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The Use of Tetra(phenylethynyl)tin as an Initiator for the Ring-Opening Polymerization of Lactide

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Summary: Tetra(phenylethynyl)tin is an efficient initiator for the ring-opening polymerization of lactide, with or without the addition of isopropanol as a coinitiator, providing high activity and high molar mass polymers.

Polylactides (PLA) are an important class of biodegradable polymers commonly used for biomedical or pharmaceutical purposes.[1,2] The most important polymerization process for the preparation of PLA materials is the ring-opening polymerization (ROP) of lactide monomers initiated by an alkoxide or an alkanoate derivative of main-group[3] or rare-earth[4] metals. Due to its simple handling, fair activity, and low toxicity, tin bis(2-ethylhexanoate) ($Sn(O_2Oct)_2$) is a widely used initiator employed with an alcohol coactivator for the commercial production of polylactide.[5,6] However, recent studies of the mechanism of $Sn(O_2Oct)_2$-initiated lactide polymerization showed that the actual active species is not $Sn(O_2Oct)_2$ but an in situ formed Sn(II) alkoxide by alcoholysis of $Sn(O_2Oct)_2$.[7] In fact, dibutoxytin, $Sn(OBu)_2$, was found to be an effective single-component initiator for ROP, but it has also a tendency to aggregate in solution and forms, therefore, multiple initiating species.[8] Lately, we demonstrated that tetra(alkoxy)tin(IV) compounds are highly efficient single-component initiators for the ring-opening polymerization of lactide.[9] In particular, compounds having sterically hindered alkoxide ligands are attractive initiators, as their monomeric structure facilitates selective and living ROP.[9] However, tetra(alkoxy)tin(IV) compounds are fairly air and moisture sensitive and need cautious handling compared to $Sn(O_2Oct)_2$. Thus, the objective of the present work was to develop a new Sn(IV)-based ring-opening polymerization initiator combining the high activity of tetra(alkoxy)tin and the easy manipulation of $Sn(O_2Oct)_2$.

Recently, Jousseaume and co-workers reported the convenient hydrolysis and alcoholysis of tin−alkynyl bonds, leading to the formation of tin−oxide and tin−alkoxide species, respectively.[10] According to this, tetra(phenylethynyl)tin ($Sn(C{\equiv}CPh)_4$) can be considered an attractive candidate for the initiation of lactide ROP. Active sites are likely to be created by the alcoholic cleavage of the tin−alkynyl bond. Furthermore, its hydrolysis forms tin oxide, generally considered to be a nontoxic compound.[11] Moreover, the stability of the phenylethynyl−tin bond allows open-air handling for a short period of time. We report herein the use of tetra(phenylethynyl)tin as an initiator for the ring-opening polymerization of lactide, which, to the best of our knowledge, provides the first example of alkynyltin-initiated ring-opening polymerization.

Tetra(phenylethynyl)tin was synthesized according to a published procedure[12] and purified by recrystallization from a mixture of chloroform and hexane. Polymerization experiments were undertaken by treatment of the tin initiator with isopropanol prior to the addition of the lactide monomer.[13] A defined initiator-to-alcohol ratio [Sn]:[iPrOH] of 1:1 was initially employed in order to examine the selectivity of the activation process for the ROP (Table 1, entries 1−6).[14] The monomer conversion increased steadily with time, and a linear relationship

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[13] ^1H NMR of the product of the reaction of the tin complex with 1 equiv of isopropanol done under the polymerization experimental conditions shows the substitution of one phenylethynyl group by an isopropoxy substituent.

