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TIN-INITIATED POLYMERIZATIONS OF LACTONES: MECHANISTIC AND PREPARATIVE ASPECTS

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Summary: A series of model reactions between pure Sn(II) 2-ethylhexanoate ($SnOct_2$) and primary alcohols was studied. At room temperature a rapid and reversible exchange between alcohol and octanoic acid was observed. At higher temperatures (studied up to 180°C) an esterification yielding alkyl octoates and a precipitate of SnO were found. With methyllactate (MeLac) as reaction partners analogous reactions were observed but a transesterification yielding methyl octoate and a tin lactate salt became the prevailing reactions at 100 - 180°C. Both SnO and the Sn lactate proved to initiate the polymerization of L-lactide at 150°C. $SnOct_2$ combined with alcohols as coinitiators yield polylactides having alkylester endgroups and CH-OH endgroups at temperatures ≤ 150°C. However, neat $SnOct_2$ yields at 180°C polylactide chains having octoate endgroups and the monomer/initiator ratio controls the molecular weight.
When Bu_4Sn was used as potential initiator its reactivity depended on the presence of oxygen. O_2 oxydizes Bu_4Sn with formation of dibutylether and Bu_2SnO which is the true initiator of the ring-opening polymerizations. It is concluded that both initiators $SnOct_2$ and Bu_4Sn initiate a normal coordination/insertion mechanism involving covalent Sn-O bonds.

INTRODUCTION

Tin compounds play an important role as initiators for ring-opening polymerizations of lactones, cyclocarbonates and cyclic depsipeptides. This role concerns both fields fundamental research and technical production of polylactides and related copolymers. In the case of Sn(IV) compounds the alkoxides (e.g. Bu_3SnOMe or $Bu_2Sn(OMe)_2$) and some distannoxanes (e.g. $XBu_2Sn\text{-}O\text{-}SnBu_2X$) are the most reactive initiators [1 - 3]. For such initiators the coordination-insertion mechanism schematically outlined in eqs. (1) and (2) is established [4]. This mechanism is based on the existence and reaction of covalent Sn-OR bonds. It is this covalent character of all active species which is typical for Sn initiators and for the racemization-free polymerization of L-lactide at temperatures up to 200°C (needed for the technical production of poly L-lactide). All ionic polymerizations of L-lactide involve at least partial racemization when conducted above 50°C [5, 6]. This situation raises the question as to which

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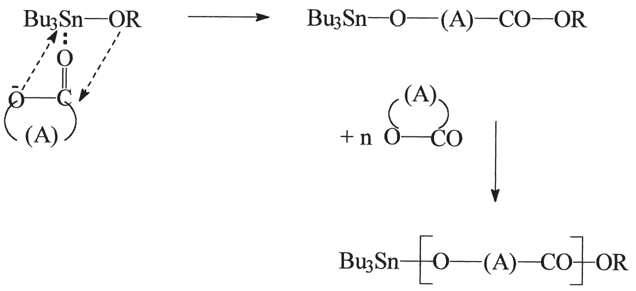
mechanism is operating when Sn compounds such as $SnOct_2$ Bu_2SnOct_2, Bu_4Sn or Ph_4Sn are used as initiators, because all these Sn-compounds do not contain a reactive tin-alkoxide or stannoxane bond. Clearly there are two fundamental alternatives. First, these initiators form a reactive Sn-OR group in the beginning of the polymerization process (for instance by the reaction with a coinitiator) and the chain growth proceeds via the mechanism outlined in eqs. (1) and (2). Second, these Sn-compounds initiate an alternative coordination-insertion mechanism where the active chain end consists of an OH-group attached to the Sn atom via a coordinative bond instead of a normal covalent bond (eqs. (3) and (4)). The present work had the purpose to study model reaction of both $SnOct_2$ and Bu_4Sn to shed more light on the polymerization mechanism.

