Kinetics and Mechanism of L-Lactide Polymerization Using Two Different Yttrium Alkoxides as Initiators

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ABSTRACT: Polymerization of L-lactide in dichloromethane at 25 °C using an initiating system comprising tris(2,6-di-*tert*-butylphenoxy)yttrium and 2-propanol was first order in monomer and initiator. A propagation rate constant of 1.92×10^3 L mol^{-1} min^{-1} was determined using in situ UV spectroscopy. In the first step the large 2,6-di-*tert*-butylphenoxy ligands are exchanged for the sterically less demanding 2-propoxide ligands. In the second step the alkoxide is able to attack the carbonyl group with formation of the ring-opened product. After the first two initiating steps the polymerization can proceed until the equilibrium conversion of monomer is reached. Evidence for these three steps is provided by ^{1}H and ^{13}C NMR spectroscopy of the reaction products of each step. The kinetic behavior of commercially available yttrium isopropoxide was more complicated.

Introduction

Homo- and copolymers of poly(lactide)s are important biomaterials and are likely to gain an important position in the biodegradable polymer field as well. The recent completion of large-scale production facilities for the raw materials required for the production of these polymers will accelerate this development. Commonly, ring-opening polymerization of L-lactide is applied for the preparation of high molecular weight poly(lactide)s. Combined with the continued interest in poly(lactides)s as biomaterials, the design of improved synthetic routes for these materials is a challenge.

Anionic polymerization of lactones by alkali-metal alkyls or alkali-metal alkoxides can be very fast but is problematic for two reasons. Inter- or intramolecular transesterification reactions, leading to the formation of macrocycles and broadening of the molecular weight distribution are usually encountered in the anionic polymerization of lactones and have to be avoided.[1−5] Additionally, proton abstraction can occur, because the proton attached to the chiral carbon atom in the ring has a high p*K* value.[6−8] This leads to loss of molecular weight control and to racemization with decrease of crystallinity.

It was shown that aluminum and zinc alkoxides can also be used for the controlled polymerization of lactide.[9−11] Although with the use of these initiators almost no side reactions are observed, it is clear that they exhibit a low activity in lactide polymerization compared to anionic initiators. Exact kinetic data are scarce and only in one limited study a propagation rate constant of 0.60 L mol^{-1} min^{-1} was determined for the polymerization of D,L-lactide in toluene at 70 °C using aluminum isopropoxide as an initiator.[9]

Recently it was reported that trivalent rare-earth alkoxides can initiate living polymerization of monomers such as ϵ-caprolactone,[12−14] L-lactide,[14−16] and β-butyrolactone,[16] with activities unprecedented in the coordination polymerization of these monomers. The use of lanthanide-based systems for the living polymerization of these monomers is a relatively new development, and only a few studies have appeared. The applicability of these systems in macromolecular engineering has been demonstrated.[17−21] Lanthanide-based systems are especially promising for lactide polymerization as these initiators potentially combine the good properties of anionic and aluminum initiators. Only general descriptions of the polymerization process are currently available.

In this study the kinetics and mechanism of lactide polymerization initiated by a commercially available yttrium alkoxide, $Y_5(\mu\text{-O})(O^iPr)_{13}$ (**1**), and by a novel catalyst system comprising tris(2,6-di-*tert*-butylphenoxy) yttrium (**2**) and 2-propanol are discussed. Kinetic data which allow a comparison with other systems are provided and NMR data are presented to support the mechanism proposed.

Experimental Section

Materials. L-(−)-Lactide (Purac Biochem b.v., Gorinchem, the Netherlands) was used as received. 2-Propanol was dried over CaH_2 prior to distillation. Tris(2,6-di-*tert*-butylphenoxy)-yttrium ($Y(OAr'')_3$) was prepared as described previously.[22] Stannous(II) ethylhexanoate (stannous octoate, $Sn(Oct)_2$, Sigma Chem. Co., St. Louis, MO) was used as received. Toluene-d_8 and dichloromethane-d_2 (Merck-Schuchardt, Darmstadt, Germany) were dried by stirring over CaH_2 and vacuum transferred in a special grease-free distillation apparatus. Chloroform-d_1 (Merck-Schuchardt, Darmstadt, Germany) was used as received. All glassware for the preparation of living oligomers was dried before use, and reactions were carried out in a Braun 150 GI drybox under nitrogen.

Preparation of Living Oligomers. In a typical experiment 50 mg (0.071 mmol) $Y(OAr'')_3$ was dissolved in 250 μL of the appropriate NMR solvent in a 2 mL mixing vessel with Teflon-coated magnetic stirrer. In a separate vessel 16.3 μL (0.213 mmol) of 2-propanol was added to a solution of a 2- or 8-fold molar excess of L-lactide relative to 2-propanol in 250 μL of the NMR solvent. The $Y(OAr'')_3$ solution was added to the monomer/co-initiator solution, and the resulting solution was stirred for 2 min and transferred to a Pyrex NMR tube with vacuum adapter. The solution was frozen in liquid nitrogen and the NMR tube was flame sealed under a pressure of 0.06 mbar and gently warmed to room temperature.

