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Macromolecular Engineering of Polylactones and Polylactides. 11. Synthesis and Use of Alkylaluminum Dialkoxides and Dithiolates as Promoters of Hydroxy Telechelic Poly(ε-caprolactone) and α,ω-Dihydroxy Triblock Copolymers Containing Outer Polyester Blocks

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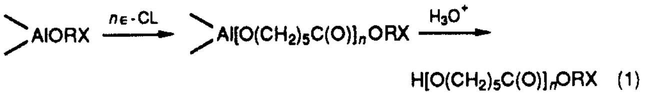
ABSTRACT: Diethylaluminum dialkoxides ($Et_2AlOXOAlEt_2$, where X is either an aliphatic radical or a polymer chain) and related dithiolates have been investigated as potential initiators for the ring-opening polymerization of ε-caprolactone. Hydroxy telechelic poly(ε-caprolactone) and α,ω-dihydroxypoly(ε-caprolactone-*b*-X-*b*-ε-caprolactone) have been accordingly prepared and characterized. A hydroxy group is selectively attached at both ends as demonstrated by IR and ^1H NMR spectroscopies and confirmed by titration of the derivatized α,ω-dicarboxylic acid (co)polymers. Polymerization of ε-caprolactone is living and yields linear polyester chains of a predictable molecular weight and of quite a narrow molecular weight distribution.

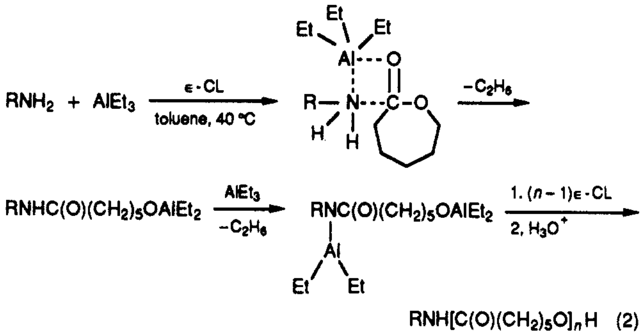
Introduction

Several years ago, some of us reported that the living polymerization of ε-caprolactone (ε-CL) could be promoted by bimetallic (Zn,Al) μ-oxo alkoxides.[1] Later on, aluminum trialkoxides and alkylaluminum alkoxides were used for the same purpose.[2–5] More recently, the selective end functionalization of poly(ε-caprolactone) (PCL) has been investigated by using aluminum alkoxides carrying functional alkoxy groups as initiators.[6–9] The functional group (–RX) associated with the active aluminum alkoxy groups of the initiator, $Et_{3-p}Al(ORX)_p$ ($1 \le p \le 3$), is selectively attached to one chain end, whereas the second end group is systematically a hydroxy function resulting from the hydrolysis of the living growing sites (eq 1). Polymerization thus proceeds through insertion of the monomer into the metal–alkoxide bond with the selective cleavage of the acyl–oxygen bond of ε-CL.



$$>AlORX \xrightarrow{n\epsilon\text{-CL}} >Al[O(CH_2)_5C(O)]_nORX \xrightarrow{H_3O^+} H[O(CH_2)_5C(O)]_nORX \quad (1)$$

Furthermore, primary amines added with triethylaluminum have been found to be effective initiators for the ε-caprolactone polymerization.[10] The alkylaluminum favors the nucleophilic attack of the amine on the carbonyl group of the monomer, leading to the formation of an amide linkage and a hydroxyl end group, respectively (eq 2). Finally, diethylaluminum ω-bromododecanoxide has been successfully used as a precursor for the synthesis of ω-primary amino PCL[11] (eq 3), which is a macroinitiator for the ring-opening polymerization of *N*-carboxyanhydrides (Leuchs anhydrides) with formation of poly(ε-caprolactone-*b*-peptide) copolymers.[12]



$$Br(CH_2)_{12}OAlEt_2 \xrightarrow[2.\ H_3O^+]{1.\ n\epsilon\text{-CL, toluene, 25 °C}} Br(CH_2)_{12}O[C(O)(CH_2)_5O]_nH \xrightarrow[\text{DMF, 30 °C}]{NaN_3} N_3(CH_2)_{12}O[C(O)(CH_2)_5O]_nH \xrightarrow[\text{DMF, 30 °C}]{HC(O)O^-NH_4^+/Pd\ (10\%)} H_2N(CH_2)_{12}O[C(O)(CH_2)_5O]_nH \quad (3)$$

