New Functional Aliphatic Polyesters by Chemical Modification of Copolymers of ϵ-Caprolactone with γ-(2-Bromo-2-methylpropionate)-ϵ-caprolactone, γ-Bromo-ϵ-caprolactone, and a Mixture of β- and γ-Ene-ϵ-caprolactone

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ABSTRACT: New functional aliphatic polyesters were prepared by chemical modification of brominated copolyesters. Poly(ϵ-caprolactone)-*co*-poly(γ-(2-bromo-2-methylpropionate)-ϵ-caprolactone) copolymer was prepared and successfully converted into copolyester bearing methacrylate double bonds by dehydrohalogenation of the pendant tertiary alkyl bromides, thus leading to cross-linkable polyester. The tertiary alkyl bromide groups of the original copolyester were also quaternized by reaction with pyridine, although some side reactions occurred which limited the reaction yield. Nevertheless, quaternization of the bromide groups of the poly(ϵ-caprolactone)-*co*-poly(γ-bromo-ϵ-caprolactone) copolymer proved to be quantitative and to occur without degradation of the polyester chains. This general strategy paves the way to either amphiphilic copolyesters or water-soluble polyesters. The poly(ϵ-caprolactone)-*co*-poly(γ-bromo-ϵ-caprolactone) copolymer was also quantitatively converted into unsaturated copolyester by dehydrohalogenation with formation of double bonds including acrylic-type double bonds. As an alternative, γ-bromo-ϵ-caprolactone was first dehydrohalogenated, and the unsaturated cyclic monomer was copolymerized with ϵ-caprolactone. Finally, the nonconjugated double bonds of the copolyesters were oxidized into epoxides, except for the acrylic-type unsaturations which remained unchanged.

Introduction

Aliphatic polyesters, such as poly(ϵ-caprolactone) (PCL), polylactides (PLA), and polyglycolide (PGA), are of great interest for biomedical applications. These materials are biodegradable, bioresorbable, and permeable to many drugs which makes them excellent candidates for components of drug delivery systems, resorbable protheses, chemotherapy, and galenic formulations.[1] These polymers have the advantage of being readily hydrolyzed into their α-hydroxy acid constituents, which are eliminated by the usual metabolic pathways. However, the biodegradation rate of these polyesters depends on their chemical structure, hydrophobicity, and degree of crystallization.

Aliphatic polyesters are commonly prepared by ring-opening polymerization (ROP) of the parent cyclic esters. Aluminum alkoxides are efficient initiators for the ring-opening polymerization of lactones and lactides, since polyesters of predictable molecular weight, narrow molecular weight distribution, and bearing functional end groups can be synthesized and random, block, and graft copolymers, as well.[2] However, only a few examples of aliphatic polyesters bearing functional pendant groups were reported,[3] although these polymers are highly desirable for tailoring properties including hydrophilicity, biodegradation rate, bioadhesion, and biological activity. Recently, synthesis, homopolymerization, and random copolymerization of γ-(2-bromo-2-methylpropionate)-ϵ-caprolactone (BMPCL) were reported.[4] The pendant 2-bromo-2-methyl propionate groups were used as macroinitiators for the ATRP of methyl methacrylate with formation of poly(ϵ-caprolactone)-*graft*-poly(methyl methacrylate) copolymers. Homopolymerization and random and block copolymerization of γ-bromo-ϵ-caprolactone (γBrCL) were also reported.[5] The purpose of this paper is to illustrate the contribution of the BMPCL and γBrCL brominated lactones to the synthesis of novel functional aliphatic polyesters by the selective derivatization of the pendant alkyl bromide groups of copolyesters into a series of nondirectly available reactive groups. As an additional approach, γBrCL will also be converted into unsaturated ϵ-caprolactone by dehydrohalogenation, followed by synthesis of unsaturated copolyester.

Experimental Section

Materials. Toluene was refluxed over sodium and distilled under nitrogen prior to use. ϵ-Caprolactone (ϵCL) was dried over CaH_2, distilled under reduced pressure, and stored under dry nitrogen atmosphere. γ-(2-Bromo-2-methyl propionate)-ϵ-caprolactone (BMPCL)[4] and γ-bromo-ϵ-caprolactone (γBrCL)[5] were prepared as reported elsewhere.

A mixture of 6,7-dihydro-2(5*H*)-oxepinone (**1**), 6,7-dihydro-2(3*H*)-oxepinone (**2**), and 4,7-dihydro-2(3*H*)-oxepinone (**3**) was prepared as follows: 10.2 g of DBU (1,8-diazabicyclo[5.4.0]-undec-7-ene, 67 mmol) was added to a solution of 10 g of γ-bromo-ϵ-caprolactone (52 mmol) in 50 mL of toluene under nitrogen. The mixture was heated at 80 °C for 2 h with formation of a white solid, which was filtered out. The organic phase was added with 50 mL of water and 1 N HCl until pH = 7. The organic phase was then washed with water (3 × 30 mL) and dried over $MgSO_4$, and toluene was eliminated under vacuum. A yellow liquid was collected and purified by chromatography through a silica gel column using CH_2Cl_2/EtOAc 85/15 as an eluent. A mixture of β- and γ-ene-ϵ-caprolactone

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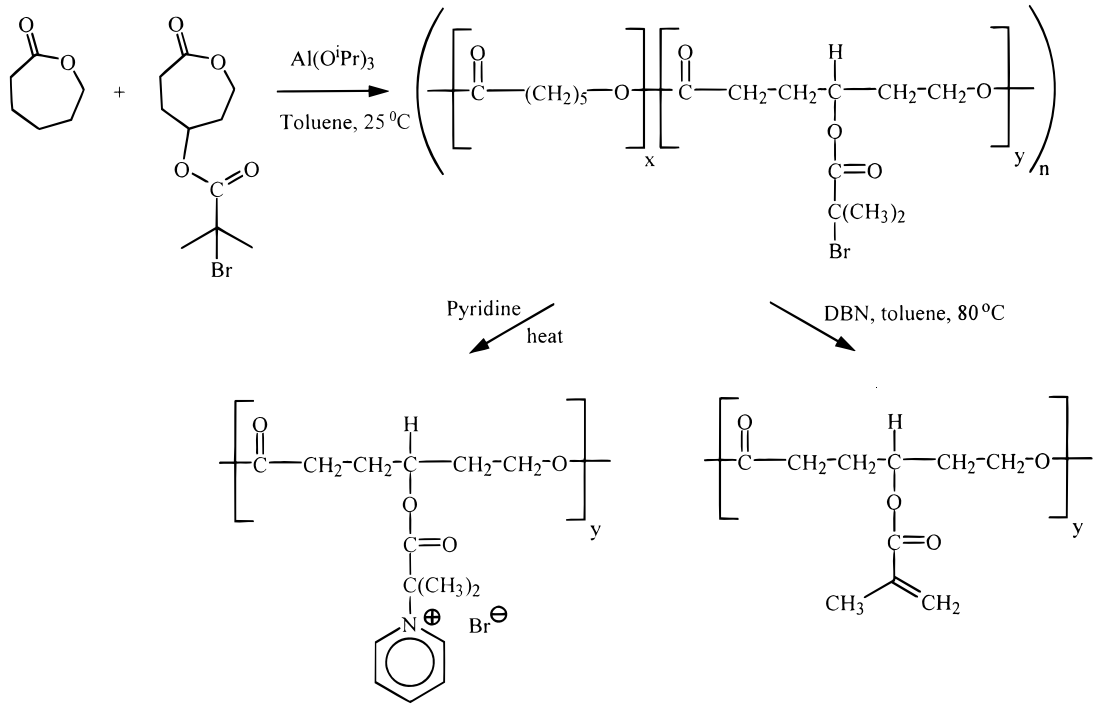
Scheme 1



(50:50) was isolated (1.3 g after distillation), together with a mixture of the α, *β*, and *γ* isomers (90:5:5) (0.4 g after distillation).