Preparation of Model Hydroxyl-Terminated Oligomers. A solution of 1 g (16.6 mmol) of 2-propanol was refluxed in the presence of a 2- or 8-fold molar excess of monomer and 100 mg of $Sn(Oct)_2$ in 15 mL of toluene for 3 h. All volatiles were removed by means of a rotavapor and the resulting oligomers were characterized by ^{1}H and ^{13}C NMR spectroscopy.

Kinetic Experiments. Glassware was dried overnight in an oven at 130 °C. A hot reaction vessel was connected to a

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high-vacuum line, cooled under argon outflow and evacuated to 10^{-5} mmHg and flushed with argon again. UV spectra were recorded with a MCPD spectro multichannel photodetector (Otsuka Electronics). Spectra were measured directly in the reaction mixture by means of an immersed fiber optics probe. The probe had been fitted to the reaction vessel in order to allow experiments in a perfectly closed system. The sampling time of the spectra was varied according to the progress of the reaction with a minimum of 1 s/spectrum and with a maximum of 80 spectra in total. An optical path length of 5.75 mm was used, which was calculated based on the absorption of styrene in hexane at 280 nm.[23] Reference and background spectra were recorded with a solution containing 2,6-di-*tert*-butylphenol (HOAr″) in the same concentration as calculated for the final polymerization mixture.

To a solution of monomer and co-initiator of known concentration, prepared in a drybox, an appropriate amount of catalyst was added, and the optical density was followed with time. The final conversion was established by ^{1}H NMR spectroscopy after quenching the polymerization with a 10-fold excess of acetic acid. The optical densities were related to the conversion by assuming a linear relationship between the variation of optical density and conversion. This assumption was verified by preparing mixtures of L-lactide and poly(L-lactide) over a range corresponding to conversions from 5 to 95%.

Characterization. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AC 250 operating at 250 MHz (^{1}H) or 62.5 MHz (^{13}C) with 60 and 2400 scans, respectively, for the living oligomers and 16 and 160 scans, respectively, for the hydroxyl-terminated model oligomers. Gel permeation chromatography (GPC) was used to determine molecular weights and molecular weight distributions (M_w/M_n). A Waters 6000A GPC apparatus equipped with three Waters μStyragel (10^3, 10^4, 10^5 Å pore diameter) columns was used, combined with a H502 viscometer detector (Viscotek Corp.) for determination of absolute values of molecular weights. Polymers were dissolved in tetrahydrofuran (1.0 wt %) and elution was performed at 25 °C at a flow rate of 2.0 mL/min using THF as eluent.

Results and Discussion

Yttrium compounds containing yttrium−hydrogen, yttrium−carbon, and yttrium−nitrogen bonds are very reactive toward substrates containing activated hydrogen atoms, predominantly by acid−base type reactions.[24] For the synthesis of well-defined poly(lactides), lanthanide catalysts with strong basic properties have to be avoided, because the side reactions encountered in traditional anionic polymerization of lactides can be expected for these compounds as well.[25] Alkoxides are ligands of potential interest, because the highly electropositive lanthanide elements are stabilized by the electronegative oxygen atoms and thus decrease the reactivity of these elements in acid−base reactions.

It was already reported that commercially available yttrium isopropoxide is a suitable initiator for the preparation of block copolymers of ϵ-caprolactone and L-lactide by sequential polymerization.[3] Yttrium isopropoxide is a cluster compound in which five yttrium atoms are attached to a single central oxygen atom,[26] $Y_5(\mu\text{-}O)(O^iPr)_{13}$ (**1**). The core structure of this molecule is depicted in Figure 1.

Complexes containing bridging oxide and chloride ions are abundant in lanthanide alkoxide chemistry,[27] and the reactivity of **1** in ring-opening polymerization could be a good example of this class of compounds.

Homopolymerization of L-lactide using yttrium isopropoxide as an initiator was carried out at various monomer over initiator ratios. End-group analysis revealed that only poly(lactide)s with isopropoxycarbonyl end groups were formed. The number of active catalytic sites was determined by measuring the degree of polymerization as a function of the monomer to initiator ratio. A linear relation between the degree of polymerization and the molar monomer to initiator ratio was found (Figure 2).

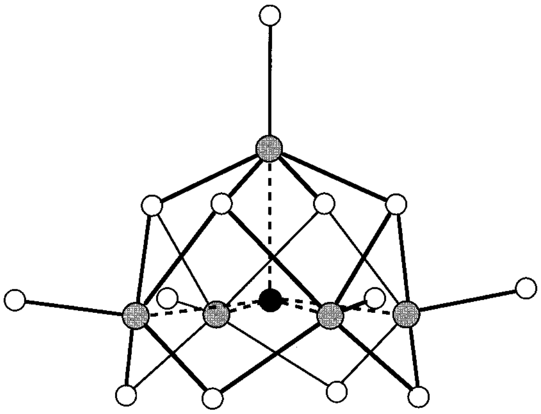


Figure 1. Core structure of $Y_5(\mu\text{-}O)(O^iPr)_{13}$ (**1**) as determined by Poncelet et al. by single-crystal X-ray diffraction.[26] Yttrium atoms are represented by gray circles, and oxygen atoms by white circles. The black circle in the center represents the μ-5 oxygen atom connecting all the yttrium atoms. All other atoms are left out for clarity.