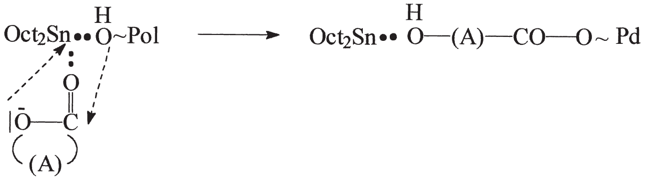
EXPERIMENTAL PART

Materials: L-lactide was a gift of Boehringer GmbH (Ingelheim, Germany) it was recrystallized from ethyl acetate and dried over P_4O_{10} in vacuo. ε-Caprolactone was purchased from Aldrich Co. (Milwaukee, WI, USA) and distilled over CaH_2. Bu_4Sn was also purchased from Aldrich Co. and subjected to fractionated distillation in vacuo. $SnOct_2$ (Aldrich Co.) was twice dried by azeotropic distillation with xylene and afterwards fractionated by distillation in a vacuum of 10^{-3} mbar. The highest boiling fraction was used. A detailed description of all experiments and measurements is given in two manuscripts recently submitted for publication [7, 8].



(1)

(2)



(3)

$$\mathrm{Oct_2Sn + HO{-}R \rightleftharpoons \underset{\mathbf{1}}{OctSn{-}OR} + Oct\,H} \qquad (4)$$

$$\mathrm{Oct_2Sn + HOR \rightleftharpoons Oct_2Sn{\bullet\bullet}\overset{H}{O}{-}R} \qquad (5)$$

$$\mathrm{OctSn{-}OR + HOR \rightleftharpoons \underset{\mathbf{2}}{RO{-}Sn{-}OR} + OctH} \qquad (6)$$

$$\mathrm{Oct_2Sn + HOR \longrightarrow \underset{\mathbf{3}}{OctSn{-}OH} + Oct{-}OR} \qquad (7)$$

$$\mathrm{OctSn{-}OR + HOR \longrightarrow \underset{\mathbf{4}}{RO{-}Sn{-}OH} + Oct{-}OR} \qquad (8)$$

$$\mathrm{OctSn{-}OH + HOR \longrightarrow \underset{\mathbf{5}}{H{-}O{-}Sn{-}OH} + Oct{-}OR} \qquad (9)$$

RESULTS AND DISCUSSION

Experiments with $SnOct_2$

$SnOct_2$ is the most widely used initiator for the technical production of poly lactides and related copolymers [9, 10] because of several advantages, such as high catalytic activity, racemization-free polymerization of L-lactide, formation of high molecular weights in combination with high yields etc. Usually a primary alcohol is added as a coinitiator, which serves three purposes. Firstly, it accelerates the polymerization process. Secondly, it allows for a control of the molecular weights and thirdly, it forms ester endgroups which can be used for further preparative or analytical purposes (e.g. ^1H NMR spectroscopic determination of the degree of polymerization).

In contrast to several authors, who have speculated about a cationic or activated monomer mechanism [11-13] Zhang et al. [14] have proposed that the alcohol reacts with $SnOct_2$ under formation of a Sn-O-R group (eq. (4)) which initiates the chain growth according to the classical coordination-insertion mechanism of eqs. (1) and (2). Yet, those authors did not provide any experimental evidence.

More recently we have shown by ^1H and ^{119}Sn NMR spectroscopy that in fact a rapid equilibration between $SnOct_2$ and benzylalcohol occurs even at 20°C and the formation of a $SnOct_2$-alcohol complex was formulated (eq. (5)). An increasing downfield shift of the OH-proton was observed with higher $SnOct_2$/alcohol ratios [10]. The continuation of this studies using ^{13}C NMR spectroscopy has now revealed that the CO-signal of $SnOct_2$ (189.1 ppm in $CDCl_3$/TMS) shifts upfield in direction of the value typical for free octanoic acid (183.6 ppm) when an alcohol is added (Fig. 1). Therefore, these NMR spectroscopic results clearly prove an extremely rapid equilibration between both octoate groups of $SnOct_2$ and the added alcohol so that octanoic acid is liberated (eq. (4)) via the transition state formulated in eq. (5).

