

## RESEARCH ARTICLE

# Ring-opening polymerizations of L-Lactide catalyzed by zinc caprylate: Syntheses of cyclic and linear poly(L-lactide)s

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**Abstract**

Alcohol-initiated ring-opening polymerizations (ROPs) of L-Lactide (LA) were conducted in bulk at 130 °C catalyzed by Zn acetate (ZnAc<sub>2</sub>), lactate (ZnLac<sub>2</sub>), or caprylate (ZnCap<sub>2</sub>). 11-undecenol (UND), 1-hydroxymethylnaphtalene (HMN), and 4-nitrobenzylalcohol (4NB) were used as alcohols. Whereas variation of the alcohols had little effect, the usefulness of the catalysts increased in the order: acetate < lactate < caprylate. Hence, further alcohol-initiated polymerizations were performed with ZnCap<sub>2</sub> alone and with variation of the lactide/catalyst (LA/Cat) ratio. With increasing LA/Cat ratio higher fractions of cyclic poly(L-lactide) (PLA) were found, so that the measured degree of polymerization (DP) is considerably lower than the theoretical value (i.e., 2 x LA/alcohol). With neat ZnCap<sub>2</sub> cyclic PLAs were the largely prevailing reaction products. For these cyclic PLAs weight average molar masses (M<sub>w</sub>) up to 134,000 were obtained and an optical purity around 99% was indicated by <sup>13</sup>C NMR spectroscopy and DSC measurements even after 48 h at 150 or 160 °C.

**KEYWORDS**

cyclization, lactide, ring-opening polymerization, transesterification, zinc catalysts

## 1 | INTRODUCTION

Poly(L-lactide) has become a widely used biodegradable material with the additional benefit to be synthesized from natural resources.<sup>1–3</sup> The technical production is based on alcohol-initiated ring-opening polymerizations (ROPs) catalyzed by tin(II) 2-ethyl hexanoate (SnOct<sub>2</sub>) and therefore, most preparative and mechanistic studies of ROPs of lactides were conducted with tin catalysts. Although tin(II) ions have low toxicity for humans, they do not belong to the human metabolism and their presence in polylactides (PLAs) used for medical or

pharmaceutical applications is not desirable.<sup>4,5</sup> ROP catalysts based on zinc have a long tradition in the chemistry of PLAs beginning with the work of Kleine et al. in 1958.<sup>6</sup> In the following decades zinc-based catalysts have been used by numerous research groups.<sup>7–28</sup> In their first paper mentioning zinc-catalyzed ROPs of lactide Kleine et al. used Zn powder as catalyst and found only negligible racemization after 24 h at 160 °C.<sup>6</sup> Zn powder was also used by Vert et al.<sup>11–14</sup> who prepared PLA for medical applications. However, for such applications they had to remove the catalyst by filtration or centrifugation from PLA solutions. The catalytic activity of zinc powder was

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attributed to the layer of ZnO covering the surface of the metal particles. Hence, the catalytic activity of ZnO and other Zn salts such as carbonate and carboxylates came into the focus of several research groups. However, the reactivity of those Zn catalysts proved to be inferior to analogous Sn salts, and ZnO showed a high tendency to racemize L-lactide. Therefore, numerous Zn complexes having ancillary ligands were synthesized and characterized over the past 20 years. Those Zn complexes showed a higher activity and enabled polymerizations at temperatures below 100 °C usually used in combination with an alcohol as initiator. However, these polymerizations were conducted in solution, and thus, were unfavorable for upscaling and unacceptable for technical production. Furthermore, the toxicity of those complexes is unknown, and it is not justified to assume low toxicity just because the “naked” Zn ion is not toxic. In contrast, Zn carboxylates derived from carboxylic acids that belong to the human metabolism have a predictably low toxicity.

The ROP experiments with zinc carboxylates were conducted before 1999 at a time, when MALDI TOF mass spectrometry was still in its infancy and not available in most laboratories.<sup>15–21</sup> Hence, information about the formation of cyclic polylactides and transesterification reactions was not provided. From alcohol-initiated and SnOct<sub>2</sub>-catalyzed ROPs of L-lactide it has been learned meanwhile that at least three different intermolecular transesterification reactions exist, when they are performed in bulk above 120 °C.<sup>29,30</sup> It was also observed that the efficiency of these transesterifications depends on the nature of the initiator.<sup>30</sup> Transesterification reactions also persisted in the solid state and caused modification of morphology, melting temperature ( $T_m$ ), and crystallinity.<sup>31–33</sup> Furthermore, increasing amounts of cycles were found with decreasing initiator/catalyst (In/Cat) ratio, and it turned out that the formation of cycles was responsible for deviation of the experimental number average molar mass ( $M_n$ ) from the theoretical value.<sup>34,35</sup>

None of these interesting aspects has been studied in the case of Zn salt-catalyzed ROPs of L-lactide. Therefore, it was the purpose of this work to study alcohol-initiated ROPs in bulk catalyzed by zinc acetate, zinc caprylate, and zinc lactate in more detail. These Zn salts were selected for two reasons, they were commercially available or easy to synthesize in a water-free form (many zinc salts form hydrates difficult to dry), and their toxicity is certainly not higher than that of the Zn ion. Variation of the anion was of interest because rapid dissolution in molten L-lactide was desirable but not predictable. Furthermore, polymerizations catalyzed by neat Zn salts should be studied to find out if, in analogy to tin(II) carboxylates,<sup>36</sup> cyclic PLA is formed via the ROPPOC mechanism (ring-opening polymerization with simultaneous polycondensation).<sup>37</sup>