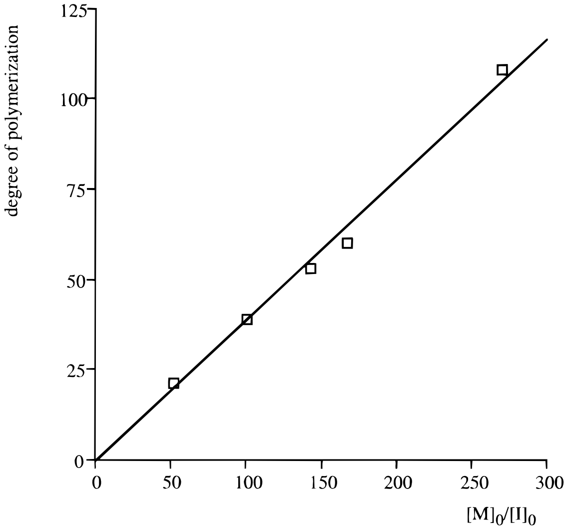


Figure 2. Degree of polymerization determined by end-group analysis using ^{1}H NMR spectroscopy as a function of monomer over initiator ratio for L-lactide polymerization using **1** as an initiator in dichloromethane at 22 °C.

The stoichiometry of the cluster compound yttrium isopropoxide is $Y_5(\mu\text{-}O)(O^iPr)_{13}$ (**1**),[26] and thus the average number of possible polymerization sites/Y is 2.6. The line through the origin has a slope of 0.39, close to the theoretical value of 0.38. Molecular weight distributions of approximately 1.15 were obtained. It was concluded that all isopropoxide groups are active as initiators in the polymerization of L-lactide and the polymerization proceeds in a living manner.

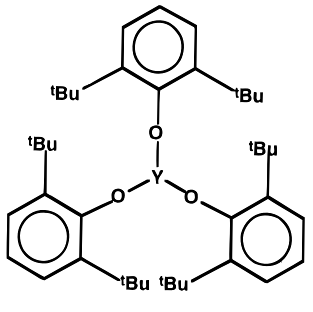
The use of tris(2,6-di-*tert*-butylphenoxy)yttrium ($Y(OAr'')_3$, **2**) as a catalyst in the ring-opening polymerization of L-lactide was evaluated, because this compound, in contrast to **1**, does not contain a bridging oxide anion and is known to be disassociated in solution.[22,28] The molecular structure of **2** in the solid state has been

Table 1. Polymerization of L-Lanthanide Initiated with Tris(2,6-di-*tert*-butyl phenolate) Lanthanides[a] and Various Alcohols ($[M]_0/[ROH]_0/[1]_0$ of 50/1/0.3) in Dichloromethane

no.	monomer	co-initiator	reaction time (min)	conversion (%)	$10^{-3}\,\bar{M}_{n,calc}$ (g/mol)	$10^{-3}\,\bar{M}_{n,NMR}$ (g/mol)	$10^{-3}\,\bar{M}_{n,GPC}$ (g/mol)	$\bar{M}_w/\bar{M}_n$
1	L-LA	^{i}PrOH	5	98	7.2	7.1	10.8	1.14
2	L-LA	^{n}BuOH	5	100	7.2	6.6	8.6	1.16
3	L-LA	Me_2NEtOH	3	99	6.5	6.9	8.4	1.11
4	L-LA	MeOEtOH	3	99	6.5	5.6	7.9	1.04
5[b]	L-LA	PEG1000	2	94	15.4	18.5	21.0	1.16
6	L-LA	^{i}PrOH	3	98	7.2	7.1	10.8	1.14

[a] All reactions were carried out using tris(2,6-di-*tert*-butylphenoxo)yttrium as an initiator, except no. 6, which was carried out using tris(2,6-di-*tert*-butylphenoxo) lanthanum. [b] In this case, a dihydroxyl-functionalized poly(ethylene glycol) was used as co-initiator.

determined by single-crystal X-ray diffraction and in solution by NMR spectroscopy and cryoscopy.



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Polymerization of L-lactide in the presence of **2** in dichloromethane did not have the expected polymerization characteristics. Slow conversion of monomer did occur (complete after 10 h), but signals for specific end groups could not be detected in the ^1H NMR spectrum of the isolated polymer. The molecular weight determined by GPC was much higher than expected from the assumption that every phenoxide ligand initiated polymerization ($M_{n,calc}$ = 7600 g/mol, $M_{n,found}$ = 29.300 g/mol, M_w/M_n = 1.71). Apparently, no direct insertion of monomer into the yttrium oxygen bond of **2** is possible. In this case, initiation seems to occur not by a coordination insertion mechanism but possibly by proton transfer from monomer or solvent or trace impurities to initiator.

The lack of reactivity of the yttrium−oxygen bond in **2** triggered a different approach. Ligand exchange in soluble lanthanide metal alkoxides with alcohols is generally very fast.[27] Addition of a sterically more accessible alcohol to **2** and in situ generation of a small alkoxide ligand by alcohol−alkoxide exchange might result in an effective initiating system.

This new concept was evaluated by the addition of **2** to a reaction mixture containing L-lactide and an alcohol the latter functioning as co-initiator. The reaction rate increased dramatically and good control over molecular weight and end-group identity was obtained.[29] Polymers prepared by this method had unimodal, symmetric molecular weight distributions with a polydispersity between 1.04 and 1.16 as shown in Table 1.

