


ORIGINAL ARTICLE

ROP of L-lactide and ϵ -caprolactone catalyzed by tin(II) and tin(IV) acetates—switching from COOH terminated linear chains to cycles

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Abstract

The catalytic potential of tin(II)acetate, tin(IV)acetate, dibutyltin-bis-acetate and dioctyl tin-bis-acetate was compared based on polymerizations of L-lactide conducted in bulk at 160 or 130°C. With SnAc₂ low-Lac/Cat ratios (15/1–50/1) were studied and linear chains having one acetate and one carboxyl end group almost free of cyclics were obtained. Higher monomer/catalyst ratios and lower temperatures favored formation of cycles that reached weight average molecular weights (Mw's) between 100,000 and 2,500,000. SnAc₄ yielded mixtures of cycles and linear species under all reaction conditions. Dibutyltin- and dioctyl tin bis-acetate yielded cyclic polylactides under most reaction conditions with Mw's in the range of 20,000–80,000. Ring-opening polymerizations performed with ϵ -caprolactone showed similar trends, but the formation of COOH-terminated linear chains was significantly more favored compared to analogous experiments with lactide. The reactivity of the acetate catalysts decreased in the following order: SnAc₂ > SnAc₄ > Bu₂SnAc₂ ~ Oct₂SnAc₂.

KEYWORDS

catalyst, MALDI-TOF MS, polylactides, ring-opening polymerization, tin acetates

1 | INTRODUCTION

The rapidly increasing pollution of our environment including living organisms with micro- and nano plastic will sooner or later enforce to replace most of the “immortal” plastics by hydrolytically degradable polymers that yield nontoxic degradation products. One of the most attractive candidates is polylactide, because its production is based on natural resources and because its properties can be varied over a broad range. This broad variation can be achieved via different chain lengths, different topologies, different stereosequences, by copolymerization with various comonomers and blending with another polymer.^{1–8} Almost all homo- and copolymers of lactic

acid are produced by ring-opening polymerization (ROP) of lactide, and for their technical production (by polymerization in bulk) tin(II) 2-ethylhexanoate (SnOct₂) is the most widely used catalyst.^{9–11} The extraordinary usefulness of this catalyst may be attributed to the following properties. First, it shows an excellent performance in terms of high rates of polymerization, high-molecular weights, absence of racemization even at 180°C and little or no discoloration at short reaction times (<2 h at 180°C) and good miscibility with molten lactide. Second, although SnOct₂ is toxic for most microbes and fungi, its toxicity is low for humans, and thus, the American FDA has admitted SnOct₂ as food stabilizer like SnCl₂. Because many billions of cans have been used for food

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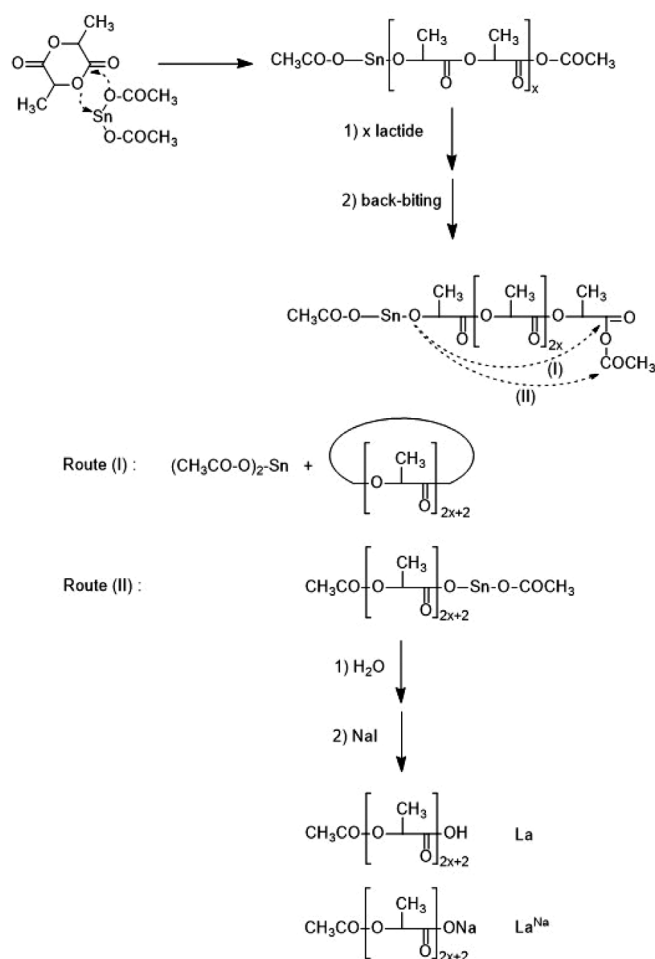
preserving over a period of 100 years, the toxicity of tin(II) ions has extensively been studied.^{9–11} Most of these cans were produced from steel, but their interior is plated with tin as anticorrosive coating.

Although the usefulness of SnOct₂ as catalyst for ROPs of cyclic esters is known for almost 50 years,^{12,13} very little is known about the catalytic activities of related tin salts such as tin(II) acetate (SnAc₂) or tin(II)chloride (SnCl₂), despite the fact that their anions belong to the human metabolism in contrast to 2-ethylhexanoate and despite the fact that these salts have been commercially available for decades.

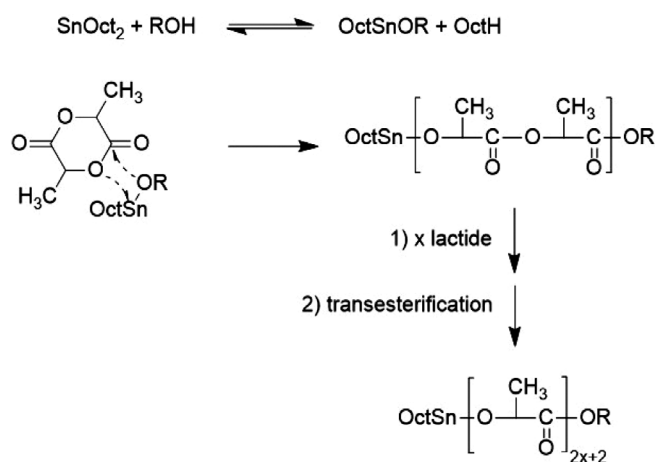
Quite recently, a few polymerizations of L-lactide were performed with anhydrous SnAc₂ for comparison with SnOct₂ and interesting results were obtained which prompted the authors to perform the present work.¹⁴ This work had the purpose to compare the three commercially available tin acetates SnAc₂, dibutyltin bis-acetate (Bu₂SnAc₂), and tin(IV) acetate (SnAc₄) with each other, and with SnOct₂. To our best knowledge, ROPs of L-lactide catalyzed by Bu₂SnAc₂ or SnAc₄ have never been published before. This comparison should include the following points: relative catalytic activities, maximum molecular masses that can be achieved, topology, and discoloration. Furthermore, a comparison of L-lactide and ε-caprolactone (CL) should be included in this study.

