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Polylactones 48. SnOct$_2$-Initiated Polymerizations of Lactide: A Mechanistic Study

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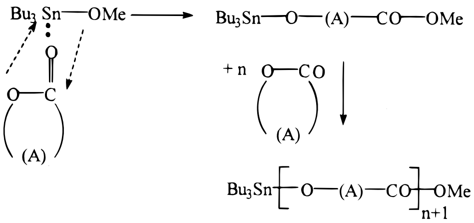
ABSTRACT: Sn(II)2−ethylhexanoate (SnOct$_2$) was reacted with 2 equiv of benzyl alcohol at 20 °C, and a liberation of octanoic acid in a rapid equilibration was found. When the temperature was raised to 180 °C in steps of 40 °C, esterification of benzyl alcohol and octanoic acid was observed up to a conversion of 90%. This esterification was catalyzed by Sn(II) and not by the protons of the free octanoic acid. The esterification liberated Sn(OH)$_2$, which finally precipitated in the form of SnO. This precipitate proved to be a good initiator for the polymerization of lactide above 120 °C. Analogous results were obtained with 1-decanol, triethylene glycol monomethyl ether, and neopentane diol. When SnOct$_2$ was reacted with methyl lactate at 20 °C, a chelate complex of one Sn with two lactate ligands was formed, liberating almost all octanoic acid. At higher temperatures, esterification of octanoic acid with methyl lactate and transesterification of the methyl group (yielding methyl octoate) were observed. The latter esterification was predominant at higher temperatures, and a Sn lactate (1:1) complex precipitated under all circumstances. This complex proved to be an initiator for polymerizations of L-lactide. Polymerization of L-lactide initiated with neat SnOct$_2$ at 180 °C yielded polylactides having octanoate end groups, and the molecular weights paralleled the monomer/initiator ratio.

Introduction

The rapidly growing interest in biodegradable materials has also increased interest in catalysts and mechanisms concerning the ring-opening polymerization of lactides and lactones. Tin compounds (including salts and complexes) have proven to be an extremely versatile and highly efficient group of catalysts or initiators. Among the numerous catalytically active tin compounds, tin(II) 2-ethylhexanoate, SnOct$_2$, plays a predominant role, because it is the most widely used initiator for research purposes and for the technical production of polylactides and related copolyesters.[1−21] However, the reaction mechanisms of SnOct$_2$ have not been fully elucidated yet despite recent progress in this direction.[9,10,12−21] Therefore, it was the purpose of the present work to continue our previous studies[12,22] of polymerization mechanisms of tin compounds and to contribute to a better understanding of SnOct$_2$-catalyzed esterification and transesterification processes.

For a long time, SnOct$_2$ was believed to initiate a cationic polymerization mechanism, and a precise formulation of such a mechanism was presented for the first time by Nijenhuis et al.,[8] but without any detailed experimental evidence. On the other hand, it was shown[23,24] that both anionic and cationic polymerizations of L-lactide involve strong racemization above 50 °C, whereas SnOct$_2$ yields optically pure poly(L-lactide) even at 180 °C when the reaction time is short. This simple fact alone lends strong support to the assumption of a coordination−insertion mechanism. For di- or tributyl tin alkoxides, it was demonstrated that a coordination−insertion mechanism according to eqs 1 and 2 is operating.[22] However, SnOct$_2$ in a pure state does not contain alkoxide (or hydroxide) groups, and it was also previously demonstrated that lactones do not insert into Sn−carboxylate bonds (eq 3) under normal polymerization conditions regardless if Sn(II) or Sn(IV) carboxylates are involved.[22] Furthermore, it has been reported by several authors[3,11,12,17] that addition of alcohols (including diols) accelerates the polymerization and allows a modification of structure and molecular weights.



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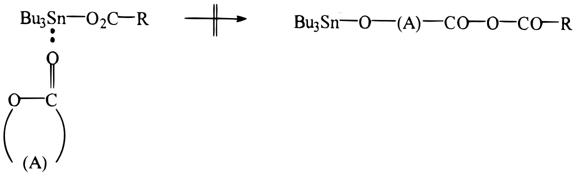
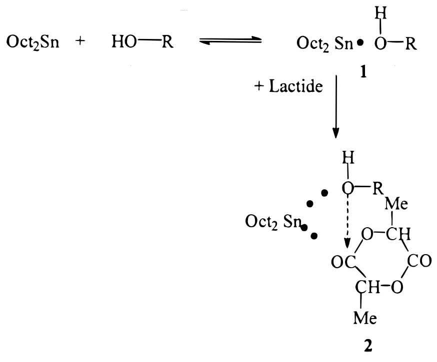


(3)

Detailed ^{1}H NMR spectroscopy studies conducted at room temperature have recently revealed[12] that SnOct$_2$ combined with an alcohol establishes a rapid complexation equilibrium (eq 4) and that this interaction is stronger than the interaction between SnOct$_2$ and lactide. This means that the interaction of SnOct$_2$ with the alcohol (when added as co-initiator) proceeds any chain growth step. On the basis of these results, a chain growth via a reaction between coordinated alcohol (or chain end) and lactone was hypothetically formulated (eq 5). On the other hand, Zhang et al.[14] have postulated that the reaction of SnOct$_2$ with alcohols yields a tin



(4)

(5)

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Table 1. ^{13}C NMR Chemical Shifts δ^a of the CO Signals of $SnOct_2$ and Mixtures of $SnOct_2$ with Various Alcohols

reaction mix (molar ratio)	δ (ppm)	reaction mix (molar ratio)	δ (ppm)
$SnOct_2$ neat	189.1	$SnOct_2$ + decanol (1:2)	185.6
2-ethylhexanoic acid (OctH, n. eg.)	183.3	$SnOct_2$ + TGMEl (1:2)	182.2
$SnOct_2$ + Bzl−OH (4:1)	188.6	$SnOct_2$ + neopentane diol (1:1)	183.3
$SnOct_2$ + Bzl−OH (1:1)	187.1	$SnOct_2$ + methyl lactate (1:2)	183.3
$SnOct_2$ + Bzl−OH (1:2)	186.3		
$SnOct_2$ + Bzl−OH (1:8)	184.8		

[a] Measured in $CDCl_3$/TMC at 23−25 °C.

alkoxide (OctSnOR) that initiates the polymerization of lactide and lactones via the "classical coordination−insertion mechanism" outlined in eqs 1 and 2. Kowalski et al.[19,20] have quite recently presented MALDI-TOF and kinetic data supporting the hypothesis of Zhang et al. at least for temperatures below 100 °C for the $SnOct_2$/butanol-initiated polymerization of ϵ-caprolactone.

