset{O}{\|}}{C}CH\begin{smallmatrix}C_4H_9\\ C_2H_5\end{smallmatrix}}$

(H-(la) $_n$-Oct, (E))

Population C dominates just after complete LA consumption (≈10 min at 150 °C). The same mixture gives, after longer reaction time (≈120 min at 150 °C), exclusively esterified chains (populations B and E). Reaction 8, parts a–c, explains formation of the populations B and C. Initiation with the ...−SnOH species, formed in reaction 9a, gives populations D and E.

$$\ldots{-}\mathrm{SnO}{-}(\mathrm{la})_n{-}\mathrm{Bu} + m\mathrm{LA} \rightleftarrows \ldots{-}\mathrm{SnO}{-}(\mathrm{la})_{n+m}{-}\mathrm{Bu} \tag{8a}$$

$$\ldots{-}\mathrm{SnO}{-}(\mathrm{la})_p{-}\mathrm{Bu} + \mathrm{OctH} \rightleftarrows \ldots{-}\mathrm{SnOct} + \mathrm{HO}{-}(\mathrm{la})_p{-}\mathrm{Bu} \tag{8b}$$

$$\ldots{-}\mathrm{SnO}{-}(\mathrm{la})_p{-}\mathrm{Bu} + \mathrm{ROH} \rightleftharpoons \ldots{-}\mathrm{SnOR} + \mathrm{HO}{-}(\mathrm{la})_p{-}\mathrm{Bu} \tag{8c}$$

and

$$\ldots{-}\mathrm{SnOct} + \mathrm{HO}{-}(\mathrm{la})_p{-}\mathrm{Bu} \xrightarrow{\substack{\text{practically}\\ \text{irreversible}}} \ldots{-}\mathrm{SnOH} + \mathrm{Oct}{-}(\mathrm{la})_p{-}\mathrm{Bu} \tag{9a}$$

$$(\text{and/or } \mathrm{OctH} + \mathrm{HO}{-}(\mathrm{la})_p{-}\mathrm{Bu} \xrightarrow{\mathrm{Sn(Oct)_2}} \mathrm{H_2O} + \mathrm{Oct}{-}(\mathrm{la})_p{-}\mathrm{Bu}) \tag{9b}$$

Taking into account the reversibility of the first two reactions and (practically) irreversibility of esterification it is only a matter of time to introduce “all” of the available octoate groups into macromolecules. Esterification is irreversible, because water is consumed—introduced as the end groups into the macromolecules.

Polymerization in the Presence of Amines. (a) BuNH$_2$ as Co-initiator and Transfer Agent—Comparison with BuOH. Co-initiation with amines is interesting for several reasons: first, because co-initiation would mean that the cationic mechanisms of cyclic esters polymerizations initiated with Sn(Oct)$_2$ have to be excluded, second, because in this way the amide end groups could be created, and finally, as an introduction to the block copolymers synthesis, starting from polymers with ...−NH$_2$ end groups.[36]

Figure 10 compares kinetics of polymerization of LA initiated with Sn(Oct)$_2$/BuOH and Sn(Oct)$_2$/BuNH$_2$ systems. Polymerization with BuNH$_2$ proceeds with almost identical rate as with BuOH taken as co-initiator.

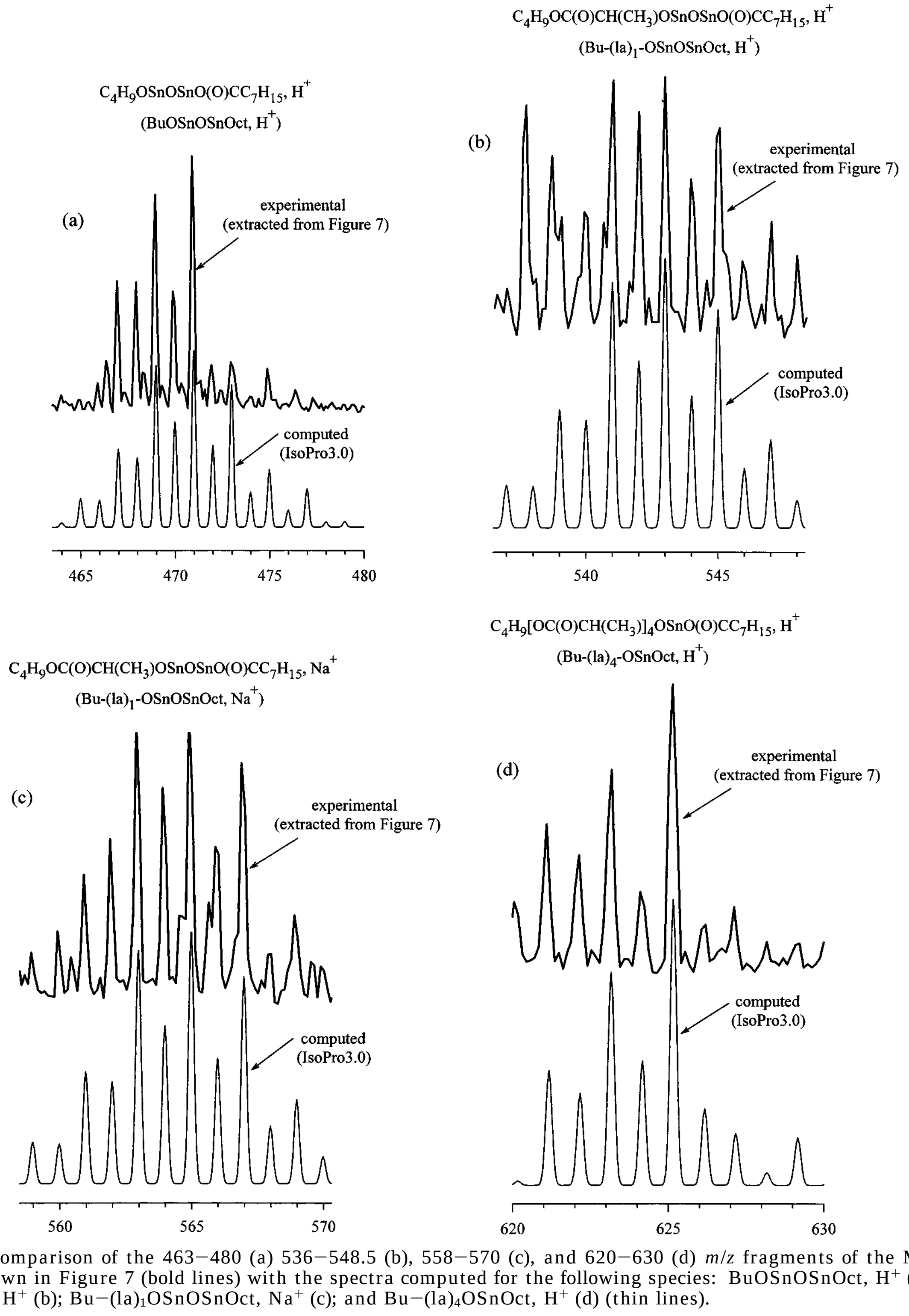
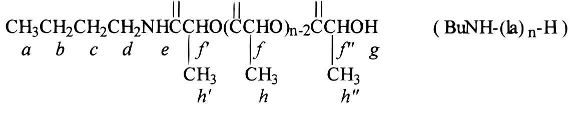


