This anion polymerized pivalolactone giving the masked polyoxyethylene/copivalolactone copolymeric salt, 3, which was isolated by precipitation in ether. After drying, a methylene chloride solution was treated with 3N HCl to convert it to a telechelomer. (A telechelomer is defined as a high molecular weight monomer which is self polymerized into high polymer to a step polymerization mechanism.)

A novel and apparent catalyst, alanine, was used to convert the telechelomer to the segmented copolymer. In the absence of alanine, no high molecular weight polymer is formed. In a typical polycondensation, the telechelomer was stirred at 185°C with dl-alanine under argon. Only the telechelomer (not alanine) melted at this temperature, and thus the reaction mixture became heterogeneous. After stirring the mixture for two hours, a vacuum was applied to sublime any unreacted alanine. A catalytic amount of titanium butoxide was added to the reaction mixture. Within about one-half hour the viscosity of the mixture increased substantially, and the contents could not be stirred with a magnetic stirrer after that time. The product obtained was characterized using GPC viscometry, and we found that the high molecular weight polymer was formed.

The function of alanine is under study, since no previous reports of amino acid or zwitterionic catalyzed polyesterifications exist. A model esterification of pivalic acid (Figure 3) and 2-(2-methoxyethoxy)ethanol has confirmed the activity of alanine, where a ten-fold increase in the ester acid ratio is observed in the presence of a catalytic quality of alanine. Alanine is heterogeneous in this case as well.

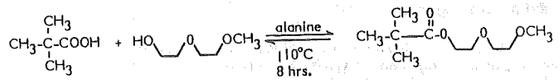

Figure 3. A Model Study of the Activity of Alanine

Acknowledgements

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MACROMOLECULAR ENGINEERING OF POLYLACTONES AND POLYLACTIDES: II- "LIVING" POLYMERIZATION AND SELECTIVE END-FUNCTIONALIZATION OF POLY-ε-CAPROLACTONE

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INTRODUCTION

Poly-ε-caprolactone (PCL) is a specially attractive polyester due to its capacity to be blended with various commercial polymers over a wide composition range.[1,2] Furthermore biodegradability, high permeability and lack of toxicity [3] are other properties that allow PCL to be used as a synthetic biomaterial[4] or in controlled release drug delivery systems.[5]

Although ε-caprolactone can be polymerized using various types of initiators,[6] living polymerization is rather an exception than a general rule. Most often, the anionic polymerization is perturbed by side intra- and intermolecular transesterification reactions leading to a mixture of linear and cyclic molecules.[7,8] It has however been found that less reactive initiators, like aluminum alkoxide functions, can favor the linear chains formation at the expense of macrocycles.[9,10] As reported by Inoue[11,12] and Penczek,[13] a living "coordination-insertion" polymerization can also be initiated by α,β,γ,δ-tetraphenylporphinatoaluminum derivatives and diethylaluminum methoxide, respectively.

Synthesis of end-reactive PCL with a precisely controlled molecular weight is of a particular interest in the macromolecular engineering of polyesters. Recently, we have reported about the end-functionalization of PCL chains using functional alkoxides as initiators.[14] We will discuss here the potentialities of that strategy in preparing PCL selectively capped at one end by a bromide, an unsaturation or a diethylamine group respectively. Using the functional aluminum alkoxides 1 and 2, the living character of ε-CL polymerization and the selective end-functionalization of the chains will be analyzed.

$$(C_2H_5)_{3-p}\ Al(O\text{-}CH_2\text{-}X)_p$$

1 : p = 1
2 : p = 3

with a : $-CH_2-Br$
b : $-(CH_2)_2-CH=CH_2$
c : $-(CH_2)_2-NEt_2$

EXPERIMENTAL

CL (Janssen Chimica) was purified according to the procedure described earlier.[14] Toluene was dried by refluxing over calcium hydride. Diethylaluminum alkoxides 1 were prepared by the equimolar reaction of triethylaluminum and the corresponding alcohol; 1,0 mmol of the required alcohol in 10 ml of toluene was slowly added to an equimolar amount of $AlEt_3$ in 90 ml of toluene (eq. 1). Aluminum trialkoxides 2 were synthesized by reaction of aluminum triisopropoxide with 3 equivalents of the appropriate alcohol (eq. 2). The toluene/isopropanol azeotrope was distilled off continuously.

