Macromolecular Engineering of Polylactones and Polylactides. 3. Synthesis, Characterization, and Applications of Poly(ε-caprolactone) Macromonomers

Ph. Dubois, R. Jérôme,* and Ph. Teyssié

Laboratory of Macromolecular Chemistry and Organic Catalysis, University of Liège, Sart-Tilman B6, 4000 Liège, Belgium

Received March 13, 1990; Revised Manuscript Received July 16, 1990

ABSTRACT: Well-defined ω-methacryloylpoly(ε-caprolactone) (or PCL) macromonomers have been prepared by using an aluminum alkoxide that bears a methacrylic double bond. The initiator results from the equimolar reaction of triethylaluminum with 2-hydroxyethyl methacrylate (HEMA). The coordination–insertion type of polymerization is living and yields exclusively linear macromonomers of a predictable molecular weight with a narrow molecular weight distribution. IR and ^{1}H NMR studies show that the methacryloyl group associated with the active alkoxy group of the initiator is selectively attached to one chain end. Should the living polymerization be terminated by methacryloyl chloride, and a α,ω-dimethacryloyl-PCL, i.e. a α,ω-macromonomer is obtained. PCL macromonomers and HEMA are easily copolymerized in the presence of AIBN, resulting in a hydrophilic poly(HEMA) backbone grafted with hydrophobic PCL subchains.

Introduction

Macromolecular engineering is the ultimate goal of the polymer chemist when he has a monomer or a family of monomers at his disposal. Once each step of the polymerization process is carefully controlled, each molecular parameter of the polymer is predictable: molecular weight, tacticity, nature of the end groups, and molecular weight distribution. Like pieces of a construction set, these properly tailored macromolecules can then be used to design new polymeric materials. Block and graft copolymers are convincing examples of well-controlled molecular architectures that comprise at least two polymeric components and lead to original materials, e.g., thermoplastic elastomers, polymeric emulsifiers, etc.

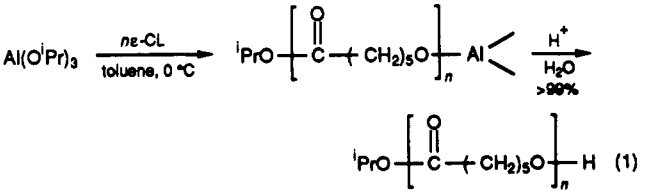
For a few years, the advent of macromonomers has marked a real breakthrough in the tailoring of graft copolymers.[1,2] They can be synthesized by either initiating a living polymer or terminating it with an organic compound that bears the required double bond.[3-5] If such a compound was not available, a macromonomer can, however, be obtained by the appropriate chemical modification of a preexisting reactive end group. In any event, the end capping must be as quantitative as possible.

Recently, we have reported the living polymerization and selective end functionalization of poly(ε-caprolactone) (PCL).[6,7] Aluminum alkoxides carrying functional alkoxy groups are effective initiators of the ε-caprolactone (ε-CL) polymerization. The coordination–insertion type of polymerization is perfectly living and yields exclusively linear polyesters of a predictable molecular weight with a narrow molecular weight distribution. This paper is concerned with the potentialities of aluminum alkoxides in the synthesis of PCL macromonomers. Unsaturated alkoxides have been purposely synthesized, whereas there are advantages from the polymerization mechanism that systematically leads to the formation of a reactive hydroxyl end group. This new type of macromonomer provides an easy access to different graft copolymers as illustrated by the copolymerization with unsaturated comonomers, such as 2-hydroxyethyl methacrylate (HEMA).

Results and Discussion

Two different pathways have been envisioned in order to prepare PCL macromonomers. The first one relies upon a two-step procedure, i.e., ε-CL polymerization using aluminum isopropoxide as an initiator, followed by the esterification by the hydroxyl end group by methacrylic acid. The second approach is direct based on the synthesis of an aluminum alkoxide bearing a double bond of the methacrylic type.