^{1}H NMR analysis of the three unsaturated isomers of *ϵ*-caprolactone in $CDCl_3$ gave the following data: 6,7-dihydro-2(5*H*)-oxepinone (α-isomer or **1**), *δ* 6.48 (1 H, dt), 5.97 (1 H, dt), 4.30 (2 H, m), 2.70−2.38 (2 H, m) and 2.28−1.97 (2 H, m) ppm; 6,7-dihydro-2(3*H*)-oxepinone (the *β*-isomer or **2**), *δ* 3.38 (2 H, m), 4.42 (2 H, m), 2.47 (2 H, m), 5.50−5.80 (2 H, m) ppm; 4,7-dihydro-2(3*H*)-oxepinone (the *γ*-isomer or **3**), *δ* 2.45 (2 H, m), 2.89 (2 H, m), 4.66 (2 H, m) and 5.81 (2 H, m) ppm. All the other chemicals were purchased from Aldrich and used without further purification.

Polymerization Technique. Homopolymerization and random copolymerization were carried out at 0 or 25 °C in dry toluene (10 wt % of monomer). BMPCL, *γ*BrCL, and unsaturated *ϵ*-caprolactone were dried by repeated (three times) azeotropic distillation of toluene in the polymerization flask. Solvent, *ϵ*-caprolactone if needed, and initiator (dissolved in toluene) were then added sequentially through a rubber septum with syringe or stainless steel capillary. After polymerization, an excess of 1 N HCl was added, and the polymer was recovered by precipitation in cold heptane or methanol.

Chemical Derivatization of the Brominated Aliphatic Polyesters. *Reaction with Pyridine (Quaternization Reaction).* In a common experiment, 0.5 g of copolymer was dissolved in 5 mL of pyridine. Reaction took place under stirring at the desired temperature. When the reaction was complete, the excess of pyridine was eliminated under vacuum, and the polymer was purified by repeated precipitation from THF in heptane.

Dehydrohalogenation of the Alkyl Bromide. The copolymer (0.3 g, 0.23 mmol of alkyl bromide) and 1,5-diazabicyclo[4.3.0]-non-5-ene (DBN) (0.155 g, 1.25 mmol) or 1,8-diazabicyclo[5.4.0]-undec-7-ene (DBU) (0.19 g, 1.25 mmol) were dissolved in 4 mL of toluene and reacted at 80 °C for 10 h. The reaction solution was concentrated, and the polymer was repeatedly precipitated in cold heptane.

Epoxidation of the Unsaturated Copolyester. The copolymer was dissolved in CH_2Cl_2 (10 wt %) and a 2 M excess of *m*-chloroperoxybenzoic acid (mCPBA) with respect to the double bonds was added dropwise. The reaction was conducted under stirring at room temperature overnight. The organic solution was then washed twice with a solution of sodium bisulfite, followed by a hydrogenocarbonate solution, and then with water. The polymer was finally recovered by repeated precipitation in cold heptane.

Characterization. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ with a Bruker AM 250 (250 MHz) spectrometer and a Bruker AN 400 (400 MHz) apparatus at 25 °C. Size exclusion chromatography was carried out with a Waters chromatograph connected to a Waters 410 differential refractometer, using polystyrene standards for calibration. Four 5 *μ*m Waters columns of increasing pore size (100, 1000, 10^5, and 10^6 Å) were used with THF as solvent. The universal calibration was used for PCL in reference to the viscometric relationships as reported elsewhere.[6]

Results and Discussion

1. Synthesis and Derivatization of Poly(*ϵ*-caprolactone)-*co*-poly(*γ*-(2-bromo-2-methylpropionate)-*ϵ*-caprolactone). Synthesis of *γ*-(2-bromo-2-methylpropionate)-*ϵ*-caprolactone (BMPCL) was reported elsewhere.[4] BMPCL was polymerized in toluene at 25 °C with $Al(O^iPr)_3$ as initiator.[7] It was also copolymerized with *ϵ*CL randomly and in a sequential way[4] (Scheme 1). In agreement with a living process, the BMPCL polymerization shows a very good fit between the experimental molecular weight calculated by ^{1}H NMR and the molecular weight predicted from the monomer to initiator molar ratio and the monomer conversion (entry 1, Table 1). Furthermore, size-exclusion chromatography shows that the elution peak is symmetrical and narrow (M_w/M_n < 1.30), supporting a combination of livingness and initiation faster than propagation. In the case of random copolymers of BMPCL with *ϵ*-caprolactone, the molecular weight is controlled, and the polydispersity is narrow, as shown in Table 1 (entry 2). The "livingness" of the BMPCL polymerization was further substantiated by the quantitative preparation of poly(*ϵ*CL)-*b*-poly(BMPCL) copolymer (entry 3 in Table 1). *ϵ*CL and BMPCL were indeed sequentially polymerized, the PCL block being prepared first followed by the addition and polymerization of BMPCL with formation of the desired block copolymer in quantitative yield.

Table 1. Ring-Opening Polymerization of γ-(2-Bromo-2-methylpropionate)-ϵ-caprolactone and Copolymerization with ϵ-Caprolactone Initiated by Al(O^{i}Pr)$_3$ in Toluene at 25 °C

entry	nature	reaction time (h)	yield (%)	f_{BMPCL}[a]	F_{BMPCL}[b]	M_n[c] theor	M_n[d] NMR	M_n[e] SEC	M_w/M_n
1	P(BMPCL)	24	95	1	1	4000	3800	4800	1.25
2	P(CL-*co*- BMPCL)	20	95	0.10	0.10	7500	7500	8700	1.30
3	P(CL-*b*- BMPCL)	24	95	0.45	0.43	4500	4300	3300	1.25

[a] γ-(2-Bromo-2-methylpropionate)-ϵ-caprolactone molar fraction in the comonomer feed. [b] γ-(2-Bromo-2-methylpropionate)-ϵ-caprolactone molar fraction in the copolymer measured by ^{1}H NMR. [c] Theoretical number-average molecular weight: $M_n = [\epsilon CL]/[init.] \times 114 + MW_{init.}$ [d] Experimental number-average molecular weight measured by ^{1}H NMR. [e] M_n determined by SEC (polystyrene standards).

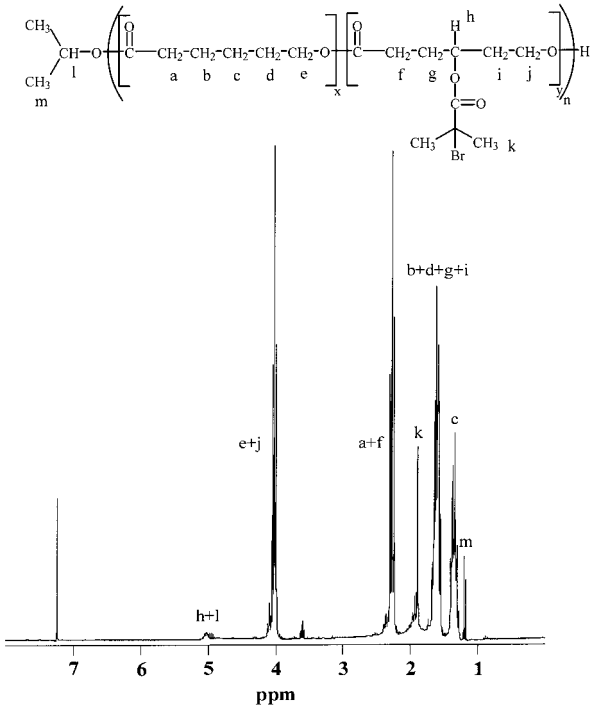


Figure 1. 250 MHz ^{1}H NMR spectrum of the poly(ϵCL)-*co*-poly(BMPCL) copolymer ($F_{BMPCL} = 0.1$, $M_n = 7500$).