This paper aims at reporting the synthesis and use of aluminum dialkoxides of the general formula $Et_2AlOXOAlEt_2$, where X is either an aliphatic radical or a polymer chain, as initiators for the ε-CL polymerization. Dithiolates of the same structure will also be investigated. The ultimate purpose is the synthesis of hydroxy telechelic PCL and α,ω-dihydroxypoly(ε-caprolactone-*b*-X-*b*-ε-caprolactone). These hydroxy telechelic polymers are nothing but macromonomers which can provide valuable polycondensates incorporating biodegradable polyester blocks, e.g., polyurethanes.[13,14] Moreover, amphiphilic poly(ε-caprolactone-*b*-oxirane-*b*-ε-caprolactone) copolymers, as such or after chain extension through the hydroxyl end groups, are expected to form hydrogels at least in some composition range.[15,16] These hydrogels might be useful for the controlled release of high molecular weight active biomolecules (proteins, enzymes, ...). They have the originality of being partially biodegradable with release of hydrosoluble poly(ethylene oxide) segments. Finally, Penczek has esterified the hydroxy end groups of α,ω-dihydroxypoly(ε-caprolactone) with pyrene derivatives in order to study the dynamics of cyclization by a fluorescence method.[17]

Experimental Part

Materials. ε-CL (Janssen Chimica) was dried over calcium hydride for 48 h at room temperature and distilled under reduced pressure just before use. Triethylaluminum (Fluka) was used without further purification. 1,4-Butanediol and 2,2′-(methylamino)diethanol (Janssen Chimica) were dried over CaH_2 for 1

Table I. Ring-Opening Polymerization of ϵ-CL As Initiated by $Et_2Al[OCH_2CH_2]_nOAlEt_2$ and Carried out to Completion, in Toluene at 25 °C

					$\bar{M}_n$(PCL subchains)		
sample	M_n(PO)	[I] (mol L^{-1})	[ϵ-CL]/[I]	polymn time (h)	theor[a]	exptl[b]	$\bar{M}_w/\bar{M}_n$
1	6 500	5.85×10^{-4}	300	48	17100	18000	1.3
2	33 000	6.1×10^{-4}	110	20	6300	6300	1.25
3	33 000	6.1×10^{-4}	210	20	12000	12000	1.3
4	26 000	7.7×10^{-4}	128	20	13000	13000	1.3
5	11 500	1.7×10^{-3}	90	100	5100	4850	1.6[c]
6	11 500	1.7×10^{-3}	150	140	8600	8400	1.4[c]
7	6 500	3.1×10^{-3}	86	160	4850	5000	1.4[c]
8	6 500	3.1×10^{-3}	48	160	2800	2500	1.4[c]
9	1 350	1.5×10^{-2}	18	20	1050	1100	1.9[c]

[a] Theoretical molecular weight: $\bar{M}_n$ = ([ϵ-CL]/[I]) × 114/2, where 114 is the ϵ-CL molecular weight and [I] is the concentration of $Et_2Al[OCH_2CH_2]_nOAlEt_2$. [b] Molecular weight as calculated by ^1H NMR. [c] Bimodal molecular weight distribution.

Table II. Ring-Opening Polymerization of ϵ-CL As Initiated by $Et_2AlOROAlEt_2$ (with R = $-(CH_2)_4-$ and $-(CH_2)_2N(Me)(CH_2)_2-$) in Toluene

							$\bar{M}_n$(PCL)		
sample	$-ORO-$	[I] (mol L^{-1})	[ϵ-CL]/[I]	polymn time (h)	convn (x) (T)	T (°C)	theor[a]	exptl[b]	$\bar{M}_w/\bar{M}_n$
10	$-(CH_2)_4-$[c]	1.51×10^{-2}	66	5	96	25	7300	7200	1.6[d]
11	$-(CH_2)_4-$[c,e]	3.62×10^{-2}	28	18	100	25	3300	3600(3750)[f]	1.1
12	$-(CH_2)_2N(Me)(CH_2)_2-$	3.85×10^{-2}	26	3	100	40	3100	3700	1.4[d]

[a] Theoretical molecular weight: $\bar{M}_n$ = [([ϵ-CL]/[I]) × 114 × x/100] + MW($-ORO-$), where 114 is the molecular weight of ϵ-CL. [b] Molecular weight as calculated by ^1H NMR. [c] Polymerization in THF (1,4-butanediol is insoluble in toluene). [d] Bimodal molecular weight distribution. [e] Previously distilled $Et_2AlO(CH_2)_4OAlEt_2$. [f] Molecular weight as determined by VPO.

Table III. Ring-Opening Polymerization of ϵ-CL As Initiated by $Et_2AlS(CH_2)_2SAlEt_2$ in Toluene at 25 °C

					$\bar{M}_n$			
						exptl[b]		
sample	[ϵ-CL]$_0$ (mol L^{-1})	[I] (mol L^{-1})	time (min)	convn (x) (%)	theor[a]	^1H NMR	SEC	$\bar{M}_w/\bar{M}_n$
13	9.61×10^{-1}	1.09×10^{-2}	5	100[c]	10 100	13 100	13 400	1.4
14	1.59×10^{-1}	3.6×10^{-3}	45	86	4 400	4 700	4 300	1.5

[a] Theoretical molecular weight: M_n = [([ϵ-CL]$_0$/[I]) × 114 × x/100] + MW($-S(CH_2)_2S-$). [b] Molecular weight as calculated by ^1H NMR and SEC. [c] Gelation of the reaction medium after a 5-min polymerization time.

night and distilled under reduced pressure. 1,2-Ethanedithiol was purchased from Janssen Chimica and dried over $CaCl_2$ for 72 h and freshly distilled. Several samples of α,ω-dihydroxypolyoxirane (PO; Hoechst) were recrystallized in ethyl acetate; the hydroxy content was determined by titration of the derivatized α,ω-dicarboxylic acid polyether. (Dimethylamino)pyridine, succinic anhydride, 1,4-dithiane, and PO were dried by two azeotropic distillations of toluene before use. Triethylamine (Janssen Chimica) was dried over BaO for 1 week and distilled under reduced pressure. Toluene and tetrahydrofuran (THF) were dried by refluxing over CaH_2 and a benzophenone/Na complex, respectively.