The present work was mainly aimed at studying the interaction between $SnOct_2$ and alcohols with a variation of the alcohol structure and a variation of the temperature. A temperature of 180 °C was selected as the upper limit because this temperature is needed for the technical production of poly(L-lactide).

Experimental Section

Materials. $SnOct_2$ was purchased from Aldrich Co. (Milwaukee, WI). It was twice "dried" by distillation with xylene under reduced pressure and finally subjected to a fractionated distillation in a vacuum of 10^{-3} mbar. In the ^{1}H NMR spectrum of the fractionated product, the proton signal at 11.3 ppm (recorded in $CDCl_3$/TMS) indicating free octanoic acid was barely detectable. Benzyl alcohol, 1-decanol, triethylene glycol monomethyl ether (TGME), and methyl L-lactate were also purchased from Aldrich and distilled before use. Neopentane diol was purchased from Merck Co. (Darmstadt, Germany) and dried over P_4O_{10} in vacuo. The L-lactide was a gift of Boehringer KG (Ingelheim, Germany) and was recrystallized from ethyl acetate. Methyl octanoate, benzyl octanoate, and the octanoate of methyl lactate (**11**) were prepared from the corresponding alcohols and octanoyl chloride with stoichiometric amounts of pyridine in dry CH_2Cl_2.

$SnOct_2$ + Benzyl Alcohol. $SnOct_2$ (20 mmol) and benzyl alcohol, Bzl−OH, (40 mmol) were mixed under dry nitrogen in a glass flask having a ground-glass joint and silanized glass walls. The reaction vessel was closed with a glass stopper and steel spring and immersed in a preheated thermostated oil bath. When the reaction time was over (see Tables 2−4), a sample was recovered for ^{1}H NMR spectroscopy. Afterward, the reaction mixture was diluted with diethyl ether and filtered, and the precipitate was intensively washed with diethyl ether and dried at 20 °C over P_4O_{10} in vacuo. All experiments with other alcohols were performed analogously.

The ^{13}C NMR spectra (Table 1 and Figure 3) were recorded in such a way that $SnOct_2$ and an alcohol (molar ratio 1:2) were mixed in $CDCl_3$ and a ^{13}C NMR spectrum was recorded immediately.

The presence of an organic component in the precipitate was checked by IR (KBr pellets) and ^{1}H NMR spectroscopies (in CF_3 CO_2D/TMS) and by elemental analyses.

Polymerizations of L-Lactide with SnO or Sn Lactate. L-Lactide (40 mmol) and dry SnO or Sn lactate (**13**) (0,4 mmol) were weighed into a round-bottom flask having silanized glass walls. The reaction vessel was closed with a glass-stopper and steel spring and immersed into an oil bath thermostated at 150 °C. After the reaction cooled, the product was dissolved in CH_2Cl_2, filtered if necessary, precipitated into cold methanol (+5 °C), and dried at 20 °C in vacuo.

Polymerizations of L-Lactide with $SnOct_2$. L-Lactide (40 mmol) and $SnOct_2$ (1 M solution in dry toluene) were mixed in a round-bottom flask having silanized glass walls. Seven reaction mixtures with M/I ratios of 10, 20, 40, 60, 100, 150, and 200 were prepared (Table 5). The reaction vessel was closed with a glass stopper and steel spring and immersed into an oil bath thermostated at 180 °C (the reaction vessel was then shortly opened to relax the pressure). In the case of M/I = 10 samples were taken for ^{13}C NMR spectroscopy after 0.5, 1.0, and 2.0 h. In all other cases, the reaction mixture was cooled after 2 or 6 h dissolved in CH_2Cl_2 precipitated into cold methanol and dried at 20 °C in vacuo. Afterward, inherent viscosities and 400 MHz ^{1}H NMR spectra were recorded.

Measurements. The inherent viscosities were measured in CH_2Cl_2 with an automated Ubbelhode viscometer thermostated at 20 °C.

The 100 MHz ^{1}H NMR spectra were recorded with a Bruker AC-100 FT NMR spectrometer in 5 mm outer diameter (o.d.) sample tubes. The 25.2 MHz ^{13}C NMR spectra were recorded with the same spectrometer in 10 mm o.d. sample tubes. The 400 MHz ^{1}H NMR spectra were obtained on a Bruker AM-400 FT NMR spectrometer. $CDCl_3$ containing TMS served as solvent and shift reference for all measurements.