In this connection, the focus on topology needs a short discussion. Recent experiments conducted with SnAc₂ in bulk at 160°C have shown that low L-lactide/catalyst (Lac/Cat) ratios (25/1) yield a polylactide mainly consisting of linear chains having one acetyl and one carboxyl end group (La in Scheme 1 and 3).¹⁴ At higher Lac/Cat ratios the fraction of cycles strongly increased and above 400/1 the polylactides almost exclusively consisted of cycles. To the best of our knowledge, a direct formation of La-type polylactides has only been reported as component of complex reaction mixtures resulting from ROP of L-lactide catalyzed by neat SnOct₂.¹⁵ In dozens of papers reporting on ROPs of lactide (and in the technical production of polylactide) an alcohol was used as initiator so that alkyl ester terminated (Lb) chains were formed as exemplarily illustrated in Scheme 2 (see also Scheme 3). Relatively few papers report on the formation of polylactides having one —COOH and one HO—CH(CH₃)— end group. Either water or lactic acid played the role of initiator, and metal complexes^{16–20} or trifluoromethane sulfonic acid served as catalyst.^{21,22}

In the case of CL the authors have not found any papers describing a one-step synthesis of polymers containing one COOH and one acyl end group (Ld in Scheme 3). However, a few papers reporting on H₂O-initiated ROPs yielding Lf chains (Scheme 3) have been found. In these papers water served as initiator and a

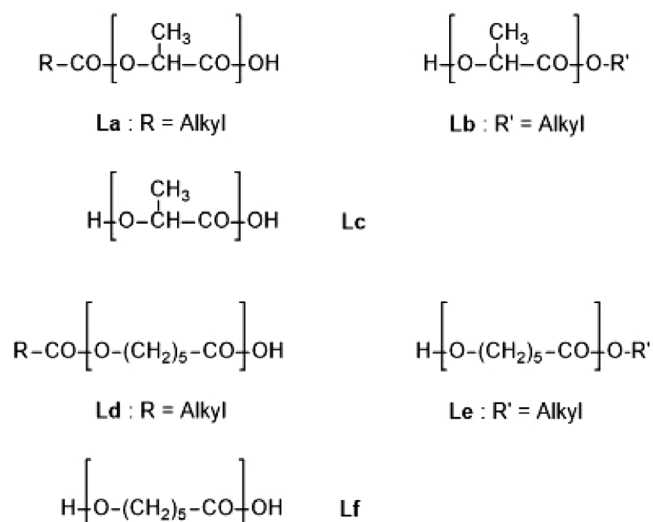


SCHEME 1 Simplified ROPPOC mechanism of L-lactide catalyzed by SnAc₂ (ROPPOC - ring-opening polymerization combined with simultaneous polycondensation)



SCHEME 2 Alcohol initiated ROPs of L-lactide initiated by SnOct₂

metal complex,^{23,24} enzymes^{25–28} or sulfonic acids²⁹ served as catalysts. However, La- or Ld-chains are of interest for various purposes. They may play the role of



SCHEME 3 Various types of linear PL and PCL discussed in this work

surfactants and, after activation of the carboxyl group, such chains may be used for numerous syntheses, such as block-copolymers, star-shaped polymers and graft-copolymers. Hence, it was of particular interest to find reaction conditions allowing for the synthesis of La- and Ld chains almost free of cyclics. The preparation of low molecular weight cycles ($M_w < 50,000$) almost free of linear chains was another goal of the present work, since syntheses of high-molar mass cyclic poly(L-lactide) have been reported several times^{30–32}, whereas the preparation of low molar mass cycles in bulk has only been reported once.³³ In contrast to alcohol or primary-amine-initiated ROPs of lactide synthetic methods yielding cyclic poly lactides do not allow for a control of the molecular weight via the monomer/initiator or monomer/catalyst ratios. Therefore, catalysts and reaction conditions allowing for an easy variation of the molecular weights over a broad range are of great preparative interest.

2 | EXPERIMENTAL

2.1 | Materials

L-lactide, a product of Corbion Purac was kindly supplied by Thyssen-Uhde AG and recrystallized from “Toluene 99.89% extra dry” purchased from Fischer ACROS Chemicals (Gel Belgium). CL was purchased from Alfa Aesar (Kandel, Germany). It was distilled in vacuum (oil pump) over a short-path apparatus in portions of ca 70 g over P_4O_{10} at a bath temperature raised from 95 to 105°C in the course of the distillation (yield 50–70% due to competing polymerization). A second distillation was conducted over powdered CaH_2 at a bath temperature of

94–98°C (yield 95%). Sn(II)acetate, Sn(IV)acetate, dibutyl tin bis-acetate, dioctyl tin oxide, bismuth(III)acetate, and zinc(II)acetate were all purchased from Sigma-Aldrich. The acetates were dried at 70°C in vacuo for 4 days in the presence of solid NaOH to remove traces of acetic acid.

2.2 | Synthesis of di(n-octyl) tin bis-acetate

Di(n-octyl)tin oxide (30 mmol) and acetic anhydride (40 mmol) were weighed into a 250 ml round bottom flask. Dry toluene 100 ml and a magnetic bar were added. This mixture was refluxed for 10 min whereupon a clear solution was obtained which was reduced to approximately 20 ml in vacuo. Then, 60 ml of toluene was added and the evaporation in vacuo was continued in a 100 ml round bottom flask to remove the excess of acetic anhydride. The viscous product was finally dried at 70°C in a vacuum of 1 mbar for 7 days and stored under nitrogen. This product did neither crystallize at 20–22°C nor at 2–3°C in the refrigerator, and it decomposed upon attempted distillation over a short-path apparatus in a vacuum <0.1 mbar. The 400 MHz 1H NMR spectrum was in perfect agreement with the expected structure and indicated a trace of toluene as the sole impurity.

2.3 | Polymerizations of L-lactide

In all polymerizations listed in Tables 1–8 a conversion around 97% (corresponding to the ring-chain equilibrium) has been reached.

(a) with $SnAc_2$ at 160°C (No. 1, Table 1).

$SnAc_2$ (3 mmol) was weighed into a 50 ml flame-dried Erlenmeyer flask and L-lactide (45 mmol) and a magnetic bar were added under a blanket of argon. The catalyst and lactide were mixed by stirring with a spatula. The closed reaction vessel was then immersed into an oil bath thermostated at 160°C. Finally, the virgin reaction product was characterized. In an alternative procedure the poly-lactide was dissolved in 50 ml of dry dichloromethane, filtered and the filtrate was precipitated into ligroin. Since part of the oligomers remain in solution M_n is higher than measured for the virgin reaction product.

When catalyst and lactide are not carefully mixed prior to heating and when the magnetic stirrer is not large enough to achieve a homogeneous dispersion of the catalyst in the molten lactide before the rapidly increasing viscosity stops it, higher molecular weights are the consequence. Mixing with a spatula was not necessary for Lac/Cat ratios >200/1.

(b) with $SnAc_2$ at 130°C (No. 6, Table 1).