I. Synthesis of a PCL Macromonomer by a Two-Step Method. It is well-known that aluminum isopropoxide is a very effective initiator of ε-CL polymerization. The propagation step is actually a living process that leads to a polymer with a narrow molecular weight distribution.[8,9] The molecular weight is predictable on the basis of the monomer to initiator molar ratio. Furthermore, the hydrolysis of the chain-growing sites results in the selective capping of one chain end with a hydroxyl group (eq 1).



(1)

1

Esterification of the hydroxyl end group by, e.g., methacrylic acid is an obvious way to PCL macromonomers. Purposely, methacrylic acid was activated by a carbodiimide, dicyclohexylcarbodiimide (DCCI), as previously reported in peptide synthesis.[10-12] The formed *O*-acylisourea 2 was identified by ^{1}H NMR and IR spectroscopy and added to the THF solution of ω-hydroxy PCL 1 in the presence of triethylamine and 4-(dimethylamino)pyridine (DMAP) under dry conditions (eq 2).

According to the ^{1}H NMR spectrum of Figure 1, the PCL chains are quantitatively (±5%) end capped with a methacryloyl unit. The signal of the α-hydroxymethylene end group ($-CH_2OH$) at 3.64 ppm has completely disappeared in favor of a new signal at 4.14 ppm, which can be assigned to the methacryloyl ester methylene. The intensity of the protons a and b of the methacryloyl end group corresponds quite closely to that of the protons i and h of the second isopropyl end group. Furthermore, molecular weight and polydispersity ($\bar{M}_w/\bar{M}_n$ = 1.1) of

0024-9297/91/2224-0977$02.50/0 © 1991 American Chemical Society

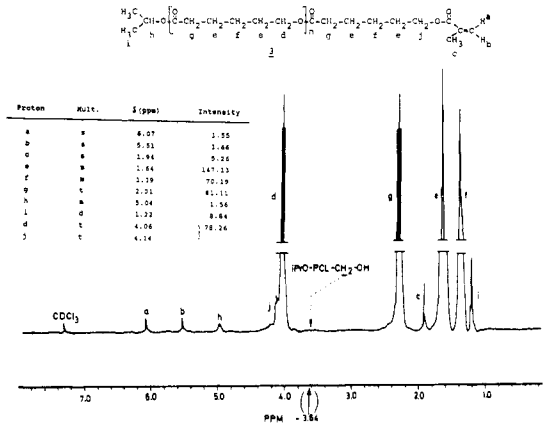
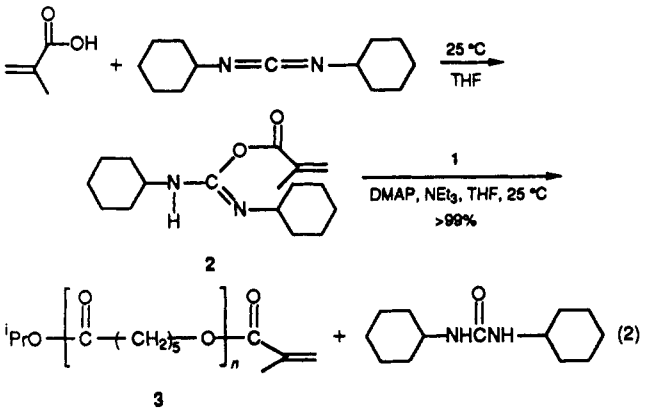


Figure 1. ^{1}H NMR spectrum of α-isopropyl ester ω-methacryloyl-PCL ($\bar{M}_n$ = 2800) (see eq 2) in $CDCl_3$.

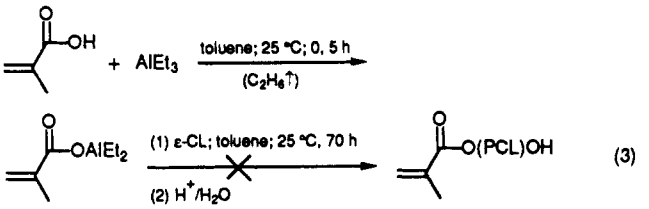


the starting PCL remain unchanged during the whole esterification process.