Results and Discussion

Reactions of Benzyl Alcohol. Benzyl alcohol (Bzl−OH) was used in our previous study as reaction partner of $SnOct_2$ because it is particularly favorable for ^{1}H NMR spectroscopic analyses of reaction mixtures and reaction products. For the present work, it had the additional advantage that the high boiling point allowed for model reactions up to 180 °C. Most model reactions discussed below were conducted with a mixture of neat $SnOct_2$ and Bzl−OH at a molar ratio of 1:2. When this mixture was stored at 20 °C for 1 week, a singlet signal became detectable in the ^{1}H NMR spectrum at 5.15 ppm, a chemical shift characteristic for the benzyl octoate. No esterification was detectable when a Bzl−OH and octanoic acid mixture was stored for 1 week at 20 °C. At 60 °C, the Bzl−OH/$SnOct_2$ mixture showed 2% esterification after 1 h, but no esterification was found for the Bzl−OH/octanoic acid mixture after 6 h. Therefore, it may be concluded that the esterification is a tin-catalyzed reaction that obviously involves a cyclic transition state based on the complex **1** (R−OH/$SnOct_2$).

This result is not particularly surprising taking into account that Bu_2SnO and other Bu_2Sn derivatives are well-known as esterification catalysts in organic chemistry.[25] The lactonization of ω-hydroxy carboxylic acids involving a four-membered transition state is particularly noteworthy at this point.[26]

The Bzl−OH/$SnOct_2$ mixture was also examined by ^{13}C NMR spectroscopy immediately after mixing at room temperature. Previous ^{1}H and ^{119}Sn NMR studies had revealed that a rapid complexation equilibration was formed, and **1** was considered to be endproduct of this equilibrium (eq 4 at 20 °C). However, neither the ^{1}H nor ^{119}Sn NMR spectra allowed for the detection of the liberated octanoic acid that was now detected by ^{13}C NMR spectroscopy. The CO signals of $SnOct_2$ (189.1 ppm) and octanoic acid (183.3 ppm) differ by 6 ppm (Table 1), and when Bzl−OH was added to $SnOct_2$, the CO signal was shifted toward the value of free octanoic acid. This shift effect increased with the molar ratio of added Bzl−OH as expected for a rapid equilibration involving all Bzl−OH molecules and both octanoate

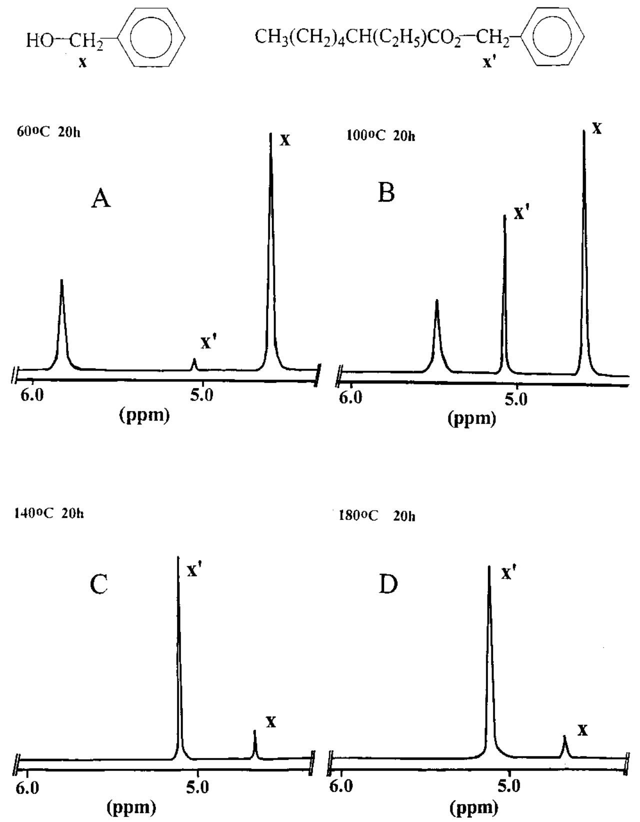
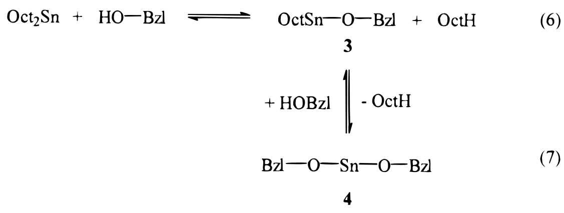


Figure 1. 100 MHz ^{1}H NMR spectra of SnOct$_2$/benzyl alcohol (1:2) reaction mixtures (all done for 20 h): (A) 60, (B) 100, (C) 140, and (D) 180 °C.

groups (eqs 6 and 7). This conclusion is also in perfect agreement with our previous ^{1}H NMR data, which also showed a rapid exchange of all acid protons. In this connection, it should be mentioned that Penczek and co-workers have recently postulated the formation of the monoalkoxide **5** as the main initiator at temperatures of 60 °C. However, the ^{1}H and ^{13}C NMR data of the present and previous work clearly indicate that the second octanoate group is also involved in the exchange process, so that the tin bis(benzyl)oxide **6** must exist in this equilibrium.



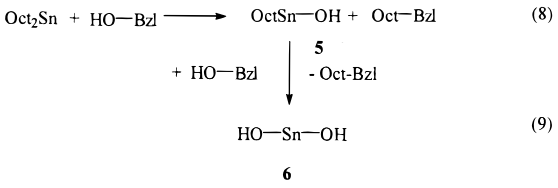
$$\mathrm{Oct_2Sn} + \mathrm{HO{-}Bzl} \rightleftharpoons \underset{\mathbf{3}}{\mathrm{OctSn{-}O{-}Bzl}} + \mathrm{OctH} \qquad (6)$$

$$\mathrm{OctSn{-}O{-}Bzl} \xrightleftharpoons[-\,\mathrm{OctH}]{+\,\mathrm{HOBzl}} \underset{\mathbf{4}}{\mathrm{Bzl{-}O{-}Sn{-}O{-}Bzl}} \qquad (7)$$

