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A Novel and Versatile Calcium-Based Initiator System for the Ring-Opening Polymerization of Cyclic Esters

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ABSTRACT: A novel and efficient calcium alkoxide initiating system, generated in situ from bis(tetrahydrofuran)calcium bis[bis(trimethylsilyl)amide] and an alcohol, for the ring-opening polymerization of cyclic esters has been developed. The solution polymerization in THF using mild conditions is living, yielding polyesters of controlled molecular weight and tailored macromolecular architecture. The polymerizations initiated with the 2-propanol−$Ca[N(SiMe_3)_2]_2(THF)_2$ system are first-order in monomer with no induction period. At high 2-propanol/$Ca[N(SiMe_3)_2]_2(THF)_2$ ratios, complete conversion of 2-propanol occurs due to fast and reversible transfer between dormant and active species.

Introduction

Biodegradable and biocompatible aliphatic polyesters have received much interest for their medical, pharmaceutical, and environmental applications.[1−3] Many of these polyesters can be synthesized by the ring-opening polymerization of cyclic esters, for which various effective initiating systems have been developed.[4−9]

However, in practice, complete removal of the catalyst residues from the polymer is not possible, and therefore a biocompatible catalyst should be used. Ca-, Fe-, and Mg-based catalysts/initiators are the most favored, since these metals participate in the human metabolism.[10−12] Recently, the ring-opening polymerization of L-lactide and/or ϵ-caprolactone with catalysts based on these metals has been described.[13−17] However, racemization is generally observed for L-lactide polymerization as a result of the high temperature and long polymerization time necessary to reach high conversion.[18]

In-situ generated yttrium alkoxides, based on fast exchange between yttrium 2,6-di-*tert*-butylphenoxides and different alcohols, have unprecedented activity in the ring-opening polymerization of lactides and lactones under very mild conditions, allowing excellent control over the polymerization process.[19,20] Very recently, the ring-opening polymerization of ϵ-caprolactone with [tris(hexamethyldisilyl)amide]yttrium in the presence of an excess of 2-propanol, which gave polymers with controlled molecular parameters, was also reported.[21] We describe here a novel and efficient calcium alkoxide initiating system, generated in situ from bis(tetrahydrofuran)calcium bis[bis(trimethylsilyl)amide] and an alcohol, for the ring-opening polymerization of cyclic esters.

Experimental Section

Materials. L-Lactide (Purac Biochem b.v., The Netherlands) was purified by recrystallization from dried toluene. ϵ-Caprolactone (Merck-Schuchardt, Darmstadt, Germany), 2-propanol, and methanol were dried over CaH_2 and distilled prior to use. Poly(ethylene glycol) with $M_n = 2.0 \times 10^3$ g/mol (Sigma-Aldrich, Steinheim, Germany) was purified by dissolution in $CHCl_3$ and precipitation from diethyl ether followed by drying under reduced pressure (∼8.0 mmHg) for more than 1 week. Bis(tetrahydrofuran)calcium bis[bis(trimethylsilyl)amide] [$Ca[N(SiMe_3)_2]_2(THF)_2$] was prepared by the transmetalation of bis[bis(trimethylsilyl)amido]tin(II) with calcium metal in THF and crystallized from *n*-hexane at 0 °C, as described previously.[22] $Ca[N(SiMe_3)_2]_2(THF)_2$ is sensitive toward moisture and air and readily soluble in common organic solvents (e.g., toluene, benzene, THF). Toluene and benzene-d_6 were dried by refluxing over a Na/K alloy. THF was dried by refluxing and distillation over sodium wire. All glassware for the polymerization was dried in an oven before use.