## 2 | EXPERIMENTAL

### 2.1 | Materials

L-Lactide, a product of Corbion Purac, was kindly supplied by Thyssen-Uhde AG (Berlin, Germany). It was recrystallized from toluene (99.89% extra dry, ACROS Chemicals) and dried in vacuo at 60 °C. Zinc caprylate (ZnCap<sub>2</sub>) was purchased from MP Biochemicals about 40 years ago. Apparently, this company does not offer this chemical today but other commercial sources such as “American Elements” still exist. 11-Undecenol (UND), 1-hydromethyl naphthalene (HMN) and 4-nitrobenzyl alcohol (4NB) were purchased from Alfa Aesar (Kandel, Germany) and used as received.

### 2.2 | Synthesis of zinc L-lactate

ZnO (50 mmol) and L-lactide (52 mmol) were suspended in distilled water (150 ml) and refluxed with stirring until a clear solution was obtained. This solution was concentrated in vacuo to ~50% of its original volume. Dioxane 70 (ml) was then added, and its concentration was reduced in vacuo likewise. This procedure was repeated twice, and the remaining suspension was diluted with dioxane up to a volume of about 150 ml. On the next day, the precipitated product was isolated by filtration and dried at 60 °C in vacuo (yield, 81%). This catalyst decomposes upon heating and does not have a sharp melting point.

### 2.3 | Alcohol-initiated polymerizations at 130 °C

Alcohol (0.8 mmol) and ZnCap<sub>2</sub> (0.08 mmol) were weighed into flame-dried 50 ml Erlenmeyer flask and L-lactide (40 mmol) and a magnetic stirrer were added under a blanket of argon. The reaction vessel was immersed into an oil bath thermostated at 130 °C. After 12 or 24 h the crystalline PLA was crashed into pieces with a spatula, removed from the reaction vessel, and characterized in the virgin state.

### 2.4 | HMN-initiated ROPs at 160 °C

HMN (0.4 mmol or smaller amounts) and ZnCap<sub>2</sub> (0.08 mmol) were weighed into flame-dried 50 ml Erlenmeyer flask and L-lactide (40 mmol) and a magnetic bar were added under a blanket of argon. The reaction vessel was immersed into an oil bath thermostated at 160 °C.

The virgin polylactides isolated after 24 h were characterized.

## 2.5 | Polymerizations catalyzed by neat ZnCap<sub>2</sub>

### 2.5.1 | At 160 °C

ZnCap<sub>2</sub> (0.04 mmol) was weight into a flame-dried 50 ml Erlenmeyer flask, L-lactide (40 mmol), and a magnetic bar were added under a blanket of argon. The reaction vessel was immersed into an oil bath thermostated at 160 °C. After 24 h ~1 g of the orange melt was removed with spatula under a blanket of argon. The remaining PLA was then thermostated again at 160 °C for 24 h. The crude PLA was characterized.

### 2.5.2 | At 150 °C

These polymerizations were performed as described above, but at a bath temperature of 150 °C, whereupon crystallization occurred within 2 days. The PLA isolated after 2 days had a number averaged molecular mass ( $M_n$ ) of 28,000 and a weight average molecular mass ( $M_w$ ) of 67,000. In a parallel experiment the time was extended to 7 days and a  $M_n$  of 23,000 and a  $M_w$  of 51,000 was obtained. The DSC data are discussed in the text.

## 2.6 | Measurements

All samples were characterized in the virgin state.

The 150 MHz <sup>13</sup>C NMR spectra were recorded with a Bruker Avance 600 FT NMR spectrometer in 5 mm sample tubes. CDCl<sub>3</sub> containing TMS served as solvent and shift reference; 10 000 scans were accumulated.

The DSC measurements were conducted with a heating rate of 10 K min<sup>-1</sup> on a Mettler-Toledo DSC-1 equipped with Stare Software version 11.00. The sample size was in the range of 8–11 mg. The system was rinsed with nitrogen at a flow rate of 50 ml min<sup>-1</sup>. Only the first heating was evaluated.

MALDI TOF mass spectrometry was performed using an Autoflex max (Bruker Daltonik GmbH, Bremen) in the linear positive mode using trans-2-[3-(4-tert-butylphenyl)-2-methyl-2-propenylidene] malononitrile (DCTB) dissolved in chloroform (20 mg ml<sup>-1</sup>) as matrix. The solution was doped with potassium trifluoroacetate to enable selective potassium adduct ion formation. The matrix solution was premixed with the analyte solution (chloroform, 4 mg ml<sup>-1</sup>) in a ratio of 5/2(vol/vol); 1 µl 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<sup>-1</sup>, refractive index detector, Optilab reX, Wyatt) was applied. Samples dissolved in chloroform were manually injected (100 µl, 2–4 mg ml<sup>-1</sup>). For instrument control and data calculation Astra 6.1 software (Wyatt Technology Europe GmbH, Dernbach) was used. The calibration was performed using polystyrene standard sets (Polymer Standards Service – PSS, Mainz, Germany).