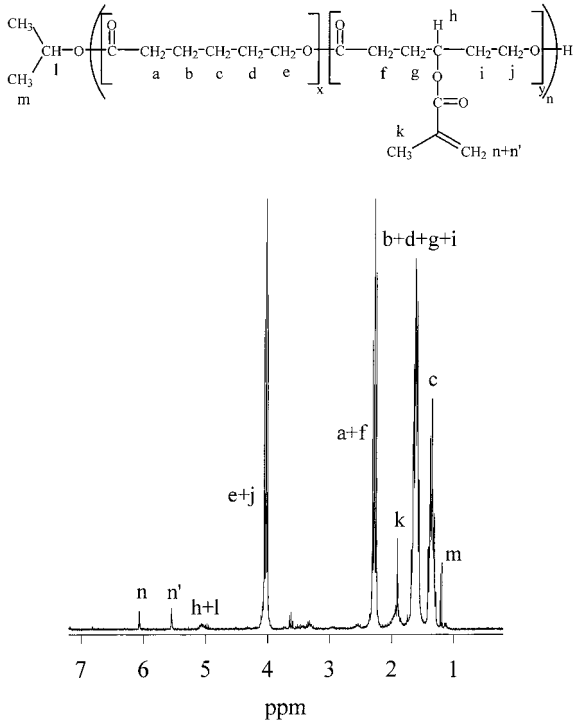
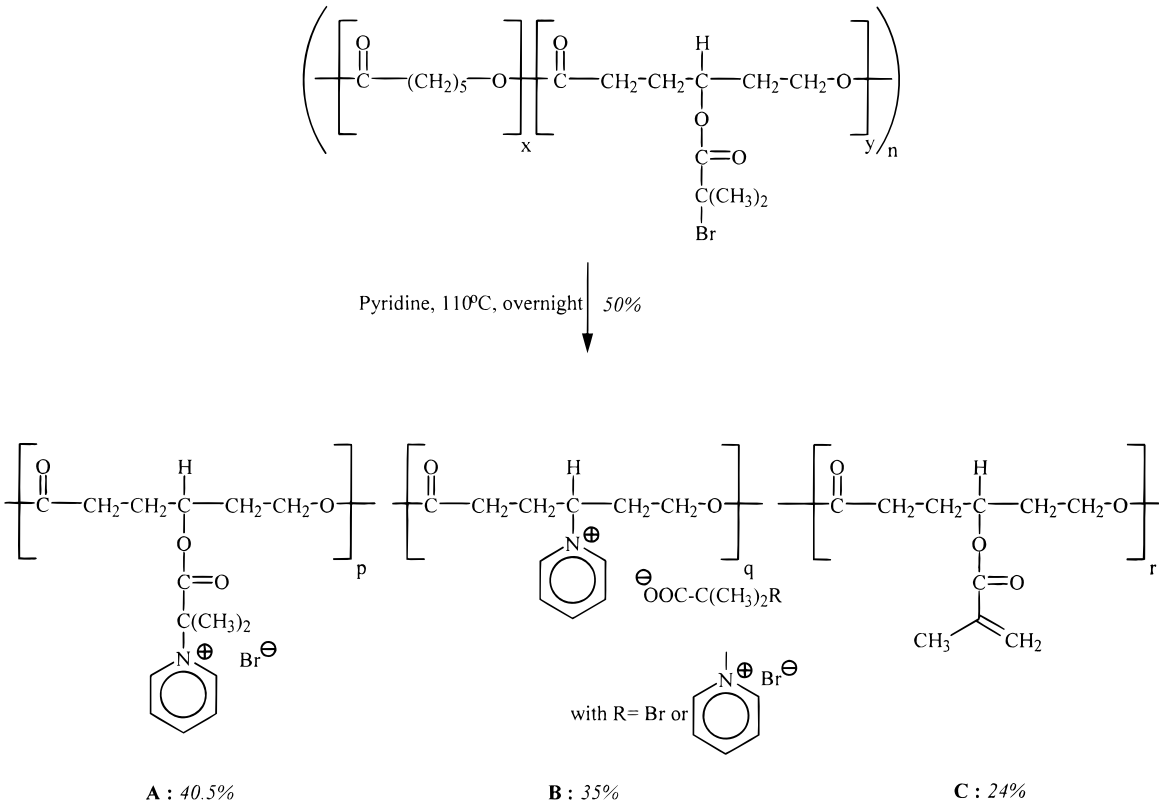


Figure 2. 250 MHz ^{1}H NMR spectrum of the poly(ϵCL)-*co*-poly(BMPCL) copolymer after dehydrohalogenation.

The pendant tertiary alkyl bromide groups of the random poly(ϵCL)-*co*-poly(BMPCL) copolymer (Table 1, entry 2) were chemically modified as illustrated in Scheme 1.The first modification was the dehydrohalogenation of the tertiary alkyl bromide with formation of methacrylic unsaturation (Scheme 1). This reaction was carried out in toluene at 80 °C in the presence of bicyclic amidine 1,5-diazabicyclo[4.3.0]non-5-ene (DBN).[8] The success of this elimination reaction was confirmed by ^{1}H NMR analysis of the copolymer before (Figure 1) and after derivatization (Figure 2). New resonances at 6.02 and 5.50 ppm characteristic of the methacrylic double bond are indeed observed. Furthermore, the relative integration of these signals and the signal at 5.02 ppm indicates that the extent of the modification reaction was 92% after 10 h of reaction. The SEC chromatogram remains unimodal and narrow, consistent with the absence of degradation and side reactions ($M_n = 7300$ and $M_w/M_n = 1.35$). Subsequent reactions of these unsaturated copolymers, such as radical cross-linking, may provide an alternative way to curable resins, biodegradable gels, and elastomers.

The second modification of the alkyl bromide pendant groups of the random poly(ϵCL)-*co*-poly(BMPCL) copolymer (Table 1, entry 2) consists of the nucleophilic substitution of the bromine atom by pyridine with formation of pyridinium salt (Scheme 2). The ^{1}H NMR analysis (Figure 3) of the quaternized copolymer shows that 50% of the alkyl bromide units are modified on the basis of the relative intensity of the peaks characteristic of the aromatic protons of the pyridinium moieties in the 8.1−9.9 ppm range and the CH proton of the polyester backbone at 5 ppm or the CH_3 protons of the tertiary alkyl bromide at 1.87 ppm. The same degree of polymerization after quaternization as before is evidence for a nondegradative derivatization process. It must be noted that the reaction time has to be short for degradation of the polyester chains to be avoided at this temperature. Two distinct sets of aromatic signals (A and B) and a significant amount of unsaturated species (C, 24%) are observed in the spectrum (Figure 3). The resonances at 8.23, 8.57, and 9.58 ppm were assigned to the species A (40.5%), which result from the nucleophilic substitution of the alkyl bromide, and the resonances at 8.15, 8.23, and 9.92 ppm to the species B (35%) formed as result of the cleavage of the O−CH bond (Scheme 2). This structure was confirmed by the ^{1}H NMR analysis of a sample of structure B, whose synthesis will be reported in the next section. The signals at 5.52 and 6.04 ppm were assigned to the vinylidene protons of the methacrylic unsaturation formed by dehydrohalogenation of the tertiary alkyl bromide. To decrease the extent of this dehydrohalogenation reaction, the quaternization was performed under milder conditions (65 °C, for 160 h). Thus, 58% of the tertiary bromides are transformed into pyri-

Scheme 2



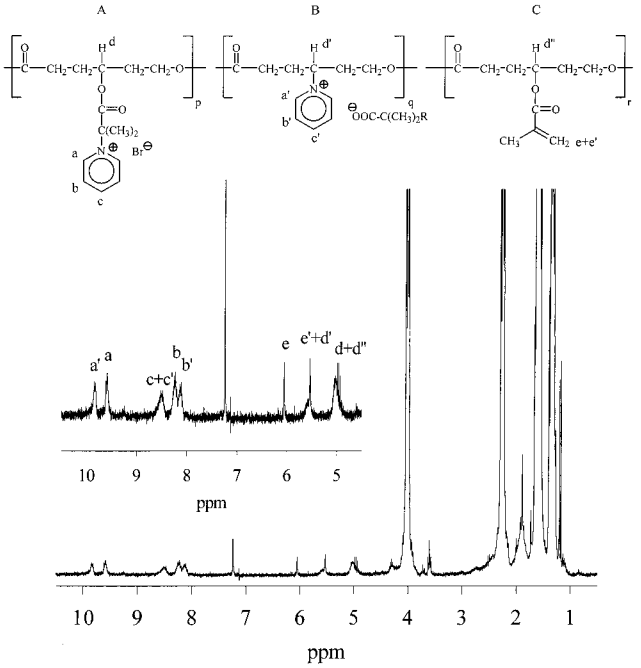


Figure 3. 250 MHz ^{1}H NMR spectrum of poly(ϵCL)-*co*-poly(BMPCL) after reaction with pyridine at 110 °C for 14 h.

dinium salts (species A) and unsaturated species in a 11.5/1 molar ratio. The pyridinium salt (species B) is no more detected under these experimental conditions. When the block copolymer 3 (Table 1) was similarly treated at 65 °C for 48 h, 53% of the bromide units were transformed into pyridinium salts of species A (91%) and unsaturated species (9%). Longer reaction time (160 h) increased the bromide conversion to 68% while keeping the unsaturated units to pyridinium species ratio constant. Despite the limited yield of quaternization and the lack of selectivity, water dispersible polyesters were collected. The ability of these copolymers to form micelles will be the topic of a forthcoming paper.