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Table 1. Ring-Opening Polymerization of Lactide with Tetra(phenylethynyl)tin as Initiator[a]

entry	catalyst	monomer	T (°C)	$[M]_0/[I]_0$[b]	reaction time (h)	conversion (%)[c]	M_n [d]	M_w [d]	MWD[d]
1	Sn/iPrOH[e] (1:1)	L-LA	75	200	2	25	2 900	3 000	1.02
2			75	200	2.5	30	3 400	3 500	1.03
3			75	200	3	35	3 800	3 900	1.03
4			75	200	5	50	5 600	5 800	1.02
5			75	200	6	62	5 900	6 100	1.12
6			75	200	20	97	15 800	23 200	1.46
7	Sn[f]	L-LA	75	200	1	11	14 500	17 700	1.11
8			75	200	2	23	24 100	27 200	1.13
9			75	200	2.5	28	29 600	32 600	1.10
10			75	200	3	33	34 500	39 400	1.13
11			75	200	6	62	38 100	43 200	1.13
12			75	200	20	85	69 900	84 600	1.21
13	Sn[g]	D,L-LA	140	5000	0.25	98	268 500	588 000	2.19
14			140	9000	0.25	98	491 400	1 007 400	2.05
15			140	10000	0.25	98	599 900	1 145 700	1.91

[a] Conditions: reaction conducted at 75 °C, initial monomer concentration $[M]_0$ of 1.0 M, ratio of monomer to initiator $[M]_0:[I]_0 = 200$. [b] Initial monomer concentration $[M]_0 = 1.0$ mol/L. $[I]_0$ is the initial initiator concentration. [c] Conversion experimentally determined by ^{1}H NMR. [d] Determined by GPC relative to polystyrene standards, with THF as the eluent, at 40 °C.[19] [e] In toluene at 75 °C, with isopropanol as the cocatalyst. [f] In toluene at 75 °C. [g] Bulk polymerization at 140 °C.

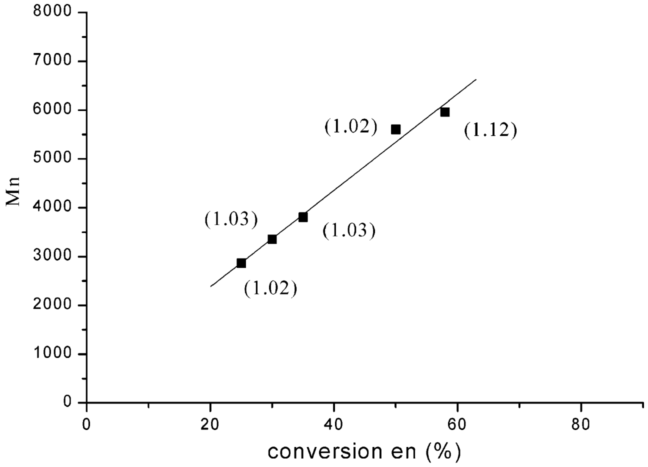
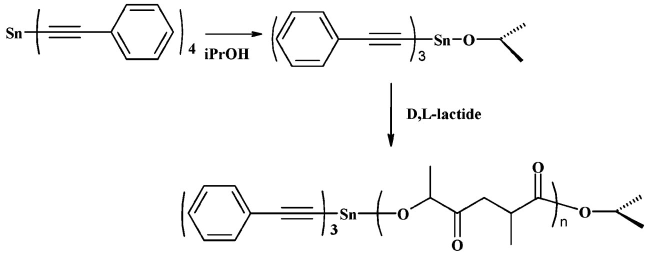


Figure 1. Plot of M_n as a function of the monomer conversion. $[M]_0:[I]_0 = 200$, in toluene, at 75 °C, with isopropanol as the cocatalyst in a 1:1 ratio with the initiator. PDI values are given in parentheses.

with M_n was found (Figure 1), indicating the occurrence of a living-type polymerization process.[15] Polylactides with narrow polydispersity indexes (PDI) were obtained, evidence of a uniform chain growth process and the absence of chain termination reactions. The broadening of PDI attained at high monomer conversions (Table 1, entry 6) is known for Sn(IV) initiators and is due to transesterification side reactions, which become more prevalent at high temperatures and low monomer concentrations.[16−18] ^{1}H NMR analysis of oligomers revealed the presence of an isopropyl ester end group (protons a and b, Figure 2). This suggests that the first monomer inserts into the Sn−O bond; thus, the ROP occurs through a coordination−insertion mechanism (Scheme 1).[9,19]

