4134 *Macromolecules* **1994,** *27,* 4134-4144

Macromolecular Engineering of Polylactones and Polylactides. 18. Synthesis of Star-Branched Aliphatic Polyesters Bearing Various Functional End Groups

Dong Tian, Ph. Dubois,† R. Jérôme,* and Ph. Teyssié

Center for Education and Research on Macromolecules (CERM), University of Liège, Sart-Tilman, B6, 4000 Liège, Belgium

Received February 15, 1994; Revised Manuscript Received April 28, 1994⊗

ABSTRACT: Three-arm star-branched aliphatic polyesters have been synthesized by an appropriate termination reaction of the living chains prepared by ring-opening polymerization with aluminum alkoxides. The use of functional aluminum alkoxides, Et_2AlOCH_2X with X = $CH_2CH_2CH{=}CH_2$ and $(CH_2)_{10}Br$, has led to X functional end-capped star-branched polyesters. Trimesic acid trichloride has proved to be an efficient termination agent for the living poly(ϵ-caprolactone) [PCL] chains ended with a reactive aluminum alkoxide group. A quantitative end functionalization has been reported for bromide and 1-pentene end-capped star-branched PCL. The bromide end groups have been converted into azido end groups, which have been subsequently reduced to the expected primary amine end-capped star-branched PCL by catalytic transfer hydrogenation in DMF. In contrast to living PCL, reaction of trimesic acid chloride with the aluminum alkoxide end group of living poly(L,L)lactide [P(L,L)LA] and living poly(ϵ-caprolactone-*b*-(L,L)lactide) [P(CL-*b*-(L,L)LA] chains has produced star-branched polyesters within a very poor yield. This result is more likely due to a steric effect of the methyl group in α-position of the terminal aluminum alkoxide. This drawback has been overcome to some extent by initiating the living polymerization of (L,L)LA with primary amine end-capped star-branched PCL in the presence of triethylaluminum. Formation of a hydroxyl end-capped star-branched poly(ϵ-caprolactone-*b*-(L,L)lactide) diblock copolymer has accordingly been reported.

Introduction

Poly(ϵ-caprolactone) (PCL) is known for biodegradation with release of nontoxic products.[1,2] Moreover, miscibility of PCL with a variety of commercial polymers, e.g. bisphenol A polycarbonate and PVC, is a unique characteristic feature that has been used in order to improve some deficient properties of these polymers such as poor stress–crack resistance and lack of gloss and adhesion.[3,4]

The main properties associated with the hydrodynamic volume of a polymer are significantly different for linear chains compared to their branched counterparts. Synthesis of well-defined molecular architectures, such as stars and dendrimers, is accordingly a key target of modern polymer chemistry. For the last few decades, star-branched polymers have been successfully prepared by living anionic polymerization[5] and living cationic polymerization.[6] One typical method relies upon the synthesis of living linear chains followed by the chemical bonding of these arms to a multifunctional core. This methodology could be possibly applied to the synthesis of star-branched aliphatic polyesters, although the anionic ring-opening polymerization of ϵ-caprolactone and lactide must be disregarded due to intra- and intermolecular transesterification side reactions.[7] Living polymerization of these monomers can however be promoted by aluminum alkoxides,[8-12] yttrium and lanthanide alkoxides,[13] zinc alkoxides,[14] and (Al,Zn)μ-oxo-alkoxides.[9,15] The living mechanism allows avoidance of formation of cyclic oligomers and leads to linear chains of a predictable molecular weight and a narrow molecular weight distribution.

Special attention has been paid to aluminum alkoxides, such as $Al(O^iPr)_3$ and $Et_{3-p}Al(O(CH_2)_2X)_p$ with $1 \leqslant p \leqslant 3$.[8,9,12,16,17] The ring-opening polymerization proceeds through a "coordination–insertion" mechanism that involves the selective rupture of the acyl oxygen bond of the monomer and its insertion into an Al–O bond of the initiator.[8] This typically "living" polymerization is a straightforward way toward block copolyesters of perfectly controlled molecular weight and composition.[8,9,16-19] Aluminum alkoxides carrying functional alkoxy groups (X = Br, CH_2NEt_2, $CH_2CH{=}CH_2$, $CH_2OC(O)C(Me){=}CH_2$, etc.) have also been successfully used to prepare ω- and α,ω-functional polyesters.[12,22]

This paper aims at reporting on the synthesis of star-branched aliphatic polyesters by the so-called "arm-first" method. Thus living chains have to be prepared by the aforementioned "coordination–insertion" mechanism and reacted with a multifunctional reagent, such as trimesic acid chloride. The efficiency of this coupling reaction has been analyzed for poly(ϵ-caprolactone), poly(L,L)lactide, and the related diblock copolymers.

Experimental Section

Materials. ϵ-Caprolactone (Janssen) was dried over calcium hydride for 48 h at room temperature and distilled under reduced pressure just before use. (L,L)Lactide was purchased from Boehringer. It was recrystallized three times from dry toluene at 70 °C, and then dried for 24 h at 25 °C under reduced pressure (10^{-2} mm Hg) before polymerization. n-Butyl alcohol (Janssen) and 4-penten-1-ol (Aldrich) were dried over calcium hydride for 48 h at room temperature and distilled under reduced pressure just before use. 11-Bromo-1-undecanol (Janssen), trimesic acid chloride (1,3,5-benzenetricarboxylic acid chloride) (Fluka), sodium azide (Janssen), and ammonium formate (Janssen) were dried by repeated (three times) azeotropic distillation of toluene just before use. Palladium on activated carbon (10 wt %) (Aldrich) was used as received. Pyridine (Aldrich) was dried over KOH for a week and freshly distilled under reduced pressure just before use. Toluene and tetrahydrofuran (THF) were dried by refluxing over calcium hydride and a benzophenone–sodium complex, respectively, and distilled under nitrogen atmosphere. Triethylaluminum (Fluka) was used without further purification and dissolved in dry toluene. Dimethylformamide (DMF) was dried over P_2O_5 for 72 h and distilled under reduced pressure just before use.

---

* To whom all correspondence should be addressed.

† "Chargé de Recherches" by the Belgian "National Fund for Scientific Research" (FNRS).

⊗ Abstract published in *Advance ACS Abstracts,* June 1, 1994.

0024-9297/94/2227-4134$04.50/0 © 1994 American Chemical Society

Table 1. Coupling of XCH_2O-PCL-$OAlEt_2$ by Trimesic Acid Trichloride in the Presence of Pyridine

						star-branched poly(ϵ-caprolactone)				
		linear poly(ϵ-caprolactone)				coupling efficiency (%)				
entries	X	$[\epsilon\text{-CL}]_0/[I]_0$	$M_{n,th}$[a]	M_n (SEC)	M_w/M_n	^{1}H NMR	SEC	M_n, (^{1}H-NMR) (1-arm)	M_n (VPO)	M_w/M_n
1	$CH_3CH_2CH_2$	17.3	2.0×10^3	2.5×10^3	1.30	100	100	2.0×10^3	7.5×10^3	1.35
2	$CH_2{=}CHCH_2CH_2$	37.8	4.4×10^3	4.5×10^3	1.20	100	100	4.0×10^3	13.0×10^3	1.25
3	$CH_2{=}CHCH_2CH_2$	30.2	3.5×10^3	3.5×10^3	1.15	100	>98	4.0×10^3	10.5×10^3	1.25
4	$CH_2{=}CHCH_2CH_2$	54.1	6.2×10^3	5.5×10^3	1.20	100	>98	5.0×10^3	16.5×10^3	1.20
5	$Br(CH_2)_{10}$	27.3	3.4×10^3	3.0×10^3	1.15	95.2	98	3.5×10^3	10.0×10^3	1.35
6	$Br(CH_2)_{10}$	17.0	2.2×10^3	2.5×10^3	1.15	100	>98	2.5×10^3	7.0×10^3	1.20
7	$Br(CH_2)_{10}$	45.5	5.4×10^3	5.5×10^3	1.20	100	>98	6.0×10^3	16.5×10^3	1.30
8	$Br(CH_2)_{10}$	85.2	10.0×10^3	10.0×10^3	1.15	100	>95	10.0×10^3	37.0×10^3[b]	1.25

[a] Theoretical molecular weight: X = $CH_2CH_2CH_3$, $M_{n,th} = [\epsilon\text{-CL}]_0/[I]_0 \times 114 + 73$; X = $CH_2CH_2CH{=}CH_2$, $M_{n,th} = [[\epsilon\text{-CL}]_0/[I]_0] \times 114 + 85$; X = $(CH_2)_{10}Br$, $M_{n,th} = [[\epsilon\text{-CL}]_0/[I]_0] \times 114 + 250$. [b] Weight average molecular weight (M_w) as measured by light scattering.