Figure 8. Comparison of the 463−480 (a) 536−548.5 (b), 558−570 (c), and 620−630 (d) *m*/*z* fragments of the MALDI−TOF spectrum shown in Figure 7 (bold lines) with the spectra computed for the following species: BuOSnOSnOct, H^+ (a); Bu−$(la)_1$-OSnOSnOct, H^+ (b); Bu−$(la)_1$OSnOSnOct, Na^+ (c); and Bu−$(la)_4$OSnOct, H^+ (d) (thin lines).

According to the analysis of the MALDI−TOF (Figure 11) and ^1H NMR (Figure 12) spectra, in the presence of $BuNH_2$, the PLA macromolecules with amide end groups (BuNH−$(la)_n$−H) are formed.



$$\underset{a\;\;b\;\;c\;\;d\;\;e}{CH_3CH_2CH_2CH_2NH}\overset{O}{\overset{\|}{C}}\underset{\underset{h'}{CH_3}}{\underset{|f}{C}}HO(\overset{O}{\overset{\|}{C}}\underset{\underset{h}{CH_3}}{\underset{|f}{C}}HO)_{n-2}\overset{O}{\overset{\|}{C}}\underset{\underset{h''}{CH_3}}{\underset{|f''}{C}}H\underset{g}{OH} \quad (BuNH\text{-}(la)_n\text{-}H)$$

The corresponding assignments are given directly in the figures (similar chemical shifts of the amide protons (−$CH_2NHC(O)$−) were reported for BuNH−PCL[37]). The resulting molar masses and chain ends are controlled by the feed composition, and therefore, $BuNH_2$ can be considered as an effective co-initiator and transfer agent. This is not a result of the direct reaction of $BuNH_2$ with LA monomer or with the PLA formed—our attempts of LA polymerization in the absence of $Sn(Oct)_2$ failed. Also in the direct reaction of PLA of $M_n = 80 \times 10^3$ with $BuNH_2$, only 5 mol % of the latter was consumed, under the otherwise identical conditions.

(b) Influence of 2,6-Di-*tert*-butylpyridine. Figure 13 illustrates the influence of the proton trap, 2,6-di-

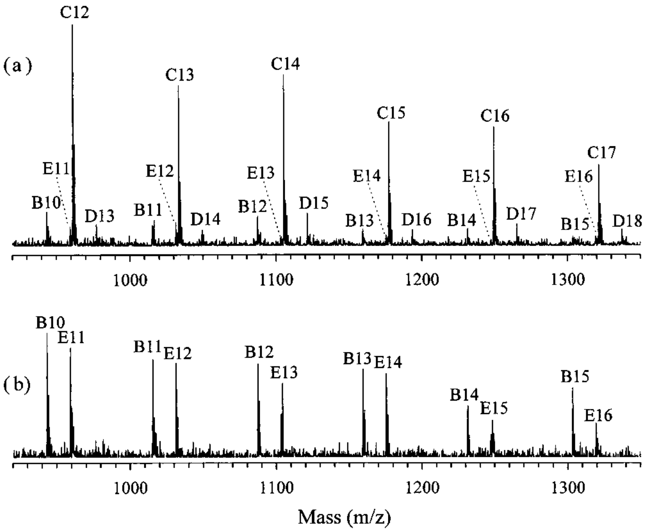


Figure 9. Comparison of the 920−1350 *m/z* fragments of the MALDI−TOF spectra L,L-dilactide/Sn(Oct)$_2$/BuOH mixtures reacted for different times at 150 °C (samples doped with NaI). All marked signals correspond to macromolecules cationized with Na$^+$; the numbers following B, C, and D denote degrees of polymerization of the PLA chains. Polymerization conditions: $[LA]_0 = 1.0$ mol·L^{-1}, $[Sn(Oct)_2]_0 = 1.0$ mol·L^{-1}, $[BuOH]_0 = 0.10$ mol·L^{-1}; *o*-dichlorobenzene solvent, 150 °C. Reaction times: 10 (a) and 120 (b) min.