Polymerizations. All polymerizations were carried out at room temperature with THF as the solvent in a glovebox under a nitrogen atmosphere. In a typical procedure, a THF (1.0 mL) solution of $Ca[N(SiMe_3)_2]_2(THF)_2$ (0.069 mmol) was added under vigorous stirring to a mixture of L-lactide (1.0 g, 6.9 mmol) and 2-propanol (0.138 mmol, added as 5 wt % stock solution in THF) in THF (6.0 mL) ($[M]_0/[2\text{-PrOH}]_0/[Ca]_0 = 100/2/1$). After the desired reaction time (35 min), polymerization was terminated by introducing acetic acid. A sample was taken for conversion determination using ^{1}H NMR. The poly(L-lactide) was isolated by precipitation from excess methanol followed by filtration and drying at 40 °C in vacuo. Monomer conversion: 100%; yield: 0.91 g; $M_{n,GPC} = 6.9 \times 10^3$, PDI = 1.05. ^{1}H NMR ($CDCl_3$): δ 0.05 (s, $HN(Si(CH_3)_3)_2$), 1.24 (t, $(CH_3)_2CHOC(O)-$), 1.56 (d, $-C(O)CH(CH_3)O-$), 2.66 (broad, $-C(O)CH(CH_3)OH$), 4.34 (q, $-C(O)CH(CH_3)OH$), 5.06 (m, $(CH_3)_2CHOC(O)-$), 5.16 (q, $-C(O)CH(CH_3)O-$). An M_n of 6.9 $\times 10^3$ was calculated based on the relative intensities of the ^{1}H NMR ($CDCl_3$) signals at δ 5.16 and 1.24. Polymerization of ϵ-caprolactone (ϵ-CL) was performed as described above to afford poly(ϵ-caprolactone). Monomer conversion: 100%, $M_{n,GPC} = 6.2 \times 10^3$, PDI = 1.24. ^{1}H NMR ($CDCl_3$): δ 0.05 (s, $HN(Si(CH_3)_3)_2$), 1.22 (d, $(CH_3)_2CHOC(O)-$), 1.37 (m, $-C(O)CH_2CH_2CH_2CH_2CH_2O-$), 1.66 (m, $-C(O)CH_2CH_2CH_2CH_2CH_2O-$), 2.30 (t, $-C(O)CH_2CH_2CH_2CH_2CH_2O-$), 3.63 (t, $-C(O)CH_2CH_2CH_2CH_2CH_2OH$), 4.04 (t, $-C(O)CH_2CH_2CH_2CH_2CH_2O-$), 4.98 (m, $(CH_3)_2CHOC(O)-$).

Synthesis of Poly(ϵ-caprolactone)-*b*-(L-lactide). A living poly(ϵ-caprolactone) prepolymer was prepared similarly as described above. To a mixture of ϵ-CL (1.54 g, 13.5 mmol) and 2-propanol (0.27 mmol, added as 5 wt % stock solution in THF) in THF (16.0 mL) ($[\epsilon\text{-CL}]_0/[2\text{-PrOH}]_0/[Ca]_0 = 100/2/1$) was

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Table 1. Polymerization of L-LA and ϵ-CL Initiated with Alcohol−Ca[N(SiMe$_3$)$_2$]$_2$(THF)$_2$ Systems ([M]$_0$/[Ca]$_0$ = 100/1)[a]

						$M_n \times 10^{-3}$			PDI
entry	mon	ROH	[M]$_0$ (mol/L)	time (min)	conv[c] (%)	NMR[d]	GPC[e]	theo[f]	GPC[e]
1	L-LA		1.0	35	71		8.4	5.1	1.16
2[b]	ϵ-CL		0.5	1	100		22.8	5.7	3.95
3	ϵ-CL		0.5	8	100		11.8	5.7	2.39
4	L-LA	2-PrOH	1.0	35	100	6.9	6.9	7.2	1.05
5	ϵ-CL	2-PrOH	0.8	6	100	6.2	6.2	5.7	1.24
6	L-LA	PEG2000	1.0	18	100	15.1	15.5	15.5	1.03
7	L-LA	MeOH	1.0	18	97	10.3	12.7	7.0	1.07
8	ϵ-CL	MeOH	0.8	10	100	8.5	9.0	5.7	1.29

[a] All polymerizations were carried out under N_2 atmosphere at room temperature (~18 °C) with THF as the solvent. Entries 1−3 without alcohol, the others with [ROH]$_0$/[Ca]$_0$ = 2/1 (molar ratio). [b] Toluene as solvent. [c] Estimated from ^{1}H NMR spectra (300 MHz, $CDCl_3$) of the crude polymerization mixtures. [d] Experimental values obtained from ^{1}H NMR end group analysis (300 MHz, $CDCl_3$). [e] Determined by GPC analysis. [f] Calculated based on the following formula: $M_{n,theor} = M_w$, alcohol + M_w, monomer × [M]$_0$/[I]$_0$ × conversion, [I]$_0$ refers to [ROH]$_0$ or 2[Ca]$_0$ (in the absence of alcohol, i.e., entries 1−3).

added a THF (1.0 mL) solution of Ca[N(SiMe$_3$)$_2$]$_2$(THF)$_2$ (0.135 mmol) under vigorous stirring. After 6 min prepolymerization, part of the reaction mixture (ca. 2.0 mL) was removed, and the polymerization was terminated by the addition of acetic acid. ^{1}H NMR analysis revealed complete monomer conversion. To the remaining mixture containing the living poly(ϵ-caprolactone) prepolymer, L-LA (1.50 g, 10.4 mmol) in 8 mL of THF was added. After another 80 min, the reaction was quenched by adding excess acetic acid, and the polymer was isolated using the procedures described above. L-LA conversion: 93%, $M_{n,GPC} = 12.6 \times 10^3$, PDI = 1.18.