Measurements. IR spectra were recorded by using a Perkin-Elmer IR197. ^1H NMR spectra were recorded in $CDCl_3$ by using a Bruker AM 400 spectrometer. Size-exclusion chromatography (SEC) was performed in THF by using a Hewlett Packard 1090 liquid chromatograph equipped with a Hewlett Packard 1037 A refractometer index detector and a set of columns of pore sizes 10^5, 10^3, 500, and 100 Å. Molecular weight and polymolecularity were calculated by using a universal calibration curve. Low molecular weights were also measured by vapor pressure osmometry (VPO; Ateliance Instruments, France) in toluene at 47 °C.

Preparation of Initiators. Diethylaluminum dialkoxides (dithiolates) were prepared by reaction of triethylaluminum with appropriate alcohols (thiols) as previously reported for monoalkoxides.[6,7] The reaction proceeded under nitrogen, with vigorous stirring, at room temperature and went to completion as proved by the volume of ethane formed as a reaction byproduct. When 1 mol of 1,4-butanediol was reacted with 2 mol of $AlEt_3$, active ethylaluminum dialkoxide species, e.g., $EtAl[O(CH_2)_4OAlEt_2]_2$, were actually formed in addition to the expected diethylaluminum dialkoxide. Pure $Et_2AlO(CH_2)_4OAlEt_2$ was isolated by fractional distillation under reduced pressure and characterized by ^1H-NMR analysis (Figure 5).

Polymerization Procedure. The ϵ-CL polymerization was carried out in toluene in a flask previously dried, purged with nitrogen, and kept at the desired temperature for a suitable period of time (for details, see Tables I–III). The reaction was stopped by adding a 10-fold excess of 2 N HCl solution with regard to Al. Catalyst residues were removed as described elsewhere.[9]

Synthesis of α,ω-Dicarboxylic Acid Poly(ϵ-caprolactone). α,ω-Dihydroxypoly(ϵ-caprolactone) (10 w/v %) was esterified by succinic anhydride (5 equiv) in dry THF in the presence of triethylamine (5 equiv) and a catalytic amount of (dimethylamino)pyridine (0.2 equiv) for 24 h at 50 °C. The polyester was purified by three successive precipitation–dissolution cycles (methanol–THF).

Results and Discussion

When the ring-opening polymerization of ϵ-CL is initiated by an aluminum alkoxide, the reaction leads to the formation of α-hydroxy-ω-RX-poly(ϵ-caprolactone) (eq 1). Accordingly, a diethylaluminum dialkoxide of the general structure $Et_2AlOXOAlEt_2$ is a potential initiator for the synthesis of α,ω-dihydroxypoly(ϵ-caprolactone) chains containing the X group from the initiator in a central position. As a result, whenever X is a prepolymer, a telechelic triblock copolymer is expected to be formed. Moreover, the use of a functional X group, such as a tertiary amine, is a possible way to incorporate an organic function inactive toward aluminum alkoxides within the telechelic polyester chains. All these opportunities are schematized by eq 4, which first describes the synthesis of the diethylaluminum dialkoxides. The difunctional initiator is prepared in a straightforward way by adding 2 mol of triethylaluminum/mol of diol. The reaction proceeds easily in toluene at 25 °C as has been previously reported

$$\mathrm{HOXOH} + 2\mathrm{AlEt_3} \xrightarrow[-2\mathrm{C_2H_6}]{\text{toluene}} \mathrm{Et_2AlOXOAlEt_2} \xrightarrow[\text{toluene}]{\epsilon\text{-CL}}$$

$$\mathrm{Et_2AlO(PCL)OXO(PCL)OAlEt_2} \xrightarrow{\mathrm{H_3O^+}} \mathrm{HO(PCL)OXO(PCL)OH} \quad (4)$$

where $\mathrm{X} = -(\mathrm{CH_2})_4-;\ -(\mathrm{CH_2})_2\mathrm{N(Me)}(\mathrm{CH_2})_2-;$
$-\mathrm{CH_2CH_2[OCH_2CH_2]}_n\mathrm{OCH_2CH_2}-$