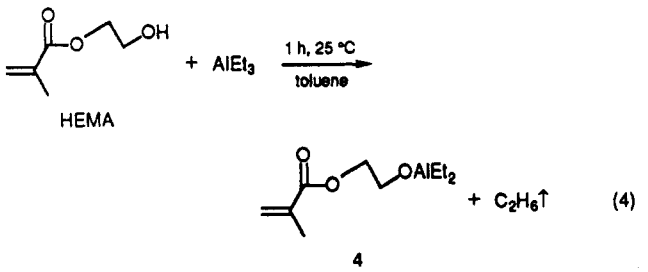
II. One-Step Synthesis of PCL Macromonomers. The two-step technique is a very time-consuming procedure, since it requires the hydrolysis of the living chain end with formation of the terminal hydroxyl group and the purification of the polymer (extraction of Al residues by EDTA) followed by a drying step and redissolution in dry THF in view of the esterification reaction. This complexity should, however, be circumvented whether the initiator bears an unsaturated and polymerizable group or alternatively an unsaturated reagent deactivates the living polymer and is attached at the related extremity.

II.a. Synthesis and Use of a Functional Aluminum Alkoxide Initiator. Synthesis of aluminum alkoxides carrying functional alkoxy groups, $Et_2AlOCH_2CH_2X$ where X = -Br, $-CH_2CH{=}CH_2$, and $-CH_2NEt_2$, has been reported recently as well as their use as initiators in the ring-opening polymerization of ε-caprolactone.[6,7] According to the polymerization mechanism, one end of each PCL chain is quantitatively capped by the functional group associated to the initiator ($-C(O)OCH_2CH_2X$), whereas the second extremity bears the hydroxyl group as already mentioned (eq 1). Asymmetric telechelic polyesters (-X, -OH) can thus be obtained in a perfectly controlled way. This strategy opens a straightforward access to PCL chains capped at one end by a methacryloyl moiety.

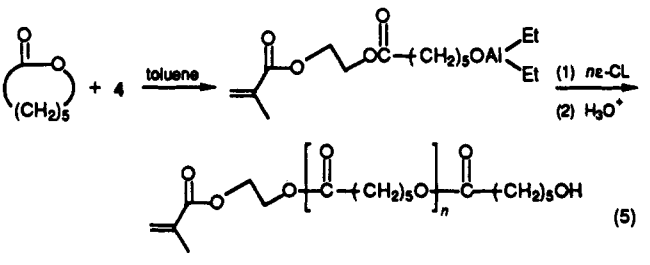
In a preliminary attempt, triethylaluminum has been reacted with an equimolar amount of methacrylic acid, in order to produce a diethylaluminum methacrylate (eq 3). This compound is, however, unreactive toward the ring-opening polymerization of ε-CL in agreement with former results from our laboratory.[13] Furthermore, Inoue et al. have also reported that ε-CL cannot be polymerized by (5,10,15,20-tetraphenylporphinato)aluminum carboxylates in contrast to (porphinato)aluminum alkoxides.[14,15]



In a second approach, diethylaluminum 2-hydroxyethyl methacrylate (4) has been prepared by substitution of one ethyl group of $AlEt_3$ by freshly distilled 2-hydroxyethyl methacrylate (eq 4) (see the Experimental Part). The



structure of compound 4 was confirmed by an ^{1}H NMR spectrum (Figure 2). The signal due to the $-CH_2OAlEt_2$ proton (H_d) at 3.76 ppm is quantitatively observed. Diethylaluminum 2-hydroxyethyl methacrylate (4) behaves as an initiator of the ε-CL polymerization, although alkylaluminum bonds are known to be inactive in the lactone polymerization under strictly anhydrous conditions.[16] It means that the lactone has likely been polymerized by insertion into the aluminum–alkoxide bond as previously reported.[7] If it is so, the acyl–oxygen cleavage of the lactone occurs in a way that maintains the binding of the growing chain to the aluminum through an alkoxide link. The hydrolysis of this active aluminum–alkoxide bond should thus lead to a hydroxyl end group, the second end group being an ester carrying the methacryloyl radical associated to the alkoxide function (eq 5).