Synthesis of Poly(L-lactide)-*b*-(ethylene glycol)-*b*-(L-lactide). To a vigorously stirred THF solution (6.0 mL) of poly(ethylene glycol) with $M_n = 2.0 \times 10^3$ g/mol (0.138 g, 0.069 mmol) and l-LA (1.0 g, 6.9 mmol) was added a THF solution (1.0 mL) of Ca[N(SiMe$_3$)$_2$]$_2$(THF)$_2$ (0.069 mmol). A rapid increase in viscosity was observed. After 18 min, the reaction was quenched by adding excess acetic acid, and the polymer was isolated using the procedures described above. l-LA conversion: 100%, yield: 0.96 g, $M_{n,GPC} = 15.5 \times 10^3$, PDI = 1.03. ^{1}H NMR ($CDCl_3$): δ 1.56 (d, −C(O)CH(C**H**$_3$)O−), 2.68 (broad, −O**H**), 3.65 (s, −OC**H**$_2$C**H**$_2$O−), 4.28−4.34 (m, −OCH(CH$_3$)C(O)OC**H**$_2$CH$_2$O− and −C(O)C**H**(CH$_3$)OH), 5.16 (q, −C(O)C**H**(CH$_3$)O−).

Measurements. ^{1}H (300 or 400 MHz) and ^{13}C (75.26 MHz) NMR spectra were recorded on a Varian Inova spectrometer with chemical shifts relative to the solvent peak. The GPC measurements were conducted with a Waters 6000A GPC apparatus equipped with a series of standard Waters Styragel HR columns and a H502 viscometer detector (Viscotek Corp.) for absolute molecular weight determinations. Polymers were dissolved in chloroform (1.0 wt %), and elution was performed at 25 °C at a flow rate of 1.5 mL/min using chloroform as eluent. Differential scanning calorimetry (DSC) was carried out with a Perkin-Elmer DSC-7 apparatus calibrated with pure indium. The sample was heated from 20 to 185 °C at a rate of 10 °C/min, kept at 185 °C for 2 min, and cooled to 20 °C at a rate of 40 °C/min, and then a second heating scan at a rate of 10 °C/min was recorded. The maximum of the endothermic peak was taken as the melting temperature.

Results and Discussion

Attempts to homopolymerize L-lactide (L-LA) or ϵ-caprolactone (ϵ-CL) with Ca[N(SiMe$_3$)$_2$]$_2$(THF)$_2$ in THF at room temperature (~18 °C) revealed a slow L-LA but fast ϵ-CL polymerization (Table 1, entries 1−3). The poly(L-LA) isolated had a narrow molecular weight distribution. The molecular weight as determined by GPC deviated largely from the theoretical value. Because the end groups could not be detected by ^{1}H NMR, no accurate M_n value could be calculated. The ϵ-CL polymerization afforded polymers of somewhat broader polydispersity index (PDI). Analogous observations have been reported for yttrium and samarium amides in ϵ-CL polymerization.[21,23,24]

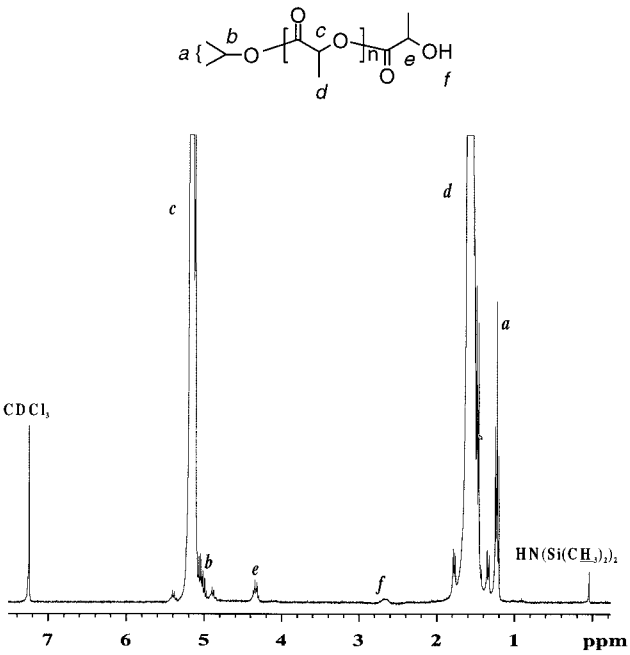


Figure 1. The 300 MHz ^{1}H NMR spectrum ($CDCl_3$) of poly(L-LA) obtained with 2-PrOH−Ca[N(SiMe$_3$)$_2$]$_2$(THF)$_2$ (molar ratio: 2/1) (entry 4, Table 1).