Quaternization of polyesters containing secondary alkyl bromide groups, not conjugated with a carbonyl group, should increase the yield in pyridinium units and restrict the extent of the elimination reaction. For this reason, γ-bromo-ϵ-caprolactone and random copolymers with ϵ-caprolactone were synthesized.

2. Synthesis and Derivatization of Poly(ϵ-caprolactone)-*co*-poly(γ-bromo-ϵ-caprolactone). γ-Bromo-ϵ-caprolactone (γBrCL) was synthesized as previously reported.[9] Homopolymerization and random and block copolymerization with ϵ-caprolactone were living in toluene at 0 °C as supported by the good agreement between the experimental and theoretical molecular weights, the low polydispersity, and the formation of well-defined poly(ϵCL)-*b*-poly(γBrCL) diblock copolymers.

Random copolymerization of γBrCL with ϵCL was initiated by Al(O^{i}Pr)$_3$ in toluene at 0 °C for 2 h. The conversion of γBrCL and ϵCL was quantitative, and the molecular weight of the copolymer agreed with the value predicted for a "living" mechanism (Table 2). Furthermore, the molecular weight distribution of the random copolymer is narrow, which is evidence for fast initiation with respect to propagation and fast propagation compared to chain transfer and/or termination reactions, if any. Scheme 3 summarizes the derivatization reactions that were carried out and will be discussed below.

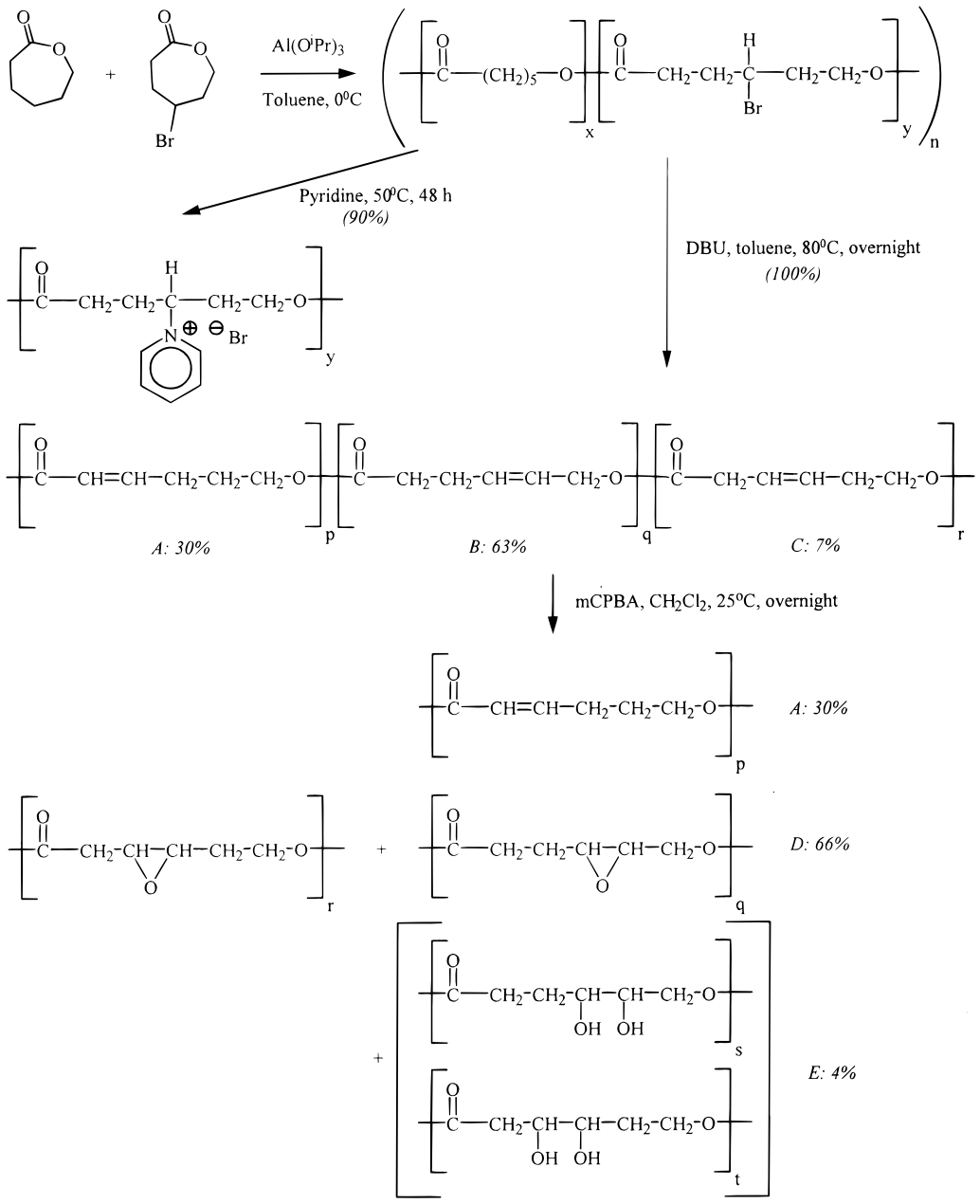
The first modification that was achieved is the quaternization of the brominated polyester by pyridine (Scheme 3). As was the case for the previous poly(ϵCL)-*co*-poly(BMPCL) brominated copolyester, the poly(ϵ-caprolactone)-*co*-poly(γ-bromo-ϵ-caprolactone) or poly(ϵCL)-*co*-poly(γBrCL) (entry 2 in Table 2) was dissolved

Table 2. Random Ring-Opening Copolymerization of γ-Bromo-ϵ-caprolactone and ϵ-Caprolactone Initiated by Al(O^{i}Pr)$_3$ in Toluene at 25 °C

entry	reaction time (h)	yield (%)	$f_{\gamma BrCL}$[a]	$F_{\gamma BrCL}$[b]	M_n(theor)	M_n(NMR)	M_n(SEC)	M_w/M_n
1	2	>99	0.1	0.09	17 000	16 800	25 500	1.15
2	2	>99	0.3	0.28	17 000	16 500	23 500	1.15

[a] γ-Bromo-ϵ-caprolactone molar fraction in the comonomer feed. [b] γ-Bromo-ϵ-caprolactone molar fraction in the copolymer measured by ^{1}H NMR.