$SnAc_2$ (0.4 mmol) was weighed into a flame-dried 50 ml Erlenmeyer flask and L-lactide (40 mmol) and a

TABLE 1 ROPs catalyzed by SnAc₂ in bulk at 130, 160, and 180 °C

Exp. No	Lac/Cat	Temp (°C)	Time (h)	M _n	M _w	Topology
1A	15/1	160	1.0	2300	6000	La chains
1B	15/1	160	2.0	1500	4800	La chains
2A	25/1	160	1.0	4000 (3500) ^a	7200 (6800) ^a	La chains
2B	25/1	160	2.0	3400	9000	La chains
3A	50/1	160	1.0	7000 (6800) ^a	13,500 (15,000) ^a	La chains + few cycles
3B	50/1	160	2.0	7500	21,000	La chains + few cycles
4	100/1	180	0.5	13,000	44,000	La chains + cycles
5	100/1	160	1.0	12,700	39,000	La chains + cycles
6	100/1	130	1.0	99,000	225,000	Mainly cycles
7	100/1	105	6.0	63,000	145,000	Cycles + chains
7	200/1	160	1.0	43,000	130,000	Mainly cycles
8	400/1	160	1.0	75,000	195,000	Cycles
9	600/1	160	1.5	85,000	250,000	Cycles

^aRepetition with another batch of lactide.

Exp. No	Lac/Cat	Time (h)	M _n	M _w	Topology
1A	25/1	1	2000	6000	Mainly chains
1B	25/1	4	3500	5900	Mainly chains
2A	50/1	1	5500	11,000	Mainly chains
2B	50/1	4	9500	13,000	Mainly chains
3	200/1	2	14,000	30,000	Mainly chains
4	400/1	4	18,000	31,000	Chains + cycles
5	1000/1	4	23,500	36,000	Chains + cycles

TABLE 2 ROPs catalyzed by SnAc₄ in bulk at 160 °C

Exp. No	Lac/Cat	Temp (°C)	Time (h)	M _n	M _w	Topology
1A	25/1	160	1	33,700	86,000	Cycles
1B	25/1	160	4	12,000	42,500	Cycles
2A	50/1	160	1	23,500	61,500	Cycles
2B	50/1	160	4	12,000	38,000	Cycles
3	100/1	160	1.0	26,000	58,000	Cycles
4	200/1	160	2.5	24,000	43,000	Cycles
5	25/1	130	2.0	10,500	20,000	Mainly cycles
6	50/1	130	4.0	8000	16,500	Mainly cycles
7	50/1	130	10.0	9500	23,000	Mainly cycles
8	100/1	130	10.0	18,500	40,000	Mainly cycles

TABLE 3 ROPs catalyzed by Bu₂SnAc₂ at 160 or 130 °C in bulk

magnetic bar were added under a blanket of argon. Lactide and SnAc₂ were mixed with a spatula. The reaction vessel was immersed into an oil bath thermostated at 130 °C. Finally, part of the extremely viscous polylactide was removed by means of spatula and pincer and characterized without purification.

(c) with SnAc₄ (No. 4, Table 2).

SnAc₄ (0.1 mmol) was weighed into a flame-dried 50 ml Erlenmeyer flask and L-lactide (40 mmol) and a magnetic bar were added. The reaction vessel was immersed into an oil bath thermostated at 160 °C, finally part of the reaction product was isolated by means of a

TABLE 4 ROPs catalyzed by Oct₂SnAc₂ at 160°C in bulk

Exp. No	Lac/Cat	Time (h)	M _n	M _w	Topology
1	25/1	1.0	7300	18,000	Cycles
2A	50/1	1.0	8500 (9500) ^a	21,000 (24,000) ^a	Cycles
2B	50/1	4.0	4300	12,000	Mainly cycles
3	100/1	1.0	15,000	43,000	Cycles
4	200/1	2.0	37,000	82,000	Cycles

^aRepetition with another batch of lactide.**TABLE 5** Comparison of SnAc₂, Oct₂SnAc₂, ZnAc₂ and BiAc₃ at 160°C in bulk; Lac/Cat = 400/1

Exp. No	Catalyst	Time (h)	M _n	M _w	Topology
1	SnAc ₂	1	54,000	165,000	Cycles
2	Oct ₂ SnAc ₂	2	39,000	99,000	Cycles
3	BiAc ₃	5	22,000	45,000	Cycles + chains
4	ZnAc ₂	24	13,000	39,000	Cycles + chains

TABLE 6 ROPs of ε-caprolactone (CL) catalyzed by SnAc₂ in bulk

Exp. No	CL/Cat	Temp (°C)	Time (h)	M _n	M _w	Topology
1A	50/1	160	0.5	12,000	23,000	La chains
1B	50/1	160	1.0	10,500	19,000	La chains
2A	200/1	180	0.5	36,000	70,000	Mainly La + few cycles
2B	200/1	180	1.0	36,000	69,000	Mainly La + few cycles
3A	200/1	160	1.0	32,000	66,000	Mainly La + few cycles
3B	200/1	160	2.0	35,000	67,000	Mainly La + few cycles
4A	200/1	130	1.5	45,000	86,000	Mainly La + few cycles
4B	200/1	130	3.0	43,500	84,000	Mainly La + few cycles
5A	600/1	160	1.0	69,000	145,000	
5B	600/1	160	2.0	70,000	140,000	

TABLE 7 ROPs of ε-caprolactone (CL) catalyzed by SnAc₄ in bulk at 160°C

Exp. No	CL/Cat	Time (h)	M _n	M _w	Topology
1A	100/1	0.5	16,500	31,500	Ld chains
1B	100/1	1.0	15,500	30,500	Ld chains
2A	400/1	1.0	35,000	73,000	Mainly Ld chains
2B	400/1	2.0	30,000	66,500	Mainly Ld chains

TABLE 8 ROPs of ε-caprolactone (CL) catalyzed by Bu₂SnAc₂ in bulk at 160°C

Exp. No	Lac/Cat	Time (h)	M _n	M _w	Topology
1A	25/1	0.5	26,500	51,000	Mainly cycles
1B	25/1	1.0	16,000	31,000	Mainly cycles
2	50/1	1	33,500	63,000	Mainly cycles
3A	100/1	0.5	61,500	117,000	Mainly cycles
3B	100/1	1.0	77,000	122,000	Mainly linear chains
4A	400	1.0	58,000	116,000	Mainly linear chains
4B	400	2.0	22,500	57,000	Mainly linear chains

spatula and/or pincer and characterized in the virgin state.

(d) with Bu_2SnAc_2 (No. 2, Table 3) and $\text{Oct}_2\text{SnAc}_2$ (Table 4).

Bu_2SnAc_2 (1 mmol) was weighed into a flame-dried Erlenmeyer flask and L-lactide (50 mmol) and a magnetic bar were added under a blanket of argon. The reaction vessel was immersed into a n oil bath thermostated at 160°C and part of the reaction product was finally isolated by means of a spatula. Polymerization catalyzed by $\text{Oct}_2\text{SnAc}_2$ was performed analogously.