For the determination of the Mark-Houwings-Sakurada (MHS) relationship a triple detector arrangement consisting of a refractive index detector (Optilab reX, Wyatt) viscometer (Viscostar, Wyatt) and a multiangle laser light scattering (MALS) detector (Dawn EOS, Wyatt) were used. Astra 6.1 software (Wyatt) also served for calculating the MHS curves.

## 3 | RESULTS AND DISCUSSION

### 3.1 | Alcohol-initiated ROPs-variation of catalyst and alcohol

The first series of nine ROPs was performed at 130 °C for comparison with previous ROPs catalyzed by SnOct<sub>2</sub>. Three different alcohols were used as initiators, namely 11-undecenol as example of an (nonvolatile) aliphatic alcohol and 1-hydroxymethyl naphthalene or 4-nitrobenzylalcohol as aromatic alcohols. These three alcohols were selected, because the SnOct<sub>2</sub>-catalyzed experiments revealed that the MALDI TOF spectra looked quite different, because the extent of transesterification depended on the nature of the initiator.<sup>30</sup> Furthermore, three different catalysts, that is, different Zn carboxylates were compared, namely Zn lactate, which is easy to synthesize from lactides and ZnO in hot water, and Zn acetate and Zn caprylate (n-octanoate) which were both commercial Zn salts. The results of these experiments were summarized in Table 1.

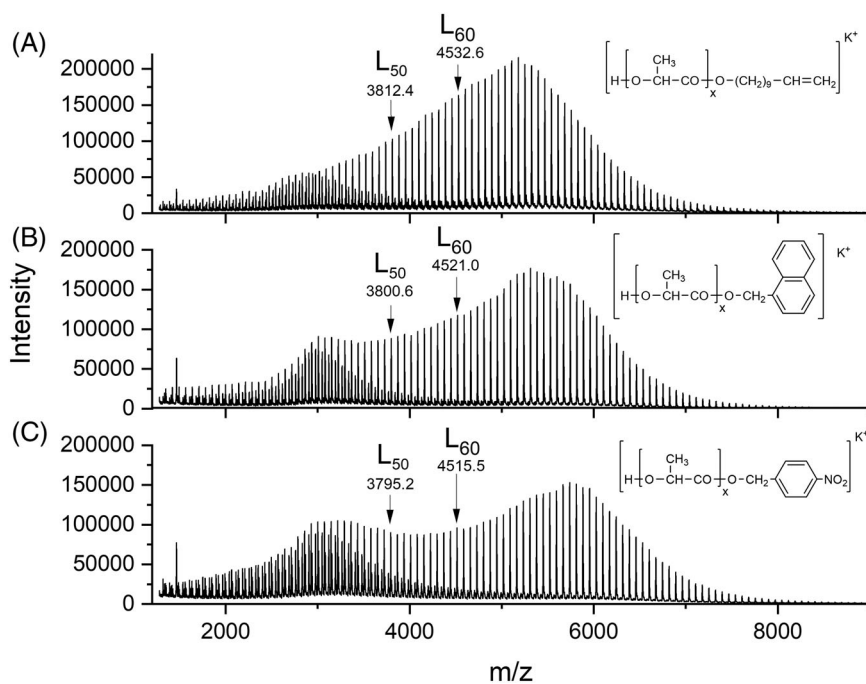
The experiments designed for the comparison of catalysts were stopped after 24 h, because previous experiments had shown that Zn carboxylates are rather sluggish catalysts that require such long reaction times to reach complete conversion (97% according to the thermodynamic equilibrium when PLA is in the molten state or > 99% when it is crystalline, because crystallized chains do not participate in the LA/chain equilibration). The evaluation of the catalysts gave the following results. Surprisingly, the reaction products obtained with ZnAc<sub>2</sub> as catalyst looked like black tar, and thus, were not

**TABLE 1** Alcohol-initiated ZnLac<sub>2</sub> and ZnCap<sub>2</sub>-catalyzed ROPs of L-lactide in bulk at 130 °C for 24 h; variation of the alcohol: LA/In = 50/1, LA/Cat = 500/1, conv. >99% in all experiments

Exp. no.	Catalyst	Initiator	Time (h)	M <sub>n</sub> <sup>a</sup> (theor.)	M <sub>n</sub> <sup>b</sup> (corr.)	M <sub>n</sub> (meas.)	M <sub>w</sub> (meas.)	Dispersity Đ	T <sub>m</sub> (°C)	ΔH <sub>m</sub> (Jg <sup>-1</sup> )
1	ZnLac <sub>2</sub>	UND	24	7400	4600	6500	10,600	1.63	-	-
2	ZnLac <sub>2</sub>	HMN	24	7350	5300	7700	11,200	1.45	-	-
3	ZnLac <sub>2</sub>	4NB	24	7350	5200	7500	9200	1.23	-	-
4A	ZnCap <sub>2</sub>	UND	12	7400	6300	9200	11,700	1.27	-	-
4B	ZnCap <sub>2</sub>	UND	24	7400	7500	10,800	15,300	1.42	166.1	59.2
5A	ZnCap <sub>2</sub>	HMN	12	7350	7800	11,500	13,800	1.20	-	-
5B	ZnCap <sub>2</sub>	HMN	24	7350	7800	11,500	14,600	1.27	172.5	62.4
6A	ZnCap <sub>2</sub>	4NB	12	7350	4600	6700	8000	1.19	-	-
6B	ZnCap <sub>2</sub>	4NB	24	7350	7700	11,200	14,200	1.27	169.0	61.1

<sup>a</sup>Calculated with 100% conversion plus end group.