Scheme 1. Reaction Pathway for the Polymerization of Lactide with an Isopropanol Activated Tetra(phenylethynyl)Tin Initiator



When a higher initiator-to-alcohol ratio [Sn]:[iPrOH] = 1:4 was utilized, with reaction conditions otherwise similar to those described above, the polymerization activity was significantly enhanced. A nearly quantitative conversion (97%) was reached after 4 h, and the polymer formed had a low molar mass ($M_n = 9500$ g/mol, PDI = 1.2). This result is in good agreement with the assumption that a higher initiator-to-alcohol ratio should generate a higher concentration of initiating species. The addition of ϵ-caprolactone monomer gave a polylactide-*block*-polycaprolactone copolymer,[20] demonstrating that the propagating centers remain in an active form.

The intriguing possibility that tetra(phenylethynyl)tin could also act as a single-component initiator was investigated with L-lactide. In this case, the polymerization activities resembled those observed for the isopropanol-activated initiator (1:1 activation), but higher molar masses were obtained (Table 1, entries 7−12).[21]

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(14) Polymerization experiments were carried out in toluene at 75 °C with an initial monomer concentration of 1.0 mol/L. The initial monomer-to-initiator ratio ($[M]_0:[I]_0$) was 200:1.

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(20) The block copolymer was prepared as following: L-lactide (200 equiv relative to Sn) was polymerized for 4 h under conditions similar to those given in Table 1, and a GPC sample was taken ($M_w = 10\,000$ g/mol, MWD = 1.1). A portion of ϵ-caprolactone (200 equiv) was then added, and the polymerization proceeded to 92% conversion over 2 h, yielding the block copolymer PLA-PCL with $M_w = 24\,000$ g/mol and MWD = 1.59 with unimodal nature of a GPC curve. The GPC chromatogram is presented as Supporting Information.

(21) Molar masses were measured by GPC relative to polystyrene standards at 35 °C in THF. This causes a certain overestimation of the M_n and M_w values when compared to molar masses determined by ^{1}H NMR, but the method is frequently found in the literature. The GPC method offers, in any event, an efficient and qualitative tool to