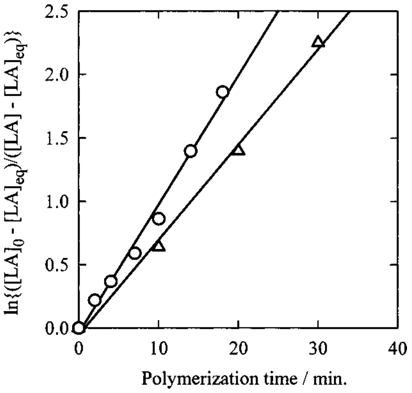


Figure 10. Comparison of the kinetics of L,L-dilactide polymerization initiated with Sn(Oct)$_2$ and carried out with BuOH (○) and BuNH$_2$ (△) as co-initiators/transfer agents. [LA] measured by polarimetry. Conditions of polymerization: $[LA]_0 = 1.0$ mol·L^{-1}, $[Sn(Oct)_2]_0 = 0.05$ mol·L^{-1}, $[BuNH_2]_0 = 0.12$ mol·L^{-1}, $[BuOH]_0 = 0.09$ mol·L^{-1}; THF solvent, 80 °C.

tert-butylpyridine (TBPY), on the kinetics of LA polymerization initiated with Sn(Oct)$_2$. TBPY is taken with a 5-fold molar excess in relation to Sn(Oct)$_2$. At lower degrees of monomer conversion, polymerizations with and without TBPY proceed with comparable rates, and then polymerization with TBPY accelerates. Tentatively, we assume that this phenomenon can be related to the trapping of the OctH formed.

This result as well as polymerization in the presence of BuNH$_2$ exclude participation of the carbocationic species or the secondary oxonium ions in the PLA chain growth.

Analysis of the Earlier Proposed Mechanisms in the Light of Results of the Present Work. Major new facts and general conclusions on the basis of these new facts are as follows:

1. Leveling off of the dependencies of the polymerization rates on concentration of one of the co-initiators in systems initiated with Sn(Oct)$_2$/BuOH mixture when one of the components of the initiating system starts to be in a sufficient excess,

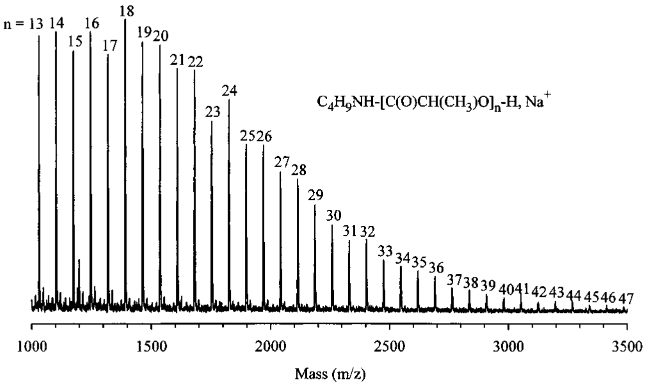


Figure 11. MALDI−TOF mass spectrum (1000−3500 *m/z* range) of the PLA prepared with LA/Sn(Oct)$_2$/BuNH$_2$ system (sample doped with NaI). Conditions of polymerization: $[LA]_0 = 1.0$ mol·L^{-1}, $[Sn(Oct)_2]_0 = 0.05$ mol·L^{-1}, $[BuNH_2]_0 = 0.12$ mol·L^{-1}; THF solvent, 80 °C.

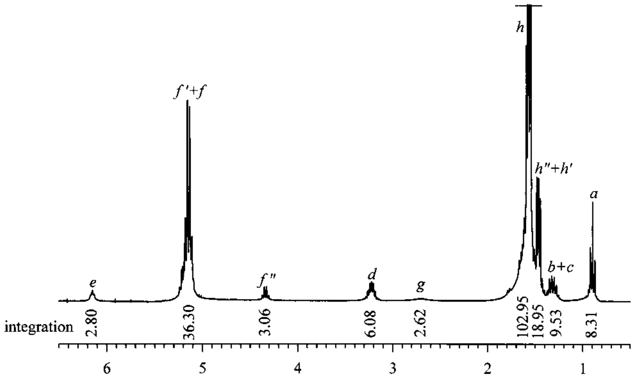


Figure 12. ^{1}H NMR spectrum (200 MHz, CDCl$_3$ solvent, 25 °C) 1000−3500 *m/z* range) of the polymer isolated from the LA/Sn(Oct)$_2$/BuNH$_2$ reacting mixture. Conditions of polymerization are given in the caption for Figure 11.

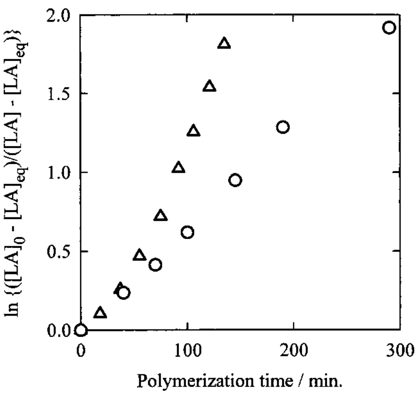


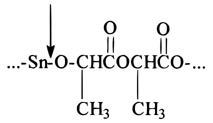
Figure 13. Comparison of kinetics of L,L-dilactide polymerization initiated with Sn(Oct)$_2$ without additive introduced (○) and in the presence of 2,6-di-*tert*-butylpyridine (TBPY) (△). [LA] measured by polarimetry. Conditions of polymerization: $[LA]_0 = 1.0$ mol·L^{-1}, $[Sn(Oct)_2]_0 = 0.05$ mol·L^{-1}, $[TBPY]_0 = 0.24$ mol·L^{-1}; THF solvent, 80 °C.