(e) with various metal acetates (Table 5).

These polymerizations were performed as described under (c).

2.4 | Polymerizations of CL

(a) with SnAc_2 (Table 6).

SnAc_2 (0.3 mmol) and CL (60 mmol) were weighed into a flame-dried 50 ml Erlenmeyer flask under a blanket of argon and a magnetic bar was added. The reaction vessel was immersed into an oil bath thermostated at 160°C . After certain time intervals (see Table 6) a sample of approx 1 g was removed under a blanket of argon.

(b) with SnAc_4 or Bu_2SnAc_2 (Tables 7 and 8).

The polymerizations conducted with SnAc_4 or Bu_2SnAc_2 catalysts (Tables 7 and 8) were performed as described above (a).

2.5 | Measurements

The 400 MHz ^1H NMR spectra were recorded with a Bruker Avance 400 in 5 mm sample tubes. CDCl_3 containing TMS served as solvent and shift reference.

The DSC measurements were conducted with a heating rate of 10 K min^{-1} on a Mettler-Toledo DSC-1 equipped with Stare Software version 11.00. Only the first heating was evaluated.

MALDI TOF mass spectrometry was performed using an Autoflex max (Bruker Daltonik GmbH, Bremen) using trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenyldiene] malononitrile (DCTB) dissolved in chloroform (20 mg ml^{-1}) as matrix in the linear positive mode. The solution was doped with sodium or potassium trifluoroacetate to promote selective adduct ion formation. The matrix solution was premixed with the analyte solution (chloroform, 4 mg ml^{-1}) in a ratio of 5/2 (vol/vol). $1\text{ }\mu\text{l}$ of the resulting solution was deposited on the sample target. Typically, 8000 single spectra recorded at four different positions within one spot were accumulated. The instrument was previously calibrated with PEO standards.

For the GPC experiments a modular system kept at 40°C (isocratic pump, 1 ml min^{-1} , refractive index detector, RI-501 -Shodex) was applied. Samples were manually injected ($100\text{ }\mu\text{l}$, $2\text{--}4\text{ mg ml}^{-1}$). For instrument control and data calculation Clarity software (GPC extension, DataApex) was used. The calibration was performed using polystyrene standard sets (Polymer Standards Service-PSS, Mainz, Germany).

For the determination of the Mark-Houwling-Sakurada (MHS) relationship a viscometer (Viscostar, Wyatt, Germany) and a multiangle laser light scattering (MALS) detector (Dawn EOS, Wyatt, Germany) were used. Astra 6.1 software (Wyatt) served for calculating the MHS curves.

3 | RESULTS AND DISCUSSION

3.1 | Polymerizations with SnAc_2

The focus of the experiments conducted with SnAc_2 concerned two correlated questions. What are the optimum reaction conditions for the preparation of linear chains having one acetyl and one carboxyl end group (La in Scheme 1)? What is the range of molecular weights that can be achieved for these La chains? From the previous experiments it was learned that low-Lac/Cat ratios (i.e., higher concentrations of catalyst) are favorable for a high ratio La-chain/cycles.¹⁴ In this work the Lac/Cat ratio was lowered to 15/1 (No. 1A and B, Table 1) and the polymerization time was varied. The MALDI TOF mass spectra (Figure 1 and Figure S1, suppl. part) revealed that the composition of the reaction product obtained with a Lac/Cat ratio of 15/1 was identical with that obtained at a Lac/Cat ratio of 25/1. At ratios of 50/1 and 100/1 the content of cycles slightly increased (Figure 2(B)). When the time was varied, it was found that after 0.5 h (not listed in Table 1) small peaks of other linear chains were present in the mass spectra, which disappeared after 1 h (A-experiments in Table 1). However, extension of the time to 2.0 h caused considerable decrease of the molecular weights (B-experiments). Hence, the optimum time for polymerizations with Lac/Cat ratios $<100/1$ seems to be around 1 h. Another interesting result is the increase of the molecular weights with the Lac/Cat ratio. This result fits in with the mass spectra in that this trend is typical for polymerizations, where the catalyst plays the role of initiator. Concerning the molecular weights of La chains that can be prepared with SnAc_2 at Lac/Cat ratios around 50/1 or below it should be considered that polystyrene-calibrated SEC measurements overestimate the real molecular weights of aliphatic polyesters by at least 50%. Therefore, the M_n

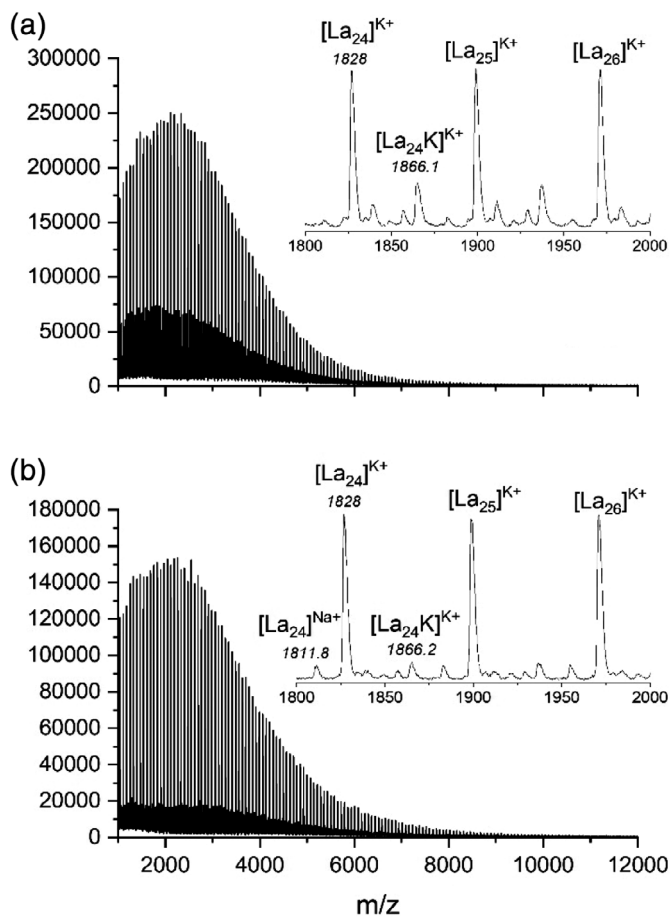


FIGURE 1 MALDI-TOF mass spectra of SnAc₂-catalyzed poly(L-lactide)s with Lac/Cat = 15/1: (A) after 1 h (No. 1A, Table 1); (B) after 2.0 h (No. 1B, Table 1)

values listed in Table 1 have to be multiplied with a correction factor of 0.68 to obtain more realistic values.³⁴ This means, in turn, that SnAc₂ enables syntheses of La-chains in the mass range of 1500–5000 g mol⁻¹. However, higher molecular weights are obtained, when lactide and catalyst are not thoroughly mixed before heating and during the first minutes of the polymerization. Higher molecular weights are also obtained when the polymerization product is dissolved, filtered, and precipitated into a nonsolvent, because parts of the oligomers remain in solution, even when ligroin is used for precipitation.