In the presence of Ca[N(SiMe$_3$)$_2$]$_2$(THF)$_2$ and 2-propanol, the polymerization of L-LA and ϵ-CL proceeded smoothly to afford the corresponding polyester with a narrow molecular weight distribution (entries 4 and 5). For example, when a THF solution of Ca[N(SiMe$_3$)$_2$]$_2$(THF)$_2$ was added to a mixture of 2-propanol and L-LA at a molar ratio [L-LA]$_0$/[2-PrOH]$_0$/[Ca]$_0$ of 100/2/1, the conversion was complete within 35 min. The polyester isolated by precipitation from methanol had an M_n of 6.9×10^3 (entry 4), close to the theoretical value (7.2×10^3) calculated from the monomer-to-alcohol molar ratio. Moreover, the polymer had a low polydispersity index (PDI) of 1.05. The ^{1}H NMR spectrum as well as detailed peak assignments of the obtained poly(L-LA) is shown in Figure 1. The two doublets appearing as a triplet at δ 1.24 and the quartet at δ 4.34, with an integral ratio close to 6:1 within the limits of the NMR experimental errors, were assignable to the methyl protons of the isopropoxycarbonyl end group and the methine proton neighboring the hydroxyl end group, respectively. A trace signal appearing at δ 0.05 was attributed to the free HN(Si(C**H**$_3$)$_3$)$_2$ residues originating from the alcoholysis of Ca[N(SiMe$_3$)$_2$]$_2$-(THF)$_2$. The M_n calculated from the relative intensities

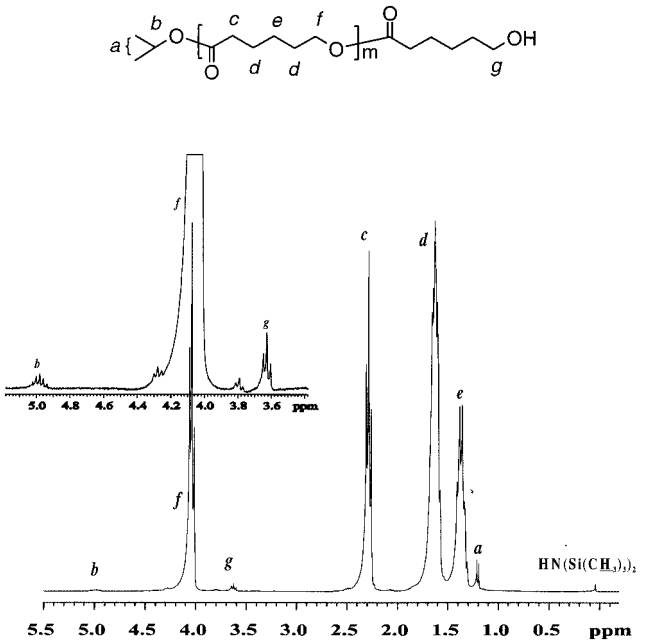


Figure 2. The 300 MHz ^{1}H NMR spectrum ($CDCl_3$) of poly(ϵ-CL) obtained with 2-PrOH−$Ca[N(SiMe_3)_2]_2(THF)_2$ (molar ratio: 2/1) (entry 5, Table 1).

of signals at δ 5.16 (main chain methine proton) and at δ 1.24 (methyl protons of the isopropoxycarbonyl end group) was 6.9×10^3. The good agreement between the theoretical value of M_n and that determined by GPC or ^{1}H NMR end group analysis unambiguously showed that the 2-propanol groups and not the bis(trimethylsilyl)amide ligands were incorporated during the initiation and that the polymerization proceeded exclusively by acyl−oxygen cleavage of the monomer. Similar results were also observed for the ϵ-CL polymerization (entry 5), with isolated poly(ϵ-CL) chains bearing an isopropoxycarbonyl group at one end and a hydroxyl group at the other end as revealed by the ^{1}H NMR analysis (Figure 2).

The ratio of the degree of polymerization (DP) of poly(L-LA) and monomer conversion increased proportionally with the initial monomer-to-alcohol ratio (Figure 3). Moreover, the molecular weight also followed a linear relationship in monomer conversion, with the PDI becoming lower during the polymerization course (Figure 4). The perfect control over molecular weight and low PDI indicate that the polymerization has a living nature. This was further confirmed by the sequential copolymerization of ϵ-CL and L-LA. In the first stage, a THF solution of $Ca[N(SiMe_3)_2]_2(THF)_2$ was added to a mixture of ϵ-CL and 2-propanol ($[\epsilon\text{-CL}]_0/[2\text{-PrOH}]_0/[Ca]_0 = 100/2/1$, $[\epsilon\text{-CL}]_0 = 0.8$ mol/L), affording after 6 min polymerization 100% monomer conversion. To this reaction mixture, a solution of L-LA (44 equiv with respect to 2-propanol) in THF was added. The polymerization of L-LA ensued to give at 93% conversion after 80 min a block copolymer with $M_n = 12.6 \times 10^3$ (M_n, theory = 12.4×10^3) and PDI = 1.18. The ^{1}H NMR spectrum of the block copolymer is shown in Figure 5. Besides resonances from the main chain, the signals at δ 1.22 (doublet) and 4.34 (quartet) characteristic of the methyl protons of the isopropyl ester end group and the lactyl methine proton neighboring the hydroxyl group, respectively, were clearly detected. The triplet assignable to α-methylene protons of hydroxyl-capped poly(ϵ-CL) at δ 3.63 completely disappeared. These results indicate