Table 2. Synthesis of Star-Branched Poly(CL-*b*-(L,L)LA) and Poly(L,L)LA by Coupling of the Living Precursors with Trimesic Acid Trichloride in the Presence of Pyridine in THF

	poly(CL-*b*-(L,L)LA)									star-branched polyester				
	first-block PCL[a]			second block[b]			poly(L,L)LA[a]			coupling reaction		coupling efficiency (%)		
entries	$M_{n,th}$	M_n (SEC)	M_w/M_n	$M_{n,th}$	M_n (^{1}H-NMR)	M_w/M_n	$M_{n,th}$	M_n (SEC)	M_w/M_n	T (°C)	t (h)	^{1}H NMR	SEC	M_w/M_n
1	3.1×10^3	3.5×10^3	1.10	3.0×10^3	2.5×10^3	1.25				25	30	6	0	1.30
2							3.5×10^3	3.0×10^3	1.25	25	40	10	0	1.30
3							5.0×10^3	4.0×10^3	1.30	25	40	5	0	1.35
4							2.5×10^3	2.5×10^3	1.20	40	65	20	12	1.65
5							3.0×10^3	3.0×10^3	1.20	50	65	25	15	1.70

[a] PCL and P(L,L)LA obtained by initiation with $Et_2AlO(CH_2)_{11}Br$ in toluene at 25 and 70 °C, respectively. [b] (L,L)LA polymerization performed in toluene at 70 °C.

Preparation of the Initiators. Diethylaluminum alkoxides were prepared by reaction of triethylaluminum with the corresponding alcohol (eq 1). One millimole of the required alcohol in 10 mL of toluene was slowly added into a carefully dried pyrex flask equipped with a rubber septum, connected to a gas burette through an oil valve and containing an equimolar amount of $AlEt_3$ in 90 mL of toluene. The reaction proceeded under nitrogen and under vigorous stirring at −78 °C. When the evolution of ethane stopped, the temperature was allowed to increase slowly up to 40 °C under stirring. The solution was kept at 40 °C for an extra hour.

$$(CH_3CH_2)_3Al + HOCH_2X \rightarrow (CH_3CH_2)_3AlOCH_2X + C_2H_6\uparrow \qquad (1)$$

$$X = CH_2CH_2CH_3,\ CH_2CH_2CH{=}CH_2,\ CH_2(CH_2)_9Br$$

Preparation of Star-Branched Aliphatic Polyesters. The living polymerization ϵ-CL, (L,L)-LA, and P(CL-*b*-(L,L)LA) was initiated by Et_2AlOCH_2X as previously reported.[12,14,18] When the monomer conversion was complete, toluene was distilled off and the "living" polyester chains were dissolved in very carefully dried THF. An aliquot of the "living" polyester solution was picked out and hydrolyzed, and the polymer was analyzed by size exclusion chromatography (SEC). The $^1/_3$ equimolar amount of trimesic acid trichloride and pyridine (as compared to the living polymer chains) were added to the living polymer solution. After reaction, this solution was treated with a small amount of aqueous HCl and the three-arm star-branched aliphatic polyester was precipitated into cold methanol.

Conversion of Bromide End-Capped Star-Branched Polyesters into the Primary Amine Counterpart. A 5-fold molar excess of sodium azide with respect to the bromide end-capped star-branched polyester was used to convert quantitatively the halogen end groups into azide functions. This reaction was performed in dry DMF (5 wt/v % of polymer in DMF) at 30 °C for 14 h. The polyester was recovered and purified by selective precipitation into methanol. The yield was quantitative within the limits of the ^{1}H NMR analysis.

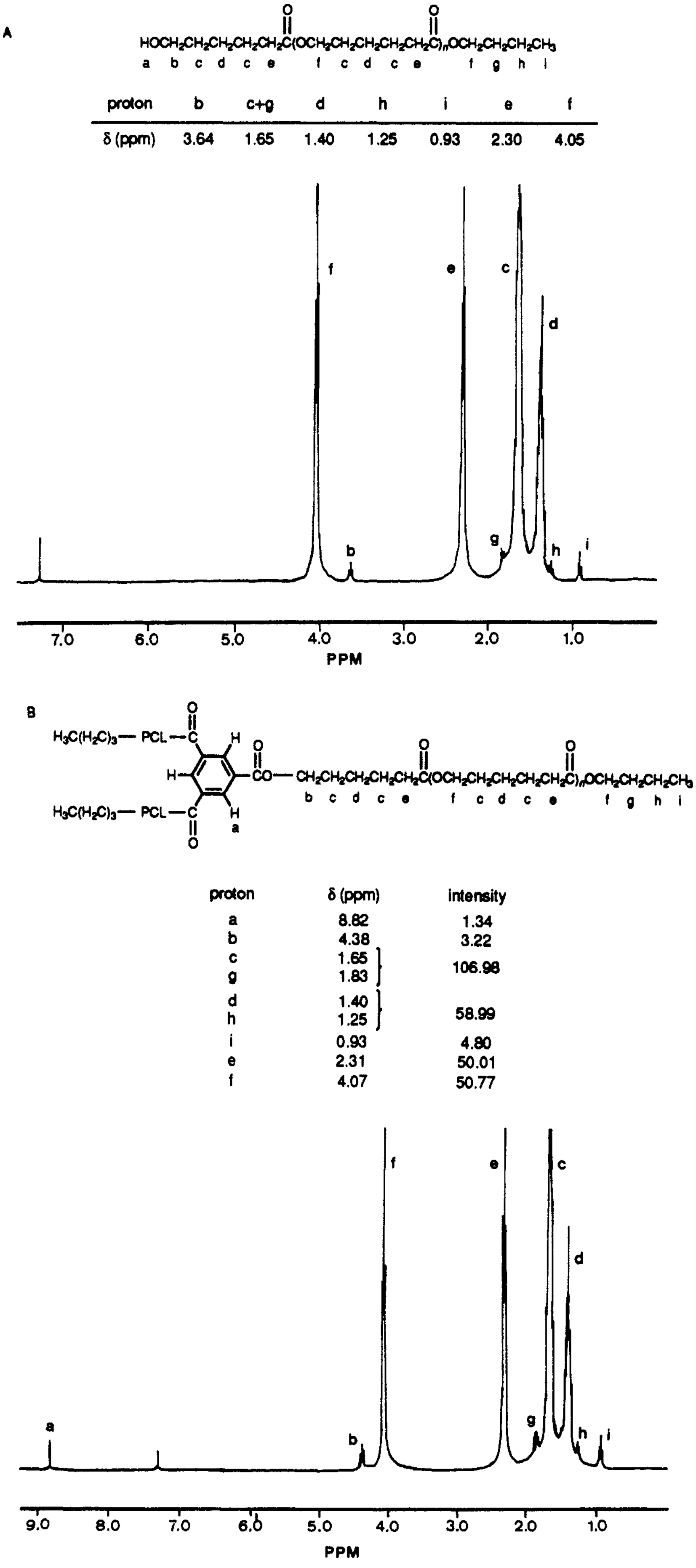
The azido end groups were then hydrogenated in dry DMF by reaction with a 5-fold molar excess of ammonium formate and 10 wt % Pd supported on activated carbon. The reaction temperature was kept at 30 °C for 17 h. Palladium residues were recovered by filtration. The polyester was selectively precipitated in methanol. The azide–amine conversion was analyzed by ^{1}H NMR and IR.

Synthesis of Star-Branched Poly(CL-*b*(L,L)LA) Diblocks. The (L,L)lactide polymerization was initiated by a primary amine end-capped star-branched PCL in the presence of triethylaluminum ($AlEt_3$/amine = 3:1 molar ratio). Copolymerization was carried out in toluene under nitrogen in a previously flamed glass reactor connected to an oil valve. After 115 h reaction time at 70 °C, the copolymer was precipitated in cold methanol.