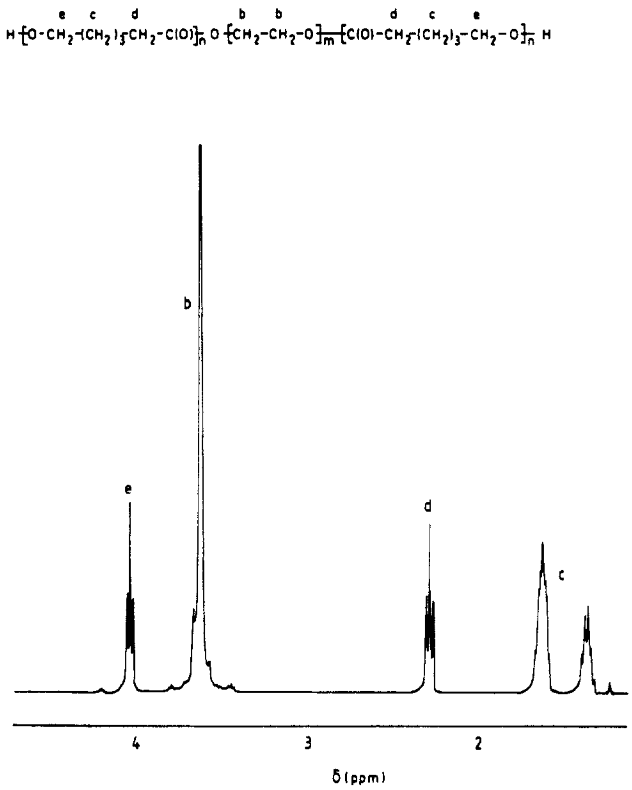
by Penczek,[17] and it goes to completion as proved by the measurement of the volume of ethane which is formed as a byproduct (see Experimental Part). Alkyl–aluminum bonds are inactive toward ϵ-caprolactone under these conditions.[6,7] The next sections report on the synthesis and characterization of hydroxy telechelic poly(ϵ-caprolactone) and derivatives.

Polyoxirane Dialkoxides as Initiators for the ϵ-CL Polymerization. When commercial polyoxiranes (PO) are the starting materials to produce block copolymers, the end-group analysis is a major concern.[18] This is the reason why the hydroxyl content of PO of various molecular weights (from 1350 to 33 000) has been measured by titration of the acid end groups formed upon reaction of the hydroxyl end groups with succinic anhydride. All the polyethers investigated in this study are of a hydroxyl functionality of 2 within the limits of experimental errors.

α,ω-Dihydroxypolyoxiranes have been reacted with a stoichiometric amount of $\mathrm{AlEt_3}$ (eq 4). Under these conditions, conversion of the hydroxyl endgroups into aluminum alkoxide functions is complete and all the polymeric dialkoxides mentioned in Table I polymerize ϵ-CL to completion in toluene at 25 °C. Figure 1 illustrates the ^{1}H NMR spectrum of the sample labeled 8 in Table I. Polyoxirane and poly(ϵ-caprolactone) are clearly identified, and the relative intensity of the methylene protons of PCL compared to the methylene protons of PO allows the number-average molecular weight ($\bar{M}_n$) of the PCL blocks to be calculated from $\bar{M}_n$ of the poly(ethylene oxide) precursor.

Interestingly, there is a good agreement between the calculated values of $\bar{M}_n$ and the theoretical values based on the monomer over initiator molar ratio. Figure 2 shows a linear dependence of the experimental $\bar{M}_n$ of the PCL subchains (i.e., initiated by the individual aluminum alkoxide groups) on the theoretical values. The slope is close to unity, which indicates that each aluminum alkoxide contributes to the ϵ-CL conversion. This behavior is in agreement with the previously demonstrated "living" character of ϵ-CL polymerization initiated by diethylaluminum alkoxides.[6-11]

It is worth pointing out that the molecular weight distribution of samples 5–9 (Table I) is bimodal in contrast to the four first samples. The first question to be addressed is whether that unexpected behavior results from the contamination of the expected block copolymer by homopolymer(s). Purposely, crude polymeric materials prepared from the macroinitiators have been fractionated, at 25 °C, by using toluene/methanol as a solvent/nonsolvent pair for PCL. For instance, the solution behavior of sample 5 (M_n of PCL = 4850) has been compared to a homopolyester of a comparable molecular weight (5000). Each sample has been dissolved in toluene (10 wt %) and added with increasing amounts of methanol (a selective solvent of PO). Although homo-PCL starts to precipitate when the methanol/toluene volume ratio is 6, the precipitation of sample 5 is observed to occur at a volume ratio of 9. Moreover, the first fraction separated from sample 5 contains PO, whereas no residual polyether is left in the supernatant at the end of the fractionation process. As a result, these experimental observations agree



assignment	multiplicity	δ (ppm)	intensity
b	T	3.62	29.88
c	M	1.6	12.81
d	T	2.3	4.3
e	T	4.04	4.1

Figure 1. ^{1}H NMR spectrum (400 MHz) of a PCL–PO–PCL block copolymer (sample 8 in table I, $\bar{M}_n$ = 2500–6500–2500).