Molecular weights determined by NMR and GPC were close to calculated values. The presence of 2,6-di-*tert*-butylphenol did not affect the polymerizations and this compound was easily removed from the polymer by precipitation. The relative inertness of the phenolic proton of 2,6-di-*tert*-butylphenol has been described in the literature.[30,31] The end groups of the resulting polymers consisted only of the alkyl ester group of the added alcohol and lactyl hydroxyl groups. On the basis of these findings, a three-step mechanism is proposed for the polymerization of lactones using the tris(2,6-di-*tert*-butylphenoxy) yttrium ($Y(OAr'')_3$, (**2**))/alcohol system (eqs 1−3).

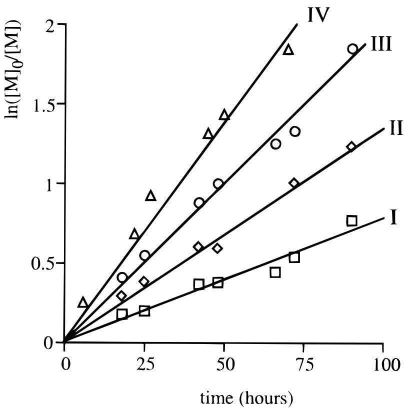
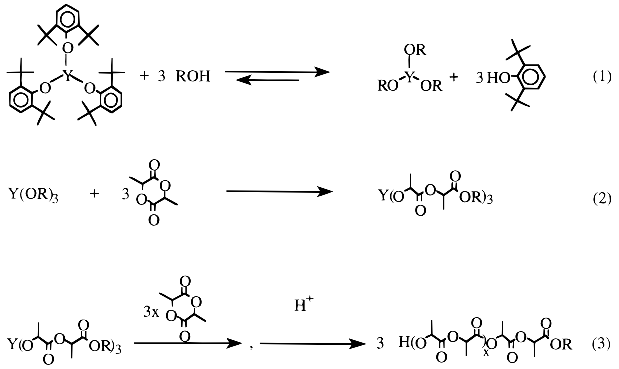


Figure 3. Semi-logarithmic plots of L-lactide ($[M_0]$ = 175 mM) conversion in time initiated by **1** at four different initiator concentrations (I: $[I]_0$ = 0.58 mM; II: $[I]_0$ = 1.16 mM; III: $[I]_0$ = 2.33 mM; IV: $[I]_0$ = 5.8 mM) in dichloromethane at 22 °C.



In the first step the large 2,6-di-*tert*-butylphenoxy ligands are exchanged for the sterically less demanding 2-propoxide ligands. In the second step the alkoxide is able to attack the carbonyl group with formation of the ring-opened product. After the first two initiating steps the polymerization can proceed until the equilibrium conversion of monomer is reached. The method has the advantages of efficiently producing polymers with control over the molecular weight, molecular weight distribution, and end groups, which allows for the preparation of polymers with a wide variety of end groups as they are determined by the chemical structure of the added co-initiator, which can be an alcohol, primary amine, or a sterically unhindered secondary amine.

Kinetics of L-Lactide Polymerization. The conversion with time of L-lactide at various concentrations of **1** in dichloromethane at 25 °C was monitored by ^1H NMR analysis of samples withdrawn from the reaction

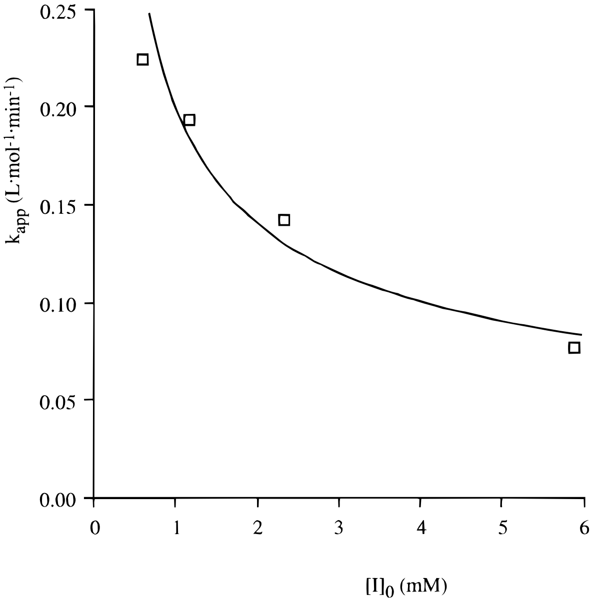


Figure 4. Apparent rate constant of L-lactide polymerization initiated by **1** at various initiator concentrations in dichloromethane at 22 °C.

mixture. The corresponding first-order kinetic plots for the polymerization are shown in Figure 3.

The polymerization is apparently first-order in monomer under the conditions studied. Apparent rate constants are plotted as a function of initiator concentration in Figure 4.