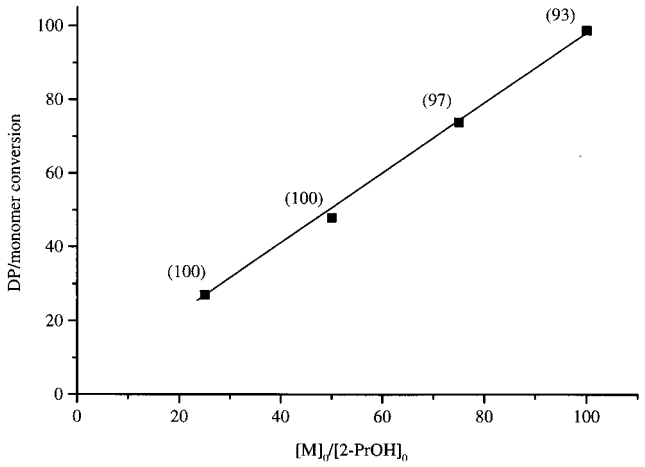


Figure 3. Dependence of the ratio of degree of polymerization (DP) of poly(L-LA) and monomer conversion on the initial monomer/2-PrOH molar ratio. The DP was determined by ^{1}H NMR end group analysis. Polymerization conditions: $[2\text{-PrOH}]_0/[Ca]_0 = 2/1$, room temperature, THF. Conversion (%) is noted in parentheses.

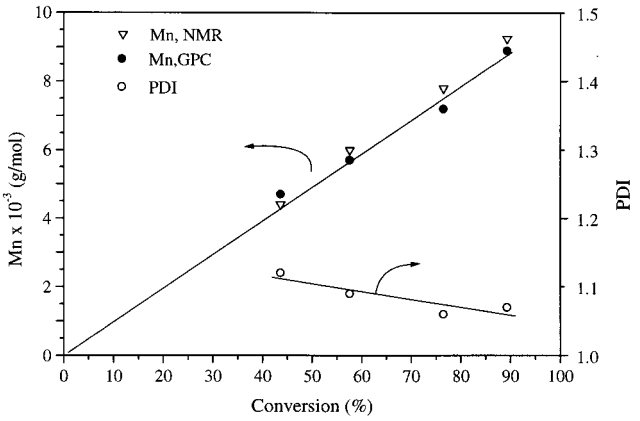


Figure 4. Poly(L-LA) molecular weight and polydispersity index (PDI) vs conversion with $[M]_0/[2\text{-PrOH}]_0/[Ca]_0 = 150/2/1$, room temperature, THF, $[M]_0 = 0.8$ mol/L.

a quantitative crossover from the living poly(ϵ-CL) end to the living poly(L-LA) end. ^{13}C NMR analysis of the copolymers of ϵ-caprolactone and L-lactide affords distinct information on the sequence distribution of ϵ-oxycaproyl and lactyl units, with the carbonyl signals proven to be the most sensitive to sequence effects.[25−27] The absence of resonances between the two carbonyl signals at δ 173.4 and 169.4, corresponding to poly(ϵ-CL) block and poly(L-LA) block, respectively, as shown in Figure 6, indicates that no random sequences due to transesterification were formed.[25−27] In contrast, attempts to prepare the block copolymer in the reverse order or to synthesize random copolymers by simultaneously polymerizing an ϵ-CL and L-LA mixture failed, both yielding exclusively poly(L-LA) homopolymer. Interestingly, the same phenomena were observed for analogous initiator systems, such as aluminum alkoxides[28] and yttrium alkoxides.[19]

The alcohol used determines the end functionalities and/or macromolecular architectures. To exemplify this, poly(ethylene glycol) ($M_{n,NMR} = 2.0 \times 10^3$, PDI = 1.03, PEG2000) was used in the present system. A THF solution of $Ca[N(SiMe_3)_2]_2(THF)_2$ was added to a mixture of PEG2000 and L-LA at a molar ratio $[\text{L-LA}]_0/[OH]_0/[Ca]_0 = 100/2/1$. The polymerization proceeded to 100% conversion within 18 min, yielding poly(L-lactide)-