2. Direct observation by MALDI−TOF mass spectrometry of the macromolecules (in the lower molar mass range) of the structure OctSnO(la)$_n$Bu and OctSnOSnO(la)$_n$Bu.

3. Initiation of polymerization with a system Sn(Oct)$_2$/BuNH$_2$, giving rates of polymerization similar to those observed with BuOH.

4. Rate of polymerization increased by the proton sponge.

These facts allow rejecting several mechanisms proposed by other authors (vide infra) and reconfirm conclusions of our work on CL polymerization with $Sn(Oct)_2$,[22−25] i.e., that initiator is formed by reaction of $Sn(Oct)_2$ with either ROH and polymerization proceeds finally on the −Sn−alkoxide bond:



$$\ldots\text{-Sn}\overset{\downarrow}{\text{-}}\text{O-}\underset{|\atop \mathrm{CH_3}}{\mathrm{CH}}\overset{\mathrm{O}\atop\|}{\mathrm{C}}\mathrm{O}\underset{|\atop \mathrm{CH_3}}{\mathrm{CH}}\overset{\mathrm{O}\atop\|}{\mathrm{C}}\mathrm{O}\text{-}\ldots$$

We were not the first ones which proposed this mechanism (see refs 2 and 13), although neither detailed kinetic measurements nor the mass spectrometric evidence were earlier available. Below, we analyze the other mechanisms put forward during approximately the last 3 decades, and we discuss reasons for which these other mechanisms cannot operate.

It has correctly been stressed many times that for the $Sn(Oct)_2$-initiated polymerization of cyclic esters almost all of the imaginable mechanisms were proposed during the last 30 years. We may add that surprisingly little kinetic measurements were made and in several works $Sn(Oct)_2$ used was contaminated with up to 30 mol % of other compounds.

All of the proposed mechanisms can be divided into the following general groups:

I. Cationic polymerization.

II. Addition of the monomer−$Sn(Oct)_2$ complex (activated monomer) into the ...−OH ended macromolecules, where several variations were offered, including the ternary complex involving monomer, ROH, and $Sn(Oct)_2$ (ROH activated by $Sn(Oct)_2$?).

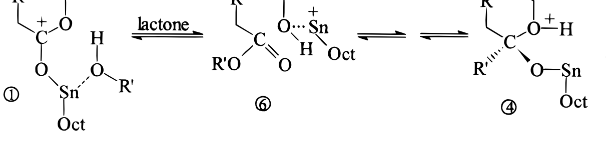
III. Direct reaction of $Sn(Oct)_2$ with monomer with formation of the anhydride end group.

IV. Conversion of $Sn(Oct)_2$ into OctSnOR (and/or OctSnOH, OctSnOSnOct, or related compounds) with polymerization proceeding eventually on the ...−Sn−OR (tin(II)−alkoxide bond) in a manner in principle similar to other covalent metal alkoxides.

These mechanisms are analyzed below on the basis of the results of the present work.

Cationic Polymerization. In one of the papers proposing this mechanism[3] it has been suggested that "... first of all coordination of lactide carbonyl to free p or d orbitals of the dissolved $Sn(Oct)_2$ will take place .... As a result of the resonance, the electron density at the carbon is decreased, making it more susceptible to nucleophilic attack by hydroxyl-containing compounds which ... are likely to be true initiators of the polymerization".[3]

Then the proposed scheme follows (we show here only the part of it relevant for our discussion). The first species in this scheme is

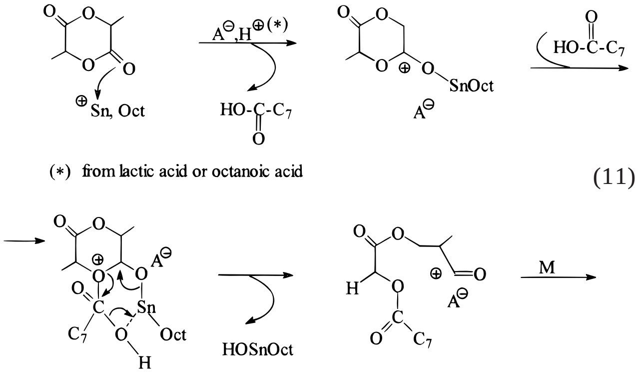


(10)

Presumably, there should also be shown the octoate anion, as the counterion. It is missing in the original paper. According to the authors of this work "After coordination complex (6) has been formed, the coordination with a new lactone will generate species (1) again, where in this case R′ is the growing polymer chain. In the proposed mechanism the catalyst is not chemically bound to the growing chain end (structure (6) ...)".[3] This cationic mechanism involves formation of species (4), being a secondary oxonium ion. This ion would not survive in the presence of the large excess of a strong base. Our data (cf. section on polymerization in the presence of $BuNH_2$ or TBPY) have shown that the rate of polymerization of LA induced by $Sn(Oct)_2$ in the presence of an amine is as fast as in the presence of an alcohol. Moreover, in the presence of TBPY the process accelerates. Other authors[36] also successfully conducted polymerization in the presence of amines. Dubois et al.[37] observed that the rate of polymerization induced by $Sn(Oct)_2$ increases in the presence of other strong bases−phosphines. None of the numerous different cations shown in the scheme of the cited paper could exist in the presence of an amine or phosphine. It would be converted quickly into the ammonium or phosphonium salt, respectively. Besides, according to this mechanism, Sn is not bound to the growing chain, in contrast to the MALDI−TOF data reported in this and our previous[25] paper.