Characterization. ^{1}H NMR spectra of polyester were recorded in $CDCl_3$ at 400 MHz in the FT mode with a Brüker AN 400 superconducting magnet system. IR spectra were recorded by using a Perkin-Elmer 106 FTIR. Size-exclusion chromatography (SEC) was performed in THF, by using a Hewlett-Packard 1090 liquid chromatograph equipped with a Hewlett-Packard 1037A 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 reference to a universal calibration curve set up with polystyrene standards and the PCL and P(L,L)LA viscometric relationships.[20,21] Low molecular weights (M_n < 15 000) were also calculated by ^{1}H NMR from the relative intensity of the signals of the α-methylene end group and the methine (PLA) or methylene (PCL) ester groups, respectively. Block copolymers were also characterized by SEC and their composition determined by ^{1}H NMR from the signal intensities of the PLA methine groups (δ = 5.17 ppm) and the PCL methylene group (δ = 4.07 ppm), respectively. From the overall composition and Mn of the first polymerized PCL block (SEC and/or ^{1}H NMR), molecular weight of the second block was calculated. Molecular weight (M_n) of small size star-branched polyesters was measured by vapor pressure osmometry (VPO, Ateliance Instruments, France) in toluene at 47 °C. Star-branched polyesters of a high molecular weight (M_w) were analyzed by laser light scattering in THF at 25 °C with a Brookhaven BI2030 system (λ = 488 nm). The refractive index increment (d*n*/d*c*) was measured in THF at 25 °C with a home-built refractometer (λ = 488 nm).

Results and Discussion

Equation 2 schematizes the reaction pathway for the synthesis of star-branched PCL. The reaction is used on



proton	b	c+g	d	h	i	e	f
δ (ppm)	3.64	1.65	1.40	1.25	0.93	2.30	4.05

proton	δ (ppm)	intensity
a	8.82	1.34
b	4.38	3.22
c	1.65	106.98
g	1.83	
d	1.40	58.99
h	1.25	
i	0.93	4.80
e	2.31	50.01
f	4.07	50.77

Figure 1. ^{1}H NMR spectrum of PCL initiated by $Et_2Al(CH_2)_3CH_3$: (A) linear PCL and (B) three-arm star-branched PCL.

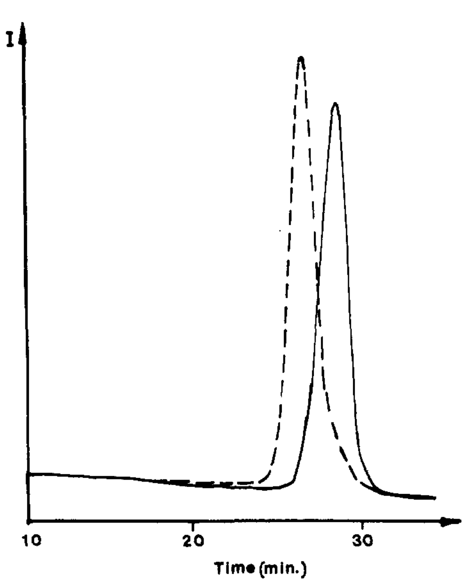


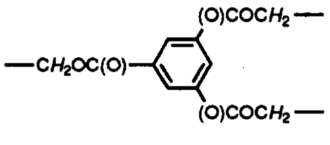
Figure 2. Size exclusion chromatograms of PCL chains before (—) and after (- - -) the coupling reaction (entry 4 in Table 1).

the controlled termination of living PCL chains previously initiated with Et_2AlOCH_2X (where X = $CH_2CH_2CH_3$, $CH_2CH_2CH{=}CH_2$, $(CH_2)_{10}Br$. $C(Y)_p$ is a multifunctional compound able to react quantitatively with the aluminum alkoxide end-groups of living PCL chains.

$$Et_2AlOCH_2X \xrightarrow{n\epsilon\text{-CL}} XCH_2O[C({=}O)(CH_2)_5O]_nAlEt_2 \xrightarrow{C(Y)_p} [XCH_2O[C({=}O)(CH_2)_5O]_n]_pC \quad (2)$$

It is worth recalling that a previous paper has reported on the synthesis of PCL macromonomers by the quantitative reaction of methacryloyl chloride with PCL chains ended with a reactive aluminum alkoxide group.[22] Similarly, substitution of methacryloyl chloride by terephthaloyl chloride has led to the very well-controlled synthesis of telechelic PCL chains.[23] As an extension of these very efficient reactions of aluminum alkoxide with an acid chloride, trimesic acid trichloride has been considered as a potential coupling agent for the synthesis of three-arm star-branched PCL.

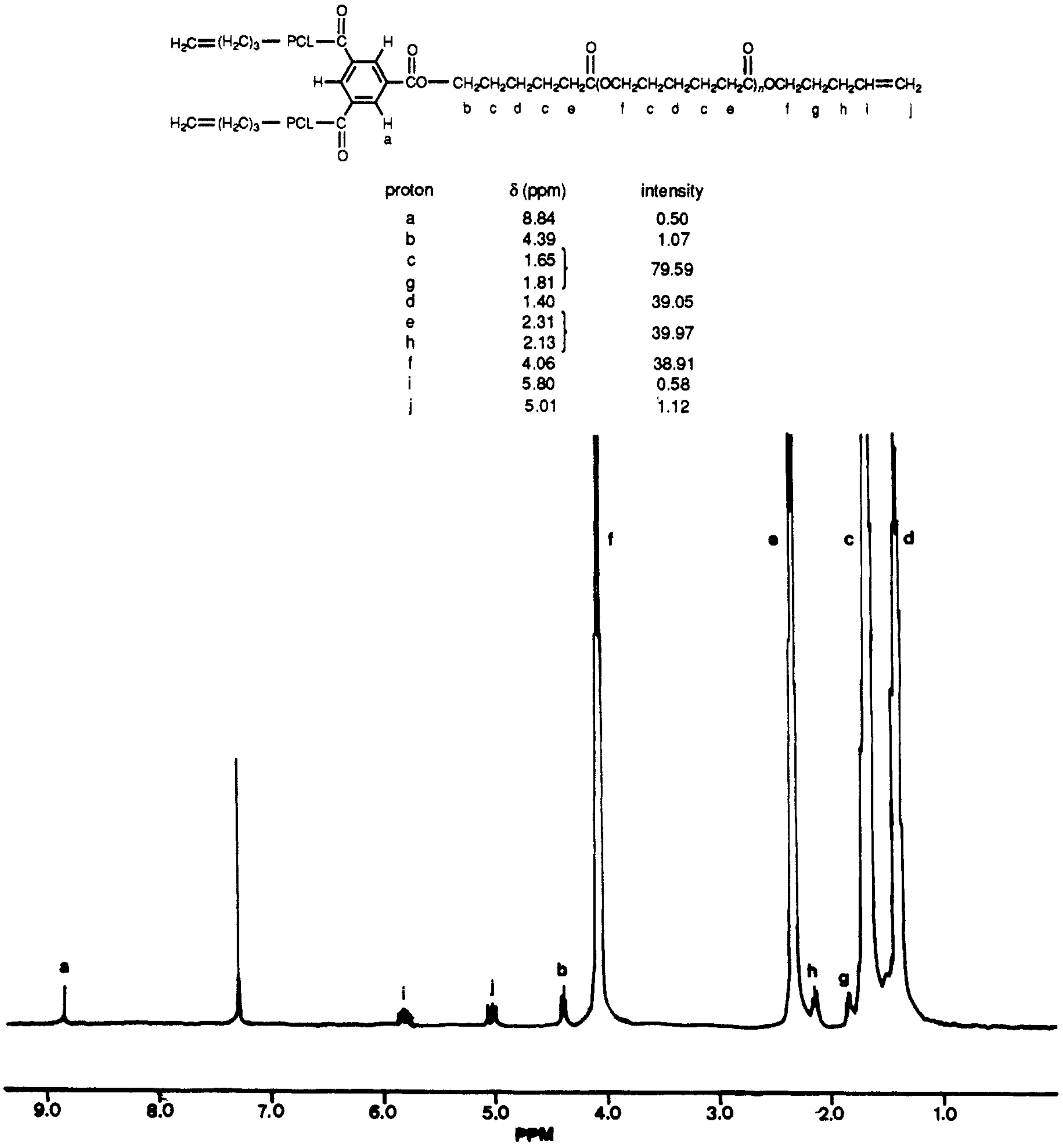
Synthesis of Three-Arm Star-Shaped PCL Bearing Alkyl, 1-Pentenyl, and Bromide End Groups. Diethylaluminum alkoxides are common initiators for the synthesis of living PCL chains.[12,22] These chains have been reacted with the stoichiometric amount of trimesic acid trichloride in THF, in the presence of pyridine. According to entry 1 in Table 1, molecular weight of the living PCL chains is in a good agreement with the value calculated from the monomer over initiator molar ratio at the complete monomer conversion. In addition to the molecular weight (2500), size-exclusion chromatography has also provided a polydispersity index (M_w/M_n) of 1.3 after reaction with trimesic acid chloride, and precipitation into cold methanol confirms that the coupling reaction is complete. Indeed, Figure 1 shows that the signal characteristic of the α-hydroxymethylene protons at 3.66 ppm has disappeared in favor of a new triplet at 4.38 ppm. This new signal has to be assigned to protons of the aromatic ester methylene group:



SEC analysis of the coupling reaction product agrees with the quantitative coupling of living PCL chains as suggested by ^1H NMR. Indeed, the trace of the initial PCL chains has been completely shifted toward smaller elution volumes. Figure 2, which however refers to PCL chains initiated with diethylaluminum 1-pentenyl oxide, is representative of the SEC results. Figure 1 has also allowed molecular weight of the individual arms to be calculated from the relative intensity of the aromatic ester methylene protons (H_b) at 4.38 ppm and the methylene protons (H_e) of the monomer unit at 2.31 ppm. The agreement with the theoretical value and with M_n measured by SEC is additional evidence for a complete coupling reaction. That the intensity of the methyl protons of the butyl end groups derived from the initiator (H_i) is 1.5 times as high as the intensity of protons (H_b) corroborates this conclusion. Absolute molecular weight as measured by vapor pressure osmometry (VPO) fits the expectation of an average of three arms per star-shaped macromolecule. Finally, the coupling reaction has not significantly changed the molecular weight distribution of the PCL precursors. This preliminary result supports that the set of reactions described by eq 2 is an effective strategy for the preparation of star-branched PCL.

It is very well known that the alkoxy group of the diethylaluminum alkoxide initiator is attached as an end group to the propagating PCL chains.[12,22] It is the reason why end-functional PCL chains have been synthesized within a 100% yield when initiated with functional aluminum alkoxides, such as the previously mentioned Et_2AlOCH_2X. Thus, in a second series of experiments, diethylaluminum 1-pentenyl oxide has been used as an initiator in order to prepare three-arm star-shaped PCL, each branch of which is ended with a double bond. Entries 2–4 in Table 1 convincingly confirm all the conclusions drawn from the first experiment. SEC analysis (Figure 2) is in a systematic agreement with a 100% coupling efficiency. No significant increase in polydispersity is reported. Figure 3 is an example (entry 2 in Table 1) of the ^1H NMR analysis of the coupled PCL chains. The signal at 3.66 ppm characteristic of the PCL chains isolated before coupling is no longer observed. Conversely, protons of the coupling agent (protons H_a at 8.84 ppm) and protons of the PCL methylene group directly attached to the coupling agent (protons H_b at 4.39 ppm) are clearly observed. Above all, osmometry (VPO) shows that the actual molecular weight of the coupled PCL chains is three times as high as the experimental value of the individual arms as measured by ^1H NMR (Figure 3), i.e. from the relative intensity of signals associated to the PCL methylene protons (H_f) at 4.06 ppm and the protons of the unsaturated end group (protons H_i at 5.80 ppm and protons H_j at 5.01 ppm), respectively. Conclusion of a three-arm star-shaped structure is also strengthened by the signal intensity of the aromatic protons (H_a) of the coupling agent which is half the intensity of the six aromatic ester methylene protons (H_b) (Figure 3). The same conclusion emerges from the relative intensity of protons (H_b) and protons (H_i and H_j) of the end group, respectively.

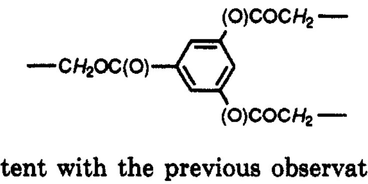
Diethylaluminum 1-bromoundecyl oxide has finally been used as an initiator for the living polymerization of ϵ-caprolactone. Entries 5–8 in Table 1 give credit to the very well-controlled synthesis of three-arm star PCL end-capped with a bromine atom. Comparison of the SEC trace of PCL chains before and after reaction with trimesic acid chloride shows that the coupling is close to completion (Figure 4). As illustrated by Figure 5, the signal characteristic of the α-hydroxymethylene protons [$\delta(CH_2OH)$



proton	δ (ppm)	intensity
a	8.84	0.50
b	4.39	1.07
c	1.65	79.59
g	1.81	
d	1.40	39.05
e	2.31	39.97
h	2.13	
f	4.06	38.91
i	5.80	0.58
j	5.01	1.12

Figure 3. ^{1}H NMR spectrum of star-branched PCL end-capped with a 1-pentene group.

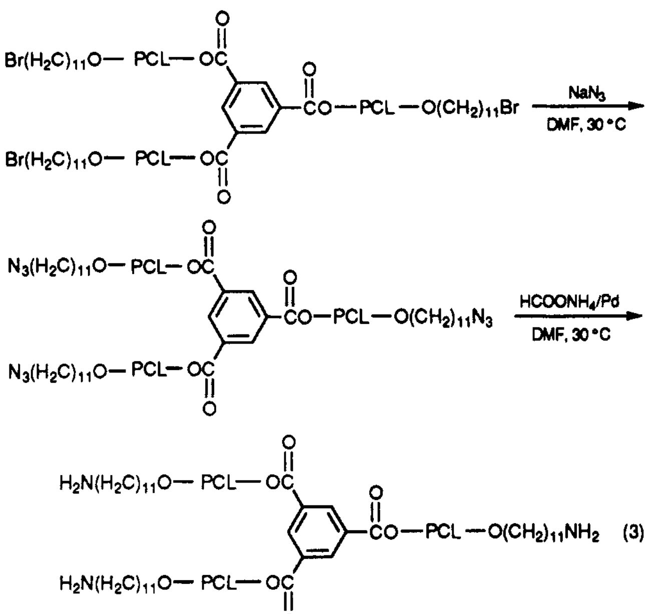
= 3.66 ppm] of PCL chains picked out before the coupling reaction has completely disappeared with the concomitant formation of the triplet (H_b) at 4.39 ppm assigned to the aromatic ester methylene protons:



Still consistent with the previous observations, the experimental molecular weight of the three-arm star-branched PCL (VPO or light scattering data) is three times the molecular weight of the ω-bromine PCL arm, within the limits of experimental errors. In this respect, the signal intensity of the methylene bromide protons (H_j) at 3.41 ppm has been compared to the intensity of the H_f protons at 4.06 ppm for the ε-CL units. The same result is obtained when intensity of the H_f protons is compared to the intensity of the protons of the second arm end (H_b at 4.39 ppm). This observation strongly supports that each PCL arm is quantitatively end-capped with one bromine atom. Even when the molecular weight of the "living" PCL precursor is as high as 10^4, the coupling reaction is still efficient enough to produce three-arm star-branched PCL selectively end-capped with bromine.

Synthesis of Star-Branched PCL with Primary Amine End Groups. Initiation of the ε-CL polymerization by a diethylaluminum aminoalkoxide has failed to provide the expected ω-amino PCL.[24] Due to the great interest of a primary amine functionality, indirect synthetic pathways have been considered.[25] Protection of the amino group of the initiator by conversion into phthalimide has proved to be inefficient because of a problem of deprotection of the amine after polymerization. In an alternate approach, diethylaluminum 11-bromo-1-undecanyloxide has been used as the polymerization initiator. The bromo end group of PCL has then been converted into an azido group, that has subsequently been reduced to the expected primary amine. For this strategy to be efficient, the original alkyl bromide must be long enough to prevent the azide from activating the nearest-neighbor ester group.[25] This pathway has thus been used in view of the synthesis of star-branched PCL end-capped with a primary amine.

The set of reactions after the coupling reaction of living PCL with trimesic acid chloride is schematized by



(3)

Conversion of the bromide into an azido end group has been achieved as reported elsewhere and found to be quantitative. ^{1}H NMR analysis shows indeed the complete disappearance of the alkyl bromide [δ(–CH_2Br) at 3.41 ppm] in favor of the azide group (CH_2N_3) at 3.27 ppm (Figure 6). Moreover, the additional IR absorption at 2096 cm^{-1} compared to the IR spectrum of the bromide end-capped precursor is characteristic of the azido group (Figure 7). The azido end-capped star-branched PCL has then been reduced by catalytic transfer hydrogenation in the presence of ammonium formate in dry DMF, at 30 °C. ^{1}H NMR analysis confirms the complete reduction of the azide since the signal characteristic of the α-azidomethylene protons at 3.27 ppm is no longer observed (Figure 8). Additional evidence is provided by IR spectroscopy, which shows formation of the primary amine end group at 3445 cm^{-1} (Figure 9) at the complete expense of the azido end group at 2096 cm^{-1} (Figure 7).