In order to confirm unambiguously that PCL is selectively and quantitatively capped by a methacryloyl group and a hydroxyl function, respectively, the recovered polyester has been characterized by ^{1}H NMR (Figure 3) and IR (Figure 4) spectroscopy. The absorption at 1625 cm^{-1} is consistent with the presence of the carbon–carbon double bond (Figure 4). The same conclusion is supported by the signals at 5.60 and 6.12 ppm of the ^{1}H NMR spectrum (Figure 3).

More interestingly, Table I shows that molecular weight determined by GPC or/and by ^{1}H NMR is in close agreement with the theoretical value ($\bar{M}_{n\ theor}$) calculated for a living polymerization taking into account the conversion (x) (eq 6).

$$\bar{M}_{n\ theor} = \frac{[CL]_0 M_{CL} x}{[4]_0} \qquad (6)$$

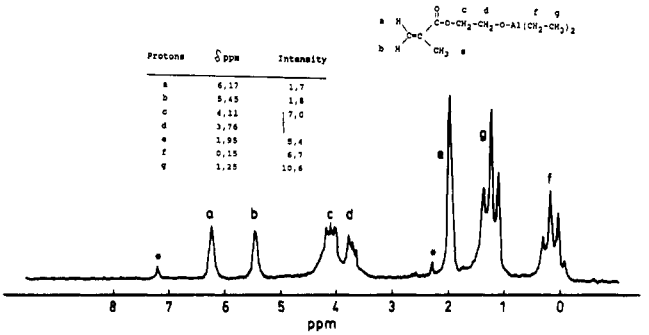


Figure 2. ^{1}H NMR spectrum of diethylaluminum 2-hydroxyethyl methacrylate 4 in toluene-d_8 (*).

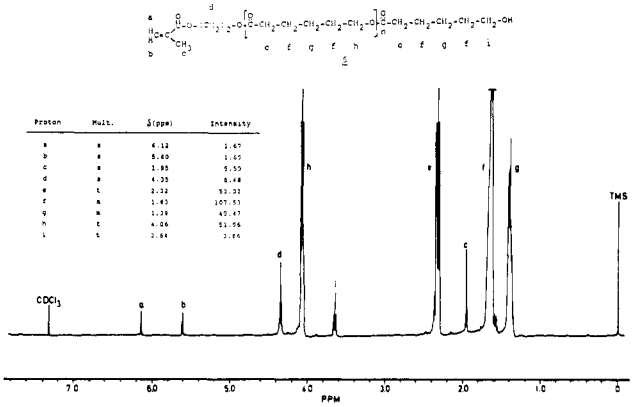


Figure 3. ^{1}H NMR spectrum of PCL 5 ($\bar{M}_n$ = 1650) as recovered after hydrolysis of PCL initiated by diethylaluminum alkoxide 4 (solvent, $CDCl_3$; reference, TMS).

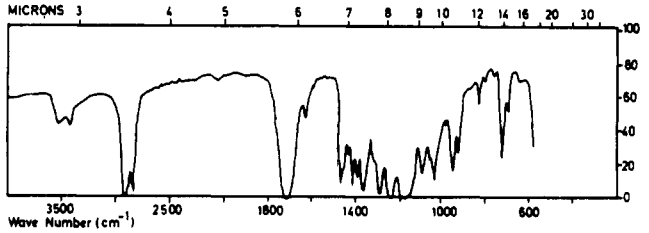


Figure 4. IR spectrum of PCL 5 ($\bar{M}_n$ = 1650) as recovered after hydrolysis of PCL initiated by diethylaluminum alkoxide 4.