Scheme 3



in pyridine and heated at 50 °C for 24 h. The ^{1}H NMR analysis (Figure 4) shows that 30% of the brominated groups were quaternized by pyridine. Longer reaction times (48 h) lead however to almost quantitative substitution (90%) of the bromide groups into pyridinium moieties, and no elimination reaction occurs. The conversion was calculated from the relative intensity of the signals of the pyridinium protons at 8.3 ppm or the CH proton of the polyester backbone at 5.6 ppm and the CH of the isopropyl ester end group at 5 ppm. Furthermore, the integration of the signals of the pyridinium protons and the CH of the isopropyl α-end group shows that the degree of polymerization was the same before and after quaternization, thus indicating that no degradation of the polyester chains occurred under these conditions. Thus, in contrast to the copolyester containing tertiary alkyl bromide (poly(ϵCL)-*co*-poly(BMPCL)), discussed in the previous section, the quaternization of the poly(ϵCL)-*co*-poly(γBrCL) copolymer by pyridine was close to completion at 50 °C after 48 h, and no elimination reaction took place. The γBrCL monomer is thus an ideal (co)monomer for the synthesis of well-defined ammonium containing (co)polyesters. Furthermore, additional functions could be attached to

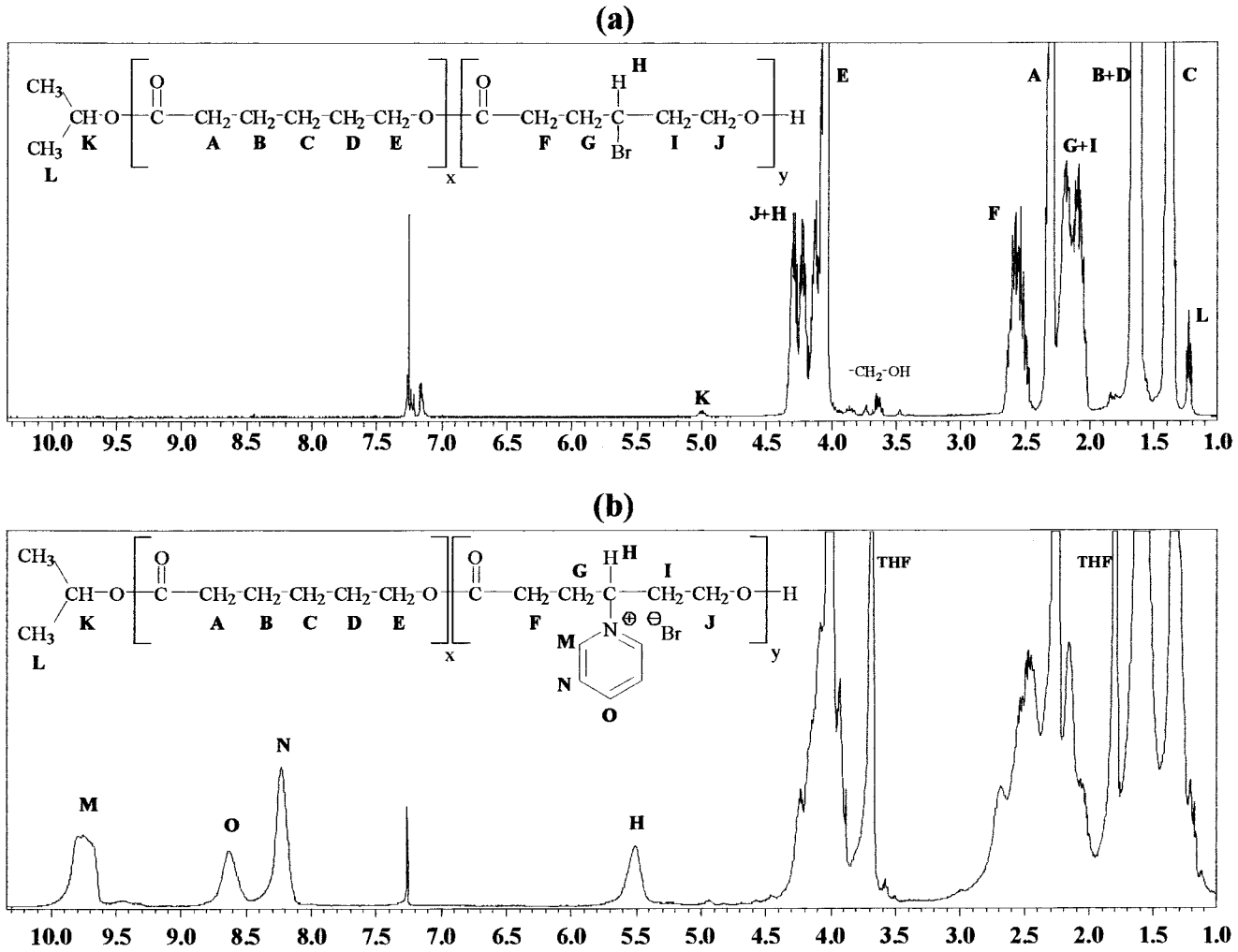


Figure 4. 400 MHz ^{1}H NMR spectrum of poly(ϵCL)-*co*-poly(γBrCL): (a) before quaternization; (b) after quaternization.

Table 3. Ring-Opening Copolymerization of Mixtures of the Lactones 1, 2, and 3 (Scheme 4) and ϵ-CL Initiated by Al(O^{i}Pr)$_3$ in Toluene at 25 °C

entry	comonomers **1**/**2**/**3**/CL	time (h)	yield (%)	$M_{n,th}$	$M_{n,NMR}$	$M_{n,SEC}$	M_w/M_n
1	26/24/50/0	2	95	10 800	11 000	14 000	1.35
2	90/5/5/0	14	60	3 800	3 500	3 000	1.40
3	0/50/50/0	2	95	7 000	7 500	8 000	1.30
4	0/50/50/0	2	95	20 000	19 000	21 500	1.20
5	0/32/32/36	2	95	15 000	14 000	16 000	1.35
6	0/24/24/52	2	95	17 000	16 000	19 000	1.20
7	0/18/18/64	2	95	15 000	13 500	18 000	1.25
8	0/7/7/86	2	95	15 000	14 000	17 000	1.31

the chains by the judicious choice of the tertiary amine and modulate accordingly the properties of the (co)-polyesters. Depending on the pyridinium salt content (ca. 10 mol %), the polyester chains are easily dispersed in water, which makes them good candidates for biodegradable flocculation agents and surfactants.[9] The behavior of these functional (co)polyesters in water is under current investigation.

Dehydrohalogenation of the brominated (co)polyester is the second modification that was considered with the purpose to make unsaturated aliphatic polyester available. This reaction was carried out by heating the poly(ϵCL)-*co*-poly(γBrCL) copolymer (entry 1, Table 2) in the presence of 1,8-diazabicyclo[5.4.0] undec-7-ene (DBU) in toluene at 80 °C overnight. When a 5 molar excess of DBU is used with respect to the brominated units, the elimination is quantitative as confirmed by the disappearance of the CH protons of the poly(γBrCL) (Figure 5a) and the appearance of new signals characteristic of the olefinic protons (Figure 5b). Three types of unsaturations are however observed (Scheme 3). Indeed, in addition to two families of internal double bonds (species B, 63%; species C, 7%), acrylic double bonds (species A, 30%) are identified by the multiplet at 6.92 ppm and the doublet at 5.81 ppm (Figure 5 and Scheme 3). The acrylic double bonds result from the rearrangement of the species C, whose double bond migrated for being conjugated with the carbonyl at the benefit of the stability of the system. The relative intensity of the signals for the protons of the double bonds and the CH proton of the α-isopropyl group at 5 ppm confirms that the degree of polymerization of the unsaturated polyester is the same as that of the original brominated polyester. Moreover, the SEC trace remains unimodal