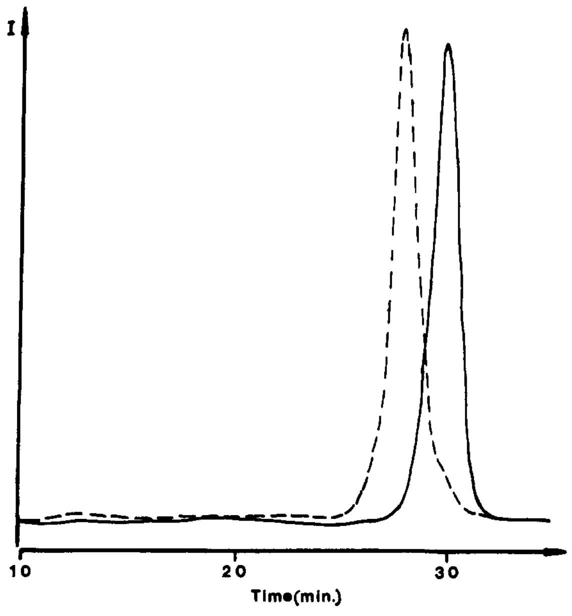
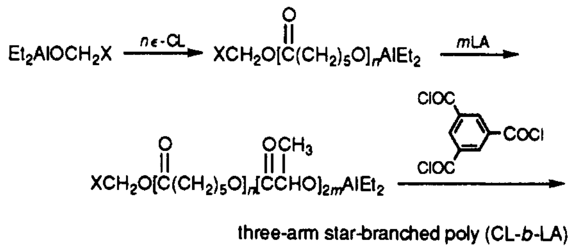


Figure 4. Size exclusion chromatograms of PCL chains before (—) and after (- - -) the coupling reaction (entry 6 in Table 1).

Furthermore, molecular weight of the individual arm has been calculated from the ^{1}H NMR spectrum of the azido end-capped star-branched PCL (Figure 6, e.g., from relative signal intensity of H_f protons and H_j protons), on one hand, and the primary amine counterpart (Figure 8, e.g., from the relative signal intensity of H_f protons and H_b protons), on the other hand. The calculated values are in agreement within the limits of experimental errors ($2.6 \times 10^3 \pm 10\%$) and fit the molecular weight of the bromide precursor (entry 6 in Table 1 and Figure 5). These data strongly support that the bromide end-capped star-branched PCL has been quantitatively converted into the primary amine end-capped three-arm star-shaped PCL and that PCL chains have not degraded during this process.

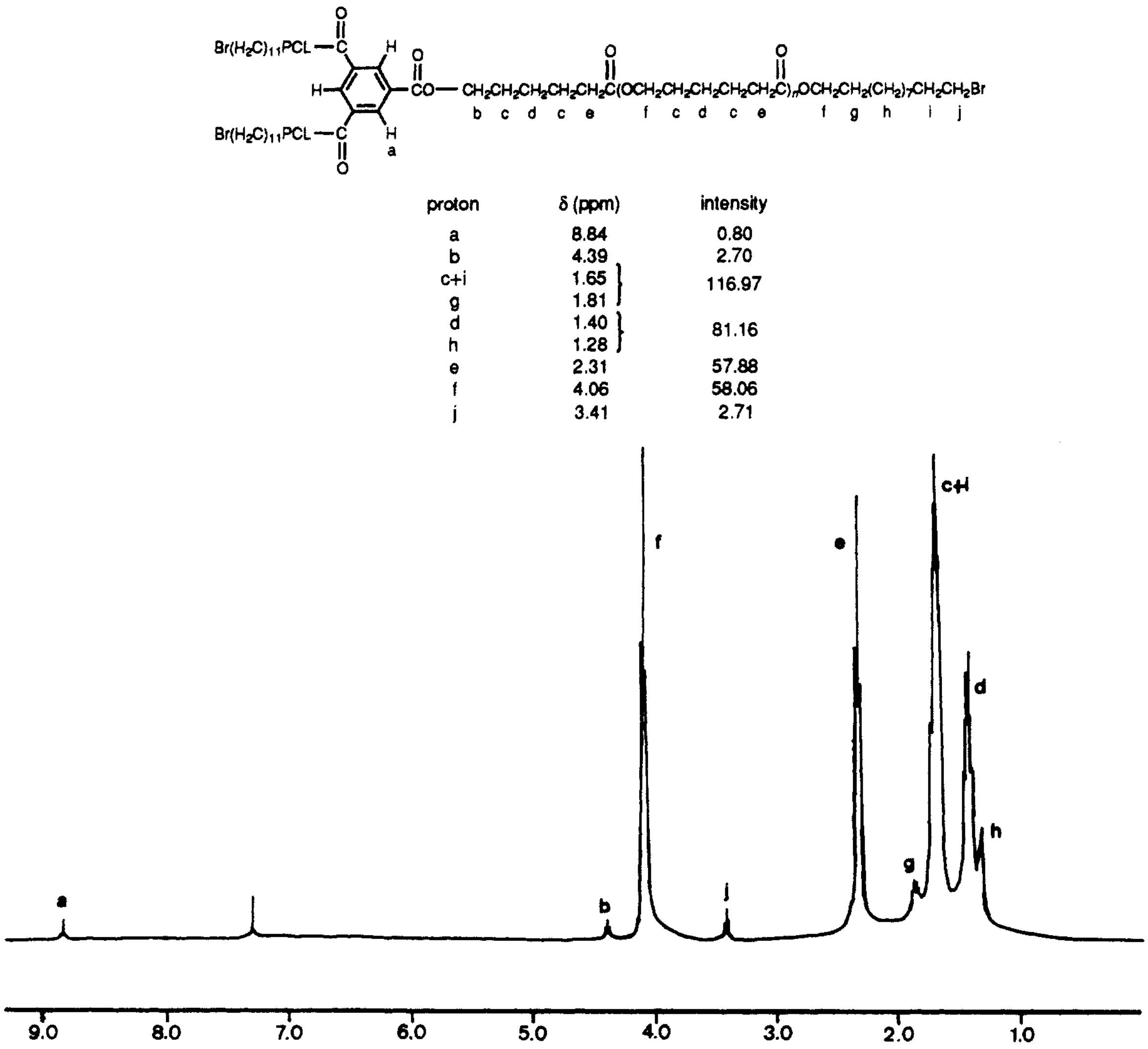
Although indirect, the end-capping of star-branched PCL with a primary amine deserves interest, since this function is an efficient initiator for the living ring-opening polymerization of amino acid *N*-carboxy anhydrides (NCA) with formation of a polypeptide chain.[26] Since the successful synthesis of poly(CL-*b*-peptide) has recently been reported,[27] the way is now paved toward the synthesis of three-arm star poly(CL-*b*-peptide) diblocks.

Synthesis of Star-Branched Polylactide and Star-Branched Poly(CL-b-LA). Due to the great similarity in the ring-opening polymerization mechanism of ϵ-CL and lactides,[16,17] the coupling reaction of living PCL chains with trimesic acid chloride has been extended to living polylactide (PLA) and poly(CL-*b*-LA) chains (eq 4). Entry 1 in Table 2 shows that there is almost no reaction between trimesic acid and the aluminum alkoxide end groups of living poly(CL-*b*-(L,L)LA) chains at 25 °C for 30 h, i.e. under the conditions requested for the quantitative coupling of living PCL chains. The same conclusion holds when living PLA chains are used, although they are of a low molecular weight (entries 2 and 3 in Table 2). The situation is slightly improved until reaching a reaction yield of 20–25% (as calculated by ^{1}H NMR) when the reaction time and temperature are increased (entries 4 and 5 in Table 2). However, secondary reactions occur as indicated by a significant broadening of the molecular weight distribution. A reasonable explanation for the failure of trimesic acid chloride to couple aluminum alkoxide-ended PLA might be the steric hindrance around the active alkoxide due to the methyl substituent in α-position (C(O)CH(CH$_3$)OAlEt$_2$). This steric effect does not prevail for the aluminum alkoxide end group of PCL (C(O)(CH$_2$)$_5$OAlEt$_2$), which is consistent with the completeness of the coupling reaction.