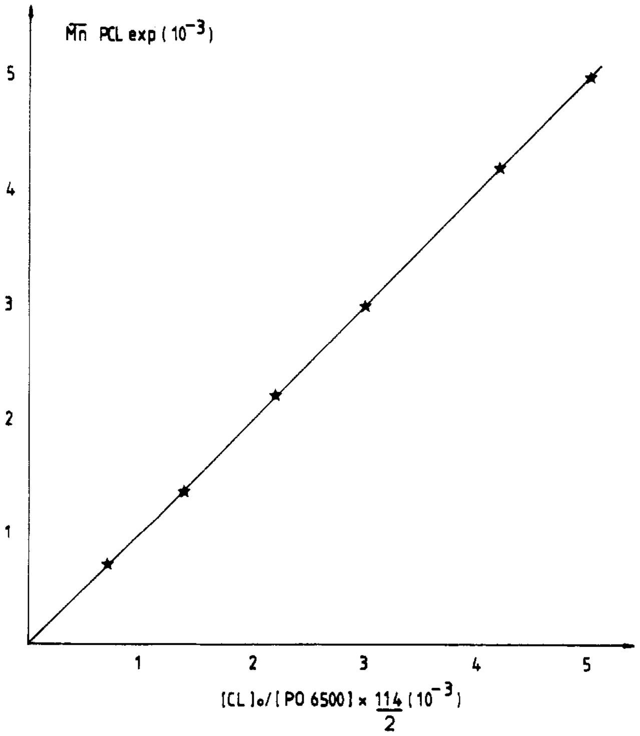


Figure 2. Dependence of $\bar{M}_n$ of PCL subchains (determined by ^{1}H NMR) on the [monomer]/[$\mathrm{Et_2AlOPO(6500)OAlEt_2}$] molar ratio in the polymerization of ϵ-CL in toluene at 25 °C.

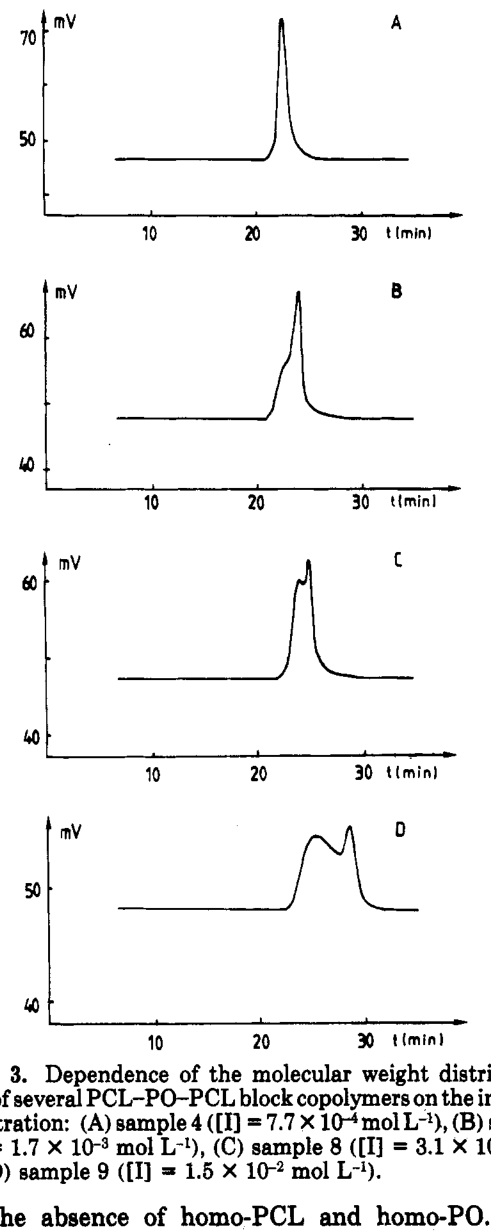


Figure 3. Dependence of the molecular weight distribution (SEC) of several PCL–PO–PCL block copolymers on the initiator concentration: (A) sample 4 ([I] = 7.7×10^{-4} mol L^{-1}), (B) sample 5 ([I] = 1.7×10^{-3} mol L^{-1}), (C) sample 8 ([I] = 3.1×10^{-3} mol L^{-1}), (D) sample 9 ([I] = 1.5×10^{-2} mol L^{-1}).

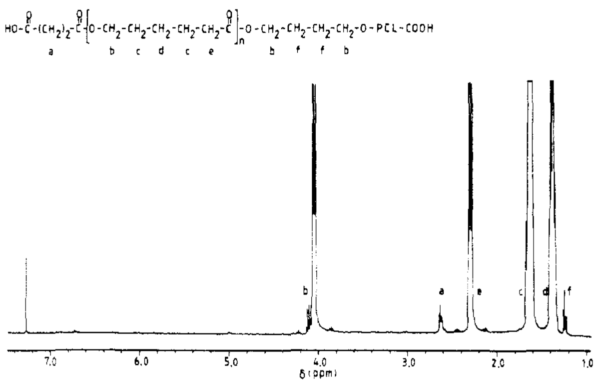
with the absence of homo-PCL and homo-PO. The bimodal distribution should therefore correspond to two distinct populations of block copolymers which would be produced from alkoxides of a different reactivity. Comparison of the size-exclusion chromatograms of samples 4, 5, 8, and 9 (Table I) clearly shows that the bimodal nature of the molecular weight distribution is closely related to the initiator concentration, i.e., the molar concentration at which the diol precursor has been reacted with triethylaluminum. Figure 3 shows that a component of a higher molecular weight emerges and its relative importance increases with the molar concentration of the initiator. In other words, a more active aluminum alkoxide is formed when the diol is reacted with triethylaluminum at a higher concentration. It is suggested that in addition to the expected diethylaluminum alkoxide, ethylaluminum dialkoxide might also be produced. The probability for ethylaluminum dialkoxide to be formed obviously increases with the concentration of the hydroxy end groups. Since ethylaluminum dialkoxide is more nucleophilic than diethylaluminum monoalkoxide, the related initiation and propagation rates are higher and consequently lead to macromolecules of a higher molecular weight.