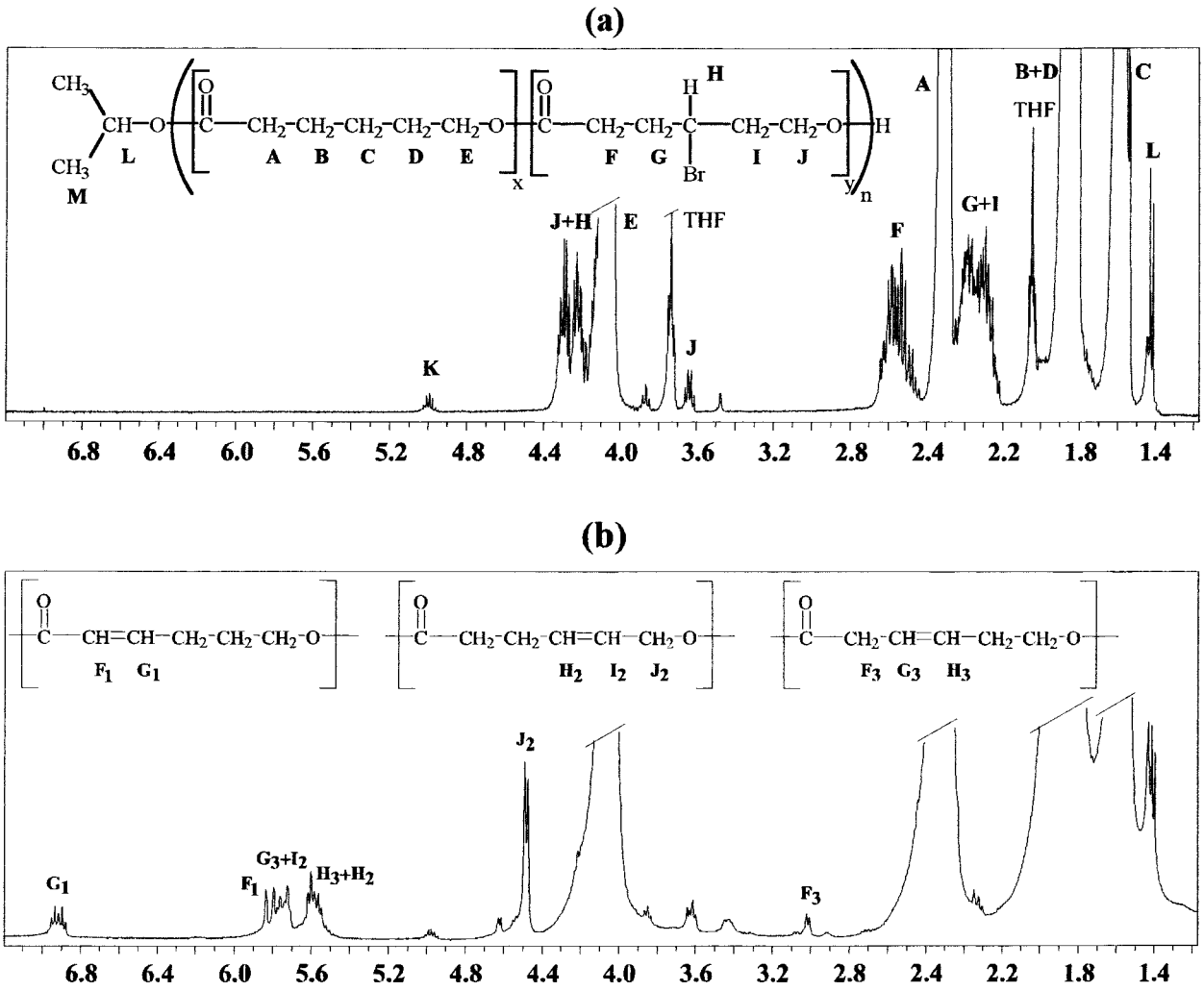


Figure 5. 400 MHz ^{1}H NMR spectrum of poly(ϵCL)-*co*-poly(γBrCL): (a) before dehydrohalogenation; (b) after dehydrohalogenation.

and narrow ($M_{n,SEC}$ = 25 000, M_w/M_n = 1.2), also in agreement with the lack of degradation during the elimination reaction. The double bonds now available in the aliphatic polyester chains open the way to further chemical modifications and modulation of the properties.

The third modification studied in this paper was the epoxidation of the unsaturated polyester by reaction with a 2-fold molar excess of mCPBA at room temperature overnight. The conversion of the internal double bonds (species B and C) into epoxides was close to completion (96%) as proved by the disappearance of the peaks at 5.6 and 5.75 ppm for the vinylic protons and the appearance of a multiplet at 2.95 ppm characteristic of the epoxide (Figure 6). The very small multiplet at 3.2 ppm (CH−OH) shows that the possible hydrolysis of the epoxide under the acidic conditions used for the epoxidation and the polymer isolation (see Experimental Section) is very limited (<4%). Expectedly, the less reactive C═C acrylic double bonds remained unreacted, as shown by the unchanged relative intensity of the acrylic protons. The narrow molecular weight distribution of the epoxidized polyester (M_w/M_n = 1.2) and the excellent agreement between the degree of polymerization before and after functionalization are consistent with a nondegradative derivatization reaction. Therefore, the epoxidation of the unsaturated polyester previously prepared by dehydrohalogenation of brominated polyester led to extensively epoxidized polyester (67%) containing acrylic double bonds (30%) and a very small amount of diol (3%). The epoxide functions are intrinsically reactive toward protic reagents, such as water, alcohols, and amines, thus allowing a series of molecules of interest (drugs for instance) to be attached to the polyester backbone. Furthermore, the acrylic double bonds can contribute to the on-purpose cross-linking of the polymer with the opportunity to prepare hydrogels or lipogels, depending on the hydro(lipo)philicity of the modified polyester.

3. Direct Synthesis of Unsaturated Copolymers of ϵ-Caprolactone. Copolymerization of ϵ-caprolactone with the parent unsaturated monomer is an alternative to the dehydrohalogenation of brominated copolyesters (cf. supra) for the synthesis of unsaturated copolyesters. With this purpose in mind, γ-bromo-ϵ-caprolactone was quantitatively dehydrohalogenated by 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) at 80 °C. A mixture of the unsaturated ϵ-caprolactones **1**, **2**, and **3** (Scheme 4) was accordingly formed. Lactone **1** results from the migration of the double bond of the lactone **2** for being conjugated with the carbonyl group.

ROP of this mixture of lactones was initiated by Al(O^iPr)$_3$ at room temperature (Table 3, entry 1). The experimental number-average molecular weight ($M_{n,NMR}$) is in good agreement with the theoretical value ($M_{n,th}$) and the molecular weight distribution is narrow, consistent with a controlled polymerization process. Figure 7 shows the ^{1}H NMR spectrum of this polyester, which contains the major peaks of the polyester back-