(4)

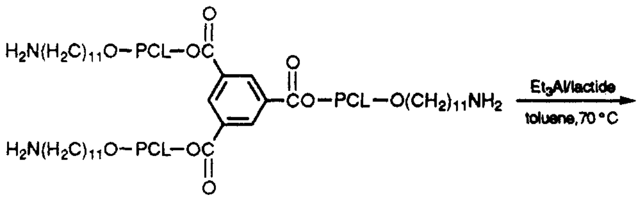
The question might be addressed to know whether there is another way for preparing star-shaped diblock copolymers. The coupling of living poly(LA-*b*-CL) chains should work, since the active Al alkoxide would then be attached to the PCL block. The problem is that living PLA chains cannot initiate the ϵ-CL polymerization.[15,17,18] Another alternative might consist in using the primary amine end-capped three-arm star-shaped PCL as a macroinitiator for the lactide polymerization. Indeed, a primary amine has been shown to initiate the ROP of ϵ-CL in the presence



proton	δ (ppm)	intensity
a	8.84	0.80
b	4.39	2.70
c+i	1.65	116.97
g	1.81	
d	1.40	81.16
h	1.28	
e	2.31	57.88
f	4.06	58.06
j	3.41	2.71

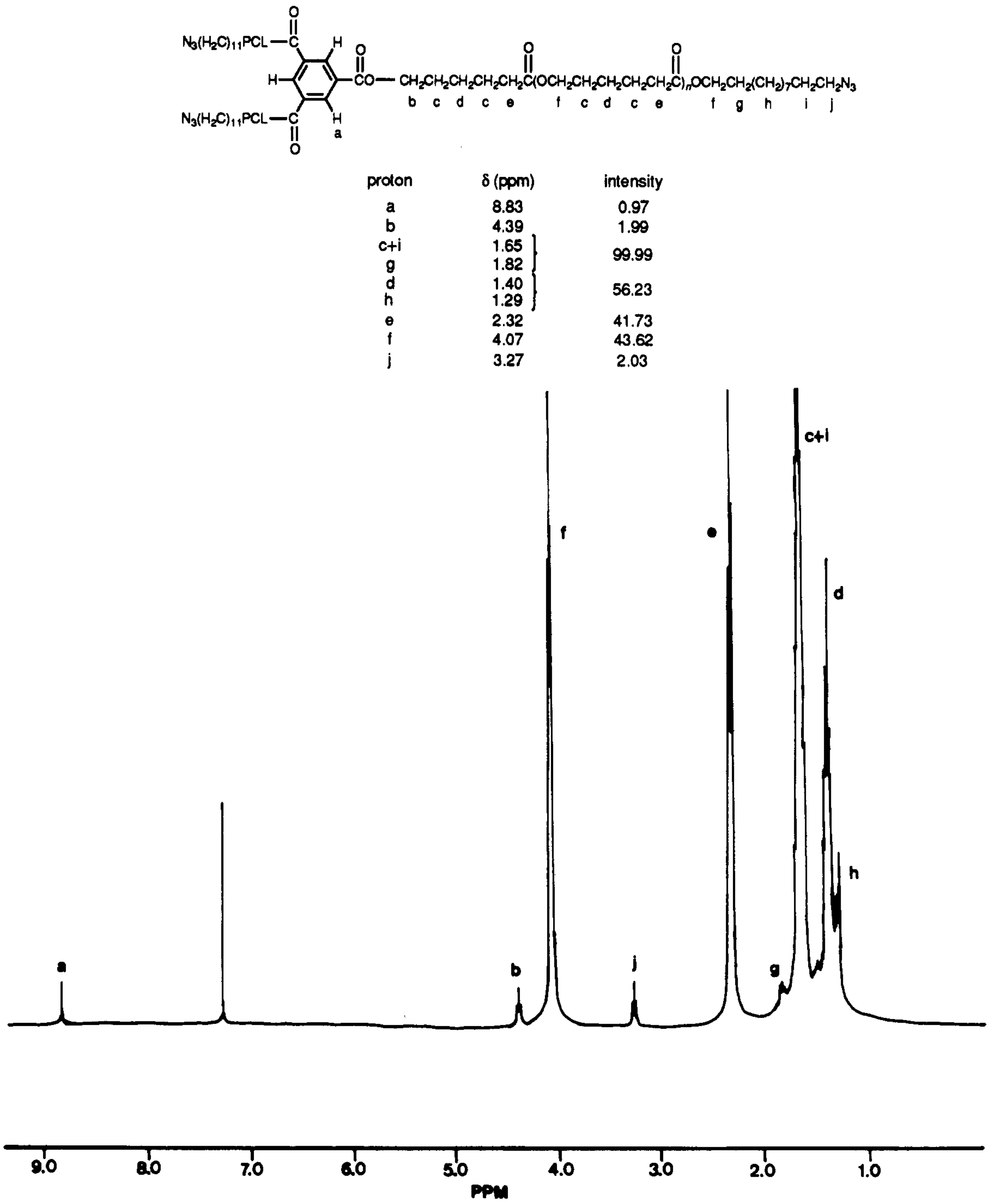
Figure 5. ^{1}H NMR spectrum of star-branched PCL end-capped with a bromine atom.

of triethylaluminum.[24] Polymerization proceeds according to the classical "coordination–insertion" mechanism with the selective rupture of the acyl–oxygen bond of the monomer. Triethylaluminum actually activates the carbonyl group of the monomer which accordingly favors the nucleophilic addition of the amine. This reaction is the actual initiation step. When the Et_3Al/amine molar ratio is 3 or higher, the propagation is living in toluene at 40 °C.[24] This polymerization mechanism has been tentatively extended to lactide in view of preparing three-arm star-shaped poly(CL-*b*-(L,L)LA), as schematized by



three-arm star-branched poly (CL-*b*-LA) (5)

Copolymerization of (L,L)lactide has been initiated by the previously mentioned primary amine end-capped three-arm star-branched PCL (M_n 7000) and triethylaluminum ($AlEt_3$/amine = 3:1 molar ratio), in toluene at 70 °C, for 115 h. The copolymerization product has been precipitated into cold methanol and recovered within a 55% (L,L)lactide conversion. The ^{1}H NMR spectrum (Figure 10) allows the comparison of the relative intensity of the PLA methine protons (H_{l+p} at 5.17 ppm) and the PCL methylene protons (H_f at 4.07 ppm), respectively, and calculation of molecular weight of the poly(L,L)lactide block. The value calculated for one arm (2.7×10^3) is in a close agreement with the theoretical molecular weight ($M_n = 2.5 \times 10^3$) within the limits of experimental errors. Furthermore, *N*-methyleneamide protons H_j ($CH_2NHC(O)$) are observed at 3.29 ppm (36%) and 3.18 ppm (64%), indicating that the amide function is localized within the chain and is more likely the amide linkage between PCL and P(L,L)LA blocks. It is indeed well known that the ^{1}H NMR chemical shifts of the cis and trans conformations of sterically hindered amides are different enough to be unambiguously distinguished.[28] Figure 10 also shows the presence of a hydroxyl group [H_q, $\delta(CH(CH)_3OH$ at 2.70 ppm)]. From the relative intensity of protons H_q compared to protons H_a of the benzene ring, the star-branched P(CL-*b*-(L,L)LA) chains appear to be quantitatively end-capped with a hydroxyl group. Moreover, the intensity of the *N*-amide methylene protons [$I(H_j) = 1.003$] may be compared to the value predicted from the intensity of the PCL protons and DP of the individual PCL block [$I(H_f) = DP_{PCL} \times I(H_j)$; thus $I(H_j)$ should be 0.88]. The same comparison holds for the P(L,L)LA block [$I(H_{l+p}) = {}^1/_2 I(H_j) \times DP_{PLA}$; thus $I(H_j) = 0.95$]. The good agreement



proton	δ (ppm)	intensity
a	8.83	0.97
b	4.39	1.99
c+i	1.65	99.99
g	1.82	
d	1.40	56.23
h	1.29	
e	2.32	41.73
f	4.07	43.62
j	3.27	2.03

Figure 6. ^{1}H NMR spectrum of star-branched PCL end-capped with an azido group.

between experimental and theoretical values is in favor of the blocky structure of the copolymer arms and precludes presence of homopolymers at least within the limits of the NMR experimental errors.