HOXOH/2AlEt$_3$ with X = $-(CH_2)_4-$ or $-(CH_2)_2N(Me)(CH_2)_2-$: Nonfunctional and Functional Aluminum Dialkoxides as Initiators for the ε-CL Polymerization. Expectedly, the behavior reported for α,ω-diethylaluminum alkoxide polyoxirane might be extrapolated to any low molecular dialkoxide. In order to support that assumption and to prove that α,ω-dihydroxypoly(ε-caprolactone) can be prepared in a straightforward way, symmetric diols, functional or not, have been reacted in a "one-pot process". Triethylaluminum has been first reacted with the diol solution in toluene or in tetrahydrofuran. When ethane has completely evolved, ε-CL has been added and polymerized in situ. The dialkoxide concentration ([I]), the monomer over initiator molar ratio, temperature, solvent, and ε-CL conversion are reported in Table II. There is again a good agreement between the experimental molecular weight calculated from the ^{1}H NMR spectrum and the value calculated on the basis of a living process. The relative intensity of the methylene protons of the hydroxy end groups (δ CH_2OH = 3.64 ppm) compared to the methylene protons of the monomeric unit (δ $CH_2C(O)-$ = 2.40 ppm) allows the molecular weight of the PCL to be calculated on the assumption that each chain end is capped by a hydroxy group. Evidence for that hypothesis has been found in the chemical conversion of these end groups into carboxylic acid ones. An excess of succinic anhydride has been used on purpose in the presence of triethylamine and (dimethylamino)pyridine (DMAP) as catalysts (eq 5).

$$HO(PCL)O(CH_2)_4O(PCL)OH + 10\ \text{equiv of succinic anhydride} \xrightarrow[2.\ H_3O^+]{1.\ NEt_3,\ DMAP,\ THF,\ 50\ ^\circ C} HOC(O)(CH_2)_2C(O)O(PCL)O(CH_2)_4O(PCL)OC(O)(CH_2)_2C(O)OH \quad (5)$$

^{1}H NMR analysis of α,ω-dicarboxylic acid poly(ε-caprolactone) shows the disappearance of unreacted hydroxy groups (δ CH_2OH = 3.64 ppm) and the appearance of a multiplet at 2.65 ppm assigned to the methylene protons in α and β positions of the carboxylic acid ($-OC(O)(CH_2)_2C(O)OH$) (Figure 4). The molecular weight of that sample (originally sample 11, in Table II) has been calculated from the relative intensity of protons a at 2.65 ppm and protons b (δ = 4.06 ppm) of the monomer unit and found to be 3500. This value is in very close agreement with $\bar{M}_n$ calculated for the hydroxy telechelic sample (3600) and the absolute molecular weight measured by vapor pressure osmometry (3750). Finally, the nonaqueous titration of the carboxylic acid chain end groups concludes to a functionality of 1.9.

From Table II, it is also obvious that the molecular weight distribution is bimodal when the diol is reacted with triethylaluminum at a concentration of 1.5×10^{-2} mol L^{-1} and higher. This observation confirms the data reported in Table I for the polymeric aluminum dialkoxides. Up to now, the coexistence of ethylaluminum dialkoxides and diethylaluminum alkoxides of a different reactivity was suggested as the primary cause for two distinct populations of hydroxy-terminated chains. In order to ascertain this hypothesis, the crude reaction product of 1,4-butanediol with triethylaluminum (2 equiv) has been carefully purified on fractional distillation under reduced pressure. As observed by ^{1}H NMR analysis, the expected diethylaluminum dialkoxide was actually contaminated by active ethylaluminum dialkoxide species, e.g., $EtAl[O(CH_2)_4OAlEt_2]_2$. When the carefully purified diethylaluminum dialkoxide (Figure 5) is used as an initiator, a α,ω-dihydroxypoly(ε-caprolactone) of a very narrow MW distribution is obtained (sample 11 compared to 10 in Table II). This observation accounts for the broad polymolecularity which is observed when the initiator has not been purified prior to polymerization. Then two species of an uneven activity contribute to the polymer-



assignment	multiplicity	δ (ppm)	intensity
a	T	2.65	3.33
b	T	4.06	25.21
c	M	1.63	53.02
d	M	1.39	24.83
e	T	2.31	24.32
f	T	1.24	1.49

Figure 4. ^{1}H NMR spectrum (400 MHz) of a α,ω-dicarboxylic acid poly(ϵ-caprolactone) (eq 5).