When the 1:2 mixture was heated to 60, 100, 140, and 180 °C for a constant time (20 h), an increasing conversion of the esterification process was observed, as demonstrated by the ^{1}H NMR spectra of Figure 1. The exact data of this esterification process were summarized in Table 2. Variation of the reaction time at 180 °C revealed that the final state of the entire reaction process was achieved after 3 h. At this equilibrium situation, approximately 90% of the Bzl–OH were esterified, which means that both octanoate groups were involved in this process. An important consequence of the esterification reaction is the (formal) liberation of water, which in the first stage of the entire process is presumably bound in the form of the tin hydroxides **5** and **6** (eqs 8 and 9). Increasing concentration of Sn–OH groups results in a condensation yielding stannoxane units, which continue the condensation process so that, finally, hydrated SnO precipitates from the reaction mixture (eqs 9 and 10). The precipitated SnO displayed the typical dark color, and the tin oxides isolated from the 140 and 180 °C/20 h experiment proved to be free of organic components as evidenced by IR and ^{1}H NMR spectroscopy. Obviously, the formation of the tin oxide is the rate-determining step of the entire process, but after 48 h at 140 °C or 4 h at 180 °C, almost all Sn had precipitated from the reaction mixture. The tin oxide isolated from this process was found to be a good initiator for L-lactides, as discussed below.

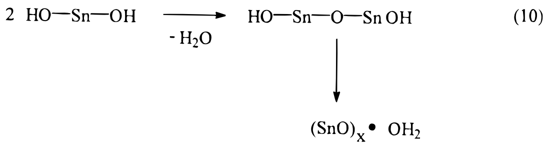
Table 2. Reactions of Benzyl Alcohol with SnOct$_2$ (molar ratio 2:1) in Bulk

exp. no.	temp. (°C)	time (h)	esterific. of Bzl–OH (%)	yield (%) of SnO
1	60	1	0.5	
2	60	4	1.0	
3	60	20	3.5	
4	100	20	38.0	37
5	140	20	81.0	92
6	180	20	92.0	94
7	180	2	85.0	
8	180	4	92.0	
9	180	8	93.0	
10	180	48	93.0	95



$$\mathrm{Oct_2Sn} + \mathrm{HO{-}Bzl} \longrightarrow \underset{\mathbf{5}}{\mathrm{OctSn{-}OH}} + \mathrm{Oct{-}Bzl} \qquad (8)$$

$$\mathrm{OctSn{-}OH} \xrightarrow[-\,\mathrm{Oct\text{-}Bzl}]{+\,\mathrm{HO{-}Bzl}} \underset{\mathbf{6}}{\mathrm{HO{-}Sn{-}OH}} \qquad (9)$$



$$2\ \mathrm{HO{-}Sn{-}OH} \xrightarrow[-\,\mathrm{H_2O}]{} \mathrm{HO{-}Sn{-}O{-}Sn\,OH} \longrightarrow (\mathrm{SnO})_x \bullet \mathrm{OH_2} \qquad (10)$$

Reactions of Various Alcohols. Model reactions between SnOct$_2$ and 1-decanol or TGME were performed to elucidate whether the above-described reactions of benzyl alcohol are somehow unusual or represent the normal case. It was found that both primary alcohols in principle react like Bzl–OH, but two slight differences are worth mentioning. First, the ^{13}C NMR spectrum of the SnOct$_2$/TGME 1:2 mixture suggests that most of the octanoic acid is liberated at room temperature, whereas approximately 50% of the octanoic acid is liberated in the case of Bzl–OH or 1-decanol. This difference may result from a complexation of the Sn atom by the ether groups of TGME that stabilize the formation of the Sn–alkoxide bonds. Second, as demonstrated by the data listed in Table 3, the rates and extent of esterification are somewhat different for all three alcohols. Third, in the case of TGME, no precipitation of SnO was observed at 100 °C after 20 h. This observation may be a result of a slower esterification, or it may be due to a weak complexation of the Sn hydroxides **5** and **6** by the ether groups of TGME.

When SnOct$_2$ was combined with neopentane diol in CDCl$_3$ at 20 °C, the ^{13}C NMR spectra indicated the liberation of certainly more than 50%, probably even

Table 3. Reactions of $SnOct_2$ with Various Alcohols in Bulk[a]

temp. (°C)	1-decanol % ester	TGME % ester	neopentane diol % monoester	% diester	% SnO[b]
20	0	0	0	0	0
60	4	1	4	0	0
100	45[b]	18	58	7	0
140	88[b]	71[b]	36[b]	58	48
180	94[b]	85[b]	16[b]	80	75

[a] Molar ratio $SnOct_2$:CH_2OH = 1:2. Time = 20 h. [b] Precipitation of SnO was observed.

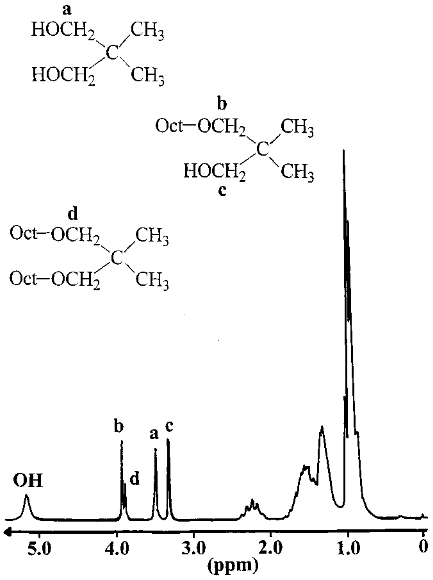
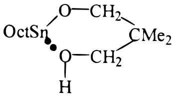


Figure 2. 100 MHz ^1H NMR spectrum of the reaction mixture of $SnOct_2$ and neopentane diol (1:1) as obtained at 100 °C after 20 h.