$$(C_2H_5)_3Al + HO\text{-}CH_2\text{-}X \longrightarrow (C_2H_5)_2Al\text{-}O\text{-}CH_2\text{-}X + C_2H_6\uparrow \quad (1)$$

$$(^iPrO)_3Al + 3\ HO\text{-}CH_2\text{-}X \underset{}{\overset{\text{toluene}}{\rightleftharpoons}} (X\text{-}CH_2\text{-}O)_3Al + 3\ {}^iPrOH \quad (2)$$

with X = $-CH_2-Br$
= $-(CH_2)_2-CH=CH_2$
= $-(CH_2)_2-NEt_2$

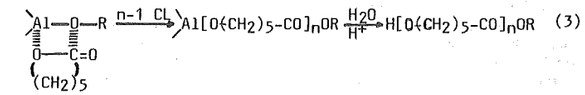
All the reactions were carried out under nitrogen using carefully dried alcohols and freshly distilled triethylaluminum (Fluka) or aluminum isopropoxide (Aldrich).

CL was polymerized under stirring in toluene solution in a flask previously dried and purged with nitrogen. Solvent, monomers and catalyst were added successively. The reaction was stopped by adding an excess (relative to the catalyst) of 2N HCl solution and the catalyst residues were repeatedly extracted with an aqueous EDTA solution (0,1 mol.l^{-1}).[14] After the reaction mixture was washed with water up to neutral pH, the polymeric product was precipitated into an excess of heptane and dried under vacuum up to constant weight.

^{1}H-NMR spectra of PCL were recorded in $CDCl_3$ using a Bruker AM 400 apparatus. GPC analyses were performed in tetrahydrofuran using a Hewlett-Packard 1090 liquid Chromatograph equipped with a 1037A Refractometer Index Detector and a set of columns: pore size 10^5 Å, 10^3 Å, 500 Å and 100 Å. Molecular weight and molecular weight distribution were calculated using a calibration curve set up with polystyrene standards. Low molecular weights ($\bar{M}_n$ < 15.000) were also estimated by ^{1}H-NMR from the comparison of the signal intensities of the α-hydroxymethylene end-group ($-CH_2-OH$) and the ester methylene ($-C(O)O-CH_2-$) in the polyester chain. Molecular weights calculated by ^{1}H-NMR spectroscopy were in close agreement with the values obtained by GPC.

RESULTS AND DISCUSSION

It is known that the ring-opening polymerization of CL is well controlled by Al alkoxides and bimetallic μ-alkoxides at relatively low temperature.[9,10,15] Kinetic and structural data indicate a typical anionic-coordinated insertion mechanism. This reaction proceeds through insertion of the lactone in a metal-alkoxide bond. The specific cleavage of the acyl-oxygen bond of CL results in the bonding of the growing chain to the catalyst through an active alkoxide link. The hydrolysis of the active aluminum-alkoxide link leads to a hydroxyl group at one end of PCL. The second end-group is nothing but an ester carrying the R radical of the initial alkoxide function (eq. 3):



(3)

Accordingly, initiators 1 and 2, carrying a functional group ($-R=-CH_2-X$) should provide a straightforward way to asymmetric telechelic polyesters.[14] Preliminary experiments suggested that opportunity[16] and confirmed that alkyl aluminum bonds were inactive in the lactone polymerization process under strictly anhydrous conditions.[14,17]

Living character of the polymerization. A perfectly "living" behavior is observed when the polymerization of ε-CL is initiated by the functional aluminum alkoxides of the 1 a,b,c and 2 a,b,c series, in toluene at 25°C. This is supported by linear dependence of the experimental molecular weight (^{1}H-NMR and/or GPC) upon monomer conversion (fig. 1). Furthermore, there is a close agreement between the mean degree of polymerization (D.P.) at total conversion and the monomer-to-initiator molar ratio (fig. 2). These relationships hold even for the preparation of molecular weights as high as 100.000.