<sup>b</sup>Corrected by multiplication of measured M<sub>n</sub> values with a factor of 0.68.<sup>38</sup>

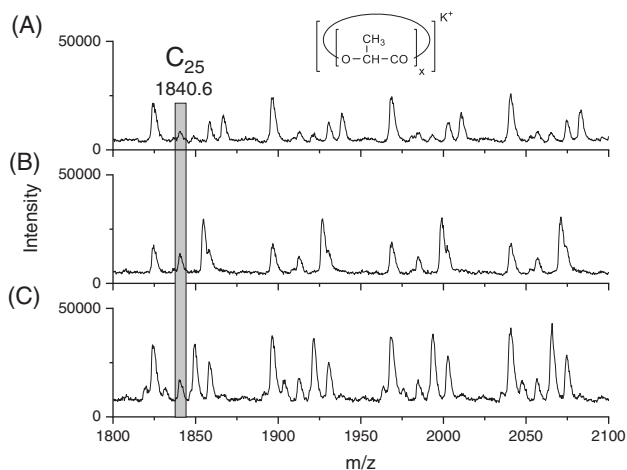


**FIGURE 1** MALDI TOF mass spectra of polyactides prepared at 130 °C with ZnCap<sub>2</sub> as catalyst: (A) UND as initiator (no. 4B, Table 1), (B) HMN as initiator (no. 5B, Table 1), (C) 4NB as catalyst (no. 6B, Table 1)

worked up and characterized. The other six polyactide samples had an orange discoloration, and three samples prepared with ZnCap<sub>2</sub> were crystalline after 24 h. The GPC measurements showed that only those samples prepared with ZnCap<sub>2</sub> had number average molar masses (M<sub>n</sub>) in agreement with the theoretical values. The theoretical values were calculated for 100% conversion and the addition of the end groups. Approximately 99% conversion were found by <sup>1</sup>H NMR spectroscopy as expected for crystalline PLA. The measured M<sub>n</sub> values were corrected with a factor of 0.68, published by Duda et al. for PLA solutions in dichloromethane.<sup>38</sup> This factor has also proven to give reasonable results in a recent study of the authors dealing with tin catalyst ROPs of L-lactide.<sup>30</sup> As

demonstrated by comparison of Figures 1 and S1, the MALDI TOF mass spectra confirmed the lower-than-expected molar masses of the polyactides prepared with ZnLac<sub>2</sub>. In summary, these results indicated that only ZnCap<sub>2</sub> is a useful catalyst, and thus, all further experiments of this work were performed with ZnCap<sub>2</sub>.

The mass spectra of the PLA's obtained with ZnCap<sub>2</sub> as catalyst after 12 or 24 h (Figures 1 and 2) allowed for the following conclusions. First, together with the M<sub>n</sub> and M<sub>w</sub> data the mass spectra indicate that the conversion was not yet complete after 12 h, so that a longer reaction time was indeed needed. Second, there is no significant difference between samples polymerized with different initiators. In this regard the ZnCap<sub>2</sub> catalyzed

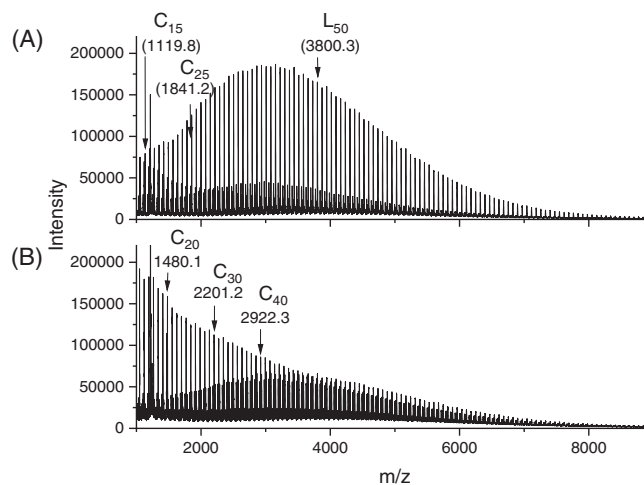


**FIGURE 2** MALDI TOF mass spectra (low mass section) of polylactides prepared at 130 °C with ZnCap<sub>2</sub> as catalyst and (A) UND as initiator (no. 4A), (B) HMN as initiator (no. 5A, Table 1), (C) 4BN as initiator (no. 6A, Table 1)

PLAs differed considerably from those prepared with SnOct<sub>2</sub> under nearly identical conditions (Figures S2 and S3). The mass spectra of Figure S2 were measured after 1 h, because the high reactivity of the SnOct<sub>2</sub> enabled 99% conversion within this short reaction time.