90%, of the octanoic acid (Table 1). Obviously, this diol can form cyclic tin alkoxides such as **7** and **8**, which for



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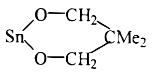

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reasons of entropy are somewhat more stable than the noncyclic bisalkoxides such as **4**. At higher temperatures, at first, a monoesterification of the neopentane diol was observed, followed by a double esterification as illustrated by Figure 2 and by the data in Table 3. Obviously, due to the higher stability of the cyclic tin alkoxide **7,** no precipitation of SnO was observed at 100 °C. At higher temperatures, the double esterification of neopentane diol became the prevailing process and SnO precipitated from the reaction mixtures. In summary, it may be said that all four alcohols followed the same reaction pathway with slight differences in the reaction rates and in the stability of the intermediately formed tin alkoxides.

Reactions of Methyl L-Lactate. L-Lactide is usually contaminated with the linear dimer (lactyl lactic acid) resulting from the hydrolysis of lactide on the surface of the lactide crystals. Furthermore, water brought into the polymerization process by air, moist glass walls by Sn–Oct_2, and by its esterification with alcohols may all contribute to the formation of the linear dimer, which may itself then play the role of a co-initiator. Therefore, the combination of $SnOct_2$ with methyl L-lactate is a particularly interesting model system. In our previous study,[12] it was demonstrated by ^1H and ^{119}Sn NMR spectroscopy that the interaction of $SnOct_2$ with ethyl lactate at room temperature is considerably stronger than that with Bzl–OH and that the CO group participates in the complex formation as a ligand. This observation was now confirmed in the present work by ^{13}C NMR spectroscopy, which showed that 2 equiv of MeLac suffice to liberate almost all octanoic acid (Figure 3). The chemical shift of the CO signal of the liberated octanoic acid was almost identical with that of neat octanoic acid (183.3 ppm). In other words, the chelated complex **10** is the most likely reaction product of this interaction (eqs 12 and 13).

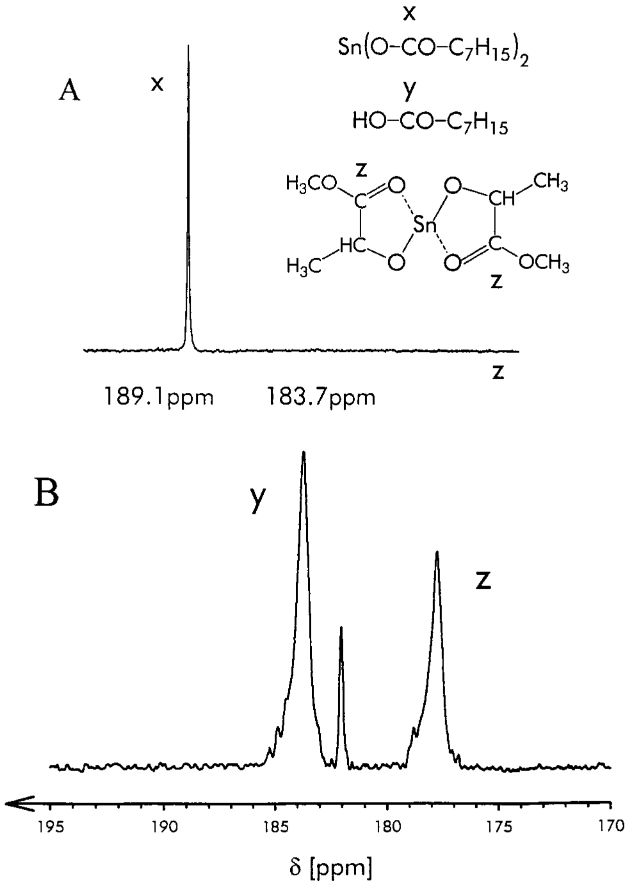
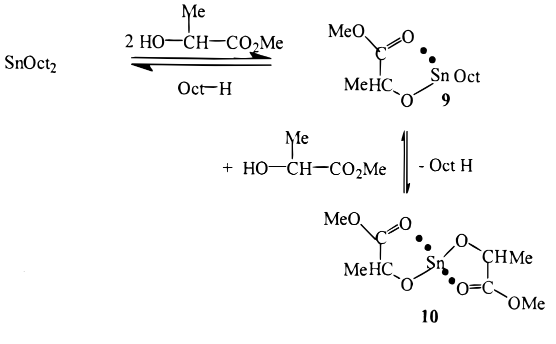


Figure 3. ^{13}C NMR spectra (CO signals only) of (A) neat $SnOct_2$ and (B) 1:2 mixture of $SnOct_2$:methyl L-lactate recorded in $CDCl_3$ at 20 °C.



(12)

(13)

In parallel to the experiments with other alcohols, the $SnOct_2$/MeLac mixture (molar ratio 1:2) was heated to 60, 100, 140, and 180 °C (Table 4). In agreement with the above-discussed result, an esterification of MeLac

Table 4. Reactions of $SnOct_2$ with Methyl L-Lactate in Bulk[a]

exp.	temp (°C)	time (h)	Lac−OM (3.77 ppm)	Oct−OLac−OMe (3.73 ppm)	Oct−OMe (3.68 ppm)	methanol (3.47 ppm)	precipitate yield (%)	elem. anal.[b] found for $SnC_3H_4O_3$ C	H
1	60	1	76	15		9			
2	100	1	67	7	5	1			
3	100	20	47	20	27	6	24	18.75	2.07
4	100	72					56	18.23	2.00
5	140	1	51	24	20	6	28	18.24	1.95
6	140	8	28	22	44	6	78	18.08	1.95
7	140	20	18	23	53	6	82	18.08	1.91
8	140	48	10	25	61	4	82	17.95	2.05
9	180	1	6	30	62	2	70	17.80	1.86
10	180	8	2	32	65	(1)	81	18.25	2.12
11	180	20	(1)	32	66	(1)	80	18.33	1.95

[a] Molar ratio 1:2 in bulk. [b] Calcd for $SnC_3H_4O_3$: C 17.34, H 2.42%. Calcd for $SnC_6H_{10}O_6$ (two lactic acid residues): C 24.28, H 3.40%.