The reaction between neat $SnOct_2$ and neat benzylalcohol was also studied at 60, 100, 140 and 180°C and slow esterification yielding benzyloctoate was observed (eqs. (7) - (8)) in addition to the rapid equilibration outlined in eqs. (4) - (6). At 20°C 1 % of esterification was observed after 4 days. Its extent increased with time and temperature and at 180°C the esterification and condensation processes had reached the final state after 2 h. This final state was characterized by approx. 90 % esterification of the $SnOct_2$/2 BzlOH mixture and an almost complete precipitation of SnO. We could also prove that this esterification is catalyzed by tin and not a simple proton catalyzed esterification of benzylalcohol and free octanoic acid (which is extremely slow at temperatures ≤ 60°C). As outlined in eqs. (7) - (8) the esterification involves the formation of tin hydroxide groups which are not stable at temperatures ≥ 100°C and undergo condensation steps with elimination of water. SnO is formed as the most stable endproduct probably via the intermediate formation of stannoxanes such as compounds 6 - 9.

The experiments performed with benzyl alcohol were repeated with 1-decanol, triethylene glycol monomethyl ether and 2,2-dimethyl-1,3-propane diol. With benzylalcohol and 1-decanol precipitation of SnO was observed at 100°C within a period of 20 h. For the other two alcohols a temperature of 140°C was needed to observe the precipitation of SnO. But in principle all four alcohols followed the same reaction pathway.

A new aspect came into sight when methyl-L-lactate (MeLac) was used as reaction partner of $SnOct_2$. It was already demonstrated in a previous publication [10] that the interaction of MeLac with $SnOct_2$ is particularly strong due to the formation of a kind of chelate complex (**10** in eq. (9)). In this work the almost complete liberation of octanoic acid was demonstrated by ^{13}C NMR spectroscopy. By analogy with the reactions of all other alcohols an esterification of MeLac yielding the octoate **11** was observed. However, this esterification proved to be of minor importance as the main reaction (up to 90 % at 180°C) consisted of a transesterification yielding methyl octoate **12** along with the tin lactate salt **13** which precipitated from the reaction mixture. The beginning of this precipitation was already observed at 100°C .

The SnO isolated from the reaction of $SnOct_2$ with various alcohols and the SnLactate **13** were used as catalysts for the polymerization of L-lactide at 150°C in bulk and high yields along with high molecular weights were obtained. These results and the aforementioned model reactions demonstrate that a $SnOct_2$ catalyzed polymerization of lactide may involve a variety of active species at least above 100°C. The formation of alkyl ester endgroups from the coinitiator does not prove that the tin alkoxides **1** or **2** are the only active species, because it was found that primary alcohols cleave polylactide chains quite rapidly above 100°C even in the absence of a catalyst (eq. (10)).

OctSn—O—SnOct

6

OctSn—O—Sn—OR

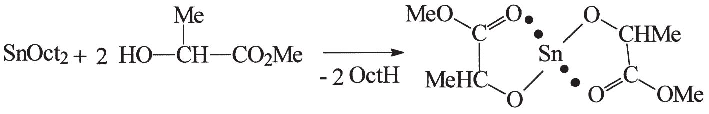
7

ROSn—O—SnOH

8

HOSn—O—Sn—OH

9



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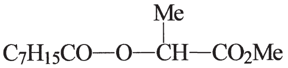
(9)

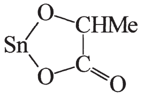


$C_7H_{15}CO-O-\overset{Me}{\overset{|}{C}}H-CO_2Me$

11

$C_7H_{15}CO-OMe$

12



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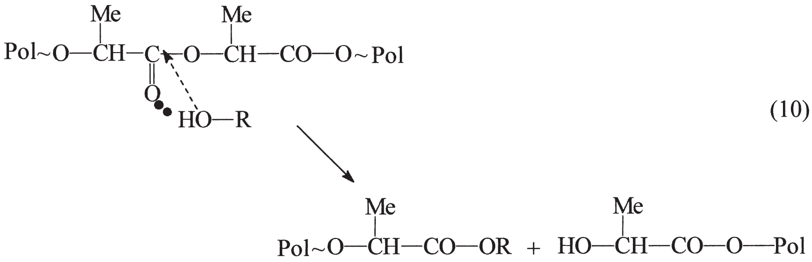
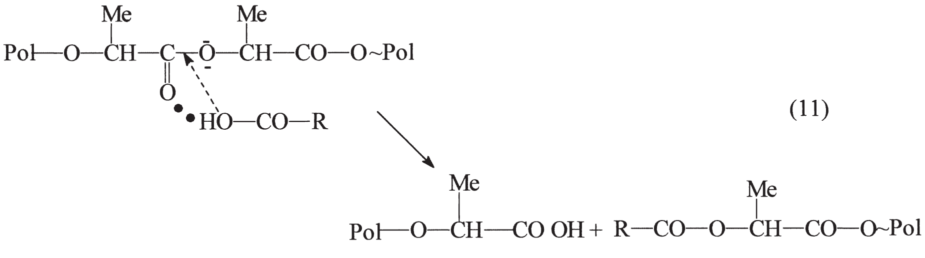