Another interesting result was obtained, when the temperature was varied at a Lac/Cat ratio of 100/1. As demonstrated by comparison of Figures 2(A),(B) and 3 (A),(B) the La chains were the predominant polymerization product at 160 or 180°C, whereas the cycles prevailed at 130°C. In other words, polymerizations of L-lactide catalyzed by SnAc₂ allow for a switching from linear COOH-terminated chains to cycles either by increasing the Lac/Cat ratio or by lowering the temperature. The temperature dependence of the topology indicates that a temperature dependent equilibrium of two reactive

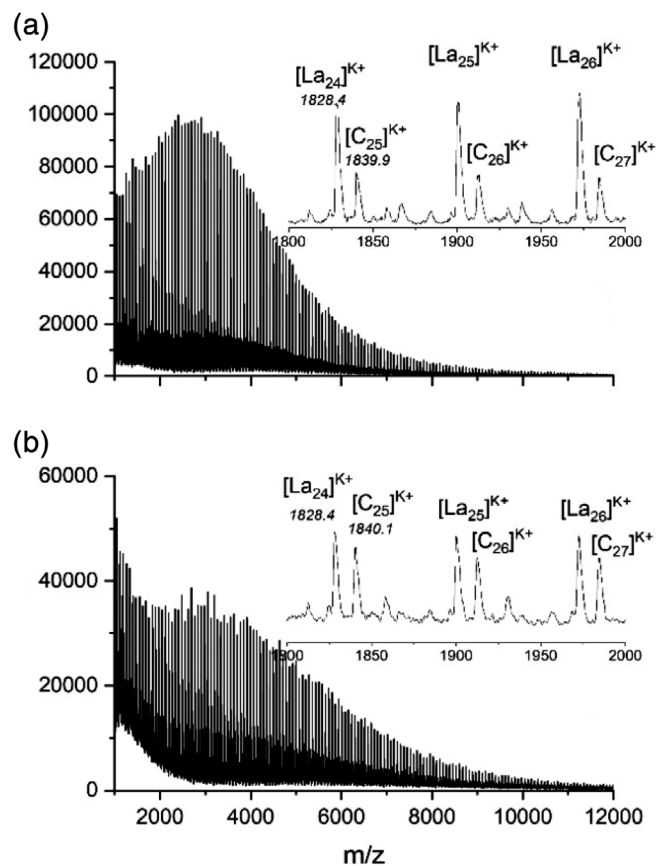


FIGURE 2 MALDI TOF mass spectra of SnAc₂-catalyzed poly(L-lactide)s with Lac/Cat = 100/1: (A) after 0.5 h at 180°C (No. 4, Table 1); (B) after 0.5 h at 160°C (No. 5, Table 1)

species exists. One hypothesis is the assumption that two SnAc₂ molecules form a cyclic dimer (Scheme 4) which produces cyclic poly lactide via a ring-expansion polymerization (REP) mechanism. However, this hypothesis is in contradiction to the fact that higher Lac/Cat ratios also favor the formation of cycles. Higher Lac/Cat ratios mean lower catalyst concentrations, which are unfavorable for the dimerization of SnAc₂. Another temperature dependent equilibrium is the intra-molecular cyclization of the active chain end via donor-acceptor interaction (Scheme 4). Theoretical and experimental evidence for the existence of this equilibrium has been published in connection with Sn(II)2-ethylhexanoate-catalyzed polymerizations.^{35,36} However, it is hard to understand, how the cyclic chain end should favor the end-to-end cyclization according to the ROPPOC mechanism shown in route I (Scheme 1). ROPPOC means ring-opening polymerization combined with simultaneous polycondensation, a new concept recently discussed and reviewed.³⁷ Hence, the observed phenomena defy a straightforward explanation on the basis of the mechanisms outlined in Scheme 1.

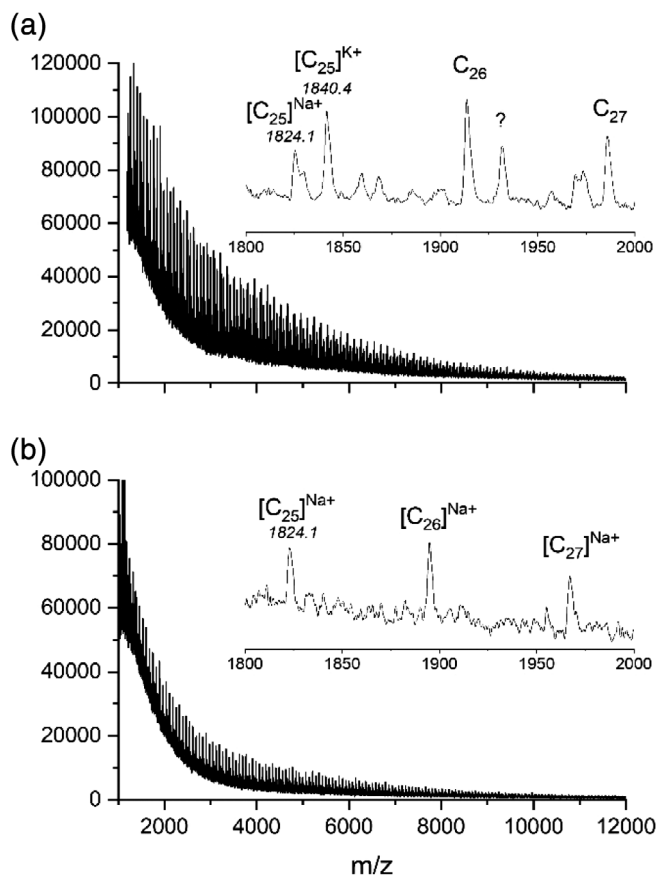
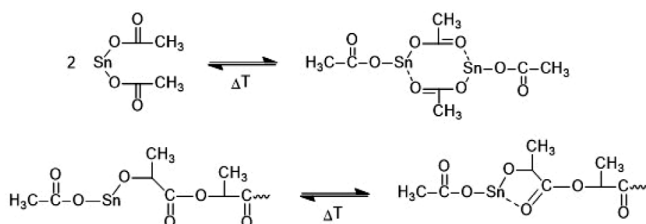


FIGURE 3 MALDI-TOF mass spectra of the SnAc_2 -catalyzed poly(L-lactide) prepared at 130°C with $\text{Lac/Cat} = 100/1$ (No. 6, Table 1): (A) recorded with K-doping, (B) recorded with Na-doping



SCHEME 4 Reversible inter- or intra-molecular donor-acceptor interactions of SnAc_2

3.2 | Polymerizations with SnAc_4

Several polymerizations catalyzed by SnAc_4 were conducted under the same conditions as those described for SnAc_2 above (Table 2). At first low-Lac/Cat ratios were used to find out, if La chains were formed as the main reaction products. However, the MALDI TOF mass spectra revealed that the composition of the polymerization product was or complex and included up to four different species, which were not studied in detail. Furthermore,

three polymerizations were performed with high-Lac/Cat ratios (No. 3–5, Table 2). Regardless of the Lac/cat ratio, the mass spectra of these samples have in common that they display peaks of four different species, namely cyclics and three kinds of linear chains (Figure S2). Moreover, the molecular weights were low relative to those obtained with SnAc_2 under the same conditions. Therefore, a simple conclusion may be drawn which says that SnAc_4 is a catalyst which in any aspect is inferior to SnAc_2 and almost useless for preparative purposes, when lactide is used as monomer.