It should be added that in principle this mechanism is very close to the "activated monomer" mechanism (group II), discussed below, since the actual propagation step requires a nucleophilic attack of a hydroxyl group on the carbonyl carbon atom.

Another "cationic" mechanism involves "... co-initiation by octanoic acid ...".[6] Detailed analysis of the NMR data of the resulting PLA leads the authors to the following conclusion: "... we propose a mechanism involving the polarization of the lactide carbonyl bond by interaction with stannous octoate and a proton with the formation of a carbocation ...".[6] Again, proton would not survive in the presence of strong bases. From the scheme given by these authors we take only its beginning:



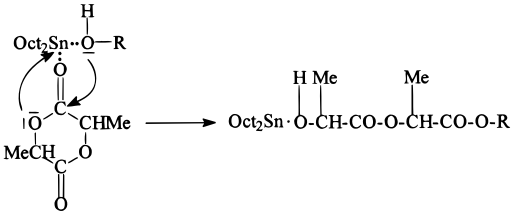
(11)

In this mechanism $Sn(Oct)_2$ is used to generate the carboxonium ion (chain end ...$O-C(CH_3)-C^+(O)A^-$ and then polymerization proceeds merely as a cationic process with carboxonium−carboxylate ions (ion pairs or pair of ions) as growing species. OctSnOH is a byproduct of initiation. This mechanism is incompatible with two experimental facts of the present work:

- Octanoic acid decreases the rate of polymerization whereas in the proposed mechanism for higher concentration of acid the rate should also be higher.
- Polymerization proceeds in the presence of an amine that would react irreversibly with carboxonium ion

(proposed to be an active species) giving an ammonium ion and stopping the polymerization.

Activated Monomer Mechanism. Another group of mechanisms assumes formation and then addition of the monomer−$Sn(Oct)_2$ complex to ROH (initiation) and addition to the ...−OH-ended macromolecules (propagation). There are again several variations of this scheme, however, including always the ternary complex in which ROH is stronger complexed with $Sn(Oct)_2$ than monomer itself. The most comprehensive description of this approach is given in the paper on "Sn(II) Octoate-Initiated Polymerization of L-Lactide: A Mechanistic Study".[7] The course of the reactions is depicted in the following way:

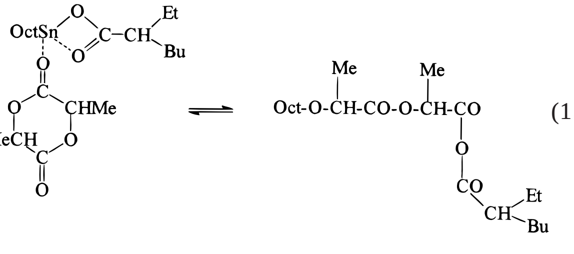


(12)

This mechanism assumes that alcohol complexed with $Sn(Oct)_2$ reacts with monomer and forms the ternary complex. Then initiation and chain growth proceed within this complex with liberation of the intact $Sn(Oct)_2$ Then, similar complexation starts the next step. The authors of the cited paper clearly state "The first step consists of a coordination between catalyst and alcohol or OH end group .... It is characteristic for this mechanism that the propagation steps exclusively involve free orbitals of the catalyst, and neither covalent nor ionic bonds. The experimental data presented in this work and by other authors[9] do not definitely prove this mechanism, but the mechanism is consistent with all experimental data and also explains the catalytic activity of Ph_4Sn[38]".[7]

The experimental data being at the disposal of the cited authors could lead to the formulation of the discussed reaction scheme. Newer results, however, described in our present paper, are not compatible with this mechanism. It is sufficient to say that $Sn(Oct)_2$ was shown to react chemically with ROH, therefore this is the chemical change responsible for the formation of the true initiator. The tin(II)-alkoxide bonds are the active sites of propagation and it is not enough that "...propagation steps exclusively involve free orbitals of the catalyst, and neither covalent nor ionic bonds".[7]

Direct Reaction of $Sn(Oct)_2$ with Monomer. In the paper discussed above,[7] polymerizations without and with co-initiator purposely added were considered. For the process "without" co-initiator (we put quotation marks around "without", since it is practically not possible to remove all of the co-initiator from the system), the following reaction was written:



(13)

Thus, it is assumed that an anhydride unit is formed (no experimental evidence is given) and that further propagation proceeds on the Sn−alkoxide bond. One of the consequences of this "direct reaction" should be the linear increase of polymerization rate with increasing $[Sn(Oct)_2]_0$. Also kinetic plots should exhibit tendency to autoacceleration. This is not the case. According to the experimental data reported in the present paper, the rate does not increase after a certain $[Sn(Oct)_2]_0$ is reached (Figure 5b) and the semilogarithmic kinetic plots are linear (Figures 1 and 2). The authors of the paper cited above realize that formation of an anhydride is energetically unfavorable and conclude that this direct initiation "... presumably plays a minor role and (co)initiation by water or other OH groups ... plays the major role".[7] Hall in his paper also noticed that formation of an anhydride is unlikely.[39]

Formally, another direct insertion mechanism, assuming attack of the carboxylate species on the monomer, followed by the alkyl−oxygen bond scission, could also be considered. This mechanism, operating for the four-membered lactones,[40,41] has been rejected for the larger rings, at least at the ambient temperature.[41−43] In two recently published papers on LA polymerization induced by the other carboxylates, namely by $La(O(O)CCH_3)_3$[44] or by $Fe(O(O)CCH_3)_2$[45] and carried out in bulk at temperatures ≥160 °C, the direct reaction of a monomer with these carboxylates was postulated again, on the basis of the alleged spectroscopic evidence. The ^1H NMR singlet at $\delta = 2.1$ ppm was ascribed in ref 45 to the CH_3 group in the anhydride chain end: $C\mathit{H}_3C(O)OC(O)CH(CH_3)O$−PLA. However, the identical chemical shift (in the same solvent) was reported for the ester chain end:[46] $C\mathit{H}_3C(O)OCH(CH_3)\mathit{C}(\mathit{O})$−PLA. Indeed, the latter could be formed by the esterification of the PLA hydroxyl chain end with $Fe(O(O)CCH_3)_2$ (or with $CH_3C(O)OH$ resulting from $Fe(O(O)CCH_3)_2$ hydrolysis).