Since the polymerization of ε-CL is living, the molecular weight of PCL can be predicted by eq. 4 :

$$\bar{M}_{n\ \text{theoretical}} = \frac{[CL]_o.M_{CL}}{[Al].p} \quad (4)$$

where M_{CL} = 114,14 (M.W. of the monomer) and p is the number of active alkoxide groups per aluminum molecule. From the slope of the D.P. vs $[CL]_o/[Al]$ (fig. 2), it appears that p = 1 (each alkoxide group is active) at 25°C when the initiator is a diethylaluminum alkoxide of the 1 a,b,c series. In contrast, the value of p depends on the functional radical R of aluminum trialkoxides of the 2 a,b,c series. It is also observed that the number of active alkoxide groups per aluminum molecule decreases at lower temperatures, i.e. at 0°C compared to 25°C. This phenomenon which results from the increasing coordinative aggregation of the initiator will be studied in more detail in a forthcoming paper.

PCL samples prepared in this study display a rather narrow molecular weight distribution ($\bar{M}_w/\bar{M}_n$ = 1,05 to 1,20). However, that distribution broadens substantially when the

polymer is left for increasing periods of time in the reaction medium. This may be due to the possible intra- and intermolecular transesterification reactions.[7]

End-group structure of poly-ε-caprolactone chains. According to the mechanism of the ε-CL ring-opening polymerization (eq. 3) each PCL chain should thus be capped at one end by the radical derived from the initiating alkoxide function. In order to state unambiguously that the functional group X associated to the alkoxide is actually attached to the PCL chain, corresponding ^{1}H-NMR data are reported in Table I for Poly-ε-CL, initiated by Et_2-Al-O-CH_2-X 1 a,b,c. They are indeed consistent with the presence of the functional R radical associated to the initiator. The same qualitative conclusion is also supported by IR spectroscopy; for instance, PCL initiated by CH_2=CH-$(CH_2)_3$-O-$AlEt_2$ 1 b shows an absorption at 1630 cm^{-1} typical of the olefinic group.

More interestingly, the theoretical molecular weight as calculated by eq. 4 is in a very close agreement (better than 95%) with the experimental value determined by GPC and by ^{1}H-NMR, i.e. from the integration of the signals corresponding to the ester methylene in the polyester chain (-C(O)O-CH_2-) at δ= 4,06 ppm, and either the α-hydroxylmethylene end-group (-CH_2-OH) at δ= 3, 64 ppm, or some of the protons $H_{(a-e)}$ of the functional ester at the end of the chain (Table I).

So each molecule of initiator initiates the polymerization, but only R-O- groups from aluminum alkoxides 1 a,b,c can open the lactone ring, as expected, each PCL chain is quantitatively capped by the functional group at one end and by a hydroxyl group at the other end.

The polymerization and selective functionalization technique reported in this paper has been extended successfully to other functional alkoxides as obtained by reaction of the appropriate functional alcohol with either alkylaluminum, alkyl aluminum hydride or aluminum trialkoxide. It is worth noting that the use of 2-hydroxyethylmethacrylate (HEMA) is a straightforward way to PCL macromonomers and, in a further step, to graft copolymers containing tailored PCL branches. Another example is the controlled synthesis of α,ω-dihydroxyl PCL using the reaction product of one mole of a diol and 2 moles of $AlEt_3$ as an initiator. 2,2'-methyliminodiethanol is another diol that offers the opportunity to insert a tertiary amine in the central position of hydroxy-telechelic PCL. All these opportunities will be reported extensively in the near future as well as the effect of the functional groups X on the kinetics of CL polymerization.