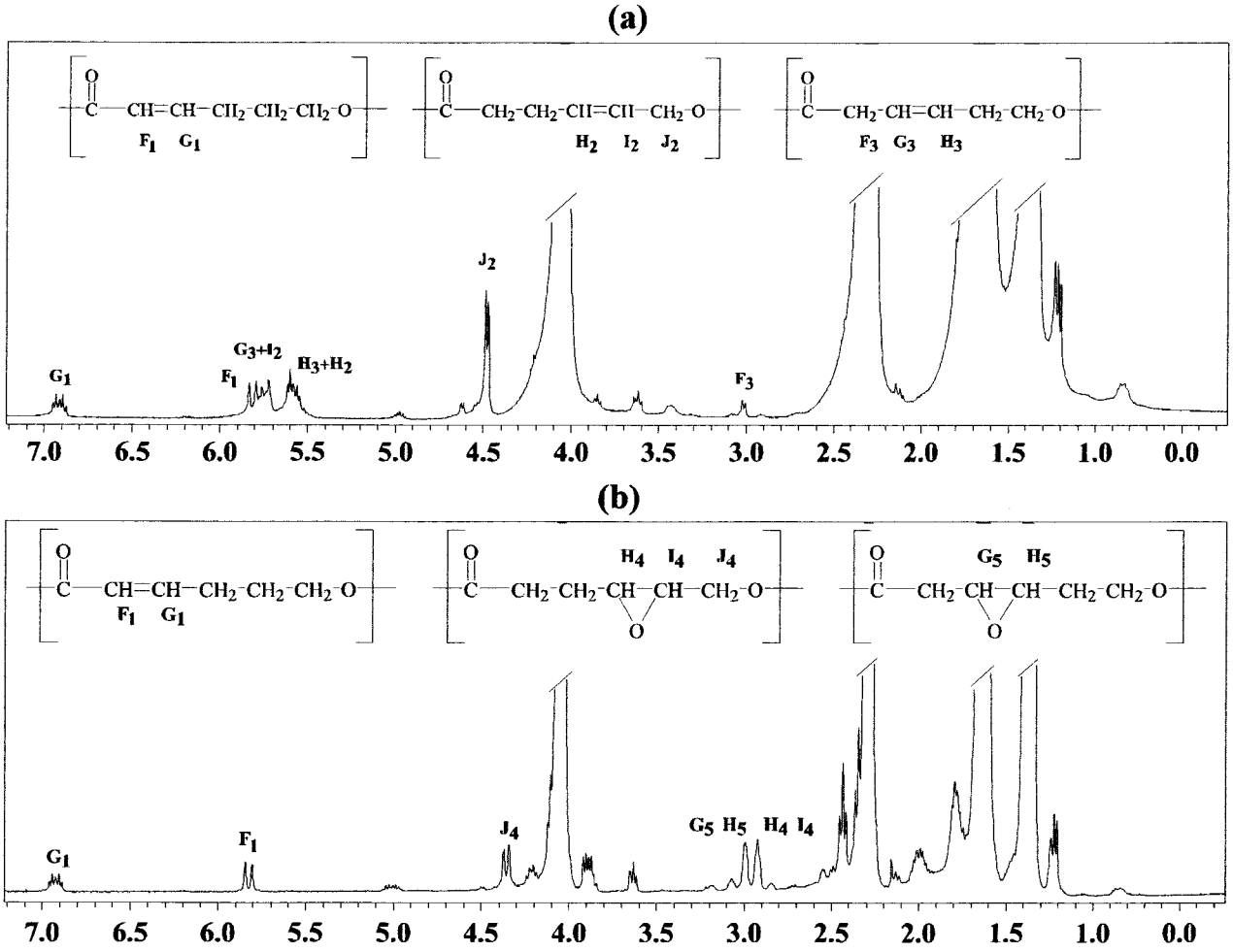
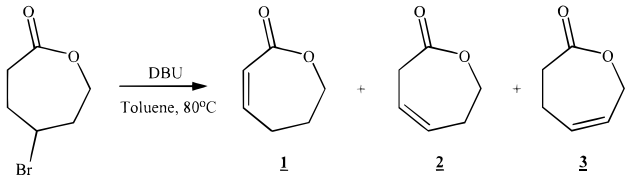


Figure 6. 400 MHz ^{1}H NMR spectrum of poly(ϵCL)-*co*-poly(γBrCL): (a) original unsaturated polyester; (b) epoxidized polyester.

Scheme 4



bone, together with the resonances typical of the isopropyl ester (δ = 1.2 and 5.0 ppm), protons attached to double bonds (δ = 5.5−5.8 ppm), and the terminal primary alcohol (δ = 3.65 ppm). These data are consistent with a coordination−insertion polymerization mechanism and confirm the assignment of the peaks for the copolyester synthesized by dehydrohalogenation of the poly(ϵCL)-*co*-poly(γBrCL) copolymer (Figure 5). To estimate the reactivity of the unsaturated lactones in ROP, effort was made to isolate each of them. Although the pure lactone **1** was collected by chromatography through silica, the quantitative separation of the lactones **2** and **3** failed, an equimolar mixture being finally recovered.

This mixture of the lactones **2** and **3** (Table 3, entries 3 and 4) was polymerized quantitatively by Al(O^{i}Pr)$_3$ in toluene at room temperature. A good agreement between the experimental molecular weight and the theoretical one was observed, and the molecular weight distribution remained narrow. The ^{1}H NMR spectrum for a typical homopolymer (**2**/**3** = 50/50) is shown in Figure 8. Finally, the time dependence of the conversion

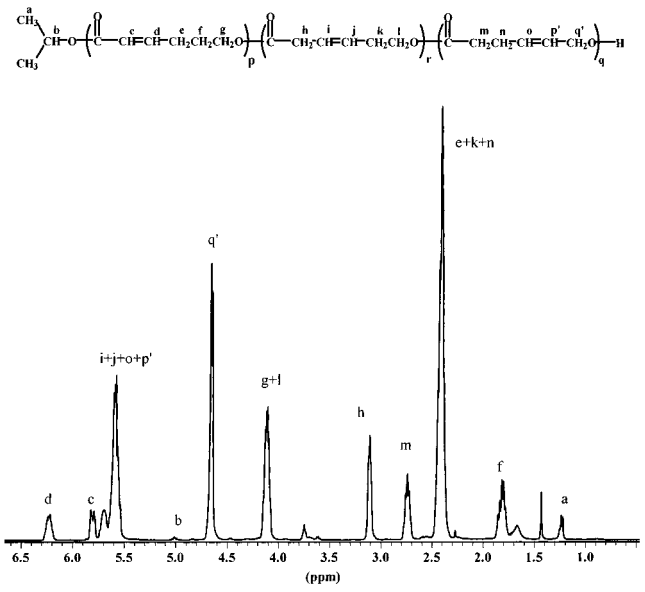


Figure 7. 400 MHz ^{1}H NMR spectrum of the random copolyester of lactones **1**, **2**, and **3**.

with the lactones **2** and **3** was analyzed at 0 °C in order to compare their reactivity (Figure 9). Conversion of the lactone **3** was quasi-complete (90%) within 1 h, in contrast to the lactone **2** that was converted only to 20% for the same period of time, thus indicating a huge difference in reactivity in favor of **3** compared to **2**. The

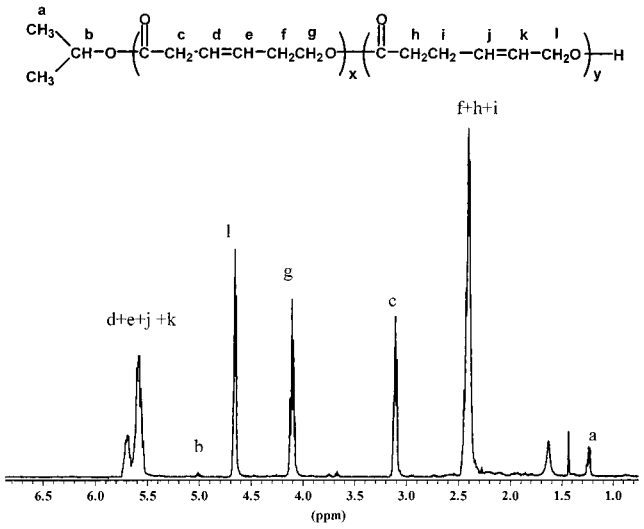


Figure 8. 400 MHz ^{1}H NMR spectrum of the poly(lactone **2**)-*co*-poly(lactone **3**).

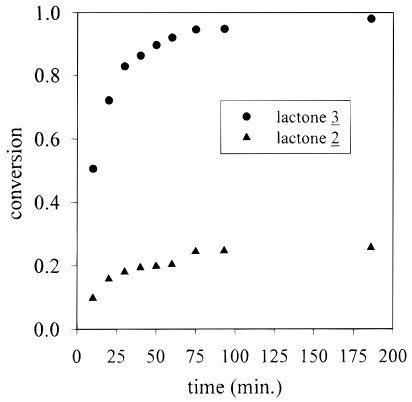


Figure 9. Time dependence of the conversion for the ROP of a 50/50 mixture of lactones **2** and **3** [0 °C, $[Al(OiPr)_3]_0 = 4 \times 10^{-5}$ M, [**2** + **3**] = 1 M].