The curved nature of this plot indicates that species of different activity are present during polymerization, possibly generated by partial or complete disassembly of **1** upon coordination of monomer and/or polymer. However, identification of these species is not straightforward. In the concentration range studied, overall rate constants of 0.076 L mol^{-1} min^{-1} ($[I]_0 = 5.8$ mM) to 0.22 L mol^{-1} min^{-1} ($[I]_0 = 0.58$ mM) were determined. For the only other yttrium compound studied so far, $Y(OEtNMe_2)_3$, the kinetics were reported to be zero order in monomer and a propagation rate constant of 30 min^{-1} was found.[12] This is the only example of lactone polymerization with kinetics zero order in monomer, which was explained by the presaturation of the metal center by coordinated monomer. On the basis of the available data, which were rather limited, it could be argued equally well that the polymerization is first order in monomer with slow initiation.[32,33] This could explain the increasing value of the apparent rate constant with time, the induction period, and the finding that not all alkoxide groups had reacted to form high molecular weight polymer. We have established that the addition of triethylamine slows down the polymerization of L-lactide by **1** by at least a factor of 2 ($[NEt_3] = [O^iPr^-]$). This means that tertiary amines can very effectively compete with lactones for metal coordination sites. If this coordination can be achieved intramolecularly in a bidentate coordination mode as in $Y(OEtNMe_2)_3$, this could drastically affect the initiation properties of the yttrium alkoxide in lactone polymerization.

In related aluminum alkoxide chemistry, only one example can be found. The polymerization of D,L-lactide in toluene at 70 °C using $Al(O^iPr)_3$ was found to proceed with a propagation rate constant of 0.60 L mol^{-1} min^{-1}.[9] Four points were measured up to only 20% conversion, and an induction period was observed.

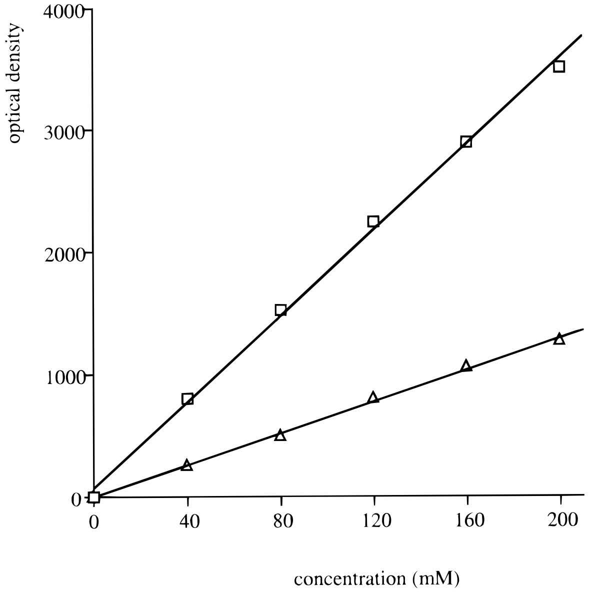


Figure 5. Dependence of the optical density for L-lactide (squares) and poly(L-lactide) (triangles) as a function of concentration at λ_{max} of 240 nm in dichloromethane.

A comparison of the kinetics of L-lactide polymerization initiated by **1** and other systems is thus hampered by lack of data. Qualitatively, it is clear that for an yttrium alkoxide initiated polymerization of L-lactide the rate of propagation by **1** is relatively low.[15,16,29] We attribute this to the cluster character of this compound, which leads to sterically very crowded polymerization sites.

Even in dilute dichloromethane solution at room temperature the polymerization of L-lactide was complete within 2 min using the **2**/2-propanol system. In this case, determination of conversion by manual sampling could not be realized. Several techniques are available to study such reactions, including flow-tube techniques, stirred tank reactors with magnetically driven valves, calorimetric devices, dilatometric devices, and specially designed reactors with an optical cell placed in the reactor.[34]

It was established that the UV extinction coefficient of the carbonyl groups of lactones is lower in the linear polymer than in the cyclic monomer (Figure 5).

This finding was used to monitor in situ monomer conversion in time by UV spectroscopy. Spectra were obtained by means of an immersed fibre optics probe placed directly in the reaction mixture. The probe is connected by an optical fibre to a UV or vis source and a spectrophotometer, which in turn are connected to a computer for control of the experiment and data processing. Up to 80 data points in one experiment can be collected, and the minimum time between spectra is about 1 s under ideal conditions. The reaction vessel is connected to a high-vacuum line and is suitable for highly air- and moisture-sensitive polymerizations. A polymerization of L-lactide in dichloromethane was carried out and the optical density was followed with time (Figure 6).

The optical density was related to the monomer conversion and in this way the kinetic plots for the polymerization of L-lactide using the **2**/2-propanol system were obtained as shown in Figure 7.

The polymerization is first order in monomer and also in initiator, because of the constant value of the apparent rate constant divided by the initial initiator con-

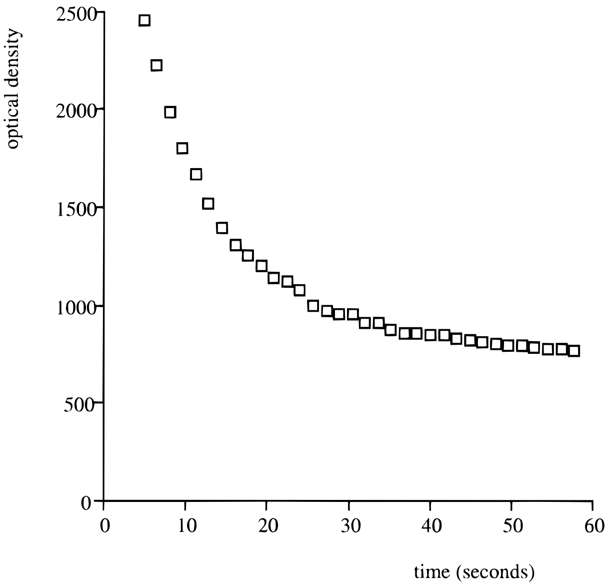


Figure 6. Variation of the optical density with time during a L-lactide (0.14 M) polymerization initiated by **2**/propanol ($[I]_0 = 0.9$ mM) in dichloromethane (25 °C).