3.3 | Polymerizations with dibutyl tin and dioctyl tin bis acetate

ROPs with Bu_2SnAc_2 as catalyst (Table 3) were again conducted under the standard conditions mentioned for Table 1. The experiments with low-Lac/Cat ratios (Nos. 1 and 2, Table 3) gave surprising results in two directions. First, the MALDI TOF mass spectra revealed that the reaction products exclusively consisted of cycles (Figure 4 (A) and Figure S3). The mass peaks of the cycles were observable up to masses around m/z 10,000. Therefore, regarding topology these results represent exactly the opposite trend to SnAc_2 . In agreement with a ROPPOC mechanism yielding cycles, the second surprising result were the high-molecular weights obtained at these low-Lac/Cat ratios. They indicate indirectly that incorporation of acetate groups into the polylactides do not play a significant role in agreement with the message of the MALDI TOF mass spectra. Starting out from the samples with the highest molecular weights (Nos. 1 and 2, Table 3).

Mark-Houwink-Sakurada (MHS) measurements were performed (comparison of the intrinsic viscosity with that of a linear standard). As illustrated in Figure 5, these measurements confirmed that also the high-molar mass fraction of these samples almost completely consisted of cycles. The intrinsic viscosities of the polylactides prepared with Bu_2SnAc_2 amount to 65–70% of that of the linear standard as predicted by theory and experimentally proven many times for polylactides and numerous other polymers.

Concerning the molecular weights, the experiments with Bu_2SnAc_2 have the advantage that they cover the mass range between 40,000 and 80,000 (uncorrected Mw's) and thus a range below that typically accessible by SnAc_2 . To find out, if even lower molecular weights are accessible by lowering the temperature, four polymerizations were performed at 130°C . Lower Mw's were indeed obtained, but the mass spectra showed weak peaks of unidentified linear species in addition to the

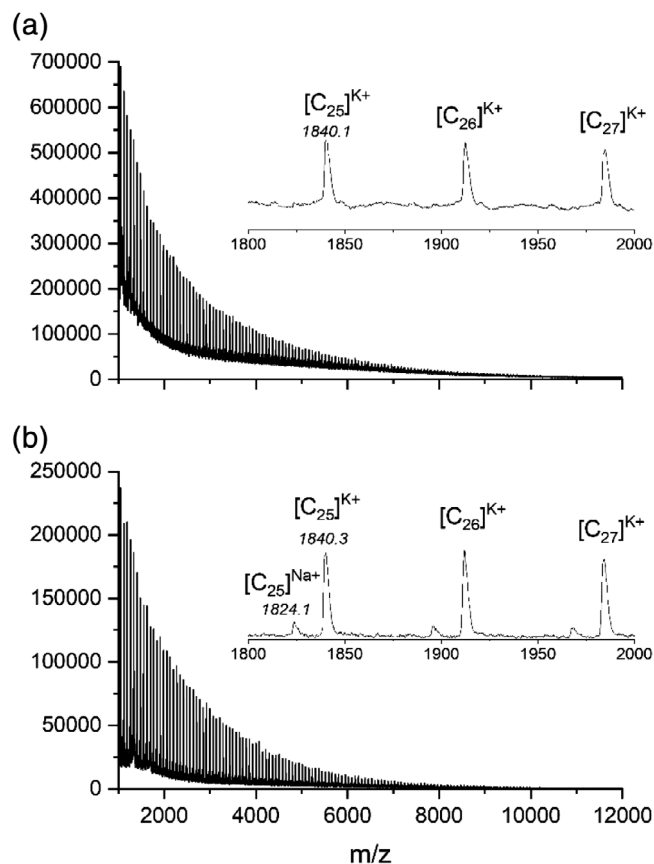


FIGURE 4 MALDI-TOF mass spectra of poly(L-lactide)s prepared at 160°C: (A) with Bu_2SnAc_2 , Lac/Cat = 25/1, 4 h (No. 1B, Table 3); (B) with $\text{Oct}_2\text{SnAc}_2$, Lac/Cat = 50/1, 1 h (No. 2B, Table 4)

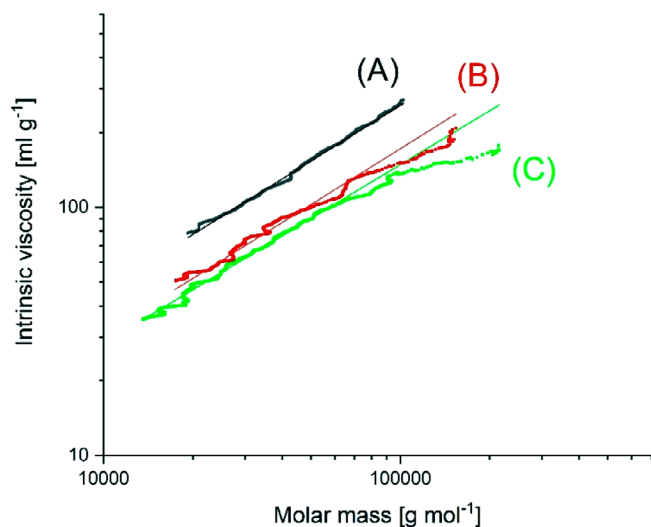


FIGURE 5 Comparison of intrinsic viscosities (MHS measurements) of: (A) linear, commercial poly(L-lactide) Purapol L105; (B) Bu_2SnAc_2 -catalyzed poly(L-lactide) No. 1B, Table 3 (see Figure 4(A)); (C) Bu_2SnAc_2 -catalyzed poly(L-lactide) No. 2B, Table 3. MHS, Mark-Houwink-Sakurada [Color figure can be viewed at wileyonlinelibrary.com]

predominant peaks of the cycles. Furthermore, long reaction times were required. Therefore, polymerizations at 130°C are not attractive from a preparative point of view.

The results obtained with Bu_2SnAc_2 prompted the authors to hypothesize that higher steric demands of the catalyst might favor cyclization with the consequence of lower molecular weights. Therefore, dioctyl tin bisacetate was synthesized and used as catalyst. The synthesis of this tin compound was easily and quantitatively achieved by heating dioctyl tin oxide with the stoichiometric amounts of acetic acid combined with azeotropic removal of water by means of toluene. With the crude, oily catalyst obtained in this way the five polymerizations listed in Table 4 were conducted. Mw values down to 20,000 were indeed obtained and the mass spectra of the four polylactides No. 1, 2A, 3, and 4, Table 4, exclusively displayed peaks of cycles (Figure 4(B)). Experiment No. 2B is not included in this comment, because after the relatively long reaction time of 4 h, small peaks of linear chains were detectable in the mass spectrum. In summary, Bu_2SnAc_2 and $\text{Oct}_2\text{SnAc}_2$ are useful catalyst for a simple preparation of cyclic polylactides in bulk with Mw values in the range of 20,000–100,000. Considering that with SnAc_2 cyclic poly(L-lactide)s with masses up to 240,000 can be synthesized, the tin acetates studied in this work allow for the preparation of cyclic polylactides with variation of the molecular weights by a factor > 10. To the best knowledge of the authors no other catalyst system reported so far enables syntheses of cyclic polylactides with such a broad range of molecular weights. This point is important, because in REP and ROPPOC type polymerizations the average molecular weights cannot easily be controlled via the Lac/Cat ratio.