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Table I : ^{1}H-NMR chemical schifts δ(ppm, relative to internal TMS) of hydrolyzed polyesters obtained by the reaction of CL and initiators 1 a,b,c :

R-O-C(=O)-CH_2-CH_2-CH_2-CH_2-CH_2-O-$]_n$-C(=O)-CH_2-CH_2-CH_2-CH_2-CH_2-O-H

δ(ppm)= 2,31 1,64 1,39 1,64 4,06 2,31 1,64 1,39 1,64 3,64

R-O-	Chemical schifts δ,ppm (Intensities) H_a	H_b	H_c	H_d	H_e	-CH_2-OH	$\bar{M}_{n\,^1H\text{-}NMR}$	$\bar{M}_{n\,theor}$(1)
Br-CH_2-CH_2-O- a b	3,52(5,74)	4,39(5,76)				3,64(5,83)	3,100	3,000
CH_2=CH-CH_2-CH_2-O- a b c d e	5,02(0,57)	5,80(0,27)	2,15(0,53)	1,74(-)(2)	4,06(-)(3)	3,64(0,58)	4,980	5,000
$[CH_3$-$CH_2]_2$-N-CH_2-CH_2-O- a b c d e	1,02(1,95)		2,51(4,25)	1,76(-)(2)	4,06(-)(3)	3,64(0,67)	8,800	8,900

(1) Molecular weight calculated from eq. 4 (p=1)
(2) Superimposed to signal at 1,64 ppm corresponding to β-ester methylene in the polymer chain (-O-C(O)-CH_2-CH_2-)
(3) Superimposed to signal at 4,06 ppm corresponding to ester methylene in the polymer chain (-CH_2-O-C(O)-)

Figure 1
Relationship between $\bar{M}_n$ and conversion (%) for the CL polymerization in toluene at 25°C, initiated by 1 a,b,c and 2 a,b,c alkoxides

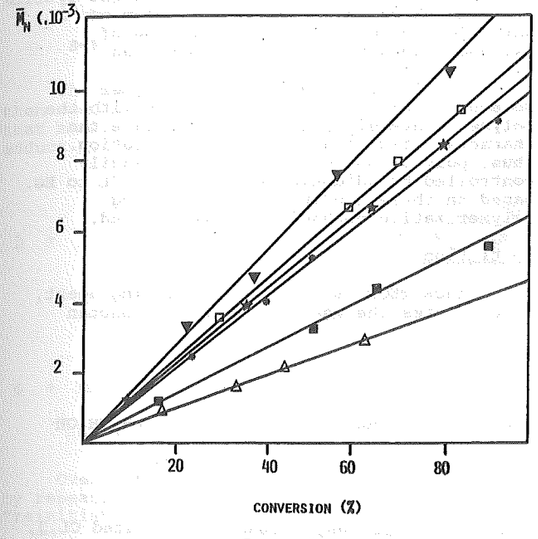
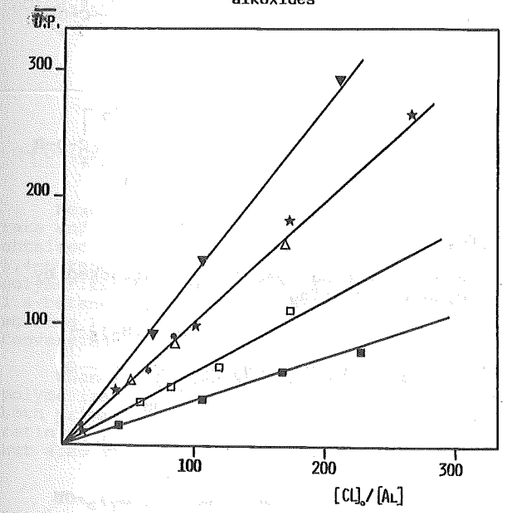


Figure 2
Dependence of $\overline{D.P.}$ on the [monomer]/[initiator] molar ratio in the polymerization of CL in toluene at 25°C initiated by 1 a,b,c ($[CL]_o$= 10,6.10^{-1}M) and 2 a,b,c ($[CL]_o$= 8,6.10^{-1}M) alkoxides



-X	$Al(O-CH_2-X)_3$	$([CL]_o/[Al])$	Et_2-Al-O-CH_2-X	$([CL]_o/[Al])$
-CH_2-Br	■	(167)	★	(88)
$(CH_2)_2$-CH=CH_2	▼	(200)(1)	△	(44)
$(CH_2)_2$-NEt_2	□	(174)	⁕	(87)(2)

(1) Polymerization at 0°C
(2) Polymerization at 35°C