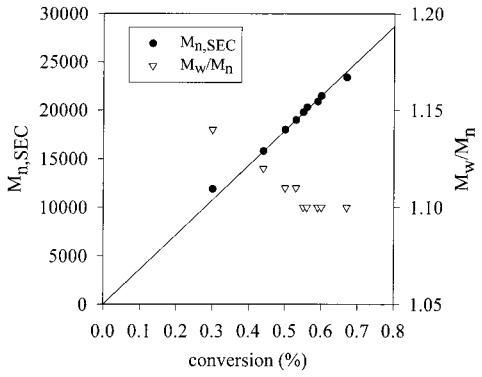


Figure 10. Dependence of $M_{n,SEC}$ on the conversion of the lactone [**2** + **3**] (0 °C, $[Al(OiPr)_3]_0 = 4 \times 10^{-5}$ M, [**2** + **3**] = 1 M).

linear dependence of the molecular weight on the monomer conversion and the narrow polydispersity agree with a living mechanism (Figure 10). A mixture of the three unsaturated lactones **1**, **2**, and **3** (90/5/5) was also polymerized under the same conditions (Table 3, entry 2). A good agreement between the experimental molecular weight and the theoretical one was again observed. Nevertheless, the polymerization was slower than for the previous mixture (**2** + **3**), which emphasizes that the unsaturated lactone **1**, which contains a double bond conjugated with the carbonyl group, is less reactive

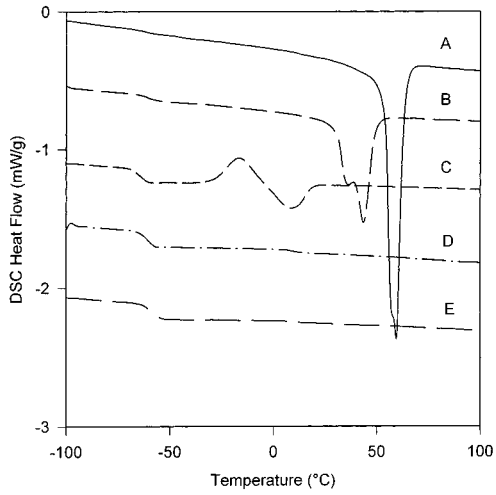


Figure 11. DSC traces for poly(ϵCL)-*co*-poly(**2** + **3**) copolyesters of various molar compositions: (A) 100% PCL, (B) 86% PCL, (C) 63% PCL, (D) 36% PCL, (E) 0% PCL.

than the two other isomers. Indeed, the electrophilicity of the carbon of the carbonyl is decreased, which is detrimental to the attack by the alkoxide.

Several random copolymers of the lactones **2** and **3** with ϵ-CL were also synthesized, the results being shown in Table 3 (entries 5−8). Once again, number-average molecular weight and polydispersity were properly controlled, and the experimental molar composition (^{1}H NMR analysis) fits the composition of the comonomer feed at the high conversion reached (95%). The thermal transitions of the copolymers were analyzed by differential scanning calorimetry (DSC). Copolymerization of ϵ-CL with increasing amounts of **2** and **3** has a strong influence on the melting temperature (T_m) (Figure 11). PCL has a T_g at −61 °C and a T_m at 57 °C, whereas the copolymer of **2** and **3** was amorphous with a T_g at −59.5 °C. Increasing the content of **2** and **3** in the copolymer resulted in decreasing T_m for PCL. At molar contents of (**2** + **3**) higher than 37%, the copolymers were amorphous.

Block copolymers of ϵCL and the mixture of the unsaturated lactones **2** and **3** were prepared by sequential polymerization, the ϵ-caprolactone being first polymerized by $Al(O^iPr)_3$ in toluene at 25 °C. The experimental molecular weight of each block is consistent with the value expected for living polymerization at complete monomer conversion (Table 4), and the molecular weight distribution is the same for the first block and the final diblock, which is in favor of lack of side reactions. That no transesterification reactions occurred was confirmed by ^{13}C NMR spectroscopy (Figure 12), which compared the carbonyl region for pure PCL, for a diblock copolymer (Table 4, entry 2), and for a random one (Table 3, entry 5). Peak A (Figure 12a) which is typical of the homodiad of PCL is also observed for the diblock without additional peak for the PCL block, consistent with the formation of "pure" diblock structure. Moreover, two series of peaks are observed for the unsaturated PCL block, which is actually a "random" copolymer of the unsaturated lactones **2** and **3**. These additional peaks have thus to be assigned to the heterodiads of **2** and **3**. In the random terpolymer, each comonomer is characterized by one homodiad peak and two heteradiad ones. So, the nine peaks observed in the carbonyl region confirm the randomness of the comonomer distribution.

Table 4. Sequential Copolymerization of Caprolactone and Mixture of the Lactones 2 and 3 (Scheme 4) Initiated by $Al(O^iPr)_3$ in Toluene at 25 °C

	first block			second block				
entries	$M_{n,th}$	$M_{n,SEC}$[a]	M_w/M_n	$M_{n,th}$	$M_{n,exp}$ (SEC)	$M_{n,exp}$ (SEC)	M_w/M_n	yield
1	20 000	20 000	1.10	4000	4 000	24 000	1.15	95
2	20 000	21 000	1.10	9500	12 500	33 000	1.15	95

[a] Universal calibration for PCL.

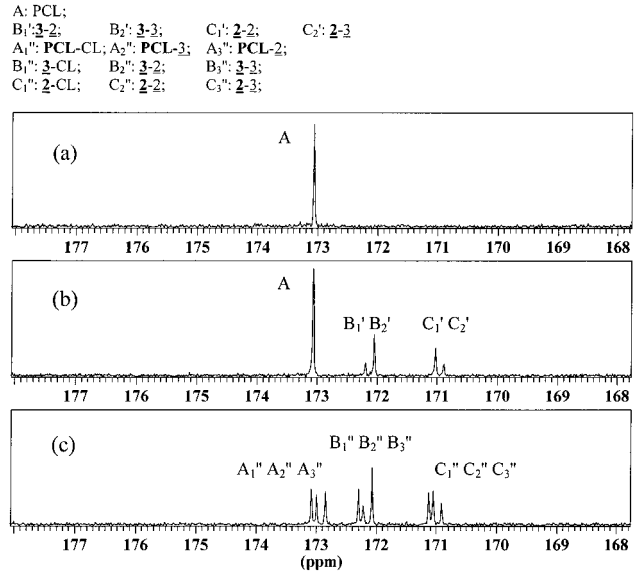


Figure 12. Expanded ^{13}C NMR spectra (carbonyl region) for (a) PCL, (b) poly(ϵCL)-*b*-poly(**2** + **3**) (copolymer 2, Table 4), and (c) poly(ϵCL)-*co*-poly(**2** + **3**) (copolymer 5, Table 3).

Conclusions

(Co)polymerization of bromine containing ϵ-caprolactone is a valuable strategy for the synthesis of a series of new functional aliphatic polyesters. For instance, poly(ϵCL)-*co*-poly(BMPCL), which contains tertiary alkyl bromide pendant groups, has been quaternized by pyridine under different experimental conditions. The quaternization is partial (50−70%) because of the occurrence of competing elimination reactions. Interestingly enough, this modified polyester can be easily dispersed in water. In contrast, the dehydrohalogenation is quantitative, so leading to (co)polyester with pendant methacrylic double bonds which can participate to polyaddition reactions.

The poly(ϵCL)-*co*-poly(γBrCL) copolyesters, in which the bromine atom is directly attached to the central methylene of the ϵCL unit, has also been quaternized in a quasi-quantitative way at 50 °C, the occurrence of side reaction being not observed. Water-soluble or at least water-dispersible polyesters can be synthesized, which have a chance of being degradable. Unsaturated copolyester has also been prepared by dehydrohalogenation. Then, three types of double bonds are formed (two types of internal double bonds (70%) plus acrylic double bonds (30%)). The epoxidation of the internal double bonds provides a polymer that contains 70% of epoxide and 30% of acrylic double bonds. Further derivatization of the epoxide groups is a possible approach to modulate the solubility and the reactivity of the cross-linkable polyester chains. All the chemical modifications of the γBrCL co-units reported in this work are selective, thus preserving the molecular characteristics (M_n, M_w/M_n) of the chains. In an alternative approach to unsaturated ϵ-caprolactone, γ-bromo-ϵ-caprolactone has been quantitatively dehydrohalogenated, and the mixture of unsaturated isomers successfully polymerized and copolymerized with ϵ-caprolactone.

So, poly(ϵCL)-*co*-poly(γBrCL) copolyesters and γ-bromo-ϵ-caprolactone are key macromolecules and monomer for the synthesis of a series of new functional polyesters with tunable properties. The analysis of the degradation and/or the biodegradation of these potential biomaterials deserves interest.

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