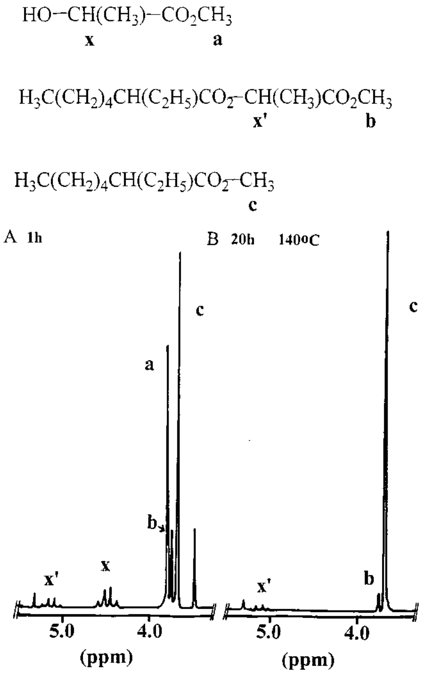
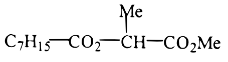


Figure 4. ^1H NMR spectra of $SnOct_2$/methyl lactate reaction mixtures (molar ratio 1:2) at 140 °C: (A) after 1 h and (B) after 20 h.

with octanoic acid was observed (**11**) that is character-


$C_7H_{15}-CO_2-CH(Me)-CO_2Me$

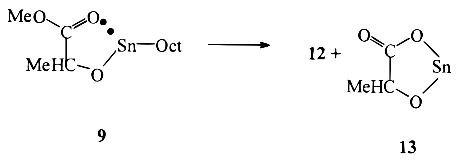
11

$C_7H_{15}-CO_2-Me$

12

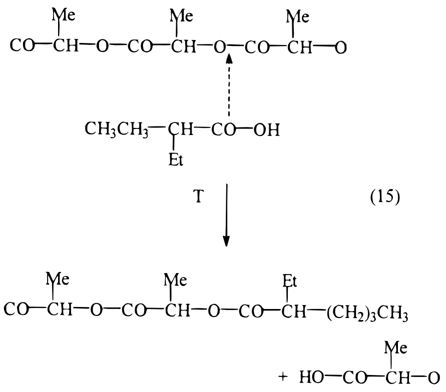
ized by a downfield shift of the Lac C−H signal (quadruplet) and by a slight upfield shift of the OMe signal (Figure 4). However, this reaction leveled off around 22−25% at 140 °C or around 30−32% at 180 °C, and another reaction became predominant, namely, the transesterification of the methyl ester group with the formation of methyl octanoate (**12**). Figure 4A represents an intermediate situation where all three methyl esters (MeLac **11** and **12**) are present, whereas Figure 4B indicates the final stage of the reaction (after 20 h at 140 °C) with methyl octanoate as the main liquid reaction product.

From all experiments conducted at 100 °C or higher, a white precipitate was isolated, which just by its color was indicated to be different from SnO. IR and ^1H NMR spectra proved the presence of lactic acid moieties in all of these precipitates. The elemental analyses listed in Table 4 suggest that at 140 °C and 180 °C the cyclic compound **13** (SnLac) was formed regardless of the reaction time. The formation of **13** may occur in several ways. The elimination of methyl octoate from the complex **9** (eq 14) is perhaps the most obvious route.



(14)

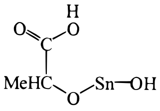
However, an intramolecular hydrolysis (eq 15) or an



(15)

intermolecular hydrolysis yielding methanol and lactic acid may contribute to the formation of **13.** The observation of a weak singlet signal at 3.47 ppm in the reaction mixture suggests the presence of free methanol (Table 4).

At this point, it should be mentioned that Schwach et al.[16] postulated a hydroxytin lactate **14** as reaction



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intermediate in their hypothetical cationic polymerization mechanism. Furthermore, those authors reported on the formation of the same compound **14** in a model reaction between free lactic acid and $SnOct_2$. However, the published elemental analyses do not agree with structure **14**, but they agree with structure **13**. Obvi-

Table 5. Polymerization of L-Lactide in Bulk at 150 °C (48 h) Initiated with SnO or Sn Lactate

polym.	init.	mon./init.	co-init.	mon./init.	yield (%)	η_{inh}[a] (dL/g)
1	SnO	200	Bzl−OH	50	86	0.22
2	SnO	200	Bzl−OH	200	94	0.30
3	SnLac	200	Bzl−OH	25	91	0.13
4	SnLac	200	Bzl−OH	50	94	0.24
5	SnLac	200	Bzl−OH	100	95	0.33
6	SnLac	200	Bzl−OH	150	95	0.36
7	SnLac	200	Bzl−OH	200	95	0.39
8	SnLac	200			93	0.57
9	SnLac	1000			92	0.58

[a] Measured at 25 °C with $c = 2$ g/L in CH_2Cl_2.

ously, those authors also had the tin lactate **13** in hand. In this connection, it should be emphasized that formula **13** does not necessarily represent the true structure. This tin lactate may have a dimeric or polymeric structure, and its poor solubility in inert organic solvent indicates that strong intermolecular donor−acceptor interactions between Sn and O atoms exist.

Polymerizations. To make sure that the Sn-containing precipitates (SnO or **13**) isolated from the model reactions with Bzl−OH or MeLac were active initiators for lactide, a small series of polymerizations was performed (Table 5). The high yields and high molecular weights obtained in most of these polymerizations clearly indicate that these products of the model reaction possess the expected high reactivity even in the absence of an alcohol as co-initiator. In the course of a normal polymerization conducted with high *M*/*I* ratios, SnO or the tin lactate **13** will certainly not precipitate. However, the formation of tin hydroxides, stannoxane bonds, and tin lactate complexes is unavoidable, when water is present or formed during the initiation/polymerization process. Therefore, the role of the alcohol needs a short discussion.