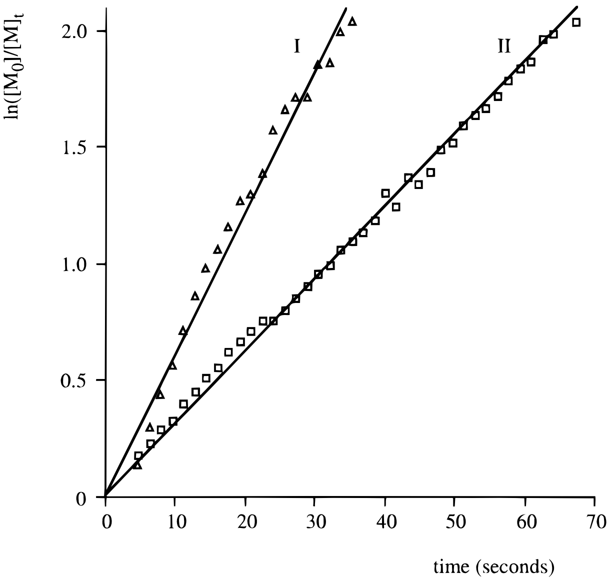


Figure 7. Semilogarithmic plots of L-lactide (0.14 M) conversion with time initiated by the **2**/2-propanol system at two different initiator concentrations (I: $[I]_0 = 2.0$ mM; II: $[I]_0 = 0.9$ mM) as monitored by in situ UV spectroscopy in dichloromethane at 25 °C.

centration. Unfortunately, we were unable to reliably measure the progression of L-lactide polymerization over a broader range of initiator concentrations. At higher initiator concentration the polymerizations became too fast even for the present measuring system. At lower initiator concentrations problems of stoichiometry were encountered, e.g., matching the concentration of **2** and 2-propanol and the absolute amount of 2,6-di-*tert*-butylphenol released by **2** used for measuring the background spectrum. Nevertheless, within the range of initiator concentration measured, a propagation rate constant of 1.92×10^3 L mol^{-1} min^{-1} was calculated from the slope of the curves.

Lactide polymerization with comparable reaction half times (on the order of minutes) have been carried out using anions generated by potassium compounds.[35] However, great care must be taken to avoid racemization or cyclization in this type of polymerization.[6-8] As far as coordination polymerization is concerned, the activity of the current initiating system is indeed unprecedented in lactide polymerization.

No induction period was observed, which is an indication that extensive rearrangement processes are not a prerequisite for polymerization. The extinction coefficient of **2** is very high but its signal disappears within the mixing period. The exchange of 2,6-di-*tert*-butylphenoxy ligands of the catalyst with 2-propanol is very fast, since the polymer molecular weights and end-group identity could be predicted from the amount of alcohol added, it is likely that the active centers are generated as unassociated species in the presence of monomer and that these species have no tendency to associate during polymerization.

It was established that the addition of of 2,6-di-*tert*-butylphenol to a reaction mixture containing L-lactide and **1** did not affect the polymerization characteristics, the kinetics of a polymerization carried out in the presence of 2,6-di-*tert*-butylphenol being virtually identical with polymerization without the addition of this compound.

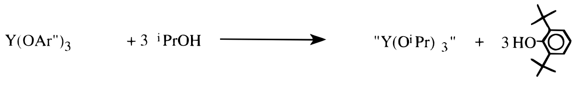
This shows that the large differences between the kinetics of L-lactide polymerization initiated by **1** and **2**/2-propanol are not due the presence of 2,6-di-*tert*-butylphenol. In general, the kinetics of lactone polymerization by lanthanide alkoxides do not seem to be related to the degree of association (as for aluminum alkoxides) in solution, but to the presence of covalently bridging atoms and nature of the ligands.

NMR Experiments. As the best results in L-lactide polymerization were achieved with the **2**/2-propanol system, it would be of great interest to identify in solution some of the species involved.

When **2** was reacted with 3 equiv of 2-propanol and the reaction mixture was analyzed in situ with ^{1}H and ^{13}C NMR spectroscopy, the 2,6-di-*tert*-butylphenoxy ligands were replaced by isopropoxide ligands. In the ^{1}H NMR spectrum recorded in CD_2Cl_2 signals are found at $\delta = 4.4$ ppm (broad, CH) and 1.2−1.7 ppm (multiplet, CH_3), clearly shifted downfield from the signals of 2-propanol (δ = 3.95, m, CH; 1.15, d, CH_3). The chemical shifts are in agreement with those reported for $Y_5(\mu\text{-}O)(O^iPr)_{13}$ (**1**), but the distinct features of the methyl group signals in this compound (three doublets at 1.50, 1.29, and 1.05 ppm) are absent.[26] It is of great importance to establish whether **1** or some other species is formed under the conditions used for the polymerization of lactones, because the activities of the **2**/2-propanol system and **1** in lactide polymerization are vastly different (vide infra). It has been reported that the solid prepared by contacting $Y[N(SiMe_3)_2]_3$ at room temperature with excess 2-propanol, after removal of all volatiles (2-propanol and $HN(SiMe_3)_2$), has a ^{1}H NMR spectrum which is complex and different from that of **1** (eq 4).[36]