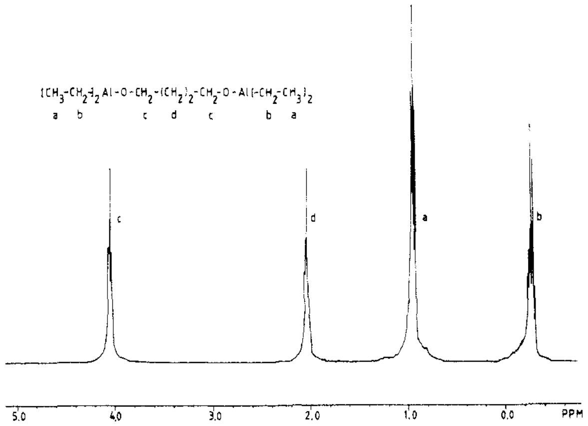
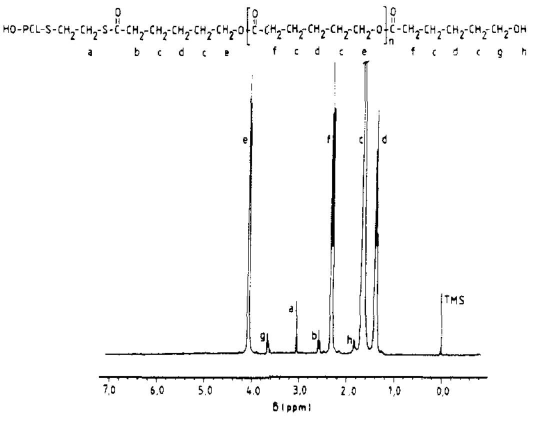


Figure 5. ^{1}H NMR spectrum (400 MHz) of $Et_2AlO(CH_2)_4OAlEt_2$ recovered by distillation from the crude reaction product of 1 mol of 1,4-butanediol and 2 mol of $AlEt_3$.

ization, resulting in a much broader and sometimes bimodal distribution.

$HS(CH_2)_2SH/2AlEt_3$: Aluminum Dithiolate as an Initiator for the ϵ-CL Polymerization. Thiols are more acidic than the related alcohol, and they are thus expected to react easily with triethylaluminum with formation of aluminum thiolates which might initiate the ϵ-CL polymerization. An alternative pathway to α,ω-dihydroxypoly(ϵ-caprolactone) would accordingly consist of the synthesis of a diethylaluminum dithiolate to be used as an initiator of the ϵ-CL polymerization. As an example, 1,2-ethanedithiol has been reacted with $AlEt_3$ in a toluene solution, under the same conditions as previously reported for diols and schematized by eq 4.

Table III shows that ϵ-CL is rapidly polymerized to completion when the tetraethyldialuminum 1,2-ethanedithiolate is used as an initiator in toluene ([ϵ-CL] = 1 mol L^{-1}) at 25 °C (sample 13). PCL samples of Table III have been characterized by ^{1}H NMR spectroscopy. Figure 6 refers to sample 14 and confirms the end-capping of the chains by a hydroxymethylene group (δ $-CH_2OH$ = 3.64 ppm). The relative intensity of the protons g compared to protons e of the ϵ-CL subunits gives access to $\bar{M}_n$ stating that there are actually two hydroxy groups per chain ($\bar{M}_n$ = 4700). This value satisfactorily agrees with size-exclusion chromatography (universal calibration; $\bar{M}_n$ = 4400). Since the end groups are unmodified when the active diethylaluminum alkoxides are substituted by diethylaluminum thiolates, the propagation mechanism would also be unchanged, i.e., insertion of ϵ-CL into the >Al–S bond through the selective cleavage of the acyl–oxygen linkage of the monomer (eq 6). If it is so, the ethyl



assignment	multiplicity	δ (ppm)	intensity
a	S	3.05	1.8
b	T	2.58	1.82
c	M	1.63	79.78
h	S	1.85	
e	T	4.06	37.23
f	T	2.32	37.82
g	T	3.64	1.94
d	M	1.39	36.93

Figure 6. ^{1}H NMR spectrum (400 MHz) of a α,ω-dihydroxypoly(ϵ-caprolactone) which has been initiated by $Et_2AlS(CH_2)_2SAlEt_2$ (sample 14, Table III).