It is obvious that the addition of an alcohol starts a reaction sequence yielding various tin compounds having reactive Sn−O bonds. Therefore, it is not "a priori" justified to attribute the initiation step under all circumstances exclusively to a tin alkoxide such as **5** or **6**. This interpretation is supported by the following experiments. A preformed poly(L-lactide) was heated with Bzl−OH in a concentrated chlorobenzene solution to 130 °C. The polylactides isolated after precipitation into diethyl ether contained almost all of the Bzl−OH in the form of benzyl ester end groups, and the molecular weights had decreased with the higher feed ratios of Bzl−OH. In other words, the Bzl−OH cleaved rapidly the polylactide chain even in the absence of a catalyst. This finding is in perfect agreement with the well-known fact that precipitation of polylactide solution into methanol at 20−25 °C involves the formation of methyl ester groups. Hence, it is clear that the formation of ester end groups by the co-initiator does not say anything about the nature of the initiator. In addition to tin alkoxides, tin hydroxides, stannoxanes, and tin lactate complexes may play this role.

Another interesting aspect of the model reaction with MeLac is the high yield of Me octoate obtained at temperatures ≥140 °C. If in a real polymerization of lactides oligo or polylactides having OH end groups are the reaction partners of $SnOct_2$, the analogous transesterification will yield oligo- and polylactides having octoate end groups. In previous studies of several authors, only traces of octanoate end groups were found when the polymerization were conducted below 150 °C and in the presence of alcohols. Obviously, the transesterification of the octanoate groups is rather slow and is suppressed by the presence of alcohols. In the present work, L-lactide was reacted with $SnOct_2$ at 180 °C at a *M*/*I* ratio of 10:1. The virgin reaction product were characterized by ^{13}C NMR spectra with the following results. After 1 h, the CO signal of the initiator had disappeared, and a new CO signal at 182 ppm was detectable (Figure 5). As revealed by comparison with the model compound **11,** this CO signal is typical for an octanoate group esterified with lactic acid derivatives.

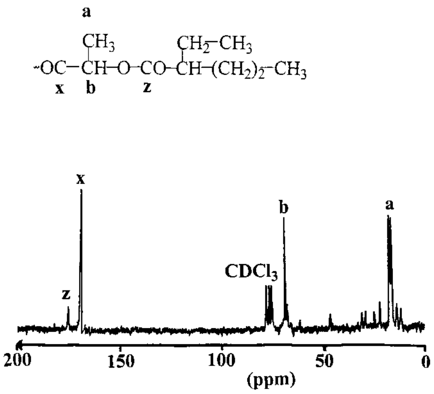

Figure 5. 25.2 MHz ^{13}C NMR spectrum of the crude reaction product obtained from L-lactide and $SnOct_2$ after 1 h at 180 °C.

Table 6. $SnOct_2$-Initiated Polymerization of L-Lactide in Bulk at 180 °C[a]

polym.	mon/init.	yield[b] st(%)	η_{inh}[c] (dL/g)	DP[d]
1	20	32	0.12	50 ± 5
2	40	83	0.24	85 ± 10
3	60	88	0.43	100 ± 10
4	100	93	0.55	160 ± 10
5	150	95	0.73	350 ± 20
6	200	95	0.91	450 ± 25

[a] Time = 1 h. [b] After precipitation into cold methanol. [c] Measured at 25 °C with $c = 2$ g/L in CH_2Cl_2. [d] Apparent degree of polymerization as determined by ^1H NMR spectroscopic end group analyses from the CH_3 signals of the octoate groups.

On the basis of this result, L-lactide was polymerized at 180 °C with neat $SnOct_2$ under variation of the *M*/*I* ratio. The results compiled in Table 6 allowed two important conclusions. First, the molecular weights depends on the *M*/*I* ratio. Second, all samples contained significant amounts of octoate end groups. The CH_3 signals consisting of a triplet and a quadruplet pattern (Figure 6B) clearly prove the covalent attachment of the octanoate groups to lactide units. This signal pattern is the consequence of a coexistence of two diastereomers, namely, lactyl units esterified with *S*- or *R*-octanoic acid (2-ethylhexanoic acid). When the octanoic acid is attached to a nonchiral alcohol as in methyl octanoate **12**, only one triplet is observable for both CH_3 groups (Figure 6A). From the signal intensities of the octanoate end groups, apparent degrees of polymerizaions (DPs) were calculated (Table 6). These apparent DPs indicate that, on the average, only one octanoate group per initiator was transformed into an end group.

In this connection, a further model reaction should be reported. Poly(L-lactide) free of octanoate groups was heated with octanoic acid (in the absence of $SnOct_2$!) for 1 h to 180 °C. Afterward, the inherent viscosity of