$$Y[N(SiMe_3)_2]_3 + x\ {}^iPrOH \longrightarrow \text{"}Y(O^iPr)_3\text{"} + (x-3)\ {}^iPrOH\uparrow + 3\ HN(SiMe_3)_2\uparrow \quad (4)$$

$$5\ \text{"}Y(O^iPr)_3\text{"} \longrightarrow 1 + O(^iPr)_2 \quad (5)$$



(6)

Only upon heating in refluxing 2-propanol, this complex was converted to **1**, and it was suggested that

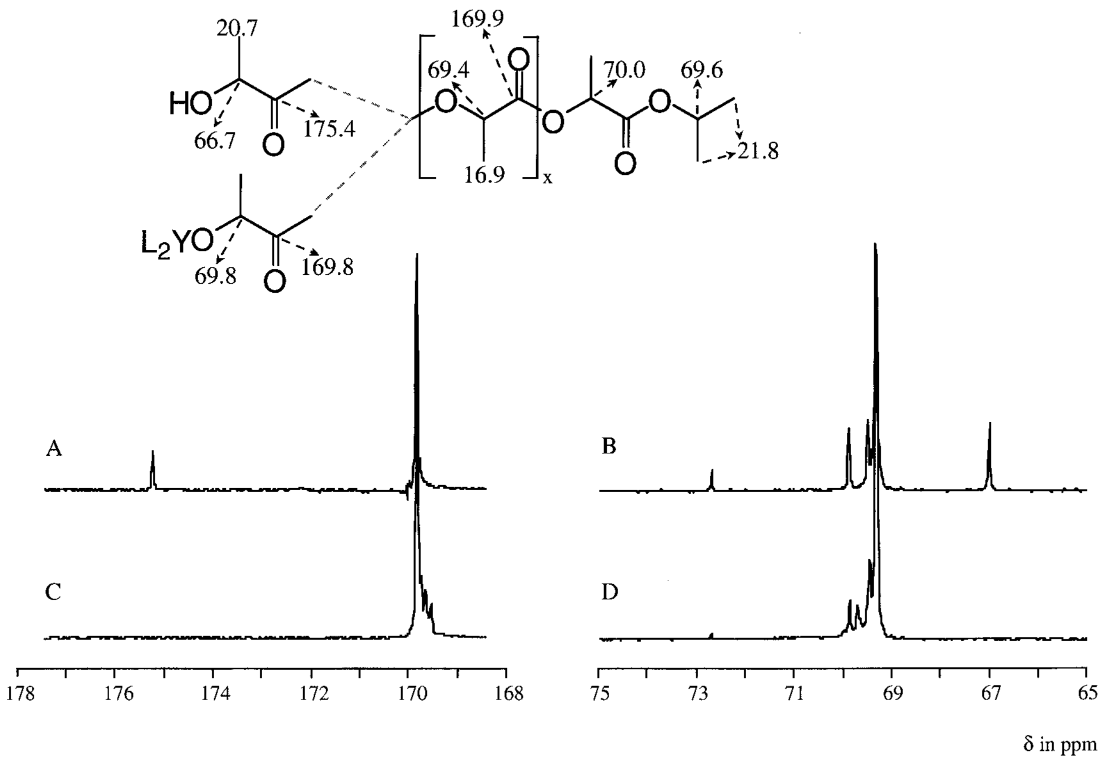


Figure 8. Full assignment of ^{13}C NMR spectra of living oligomers of L-lactide inititated with the **2**/2-propanol system in dichloromethane-d_2 (C and D) and details of hydroxyl-terminated oligomers) (A and B), A and C carbonyl region, and B and D methine region. A signal for residual monomer can be discerned at 72.6 ppm, which in the case of the living oligomer corresponds to the equilibrium concentration of L-lactide in the reaction mixture.

this conversion was accompanied by the formation of diisopropyl ether (eq 5).

It is likely that the reaction product of the reaction of **2** with 3 equiv of 2-propanol is very similar to the product formed in eq 4, because the reactions are carried out under similar mild conditions (eq 6).

The ^{13}C NMR spectrum of the yttrium isopropoxide generated by the **2**/2-propanol system shows two multiplets centered around $\delta = 67.0$ (CH) and 28.4 (CH_3) ppm, but again with a fine structure different from **1** (separate signals at 67.6, 67.3, 67.0 (CH) and 29.0, 28.5, 27.7 (CH_3) ppm, respectively). Probably the presence of various aggregation forms in equilibrium in the absence of monomer, fast reversible coordination or exchange with the 2,6-di-*tert*-butyphenol and overlap of signals hinder a detailed interpretation of the NMR spectra. Similar observations have been made repeatedly for other lanthanide alkoxides.[27] In a control experiment, the activity of a **2**/2-propanol mixture for lactide polymerization did not decrease for at least 2 h, again indicating that formation of **1** does not occur under the polymerization conditions. Also, a **2**/2-propanol mixture was kept in toluene-d_8 at 100 °C for a week, but even at these conditions the formation of **1** could not be established.