Initiation with OctSnOR, $Sn(OR)_2$, and/or OctSnOH, OctSnOSnOct, or Related Compounds. The fundamental difference between this mechanism and the three discussed above is that the active species are formed by chemical reaction of $Sn(Oct)_2$ with H_2O or ROH (alcohols) either present as impurities in the system or added purposely. Eenink in his Ph.D. work[47] has given indication, on the basis of atomic absorption data, that Sn is bound to macromolecules.

Apparently, the only earlier paper explicitly proposing the interconversion

$$Sn(Oct)_2 + ROH \rightleftharpoons OctSnOR + OctH \qquad (14)$$

with further polymerization on the −Sn−OR bond was published in 1994 by McAuley et al.[13] (however, some suggestions considering equilibria, such as depicted in eq 14, are already given in the Pennings work from 1987[2]). In the paper of McAuley et al. on the mechanism of "LA polymerization in the presence of $Sn(Oct)_2$ ..." the effect of 1-hexadecanol and stearic acid on PLA yield and molar masses was studied. The novelty of their work was to show the decrease of the rate of polymerization under the influence of carboxylic acid. Since these authors used $Sn(Oct)_2$ as supplied and of unspecified purity, some of their results suffer from the presence of cocatalytic impurities in $Sn(Oct)_2$. Nevertheless, the observed decrease in rate in the presence of stearic acid and consideration of the known reaction of $Sn(Oct)_2$ with hydroxy substances[48,49] lead these authors to the following major conclusion "The above considerations indicate the possibility that the true initiator in the polymerization might be stannous alkoxide, which would act as an insertion coordination mechanism...".[13] Later, for the polymerization of CL, Storey reached a similar conclusion.[21]

During evaluation of the present work in the editorial office, a paper entitled "Sn(II) Octoate-Initiated Polymerization of L-Lactide: A Mechanistic Study"[8] by the authors of ref 7 appeared. In the introduction to this paper, the authors maintain the previously proposed mechanism[7] (cf. eq 12), but then later in the text come to the opinion similar to that expressed earlier by us in refs 22 and 23, stating that at least one carboxylate group in $\mathrm{Sn(Oct)_2}$ is replaced by alkoxide group and then polymerization proceeds by monomer insertion into the resulting tin(II)−alkoxide bond. ref 8 confirms also formation of the OctR esters and octanoate end groups observed originally by Storey[21] and in our own research.[22,23]

Nevertheless, we have to agree with Vert and other authors, stressing the complexity of the system and difficulties in understanding the detailed mechanism "... since it is not possible to check the chemical nature of the end groups for high molecular weight polymers".[6] The criticism of the insertion mechanism was finally based on the following reasoning: "... rule out the insertion mechanism since no tin containing end groups were identified".[6] Again, the evidence available at that time forced one to apply mechanisms that had to explain polymerization without tin being at the active chain ends. However, the new facts brought to light by the present paper and by our recent work on $\mathrm{Sn(Oct)_2}$-initiated polymerization of CL[25] show that tin containing end groups could be detected in macromolecules. It is true for the lower molar masses, but the observation of the polyester chains—$\mathrm{OctSnO(cl)}_n\mathrm{OBu}$ and $\mathrm{OctSnO(la)}_n\mathrm{OBu}$, the former to molar masses of at least 2000 and the latter to 1000—is removing the major difficulty with accepting the simplest mechanism: propagation on the ...−*SnOR* species, as described in this paper. The kinetic evidence, based on the similarity of the $\mathrm{Sn(Oct)_2/BuOH}$ and $\mathrm{Sn(OBu)_2/OctH}$ systems, is an equally strong point.

Conclusions

Polymerization of LA initiated with $\mathrm{Sn(Oct)_2/BuOH}$ and studied in THF solvent below 100 °C shows qualitatively the same features as polymerization of CL initiated with the same system in the same solvent.[23,25] The major conclusions are given below.

When purified $\mathrm{Sn(Oct)_2}$ was used (less than 2 mol % of impurities) without any co-initiator purposely added, polymerization is very slow and shows the basic features of living polymerization: M_n increases linearly with conversion (no transfer changing the number of chains), and first-order kinetic plots are linear (no measurable termination).

$\mathrm{Sn(Oct)_2}$ under conditions typical for polymerization reacts with BuOH giving the corresponding Sn compounds, acting as initiators: OctSnOBu, $\mathrm{Sn(OBu)_2}$, and OctSnOSnOBu. Some of these and similar compounds were observed in MALDI−TOF. Moreover, $\mathrm{OctSnO(la)}_n\mathrm{OBu}$ and $\mathrm{OctSnOSnO(la)}_n\mathrm{Bu}$ species were detected. Only products with lower *n* were clearly identified, indicating substantially lower stability (hydrolytic and/or thermal) of these species bound to the PLA chains than stability of the same species bound to the PCL chains. This could be expected, because secondary alkoxides (LA) are less hydrolytically stable than the primary ones (CL).

The rate of polymerization, studied as a function of $[\mathrm{Sn(Oct)_2}]_0$ for fixed $[\mathrm{BuOH}]_0$, first increases almost linearly and then levels off, indicating that $\mathrm{Sn(Oct)_2}$ alone does not initiate polymerization.