The mass spectra of Figure S3 were recorded after 24 h and thus, were exactly comparable with the reaction conditions underlying Figure 1. Regardless of whether Figure S2 or S3 is considered, it is obvious that the shapes of the mass spectra and the extent of even-odd equilibration depended on the initiator when SnOct<sub>2</sub> was used as catalyst. In contrast the even-odd equilibration is complete for all initiators, when ZnCap<sub>2</sub> is used. This result is neither trivial nor was it predictable, because it can be estimated from the increase of the melt viscosity that SnOct<sub>2</sub> is ~50 times more active as polymerization catalyst than ZnCap<sub>2</sub>. When different types of tin catalysts were compared it was found that a higher catalyst activity is combined with a higher reactivity as transesterification catalyst. Obviously, this correlation does not hold, when Sn and Zn catalysts of nearly identical structure are compared.

Another interesting and important result concerns the formation of cycles. In the mass spectra obtained with ZnCap<sub>2</sub> after 24 h tiny peaks of cycles were detectable in the mass range below 2000 Da (Figure 2). However, after 12 h peaks of cycles were still absent, whereas even-odd equilibration had occurred as demonstrated in Figures 1 and 3. This observation indicates that intermolecular transesterification was far more efficient than equilibration via formation of cycles by “back-biting.” The same trend was found for Sn(II) and Sn(IV) catalysts<sup>39</sup> and also for toluene sulfonic acid.<sup>40</sup> The relationship between



**FIGURE 3** MALDI TOF mass spectra of the PLAs prepared at 160 °C for 24 h with HMN as initiator and ZnCap<sub>2</sub> as catalyst: (A) La/In ratio = 50/1, (B) LA/In ratio = 300/1

intramolecular transesterification via ring chain equilibration and intermolecular transesterification is decisive for the proper understanding of reversible polycondensations. Jacobson and Stockmayer have published a first and widely accepted concept of reversible polycondensations based on the assumption that ring-chain equilibration is the only source of reversibility for the formation of ester groups.<sup>41</sup> The results obtained in this work with ZnCap<sub>2</sub> confirm the critique of the Jacobson-Stockmayer theory recently published by the authors.<sup>39,40</sup>

### 3.2 | Alcohol-initiated and ZnCap<sub>2</sub>-catalyzed ROPs: Variation of the LA/Cat ratio

A second, smaller series of polymerizations catalyzed with ZnCap<sub>2</sub> was performed with HMN as initiator, so that the LA/HMN ratio was varied, whereas the LA/Cat ratio was kept constant (see Table 2).

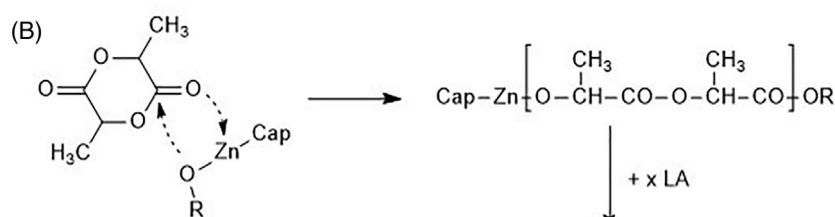
The temperature was raised to 160 °C to accelerate the polymerization and a conversion around 97% (thermodynamic equilibrium) was achieved in all experiments. The purpose of these ROPs was to find out to what extent the real  $M_n$  values agree with the theoretical  $M_n$ 's, or in other words, to find out, to what extent  $M_n$  can be controlled via the LA/In ratio. The results summarized in Table 2 demonstrate that the measured  $M_n$  values are significantly lower than the theoretical values even before correction. The main reason for this discrepancy became evident from the mass spectra. In contrast to the 130 °C experiments, the ROPs performed at 160 °C contain considerably more cyclic PLA and their fraction

**TABLE 2** 1-hydroxyethyl naphthalene-initiated ROPs at 160°C for 24 h catalyzed by ZnCap<sub>2</sub> (LA/Cat = 500/1); variation of LA/In ratio; conversion ~97% in all experiments

Exp. no.	LA/Cat	LA/In	Time (h)	$M_n^a$ (theor.)	$M_n^b$ (corr.)	$M_n$ (meas.)	$M_w$ (meas.)	Disp Đ
1	500/1	50/1	24	7300	3800	5700	13,600	2.4
2	500/1	100/1	24	14,600	9300	13,500	31,500	2.4
3	500/1	200/1	24	29,000	12,300	18,500	45,000	2.4
4	500/1	300/1	24	43,400	15,200	22,000	54,000	2.4
5	500/1	400/1	24	59,800	15,500	23,000	52,000	2.3
6	500/1	400/1	48	59,800	12,300	18,000	44,000	2.4

<sup>a</sup>Calculated with 100% conversion plus end group.