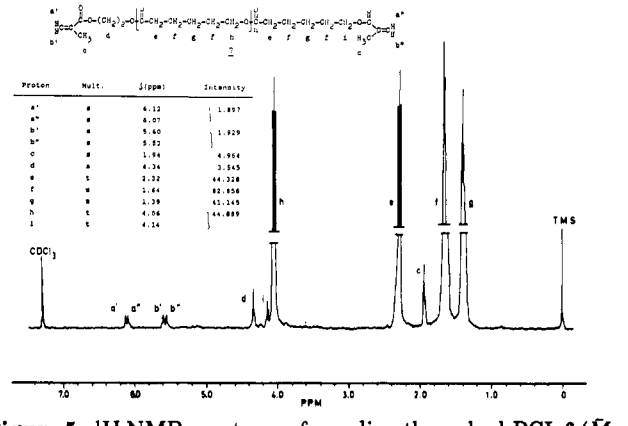


Figure 5. ^{1}H NMR spectrum of α,ω-dimethacryloyl-PCL 6 ($\bar{M}_n$ = 2900) (see eq 7) in $CDCl_3$ (reference, TMS).

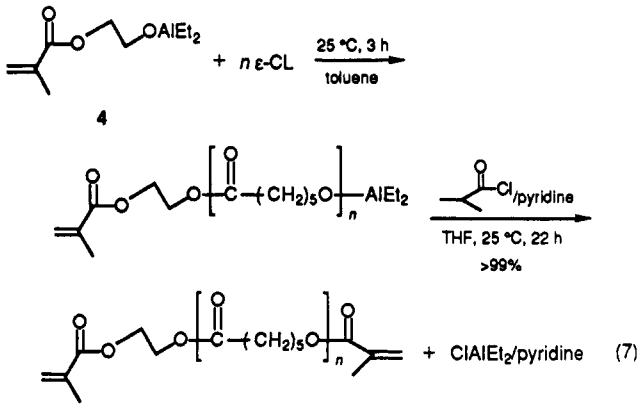
At least in the $\bar{M}_n$ range up to 20 000, the polymerization obeys a perfectly living mechanism and the molecular weight of the PCL macromonomer can be predicted by the initial monomer to initiator 4 molar ratio.

It must be stressed that the polymerization is only living under strictly anhydrous conditions and particularly when 2-hydroxyethyl methacrylate is carefully dried and freshly distilled before use.

II.b. Simultaneous Control of the Initiation and Termination Steps. It would also be of great interest to control the termination step, i.e., to substitute the usual acid hydrolysis of the propagating sites by a specific reaction of the aluminum alkoxide group with a functionalized reagent, e.g., methacryloyl chloride.

Such a procedure would allow us to prepare a PCL macromonomer when the polymerization has been initiated by aluminum isopropoxide. More interestingly, combination of initiation by functional aluminum alkoxide 4 and termination by methacryloyl chloride is a one-pot technique for the synthesis of α,ω-dimethacryloyl-PCL, i.e., a prepolymer that could be used in a photochemically or thermally cross-linked resin.

As an example, ϵ-CL was polymerized in toluene at 25 °C by using the aluminum alkoxide 4 as an initiator, followed by reaction with methacryloyl chloride (eq 7). After hydrolysis, the quantitatively recovered PCL di-



(7)

functional macromonomer (α,ω-dimethacryloyl PCL or α,ω-macromonomer) 6 was characterized by ^{1}H NMR (Figure 5). The signal at 3.64 ppm corresponding to the α-hydroxymethylene protons (see Figure 3) has been accordingly shifted to lower field (δ_{H_f} = 4.14 ppm). Furthermore, extra signals observed at $\delta_{H_a''}$ = 6.07 ppm and $\delta_{H_b''}$ = 5.53 ppm can be assigned to the methacrylic unsaturation.

Still another possible pathway to PCL, α,ω-macromonomers could consist of coupling, provided a very high yield (>95%), of the asymmetric ω-hydroxy α-methacryloyl-PCL or better the living ω-aluminum alkoxide α-methacryloyl-PCL by a difunctional agent. These coupling reactions will be discussed in detail in a forthcoming paper.

III. Application: Synthesis of "Graft" Copolymers. Free-radical copolymerization of a macromonomer with a vinylic or (meth)acrylic comonomer has been and is still a major field of application providing an easy access to a variety of regular graft copolymers. The original properties of graft (and also block) copolymers has to be found in the incompatibility of the constitutive polymer chains. Among other opportunities, let us recall the possible surface modification of a polymer matrix by a small amount of an appropriate graft copolymer. For instance, Yamashita et al. have copolymerized an ω-methacryloylpoly(methyl methacrylate) macromonomer with 2-hydroxyethyl methacrylate[4,17] and have proven that these copolymers could diffuse to and reorganize at the surface of PMMA films. The PMMA grafts play the role of anchoring segments whereas the more hydrophilic backbone can constitute the interface with water.