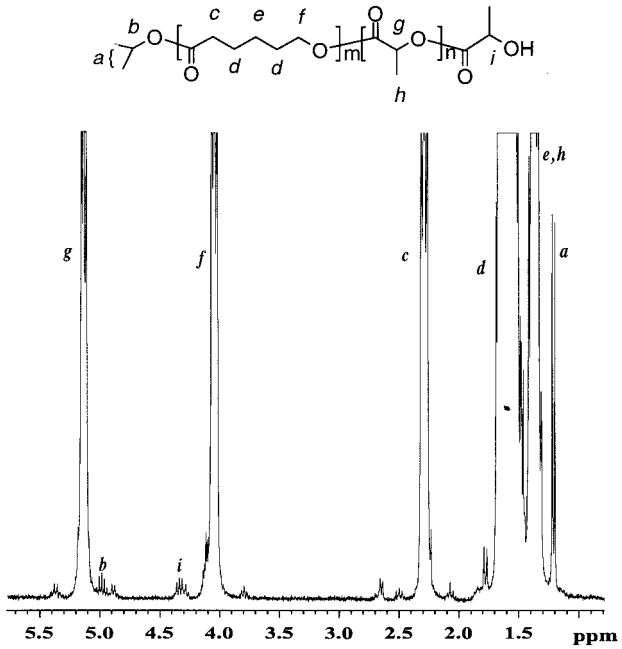


Figure 5. The 300 MHz ^{1}H NMR spectrum ($CDCl_3$) of poly(ϵ-CL)-*b*-(L-LA) block copolymer prepared by sequential ring-opening polymerization of ϵ-CL and L-LA employing 2-PrOH−$Ca[N(SiMe_3)_2]_2(THF)_2$ (molar ratio: 2/1).

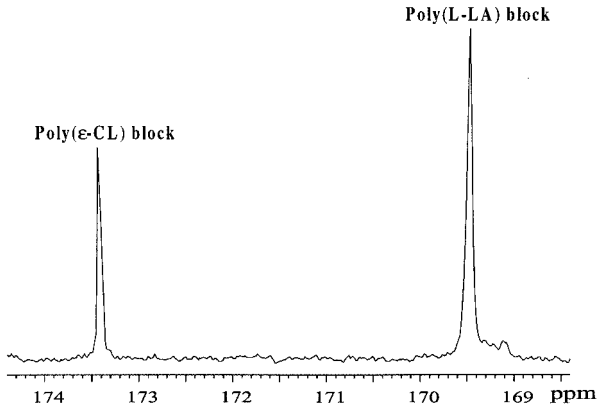


Figure 6. Carbonyl region of ^{13}C NMR spectrum (75.26 MHz, $CDCl_3$) of poly(ϵ-CL)-*b*-(L-LA) block copolymer prepared by sequential ring-opening polymerization of ϵ-CL and L-LA employing 2-PrOH−$Ca[N(SiMe_3)_2]_2(THF)_2$ (molar ratio: 2/1).

b-(ethylene glycol)-*b*-(L-lactide) triblock copolymer capped with hydroxyl groups at both ends and with a M_n and PDI of 15.5×10^3 and 1.03, respectively (entry 6).

The combination of $Ca[N(SiMe_3)_2]_2(THF)_2$ and methanol in the homopolymerizations of L-LA or ϵ-CL yielded polyesters having a much higher M_n than expected (entries 7 and 8). This may result from the aggregation of in-situ generated calcium methoxide and/or growing species, since calcium alkoxides containing sterically compact groups (−OMe, −OEt, etc.) are oligomeric or polymeric.[29,30] The alcohol used in this catalyst/initiator system apparently plays an important role. Sterically more crowded alcohols, such as 2-propanol and poly(ethylene glycol), can sufficiently suppress the formation of coordinative aggregates and thus lead to good control over the polymerization.

In another experiment, polymerization of L-LA was carried out with a large excess of 2-propanol relative to $Ca[N(SiMe_3)_2]_2(THF)_2$ ($[L\text{-LA}]_0/[2\text{-PrOH}]_0/[Ca]_0 = 192/8/1$). After 1.5 h, a ^{1}H NMR spectrum of the crude

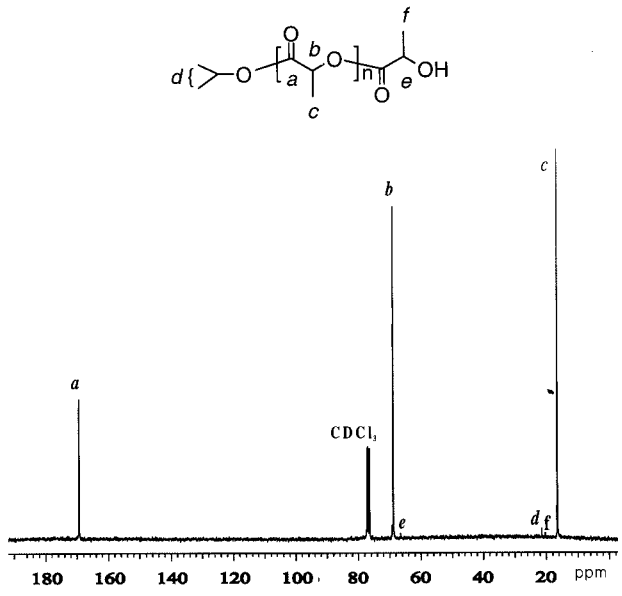


Figure 7. The 75.26 MHz ^{13}C NMR spectrum ($CDCl_3$) of poly(L-LA) obtained with 2-PrOH−$Ca[N(SiMe_3)_2]_2(THF)_2$ (molar ratio: 2/1) (entry 4, Table 1).