<sup>b</sup>Corrected by multiplication of measured  $M_n$  values with a factor of 0.68.<sup>38</sup>



**SCHEME 1** Mechanism of alcohol-initiated and ZnCap<sub>2</sub>-catalyzed ROP of lactide

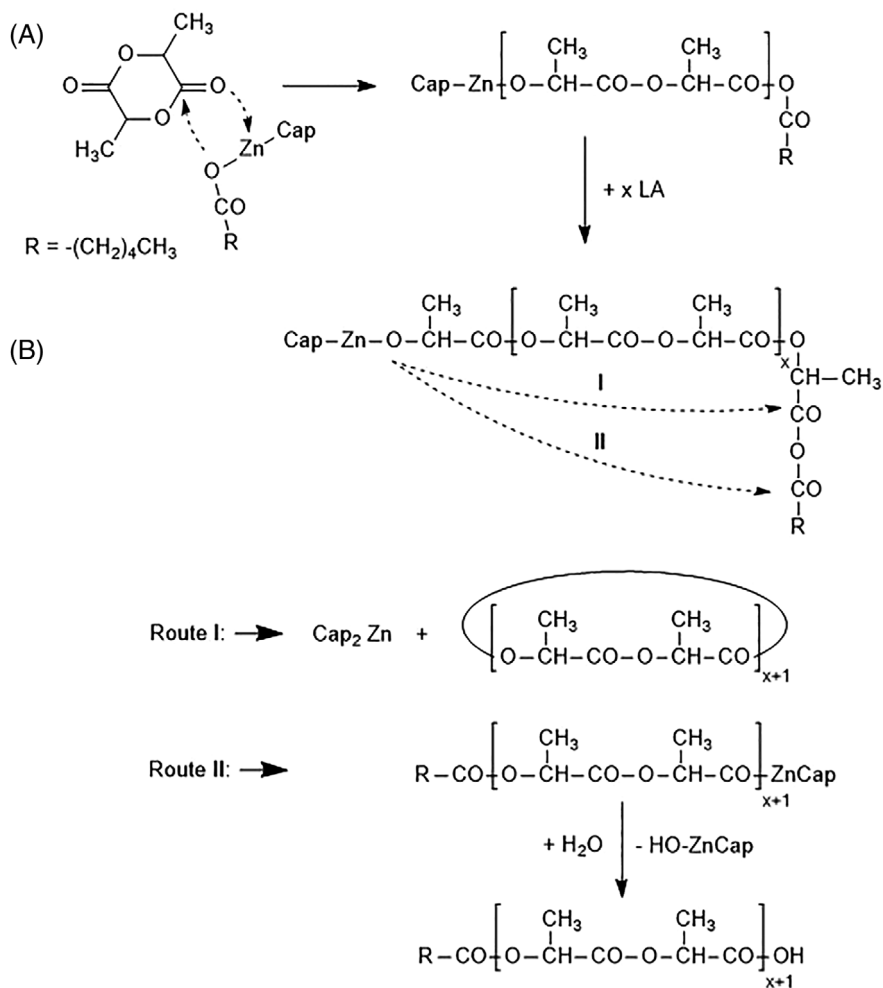
dramatically increases with LA/In ratio as demonstrated in Figures 3 and S5.

This strong increase suggests the following mechanistic explanation. In analogy to what is known about SnOct<sub>2</sub> it may be assumed that the alcohol-initiated polymerization obeys the reaction pathway outlined in Scheme 1. The alcohol reacts with ZnCap<sub>2</sub> yielding an equilibrium, which contains a Zn alkoxide group ((a) in Scheme 1). The Zn alkoxide species is the real initiator and starts the ROP via the coordination insertion mechanism ((b) and (c), Scheme 1). The equilibrium (a) is shifted to the left side, because the ionic tin carboxylate bond is thermodynamically more stable than the covalent Zn alkoxide bond. Increasing LA/In ratio means decreasing concentration of the alcohol, so that the equilibrium (a) further shifted to the left side.

As demonstrated in the next section also neat ZnCap<sub>2</sub> can catalyze a polymerization of LA, which yields cyclic PLA via the ROPPOC mechanism formulated in

Scheme 2. The ROPPOC mechanism competes with the ROP via Scheme 1 and higher LA/In ratios favor the ROPPOC process due to a lower concentration of the Zn alkoxide species. However, it should be emphasized that a small part of the cycles may also result from “back-biting.” Concerning the consequences for  $M_n$  it must be considered that the number fraction of cycles are considerably higher than their weight fraction, because their molar masses are on the average lower than that of the linear chains as evidenced by the mass spectra. For  $M_n$  the number fraction is decisive, and thus even a weight fraction of only a few percent can cause a significant reduction of  $M_n$ . The same trends were observed for alcohol-initiated ROPs of LA catalyzed by SnOct<sub>2</sub>, but in the latter case ring formation is far less efficient and the real  $M_n$ 's agree with the theoretical ones up to LA/In ratios around 200/1. Hence, the results of Table 2 indicate that ZnCap<sub>2</sub> favors formation of cycles more than Sn(II) carboxylates, a result which may be explained by

**SCHEME 2** Mechanism of ring opening polymerization combined with simultaneous polycondensation (ROPPOC) catalyzed by neat  $\text{ZnCap}_2$



the assumption that the equilibrium (a) in Scheme 1 is shifted more to the left side for Zn than for Sn.