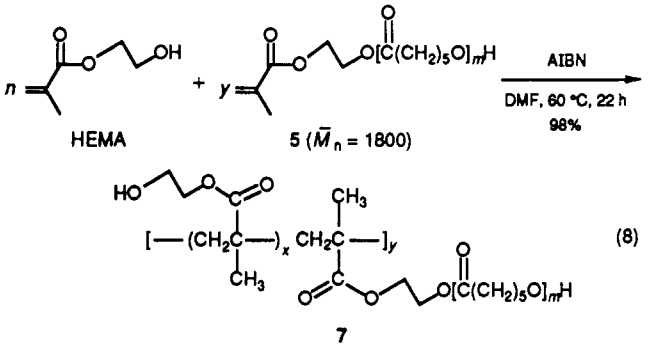
Among the various monomers that can be copolymerized with the PCL macromonomers, we selected HEMA. HEMA is a very interesting hydrophilic monomer due to the biocompatibility of the polymer it generates.[18,19]

Table I
Polymerization of ε-CL Initiated by the Diethylaluminum Alkoxide 4 in Toluene at 25 °C

$[CL]_0 \times 10^1$ mol L^{-1}	$[4]_0$, mol L^{-1}	time, h	convn (x), %	$\bar{M}_{n\ theor}$[a]	$\bar{M}_n$ ^1H NMR[b]	$\bar{M}_n$ GPC	$\bar{M}_w/\bar{M}_n$
7.85	6.05×10^{-2}	2	>99	1500	1650	1800	1.2
9.04	3.43×10^{-2}	3	98	2940	2950	2850	1.3
8.00	9.09×10^{-3}	23	79	7900	8000	7500	1.2
8.08[c]	4.61×10^{-3}	71	>99	20000	21300	20000	1.5

[a] Molecular weight calculated from eq 6. [b] Molecular weight determined from the relative intensity of the α-hydroxymethylene end group ($-CH_2OH$: δ_{H_i} = 3.64 ppm) and the ester methylene ($-C(O)OCH_2-$; δ_{H_h} = 4.06 ppm) of the polyester chain. [c] In THF solution.

The ω-methacryloyl-PCL macromonomer **5** was thus copolymerized with 2-hydroxyethyl methacrylate in dimethylformamide (DMF) at 60 °C for 22 h, using azo-2,2′-bis(isobutyronitrile) (AIBN) as a free-radical initiator (eq 8).



(8)

DMF was replaced by THF, i.e., a nonsolvent of the poly(HEMA). At a structural unit ratio (nHEMA/(ym)CL) of 1.74, no homopoly(HEMA) was observed (clear solution in THF) and no PCL macromonomer or comonomer was left, as confirmed by the absence of the unsaturation signals in the IR and ^1H NMR spectra. Characterization and applications of the graft copolymer will be the topic of another paper.

In conclusion, PCL macromonomers of the methacrylic type can be efficiently prepared according to various pathways. In particular, a direct access has been made possible by the synthesis and the ring-opening capability of a diethylaluminum methacryloyl alkoxide. Furthermore, α,ω-dimethacryloyl-PCL, i.e., a α,ω-macromonomer, has also been successfully synthesized by the simultaneous control of the initiation and the termination steps.

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) and aluminum isopropoxide (Aldrich) were purified by distillation under reduced pressure. 2-Hydroxyethyl methacrylate (HEMA) was dried over molecular sieves (4 Å) at room temperature and distilled under reduced pressure just before use. The ethylene dimethacrylate (EGDMA) content in the purified HEMA was estimated to be lower than 0.02 mol %. Nevertheless, this byproduct did not react during the polymerization and was eliminated by precipitation of the polyester. Methacryloyl chloride (dried over CaH_2) and methacrylic acid were freshly distilled before use. Toluene and tetrahydrofuran (THF) were dried by refluxing over calcium hydride and a benzophenone–sodium complex, respectively.