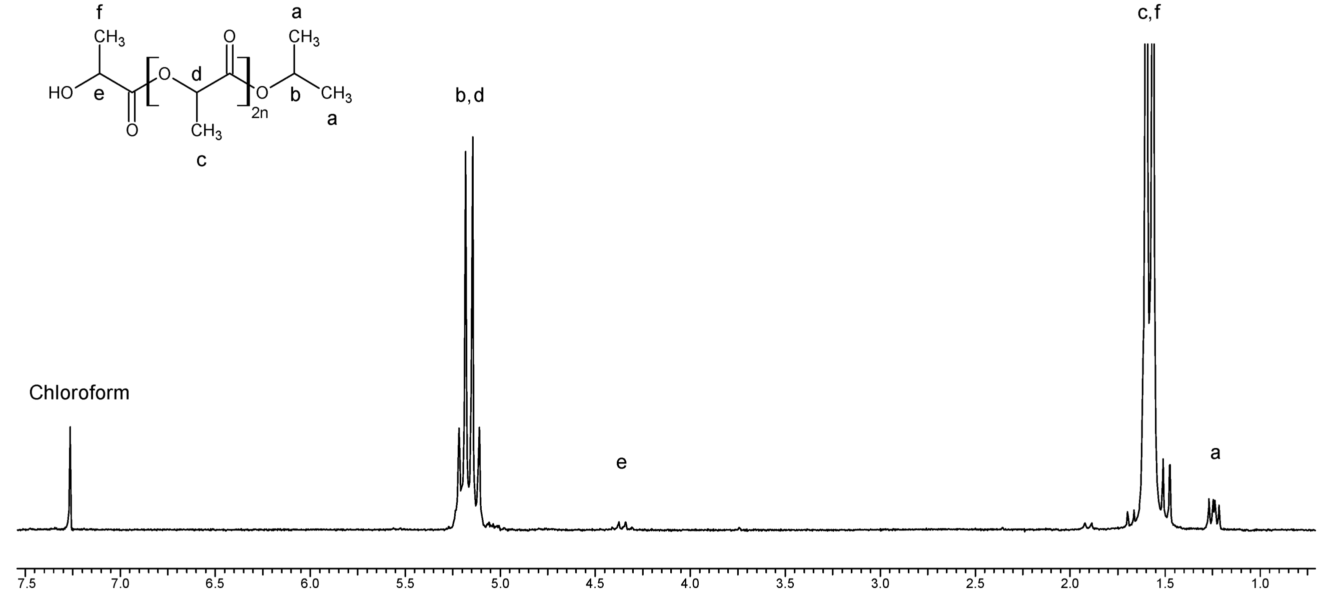

Figure 2. 200 MHz ^{1}H NMR spectrum of polylactide in $CDCl_3$ at 25 °C.

^{1}H NMR monitoring of the polymerization showed a clear time dependence for both the monomer conversion and the increase of molar mass (Table 1). The PDI values remain relatively narrow, indicating that the transfer reaction (transesterification) is suppressed throughout the polymerization reaction. The presence of phenylethynyl functions in the polymers was determined by ^{1}H NMR spectroscopy from a low-molecular-weight PLA sample prepared by using the monomer-to-initiator ratio $[M]_0:[I]_0 = 20$. The activation process was subsequently studied by the reaction of lactide with the tin initiator in a 4:1 ratio under reaction conditions similar to those for the polymerization experiments. The ^{13}C NMR spectrum of the resulting oligomer displays minor peaks at δ 35 and 97 ppm, consistent with an alkoxyethynyl bond $PhC{\equiv}C{-}O{-}C$,[22] which clearly underlines the occurrence of a first monomer insertion into the Sn−C bond. Interestingly, when a 1:1 ratio was employed, no insertion product was detected. Other examples concerning the use of compounds containing only Sn−C bonds as an initiator for ROP of lactides are rather sparse; to the best of our knowledge only tetraphenyltin has been used, resulting in a nonliving polymerization behavior.[23,24]

Bulk polymerization of D,L-lactide with tetra(phenylethynyl)tin without coinitiator was also investigated under various initiator-to-monomer ratios at 140 °C (Table 1, entries 13−15). In this case, the polymerization proceeds quite fast and a quantitative conversion of the monomer (>98% according to ^{1}H NMR) was obtained after less than 15 min. Molar masses measured by GPC increase with the $[M]_0/[I]_0$ ratio, and polymers with very high molar masses ($M_n = 2{,}7 \times 10^5$ to 6×10^5 g/mol) were obtained. The PDI values are higher than those obtained in toluene solutions at 75 °C. This phenomenon can be attributed to transesterification side reactions favored by the higher temperature.

In summary, this work describes the use of tetra(phenylethynyl)tin as a novel initiator for the ring-opening polymerization of lactides. This preliminary study shows that the polymerization occurs with or without the addition of isopropanol as the cocatalyst. Apparently, the polymerization proceeds through a classic coordination−insertion type mechanism when the isopropanol cocatalyst is used. Under the bulk conditions tetra(phenylethynyl)tin is a rather efficient initiator for ROP and produces high molar mass PLA. Further studies of kinetics and mechanistic details are currently in progress.

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Supporting Information Available: Figures giving NMR spectra of phenylethynyl terminated lactide oligomers and a GPC chromatogram of poly(lactide-β-caprolactone). This material is available free of charge via the Internet at http://pubs.acs.org.

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