### 3.3 | Polymerizations catalyzed by neat $\text{ZnCap}_2$

Although polymerizations catalyzed by  $\text{SnOct}_2$  were known for almost 50 years, the detection that neat Sn(II) carboxylates favor formation of cyclic PLAs via the ROPPOC mechanism was only published 2 years ago.<sup>36,42</sup> Weight average molar masses  $M_w$  up to 325,000 were reported. In this work, eight experiments with neat  $\text{ZnCap}_2$  were conducted, whereupon the LA/Cat ratio and the time were varied (see Table 3). The data compiled in Table 3 indicate the following trends. First, the molar masses increase with the LA/Cat ratio but do not parallel it. Second, longer reaction times (48 h) cause reduction of the molar masses. However, this effect decreases with increasing LA/Cat ratios, because the lower concentration of catalyst entails a lower rate of side reactions responsible for the degradation of the molar

masses. Third, the mass spectra exclusively display peaks of cycles as demonstrated in Figure 4 and S6. It is worth mentioning, that the linear chains formed via reaction path-way II in Scheme 2, have the same mass (at identical degree of polymerization) as the cycles, so that the cycles and linear chains cannot be distinguished by MALDI mass spectrometry. However, the number or weight of the linear chains fall below 1%, when the LA/Cat ratio was increased beyond 400/1 and thus, do not affect the properties of these PLAs. This conclusion is, for example, confirmed by comparison of the intrinsic viscosity with that of a commercial, linear PLA (Purapol L105) as illustrated by Figure 5 and S7. The intrinsic viscosity of the cycles amounts to a value of 0.65(+/-0.01) relative to that of the linear species as expected for cyclic PLAs. The lower  $M_w$  values compared with those obtained by  $\text{SnOct}_2$  under identical conditions may be explained by a higher rate of cyclization due to a higher nucleophilicity of the Zn—O—CH end group relative to the Sn—O—CH end group. Finally, it should be mentioned that the  $M_n$  and  $M_w$  data listed in Table 3 do not need correction, because the hydrodynamic volume of

TABLE 3 ROPPOCs catalyzed by neat ZnCap<sub>2</sub> in bulk at 160 °C; variation of LA/Cat and time; conv. >97% in all experiments

Exp. no.	LA/Cat	Time (h)	M <sub>n</sub>	M <sub>w</sub>	Disp. Đ
1A	400/1	24	25,000	63,000	2.6
1B	400//1	48	19,000	53,000	2.8
2A	600/1	24	36,000	75,000	2.1
2B	600/1	48	27,000	66,000	2.4
3A	1000/1	24	45,000	97,000	2.1
3B	1000/1	48	40,000	88,000	2.2
4A	2000/1	24	66,500	134,000	2.0
4B	2000/1	48	65,000	130,000	2.0
5A	4000/1	24	55,000	109,000	2.0
5B	4000/1	48	48,000	95,000	2.0

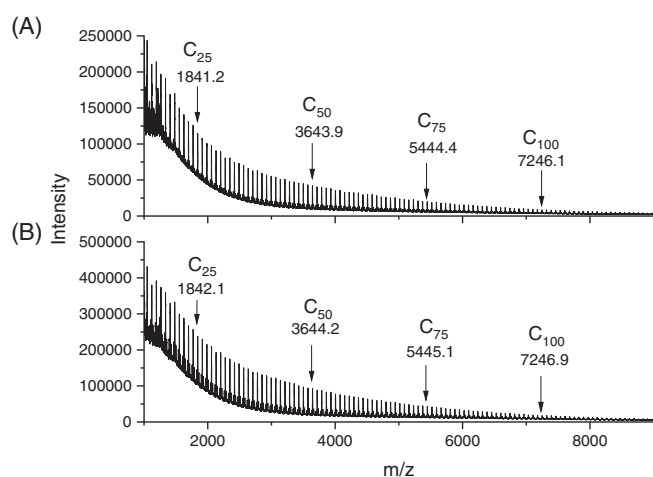
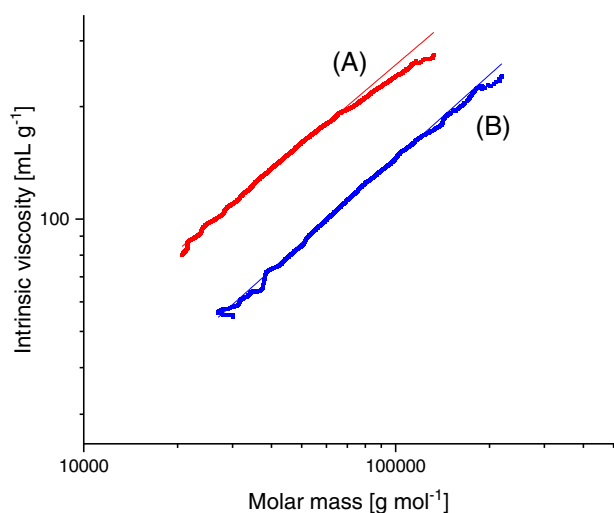
FIGURE 4 MALDI TOF mass spectra of PLAs prepared in bulk with neat ZnCap<sub>2</sub> (LA/Cat ratio 2000/1): (A) after 24 h, (B) after 48 h

FIGURE 5 Comparison of the intrinsic viscosity/molar mass relationship (Mark-Houwink-Sakurada plot) for (A) commercial Purapol L105, (B) cyclic PLA no. 5A, Table 3