polymerization mixture showed that conversion was complete and all 2-propanol molecules had taken part in the polymerization ($M_{n,NMR} = 3.9 \times 10^3$, $M_{n,theory} = 3.5 \times 10^3$, PDI = 1.13). This implies that the alcohol−$Ca[N(SiMe_3)_2]_2(THF)_2$ initiator system promotes living ring-opening polymerization of cyclic esters with fast reversible transfer between dormant species and active species ("immortal" polymerization[8,31]). A ^{1}H NMR spectrum of a 2-propanol−$Ca[N(SiMe_3)_2]_2(THF)_2$ mixture (10/1) in C_6D_6 at room temperature revealed that the isopropyl groups are in a single average environment, supporting the rapid and reversible exchange between coordinated alkoxides and free alcohols.

Another important issue for L-LA polymerization is the possible racemization during the reaction. ^{13}C NMR spectroscopy has been established as a useful method to identify the stereosequence distribution in poly(lactide).[32−35] ^{13}C NMR spectra (Figure 7) of all poly(L-LA)s obtained in this study showed only three sharp signals corresponding to the carbonyl, methyl, and methine carbons, respectively, indicating the formation of isotactic poly(L-LA) and no base-promoted epimerization of the L-LA monomer or poly(L-LA).[34] The introduction of stereochemical defects into poly(L-LA) chains as a result of racemization would dramatically alter the thermal behavior such as a decrease of melting point and the degree of crystallinity.[36,37] Therefore, the characteristic thermal properties are good indexes for the structural perfectness. DSC of a poly(L-LA) sample revealed a crystallization exotherm at 106 °C and a single melting peak at 165 °C (Figure 8). This is in close agreement with the melting behavior of optically pure poly(L-LA) reported by Prud'homme et al.[37]

Kinetics of ϵ-CL polymerization in THF initiated with a low concentration of $Ca[N(SiMe_3)_2]_2(THF)_2$ was investigated at room temperature and monitored by manual sampling followed by ^{1}H NMR analysis ($CDCl_3$) to determine the monomer conversion. In the presence of 2 equiv of 2-propanol with respect to $Ca[N(SiMe_3)_2]_2(THF)_2$, the polymerization is first-order in monomer, and no induction period is observed (Figure 9). This is in sharp contrast to polymerizations with aluminum alkoxides[38,39] or commercial yttrium isopropoxides[40]

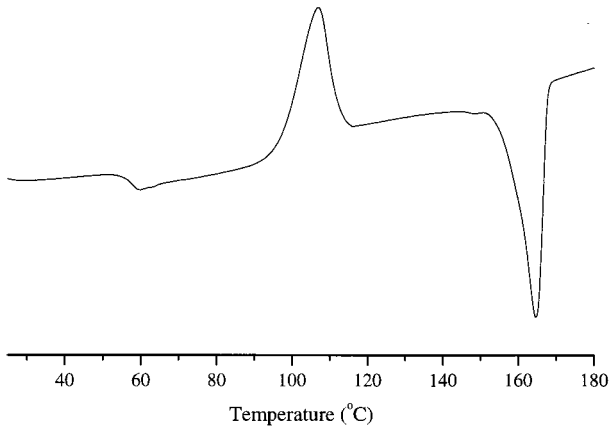


Figure 8. DSC thermogram (second scan) of a poly(L-LA) sample recorded at a heating rate of 10 °C/min under N_2 flow.

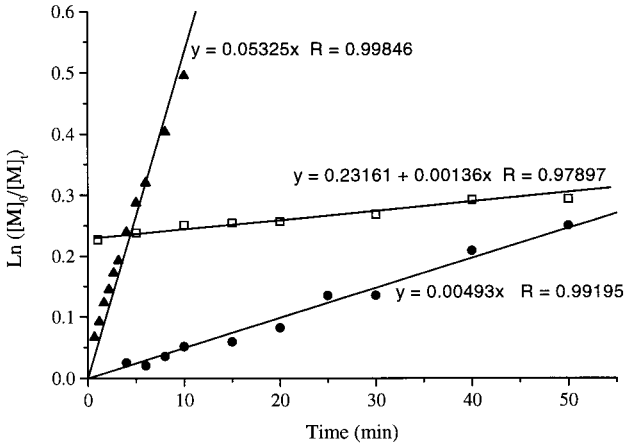


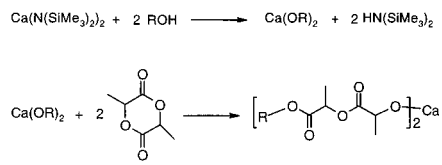
Figure 9. Kinetics of ϵ-CL ([ϵ-CL]$_0$ = 200 mmol/L) polymerization initiated with Ca[N(SiMe$_3$)$_2$]$_2$(THF)$_2$ in THF at room temperature: [Ca]$_0$ = 1.0 mmol/L, in the absence of alcohol (□); [Ca]$_0$ = 1.0 mmol/L, [2-PrOH]$_0$ = 2.0 mmol/L (●); [Ca]$_0$ = 1.35 mmol/L, [2-PrOH]$_0$ = 2.70 mmol/L (▲).