Comparison of the rates of polymerization for a system $\mathrm{Sn(Oct)_2/BuOH}$ and $\mathrm{Sn(OBu)_2/OctH}$ revealed that rates are identical when $2[\mathrm{Sn(Oct)_2}]_0 = 2[\mathrm{Sn(OBu)_2}]_0 = [\mathrm{BuOH}]_0 = [\mathrm{OctH}]_0$. These are conditions required to have exactly the same concentrations of identical species, namely (at least) $\mathrm{Sn(Oct)_2}$, $\mathrm{Sn(OBu)_2}$, OctSnOBu, OctH, and BuOH in both systems.

Thus, the combined kinetic and spectroscopic data show that $\mathrm{Sn(Oct)_2}$ is by itself neither an initiator nor a catalyst of LA polymerization; reaction of $\mathrm{Sn(Oct)_2}$ with ROH (R can also be H), studied in this work, provides the initiating species. These are OctSnOR, $\mathrm{Sn(OR)_2}$, and their derivatives (like OctSnOSnOct) converting eventually into growing species, in which polymerization proceeds on the ...−Sn−O−polymer (tin(II)−alkoxide) bond, presumably in an insertion manner similar to that for other covalent metal alkoxides.

Eventually, the following general scheme of polymerization in $\mathrm{LA/Sn(Oct)_2/ROH}$ system could be presented:

$$
\begin{gathered}
\mathrm{Sn(Oct)_2 + ROH \leftrightarrows OctSnOR + OctH} \\
\mathrm{OctSnOR + ROH \leftrightarrows Sn(OR)_2 + OctH} \\
\ldots{-}\mathrm{SnOR + nLA} \rightleftarrows \ldots{-}\mathrm{SnO{-}(la)}_{n}{-}\mathrm{R} \\
\ldots{-}\mathrm{SnO{-}(la)}_{n}{-}\mathrm{R + OctH} \rightleftarrows \ldots{-}\mathrm{SnOct + HO{-}(la)}_{n}{-}\mathrm{R} \\
\ldots{-}\mathrm{SnO{-}(la)}_{n}{-}\mathrm{R + ROH} \rightleftharpoons \ldots{-}\mathrm{SnOR + HO{-}(la)}_{n}{-}\mathrm{R} \\
\ldots{-}\mathrm{Sn{-}(la)}_{n}{-}\mathrm{R + OctH} \rightarrow \ldots{-}\mathrm{SnOH + Oct{-}(la)}_{n}{-}\mathrm{R} \\
\ldots{-}\mathrm{SnOH + nLA} \rightleftarrows \ldots{-}\mathrm{SnO{-}(la)}_{n}{-}\mathrm{H} \\
\ldots{-}\mathrm{SnO{-}(la)}_{n}{-}\mathrm{H + OctH} \rightleftarrows \ldots{-}\mathrm{SnOct + HO{-}(la)}_{n}{-}\mathrm{H} \\
\ldots{-}\mathrm{SnO{-}(la)}_{n}{-}\mathrm{H + ROH} \rightleftharpoons \ldots{-}\mathrm{SnOR + HO{-}(la)}_{n}{-}\mathrm{H} \\
\ldots{-}\mathrm{SnO{-}(la)}_{n}{-}\mathrm{H + OctH} \rightarrow \ldots{-}\mathrm{SnOH + Oct{-}(la)}_{n}{-}\mathrm{H}
\end{gathered}
\tag{15}
$$

(other possible reactions involving OctSnOH (e.g., formation of distannoxanes: OctSnOSnOct) are omitted). Importance of a given reaction may vary from one particular polymerizing system to another, depending on the feed composition, solvent, temperature, and degree of conversion.

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References and Notes

(1) Tunc, D. C.; Rohovsky, M. W.; Jadhaw, B.; Lehman, W. B.; Strongwater, A.; Kummer, F. In *Advances in Biomedical Polymers; Polymer Science and Technology*; Gebelein, C. G., Ed.; Plenum Press: New York and London, 1987; Vol. 35, pp 87−100.