Measurements. IR spectra were recorded by using a Perkin-Elmer IR 197. ^1H NMR spectra of PCL were recorded in $CDCl_3$ or in toluene-d_8 by using Bruker AM400 or Varian EM360L spectrometers. Gel permeation chromatography (GPC) 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: pore sizes 10^5, 10^3, 500, and 100 Å. Molecular weight and molecular weight distribution were calculated by using a calibration curve set up with polystyrene standards. Molecular weights of oligomers were also estimated by ^1H NMR from the comparison of the signal intensities of protons adjacent to a characteristic end group (particularly the α-hydroxymethylene end group ($-CH_2OH$) and the ester methylene ($-C(O)OCH_2-$)) in the polyester chain. The molecular weights calculated by ^1H NMR spectroscopy were in close agreement with the values obtained by GPC.

Synthesis of α-Isopropyl Ester ω-Hydroxy-PCL 1. ε-CL polymerization initiated by aluminum isopropoxide in toluene at room temperature has been previously described.[8]

Preparation of α-Isopropyl Ester ω-Methacryloyl-PCL Macromonomer 3. The α-isopropyl ester ω-hydroxy PCL **1** was esterified with methacrylic acid using the dicyclohexylcarbodiimide (DCCI) method: freshly distilled methacrylic acid (9 mmol) and DCCI (9 mmol) were dissolved in anhydrous THF at 25 °C. The reaction product was identified by ^1H NMR and IR spectroscopy as the *O*-acylisourea **2**. It was slowly added to a THF solution of DMAP (0.7 mmol), NEt_3 (1.8 mmol), and ω-hydroxy PCL of 2800 $\bar{M}_n$ (5.0 g, 1.8 mmol), previously dried by repeated toluene azeotropic distillation, and kept for 1 night under vacuum. After a 22-h reaction time, the reaction medium was hydrolyzed, the precipitated dicyclohexylurea was filtered, and the polymer was finally recovered from THF by precipitation in cold heptane. After filtration, it was dried for 24 h at room temperature under reduced pressure.

Preparation of ω-Hydroxy α-Methacryloyl-PCL Macromonomer 5. Polymerization of CL Initiated by Aluminum Alkoxide 4 in Toluene at Room Temperature. Preparation of the initiator **4**: 1.0 mmol of strictly anhydrous and freshly distilled 2-hydroxyethyl methacrylate in 100 mL of toluene was slowly added into a carefully flamed Pyrex flask equipped with a rubber septum, connected to a gas buret through an oil valve and containing an equimolar amount of $AlEt_3$ in 90 mL of toluene. The reaction proceeded under nitrogen and under a vigorous stirring at room temperature ($^1/_2$ h) and at 40 °C ($^1/_4$ h) to quantify the reaction as determined by volumetry experiments. When the evolution of ethane stopped, the catalyst solution was kept under stirring for an extra 1 h at room temperature.

Polymerization Procedure. ε-CL polymerization, initiated by a desired quantity of aluminum alkoxide **4** (calculated from eq 6), was carried out under stirring in toluene solution in a flask previously dried, purged with nitrogen, and kept at 25 °C for a suitable period of time. The reaction was stopped by adding a 10-fold excess of 2 N HCl solution with regard to Al.

The catalyst residues were removed by repeated extractions with an aqueous EDTA solution (0.1 mol L^{-1}), and the polymeric solution was washed with water up to neutral pH. Two-thirds of the initial toluene was removed under reduced pressure, and the macromonomer **5** was further recovered from toluene by precipitation. It was finally dried for 24 h at room temperature under reduced pressure.

Synthesis of α,ω-Dimethacryloyl-PCL α,ω-Macromonomer 6. The PCL α,ω-macromonomer **6** was synthesized as the macromonomer **5** except for the termination reaction. The aluminum alkoxide polymerization site was indeed reacted with methacryloyl chloride instead of being hydrolyzed.