From the kinetic experiments it was concluded that association of the initiator generated by reaction of **2** and 2-propanol in the *presence* of monomer does not occur. In the *absence* of monomer, association probably does occur as indicated by the complicated NMR spectra of mixtures of **2** and 2-propanol. This appears to be a dynamic process because the initiating activity of the solution is retained. This is in sharp contrast with the association behaviour of aluminum trisisopropoxide in which very slow interconversion occurs between different associated species, with very different initiating properties. The dynamic behavior of the yttrium alkoxides might be related to the much larger coordination sphere of yttrium compared to aluminum. When the most common coordination numbers for Al^{3+} and Y^{3+} are compared, it is striking that the ionic radius of Al^{3+} increases from 53 pm for four-coordinate aluminum to 68 pm for six coordinate Al^{3+}, while the ionic radius increases from 90 pm for six coordinate Y^{3+} to 108 pm for nine-coordinate Y^{3+}.[37]

Similar ^{1}H NMR spectra were obtained for oligomers of L-lactide prepared in CD_2Cl_2 by the **2**/2-propanol system and the model hydroxyl-terminated oligomers prepared by mixing L-lactide and 2-propanol in toluene in the presence of stannous octoate. The only differences are the distinct signals of the HOC*H*(Me)– (4.35 ppm) end groups of the hydroxyl-terminated oligomers signals upfield relative to the polymer backbone signal, which are absent in the living oligomers. Probably, in the living oligomer the signal of the yttrium-terminated end group coincides with the polymer backbone signal. The ^{13}C NMR spectra of these oligomers appeared much more informative than the corresponding ^{1}H NMR spectra. The living oligomers and model hydroxyl-terminated polymers with degrees of polymerization of approximately two and eight allowed the complete assignment of the signals in the ^{13}C NMR spectra.

For the oligomers the most informative parts of the spectrum are the α-oxygen methine region (65–72 ppm) in which four signals are visible and the carbonyl region (167–177 ppm). These regions are shown in Figure 8, combined with a full assignment of all signals.

The NMR spectra of hydroxyl-terminated oligomers are obviously different from the living oligomers. From the sharp signals of the yttrium-terminated chain ends, as well as from the 2,6-di-*tert*-butylphenol signals (data not shown) it can be concluded the 2,6-di-*tert*-butylphenol does not interact with the metal centers.

An interesting feature in the ^{13}C NMR spectra of the oligomers with a degree of polymerization of two is the presence of some additional signals at 70.1 ppm in the "living" oligomer and at 69.6 ppm in the hydroxyl-terminated oligomer. These are attributed to the methine group of the isopropyl end group if there is only one lactyl unit between this group and the other end group ($XOCH(Me)C(O)OC\mathit{H}(Me)_2$, X = H or Y). Such a sequence can only be a result of intermolecular transesterification, because for intramolecular transesterification no favorable conformation can be achieved. It was observed that upon prolonged standing of living polymerization mixtures, broadening of the molecular weight distribution occurred. It is still an open question if this can happen in the presence of monomer or other coordinating compounds as well.

So far the oligomers prepared were described as "living". To investigate if this is indeed a proper designation, the activity of the living oligomers in lactide polymerization was determined. The reactions were carried out at room temperature by adding the contents of a NMR tube to a L-lactide solution in dichloromethane in such a way that if the polymer would form in a living manner, it would have a molecular weight of approximately 8000 g/mol. The time elapsed between the preparation of a solution for NMR analysis and the activity test was at least 10 days. All living oligomers of L-lactide were able to reinitiate L-lactide polymerization. Near complete conversion of lactide monomer ($t^{1/2}$ between 5 and 30 min) was reached with formation of poly(lactide) block copolymer with the molecular weight calculated from the stoichiometric ratios. The activity of the initiator solutions thus has decreased in time compared to the activity of a freshly prepared initiator solution. Probably this is caused by reversible aggregation of metal centers after depletion of monomer. In view of the fact that the activities are still at least comparable to those reported for other yttrium-based systems such as $Y(OEtNMe_2)_3$, the oligomers prepared can be regarded as living systems.

Conclusions

L-Lactide polymerization using the **2**/2-propanol system in dichloromethane at 25 °C is first order in monomer and initiator. A propagation rate constant of 1.92×10^3 L mol^{-1} min^{-1} was established, showing exceptional activity in the polymerization of L-lactide. In the polymerization process a three-step mechanism is operative. In the first step, the large 2,6-di-*tert*-butylphenoxy ligands are exchanged for the smaller 2-propanol. In the second step the polar alkoxide residues are able to attack the carbonyl group and to form the ring-opened product. After the first two initiating steps, the polymerization can proceed until the equilibrium conversion of monomer is reached. It was shown that association of metal centers is not as important as in aluminum alkoxide initiated polymerization of lactones, probably because of the much more dynamic nature of yttrium alkoxides. Only in the case of bridging oxide ions, a strong effect on the polymerization activity of an yttrium alkoxide can be expected as was shown for the commercially available compound **1**.

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