where a pronounced induction time to rearrange the ligands of the initiator thereby allowing the monomer to access the coordination sphere of the metal is present. Interestingly, no retardation was observed for either ϵ-caprolactone or L-lactide polymerization with the in-situ yttrium isopropoxides generated from yttrium 2,6-di-*tert*-butylphenoxides and 2-propanol.[20,40] It appears that in-situ generated initiators have superior polymerization kinetics in that the polymerization reaction starts immediately upon mixing catalyst and monomer. These features are in line with the absence of termination reactions and the conclusion that fast exchange of the free 2-propanol with bis(trimethylsilyl)amide ligands occurs and that the initiation is fast compared to propagation. The apparent propagation rate constants (k_p^{app}), calculated according to $\ln([M]_0/[M]_t) = k_p^{app}[2\text{-PrOH}]_0 t$, are 0.041 L mol^{-1} s^{-1} ([2-PrOH]$_0$ = 2.0 mmol/L) and 0.33 L mol^{-1} s^{-1}([2-PrOH]$_0$ = 2.7 mmol/L), respectively, which are lower than that determined for the yttrium isopropoxide polymerization of ϵ-CL using CH_2Cl_2 as the solvent[40] but comparable to those of aluminum alkoxides in THF.[38,41,42] In contrast, in the absence of 2-propanol, the polymerization appears to proceed in two stages. A rapid initiation and early propagation is followed by a very slow first-order propagation.

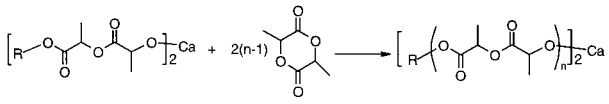
On the basis of the results and by analogy with the mechanisms accepted for the ring-opening polymerization of cyclic esters mediated with other metal alkoxides,[4,40,43] an initiation mechanism in which the bis(trimethylsilyl)amide ligands in Ca[N(SiMe$_3$)$_2$]$_2$(THF)$_2$ are irreversibly exchanged for the alcohol and the in-situ formed calcium alkoxides subsequently promote the ring-opening polymerization of cyclic esters through exclusive acyl−oxygen cleavage of the monomer and insertion into the calcium−alkoxide bond (Scheme 1) is proposed. In the case of excess alcohol with regard to bis(trimethylsilyl)amide ligands, the active species (coordinated alkoxides and/or growing polymer ends) exchange rapidly and reversibly with the dormant species (free alcohol molecules and/or hydroxyl-capped polymers). This feature ensures that more than two polymer chains can be produced by each Ca[N(SiMe$_3$)$_2$]$_2$(THF)$_2$ molecule. The living species can be hydrolytically deactivated by adding an acid, which leads to the formation of the hydroxyl end group.

Scheme 1. Polymerization Reactions

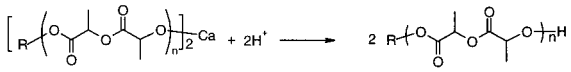
(1) Initiation:



(2) Propagation:



(3) Termination:



(4) Reversible transfer:

Conclusions

Aggregation and/or insolubility of calcium alkoxide derivatives was circumvented by generating them in situ from Ca[N(SiMe$_3$)$_2$]$_2$(THF)$_2$ precursor and an adequate alcohol using THF as the solvent. In-situ formed calcium alkoxides are highly active, initiating a fast living ring-opening polymerization of both ϵ-caprolactone and L-lactide under mild conditions. Polyesters and block copolyesters of expected molecular weight and tailored chain structure can be readily prepared. The ring-opening process involves selective acyl−oxygen rupture of the monomer and insertion into the calcium−alkoxide bond initially obtained after the alcoholysis of calcium amides. Kinetic profiles with first-order propagation in monomer and no induction period were established for ϵ-caprolactone polymerization with a 2-PrOH−Ca[N(SiMe$_3$)$_2$]$_2$(THF)$_2$ initiating system. No

racemization was observed in L-LA polymerization, as revealed by NMR and DSC analyses. The high catalytic activity of the calcium−oxygen bond of alkoxide in the polymerization of cyclic ester substrates as demonstrated by the present study offers great potential of calcium-based initiators in the synthesis of biomedical and pharmaceutical polyesters. Detailed mechanistic and kinetic investigations for L-lactide polymerization as well as the development of structurally well-defined single-site calcium alkoxide with a formula Ln*−Ca−OR (Ln* refers to a bulky ligand set) are currently in progress.

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