(10)



(11)

The most interesting results from polymerization experiments were obtained, when neat $SnOct_2$ was used as initiator at 180°C. As illustrated by the data in Tab. 1 the molecular weights increased with the monomer/initiator ratio and were higher than those obtained with SnO or SnLac. Furthermore, octoate endgroups were found by ^1H NMR spectroscopy in the precipitated polylactide samples. This result agrees well with the transesterification reactions yielding **11** or **12,** but it was quite unexpected, because several research groups have reported, that $SnOct_2$ initiated polylactones are free of octoate endgroups [10, 12 - 14]. The discrepancy between the literature and our new results is mainly a consequence of different reaction temperatures. All previous mechanistic studies were conducted at temperatures ≤ 150°C. Furthermore, it must be taken into account that the presence of a coinitiator suppresses the formation of octoate endgroups. The new results indicate that the polymerization process proceeding at 180°C is partially different from the mechanistic course below 100°C. The elucidation of the details requires further intensive studies.

Table 1: $SnOct_2$-initiated polymerization of L-Lactide in bulk at 180°C (time: 1h)

Polym. No.	$\frac{\text{Mon}}{\text{Ini.}}$	Yield$^{a)}$ (%)	$\eta_{inh}$$^{b)}$ (dL/g)	DP$^{c)}$
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) after precipitation into cold methanol
b) measured at 25°C with c = 2g/L in CH_2Cl_2
c) apparent degree of polymerization as determined by ^1H NMR spectroscopic endgroup analyses from the CH_3-signals of the octoate groups

Experiments with Bu_4Sn

Ph_4Sn was reported by Kohn et al. [15] to catalyse the polymerization of L-lactide in bulk at temperatures ≥ 120°C, but mechanistic studies were not conducted. When we tried to investigate the reactivity of Ph_4Sn it turned out that this compound is poorly soluble in all typical NMR solvents, so that NMR spectroscopic studies were not feasible. Therefore, we have concentrated our interest on Bu_4Sn which is a commercial chemical, a liquid which is soluble in many solvents and which allows purification by fractionated distillation.

When Bu_4Sn was mixed with benzylalcohol in $CDCl_3$ the ^1H NMR spectrum of benzylalcohol exhibited characteristic changes, because the coupling between OH and CH_2 protons became detectable indicating that the rapid exchange between the OH protons (typical for the neat alcohol) was interrupted. This observation suggests a weak complexation between Bu_4Sn and benzyl alcohol which is a prerequirement of the alternative coordination-insertion mechanism formulated in eq. (3). Furthermore, an acceleration of the polymerization process was observed when benzylalcohol was used as coinitiator of the Bu_4Sn-initiated polymerizations of ε-caprolactone. Also this finding is in agreement with the hypothetical mechanism of eg. (3) but it can not serve as a definite proof.

Regardless, if an alcohol was added as a coinitiator or not Bu_4Sn proved to be a sluggish initiator so that reaction temperatures ≥ 100°C were needed for polymerizations of ε-caprolactone with high conversions.

When tin alkoxides, such as Bu_3Sn-OMe or Bu_3Sn-OBzl were used as initiators under the same conditions far higher polymerization rates (at least by a factor of $10^{3)}$ were found. This finding means that a contamination of Bu_4Sn or a reaction byproduct in a concentration of O.1 mol % might also be responsible for the catalytic activity of Bu_4Sn yielding reactive covalent Sn-OR groups. For this purpose neat Bu_4Sn was heated with benzylalcohol to 120°C for 24 h. However, a cleavage of the Bu-Sn bond according to eq. (12) was not detectable by ^1H NMR spectroscopy (400 MHz, signal-to-noise ratio 10^5:1). Furthermore, Bu_4Sn was heated with benzylacetate to 120°C, to find out if a cleavage of the Bu-Sn bond according to eq. (13) may occur, but again no evidence was found. Moreover, dry CO_2 was bubbled through Bu_4Sn at 120°C with the purpose to detect a reaction according to eq. (14). Again no reaction was detectable.