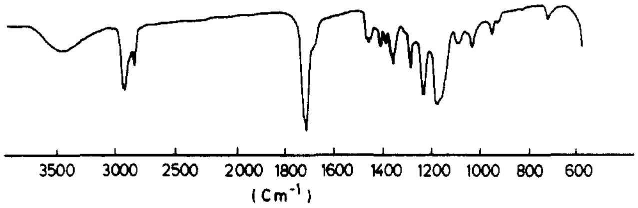


Figure 7. IR spectrum (film) of a α,ω-dihydroxypoly(ϵ-caprolactone) ($\bar{M}_n$ = 4400) containing two thioester groups within the polymer chain (sample 14, Table III).

$$>AlSCH_2CH_2SAl< + n\epsilon\text{-CL} \rightarrow$$

$$>Al[O(CH_2)_5C(O)]_{n/2}SCH_2CH_2S[C(O)(CH_2)_5O]_{n/2}Al<$$

$$\xrightarrow{H_3O^+} H[OCH_2C(O)]_{n/2}SCH_2CH_2S[C(O)(CH_2)_5O]_{n/2}H \quad (6)$$

radical of 1,2-ethanedithiolate should be incorporated within the chains as a dithioester group (eq 6). Actually, methylene protons directly adjacent to a thioester are observed by ^{1}H NMR (δ [$-CH_2SC(O)-$] = 3.05 ppm and δ [$-SC(O)CH_2-$] = 2.58 ppm) (Figure 6). These protons (a and b) are of the same relative intensity as the hydroxymethylene protons (g), which indicates that there are two hydroxy end groups per initiator residue within the limits of experimental errors.

Finally, a large IR absorption at 3400 cm^{-1} and a shoulder at 1625 cm^{-1} (Figure 7) are additional evidences for the hydroxyl end groups and the thioester functions, respectively. It is worth noting that the mechanism proposed for the ring-opening polymerization of ϵ-CL is supported by the well-known conversion of esters into thioesters by trimethylsilyl sulfur[19] or aluminum thiolate.[20,21]

Unexpectedly, a substantial increase in the polymerization rate together with the rapid gelation of the final polymerization medium has been promoted by increasing the monomer and initiator concentrations from sample 14 to sample 13 (Table III). These effects have been accounted for by coordinative interactions between the thioester groups within the PCL chains and aluminum atoms of the active centers. Indeed, gelation is not due to primary covalent bonds, since the gel disappears upon the addition of a diluted aqueous solution of HCl or upon dilution with dry THF. An additional proof for the decisive role of sulfur atoms in the gelation process has been found in the following experiment. When the ϵ-CL polymerization is initiated by diethylaluminum 1,4-butanedioxide ($[\epsilon\text{-CL}]_0 = 1.0$ mol L^{-1} and $[\epsilon\text{-CL}]_0/[I]_0 = 35$) in toluene at 0 °C, no gel is observed. In contrast, within the same conditions, the addition of 0.5 equiv of 1,4-dithiane per Al promotes an initial increase in viscosity which ultimately leads to gelation. This gel is again unstable in acidic conditions or upon addition of THF.

Sulfur atoms of the ethane dithioester within the chains and of the 1,4-dithiane additive do not only modify the physical properties of the polymerization medium, but they also affect the polymerization kinetics. For instance, the addition of 1 equiv of 1,4-dithiane per mole of diethylaluminum 1,4-butanedioxide increases the monomer conversion from 50 to 95% within a polymerization time of 20 min, under previously mentioned conditions of concentration, solvent, and temperature. Similar figures have been observed for the substitution of a diethylaluminum alkyldialkoxide (sample 11 in Table II) by a diethylaluminum dithiolate (sample 14 in Table III). The polymerization rate enhancement is clearly related to the coordinative $>S\rightarrow AlO-$ interactions, which expectedly increase the nucleophilicity of the parent alkoxide. As will be reported in a separate paper, pyridine has a kinetic effect comparable to 1,4-dithiane in the ring-opening polymerization of ϵ-CL and lactides.[22]

Finally, the use of α,ω-diethylaluminum thiolate derivatives as initiators for the ϵ-CL polymerization produces telechelic PCL of a monomodal molecular weight distribution. This observation supports the selective formation of diethylaluminum thiolate end groups in contrast to the reaction between diols and triethylaluminum which produces, under the same conditions of concentration, ethylaluminum dialkoxide functions (OAl(Et)O–: chain extenders) in addition to the expected diethylaluminum alkoxide end groups ($-OAlEt_2$). In this respect, it is worth pointing out that Penczek et al. do not mention the formation of bimodal α,ω-dihydroxypoly(ϵ-caprolactone) when they use $(CH_3CH_2)_2AlO(CH_2CH_2O)_3Al(CH_2CH_3)_2$ as an initiator, in THF, at room temperature.[17]

In conclusion, a straightforward strategy is available for the controlled synthesis of α,ω-dihydroxypoly(ϵ-caprolactone) and expectedly polylactides. It relies upon the quantitative reaction of triethylaluminum with a diol or a dithiol, followed with the initiation of the ring-opening polymerization of ϵ-CL. Although this one-pot procedure allows the hydroxyl functionality of the polyester chains to be carefully controlled, the polymolecularity is broad. This drawback can however be avoided by the previous purification of the initiator by fractional distillation. The replacement of aluminum alkoxide by aluminum thiolate enhances the polymerization rate by a coordinative interaction of the aluminum and sulfur atoms. When a α,ω-dihydroxy prepolymer is used as a diol, a α,ω-dihydroxy triblock copolymer consisting of lateral biodegradable PCL chains is produced.

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