3.4 | Comparison of various metal acetates in ROPs of L-lactide

The purpose of these experiments was to compare SnAc_2 and $\text{Oct}_2\text{SnAc}_2$ with the nontoxic acetates of zinc and bismuth(III) under identical conditions. Magnesium acetate was not included, because it was shown that MgAc_2 causes severe racemization when used for polymerization of L-lactide in bulk at 150°C.³⁸ Iron(II) acetate was not included because iron salts are pretty toxic when not resorbed by a special mechanism in the intestines. For the experiments listed in Table 5 the standard temperature of 160°C was used and a Lac/Cat ratio of 400/1, because it was found in preliminary experiments that ZnAc_2 is rather sluggish catalyst, so that significantly higher Lac/Cat ratios did not make sense. Estimated from the increase of melt viscosity the following order of reactivity was found:

$\text{SnAc}_2 > \text{Oct}_2\text{SnAc}_2 > \text{BiAc}_3 > > \text{ZnAc}_2$.

The long reaction time required for ZnAc_2 caused a brownish discoloration. Furthermore, the molecular weights obtained from Zn and Bi acetates were considerably lower than those achieved with SnAc_2 . The slower polymerization rate, the lower molecular weight, and the discoloration found for ZnAc_2 when compared with SnAc_2 parallel the results of a previous comparison of Zn octanoate with Sn octanoate.³⁹ Moreover, the MALDI-TOF mass spectra revealed that in the case of Zn and Bi acetates mixtures of cyclic and linear species were formed, whereas a rather uniform topology, namely cycles, was achieved when SnAc_2 was used as catalyst. In summary, for several reasons SnAc_2 proved to be the most useful and attractive acetate catalyst for ROPs of L-lactide. First, it is the most active catalyst. Second, it is much less toxic than the alkyl and aryl tin compounds. Third, it gives higher molecular weights than all other acetates studied in this work. Fourth, it yields a rather uniform topology either at low-Lac/Cat ratios (<100/1) and relatively low temperatures or at high-Lac/Cat ratios (> 400/1) and higher temperatures.

3.5 | Polymerizations of CL with SnAc_2

The properties of CL are different from those of lactide. CL is more basic and thus, more sensitive to cationic catalysts than lactide as evidenced by polymerizations catalyzed by protic acids (e.g., 4-toluene sulfonic acid) that do not react with lactide. On the other hand, CL is less electrophilic than lactide as indicated by the significantly lower sensitivity of CL and poly-CL to hydrolysis when compared with polylactides. Hence, the question arises to what extent the characteristic features of SnAc_2 -catalyzed polymerizations of lactide are also valid for SnAc_2 -catalyzed polymerizations of CL. The 10 experiments performed with variation of CL/Cat ratio, temperature and time are summarized in Table 6, and give the following trends. First, at the lowest CL/Cat ratio, COOH terminated chains (Ld, Scheme 3) are the only kind of reaction product observable in the mass spectra as illustrated in Figure 6(A). The mass peaks of the Ld chains are detectable up to masses around m/z 16,000. This mass range exceeds the real M_n 's of experiments No. 1A and B by approx. 100%. This conclusion takes into account that polystyrene-calibrated SEC measurements overestimate the real M_n 's and M_w 's by at least 50%, so that the measured values need to be multiplied with a correction factor at least 0.68 to approach the real molecular weights.⁴⁰ Hence, the mass spectrum of Figure 6(A) proves that almost all molecules of this sample have the Ld structure. Second, at Lac/Cat ratios of 200/1 or 600/1 small peaks of cycles appear (Figure 6(B)) demonstrating the same trend

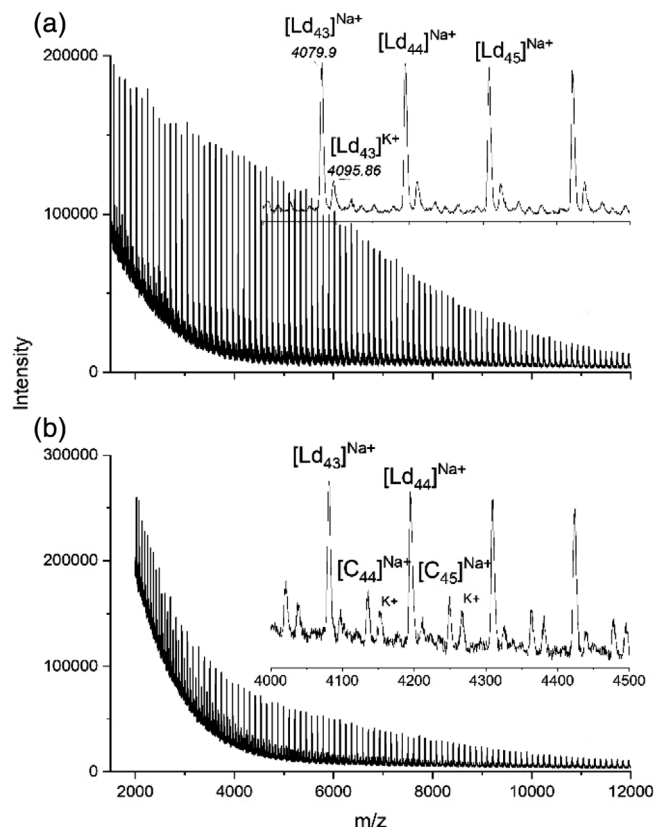
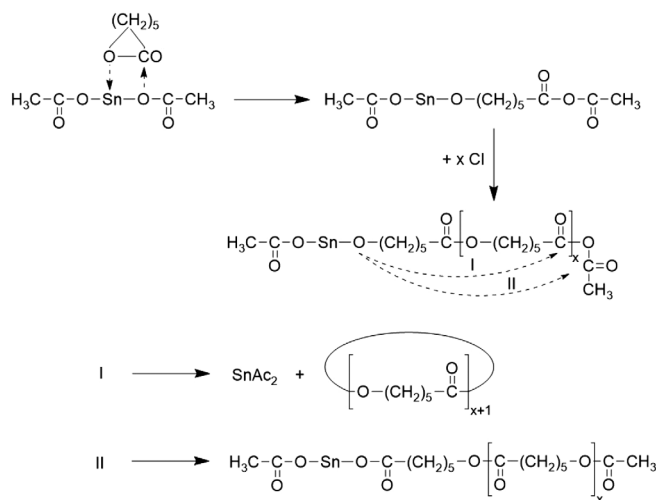


FIGURE 6 MALDI-TOF mass spectra of SnAc_2 -catalyzed poly(ϵ -caprolactone)s prepared at $160^\circ\text{C}/1\text{ h}$: (A) CL/Cat = 50/1 (No. 1A, Table 7); (B) CL/Cat = 200/1 (No. 2A, Table 7)

already observed for SnAc_2 catalyzed ROPs of L-lactide. However, in the case of CL, formation of the linear chains is more favored than in the case of lactide. This difference may be understood based on the reaction mechanisms outlined in Schemes 1 and 5. The lower electrophilicity of caproyl units favors the transfer of acetyl groups via route II. Third, in agreement with a polymerization process where the catalyst mainly plays the role of initiator, the M_n and M_w values increase with Lac/Cat ratio.