It may be concluded that the approach described by eq 5 is an original and effective strategy for the synthesis of three-arm star-shaped poly(CL-*b*-LA) copolymers. It is also obvious that the lactide polymerization can be initiated by an aliphatic primary amine added with triethylaluminum.

Conclusions

Three-arm star-branched poly(ϵ-caprolactone) end-capped with various functional groups can be prepared by the quantitative coupling of living α-X functional-ω-aluminum alkoxide PCL chains with trimesic acid trichloride. When the termination reaction of the living chains is catalyzed with a Lewis base (pyridine), a 3-fold increase in molecular weight is observed within the limits of experimental errors and the molecular weight distribution remains essentially unchanged. In sharp contrast, synthesis of star-branched poly(L,L)lactide and poly(CL-*b*-(L,L)LA) based on the same strategy is quite a problem, more likely due to the steric hindrance around of the active aluminum alkoxide by the methyl substituent in α position. Bromide end-capped star-branched PCL has proved to be a valuable precursor for the preparation of the primary amine counterpart. This indirect approach is based on the conversion of the bromide end-group into an azido group, which is then reduced into a primary amine. These reactions are essentially quantitative. It is worth pointing

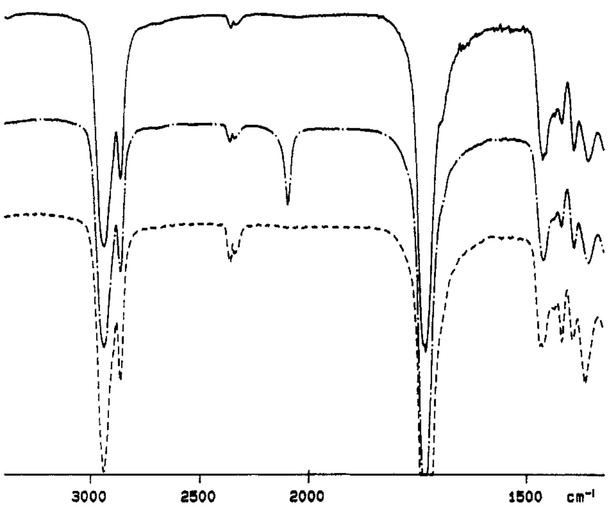


Figure 7. Cumulative IR spectrum of star-branched PCL end-capped with various functional end-groups: (- - -) bromine; (- · -) azide [$\nu(N_3)$ = 2096 cm^{-1}]; (—) primary amine.

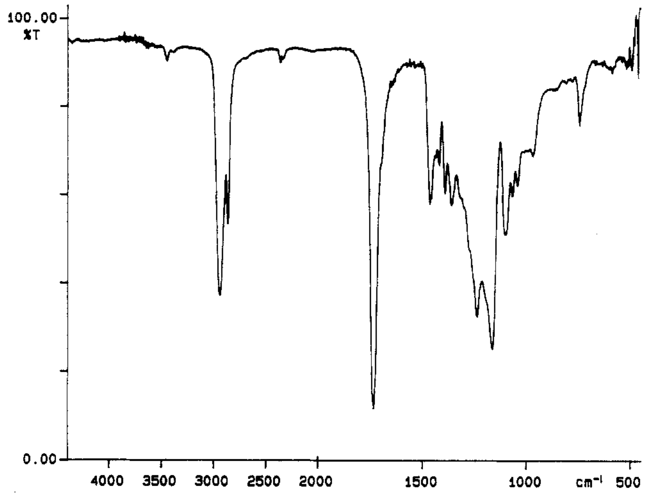
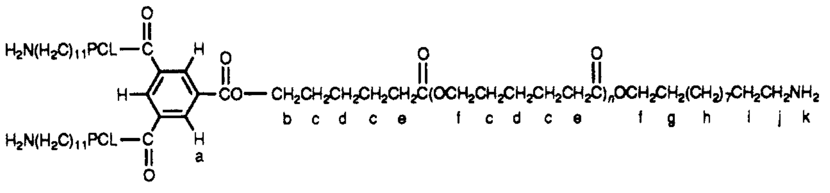


Figure 9. IR spectrum of star-branched PCL end-capped with a primary amine.

out that the primary amine end-capped star-branched PCL is a potential macroinitiator for the ring-opening polymerization of *N*-carboxy-γ-benzylglutamate anhydride with formation of biocompatible and biodegradable star-branched poly(caprolactone-*b*-peptide). Still more interesting, the primary amine end-capped star-branched PCL is a very effective initiator for the lactide polymerization in toluene when combined with a molar excess of triethylaluminum. Hydroxyl end-capped star-branched poly(CL-*b*-(L,L)LA) can then be made available. This initiation pathway also opens the way to the synthesis of polylactide from an aliphatic primary amine. It might also allow to prepare the star-branched poly(CL-*b*-(L,L)LA) copolymer, the synthesis of which failed according to the herein reported coupling reaction. Initiation of the ϵ-caprolactone polymerization by aluminum polyalkoxide or a polyamine in the presence of a molar excess of $AlEt_3$, followed by the addition of lactide, is indeed a possible strategy, which will be discussed in the near future.

Acknowledgment. The authors are grateful to the "Services de la Programmation de la Politique Scienti-



proton	δ (ppm)	intensity
a	8.83	0.75
b	4.39	1.61
c+i	1.66	67.59
g	1.84	
d+k	1.41	43.94
h	1.28	
e+j	2.32	32.31
f	4.06	31.33

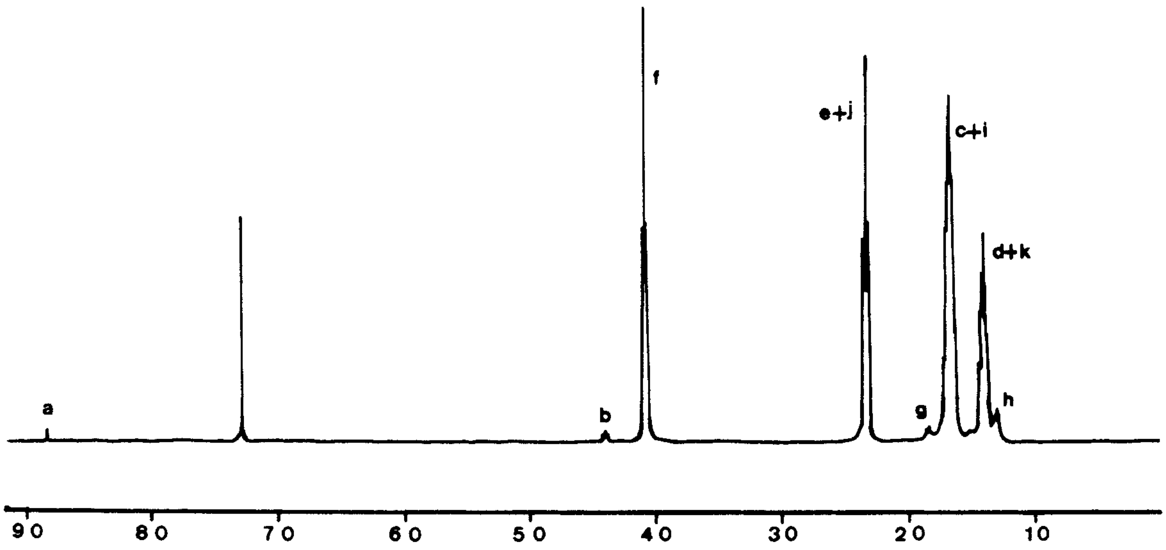
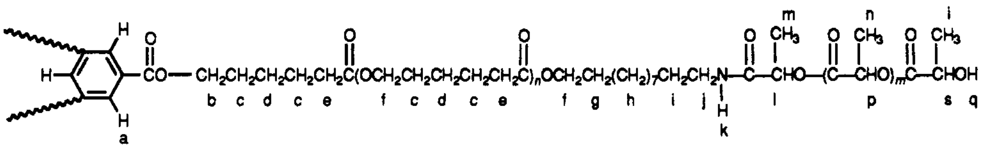


Figure 8. ^1H NMR spectrum of star-branched PCL end-capped with a primary amine.



proton	δ (ppm)	intensity
a	8.84	0.45
b+s	4.39	1.12
c+i	1.65	93.39
g	1.84	
m+n+r	1.58	
d	1.40	27.89
h	1.28	
f	4.07	17.69
e	2.32	18.38
l+p	5.17	16.54
j	3.29	0.36 (36%)
	3.18	0.64 (64%)
q	2.70	0.47