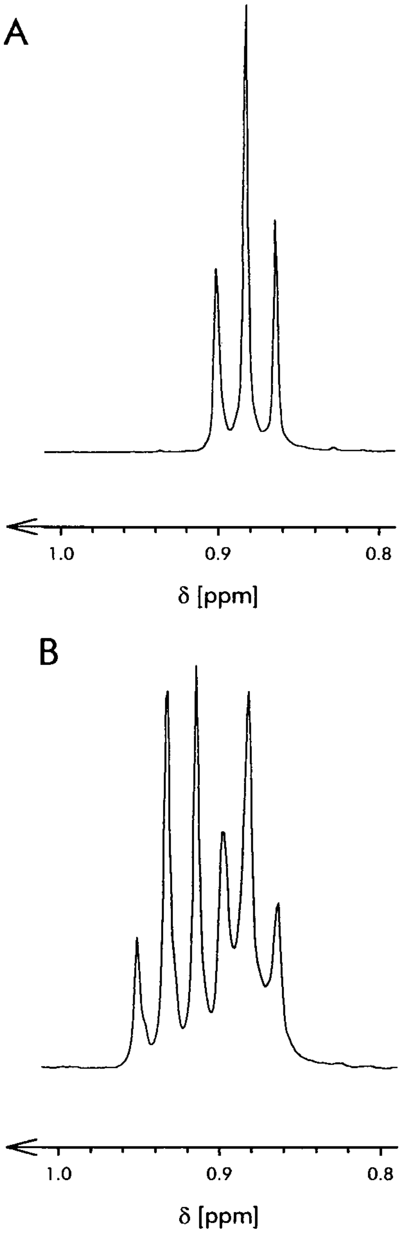

Figure 6. 400 MHz ^1H NMR spectra (CH_3 signals only) of (A) methyl octanoate (**12**) and (B) octanoate end groups in polylactides prepared at 180 °C (Table 6).

the starting material had dropped from 1.6 to 0.90 dL/g, and the precipitated polylactide contained traces of octanoate end groups. This means that octanoic acid can react with polylactide at 180 °C by acidolytic transesterification (eq 15), but this process is pretty slow. Therefore, it may be concluded that the rather high concentration of octanoate end groups in the $SnOct_2$-initiated poly(L-lactide)s result from a tin-catalyzed transesterification process in agreement with the efficiency of the model reactions summarized in Table 4.

Finally, it should be mentioned that also CH−OH end groups were detected in the ^1H NMR spectra (4.30 ppm, $J = 7.0-7.5$ Hz). However, a reliable quantification of the original end groups was not possible for the following reasons. When the polylactides were precipitated into methanol, a methanolytic cleavage of ester groups took place even when cold methanol (+4 °C) was used and the samples were dried at 20 °C in vacuo. The polymerizations were then repeated, and 1,2-dimercapto-ethane was added to the CH_2Cl_2 solutions of the polylactides to complex the tin. Afterward, the polylactides were precipitated into dry diethyl ether. However, the isolated polylactides contained even more CH−OH end groups, suggesting that also the 1,2-dimercaptoethane had cleaved ester groups. Finally, the $SnOct_2$-initiated polymerizations at 180 °C were conducted a third time, and ^1H NMR spectra of the virgin reaction products were recorded. The ^1H NMR spectra displayed a quadruplet at 4.36 ppm which may be attributed to CH−O−Sn groups. The intensity of this signal fell into the range of 0.2−0.3% of the main chain CH signal (5.16 ppm) regardless of the M/I ratio. Because both the amount of octanoate end groups and the molecular weights vary with the M/I ratio, it may be concluded that it is mainly the formation of octanoate end groups that controls the molecular weights. These results clearly indicate that the reaction mechanism at 180 °C is partially different from that below 100 °C, and further intensive investigations are needed to elucidate these complex processes.

Despite the complexity of the $SnOct_2$-initiated polymerization process, the results of this study and of previous publications[12,14,19,20] clearly demonstrate that the chain growth proceeds by a classical coordination−insertion mechanism (eqs 1 and 2), as was previously formulated and proven for Sn(IV) alkoxides.[22] The cationic or pseudocationic mechanism postulated by several authors[8,16] may be excluded for the following reasons. First, these mechanisms are in total contradiction to the NMR spectroscopic results and MALDI-TOF measurements presented here and in previous publications.[12,19] Second, the end groups identified by Schwach et al.[16] can be explained by the nonionic esterification and transesterification reaction discussed in this study. Third, only extremely strong acids and carbenium ion donors were found to initiated a true cationic polymerization of lactide.[23] Fourth, L-lactide is highly sensitive to the presence of bases such as carboxylate ions, which cause deprotonation in the α-position and thereby racemization. Potassium benzoate was found to cause partial racemization even at 20 °C.[24] Various Fe,[24] Mn[24], Mg,[24] and Ca[24] carboxylates were found to cause partial racemization of L-lactide at higher temperatures.[27−30] It is clearly the covalent character of $SnOct_2$ and its reaction intermediates that allow the preparation of optically pure poly(L-lactide) at temperatures up to 180 °C.

Conclusion

The results of the present work demonstrate that the combination of alcohols with $SnOct_2$ yields a complex system of reactions. A rapid equilibration involving a liberation of octanoic acid is followed by a slower tin-catalyzed esterification of alcohol and octanoic acid. The liberated water yields tin hydroxide groups that at high concentrations and temperatures undergo condensation steps yielding stannoxanes and, finally, insoluble SnO. However, this reaction sequence is modified by alcohols capable of forming chelate-type Sn complexes. With MeLac as co-initiator, an additional transesterification yielding methyl octanoate and a Sn lactate complex become the main reaction. At temperatures below 100 °C, tin alkoxides such as **3** and **4** (or **10**) may play a predominant role as initiators. However, at higher temperatures, a broad variety of Sn compounds having covalent Sn−O bonds are formed (e.g., Sn hydroxides, stannoxanes, and lactate complexes) that all can contribute to the initiation process. The Sn lactate **13** may play a particularly important role above 100 °C. Addition of alcohol will control the molecular weights and yield ester end groups regardless if they are involved in the initiation step or not. Particularly noteworthy is the efficient transesterification of octanoic acid with ester groups of lactic acid, which has the consequence that at temperatures around and above 140 °C polylactide chains containing octoate end groups are formed. Hence, the molecular weights of $SnOct_2$-initiated polymerizations at 180 °C parallel roughly the *M*/*I* ratio, a course that has never been reported before. In summary, it may be concluded that the $SnOct_2$-based initiators are a complex dynamic system that responds to all changes of the reaction conditions by a change of structure and concentration of the active species.

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