3.6 | Polymerization of CL with SnAc_4 or Bu_2SnAc_2

Characteristic for the ROPs of L-lactide catalyzed by SnAc_4 is the complexity of the polymerization products, irrespective of the reaction conditions. Up to for different polymeric species were detected (Figure S2). The four experiments performed with CL were compiled in Table 7. The MALDI TOF mass spectra revealed a considerably higher uniformity of the reaction products. The Ld chains were the predominant species up to a CL/Cat ratio of 100/1 as illustrated by the mass spectrum of Figure 7 (A). At higher Lac/Cat ratios the polymerization product



SCHEME 5 Hypothetical ROPPOC mechanism of SnAc_2 catalyzed polymerizations of ϵ -caprolactone

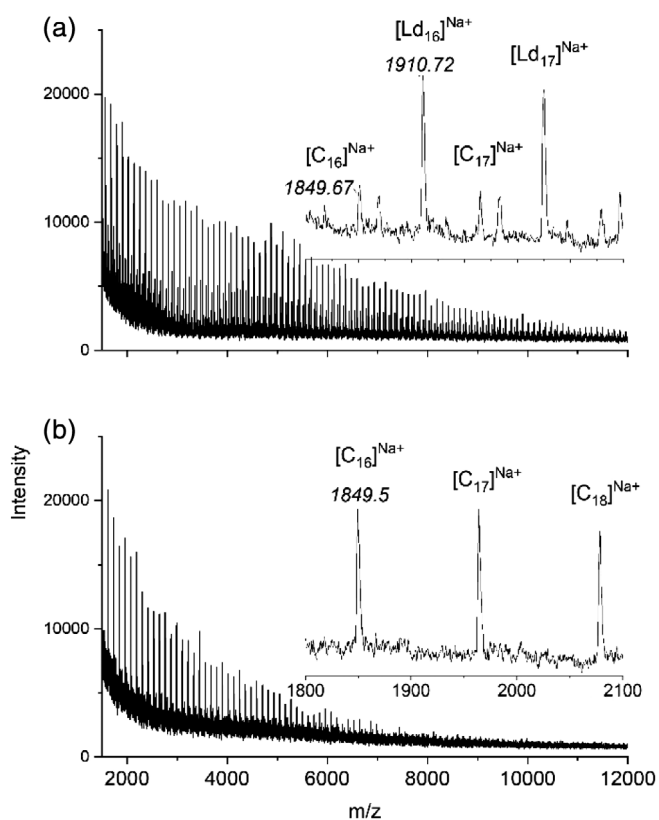


FIGURE 7 MALDI TOF mass spectra of poly(ϵ -caprolactone) prepared at $160^\circ\text{C}/0.5$ h in bulk: (A) with SnAc_4 (Lac/Cat = 100/1, No. 1A, Table 8); (B) with Bu_2SnAc_2 (Lac/Cat = 100/1, No. 3A, Table 8)

became more complex and the fraction of cycles considerably increased (Figure S4). These results mean that the trends observed for SnAc_2 or SnAc_4 -catalyzed polymerizations of L-lactide also exist when CL is used as monomer, but formation of linear (Ld) chains is more favored. Experiments with Bu_2SnAc_2 gave quite different results

(Table 8). As demonstrated by the MALDI-TOF mass spectrum of Figure 7(B) polymerizations conducted with Lac/Cat ratios around 100/1 or below yielded reaction products mainly consisting of cycles. Since the signal/noise ratios of these mass spectra were relatively low, ^1H NMR spectra were recorded which showed that approximately 15–25% (increasing with the Lac/Cat ratio) of the acetate groups added in the form of Bu_2SnAc_2 (signal “a” at 2.10 ppm) were transformed into acetate end groups (signal “b” at 2.04 ppm, Figure S6). At higher CL/Cat ratios the fraction of Ld chains and another kind of linear species increased in intensity.

Therefore, it may be said that Bu_2SnAc_2 is certainly not an optimum catalyst for syntheses of cyclic polycaprolactone. Yet, the relatively high-molecular weights are conspicuous, because they exceed the values expected from the Lac/Cat ratio. Such a trend is characteristic for polymerizations, where the catalyst does not play the role of initiator as it is true for REP. These findings confirm two trends. First, they indicate that Bu_2SnAc_2 is an acetate, which favors formation of cycles regardless, whether lactide or CL are used as monomers. Second, all the results obtained with SnAc_2 , SnAc_4 , and Bu_2SnAc_2 together indicate that in the case of CL the formation of COOH terminated chains is more favored than for lactide. This overriding trend may be explained by the reaction mechanism outlined in Schemes 1 and 5. The electrophilicity of the CO group of poly-CL is lower than that of polylactide as evidenced by the lower sensitivity of poly-CL toward hydrolytic degradation. A lower electrophilicity has, in turn, the consequence that route I (see Schemes 1 and 5), which results in the formation of cycles, is less effective.

4 | CONCLUSIONS

The present work demonstrates that from the preparative point of view the Sn-acetates studied in this work may be subdivided into three classes. SnAc_4 is less attractive, because it yields mixtures of cyclic and linear polylactides of relatively low molecular weight ($M_w < 50,000$). Dialkyl tin bis acetates (R_2SnAc_2) yielded cyclic polylactides under all reaction conditions. Characteristic and useful are the relatively low molecular weights ($M_w < 80,000$), whereas SnAc_2 allows for preparation of high-molar cycles ($M_w \sim 100,000$ – $250,000$), when high-Lac/Cat ratios and temperatures around or above 160°C are applied. Hence variation of tin acetates and reaction conditions allow for the preparation of cyclic poly(L-lactide)s having M_w 's in the range of 20,000–250,000 ($320,000^{14}$). Such a broad range cannot be realized by other catalysts described so far, and this result is of interest, because synthetic methods yielding cyclic

polylactides do not allow for a control of the molecular weight via the Lac/Cat ratio. Another important advantage of SnAc₂ is the direct synthesis of linear polylactides having one COOH and one acetyl end group. This new course of a ROP of cyclic esters does not only work with lactide, it is even more successful with CL and thus, represents a new approach to polyester chains that have never been synthesized by another one-step polymerization process before.

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