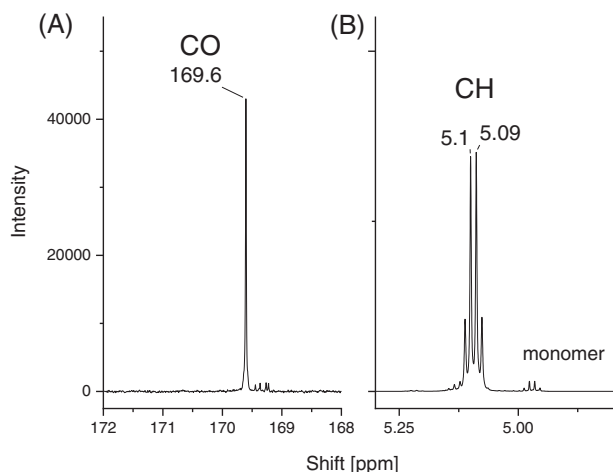
cyclic PLA is quite similar to that of linear polystyrene. Hence, the GPC measurements calibrated with linear polystyrene are close to the real molar masses. An example of a GPC curve of a cyclic PLA is given in Figure S4B.

### 3.4 | Optical purity

The higher basicity of the Zn—O group relative to Sn—O has the consequence that Zn carboxylates (and alkoxides or phenoxides) have a higher tendency to cause racemization of LA than analogous Sn—O compounds, because racemization of LA proceeds via reversible deprotonation of the CH group. In a previous study, the first author compared the influence of 14 different metal salts on the racemization of LA under the conditions of polymerization in bulk with variation of time.<sup>15</sup> That study included ZnO and Zn stearate which is comparable with ZnCap<sub>2</sub> with regard to its basicity. It was found that the stearate did not cause racemization at 120 °C and slight racemization at 150 °C. However, the catalyst concentration was much higher corresponding to a LA/Cat ratio of 100/1 and the reaction time was 48 h. In later experiments conducted with a LA/Cat ratio of 1000/1 no racemization was found at 150 °C even after 96 h. With a LA/Cat ratio of 4000/1 racemization did not occur up to 192 h.

In the present work high resolution <sup>13</sup>C NMR spectra of four PLAs (No. 2A, B and 4A, B, Table 3) were recorded with a 600 MHz FT-NMR spectrometer and more than 10,000 scans, so that a signal-to-noise ratio > 150/1 was achieved. As exemplarily demonstrated in Figure 6 (A), perfectly symmetrical CO-signals were found indicating at least an optical purity of 99%. It has been demonstrated previously that presence of D-units may cause nonsymmetrical broadening of the CO-signal due to tetrads of different stereo-sequences. The tiny sharp signals on the right side of the main CO signal





**FIGURE 6** 150 MHz  $^{13}\text{C}$  NMR spectrum (CO signal) (A) and 400 MHz  $^1\text{H}$  NMR spectrum (CH signal) (B) of a PLA prepared with neat ZnCap<sub>2</sub> in bulk at 160°C (no. 5 B, Table 3)

result from CO signals of the monomer and most likely of the cyclic trimer and tetramer. The presence of 3% of LA is quite normal due to the thermodynamic equilibrium and its presence is also documented in the  $^1\text{H}$  NMR spectrum (Figure 6B). Hence, the perfect symmetry observed for the CO signals of all four samples indicates absence of significant racemization in good agreement with previous measurements.<sup>15,18</sup>

Furthermore, a polymerization conducted with a LA/Cat ratio of 200/1 at 150 °C in bulk yielded a crystalline PLA in contrast to the experiments performed at 160 °C (Table 3). The DSC measurement performed with a heating rate of 10 K min<sup>-1</sup> (as usual for PLA) gave a melting temperature of 188.5 °C and a melting enthalpy of 89.8 Jg<sup>-1</sup> after polymerization and annealing for 2 days. In a parallel experiment, a  $T_m$  of 189.9 °C and a  $\Delta H_m$  of 98.0 Jg<sup>-1</sup> were obtained after 7 days. The corresponding DSC curve is presented in Figure S8B in comparison with that of low molar mass linear species listed in Table 1. Kalb and Pennings reported for a PLA (prepared racemization-free with SnOct<sub>2</sub>) isothermally crystallized at 150 °C a  $T_m$  in the range of 188–191°C.<sup>43</sup> Therefore, the  $T_m$  values of 188.5 and 189.9 °C agree well with an optical purity of at least 99%.

## 4 | CONCLUSION

The results obtained in this work allow for the following conclusions. First, ZnCap<sub>2</sub> is the most attractive catalyst of the three Zn carboxylates studied in this work. When compared with SnOct<sub>2</sub>, ZnCap<sub>2</sub> is far less reactive as polymerization catalyst but surprisingly more reactive as catalyst of even-odd equilibration. Third, ZnCap<sub>2</sub> enables

the preparation of cyclic PLAs having moderate to high molar masses almost free of racemization.

## AUTHOR CONTRIBUTIONS

**Steffen M. Weidner:** Data curation (equal); investigation (equal); methodology (equal); visualization (lead); writing – review and editing (equal). **Felix Scheliga:** Investigation (equal); methodology (equal); resources (equal); writing – review and editing (equal). **Hans R. Kricheldorf:** Conceptualization (lead); investigation (equal); methodology (equal); resources (equal); supervision (lead); writing – original draft (lead); writing – review and editing (equal).

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