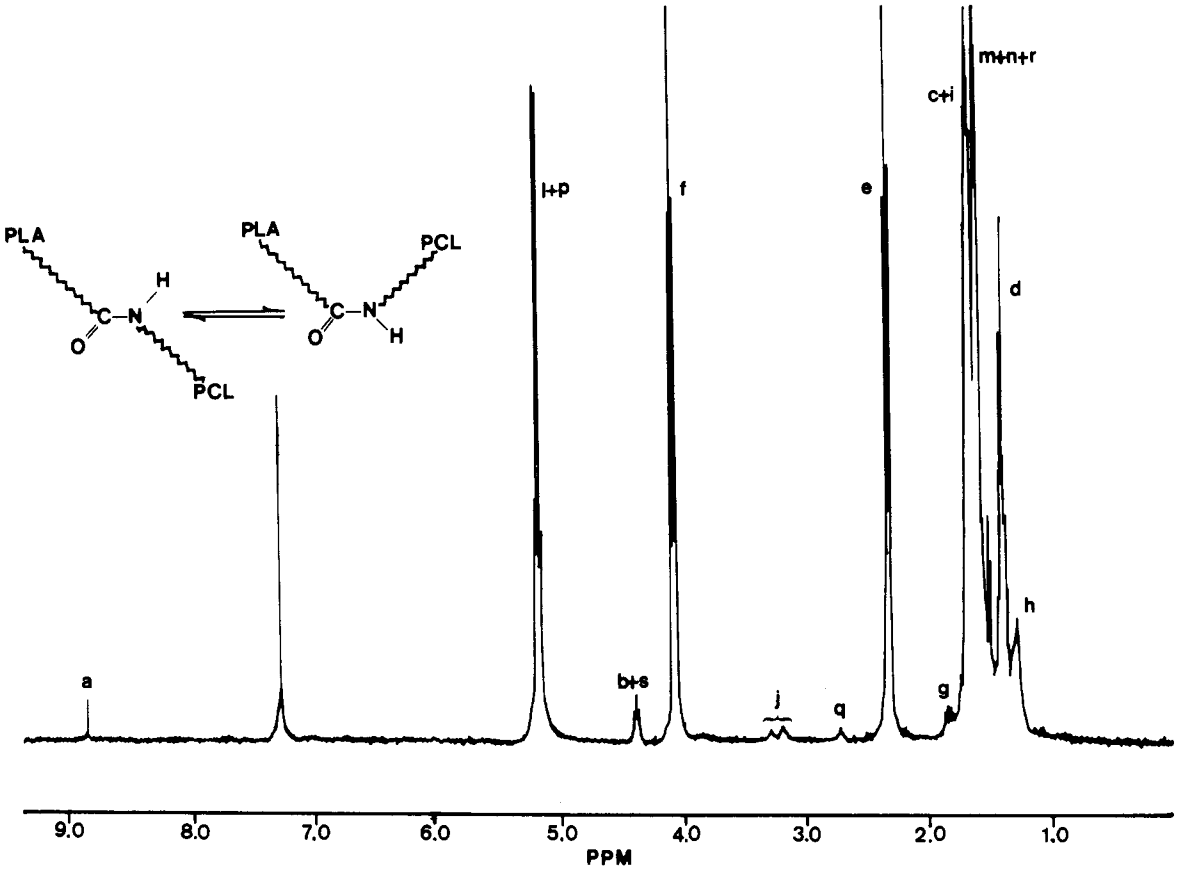


Figure 10. ^{1}H NMR spectrum of star-branched P(CL-*b*-(L,L)LA) end-capped with a hydroxyl group.

fique" for general support in the frame of the "Pôle d'Attraction Interuniversitaire-Polymères".

References and Notes

(1) Pitt, C. G.; Marks, T. A.; Schindler, A. Biodegradable Drug Delivery Systems Based on Aliphatic Polyesters: Application of Contraceptives and Narcotic Antagonists. In *Controlled Release of Bioactive Materials*; Baker, R., Ed.; Academic Press: New York, 1980.

(2) Schindler, A.; Jeffcoat, R.; Kimmel, G. L.; Pitt, C. G.; Wall, M. E.; Zweidinger, R. Biodegradable Polymer for Sustained Drug Delivery. *Contemporary Topics in Polymer Science*; Plenum Press: New York, 1977; Vol. 2, p 256.

(3) Olabisi, O.; Robeson, L. E.; Shaw, M. T. *Polymer-Polymer Miscibility*; Academic: New York, 1979.

(4) Brode, C. L.; Koleske, J. V. *J. Macromol. Sci.-Chem.* **1972**, *A6*, 1109.

(5) For review, see: (a) Bauer, B. J.; Fetters, L. J. *Rubber Chem. Technol.* **1978**, *51*, 406. (b) Bywater, S. *Adv. Polym. Sci.* **1979**, *30*, 90.

(6) Kanaoka, S.; Sawamoto, M.; Higashimura, T. *Macromolecules* **1991**, *24*, 2309.

(7) Kricheldorf, H. R.; Mang, T.; Jonte, J. M. *Macromolecules* **1984**, *17*, 2173.

(8) Ouhadi, T.; Stevens, C.; Teyssié, Ph. *Makromol. Chem. Suppl.* **1975**, *1*, 191.

(9) Hamitou, A.; Ouhadi, T.; Jérôme, R.; Teyssié, Ph. *J. Polym. Sci., Polym. Chem. Ed.* **1977**, *15*, 865.

(10) Endo, M.; Aida, T.; Inoue, S. *Macromolecules* **1987**, *20*, 2982.

(11) Hofman, A.; Slomkowski, S.; Penczek, S. *Makromol. Chem., Rapid Commun.* **1987**, *8*, 387.

(12) Dubois, Ph.; Jérôme, R.; Teyssié, Ph. *Polym. Bull.* **1989**, *22*, 475.

(13) McLain, S. J.; Drysdale, N. E. US Patent 5,028,667, 1991; assigned to E.I. Du Pont de Nemours and Co.

(14) Barakat, I.; Dubois, Ph.; Jérôme, R.; Teyssié, Ph. *Macromolecules* **1991**, *24*, 6542.

(15) Song, C. X.; Feng, X. D. *Macromolecules* **1984**, *17*, 2764.

(16) Barakat, I.; Dubois, Ph.; Jérôme, R.; Teyssié, Ph. *J. Polym. Sci., Part A: Polym. Chem.* **1993**, *31*, 505.

(17) Dubois, Ph.; Jacobs, C.; Jérôme, R.; Teyssié, Ph. *Macromolecules* **1991**, *24*, 2266.

(18) Jacobs, C.; Dubois, Ph.; Jérôme, R.; Teyssié, Ph. *Macromolecules* **1991**, *24*, 3027.

(19) Vanhoorne, P.; Dubois, Ph.; Jérôme, R.; Teyssié, Ph. *Macromolecules* **1992**, *25*, 37.

(20) Heuschen, J.; Jérôme, R.; Teyssié, Ph. *Macromolecules* **1981**, *14*, 242.

(21) Van Dijk, J. A. P. P.; Smit, J. A. M.; Kohn, F. E.; Feijen, J. J. *Polym. Sci., Polym. Chem. Ed.* **1983**, *21*, 197.

(22) Dubois, Ph.; Jérôme, R.; Teyssié, Ph. *Macromolecules* **1991**, *24*, 977.

(23) Dubois, Ph.; Jérôme, R.; Teyssié, Ph. *Polymer*, accepted for publication.

(24) Dubois, Ph.; Degee, Ph.; Jérôme, R.; Teyssié, Ph. *Macromolecules* **1992**, *25*, 2614.

(25) Degee, Ph.; Dubois, Ph.; Jérôme, R.; Teyssié, Ph. *Macromolecules* **1992**, *25*, 4242.

(26) Kricheldorf, H. R. *α-Amino acid N-carboxy anhydrides and related heterocycles*; Springer Verlag: Berlin, 1987; p 57.

(27) Degee, Ph.; Dubois, Ph.; Jérôme, R.; Teyssié, Ph. *J. Polym. Sci. Part A: Polym. Chem.* **1993**, *31*, 275.

(28) Bovey, F. A. *High Resolution NMR of Macromolecules*; Academic Press: New York, 1972; Part I, Chapter III, p 71.