When the ε-CL polymerization initiated by the initiator **4** was complete, toluene was distilled off and the polymer dissolved in an equal amount of THF. An excess of 10 equiv of methacryloyl chloride and pyridine (previously refluxed over NaOH and distilled) in THF was slowly added to the PCL solutin at 25 °C.

After 22 h, the polymerization medium was hydrolyzed and filtered and the PCL α,ω-macromonomer **6** was isolated by repeated precipitation in heptane. The α,ω-macromonomer **6** was purified as previously described.

Copolymerization of HEMA with PCL Macromonomer 5. α-Hydroxy ω-methacryloyl-PCL macromonomer **5** (1.0 g, 0.6 mmol), distilled HEMA (15.4 mmol), and AIBN (100 mg) in DMF solution were stirred overnight (22 h) at 60 °C. DMF was distilled off and the polymeric product redissolved in THF, precipitated in heptane. It was filtered and dried overnight under reduced pressure. The "graft" copolymer **7** was finally analyzed by IR, ^{1}H NMR, and DSC.

Acknowledgment. We are indebted to the IRSIA for a fellowship to Ph. D. and to the "Services de la Programmation de la Politique Scientifique" for financial support.

References and Notes

(1) Milkovich, R. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1980**, *21* (1), 40.
(2) Schulz, G. O.; Milkovich, J. *J. Polym. Sci., Polym. Chem. Ed.* **1984**, *22*, 1633, 3795.
(3) Rempp, P. F.; Franta, E. *Adv. Polym. Sci.* **1984**, *58*, 1.
(4) Yamashita, Y. *J. Appl. Polym. Sci., Appl. Polym. Symp.* **1981**, *36*, 193.
(5) Chujo, Y.; Shishino, T.; Tsukahara, Y.; Yamashita, Y. *Polym. J.* **1985**, *17*, 133.
(6) Dubois, Ph.; Jérôme, R.; Teyssié, Ph. *Polym. Bull.* **1989**, *22*, 475.
(7) Dubois, Ph.; Jérôme, R.; Teyssié, Ph. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1990**, *31* (1), 7.
(8) Ouhadi, T.; Stevens, C.; Teyssié, Ph. *Makromol. Chem.* **1975**, Suppl. 1, 191.
(9) Vion, J. M.; Jérôme, R.; Teyssié, Ph.; Aubin, M.; Prud'homme, R. E. *Macromolecules* **1986**, *19*, 1828.
(10) Sheerhan, J.; Hess, G. *J. Am. Chem. Soc.* **1955**, *77*, 1067.
(11) Mathias, L. *J. Synthesis* **1979**, 561.
(12) Gnanou, Y.; Rempp, P. *Makromol. Chem.* **1987**, *188*, 2111.
(13) Heuschen, J.; Jérôme, R.; Teyssié, Ph. *Macromolecules* **1981**, *14*, 242.
(14) Endo, M.; Aida, T.; Inoue, S. *Macromolcules* **1987**, *20*, 2982.
(15) Yasuda, T.; Aida, T.; Inoue, S. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3931.
(16) Hsieh, H. L.; Wang, I. W. *Ring-Opening Polymerization*; McGrath, J. E., Ed.; ACS Symposium Series 286; American Chemical Society: Washington, DC, 1985; p 161.
(17) Yamashita, Y.; Tsukahara, Y.; Ito, K.; Okada, K.; Tajima, Y. *Polym. Bull.* **1981**, *5*, 335.
(18) Kataoka, K.; Sakurai, Y.; Tsuruta, T. *Makromol. Chem.* **1985**, Suppl. 9, 53.
(19) Maruyama, A.; Tsuruta, T.; Kataoka, K.; Sakurai, Y. *Makromol. Chem. Rapid Commun.* **1987**, *8*, 27.

Registry No. 4, 131458-77-0; **5** (SRU), 81984-60-3; **6** (SRU), 131458-60-1; **8** (graft copolymer), 113253-80-8; $H_2C{=}C(CH_3)CO_2(CH_2)_2OH$, 868-77-9; $AlEt_3$, 97-93-8.