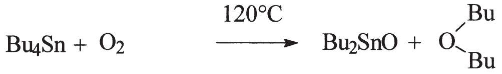
When attempts were made to elaborate time/conversion curves for ε-caprolactone initiated either by neat Bu_4Sn or by Bu_4Sn + benzylalcohol, an unusual poor reproducibility was found. This observation and the well known sensitivity of Sn-alkyl compounds to radical reaction [16] suggested to study the influence of oxygen on the reactivity of Bu_4Sn. In a model experiment air was bubbled through neat Bu_4Sn at 100 or 120°C and after 48 h a precipitate of Bu_2SnO was obtained along with the formation of dibuthyl ether (eq. (15)). Bu_2SnO is an oligomeric species which is poorly soluble in all inert organic liquids. However, it was found by ^{119}Sn NMR spectroscopy that approx. 1 % of Bu_2SnO remained dissolved in Bu_4Sn even at room temperature. Such an "impurity" may be responsible for the catalytic activity of Bu_4Sn because Bu_2SnO is known to be a good esterification catalyst [17] and it is also known as good initiator of β-lactones [18].

This interpretation was confirmed by measurements of time-conversion curves using four different samples of Bu_4Sn. One sample was partially oxidized with air at 100°C, the second sample was handled in air at 20°C, the third sample was handled under nitrogen and the fourth sample was handled under argon beginning with the opening of the original "Aldrich bottle". The polymerization rate of ε-caprolactone showed indeed a strong dependence on the pretreatment of Bu_4Sn samples. A more intense exposure to oxygen caused higher rates of polymerizations and the sample handled under argon was absolutely inactive. All these results together suggest that a partial oxidation of Bu_4Sn is in fact the origin of its catalytic activity in polymerizations of lactones. The exact mechanism of Bu_2SnO-initiated polymerizations is still unknown and deserves further investigations.

$$Bu_4Sn + HO\text{—}Bzl \overset{120°C}{\not\longrightarrow} Bu_3Sn\text{—}O\,Bzl + H\text{—}Bu \qquad (12)$$

$$Bu_4Sn + AcO\text{—}Bzl \overset{120°C}{\not\longrightarrow} Bu_3Sn\text{—}O\,Bzl + \text{—}CO\text{—}Bu \qquad (13)$$

$$Bu_4Sn + CO_2 \overset{120°C}{\not\longrightarrow} Bu_3Sn\text{—}O_2C\text{—}Bu \qquad (14)$$



$$Bu_4Sn + O_2 \xrightarrow{120°C} Bu_2SnO + O\begin{smallmatrix}\diagup Bu\\ \diagdown Bu\end{smallmatrix} \qquad (15)$$

CONCLUSION

The recently elaborated results summarized in this paper do not support the existence of the coordination-insertion mechanism of eq. (3). On the other hand, they do not allow a definite elimination of this mechanism. Most important is the observation that both initiators $SnOct_2$ and Bu_4Sn are capable of forming covalent and highly reactive Sn-OR bonds in the first stage of the polymerization process and these Sn-OR bonds (alkoxides or stannoxanes) initiate an efficient chain growth via the classical coordination-insertion mechanism outlined in eqs. (1) and (2). In the case of $SnOct_2$ it should be emphasized, that its activation by alcohols, water or other byproducts (e.g. linear oligolactones) is a complex process and several active species such as Sn-alkoxides, Sn-hydroxides and stannoxanes may be involved in the polymerization process. Furthermore, the temperature plays a role, and polymerizations conducted at 180°C or at 80°C differ in a variety of aspects, such as endgroups and formation of additional active species. Regardless of the details, it is the covalent character of all active species which allows for a racemization-free polymerization of L-lactide at temperatures up to 200°C (with optimization of the reaction time).

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