(2) Leenslag, J. W.; Pennings, A. J. *Makromol. Chem.* **1987**, *188*, 1809.
(3) Nijenhuis, A. J.; Grijpma, D. W.; Pennings, A. J. *Macromolecules* **1992**, *25*, 5, 6419.
(4) Doi, Y. J.; Lemstra, P. J.; Nijenhuis, A. J.; van Aert, H. A. M.; Bastiaansen, C. *Macromolecules* **1995**, *28*, 2124.
(5) Chabot, F.; Vert, M.; Chapelle, S.; Granger, P. *Polymer* **1983**, *24*, 53.
(6) Schwach, G.; Coudane, J.; Engel, R.; Vert, M. *J. Polym. Chem., Part A: Polym. Chem.* **1997**, *35*, 3431.
(7) Kricheldorf, H. R.; Kreiser-Saunders, I.; Boettcher, C. *Polymer* **1995**, *36*, 1253.
(8) Kricheldorf, H. R.; Kreiser-Saunders, I.; Stricker, A. *Macromolecules* **2000**, *33*, 702.
(9) Dahlman, J.; Rafler, G.; Fechner, G.; Meklis, B. *Br. Polym. J.* **1990,** *23*, 235.
(10) Rafler, G.; Dahlman, J. *Acta Polym.* **1992**, *43*, 91.
(11) Dahlman, J.; Rafler, G. *Acta Polym.* **1993**, *44*, 103.
(12) Zhang, X.; Wyss, U. P.; Pichora, D.; Goosen, M. F. A. *Polym. Bull. (Berlin)* **1992**, *27*, 623.
(13) Zhang, X.; MacDonald, D. A.; Goosen, M. F. A.; McAuley, K. B. *J. Polym. Sci., Part A: Polym. Chem.* **1994**, *32*, 2965.
(14) 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.
(15) Shinno, K.; Miyamoto, M.; Kimura, Y.; Hirai, Y.; Yoshitome, H. *Macromolecules* **1997**, *30*, 6438.
(16) Witzke, D. R.; Narayan, R.; Kolstad, J. J. *Macromolecules* **1997**, *30*, 7075.
(17) Degee, Ph.; Dubois, Ph.; Jacobsen, S.; Fritz, H.-G.; Jerome, R. *J. Polym. Sci., Part A: Polym. Chem.* **1999**, *37*, 2413.
(18) Duda, A.; Penczek, S. *Macromolecules* **1990**, *23*, 1636.
(19) Brode, G. L.; Koleske, J. V. *J. Polym. Sci., Part A: Polym. Chem.* **1972**, *35*, 1109.
(20) Schindler, A.; Hibionada, Y. M.; Pitt, C. G.; Langer, R. J. *J. Polym. Sci., Part A: Polym. Chem.* **1982**, *20*, 319.
(21) Storey, R. F.; Taylor, A. E. *J..Macromol. Sci.—Pure Appl. Chem.* **1996,** *A33*, 77; **1998**, *A35*, 723.
(22) Kowalski, A.; Libiszowski, J.; Duda, A.; Penczek, S. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1998**, *39* (2), 74.
(23) Kowalski, A.; Duda, A.; Penczek, S. *Macromol. Rapid Commun.* **1998**, *19*, 567.
(24) Duda, A.; Penczek, S.; Kowalski, A.; Libiszowski, J. *Macromol. Symp.* **2000**, *153*, 41.
(25) Kowalski, A.; Duda, A.; Penczek, S. *Macromolecules* **2000**, *33*, 689.
(26) Kharash, G. B.; Sanchez-Riera, F.; Severson, D. K. In *Plastics from Microbes;* Mobley, D. P., Ed.; Hanser Publishers: Munich, Germany, and New York, 1994; p 93.
(27) Zhang, X.; Wyss, U. P.; Pichora, D.; Goosen, M. F. A. *J. Macromol. Sci.—Pure Appl. Chem.* **1993**, *A30*, 933.
(28) Benoit, J. P.; Thies, C. In *Microencapsulation. Methods and Industrial Applications*; Benita, S., Ed.; Marcel Dekker: New York, 1996; p 133.
(29) Sinclair, R. G. *J. Macromol. Sci.—Pure Appl. Chem.* **1996**, A33, 585.
(30) Hartmann, H. In *Biopolymers From Renewable Resources*; Kaplan, D. L., Ed.; Springer: Berlin 1998; p 367.
(31) Mecerreyes, D.; Jerome, R.; Dubois, P. *Adv. Polym. Sci.* **1998**, *147*, 1.
(32) Lunt, J. *Polym. Degrad. Stab.* **1998**, *59*, 145.
(33) Takeuchi, D.; Aida, T.; Endo, T. *Macromol. Rapid Commun.* **1999**, *20*, 182.
(34) Duda, A.; Florjanczyk, Z.; Hofman, A.; Slomkowski, S.; Penczek, S. *Macromolecules* **1990**, *23*, 1940.
(35) Kowalski, A.; Duda, A.; Penczek, S. *Macromolecules* **2000**, *33*, 1964.
(36) Rypacek, F. (a) In *5th International Scientific Workshop on Biodegradable Plastics and Polymers, Stockholm (Sweden)*; June 1998. (b) personal information, May 2000.
(37) Dubois, P.; Degee, P.; Jerome, R.; Teyssie, Ph. *Macromolecules* **1992**, *24*, 2614.
(38) Kohn, F. E.; van den Berg, J. W. G.; van der Ridder, G.; Feijen, J. *J. Appl. Polym. Sci.* **1984**, *29*, 4265.
(39) Bassi, M. B.; Padias, A. B.; Hall, H. K., Jr. *Polym. Bull. (Berlin)* **1990**, *24*, 227.
(40) Slomkowski, S.; Penczek, S. *Macromolecules* **1976**, *9*, 367; **1980**, *13*, 229.
(41) Sosnowski, S. Ph.D. Thesis, Center of Molecular and Macromolecular Studies, Polish Academy of Sciences, Lodz, Poland, 1990.
(42) Endo, M.; Aida, T.; Inoue, S. *Macromolecules* **1987**, *20*, 2982.
(43) Tortosa, K.; Miola, C.; Hamaide, T. *J. Appl. Polym. Sci.* **1997**, *65*, 2357.
(44) Deng, X. M.; Yuan, M. L.; Xiong, C. D.; Li, X. H. *J. Appl. Polym. Sci.* **1999**, *71*, 1941.
(45) Stolt, M.; Sodergard, A. *Macromolecules* **1999**, *32*, 6412.
(46) Stassen, S.; Archambeau, S.; Dubois. P.; Jerome, R.; Teyssie, P. *J. Polym. Sci., Part A: Polym. Chem.* **1994**, *32*, 2443.
(47) Eenink, M. J. D. Ph.D. Thesis, Twente University (The Netherlands), 1987.
(48) Weij, V. W. V. D. *Makromol. Chem.* **1980**, *181*, 2541.
(49) Dub M.; Weiss, R. W. *Organometallic Compound*; 2nd ed.; Springer-Verlag, New York, 1967; Vol II, p 395; 1973; First Supplement, Vol II, p 623.

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